# IMAGING FOR BREAST CANCER HELPS IN DIAGNOSIS AND TREATMENT

## II-1. Background

The purpose of this report is to provide an overview of the role of imaging for diagnosis, treatment planning and follow-up of breast cancer. Breast cancer is the most common non-skin type malignancy and the second leading cause of cancer mortality in women, as well as the most common female cancer in both developing and developed countries [II-1]. It arises from the breast tissue, most commonly from the inner lining of milk ducts (ductal carcinoma) or, less frequently, from the lobules that supply milk to the ducts (lobular carcinoma) [II-2].

Although breast cancer incidence, mortality and survival rates vary by as much as four-fold in different geographical regions of the world, its incidence is increasing in the world as a whole. Nevertheless, the age-standardized rate (ASR) still remains almost three-fold higher in developed than in developing areas (more than 80 versus less than 30 new cases per 100 000 per year, respectively) [II-3]. On the other hand, mortality is growing especially in those regions of the world without early detection programmes [II-4], so that the pattern of mortality across different countries does not consistently mirror incidence (see Fig. II-1).

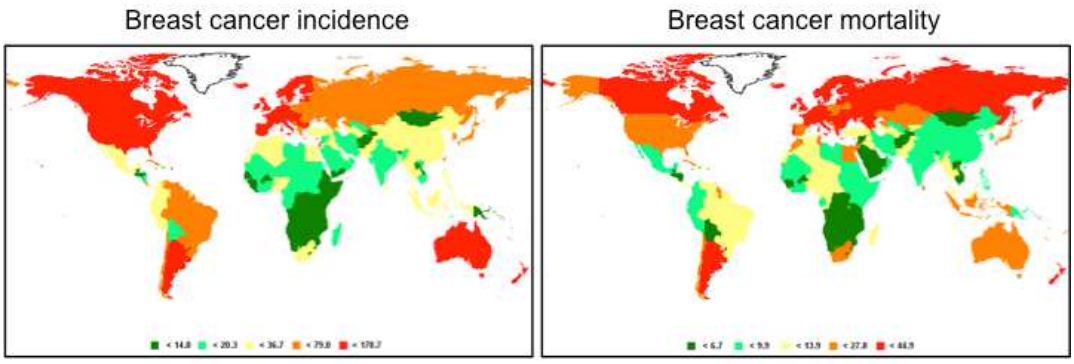


*FIG. II-1. Patterns of distribution of breast cancer incidence and mortality worldwide (modified from WHO/IARC data retrieved from <http://globocan.iarc.fr/>, last access on 18 November 2011).*

Interestingly, higher socioeconomic conditions have been reported to be associated with an increased risk of breast cancer mortality. In fact, longitudinal data on breast cancer mortality according to educational level and marital status obtained from different European countries (Austria, Belgium, Denmark, England, Wales, Finland, France, Norway, Switzerland) or from individual cities (Barcelona, Madrid, Turin) showed a positive association in all populations, except for Finland and France (and for Barcelona among the cities). As a persistent and generalized observation across Europe in the 1990s, women with a higher educational level had an approximately 15% greater risk of dying from breast cancer than those with lower education, a common feature for both married and unmarried women [II-5].

## II-2. Risk Factors

Age, family history and genetics, late first pregnancy and obesity are well-established risk factors for breast cancer [II-6]. Most women with breast cancer are postmenopausal although breast cancer is not uncommon in premenopausal women and is often more aggressive in this group. The recognition of gene mutations in the germ cell line [II-7] (for example, in the BRCA1 gene) is a major advance in understanding the basis of inherited disease; in this regard, the genetic profile is now being increasingly incorporated in breast cancer risk assessments, particularly for families prone to breast cancer at an early age.

## II.-3. Staging and Prognosis

The most crucial parameters for newly diagnosed breast cancer are staging at the time of diagnosis and receptor status.

***Stage***: According to the American Joint Committee on Cancer, the TNM parameters for staging breast cancer include size of the tumour (parameter T), whether or not the tumour has spread to the axillary lymph nodes (parameter N), and whether or not the tumour has metastasized (parameter M) (i.e. spread to a more distant part of the body). Larger tumour size, nodal spread, and distant metastasis have worse prognosis, as also have increasing levels of overall stage, from early-stage disease (stage I) to late-stage metastatic disease (stage IV). In this regard, improved diagnosis and staging, especially sentinel lymph node mapping, has resulted in recent updates in the staging definitions [II-8].

***Prognosis***: Breast cancer cells have receptors on their surface and in their cytoplasm and nucleus. Binding of specific ligands (such as hormones) to these receptors causes changes in cell biology. The most important receptors for breast cancer cells are: estrogen receptors (ERs), progesterone receptors (PRs), and epidermal growth factor receptors (HER2/neu). