

Abstracts 1 to 8  
President's Plenary Session  
Friday, March 13, 2009 7:45–9:30 AM

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1

### Second hepatic resection for recurrent hepatocellular carcinoma

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While several Asian studies have shown promising results for second resection for recurrent hepatocellular carcinoma (HCC), there are no Western series on this topic. The purpose of this study was to determine the outcome of patients undergoing a second hepatic resection for recurrent HCC at a Western center and to identify prognostic variables.

**Methods:** A retrospective review of all patients undergoing hepatic resection for HCC from 1/1990 to 1/2008 was conducted. Patients underwent second resection if they had a single tumor on imaging, Child's A liver function, platelets > 100 000 and no extrahepatic disease.

**Results:** During this period, 487 patients underwent resection with 221 having documented recurrence. Of these, 30 underwent second resection. Underlying liver disease included HBV ( $n = 18$ ), HCV ( $n = 6$ ), none ( $n = 4$ ), and other ( $n = 2$ ). Mean tumor size was 9.6 cm at first resection and 4.0 cm at second resection. Median interval between first resection and recurrence was 15.5 months. There were no perioperative mortalities and 1, 3, and 5 years survivals were 88%, 65%, and 65%. Recurrence rate at 3 year was 80%. Univariate predictors of survival included < 1 year interval from first resection to recurrence, gross vascular invasion at second resection, tumor > 5cm at second resection, and blood transfusion at second resection. Multivariate analysis found gross vascular invasion at second resection as the only independent predictor of mortality (HR 76.9,  $P = 0.002$ ). Patients without gross vascular invasion at

2nd resection had median survival of 76.8 months and 5 year survival of 74%.

**Conclusions:** Second resection for recurrent HCC has excellent outcomes in well selected patients. Gross vascular invasion is the only independent predictor of outcome after second resection.

2

### Incorporating an HPB fellowship does not diminish surgical residents' HPB experience in a high-volume training program

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**Background:** A major paradigm shift in surgical education has recently been instituted by the American Board of Surgery and the Surgical Council on Resident Education (SCORE). Specific surgical procedures have been defined as ESSENTIAL (Common/Uncommon – specific procedural competency required by the end of training) and COMPLEX (generic competence required, but not competence in individual procedures). Importantly, virtually all elective HPB procedures fall into the SCORE 'COMPLEX' category. Trainees who wish to practice HPB surgery will therefore be required to obtain advanced training. As this training paradigm evolves, it is equally crucial that incorporation of an HPB fellowship into an established surgical residency program does not diminish surgical residents' exposure to complex HPB procedures. We hypothesized that incorporation of an HPB fellowship into a high volume clinical training program would not detract from residents' HPB experience.

**Methods:** Our institution incorporated an HPB training program in 2005–2006. Resident operative case logs (provided by the American Council of Graduate Medical Education) and HPB fellow case logs were reviewed. Resident exposure to complex HPB procedures for 3 years prior to and 3 years after fellowship incorporation were compared. Student's  $t$ -test was applied where appropriate;  $P < 0.05$  was accepted as statistically significant.

**Results:** The ACGME requires graduating residents' exposure to a minimum of three pancreas and four liver cases (complex biliary cases are not subdivided from the category 'alimentary'). In 2007, the national average exposure of graduating chief residents was: pancreas – 11; liver – 9; biliary – 5. The International Hepatopancreatobiliary Association (IHPBA) guidelines for HPB fellowship training call for exposure to: pancreas – 30; liver – 25; and biliary – 20. Our institutional resident and fellow HPB experience is shown in the Table 1.

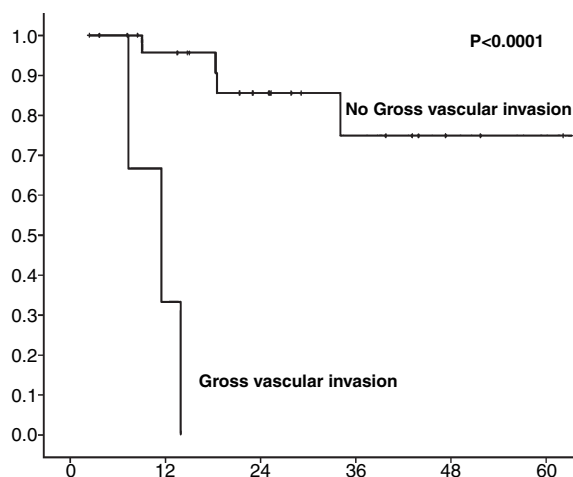


Figure 1.

**Table 1.** Resident and fellow HPB experience 2002–2008.

	Pancreas		Liver		Complex Biliary	
	Resident	Fellow	Resident	Fellow	Resident	Fellow
2002–2003	20	—	13	—	8	—
2003–2004	25	—	22	—	11	—
2004–2005	27	—	15	—	9	—
2005–2006	23	100	14	40	4	38
2006–2007	23	109	14	42	8	44
2007–2008	19	114	13	40	**	56
P value	0.39		0.34		0.17	

\*\*Data will be available 12/2008.

**Conclusions:** These data show that an HPB fellowship program can be incorporated into a high volume clinical training program without detracting from resident HPB experience. Prior to initiating an HPB fellowship program, individual training programs must carefully assess their capability to provide an adequate clinical experience for fellows without diminishing resident exposure to complex HPB procedures.

### 3

#### Improved survival with aggressive resection of hilar cholangiocarcinoma

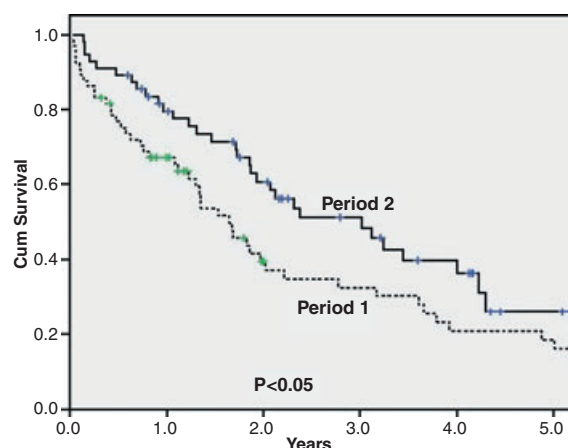
Y. L. CHEAH, MD, M. AKOAH, MD, K. VAKILI, MD, J. J. POMPOSELLI, MD, PHD, E. A. POMFRET, MD, PHD, W. D. LEWIS, MD and R. L. JENKINS, MD

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**Background:** Complete surgical resection with negative histologic margins is a major determinant of long-term survival for patients with hilar cholangiocarcinoma. As our experience with surgical resection for hilar cholangiocarcinoma evolved, we adopted a more radical surgical approach with the addition of hepatectomy and complex vascular reconstruction to achieve negative surgical margins. In this study we sought to examine the results of this aggressive surgical approach and its impact on patient survival.

**Methods:** All patients with the diagnosis of hilar cholangiocarcinoma evaluated and treated by a single team of surgeons between 1986 and 2007 were identified from our computerized database. A total of 120 patients underwent resection with curative intent; 65 patients between 1986 and 1998 at the former New England Deaconess Hospital (period 1), and 55 patients between 1999 and 2007 at the Lahey Clinic (period 2). Patient demographics, extent of surgical resection and outcomes were retrospectively analyzed and compared between periods 1 and 2. Survival is calculated using the Kaplan–Meir method and curves were compared using the log rank test.

**Results:** The overall 1, 3, and 5-year survival rates of patients with R0 resection were 85.5%, 63.7% and 35.5% compared to 56.6%, 8.2% and 0% for R1 resection ( $P < 0.001$ ). Patients in period 2 received more extensive surgical resections; hilar combined with hepatic resection was performed in 69.1% of patients in period 2 compared to 48.6% in period 1. Concomitant vascular resection was performed in 17 patients (three in period 1 and 14 in period 2), with portal vein resection in 13



**Figure 1.** Difference in survival between periods 1 and 2.

patients, hepatic artery resection in two patients, and both hepatic artery and portal vein resection in two patients. Negative margins were achieved in 81.8% in period 2 compared to 50.0% in period 1 ( $P < 0.05$ ). The perioperative mortality rate improved from 6% in period 1 to 1% in period 2. The 1, 3 and 5 year survival in period 1 was 67.1%, 39.4%, and 18.5% compared to 79.6%, 48.4%, and 31.1% in period 2 ( $P < 0.05$ ). Post-operative complications occurred in 22 (40%) patients in period 2; the most common complication was bile leak in eight patients.

**Conclusion:** Aggressive surgery with the addition of partial hepatectomy and vascular resection in treating hilar cholangiocarcinoma improves patient survival with acceptable morbidity and mortality.

### 4

#### Validation of a predictive algorithm to maximize resectability of pancreatic adenocarcinoma

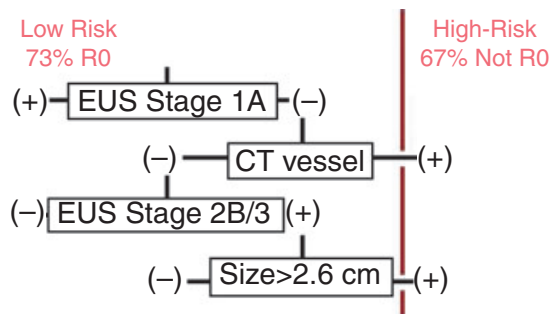
P. BAO, MD, D. POTTER, PHD, J. YOUNG, D. EISENBERG, MD, D. LENZNER, MS, K. LEE, MD, H. ZEH, MD, M. SANDERS, MD, S. HUGHES, MD and A. J. MOSER, MD

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**Introduction:** The surgeon's major contribution to patients with localized pancreatic cancer is a margin negative resection. We hypothesized that a prediction algorithm based on preoperative computed tomography (CT) and endoscopic ultrasound (EUS) could maximize the rate of R0 resection while reducing the risk of non-therapeutic surgery.

**Methods:** 197 patients with biopsy-proven pancreatic adenocarcinoma (157 head; 40 body/tail) underwent exploration with intent to resect from 2002 to 2007. All patients had staging helical CT and 143 had EUS. A prediction model was developed from the imaging data of 65 patients during 2002–2005. This algorithm classified patients as high or low risk for noncurative surgery. It was validated in a subsequent cohort of 78 patients between 2005 and 2007. Model performance was evaluated using contingency table and survival analysis.

**Results:** Predictors of resectability in the development cohort were: *any* evidence of vascular involvement on CT scan, EUS stage IIB by AJCC criteria, and EUS tumor size greater than 2.6 cm. The resectability rate in the validation cohort was 77% with a 58% R0 resection rate. Compared to these outcomes, selecting operative patients classified by the model as favorable for curative surgery would have increased the resectability rate from 77% to 92% ( $P = 0.03$ ) and the R0 resection rate from 58% to 73% ( $P = 0.08$ ). The model was 71% accurate with 78% sensitivity and 61% specificity for R0 resection. There was a 40% difference in R0 resectability between high risk and low risk patients ( $P = 0.001$ ). High risk classification was associated with unresectable locally-advanced disease ( $P = 0.007$ ), metastasis ( $P = 0.012$ ), and the need for mesenteric vein resection ( $P = 0.012$ ). Compared to patients at low risk, those at high predicted risk had a 67% rate of noncurative surgery and experienced significantly shorter median survival (12.3 vs. 20.6 months,  $P = 0.022$ ).



Prediction algorithm for Risk of Nontherapeutic Laparotomy

**Figure 1.**

**Conclusion:** This validated prediction algorithm uses standard CT and EUS criteria to identify patients most likely to benefit from resection for pancreatic adenocarcinoma. The model significantly increased the R0 resection rate and reduced the rate of nontherapeutic surgery. Prediction models may be used to classify patients entering neoadjuvant therapy trials.

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### Serial molecular analysis of EUS guided FNA aspiration of pancreatic cysts: quantitative molecular evidence detects neoplastic cyst progression, stability or regression

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**Introduction:** The biological behavior of pancreatic cystic neoplasms, particularly those of mucinous origin, is difficult to predict. Progression rates of 30% and higher have been reported in mucinous cystic processes leading to recommended surgical excision in all cases. Regression of mucinous cysts over time is suspected to occur, however objective support has been lacking.

Molecular analysis of aspirated pancreatic cyst fluid (point mutation, loss of heterozygosity) is used here to evaluate the presence and rate of that mutational change over time.

**Design:** The fluid from 52 patients with EUS-FNA pancreatic cysts underwent molecular analysis consisting of measurement of 1) DNA quantity, 2) DNA quality (extent of degradation), 3) Kras point mutation, 4) allelic imbalance (loss of heterozygosity determination [LOH]) for a panel of 16 markers and 5) degree of clonal expansion of DNA alterations when present (PathFinderTG®). In each patient, serial aspirations were available (40-two serial, 8-three, 4-four) totaling 120 separate cyst fluid genotyping reactions. The interval between serial analyses ranged from 3 to 36 months. Mucinous cysts were defined as cysts containing gross or microscopically visible mucin, elevated CEA, Kras point mutation and/or multiple LOH alterations. Cysts not meeting these criteria were classified as serous/reactive processes.

**Results:** Forty-two of 52 patients had cysts meeting the criteria for mucinous etiology. 20 (48%) manifested neoplastic regression by reduction in DNA amount, shift from good to poor quality, elimination of some or all of the point mutations/LOH change present previously and/or lowering in the degree of clonality. The mucinous cysts of 19 patients (45%) remained essentially stable while three patients (7%) manifested molecular evidence of progression at 6, 8 and 10 months. All 10 non-mucinous cyst fluids showed stable indolent molecular features (low DNA, poor quality, 0–2 low clonality alterations). Mucinous cysts with indolent molecular features did not manifest neoplastic progression.

**Conclusions:** Molecular analysis provides a useful ancillary tool with which to characterize aspirated pancreatic fluid. The vast majority of mucinous cysts did not manifest neoplastic progression for up to 36-month follow-up. Only 7% of mucinous cysts showed molecular progression which was predicted in the initial sample by aggressive molecular changes. The results support integrated molecular pathology risk stratification of patients with pancreatic cysts including mucinous cystic lesions.

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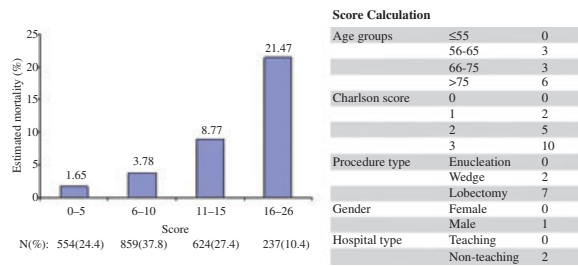
### A simple risk score predicts inpatient mortality after liver resection for hepatocellular carcinoma

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**Objective:** To develop an integer-based risk score based on national data to estimate the risk of in-hospital mortality in patients undergoing procedures for hepatocellular carcinoma.

**Background:** There is a wide spectrum of disease burden in hepatocellular carcinoma accompanied by several options for surgical management. However, the associated mortality of such procedures is not well-defined. Accurate predictions of patients' perioperative risk would be helpful to guide decision-making.



**Figure 1.**

**Methods:** The Nationwide Inpatient Sample, the largest all-payer discharge database in the U.S., was queried from 1998 to 2005. A cohort of patient-discharges for hepatic procedures with a diagnosis of primary liver neoplasm was assembled. Procedures were categorized as hepatic lobectomy, wedge resection, or enucleation/ablation. Logistic regression and bootstrap methods were used to create an integer risk score for estimating the risk of in-hospital mortality using procedure type, patient demographics, comorbidities, and hospital type. A randomly selected sample of 80% ( $n = 2274$ ) of the cohort was used to create the risk score with validation of the score conducted in the remaining 20% ( $n = 560$ ).

**Results:** A total of 2834 patient-discharges were identified. Overall in-hospital mortality was 6.53%. Factors included in the final model were age, gender, Charlson comorbidity score, procedure type, and teaching hospital status. Integer values were assigned to these characteristics, and then used for calculating an additive score (Figure, right panel). Four clinically relevant score groups were then assembled to stratify risk of in-hospital mortality, with a 13-fold gradient of mortality ranging from 1.6 to 21.5% (Figure, left panel;  $P < 0.0001$ ). In the derivation set, as in the validation set, the score discriminated well, with a c-statistic of 0.74 and 0.72, respectively.

**Conclusion:** An integer-based risk score can be used to predict in-hospital mortality after surgical procedure for hepatocellular carcinoma, and may be useful for preoperative risk stratification and patient counseling.

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### SNPs in *RecQL* predict survival in pancreatic adenocarcinoma

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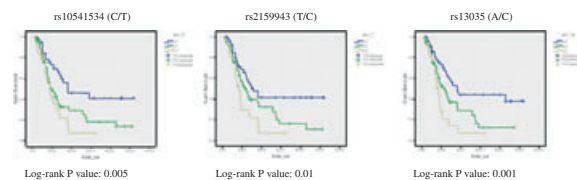
**Introduction:** *RecQL* is a DNA helicase involved in DNA mismatch repair. The *RecQL* 3'UTR A159C genotype has previously been associated with overall survival of patients with pancreatic cancer. However, the functional significance of this SNP remains unknown.

**Hypothesis:** The *RecQL* A159C SNP is in linkage disequilibrium with other functional SNPs of the gene. Somatic mutations of the *RecQL* gene in tumors may influence the clinical outcome of pancreatic cancer.

**Methods:** We sequenced the entire coding regions of the *RecQL* gene in paired blood and tumor DNA of 35 patients with resectable pancreatic cancer treated with surgery and adjuvant chemoradiation. DNA was isolated from blood using the PAXgene Blood DNA kit (Pre-AnalytiX) and from matched tumors using the QIAamp

DNA Mini kit (Qiagen). Primer sets were designed to cover the 15 *RecQL* exons with their surrounding intronic regions. Sequencing was performed on ABI 3700 DNA Sequencers. SNPs and somatic mutations were validated with Biotage pyrosequencing. SNPs that showed significant association with overall survival were further tested in blood DNA samples of 120 patients with resectable pancreatic adenocarcinoma who received neoadjuvant chemoradiation. Univariate analysis of the effect of genotype on time to recurrence and overall survival was performed using the Cox proportional hazards models.

**Results:** Several previously reported and newly identified SNPs but no nonsynonymous SNPs were found in this study. In addition to the *RecQL* A159C SNP (rs13035), 2 SNPs, located in introns 2 and 11 (rs10841834, rs2159943) showed a significant association with overall survival. The three SNPs are part of the same haplotype block (linkage disequilibrium). The variant allele of each SNP had a similar effect on overall survival of patients receiving either adjuvant or neoadjuvant therapy. No mutations were detected in the tumors in the exonic regions of the *RecQL* gene.



**Figure 1.**

**Conclusion:** The SNPs from the 3'UTR and intronic 2 and 11 regions (CC, TT, and AA genotypes) of *RecQL* are associated with improved overall survival of patients with resectable pancreatic cancer. The functional significance of these SNPs warrants further investigation.

8

### Biliary complications including a single donor mortality: experience of 207 adult-to-adult living donor liver transplantation

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**Introduction:** Donor safety is crucial in Living donor liver transplantation (LDLT) with 'do no harm' aphorism printed in the transplant team mind. Biliary anomalies are more common in right liver compared to left liver grafts. Biliary complication is the main cause of morbidity following right lobe donation. Mortality following right lobe donation has been estimated to be less than 0.5%.

**Patients and methods:** Between November 2001 to date, 207 adult-to-adult LDLT has been done using right lobe grafts. The donors included 173 men and 34 women with mean age  $28.4 \pm 5.2$  years. Siblings were 144 (69.6%) cases while unrelated donors were 63 (30.4%) with a mean body mass index  $25.2 \pm 2.4$ . Liver biopsy is

routinely done and steatosis less than 15% is accepted. Single and multiple right bile duct (RBD) were present in 82 (39.6%) and 125 (60.3%) donor, respectively. Multiple RBD included 2 or 3 RBD in 116 (56%) and 9 (4.3%) cases, respectively. The mean operative time was  $360 \pm 50$  min. with an estimated blood loss around  $950 \pm 450$  mL and returned cell-saver amount of  $450 \pm 334$  mL. Two donors (0.9%), each received two blood bank units. Donor remnant liver volumes (RLV) were  $33.5 \pm 3.2\%$ . Mean ICU stay was  $3 \pm 0.7$  days and mean hospital stay was  $14 \pm 3.5$  days.

**Results:** The overall biliary complications occurred in 27 (13.04%) cases. Following modified Clavien classification, biliary complications were graded as grade I ( $n = 10$ ), grade II ( $n = 2$ ), grade III ( $n = 14$ ) and grade V ( $n = 1$ ). Grade I and II ( $n = 12$ ) biliary complications were successfully managed conservatively. Grade III cases were treated by ultrasound guided aspiration,

ERCP and surgery in 10, 2 and 2 donors, respectively. The later 2 donors were treated by t-tube insertion in one case and duct-to-duct anastomosis following transaction of the CBD in the other case. The later case needed ultrasound guided dilatation and 10F stent insertion twice with normal liver profile thereafter. Single donor mortality (Grade V) (0.4%) occurred following biliary leakage from RBD stump followed by peritonitis that necessitated exploration on day 11, re-exploration on day 31 and ERCP with stent insertion on day 38 and the donor succumbed on day 43 due to uncontrolled sepsis.

**Conclusion:** Donor biliary complications accounts for up to 43% of all complications. The majority of biliary complications is minor and could be managed conservatively. However, uncontrolled biliary leakage is a serious morbidity that should be avoided as it could lead to a mortality.



Abstracts 9 to 16  
Free Papers – Liver I  
Saturday, March 14, 2009 8:10–10:10 AM

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9

**Surgical downstaging and neo-adjuvant therapy in metastatic colorectal carcinoma with irinotecan drug eluting beads: a multi-institutional study**

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**Background:** Neoadjuvant chemotherapy for potentially resectable metastatic colorectal cancer (MCC) is becoming a more common treatment algorithm. However, with the ever increasing hepatic toxicity with systemic chemotherapy a more target approach with maximum response and minimal hepatic toxicity is needed. The aim of this study was to evaluate the efficacy of precision hepatic arterial Irinotecan therapy in potentially resectable MCC.

**Methods:** An open-label, multi-center, multi-national single arm study of MCC patients, who received hepatic arterial Irinotecan. Primary endpoints were safety, tolerance and metastatic tumour resection.

**Results:** Fifty-five patients with metastatic colorectal to the liver underwent a total of 90 hepatic arterial Irinotecan treatments. Thirty (55%) Women, 25 (45%) Men, 39 (71%) Caucasian, with a median age of 52 years (range 42–75) were treated. The extent of liver involvement was 41 (75%) of patients had < 25% Tumor Replacement, 15% (< 26–50% tumor replacement), 10% (> 50% replacement), with median number of hepatic lesions being 4 (range 1–20), total size of all target lesions being 9 cm (range 5.5–28 cm), and 50% of patients having bilobar tumor distribution. Median number of irinotecan treatments were two (range: 1–5), median treatment dose was 100 mg (range 100–200), with total hepatic treatment of 200 mg (range 200–650), with 86% of treatments being performed in a lobar infusion treatment, and 30% of patients treated with concurrent simultaneous chemotherapy. Eleven (20%) patients demonstrated significant response and downstage of their disease or demonstrated stable disease without extra-hepatic disease progression that they underwent resection, ablation, or resection and ablation. There were no deaths with morbidity occurring in 20% of patients, with none of them being hepatic related. Non-tumorous liver resected demonstrated no evidence of steatohepatitis from the Irinotecan arterial infusion.

**Conclusions:** Hepatic arterial infusion with Irinotecan was safe and effective in the treatment of MCC as demonstrated by a minimal infusion complication rate, acceptable tumor response and sustained disease stabilization. Hepatic arterial infusion is an acceptable therapy for evaluating the biology of metastatic colorectal to the liver prior to planned hepatic resection.

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**Exsanguination protocol improves survival after major hepatic trauma**

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*Vanderbilt University Medical Center, Nashville, TN, USA*

**Background:** Hepatic injury remains an important cause of exsanguination after major trauma. Recent studies have noted a dramatic reduction in mortality among severely injured patients when trauma exsanguinations protocols (TEP) are employed. We hypothesized that utilization of our institution's TEP at the initiation of hospital resuscitation would improve survival in patients with significant hepatic trauma.

**Methods:** TEP, which involves immediate and sustained release of blood products to the hemodynamically unstable trauma patients in the operating room in pre-defined ratios, was initiated in February 2006. All patients who (1) underwent immediate operative intervention, (2) sustained intra-abdominal hemorrhage with Grade 3–5 hepatic injury, and (3) received the TEP between February 2006 and January 2008 were prospectively identified. A pre-TEP cohort was retrospectively identified from among all trauma patients admitted between February 2004 and January 2006 who (1) received immediate operative intervention, (2) were treated for major intra-abdominal hemorrhage with a Grade 3–5 hepatic injury, and (3) received more than 10 units packed red blood cells in the first 24 h. Univariate and multivariate analyses were used to examine the effects of TEP on blood product use during the first 24 h of resuscitation and evaluated the effects of demographic and clinical covariates on survival.

**Results:** Seventy-five patients were included in the analysis: 39 constituted the pre-TEP cohort (31% 30-day survival) and 36 were treated with the TEP protocol (53% 30-day survival). There were no differences in age, gender, mechanism, grade of injury, lobar involvement, or injury to major hepatic vasculature between the two cohorts (all  $P > 0.25$ ). However, patients treated with TEP had higher injury severity scores ( $P < 0.01$ ). While 24-hour use of blood products did not differ between cohorts, TEP patients received more FFP and platelets during operative intervention and significantly less crystalloid (all  $P < 0.01$ ). After adjusting for age, gender, mechanism, and injury severity score; Grade 5 injury and involvement of major hepatic vasculature had significant negative effects on survival (both  $P \leq 0.02$ ), while utilization of TEP improved the odds of 30-day survival by 78% (OR = 0.22, CI: 0.06–0.81,  $P = 0.02$ ).

**Conclusions:** An exsanguination protocol allows for more effective utilization of FFP and platelets during intra-operative management of major hepatic injury. TEP was associated with a significant improvement in 30-day survival among patients treated for intra-abdominal hemorrhage associated with significant hepatic trauma.

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### Evaluation of perioperative chemotherapy using a prognostic nomogram for survival following resection of colorectal liver metastases

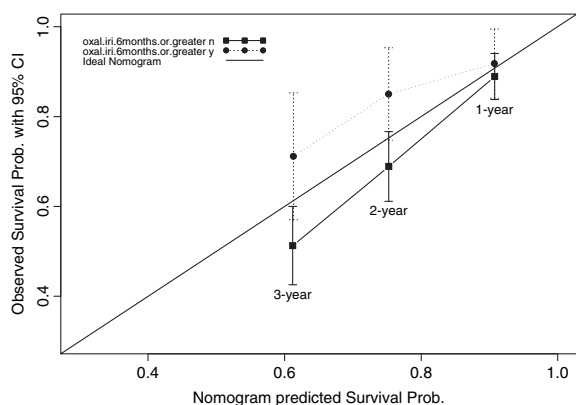
S. K. REDDY, MD, M. W. KATTAN, PHD, C. YU, PHD, E. P. CEPPA, MD, S. G. DE LA FUENTE, MD, Y. FONG, MD, B. M. CLARY, MD and R. R. WHITE, MD

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**Introduction:** Nomograms are statistical tools designed to predict outcomes and risk stratify patients for clinical trials and multi-modality therapy. The aim of this study was to evaluate the effects of perioperative chemotherapy on disease-specific survival (DSS) after resection of colorectal liver metastases (CLM) using a prognostic nomogram incorporating demographic and clinicopathologic variables established at Memorial-Sloan Kettering Cancer Center (MSKCC).

**Methods:** An external cohort comprised of 203 consecutive patients who underwent resection of CLM between 1996 and 2006 at Duke University Medical Center was used to validate the nomogram and to evaluate the effects of perioperative chemotherapy on DSS after resection.

**Results:** Similar to the MSKCC population, the external cohort included patients with node-positive primary disease (61.1%), rectal primary tumors (22.2%), disease-free interval < 12 months (63.5%), size greater than 5 cm (30.0%), multiple CLM (39.4%), bilobar disease (26.1%), and age greater than 70 (20.7%). After a median follow-up of 30.4 months (range 0.33–150), Kaplan-Meier (KM) estimates for 3, 5, and 8-year post-resection DSS were 56%, 41%, and 32%; similar to nomogram predicted probabilities for DSS. The nomogram concordance index was higher (0.602) than the concordance index for the Fong colorectal risk score (CRS; 0.533). KM DSS was longer for the 50 patients treated with at least six months of peri-operative irinotecan and/or oxaliplatin (iri/oxal) based chemotherapy regimens compared to patients who were not (median 66 vs. 40 months,  $P = 0.06$ ). KM DSS was greater than nomogram predicted DSS for treated patients ( $P = 0.32$ , Figure 1).



**Figure 1.** Observed KM DSS versus nomogram predicted DSS stratified by treatment with at least 6 months of peri-operative iri/oxal. The KM estimate of survival at each time point with 95% confidence intervals is represented.

**Conclusions:** The CLM nomogram was validated by an external cohort and more accurately predicted post-resection survival than the commonly used CRS. Peri-operative contemporary chemotherapy treatment may improve outcomes beyond that predicted by the nomogram.

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### Hepatectomy after neoadjuvant chemotherapy for initially unresectable liver metastases from colorectal cancer

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**Hypothesis:** Multiple, bilateral and synchronous disease is not an absolute contraindications to hepatectomy and neoadjuvant chemotherapy followed by hepatectomy could provide significant survival in those not previously considered for cure.

**Results:** From 1996 to 2008 75 patients had 102 hepatectomies for colorectal liver metastases with 55 (73.3%) not initially considered for cure based upon the number, location and size of these lesions. They were only offered palliative chemotherapy by other institutions. Despite previous opinions, 33 (44.0%) patients had primary hepatectomy (PH) while the 42 (56.0%) others received neoadjuvant chemotherapy (NCH) prior to liver resection. A major response occurred in 26/42 (61.9%) patients, partial and total tumor necrosis in 14/42 (33.3%) and 4/42 (9.5%) others respectively on final pathology. Major hepatectomy was performed in 46 (61.3%) patients and minor in 29 (38.7%) including discontinuous bilateral hepatectomy in 34 (45.3%) patients. Morbidity was 31.1% with mortality of 1.4%. 5 and 10-year survival was 41.4% and 25.3% respectively for the series. With 5 and 10-year survival of 51.2% and 42.7% for PH and 34.2% and 17.1% for the NCH groups respectively. Disease-free survival at 5 and 10 years was 39.7% and 24.3% that was 45.8% and 38.2% for PH and 24.5% and 12.3% for the NCH group. The difference in survival was not statistically significant for overall ( $P = 0.40$ ) and disease-free survival ( $P = 0.18$ ). At the last follow-up 33 (44.6%) were alive with a mean survival of  $5.9 \pm 0.5$  years (range 0.8–11.4 years) 41 (55.4%) were dead, 24 (32.4%) were disease-free with a mean survival of  $5.0 \pm 0.6$  years (range 0.8–11.1 years) and 9 (12.2%) were alive with disease with a mean survival of  $3.6 \pm 1.3$  years (range 1.2–4.8 years).

**Conclusions:** Initially resectable patients can undergo PH with good survival while others are down-staged with neoadjuvant chemotherapy prior to liver resection. Removing all disease can produce long-term survival in patients deemed initially unresectable for cure. Multiple and bilateral tumors from colorectal metastases benefit from neoadjuvant chemotherapy before hepatectomy. Survival benefit was statistically similar in both the PH and NCH groups. Salvage of these patients for cure is encouraging when the only other alternatives are locoregional and palliative chemotherapy where the likelihood of obtaining a long-term survival is hopeless.

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### Resection of colorectal cancer (CRC) liver metastases: What is an adequate margin?

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Traditionally a 1cm margin has been accepted as the goal when resecting CRC liver metastases. Evidence is emerging that a lesser margin may provide good outcomes, but a critical margin, below which recurrence is higher and survival poorer, has not been universally agreed. In a recent publication<sup>1</sup> we reported peri-operative morbidity and clear margin as the two independent prognostic factors. In this study we defined a clear margin as an absence of tumor cells within 1 mm of the transected surface. The aim of the current study is to further analyse the effect of the width of the surgical margin on patient survival to determine whether a margin of 1 mm is adequate.

**Methods:** Two hundred and sixty-one consecutive primary liver resections for CRC mets from 1992 to 2007 were analysed (including 197 patients from<sup>1</sup>). 163 (62.5%) were male. The median age was 64 (22–92) years. The 30 day (in-hospital) mortality was 1.5%. The primary CRC Duke staging include 11 As, 70 Bs, 110 Cs and 70 Ds. Initial analysis was performed on five groups according to the resection margins; involved, minimal margin (0–1mm), > 1–4mm, > 4 to < 10mm and ≥10mm. Subsequent analysis was based on two groups: margin ≤ 1mm and > 1mm.

**Results:** With a median follow-up of 4.7 years, the overall 5 year patient & disease free survival (DFS) were 38% & 22% respectively. The 5 year patient and DFS was significantly better in patients with ≥ 10mm resection margin compared with those of involved margin (43.4% vs. 19.4%  $P < 0.03$ ; 28.7% vs. 16.9%  $P < 0.02$  respectively). There was no significant difference in patient or DFS between the three groups with margin > 1mm. The 5-year patient survivals in these groups were similar. When a comparison is made between patient with either involved or ≤ 1mm margin with patients with > 1mm margin, there is a significant 5 year patient survival difference of 25% versus 43% ( $P < 0.04$ ). The DFS difference however did not reach statistical significance ( $P = 0.14$ ).

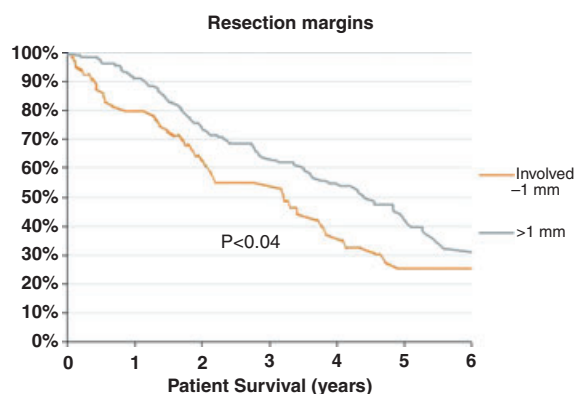


Figure 1.

**Conclusions:** In this cohort with a medium follow-up of 5 years, we can demonstrate that a margin of > 1 mm is associated with significant better 5 year survival. The possible beneficial effect of greater margin beyond 1mm could not be clearly demonstrated in this cohort.

#### Reference:

1. Scheisser M, Chen JW, Maddern GJ, Padbury RT. Perioperative morbidity affects long term survival in patients following liver resection for colorectal metastases. *J Gastrointestinal Surg* 2008; **12**: 1054–60.

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### Locally advanced intrahepatic cholangiocarcinoma: survival benefit with aggressive hepatic resection

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**Introduction:** Intrahepatic cholangiocarcinoma (ICC) is rare and often presents as locally advanced disease. We hypothesized that aggressive major hepatic resection may improve the survival of patients with ICC.

**Methods:** All consecutive patients who underwent hepatic resection for ICC from Jan 1993 to Jan 2003 were retrospectively reviewed. All pathological specimens were re-examined by two independent pathologists.

**Results:** There were 100 patients (male = 40, female = 60) with a mean age of 63 years old. Eighty-six patients had major hepatic resections, of which 30 were extended hepatic resections and eleven involved resection and reconstruction of an extrahepatic structure (vena cava = 7, main portal vein = 2, and common bile duct = 2). The mean tumor size was 7.7 cm; multifocal disease was present in 27 and regional invasion in 17. There were 89 R0 resections and eight R1 resections despite an extended hepatic resection. Perioperative morbidity and mortality were 37% and 3%, respectively. Mean hospitalization was 9 days. Multivariate analysis demonstrated that the factors significantly predicting survival were R0 resection ( $P < 0.0001$ , HR 3.92), tumor size ( $P = 0.0001$ , HR 3.74), metastasis to lymph node(s) ( $P = 0.0001$ , HR 3.241), older age ( $P = 0.002$ , HR 3.11), and tumor multiplicity ( $P = 0.02$ , HR 1.78). The median survival rate for R0 and R1 resections was 4.97 years vs. 8.9 months, respectively. Overall 1-, 3-, and 5- year survival rates for R0 and R1 resection were 84% vs. 45%, 57% vs. 18% and 49% vs. 0%, respectively. Disease recurred in 59% of patients after a mean follow up of 4 years (hepatic recurrence = 53%, extrahepatic = 47%).

**Conclusions:** Multivariate analysis demonstrated both tumor and patient factors as critical predictors of long term outcome in the management of locally advanced ICC. However, the most significant factor predicting survival was ability to achieve an R0 resection. Effective preoperative multimodality therapy is needed to downstage tumors, and patients should undergo aggressive major hepatic resection with the goal of R0 resection.



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### Long-term outcome following sequential resections of liver and lung metastases from colorectal carcinoma

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**Background:** Surgical resection of colorectal liver metastases (CLM) is an established form of treatment. Limited data exists on the value of sequential hepatic and pulmonary metastatectomy. We analysed patients who underwent sequential liver and lung resections for CLM.

**Methods:** A total of 910 patients who underwent liver resection for CLM between January 2000 and December 2007, were analysed to identify patients with resectable pulmonary metastases ( $n = 43$ ; 4.7%). Patient demographics, overall survival and survival difference between synchronous and metachronous pulmonary metastatectomy group and between 'liver and lung resection' group and matched 'liver resection only' group without pulmonary metastases (matched for age, primary disease stage, interval to liver resection, and liver disease stage) were analysed.

**Results:** Forty-three patients underwent sequential liver and lung resections. The median age was 62 years. The median number of liver lesion detected was three and the most commonly performed procedure was right hemihepatectomy (41.9%). Right upper lobe was the predominant site of lung metastasis (51%). Ten patients had synchronous lung metastasis. The median interval between liver and lung metastatectomy was 25 months. The 1-, 3- and 5-year overall survival rates after first metastatectomy were 100%, 87.1% and 53.9% respectively with a median survival of 42 months. Metachronous pulmonary metastatectomy group had better 1-, 3- and 5-year survival rates than the synchronous group (100%, 88.9% and 60.9% vs. 100%, 75% and 0% respectively). There was no significant survival difference between the 'liver and lung resection' and the 'liver resection only' groups.

**Conclusion:** Sequential liver and lung resections for metastases from colorectal carcinoma have good long-term survival for selected patients. Presence of synchronous lung and liver metastases was not associated with long term survival.

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### Predictors of blood transfusion requirement in elective liver resection

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**Background:** Liver resection for primary and secondary malignancy remains major surgery frequently requiring intra-operative blood transfusion. The balance between safer surgical techniques and more extensive resections

has direct implications on blood transfusion requirements. In addition to increasing shortage of blood stocks, and the cost and side effects of blood transfusion, there is concern that perioperative blood transfusion has an immunomodulatory effect which adversely affects tumour recurrence and prognosis.

**Aim:** To identify predictors of perioperative blood transfusion.

**Methods:** A retrospective review of a prospectively collected database of all elective hepatic resections undertaken in a tertiary referral centre over a 4-year period was performed. Data analysed included patient demographics, comorbidities, underlying liver disease, haematological parameters, preoperative radiological intervention, chemoradiotherapy, previous liver resection, number of tumours, extent and method of resection, use of haemostatic agents and histological diagnosis and grade. Number of units of blood crossmatched and transfused were collected from the hospital's blood bank database. Multivariate regression analysis was performed on significant factors on univariate analysis to determine independent predictors of blood transfusion in the immediate perioperative period (48 h).

**Results:** 599 patients were identified with a median age of 64 years and a male: female ratio of 8:5. In the perioperative period patients were crossmatched a median of 10 units blood. Ratio of units crossmatched: units transfused was 13:1. Fifteen percent of patients received a blood transfusion with a median transfusion of two units. Transfusion requirement varied by operation from 12% of patients undergoing hemihepatectomy or metastectomy to 48% of patients undergoing trisectionectomy. Multivariate regression analysis identified seven independent factors predictive of transfusion requirement (Table 1).

**Table 1.** Independent predictors of blood transfusion requirement.

Predictor	P-value	Odds ratio	95% CI
Coronary artery disease	0.009	2.769	1.287–5.960
Preoperative biliary drainage	< 0.001	6.120	2.276–16.452
Previous liver resection	0.001	4.450	1.830–10.824
Preoperative platelet count	0.002	1.005	1.002–1.008
No. of segments resected: 3–4	0.507	1.300 <sup>a</sup>	0.599–2.824
a) compared to 1–2 segments resected			
No. of segments resected: 5+	< 0.001	4.182 <sup>a</sup>	1.874–9.328
Hepatocellular carcinoma	0.03	2.443	1.092–5.464
Preoperative haemoglobin < 10 g/dL	0.021	6.556 <sup>b</sup>	1.325–32.440
b) compared to Hb > 12.5 g/dL			
Preoperative haemoglobin 10–12.5 g/dL	0.041	2.019 <sup>b</sup>	1.030–3.958

**Conclusions:** Results from this single centre study suggest that major liver surgery may be safely performed with fewer crossmatched units of blood. Here we have identified seven independent predictors of transfusion requirement. These factors could be used as criteria for cross matching of blood, with group and save being a safe and more cost effective measure in certain groups of patients.

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**Targeting focal adhesion kinase inhibits pancreatic cancer growth and metastasis**

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**Background:** Focal adhesion kinase (FAK) is a cytoplasmic protein tyrosine kinase involved in the regulation of cellular signaling, migration, apoptosis, and cell cycle progression. FAK has been shown to activate proliferation and inhibit apoptosis in cancer; however, its role in pancreatic cancer is not well understood. We analyzed the effects of PF-562,271, an inhibitor of FAK, on pancreatic cancer growth, invasion and metastasis.

**Methods:** The human pancreatic adenocarcinoma cell lines L3.6pl and MPanc 96 were investigated *in vitro*, while MPanc 96 was used for *in vivo* investigation. FAK phosphorylation was assessed by Western blot analysis. Transwell migration assays were used to evaluate the role of FAK inhibition in pancreatic cancer cell migration and invasion after stimulation with growth factors and extracellular matrix proteins. To evaluate the effects of FAK inhibition *in vivo*, we used an orthotopic mouse model in which 33 mg/kg of PF-562,271 was administered twice daily by gastric lavage. Tumor volume was evaluated by magnetic resonance imaging (MRI) and tumor size, retroperitoneal invasion, and metastasis were evaluated at necropsy. PF-562,271 was generously provided by Pfizer Inc.

**Results:** In pancreatic cancer cell lines FAK phosphorylation was significantly reduced by PF-562 271 administration exhibiting an IC<sub>50</sub> of 0.1 uM. Stimulation by IGF-I resulted in a 7-fold increase ( $P < 0.05$ ) in cell migration which was inhibited 94% by pretreatment with PF-562 271. Coating of transwell migration chamber membranes with collagen-I increased migration 6-fold and this was inhibited 32% by PF-562 271. In mice bearing orthotopic pancreatic tumors, PF-562,271 therapy (*vs.* control) significantly inhibited tumor growth by MRI volumetric analysis (58.75 mm<sup>3</sup> *vs.* 127 mm<sup>3</sup>,  $P < 0.05$ ) and by pathologic examination (325 mm<sup>3</sup> *vs.* 816 mm<sup>3</sup>,  $P < 0.05$ ). Treatment with PF-562,271 also yielded significantly fewer abdominal metastases (29%

*vs.* 100%,  $P < 0.05$ ), less retroperitoneal invasion (0% *vs.* 83%,  $P < 0.05$ ), and showed a trend towards fewer liver metastasis (0% *vs.* 50%,  $P = 0.06$ ), compared to control.

**Conclusions:** Our study demonstrates the important role of FAK in pancreatic cancer growth, invasion and metastasis. These findings support FAK as a potential target for therapy in patients with pancreatic cancer.

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**The molecular mechanism of HIF-1-independent VEGF expression in hepatocellular carcinoma cell line**

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**Purpose:** Hypoxia-inducible factor-1 (HIF-1) is a master transcription factor that plays a central role in hypoxic expression of various genes. The aim of this study was to provide molecular pathway of vascular endothelial growth factor (VEGF) expression of HIF-1 independent pathway in hepatocellular carcinoma cell line (Hep3B).

**Methods:** HIF-1 $\alpha$ , HIF-2 $\alpha$  dominant negative lentiviral vector was introduced to decrease the expression of HIF in Hep3B cell line. Cells were incubated at 37°C under normoxic and hypoxic condition. We performed VEGF ELISA using supernatant, and Western Blotting to demonstrate the difference of protein expression in normoxic or hypoxic condition. To validate the HIF-1 dependent or HIF-1 independent pathway, we treated the cells with PI3K inhibitor and Erk kinase inhibitor.

**Results:** VEGF level was increased under the hypoxic condition. HIF-1 $\alpha$  protein expression was induced in Hep3B cell line after 24 h of exposure of hypoxia. We used siHIF-1 $\alpha$  and siHIF-2 $\alpha$  transfected Hep3B cell line which was incubated in the normoxic or hypoxic condition. The production of the VEGF was done by the HIF-1 pathway. However significant portion of the VEGF was produced by HIF-1 independent pathway. We treated the vector, siHIF-1 $\alpha$  and siHIF-2 $\alpha$  transfected cells with ERK inhibitor before incubating normoxic or hypoxic condition. The VEGF expression was not different in each cell lines in hypoxic condition. Therefore the regulation of VEGF expression was not influenced by ERK pathway. We treated the vector, siHIF-1 $\alpha$  and siHIF-2 $\alpha$  transfected cells with PI3K inhibitor before incubating normoxic or hypoxic condition. The PI3K inhibitor decreased VEGF expression in the siHIF-1 $\alpha$  transfected cells in the hypoxic condition. We treated the vector, siHIF-1 $\alpha$  and siHIF-2 $\alpha$  transfected cells with siSP1 transient transfection before incubating normoxic or hypoxic condition. The siSP1 transient transfection decreased VEGF expression in the siHIF-1 $\alpha$  transfected cells in the hypoxic condition. Therefore the VEGF regulation of Hep3B cell line was mainly controlled by

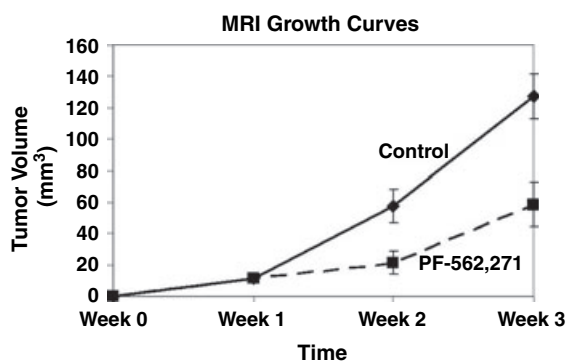


Figure 1.

Akt/PI3K and SP1 pathway which was independent on HIF-1 in hypoxic condition.

**Conclusions:** Under the hypoxic condition, VEGF expression was controlled by HIF-1. However the VEGF expression by Akt/PI3K and SP1 pathway is not mediated by HIF-1 in the Hep3B cell line.

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### **Proteasome inhibition in combination therapy of experimental pancreatic cancer: *in vitro* and *in vivo* evaluation**

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**Background:** Use of targeted therapy to enhance clinical benefits of cytotoxic chemotherapy has failed to improve responses in pancreatic ductal adenocarcinoma (PDAC). Proteasome inhibition (PI) with agents such as bortezomib (B, Velcade) has shown anticancer benefits through increase in proapoptotic mechanisms and cell cycle-related antiproliferative effects. This and the possibility for an increased biologic activity of other agents after PI provide the rationale for PI combination therapy. We have previously shown that endothelial monocyte activating polypeptide II (EMAP II, E), an antiangiogenic cytokine, enhances combination treatment effects in experimental PDAC through VEGF and integrin-related mechanisms. Testing E and B for combination benefits *in vivo* and *in vitro* was the purpose of this study.

**Methods:** *In vitro* studies used WST-1 proliferation assays with three human PDAC lines and HUVECs endothelial cells (ECs) in a dose escalation matrix. Human ASPC PDAC cells were used in a murine xenograft survival model. Twelve days after i.p. or s.c. injection of  $7.5 \times 10^5$  tumor cells, animals underwent treatment with various combinations of E (80  $\mu\text{g/kg}$  i.p. daily), B (0.8 mg/kg i.p. twice weekly), or gemcitabine (G, 100 mg/kg i.p. twice weekly) for maximally 30 days. The resulting group survival ( $n = 6/\text{group}$ ) was compared via logrank statistic.

**Results:** In 48-h. assays, B showed strong activity against various PDAC cells (IC<sub>50</sub> range: 0.5–50  $\mu\text{M}$ ) and ECs (25 nM). In a 72-h. combination assay, IC<sub>50</sub>s against ASPC (in  $\mu\text{M}$ ) were: B = 0.1, G = 10, E = not reached at > 50; addition of G and/or E to B at various doses did not affect proliferation differently. In a 48-hr. combination assay, IC<sub>50</sub>s against ECs (in  $\mu\text{M}$ ) were: B = 0.025, G = 5, E = 10; addition of G or E (at their IC<sub>20</sub>) increased B toxicity by 20%, and the triple combination by 42%, suggesting some additive effects. After initiation of *in vivo* PDAC therapy, median group survival (d) was: control = 19, B = 18, E = 20, G = 28; of all three monotherapy groups, only G had a significant survival impact ( $P = 0.02$ ). All combination groups except B + E led to extended survival compared to monotherapies or control ( $P = 0.003$ ). However, addition of B to E, G, or E + G did not enhance survival ( $p = \text{NS}$  for all three comparisons).

**Conclusions:** PI with bortezomib mediates strong antiproliferative effects against PDACs and ECs *in vitro*, but fails to enhance survival. Although combinations are more effective than monotherapies, the *in vivo* synergistic potential is limited. The findings highlight both benefits and challenges of combination therapy approaches, while suggesting limitations of cancer cell *in vitro* assay efficacy predictions.

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### **Anti-inflammatory effects of the nigella sativa seed extract, thymoquinone, in pancreatic cancer cells**

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**Background:** Both hereditary and sporadic forms of chronic pancreatitis are associated with an increased risk of developing pancreatic ductal adenocarcinoma (PDA). Inflammation has been identified as a significant factor in the development of solid tumor malignancies. Thymoquinone (Tq), the major constituent of the *Nigella sativa* oil extract induces apoptosis and inhibits PDA cell proliferation. Tq also increases p21<sup>WAF1</sup> expression, inhibits histone deacetylase (HDAC) activity, and induces histone hyperacetylation. HDAC inhibitors have been shown to ameliorate inflammation-associated cancer in several animal models.

**Objective:** To evaluate the anti-inflammatory potential of Tq in PDA cells in comparison to a specific HDAC inhibitor, trichostatin A (TSA).

**Methods:** PDA cells (AsPC-1, HS766T; MiaPaca) were cultured and treated with or without Tq (25–75  $\mu\text{M}$ ), with or without pre-treatment of TNF- $\alpha$  (30 nM). The effect of Tq on the expression of different proinflammatory cytokines and chemokines was analyzed by real time PCR. Luciferase-labeled promoter studies evaluated the effect of Tq on the transcription of monocyte chemoattractant protein-1 (MCP-1) and nuclear factor- $\kappa\text{B}$  (NF- $\kappa\text{B}$ ). The effect of Tq on the endogenous and TNF- $\alpha$ -induced activation and nuclear translocation of NF- $\kappa\text{B}$  was examined by ELISA and immunohistochemistry.

**Results:** Within 6 h, Tq significantly and dose-dependently reduced PDA cell production of TNF- $\alpha$  ( $P < 0.02$ ), interleukin (IL-1 $\beta$ ) ( $P < 0.02$ ), IL-8 ( $P < 0.05$ ), Cox-2 ( $P < 0.002$ ), and MCP-1 ( $P < 0.005$ ). There was no reduction in interferon- $\gamma$  (IFN- $\gamma$ ) in the same cultures. Within the same time period, TSA reduced the production of Cox-2 ( $P < 0.02$ ) and MCP-1 ( $P < 0.05$ ), but had no effect on TNF- $\alpha$ , IL-8, or IL-1 $\beta$ . Tq, but not TSA, significantly and dose-dependently reduced the intrinsic activity of the MCP-1 promoter. Tq also inhibited the intrinsic and the TNF- $\alpha$ -mediated activation of NF- $\kappa\text{B}$  in PDA cells and reduced the transport of NF- $\kappa\text{B}$  from the cytosol to the nucleus.

**Conclusions:** Our data demonstrate previously undescribed anti-inflammatory activities of Tq in PDA cells, which are paralleled by inhibition of NF- $\kappa\text{B}$ . Tq as a novel inhibitor of proinflammatory pathways provides a promising strategy that combines anti-inflammatory and proapoptotic modes of action.

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### **A proteomic based platform for marker discovery in cholangiocarcinoma**

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Cholangiocarcinoma (CCA) is the second commonest primary malignancy of the liver with a rising incidence worldwide and a dismal prognosis. There remains a lack

of sensitive and specific biomarkers for this disease particularly in distinguishing it from patients with benign and predisposing diseases such as Primary Sclerosing Cholangitis.

Bile, directly draining the liver, may contain higher concentrations of biomarkers than those found in the general circulation, as these may be tumour derived, shed or secreted proteins. The proteomic analysis of bile in disease pathogenesis (i.e. malignancy and gallstone disease), drug metabolism and biomarker discovery has received recent interest. We have developed a reproducible and accurate method of quantifying, desalting and delipidating bile prior to proteomic analysis. Using this method we ran two parallel proteomic based approaches, with the aim of marker discover in CCA.

The first, using Differential In Gel Electrophoresis (DIGE), was a study comparing bile from 4 groups of patients: healthy liver donors ( $n = 5$ ), benign obstruction ( $n = 5$ ), Primary Sclerosing Cholangitis ( $n = 3$ ) and CCA ( $n = 5$ ). This study resulted in six proteins that were significantly differentially expressed between groups (downregulated  $n = 5$ , upregulated  $n = 1$ ) which were then identified by mass spectrometry. Downstream validation of the upregulated protein was performed by Western blotting, which confirmed a significant difference in abundance of this protein between the four groups.

The second method used a Shotgun based approach, namely GeLC-MS/MS. For this, a sample of bile from a patient with CCA was analysed and over 1200 proteins identified. In validation studies, by Western blotting, two of these biliary proteins were differentially upregulated in CCA when compared to other disease groups. Using a proteomic based approach we have identified 3 differentially expressed proteins in the bile of patients with CCA compared to normal, benign and predisposed patient groups.

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### Microenvironment-induced gene expression changes in breast cancer liver metastases

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**Introduction:** Breast cancer is the most common cancer affecting Canadian women and is the second leading cause of cancer related deaths in these patients. The acquisition of metastatic abilities by breast cancer cells is the most deadly aspect of the disease. Upon dissemination from the primary tumor, breast cancer cells display preferences for specific metastatic sites. The liver represents the third most frequent site for breast cancer metastasis, following bones and lungs. Despite the evidence that hepatic metastases are associated with poor clinical outcome in breast cancer patients, little is known about the molecular mechanisms governing the spread and growth of breast cancer cells within the liver.

**Methods:** We have employed 4T1 murine mammary carcinoma cells that were subjected to three rounds of splenic injection, which permitted the isolation of breast cancer cells that aggressively grow in the liver. Laser Capture Microdissection (LCM) was used to identify gene expression changes within breast cancer liver

metastatic cells that occur *in situ* in response to the liver microenvironment. 4T1 breast cancer cells located at the margin and the centre of several metastatic lesions have been individually sampled by LCM and the recovered RNA subjected to linear amplification, labeling and hybridization to Agilent microarrays. To date, we have analyzed four matched sets of margin vs. core liver metastases samples. Moreover, we have complemented the analyses of 4T1-derived lesions with LCM experiments performed on liver metastases isolated from breast cancer patients.

**Results:** Among several candidate genes that were differentially expressed between the margin and core of the liver metastases, the gene encoding for the leptin receptor appeared to be up-regulated in the margin. The Leptin/LEPR axis has gained considerable attention as an important regulator of breast cancer progression. Indeed, Leptin and LEPR are over-expressed in breast cancers compared to normal breast epithelium and Leptin has been shown to stimulate the proliferation of breast cancer cells. We have validated LEPR expression in the 4T1-derived liver lesions, and more importantly, observe LEPR positivity in multiple liver metastases obtained from breast cancer patients.

**Conclusion:** The identification and functional validation of candidate genes important for the ability of breast cancer cells will provide basic insights into the pathways required for breast cancer cells to metastasize to the liver. Our results suggest that the LEPR may play an important role in enabling breast cancer cells to metastasize to the liver.

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### Validation of a novel, physiologic model of experimental acute pancreatitis in the mouse

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**Background:** Acute pancreatitis is a devastating disease that affects 240 000 Americans each year. No specific treatment for acute pancreatitis currently exists, largely because its precise pathophysiology is poorly understood. Murine experimental models are attractive, as complete knowledge of the mouse genome permits precise genetic manipulation. Unfortunately, current methods used to induce acute pancreatitis in the mouse (cerulein hyperstimulation, intravascular bile salt infusion, supraphysiologic arginine administration) are of questionable clinical relevance. Therefore, the aim of the current study was to validate a recently reported murine model of acute pancreatitis that is more representative of the human disease process.

**Methods:** Twenty C57BL/6J and 11 CF-1 mice were studied. Under general anesthesia, transduodenal cannulation of the pancreatic duct was accomplished with a 30-gauge catheter, and 50  $\mu$ L of 5% Sodium Taurocholate (NaT) or 0.9 normal Sodium Chloride (NaCl) was infused. Mice were euthanized 24 h later. Three observers rated pancreatitis severity by light microscopic evaluation of H&E sections. A validated scale incorporating degree of edema, vacuolization, and inflammatory cell infiltrate comprise the total pancreatitis score. Pancreatic tissue concentration of the chemoattractant molecule

monocyte chemoattractant protein-1 (MCP-1) and the proinflammatory cytokine interleukin-6 (IL-6) were determined by ELISA. ANOVA and Student's *t*-test were applied where appropriate; *P* value < 0.05 was accepted as statistically significant.

**Results:** Thirteen mice (NaCl – 6; NaT – 7) survived for 24 h. The total pancreatitis score was significantly greater in mice undergoing retrograde pancreatic duct infusion of NaT (Table 1). Pancreata of mice infused with NaT demonstrated significant necrosis, consistent with severe acute pancreatitis. Pancreatic concentrations of MCP-1 and IL-6 are shown in the Table 1.

**Table 1.** Pancreatic concentrations of MCP-1 and IL-6.

	Pancreatitis score	MCP-1 (pg/mg)	IL-6 (pg/mg)
NaCl ( <i>n</i> = 6)	1.2 ± 0.4	2350 ± 1386	452 ± 269
NaT ( <i>n</i> = 7)	6.3 ± 1.2*	3633 ± 1853	2028 ± 1612*

\**P* < 0.05 vs. NaCl

**Conclusions:** Retrograde pancreatic duct infusion of Sodium Taurocholate induces severe acute pancreatitis in the mouse. Though associated with a discrete learning curve, this model is likely more representative human pancreatitis pathophysiology, and therefore provides a powerful tool with which to elucidate clinically important basic mechanisms underlying the pathogenesis of acute pancreatitis.

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### The expression of interferon receptor alpha/beta in human pancreatic cancer in nude mice is essential for tumor response to interferon alpha treatment

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**Introduction:** Adjuvant interferon (IFN) therapy and chemoradiation status post pancreaticoduodenectomy

for patients with pancreatic cancer have rendered promising results. The aim of this study was to evaluate the *in vivo* effect of interferon alpha on human pancreatic carcinoma implanted orthotopically into nude mice.

**Material and methods:** Human pancreatic cancer cell lines MiaPaCa-2 and Panc-1 were used. MiaPaCa-2 is known to express the interferon alpha/beta receptor and Panc-1 cells do not. The cells were implanted into the pancreas of nude mice and treatment was initiated seven days later. Regimen I consisted of intraperitoneal single-agent gemcitabine (125-mg/kg biweekly) and Regimen II consisted of IFN-alpha (10 000-units daily, subcutaneously) and gemcitabine biweekly for 30 days. Animals were sacrificed after 30 days or if they became moribund. Body weight was determined and the primary tumors in the pancreas were excised, measured, and weighed. Visible metastases or adjacent organ invasion were counted and processed for H&E staining. All macroscopically enlarged regional (celiac and para-aortal) lymph nodes were harvested and the presence of metastatic disease was confirmed by histology.

**Results:** The mice that were implanted with MiaPaCa-2 cells showed a more dramatic response to Regimen II when compared to Panc-1 implanted mice. The MiaPaCa-2 group that was treated with Regimen II showed an 87% reduction in tumor volume compared to 50% in the Panc-1 group treated with the same regimen (*P* < 0.001). Mice implanted with MiaPaCa-2 and treated with Regimen II showed less metastasis, less local invasion, and a longer survival compared to mice implanted with Panc-1 treated with same regimen. Regimen II was more effective on MiaPaCa-2 compared to Regimen I (*p* < .001). There were no differences between regimen I and II in the Panc-1 group.

**Table 1.** Tumor reduction after treatment based on regimen.

Regimen/cells implanted	Regimen 1 ( <i>n</i> = 7), %	Regimen 2 ( <i>n</i> = 7), %
MiaPaca - 2	48	87
Panc- 1	40	50

**Conclusions:** Treatment of human pancreatic cancer in nude mice with interferon alpha and gemcitabine was associated with a reduction in tumor volume. This process occurs in those cells that express the appropriate interferon receptors.



Abstracts 25 to 31  
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**Is the use of donors with high donor risk indices cost-effective in liver transplantation?**

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**Background:** The ever widening gap between the availability of donor organs and the number of liver transplant candidates requires the maximal use of all available grafts, including those with high donor risk indices (DRI). High DRI organs are classified as those having DRIs greater than 2.0, while low DRI organs have DRIs less than 2.0. Organs with a DRI above 2.0 account for about 10% of the donor pool. Recipients receiving high DRI organs have been shown to have twice the length of stay and a two fold increase in hospital costs when compared to recipients of low DRI organs. Unless these grafts are used judiciously, outcomes and transplant resource utilization will be negatively affected. The aim of this study was to evaluate the cost-effectiveness of an organ allocation scheme using high and low DRI organs compared to an allocation scheme using only low DRI organs. Additionally, the impact of these schemes on wait list mortality will be evaluated.

**Methods:** A Markov-based decision analytic model was created to simulate outcomes for liver transplantation in recipients of organs from low and high DRI donors versus recipients of organs from low DRI donors. A second model was created to simulate outcomes that reflect alterations in wait list mortality under both organ allocation schemes. Baseline values and ranges were determined from the UNOS database (19 000 recipients transplanted between 2002 and 2007) and Medicare cost data. Sensitivity analyses were conducted to test model strength and parameter variability.

**Results:** Recipients of organs from low DRI donors had a three year survival of 75% versus 65% for recipients of organs from high DRI donors. After transplantation, recipients of high DRI organs gained 5.1 QALYs (Quality Adjusted Life Years) at a cost of \$75,000/QALY versus 5.9 QALYs at a cost of \$52 000/QALY for recipients of low DRI organs. However, the allocation scheme in which both low and high DRI organs were used together proved more cost-effective when compared to the scheme in which only low DRI organs were used and there was a 25% increase in wait list mortality; 5.8 QALYs at a cost of \$54 000/QALY versus 5.6 QALYs at a cost of \$59 000/QALY.

**Conclusions:** High DRI donors provide a significant number of grafts. While these grafts may represent an increased cost per individual transplant, the overall contribution of these grafts to the donor pool and a subsequent reduction in wait list mortality make them cost-effective.

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**The development of a classification system for biliary complications following orthotopic liver transplantation**

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**Introduction:** Biliary tract complications remain a significant source of morbidity and mortality following orthotopic liver transplantation (OLTx). Even though these occur with an estimated incidence of 10–40% and may lead to graft failure, there exists no universally accepted classification system. As such, descriptions of biliary complications in the literature often lack consistency and clarity which limits evaluation and comparison of post-transplantation outcomes. We propose a structured classification system for biliary complications following choledocho-choledochal anastomosis (CCA) at OLTx. The classification is based on four major components: leaks (anastomotic or cystic duct, anastomotic disruption), filling defects (stones/sludge/casts in the intrahepatic, recipient or donor common ducts), strictures (unilateral intrahepatic, common hepatic or anastomotic) and development of sclerosing cholangitis. Complications are identified and classified based on their appearance on a contrast cholangiogram, mostly endoscopic cholangiopancreatography (ERCP). The goal of this initial report is to ensure that the proposed classification is consistent and reliable.

**Methods:** Patients having undergone OLTx with CCA at the McGill University Health Center from 2004 to 2007 and who had at least one contrast cholangiogram post-operatively were candidates for the study. ERCP films were assessed by two independent reviewers to determine inter-rater reliability and the kappa coefficient of agreement of classification of the complication.

**Results:** One hundred and eight ERCP films were reviewed. Overall inter-rater reliability (percent agreement) among the reviewers was 88.5%. Agreement on specific elements of the classification scheme (leak, stricture, filling defect) was similarly high. Agreement among study reviewers was greater than agreement between study reviewers and the official radiographic report (77.9%), although this was not statistically significant. The kappa coefficient was 0.87 (95% confidence interval 0.79–0.94).

**Conclusion:** The proposed classification system demonstrates high reliability and would allow for consistent interpretation and reporting of biliary complications following OLTx. Validation of this classification system is ongoing through correlation of complications with the end-points of patient survival, graft survival, number of additional interventions required, length of hospital stay and number of readmissions.

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### Regionalization of liver transplantation to high volume centers is associated with diminished volume-outcomes relationship and underutilization of high volume centers by minority patients

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**Introduction:** Our purpose was to determine the temporal trends in liver transplant center volume as well as the effect of those trends on both the volume-outcomes relationship and the utilization of high volume centers by minority patients.

**Methods:** We performed a retrospective analysis of 35 374 adult orthotopic liver transplant procedures included in the Scientific Registry of Transplant Recipients (SRTR) for three consecutive 30-month time periods between 1999 and 2006. Transplant centers were divided into five categories based on annual volume (very low-volume < 36 procedures per year, low volume = 37–55, moderate-volume 56–79, high-volume group = 80–129, very high volume > 130). One-month and 1-year observed-to-expected patient death ratios (provided by the SRTR), were calculated for each time period. Comparisons between volume groups in each time period were made using chi square analysis. Trends in the demographic characteristics were also assessed.

**Results:** The percentage of liver transplants performed at lower volume centers decreased significantly from 51% in Period 1 to 33% in Period 3 ( $P < 0.0001$ ), while those performed at higher volume centers increased significantly from 27% in Period 1 to 44% in Period 3 ( $P < 0.0001$ ). In Period 1, the 1-month and 1-year O:E patient death ratios at very low-volume centers (1-month ratio 1.33, 1-year ratio 1.18) were significantly higher than the ratios at very high volume centers (1-month ratio 0.89, 1-year 0.93,  $P < 0.0001$  at both 1-month and 1-year). By Period 3, the disparity between very low and very high volume centers was no longer statistically significant at either 1 month or 1 year. Meanwhile, in Period 1 the percentage of Black or Hispanic patients at very high-volume centers (28.4%) was significantly greater than at very low-volume centers (20.6%,  $P < 0.0001$ ). By Period 3, the percentage of Black or Hispanic patients at very high volume centers had become significantly lower (18.1%) than at low volume centers (22.7%,  $P = 0.0004$ ).

**Conclusions:** As the percentage of liver transplants performed at higher volume centers has increased over time, the volume-outcomes relationship has become less prominent. However, regionalization of liver transplantation does appear to be associated with a growing underutilization of high volume centers by minority patients.

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### Is magnetic resonance imaging superior to computed tomography for preoperative evaluation of cystic lesions of the pancreas?

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**Purpose:** Cystic lesions of the pancreas (CLP) represent a diverse range of pathologies. Appropriate management depends on accurate diagnostic imaging. Although magnetic resonance imaging (MRI) provides a theoretical advantage in improved soft-tissue contrast, no definitive superiority in its diagnostic capability has been established over computed tomography (CT) in evaluation of CLP.

**Methods:** Database review identified patients undergoing surgical management at our institution between 1/1/00 and 12/31/07 for CLP as confirmed by postoperative pathologic analysis. Records of patients who also underwent same-institution preoperative CT and/or MRI were selected for study. Diagnostic accuracy and confidence were rated on a 5-point scale (Table 1) for each radiologic study as compared with histologic review. Mann-Whitney U and Chi-square tests were used to compare scores for CT and MRI.

**Results:** One hundred and forty-eight patients received operative interventions for CLP. Of these, 96 (65%) underwent preoperative CT and/or MRI (43 CT only, 41 MRI only, 12 both) at our institution with a total of 108 radiologic studies. Histologically, 24 patients (25%) had serous cystadenomas; 23 (24%), intraductal papillary mucinous neoplasms (IPMN); 20 (21%), mucinous cystadenoma/adenocarcinomas; 19 (20%), pseudocysts; 7 (7%), solid pseudopapillary tumors; 2 (2%), simple cysts; and 1 (1%), lymphoepithelial cyst. No significant difference between diagnostic scores of CT and MRI was detected (median 3 vs. 2,  $P = 0.14$ ). However, only 43.6% of CT studies received scores of 1 or 2, while 62.3% of MRI studies achieved the same ( $P = 0.05$ ). There was a trend towards improved preoperative identification of IPMN using MRI as evidenced by percent of score 1 (50% by MRI vs. 13% by CT,  $P = 0.075$ ). No such trend was observed among cystadenomas.

**Conclusions:** MRI may provide greater diagnostic accuracy and confidence in preoperative evaluation of cystic lesions of the pancreas. MRI is prudent when uncertainty regarding diagnosis and management of CT-visualized lesions arise. Additionally, cystic lesions suspicious for IPMN may be better evaluated for ductal involvement with MRI than CT.

**Table 1.** Diagnostic scoring system used for CT and MRI.

Score	Degree of accuracy and confidence of radiologic report results in comparison to surgical pathology results
1	Definitive: correct answer proposed as single or top diagnosis
2	Suggestive: mentions correct answer within a narrow range (3 or less) possible diagnoses of equal likelihood
3	Somewhat suggestive: mentions correct answer within a wide range (greater than 3) of possible diagnoses
4	Vague: does not mention possibility of correct diagnosis anywhere within report
5	Contradictory: correct diagnosis not proposed as possibility, and top proposed diagnosis inaccurate or contradictory to correct diagnosis

( $n = 58$ ), 1 ( $n = 219$ ),  $\geq 2$  ( $n = 89$ ). Except for the AJCC system, all established staging systems performed poorly as judged by the  $c$ -statistics (Table 1). The proposed scoring system for early HCC demonstrated the best prognostic discrimination of all the evaluated systems (Table 1).

**Table 1.** Survival by stage for five existing staging systems and a proposed scoring system for early HCC.

5-year survival, by stage/score (%)						
	AJCC	IHPBA	JIS	CLIP	Okuda	Early HCC Scoring System
T1/Score 0/B 59	59	64	52	45	67	
T2/Score 1/B 40	52	50	47	53	55	
Score 2/C	No pts.	51	57	50	67	39
Score 3	No pts.	No pts.	47	100	No pts.	No pts.
$c$ -Statistics	0.585	0.518	0.502	0.510	0.508	0.592

**Conclusions:** Most staging systems perform poorly when used for prognostic stratification of pts with early HCC. Although the AJCC staging provides moderate discriminative ability, it only includes two groupings (T1 and T2) that constitute early HCC. A simple scoring system for early HCC provides superior discriminative power than existing staging systems.

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### Comparative performance of staging systems for early hepatocellular carcinoma

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**Introduction:** While several staging systems for hepatocellular carcinoma (HCC) have been proposed for patients (pts) with a wide spectrum of HCC disease, most surgical candidates in fact have early HCC. The ability of staging systems to discriminate prognosis after surgery for early HCC is unknown. We sought to assess the performance of major HCC staging systems in a large cohort of pts with early HCC.

**Methods:** Data on pts undergoing liver resection (LR) or transplantation (LT) for early HCC ( $\leq 5$  cm, N0M0, no major vascular invasion) with well-compensated cirrhosis were collected from an international group of seven hepatobiliary centers. We evaluated five staging systems: American Joint Committee on Cancer (AJCC), International Hepato-Pancreato-Biliary Assoc. (IHPBA), Japanese Integrated Staging (JIS), Cancer of the Liver Italian Program (CLIP), and Okuda. A previously proposed scoring system for early HCC was also evaluated; this system allots 1 point each for size  $> 2$  cm, multifocality, and microscopic vascular invasion (mVI). The discriminative abilities of the systems were quantified via bootstrap-corrected concordance indices ( $c$ ).

**Results:** Of 366 eligible pts, 236 underwent LR and 130 LT. Overall survival was 74% at 3 years and 53% at 5 years (median 63 months). While most pts had size  $> 2$  cm ( $n = 278$ , 76%), a minority had multifocality ( $n = 47$ , 13%) or mVI ( $n = 76$ , 21%). The distribution of pts among stages was: AJCC: T1 ( $n = 250$ ), T2 ( $n = 116$ ); IHPBA: T1 ( $n = 67$ ), T2 ( $n = 273$ ), T3 ( $n = 26$ ); JIS 0 ( $n = 51$ ), 1 ( $n = 249$ ), 2 ( $n = 54$ ), 3 ( $n = 12$ ); CLIP: 0 ( $n = 206$ ), 1 ( $n = 81$ ), 2 ( $n = 19$ ), 3 ( $n = 2$ ); Okuda: A ( $n = 69$ ), B ( $n = 219$ ), C ( $n = 3$ ); early HCC scoring system: 0

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### Liver retransplantation – a 25-year experience

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Retransplantation (re-LT) is the only viable option for irreversible graft failure after primary transplantation. Due to the growing disparity between the number of people listed for primary Liver transplantation and organs available and its inferior outcomes when compared to primary transplantation, re-LT is certainly controversial. The aim of this study was to analyse the indications and outcomes of re-LT since the beginning of our programme.

**Methods:** The clinical and demographic data for this retrospective study from 1982 to 2007 was collected from our dedicated transplant database. During this period a total of 2420 adult transplants were performed at our centre.

**Results:** A total of 196 re-LT patients underwent 225 transplantations (8.09%). The mean age was 42.99 years ( $SEM \pm 0.09$ ) with the median age of 44.85 years (16.4–68.3). The number of retransplants has gone down steadily due to the better techniques and newer immune suppression. Out of 196 re-LT, 23 had second re-LT (0.95%) and 6 had their fourth re-LT grafts (0.24%). More than 1/3 in our study (37.6%) required regrafting within the 6 months of primary transplant. The most common indication was Hepatic artery thrombosis (31.5%), followed by chronic rejection (22.6%) and recurrent disease (14.2%). The patient survival and graft survival are as shown in Table 1.

Early retransplants ( $< 7$  days) of the primary transplant had a worse outcome than late retransplants

( $P = 0.001$ ). Patient survival after retransplantation in patient with PNF and Haemorrhagic necrosis had poor outcome in comparison to others ( $P = 0.008$ ). MELD did not have any impact on patient survival ( $P = 0.2$ )

**Conclusion:** Long terms graft as well as patient survival in patients with regraft populations is significantly lower than patients with primary grafts. Patient survival depends on the indication for retransplantation. Retransplants within 7 days had a poor outcome than the late transplants. Higher MELD did not have any impact on patient's survival. Retransplantation is necessary but the clinical selection of recipient remains of paramount importance.

**Table 1.** Patient (PS) and graft survival (PS).

	First Re		Second Re		Third Re	
	LTx		LTx		LTx	
	PS	GS	PS	GS	PS	GS
30 days	83%	82%	64%	59%	67%	60%
90 days	73%	72%	59%	59%	24%	40%
1 year	66%	65%	45%	45%	24%	20%
3 years	61%	59%	40%	36%	0%	
5 years	57%	54%	40%	32%	0%	
10 years	47%	43%	25%	24%	0%	
Total no of patients	196		23		6	

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### Initial experience using Hepatitis C positive renal allografts in elderly Hepatitis C negative recipients

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**Introduction:** First year mortality for elderly end stage renal disease (ESRD) patients is 1.62–2.53 fold higher as compared to younger ESRD patients. Renal transplantation is an option that provides improved survival,

however, the lack of suitable organs, longer wait-times and worsening co-morbidities are great impedances for the elderly. Considering these difficulties, the use of kidneys from donors with serology positive for Hepatitis C virus (HCV) has been explored. We report our experience with nine HCV negative elderly patients whom underwent renal transplantation receiving an HCV positive allograft.

**Methods:** At the University of Virginia Health System, 542 patients underwent renal transplantation between January 2003 and September 2008. The number of patients  $\geq 60$  years transplanted was 137, including 9 HCV negative patients receiving allografts from HCV positive donors (D+/R-) and 123 HCV negative patients receiving allografts from HCV negative donors. This study retrospectively reviewed those recipients' clinical course, graft function, HCV status, liver function and outcome.

**Results:** The average age of the nine D+/R- patients was  $69.67 \pm 5.96$  years. The average age of the 123 D-/R- patients was  $65.65 \pm 4.24$  years. All D+/R- transplants were from cadaveric donors while D-/R- transplants were divided into 54% cadaveric, 28% living related donors and 18% living unrelated donors. Follow-up ranged between 3 months and two years. Three D+/R- patients (30%) died during the follow-up period: one from causes unrelated to transplantation, two from sepsis. Nineteen of 123 D-/R- patients (15%) died during the follow-up period. The two D+/R- patients who died from sepsis had the only graft function loss and were both treated for rejection (one cellular, treated with high dose steroids and one humoral, treated with plasmapheresis, intravenous immunoglobulin and rituximab). Four D+/R- patients were diagnosed with HCV by HCV-RNA reverse transcriptase polymerase chain reaction. Recipient HCV serology in patients with detectable viral loads was negative for all patients tested. Two D+/R- patients had overt signs of liver disease; one died with transaminitis and one is alive with cirrhosis and portal hypertension.

**Conclusions:** Undoubtedly, elderly patients can achieve improved outcomes with renal transplantation as compared to dialysis. This study size was small and observational only. However, the effect of using allografts from HCV positive donors to reduce wait-time and improve survival may put elderly patients at greater risk for morbidity.

# Abstracts 32 to 40

## Free Papers – Biliary

### Saturday, March 14, 2009 2:00–4:00 PM

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#### Repair of laparoscopic bile duct injuries: timing of surgical repair does not influence success rate

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**Purpose:** Many factors contribute to the success of biliary reconstruction following laparoscopic bile duct injury. We previously reported that control of intra-abdominal infection, complete preoperative cholangiography, surgical technique, and surgical experience affected the result. There is no consensus, however, on whether timing of the operation is important.

**Methods:** We examined factors influencing the success of the first repair of 307 major bile duct injuries following laparoscopic cholecystectomy. The influence of timing of the reconstruction was assessed for cases initially repaired by the primary surgeon or a biliary surgeon. Bivariate and multivariate analysis were used to determine the influence of the factors just mentioned.

**Results:** One hundred and thirty-seven injuries were initially repaired by a biliary surgeon, 163 injuries were initially repaired by the primary surgeon, and seven were managed non-surgically. The repairs by primary surgeons were done earlier than those by biliary surgeons (11 vs. 68 days,  $P < 0.0001$ ). Bivariate analysis of the entire cohort suggested that later repairs might have been more successful than earlier ones (17 vs. 57 days,  $P = 0.003$ ). Multivariate analysis, however, showed that timing of the repair was not important ( $P = 0.931$ ). Instead, success correlated with: eradication of intra-abdominal infection ( $P = 0.0001$ ), complete preoperative cholangiography ( $P = 0.002$ ), correct surgical technique ( $P = 0.0001$ ), and repair by a biliary surgeon ( $P = 0.0001$ ). Separate multivariate analyses of outcomes for primary and biliary surgeons, revealed that timing was unrelated to success in either case (see Table 1); although there was a trend towards significance for primary surgeons ( $P = 0.103$ ) but not biliary surgeons.

**Table 1.** Separate multivariate analysis of outcomes for primary and biliary surgeons.

Time of Biliary surgeon repair			Primary surgeon		
	Success	Bivariate	Success	Bivariate	
	with	P value	with	P-value	
	Success	dilatation	Success	dilatation	
OP	- -	- -	10%	13%	0.103
repair					
< 1	93%	96%	21%	29%	
week		0.854			
< 1	90%	93%	20%	31%	
month					
≤ 6	91%	93%	18%	28%	
weeks					
> 6	88%	95%	0%	33%	
weeks					

**Conclusion:** Thus, the success of biliary reconstruction for iatrogenic bile duct injuries depended on complete eradication of abdominal infection, complete cholangiography, correct surgical technique, and repair by an experienced biliary surgeon. If these objectives were achieved, the repair could be performed at any time with the expectation of an excellent outcome. We see no reason to delay the repair for some arbitrary period in hopes that the operation will become easier and the outcome better. The operation is difficult at any time, but the results are good when it is performed by a biliary surgeon.

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#### Role of preoperative biliary drainage of liver remnant prior to extended liver resection for hilar cholangiocarcinoma

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B. ZAO, SCD, M. D'ANGELICA, MD, Y. FONG,  
MD, P. ALLEN, MD, R. DEMATTEO, MD,  
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**Background:** In patients with hilar cholangiocarcinoma (HCCA), concomitant hepatic resection improves survival but is associated with increased morbidity. Preoperative biliary drainage (BD) of the future liver remnant (FLR) and contralateral portal vein embolization (PVE) may improve perioperative outcome, but their routine use is controversial. This study analyzes the impact of FLR volume and preoperative BD on postoperative hepatic insufficiency and death.

**Methods:** Patients with HCCA who underwent hepatic resection and had adequate imaging available for FLR calculation were identified retrospectively. Patient demographic, operative and perioperative data were recorded and analyzed. The FLR was calculated based on the total liver volume and the volume of the resection performed using semi-automated contouring of the liver on preoperative helical acquired scans. Hepatic insufficiency was defined as a postoperative increase in bilirubin of  $> 5\text{mg/dl}$  that persisted for longer than 5 days. Operative mortality was defined as death related to the operation, whenever it occurred.

**Results:** Between 1997 and 2007, 60 patients with HCCA were identified who underwent hepatic resection and had imaging available for analysis. Preoperative BD of the FLR was used selectively and PVE was used in only 1 patient. The median LOS was 14 days and the overall morbidity and mortality was 53% and 10%. Preoperative



FLR volume was a predictor of hepatic insufficiency and death ( $P = 0.012$ ). 65% of patients had an FLR  $\geq 30\%$  (39/60). No patient in this group had hepatic insufficiency, but there were two operative deaths (5%) in patients who had preoperative BD (Figure). By contrast, in the group with FLR  $< 30\%$  (21/60, 35%), hepatic insufficiency was seen in five patients and operative mortality in four patients (Figure) which was strongly associated with a lack of preoperative BD of the FLR ( $P = 0.009$ ).

**Conclusions:** In patients undergoing liver resection for HCCA, FLR volume  $< 30\%$  is associated with increased risk of hepatic insufficiency and death. Preoperative BD of the FLR appears to improve outcome if the predicted FLR is  $< 30\%$ . However in patients with FLR  $\geq 30\%$ , preoperative BD and PVE do not appear to improve perioperative outcome.

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#### Elevated CA 19-9 portends poor prognosis despite surgical resection of biliary malignancies

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**Background:** Biliary tree malignancies are aggressive cancers with a high disease-specific mortality despite resection. We sought to evaluate our experience and identify predictors of survival following resection.

**Methods:** We reviewed the records of all patients that underwent radical resection of biliary tree malignancy including extrahepatic, intrahepatic cholangiocarcinomas and gallbladder cancers. Demographics, treatment and outcome data were collected and compared by tumor location. Kaplan-Meier survival curves were created and compared by log-rank analysis. Multivariate analysis was undertaken using Cox proportional hazards.

**Results:** Ninety-one patients with biliary malignancies underwent surgical resection between 1992 and 2007. There were 46 extrahepatic cholangiocarcinomas, 23 intrahepatic cholangiocarcinomas, and 22 gall-

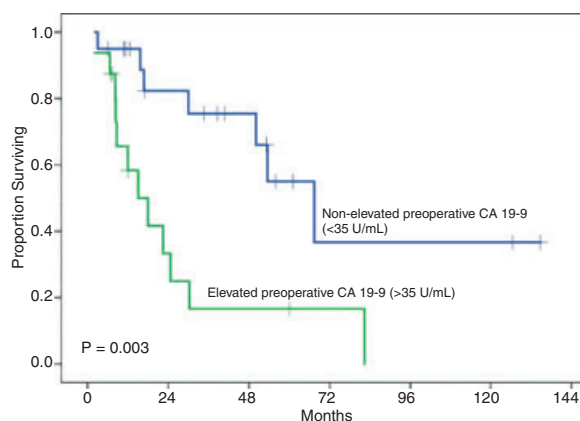


Figure 1.

bladder cancers. All 3 groups were similar in terms of age, gender, preoperative CA 19-9 level, completeness of resection and tumor histology (Table 1). Gallbladder cancer histology correlated with the shortest median survival (14.3 months) followed by extrahepatic cholangiocarcinoma (24.8) and intrahepatic cholangiocarcinoma (30.4) however this did not meet statistical significance ( $P = 0.971$ ). Only elevated preoperative CA 19-9 level ( $> 35 \text{ U mL}^{-1}$ ) was predictive of poor median survival by univariate ( $P = 0.003$ , figure) and multivariate analysis (15.1 months vs. 67.4,  $P = 0.047$ ).

**Conclusions:** While location (i.e. intrahepatic or extrahepatic) of Cholangiocarcinoma is often considered predictive of survival, we did not find a difference in biologic behavior based upon location or histology. Only high preoperative CA 19-9 levels predicted poor survival, thus should be routinely measured prior to resection.

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#### Identification of intraductal papillary mucinous neoplasm in resected biliary tract lesions

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**Background:** The pathologic similarities between mucin secreting cholangiocarcinoma and intraductal papillary mucinous neoplasm (IPMN) of the pancreas have been reported with increasing frequency. Despite this, bile duct IPMN (BD-IPMN) is not recognized currently as a unique medical disease. Our aim was to review the presence of BD-IPMN in a large series of resected biliary neoplasms.

**Methods:** BD-IPMN cases from January 1996 to October 2006 were identified by reviewing pathology specimens of all resected cholangiocarcinomas, and additionally by reviewing liver or bile duct lesions other than cholangiocarcinoma when cystic, papillary, or mucinous features were cited in pathology reports. Diagnostic information, presenting symptoms, operative details, and survival were analyzed via review of medical records. Follow-up and survival were analyzed by Kaplan-Meier techniques.

**Results:** BD-IPMN was identified in 23 of 253 specimens reviewed (48% men; median age = 68 years; range 31–81 years). Symptoms were present for a median of 30 days prior to diagnosis (range 3 days to 7 years). Presenting symptoms included abdominal discomfort in 15 patients (65%), jaundice in 9 (39%), and weight loss in 8 (35%). Preoperative biopsies were performed in 14 patients. None of the original preoperative pathology reports used the term IPMN; 4 (29%) used the terms cystic, mucinous, and/or papillary. Only one of the original pathology reports of the surgical resection specimens used the term IPMN; 13 (57%) used the terms cystic, mucinous, and/or papillary. BD-IPMN was located only in the extra-hepatic bile ducts in 12 (52%), only in the intra-hepatic bile ducts in 6 (26%), and in

both intra and extra-hepatic bile ducts in 5 (22%). Pancreatoduodenectomy was performed in six, combined major hepatic resection and extra-hepatic duct resection in six, radical common bile duct resection in four, hepatic lobectomy in four, segmentectomy in one, cholecystectomy in one, and hepatic duct excision in one. Carcinoma was found in association with BD-IPMN in 18 patients (78%) with a median follow-up of 5.5 years (range 1 month to 9.2 years). Of the patients with confirmed carcinoma, the median survival was 2.8 years; 5-year survival was 40% (95% CI 21-76%).

**Conclusion:** BD-IPMN occurs throughout the intra and extra-hepatic biliary system, and with an understanding of recent trends in pathology, is identified readily. BD-IPMN is found typically in association with carcinoma, but like its pancreatic counterpart, can occur as a benign lesion. Broader acceptance of BD-IPMN as a unique medical disease may lead to a better understanding of the pathogenesis of biliary malignancies.

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### Iatrogenic bile duct injury with loss of confluence: a surgical challenge

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**Background:** One of most feared type of injury is that that involves the confluence (Bismuth IV, Strasberg E-4). The injury that produces two separated right and left ducts is of multifactorial etiology, and the result of ischemic or thermal damage, an inflammatory reaction, as well as anatomical variants. The treatment options are several, mainly surgical. We here in describe our experience with this type of injury.

**Methods:** In an 18 year period, among 510 patients referred to our hospital for surgical treatment of complex bile duct injuries, 39 presented involvement of the hilar confluence. Imagenological studies, mainly MRI showed a loss of confluence. The files of these patients were analyzed and general data was recorded, including type of operation and postoperative outcome with emphasis on postoperative cholangitis, liver function test and quality of life.

**Results:** Patients were divided in five groups: GI ( $n = 16$ ): Construction of neoconfluence + Roux en Y hepatojejunostomy. GII ( $n = 13$ ): Roux en Y portoenterostomy. GIII ( $n = 6$ ): Double (right and left) Roux en Y hepatojejunostomy. GIV ( $n = 2$ ): Major + Roux en Y hepatojejunostomy. G-V ( $n = 2$ ): Associated right posterior injury: portoenterostomy. Postoperative outcome for each of these groups is as follows: GI: 1 cholangitis, treated medically, one lost, 14 asymptomatic. GII: one cholangitis, one death (40th post-op, month due to liver failure). GIII: one cholangitis, one liver transplant. GIV: Asymptomatic. GV: one cholangitis, one asymptomatic. In all patients the outcome was four cases of cholangitis, one death, two lost to follow-up, one liver transplant, 32 asymptomatic.

**Discussion:** Loss of confluence represents a surgical challenge. There are several treatment options at different

stages. Roux en Y bilioenteric anastomosis (neoconfluence, double anastomosis, portoenterostomy, associated major hepatectomy), is the treatment of choice, but liver transplantation should also be considered.

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### *Helicobacter* spp. in gallbladder tissue of patients with symptomatic gallbladder disease

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**Purpose:** Evidence suggests that chronic gallbladder disease may be associated with gastroesophageal reflux disease and gastritis. Since these processes are chronic inflammatory disorders of the upper gastrointestinal tract, we questioned if bacteria such as *Helicobacter* spp might play a role. We attempted to assess for the presence of *Helicobacter* spp. in bile, gallstones, and gallbladder tissue from patients with symptomatic gallbladder disease.

**Methods:** From February, 2008, to May, 2008, at New York University Medical Center, twenty nine patients (mean age = 50 years, 13 female, 16 male) scheduled for elective cholecystectomy for benign gallbladder disease were recruited after obtaining written informed consent. Immediately after gallbladder removal, bile, gallstones if present, and gallbladder tissue were collected in sterile manner and stored whole and unprocessed at -80°C. DNA was isolated from bile using the Qiaamp DNA Stool Minikit (Qiagen Valencia, CA, USA); from gallstones and tissue, the DNeasy Blood and Tissue Kit (Qiagen) was used. DNA was amplified via PCR technique using primers specific for 16sRNA gene of *Helicobacter* spp. Products were analyzed with agarose gel electrophoresis. Genewiz was used for product sequencing, and results were aligned using Sequencher program with Clustal X program. For plasma analysis, 10 mL of blood was collected preoperatively. The resultant plasma was used to assess the immune response to *H. pylori* by enzyme linked immunosorbent assay (ELISA) analysis.

**Results:** Of 29 patients with benign gallbladder disease recruited, three did not have gallstones for analysis. Zero of 29 (0%) bile samples and zero of 26 (0%) gallstone samples were positive for *Helicobacter* spp. Five of 29 (17.2%) tissue samples were positive for *Helicobacter* spp. Two of these five samples were sent to Genewiz for product sequencing and aligned with Sequencher program, revealing *Helicobacter* genus signal. Using Clustal X program for sequence comparison, the products were found to be nearly identical. Lastly, ELISA technique was used to analyze plasma of these two patients for the presence of *Helicobacter pylori*, and only one of the two patients' plasma demonstrated antibodies reactive to this single bacterial species.

**Conclusions:** *Helicobacter* spp, not necessarily *H. pylori*, may play a significant role in the development of benign, symptomatic gallbladder disease. This is clinically important as people who have colonization/infection of their gallbladder with this/these organism(s) might benefit from antibiotic treatment instead of surgery.

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### What is the benefit of radical resection for T1b gallbladder cancer: a decision analysis

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**Background:** Gallbladder cancer is the fifth most common gastrointestinal malignancy. Radical surgery (including liver resection and regional lymphadenectomy) is applied for some gallbladder cancers, but the benefits of these procedures are unproven. In particular, for patients with T1b cancers on cholecystectomy specimens, the utility of radical surgery remains debated.

**Methods:** Using published data collected from a systematic Medline search, we carried out formal decision analysis in order to compare two management strategies for patients discovered to have T1b gallbladder cancer at cholecystectomy: Group 1 underwent no further surgical therapy while Group 2 underwent additional radical surgery. The primary outcome of interest for this study was 5-year survival. Sensitivity analyses were conducted for variables in which weighted means were calculated from the literature.

**Results:** Seventeen studies (114 patients) and eight studies (28 patients) were included in the analyses for Groups 1 and 2, respectively. Weighted 5-year survival rates were 65% (range: 0–100%) and 93% (range: 0–100%) for Groups 1 and 2, respectively. Perioperative mortality for those patients undergoing radical resection was calculated from 31 studies (981 patients), yielding a weighted mean of 2.5% (range: 0–10%). Overall decision analysis favored additional radical resection over no further surgical resection for this patient subset. Sensitivity analysis demonstrated that this decision is contingent on the perioperative mortality rate.

**Conclusions:** Data available for the subset of patients with T1b gallbladder cancer suggest a potential survival benefit for further radical resection.

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### Epidemiologic differences on presentation of gallbladder cancer between a high-risk (Temuco, Chile) and a low-risk population (Georgia, USA); not all cancers are created equal

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**Introduction:** The presentation of Gallbladder cancer (GBCA) differs among world regions; the south of Chile is likely the location with the highest incidence worldwide. This being likely environmentally related, there is no clear comparison with less prevalent regions, including USA.

**Methods:** All patients presenting with the diagnosis of GBCA in a period between 2000 and 2007 were entered in the database. Same variables were used and compared for two academic institutions, one in the south of Chile (Ch) and one in the Southern region of the USA (US).

**Results:** Four hundred and sixty patients were identified; 436 (95%) belong to Ch. The demographic data is shown in the Table 1. In general, the histologic features were more favorable in Ch, having an earlier stage at presentation and less invasive tumors. Lithiasis is not always constant in US.

**Conclusions:** There are drastic differences in the presentation of GBCA in prevalent (Ch) and low incidence (US) regions. With a surveillance program, GBCA is discovered earlier. In addition, the histologic markers for aggressiveness are less pronounced on tumors with a higher incidence of GBCA (degree of differentiation, perivascular -, perineural -, lymphatic invasion). Probably more sophisticated studies are necessary to elucidate the different behavior in these two populations.

**Table 1.** Demographic data.

Variable	Ch (n = 436)	US (n = 24)
Gender (male)	74 (17%)	7 (29%)
Age (mean-SD)	62 (13) year	64 (11)
Lithiasis (present)	431 (99%)	19 (79%)
Early T (0-1B)	126 (29%)	5 (20%)
Degree of diff. (well-mod)	308 (71%)	11 (46%)
Perivasc invasion (absence)	383 (88%)	10 (42%)
Perineural infiltr. (absence)	403 (92%)	4 (17%)
Lymphatic invas (absence)	391 (90%)	10 (42%)
Nodal mets (-)	331 (76%)	12 (50%)
Preop dx unsuspected	402 (92%)	15 (63%)

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### The role of pet-ct in patients with incidental gallbladder cancer

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**Introduction:** Incidental gallbladder cancer (IGC) after a cholecystectomy requires adequate imaging studies to determine the actual extent of the disease to properly tailor subsequent treatment. The aim of this study was to evaluate the utility of PET-CT to provide optimal pre-treatment staging in patients with IGC.

**Material and methods:** Between January 2006 and August 2008, all patients with IGC and at least muscular layer invasion were studied with <sup>18</sup>F FDG PET-CT. The exam was considered positive when the standardized uptake values (SUV) were  $\geq 2.5$ . In all instances patients were offered to undergo definitive exploration and possible resection. Final pathologic findings were reported (final pathology report = FPR).

**Results:** The series included 32 patients, 26 women and 6 men, with a mean age of 58 years (range 30–81 years). The exam was performed on average 10 weeks after cholecystectomy (range 2–52 weeks). PET-CT was negative in 13 patients and positive in 19 patients: nine with localized potentially resectable disease (PRD) and in 10 with disseminated disease. Of the 13 patients with

negative exam, nine refused surgery and four underwent formal exploration: three patients were resected with no disease identified in the FPR and one was not resected due to carcinomatosis. Of the nine with PRD, four patients refused reoperation and five underwent exploration: three were resected with residual disease noted in the FPR and two did not undergo resection due to dissemination. Two patients with disseminated disease were reoperated and in both instances disseminated disease

was confirmed. For the entire group, the median survival and the 2 years overall survival (OS) was 20.3 months and 45%, respectively. Fifteen months OS was 90% for negative findings, 67% for localized potentially resectable disease and 0% for disseminated disease found in CT-PET ( $P < 0.003$ ).

**Conclusions:** PET-CT finding is a useful prognostic factor in IGC. PET-CT might be a helpful tool for selection patients for potentially curative treatment.

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**HPB NSQIP: potential for quality improvement, registries, and clinical trials**

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**Background:** The American College of Surgeons – National Surgical Quality Improvement Program (ACS-NSQIP) was started in 2004. In the first 2 years, 37 hospitals were participating, and data had been accumulated on over 30 000 operations. By June, 2008, ACS-NSQIP had 173 hospitals with reliable data on over 200 000 operations. Presently, 60% of the hospitals participating in ACS-NSQIP are academic/teaching hospitals. In addition to general and vascular surgery, ACS-NSQIP has developed multispecialty, bariatric and pediatric surgery options. Recently, ACS-NSQIP made risk-adjusted data available for use by participating hospitals. Therefore, the aim of this analysis was to explore the ACS-NSQIP database for utility in hepato-pancreato-biliary (HPB) surgery.

**Methods:** The ACS-NSQIP Participant Use File was queried for patient demographics and outcomes for 18 major HPB operations from January 1 through December 31, 2007. The procedures included four hepatic and six pancreatic resective as well as eight complex biliary operations.

**Results:** During this 12-month period, data were accumulated on 4204 patients undergoing major HPB surgery. The operations included 1285 hepatic resections (31%), 2482 pancreatic resections (59%), and 437 complex biliary procedures (10%) with the majority being performed at academic/teaching hospitals. Patients undergoing hepatic resections were more likely to have metastatic disease (42%) and recent chemotherapy (7%) whereas those having complex biliary procedures were most likely to have diabetes (13%), ascites (5%) and significant weight loss (20%). Thirty-day (30d) morbidity and mortality as well as risk-adjusted morbidity and mortality (Observed/Expected = Index) are shown in the Table 1.

**Conclusions:** These data suggest that major HPB operations being performed at ACS-NSQIP hospitals have acceptable morbidity and mortality rates. We conclude that creation of an HPB NSQIP has the potential to further improve quality, provide risk-adjusted registries and facilitate multi-institutional clinical trials.

**Table 1.** Observed/expected data.

Outcomes	Hepatic	Pancreatic	Biliary	HPB
30-day morbidity	24%	35%	30%	34%
Morbidity index	0.69	1.04	0.79	0.91
30-day mortality	1.9%	2.8%	3.0%	2.5%
Mortality index	0.79	1.08	0.75	0.96

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**Clinical factors predictive of malignant and premalignant cystic neoplasms of the pancreas**

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**Background:** As cystic neoplasms of the pancreas continue to be more commonly found with advanced imaging techniques, pancreatic surgeons often struggle with identifying who is at risk of having or developing pancreatic cancer. The utility of endoscopic ultrasound (EUS) with fine needle aspiration and cyst fluid analysis has been well documented, but preoperative diagnosis of cystic lesions of the pancreas remains unreliable. As such, we sought to review our experience with the surgical management of cystic neoplasms of the pancreas to determine preoperative clinical indicators of malignancy or premalignant (i.e. mucinous) lesions.

**Methods:** Between 1996 and 2007, 114 consecutive patients with cystic neoplasms of the pancreas underwent pancreatectomy. Invasive adenocarcinoma was identified in 35 while 79 had benign lesions. Mucinous lesions were considered premalignant and consisted of 29 intraductal papillary mucinous neoplasms (IPMN) and 17 mucinous cystic neoplasms (MCN). The remaining 33 benign lesions were serous microcystic adenomas. Clinicopathologic characteristics were reviewed and compared using Student's T and Fisher's Exact tests.

**Results:** Patients found to have pancreatic cancer arising from a cystic neoplasm were significantly older than those with benign cysts but with a similar gender distribution (Table 1). Benign cysts were more commonly asymptomatic, less likely to have an elevated CA19-9, more commonly located in the left pancreas, and tended to be smaller than those with associated malignancy (Table 1). Premalignant (i.e. mucinous) cysts more commonly presented with symptoms and elevated CA19-9 than those without malignant potential (i.e. serous) (Table 1). At a median follow-up of 33 months, three (7%) mucinous tumors recurred while no serous neoplasms recurred ( $p = \text{NS}$ ).

**Conclusions:** Based upon our modern single institution experience with resection of cystic neoplasms of the pancreas, we advocate an aggressive surgical approach to any patient presenting with a symptomatic cyst or elevated CA19-9, particularly in an older patient and in the head of the pancreas. Resection for small asymptomatic cysts located in the left pancreas in younger patients can be undertaken on a selective basis.



**Table 1 for abstract 42.** Characteristics of patients undergoing pancreatectomy for cystic lesions of pancreas.

	<i>All</i>	Benign			Malignant	
		<i>Serous</i>	<i>Mucinous</i>	<i>P (vs. serous)</i>		<i>P (vs. benign)</i>
N	79	33	46		35	
Age	59 (24–84)	59 (38–83)	59 (24–83)	NS	68 (36–84)	0.03
Female	68%	79%	61%	NS	57%	NS
Asymptomatic	25%	42%	6%	0.0002	6%	0.02
Elevated CA 19-9	24%	0%	27%	0.03	67%	0.002
Head of pancreas location	31%	24%	35%	NS	71%	< 0.0001
Size	3.5 (0.6–15)	3.5 (1–8.5)	3.6 (0.6–15)	NS	4.5 (2–18.5)	0.04

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### Escalating computed tomography angiogram (CTA) grade predicts unresectability and positive margins for pancreaticobiliary neoplasms

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**Background:** The CTA grading system of pancreaticobiliary cancers was conceived to predict resectability based on tumor involvement of critical vasculature. As this has not yet been rigorously assessed clinically, our goal was to examine the relationship between CTA grade and resectability, as well as margin status and other surgical outcomes, in pancreas resections.

**Methods:** 370 patients with presumed pancreaticobiliary malignancy and a pancreas protocol CTA at our institution underwent attempted curative resection from 10/01 to 08/07. The relationship between radiographic resectability, according to the 5-point Raptopoulos scale, and *actual* resectability, margin status, and other metrics was assessed.

**Results:** Overall, 271 patients (73.2%) were resectable. 11% of these had benign final pathology. As CT grade worsened, unresectable cases increased, from 16.6% of Grade 0 cases, to 79.3% of Grade 3 cases,  $P < 0.00001$  (Figure). Five Grade 4 cases underwent laparotomy for palliative purposes and were all confirmed to be unresectable by vascular invasion, as anticipated preop. Of unresectable Grade 0 cases, 72% were excluded from resection by peritoneal/ liver metastases/nodes not recognized on CT, but surprisingly, 28% were due to vascular involvement. For Grade 2 and 3 cases which are potentially resectable radiographically, 30/48 Grade 2 (62.5%) and 23/29 Grade 3 (79.3%) were unresectable – most often due to vascular involvement (67% and 61%, respectively). The 241 patients with either malignant or premalignant diagnoses were considered for margin analysis. 72.3% were R0

resections. The positive margin (R1/R2) rate did not differ appreciably among Grades 0–2, but was significantly higher (83%,  $P = 0.004$ ) for Grade 3 (Fig). The rate of multiple positive margins differed significantly between grades 0–1 and 2–3 (14.3% vs. 50%,  $p = .01$ ). Among resectable cases, surrogates of operative difficulty (EBL, transfusion, operative time) did not differ significantly by CT grade.

**Conclusions:** Escalating CTA grade accurately predicts unresectability. In resectable cases, positive margins are regularly encountered, even at lower CT grades (20–37%), and almost always with Grade three lesions. These findings suggest that attempted surgical resection has limited efficacy with advanced presentations as graded by CTA.

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### Neoadjuvant therapy may lead to successful surgical resection and improved survival in patients with borderline resectable pancreas cancer

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**Background:** Borderline resectable pancreatic cancers are tumors that are technically amenable to surgical resection but may be associated with increased risks of locoregional recurrence. Patients with borderline resectable tumors are usually treated with neoadjuvant therapy in an attempt to improve margin negative resection rates. It is not clear how effective this strategy is and whether it is associated with long-term survival.

**Objective:** This study aims to retrospectively review our institutional experience with patients demonstrating borderline resectable pancreatic cancer.

**Methods:** Pancreas cancer databases from the past 5 years were retrospectively reviewed. The diagnosis of borderline resectable disease was based upon the presence of 1 of 4 criteria on abdominal CT or endoscopic ultrasound: short segment occlusion of the superior mesenteric vein (SMV) and/or portal vein (PV), short segment involvement of the hepatic artery (HA), superior mesenteric artery (SMA) involvement of  $< 180$  degrees, or SMV involvement of  $> 180$  degrees.

**Results:** Twenty-eight patients were identified for inclusion in the study. Of the included patients, 24 underwent a full course of neoadjuvant therapy. Eleven (46%) underwent surgical resection, and 13 either had tumor progression or were deemed unresectable at laparotomy. The anatomic tumor characteristics did not differ

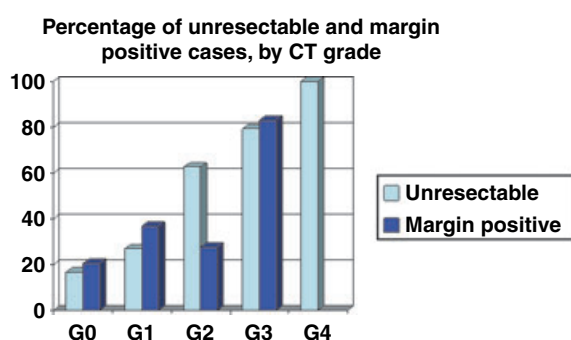


Figure 1.

between groups. The most common systemic chemotherapy regimens were gemcitabine alone (36%), gemcitabine and Tarceva (27%), and gemcitabine with Tarceva and oxaliplatin (18%). In addition, 50% of patients received neoadjuvant chemoradiation, given only if patients did not respond to the initial chemotherapy regimen. Forty-one percent of patients ( $n = 9$ ) underwent resection following chemotherapy alone, with an additional 9% ( $n = 2$ ) undergoing resection after subsequent chemoradiation. Of those undergoing surgery ( $n = 11$ ), 63% had margin-negative (R0) resection and 45% required venous resection and reconstruction. Median survival was  $14.1 \pm 2.6$  months for unresected patients and  $23.3 \pm 9.0$  months for those undergoing resection.

**Conclusion:** Patients with borderline resectable pancreatic cancer can be successfully treated with neoadjuvant therapy, resulting in margin negative resection, associated with long-term survival. Further prospective studies are needed to further study this subset of patients.

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#### Multimodal therapy for treatment of hepatocellular carcinoma: A ten-year survival analysis.

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**Introduction:** There are multiple treatment options for hepatocellular carcinoma (HCC) including resection, radiofrequency ablation (RFA), ethanol injection (EI), chemotherapy (CTx), transarterial chemoembolization (TACE), liver transplantation (OLT) or observation (obs). This study was performed to evaluate the survival benefit of multimodal therapy for HCC.

**Methods:** A retrospective review was conducted on 251 consecutive patients treated for HCC between 1996 and 2006 at Vancouver General Hospital (VGH) and the BC Cancer Agency (BCCA). There was a complete data set available on 247/251 patients. Data were retrieved from clinical charts and Information Systems from VGH and BCCA. All patients underwent primary treatment by resection, RFA, EI, CTx, or TACE. A subset of patients with persistent or recurrent disease underwent salvage therapy.

**Results:** Mean overall survival was 76.8 months. Poor survival was associated with symptoms at diagnosis, chronic HCV vs. HBV infection, lack of antiviral therapy in early TNM stage HBV/HCV patients, portal venous thrombosis, poor Child-Pugh status, and higher TNM stage (all  $P < 0.001$ ). Among primary treatment modalities, survival was comparable for resection, RFA, and EI; with significantly shorter survival for CTx, TACE, or observation. Among salvage treatment modalities, RFA of dominant lesions was associated with improved survival.

**Conclusions:** These results underscore the value of early detection of HCC in at-risk patients. The data suggest that patients may be stratified based on tumor stage and underlying liver function to curative intent or disease control strategies to optimize survival and minimize risk. Multimodal therapy may also delay or obviate the need for OLT.

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#### Results of total pancreatectomy: a single center experience

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**Introduction:** Total pancreatectomy (TP) is associated with major metabolic abnormalities resulting in difficulties in glucose control and malabsorption, leading to multiple medical problems and decreased quality of life. However, with the availability of modern pancreatic enzyme formulations and improvements in control of diabetes mellitus, the metabolic drawbacks of TP have diminished. As indications for TP have increased, we have examined our results of patients undergoing TP.

**Methods:** A retrospective chart review of 47 patients undergoing TP from 1/02 to 1/08 was performed. Patient demographics, perioperative morbidity and mortality, and long term follow up was obtained.

**Results:** In this 6-year period, TP was performed on 15 males and 23 females with a mean age of 67.3 years. Indications were pancreatic adenocarcinoma (18), IPMN (18), other neoplasm (7), and benign (4). The mean BMI was 25.5 and most common symptoms were abdominal pain, weight loss, and new onset diabetes. 23 were performed with pylorus preserving technique and nine involved venous resection. Mean blood loss was 1150 mL and operative time was 390 mins. Mean units of blood transfused intraoperatively were 3.3 units and 4.3 units for the whole hospital stay. Mean ICU stay was 1.68 days and total length of stay was 13 days. Most patients were maintained on an insulin drip for a mean of 5.1 days postop. Parenteral nutrition was needed in 5. Medical complications resulting in prolonged hospitalization occurred in 14 and surgical complications occurred in 4. Reoperation within 30 days was needed in two patients and postoperative inpatient mortality was 0%. Most were discharged with a combination of long acting and sliding scale insulin and average units of long acting insulin preparation was 13.7 at discharge. Mean follow up was 22 months. 14 patients required hospitalization within 3 months of discharge resulting in 1 death. Mean weight loss at 3, 6, and 12 months was 5.0, 7.7, and 9.7 kg respectively from preoperative weight. Mean Hb<sub>A1C</sub> at 6 months, 12 months, and 24 months was 7.1%, 7.2%, and 7.6% respectively. Survival varied based on underlying disease process.

**Discussion:** TP results in significant metabolic derangements which require multidisciplinary management for

**Table 1 for abstract 45. Survival (months).**

Symptoms		PV thrombosis		Child-pugh		TNM stage		Primary treatment					
		No	Yes	A	B + C	I + II	III + IV	Resect	RFA	EI	CTx	TACE	Obs
92.1	30.7	80.6	20.3	82.8	25.5	76.2	35.4	93.2	66.2	80.1	24.9	47.4	31.4

improved outcomes. Diabetic control and weight maintenance remain a challenge. Intensive diabetic and nutritional counseling combined with advanced insulin delivery systems, pancreatic exocrine formulations, and vitamin supplementations are essential. Readmission rates are high and a closer look must be taken at prolonging hospitalization and providing additional nutrition for these patients. However, the risks of TP appear acceptable compared to the benefits of resection.

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### Predicting poor outcome following hepatectomy: analysis of 2313 hepatectomies in the NSQIP database

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**Background:** For the past two decades multiple series have documented that liver resection has become safer. The purpose of this study was to determine the current status of hepatic resection in the US by analyzing the multi-institutional experience within the National Surgical Quality Improvement Program (NSQIP) dataset.

**Methods:** Of the 363 897 cases in the 2005–2007 NSQIP Participant Use File, 2313 elective open hepatectomy cases were identified (1344 partial, 230 left, 510 right and 229 extended hepatectomies). 36 perioperative risk factors and 52 postoperative complications were compared. To determine the applicability of NSQIP general risk models to hepatic surgery, the prognostic value of standard multivariate analysis was compared to the novel NSQIP aggregate risk index (*morbprob*).

**Results:** The median age of pts contained in the database was 60 years, the sex distribution was equivalent, and 78% were Caucasian. With regard to preoperative risk factors, 65% of pts had an ASA score of 3 or 4. The most prevalent comorbidity was hypertension (46%). 41% of pts underwent hepatectomy for disseminated cancer, 19% of whom had received chemotherapy within 30 days of surgery. The overall 30-day mortality rate was 2.5% (57/2313) and the 30-day major morbidity (MM) rate was 19.6% (453/2313). Multivariate analysis identified six independent preoperative risk factors for MM (Table 1). Operative factors associated with MM included operative time, intraoperative red blood cell transfusion, and early postoperative transfusion (Table 1). A 75th percentile *morbprob* (0.40) was associated with a major complication PPV of 30.4%, NPV of 85.5%, sensitivity of 49.8% and specificity of 72.3%. For those pts who developed MM, the median length of stay was longer (10 vs. 6 days,  $P = 0.001$ ) and the mortality rate was higher (0.3% vs. 11.3%,  $P = 0.001$ ).

**Conclusions:** Analysis of the NSQIP experience with hepatectomy indicates that the current mortality and major morbidity rate benchmarks are 2.5% and 18%, respectively. Poor outcomes were not associated with age or body mass index, and were most dependent on nutritional status, liver function, and the extent of hepatectomy. The NSQIP *morbprob* value was a relatively poor predictor of observed morbidity, indicating the need for specialty-specific NSQIP modeling.

**Table 1.** Multivariate analysis-NSQIP hepatectomy.

Strata	Risk factor	MV P-value	Odds ratio
Preop	Elevated alk phos	0.0001	4.9
	Low albumin	0.006	2.8
	Elevated PTT	0.047	2.0
	Extended resection	0.0001	1.8
	Smoking	0.0001	1.7
	ASA 3/4	0.001	1.4
Periop	Intraop transfusion	0.0001	2.2
	Prolonged OR time	0.011	1.6
	Early postop transfusion	0.001	1.4

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### Validation of the meld based objective scoring system (moss): unresectable hepatocellular carcinoma in patients with cirrhosis

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**Introduction:** The novel MELD-based objective scoring system (MOSS) was recently shown to be accurate in stratifying survival in patients with hepatocellular carcinoma (HCC) and cirrhosis undergoing non-liver transplant modalities. The primary aim of this study is to validate the predictive value of MOSS in patients with cirrhosis and unresectable HCC.

**Methods:** A survival analysis of 251 patients with HCC and cirrhosis diagnosed between 2004 and 2008 at two university-based institutions was performed. There were 152 patients in the no-therapy group and 99 patients in the transarterial chemoembolization (TACE) group.

**Results:** There were 64 females and 187 males with a mean age of 59 years. The mean MELD score and tumor size for the no-therapy group and the TACE group were (12.6 vs. 10) and (5.9 cm vs. 5.4 cm), respectively. The median survival for the no-therapy group was 4.8 months and for the TACE group 15.7 months ( $P < 0.0001$ ). In the multivariable analysis independent prognostic factors that predict long-term survival were tumor size ( $P = 0.047$ , HR 1.476), vascular invasion ( $P = 0.021$ , HR 1.669), T-stage ( $P = 0.005$ , HR 1.331), MOSS Class ( $P < 0.001$ , HR 1.901). The overall median survival according to the MOSS Class I, II, III and IV were 21, 8.7, 5.2 and 0.2 months respectively ( $P < 0.0001$ ). Table 1 demonstrates the median survival for the no-therapy and TACE groups according to their MOSS Class I, II, III and IV.

**Conclusions:** MOSS class, an objective clinical scoring system that combines MELD and tumor characteristics, accurately stratifies outcomes in cirrhotic patients with unresectable HCC. Once externally validated, the MOSS classification scheme can be used clinically to guide decisions regarding non-transplant treatment modalities. In addition, the objectivity of this scoring system will afford its use as a common platform for international data sharing and comparison and to design clinical trials of novel treatments.

**Table 1 for abstract 48:** The median survival for patients with cirrhosis and HCC treated with no-therapy or TACE according to MOSS class

	MOSS Class I	MOSS Class II	MOSS Class III	MOSS Class IV	P value
No-therapy (n = 152), months	21.6	4.1	4.7	0	< 0.0001
TACE (n = 99), months	21	17.3	7.1	0	0.0004

MELD score (6, 7, 8 = 3 points), (9, 10, 11 = 6 points), (12, 13, 14 = 9 points), (> 15 = 12 points)

Tumor Size (< 5cm = 0 points), (≥ 5 cm = 2 points)

Multiplicity (single lesion = 0 point), (≥ 2 lesions = 1 point), (diffuse HCC = 2 points)

Portal Invasion (No = 0 points), (Yes = 1 point)

Class I = Total points = < 5 points

Class II = Total points = 6–9 points

Class III = Total points = 10–14 points

Class IV = Total points = ≥ 15

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### **Interpreting three-dimensional structures from two-dimensional images: a web-based interactive 3D model of the liver to enhance surgical residents' spatial understanding of structural inter-relationships**

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**Background:** Learning intra-hepatic anatomy and developing an understanding of the relationships that exist between the key structures is a difficult process that is required of surgical residents. They need to mentally reconstruct 3D images from available CT scans and this may not be an effective way of understanding the liver. A

web-based interactive 3D model of the liver was created to facilitate understanding of the complex spatial anatomy of the liver and to help visualize this anatomy in 3D when viewing CT scans.

**Methods:** By importing CT scans into Osirix, 3D surface renderings of the liver were obtained. Using these images as reference, anatomical structures were modeled in Cinema4D. This included the liver surface and the intra-hepatic structures; portal veins, hepatic veins, hepatic arteries and the biliary system. Interactivity was created in Flash.

**Implications:** Users can view common liver anatomy and common variations online in interactive 3D rotational model to observe the complex interactions of the vascular and biliary systems. This model will be useful for surgical trainees learn the difficult and complicated intra-hepatic anatomy and will optimize learning opportunities for all trainees requiring knowledge of liver structures.

# Abstracts 49 to 57

## Free Papers – Pancreas

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### Surgery residency training programs greatly impact outcomes after pancreaticoduodenectomy, greater than hospital volume or surgeon frequency

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**Introduction:** Hospital volume of pancreaticoduodenectomy (PD) and the frequency with which surgeons undertake PD have been shown to impact outcomes. However, the impact that surgery residency training programs have on outcomes after PD is not established. This study was undertaken to determine the impact of surgery residency training programs on outcomes after PD as well as their importance relative to hospital volume and surgeon frequency of PD.

**Methods:** The State of Florida Agency for Healthcare Administration database was queried for patients undergoing PD (ICD-9 code 52.51 [proximal PD] or 52.7 [radical PD]) from 2002 through 2007. Measures of outcome were compared for patients undergoing PD at centers with vs. without surgery residency training programs. Data are presented as median, mean  $\pm$  SD.

**Results:** 1478 (63%) PD were undertaken at centers with surgery residency training programs and 867 (37%) at centers without surgery residency training programs. Relative to centers without surgery training programs, patients undergoing PD at centers with surgery residency training programs had shorter lengths of stay, less hospital charges, and lower in-hospital mortality (Table 1). Relative to the frequency with which surgeons undertook PD, surgery residency training programs had a greater favorable impact on hospital length of stay, hospital charges, and in-hospital mortality ( $P < 0.001$  for each, ANCOVA). As well, relative to hospital volume of PD undertaken, surgery residency training programs had a greater impact on hospital charges ( $P < 0.001$ , ANCOVA).

**Table 1. Results.**

	Length of stay (days)	Hospital charges (dollars)	In-hospital mortality
Training centers	12 (15 $\pm$ 11.8)	87,685 (111,703 $\pm$ 98,146)	2.7%
Non-training centers	17 (20 $\pm$ 12.3)	120,367 (150,451 $\pm$ 113,557)	11.0%
P-value	$P < 0.001$ (Mann-Whitney)	$P < 0.001$ (Mann-Whitney)	$P < 0.001$ (Chi-square)

**Conclusions:** Most PD in Florida are undertaken at centers with surgery residency training programs. Relative to centers without training programs, centers with training programs have shorter hospital stays, less hospital charges, and less in-hospital mortality. Surgery

residency training programs have a greater impact on hospital length of stay, hospital charges, and in-hospital mortality than do the frequency with which surgeons undertake PD and the hospital volume of PD. Therefore, surgery residency training programs, and all they entail, have a favorable impact on outcome after PD, which is greater than hospital volume of PD or the frequency with which surgeons undertake PD.

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### Pyogenic liver abscess following pancreaticoduodenectomy: risk factors, treatment, and long-term outcome

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**Background:** Pancreaticoduodenectomy (PD) remains a challenging operation with a 40% postoperative complication rate. Pyogenic liver abscess (PLA) is an uncommon complication following PD, and little information exists on its incidence and treatment. This study was performed to examine the incidence, risk factors, treatment and long-term outcome of PLA after PD.

**Methods:** We retrospectively reviewed 1189 patients undergoing PD ( $n = 839$ ) or distal pancreatectomy (DP) ( $n = 350$ ) at a single institution over a 14-year period (1/1/1994 - 1/1/2008). Two pancreatic databases (PD & DP) were queried for postop complications and cross-checked through a hospital wide database using ICD-9 codes 572.0 (PLA) and 006.3 (amebic liver abscess) as primary or secondary diagnoses. No PLA occurred following DP. Twenty-four patients (2.9%) developed PLA following PD. These 24 patients were matched (1:3) with 72 patients without PLA following PD. Patient groups were equivalent with respect to age, gender, year of operation, and indication for surgery. Student's t-test and chi square analysis were used with  $P < 0.05$  taken as significant.

**Results:** There were no differences in eight pre-operative variables between the groups including: jaundice, pre-operative biliary stenting, or episodes of cholangitis. Intra-operative blood loss (1128 mL vs. 827 mL,  $P = 0.05$ ) was significantly higher in patients who developed PLA compared to matched controls. Postoperatively, patients with anastomotic complications had a significantly higher rate of PLA (33% vs. 7%,  $P = 0.001$ ) while the incidence of pancreatic fistula (13% vs. 4%,  $P = 0.14$ ), delayed gastric emptying (13% vs. 6%,  $P = 0.19$ ), and superior mesenteric/portal venous thrombosis (8% vs. 3%,  $P = 0.24$ ) were similar between groups. Fifteen patients (63%) developed a solitary abscess and nine patients (38%) had multiple abscesses. Treatment involved antibiotics and percutaneous drainage ( $n = 16$ ,

67%), antibiotics alone ( $n = 6$ , 25%), or percutaneous drainage alone ( $n = 2$ , 8%) with a mean hospital stay of 12 days. No patient required surgical drainage and all abscesses resolved. Long-term follow-up showed equivalent 1- (79% vs. 74%), 2- (50% vs. 57%), and 3-year (38% vs. 33%) survival rates and hepatic function (liver function tests) between patients with PLA and matched controls.

**Conclusions:** Intra-operative blood loss and postoperative anastomotic complications are risk factors for the development of PLA following PD. Treatment utilizing antibiotics and selective percutaneous drainage is 100% effective with no adverse effects on long-term hepatic function or survival.

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### Admission volume as a determinant of outcome for patients with acute pancreatitis

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The optimal management of acute pancreatitis (AP) remains controversial with degrees of medical and surgical management. Our group has previously shown that high volume (HV) hospitals have lower mortality after pancreatectomy. We sought to examine if a similar mortality benefit exists for patients admitted with AP.

**Methods:** Using the Nationwide Inpatient Sample (NIS), discharge records for all adult admissions with a primary diagnosis of AP from 1998 to 2006 were examined. Unique hospital identifiers were used to divide hospital volume into equal tertiles based on # of admissions for AP per year (lowest tertile (LV) < 65/year; 64/year < medium tertile (MV) < 118/year; highest tertile (HV) > 117/year). Adjusted mortality was the primary outcome measure while adjusted length of stay (LOS) was a secondary measure.

**Results:** There were 416 489 primary admissions for AP during the study period. In-hospital mortality for the cohort was 1.6%. The leading causes of AP reported were alcohol (25.4%) and gallstones (22.6%). Hospital admissions for AP increased over the study period ( $P < 0.0001$ ). HV hospitals tended to be large (82%), urban (99%), teaching centers (59%) ( $P < 0.0001$ ) which cared for patients with greater comorbidities (35.9% with > 2 comorbidities vs. 29.1% at LV hospitals) ( $P < 0.0001$ ). Overall, cholecystectomy was the most commonly performed primary procedure ( $n = 45\,579$ ) (26.2%). LV centers appeared more likely to perform pancreatic operations than HV hospitals (OR 1.50; 95% CI 1.32–1.70). There was a lower likelihood of a prolonged adjusted LOS at HV hospitals compared to LV (OR 0.75; 95% CI 0.71–0.79) or MV hospitals (OR 0.82; 95% CI 0.79–0.85). After adjusting for patient and hospital factors, there was an in-hospital mortality benefit for being treated at a HV center (HR 0.68; 95% CI 0.62–0.76). The decision to operate on a given patient did not alter the mortality benefit of the HV hospital.

**Conclusions:** The rates of admissions for AP in the US are increasing. High annual hospital volume of AP confers a shorter LOS and an in-hospital mortality benefit to patients admitted with AP. Although HV hospitals performed less pancreatic surgery compared to lower

volume groups, the role of surgery remains unclear. Further studies should examine other possible reasons for this mortality benefit such as the availability of specialists, the quality of critical care and timing of surgery.

**Table 1.** Multivariable analysis of factors associated with mortality.

Variable	HR	95% CI
Age	1.04	1.04–1.05
Female gender	1.35	1.27–1.43
Black race	0.79	0.73–0.87
Private insurance	0.83	0.76–0.91
Comorbidity	3.60	3.16–4.12
Teaching hospital	1.46	1.36–1.56
Large bedsize	1.62	1.46–1.80
High volume hospital	0.68	0.62–0.76

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### Benign pancreatic islet cell tumors: resect or enucleate?

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**Introduction:** The optimal management for benign pancreatic islet cell tumors is controversial. Classically, surgeons enucleated such lesions; however, more recently, pancreatic resection has become the standard therapy. Data comparing these two surgical approaches are lacking. Therefore, the purpose of this study was to document the morbidity, mortality, and outcomes of enucleation versus resection for benign pancreatic islet cell tumors.

**Methods:** Multi-institutional retrospective review identified 113 patients with benign pancreatic islet cell tumors who were operated on between January 1990 and June 2008. Patients with positive lymph nodes, distant metastases, or primary tumors greater than 3 cms were excluded. The enucleation group included patients who underwent enucleation, duodenal wall excision, or transduodenal ampullary tumor excision, while the resection group was comprised of patients treated by pancreaticoduodenectomy, distal pancreatectomy, or partial pancreatectomy.

**Results:** Thirty-three patients underwent enucleation of their islet cell tumors, and 80 patients were resected. These groups did not differ with respect to age, gender, or mean tumor size (1.8 cm vs. 1.7 cm in the enucleated and resected groups, respectively). Tumors that were enucleated were a) more likely to be functioning (enucleation vs. resection: 74% vs. 26%,  $P = 0.0001$ ), b) in the head, ampulla, or uncinate process of the pancreas (59% vs. 25%,  $P = 0.004$ ), and, c) when applicable, less likely to result in splenectomy (0% vs. 63%,  $P = 0.005$ ). The two groups were statistically similar with respect to



all outcome measures examined: operative (OR) time, blood loss, morbidity, mortality, hospital stay, and 5-year survival (see Table 1).

**Table 1.** Outcome measures.

	OR time (mins)	Blood loss (mL)	Morbidity (%)	Mortality (%)	Hospital stay (days)	5-year survival (%)
Resection	251	708	40	1.3	10.2	97.5
Enucleation	228	379	53	0	8.9	100

**Conclusion:** These data suggest that enucleation of benign pancreatic islet cell tumors is comparable to resection in terms of operative time, blood loss, morbidity, mortality, length of stay, and long-term survival. However, enucleation has the advantages of preserving pancreatic and splenic function. Therefore, we conclude that enucleation of small, benign, pancreatic islet cell tumors is an acceptable operative option.

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### Revision of anastomotic stenosis after pancreatic head resection for chronic pancreatitis: is it futile?

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**Introduction:** Because long-term survival after pancreaticoduodenectomy (PD) for cancer is limited, it is difficult to assess pancreaticojejunal anastomotic patency after pancreatic head resection. However, in patients with benign disease pancreaticojejunal anastomotic stenosis may become problematic post-operatively. What happens when pancreaticojejunal anastomosis revision is undertaken for anastomotic stenosis?

**Methods:** Patients undergoing pancreatic anastomotic revision after pancreatic head resection for chronic pancreatitis between 1997 and 2007 at the Medical University of South Carolina were identified. A retrospective chart review and analysis was undertaken with the approval of the Institutional Review Board for the evaluation of human subjects. Long term follow up was obtained by patient survey at the time of a clinic visit or by phone follow-up.

**Results:** During the study time period, 237 patients underwent pancreatic head resection. Twenty-seven patients (17 women, median age 42) were identified who underwent revision of their pancreaticojejunal anastomosis. Six patients (22%) had a pancreatic leak or abscess at the time of their index pancreatic head resection. Indication for revision of anastomosis was intractable pain. Twenty-four patients underwent preoperative magnetic resonance cholangiopancreatography (MRCP) which indicated anastomotic stricture in 15 patients (63%). Fourteen other patients underwent exploration based on clinical suspicion due to recurrent pancreatitis and had stenosis confirmed at the time of surgery. Six patients (22%) had perioperative complications after revision and length of stay was median 12 days. There was no perioperative death; however late mortality occurred in four patients (15%). Six of 23 survivors

(26%) at time of follow-up (median 56 months) reported long term pain relief after revision of their pancreaticojejunal anastomosis.

**Conclusions:** Stricture of the pancreaticojejunal anastomosis after pancreatic head resection presents with recurrent pancreatitis and pancreatic pain. MRCP has good specificity in the diagnosis of anastomotic obstruction but lacks sensitivity. Pancreaticojejunal revision is safe, but rarely effective as a means of pain relief in patients with the pain syndrome associated with chronic pancreatitis.

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### Outcome of radical vs. limited pancreatic head resection for chronic pancreatitis – a meta-analysis

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**Aim:** A meta-analysis on available published literature to examine the outcome of surgical management of chronic pancreatitis (CP) involving the head of pancreas.

**Background:** There is no consensus in the best surgical management for intractable pain and other major complications from CP. Surgical interventions include pancreaticoduodenectomy (Whipple's) and pylorus-preserving pancreaticoduodenectomy (PPPD); duodenum-preserving pancreatic head resection (Beger's) and longitudinal pancreaticojejunostomy (Frey's procedure). **Methods:** PubMed was used to search for published studies in English between 1990 to 2006. 'MeSH' search with 'chronic pancreatitis', and above procedural terms were used. Outcomes of interest included: indication for surgery, morbidity and mortality, long-term pain control, and pancreatic function.

**Results:** Thirty-three published series which fulfilled our inclusion criteria were evaluated. 2215 patients underwent surgical procedures including Whipple's ( $n = 421$ ), PPPD ( $n = 383$ ), Beger's ( $n = 1172$ ) and Frey's ( $n = 239$ ). There were three randomized controlled studies comparing pancreatic head resection (PHR) and Beger's procedure; three cohort studies, and six reviews. Between Whipple's and PPPD, there was no significant difference in morbidity ( $P = 0.07$ ), mortality ( $P = 0.13$ ), postoperative pain ( $P = 0.15$ ), endocrine ( $P = 0.99$ ) or exocrine functions ( $P = 0.29$ ). Similarly, postoperative endocrine, exocrine functions were comparable in PHR and Beger's ( $P = 0.16$ ;  $P = 0.95$ ), as was postoperative pain relief ( $P = 0.18$ ). Importantly, morbidity rate was significantly reduced in Beger's group when compared with PHR ( $P = 0.01$ ), albeit a similar mortality rate ( $P = 0.52$ ). Comparing PHR and Frey's, there was no significant difference for postoperative morbidity ( $P = 0.3$ ), mortality ( $P = 0.18$ ), long-term pancreatic function ( $P = 0.77$ ) or pain relief ( $P = 0.27$ ). Between Beger's and Frey's, there was no difference in postoperative morbidity ( $P = 0.49$ ), mortality ( $P = 0.28$ ), endocrine or exocrine function ( $P = 0.92$ ;  $P = 0.7$  respectively). A significantly higher proportion of patients had better pain control following Frey's

compared with Beger's procedure (89 vs. 85%,  $P = 0.009$ ).

**Conclusion:** There was no significant difference in outcome with Whipple's procedure compared to PPPD. Beger's procedure offered significant reduction in post-operative morbidity rate. Radical or limited resection had no impact on postoperative mortality or pancreatic function. Frey's procedure provided improved long-term pain relief.

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### A simplified prognostic system for resected pancreatic neuroendocrine neoplasms

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**Background:** A number of clinicopathological variables have been proposed for purposes of prognostication for patients with pancreatic neuroendocrine neoplasms. Previous analyses have been drawn from heterogeneous populations that have included patients with metastatic disease. A consistent and clinically applicable staging system has yet to be defined for patients undergoing potentially curative resection of pancreatic neuroendocrine neoplasms.

**Method:** We examined a prospectively maintained single institution database to identify patients who underwent potentially curative resection of non-metastatic primary pancreatic neuroendocrine neoplasms. All pathological specimens were independently reviewed and histological grade was defined as low grade or intermediate grade using previous defined criteria of mitotic activity and presence of necrosis. Patient, operative, and tumor characteristics were analyzed to identify factors associated with disease-specific and disease-free survival.

**Results:** Between 1991 and 2007, 43 patients underwent potentially curative resection of primary pancreatic neuroendocrine neoplasms. After a median follow-up of

68 months, 5-year disease-specific survival was 94%, and 5-year disease-free survival was 72%. The only variable associated with significant differences in disease-specific survival was tumor size  $> 5$  cm. Tumor size  $> 5$  cm, presence of nodal metastases, and positive resection margins were associated with significant differences in disease-free survival. The association between histologic grade and recurrence neared but did not reach statistical significance ( $P = 0.091$ ). The onset of disease recurrence was associated with decreased overall survival; median survival after disease recurrence was 49 months. A simplified scoring system consisting of tumor size  $> 5$  cm, histologic Grade, presence of Nodal metastases and resection Margin positivity (SGNM) permitted stratification of expected disease-specific ( $P = 0.047$ ) and disease-free survival ( $P = 0.0004$ ) outcomes.

**Conclusion:** A simplified scoring system based on tumor size, histologic grade, presence of nodal metastases and resection margin status permits accurate prognostication of outcomes for patients undergoing resection of primary pancreatic neuroendocrine neoplasms.

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### Routine intra-operative biliary cultures during pancreaticoduodenectomy: a guide to avoid postoperative complications

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**Introduction:** Multiple pre-, intra-, and post-operative factors have been identified to be potentially predictive of morbidity and mortality associated with pancreaticoduodenectomy. Biliary stenting has been demonstrated to potentially be one of those predictive factors. However, there have been no reports evaluating the effect of intra-operative bile culture on preventing post-operative complications. The aim of this study was to evaluate the effects of intra-operative bile cultures on the outcome of patients undergoing pancreaticoduodenectomy.

**Methods:** A review of our 1430 hepato-pancreatic-biliary database from 1/1998 to 8/2008 was performed for patients who had data on the presence/absence of biliary stenting, use of intra-operative bile culture, and microbiology of the bile culture. All clinico-pathologic data, as well as all complications 90 days from operation were recorded and evaluated. Complications were graded using our established 5-point grading scale. Chi-square and log rank were used to evaluate the effects of biliary stents, presence/absence infected bile, and the type of organism identified.

**Results:** We identified 228 patients who met our data requirements. There were 55% men, 45% women, median age of 59 years (range 42–91). Preoperative biliary stenting was performed in 129 out of 228 patients (57%). Of this 129 patients, 66 (51%) had bile cultures taken intraoperative, with 56 (85%) of these patients having positive bile cultures. Neither Preoperative biliary stenting (incidence complication: 54% w/stent vs. 51% w/o,  $P = 0.9$ ) or infected bile (incidence complication: 54% w/infection vs. 53% w/o,  $P = 0.9$ ) were predictors of overall complications. Length of operating time, length of hospital stay, blood loss, blood transfusion, and severity of complications were all similar. There were 18

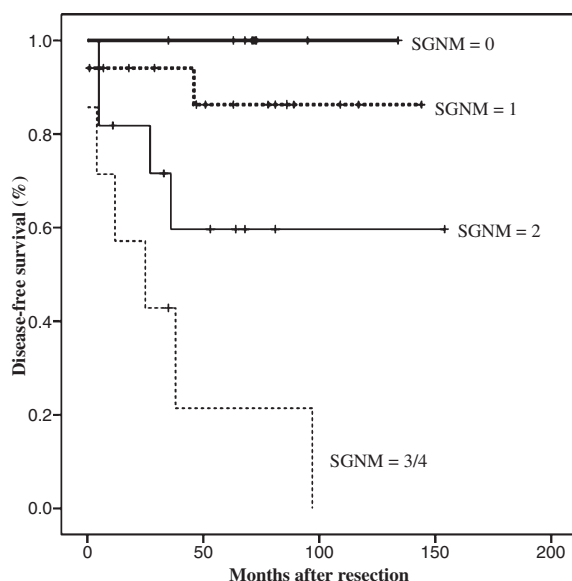


Figure 1.

different organisms identified with the most common being *Enterococcus* (23%), *Candida* (16%), *Escherichia coli* (16%), and *Staph* (13%). Only a *Candida* infection within the bile was a statistically significant predictor of severity of complication and increased length of stay.

**Conclusions:** Preoperative biliary stenting correlates with a higher rate of biliary infections, however intra-operative bile cultures allows for early appropriate antibiotic use, which maintains a similar morbidity and infectious incidence as non-stented patients. Treatment of extrahepatic biliary obstruction with preoperative stenting should not be abandoned; however, obtaining intraoperative bile cultures is important to further guide treatment of postoperative complications.

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### **Pancreatic resection: a key component to reducing racial disparities in pancreatic adenocarcinoma**

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**Introduction:** Pancreatic adenocarcinoma is more common and outcomes are less favorable among Blacks. Potential cures require resection. If surgical disparities exist, they may provide insight into outcome discrepancies.

**Methods:** Pancreatic adenocarcinoma patients were identified using Surveillance, Epidemiology, and End

Results (SEER) 1992–2002. Univariate analyses compared demographics, tumor characteristics, and operative data; logistic regression was used to determine independent predictors for recommendation/performance of surgery. Kaplan–Meier survival was assessed; a Cox proportional hazards model examined adjusted predictors of survival.

**Results:** A total of 27 828 patients were identified; 81.4% were White and 11.5% were Black. Whites and Blacks presented at equivalent stages, and resection was recommended at similar rates (34.5% vs. 34.0%,  $P = 0.93$ ). However, Blacks underwent fewer resections (10.6% vs. 12.7%,  $P = 0.0007$ ) and multivariable analysis confirmed they were less likely to undergo resection (adjusted odds ratio 0.69,  $P = 0.0002$ ). Overall, Blacks had worse univariate survival (log rank,  $P < 0.0001$ ). Resected Blacks' survival did not statistically differ from Whites', although median survival trended lower (Black median 11 months vs. 13 months for Whites,  $P = 0.1291$ ). In a multivariable Cox model, Black race independently predicted worse survival (HR 1.11, 95% CI 1.07–1.16); pancreatic resection was independently protective (HR 0.56, 95% CI 0.53–0.59).

**Conclusions:** In the SEER registry 2002–2006, Blacks and Whites were recommended for pancreatectomy at similar rates, yet Blacks were less likely to undergo resection. Resected Blacks and Whites had crude survivals that did not differ significantly, although in multivariable analysis a survival disadvantage remained for Black race despite adjusting for resection. Our results suggest that pancreatectomy may be underutilized for Blacks with pancreatic adenocarcinoma. Maximizing rates of pancreatic resection for appropriate patients may be an important component in reducing outcome disparities for this disease.

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**Perioperative bevacizumab containing chemotherapy for colorectal cancer liver metastasis**

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**Background:** Colorectal cancer liver metastases (CRCLM) when treated aggressively have a potential long-term survival. Liver resection combined with Oxaliplatin based adjuvant chemotherapy proved to increase disease-free survival, and neoadjuvant therapy improved progression-free survival. Bevacizumab (Bev) when added to Oxaliplatin based chemotherapy improved median survival in patients with CRCLM. Our goals are to determine safety and efficacy of adding Bev to the adjuvant therapy following liver resection for CRCLM and its impact on survival.

**Methods:** In a single arm feasibility study, all patients with detectable liver metastasis eligible to receive adjuvant chemotherapy and Bev were reviewed. Results: Thirty-six patients were identified: 26 male, median age 57 years, ECOG < 2. Thirty-one patients had synchronous liver metastases and five metachronous disease. All patients underwent perioperative Bev containing chemotherapy, Oxaliplatin based in 29 patients (80%) and CPT-11 in seven patients (20%). Twenty-eight (78%) had neoadjuvant therapy, and all had adjuvant chemotherapy. Median treatment duration pre and postoperatively was 3 and 6 months respectively. Bev was discontinued 6 weeks before and restarted 8 weeks after surgery. Seven patients underwent staged liver resection. Grade 3/4 Bev related complications were seen in four patients (epistaxis, anaphylactic reaction, and hypertension). Overall postoperative complication rate was 48%, grade 3/4 postoperative complications as per Clavien system was in two patients (5%). Overall response rate was 70% (22/31): 35% partial and 35% complete response, with a median follow up of 25 months. No patients progressed prior to surgery. Overall survival rates at 12, 24, 36 and 48 months were 100%, 89%, 80% and 77% respectively and 5-year median survival of 55%. Three patients relapsed, 4, 5 and 12 months post treatment, two patients died due to sepsis, and disease progression.

**Conclusions:** Bev containing chemotherapy and hepatectomy is well tolerated and effective in patients with CRCLM. Our 70% response rate is one of the highest reported, with only three patients progressing. Perioperative Bev containing chemotherapy seems to be justifiable in selected patients and warrants further investigation in phase-III trials.

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**Fast track liver resection: single dose intrathecal morphine with gabapentin vs. continuous epidural analgesia**

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**Introduction:** Historically liver resection has been associated with significant blood loss requiring large volumes

of intravenous fluid both pre and intraoperatively. With the advent of low CVP anaesthesia fluid has been restricted preoperatively but patients are volume loaded at the completion of the resection. While lowering CVP, the use of epidural anaesthesia may further increase post-operative fluid requirements to maintain blood pressure. This may unnecessarily prolong hospital stay delaying return of gut function, removal of bladder catheter and full mobility.

**Aim:** To compare the perioperative course and hospital stay in patients managed with continuous epidural infusion of bupivacaine 0.125% & fentanyl 2 mcg ml<sup>-1</sup> at 0.1 ml kg<sup>-1</sup> h<sup>-1</sup> or single dose intrathecal morphine 300 mcg in combination with oral gabapentin (1200 mg preop & 400 mg bd postop) and postoperative diclofenac SR 75 mg bd. All patients received paracetamol 1 g qid. **Methods:** Data on 100 consecutive patients managed with continuous epidural infusion (*n* = 50) or single dose intrathecal morphine (*n* = 50) were entered on a computerised database. Intergroup comparisons were performed using ANOVA.

**Results:** The epidural and intrathecal morphine groups were equivalent in terms of patient age, sex, major (≥ 4 segments resected) and minor hepatectomy and intra-operative blood loss (Table 1). There were no complications related to either form of analgesia and pain scores were uniformly low. However patients receiving intrathecal morphine received less intraoperative intravenous fluids [median 1.5 L (range 1.2–2.8 L) vs. 2.2 L (range 1.5–3.2 L) *P* = 0.06], less postoperative fluids [median 1.2 L (range 0.8–1.5 L) vs. 4.3 L (range 3.5–5.2 L) *P* = 0.03] than patients receiving epidural infusion. Patients receiving intrathecal morphine also established a normal dietary intake earlier (16 h vs. 20h, *P* = 0.05) and had shorter hospital stays than those managed with epidural infusions (4.2 ± 0.6 days vs. 6.8 ± 1.2 days, *P* = 0.02).

**Conclusions:** Single dose intrathecal morphine in combination with oral gabapentin is a safe and effective alternative to epidural analgesia in patients undergoing hepatectomy. Patients managed with intrathecal morphine resume an oral diet sooner and have shorter hospital stays than those managed with continuous epidural analgesia possibly because of a decreased requirement for intravenous fluid administration.

**Table 1. Results.**

Group	Sex M:F	Age Median ± SEM	Hepatectomy Major:Minor	Intraoperative blood loss Median ± SEM
Epidural ( <i>n</i> = 50)	27:23	61 ± 5 years	21:29	352 ± 73 mL
Intrathecal ( <i>n</i> = 50)	24:26	60 ± 6 yr	20:30	277 ± 88 mL

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### Surgical dilemma: liver resection or liver transplantation for hepatocellular carcinoma and cirrhosis. intention to treat analysis in patients within and outside milan criteria

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**Background:** The optimal role of surgery in the management of hepatocellular carcinoma (HCC) is in continuous evolution.

**Objective:** The objective of this study was to analyze the survival after liver resection (LR) and liver transplantation (OLT) for HCC within and outside Milan criteria in an intention to treat analysis.

**Methods:** From 1997 to 2007, 179 patients with cirrhosis and HCC underwent either LR ( $n = 60$ ) or were listed for OLT (119). After eliminating incidental HCC after OLT, preoperative macrovascular invasion before LR, non cirrhotics and Child-Pugh Class C cirrhosis prior to OLT, 51 patients primarily treated with LR, and 107 patients listed for primary OLT (81 transplanted) were included in this analysis. Sixty-six patients exceeded Milan criteria (26 LR; 40 OLT), while 92 patients continued to meet Milan criteria (25 LR; 57OLT)

**Results:** The median follow up time was 22 months. The mean waiting time for OLT was 7 months. During that time, 21 patients were removed from the waiting list due to tumor progression. The drop out probability was 2% and 13% at 6 and 12 months for patients within Milan, and 34% and 57% at 6 and 12 months for patients outside Milan ( $P < 0.01$ ).

Overall survival from time of listing for OLT or LR was not different between the two groups ( $p < 0.99$ ); within Milan criteria, 1 and 4 year survival after LR was 88% and 67% compared with 92% and 63% for OLT ( $p 0.84$ ). Outside Milan criteria, 1 and 4 year survival after LR was 67% and 54% compared with 67% and 45% for OLT ( $p < 0.56$ ).

**Conclusion:** The survival of patients with HCC is similar between LR and OLT. Particularly in patients outside Milan criteria, LR can potentially decrease the dropout rate and serve as a bridge for future salvage liver transplantation.

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### Chemotherapy within 30 days prior to liver resection does not increase postoperative morbidity or mortality

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**Introduction:** Liver resections (LRsxn) are increasingly performed for metastatic disease. To minimize the risk of postoperative complications, six weeks between the last dose of chemotherapy (CTX) and LRsxn is

recommended. The current study sought to examine postoperative morbidity and mortality following LRsxn in patients (pts) who received CTX within 30 days prior to resection.

**Methods:** The validated, risk-adjusted, multi-institutional National Surgical Quality Improvement Program (NSQIP) merged 2005–2007 Participant Use File was queried for preoperative risk factors, laboratory values, and postoperative complications in pts who underwent LRsxn (CPT 47120, 47122, 47125, 47130). Pts were grouped based upon receipt of CTX within 30 days prior to LRsxn and the occurrence of major postoperative complications.

**Results:** 2331 patients underwent LRsxn; 2147 (92%) did not receive CTX within 30 days of resection (No Chemo) and 184 (8%) did receive CTX prior to LRsxn (Chemo). The groups were similar with regard to preoperative comorbidities (e.g. diabetes, cardiac disease) and operative factors (e.g. operative length, intraoperative transfusion). The median value for the NSQIP statistically-computed morbidity probability was similar between the groups (No Chemo 0.32, Chemo 0.34,  $P = 0.07$ ) while the median mortality probability was higher among the Chemo group (0.02) vs. the No Chemo group (0.014,  $P = 0.001$ ). Thirty-day survival was similar between the two groups (No Chemo 97%, Chemo 98%,  $P = 0.44$ ). The major complication rate did not differ between the groups (No Chemo 20%, Chemo 18%,  $P = 0.51$ ) and there were no differences in the following major postoperative complication types: infectious complications, thromboembolic events, or pulmonary complications (Table 1). Factors associated with major complications in the Chemo group included: extent of LRsxn, intraoperative transfusion, preoperative ascites, and preoperative hematocrit (Table).

**Table 1.**

No chemotherapy vs. chemotherapy data	No chemotherapy $n = 2147$	Chemotherapy $n = 184$	P-value
Major complication	428 (20%)	33 (18%)	0.51
Infectious complications	438 (20%)	36 (20%)	0.79
Thromboembolic complications	66 (3%)	8 (4%)	0.34
Pulmonary complications	194 (9%)	13 (7%)	0.37
Chemotherapy group morbidity data	No major complication $n = 151$	Major complication $n = 33$	
Extent of hepatectomy	94 (62%)	13 (39%)	0.02
Partial hemihepatectomy	57 (38%)	20 (61%)	
Hemi or extended hepatectomy			
# packed red blood cells transfused intraoperatively (mean $\pm$ SD)	0.8 $\pm$ 2.1 0–17	3.7 $\pm$ 7.5 0–40	<0.001
Range			
Preoperative ascites	0	2 (6%)	0.002
Preoperative hematocrit	39.1 $\pm$ 3.9	37.1 $\pm$ 5.4	0.02

**Conclusions:** Despite slightly higher predicted risk, major morbidity was not increased in Chemo pts. The strongest predictors of major postoperative complications in Chemo pts were extent of resection and intraoperative transfusion. These data suggest that LRsxn may be safely performed within 30 days of CTX, thereby minimizing the time that pts with liver metastases are off systemic treatment.

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**Pancreaticoduodenectomy for suspected periampullary cancers: the mimes of malignancy**

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**Introduction:** Given the risks and difficulty with preoperative confirmation of cancer, pancreaticoduodenectomy are often undertaken for suspicion of malignancy without histological diagnosis. We undertook this study to review preoperative presentations and diagnostics and ascertain if non-therapeutic resections can be avoided.

**Methods:** Data from patients undergoing pancreaticoduodenectomy were prospectively collected and patients undergoing resections without histological evidence of premalignant or malignant disease were identified. Operative indications, including presenting symptoms, serum tumor markers, results with ERCP/EUS with or without biopsy/genetic testing, and radiographic data, were reviewed. Data are presented as median, mean  $\pm$  SD.

**Results:** From 1996 through 2007, 729 patients underwent pancreaticoduodenectomy at our institution. Malignant lesions were present in 77% of patients; premalignant lesions were identified in 11% patients. Chronic pancreatitis was the operative indication in 3% of patients. 64 (9%) patients underwent pancreaticoduodenectomy with preoperative constellation of signs and symptoms mimicking cancer, although they were without premalignant or malignant disease on final report by Pathology; their clinical and radiographic data are depicted in the table. The most common final diagnoses for patients undergoing pancreaticoduodenectomy without premalignant or malignant disease were pancreatitis (59%) and serous cystadenomas (18%). Of the 64 patients, 17% had preoperative brushings/biopsies “documenting” adenocarcinoma and 41% had a constellation of biliary stricture, jaundice, and pancreatic head mass, without history of pancreatitis. However, 17% had clinical histories and imaging studies sufficient to diagnose chronic pancreatitis, 16% had clear misinterpretations of their imaging studies, and 6% had inadequate preoperative evaluations.

**Table 1.** Clinical and radiographic data.

Patients (n)	Age (years)	Weight loss	Jaundice	Pain	Symptom duration (months)	History of pancreatitis	Mass on CT
64	58 (59 $\pm$ 12.1)	45%	52%	69%	1 (5 $\pm$ 11.9)	20%	96%

**Conclusion:** Only a small minority of patients treated at a tertiary referral center for suspicion of periampullary cancer undergo non-therapeutic or inappropriate pancreaticoduodenectomy and are, as of now, generally unidentifiable prior to resection. Advances in imaging, imaging interpretation, and/or evolving molecular diagnostics should unmask the mimes of periampullary cancer.

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**Incidence of benign disease in patients diagnosed with presumed pancreatic adenocarcinoma by endoscopic ultrasonography (EUS) and fine-needle aspiration (FNA)**

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**Introduction:** The lack of accurate markers makes preoperative differentiation between pancreatic cancer and non-malignant head lesions clinically challenging. Several series have demonstrated the superiority of EUS over CT scan and MRI in the diagnosis of pancreatic neoplasms; however, these diagnostic modalities are poor in distinguishing malignant from benign disease and in diagnosing superimposed cancer in patients with underlying pancreatitis. In this study, we investigated the incidence of benign disease in patients that underwent resection for presumed pancreatic cancer diagnosed by EUS and EUS-guided FNA.

**Methods:** Medical records of consecutive patients who underwent pylorus-preserving pancreaticoduodenectomy at Duke University Medical Center from 1992 to 2007 were reviewed. Demographics, clinicopathologic characteristics, preoperative imaging, EUS, EUS-guided FNA, and postoperative outcomes were analyzed.

**Results:** A total of 494 patients were operated on for presumed pancreatic cancer within the study period. Of these, 37 patients (7.4%) were found to have benign disease on postoperative pathology. The majority of these patients were white males with a mean age of 53 years old. The most common presenting symptom was obstructive jaundice, but 35% of the patients presented with multiple symptoms. Fifty-nine percent of these patients ( $n = 22$ ) with benign disease underwent preoperative EUS. EUS was positive for a head mass in 70%, demonstrated enlarged lymph nodes in 27% and showed signs concerning for vascular invasion in 13%. FNA was suspicious or indeterminate for cancer in 63% of patients. The mean follow up was 23 months. Early complications occurred in 47% and one patient died after surgery. The overall pancreatic leak rate was 15%.

**Conclusions:** In the present series, up to 7% of patients undergoing pancreaticoduodenectomy for presumed pancreatic cancer had benign disease on postoperative pathologic examination. Despite the common use of endoscopic ultrasonography, most of these patients have the appearance of malignancy on preoperative assessment. Even with aggressive use of preoperative evaluation there is still a small subset of patients where malignancy cannot be excluded without pancreaticoduodenectomy.



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### Aetiology and outcome of acute liver failure

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**Background:** Acute liver failure is a clinical syndrome characterized by the sudden onset of coagulopathy and encephalopathy. The outcome is unpredictable and is associated with high morbidity and mortality. We reviewed our experience to identify the aetiology and study the outcome of acute liver failure.

**Methods:** A total of 1237 patients who presented with acute liver failure between January 1992 and May 2008 were included in this retrospective study. Liver transplantation was undertaken based on the King's College Hospital criteria. Data was obtained from the hospital liver database. The following parameters were analyzed: patient demographics, aetiology, operative intervention, overall outcome, 30-day mortality and regrafts.

**Results:** There were 558 men and 679 women with a mean age of 37 years (range: 8–78 years). The most common aetiology was drug induced liver failure (68.1%), of which 90% was due to paracetamol overdose. Other causes include seronegative hepatitis (15%), hepatitis B (2.6%), hepatitis A (1.1%), acute Budd-Chiari syndrome (1.5%), acute Wilson's disease (0.6%), subacute necrosis (3.2%) and miscellaneous (7.8%). 327 patients were listed for liver transplantation, of which 263 patients successfully had the procedure (80.4%). The current overall survival following transplantation was 70% with a median follow-up of 57 months. The 30-day mortality was 13.7%. Drug induced hepatic failure (21.6%) and age over 60 years (21.4%) were associated with significantly higher 30-day mortality. The overall survival of the 974 patients who were not transplanted was 71.1% with a median follow-up of 85 months. Regrafting was performed in 31 patients (11.8%), the most common indication being hepatic artery thrombosis (11 patients).

**Conclusion:** Paracetamol overdose was the most common cause of acute liver failure. Liver transplantation, when performed for acute liver failure, has good long-term survival.

treatment options for patients with unresectable HCC. The purpose of this study was to examine the impact of TACE and SIRT on overall survival (OS), health-related quality of life (HRQL), and cost-effectiveness.

**Methods:** A retrospective analysis was performed on 788 patients treated with TACE or SIRT between 1989 and 2008 at a large tertiary care center. A subset of patients were administered the Functional Assessment of Cancer Therapy-Hepatobiliary (FACT-Hep) at diagnosis, 3- and 6-months follow-up in a randomized ( $n = 19$ ) and non-randomized trial ( $n = 83$ ) of TACE vs. SIRT. Survival was assessed with Kaplan-Meier and Cox Regression analyses. Differences in HRQL were tested using repeated measures ANOVA. Costs were calculated by using the mean charged cost and number of treatments by days of survival.

**Results:** Using Kaplan-Meier analyses, a significant difference in survival was observed between TACE and SIRT ( $P = 0.009$ ) with SIRT patients having a longer survival (median = 466 days, 95% CI = 345–587 days) compared to the TACE patients (median survival = 392 days; 95% CI = 353–431 days). Untreated patients ( $n = 14$ ) had a median survival of 137 days. However, using Cox regression to control for baseline demographic (i.e. gender, age, ethnicity) and disease-specific differences (i.e. cirrhosis, lesion size and number, PV thrombosis, ascites), a trend toward significance was observed in which treatment with SIRT continued to contribute to longer survival when compared to TACE ( $P = 0.11$ ). Although statistically and clinically meaningful differences in HRQL were not observed, patients treated with SIRT consistently had improved HRQL from baseline to 6-months while patients treated with TACE had decrements in HRQL. The average cost for SIRT patients was \$74 155 (mean # of tx = 2) compared to TACE which was \$135 900 (mean # of tx = 5). The cost of SIRT was \$9548 per month of life compared to TACE which was \$10 401 per month of life.

**Conclusion:** After controlling for demographic and disease-specific differences, there appears to be a trend toward significance for overall survival and HRQL for unresectable HCC patients treated by SIRT compared to TACE. In addition, the average cost per month of additional life with SIRT was less than that of TACE, suggesting that SIRT may be a more cost-effective palliative loco-regional therapeutic choice.

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### Overall survival and health-related quality of life in unresectable hepatocellular carcinoma (HCC) treated with transarterial chemo-embolization (TACE) vs. selective internal radiation therapy (SIRT) with Yttrium-90 microspheres

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**Background:** Locoregional therapies, such as TACE and SIRT with Yttrium-90 microspheres, are recognized

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**Partial liver resection for HCC in patients with good liver function can challenge liver transplantation**

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**Introduction:** The practice of liver resection for HCC continues to evolve, but few large, contemporary studies have specifically evaluated the impact of these changes.

**Methods:** From 1990 to 2007, 556 patients underwent liver resection for HCC in our institution. There were 415 men and 141 women; the mean age was  $58 \pm 9$  years. Chronic liver disease (CLD) was present in 367 patients, including 229 with cirrhosis. Etiology of CLD included HCV ( $n = 157$ ) HBV ( $n = 114$ ), alcohol ( $n = 63$ ), cryptogenic ( $n = 182$ ), hemochromatosis ( $n = 30$ ), and other ( $n = 32$ ). Major liver resection was performed in 275 patients and resection was performed in 53. Mean tumor size was 7.5 cm and 70 patients had more than one lesion. Clinical features and outcomes of patients who underwent liver resection before 2000,  $n = 329$  (59%) and after 2000,  $n = 227$  (41%) were compared in table.

**Results:** The incidence of cryptogenic CLD increased significantly after the 2000s (44% vs. 25%,  $P < 0.001$ ). After 2000s, use of Pringle maneuver was less frequently (66 vs. 77%,  $P < 0.002$ ). Perioperative blood transfusion decreased significantly (20% vs. 30  $P < 0.05$ ). Preoperative portal vein embolization (PVE) ( $n = 36$  vs.  $n = 44$ ,  $P < 0.001$ ) as well as the rate of major liver resection (56% vs. 44%,  $P < 0.040$ ) and the mean tumor size (8.6 cm vs. 7 cm,  $P < 0.003$ ) increased significantly. Before 2000s, 9 patients and 35 after 2000s underwent liver transplantation following liver resection. The hospital mortality was reduced from 7.9% before 2000s to 3.3% after 2000s ( $P < 0.05$ ). Overall survival at 1, 3 and 5 years were 79%, 62% and 44% before 2000s and 95%, 89% and 70% after 2000s ( $P = 0.0001$ ).

**Conclusions:** Results of the present series showed that with a better patient selection and preparation, including PVE, the operative mortality decreased. The 5 years survival of 70% resulted from operative technical changes and specific managements of recurrence.

**Table 1. Results.**

	Before 2000 ( $n = 329$ )	After 2000 ( $n = 227$ )	<i>P</i>
Age	56.5	60	0.023
PVE	4	46	0.0001
Pringle maneuver	256	146	0.002
Blood transfusion	90	46	0.05
Major liver resection	151	124	0.04
Positive margin	55	14	0.0001
LT after resection	9	35	0.001
Disease free 1, 3, 5 yrs	78/39/26	75/76/39	0.0001
Survival free 1, 3, 5 yrs	79/62/44	95/89/70	0.0001

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**Reappraisal of pringle maneuver: effect of ischemic time on late oncological outcomes following hepatic resection for metastatic colorectal cancer**

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**Background and aim:** Portal pedicle clamping (Pringle maneuver, PM) is commonly used to reduce bleeding liver resection. PM is well known to cause ischemia/reperfusion injury, but its effect on long-term oncological outcomes is poorly defined. The aim of this study was to evaluate the effect of ischemic time during liver resection on late oncological outcomes for metastatic colorectal cancer (MCRC).

**Methods:** Medical records of patients who underwent R0 liver resection for MCRC between 1991 and 2002 were reviewed. Patients without documented Pringle time were excluded; operative and peri-operative data, including total occlusion time, number of PM applications, peri-operative morbidity, mortality, and clinicopathological variables were analyzed. Long-term progression free (PF) and disease specific (DS) survival were analyzed using Log-Rank test and Cox-regression.

**Results:** Nine hundred patients were included in the study, and the median follow-up period was 44 months. Five hundred and fifty-eight patients (65%) underwent a hemihepatectomy or greater, 373 patients (41%) had bilobar resection and 273 patients (30%) had complex resection. Intermittent PM was used in 781 patients (87%) (median number of applications = 4 (range = 2–16)), while continuous PM was used in 58 patients (6%) and 61 patients (7%) had no occlusion at all. Median of total PM time was 34 min (range = 2–181 min). The factors associated with prolonged PM time ( $> 60$  min) included hemihepatectomy or greater resection, bilobar resection, greater blood loss, longer operation time, multiple tumors, perioperative transfusion, preoperative and postoperative chemotherapy. Univariate and multivariate analysis for long-term PFS and DSS are shown in the Table 1. The total portal pedicle occlusion time was a significant predictor of reduced PFS [ $P = 0.028$ , HR 1.1 (95% CI; 1.0–1.2)], independent of disease and resection extent.

**Conclusions:** Prolonged portal pedicle occlusion is an independent predictor of recurrence and reduced PFS following hepatic resection for MCRC. The mechanism by which this occurs is uncertain but appears likely related to liver ischemia.

**Table 1 for abstract 67.** Significant predictors for PFS and DSS (only significant factors are shown).

Factors	PFS UVp	PFS MVp	HR (95% CI)	DSS UVp	DSS MVp	HR (95% CI)
Pringle time (as continuous, increment of 20 min)	<0.0001	0.028	1.1 (1.0–1.2)	0.01	0.30	1.0 (0.96–1.1)
Preoperative chemotherapy	0.0065	0.014	1.3 (1.1–1.6)	0.050	0.18	1.2 (0.93–1.4)
Adjuvant chemotherapy	0.14			0.024	0.04	0.72 (0.57–0.90)
Bilobar resection	<0.0001	0.13	1.2 (0.95–1.5)	<0.0001	0.005	1.4 (1.1–1.8)
Complex resection	<0.0001	0.004	1.3 (1.1–1.7)	0.0018	0.14	1.2 (0.95–1.5)
Primary node (+)	<0.0001	<0.001	1.6 (1.3–1.9)	<0.0001	<0.001	1.7 (1.4–2.1)
CEA > 200	0.0024	0.035	1.4 (1.0–1.8)	0.0001	0.002	1.6 (1.2–2.3)
Multiple tumors	<0.0001	0.095	1.2 (0.97–1.5)	<0.0001	0.026	1.3 (1.0–1.6)
Tumor size > 5 cm	0.0001	0.002	1.4 (1.1–1.7)	<0.0001	0.017	1.3 (1.1–1.7)

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### Two-stage liver resection for colorectal liver metastases: experience at a single center

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**Aim:** To assess the outcome of patients undergoing two-stage liver resection (2-SLR) for multiple colorectal liver metastases (CLM).

**Background:** Only 10–20% of patients were suitable for liver resection for CLM. The remainder of patients was excluded due to extensive bilobar disease, or insufficient future liver remnant (FLR) which increases the risk of postoperative liver failure. The technique of 2-SLR with portal vein embolization (PVE) can increase the number of patients eligible for resection.

**Methods:** Between January 2001 and May 2008, patients with multiple CLM considered suitable for 2-SLR were prospectively followed up. Stage 1 resection involved resection of metastasis in the left lobe of liver with or without radiofrequency ablation (RFA) which was followed by right PVE immediately postoperatively. The final stage of liver resection with curative intent ensues with a right or extended right hepatectomy to remove all metastases. All patients received neoadjuvant chemotherapy prior to initial hepatic resection and 3 patients received adjuvant chemotherapy following stage 2.

**Results:** Twenty-nine patients (11 male, 18 female), median age of 61 (range 36–82; 7 above age 70) underwent a staged liver resection. The median average number of metastases after chemotherapy was 4 (range 1–31), and the median size of the largest metastasis was 30mm (range 10–87). 25 patients (86%) completed staged 2 resection, 18 (62%) of which were with curative intent. Seven patients (24%) were found to have disease progression, but proceeded to undergo resection of tumors. Stage 2 was abandoned in 4 (14%) patients due to progressive extra/intrahepatic disease. Overall survival (OS) after limited stage 2 resection was 67 and 33% at 1 and 2 years. In patients who underwent curative resection, the OS after hepatectomy was 83, 28 and 6% at 1, 2 and 3 years. The mean OS was 20.4 months (range 2–79) with 2-SLR, with median follow-up of 19 months. Disease free survival after 2-SLR was 24 and 4% at 1 and 2 years respectively. There was one major complication of bile leak requiring repeated percutaneous drainage, and no

perioperative mortality. Four patients later developed recurrence in the left lobe of the liver and underwent further RFA.

**Conclusion:** This study confirms the safety and benefits of 2-SLR in patients with CLM where previously would be unsuitable for curative resection. The use of preoperative staging modalities, as well as molecular tumor markers may help in the decision to proceed with 2-SLR. The role of adjuvant chemotherapy in 2-SLR should also be considered.

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### Predictive factors for outcome after surgery for colorectal liver metastases: reassessment in a recent cohort

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**Aim of the study:** Constant progresses in the management of patients with colorectal liver metastases (CRLM) justify to regularly reevaluate the value of predictive factors for selecting patients for surgery. We reviewed several established prognostic factors and scores in a recent series of patients operated for CRLM.

**Methods:** Sixty-one consecutive patients undergoing a first liver resection for CRLM were reviewed. Classical factors were analyzed to assess their predictive values on operative morbidity and mortality and overall (OS) and disease free survivals (DFS). The accuracy of two prognostic scores was evaluated, Score I: node positive primary tumor, disease free interval < 12 months, number of CRLM > 1, largest tumor > 5 cm and CEA > 200 ng mL<sup>-1</sup> (Fong, *Ann Surg* 1999) and Score II: inflammatory response to tumor and number of CRLM > 8 (Malik, *Ann Surg* 2007). Univariate and multivariate comparisons were made with chi square or Fischer's exact tests and Cox model. Predictive values of scores I and II were analyzed with Wilcoxon-Mann-Whitney test.

**Results:** CRLM were synchronous in 70%, multiple in 63% and bilobar in 30%; 84% of the patients received preoperative chemotherapy (response rate: 84%). Major

resections were performed in 48% and 2-steps hepatectomy in 12%. In 12% of the cases, a combined Radio-frequency was performed on additional non resectable lesion. Operative mortality and morbidity were 3 and 30% respectively. A largest tumor > 50 mm and a 2-steps hepatectomy were the only significant univariate prognostic factors for operative morbidity. Median follow-up was 15 months. One and 2-years OS and DFS were 92 and 89% and 47 and 30% respectively. Positive lymph nodes at primary tumor, number of CRLM, bilobar distribution, increased CEA level and use of RF were significantly associated with tumor recurrence in univariate but not in multivariate analyses. Score I was found predictive of tumor recurrence, with a most discriminative score of 2 ( $P = 0.001$ ) but no prognostic value was demonstrated for Score II.

**Conclusion:** In this recent series of patients operated for CRLM, none of the classical risk factors used to predict tumor recurrence after resection were found significant in multivariate analysis. Only clinical score I (Memorial Sloan-Kettering Cancer Center) was found predictive. While the large majority of the patients received active neoadjuvant chemotherapy, a preoperative score > 2 remained associated with high short-term tumor recurrence rate, questioning the benefit of surgery and underlying the need to consider other adjuvant therapies and more sensitive biomarkers in these cases.

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#### Increased survival by clip score category after stereotactic body radiotherapy in patients with hepatocellular carcinoma

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**Introduction:** The absolute impact of cancer therapy is measured by how long a patient lives compared to their pre-treatment life expectancy. For patients with hepatocellular carcinoma (HCC), life expectancy is often determined by a combination of liver and tumor related variables. The Cancer of the Liver Italian Program (CLIP) score is a validated measure of survival in patients with HCC and has been used to assess survival in large cohorts of patients. The objective of this study was to evaluate the impact of treatment with stereotactic body radiotherapy (SBRT) on survival of HCC patients by comparing pretreatment CLIP score estimates of life expectancy to post therapy survival.

**Methods:** Records from forty patients treated with SBRT at Indiana University between March 2005 and July 2008 were reviewed. Eligible patients had one to three lesions with a maximum sum of diameters up to 6cm. Patients were treated by receiving either 1200–1600 cGy per fraction, 3 fractions or 800 cGy, 5 fractions. CLIP scores were calculated for each patient and patients were stratified by scores 0–4. Life expectancy was estimated based on published survival rates for each CLIP category. Post treatment survival was calculated using Kaplan Meier methodology. The absolute survival benefit for each subgroup was evaluated by comparing the predicted survival of patients based on their CLIP score to the post treatment survival.

**Results:** The median follow-up for the entire population was 10.7 months from the last SBRT treatment date.

Eight patients (20%) have died. No patient died of cancer progression. Thus far, our population does not include enough events in the CLIP 0 category to report survival data. However, survival in the CLIP 1, 2 and 3 groups has been 90% at 32.4 months follow-up for CLIP 1, 67% at 19.1 months follow-up for CLIP 2 and 50% at 25.2 months for CLIP 3. The sole CLIP 4 patient survived 13.9 months. Comparatively, pre-treatment life expectancies for CLIP 1, 2, 3, and 4 are 32, 16.5, 4.5, and 2.5 months, respectively. This translates to a net survival benefit of 0.4, 2.6, 20.7, and 11.4 months in CLIP 1–4, respectively.

**Conclusions:** SBRT has the potential to prolong survival in the majority of patients with HCC compared to pre-treatment survival estimates. This increase may provide immeasurable benefit for individual patients. Furthermore, as many of these patients may be potential transplant candidates, the additional time may provide a cushion for patient work-up, health optimization, and time spent on the wait-list prior to transplant.

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#### Use of oxaliplatin and irinotecan prior to hepatic resection of colorectal cancer metastases is not associated with chemotherapy-associated steatohepatitis (CASH) in a clinic-based Canadian population

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**Background:** Newer chemotherapeutic agents have been linked to liver parenchymal injuries. In particular chemotherapy-associated steatohepatitis (CASH) and diffuse sinusoidal injury have been linked to use of irinotecan and oxaliplatin, respectively. We assessed the prevalence of parenchymal liver injury and correlated findings with chemotherapy use, tumor response, and postoperative complications.

**Methods:** Two hundred and forty-six hepatic resections for metastatic colorectal carcinoma from 2004 to 2007 were reviewed in a blinded fashion. Each case was scored for steatohepatitis, vascular injury, and tumor response using established histological criteria. Chemotherapy and perioperative complication data were available for retrospective analysis in 206 cases.

**Results:** In the year prior to hepatic resection 25 patients received 5-fluorouracil (5FU) alone, 33 irinotecan with 5FU, 24 oxaliplatin with 5FU, 8 all 3 agents, and 116 did not receive chemotherapy. Significant tumor response was seen only in cases that received newer agents prior to surgery (15/65, 23%). Steatohepatitis was identified in four cases (1.9%) – one case who received irinotecan and three that did not receive chemotherapy. Vascular injury was seen in all treatment groups but was significantly associated with oxaliplatin ( $P < 0.05$ ). Multivariate analysis of complications using logistic regression showed a significant association with male gender ( $P = 0.019$ ) and increased body mass index ( $P = 0.046$ ), but not with chemotherapy.

**Conclusions:** No significant association was demonstrated in this series between the use of newer chemotherapeutic agents and CASH. While the vascular hepatic injuries identified were associated with oxaliplatin, the use of chemotherapy prior to surgery was not associated with increased post-operative complications.

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### National trends in inpatient treatment and procedure-related mortality for hepatocellular carcinoma

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**Introduction:** Although therapeutic options for hepatocellular carcinoma (HCC) have evolved over the last decade, the population-level impact of these changes on treatment patterns for HCC has not been studied. We sought to characterize national trends in the application and procedural mortality of inpatient therapeutic interventions for HCC.

**Methods:** The 1998–2006 Nationwide Inpatient Sample was used to identify all HCC-related hospitalizations. Population estimates of in-hospital therapy – major hepatectomy (MH), hepatic wedge resection (WR), ablation, liver transplantation (LT), and chemotherapy/transcatheter arterial chemoembolization (TACE) – and mortality were calculated for each year. Averages over all years were calculated using inverse variance weighting, and trends were analyzed using variance-weighted least squares regression.

**Results:** The annual number of HCC-related hospitalizations increased from 17 510 in 1998 to 30 339 in 2006 ( $P < 0.001$ ). The number of HCC-related procedures similarly increased from 3905 to 7168 ( $P < 0.001$ ), and the number of procedure-related hospitalizations rose from 3056 to 5694 ( $P < 0.001$ ). Although the number of MH remained constant at 489 ( $P = 0.3$ ), the share of procedure-related hospitalizations attributable to MH declined from 16% to 8% ( $P = 0.01$ ). The number of WR increased (499 to 697,  $P = 0.001$ ), as did the number of TACE (1692 to 2898,  $P = 0.002$ ), but the share of procedure-related hospitalizations remained constant for both ( $P > 0.05$ ). For ablation, in contrast, both the number (226–1287,  $P < 0.001$ ) and share of hospitalizations (7–23%,  $P < 0.001$ ) rose dramatically. Similarly, for LT, both the number (212–659,  $P < 0.001$ ) and share of hospitalizations (7–12%,  $P = 0.001$ ) increased. While mean hospital volume remained constant at 17 for MH ( $P = 0.5$ ), it increased for both ablation (13–21,  $P = 0.02$ ) and LT (40–81,  $P < 0.001$ ) and actually declined for WR (44–30,  $P = 0.009$ ). Teaching hospitals performed a smaller share of WR over time (91–85%,  $P = 0.001$ ) but a larger share of ablations (77–83%,  $P < 0.001$ ); there was no change for MH (88%), LT (100%), or TACE (88%) (all  $P > 0.05$ ). In-hospital mortality for MH (9.6%) was higher than for WR (5.1%), ablation (4.1%), LT (3.7%), and TACE (2.4%) (all  $P < 0.05$ ). No changes in procedural mortality rates occurred over time (all  $P > 0.05$ ).

**Conclusions:** The overall increases in HCC-related hospitalizations and procedures have been characterized by a shift toward ablation and LT. An increase in WR

has also occurred with a notable decentralization towards lower-volume and non-teaching hospitals. MH remains associated with increased in-hospital mortality as compared with other HCC therapies.

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### The role hepatic intra-arterial injection of doxorubicin eluting beads in hepatocellular cancer: results of multi-institutional study

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**Purpose:** Hepatic intra-arterial therapy for unresectable hepatocellular cancer (HCC) has been demonstrated to improve overall survival, but can have significant toxicity. Results from the recent prospective randomized control trial comparing conventional chemoembolization to doxorubicin eluting beads (DEB) has demonstrated superior response rates and significantly less morbidity and less doxorubicin related adverse events. The aim of this multi-institutional study was to assess the safety and efficacy of DEB delivered by trans-arterial infusion for the treatment of unresectable HCC.

**Methods:** This open-label, multi-center, multi-national single arm study included 41 HCC patients (Pt's) who were not a candidate for transplantation or resection. Patients received DEB (max 150 mg per infusion) at each treatment. Complications were graded by the Cancer Therapy Evaluation Program Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Response rates were graded by the modified RECIST criteria.

**Results:** These 41 pt's received a total of 88 DEB (range 1–12) treatments. Six patients with portal vein thrombosis (PVT) underwent 15 treatments with no complications. Eight patients while on concurrent sorafenib underwent 18 treatments and tolerated both therapies without major complications. Fourteen patients had prior Yttrium-90 therapy and had failed or progressed and were treated with 23 treatments with one major complication. After a median follow up of 12 months we have seen an overall response of 72% (9CR, 20PR), Stable Disease: 16% ( $n = 7$ ), and progression in five patients with three in the peritoneum, and two with new sites of liver disease. Five patients have been downstaged with additional liver therapy, two transplant and three patients resection/ablation. There was a non-significant reduction in alpha fetoprotein levels of 3143 ( $P = 0.27$ ). PVT did not affect overall survival (9.3 vs. 6.2 months with and without respectively,  $P = 0.83$ ).

**Conclusions:** Hepatic intra-arterial injection of DEB's is safe and effective in the treatment of HCC as demonstrated by a minimal complication rate and tumor response. DEB appear safe in patients with PVT, prior Yttrium therapy, and while receiving concurrent sorafenib treatment, but further larger studies are needed to confirm this data, and establish where hepatic arterial precision chemotherapy should be utilized in the algorithm of the HCC patient.

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### Obesity and its impact on cancer-specific outcomes following liver resection

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While obesity may affect perioperative outcomes following hepatectomy, its effect on cancer-specific outcomes is unknown. We hypothesized that obesity may impact recurrence and survival following hepatectomy for malignancy.

**Methods:** We retrospectively reviewed 660 patients undergoing hepatic resection from 1996 to 2006 at our center. Patient factors including diagnosis, age, resection type, comorbidities, and obesity (BMI > 30) were evaluated. Post-resection recurrence was assessed by CT or MRI. Mortality was determined using the Social Security Death Master File. Risk-adjusted models for recurrence and mortality were constructed using the Cox proportional hazards method.

**Results:** 359 patients had adequate BMI data. 76 (20.7%) patients had benign disease, 82 (22.3%) had primary hepatobiliary cancers (HB), 137 (37.2%) had colorectal metastases (CRM), and 73 (19.8%) had other resectable liver metastases (OM). 33.3% of patients with malignant disease ( $n = 291$ ) were obese. Mean age was  $59.1 \pm 12.3$  years, and was similar by obesity group ( $P = 0.99$ ). Obesity was more common in males (61.8%

males vs. 49.8% females,  $P = 0.04$ ), but was similarly distributed across diagnoses (37.8% HB vs. 34.3% CRM vs. 26.3% OM,  $P = 0.31$ ). The existence of comorbidities or liver disease was not significantly different between groups. Extent of resection, margin status, and receipt of adjuvant chemotherapy were similar across the cohort. Obese patients had more biliary leaks (18.9% vs. 9.0%,  $P = 0.02$ ), intra-abdominal abscesses (7.2% vs. 1.5%  $P = 0.01$ ), urinary tract infections (17.5% vs. 7.2%  $P = 0.007$ ), and pneumonias (8.2% vs. 3.1%  $P = 0.05$ ). Postoperative peak AST, ALT, and total bilirubin were higher in the obese ( $P = 0.04$ ,  $P < 0.001$ ,  $P = 0.02$ , respectively). Median follow-up was 29 months. 53.1% patients recurred and 51.2% died. Overall, obese patients had significantly longer time to recurrence vs. the non-obese (14.5 months vs. 12 months,  $P = 0.01$ ). Overall survival was not significantly different. Independent predictors of recurrence in the multivariate risk-adjusted model were CRM diagnosis [HR 0.45, 95% CI (0.28–0.72)], male sex [HR 2.0, 95% CI (1.34–3.00)], and post-operative liver failure [HR 15.8, 95% CI (2.03–123.0)]. Obesity was independently associated with a decreased recurrence rate (HR 0.58, 95% CI (0.38–0.89)).

**Conclusions:** Our study suggests that while the obese may have a higher rate of perioperative complications post hepatectomy, obesity independently confers a reduced risk of cancer recurrence. Further study is required to determine whether the obese have a greater tolerance for adjuvant therapies or have an inherently different susceptibility to cancer progression.



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**Long-term outcomes after RFA compared to resection of colorectal liver metastases**

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Recently some have called for randomized controlled trials comparing RFA to hepatic resection, particularly for patients with only a few small metastases. The objectives of this study were to compare local recurrence rates and overall survival following open RFA and hepatic resection for colorectal liver metastases.

**Methods:** This was a retrospective review of open RFA and hepatic resection for CRC liver metastases between January 1999 and May 2007 at two University hospitals in Winnipeg, Manitoba. All patients who had RFA were considered to have unresectable disease. A subgroup analysis comparing outcomes of patients with solitary metastases who underwent RFA to those who underwent hepatic resection was planned *a priori*.

**Results:** Fifty-eight patients had hepatic resection and 43 had RFA. Mean follow-up was 32 months. The only operative mortality was seen in a patient who had RFA alone. OR time, blood loss, and transfusions were higher for resection. Rates of ICU admission and length of stay were not different. Complications were not significantly different between groups. OS and DFS were significantly better after resection than RFA. 5-year survival after resection was 43% compared to 23% after RFA. On univariate analysis, surgical resection, age under 70, metastases smaller than 5 cm, less than five lesions, and synchronous lesions were positive prognostic factors. See Table 1 for the results of the multivariate analysis. For patients with solitary lesions, 5-year survival was 48% after resection and 15% after RFA. Even when limited to solitary lesions that were 3 cm or less in diameter, the survival associated with resection was significantly greater than with RFA. While the proportions of patients with distant recurrences and recurrences elsewhere in the liver were not different between groups, the incidence of local recurrence was dramatically different. Over the course of the study, 60% of patients who had RFA suffered local recurrences compared to 7% of patients who underwent hepatic resection ( $P < 0.0005$ ). The local recurrence rate in small ( $\leq 3$  cm) solitary lesions treated by RFA was still 50%.

**Conclusions:** RFA is not equivalent to hepatic resection. Although RFA was done in patients with unresectable disease, the high local recurrence rates and inferior survival rates raise serious doubt as to the feasibility of performing a randomized trial at the present time.

**Table 1.** Multivariate cox proportional hazards regression model for overall survival.

Variable	Hazard Ratio*	(95% Confidence Intervals)	p Value
Procedure			
RFA	1.00		
Hepatic Resection	0.36	0.19–0.70	0.0023
Size of Lesion			
< 5 cm	1.00		
$\geq 5$ cm	2.43	1.26–4.67	0.0081
Number of Lesions			
< 5	1.00		
$\geq 5$	6.08	2.21–16.70	0.0005
Timing of Lesion			
Synchronous	1.00		
Metachronous	2.92	1.50–5.70	0.0017

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**Precision trans-arterial chemotherapy with doxorubicin-eluting beads (ptace) for hepatocellular carcinoma (hcc) in cirrhotics**

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Liver transplantation (LT) is curative for many patients with HCC and cirrhosis; due to a worsening organ shortage, LT can't be utilized immediately upon diagnosis, if at all in some patients. Thus, therapy to control disease while awaiting LT is warranted. Ideally, these efforts will cure the target lesion(s) to eliminate the risk of subsequent metastasis or local progression outside Milan criteria. If consistently curative, the therapy may eliminate/postpone the need for LT in patients with a low laboratory-based MELD score, and it would be an obvious advance in treating non-transplant candidates. pTACE may provide an advance in this regard.

**Methods:** This is a retrospective review of 69 LT and non-LT candidates with cirrhosis/HCC that underwent pTACE (106 procedures) at our institution, including 11 who subsequently underwent LT.

**Results:** Fifty patients were male; mean age = 60.4 - years; mean tumor size = 4.6 cm; 16 had portal vein thrombosis; 35 were Child's A, 27 were Child's B and 7 were Child's C. 41 of 113 evaluable lesions had a radiographic complete response (CR). Two patients were downstaged to within Milan criteria and successfully transplanted. Eight of 11 LT patients had no viable tumor in their treated lesion(s) on explant histology. Two patients died following LT (fungal sepsis; recurrent

hepatitis C in a patient with a laboratory-based MELD < 15;  $n = 1$  each); there has been no post-LT HCC recurrence (median follow-up = 612 days; mean = 604 days). Two patients (2.9%) died within 30 days after pTACE (untreated SBP; pancreatitis;  $n = 1$  each). 25 pTACE patients have died, the majority from cirrhotic complications. Non-fatal adverse events included acute renal failure, gastric ulceration, groin infection, metabolic acidosis, gallbladder necrosis/perforation ( $n = 1$  each); and pancreatitis ( $n = 2$ ).

**Conclusions:** pTACE is a relatively safe and potentially curative HCC therapy in cirrhotics. It may be used as a bridge to LT or as a stand-alone potentially curative HCC therapy in non-transplant candidates. Radiographic CR may allow watchful waiting in listed transplant candidates with a low laboratory-based MELD. Underlying cirrhosis often limits survival more than HCC after pTACE in cirrhotics.

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### Impact of obesity on outcomes following hepatic resections for metastatic colorectal cancer

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**Introduction:** Obesity has become an increasingly common health problem in the United States. The purpose of this study was to evaluate the surgical and oncologic outcomes of patients with resections for colorectal liver metastasis when stratified by body mass index (BMI).

**Methods:** Our 1410 patient prospectively maintained Hepato-Pancreato-Biliary database from 8/1996 to 12/2007 was reviewed for patients with colorectal metastasis. Patient's weight was recorded at the time of hepatectomy. Data included resection type, BMI, operative time, perioperative complication rate, blood loss, length of stay, recurrence rate, and overall survival. Complications were graded using our established 5 points grading scale. Patients with non-anatomic resections, ablations, and ablations with resections were excluded from the study.

**Results:** Overall, 148 patients underwent anatomic hepatic resection for colorectal metastasis with a median follow up of 26 months. A total of five central resections, 57 right lobe lobectomies, 19 left lobectomies, 29 left lateral lobectomies, 15 right posterior sectorectomies, and 23 trisegmentectomies were performed. Patient groups were divided based on the National Institutes of Health BMI class with 46 (31%) of the patients classified as obese (BMI  $\geq 30$  kg m<sup>-2</sup>). There was no difference in mean operative times (176 vs. 166 mins,  $P = 0.5$ ), mean estimated blood loss (428 mL vs. 421 mL,  $P = 0.9$ ), length of stay (8 vs. 10 days,  $P = 0.2$ ), or major complication rate (22% vs. 30%,  $P = 0.5$ ). A difference was not found in the rate of recurrence at last follow up (54% vs. 51%,  $P = 0.7$ ), but obese patients did show a longer median overall survival (63 vs. 39 months,  $P = 0.01$ ).

**Conclusions:** Obese patients have similar peri-operative outcomes as measured by operative time, blood loss, and complications when compared to non-obese patients. Interestingly, when compared to non-obese patients, obese patients have improved overall survival which may be a reflection of worse nutritional status of non-obese patients.

**Table 1. Results.**

Patients demographics $n = 148$			
	BMI < 30 $n = 102$	BMI $\geq 30$ $n = 46$	P-values
Mean length of stay	9.9 days	8.1 days	0.2
Mean operative time	166 mins	176 mins	0.5
Mean estimated blood loss	421	428	0.9
Perioperative mortality	4 (4%)	0	0.3
Median overall survival	39 months	63 months	0.01
Major complication	46 in 31 (Grade 3–5) patients (30%)	11 in 10 patients (22%)	0.5
Minor complication	67 in 40 (Grade 1–2) patients. (39%)	20 in 17 patients (37%)	0.8

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### Single center experience with living donor right lobe liver resection

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**Background:** The first living donor right lobe liver resection (LDLR) was performed in Hong Kong in 1991. Since then, this procedure has been the subject of debate. Questions related to indications, safety, outcomes and donor risks continue to be a major concern for the transplant community. In this study, we report our experience with LDLR as it is not included in the A2ALL registry.

**Material and methods:** The adult-adult living donor liver transplant program was initiated at our center in October 2000. Program implementation followed guidelines published by the American Society of Transplant Surgeons. A retrospective review of living liver donors at our center was done. Patient demographics, procedure details, complications, and outcomes were reviewed.

**Results:** Between December 2000 and August 2008, 698 orthotopic liver transplants were performed with 35 from living donors. Donor mean age was  $42 \pm 3.2$  years, with 11 males (31%) and 24 females (69%) in the group; 33 (94%) were Caucasian and 2 (6%) were African-American. The follow up period was from the date of surgery until present. Three donors (9%) chose to follow up with their own doctors and no long-term information is available but all had no immediate complications. The mean hospital stay was  $6.6 \pm 0.7$  days. Procedures consisted of standard open right hepatic lobectomy (31), extended right hepatic lobectomy (1) and laparoscopic-assisted right hepatic lobectomy (3). The mean post-operative peak SGOT, SGPT, and Bilirubin for the group was  $326.1 \pm 45.7$ ,  $321.8 \pm 54.7$ , and  $2.8 \pm 0.5$  respectively. Smooth uneventful course was seen in 25 donors (71%), while 10 (29%) developed one or more complications; 6 (17%) of whom required readmissions. Grading of complications was according to Clavien's classification post LDLR; CLAV II in 2 (6%), CLAV IIIa in 5 (14%), and CLAV IIIb in 3 (9%), with reoperations for bile leak, post-operative bleeding, and incisional hernia respectively. Interventions included ERCP, thoracentesis and percutaneous drainage of perihepatic fluid. All donors resumed their prior employment. There were no long-term disability

issues. None of the donors expressed regrets about donation.

**Conclusion:** Despite the ongoing debate, we think that LDLR is a safe procedure if performed in highly specialized centers with expertise; knowing that this procedure is associated with complications and full disclosure to donors and education are important. LDLR would help expand the donor pool and with introduction of the laparoscopic-assisted procedure, the donors' acceptance and sense of well-being have improved. Our experience was comparable to the A2ALL published report.

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### Peri-operative analysis of laparoscopic vs. open liver resections: are laparoscopic liver resections cost-effective?

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**Introduction:** Over the past decade there has been an increasing trend toward a minimally invasive approach to liver surgery. While initially limited by technical challenges, advances in laparoscopic techniques and instrumentation have rendered this approach safe and feasible. However, as health care costs approach 50% of some provincial budgets, surgical innovation must be justifiable in terms of costs and patient outcomes. With introduction of standardized post-operative liver resection guidelines (fast-track) to optimize patient length of stay in hospital, the advantages of laparoscopic liver resection (LLR) compared to open liver resection (OLR) measured by peri-operative clinical outcomes and resource utilization are not well-defined. It remains to be established whether LLR is superior to OLR by these measurements.

**Methodology:** A prospective analysis of eighteen LLRs performed at the Vancouver General Hospital from 2005–2007 was performed. These data were compared to an equivalent group of twelve consecutive OLRs undertaken immediately prior to and in preparation for the introduction of the LLR. Outcomes were evaluated for differences in peri-operative morbidity, hospital length of stay, and operative costs.

**Results:** There were no differences between LLRs and OLRs in demographics, pathology, underlying cirrhosis, tumour location, or extent of resection. There were no deaths. LLRs had significantly decreased intra-operative blood loss (287 mL vs. 473 mL,  $P = 0.03$ ) and post-operative complications (6% vs. 42%,  $P = 0.03$ ) compared to OLRs. There was a trend toward reduced hospital length of stay in LLRs (4.3 vs. 5.8 days,  $P = 0.07$ ). There were no differences in operating time for LLRs compared to OLRs (135 vs. 138 min, respectively), total time in the operating theatre (214 vs. 224 min respectively), or costs related to trocars and stapling devices (\$1267 vs. \$1007 respectively).

**Conclusions:** LLR is associated with decreased morbidity and decreased resource utilization compared to OLR. Peri-operative patient outcomes and cost-effectiveness justify LLR despite introduction of standardized post-

operative liver resection guidelines and decreased length of stay for OLR.

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### Evidence of lipid metabolism reprogramming in hepatitis C associated hepatocellular carcinoma

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**Background and aim:** Under normal physiological conditions, the liver ensures homeostasis of lipid and lipoprotein metabolism. The relationship between hepatitis induced alterations in lipid signaling and hepatocellular carcinoma (HCC) are unclear. The goal of this study was to systematically explore lipid metabolism and altered expressions of genes speculatively participating in hepatitis C associated HCC.

**Methods:** Three groups of human samples were used for microarray experiment: normal, non-hepatitis infected livers ( $n = 9$ ), hepatitis C virus related HCC tumor samples ( $n = 9$ ) and adjacent non-tumor liver samples ( $n = 11$ ). Total RNA was isolated from these three groups of samples and microarray was performed using Affymetrix Human Genome HG U133 Plus 2 GeneChip. GeneSifter software was used to identify differentially expressed genes according to Gene Ontology and the Kyoto encyclopedia of genes and genome (KEGG) pathways.<sup>1</sup>H and <sup>31</sup>P NMR experiments were performed using a CMX 400 MHz NMR spectrometer.

**Results:** Using 1.5-fold change cutoff and the adjusted  $P$ -value  $< 0.001$ , one way ANOVA analysis showed 3989 genes were differentially expressed. Gene Ontology analysis showed metabolic process is a major category with the highest Z-scores (5.75) in biological process ontology. Genes related with lipid metabolism were found to be over-represented. KEGG pathways such as fatty acid metabolism, PPAR signaling pathway and bile acid biosynthesis were significantly enriched in the differentially expressed genes. Further analysis revealed genes related to fatty acid synthesis such as fatty acid synthase were up-regulated, while genes coding the enzymes involved in fatty acid oxidation were down-regulated in HCC tumor samples compare to normal control. Genes involved in phospholipids synthesis such as acyltransferase like 2, phosphoinositide-3-kinase, class 2 beta polypeptide and phosphatidylglycerophosphate synthase 1 were overexpressed, but genes related to cholesterol or bile acid biosynthesis were down-regulated in HCC tumor. NMR spectroscopy revealed detectable and dynamic changes in the lipid metabolome in HCC tumor specimens compared to adjacent samples. Specific flux modulations were detected such as glycolysis, phospholipid synthesis and fatty acid synthesis.

**Conclusion:** Whole genome mRNA profile analysis as well as NMR analysis showed the extensive reprogramming of lipid metabolic pathways in HCC. These results provided further insight into deviations in lipid metabolism that may contribute to the development of cancer.

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### Comparison of result of hepatic and lung resection to recurrences after first hepatectomy to liver metastases of colorectal origin

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**Introduction and aim:** More than 60% of patients undergoing hepatectomy for colorectal liver metastases experience recurrence with the liver and lung being the most frequent site of recurrence. Although repeated resection provides the only hope for cure, the prognoses of patients with liver and lung recurrence have not been correctly compared. We tried to address this question.

**Patients:** Patients in whom the recurrence was detected ( $n = 166$ ) after hepatectomy to colorectal liver metastases conducted in 216 patients.

**Methods:** We investigated (i) the pattern of recurrences; (ii) the proportion of patients undergoing repeated resection and (iii) survival rates of patients after repeated resection.

**Results:** (i) Seventy-one had isolated hepatic recurrence (Liver Rec.), 25 had isolated lung recurrence (Lung Rec.), 13 had isolated hepatic and lung recurrence (Liver & Lung Rec.), and the remaining 57 had other organ recurrence. (ii) 60 of 71 (85%) with Liver Rec., 21 of 25 (84%) with Lung Rec., and 9 of 13 (69%) with Liver & Lung Rec. underwent repeated resection. In these 90 patients, the imbalance between groups was found in the following variables: disease free interval (DFI) from the primary tumor resection, DIF from the first hepatectomy, CEA values, the size and the number of metastases at repeated resection. (iii) The 3- and 5-year survival rates from the repeated liver resection are as follows: 58 and 39%, 60 and 37%, and 20 and 20% (Liver Rec., Lung Rec. and Liver & Lung Rec., respectively). Multivariate Cox analysis revealed that four variables contributed to the poor prognosis (hazard ratio [95% CI]): the number (1.20 [1.11–1.29]) and the maximum size (1.26 [1.02–1.48]) of tumor nodules at repeated resection, the lung recurrence (2.36 [1.41–3.20]), both lung and liver recurrence (4.01 [2.86–5.17]).

**Conclusion:** Patients with lung and liver/lung recurrences portend poorer prognoses than those with hepatic recurrence. However, the re-resection is the only potentially curative treatment and under the more strict indication criteria especially regarding the number of tumor nodules, the comparable long-term outcome to those with hepatic recurrence can be expected.

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### Effect of minimally invasive liver surgery (mils) on hospital resource utilization

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**Introduction:** Minimally Invasive Liver Surgery (MILS) is slowly becoming widely accepted at specialized centers. There are very few studies analyzing the costs and resource utilization of this approach. In order to determine the financial impact of these techniques, we compared the hospital charges of the open and MILS techniques at our program.

**Methods:** A retrospective review of all the charges associated with each case was performed. Data was obtained from the hospital database and under IRB approval. ANOVA and chi-square tests were used for statistical analysis. All figures are reported in US dollars (USD).

**Results:** A total of 101 liver resections were performed between 7/05 and 8/08 (open 47%; MILS 53%) at Methodist Dallas Medical Center. Length of stay (3.2 vs. 5.5 days) and blood loss were significantly less for MILS vs. open ( $P < 0.001$ ;  $P = 0.003$ , respectively). Tumor size was larger for the open group (6.1 vs. 4.6 cm;  $P = 0.04$ ). Results of the charges analysis is shown in Table 1. The MILS group revealed a significantly higher operative room charge, but a significantly lower charge in all other categories. However, total hospital charges are not significantly different for both techniques ( $P = 0.93$ ).

**Table 1.** Resource utilization in liver surgery in USD.

	MILS ( $n = 54$ )	OPEN ( $n = 47$ )	P-value
OR Charges	20648	14513	$< 0.001$
Blood Bank	846	1853	0.005
Laboratory	2232	3150	0.005
Respiratory	756	1519	$< 0.001$
ICU charges	3042	8528	$< 0.001$
Pharmacy	3806	5322	0.001
Total Hospitalization	36868	36637	0.93

**Discussion:** MILS techniques require the use of expensive tools in order to make the procedure safer, causing an increase in the cost of the actual procedure. However, all the charges following the surgical procedure are significantly lower than the open cases. From the economical standpoint, the higher charges in the operating room offset the lower charges associated with a shorter hospital stay resulting in no difference between both techniques. From the medical standpoint, the patients spend less time in the hospital, in the ICU and require less hospital resources when the MILS is used. As techniques are better refined, the goal should be a better outcome, a safe operation and ideally a less expensive procedure.

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**‘Close shave’ in liver resection for colorectal liver metastases**

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**Introduction:** Metastatic spread to the liver occurs in about 50% of patients with colorectal cancer. The optimal size of a clear liver resection margin remains controversial. The aim of this study was to investigate the effect of clear margin width on long-term survival after liver resection for colorectal liver metastases (CRLM) with a policy of standard neo-adjuvant chemotherapy.

**Methods:** Consecutive patients ( $n = 319$ ) who underwent exploration with a view to liver resection for CRLM were included over a 10 year period. All patients with synchronous or early ( $< 2$  years) metachronous tumours were treated with neo-adjuvant chemotherapy. Data were recorded prospectively and analysed retrospectively. Uni- and multivariate analyses were carried out.

**Results:** Overall survival of the cohort at 1, 3 and 5 years were 90.3%, 68.1% and 56.1% respectively. The incidence of cancer involved resection margins (CIRM) was 5.8%. 12 patients who were excluded from the survival analysis had no residual disease. Patients with macroscopically involved resection margins (R2) had a poorer overall survival than those with microscopically involved margins (R1) ( $P = 0.04$ ). Involved resection margins (R1 and R2) had a poorer overall survival ( $P = 0.002$ ) than patients with clear margins. Clear resection margins of any width did not affect long-term survival.

**Conclusion:** CIRM is an independent predictor of poor outcome in patients with CRLM, while the size of clear margin does not affect survival. A standard policy of neo-adjuvant chemotherapy may be associated with a low incidence of CIRM and may improve the long-term outcome of patients with sub-centimetre clear resection margin widths to resemble those with  $> 1$  cm clear liver resection margins.

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Oral Posters – Liver III  
Friday, March 13, 2009 4:15–5:30 PM

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**The efficacy of anatomical resection for hepatocellular carcinoma within the Milan criteria**

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**Objective:** The long patients survival (PS) and disease free survival (DFS) must be hoped when hepatectomy was performed for the patients with HCC which was within Milan criteria and transplantable. We analyzed the efficacy of anatomical resection for hepatocellular carcinoma (HCC) within the Milan criteria.

**Methods:** Between 1990 and 2006, consecutive 322 patients within the Milan criteria underwent curative resection and were classified to Group A (a tumor 5 cm or less in diameter in patients with single HCC) and Group B (no more than three tumor nodules, each 3 cm or less in diameter, in patients with multiple tumors). PS, DFS, and risk factors were analyzed.

**Results:** In Group A and B, PS rates and DFS of patients who underwent anatomical resection were significantly higher than those of patients who underwent non-anatomical resection ( $P < 0.01$ ,  $P < 0.05$ ). While the significant factors related with PS of Group A were ICGR15, T.Bil, HCV, anatomical resection, and non-cancerous liver, those with DFS were ICGR15, T.Bil, Alb, anatomical resection, tumor size, portal invasion, and non-cancerous liver by univariate analysis. In Group A, anatomical resection was significant favorite factor of PS and DFS by multivariate analysis. Whereas the significant factors related with PS of Group B were ICGR15, AFP, and anatomical resection, those with DFS were AFP and anatomical resection by univariate analysis. Anatomical resection was significant favorite factor of DFS by multivariate analysis. Group A was classified to four subgroups according to anatomical / non-anatomical resection and the value of ICGR15: Group IA (anatomical resection, ICGR15 < 15%:  $n = 109$ ), Group IIA (non-anatomical resection, ICGR15 < 15%:  $n = 47$ ), Group IIIA (anatomical resection, ICGR15  $\geq 15\%$ :  $n = 45$ ), and Group IVA (non-anatomical resection, ICGR15  $\geq 15\%$ :  $n = 86$ ). The PS and DFS curve of Group IVA was significantly worse than other three groups ( $P < 0.05$ ). The PS curve of Group IIIA was almost the same as that of Group IIA until 8 years after LR. The DFS of Group IIIA was better than that of Group IIA, and the curve of the DFS up to about 5 years was similar to Group IA. Group B was also classified to 4 subgroups; Group IB ( $n = 9$ ), Group IIB ( $n = 6$ ), Group IIIA ( $n = 6$ ), and Group IIV ( $n = 14$ ). The PS and DFS curve of Group IB was significantly better than the other groups.

**Conclusion:** Anatomical resection should be performed for the patients with HCC which was within Milan criteria and transplantable.

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**Characteristics and frequency of chemotherapy-associated liver injury following neo-adjuvant therapy for colorectal metastasis**

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**Background:** Neoadjuvant FOLFOX (folinic acid, 5-fluorouracil, and oxaliplatin) chemotherapeutic regimens are used to improve tumor resectability and reduce recurrence in patients with colorectal liver metastasis (CLM). However, systemic FOLFOX treatment frequently results in parenchymal injury.

**Methods:** Clinicopathological data was retrospectively collected on patients undergoing major liver resection ( $\geq 2$  segments) for CLM between January 2003 and January 2008. Patients who received neoadjuvant FOLFOX-based chemotherapy were selected; resected specimens were evaluated for sinusoidal injury, steatosis, and subcapsular hemorrhage by a single pathologist. The presence of injury was correlated with the treatment regimen.

**Results:** Neoadjuvant FOLFOX was given to 49 patients and major liver resection was performed in 16 patients (median age 54.4 years; male 50%; right hepatectomy, 12; left hepatectomy, 1; left lateral sectionectomy, 3). Bevacizumab (6 patients, 38%) or cetuximab (9 patients, 56%) was commonly used with FOLFOX chemotherapy. Fourteen patients (88%) were observed to have parenchymal injury: sinusoidal obstruction (11 patients, 69%), steatosis (11 patients, 69%), and subcapsular hemorrhage (10 patients, 63%). There was no correlation between the type of injury and the addition of bevacizumab or cetuximab. Median time from oxaliplatin administration to surgery was 32 days (range 15–70 days). The presence of sinusoidal injury decreased with increasing time between final oxaliplatin administration and surgery (< 30 days, 80%; 30–60 days, 67%; > 60 days, 50%); however, there was no difference in median length of stay of patients with sinusoidal injury: 10 days, 8 days, or 11 days, respectively (NS).

**Conclusion:** Neoadjuvant FOLFOX administration for CLM is associated with combined hepatic injuries including sinusoidal obstruction, steatosis, and subcapsular hemorrhage. Although fewer patients were observed to have sinusoidal injury with increasing time between final oxaliplatin administration and surgery, about 50% of patients had persistent injury. Further studies are needed to investigate the optimum administration of FOLFOX chemotherapy.



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### Systematic review of combined liver and vena caval resection for malignancy

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**Purpose:** To perform a systematic review of the existing literature to identify the best available evidence regarding combined liver and vena caval resection for malignancy.

**Methods:** A Medline search was performed to identify all relevant articles. Search terms used were 'cava' and 'liver resection'. In addition, the references of those articles identified were searched for additional pertinent papers. Articles up to January 2008 were considered.

**Results:** A total of 39 articles were identified, of which 22 were excluded (redundant series, lack of survival data, case reports). Seventeen articles were identified for analysis. All were retrospective case series published between 1990 and 2007. A total of 185 patients underwent combined resection, with a median age of 56 years, and a 56% predominance of males. Colorectal metastases accounted for 48% of the operative indications, with the remainder being split amongst cholangiocarcinoma (20%), hepatocellular carcinoma (17%), leiomyosarcoma of the cava (7%), and other pathologies (8%). The median number of tumors resected was  $1.9 \pm 0.5$ , and the median tumor size was  $7.5 \pm 2.6$  cm. Extended hepatectomy accounted for the majority of resections (52%). With regards to caval reconstruction, 51% of patients received a tube graft, 33% were repaired primarily, and 16% were patched. Ex vivo procedures were performed in 6.5%. Peri-operative mortality ranged from 0 to 50% (median  $7.7 \pm 2.9\%$ ), with an average operating time of 505 min and an average blood loss of 2599 mL. With regards to outcome, the median survival of patients undergoing combined resection is  $26.3 \pm 7.8$  months, with a recurrence free survival of  $15.8 \pm 7.6$  month. The 1, 3 and 5 year survivals were  $68\% \pm 10.8$ ,  $35\% \pm 15$ , and  $26\% \pm 8$ , respectively.

**Conclusions:** Combined liver and vena caval resection can be performed safely in experienced centres with peri-operative mortalities similar to that of liver resection alone. In addition, resection appears to provide a survival advantage. Median survival with no treatment is less than 12 month, with no 5 year survivors reported even with chemotherapy. With surgery, the median survival surpasses 2 years (26 month). Caval involvement should not preclude resection in those patients who would otherwise be surgical candidates.

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### Myoglobinuria after radiofrequency ablation of liver tumors

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**Background:** There is scant data in the literature about myoglobinuria after radiofrequency ablation (RFA) of liver tumors. The aim of this study is to analyze the incidence and identify the risk factors involved in this complication after RFA.

**Patients and methods:** An initial case of myoglobinuria and acute kidney injury (AKI) during laparoscopic liver RFA after 10 years of the liver ablation program led to the design of this study. Prospective data were collected on 41 consecutive patients undergoing laparoscopic RFA at our institution over a 9-month period. Urine myoglobin, serum creatinine kinase, and serum creatinine levels were obtained pre- and post-ablation. Variables were compared between patients to identify possible risk factors that might be related to this rare complication. Data are expressed as mean  $\pm$  standard error of the mean (SEM).

**Results:** Two patients were excluded from the study due to pre-operative myoglobinuria of unknown etiology. Of the remaining 39 patients, 3 developed dark urine with significant myoglobinuria on post-operative day 1. Two of these patients had carcinoid liver metastases; the remaining patient had a metastatic colorectal lesion. The number of tumors ablated in these patients was 14, 11 and 3 vs.  $2.4 \pm 0.4$  in the rest of the patients. Cumulative tumor volume was larger in the group of patients that developed the complication vs. who did not ( $127.9 \pm 59.5$  cm<sup>3</sup> vs.  $48 \pm 3$  cm<sup>3</sup>). Two grounding pads were used in the 3 patients that had a complication vs. 4 pads in the rest of the patients. Dark urine was identified promptly intra-operatively and treated aggressively. All of these patients required intensive care unit (ICU) admission and had a prolonged hospital stay. Marked elevation of transaminases and creatinine kinase as well as a drop in hematocrit and platelet count was observed in patients with myoglobinuria. In our retrospective review of 706 patients that underwent liver RFA in the past 10 years we detected 27 patients (3.8%) with ten or more lesions ( $11.9 \pm 0.4$ ). None of these patients had significant elevation of serum creatinine post-operatively. In the whole series of 706 patients, 22 (3.2%) were found to have elevated creatinine after liver RFA, with return to baseline in all but 7 patients in follow up.

**Conclusion:** Myoglobinuria after liver RFA is a rare but potentially devastating complication that may lead to AKI with significant morbidity and prolonged hospital stay. Patients with large tumor volumes requiring longer ablation times need to be monitored closely for the development of this complication. The fact that this was not observed in other patients with similar tumor characteristics suggests that individual patient related factors might play an important role.

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### Bipolar radiofrequency ablation: procedure and outcome in 17 patients with 26 ablations

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**Introduction:** Monopolar radiofrequency ablation (RFA) is lengthy and cumbersome due to 'radial energy deposition' from ionic friction. Microwave ablation (MWA) based on electromagnetic energy produced from rotational friction has been proposed as a superior method of thermal ablation; however, the relatively lengthy time to achieve complete ablation remains a concern; especially for multiple same patient ablations. In the present study we evaluated the role of laparoscopic

bipolar RFA (BRFA) using 'line of sight' energy deposition for hepatic tumors; ablation time and efficacy were compared to known published data for MWA (MWA-7 min for 3 cm lesions-10 min for larger lesions).

**Methods:** Using a prospectively maintained hepatobiliary database, 17 patients undergoing 26 laparoscopic BRFA were identified over the interval (9/07-8/08). Patient characteristics were studied. Lesion size, time to complete ablation (initial and confirmatory deployment) and hepatic associated post-operative complications were evaluated. For patients subsequently undergoing a staged hepatic resection, pathological evaluation for viable tumor in the previously ablated area was performed.

**Results:** Seventeen patients (9 M : 8 F) mean age of 63 years had 26 laparoscopic BRFA. Patient diagnoses included: metastatic colorectal cancer (12/17), HCC (2/17), symptomatic isolated gallbladder cancer (2/17), and adenoma (1/17). The size of the hepatic lesions were > 3 cm in 16 ablations and < 3 cm in 10 ablations. Mean ablation time was 6 min  $\pm$  2, and there was no significant difference in time needed for ablation between lesions < 3 cm and those > 3 < 5 cm larger (mean ablation time for lesions < 3 cm; 5 min 39 s  $\pm$  57 s vs. 6 min 17 s  $\pm$  2 min for lesions > 3 cm;  $P$  = NS). There were no peri-operative mortalities and no hepatic associated morbidities. In 5/17 high risk patients (ASA 3, age > 65) staged liver resection was performed after a mean period of 6 months. Pathologically, there was no evidence of viable tumor the previously ablated areas.

**Conclusion:** Bipolar RFA achieves the most time efficient ablation to what has been reported in the literature. Line of sight energy delivery enables a safe means of energy delivery and rapid ablation for lesions studies (up to 5 cm). The relative shorter ablation time, the absence of ablation induced inflammatory necrosis-zone and the pathologic absence of viable tumor in resected specimens supports BRFA as a potential preferred ablation method for primary and metastatic hepatic tumors.

each TACE procedure. Response rate (RR) was assessed using radiologic criteria, including presence of arterial enhancement during 3-phase CT/MR follow-up studies. Radiologic responses were categorized as follows: (i) complete response (CR) if no enhancement in residual tumor, no tumor growth; (ii) partial response (PR) if arterial enhancement still present, no tumor growth; (iii) stable disease (SD) if previous (CR) or (PR) is maintained at time of last study; (iv) progressive disease (PD) if increased, vascular tumor growth or new lesion. The data was retrospectively evaluated. Response rates were determined based on change in lesion size and and/or enhancement.

**Results:** The procedure was technically successful in 96% of the cases. The mean follow up time was 251 days. The one technical failure was due to hepatic artery dissection. 30 day mortality was 0%. Major Complications included one instance of pancreatitis and one case of flash pulmonary edema occurring within 30 days of the procedure (8%). Another patient developed a transient fever treated with antibiotics. Of the 18 patients with imaging follow up data available, 17 (94%) initially responded favorably with either a CR or PR. Of all 25 patients treated, two were eventually resected (8%), and two received liver transplants (8%). A partial response was seen in six patients (33%), complete response in 11 patients (61%), with stabilizing of disease on follow-up imaging sixteen patients (89%), and progressive disease in one (5.6%) of those with follow up imaging data. Two patients showed dramatic decreases in alpha fetoprotein levels after DEB-TACE.

**Conclusion:** TACE using LC beads is a safe and effective method for palliation of HCC. The treatment may downsize tumor to resectability or be used as a bridge to liver transplantation. Further study is needed to determine the effect of DEB-TACE on survival.

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### Transarterial Chemoembolization (TACE) of Hepatocellular Carcinoma (HCC) using Doxorubicin Eluting Microspheres (DEB): initial results

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**Methods:** Patients with HCC not amenable to other therapy were treated using doxorubicin-eluting microspheres (DEB-TACE). Twenty-five patients, mean age 64.1 year, were treated between 2/27/07 and 12/06/07 for unresectable HCC. Average number of sessions 1.4. Average dose 55.0 mg (range 25-130 mg) per session. DEB-TACE was performed using 1-2 vials of 100-300  $\mu$  LC beads mixed with 50 mg of Doxorubicin. The mixture was injected via a microcatheter positioned as selectively as possible into arteries supplying each tumor. Clinical and radiologic data were recorded at 24 h, 1 month, 3 months, 6 months, and 12 months following

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### Complications related to radiofrequency ablation of liver tumors. Review of the current literature and personal experience

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**Introduction:** The rates of complications in the treatment of liver tumors by Radiofrequency Ablation (RFA) are significantly lower when compared to the surgical approach although the recurrence rates are higher.

**Methods:** We raised and analyzed 11 902 cases performed by percutaneous, laparoscopic, and open surgery and evaluated the rates of local and systemic complications reported.

**Results:** Were found biliary/biloma - 0.75%, vascular lesions - 1.35%, hepatic abscess - 1.18%, difficulty in removing the needle - 0.03%, hepatic infarct - 0.03%, aneurysm - 0.03%, pleural effusion - 1.5%, ascites - 1%, intra-peritoneal hemorrhage - 0.75%, skin and abdominal wall burn - 0.5%, injuries in extra liver bodies - 0.84%, hemothorax - 0.2%, subscapular hematoma - 0.1%, pneumothorax - 0.15%, intra-peritoneal bleeding

– 0.62% – tumor seeding along the needle tract – 0.78%, jaundice – 0.3%, liver failure – 1.49%, decreased blood pressure – 0.07%, cardiac complications – 0.21%, arrhythmias – 0.41%, acute respiratory failure – 0.41%, seroma – 4.8%, pneumonia – 2.4%. The overall rate of mortality among the 11.902 cases evaluated was 0.34%.

**Conclusion:** The mortality and complication rates are low when compared to surgery, but the recurrence of the injuries reach values four times higher than the figures obtained in open surgeries. Therefore RFA should be reserved just for patients in whom surgery does not represent an option for the treatment.

# Abstracts 91 to 100

## Oral Posters – Biliary

### Friday, March 13, 2009 4:15–5:30 PM

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#### Mid duct cholangiocarcinoma: is limited bile duct resection adequate?

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**Purpose:** To determine the optimal surgical management of mid duct cholangiocarcinoma (MC).

**Introduction:** The overall incidence of MC is low and few reports specifically address its treatment. Reports in hilar cholangiocarcinoma and gallbladder cancer suggest that aggressive resection may also have improved survival benefits in MC, based on related embryology. MC may directly involve the liver, pancreas, duodenum or regional vasculature. Although central bile duct resection (CBR) with regional lymphadenectomy and hepaticojunostomy for MC may be appropriate selectively, pancreaticoduodenectomy (PD) may be superior oncologically and more widely applicable.

**Patients and methods:** This retrospective, case-control study reviewed the medical records of 89 patients with MC or distal cholangiocarcinoma (DC) who underwent surgical resection at our institution from 1993–2003. Demographics, patient and tumor features, operative morbidity, and mortality were assessed for the primary outcome, survival, and the secondary outcomes, recurrence and adequacy of surgical resection.

**Results:** MC was resected by CBR in 34 patients, PD in 5 patients and DC by PD in 45 patients. Five patients were excluded for complex tumors. Demographics, clinical presentation, performance status and tumor grade were similar between groups. Overall AJCC stage and T-stage were significantly greater for DC. Although operative mortality and morbidity were similar, duration of hospitalization was significantly shorter for CBR ( $P < 0.001$ ). CBR was significantly associated with positive resection margins ( $P = 0.005$ ) and fewer lymph nodes harvested than PD ( $P < 0.001$ ). Overall 5-year survival after CBR for MC and PD for DC was 21% and

28%, respectively. Five-year survival after R0 resection for CBR and PD was 29% and 30%, respectively. Local recurrence was greater for CBR than for PD ( $P = 0.055$ ). Disease-free survival did not differ significantly between CBR and PD (20% and 27%, respectively).

**Conclusion:** Overall, survival after CBR for MC and PD for DC is similar. Local disease failure for MC after CBR likely results from increased margin positivity and fewer lymph nodes harvested at surgical resection. PD may address the local failure associated with these findings without increased operative morbidity and mortality and should be employed more widely for MC.

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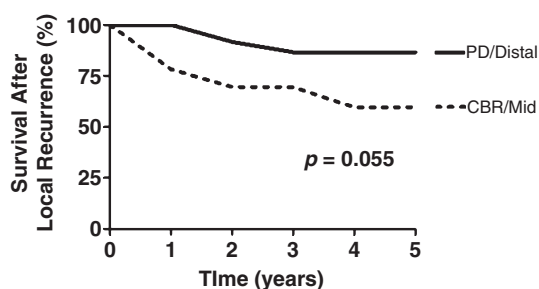
#### Getting to pure notes transvaginal cholecystectomy, without laparoscopic or needleoscopic-assistance

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**Introduction:** Initial excitement for Natural Orifice Transluminal Endoscopic Surgery (NOTES) has been partly tempered by the reality that a NOTES procedure without laparoscopic or needleoscopic-assistance has not been performed by most groups. After safely performing laparoscopically-assisted transvaginal cholecystectomy in an IACUC-approved porcine model, we embarked on an IRB-approved protocol to ultimately perform a pure NOTES cholecystectomy.

**Materials and methods:** We describe our experience with performing a true NOTES transvaginal cholecystectomy after safely accomplishing three laparoscopically-assisted or hybrid procedures in humans. To overcome the retracting limitations of currently available endoscopes, we used a 5 mm curved or articulating retractor that was placed into the abdomen via a separate colpotomy in the second and third patient. In a fourth patient, pneumoperitoneum to 15 torr was obtained via a transvaginal trocar placed through a colpotomy made under direct vision and endoscopically-placed clips were used for both the cystic duct and artery, thus, obviating the need for any transabdominally placed instruments or needles.

**Results:** This patient was the first patient to undergo a completely NOTES cholecystectomy at our institution and to our knowledge in the U.S. She was discharged on the day of surgery and has not suffered any complication after 1 month of follow-up.



No. at Risk						
CBR/Mid	27	27	15	8	7	6
PD/Distal	37	28	20	13	10	6

Figure 1.

**Conclusion:** NOTES Transvaginal Cholecystectomy without aid of laparoscopic or needleoscopic instruments is feasible in humans. Additional experience with this technique will be required before comparative studies to standard laparoscopy and hybrid techniques are appropriate.

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### **Cirrhosis is not a contraindication to laparoscopic cholecystectomy: results and practical recommendations**

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**Background:** Gallstones occur more frequently in patients with cirrhosis compared to the general population. Open cholecystectomy in cirrhotic patients is associated with a high morbidity and mortality. Several studies have suggested that laparoscopic cholecystectomy (LC) in cirrhotic patients is feasible and safe. We present a large series of cirrhotic patients who underwent LC and provide practical recommendations for the practicing surgeon based on our experience with these cases.

**Methods:** A retrospective review was performed of all cirrhotic patients undergoing LC since 1999. Seventy-one patients with gallbladder disease and Child's A/B cirrhosis underwent LC. Pre-operative characteristics, intra-operative findings, and post-operative outcomes were analyzed.

**Results:** Median age was 54 years (range 23–87) with 37 males. The majority of patients were Child's A cirrhotics (93%). Pre-operative imaging (CT/MRI) was obtained to evaluate abdominal wall varices for port placement and to rule out concurrent hepatoma. The primary indication for LC was symptomatic or chronic cholelithiasis (69%). Median operative time was 120 min (range 45–300 min) with a median blood loss of 50 mL. pRBC transfusion was required in 1.4% of patients. TissueLink cautery or Argon beam coagulation was used in all patients to ensure hemostasis. An additional fifth port was used in 11.3% of patients to improve retraction and exposure. Intra-peritoneal drains were placed in 34% of patients. Conversion to an open cholecystectomy was required in 4 patients (5.6%). Post-operatively, there was no 30-day mortality. Complications occurred infrequently and included: 2 urinary tract infections, 1 pneumonia, and 1 wound infection. No patients developed acute liver failure. ICU admission was required in 5.6% of patients, and median length of stay was 1 day (range 1–13).

**Conclusion:** With proper planning, LC for gallbladder disease can be performed safely with minimal morbidity in patients with Child's A/B cirrhosis. Pre-operative imaging, selective drain placement, and use of an additional port or coagulation devices represent important elements in the laparoscopic management of biliary disease for Child's A/B cirrhotics.

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### **The changing presentation of choledochal cysts in adults**

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**Background:** Choledochal cysts are uncommon biliary lesions associated with an increased lifetime risk of cholangiocarcinoma. Recent large series from North America have described the presentation and management of this disease in adults and children over more than a 30 year period. Due to the evolution of imaging and laparoscopic surgery, we sought to describe our last 3 years experience with the presentation and management of choledochal cysts in adults.

**Methods:** A retrospective review of a prospectively established database of adults who were managed for primary choledochal cyst disease was performed. We analyzed patient demographics, presentation, type of cyst, pathology, operation, and complications. The Todani modification of the Alonso-Lej classification system for choledochal cysts was used.

**Results:** Between 8/2005 and 8/2008, 14 adults were managed for primary choledochal cyst disease. The average age was 41 years (range 17–86) and 79% were female. All three men presented with biliary sepsis, while women presented with pancreatitis (2), abdominal pain (3), or painless jaundice (1). Three of the women had the cyst found during laparoscopic cholecystectomy at an outside institution. Two women had an incidental finding after a CT scan for an unrelated issue. 58% of the patients had an ERCP, 29% had MRCP only, and no patients were diagnosed or further evaluated by ultrasound. Nine patients had Todani type I cysts and had excision with a Roux-en-Y hepaticojejunostomy. One patient had a type III cyst and underwent a Whipple procedure; one patient had a type IV cyst and one had a type V cyst and had hepatic lobectomies with or without Roux-en-Y reconstruction. The one patient with a type II cyst did not have it removed because of decompensated liver cirrhosis, and was found after laparoscopic cholecystectomy to have HCC. The length of stay for those who had the cyst removed was 7.8 days (range 5–11). There were no operative or post-operative complications. All pathology has revealed benign disease, and all patients have had an uneventful follow-up.

**Conclusions:** Over the last 3 years 36% of our patients with choledochal cysts presented after incidental finding, either during a laparoscopic operation or after a CT scan for an unrelated problem. These patients did not have the classic findings of abdominal pain, jaundice, and a palpable mass. Increasing utilization of laparoscopy for gallbladder disease, CT scan for abdominal complaints, and less use of ultrasound has lead to a change in the pattern of presentation and ultimate treatment of choledochal cysts.

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**Gallbladder cancer – still a bad disease**

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**Background:** The aim of this retrospective study is to review our institutional experience with gallbladder cancer (GC) in the modern era of sophisticated imaging. Specifically, the issue of resectability and ability to achieve R0 resection in this condition was examined.

**Methods:** Patients diagnosed with gallbladder cancer (GC) from January 2005 to May 2008 were identified by diagnosis code in the hospital database and a case review was performed. Presentation, operative data, and pathology results were of particular interest in this review.

**Results:** Twenty-two cases were reviewed, 16 female and 6 male, with a mean age of 61 years (range 29–87). The diagnosis of GC was established pre-operatively in 1 case (palliative procedure), intra-operatively in 11, incidentally following pathologic examination of cholecystectomy (LC) specimens in 9, and liver explant in 1 (OTL). 9/22 (41%) cases were resected with radical resection (en-bloc cholecystectomy, bile duct resection, segment 4b/5 liver resection, and lymphadenectomy) (7 LC, 2 jaundiced). Palliative surgery was performed in 1 (known metastatic), and 1 was removed incidentally (OTL). The 11 unresectable cases were deemed such due to local invasion in 8 (36%) (liver, duodenum, local LN), metastatic disease in 2 (9%) (ascites, widespread peritoneal disease), and both in 1 (5%). Of those treated with radical resections, 7 achieved negative margins (R0 resection, 78 %), and 2 were margin positive (22%). Of note, all of the 9 patients with incidental GC found after LC had residual cancer following exploration, and 5/9 (56%) were resected with negative margins.

**Conclusions:** Even in the modern era of excellent imaging, 32% (R0) of patients with GC are found to be resectable in this cohort of patients. In this study, all patients that have GC diagnosed at LC had residual disease (9/9). However they can be deemed R0 with aggressive surgery.

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**The incidence of gallbladder carcinoma has not increased in the laparoscopic cholecystectomy era**

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**Background:** An incidental carcinoma is said to be identified in approximately 1–2% of cholecystectomy specimens. With the advent of the laparoscopic approach to the gallbladder, many have reported an increase in the annual number of resections performed and hence it may be expected that the incidence of gallbladder carcinoma will have increased.

**Aims:** To examine longitudinal trends in the incidence of gallbladder carcinoma and dysplasia.

**Patients and methods:** All patients undergoing cholecystectomy in the period 1999–2007 were identified from a prospectively maintained histopathology database. Data collected included: gender, age, and presence of carcinoma or dysplasia in the specimen on histopathological analysis.

**Results:** During the period of the study 4000 cholecystectomies were performed. The cohort consisted of 8 males and 21 females with a mean age of 63.6 years. There was a year-on-year increase in the annual cholecystectomy rate from 214 to 269 cases per annum. A carcinoma was identified as an incidental finding in 21 (0.5%) patients, the histological subtypes consisting of: adenocarcinoma ( $n = 16$ ); carcinosarcoma ( $n = 1$ ); small cell carcinoma ( $n = 1$ ); anaplastic carcinoma ( $n = 1$ ); papillary carcinoma ( $n = 1$ ); metastatic ( $n = 1$ ). Furthermore, dysplasia was seen in 8 (0.2%) cases and was classified as mild ( $n = 7$ ) or moderate ( $n = 1$ ).

**Conclusions:** During the course of the study there has been a 26% increase in the number of cholecystectomies performed, however there has been no increase in the incidence of gallbladder carcinoma or dysplasia during this period. Indeed, the incidence of incidental carcinoma may be significantly less than previously believed in the UK.

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**The development of a novel endoscopic bipolar radiofrequency catheter for the palliation of malignant biliary obstruction**

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**Background:** EndoHPB is an endoscopic bipolar radiofrequency (RF) catheter designed to ablate malignant tumors within the biliary tree. It is anticipated that EndoHPB will have a role in conjunction with standard stent deployment in the palliation of malignant biliary obstruction and if effective, may compete with photodynamic therapy in the management of unresectable cholangiocarcinoma. The aim of these *in vivo* experiments was to determine the ability of the device to heat and coagulate tissue in the common bile duct (CBD), to determine the power requirement and time parameter to achieve coagulation, and to assess its ease of operation via a side endoscope.

**Methods:** Three female pigs were anaesthetised and prepared. A Pentax side viewing endoscope (ED3440T) was used and the opening of the CBD identified. The duct was opened and enlarged using cutting forceps introduced via the biopsy channel of the endoscope. A 0.035" × 260 cm Hydra Jagwire (Boston Scientific) was inserted into the duct and the EndoHPB catheter was inserted over this guidewire into the CBD. The device was connected to the power source (RITA 1500× RF generator) and varying wattage and time parameters of EndoHPB activation were applied at different locations along the CBD within the same animal. On completion of the experiment the pig was killed, the abdomen opened and the CBD resected.

**Results:** The EndoHPB catheter is compatible with the Pentax ED3440T side viewing endoscope which has a 3.2 mm biopsy channel. Given the short length of the pig CBD, it was only possible to test the catheter's ability to coagulate tissue without compromising the lumen at two levels of the duct. The power setting of 5 W for 2 min appeared to be ideal, with higher power settings above 10 watts producing heating outside the CBD with complete coagulation of the CBD.

**Conclusion:** EndoHPB is compatible with any endoscope with 3.2 mm biopsy channel and a working length of 1500 mm. In the porcine model, the ideal bipolar RF power setting appears to be 5 W for 2 min. Based on this early data, a pilot clinical study to assess the safety and effectiveness of EndoHPB in the palliation of malignant biliary obstruction is to be undertaken, data of which should be available at the beginning of 2009.

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### **Surgical treatment of congenital choledocal cyst in adults: an 11-year single surgeon experience**

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**Purpose:** A single surgeon experience over an 11-year period is reviewed with adult patients treated surgically for congenital choledocal cysts with emphasis on long-term outcome.

**Method:** From 1996 to 2007 adult congenital choledocal cysts were completely excised in 7 patients. There were 6 (85.7%) women and 1 (14.3%) man with mean age of  $46.4 \pm 18.3$  years (range 18–71 years). Pain was the most common symptom in all patients and was associated with pancreatitis in 2 (28.6%) and cholangitis in 3 (42.9%) others. All patients were diagnosed before operation and none had prior surgery for this condition or evidence of cancer at the time of diagnosis. According to Todoni there were 6 (85.7%) with type IA and 1 (14.3%) with type II cysts. One patient (type IA) had a second accessory cystic duct originating from right hepatic duct that entered the dome of the gallbladder fundus. Another (type II) had a 12 cm sacular dilatation emanating from the most distal portion of the common bile duct just above the confluence of the pancreatic duct well within the pancreas parenchyma and associated pancreas divisum. Complete cystectomy was performed in all patients and bilio-enteric bypass was created with 6-0 polypropylene sutures in an interrupted fashion using the Hepp-Couinaud technique in 6 (85.7%) patients. The other (type II) had complete intra-pancreatic enucleation of a large sacular cyst without biliary anastomosis. No malignancies were detected on final pathology and there were no post-operative complications or deaths. Long-term results were evaluated by serial serum liver function tests and sonogram every 3 months for 2 years then every 6 months thereafter if no biliary abnormalities existed. Mean follow-up was  $53.9 \pm 33.9$  months (12.6–107.5 months) and no patient had evidence of stricture or cancer during this period. Two (28.6%) patients were considered to have fair results based upon recurrent symptoms: one with fever from episodic

ascending cholangitis (type IA) and another with pain from pancreatitis (type II). All symptoms resolved by 4 and 10 months respectively after surgery. Results were excellent in the other 5 (71.4%) patients (type IA) who remained asymptomatic during the whole follow-up period.

**Conclusion:** Choledocal cysts in adult patients are exceedingly rare and series representing single surgeon experience is limited. Once diagnosed cysts must be completely excised due to their malignant potential and variations of biliary tract anatomy might alter operative techniques. Management of post-operative symptoms can be treated medically as no patient required operative re-intervention. Type IA lesions seem to have the best overall long-term symptom-free prognosis.

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### **Management of pseudoaneurysms after hepatobiliary surgery**

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**Background:** Life threatening post-surgical hemorrhage after hepatobiliary surgery can be caused by a ruptured pseudoaneurysm. Although a rare complication with a high mortality rate, there is no standard of care for the optimal management of post-surgical pseudoaneurysms.

**Purpose:** The novel approach of stent placement alone or in combination with transcatheter arterial embolization (TAE) has been minimally investigated. In this study we review management and outcome of patients who have suffered a gastrointestinal hemorrhage after hepatobiliary surgery to compare stent placement and/or TAE and surgery.

**Methods:** This is a retrospective chart review of 8 patients who suffered a gastrointestinal hemorrhage out of a total of 125 patients who underwent hepatobiliary surgery at the University of Utah Huntsman Cancer Hospital between 2002 and 2008. Data was retrieved from patient electronic charts in collaboration with the National Surgical Quality Improvement Program (NSQIP).

**Summary:** Six out of the 8 patients underwent a pancreaticoduodenectomy. One patient underwent a duodenal sparing pancreatic head resection and one patient underwent a distal pancreatectomy and splenectomy. All 8 patients suffered a gastrointestinal hemorrhage within 25 days of their initial surgery involving the gastroduodenal artery (GDA), the superior mesenteric artery (SMA), or the left gastric artery. To control their hemorrhage, 3 patients underwent surgical exploration, 4 patients underwent TAE of the bleeding artery and/or stent placement across the bleeding vessel, and 1 patient underwent both TAE and stent placement followed by surgery. Surgical exploration controlled hemorrhage in all three cases. Stenting of the common and proper hepatic arteries alone or in combination with TAE of the GDA controlled hemorrhage without further bleeding complications in two patients. While TAE and stenting of the SMA in one



patient failed to control bleeding from multiple pseudoaneurysms and the patient ultimately required surgical intervention. TAE alone of the GDA and left gastric artery controlled bleeding in the remaining 2 cases. No patient developed a delayed liver abscess or organ ischemia after stenting or TAE. Of the 8 patients, 7 survived and for one patient, support was withdrawn per the request of family.

**Conclusions:** There are no established criteria which guide treatment of patients with a bleeding pseudoaneurysm. We found no survival benefit of interventional radiology techniques over surgical management. Stent placement alone or in combination with TAE is a viable option to control pseudoaneurysm related hemorrhage after hepatobiliary surgery and less invasive than repeat surgical exploration.

# Abstracts 101 to 109

## Oral Posters – Transplant I

Friday, March 13, 2009 4:15–5:30 PM

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### Meta-analysis of ischemic pre-conditioning in liver transplantation

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**Background:** Hepatic ischemic pre-conditioning (IPC) during organ procurement is one of the strategies used to prevent ischemia-reperfusion injury (IRI). IPC has been shown to protect grafts against ischemic injury in animal models. The value of this strategy on humans is still controversial.

**Methods:** A meta-analysis of six RCTs was performed to assess the efficacy of IP in cadaveric donor hepatectomies. Included studies were identified by a systematic literature search of Medline, EMBASE, PUBMED and Cochrane databases from 1966 until May 2008. Six RCTs comparing IPC followed by liver procurement mL liver procurement alone satisfied inclusion criteria ( $n = 338$  patients). Primary outcomes were: mortality, initial poor function (IPF), primary graft non-function (PGNF) and re-transplantation. Secondary outcomes were biochemical markers: AST, ALT, total bilirubin and INR.

**Results:** Peri-operative mortality, IPF, PGNF, rate of re-transplantation and liver function tests were similar in the two groups. Among five studies ( $n = 285$  patients) the OR for mortality was 0.19 (CI 0.02–1.71). Three studies ( $n = 163$  patients) showed no difference in IPF (OR 0.69, CI 0.25–1.92) and among 6 studies ( $n = 338$  patients) the OR of PGNF was 0.50 (CI 0.15–1.69). The rate of IPF and PGNF were 8.4% (7/83) and 1.8% (3/167) in IPC compared to 12.5 % (10/80) and 4.1 % (7/171) in controls. Re-transplantation rate was 3% (5/167) in the ischemic pre-conditioning group and 3.5% (6/171) in the control group with OR of 0.98 (CI 0.28–2.89) (six studies,  $n = 338$  patients).

**Conclusions:** The results of this meta-analysis from six RCTs indicate that the potential benefits of IPC in cadaveric liver transplantation do not translate in measurable improved peri-operative clinical outcomes.

**Table 1.** Results.

Outcome	Odds Ratio (95% confidence interval)
Peri-operative Mortality	0.19 (0.02–1.71)
IPF	0.69 (0.25–1.92)
PGNF	0.50 (0.15–1.69)
Re-transplantation	0.98 (0.28–2.89)

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### Early outcomes with laparoscopic-assisted living donor hepatectomy

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Living donor liver transplantation has become an increasingly common therapeutic modality. We have performed 37 living donor liver transplants between 1999 and 2008. While open live donor hepatectomy is well described and can be performed safely, donor risk and complications continue to serve as a barrier to its routine use.

**Aims:** We describe our experience with laparoscopic-assisted donor hepatectomy and its potential as a safe alternative in living donor liver transplantation.

**Methods and results:** We performed a retrospective review of our last 12 successive living donor liver transplants between 2006 and 2008. Six donors underwent standard open liver resection (OLR), and six underwent laparoscopic-assisted liver resection (LALR). We compared donor morbidity, length of surgery, hospital days, blood transfusions, and need for continuous intravenous analgesics post-operatively. We then evaluated early graft function and recipient morbidity/mortality between the open and laparoscopic groups. Laparoscopic-assisted liver resection was successfully performed in all six cases. No specific complication related to laparoscopy was observed. Length of surgery in LALR, however, was longer compared to OLR ( $5.8 \pm 0.76$  vs.  $4.2 \pm 0.75$  h,  $P < 0.05$ ). Blood loss, length of hospital stay, and analgesic use was not significantly different between groups. One liver graft in the OLR group failed post-operatively and required emergent return to the operating room for revision of the portal vein and hepatic artery anastomosis, while another developed biliary stricture requiring ERCP and stent placement. Total bilirubin was slightly more elevated on post-operative day 2 in grafts from OLR compared to those from LALR ( $6.2 \pm 2.1$  vs.  $2.8 \pm 1.1$ ,  $P < 0.05$ ). No significant complications were observed in LALR recipients.

**Conclusions:** Given the early outcomes of laparoscopic-assisted living donor hepatectomy, our experience demonstrates that it is a safe procedure with minimal morbidity compared to standard open liver resections and therefore, can be recommended as a new procedure in living donor liver transplantation.

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### Successful use of super elderly grafts in OLT

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Increasing demand for LTX has not been paralleled by supply, and the extension of donor criteria became more than necessary to prevent the mortality of patients being on the waiting list.

**Aim:** The purpose of our study is to retrospectively examine the outcomes of patients who were offered a graft from donors older than 75 years of age.

**Materials and methods:** We analyzed retrospectively the clinical data of the patients who received an elderly graft, including indication for transplantation, MELD score, cold and warm ischemic times, liver function during the first post-operatively, and survival. During the period January 2006 to June 2008, and among 297 consecutive orthotopic liver transplantations that performed for adults, 23 patients received a graft from a donor who was over the age of 75.

**Results:** Twelve males and 11 females from 50 to 71 years of age were offered a graft from donors whose age ranged between 75 and 86 years (average 78.8 year). Indications for transplantation included: HCC of various underlying cause (11 cases), alcoholic cirrhosis (4 cases), cholangiocarcinoma (2 cases), autoimmune hepatitis (2 cases), steatohepatitis (1 case), cryptogenic cirrhosis (1 case), and antitrypsin deficiency (1 case). MELD score of the recipient ranged between 6 and 35. The cold ischemic time in all cases was kept below 9 h, with half of them being under 6 h. The average warm ischemic time was 44 min. Since imported grafts were highly used, donor biopsy was useful and showed low incidence of steatosis of the liver. The peak post-operative AST value averaged 1393.48 U/L, and the average AST, bilirubin and INR values at post-operative day seven were 52.43 U/L, 3.61 mg/dL, and 1.32 respectively. Two deaths occurred on day 10 and 77 post-operatively. All the other 21 patients are alive. The 1 month and 1 year graft and patient survival rates are 95.6% and 87.5% respectively.

**Conclusions:** Careful selection of elderly grafts for liver transplantation in patients suffering from hepatic failure, and by keeping the cold and warm ischemic times as low as possible, can produce similar results to the transplantation of patients using the standard criteria, especially in non-hepatitis C induced cirrhotic patients.

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### Biliary reconstruction and complications after living-donor liver transplantation

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**Background:** The technique of biliary reconstruction is remains controversial in LDLT. The objective of this review was to assess the incidence of biliary complications after LDLT.

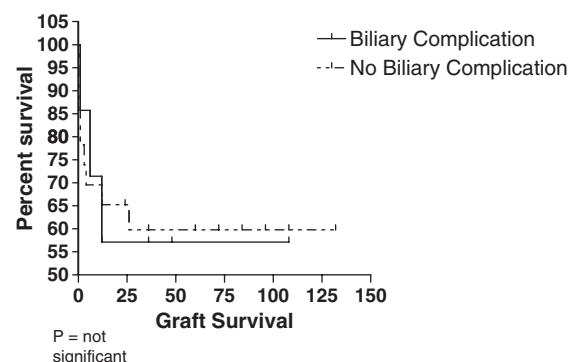
**Methods:** Thirty patients underwent LDLT between 1997 and 2007. The type of allograft was the right lobe in 14, left lobe in 4, and left lateral sector in 12 patients. There were 18 adults and 12 pediatric recipients. The mean follow-up was 48 months (range 6–120 months).

**Results:** Biliary reconstruction was achieved with Roux-en-Y choledochojejunostomy in 17 patients (Group I), and choledochocholedochostomy in 13 patients (Group II). A external biliary stent was placed in all patients (except one) in Group I and reconstruction over a T-tube was done in 6/13 of patients in Group II. Twenty-five (83.3%) patients had one biliary anastomosis and the remaining 5 (16.7%) had multiple anastomoses (one in Group I and four in Group II). The overall incidence of biliary complications was 30%; 29.4% in Group I and 30.8% in Group II. The incidence of biliary leakage was 23.5% for Roux-en-Y, and 15.4% for Group II ( $P > 0.05$ ). However, the incidence of biliary stricture was significantly higher in Group II (15.4%) compared to Group I (5.9%) ( $P < 0.01$ ). In Group II, biliary complications occurred equally in patients with and without T-tube stenting. Overall, 93.3% of the strictures were managed with endoscopic treatment alone. One patient in each group needed revision of the biliary anastomosis. Biliary complications did not affect the graft and patient survival.

**Table 1.** Comparison between two biliary reconstruction methods.

Biliary Anastomosis	Biliary stent/ t-Tube	Biliary complications	Biliary leak	Biliary stricture	Need anastomotic revision
Roux-en-Y choledochojejunostomy (n = 17)	94.1% (n = 16)	29.4% (n = 5)	23.5% (n = 4)	5.9% (n = 1)	5.9% (n = 1)
duct-to-duct choledochocholedochostomy (n = 13)	46.2% (n = 7)	30.8% (n = 4)	15.4% (n = 2)	15.4%* (n = 2)	7.7% (n = 1)

\* $P < 0.01$ .



**Figure 1.** Survival of data: survival populations.

**Conclusions:** Although there was a higher rate of biliary stricture in the choledochocholedochostomy group, we feel that because of physiologic bilioenteric continuity, comparable incidence of leakage, and easy endoscopic access, duct-to-duct reconstruction represents a feasible technique in LDLT. The endoscopic approach has been shown to be a first-line therapy for the management of biliary complications after LDLT. Placement of T-tubes did not appear to be beneficial.

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### Incidence and impact of biliary complications following pediatric living-donor liver transplantation (LDLT): analysis of 44 consecutive cases with 5-year follow-up

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**Purpose:** To characterize biliary complications in pediatric patients following LDLT and observe potential effects on patient and graft survival.

**Methods:** A single surgical team performed forty-four consecutive pediatric living-donor liver transplants over a 6-year period. Those patients were followed for occurrence, diagnosis and treatment of biliary complications and for patient and graft survival.

**Results:** Pediatric patients received mostly left lateral segment grafts (89%). Biliary reconstruction to a single duct was performed in 38 of 44 patients (86%). The overall incidence of biliary complications per ductal anastomosis was 68%. Fourteen cases were complicated by persistent biliary leaks (28% per ductal anastomosis). These were most commonly cut-surface leaks (64%) and were typically managed with early reoperation (79%). Eighteen cases were complicated by strictures, which were managed successfully with primary percutaneous

or endoscopic balloon dilation (PTC or ERCP) in 67% of occurrences requiring a mean of  $2.2 \pm 1.1$  dilations for resolution. One, 3 and 5-year graft and patient survivals were 88, 85, and 83% and 88, 88, and 88%. There was no significant difference in either patient or graft survival for those with or without biliary complications ( $P$ -values 0.91 and 0.80 respectively) (Figures 1 and 2).

**Conclusions:** Pediatric living-donor liver transplants have a significant incidence of biliary complications. PTC has proved to be effective as the first line treatment for biliary stricture. Overall, if identified and treated promptly, biliary complications do not portend any difference in prognosis with respect to graft or patient survival.

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### Steatotic liver graft use does not affect long-term outcomes, but may require increased resources following liver transplantation

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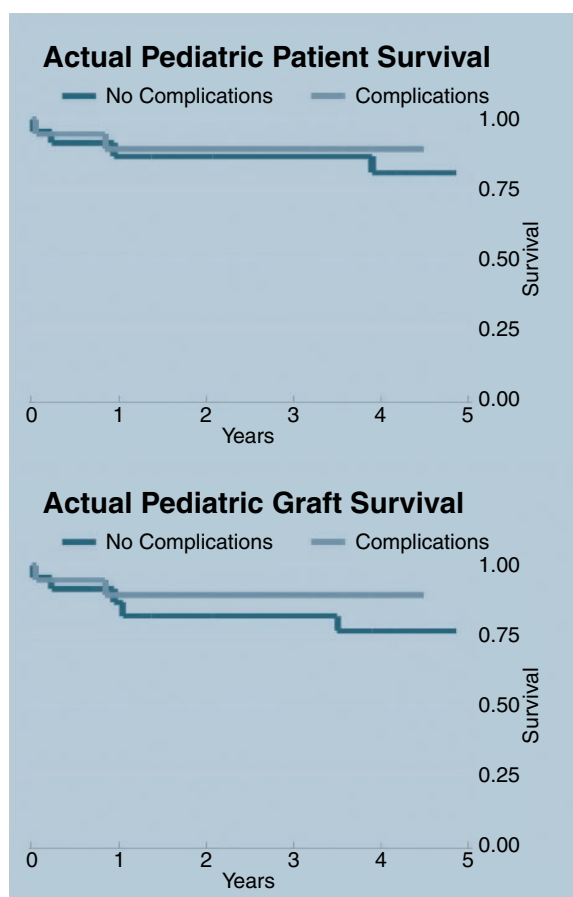
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With a continuing organ shortage and an ever increasing recipient population, many centers are using marginal grafts to avoid deaths on the waiting list. Hepatic steatosis is encountered in  $> 30\%$  of potential donors, and appears to be an increasing problem. Livers with less than 20% steatosis are routinely used, however livers with  $> 30\%$  macrovesicular steatosis are often discarded, for fear of primary non-function and increased complication rates. The aim of this study was to determine if the use of moderate to severe steatotic livers would adversely affect short- and long-term outcome in liver transplantation.

**Methods:** From Jan 2002–Dec 2007, 483 liver transplants were performed at our institution. Pre-transplant donor biopsies were identified in 65 patients and classified into 0% ( $n = 29$ ),  $< 30\%$  ( $n = 26$ ) or  $\geq 30\%$  ( $n = 10$ ) macrovesicular steatosis. Patient and graft survival, post-operative complication rates, transaminase peaks and pro-thrombin times were assessed in all groups.

**Results:** One, and 3-year patient survival was similar in all three groups, (91% and 84% respectively,  $P = 0.28$ ). Similarly there was no significant difference in 1 and 3-year graft survival (91% and 82% respectively,  $P = 0.24$ ) between groups. Significantly increased AST, ALT, and INR were encountered in the  $> 30\%$  steatosis group. No cases of primary non-function were seen however steatotic graft use was associated with increased reoperation for hemoperitoneum and longer hospital stays ( $P = 0.008$ ).

**Conclusion:** In our experience, use of liver grafts with  $> 30\%$  macrosteatosis was not associated with increased rates of primary non-function or worsened mid- and long-term outcomes. However use of such grafts does appear to be associated with increased resource utilization in the peri-operative period.



Figures 1 and 2.

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### Biliary complications in 100 liver transplants. An old problem in a new era

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**Aim:** To review the incidence, clinical outcomes and management of biliary complications in liver transplantation.

**Background:** Biliary complications are a major source of morbidity after liver transplantation. In the current era of the MELD system and use of extended criteria donors (ECD) few have addressed the presentation, risk factors and management of biliary complications, specially in cases of patients that received ECD in which ischemic cholangiopathy is becoming a common problem in centers using donation after cardiac death (DCD).

**Methods:** We retrospectively reviewed the charts and electronic database of 100 patients transplanted from August 2006 to December 2007. Pre-transplant data included demographics, etiology of liver disease, laboratory, and MELD score. Donor factors (use of Extended Criteria Donors and Ischemia Time) were evaluated in the group. Post-transplant variables including type of complications, time of presentation, treatment and outcomes were studied.

**Results:** A Total of 100 adults and pediatric patients were transplanted during the study period. 59 patients were male, mean age of 55 years of age (4 month–76 yo). HCV was the most common diagnosis (48%). Average MELD in the study group was 23.3. 35% of the donors were ECD (6 DCD). Three patients received living donor liver transplants. Eighteen patients had biliary complications. Two patients had anastomotic leak, 11 had anastomotic strictures, 4 had ischemic cholangiopathy (IC) and one patient had and early leak (duct of Luschka) and later developed a stricture. All biliary leaks presented within the first 30 days of transplant and were managed with ERCP stenting. All the extrahepatic strictures (12%) were managed with ERCP interventions. Of the 4 patients with IC, 3 received ECD (2 DCD, 1 HCV + Donor) and one patient had partial thrombosis of her arterial inflow. The 2 patients that received DCD were retransplanted within a year. One patient has been relisted for transplant and one patient died of biliary sepsis.

**Conclusions:** The management of traditional biliary complications (early leaks and late strictures) has changed with time. Currently a small number of patients require surgical intervention. However in this era of ECD (viz. DCD), we are witnessing a subset of intrahepatic ischemic complications, that lead to graft loss and require retransplantation.

(DRI). This however fails to take into account factors related to recipient characteristics and peri-operative events. We therefore studied the performance of the Schindl scoring system, to predict graft survival after OLTx. This score has been validated after liver resection to allow for early prediction of subsequent mortality.

**Method:** All OLTx done at the McGill University Health Center from 92 to 07 were included (600 patients). Multiorgan transplants, re-do OLTx, early failures due to vascular thrombosis, and fulminant liver failure requiring pre-transplant endotracheal intubation (Canadian list status 4) were excluded, leaving 451 patients for analysis.

Retrospectively, we calculated the post-transplant liver function score (PTLF) based on the most elevated results in the first 7 post-operative days, (Table 1). Patients were labeled as normal if total points were < 4 and as having liver dysfunction if total points were ≥ 4. Graft survival analysis using log-rank test was used to test relative variables. Graft loss was defined as the need for re-transplant or patients' death.

**Results:** Thirty-two percent of patients were male with mean age 54 years. 34% of patients had Hepatitis C, 24% had Hepatocellular carcinoma, and 46% had either diagnosis. None of these variables alone was able to significantly predict graft survival. The average MELD was 20.9, and mean DRI was 1.51. Mean blood loss was 2300 mL, and mean cold ischemia time was 9.8 hours. DRI was the only pre-operative significant predictor of graft survival ( $P = 0.034$ ). The median PTLF score was 4 with 42% patients showing a score < 4 (normal), and 58% scoring ≥ 4 (dysfunction). The 1 and 3-year graft survival were 85% and 74% respectively for the normal group, and 65% and 58% respectively for the dysfunction group. The difference was significant ( $P < 0.001$ ). Survival analysis showed that PTLF alone was a significant predictor of graft survival. On final survival modeling with both pre-operative and post-operative co-variables, only PTLF remained significant ( $P = 0.018$ ).

**Table 1.** Point system for liver function score calculations.

Total serum bilirubin	< 20	21–60	> 60
INR	< 1.8	1.8–2.3	> 2.3
Serum lactate	< 1.5	1.6–3.5	> 3.5
Given point	0	1	2

**Conclusion:** The PTLF scoring system is an easy and clinically practical tool to help predict long-term graft survival based on early post-operative events. It may allow to better tailor aggressive treatment intervention in selected patient groups.

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### Post-operative liver transplant function score can predict long-term outcomes

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**Introduction:** The best predictor of graft survival after liver transplantation (OLTx) is the Donor Risk Index

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**Usefulness of 3D-fusion images of MDCT 3D-cholangiography and 3D-angiography for operative designing of carcinoma in the region of hepatic hilum**

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**Background:** Hepatic hilum has a complex anatomical relation with biliary system, portal system, and hepatic arteries. To operate the malignancies of hepatic hilum, precise evaluation of tumor extension and anatomy are required for operative designing. We evaluated the efficacy of 3D-fusion images of MDCT 3D-cholangiography and 3D-angiography for operative designing of the malignancies of hepatic hilum.

**Methods:** Twenty-two patients of hilar cholangiocarcinoma, cholangiocellular carcinoma and gall bladder carcinoma invaded to hepatic hilum were constructed 3D-fusion images of 3D-cholangiography and 3D-angiography using MDCT. Seventeen patients of 22 patients who underwent the en-block resection with hepatic resection were evaluated the accordance and accuracy of bile duct extension of tumor with direct cholangiography

and 3D-cholangiography, and of vascular invasions with MDCT and 3D-angiography. Anatomical relations with 3D-fusion image were also examined.

**Results:** Fifteen patients of 17 patients (88.2%) could obtain the 3D-cholangiography by direct cholangiography ( $n = 14$ ) or DIC-CT ( $n = 1$ ). Two patients performed EST failed to obtain evaluative 3D-cholangiography. Fourteen patients could be compared the biliary images with direct cholangiography and 3D-cholangiography. All patients (100%) were obtained the identical image of tumor extension and 16 in 17 patients (94.1%) were achieved the negative margin of hepatic bile duct. The expected numbers of bile duct cutting orifices were accordant with 13 in 15 patients (86.7%). The sensitivity and specificity of vascular invasions of 2D-MDCT were 40% and 100% in portal vein invasion, 66.7% and 100% in arterial invasion, and of 3D-angiography were 50% and 100% in portal vein invasion and 100% and 92.9% in arterial invasion. 3D-fusion image expressed precise anatomical relations and variations of biliary system, portal system, and hepatic arteries and was helpful for pre-operative designing.

**Conclusion:** MDCT 3D-cholangiography and 3D-angiography has high accuracy to evaluate tumor extension to bile ducts and surrounding vessels. Moreover, 3D-fusion images provide useful information of anatomical relations and variations for operative designing of carcinoma in the region of hepatic hilum.

Abstracts 110 to 117  
Oral Posters – Pancreas I  
Friday, March 13, 2009 4:15–5:30 PM

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**Pancreatectomy with venous resection and reconstruction: a single institution 15-year experience**

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**Purpose:** We conducted a retrospective review to assess outcomes and survival of patients who underwent pancreatectomy with concomitant venous resection at our institution.

**Methods:** We reviewed all patients who underwent pancreatectomy requiring vascular resection for any pathology from 1994 to 2008. Patients who required arterial resection were excluded. We noted operation, venous reconstruction, length of stay, morbidity, and mortality. For patients with adenocarcinoma, oncologic survival was compared to patients who underwent pancreatectomy without venous resection and to patients who were explored but not resected.

**Results:** A total of one hundred and twenty three patients required vascular resection during pancreatectomy. Thirteen of these patients required resection of the hepatic and/or superior mesenteric arteries and were excluded. One hundred and ten patients required superior mesentericoportal venous resection for varying pathology. Ninety underwent pancreaticoduodenectomy, 11 total pancreatectomy, 5 distal pancreatectomy, and 4 subtotal pancreatectomy. Resections of the superior mesentericoportal veins included tangential resection with primary repair ( $n = 28$ ), tangential resection with autologous vein patch ( $n = 21$ ), segmental resection with primary anastomosis ( $n = 19$ ), and segmental resection with autologous interposition graft ( $n = 40$ ). Median length of stay for all venous resection patients was 11 days (95% CI: 1, 58). Peri-operative morbidity and mortality for all venous resection patients were 31.8% and 4.5%, respectively. For patients with adenocarcinoma, median survival was 16.6 months (95% CI: 12.3, 23.7) in those requiring venous resection and 20.1 months (95% CI: 14.1, 24.3) in those not requiring venous resection ( $P$ -value = not significant). Median survival was 6.5 months (95% CI: 12.3, 23.7) in patients explored but not resected due to vascular invasion, which was significantly shorter than patients requiring venous resection ( $P$ -value < 0.0001).

**Conclusion:** Median survival of patients with adenocarcinoma who undergo pancreatectomy with venous resection is comparable to those who undergo pancreatectomy without venous resection and is superior to those who are explored but not resected. Pancreatectomy with venous resection can be performed with acceptable morbidity and mortality in select patients.

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**Total pancreatectomy: a national study**

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**Background:** Total Pancreatectomy (TP) is performed for various indications including malignant and non-malignant pancreatic disease. Historically, morbidity and mortality associated with TP has been high. No nationwide data on TP are currently available. The objective of this study was to evaluate in-patient mortality, predictors of mortality, and review national trends for TP.

**Methods:** The Nationwide Inpatient Sample (NIS) was queried to identify all TPs performed during 1998–2006. Univariate analyses and multivariable logistic regression were performed adjusting for diagnosis, gender, race, payer, hospital teaching status, and comorbidities to evaluate in-hospital mortality (SASv9.1, Cary, NC, USA).

**Results:** By weighted national estimate, 3241 patient discharges occurred for TP during 1998–2006. 50.5% of patients were men; mean age was 61.6 years [SEM = 0.19]. 49.6% of TPs were for malignant pancreatic disease (defined as ICD-9 codes for primary and secondary malignancies, including carcinoma *in situ* and neoplasms of uncertain behavior). 35.2% of TPs were for non-malignant disease (defined as pancreatic cysts, pseudocysts, benign neoplasms, and pancreatitis), and 15.2% for other/unknown indications,  $P < 0.0001$ . Mean length of stay (LOS) for all TP was 15.6d; (18.0 d for non-malignant indications and 14.4 d, malignant). The overall number of TPs varied over time with 283 performed in 1998 and 432 performed in 2006,  $P = 0.4802$ . Overall, in-hospital mortality was 8.6%, with a decreasing trend from 1998(17.5%) to 2006 (6.3%),  $P = 0.3381$ . Mortality was not influenced by gender, race, payer, hospital teaching status, or hospital size. Increasing age was independently associated with increased mortality; age 60–79 vs. < 59 (OR 2.58; 95% CI 1.15–5.79) and > 80 vs. < 59 (OR 4.03; 95% CI 1.10–14.97). The presence of medical co-morbidities including renal failure, congestive heart failure, and liver disease were significant predictors of increased mortality.

**Conclusion:** Total pancreatectomy continues to be performed for both malignant and non-malignant pancreatic disease. In-hospital mortality remains substantial. Increasing age and the presence of medical comorbidities were significantly associated with increased mortality. Additional studies including patient-level data and overall survival are warranted to provide a better understanding of the specific predictors of outcome after TP.



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### Higher expression of RRM2 predicts effect in pancreatic cancer treated with gemcitabine

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**Background:** Gemcitabine is now considered to be the standard adjuvant therapy for advanced pancreatic cancer worldwide. Randomized controlled studies have demonstrated that gemcitabine is effective in palliating symptoms and prolonging survival in patients with advanced pancreatic cancer. Gemcitabine as adjuvant therapy brings about a longer survival rate compared to surgery alone. Although the key enzyme of gemcitabine sensitivity *in vitro* is known well, it has not been defined yet *in vivo*. The aim of this study is to clarify which enzyme is the key in gemcitabine as adjuvant therapy for the resectable pancreatic cancer.

**Patients and methods:** Patients were given gemcitabine at 100 mg/body weekly for 2 weeks followed by a week rest and for at least three cycles. RNA was extracted by microdissection from tumoral and normal surgical fresh-frozen pancreatic tissue of 32 patients. The expression of genes such as RRM1, RRM2, dCK and hENT were determined by real-time quantitative polymerase chain reaction. The association between clinical outcome and gene expression levels was estimated by Kaplan–Meier method.

**Results:** RRM1, RRM2, dCK and hENT were detectable in most tumor specimens. RRM1, dCK and hENT expression in tumor tissue were lower than in normal, while RRM2 expression in tumor was so higher than in normal as to be significantly correlated with clinical outcome. Patients with high levels of RRM2 had a significantly shorter overall survival [median, 8.4 months in the higher expression *vs.* 14.5 months in the lower expression]. However, patients with high levels of RRM2 who were given gemcitabine had a longer overall survival as well as that of patients with low levels of RRM2.

**Conclusions:** This result suggests that tumoral RRM2 expression is a clinically important determinant of malignant behavior in pancreatic cancer and a major predictor of disease response to gemcitabine treatment.

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### Pancreatic neuroendocrine tumors: a national survey

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**Purpose:** Pancreatic neuroendocrine tumors (PNETs) have a prolonged natural history, and the benefit of resection remains controversial. As a result, treatment approaches are not standardized. The purpose of this study is to assess surgical resection of PNETs on a national level.

**Methods:** This is a retrospective observational study utilizing the Nationwide Inpatient Sample (1998–2006). The primary outcome measure was in-hospital mortality. As a secondary outcome, length of stay (LOS) was assessed. Univariate analyses were performed using Rao-Scott Chi-square and the Cochran-Armitage Trend tests. Multivariable logistic regression was used to evaluate predictors of outcomes.

**Results:** A total of 3306 unweighted observations for patient admissions associated with PNETs were identified. Mean age was 58.5; 54.1% were female. Of patients with race/ethnicity available (83.3%), 81.9% were white. Most PNET admissions were at teaching and urban hospitals (59.8 and 91.8%, respectively). Overall, 470 patients (14.2%) underwent resection. Distal pancreatectomy and pancreaticoduodenectomy accounted for 56.4% and 24.5% of resections, respectively. Over the study time course, the proportion of patients receiving resection increased ( $P = 0.0026$ ). Predictors of resection in multivariable analysis included age  $< 70$  (*vs.*  $\geq 70$ ; adjusted odds ratio (OR) 1.7 [95% confidence interval (CI) 1.3–2.3]), hospital teaching status [*vs.* non-teaching; OR 2.3 (CI 1.7–3.2)], and urban hospital [*vs.* rural; OR 2.4 (CI 1.2–4.6)]. Mean LOS for patients undergoing resection was 12.3 *vs.* 6.6 days for non-resection admissions ( $P \leq 0.0001$ ). On univariate analysis, the in-hospital mortality rate for resected patients was 1.7% compared to 5.2% for the non-resected group ( $P = 0.0009$ ). Non-resection admission status remained a significant predictor of in-hospital mortality by logistic regression [*vs.* resection; OR 3.9 (CI 2.0–7.7)], as were age  $\geq 70$  [*vs.*  $< 70$ ; OR 2.2 (CI 1.6–3.1)] and length-of-stay  $> 14$  days [*vs.*  $\leq 2$  weeks; OR 3.7 (CI 2.5–5.5)].

**Conclusions:** More resections for PNETs are being performed over time. In-hospital mortality is higher for the cohort of patients not undergoing resection, suggesting disease-related factors such as advanced or recurrent disease. Peri-operative mortality for patients undergoing resection is acceptably low, supporting the role of aggressive treatment for PNETs.

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### Laparoscopic distal pancreatectomy for benign lesions – does splenic preservation effect outcomes?

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Although the spleen is often routinely resected during both open and laparoscopic distal pancreatectomies, a splenectomy can increase the risk of post-operative and life long infectious complications. In the open pancreatectomy literature, spleen preserving or conservative distal pancreatectomy is advocated if possible for benign lesions. Spleen preserving laparoscopic pancreatectomies are technically more difficult because of the delicate dissection of the splenic vessels. We performed a retrospective review of 27 laparoscopic pancreatectomies done at our institution, all for benign disease. Patient characteristics are listed in Table 1. All procedures were done laparoscopically without hand assistance. There was only one conversion to open for a positive proximal margin. Attempts were made in all patients to conserve the

spleen, which was successful in seven patients (35%). Overall, nine patients had complications (33%), including four patients with a pancreatic leak (15%) and two with post-operative hemorrhage requiring re-exploration (7.4%). Two patients had complications unrelated to the pancreatectomy (myocardial infarction and pulmonary embolism). Interestingly the only complication in the spleen-preserving cohort was a splenic vein thrombosis in a patient with a hypercoagulable state that was unknown prior to surgery. The results are listed in Table 1. Patients with spleen-preserving pancreatectomies had a trend toward fewer complications, significantly less blood loss and shorter operative time compared to patients who underwent concomitant splenectomy. Length of stay was not significantly different between the two groups. Obviously due to anatomic and other intra-operative factors during distal pancreatectomy, the spleen cannot always be preserved. However in this small study patients with spleen-preserving distal pancreatectomies had shorter operative times, less blood loss and fewer complications. These findings support splenic preservation when possible during laparoscopic distal pancreatectomy.

**Table 1.** Patient characteristics.

	Spleen preserving (7)	Splenectomy (20)	P-value
Age	30–68 (59)	22–76 (59)	0.9733
Male	57%	40%	0.6618
Diagnosis			
Serous	3	6	
cystadenoma			
Neuroendocrine	0	5	
IPMN	1	3	
Mucinous cyst	2	2	
Stricture	0	2	
Other	1	2	
Overall	1 (14%)	8 (40%)	0.3632
complications			
Surgical	1 (14%)	6 (30%)	0.6334
complications			
Operative time (min)	140–233 (174)	145–515 (276)	0.0076
Estimated blood loss (mL)	25–150 (59)	50–350 (169)	0.0024
Length of stay (days)	(3–7) 4.7	3–11 (4.8)	0.9256

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### **Pancreatic leak as an additional risk factor in elderly patients undergoing pancreaticoduodenectomy**

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The aim of this study was to investigate risk factors for mortality among elderly (greater than 70 years old) patients who underwent pancreaticoduodenectomy compared to younger (less than seventy) patients. Data were analysed from our database for all patients who underwent pancreaticoduodenectomy at a single institution between January 1997 and May 2008. A total of 706

cases were identified – 489 in the young group (mean age 58) and 217 in the elderly group (mean age 75). There were 289 (59%) men in the young group and 108 (50%) in the elderly group. The prevalence of diabetes, ischemic heart disease, renal disease and chronic airways disease were similar between the two groups. Hypertension was significantly more frequent in the elderly (29% vs. 18%). Both groups had a similar range of pathology in the resected specimens. Overall 85% of the elderly had a malignancy compared to 83% of young patients. The diagnosis of chronic pancreatitis was less frequent in the elderly group (1.4% vs. 8.2%). Mean post-operative hospital stay was 14.7 days for the elderly and 13.6 for younger patients. Both groups had similar rates of intensive care unit admission (16% vs. 17%). The post-operative mortality rate (30-day or inpatient) was significantly higher in the elderly group (10.6% vs. 4.3%). Both the elderly and younger groups experienced a similar rate of overall morbidity (36% vs. 36%). There was no significant difference in the rate of pancreatic, biliary or enteric leakage. The rate of pancreatic leak was 10.6% for the elderly group compared to 9.8% for the young. Elderly patients who did suffer from a pancreatic anastomotic leak were significantly more likely to die than younger patients (39% vs. 13%). Amongst the patients who did not suffer from a pancreatic leak the elderly also had a higher mortality (7.2% vs. 3.4%) however the difference was less pronounced. Pancreaticoduodenectomy in elderly patients will become a more frequent procedure as the population ages. This study shows that even in those patients judged fit for the procedure it carries a substantial risk of mortality (10.6%). Our data suggests that the elderly patients are particularly at risk if they suffer a leak from the pancreatic anastomosis.

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### **Uncinate or body/tail location and node ratio predict margin positivity and poor outcome in resected pancreas cancer**

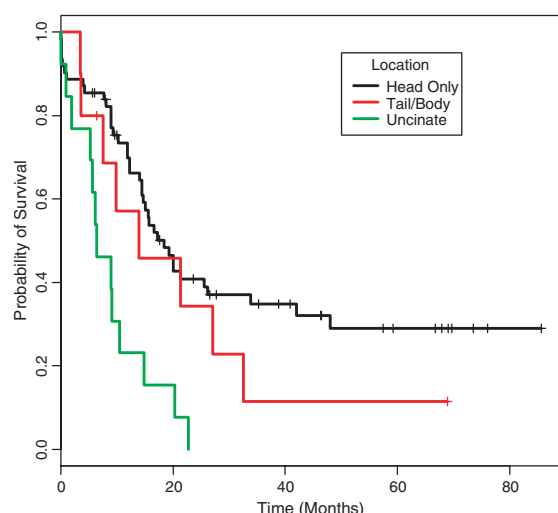
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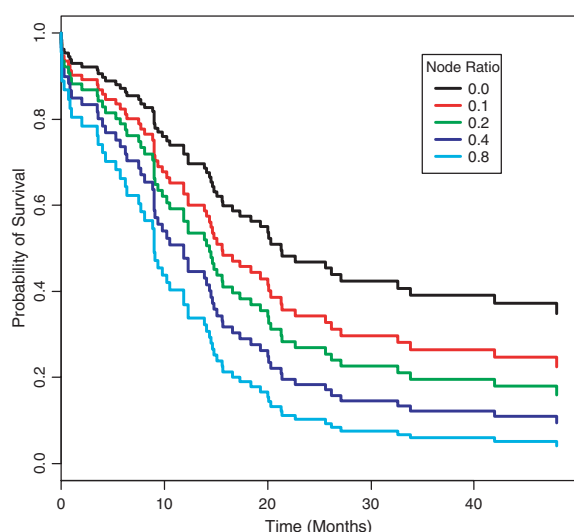
Pancreatectomy for cancer is associated with a 20–40% risk of positive surgical margins (PSM). This study identifies clinicopathologic factors predicting PSM and poor outcome.

**Methods:** Clinical data for 86 patients undergoing pancreatic cancer resection from 1999–2005 were reviewed. Data included tumor location and size, grade, morphology, node ratio, and the use of neoadjuvant and adjuvant therapy. Variables were correlated with PSM and survival using logistic regression, Kaplan–Meier and log rank analyses.

**Results:** The 86 patients had a median age of 64.5 years and median follow-up of 14.3 months. Tumor location included head only ( $n = 62$ ), uncinate involvement ( $n = 13$ ) or body/tail ( $n = 10$ ). Neoadjuvant chemoradiation (CRT) was used in 10 cases and 38 received post-operative adjuvant therapy including CRT ( $n = 36$ ) or chemotherapy only ( $n = 2$ ). Surgical margins were positive in 9 (15%) head, 8 (62%) uncinate, and 5 (50%) body/tail tumors. Tumors in the uncinate or body/tail



**Figure 1.** Overall survival versus tumour location.



**Figure 2.** Overall survival versus node ratio.

( $P < 0.001$ ) and increasing node ratio ( $P < 0.01$ ) were strong predictors of a PSM. Patients with PSM had a 7.6 month median survival compared to 18.4 months for R0 resections ( $P < 0.005$ ). Median survival was worse for uncinete (6.4 months) and body/tail (13.9 months), compared to tumors of the head (18.4 months). Tumors  $> 2$  cm ( $P < 0.05$ ), positive nodes ( $P < 0.05$ ), increasing node ratio ( $P < 0.005$ ), and poor differentiation ( $P < 0.02$ ) were all associated with worse survival. Median survival with neoadjuvant therapy (14.6 months) was no different than without (15.6 months). Adjuvant therapy (18.4 months) was associated with a marginal ( $P = 0.05$ ) increase in median survival compared to surgery alone (9 months).

**Conclusions:** Surgically resected pancreatic cancers involving the uncinete process and body/tail have a higher incidence of positive surgical margins and worse overall survival compared to isolated head lesions. Higher node ratio is also associated with positive margins and poor survival. When identified pre-operatively, patients with uncinete or body/tail lesions should be considered for neoadjuvant protocols.

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### An analysis of surgeon volume, predictors of morbidity, and cost for patients undergoing pancreaticoduodenectomy at a teaching community hospital

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**Background:** Most studies in the literature looking at volume and cost analysis for pancreaticoduodenectomy (PD) are from large academic centers or state/national databases, which do not reflect the experience of the individual teaching community hospital. Despite trends toward regionalization of care, the majority of pancreaticoduodenectomies are performed in community hospitals by surgeons with a variety of experience. Our goal was to analyze the impact of several peri-operative variables, including surgeon volume, on morbidity, mortality, length of stay and cost of PD within a community based, teaching hospital system.

**Methods:** Patients who underwent PD at Providence Medical Center from 2005–2008 were reviewed retrospectively. Patient demographics, operative and peri-operative data were analyzed. Surgeon experience was categorized as either high volume (HV) or low volume (LV) based on an average of 10 PD per year. Operative mortality was defined as death related to the operation, whenever it occurred. Complications were divided into minor and major based on the need for significant intervention or prolongation of hospital stay. Hospital cost data was queried for total cost, total charges and itemized departmental charges.

**Results:** Ninety-four patients underwent PD with an operative mortality rate of 9.6% (HV 2.2%, LV 16.0%), major complication rate of 32% (HV 18%, LV 44%), average length of stay of 14.1 days (HV 12.6 days, LV 15.4 days) and average cost of \$36 300 (HV \$33 680, LV \$39 340). Peri-operative factors predictive of death were age ( $P = 0.022$ ), body mass index ( $P < 0.001$ ), surgeon volume ( $P = 0.008$ ) and ASA grade ( $P = 0.011$ ). Factors predictive of major complication were surgeon volume ( $P = 0.005$ ) and body mass index ( $P < 0.001$ ). Factors predictive for increased length of stay for patients discharged from the hospital were surgeon volume ( $P = 0.016$ ), pre-operative albumin ( $P < 0.001$ ) and body mass index ( $P = 0.029$ ). Factors predictive for higher total cost were body mass index ( $P = 0.013$ ) and pre-operative albumin ( $P = 0.018$ ). The difference in hospital costs between high and low volume surgeon was \$5660. A detailed analysis of hospital charge data revealed that pharmacy was responsible for most of this cost difference, specifically the utilization of antibiotics, TPN, and octreotide.

**Conclusions:** Surgeon volume and patient body mass index are the peri-operative variables that are most responsible for increased morbidity from PD. This increased morbidity is reflected in higher mortality, length of stay and costs. Increased costs are driven primarily by pharmacy.

# Abstracts 118 to 125

## Oral Posters – Pancreas II

### Friday, March 13, 2009 4:15–5:30 PM

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#### Laparoscopic approach to distal pancreatectomy and splenectomy provides less invasive means for resection of pancreatic pathology

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**Introduction:** The journey from conventional 'open' to 'minimally invasive' operations, conferring 'fast track care' in pancreatic surgery, is now a reality. Due to the complex nature and infrequency of indications for laparoscopic distal pancreatectomy and splenectomy (LDPS), embracement by the surgical community has been slow despite technologic advances. This study was undertaken to evaluate our experience with distal pancreatectomy and splenectomy undertaken with laparoscopic intent to compare outcomes with concurrent open distal pancreatectomy and splenectomy (ODPS).

**Methods:** From 2005 to 2008, 30 consecutive patients undergoing LDPS were compared to the 30 most recent consecutive patients undergoing ODPS at our institution. Demographic and post-operative data were compared utilizing the Mann–Whitney *U*-test. Data are presented as median, mean  $\pm$  SD.

**Results:** There was no difference in gender, age or BMI of patients undergoing LDPS or ODPS (Table 1). Time under anesthesia and estimated intra-operative blood loss were less in patients undergoing LDPS; length of hospital stay was 25% shorter (Table 1). 47% of patients undergoing LDPS and 57% undergoing ODPS had malignant or pre-malignant disease; microscopic negative margins of resection (R0) were obtained in all patients. 37% of patients undergoing LDPS underwent conversion to ODPS; five were converted due to technical difficulties associated with malignancies. No patients undergoing LDPS had pancreatic fistula; however, two patients had extended lengths of hospital stay for myocardial infarction and atrial fibrillation. No patients died after LDPS.

**Table 1.** 30 Laparoscopic distal pancreatectomy splenectomy vs. 30 open distal pancreatectomy splenectomy.

	LDPS	ODPS	P-value
Gender	57% Male	60% Male	NS
Age	64 years (63 years $\pm$ 16.1)	62 years (61 years $\pm$ 14.6)	NS
BMI	25 kg/m <sup>2</sup> (26 kg/m <sup>2</sup> $\pm$ 4.8)	24 kg/m <sup>2</sup> (25 kg/m <sup>2</sup> $\pm$ 7.6)	NS
Anesthesia time	205 min (210 min $\pm$ 41.6)	281 min (289 min $\pm$ 78.9)	<i>P</i> = 0.001
Blood loss	200 cc (276 cc $\pm$ 283.4)	300 cc (433 cc $\pm$ 321.9)	<i>P</i> = 0.007
Length of stay	6 days (7 days $\pm$ 6.1)	8 days (12 days $\pm$ 19.8)	<i>P</i> = 0.02
Pancreatic leak	None	None	

**Conclusions:** LDPS is a safe, effective, and technically feasible operation providing the benefits of minimally invasive surgery. It can be successfully undertaken in patients for resection of benign, pre-malignant, or malignant disease, though conversions to 'open' operations may be required especially for malignant disease. Application of LDPS is encouraged as it provides less invasive means for resection of pancreatic pathology.

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#### Additional organ resection combined with pancreaticoduodenectomy does not increase post-operative morbidity and mortality

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**Background:** The mortality associated with pancreaticoduodenectomy (PD) has decreased substantially in recent times, but high morbidity continues to be a significant problem. With reductions in mortality there is increasing willingness to combine organ resections with PD when indicated. There is however a paucity of information regarding the morbidity and mortality of multi-visceral resection (MVR) that involves pancreaticoduodenectomy (MVR-PD).

**Methods:** Patients undergoing PD between January 2002 and November 2007 by a single surgeon were reviewed and peri-operative outcomes determined. Those treated by PD alone were compared to those undergoing MVR-PD.

**Results:** There were 105 patients overall who underwent PD during the study period, with MVR-PD performed in 19 patients. Twelve patients (63%) required PD combined with right colectomy, two (10%) underwent PD combined with right nephrectomy, two (10%) required liver resection with PD, and the remaining 3 (11%), had combinations of liver, kidney, colon, and small bowel resection in addition to PD. In both groups the main indication for surgery was pancreatic cancer, however there were proportionally more patients in the MVR-PD group with gastrointestinal stromal tumors (2 patients, 11%), sarcomas (2 patients, 11%) and metastases to the periaampullary region (3 patients, 16%). The overall complication rate in this study was 60%. Delayed gastric emptying (DGE) (39%) and pancreatic fistula (16%) were the most common complications. There was no significant difference in complications between the two groups. A non-pylorus preserving PD was more commonly performed in cases of MVR-PD (53% vs. 28%; *P* = 0.007), operating times were longer (9.5 h vs. 8 h; *P* = 0.002), and surgical intensive care unit stay was greater (1 day vs. 2 days, *P* < 0.001). The overall median length of hospital stay (7 days) and readmission rate were similar between the groups.

**Conclusion:** MVR-PD can be performed without significant added morbidity compared to PD alone. The main indication for MVR-PD is locally advanced pancreatic cancer requiring PD combined with right hemicolectomy.

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### Influence of node status, anatomical site and tumor size on long term outcome of resection for pancreatic neuroendocrine cancers

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**Purpose:** Pancreatic neuroendocrine malignancies are rare, indolent malignancies for which there is no effective systemic therapy and from which the mortality is significant. Here, we identify prognostic factors in pancreatic neuroendocrine malignancies.

**Methods:** Demographics, surgical data, pathologic diagnosis, post-operative course and long term outcome for patients who underwent pancreas resection for neuroendocrine malignancy from 11/1/1997 to 4/1/2008 at our institution were reviewed.

**Results:** Sixty-six patients were identified as having had surgical resection of a neuroendocrine malignancy, 42 with proximal lesions and 24 with distal lesions. Thirty-eight percent (12/32) of patients with nodal disease had recurrent disease in contrast to no disease recurrence in patients without nodal disease (0/34,  $P < 0.01$ ). Patients with node positive disease have a decreased 5-year survival (37.5% vs. 85.7%,  $P = 0.03$ ). In patients with node positive disease, those with a lesion in the distal pancreas were more likely to have disease recurrence [67% (8/12)] than those with lesions in the head or neck of the pancreas [10% (2/20),  $P < 0.01$ ]. There was no difference in the percentage of patients with positive lymph nodes based on location of tumor (proximal lesion 49% positive nodes, distal lesion 48%,  $P = 0.95$ ). Recurrence was not related to the number of positive nodes (2.8 positive nodes for recurrence vs. 4.3 positive nodes for no recurrence,  $P = 0.24$ ), nor was there a recurrence benefit related to the number of nodes sampled (11.6 nodes sampled in recurrent disease vs. 18.2 nodes sampled in those without recurrent disease,  $P = 0.15$ ). Larger primary tumors were found in node positive distal lesions than in patients with distal lesions and negative nodes (5.5 cm  $\pm$  0.9 cm vs. 2.9 cm  $\pm$  0.6 cm,  $P = 0.02$ ). This was not true for patients with proximal disease (3.9 cm  $\pm$  0.7 cm, node positive vs. 3.6 cm  $\pm$  0.7 cm, node negative,  $p = 0.78$ ). Patients with recurrent disease had larger tumors (5.4 cm  $\pm$  0.9 cm) than did those without disease recurrence (3.5 cm  $\pm$  0.4 cm,  $P = 0.05$ ).

**Discussion:** Patients with node positive disease at the time of surgery are more likely to develop recurrent disease and have an overall decreased survival. Patients with positive lymph nodes and a lesion in the distal pancreas have decreased disease free survival when compared to patients with node positive disease in the head or neck of the pancreas. Tumors are larger in patients with node positive disease of the distal pancreas than in those with node negative disease and are larger in patients who develop recurrent disease than those who do not have a recurrence.

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### Malignant pancreatic cystic neoplasms: histopathologic subtypes and associated survival outcomes

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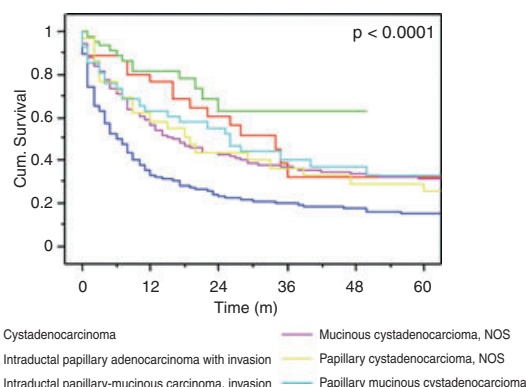
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**Background:** Cystic neoplasms (CNs) of the pancreas encompass a spectrum of various tumor types. The low incidence of malignant CNs represents a challenge to precise post-operative survival prediction and to appropriate choice of post-operative adjuvant therapy.

**Methods:** A pancreatic CN data set was created from the SEER 1970-2004 database. Prognostic factors with survival impact, and relationships between surgical therapy and overall survival (OS) were analyzed with univariate and multivariate statistical methods.

**Results:** Out of a cohort of 109 596 patients with a primary pancreatic malignancy, 16 CN histologic subgroups with 815 individuals were identified. After exclusion of those with  $< 15$  cases, eight subgroups with 767 patients remained. These histologic designations included mucinous cystadenocarcinomas ( $n = 346$ ), cystadenocarcinomas NOS ( $n = 195$ ), intraductal papillary mucinous carcinoma (IPMC), invasive ( $n = 47$ ), non-invasive IPMC ( $n = 45$ ), papillary mucinous cystadenocarcinoma ( $n = 42$ ), intraductal papillary adenocarcinoma ( $n = 36$ ), papillary cystadenocarcinoma NOS ( $n = 30$ ), and non-infiltrating intraductal papillary adenocarcinoma ( $n = 26$ ). The median age was 69 years (range 24–96), 64% of patients were female, and the median tumor size was 5 cm (0.1–35). The disease extent varied by histologic group ( $P < 0.0001$ ); localized disease was present in 45% (range 24–100), regional involvement in 26% (0–39), and distant metastases in 29% (0–46). Resection frequency (mean: 53%, range 15–100) varied by tumor type ( $P < 0.0001$ ). At a median follow up of 12 months (31 for survivors), the median OS was 17 months (invasive groups range: cystadenocarcinomas (6) to intraductal papillary adenocarcinoma (34; IPMC: not reached);  $P < 0.0001$ ; see Figure 1). Multivariate OS variables were: age, disease extent ( $P < 0.0001$ ), histologic type, grade ( $P = 0.0002$ ), gender ( $P = 0.001$ ), surgical treatment, ( $P = 0.006$ ), primary site ( $P = 0.02$ ), and primary site node involvement ( $P = 0.03$ ).

**Conclusions:** When controlled for other established prognostic parameters, the histopathologic subtype



**Figure 1.** Survival of invasive pancreatic cystic neoplasms.

assignment of pancreatic CNs significantly affects survival prediction. Resective local treatment is associated with superior survival for all tumor types and remains the standard of care.

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### En-bloc pancreatic resection for locally advanced primary and recurrent sarcoma

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**Purpose:** Primary and locally recurrent sarcoma involving the pancreas is a rare occurrence. The feasibility of treating these patients surgically with en bloc pancreatic resection is examined and may provide an opportunity for significant palliation or cure.

**Results:** Over a 10-year period from 1997 to 2007 a total of 122 patients were treated surgically for sarcoma involving the retroperitoneum, abdomen and pelvis at our institution. Of these 20 (16.4%) had primary or locally advanced disease involving the pancreas. There were 8 women and 12 men with a mean age of  $49.5 \pm 14.9$  years (range 25–75 years) and all patients had been turned down for surgery by other centers. This included 9 (45%) patients with recurrent disease from a previously resected tumor of which 6 (30%) had neoadjuvant chemotherapy prior to surgery. En-bloc resection of the distal pancreas along with other contiguous organs for locally advanced disease was performed in 18 (90%) patients while 2 (10%) others had pancreaticoduodenectomy. The average size of the lesions was  $13.4 \pm 10.4$  cm (range 1–40 cm). En bloc resection most commonly included the small bowel, stomach, spleen, colon, diaphragm, liver, adrenal and kidney that varied with each patient according to organ involvement with the goal to achieve clear margins. Blood loss averaged  $2600 \pm 2900$  cc (range 400–10 000 cc) with average blood transfusion of  $3.7 \pm 4.0$  units. There was 1 (5%) operative death and 5 (25%) non-lethal peri-operative complications. Pathology included gastrointestinal stromal tumor in 12 (60%) patients, spindle cell sarcoma in 4 (20%), liposarcoma in 2 (10%), malignant hemangiopericytoma in 1 (5%) and Ewing sarcoma in 1 (5%) other. The tumors were low grade in 7 (35%), intermediate in 4 (20%) and high in 9 (45%) others. All patients received chemotherapy post-operatively. Presently 7 (35%) patients remain alive: two (10%) with disease and 5 (25%) without evidence of recurrence. Nine patients had tumor recurrence at a mean of  $14.5 \pm 15.8$  months (range 4.0–54.5 months) after surgery at our institution. Recurrence occurred in the liver in 5 (25%) patients and locally at the surgical site in 4 (20%) others. Reoperation for local recurrence was performed in 2 (10%) patients. The overall median survival was  $27.5 \pm 10.8$  months with overall survival at 5 and 10 years of 35.2% and 23.5% respectively.

**Conclusion:** En bloc pancreatic resection for locally advanced sarcoma involving the pancreas is feasible in properly selected patients. The ability to perform a complete resection seems to provide worthwhile palliation or long term survival where the prognosis is otherwise dismal.

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### Updated initial experience with laparoscopic distal pancreatectomy at an academic institution

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**Background:** Laparoscopic distal pancreatectomy is increasingly utilized as a mode of resection for diseases localized to the body and the tail of the pancreas. Here we report our initial experience with laparoscopic distal pancreatectomy within the first 2 years and compare outcomes to patients who underwent a traditional open approach.

**Methods:** A retrospective review of a prospectively collected database was conducted of 26 patients who underwent laparoscopic distal pancreatectomy and splenectomy or laparoscopic spleen sparing distal pancreatectomy at a single academic institution from August 2006 to July 2008. Three patients were excluded from the study because they were converted to open approach. The remaining 23 patients were compared to 23 consecutive patients who underwent open distal pancreatectomy and splenectomy or spleen sparing distal pancreatectomy in the same time period. Patients who underwent resection of any additional organs were excluded from the open group. The charts were analyzed for demographic information, pathology, operative time, estimated blood loss (EBL), length of hospital stay, and pancreatic fistula formation. P-values were determined using Student's t-test or Fisher's exact test as appropriate.

**Results:** The average age of the study group was 58 years (range 19–78) vs. 62.9 years in the open group (range 28–83). The mean BMIs for the study and the open group were 29.7 (range 20.9–40.6) and 28.4 (range 22.2–46.5), respectively. The pathology in the open and the study group included both benign and malignant processes. The data are summarized in the table below.

**Conclusions:** Our initial experience indicates that laparoscopic distal pancreatectomy with or without splenectomy can be safely performed, with significantly less blood loss. The laparoscopic approach was associated with trends toward more splenic preservation, shorter operative time, and less blood loss. The laparoscopic technique resulted in higher rate of pancreatic leak. The different methods of pancreatic transaction and closure of the pancreatic stump need to be further explored to decrease the rate of pancreatic fistula formation.

**Table 1.** Comparison of laparoscopic vs. open distal pancreatectomy.

	Laparoscopic <i>n</i> = 23	Open <i>n</i> = 23	<i>P</i> -value
Spleen sparing distal pancreatectomy	9 (39%)	5 (22%)	NS
Pathology			
Benign	22 (96%)	18 (82%)	NS
Operative time (min)	267	287	NS
EBL (mL)	145	461	0.01
Median LOS (day)	5	6	NS
Pancreatic leak	5 (22%)	0	0.049

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### An evaluation of the modified POSSUM scoring system for pancreatic resection

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**Aim:** No useful indicator is available for pre-operative risk evaluation when considering treatment with pancreatic surgery. The aim of this study was to clarify a usefulness of the POSSUM audit system (Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity) in patients with pancreatic resection. **Methods:** From June 1996 to December 2006, 256 patients underwent pancreatic resection. The operative procedure was pancreaticoduodenectomy (PD) in 188 cases and distal pancreatectomy (DP) in 68 cases. The underlying disease was pancreas cancer in 106 cases, intrapapillary mucinous tumor (IPMT) in 34 cases, bile duct cancer in 30 cases, ampullary cancer in 29 cases, gastric cancer in 35 cases, duodenal cancer in 7 cases and chronic pancreatitis in 15 cases. There were 10 hospital deaths (3.9%). Post-operative complications were seen in 90 cases (35.2%). Eighteen pre-operative factors and 5 operative factors, and POSSUM parameters were evaluated. **Results:** In terms of the pre-operative factors, there was no significant difference between the PD group and the DP group. Observed-to-expected ratio (O/E ratio) of hospital death was 0.27 by original POSSUM and 0.91 by modified POSSUM (Portsmouth POSSUM). The O/E ratio of post-operative morbidity was 0.64 by original POSSUM. The subjects were divided into two risk groups by pre-operative physiological score (high-risk group is more than 20). Morbidity of the high-risk group (25/44, 57%) was significantly higher than the low-risk group (65/212, 31%), and the hospital death rate of both groups were 9.1%, 2.8%. **Conclusion:** The modified POSSUM is useful as a means of risk assessment in individuals scheduled to undergo pancreatic resection.

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### Quality of life after surgical intervention for chronic pancreatitis

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**Background:** Surgical intervention offers durable therapy for the pain and disability caused by chronic pancreatitis. Organ resection (either Whipple or distal pancreatic resection), internal drainage procedures (either by pseudocyst-enterostomy or pancreaticojejunostomy), or duodenum-preserving pancreatic head resection may be used. The quality of life (QOL) of these post-surgical

patients is uncertain. We sought to determine the QOL of our patients to provide a standard to which emerging endoscopic and NOTES procedures can be compared.

**Methods:** We reviewed our hospital database for patients treated for chronic pancreatitis over a 10 year period and contacted them to complete a SF-36 questionnaire. 135 patients were identified. 21 patients had died and 32 responded to the SF-36 survey. Of the responses, 18 had internal drainage, 12 had organ resection and 2 patients had external pseudocyst drainage. We analyzed the patients' data and then scored the SF-36 responses and compared these with US Population Norms, patients reporting long standing illness, and patients with heart disease.

**Results:** Our group was significantly worse than the US Population Norms in all 8 SF-36 measures. There was no significant difference in 6 of the SF-36 measures between the surgical group and a group reporting long standing illness. There was no significant difference in 6 of the SF-36 measures between the surgical group and a group with NYHF Class II heart disease. (See Table 1) The internal drainage and organ resection groups were also compared to the US Population Norms. Drainage patients were significantly worse than US Population norms on 4 of the 8 SF-36 summary measures while resection patients were significantly worse on only 1 measure.

**Conclusions:** The quality of life of patients after surgical intervention for chronic pancreatitis is comparable to that of patients with common chronic disease. While indications for each differ, organ resection may provide an improved QOL than internal drainage procedures for chronic pancreatitis. This QOL may serve as a standard for comparison of emerging endoscopic and NOTES procedures.

**Table 1.** Comparison of mean SF-36 scores with US Population Norms, patients reporting long standing illness, patients with heart disease, and patients having had surgery for chronic pancreatitis (CP).

SF-36 Measure	CP patients	US Norms <sup>1</sup>	Disease <sup>2</sup>	NYHA Class II <sup>3</sup>
Physical Functioning	73.8 (24.7)	83.2 (23.7)*	78.3 (23.2)	56.7 (21.3)*
Role functioning/physical	52.2 (42.6)	82.5 (25.5)*	71.9 (38.9)*	28.9 (37.4)*
Role functioning/emotional	58.9 (45.2)	87.3 (21.4)*	76.3 (36.4)*	55.0 (45.7)
Vitality	48.4 (23.5)	58.3 (20.0)*	54.0 (21.1)	49.5 (19.6)
Mental Health	66.1 (25.7)	74.9 (17.7)*	69.9 (18.7)	66.3 (17.9)
Social Functioning	70.0 (29.3)	84.3 (22.9)*	80.2 (24.8)	75.4 (23.9)
Bodily Pain	63.3 (26.3)	71.3 (23.6)*	69.8 (25.4)	65.7 (28.9)
General Health	52.0 (24.9)	70.8 (20.9)*	60.8 (23.0)	44.5 (17.1)

Values are mean and SD.

<sup>1</sup>1998 US General Population Means.

<sup>2</sup>Jenkinson C. Short Form 36 (SF 36) Health Survey Questionnaire: Normative data for adults of working age. *BMJ*, Vol. 306 (6890)1437–1430. May 29, 1993.

<sup>3</sup>Juenger J. Health related quality of life in patients with congestive heart failure: comparison with other chronic diseases and relation to functional variables. *Heart* 2002;87:235–241.

\**P* > 0.05 for t-test between group and CP.



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Oral Posters – Liver IV  
Saturday, March 14, 2009 7:00–8:00 AM

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**Steatosis in hepatocellular cancer patients**

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**Introduction:** Non-alcoholic steatohepatitis and steatosis associated with hepatitis C have been described as risk factors for hepatocellular cancer (HCC). However little is known about steatosis, including the prevalence, risk factors, or impact on outcome in patients with HCC.

**Methods:** A retrospective review of 106 patients who underwent liver resection for HCC between 1993 and 2008 was performed. Pathology reports were analyzed for size of tumor, cirrhosis, fibrosis, vascular invasion, steatosis, margins and iron deposition. Steatosis was classified as none, mild (1–9%), moderate (10–30%) and severe (> 30%). Binomial logistic regression was performed to identify risk factors associated with steatosis. Factors associated with survival were determined utilizing Cox regression analysis.

**Results:** Of the 106 patients 68.9% had evidence of steatosis, 13.2% had no steatosis, and in 17.9% of the reports presence of steatosis was not addressed. In the patients with steatosis, 8.2% were classified as severe, 21.9% as moderate, 57.5% as mild, and 12.4% were not quantified. Age, sex, ethnicity, body mass index, history of diabetes, history of alcohol use, and hepatitis status were not predictive of steatosis. The presence of steatosis was associated with smaller tumors, mean size 6.0 vs. 9.6 cm in patients without steatosis ( $P = 0.0045$ ), and a lower platelet count (192,000/L vs. 262 000/L,  $P = 0.0055$ ). In this cohort, lower serum albumin, larger tumor size, presence of cirrhosis and iron deposition were predictive of survival, but the presence of steatosis did not affect survival.

**Conclusions:** Steatosis was frequently found in the resected HCC specimens, but most patients had mild steatosis. The usual metabolic factors were not predictive of the presence or amount of steatosis. Steatosis was associated with lower platelet count and smaller tumors. Steatosis did not appear to affect survival or recurrence in HCC patients who underwent liver resection.

regional therapies are employed for palliation. In more advanced stages, best supportive care is the only option. Sorafenib has emerged as the treatment of choice in the treatment of advanced HCC and has demonstrated an anti-angiogenic and anti-proliferative effect. Anti-angiogenic agents have been shown to decrease hypoxia in the center of tumors, and theoretically would increase sensitivity to radiation. This provides a logical rationale for the use of combined therapy.

**Aim:** To evaluate the safety and tolerability of combining sorafenib with Yttrium-90 TheraSphere radioembolisation (Y-90).

**Methods:** Consecutive eligible patients were enrolled from the McGill University Health Centre HCC Clinic from March 2008 to September 2008. Patients with HCC who were candidates for Y-90 therapy were eligible for the study. Patients began sorafenib (400 mg po BID) 6–8 weeks prior to Y-90 treatment. Sorafenib was continued post-Y-90. The dose was adjusted if toxicity occurred. Follow-up scans and lab work were obtained at 1-month post-Y-90.

**Results:** Eight patients have completed treatment, and 4 are awaiting Y-90 treatment. All patients are male, mean age 61.4 years. Seven patients are Child-Pugh A, and all have ECOG status 0 or 1. The mean AFP pre-treatment was 1798 ug/L. 6 patients required sorafenib dose adjustment. The most common toxicities observed were GI (diarrhea) and hand foot syndrome. Toxicities occurred pre-Y-90, and were generally self-limited and responded to dose adjustment. No patient required drug discontinuation or experienced grade 4 toxicity. AFP levels began to decrease on sorafenib alone in 4 patients. The mean dose of Y-90 was 150 Gy. 1 patient experienced worsening ascites post-Y-90. 7 patients demonstrated tumor necrosis, and 4 had 100% necrosis. 5 had stable disease. 1 patient progressed after treatment (extrahepatic and contralateral liver). The mean decrease in AFP post-Y-90 treatment was 1470 ug/L.

**Conclusion:** These preliminary results demonstrate the safety and tolerability of combining Y-90 with sorafenib in the treatment of advanced HCC. 88% of patients demonstrated radiologic evidence of necrosis. They continue to be followed to assess progression-free survival. Based on the encouraging tumor response and tolerability, a further Phase II study will soon be started.

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**Combined sorafenib and Yttrium-90 radioembolization in the treatment of advanced HCC: preliminary results**

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**Background:** Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer and the third leading cause of cancer-related death globally. Curative treatment (liver transplant and liver resection) can only be performed in 30% of cases. In the remainder, loco-

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**A meaning of ischemic pre-conditioning in patients undergoing major hepatectomy under total vascular isolation of the liver: a retrospective study**

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Bleeding and transfusion during major hepatectomy are the most significant risk factors for poor outcome. To

reduce bleeding and transfusions, major hepatectomy is performed under Pringle maneuver in combination with a low central venous pressure in many centers. In specialized centers which have many experiences in liver transplantation, Pringle maneuver and concomitant clamping of inferior vena cava below and above the liver, i.e. total vascular isolation (TVI), have been popularized. But Pringle maneuver during hepatectomy cause ischemia reperfusion (IR) injury. Ischemic pre-conditioning (IPC) is one of protective strategies that have been employed to reduce IR injury. Several patient series to date have argued the merits of IPC for hepatectomy. The aim of this study is to evaluate whether the ischemic pre-conditioning has the protective effect on post-operative outcomes in patients who underwent major hepatectomy under TVI. The records of 79 patients who underwent major hepatectomy under TVI were reviewed. They were divided into TVI alone (group A:  $n = 46$ ) and TVI with IPC (group B:  $n = 33$ ). The IPC group received 10 min of hepatic pedicle clamping and 3–5 min of reperfusion prior to hepatectomy under TVI. Operation time, blood loss, transfusion and clamping time were reviewed. The serum concentration of aspartate aminotransferase, alanine aminotransferase, total bilirubin, prothrombin time and creatinine were regularly determined. Hospital stay and complications including mortality and morbidity were determined. Post-operative laboratory results of liver function tests were not significantly different between groups. The concentrations of aspartate aminotransferase tended to be higher in the group 1 than in the group 2. The reverse trend was observed for alanine aminotransferase. The concentration of bilirubin tended to be higher in the group 1 than in the group 2. The hyperbilirubinemia developed less in the group 2 than in the group 1. There were no differences in prothrombin time, creatinine level between the two groups. The duration of ischemia was shorter in the group 2. But IPC had no impact on the duration of operation, intra-operative blood loss, and hospital stay. Our clinical use of IPC as a protective strategy against IR injury under hepatic TVI did not show any benefit of operative, laboratory parameters and clinical outcomes. More clinical study will be required to verify or disprove the merits of IPC far suggested primarily by animal studies.

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### Re-evaluation of standard liver volume (SLV) in patients undergoing living donor liver transplantation (LDLT) and liver resection

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**Introduction:** SLV denotes the ideal liver volume of each patient adjusted for body surface area (BSA). SLV was first applied by us to select the donor and/or the type of graft in LDLT. This concept has been extended by others to candidates for liver resection to assess the safe minimal size of future liver remnant. By contrast, we have been

using total liver volume (TLV) in candidates for liver resection.

**Aim:** To re-evaluate the validity of SLV as compared with TLV.

**Methods:** (i) In LDLT donors ( $n = 301$ ; age:  $37 \pm 12$  [17–66] years old), the relationship between BSA and TLV calculated by CT volumetry was explored. (ii) In LDLT recipients ( $n = 362$  age:  $40 \pm 21$  [0.6–67] years old), the relationship between BSA and TLV assessed by weight of explanted liver was explored. (iii) In LDLT donors, liver volumetry was conducted on 0.25 post-operative month (POM) ( $n = 33$ ), 0.5 POM ( $n = 33$ ), 1 POM ( $n = 31$ ), 3 POM ( $n = 28$ ), 6 POM ( $n = 25$ ), 12 POM (25), and 57 POM ( $n = 13$ ).

**Results:** (i, ii) The relationship between TLV and BSA was as follows: donor,  $TLV = -404.8 + 961.3 \times BSA$  ( $m^2$ ).  $R^2 = 0.58$ ; recipients,  $TLV = 387.4 + 362.2 \times BSA$  ( $m^2$ ).  $R^2 = 0.16$ . 3) The donor liver volume regeneration was as follows (mean  $\pm$  SD/TLV vs. /SLV): 0 POM,  $0.49 \pm 0.11$  vs.  $0.48 \pm 0.12$ ; 0.25 POM,  $0.57 \pm 0.097$  vs.  $0.56 \pm 0.098$ , 0.5 POM,  $0.62 \pm 0.087$  vs.  $0.61 \pm 0.095$ ; 1POM,  $0.68 \pm 0.091$  vs.  $0.65 \pm 0.10$ ; 6; 3 POM,  $0.75 \pm 0.075$  vs.  $0.73 \pm 0.088$ ; 6 POM,  $0.79 \pm 0.073$  vs.  $0.77 \pm 0.10$ ; 12 POM,  $0.82 \pm 0.068$  vs.  $0.81 \pm 0.091$ ; 56 POM,  $0.89 \pm 0.057$  vs.  $0.90 \pm 0.099$ .

**Conclusion:** In normal subjects such as donors of LDLT, body size (BSA) can explain 58% of interindividual difference in liver volume. After the extended liver resection, the liver volume increases irrespective of the extent of resection until 5 years. However, the model that the volume regeneration converges to their TLV is more appropriate than to their SLV as judged by chronological alteration in SD. In LDLT recipients, the liver size became abnormally large or small due to the underlying disease and SLV should be used as a notion of ideal liver volume. In patients indicated to liver resection, TLV instead of SLV should be used as reference volume.

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### Acute normovolemic hemodilution in major hepatic resections; risk factors for transfusion

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Major hepatic resection carries the risk of intra-operative hemorrhage and often requires transfusion. Acute Normovolemic hemodilution (NVH) has been shown to be safe and effective at reducing transfusion requirements during liver resection. However, risk factors for transfusion in patients undergoing NVH have not been previously reported.

**Methods:** Patients were selected for NVH if resection of 4 or more hepatic segments was intended. Patient outcomes were analyzed to determine risk factors for the need for transfusion. Variables were analyzed by logistic regression with forward selection of predictors of transfusion.

**Results:** A total of 254 patients underwent hepatic resection during the study period and 134 patients underwent NVH. Twenty-eight (20.9%) required transfusion. Age, Gender, OR Time, Central Venous Pressure, BMI, Type of Resection, Estimated Blood Loss (EBL) and Presence of Cirrhosis were evaluated as risk factors for transfusion during hospitalization. Only EBL was significantly related to the need for transfusion

( $P < 0.001$ ). The likelihood of transfusion was 0%, 8.33% and 50.0% when EBL was 925cc, respectively. In a multiple regression model with the dependent variable EBL, the only predictors that made a significant contribution to the regression equation were OR-time ( $P < 0.001$ ) and Tumor-size ( $P < 0.05$ ).

**Conclusions:** EBL is an independent risk factor for transfusion in patients undergoing NVH. EBL > 925 cc has a strong and significant relationship to the need for transfusion in patients undergoing NVH during major hepatic resection. OR time and Tumor size were independent and significant predictors of EBL.

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### Validating the MELD-based Objective Scoring System (MOSS) in patients with hepatocellular cancer treated with radiofrequency ablation

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**Introduction:** In an attempt to stratify survival in hepatocellular cancer (HCC) patients treated with non-liver transplant modalities, Oregon Health Sciences University (OHSU) developed the MELD-based objective scoring system (MOSS). In addition to MELD score MOSS incorporates tumor size (< vs.  $\geq 5$  cm), portal vein invasion, and the number of tumors (single vs. multiple). It was initially derived from a cohort of patients treated with transarterial chemoembolization or hepatic resection. The current study attempts to validate MOSS on HCC patients treated with radiofrequency ablation (RFA).

**Methods:** A retrospective analysis of 78 patients with HCC diagnosed between 1998 and 2008 who underwent RFA as a first treatment was performed. Patients who subsequently underwent a liver transplant were excluded. Patients were classified into MOSS group I, II, or III as described by OHSU. Survival between the three groups was compared using Kaplan–Meier and log-rank test. Variables associated with survival were determined using a Cox proportionate hazard regression model.

**Results:** Mean MELD and tumor size were 10 and 3.0 cm respectively. None of the RFA patients had portal vein invasion, 91% had tumors less than 5 cm in greatest diameter, and 77% had only one tumor. Similar to the results of OHSU, multivariate analysis demonstrated that tumor size and MELD score were associated with survival. Additionally, in this cohort age and albumin were also associated with survival. Median survival with 95% confidence intervals categorized by MOSS group is summarized in Table 1. Log-rank test showed a significant difference in survival between MOSS group I and III ( $P = 0.003$ ).

**Table 1.** Median survival of HCC patients treated with RFA stratified by MOSS class.

MOSS Group	Median survival (months)	95% Confidence Interval
MOSS I ( $n = 34$ )	59	32–67
MOSS II ( $n = 23$ )	29	9.7–42
MOSS III ( $n = 21$ )	20	6.1–23

**Conclusion:** Although MOSS group suggested a trend toward survival in HCC patients treated with RFA, the difference was only statistically significant between group I and III. Most of the patients who underwent RFA (69%) had single tumors less than 5 cm and no portal vein invasion. In these patients MOSS group is based entirely on MELD score. Further stratification and heavier weighting of tumor size in the scoring system might improve its ability to predict survival in HCC patients treated with RFA.

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### Spontaneous rupture of the non-malignant liver: our 13 year experience

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**Background:** Spontaneous rupture of the liver is a rare but potentially fatal condition. The aim of this study was to review the pathology and management of benign liver lesions presenting with rupture with particular reference to the role of delayed surgery.

**Methods:** Data were collected from a prospectively maintained database on patients presenting with liver rupture that were treated at Liver unit, Queen Elizabeth Hospital, Birmingham, UK between April 1995 and May 2008.

**Results:** The study included 21 females and 2 males. Nine patients were operated on during the same admission. The remainder fourteen were managed conservatively of these 10 patients had delayed surgical resection. The surgical treatment included ligation of right hepatic artery (1), partial hepatectomy (5), hemi-hepatectomy (8), hemi-hepatectomy with non-anatomical resection (2), extended hemi-hepatectomy (2) and total hepatectomy (1). Two patients who bled following eclampsia died after emergency resection. Surgical resection was facilitated following resolution of sub capsular haematoma in elective resection. Histological examination of the 19 lesions showed liver cell adenoma (LCA) in twelve, focal nodular hyperplasia (FNH) in four, peliosis hepatis in one, and pregnancy related intra-hepatic haemorrhage/infarction in two patients.

**Conclusion:** LCA is the most common benign lesion to present with spontaneous rupture, however atypical variants of FNH too can rarely rupture and present with bleeding. There is a role for conservative management in a haemodynamically stable patient.

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### Hepatic resection for the treatment of common bile duct injuries

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**Background:** Endoscopic, percutaneous and surgical procedures are used in the management of common bile duct injury (CBDI) diagnosed in late post-operative.

Hepatic resections are not indicated frequently. Indications for resection are: irreversible liver and biliary pathology generated by a vascular and/or biliary injury.

**Objective:** To analyse indication, outcome, technical and tactical aspects of mayor hepatic resections, to treat CBDI.

**Design:** Descriptive and retrospective study.

**Population:** A total of 205 patients with CBDI were treated between January 1988 and September 2008. Thirteen patients (6.4%) required mayor hepatic resections.

**Methods:** Six were men, mean age was 41.8 years old (range 6–62). Five open surgery and eight laparoscopic surgery were the causes of the CBDI. Probable mechanism of the injury were: ligatures in three patients, resection and thermal injury in 4, resection and arterial injury in 2, section in 2 and 2 unknown mechanism. Arterial injury was associated in 37.5% and portal injury in 12.5%, all of them diagnosed with angiography. The time (median) between the injury and the resection was 24 months (range 2–407). Previous surgeries: 2.4 (range 1–4). Clinical presentation: recurrent cholangitis in 8 patients, abdominal pain and jaundice in 2, biliary leak in 3. The indications to perform the hepatic resection were: 6 patients with intra-hepatic strictures, 5 with unilateral stricture with bilio-digestive derivation (after failed percutaneous dilatation), 1 with complex CBDI, 1 with right hepatic artery injury, and 1 with a probable tumor.

**Results:** We performed nine right hepatectomies and 4 left hepatectomies. Pringle's Maneuver was used in 7 patients. Mean operative time was 305 min (range 270–360). Any patient need red blood cell transfusions. Biliary reconstruction: in 11 cases hepatic-jejunostomy, and 1 case bi-hepatic-jejunostomy. Mortallity was 0% and morbidity was 37.5%. Mean follow-up 59.9 months (range 3–129).

**Conclusions:** Hepatic resection is a good treatment for complex CBDI (those associated with vascular injury and biliary confluence injury) followed by intra-hepatic strictures and/or lobar atrophy. Mayor hepatic resections are complex procedures because of the hepatic pedicle sclerosis, adhesences and atrophy-hipertrophy phenomenon.

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### **Tumor neo-angiogenesis is a key factor in the induction of tumor-specific t-cell tolerance**

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**Introduction:** Current literature suggests that tumor angiogenesis might differ from earlier to later stages of tumor development. We have developed a murine tumor model for Hepatocellular cancer (HCC) inoculating

syngeneic tumorigenic cells into the spleen of C57BL/6 mice. Four weeks after inoculation liver tumors reach a mean diameter of 1mm. At this point endogenous T cells remain ignorant of tumor associated antigens. However at 8 weeks post inoculation, when tumors have a diameter of 1 cm, T cells become immunologically tolerant. To explore the mechanisms of this transition we evaluated the pattern and level of tumor neo-angiogenesis at different stages of tumor development and the fate of adoptively transferred naïve tumor antigen specific T cells.

**Methods:** Four cohorts of three C57BL/6 mice were inoculated with syngeneic HCC cells expressing the T antigen (T-ag) of the SV40 virus via splenic injections (ISPL). Four and eight week later tumor growth in the liver was evaluated with magnetic resonance imaging. Two cohorts were adoptively transferred with naïve T cells specific for the epitope-I of the T-ag: one 4 weeks and one 8 weeks post-ISPL. The cohorts that did not receive any adoptive transfer were used as negative controls. C57BL/6 mice adoptively transferred with naïve T cells and immunized with cells expressing the full-length T-ag were used as a positive control. Seven days after transfer, epitope-I specific T cells proliferation and  $\gamma$ -interferon ( $\gamma$ -IFN) production assays were performed. Immunofluorescent staining for CD105 and VEGF3 was performed for liver specimens.

**Results:** All animals injected ISPL developed HCC. Liver tumors with 1 mm in diameter were negatively stained for both, VEGF3 and CD105. Normal liver parenchyma surrounding the tumor showed multiple vascular structures positively stained for CD105 and VEGF3. Adoptively transferred cells proliferated and produced  $\gamma$ -IFN in the spleen of these mice. Liver tumors with 1 cm in diameter showed an intense positive staining of CD105 and VEGF3. The periphery of tumors was stained more intensely in comparison with the core of tumors. The normal liver immediately surrounding the tumors also showed a marked increase in the level of expression of these markers. In this group of mice adoptively transferred cells failed to proliferate and produce  $\gamma$ -IFN.

**Conclusion:** At early stages of tumor development in the liver, low levels of neo-angiogenesis are present. As tumors grow, neo-angiogenesis starts predominantly in the periphery of tumors and in the surrounding liver parenchyma. These phenomena are correlated with the induction of tolerance to naïve tumor antigen specific T cells.

# Abstracts 136 to 145

## Oral Posters – Liver V

Saturday, March 14, 2009 7:00–8:00 AM

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### The biliary complications of radiofrequency assisted hepatectomy

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**Introduction:** A number of technology reliant techniques for liver transection have been developed, which has contributed to a reduction in the morbidity and mortality of liver surgery. However, the occurrence of biliary complications has remained essentially static, with an incidence of 4–10% being reported. The aim of this single institution study was to document the incidence and pattern of biliary complications following RF assisted hepatectomy.

**Methods:** Data were extracted from a prospectively maintained database. Bile leak related to hepaticojejunostomy were excluded from this analysis. Univariate analysis (Fisher exact and Mann–Whitney test.) was performed using SPSS (Statistical Package for Social Sciences for Windows 11.0.1, SPSS Inc, Chicago, IL, USA).

**Results:** From January 2002 to October 2007, 384 RF assisted liver resections were performed. There were 150 major and 234 minor resections, of which 36 were performed laparoscopically. The indication for liver resection were colorectal metastases in 228 (59%), neuroendocrine metastases in 15 (4%), non-colorectal non-neuroendocrine metastases in 52 (14%) and primary hepatobiliary tumors in 58 (15%) (hepatocellular carcinoma  $n = 30$ , intra-hepatic cholangiocarcinoma  $n = 2$ , extrahepatic cholangiocarcinoma  $n = 21$ , gallbladder cancer  $n = 5$ ). 31 (8%) resections were done for benign pathologies. There were six bile leaks (incidence 1.6%). Three were from the hilus, which presented in the immediate post-operative period with bile in the drain and were managed by ERCP. The remaining three bile leaks were parenchymal and presented 2–4 weeks post-discharge with infection in the ablation zone, after initial radiological drainage of pus, bile would then follow. There was one late RF biliary stricture (incidence 0.26%) at 4 months post-surgery, which had not been preceded by bile leak. The average length of follow up was 672 (range 4–2427) days. On statistical analysis, the categorical variables of portal vein embolization ( $P = 0.004$ ), major resection ( $P = 0.003$ ) and intra-abdominal collection ( $P = 0.019$ ) were found to have an association with the occurrence of bile leak.

**Conclusion:** In this series of RF assisted hepatectomies, the incidence of bile leak was low (1.6%) and late biliary strictures (0.26%) were rare. If used appropriately and paying respect to hepatobiliary anatomy, RF assisted hepatectomy appears to have equivalent, if not better biliostasis, compared with other techniques of liver transection.

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### Lysophosphatidic acid biosynthesis in hepatocellular carcinoma

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**Aim:** Lysophosphatidic acid (LPA) is an intercellular lipid mediator with growth factor-like activities, and has frequently been linked to the formation of cancer. However, to date, its role and biosynthetic pathway has not been fully investigated in hepatocellular cancer. One of the main LPA biosynthetic pathways is choline  $\Rightarrow$  phosphatidylcholine (PC)  $\Rightarrow$  lysophosphatidylcholine (LPC)  $\Rightarrow$  LPA. The aim of this study was to quantify LPA and LPA precursors in order to better understand hepatic malignancies.

**Methods:** Liver and bile samples were collected at the time of hepatic resection for hepatocellular carcinoma (HCC). All bile specimens were collected from the gallbladder at the beginning of the case. Normal bile was collected from patients undergoing cholecystectomy for non-neoplastic disease ( $n = 5$  per group). Liver biopsy samples were taken from both tumor and adjacent normal tissue. Bile and hepatic lipids were extracted in chloroform : methanol (2 : 1) and separated from amino acids, carbohydrates and bile acids by adding KCl. Choline and LPA were quantified by ELISA. Lipids were developed on silica gel G plates with chloroform : methanol : H<sub>2</sub>O (65 : 25 : 4), with phospholipid standards run in parallel. Phospholipids were detected with ammonium molybdate/mercury phosphate detection stain and quantitated by volume densitometry.

**Results:** Biliary choline and PC levels were similar between HCC and control patients. In contrast, biliary LPC and LPA was significantly increased 78.8% and 48% in patients with HCC when compared to controls. In HCC tumor PC and PE were both increased when compared to adjacent liver control. LPC was below detectable levels in adjacent liver but was detected in tumor tissue.

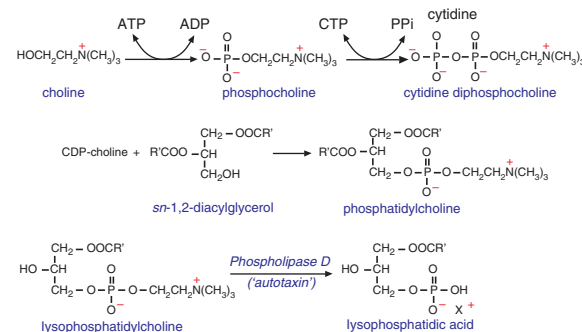


Figure 1.

**Conclusion:** LPA may be of great significance in the induction of hepatobiliary malignancies, including HCC. Increased PC and LPC biosynthesis would potentially increase LPA via the phospholipase D autotaxin.

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### Hepatic resection for recurrent metastatic gastrointestinal stromal tumors

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**Introduction:** Gastrointestinal stromal tumors (GISTs) have been associated with both a high rate of resistance to standard chemotherapy and radiation as well as a high recurrence rate following surgical resection. Therapy has evolved following the discovery that the oncogenic mutation of the c-kit gene was responsible for much of the malignant behavior of GISTs – improved survival has been realized with targeted therapies using imatinib, a tyrosine kinase inhibitor. Currently, the role of hepatic resection for non-colorectal, non-neuroendocrine metastases is less defined and at times controversial. Given that recurrent metastatic GISTs develop resistance and progression to imatinib, determining the utility of hepatic resection in recurrent metastatic GISTs remains unanswered.

**Objective:** Demonstrate the effect of hepatic resection on survival in recurrent metastatic GIST from a single institution.

**Methods:** Following IRB approval, consecutive patients who underwent hepatic resection for non-colorectal, non-neuroendocrine liver metastases from a single institution from 1998–2006 were identified. From this cohort, patients with a pathologic diagnosis of recurrent metastatic GIST were identified. Data were retrospectively reviewed and abstracted from the medical, surgical and pathologic records.

**Results:** Seven patients were identified with a median age of 48 (range 21–76 years) with the primary tumor location in the stomach. All patients considered for hepatic resection had demonstrated tumor progression despite imatinib therapy. The median interval between primary diagnosis and liver resection was 28 months (range 14–55 months). The types of liver resection performed were: trisegmentectomy-1, right hepatic lobectomy-3, left hepatic lobectomy-3. Six of the patients had radiofrequency ablation therapy for smaller, intra-parenchymal tumors identified intra-operatively. While there was no peri-operative mortality, 1 patient experienced a post-operative pneumothorax. The overall median survival was 19 months after hepatic resection-2 patients were dead of disease at 11.5 months and 5 patients were alive with disease at a median follow-up of 27 months. Following univariate analysis, no prognostic factors for improved overall survival were identified.

**Conclusion:** Hepatic resection for recurrent metastatic GIST does not result in increased morbidity or mortality. Furthermore, hepatic resection may allow for sufficient debulking to permit additional therapy with alternative therapies of GISTs that become resistant to imatinib. Larger cohort analysis may result in the identification of prognostic factors associated with improved outcomes.

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### Colorectal cancer liver metastases resection and systematic hilar lymphadenectomy. Analysis of lymph nodes micrometastases

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Hepatectomy is considered the best treatment of metastatic colorectal cancer. Several prognostic factors have been investigated, and many studies have shown that involvement of regional lymph nodes at the hepatic hilum represents a negative prognostic factor. The present study evaluated the frequency and characteristics of microscopic involvement of hilar lymph nodes, through systematic lymphadenectomy and analysis of micrometastases in patients undergoing hepatectomy due to colorectal metastases. A total of 28 patients underwent hepatic resection associated to lymphadenectomy of the hepatic hilum. Lymph nodes considered negative by conventional hematoxylin and eosin (HE) staining were analyzed by serial sectioning with 100-micron intervals and immunohistochemistry (IHC) with the anti-human pancytokeratin antibody AE1/AE3. In average, 6.18 lymph nodes were dissected per patient. Lymphadenectomy increased surgical time by 48 min in average, but no morbi-mortality was associated to the procedure. In two patients, conventional HE analysis showed the presence of microscopic lymph node metastases. IHC analysis allowed the identification of three other patients with lymph node micrometastases. The overall frequency of microscopic metastases, including micrometastases, was 18%. No statistically significant relationship was observed between other prognostic factors and the presence of microscopic metastases. Results show that systematic lymphadenectomy improved the detection of microscopic lymph node metastases, resulting in more accurate staging of extrahepatic disease. The inclusion of IHC for detection of micrometastases increased diagnostic sensitivity of lymph node involvement.

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### Pre- and post-chemotherapy computed tomography findings in the livers of patients with colorectal carcinoma undergoing adjuvant therapy: is steatosis always related to chemotherapy?

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**Background:** Recent literature suggests that chemotherapy-related changes in the livers of patients receiving adjuvant chemotherapy for colorectal carcinoma, in particular steatosis/steatohepatitis, may compromise the results of hepatic resection. However, current studies have relied on post-resection histopathology and thus it cannot be certain whether the changes were present prior to the commencement of chemotherapy.

**Aims:** To quantify steatotic changes in the livers of patients with colorectal carcinoma pre- and post-chemotherapy and to relate these to the type of chemotherapy received.

**Methods:** The pre- and post-chemotherapy computed tomography (CT) scans of patients receiving adjuvant chemotherapy following resection of colorectal carcinomas were reviewed independently by two consultant radiologists. All scans were performed on the same CT scanner using a standardised protocol. Liver attenuation was measured in 3 locations in the right and left lobes and splenic attenuation was measured likewise. A hepatic: splenic ratio < 1 as was indicative of steatosis. All measurements were made on the workstation. The distribution of steatosis was also noted.

**Results:** Forty-five consecutive patients were studied of which 25 received 5-fluorouracil, 14 oxaliplatin and 6 irinotecan-based chemotherapy. 16 patients (35%) had evidence of steatosis as indicated by a hepatic-splenic ratio < 1 prior to chemotherapy. This was diffuse and homogenous in 15 cases and with areas of focal sparing in 1 case. A further 7 (15%) patients developed CT evidence of steatosis following chemotherapy, 4 of which had received 5-fluorouracil and 1 was treated with oxaliplatin-based chemotherapy. In 6 cases this diffuse and homogenous and in 1 case was geographic.

**Conclusions:** Although 15% of patients developed steatotic changes whilst receiving chemotherapy, one third of patients already exhibited steatosis prior to commencement of therapy thus suggesting that it is imperative to consider baseline characteristics in planning adjuvant treatment.

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### Laparoscopic management of segment VII tumors

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**Background:** While laparoscopic ablation and resection of liver tumors is rapidly gaining momentum, the 'safe' areas for laparoscopy are typically limited to the left lobe and segments V and VI. However, as experience grows, the benefits of laparoscopy may be applied to patients with tumors outside of the 'safe' areas. We describe our early experience with laparoscopic treatment of segment VII tumors.

**Methods:** Reviewing our prospectively gathered databases, we identified 22 patients that underwent laparoscopic RFA or resection of segment VII tumors. RFA was used in patients with contraindications to resection or as bridge therapy toward transplantation. We analyzed the indications and operative approach for these operations. All procedures were done with the patient in the left lateral decubitus position. The liver is fully mobilized off of the retroperitoneum and diaphragm as necessary to fully access segment VII, the IVC, and right vein. RFA was done with either RITA (Angiodynamics) monopolar probes or InCircle (RFA-medical) bipolar probes. During resection, the parenchyma was pre-coagulated with either the lap Habib (Angiodynamics), TissueLink hook (Salient) or Monarch (RFA-medical). In some cases parenchymal division was done using Gyrus cutting bipolar forceps (Olympus) depending on nature of the liver parenchyma and surgeon preference.

**Results:** Fourteen patients underwent laparoscopic RFA and eight laparoscopic resections. The median age was 61 (range 59–88). The indications for surgery included primary tumors in 19 cases (HCC = 18; cholangiocarcinoma = 1) and metastatic tumors in three cases (breast, neuroendocrine, and colorectal). All hepatomas arose in the context of chronic HCV and thus some degree of fibrosis/cirrhosis. Among the RFAs, the average tumor was 4.2 cm (range 2–8). Eight underwent concomitant procedures (additional RFA elsewhere in 3; lap resection of seg 3 tumor in 1; cholecystectomy in 3; placement of gold fiducials in 1). Laparoscopic resections were completed in 7, while 1 patient required conversion. The average tumor size was 3.4 (range 2–5). Of these, 5 were posterior sectorectomies (seg 6 & 7), while 3 were isolated wedge resections of segment 7 tumors). In one case (posterior sectorectomy for 5 cm HCC), the case was converted to open for bleeding from the right hepatic vein.

**Conclusion:** Laparoscopic treatment of patients with tumors in segment VII can be applied to carefully selected patients. In fact, laparoscopy allows ablation or resection of these challenging posteriorly situated tumors in patients that would otherwise not be candidates for (open) surgery due to comorbidities and/or underlying chronic liver disease.

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### The role of percutaneous biopsy in the evaluation of liver lesions

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**Objective:** The objective of this study was to define the utilization and timing of diagnostic modalities (serum tumor markers, ultrasonography (U/S), computerized tomography (CT), magnetic resonance imaging (MR), percutaneous biopsy) employed in the evaluation of patients with liver lesions referred to a hepatopancreatobiliary (HPB) surgical practice. Our primary objective was to determine the role that percutaneous biopsy played in the assessment of these patients.

**Methods:** The medical records of a consecutive series of 201 patients presenting to a tertiary care HPB surgical practice with liver lesions from July 2004 to June 2007 were retrospectively reviewed. Data pertaining to the utilization, timing and results of serum tumor markers (CA 19-9, CEA, AFP), diagnostic imaging modalities (U/S, CT, MR), and liver biopsy were extracted for each patient. Details of management and the final diagnosis, defined by surgical pathology or serial follow-up, were recorded. For the patients that underwent percutaneous biopsy we determined its contribution to the establishment of the final diagnosis.

**Results:** Tumor markers were assayed in 128 of the 201 patients (64%). CT was the most commonly utilized imaging modality with at least one CT being obtained in 180 of the 201 patients (90%) followed by U/S in 104 (52%) and MR in 56 (28%). Twenty-nine patients in the series of 201 (14%) had a total of 34 percutaneous biopsies. Twenty patients (10%) had 24 biopsies prior to consultation and 10 had biopsy after consultation (one



patient had two biopsies performed prior to consultation and one after). Of the 24 biopsies performed prior to HPB surgical consultation, the results of nine contributed to establishing the final diagnosis (38%). When biopsy was carried out after HPB surgical consultation the results contributed to the final diagnosis in 8 of the 10 patients (80%). The difference between these two proportions is statistically significant ( $P = 0.024$ ). In the 172 patients that did not have a biopsy performed diagnostic accuracy was 91% (156 of 172 correct) vs. 86% (25 of 29 correct) when biopsy was utilized ( $P = 0.455$ ).

**Conclusions:** The results of this study suggest that, in the vast majority of cases, the accurate evaluation of liver lesions can be achieved without percutaneous biopsy. In this series percutaneous biopsy had a significantly greater utility when it was performed after consultation with a specialist in HPB surgery. We encourage the involvement of a specialist in HPB surgery in the evaluation of liver lesions, particularly if percutaneous biopsy is being considered.

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### Hepatocellular cancer in pacific islanders

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**Purpose:** Hepatocellular cancer (HCC) has a high incidence in Asian countries and is increasing in incidence in the US. The ethnicity broadly described as 'Asian and Pacific Islanders' is known to have an especially high incidence in the US, but no study has characterized HCC in the subgroup of Pacific Islanders alone.

**Methods:** This is a retrospective study of a prospectively collected database on HCC patients from 1993 to 2008. Data collected included demographics, risk factors, tumor characteristics, laboratory studies, treatment and survival. Of 523 patients with HCC, 72 were identified as Pacific Islanders and this group was compared to 85 patients in the cohort who were Caucasian. Chi-square analyses were used to identify differences in the above characteristics between the groups. Cox proportional hazards model was used to determine regression analysis of survival data.

**Results:** In Pacific Islanders, mean age was 55.6 years with males : females of 58 : 14 which was not significantly different in distribution from Caucasians. Pacific Islanders were more likely to have hepatitis B (36.1% vs. 5.9%,  $P < 0.05$ ), symptoms at presentation (59.7% vs. 41.2%,  $P = 0.003$ ), and larger tumors ( $P = 0.02$ ). Caucasians were more likely to have hepatitis C (64.7% vs. 43.1%,  $P = 0.012$ ) and encephalopathy (30.9% vs. 12.7%,  $P = 0.007$ ). Although more HCC was found on screening in Caucasians (16.7%) compared to Pacific Islanders (6.9%), this was not statistically significant. Mean survival was not different between Pacific Islanders (10.9 months, 95% CI 6.77–24.1) and Caucasians (43.3 months, 95% CI 21.2–75.5). Using backwards multivariate regression analysis, factors that were associated with decreased survival included late stage III/IV at presentation (Hazard ratio 3.2), female gender (HR 2.58), increased Childs-Turcotte-Pugh score (HR 2.52), smoking (HR 2.1), and alcohol use (HR 2.0). Ethnicity did not independently affect survival.

**Conclusion:** Pacific Islanders were more likely to have hepatitis B and present with symptoms and larger tumors, though they were just as likely to have their HCC

found upon screening. Although ethnicity did not independently affect survival, efforts should be made to better educate the community on the importance of identifying hepatitis B in Pacific Islanders, vaccinating against preventable hepatitis B and recognizing the risk for HCC in this group.

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### Liver hanging maneuver improves the outcomes of complex right upper quadrant resections

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**Background:** While the feasibility and technique of the liver hanging maneuver (HM) have been reported, its indications and advantages have not been defined for resection of hepatic and perihepatic malignancies.

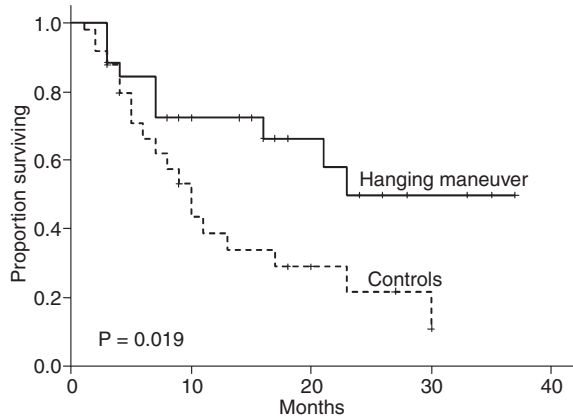
**Methods:** Medical records of patients who underwent right or extended right hepatectomy at a single institution between January 2000 and February 2007 were reviewed. HM was performed by passing a Penrose drain through the avascular retrohepatic space to suspend the liver during parenchymal transection. Patients who underwent HM were identified and compared with a group of matched controls who underwent hepatic resection via a conventional approach.

**Results:** Right or extended right hepatectomy was performed by HM in 26 patients and conventional approach in 127 patients. The two groups were similar with respect to age, gender, number of tumors, operative time, repeat liver resection, and post-operative morbidity and mortality. Compared to the conventional group, more patients in the HM group underwent hepatectomy for adrenocortical carcinoma ( $P = 0.002$ ), resection of contiguous structures ( $P < 0.001$ ), and had larger tumors (median size 7.5 cm, HM vs. 4 cm, conventional,  $P = 0.001$ ). Based on these clinicopathologic variables, the 26 HM patients were matched with 26 control patients. Compared to matched controls, HM patients had less intra-operative tumor rupture, intra-operative blood loss, and blood transfusions (Table 1). Fewer patients in the HM group had positive margins and tumor recurrence, resulting in a longer disease-free survival (median 23 months, HM vs. 10 months, control,  $P = 0.019$ ).

**Conclusion:** Indications for the liver hanging maneuver during right or extended right hepatectomy include large tumor size and resection of contiguous structures. For complex right upper quadrant malignancies, the liver hanging maneuver results in superior peri-operative and oncologic outcomes compared to conventional hepatectomy.

**Table 1. Results.**

Peri-operative and oncologic factors			
	Hanging maneuver, n (%)	Matched controls, n (%)	P-value
Intra-operative tumor rupture	0	3 (12%)	0.074
Median blood loss, mL (range)	475 (150–2500)	770 (200–4000)	0.013
Intra-operative blood transfusion	8 (31%)	15 (58%)	0.039
Positive margins	2 (8%)	12 (46%)	0.013
Disease recurrence	10 (38%)	18 (69%)	0.008



**Figure 1.** Disease-free survival after hepatectomy.

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### Impact factors influencing the results of radio-frequency ablation of primary and metastatic liver tumors – review of 17152 cases of the literature

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**Introduction:** The radiofrequency ablation (RFA) of primary and metastatic hepatic tumors is a well-known method used as treatment or palliation.

**Methods:** Review of 17.152 cases, in which the radio-frequency ablation (RFA) was performed percutaneously, laparoscopically or by laparotomy on the treatment of focal primary and metastatic hepatic lesions. The group was composed by 9959 cases of hepatocellular carcinoma, 4334 cases of colorectal liver metastasis and 2579 cases of other kinds of metastasis, such as neuroendocrine carcinoma, metastasis of breast tumor, cholangiocarcinoma; pancreatic tumor metastasis; metastasis of renal cell carcinoma, endometrial tumor metastasis, leiomyosarcoma hepatic metastasis and others.

**Results:** The way of approach most commonly used was the percutaneous route with 86.6%, followed by laparotomy 48% and laparoscopic with 25.3%. Among the groups that describe the mean of lesions treated, that represented 1.40 lesions by case, with a mean size of 2.65 cm per lesion. In the overall average size of the lesions was 3.05 cm. The recurrence rate after the procedure was 26% on average.

**Conclusion:** The RFA is a safe procedure, however, the size of the lesion less than 3 cm and the means of approach carry an important factor in the recurrence rates. Laparotomy is related with the lower recurrence rate due to the best placement of the electrodes and may be considered the most appropriate however more invasive way to approach the lesions when compared to percutaneous and laparoscopic methods.

Abstracts 146 to 153  
Oral Posters – Pancreas III  
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**The microbiology of secondary and tertiary pancreatic infections: implications for antimicrobial therapy**

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Infections within the pancreatic bed following acute pancreatitis and after elective resection remain common. Prior data has suggested a shift from enteric to gram-positive organisms in those receiving antibiotic prophylaxis for severe acute pancreatitis (SAP). The flora responsible for tertiary infections following elective resection have been ill defined. We retrospectively reviewed patients developing secondary and tertiary pancreatic infections at the University of Tennessee, Memphis affiliated hospitals from 1997–2008. Factors examined relating to secondary pancreatitis included pre-operative antibiotic use and antecedent extra-pancreatic infections potentially implicated in seeding the pancreatic bed. All patients having elective resection received 24–48 h of antibiotic prophylaxis. All infections were scrutinized for the incidence of non-enteric, resistant and fungal organisms. Twenty patients (8 pancreatic necrosis, 12 pseudocyst) required surgery for secondary infections with the recovery of 33 isolates. Fourteen patients received vancomycin prior to surgical intervention either to treat extra-pancreatic infection or as prophylaxis for SAP. Six of these 14 had surgical isolates positive for *Enterococcus faecalis* – 4 of which were vancomycin resistant (VRE). Eight patients received antifungal prophylaxis with no fungi recovered from intra-operative culture. In contrast, 2 patients not receiving empiric therapy had positive fungal isolates. Four patients with pseudocysts requiring urgent operation for sepsis had organisms similar to those recently recovered from central lines. Tertiary infections occurred in 38 (17.8%) of 213 patients having elective resection with the recovery of 73 pathogens. Twenty-one (55.2%) patients had polymicrobial infections. Thirty-five (47.9%) and 16 (21.9%) of the isolates obtained were Gram-positive and fungal organisms respectively. Sixteen (21.9%) comprised resistant bacteria including methicillin-resistant *Staphylococcus aureus*, VRE and extended spectrum  $\beta$ -lactamase producing Gram-negative bacilli. We conclude the following: (i) Prolonged vancomycin use in those with SAP is associated with the development of VRE. (ii) Empiric antifungal therapy may reduce the incidence of secondary fungal pancreatic infections. (iii) Systemic bloodstream infections from extra-pancreatic sites can lead to the rapid seeding of pancreatic pseudocysts (iv) Tertiary infections of the pancreas frequently include Gram-positive, fungal and resistant organisms. (v) Empiric therapy directed at these tertiary pathogens should be utilized until definitive cultures are obtained.

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**Laparoscopic vs. open distal pancreatectomy for pancreatic adenocarcinoma of the body or tail**

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**Introduction:** Utilization of the laparoscopic approach for distal pancreatectomy in patients with benign or premalignant lesions is increasing. However, the feasibility and oncologic outcomes of this approach with specific regard to pancreatic adenocarcinoma are not known. The aim of this study is to compare the technical aspects and outcome of patients undergoing open (ODP) or laparoscopic (LDP) distal pancreatectomy for pancreatic adenocarcinoma.

**Methods:** We conducted a retrospective review of patients having undergone LDP or ODP for pancreatic adenocarcinoma at a single institution from May 2005 to May 2008. Follow up was complete for a mean of 14 months.

**Results:** A total of 45 patients were identified having undergone a distal pancreatectomy and splenectomy for adenocarcinoma during the study time period. LDP was performed in 10 patients and ODP in 35 patients, with a mean age of 66 vs. 65 years respectively. In all patients, an R0 resection was achieved; adjacent organ resection was performed when necessary. There were no statistical differences in operative time (228 vs. 225 min), tumor size (3.4 vs. 4.5 cm), or number of lymph nodes harvested (14 vs. 11) between the LDP or ODP groups respectively. Patients undergoing LDP demonstrated reduced operative blood loss (150 vs. 750 mL;  $P < 0.001$ ), and shorter length of hospital stay (7 vs. 8 days;  $P = 0.05$ ). The overall incidence of peri-operative complications did not differ between groups. Peri-operative 30-day or in-hospital mortality occurred in 1 patient in the LDP and no patients in the ODP group. Median survival was similar for both groups (14.9 vs. 14.6 months;  $P = 0.64$ ).

**Conclusion:** Laparoscopic distal pancreatectomy for pancreatic adenocarcinoma of the body or tail is feasible and appears to result in equivalent oncologic resection and patient outcomes. Advantages of the laparoscopic approach include reduced operative blood loss and shorter hospital stay. Further investigation in a large, controlled trial is warranted.

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**Office-based, mini-laparoscopy without general anesthesia for staging of pancreatic carcinoma**

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Expedient diagnosis of patients with metastatic pancreatic carcinoma would facilitate patient management and avoid unnecessary interventions. We studied the use of mini-laparoscopy for early staging of suspected pancreatic carcinoma. A prospective trial was initiated to study the feasibility of low insufflation pressure mini-laparoscopy without general anesthesia. An initial pilot study was performed in an ambulatory operating room with an anesthesiologist with the aim of extending this to an office-based setting using nurse-monitored sedation. Following local anesthetic administration (1% lidocaine and 0.25% marcaine), Veress needle insufflation to 8 mm Hg was achieved. Diagnostic laparoscopy was performed using a 2 mm laparoscope. General inspection of the peritoneal cavity, liver and diaphragm were performed as well as directed biopsies and peritoneal washings. Intravenous sedation was utilized in two temporal phases: Phase 1 with meperidine and midazolam, and Phase 2 with dexmedetomidine (Precedex). Post-operative pain and outcome of laparoscopic findings were compared to standard laparoscopy done under general anesthesia. Twenty-five patients underwent diagnostic mini-laparoscopy with a mean age of 66 years (range 43–83). The mean pancreatic mass size was 3.03 cm. Four patients had prior abdominal incisions, and the mean BMI was 24.5. All patients had a supra-umbilical trocar placed, and 22 patients had a second trocar in the epigastrium or RUQ. A forceps liver biopsy was done in 9 (36%) and a peritoneal biopsy in one. Peritoneal washings were done in 16 (64%) with mean volume of 73 cc's aspirated. Metastatic carcinoma was identified in 4 (16%) and all findings from the mini-laparoscopy were consistent with those at standard diagnostic laparoscopy. Twelve patients were performed during Phase 1 anesthesia. A total dose of 117.8 mg of meperidine or 281.2 mcg of fentanyl, 4.0 mg of midazolam, and 30 mg of ketorolac (Toradol) were used. Thirteen patients during Phase 2 required a total mean dose of 157 mcg Precedex and 100 mcg of fentanyl. The pre-operative pain scale was zero in eleven patients (44%) and averaged 3.6 in those with pain (range 2–8). The post-operative pain scale was 0 in 6 (24%) and averaged 4.5 in those with pain (range 1–9). The mean time to pre-operative pain level was 1.8 days. There was no peri-operative morbidity and the mean length of mini-laparoscopy was 14.2 min (range 7–40). In conclusion, mini-laparoscopy with biopsy and washings is safe and accurate. Patient tolerance is suboptimal with meperidine and midazolam, and only minimally improved with Precedex administration. Current state of the art does not foresee use as an office based procedure with nurse managed sedation.

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**Analysis of adjuvant gemcitabine chemotherapy concomitant with gemcitabine-based chemoradiation therapy for resected pancreatic cancer: a retrospective study**

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**Introduction:** Pancreatic cancer has a very poor prognosis. Improving the outcome for patients with pancreatic cancer depends on increasing the rate of complete surgical resection and reducing the rate of local recurrence and distant metastasis. After resection of pancreatic cancer, we treated patients with gemcitabine chemotherapy concomitant with gemcitabine-based chemoradiation therapy since 2001.

**Aims and methods:** Thirty-six patients (mean age: 60.7, range: 43–75, pancreatic head tumors:  $n = 26$ , body and tail tumors:  $n = 10$ ) with stage 3 or 4 cancer (Japan Pancreatic Society, the fifth edition) treated between April 2001 and December 2007 were included in this study. In the group with pancreatic head tumors, patients were given a single post-operative course of gemcitabine chemotherapy consisting of gemcitabine 1000 mg/m<sup>2</sup> on Days 1, 8 and 21 after surgery. Then extra beam radiotherapy at a dose of 41.4Gy/23fr to the tumor bed and regional node was performed concomitant with the administration of gemcitabine 250 mg/m<sup>2</sup> weekly. After completion of chemoradiation therapy, patients received five more courses of gemcitabine chemotherapy. In the group with pancreatic body and tail tumors, intra-operative radiation therapy at a dose of 20Gy was performed after resection of the tumor then patients received six courses of gemcitabine chemotherapy after surgery. In eight cases a combination of systemic and intra-arterial chemotherapy with gemcitabine was given. Patients were followed with CT scanning at 3-month intervals for 1 year. We evaluated disease-free survival and an overall survival determined by the Kaplan-Meier method retrospectively.

**Results:** This regimen was well tolerated and all patients completed radiation therapy as planned. Local relapse occurred 23% of patients and Liver metastasis occurred 46% of patients. The median disease-free survival (DFS) was 15.3 months, median overall survival (OS) was 28.6 months and the overall 5-year survival was 12.1%. Patients had a DFS of 16.6 months in local relapse group vs. a DFS of 8.3 months in liver metastasis group.

**Conclusion:** Although our findings suggest a survival benefit for patients with resected pancreatic cancer, it is necessary to perform a prospective trial of gemcitabine concomitant with gemcitabine-based chemoradiation vs. gemcitabine alone following surgery in order to verify this finding.

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### Malignant potential in intra-ductal papillary mucinous neoplasm (IPMN): why observe?

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**Background:** IPMNs are well established as lesions with an evolving natural history and treatment options include surgery. IPMNs when present as cystic lesions may still bear a malignant tumor which may go undetected, even with endoscopic ultrasound (EUS). Various studies have cited factors which may suggest a slow progression and warrant observation of IPMN. IPMN are sub typed based on their location as main duct type, branch duct type and mixed type. There are conflicting studies as to which subtype suggests slow progression. The purpose of this study was to look at the incidence of IPMN, presence of malignancy in IPMN and incidence of its subtypes based on location, in our cohort of patients that underwent pancreaticoduodenectomy (PD).

**Methods:** A retrospective chart review of 122 patients that underwent a pancreaticoduodenectomy from September 2005 to August 2008 at a Non University tertiary training center was performed. Pre-operative workup included EUS with FNA and ERCP. The demographic parameters and outcome of this group was studied.

**Results:** After a pancreaticoduodenectomy, twenty two patients (18%) were diagnosed with IPMN located in the pancreatic head. Seven patients had IPMN of main duct type, 4 had branch type and 11 had a mixed type. The incidence of cancer with IPMNs was 18% (4 patients), of which, 2 had the main duct type and two had the mixed duct type. Two patients had a pre-operative diagnosis of established. Two of the patients with malignancy were pre-operatively jaundiced (50%), while only one (6%) was jaundiced in the non-malignant group. Overall four patients underwent a total Pancreatectomy for papillary features on frozen section at the resection margin, of which one was from the malignant group.

**Conclusion:** IPMN is an entity that needs to be managed with a PD. The incidence of malignancy with IPMN was 18% in our series. IPMNs of the pancreatic head should be managed with low threshold for resection irrespective of their type or location even with a negative cytology.

**Methods:** Between 1994 and 2007, 21 patients were treated for NFNEPTs. Their investigations, surgery, histology and clinical outcome were reviewed retrospectively.

**Results:** There were 11 men and 10 women of median age 49 (range 26–76) years. Gut hormone profiles were normal in all patients. Contrast-enhanced computed tomography localised the tumour in 20 patients and visceral angiography in 15 of 16. The NFNEPTs were located in the head in 16 patients, body in 2 and tail in 3. Eleven patients underwent curative resection (pancreaticoduodenectomy [PD]  $n = 8$ , distal pancreatectomy  $n = 2$  and laparoscopic enucleation  $n = 1$ ) and 10 palliative resection (PD  $n = 6$ , total and distal pancreatectomy two each). Four patients had concomitant liver resections (curative and palliative two each). There were no operative deaths. The median tumour size was 4.5 (1–17) cm. Seventeen tumours were malignant (angioinvasion = 14, perineural invasion = 2 and positive lymph nodes = 10). Ten patients received adjuvant therapy (chemotherapy  $n = 2$ , embolisation  $n = 2$ , chemotherapy and embolisation  $n = 1$ ,  $\alpha$ -interferon  $n = 2$ , targeted radionuclide therapy  $n = 1$ , targeted radionuclide therapy and radiation  $n = 1$ ). Nine patients have died from disease a median of 43 (range 10–141) months after operation. The 12 survivors, 7 of whom had curative resections, have been followed for a median of 46 (range 24–95) months. Ten patients are asymptomatic but only five are free from disease.

**Conclusions:** Although surgical cure is rare in NFNEPTs, long-term palliation can be achieved with an aggressive surgical approach and adjuvant therapy.

**Table 1.** Immunohistochemical markers.

Marker	No (%)
Chromogranin A	14 (66)
Neuron specific enolase (NSE)	13 (61)
Synaptophysin	9 (42)
Cytokeratin	7 (33)
Protein-gene product (PGP)9.5	6 (28)
VIP	1 (5)
Pancreatic Polypeptide	1 (5)
Somatostatin	1 (5)

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### Surgical management of non-functioning neuroendocrine pancreatic tumours

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**Introduction:** Due to their slow growth and inability to produce hormone-dependent symptoms, non-functioning neuroendocrine pancreatic tumours (NFNEPTs) usually have an indolent natural history. Surgical treatment of these tumours has become increasingly important for symptom palliation and survival. The aim of this study was to assess the role of surgery, adjuvant therapy and outcomes of NFNEPTs based on the experience of a single institution.

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### Vascular endothelial growth factor (VEGF) and placental growth factor (PIGF) in patients with pancreatic cancer

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**Purpose:** To determine if pancreatic adenocarcinoma produces VEGF and/or PIGF and if levels of these factors are elevated in plasma of patients with this disease.

**Methods:** From November, 2006, to May, 2008, at New York University Medical Center, patients with pancreatic adenocarcinoma undergoing potential tumor resections were recruited for study. Healthy patients

$\geq 50$  years old scheduled for elective hernia repair were recruited as controls. Immunohistochemistry (IHC) was performed on cancer specimens using anti-human VEGF and anti-human PlGF (Santa Cruz Biotechnology Santa Cruz, CA, USA). A biotin-streptavidin system was used for visualization. Staining was measured as the overall percent of cells staining within one high-power field, and the scale used was 0 = no staining, 1+ =  $< 1\%$ , 2+ = 1–10%, 3+ = 11–50%, and 4+ =  $> 50\%$ . For plasma, 8 mL of venous blood was collected pre-operatively in K2-EDTA containing Vacutainer tubes (Becton, Dickinson and Company Franklin Lakes, NJ, USA) with platelet depletion via high-speed centrifugation. Human Quantikine Kits (R&D Systems Minneapolis, MN, USA) targeting VEGF or PlGF were used. Mann-Whitney test was used for comparison of pancreatic cancer patients vs. controls. Two-sided tests were performed and run at a significance level of 0.05.

**Results:** IHC of normal pancreas demonstrated VEGF staining in ductular and acinar cells and PlGF staining in Islets of Langerhans. Tumor cells in all cancers ( $n = 8$ ) stained for VEGF and PlGF. Five of eight tumors had  $\geq 11\%$  of cancer cells positive for these factors. Inflammatory cells associated with tumor did not stain for VEGF (between 0 and  $< 1\%$ ), although they did stain for PlGF (between 1 and 50%). Plasma samples demonstrated no differences in VEGF levels between the cancer group ( $n = 10$ ) and the control group ( $n = 9$ ), but cancer patients demonstrated elevated levels of PlGF. Median VEGF plasma levels were 37.85 pg/mL for the cancer group and 42.93 pg/mL for controls. The median PlGF plasma level was elevated to 12.74 pg/mL for the cancer group compared to 8.71 pg/mL for controls ( $P = 0.053$ ).

**Conclusions:** (i) Pancreatic cancer is a source of pro-angiogenic VEGF and PlGF. (ii) Tumor-associated inflammatory cells may contribute to neovascularization via PlGF production. (iii) PlGF, which is thought to act synergistically with VEGF, is elevated in the plasma of pancreatic cancer patients. (iv) Realizing that bevacizumab, which targets only VEGF, does not affect patients with pancreatic cancer, targeting both VEGF and PlGF and/or their receptors may be important for successful anti-angiogenic therapy in patients with this disease.

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### Laparoscopic pancreatectomy under the scrutiny

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**Aim:** A systematic review carried out to assess the published evidence for safety, feasibility and reproducibility of laparoscopic pancreatectomy.

**Material and methods:** Literature search used Medline, EMBase and Pre-medline databases. A total of 397 patients (22 series) of laparoscopic distal pancreatectomy and Laparoscopic Enucleation (LEn) and 50 patients (5 series) of laparoscopic pancreaticoduodenectomy (LPD) were included.

**Result:** In over 90% of cases the disease was benign (45% are neuroendocrine lesions). The mean tumor size ranged from 1.8–5.8 cm. Spleen preservation was reported in around 37% of the LDP. The mean blood loss and average operative time was 278 mL (100–1800) and 192 min (104–354) respectively. Approximately 16% (0–40%) of the procedures were converted to open. LEn was feasible in around 22% of the cases. When compared with LDP, LEn incurred significantly less operative blood loss [10 vs. 38 mL; ( $P < 0.001$ )], shorter mean operative time [152 vs. 251 min ( $P < 0.001$ )] and shorter mean post-operative hospital stay [4.7 vs. 0.4 days ( $P < 0.001$ )]. Post-operative complications, pancreatic fistula and Re-operation were 26%, 13% (0–33%) and 8% respectively. The first 30-days mortality rate was around 0.5%. Mean post-operative hospital stay ranged between 4.1 and 11.8 days. Recurrence of the original pathology was observed in only 8 patients. In LPD cancer was the indication in over a third of patients. The mean operative time and blood loss were 410 min and 222 mL respectively. In 14% the procedure was converted to open. The recovery was uncomplicated in 76% of the patients, only 4 patients (8%) requiring re-operation. The operative mortality and mean post-operative hospital stay was 6% and 16.5 days respectively. The disease recurred in six patients (12%).

**Conclusion:** LDP is a feasible primary approach. The procedure requires a very skillful surgeon and advanced laparoscopic setting. In LPD it is still experimental in approach and need to be investigated further.

# Abstracts 154 to 163

## Oral Posters – Transplant II/Basic Science

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#### Post-operative complications in live liver donors after partial hepatectomy for liver transplantation

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**Introduction:** Donor safety is the first priority in living donor liver transplantation (LDLT). We evaluated the post-operative morbidity after partial hepatectomy for LDLT in our unit.

**Method:** Thirty patients underwent LDLT between 1997 and 2007 at our institution. This represented approximately 8% of the total liver transplant experience during that period. The type of graft was the right lobe (segments 5–8) in 14, left lobe (segments 1–4) in 4, and left lateral sector (segments 2 and 3) in 12 patients. There were 18 adults and 12 pediatric recipients. Mean donor age was 36 years (26–57). The mean follow-up was 48 months (range 6–120 months). Complications were classified according to Clavien's system: grade I, deviation from the normal post-operative course but without the need for therapy; grade II, complication requiring pharmacologic treatment; grade III, complication with the need for surgical, endoscopic or radiological intervention (IIIa/b: without/with the need for general anesthesia); grade IV, life-threatening complication requiring intensive care; grade V, death.

**Results:** No deaths occurred. Overall 8 (26.6%) patients experienced a total of 14 post-operative complications. Mean length of hospitalization was 7.5 days (5–12 days). Donor complications based on graft type were as follows: left lateral sector (16.7%), left lobe (25%), and right lobe (35.7%). Type of and grade of complications are summarized in the Table 1. The experience was divided into two periods 1997–2001 (15 patients) and 2002–2007 (15 patients). Overall complications during two periods were 40% and 13.3%, respectively ( $P < 0.001$ ). The incidence of grade III complication also decreased significantly, 63.6% vs. 33.3 ( $P < 0.01$ ).

**Table 1.** Complications.

Grade of complications: n (%)	Complications (1997–2001) (n)	Complications (2002–2007)
I: 4 (28.6%)	atelectasis (2), superficial phlebitis (1)	a
II: 1 (7.1%)	Ileus (1)	0
IIIa: 7 (50%)	Biloma (3), perihepatic fluid collection (1), pleural effusion (1), GI bleeding (1)	peripancreatic fluid collection (1)
IIIb: 2 (14.3%)	wound dehiscence (1)	ventral hernia (1)
IV: 0	0	0
V: 0	0	0

**Conclusion:** Partial hepatectomy in living donors has a learning curve which appears to approximate is about 15 cases. This learning curve is not restricted to the surgeons performing the procedure but involves all areas of peri- and post-operative patient care. Our experience emphasizes that LDLT can be safely provided by active liver transplant programs performing only modest number of LDLT.

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#### Retransplantation of the liver: the Columbia University experience

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Primary graft failure, recurrence disease and technical complications contribute significantly to decreased graft and patient survival after liver transplantation. Re-transplant is only option for patient with end-stage liver disease after transplantation. Retransplantation is historical associated with worse outcomes than primary transplant.

**Aim:** The purpose of our study is to present our experience of re-OLT for patients with graft failure after primary transplantation.

**Materials and methods:** We analyzed retrospectively the clinical data of 54 patients who were offered re-OLT for liver failure, including the indications, timing, causes of death and survival rates. Between the period June 1998 and June 2008, 817 adult patients were treated with liver transplantation, and 54 (6.6%) underwent re-transplantation. One of them needed a second re-OLT.

**Results:** The indications for re-OLT included: recurrence of viral induced hepatitis C (24 cases), primary non-function (15 cases), biliary cast syndrome (5 cases), biliary obstruction (4 cases), hepatic artery thrombosis (3 cases), outflow obstruction (1 case), chronic rejection (1 case), acute graft failure following portal vein thrombosis reconstruction (1 case), and refractory ITP (1 case). The timing of re-OLT was between 2 days and 6 years. The most common cause of death was sepsis (65%), usually associated with multi-organ failure. The 1-month, 1-year, and 3-year survival rates were 86.9%, 64.4% and 56% respectively. How common was recurrent hepatitis C as cause of retransplant failure/death?

**Conclusions:** Retransplantation remains a challenging clinical entity but sepsis rather than recurrent disease is the primary cause of death. Efforts in the future should focus on novel and reduced immunosuppression for patients undergoing retransplantation.

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#### Approach to management of excluded bile ducts in pediatric orthotopic liver transplantation

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Wider application of orthotopic liver transplantation (OLT) with living donor, cadaveric reduced and split allografts has reduced pediatric waiting list mortality. Segmental grafts have increased risk of biliary complications. A complication which can lead to graft



loss is exclusion of a major segmental bile duct. We present three cases and describe an algorithm to correct these complications.

**Case 1:** A 6-month-old girl underwent OLT for biliary atresia with a segment 2/3 graft from an *in situ* cadaveric split liver. She became jaundiced 1 month later. Hepatic ultrasonography revealed a dilated biliary tree and percutaneous transhepatic cholangiography (PTC) demonstrated complete obstruction of the segment two bile duct system. Following external biliary decompression, she was explored and the excluded duct was anastomosed to the existing Roux limb using the indwelling PTC catheter as a guide.

**Case 2:** A 5-month-old boy with biliary atresia received a segment 2/3 graft from a living donor. Reexploration for fevers and leukocytosis revealed a biloma, but no identifiable leak. An area of bile staining on the cut surface was oversewn and drained. Persistent drainage prompted a PTC which demonstrated an aberrant biliary tree draining a large portion of segment 3. This was not evident on the donor MRCP. It was managed with external biliary drainage followed by exploration and hepaticojejunostomy using the PTC catheter as a guide.

**Case 3:** A 4 year-old girl with OTC deficiency received a segment 2/3 graft from an *in situ* cadaveric split liver. Two bile ducts were identified during procurement and Roux-en-Y hepaticojejunostomy was performed for each. She required percutaneous drainage of a biloma post-operatively. An abdominal CT scan revealed an isolated dilated biliary tract. The excluded system drained the medial graft; the other two systems appeared normal. This was again managed with PTC for external drainage and interval revision hepaticojejunostomy. The patient developed a post-operative anastomotic stricture requiring PTC and dilation. Segmental allografts have an increased incidence of biliary complications. Although unusual, suspicion should remain high for an excluded bile duct if the patient develops jaundice or increased liver enzymes. Aggressive diagnosis, percutaneous decompression, and interval revision hepaticojejunostomy are the main tenets of management. Careful revision hepaticojejunostomy over a percutaneous biliary stent can result in restoration of biliary continuity and allograft survival.

complication rates such as bile leaks, vascular thrombotic events and bowel obstructions. Because most pediatric liver transplants are re-operative procedures, diaphragmatic complications such as paralysis or the development of a diaphragmatic hernia can occur. However, the incidence of diaphragmatic hernia (DH) remains unknown. We present three patients with this complication and a review of the literature. Our center has performed 122 liver transplants in children < 17 years of age between 1996 and 2007. Of these, 59 were whole organ grafts and 63 were reduced size grafts (16 were *ex situ* split or cut-down grafts, 18 were *in situ* split grafts and 29 were living grafts). Patient 1 is a 10 y/o girl who received an OLT with (left lateral segment) from an *in situ* split graft for Alagille's syndrome. A CT scan was unrevealing. After failure to improve she was explored and a right sided DH was identified and repaired primarily. Patient 2 is an 18-month-old girl with a history of biliary atresia s/p Kasai procedure who received an OLT with a left lobe reduced size graft obtained from an *ex situ* split. Her DH was repaired with a bridge of Alloderm to prevent tension on the repair. Patient 3 is a 5-year-old girl who underwent an OLT for an unresectable 15 × 10 cm embryonal sarcoma with a left lateral segment obtained from an *in situ* split. Her DH was performed primarily. To date there are only seven reported cases of children developing right sided diaphragmatic hernias following partial liver transplantation. The treatment of this complication can include: primary closure, with or without pledgets, to reapproximate the edges and bridge the gap with either an artificial mesh (gortex, prolene) or a biological mesh (i.e. Alloderm). Right sided DH acquired after a partial liver transplant within the pediatric population remains uncommon. This diagnosis should be considered in pediatric recipients of partial liver grafts who develop pulmonary complications or abdominal symptoms of bowel obstruction. Expedient exploration and repair should be performed to prevent bowel infarction.

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### Right-sided diaphragmatic hernias after orthotopic liver transplant in children: an under-reported problem after reduced size grafts

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Liver transplantation in children is being performed at increasing rates and at earlier ages. Between 1996 and 2007 there were 6863 liver transplants performed in children under the age of 17. Of these, 4333 were whole organ grafts and 2492 were reduced size grafts (living donor, *in situ*, *ex situ* split and cut-down). In general, partial grafts are associated with slightly increased

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### Piggy back technique with three suprahepatic veins: systematic use in adult orthotopic liver transplantation

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Piggy Back technique (PBT), a procedure that preserves the recipient inferior cava vein, could be performed selectively with 1, 2 or 3 suprahepatic veins (SHV). Advantages of PBT are haemodynamics stability, preserved kidney function, shorter operation time and reduction of blood loss. However, PBT is not used routinely in all liver transplant centers and some authors advocate more complications in using three SHV. The aim of this study was to describe and analyze a single center experience with PBT with three SHV.

**Methods:** PBT was used in adults with acute or chronic hepatic failure. Technique was as follows: after the common bile duct and hepatic artery were dissected and divided, accessory hepatic veins were approach from the

right side of the cava. According to the size of segment I, portal vein section was intended to be performed at the end of IVC dissection. A german clamp was applied proximally across the confluence of the three recipient SHV without occluding the flow. Intra-parenchyma vein section allowed appropriate cuffs for the upper side of the anastomoses. It was performed with the suprahepatic donor IVC and the joined cuff of the three recipient's SHV. There was no requirement of venous-venous bypass. Graft revascularization was performed via portal vein reperfusion and subsequent reconstruction of hepatic artery inflow. Variables of recipient, surgical procedure and post-operative outcome were analyzed.

**Results:** A total of 161 consecutive adult OLT with PBT were performed from May 2002 to June 2008. Eleven were second transplants, five combined liver-kidney and one liver-heart transplant. Average operating time was  $373 \pm 89$  min, cross clamp time  $73 \pm 23$  min. Red blood cell requirement  $6.2 \pm 3$  U and fresh frozen plasma  $9.5 \pm 8.5$  U. There were no intra-operative complications related to the recipient vena cava outflow. In the post-operative period there was arterial thrombosis in 3.1%, portal thrombosis in 0.6% and no caval thrombosis was detected. Three cases developed severe post-operative ascites but none showed caval obstruction in the hemodynamic studies.

**Conclusion:** OLT with PBT with three SHV is a safe procedure and can be used routinely in adults.

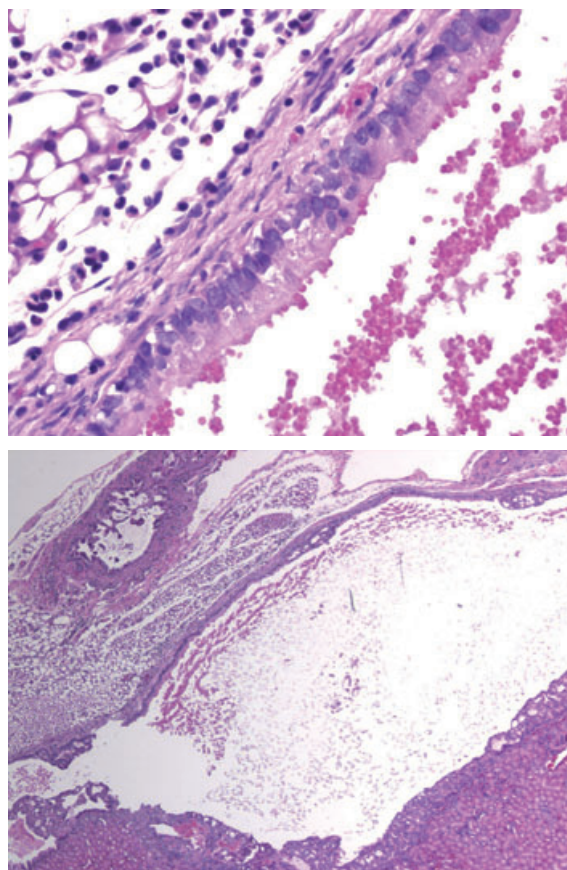


Figure 1.

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### A novel mouse model of mucinous cystic neoplasms

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We sought to create a reproducible animal model of human mucinous cystic neoplasms to study cyst injection ablation techniques which may serve as alternatives to surgical resection. A mucinous cystic neoplasm cell line (MCC1) was developed at the University of Verona from a patient with a 7 cm non-invasive mucinous tumor. The MCC1 cell suspension was grown in tissue culture using RPMI 1640 media with fetal bovine serum and other additives. Once confluent, cells were trypsinized, counted, and resuspended in 200 microliter aliquots of PBS buffer and centrifuged in flexible capillary tubing in preparation for implantation. Five-week-old female Swiss nude mice were used as the hosts. Samples of 0.25, 0.5, or  $1.0 \times 10^6$  cells were implanted under the renal capsule via the capillary tube centrifuged aliquot under general anesthesia. Animals were sacrificed at a mean of 27 days (range 22–41 days). Cysts, if present, were aspirated and samples analyzed for cytology and mucin content. The entire kidney was explanted, fixed in 10% formalin, sectioned, and stained with H&E. A single staff pathologist (CB) reviewed each pathology specimen. A total of eight renal subcapsular implantations were performed in four mice. Four cysts formed in two mice. In the other two mice there was either minimal growth or grossly solid tumors formed. Among the four cysts, maximum cyst diameter was 0.8–1.2 cm. Alcian blue/PAS staining of cyst contents revealed abundant mucin. Histology revealed columnar epithelium with varying degrees of

dysplasia. In two cysts there was no component of carcinoma whereas in the other two there were small foci of invasive carcinoma. We have demonstrated that mucinous cystic neoplasms can be reproduced in a renal capsule model of nude mice. In the future this model can be used to study cyst injection ablation techniques.

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### Adipokines and cytokines in human pancreatic juice: unraveling the local pancreatic inflammatory milieu

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**Background:** Obesity is an independent risk factor both for increased severity of pancreatitis as well as for development and progression of pancreatic cancer. The mechanisms underlying this association are incompletely understood; however, the generalized proinflammatory state of obesity appears to play an important role. Precise evaluation of human pancreatic physiology is challenging, and current understanding of the altered pancreatic inflammatory milieu in obesity is based exclusively on experimental animal data. Evaluation of adipokines and cytokines in pancreatic juice offers a relatively non-invasive method to assess the pancreatic inflammatory

profile. However, to date there has been no study of adipokines or cytokines in human pancreatic juice. This proof of concept study was therefore designed to determine the presence of adipokines and cytokines in human pancreatic juice.

**Methods:** With institutional review board approval, pancreatic juice was obtained from nine patients at the time of endoscopic retrograde cholangiopancreatography. Clinical diagnoses included: intra-ductal papillary mucinous neoplasm ( $n = 3$ ), normal ( $n = 2$ ), sphincter of Oddi dysfunction ( $n = 2$ ), chronic pancreatitis ( $n = 1$ ), and adenocarcinoma ( $n = 1$ ). Pancreatic juice was assayed by ELISA for the proinflammatory adipokine leptin, anti-inflammatory adipokine adiponectin, proinflammatory cytokines interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF- $\alpha$ ), and the chemoattractant molecule monocyte chemoattractant protein-1 (MCP-1). Correlation of adipokine, chemokine, and cytokine concentration was performed by regression analysis. Data are presented as mean  $\pm$  SEM;  $P < 0.05$  was considered statistically significant.

**Results:** Leptin was expressed in pg/mL and adiponectin in  $\mu$ g/mL concentrations (leptin  $11.0 \pm 0.6$  pg/mL, adiponectin  $61.3 \pm 1.1$   $\mu$ g/mL). IL-6 ( $112.6 \pm 28.1$  pg/mL), TNF- $\alpha$  ( $49.0 \pm 18.8$  pg/mL), and MCP-1 ( $32.2 \pm 0.9$  pg/mL) were all detected. Paradoxically, the anti-inflammatory adipokine adiponectin had a strong positive correlation with the proinflammatory cytokine IL-6 ( $r^2 = 0.977$ ,  $P < 0.001$ ).

**Conclusion:** This is the first report of adipokine and cytokine levels in human pancreatic juice. Leptin and adiponectin are expressed in pancreatic juice in concentrations similar to those observed in serum. Pancreatic juice IL-6 expression paradoxically showed a strong positive correlation with adiponectin. Adipokine and cytokine concentration in pancreatic juice likely provides an important reflection of the local pancreatic inflammatory milieu.

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### Analysis of genomic abnormal area concerning biological malignant potential and prognosis of hepatocellular carcinoma by high sensitivity array CGH

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**Background and purpose:** Array Comparative Genomic Hybridization method (aCGH) is a genomic analysis technology that measures minute abnormalities (loss: -, gain: +) of the number of copies of chromosomes. It is covered by BAC (bacterial artificial chromosome) clones that make the fragment of all genomes (some hundreds of kb). Hepatocellular carcinoma (HCC) has a poor prognosis. Though there were a lot of clinical pathologic analysis of prognostic factor, the result had not been still enough. The aim in this research is that genomic abnormal areas concerning about biological malignancy and the prognostic factor were analyzed by aCGH, and

there made comparative study with the result of a clinicopathologic examination.

**Objective and method:** Fifty-eight HCC samples were analyzed by using aCGH of 4000 clones that had the resolution of about 1Mb. These samples were collected from liver resections carried out at Hokkaido university hospital from 1999 to 2001, and DNA was obtained from frozen tumor tissues.

**Result:** There were 48 males and 10 females, and average age was 59.9 years old. 28 samples were obtained from patients with HBV infection, and 22 samples from patients with HCV infection. Using Japanese TNM staging system for primary liver cancer (Ref: Ann Surg. 245: 909-22, 2007), the number of Stage 1, 2, 3, 4A were 3, 28, 17, and 1 respectively. The average observation period was 1808 days, and the accumulation survival rate for 3 or 5 years was 80.3, and 70% respectively. The univariate and multivariate analysis revealed that serum concentration of albumin ( $< 4.0$  mg/dL), and positive pathological portal invasion (vp) were independent poor prognostic factors. The areas of 40% or more in the frequency of gain or loss of the number of copies were +1q, -4q, 8p and +8q, -13q, -16p, -16q, -17p, and -19p. Specific BAC clones correlated with vp, intra-hepatic metastasis, and the degree of histological differentiation was shown respectively, but there was little common BAC clones among them. In addition, the areas that significantly related to the prognosis were +2q +3q, -4q, -6q, -12p, -16p, -16q and -19q. E-cadherin and P27, etc. that were the already-known cancer related genes were included in these BAC clones.

**Conclusion:** It was suggested that aCGH was a promising method of getting more information about biological malignant potential and prognostic factor, included a new prognostic marker genes.

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### Microwave ablation – the state of the art

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Although many techniques for soft tissue ablation have been extensively investigated, by far the most dominant modality over the last decade has been radio frequency ablation (RFA). Whilst being reasonably efficacious in the treatment of small hepatocellular carcinoma (HCC), RFA has serious limitations in large tumour ablations and in coping with the different environments encountered in various soft tissue types. This paper demonstrates theoretical, computational, experimental, and clinical evidence in support of the hypothesis that microwave ablation (MWA) successfully addresses the major problems experienced with RFA. The physical principles of radio frequency and microwave tissue heating are presented, indicating expected differences in heating performance. Finite element modelling (FEM) is used to confirm the theoretical expectations and is compared with microwave bench experimentation and published literature for RFA. Finally, clinical comparison of MWA and RFA in an interventional radiology (IR) setting indicates that for any given ablation volume the time required for MWA is approximately 33% of that for RFA. In addition, the maximum achievable ablation volume for MWA is approximately 290% of that for RFA. The study therefore indicates that MWA is capable of larger and faster ablations.

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**Identification of candidate genes in familial pancreatic cancer with analysis of germline genomic copy number variation**

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The genetic basis of Familial Pancreatic Cancer (FPC) is largely unknown. Germline genomic copy number variation (CNV) is a widespread form of human genetic variation, and may influence cancer risk. High-resolution SNP-based DNA arrays can be used for genome-wide detection of CNVs in germline DNA. We hypothesize that one or more FPC genes are altered in the germline by large genomic deletions (affecting tumor suppressor genes) or gains (impacting dose-sensitive oncogenes), both detectable using CNV analysis of SNP platforms. Lymphocyte DNA was extracted from 128 Pancreas Cancer Genetic Epidemiology (PACGENE) Consortium FPC patients and assayed on the Affymetrix 500K SNP microarray, consisting of two chips. Raw intensity data

were analyzed with two algorithms using a Hidden Markov Model to estimate copy numbers. Only deletions were examined in the present analysis, and only regions at least 1000 base pairs in size were included. Results were compared to deletions previously identified in 1200 healthy controls. Genomic regions exclusively deleted in FPC cases were annotated using bioinformatic tools, identifying genes with potential involvement in cancer. Interesting deletions were biologically confirmed with qPCR. A total of 425 non-overlapping deletions were detected, of which 131 were detected by two algorithms and/or on both SNP chips. Thirteen percent of deletions (55/425) were detected in more than one FPC case. Importantly, 166/425 (39%) deletions were not present in any control samples, of which 74 contained 101 known genes. At least 13 deletions affect known or putative tumor suppressor genes, two of which have been validated biologically with qPCR. Validation of the other interesting regions is ongoing. Unique or rare germline copy number losses in FPC patients may lead to the discovery of putative tumor suppressor genes predisposing to FPC. Further annotation and characterization of these CNVs is in progress.

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**Pancreatic necrosectomy: North American mortality is much lower than expected**

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**Background:** Necrotizing pancreatitis is a highly lethal disease. Single institution series suggest that the mortality of patients undergoing pancreatic necrosectomy has improved, but remains at 15–20%. No national data currently exist regarding the outcome of patients requiring pancreatic necrosectomy. The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) currently accrues demographic and outcome data from 171 United States and two Canadian hospitals. In 2007 a CPT code specific for debridement of pancreatic and peripancreatic necrosis became available. Therefore, the aim of this analysis was to explore the ACS-NSQIP database to determine contemporary outcomes of a North American sample of patients undergoing debridement for pancreatic and peripancreatic necrosis.

**Methods:** The ACS-NSQIP Participant Use File was queried for all patients who had debridement of pancreatic and peripancreatic necrosis (CPT code 48105) from January 1, 2007 through December 31, 2007. Patient demographics, observed (O) and expected (E) morbidity and mortality as well as indices (O/E) were evaluated. An O/E ratio of less than 1.0 suggests that outcomes were better than expected.

**Results:** During this 12-month period, data were accumulated on 161 patients. The mean age was 54 years; 71% were male; and 75% were Caucasian. The mean Body Mass Index was 30.3; 29% had diabetes; and 10% abused alcohol. Forty-two percent were transferred to NSQIP hospitals from other facilities. Systemic Inflammatory Response Syndrome (SIRS), sepsis or septic shock were present pre-operatively in 14%, 30% and 23% of patients, respectively. Overall morbidity was 62%, and 30-day mortality was 6.8%. However, morbidity and mortality indices were 0.86 and 0.33, respectively.

**Conclusions:** These data suggest that patients undergoing debridement for pancreatic and peripancreatic necrosis at ACS-NSQIP hospitals (i) provide a new North American sample and (ii) have better than expected outcomes, especially with respect to 30-day mortality. We conclude that ACS-NSQIP is a powerful tool to assess contemporary outcomes of uncommon, high-risk procedures.

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**Reducing ICU admissions in higher ASA class patients after pancreaticoduodenectomy: impact of a team based approach**

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**Background:** Peri-operative outcome of a pancreaticoduodenectomy (PD) may be impacted by several factors, such as co-morbidities, operative technique, and post-operative care. The purpose of this study is to evaluate whether the development of a dedicated multidisciplinary team can increase direct admission to the floor and reduce the ICU admission after PD.

**Methods:** Medical records of 122 patients, who underwent PD by a single surgeon between September 2005 and August 2008 at a high volume non-university tertiary training center (NUTTC), were analyzed. The records were reviewed with respect to number of patients who were transferred to the floor directly, bypassing the ICU. During the first year 45 PD were performed and this data was compared with the 31 PD cases performed during the second year and 46 cases in the third year. The multidisciplinary team consists of a gastroenterologist, surgeon, hepatobiliary fellow, general surgery residents, ICU nursing staff, operating room team, and a surgery floor nursing staff. Standardized algorithms and a dedicated floor nursing staff were developed during this time period.

**Results:** A total of 122 patients underwent PD. The total of 55 (45%) patients transferred directly to the floor managed by a dedicated team, without being admitted to the ICU. The yearly distribution of patients was 10 (22%), 16 (52%), 29 (63%) in years I, II and III respectively. Hence the ICU admission rate has sequentially dropped from 78% in Year I to 48% in year II and 37% in year III. Overall 12% of these patients were ASA class II, 75% were ASA class III, and 13% were ASA class IV respectively. Every subsequent year a higher number of patients of ASA III (Year I – 25%, Year II – 60%, Year III – 75%) and ASA IV (Year I – 0, Year II – 33%, Year III – 70%) were transferred to the floor directly when compared to the previous year.

**Conclusions:** This study demonstrates that a multidisciplinary team can be developed in a NUTTC for patients with pancreatic disease. This process results in improved peri-operative outcomes. This outcome can be achieved with decreased use of the ICU if a dedicated floor nursing team is developed, even in patients with significant comorbidities and poor ASA status. This will translate to decreased hospital charges, earlier mobilization, and a more streamlined pathway for patients after PD.

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### Routine nasogastric decompression is unnecessary after pancreatic resections

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**Introduction:** Many major operative procedures in the upper abdomen are routinely accompanied by nasogastric tube (NGT) decompression intra- and post-operatively, although the benefit of prolonged post-operative NGT decompression is unproven.

**Methods:** Clinical information of all operative procedures involving the pancreas in a single-surgeon oncologic practice were collected in a prospective database. NGTs were placed routinely intra-operatively throughout the first part of the study interval, and removed based on clinical recovery progress; orogastric tubes (OGTs) were used intra-operatively whenever possible since April 2006, and removed prior to endotracheal extubation. Post-operative NGT duration and reinsertion rate, morbidity, length-of-stay, and later outcomes were analyzed between groups.

**Results:** The analysis includes 189 operations between 1997 and 2008, including 138 pancreatoduodenectomies (PD), 39 distal pancreatectomies (DP), two total pancreatectomies (TP), and 10 other procedures. The mean age was 65 years, there were 60% females, and 73% of patients had a cancer diagnosis. Forty patients (21%) received no NGT, compared to 149 who did; there were no differences between resection types. The median post-operative NGT duration was 1 day (range 0–79, no group differences), the median length of stay 9 days (4–100, group differences:  $P < 0.0001$ ). The mean proportion of in-hospital time with NGT was 19% (PD: 18.5, DP: 17.5, TP: 35, others: 29;  $P = \text{NS}$ ). NGT reinsertion was necessary in 30 patients (16%), and more common after PD (20%) than after DP (3%,  $P = 0.04$ ). NGT reinsertion needs did not differ between patients after routine NGT and OGT use (17 vs. 13%). The complication rate was 38% (major: 12, minor: 26), with lethal outcomes in 3%. NGTs were reinserted in 73% of major vs. 24% of minor complications ( $P < 0.0001$ ). Pyloric preservation (PP) during PD did not affect OGT use (18 vs. 26%), median NGT duration (2 day vs. 1 day), or NGT reinsertion rate (21% vs. 19%). Delayed gastric emptying (DGE) was observed in two patients after PPPD (2.9%), and in three patients past classic PD (4.3%).

**Conclusion:** This experience demonstrates that NGTs can be safely avoided in patients undergoing pancreatic resective procedures, since post-operative NGT reinsertion need, DGE rate, total NGT duration and length of stay are not negatively affected. Based on the results, we prefer to place OGTs intra-operatively, and attempt to routinely avoid post-operative nasogastric decompression.

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### Dissecting the role of cancer-directed surgery in pancreatic cancer – a case-controlled population based analysis using propensity-score matching

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**Background:** Cancer-directed surgery (CDS) improves survival in pancreatic cancer (PaCa). Those who present

with localized tumors are thought to derive the greatest benefit from CDS. The use of population-based datasets allows estimation of the effect of CDS among large cohorts, but these analyses are confounded by non-uniformity in patient profiles among the groups compared. Using data from the SEER registry, we performed a retrospective, matched study to mitigate the effects of baseline heterogeneity in the study population and to examine the true effect of CDS on survival in PaCa.

**Methods:** A total of 2856 patients with localized PaCa were identified over a 12-year period. 34% received CDS. The patient, tumor, and treatment profiles, as well as survival, of these two cohorts were compared. Then, using propensity score matching (PSM), we performed a case-controlled analysis to delineate the effect of CDS on survival. Matching 1 : 1 produced a final cohort of 715 patients (358 no CDS and 357 CDS). The matched groups were once again compared to ensure equality between the groups. After matching, survival functions were plotted for the CDS and no CDS groups and compared. Chi square tests were used for comparison of groups. Survival functions were derived using the Kaplan–Meier method and compared by the log-rank test.

**Results:** At baseline, there were significant differences between the CDS and no CDS groups in terms of patient demographics, year of diagnosis, tumor size and grade, and receipt of radiation. This heterogeneity among the groups makes direct comparison between CDS and no CDS prone to bias, calling into question the improved median survival in patients receiving CDS (27 months vs. 6 months,  $P < 0.001$ ). When matched 1 : 1 (no CDS: CDS), no statistically significant differences remained between the two populations for any of the baseline variables. In this well-matched cohort, the survival advantage in the CDS group was maintained (median 26 months vs. 7 months,  $P < 0.001$ ) (Figure 1).

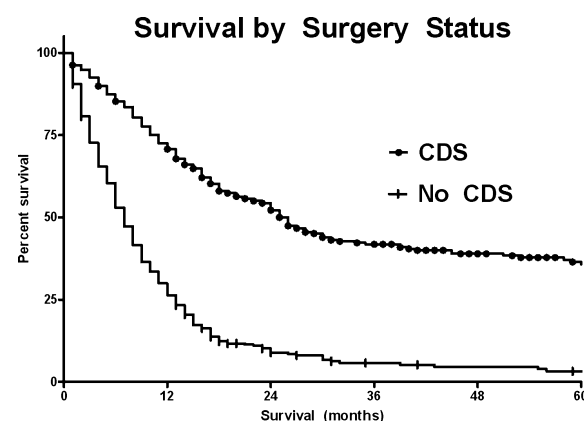


Figure 1.

**Conclusion:** Through PSM, a large cohort of well-matched patients with localized PaCa from the SEER database was examined to show that CDS results in a significantly improved survival compared to patients not receiving CDS. This study provides further evidence for the critical role of CDS in the treatment of early-stage PaCa.

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### Novel economic model of observation vs. immediate laparoscopic resection of hepatic adenomas

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**Background:** Elective surgical resection of hepatic adenomas (HA) is well-accepted in the context of uncertain diagnosis, presence of symptoms, large or increasing size, and occurrence of major complications. However, in the absence of such criteria, the management of HAs is controversial with a wide variation in clinical practice concerning the use of elective surgery. Given the absence of randomized data and the inability of existing case series to support or refute elective surgery for patients with small asymptomatic HAs, we sought to investigate whether the cost-effectiveness of observation vs. immediate surgery could be used to further clarify the preferred management of asymptomatic HAs.

**Objective:** Compare the societal costs of immediate surgery vs. routine screening in a theoretical cohort of patients with hepatic adenomas amenable to limited laparoscopic hepatic resection using evidence-based and institutional-specific assumptions.

**Methods:** Economic model comparing the net present value (NPV) of either observing a theoretical cohort of 100 patients with hepatic adenomas using a variety of imaging modalities vs. immediately operating on a comparable theoretical cohort of 100 patients whose lesions are amenable to limited laparoscopic hepatic resection. The assumptions underpinning the model are based on Deviation-Based Cost Modeling of our large institutional experience with minimally invasive liver surgery and include a major deviation rate of 2% and a 0% mortality rate.

**Results:** Assuming an initial progression rate of 5% followed by a rate of 2% after year 3, the NPV of observation using yearly computed tomography and magnetic resonance imaging is \$1 537 711 and \$1 644 922 respectively after 5 years of follow-up and \$2 448 960 and \$2 630 514 respectively at 10 years of follow-up. The NPV of immediate surgery is \$1 717 021. The break-even point at which point the present costs of yearly observation and immediate surgery intersect is after 6 years of follow-up for CT and 5 years for MRI.

**Conclusion:** There is considerable controversy regarding the management of asymptomatic hepatic adenomas. The risks of spontaneous rupture, malignant transformation, and elective surgery must be weighted against the societal economic burden of frequent monitoring and public health issue surrounding long-term exposure to radiation from screening. In light of the young age of patients afflicted with hepatic adenomas and the need for long-term serial follow up, immediate surgery in a highly selective cohort of patients is cost-beneficial assuming the operation can be performed laparoscopically and with minimal morbidity and no mortality.

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### Impact of intra-operative blood transfusion on survival following pancreaticoduodenectomy for cancer

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**Aim:** To compare the outcomes of patients with and without intra-operative blood transfusion (BT) following pancreaticoduodenectomy (PD) for cancer in a single tertiary referral centre.

**Background:** Peri-operative blood transfusion (BT) has been implicated in reduced disease free (DF) and overall survival (OS) in patients with colorectal malignancies. Increased threshold for transfusion and the use of autologous blood aims to prevent complications of immunosuppression, cancer recurrence and infective complications of BT. Few studies to date have investigated whether allogenic peri-operative BT is an independent risk factor for reduced survival in patients with pancreatic carcinoma undergoing pancreaticoduodenectomy (PD).

**Methods:** A total of 64 patients (43 male, 21 female) who underwent PD in our institution between 2002 and 2007 were prospectively followed up. Those received BT were compared with those who did not have transfusion of blood or blood products (NBT). The two groups were case-matched for all clinicopathological data including age, histology (pancreatic vs. ampullary carcinoma), type of surgical procedures (pylorus-preserving PD vs. Whipples); tumour and nodal stage, bilirubin, albumin and pre-operative haemoglobin level. Outcome measures were post-operative morbidity, mortality, DF and OS. Data were analyzed using a multivariate linear regression model (SPSS).

**Results:** There was no statistically significant difference in demographics data. The median age was 67.5 years (range 40–82) in BT, 68 years (range 36–81) in NBT group. There was no significant difference in the early complication rates in wound infection, abscess and collection, relaparotomy, morbidity or mortality rate. Intra-operative blood loss ( $P < 0.001$ ) and operative time ( $P < 0.0001$ ) were significantly higher in the BT group. However, there was no difference in intensive care ( $P = 0.08$ ) or hospital stay ( $P = 0.4$ ). The median DF survival was 13 vs. 8 months in NBT vs. BT groups post-surgery for pancreatic adenocarcinoma ( $P = 0.61$ ); and 22 vs. 10.5 months in NBT vs. BT groups in ampullary carcinoma ( $P = 0.04$ ). The median OS is 19 vs. 18.5 months in NBT vs. BT groups in patients with pancreatic adenocarcinoma ( $P = 0.78$ ); compared to 28 vs. 24 months in NBT vs. BT groups in patients with ampullary carcinoma ( $P = 0.21$ ). Multivariate analysis revealed BT significantly reduces DF survival in ampullary carcinoma, but has no significant impact on DF or OS in pancreatic adenocarcinoma.

**Conclusion:** This study shows BT significantly reduces DF survival after PD for ampullary carcinoma. Meticulous dissection and care in haemostasis reduce blood loss and prevents the need for BT; this in turn prolongs DF survival.



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### Early nutrition support after pancreaticoduodenectomy can improve patient status.

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**Background:** Various post-operative complications occur after pancreaticoduodenectomy (PD). Although surgical techniques mainly contribute to its outcome, nutrition factor cannot be neglected. Onodera's Prognostic Nutrition Index (PNI) is a convenient nutritional assessment index which predicts post-operative modality by calculating pre-operative albumin level and lymphocyte counts.

**Aim:** We aimed to clarify whether early nutrition support after PD can improve post-operative patient status whose pre-operative PNI were poor.

**Patients and method:** Eighteen consecutive patients who underwent PD (conventional or pylorus preserving) were evaluated. Duct-to-mucosa anastomosis was carried out in all patients. Enteral feeding was started within 2 days after operation. PNI, post-operative hospital stay, modality (delayed gastric emptying, failure of anastomosis, abdominal abscess) were investigated. Onodera's PNI is calculated as  $10 \times \text{alb (g/dL)} + 0.005 \times \text{peripheral lymphocyte count (/mm}^3\text{)}$ . PNI is originally described as a pre-operative modality prediction factor for advanced colorectal cancer patients. Values under 40 are considered dangerous and 45 or above are considered safe.

**Results:** There were eight conventional PD and ten pylorus preserving. Ten patients were pancreatic cancer. There were three patients whose PNI was less than 40. On the other hand, eight patients were above 45. Average PNI of pancreatic cancer patients were 40.9, whereas 45.1 in other diseases. Delayed gastric emptying occurred in seven patients (average PNI; 44.9), pancreatojejunal anastomosis failure in three patients (average PNI; 44.5), abdominal abscess in three patients (average PNI; 42.3). Every patient with PNI below 40 experienced post-operative complication. Even with good PNI (above 45), modality rate was 37%. Hospital stay of patients with PNI less than 40, between 40 and 45, and above 45 were 40 days, 37 days, and 43 days, respectively.

**Conclusion:** PNI below 40 can also be classified as dangerous range, as in original definition, for performing PD. However, patients with PNI above 45 cannot be classified as safety range for relatively high modality rate. Interestingly, length of hospital stay with PNI below 40 patients is shorter than PNI above 45 patients. Early nutrition support may contribute to early recovery from adverse events even with PNI below 40.

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### Results of liver surgery at a low-volume center

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The paper reports results from a series of 52 patients, which were prospectively collected between January 2003 and December 2007, in order to determine whether liver resection might be a safe procedure at a low-volume hospital. The mean age was 62.5 years; in 34 patients there was comorbid disease, mainly cardiovascular. Pre-operative impairment of liver function related to chronic liver disease or to steatohepatitis induced by pre-operative chemotherapy was present in 12 patients. Pre-operative right portal vein embolization was employed in six patients. Twenty-eight patients (53%) underwent major liver resections. A two-stage hepatectomy was necessary in two patients, while in 19 patients, liver resection was synchronous with other abdominal operations. Intra-operative radiofrequency thermal ablation was used with resection in five patients. Mean intra-operative blood loss was 334.8 mL, twelve patients required peri-operative blood transfusions. There was one post-operative death (1.9%), of a cirrhotic patient due to a biliopleural fistula, resulting in a lung abscess and sepsis. Overall complications, most of which were minor, occurred in 17 patients (32.7%) (Table 1) and they were always managed conservatively. Pre-operative impairment of liver function was the only factor affecting operative morbidity by univariate analysis ( $P = 0.03$ ; odds ratio [OR]: 4.2; 95% confidence interval [CI]: 0.9–20.2). The mean hospital stay was 9.7 days. A stay of more than 7 days was associated with the presence of post-operative complications ( $P < 0.001$ ) and to pre-operative impairment of liver function ( $P < 0.001$ ). According to the studies with the largest numbers of patients to date, the overall mortality and morbidity rates following hepatectomy range from 0–4.9% and 32.4–39%, respectively; our results are similar to those reported in major series. Liver resection may be safely performed at low-volume hospitals, provided that there is an ICU available, and trained surgeons, anesthesiologists, and nursing staff experienced in managing patients with complex conditions. Mortality and morbidity rates are acceptable and comparable with those of high-volume hospitals, even in cases of major hepatectomy or associated procedures.

**Table 1.** Post-operative complications.

Complication	<i>n</i>
Wound infection	4
Pleural effusion	4
Biliary fistula	4
Abdominal collection	2
Persistent ascites	2
Gastric ulcer bleeding	1
Central venous catheter infection	1

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**Outcomes of hepatic resection for metabolic disorders related to hepatocellular carcinoma**

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**Purpose:** The incidence of hepatocellular carcinoma (HCC) is increasing dramatically in Western countries because of the hepatitis C virus epidemic and screening policy of high risk populations. Recently, metabolic disorders such as obesity and insulin resistance have been identified as contributing to the increase in HCC incidence. We assessed the outcome of liver resection for HCC among patients with metabolic disorders but without other HCC risk factors.

**Patients and methods:** The records of all patients who underwent liver resection for HCC at our institution between 1998 and 2008 were reviewed. Patients with known HCC risk factors (alcohol use, hepatitis, immunologic factors, and estrogen use), as well as patients with fibrolamellar HCC were excluded. The remaining patients were included if they were overweight (body mass index [BMI] > 25 kg/m<sup>2</sup>) and had at least one of the following: type II diabetes, hypertension, or dyslipidemia.

**Results:** Among 36 patients meeting inclusion criteria, 26 (72%) were male and 24 (67%) were Caucasian. Sixteen patients (44%) were obese (BMI > 30 kg/m<sup>2</sup>), 15 (42%) had diabetes mellitus, 30 (83%) had hypertension, and 19 (53%) had dyslipidemia. Alpha-fetoprotein values were within normal range in 20 patients (56%). Pre-operative right portal vein embolization was performed in twelve patients (33%), transarterial chemoembolization in 6 (17%), and sequential arterio-portal embolization in 3 (8%). Twenty-four patients (67%) underwent major liver resection (≥ 3 segments). On pathological examination of the resected specimen, only 4 patients (11%) had cirrhosis, and mean tumor size was 81 ± 8 mm. Seven patients (19%) had satellite nodules, and 12 (33%) had vascular invasion. Post-operative morbidity and 90-day mortality rates were 50% and 11%, respectively. After median follow-up of 25 months, median overall (OS) and disease-free survival (DFS) had not been reached. OS rates at 1, 3, and 5 years were 82%, 78%, and 70%, respectively. Satellite nodules ( $P = 0.06$ ) and vascular invasion ( $P = 0.05$ ) were associated with worse DFS.

**Conclusion:** Owing to lack of screening, HCC in patients with metabolic disorders is diagnosed at an advanced stage and often requires major resection. However, the long-term prognosis is good, and aggressive surgical strategies are justified.

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**Operative mortality after resection of biliary tract cancer in the United States**

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and J. F. TSENG, MD

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**Objective:** To assess peri-operative mortality following resection of biliary tract cancer within the US.

**Background:** Resection remains the only curative treatment for biliary tract cancer [BTC]. Early detection to offer operative intervention may contribute to improved survival. However, current data on operative mortality after surgical resections for BTC are limited to small and single-center studies.

**Methods:** Using the Nationwide Inpatient Sample 1998–2006, a cohort of patient-discharges was assembled with a diagnosis of BTC, including intra-hepatic bile duct, extrahepatic bile duct, and gallbladder cancers. Patients undergoing resection, including hepatic resection, bile duct resection, pancreaticoduodenectomy, and cholecystectomy, were retained. The primary outcome measure was in-hospital mortality. Continuous variables were analyzed by t-test; categorical variables were analyzed by chi-square. Multivariable logistic regression was performed to identify independent predictors of in-hospital mortality following resection.

**Results:** A total of 31 870 patient-discharges occurred for the diagnosis of BTC, including 31.1% intra-hepatic ductal, 36.2% extrahepatic ductal, and 26.7% gallbladder. Of the total, 18.6% underwent resection: mean age was 69.3 years; 60.9% were female; 73.7% were white. Overall inpatient surgical mortality was 5.62%. Independently predictive factors of increased peri-operative mortality included patient age ≥ 70 (vs. < 50; odds ratio [OR] 8.99, 95% confidence interval [CI] 2.84–28.48), the presence of identified comorbidities (congestive heart failure, OR 3.66, 95% CI 2.58–5.18; acute renal failure, OR 4.68, 95% CI 2.93–7.43), and admission designated as emergent (vs. elective; OR 1.84, 95% CI 1.40–2.41).

**Conclusion:** Increased in-hospital mortality for patients undergoing BTC resection corresponded to age, comorbidity, and emergent admission. Further study is warranted to utilize these observations in promoting early detection, diagnosis, and elective resection.

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### Outcomes of liver resection for HCC in patients with metabolic disorders

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**Background:** Although, it is well established that HCC can be discovered in patients with metabolic disorders (MD), including type 2 diabetes, obesity and dyslipidemia, homogeneous series of patients of this group are lacking. Moreover the outcome of surgical series is not known.

**Aim:** To assess outcome of liver resection among a stringently selected population of patients with MD related HCC.

**Patients and methods:** From 2000 to 2008, among 240 patients who underwent partial liver resection for HCC, 31 patients fulfilling the criteria of MD were resected. A single pathologist reviewed pathological features of HCC and non-tumoral liver. Post-operative morbidity was stratified with the Dindo's classification. To study the survival, all patients were reviewed every 6 months for a mean duration of 3 years and there were no lost of follow-up.

**Results:** These 31 patients were characterized by 97% ( $n = 30$ ) men, a mean age of  $67.4 \pm 1.7$  years old (ranging from 50 to 81 mm), including 19  $> 65$  years, a BMI  $> 25 \text{ kg/m}^2$  in 77% ( $n = 24$ ) of cases. Diabetes, High blood pressure and dyslipidemia were found in 24 (77%), 26 (84%) and 20 (65%), respectively. AFP was elevated in 23% ( $n = 7$ ) of cases including, 3  $> 500 \text{ ng}$ . Mean tumor size was  $85 \pm 6 \text{ mm}$  (ranging from 20 to 350 mm) and 15 required (48%) major resection (more than three segments). Post-operative morbidity was 52% (Dindo I, II, III, IV in 6 (19%), 2 (7%), 1 (3%) and 4 (13%) cases respectively) and 4 patients died within 90 post-operative days (13%). Pathological examination showed that the tumor was well differentiated in 20 (64%) cases, with macro/micro vascular invasion in 6 (19%)/4 (45%) and satellite nodules in 11 (35%). Non-tumoral liver showed that chronic liver parenchyma disease was present in 11 cases (35%), while steatosis  $> 30\%$  was present in 5 (16%). After a mean follow-up of 33 months, three patients died from recurrence. Overall survival at one, 3 and 5 years was 87%, 79%, 70% whereas disease free survival (DFS) was 84%, 53%, and 35% respectively. DFS was negatively influenced by the presence of satellite nodules ( $P = 0.004$ ). Size of the tumor, differentiation, vascular invasion and the status of non-tumorous parenchyma were not correlated to DFS. OS was impaired in patients with absence of capsule ( $P = 0.02$ ), multinodular disease ( $P = 0.059$ ), vascular invasion ( $P = 0.053$ ) and satellite nodules ( $P = 0.077$ ).

**Conclusion:** According to the results of this first surgical series of HCC resected in patients with MD, surgical risk is important but long term outcome is favourable.

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### Resection of tumors of the Ampulla of Vater: retrospective review of a single institution's experience

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**Purpose:** Tumors of the Ampulla of Vater are amenable to treatment by both endoscopic techniques as well as conventional surgical management. This study evaluates a single tertiary referral center's recent experience with tumors of the Ampulla of Vater and presents a strategy for optimal treatment choice to guide therapy.

**Methods:** Demographics, treatment course, and outcomes for all patients presenting with a diagnosis of tumor of the Ampulla of Vater during a 64 month period (January 1, 2003–April 1, 2008) were analyzed ( $n = 108$ ).

**Results:** Benign adenomas and dysplastic / atypical adenomas were treated by endoscopic papillectomy ( $n = 29$ , 27%). Ampullary adenocarcinomas were treated with pancreaticoduodenectomy ( $n = 79$ , 73%). No single demographic factors favored either treatment group (age, gender, or race). Signs that were predictive of pancreaticoduodenectomy included jaundice (80% vs. 3%,  $P < 0.01$ ) and steatorrhea (33% vs. 3%,  $P < 0.01$ ). Patients that presented with GI bleed trended toward treatment with endoscopic papillectomy (14% vs. 6% for pancreaticoduodenectomy,  $P = 0.25$ ). Symptoms that favored malignancy and treatment by pancreaticoduodenectomy included pruritis (37% vs. 3% for endoscopic papillectomy,  $P < 0.01$ ) and fever (19% vs. 0% for endoscopic papillectomy,  $P < 0.01$ ). Length of stay and complication rates were higher in the pancreaticoduodenectomy group. No 30-day mortalities occurred in the endoscopic group (0/22) vs. a single 30-day mortality in the pancreaticoduodenectomy group (1/79, 1.2%).

**Conclusions:** Endoscopic papillectomy is a safe and effective treatment of benign and dysplastic/atypical adenomas. Pancreaticoduodenectomy can be effectively performed for adenocarcinoma of the ampulla and should be considered the treatment of choice for cancerous lesions. Jaundice, steatorrhea, pruritis, and fever are statistically significant predictors of malignancy as treated by pancreaticoduodenectomy compared to adenomatous lesions.

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### Maternal abdominal surgery during gestation outcomes relate to emergent nature and imply cytokine influence

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**Introduction:** Major non-obstetric abdominal operations during pregnancy impose inherent risks upon mother and fetus. This Gestational Surgical Risk Assessment (GSRA) has been correlated with gestational age during

pregnancy, but other factors may play important roles. Based on a hypothesis that inflammatory states may induce cytokines with abortifacient and other properties, we propose that emergency operations for inflammatory conditions may carry risks not shared by elective operations for conditions of non-inflammatory states, regardless of trimester.

**Methods:** We combined our experience ( $n = 32$  patients) with a literature meta-analysis ( $n > 2000$  patients) to evaluate outcomes as a function of maternal surgical indication. All patients had major non-obstetric procedures during gestation and were divided into inflammatory and non-inflammatory cohorts. Maternal death as well as fetal prematurity and spontaneous abortion were endpoints.

**Results:** Inflammatory etiologies included appendicitis, cholecystitis, intestinal obstruction, inflammatory bowel disease, and spontaneous hepatic rupture. There was a significantly higher risk of pre-term labor and spontaneous abortion for those patients with inflammatory and infectious indications for surgery, as compared to major oncologic procedures. Peritonitis proved to be an even more significant risk factor for not only fetal complications, but maternal death (Table 1).

**Table 1.** Procedures for inflammatory processes.

Indication	Number	Fetal death (%)	Maternal death (%)
Appendicitis – perforated	1653	67 (4.0)	0 (0)
Appendicitis – non-perforated	182	18 (9.9)	0 (0)
Biliary stone disease	279	12 (4.3)	1 (0.36)
Volvulus	16	4 (25)	2 (12.5)
Adhesions	39	11 (28)	2 (5.1)
Toxic obstruction	16	10 (62.5)	5 (31.2)
Obstruction (other)	21	6 (28.5)	0 (0)
Inflammatory bowel disease	12	2 (16.7)	0 (0)
Hepatic rupture	35	7 (20)	7 (20)

**Conclusions:** While major hepatobiliary operations can be tolerated well by mother and fetus, operations for perforated appendicitis and bowel obstruction prove to be extremely high risk for mother and fetus. We believe that the inflammatory cytokines and proinflammatory mediators associated with peritonitis are responsible for many of the complications experienced during emergent operations in gravid patients. Cytokines, specifically TNF- $\alpha$ , IL-1 $\beta$ , and IL-6, have long been implicated as factors contributing to the common signs of infection and inflammation in cases of sepsis, shock, and trauma. Cytokines have also recently been suspected to play a crucial role in pre-term labor and delivery. We believe that it is important to consider not only the underlying condition, but the association with physiologic stress and inflammation when assessing the risk maternal and fetal risk of a procedure.

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### Major hepatobiliary surgery without blood transfusion in Jehovah witness patients

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Major life-threatening conditions that require extensive hepatobiliary and oncologic procedures in the Jehovah Witness patient can be safely performed with a low operative risk. Over a 2.5-year period 12 Jehovah Witness patients had 14 major hepatobiliary surgeries. All of these patients were considered high risk for surgery by any standard regardless of their religious beliefs. Accordingly all of these patients were refused surgery at other major centers in the United States due to their reluctance to respect their religious belief of not accepting blood transfusions and due to the size and locations of their lesions. During the initial evaluation patients were considered for surgery depending upon the ability to technically perform the extensive surgeries based upon imaging criteria and clinical data at the time of presentation. All patients were pre-treated with epoetin alfa (Epogen) according to our protocol to optimize the hemoglobin level above 12.0 g/dl prior to any surgical intervention. The pre-operative goals were to maximize red blood cell mass, delineate tumor extension and develop a plan to incorporate blood conservation strategies and minimize blood loss. There were 5 (29%) patients that had prior unsuccessful surgery before presentation. The patients had various diagnoses that included 2 benign biliary strictures, 3 liver neoplasms, 5 pancreas tumors, and 4 with retroperitoneal tumors associated with the liver and pancreas. A total of 12 Jehovah Witness patients underwent 14 major hepatobiliary and oncologic surgeries for various diagnoses. The primary surgical procedures consisted of three complex biliary reconstructions, three hepatectomies, three distal pancreatectomies, one pancreaticoduodenectomy and three retroperitoneal tumor resections associated with the liver or pancreas. The mean blood loss was  $641 \pm 550$  cc and cell saver transfusion was necessary in only 7 (50%) patients with a mean transfusion of  $111 \pm 150$  cc of salvaged blood. Pre-operative and post-operative hemoglobin levels averaged  $13.1 \pm 1.5$  and  $11.0 \pm 1.6$  respectively. The mean decrease in hemoglobin was  $1.7 \pm 1.9$  after surgery. Post-operative complications occurred in 4 (24%) and there was one death within 30 days of surgery. Multiple blood conservation techniques were employed for these procedures that were denied at other institutions. Complex hepatobiliary surgery can be successfully performed in these patients while respecting the right to refuse allogeneic blood products. These results demonstrate that these complex procedures can be performed with acceptable morbidity and morality when compared to other individuals with similar diagnoses when the use of blood transfusion is not an option.

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**Digital 3D anatomical images of the liver – a didactic tool**

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Three-dimensional images of complex anatomical sites aid with correct understanding of depth during surgical procedures. This paper describes a simple method to obtain stereoscopic anatomical images for teaching purposes using common photographic equipment. The stereoscopic pairs were produced using a simple sliding

tray with an adapted millimeter scale to control the distance between the pictures. The initial still image was captured and the tray shifted laterally to capture the second image. Frozen isolated cadaveric livers and liver corrosion casts were used to obtain the 3D images. Binocular vision is the result of adding two slightly different images of the same object, produced by the alignment of eyes and orbits, which 'see' the same object from slightly different points of view. The distance between pictures must approximate the interpupillary distance in normal conditions. The distance between pictures is variable and depends on the distance between the lens and the object to be depicted. The resulted images can be projected or printed.

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**3D operative planning for liver surgery from your laptop**

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**Background:** The unique surgical anatomy of the liver has led to efforts to perform 3D rendering for operative planning and volumetrics. Typically, these 3D reconstructions require specialized computer equipment and training. The authors report early experience with a novel technology to allow high quality 3D operative planning performed by the surgeon using consumer-grade computers.

**Methods:** Standard thin-cut triphasic liver CT scans were obtained in 21 consecutive patients before resection ( $n = 13$ : 7 open; 6 laparoscopic) or laparoscopic radiofrequency ablation (8). The DICOM images, whether 'in-house' and on CD from elsewhere, were imported into OsiriX software on Apple computers (iMac and MacBook). 3D reconstructions were produced to characterize the anatomy of the liver and location of tumor(s) (Fig. 1). In five cases, PET images were also fused into contrast-enhanced CT. In three cases, volumetrics of the future

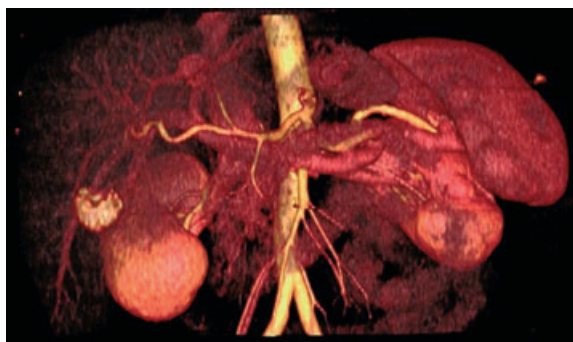


Figure 1. 3D reconstruction showing segment V HCC prior to laparoscopic resection.

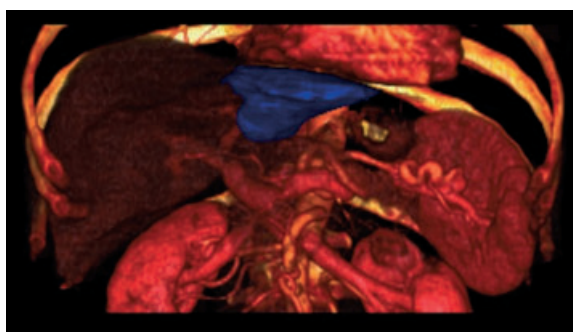


Figure 2. Volume of left lateral segment in patient requiring right triseg. Volume is only 191 cc, prompting left and seg. IV PVE.

liver remnant were performed pre- and post-portal vein embolization (Fig. 2), and the results compared to the Department of Radiology 3D lab. All reconstructions and volumetrics were performed by the operating surgeon himself.

**Results:** The OsiriX software proved very easy to learn with little ( $< 2$  h) training. 3D rendering accurately depicted anatomic details and the relationship between the tumor(s) and vasculature in all cases. The 3D reconstructions can be rotated  $360^\circ$  to facilitate planning of the operative approach, particularly in lap RFA and resection. Surgeon-measured volumetrics matched those of the 3D lab ( $< 5\%$  difference). 3D reconstructions greatly assisted in teaching residents the relevant anatomy.

**Conclusion:** In early experience, OsiriX software allows accurate 3D rendering of liver/tumor anatomy and accurate volumetrics. These reconstructions are simple to perform and offer evident utility for both operative planning and teaching.

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**Pre-liminary clinical data on the use of a novel endovascular radiofrequency catheter in the management of unresectable primary and secondary cancers of the liver**

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**Introduction:** A number of different transarterial techniques have been developed for the locoregional control of liver tumors. Presently available endovascular techniques rely on the delivery of embolic material which has the risk of collateral damage to non-tumoral liver or other non-target organs. This study reports our initial assessment of the endovascular use of a novel radiofrequency catheter (VesCoag) in the management of primary and secondary cancers of the liver.

**Methods:** Multicentre pilot study to assess the technical feasibility of manipulating VesCoag into the target vessel and to determine the parameters of activation to produce the angiographic endpoint of target vessel occlusion. Patients considered for inclusion in the study had primary or secondary cancer of the liver, which were not suitable for surgical resection.

**Results:** In this series VesCoag was used to occlude the tumor arterial blood supply ( $n = 13$ ). The average age of the patient was 68.5 years (range 48–80), five patients were female and eight were male. The indications for treatment were metastatic disease in 4, hepatocellular carcinoma in 7 and intra-hepatic cholangiocarcinoma in 2. In all cases, VesCoag was able to be manipulated into the target vessel for probe activation. There were no technical problems such as vessel dissection or rupture. The average fluoroscopic time was 12.86 min and the

mean duration of probe activation was 240 (range 20–600) seconds. The lowest wattage used was 2W and the highest 120 W. In no cases was bipolar radiofrequency activation sufficient to produce vessel sealing, so in all patients ( $n = 13$ ), VesCoag was used in monopolar mode. There were four minor complications of pain. The angiographic endpoint of occlusion of the targeted vessel after VesCoag activation was achieved in 11 patients. In 12 out of 13 cases an additional endovascular therapeutic manoeuvre was performed after VesCoag activation. These additional therapies were chemoembolization  $n = 10$ , chemotherapy  $n = 1$  and lipiodol  $n = 1$ .

**Conclusion:** This initial assessment of VesCoag shows it to be safe and fulfil its design remit of being able to produce precise occlusion of the target vessel.

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### **Intra-operative ultrasonographic characteristics determine its sensitivity in detecting colorectal liver metastases**

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**Background:** In an era of improved pre-operative cross-sectional imaging, the clinical value of intra-operative ultrasonography (IOUS) in the treatment of patients undergoing liver resection for colorectal liver metastases (CRLM) is unclear. Whether IOUS allows for the identification of additional lesions, as well as the relationship between lesion-specific ultrasonographic features and IOUS sensitivity also remain ill-defined. The purpose of the current study was to determine the association of tumor echogenicity with the ability of IOUS to detect occult CRLM.

**Methods:** Prospective data, including IOUS images and clinicopathological information, were collected on 149 patients who underwent liver surgery for CRLM between 1998 and 2007. In each instance, IOUS images were digitally recorded at the time of surgery; the images were subsequently blindly reviewed and scored for echogenicity (hypo-, iso-, or hyperechoic). Patients with isoechoic lesions were compared with patients who had non-isoechoic (hyper- plus hypo-) lesions with regard to the overall IOUS yield of detecting additional metastases intra-operatively. Routine CT scans were obtained on all patients, and early (< 6 months) intra-hepatic recurrence was used as a surrogate for residual disease (e.g. small metastases that were undetected on initial IOUS). The rate of early intra-hepatic were then compared among the iso- and non-isoechoic groups.

**Results:** Compared with pre-operative cross-sectional imaging, the detection of additional metastases by IOUS was significantly less in the isoechoic group ( $n = 67$ ; 4.6%) compared with patients who had non-isoechoic lesions group ( $n = 82$ ; 14.6%) ( $P = 0.05$ ). While late recurrence, extrahepatic recurrence and overall survival were not different among the groups, early intra-hepatic recurrences were significantly more common in patients following resection of isoechoic tumors (22.6%) compared with patients who had non-isoechoic lesions (8.3%) ( $P = 0.03$ ).

**Conclusions:** The sensitivity of IOUS to detect otherwise occult intra-hepatic CRLM lesions is dependent on tumor echogenicity. The use of IOUS in patients with isoechoic tumors is not reliable in the detection of additional CRLM metastases compared with pre-operative cross-sectional imaging. These data suggest that early intra-hepatic recurrence following resection of CRLM in patients with isoechoic lesions compared with non-isoechoic lesions is due to differences in lesion detection rather than tumor biology.

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### **Advanced imaging guidance system improves accuracy of needle placement for hepatic tumors**

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*InnerOptic Technology Inc, Chapel Hill, NC, USA*

This study measures the effectiveness of a novel guidance system which fuses virtual reality, ultrasound and real time position location. Ultrasound guided procedures such as hepatic tumor ablation or biopsy can be limited by the user's ability to accurately place the needle into the target. Three users with various levels of experience in ultrasound guidance made microwave needle antenna placements into a target both with and without advanced guidance. We hypothesized increased accuracy with the guidance system for needle placement at all angles of approach regardless of experience.

**Methods:** Seven millimetre targets 3 cm deep to the surface were created in agar gel. An InVision guidance system (InnerOptic, Chapel Hill, NC, USA) was attached to the ultrasound probe and microwave needle antenna of a B-K Pro Focus 2202 (B-K Medical, Denmark) with surgical T probe (#8659). Real time guidance was viewed on a stereoscopic monitor. A 13 gauge 22 cm surgical microwave needle antenna (Valley Lab, Boulder, CO, USA) was used for all procedures. Three users, a novice, amateur, and expert in experience with ultrasound guidance were selected. Placements were randomized between use of enhanced image guidance vs. standard ultrasound and three angles of approach relative to the ultrasound plane: 0, 45 and 90 degrees. Users could not alter the needle course once an angle of approach was chosen. Accuracy data was collected by ultrasound confirmation in two planes. Descriptive statistics comparing guided vs. non-guided were calculated using chi-square test.

**Results:** Users made 10 placements each for the three angles with and without advanced image guidance. For all users at all angles the accuracy improved significantly when using the guidance system: 40% to 90% ( $P < 0.0001$ ) at 0 degrees, 40% to 97% ( $P < 0.0001$ ) at 45 degrees, and 27–77% ( $P = 0.0001$ ) at 90 degrees. In addition, the accuracy of the novice and amateur using the system was better than that of the expert not using the system.

**Conclusions:** This advanced needle guidance system significantly improved accuracy of microwave needle placement regardless of the angle of approach or the surgeon's level of experience. Clinical trials are needed to



assess the usefulness of improved accuracy for both surgeons and interventionalists.

**Table 1.** Results.

Angle	0 degrees	45 degrees	90 degrees
Novice non-guided	30%	30%	0%
Novice guided	90%	100%	60%
Amateur non-guided	40%	20%	20%
Amateur guided	80%	90%	70%
Expert non-guided	50%	70%	60%
Expert guided	100%	100%	100%
Totals			
Non-guided	40%	40%	27%
Guided	90%	97%	77%

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### Accuracy of pre-operative automatic measurement of the liver volume by CT-scan with a 3D surgical planification software

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**Introduction:** The evaluation of the volume of remnant liver is very important in the case of major hepatectomy. We used a software developed for the 3D visualisation and analysis of the liver, vessels and tumors from a contrast CT-Scan. Therefore, pre-operative hepatectomy simulation can be done and different volumes of the liver are automatically calculated before surgery. The aim of this study were first, to compare different hepatic volumes between automatic (AC) and manual (MC) calculation techniques, and secondly operative or post-operative data.

**Material and methods:** This prospective study included 34 patients (16 females and 18 men; mean age: 55 years  $\pm$  13). Pre-operative total, resected, remnant liver and tumor volumes were calculated by both techniques and compared. The volume of resected liver was obtained by its weight at surgery. A Ct scan was performed on the 2nd post-operative day in order to evaluate the real remnant liver volume. Wilcoxon's test and Pearson's correlation were used for statistical analysis.

**Results:** Resected AC liver volume was significantly correlated to the resected MC volume (943 cm<sup>3</sup> vs. 1010 cm<sup>3</sup>, difference of 4%,  $r = 0.971$ ) and to the weight of the liver specimen (943 cm<sup>3</sup> vs. 748 cm<sup>3</sup>,  $r = 0.734$ ). Resected AC and MC volumes were significantly more important than the weight of the liver specimen (748 cm<sup>3</sup>) ( $P < 0.0001$ ). The mean of percentage of remnant AC and MC liver volume was not significantly different (54.6% vs. 52.8%,  $P = 0.5$ ,  $r = 0.926$ ). The difference between pre-operative AC and MC tumor volumes (194 cm<sup>3</sup> vs. 189 cm<sup>3</sup>) was 2.6% ( $P = 0.395$ ). These volumes were not significantly different from the pathological tumor volume (217 cm<sup>3</sup>) ( $P = 0.381$ ). Pre- and post-operative AC remnant volume were not significantly different (971 cm<sup>3</sup> vs. 1047 cm<sup>3</sup>;  $P = 0.182$ ;  $r = 0.854$ ), but the post-operative AC width of the remnant liver was 2.6 cm more than the pre-operative AC width ( $P = 0.005$ ).

**Conclusions:** The automatic calculation of liver volume by this software is accurate and reliable with a good

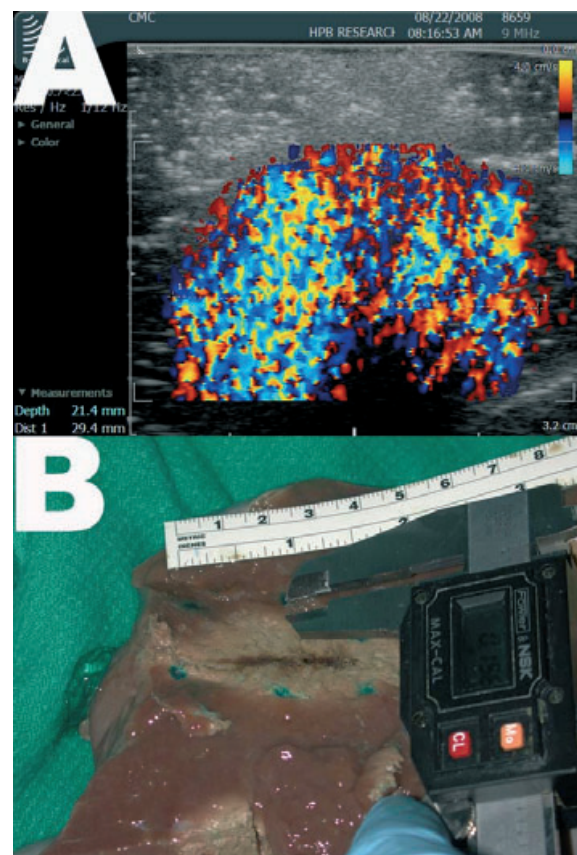
correlation to the manual technique of liver volume measurement. It allows an easy and fast calculation of different liver volumes and a 3D visualisation of the foreseen liver resection. This software appears to be very useful for a better planning of hepatic surgery. The full potential of this tool is still under assessment.

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### Color Doppler ultrasound provides real time measurement of microwave field in ablation therapy

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Microwave generators create an energy field around the active tip of an antenna via pulsed electromagnetic waves. Tissue thermocoagulation is achieved as water molecules within the field oscillate according to the frequency and energy delivered. This differs from RadioFrequency ablation where electric current passing through the tissue results in tissue heating. Through clinical experience with hepatic microwave ablation (MWA) it was suspected that color Doppler ultrasound (US) demonstrated the active microwave field in real time. This study tests the hypothesis that the visualized field seen in color Doppler US during MWA correlates with measured zone of thermocoagulation.



**Figure 1.**

**Methods:** Microwave ablations with a single needle 915 MHz surgical antenna (ValleyLab, Boulder, CO, USA) at 45W for 6 min were performed in *ex vivo* bovine liver. Ultrasound (BK Pro Focus 2202, BK Medical, Denmark) was used to monitor the ablation using color Doppler mode. A clear demarcation was observed at the edge of the microwave field (A in Fig. 1). This edge was marked circumferentially in the tissue with methylene blue soaked probes with US guidance. The tissue was then transected along the plane of needle placement and the distance between each mark and the edge of thermocoagulation zone was measured with digital calipers (B in Fig. 1).

**Results:** Twenty MW ablations were performed with an average of five markings per ablation. Measured distance from the markings to the edge of the thermocoagulation zone averaged 1.62 mm (range 0.00–5.5, SD 1.34). Additionally the field seen on Doppler US was measured at its widest point to be 2.94 cm. The width of the thermocoagulation zone seen in the beef liver was 3 cm at its widest point.

**Conclusions:** The visualized field observed in the color Doppler mode of US during MWA correlates with the MW field as well as the zone of thermocoagulation. To date this has not been described. Live feedback of the treatment area during microwave ablation can be used to create target specific probes, generator modulated ablations, and more efficient methods for shielding. In-vitro studies with active bloodflow may further delineate this observed effect.

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### Comparison of radiologic and pathologic response following 90Y microspheres therapy for hepatocellular carcinoma

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**Background:** Selective internal radiation therapy (SIRT) with intra-hepatic arterial administration of radioactive Yttrium-90 (90Y) labeled microspheres has been evaluated and used as an alternative treatment modality for advanced primary or metastatic hepatic tumors. Favorable outcomes following SIRT for inoperable hepatic tumors have been reported, but there has been difficulty regarding evaluation of response after treatment.

**Purpose:** We compared radiologic and pathologic response after microsphere (90Y) therapy for hepatocellular carcinoma (HCC) to evaluate accuracy and reliability of imaging modalities assessing therapeutic response.

**Methods:** Four patients were identified from database, who received hepatic arterial delivery of 90Y microspheres for HCC and subsequent orthotopic liver transplantation (OLT). Three patients received SIRT for downstaging of advanced HCC before OLT. One patient received SIRT due to recurrence of HCC after initial resection, and subsequently underwent OLT. All imaging studies including computed tomography (CT) and F18-2-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) were reviewed. All four patients had pre- and post-SIRT CTs and two patients had FDG PET scan available. Complete pathologic evaluation of the explanted liver was performed.

**Results:** Two patients showed good correlation between imaging and pathologic findings following SIRT. However, Two patients showed new-onset enhancement lesions surrounding tumor after SIRT, which was concerning for progressive disease. One patient underwent laparoscopic exploration and multiple biopsy of lesion to confirm the tumor status, which was negative for malignancy. Pathologic findings of explanted liver of those two patients showed almost complete necrosis of tumor with numerous neoangiogenesis at the periphery of tumor and fibrosis at the same time.

**Conclusion:** Radiologic response after SIRT can be confusing and can mislead clinical judgment. If SIRT was administered for downstaging modality, histologic confirmation of non-responder is recommended before changing treatment plan. Larger number of case study is recommended to define response to SIRT better.

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### Margin status with a standardized protocol for the sectioning of pancreaticoduodenectomy specimens

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**Background:** Margin positivity is associated with poor prognosis in periampullary cancer. Every effort should be made by the surgeon to attain a margin negative status. Ensuring microscopic margin negativity is however challenging due to anatomical limitations and proximity to major vessels. Various centers have reported on their experience with a standardized protocol for the sectioning of PD specimens. We report our experience and the impact on Superior mesenteric margin (SMA) status.

**Methods:** Medical records of Patients who underwent pancreaticoduodenectomy (PD) by a single surgeon between September 2005 and August 2008 were retrospectively reviewed. Pathologic data including tumor type, and margin status was collected. After the resection of the specimen, the circumferential soft tissue margins and surfaces were stained according to a fixed color protocol. The superior mesenteric artery margin was specifically inked.

**Results:** Seventy-eight PDs were performed for periampullary carcinoma. Thirty-two percent (25) patients with periampullary carcinoma had positive margins. Positive margins were more frequent with carcinoma of the pancreatic head. Of the patients with positive margins 21 patients had a diagnosis of carcinoma of the head of pancreas, 3 had duodenal carcinoma and 1 had carcinoma of the Ampulla of Vater. Overall 13/25 patients had a positive SMA margin, 12 of whom had a carcinoma of the pancreatic head. SMA positivity in the first 2 years was associated with a one and 2 year survival of 70% and 0% respectively which portends a poor outcome.

**Conclusion:** The use of a standardized inking and sampling protocol of resected PD specimens which includes specifically inking the SMA margin leads to a high incidence of margin positivity. The use of a standardized protocol, including specifically inking the SMA margin should be routinely performed on PD specimens.

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**Radical distal pancreatectomy with en bloc celiac axis resection for locally advanced cancer of the pancreatic body**

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Despite the development of surgical technique, locally advanced cancer of the pancreatic body is still associated with a low resectability and dismal prognosis. The main reason for unresectability is the invasion of major vessels such as the common hepatic artery (CHA) and celiac axis (CA). Resection of the involved arteries can increase respectability and thus might improve prognosis and quality of life (excellent pain control) in such patients. A 49-year-old woman was admitted to our hospital because of persistent epigastric and back pain, as well as weight loss. Contrast-enhanced computed tomography showed a tumor, 4 cm in diameter, in the body of the pancreas with encasement of the CA and CHA. An en bloc subtotal pancreatectomy with splenectomy and resection of the CA was performed. The stomach was preserved. Surgical margins were free of tumor. Intra-operative Doppler ultrasonography measurement of the hepatic arterial flow was obtained before and after clamping of the CA. No significant change in the color and tension of the liver was observed. The hepatic arterial flow via the pancreatic arcade from the SMA was sufficient and no re-arterialization of the liver was performed. The patient had an uneventful post-operative course and was discharged on post-operative day 12. 34 months after the operation, the patient is free from epigastric and back pain, without evidence of tumoral recurrence.

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**Laparoscopic robot-assisted Whipple procedure**

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**Purpose:** Advances in robotic surgery have allowed the frontiers of minimally invasive surgery to expand. We present a video demonstrating the key technical maneuvers during a Laparoscopic Robot-assisted Whipple procedure (da Vinci S System, Intuitive Surgical, Sunnyvale, CA, USA). The video demonstrates utilization of the robot assistance for pancreaticoduodenectomy, as well as the reconstruction, including the pancreatic duct to small bowel mucosa anastomosis.

**Case presentation:** The Robotic Whipple is performed on a 69-year-old male with a pre-operative diagnosis of a main duct intraductal papillary mucinous neoplasm

(IPMN) with ominous features, including pancreatic duct obstruction. Pre-operative symptoms included steatorrhea and 15 lbs weight loss over the proceeding 4 months. Endoscopic ultrasound and pre-operative imaging revealed a 6.2 × 3.3 cm nodular cystic structure in the head of the pancreas. Cyst fluid aspiration demonstrated an elevated CEA level. Relevant past medical history also includes a right hemicolectomy for colon cancer 6 years prior to the Whipple.

**Results:** The Robotic Whipple utilized 9 h and 47 min of robotic time, 6 min Robotic docking time, and blood loss was approximately 200 cc. Pathology assessment revealed a main duct IPMN without evidence of malignancy and widely negative margins. The patient had an uneventful hospital stay, used no pain medication after post-operative day 2, and was discharged home post-operative day 6 with no post-operative complications.

**Conclusions:** The video demonstrates that, with robotic assistance, the minimally invasive Whipple procedure can be completed safely and effectively, incurring all of the advantages of laparoscopic pancreas resections.

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**Pancreatic head resection with segmental duodenectomy (PHRSD) for intraductal papillary mucinous neoplasms (IPMN) of the pancreatic head**

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We proposed pancreatic head resection with segmental duodenectomy (PHRSD) for benign or low grade malignancy tumor of the pancreatic head region as a function-preserving operation instead of pylorus preserving pancreatoduodenectomy (PpPD). This operation is simple, easy and safe procedure compared with duodenum preserving pancreatic head resection (DpPHR). Laparotomy is done by upper midline skins incision. The gastroduodenal and duodenocolic ligament is divided. Intra-operative US study is done. By conserving the right gastric artery and gastroduodenal artery, 5–7 cm of the first portion of the duodenum is preserved with good arterial circulation. The anterior superior pancreatoduodenal artery and posterior superior pancreatoduodenal artery are ligated and divided. In addition, by conserving the anterior inferior pancreatoduodenal artery, the third portion and anal side of the second portion of the duodenum are preserved with good arterial circulation. Resection of the pancreatic head with 3–4 cm of segmental duodenectomy including minor and major papilla completes PHRSD. The distal pancreas is examined by ultrathin pancreatoscope. Reconstruction of the alimentary tract is then performed with pancreatogastrostomy, end to end duodenoduodenostomy and end to side choledochoduodenostomy. PHRSD is simple, easy,

safe and function-preserving operations for benign or low grade malignancy tumor of the pancreas. In this video, PHRSO for the branch type of IPMN of the pancreatic head is presented.

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### Laparoscopic middle pancreatectomy

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A middle pancreatectomy provides a pancreas-sparing treatment for low grade neoplasms arising in the body and neck of the pancreas. We demonstrate a middle pancreatectomy performed laparoscopically for treatment of a pancreatic endocrine tumor arising in the neck of the pancreas. A 40-year-old woman undergoing evaluation of left-sided abdominal pain was found to have a hypervascular mass in the neck of her pancreas causing upstream pancreatic ductal dilatation. Endoscopic ultrasound confirmed obstruction of the pancreatic duct by the mass, and biopsy of the mass confirmed the diagnosis of a pancreatic endocrine tumor. The patient was positioned supine and using five ports placed in standard positions for a laparoscopic distal pancreatectomy, the neck of the pancreas was elevated and separated from the splenoportal confluence. The pancreatic endocrine tumor was localized using a laparoscopic ultrasound probe, and the pancreas was then divided to the left and right of the mass using a laparoscopic stapler, allowing the neck of the pancreas containing the mass to be passed off of the operative field. After further mobilizing the body of the pancreas, a Roux limb was created using additional applications of the stapler and was passed in retrocolic fashion to the pancreas. The staple line was excised from the end of the pancreas, and a two layer interrupted hand sewn end to side pancreaticojejunostomy was then completed in duct to mucosal fashion. The procedure was completed without complication and with minimal blood loss. The patient's post-operative course was uneventful and she was discharged home on post-operative day 4. She has since shown no signs of pancreatic endocrine or exocrine insufficiency, and a follow-up CT scan obtained 6 months post-operatively has shown marked improvement in the pancreatic ductal dilatation consistent with a patent pancreaticojejunostomy. A middle pancreatectomy preserves pancreatic parenchyma and thereby reduces the likelihood of subsequent pancreatic endocrine or exocrine insufficiency. Performing this operation laparoscopically confers the additional benefits associated with minimally invasive surgery. Moreover, the magnification provided by laparoscopy facilitates completion of a precise pancreaticojejunostomy and may decrease the risk of leakage from this anastomosis.

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### Totally laparoscopic pancreatoduodenectomy

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I. FERNÁNDEZ, MD and C. BOZA, MD

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The development of laparoscopic surgery has allowed incorporating this technology to the surgical treatment of

diverse pathologies. The use of laparoscopic approach for pancreatic resections has remained limited for selected patients with left-sided (body and tail) lesions. Pancreatoduodenectomy (PD) is a high demanding operation with multiple anastomoses which require advance experience in laparoscopic as well as pancreatic an hepatobiliary surgery. Most of literature reports in laparoscopic PD include hand assisted support especially for reconstruction step (pancreas, biliar and gastro-anastomoses). This video shows a totally laparoscopic PD in a 16-years-old woman with a 5 cm pseudopapillary tumour of the head of the pancreas. Her history was abdominal pain and gastric outlet obstruction. After surgery she had full recovery with no post-operative complications. So far we have performed 4 totally laparoscopic PD for both benign and malignant disease of the head of pancreas.

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### Robotic-assisted laparoscopic spleen-preserving distal pancreatectomy for solid pseudopapillary neoplasm

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**Objective:** An 8-min video will be presented to demonstrate a robotic-assisted laparoscopic spleen-preserving distal pancreatectomy (LSPDP) using the daVinci® robot (Intuitive Surgical, Inc, Sunnyvale, CA, USA) for a case of solid pseudopapillary neoplasm (SPN) of distal body of pancreas.

**Background:** SPN is a rare tumor accounting for less than 1–2% of primary pancreatic neoplasms. The etiology and biologic behavior are still not completely understood. With latest advances in minimally invasive surgery, laparoscopic pancreatic surgery (LPS) is now established as a safe and feasible operative procedure. Laparoscopic distal pancreatectomy is an appropriate treatment option for benign or low-grade malignant pancreatic lesions. In addition, there has been an increasing trend towards adopting LSPDP due to the importance of spleen for its immunologic functions. Robotic-assisted LPS is the latest development in this field of pancreatic surgery.

**Materials and methods:** The patient, a 22-year-old woman was evaluated for intermittent left upper quadrant abdominal pain, hot flashes and diarrhea of 3 months duration. She was in otherwise good health with no past medical history. CT scan of the abdomen revealed a 4 cm solid mass in the distal body of pancreas, hypointense in the delayed venous phase, with no lymphadenopathy, free fluid or hepatic metastases. Endoscopic ultrasound (EUS)-guided fine needle aspiration cytology (FNAC) confirmed SPN, staining strong-positive for vimentin, CD10, alpha-1-antitrypsin and CD56, and focal-positive for synaptophysin and chromogranin. To help with the complexity of the dissection involved, the daVinci® robot was utilized. Dissection was performed using three robotic instrument arms via 8 mm ports, as well as a single assistant port for suction/irrigation device, laparoscopic ultrasound probe and endostaplers. The spleen was carefully preserved following Warshaw's procedure with division of splenic vessels.

**Discussion:** To our knowledge, this case represents the first report of robotic-assisted LSPDP in an adult female patient for SPN. The entire procedure was completed laparoscopically, with no complications, and the patient was discharged home 4 days later. Surgical pathology confirmed a 4 cm sized SPN with no lympho-vascular invasion and all ten lymph nodes negative for metastasis. She remains symptom-free during the follow-up. Robotic-assisted LSPDP is a safe and feasible option for pancreatic neoplasms of benign or low-grade malignant potential.

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### **Transduodenal ampullectomy and exploration of the common bile duct for treatment of an ampullary adenoma and impacted common bile stone**

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A transduodenal ampullectomy is an effective and potentially less morbid alternative to a pancreaticoduodenectomy for treatment of a benign ampullary adenoma. We demonstrate the technique of a transduodenal ampullectomy performed together with exploration of the common bile duct for treatment of a benign ampullary adenoma and a concurrent impacted common bile duct stone. A 75-year-old woman presented with jaundice and was found on CT scan to have a large common bile duct stone. An ERCP confirmed the presence of the stone but also identified a large ampullary mass that was unsuitable for endoscopic removal. Biopsies, however, showed only benign adenomatous changes. After placement of a stent across the obstructing stone, an endoscopic ultrasound was performed. This showed the ampullary abnormality to be confined to the mucosa of the duodenum without extension into the deeper wall layers. Extension up the bile duct could not be determined. In light of these findings, a transduodenal ampullectomy and transduodenal exploration of the common bile duct were performed for treatment of the ampullary mass and common duct stone. After performing a Kocher maneuver, the duodenum was opened transversely over the palpable ampullary abnormality. The mass was delivered out through the duodenotomy, and the mucosa around the mass was incised circumferentially where it appeared normal. The bile and pancreatic ducts were transected and the mass was removed. Frozen section evaluation of the deep margin did not show adenomatous changes, but some frond-like changes

were visible extending up the bile duct. A short segment of the bile duct was excised to remove these changes. The bile duct was then explored and the large stone was removed using stone forceps, a biliary catheter, and a mechanical lithotripsy catheter. Duct clearance was confirmed by cholangioscopy. Next, the septum between the bile and pancreatic duct openings was incised to create a single common opening to which the surrounding duodenal mucosa was then sewn, thereby completing reconstruction of the two ducts. Finally, the anterior duodenotomy was closed transversely in two layers. The patient recovered uneventfully from the procedure, and final pathologic evaluation showed a benign ampullary adenoma with negative margins of resection. This patient illustrates the usefulness of a transduodenal ampullectomy for treatment of a benign ampullary adenoma unsuitable for endoscopic resection.

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### **Laparoscopic treatment of todani type 1 choledochal cyst**

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The choledochal cyst are uncommon congenital disorder characterized by a globular or fusiform dilatation of the common bile duct just below the site of entry of the cystic duct. It is detected with an incidence of 0.2–0.5% per 1 000 000 population. There is a 3 : 1 female predominance. The diameter of the dilatation varies between 2 and several centimeters. The etiology is unknown but may be related to a mal-junction of the pancreaticobiliary channel. Total excision of the cyst in types I, II, and IV followed by reconstruction of the biliary tree with hepaticojejunostomy in a Roux-en-Y fashion has been widely accepted as the procedure of choice in treating choledochal cysts and has been found to be superior to hepaticoduodenostomy. In selected patients with a favorable anatomy we will consider a laparoscopic approach for removal of the cyst. We present two cases of choledochal cyst type I (according to Todani's classification) that were successfully excised by laparoscopy including hepaticojejunostomy. The patients had an uneventful recovery. The laparoscopic management of the choledochal cyst is feasible. Surgeon may reproduce every single step of the open technique with all the benefits of the laparoscopic approach.

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Competitive Video Session 2: Liver  
Sunday, March 15, 2009 7:00–9:00 AM

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**Bilobar totally laparoscopic anatomic segmental resection of hepatocellular carcinoma in cirrhotics**

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Hepatic resection remains the gold standard for curative resection for hepatocellular carcinoma (HCC) in non-transplant candidate patients. Data is emerging showing that radiofrequency ablation (RFA) is competitive with resection in the treatment of small HCC (< 5 cm). Laparoscopic hepatic resections are gaining popularity as laparoscopic techniques and vessel sealing instruments improve. Anatomic and non-anatomic resections as well as major lobectomies can now be done safely laparoscopically for both benign and malignant disease. Because HCC often presents as multifocal disease, we combine laparoscopic resection and RFA in patients with preserved liver function. In a subset of patients with limited bilobar disease, laparoscopic resection is our preferred treatment choice.

**Methods:** We present two cases of patients with bilobar HCC that were treated by laparoscopic hepatic resection.

**Position:** Patients were placed on a bean-bag in a partial left lateral position (~70°) with the bed slightly flexed. With the bed rotated fully to the right, the patient assumes a near supine position.

**Procedure:** A 4–5 cm vertical incision is made at the umbilicus and gel hand port device is inserted. Although the surgeons hand is not inserted, we prefer the gel port because we can use up three working ports at this location. Moreover, the intact specimens are extracted through our periumbilical port site. When appropriate, anatomic segmental resections are done with the primary goal of achieving complete histological negative margins. Intra-operative ultrasonography is done and the disease distribution verified. Lines of transection are marked on the surface of the liver using electrocautery. Inflow occlusion is not required and the liver parenchyma is transected using a bipolar cautery device (Gyrus) to expose portal structures. Segmental portal pedicles are then divided with a vascular stapler. Division of the liver parenchyma is continued and the hepatic veins are identified and divide with a vascular stapler. Specimens are individually placed into a nylon bag and extracted through the wound protected umbilical incision.

**Conclusion:** Bilobar laparoscopic hepatic resection is an aggressive treatment modality for patients with multifocal HCC who generally have a poor prognosis. These procedures are still high-risk and should only be done on highly selected patients with preserved liver function. In these carefully selected patients, laparoscopic resection often combined with RFA offers an extended disease free interval and possible extend overall survival.

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**Right hepatectomy extended to segment 4a for hepatocellular carcinoma**

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The video shows a right hepatectomy extended to segment 4a for hepatocellular carcinoma in a 50-year-old woman with HBV+ chronic hepatitis A2F1. In March 2008, screening abdominal US and MRI showed a 4 cm HCC in segment 8 in contact with the right and the middle hepatic veins. AFP was 26.9 ng/mL and liver function tests were normal. Liver resection was planned. A J-shaped incision was performed. The confluence of the hepatic veins and the space between the right and the middle hepatic veins were dissected. A tape was passed between the liver and the IVC in order to perform a hanging maneuver. Right portal branch and right hepatic artery were taped and divided. Ischemic demarcation along the Cantlie's line was obtained. Cautery incision of Glisson's capsule was performed along the right side of the upper part of falciform ligament. The middle hepatic vein was exposed along its final 4 cm up to its confluence into the inferior vena cava. Transection line was then conducted along the Cantlie's line between segments 5 and 4b, and then transversally between segment 4a and 4b to reach transection line along falciform ligament previously marked. Parenchymal transection was performed with bipolar coagulation and ultrasonic dissector. Encountered structures were treated with the application of clips or sutures according to their size. In the horizontal part of transection plane, the middle hepatic vein was identified and divided between ligatures. The right hepatic duct and the portal pedicles of segment 4a were intra-parenchymally divided. The scissural vein was exposed along transection line and preserved. At the end of parenchymal transection the middle and the right hepatic veins were divided by linear stapler. The hepatocaval ligament was divided between clips. Right hepatectomy was completed by mobilisation of the specimen. Operative time was 210 min. A single session of pedicle clamping (20 min) was needed during the final part of parenchymal transection. Blood loss was 250 mL and no transfusions were required. Post-operative course was uneventful and the patient was discharged on post-operative day 10. Final pathology confirmed diagnosis of hepatocellular carcinoma infiltrating the right hepatic vein. Surgical margin was 2 mm.



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**Hepatic resection in polycystic liver disease**

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Surgical treatment of Adult Polycystic Liver Disease (APLD) may include different procedures such as percutaneous drainage, laparoscopic or open fenestration, liver resections and also transplant. Surgeons must have many different skills in order to achieve the best outcomes. Patient selection and Gigot classification may be the key for the best results. We present a single case of a 42-year-old female with APLD associated with kidney polycystic disease. Patient presented mass effect symptoms, right upper quadrant pain, tenderness and fever episodes. US and MRI were performed and patient underwent open surgery combining fenestration and central hepatic resection. Total surgery time was 220 min, Pringle maneuver was done twice (7 and 9 min). Post-operative course with no further complications. Discharged at 5th day. In the follow-up patient was asymptomatic.

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**Two-stage laparoscopic liver resection for bilobar colorectal liver metastasis**

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**Background:** Hepatectomy may prolong survival time of colorectal cancer patients with liver metastases. Two-stage liver surgery is a valid option for the treatment of advanced or synchronous colorectal liver metastasis. Its goal is to achieve a complete tumor clearance in those cases in which a complete resection with a single hepatectomy would have left a remnant post-resection liver too small for patient survival.

**Aim:** To present a video of two-stage laparoscopic liver resection for bilobar liver metastasis.

**Patient and method:** A 54-year-old male suffering from right colon cancer and synchronous bilobar colorectal liver metastasis underwent laparoscopic right colon resection followed by oxaliplatin-based chemotherapy. The patient was then referred for surgical treatment of liver metastasis. Liver volumetry showed a small left liver remnant and CT scan disclosed moderate liver steatosis. Surgical decision was to perform a totally laparoscopic two-stage liver resection. The first stage: laparoscopic resection of segment 3 and ligation of right portal vein. Post-operative pathology confirmed high-grade liver steatosis. After 4 weeks the patient was re-evaluated and the left liver has regenerated. Volumetry of the future liver remnant was 43%. Second stage: Laparoscopic right hepatectomy using intra-hepatic Glissonian approach without Pringle maneuver and without hilar dissection. Intra-hepatic access to the main right Glissonian pedicle was achieved with two small incisions and an endoscopic vascular stapling device is inserted between these incisions, and the stapler is fired. Line of liver transection is marked along the liver surface following ischemic area.

Liver transection is accomplished with harmonic scalpel and endoscopic stapling device as appropriate. The specimen is extracted through a suprapubic incision. Falciform ligament is then fixed to maintain the left liver in its original anatomical position, avoiding hepatic vein kinking.

**Results:** Operative time was 90 and 240 min, respectively. The recovery after the first and the second operations were uneventful and the patient was discharged on the 2nd and 7th post-operative day, respectively.

**Conclusion:** Two stage liver resections can safely be done by laparoscopy. Intra-hepatic Glissonian approach is a useful tool for pedicle control of the right liver, especially after previous dissection of the hilar plate.

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**En-bloc right nephrectomy/right hepatectomy with hanging liver technique**

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The patient is a 60-year-old man with a biopsy-proven renal cell carcinoma extending from the upper pole of the right kidney into the right liver. The hanging liver technique is employed, as the mass precludes mobilization of the right liver prior to parenchymal transection. Surgical technique is highlighted.

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**Transabdominal and intra-pericardial surgical approach without the use of cardiopulmonary bypass in the management of retrohepatic and supraphrenic inferior vena cava thrombus extending into right atrium**

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Management of thrombus of the inferior vena cava represents a serious challenge for the surgeons. Operative strategy is determined by the proximal and distal extension of the thrombus. When the thrombus extends into the suprahepatic inferior vena cava and right atrium, it is widely accepted that cardiopulmonary bypass is essential to safely and completely thrombectomy. However, the use of cardiopulmonary bypass in this procedure, is associated with high morbidity and mortality. The video shows the pre-operative diagnostic procedures to evaluate the location of the hepatic cyst, the vascular invasion and extent of thrombus as well as the surgical procedure. Ultrasonography, CT and MRI demonstrated a thrombus extending into retrohepatic, supraphrenic-intrapericardial IVC and right atrium. Through a bilateral subcostal laparotomy, total cystoperiostectomy and resection of retrohepatic IVC was performed with total liver vascular exclusion. The transabdominal and



transpericardial approach to the intrapericardial IVC and right atrium avoided median sternotomy. Total thrombectomy with intra-operative transesophageal echocardiogram control was performed. The post-operative course was uneventful and he was discharged on the 15th day after the surgery. Three years after the operation, the patient remains alive without evidence of hydatid disease recurrence.

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### **Totally laparoscopic right trisectionectomy using intra-hepatic glissonian approach**

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**Background:** Laparoscopic right liver trisectionectomy is a very complex procedure with few technical descriptions so far in the English literature. To facilitate pedicle control and to reduce operating time, we have previously described a technique for laparoscopic right liver resections using intra-hepatic Glissonian approach. This video demonstrates technical aspects of a totally laparoscopic right trisectionectomy. Our technique uses intra-hepatic Glissonian approach and total control of venous outflow.

**Method:** This technique uses five trocars. Round and falciform ligaments are taken down close to the abdominal wall in order to facilitate left liver fixation at the end of the procedure. Due to previous right portal vein embolization, hepatic pedicle is not fully dissected. Main right hepatic vein is divided with vascular endoscopic stapler. Main trunk is encircled and its traction or temporary clamping permits complete outflow control of the liver, minimizing bleeding during liver transection. Intra-hepatic access to the main right Glissonian pedicle is achieved with two small incisions and an endoscopic vascular stapling device is inserted between these incisions, and the stapler is fired. Line of liver transection is marked along the liver surface and to avoid possible damage to pedicles from segments 2 and 3, the line of transection should be placed at 1 cm right from falciform ligament. Glissonian pedicle from segment 4 is divided within liver substance. Liver transection is accomplished with harmonic scalpel and endoscopic stapling device as appropriate. The specimen is extracted through a

suprapubic incision. Falciform ligament is then fixed to the abdominal wall in order to prevent remnant liver to rotate spontaneously into the right subphrenic space and cause left hepatic vein kinking. Right hepatic trisectionectomy is then completed.

**Results:** Operative time was 360 min and hospital stay was 7 days. Apart from self-limited biliary leakage, post-operative recovery was uneventful.

**Conclusion:** A totally laparoscopic right trisectionectomy is safe and feasible in selected patients and should be considered for patients with benign or malignant liver neoplasms. The described technique with the use of intra-hepatic Glissonian approach and control of venous outflow may facilitate laparoscopic extended liver resections by reducing the technical difficulties in pedicle control and may diminish bleeding during liver transection.

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### **Robotic resection of colon cancer metastasis to the caudate lobe**

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**Purpose:** To present our experience with laparoscopic robotic assisted resection of a colorectal metastasis to the caudate lobe of the liver.

**Patient:** The patient is a 44-year-old man with a history of stage III colon cancer, status post-transverse colectomy 2 years prior. He received adjuvant FOLFOX and on follow up at 15 months was found to have multiple liver metastases. He underwent laparoscopic radiofrequency ablation of the lesions. One year later he developed metastases to the caudate lobe and segment VI. We present only the resection of the caudate lobe metastasis.

**Results:** Four 12 mm ports were used. The lesser sac was entered through the lesser omentum. A stay suture was placed for traction and a bipolar radiofrequency device was used to circumferentially coagulate the surrounding parenchyma. The parenchyma was then divided using a combination of cautery, Ligasure and clips. Hemostasis and ablation of the resection margin was achieved using the bipolar radiofrequency device.

**Conclusion:** Laparoscopic resection of masses located in the caudate lobe may be achieved with robotic assistance.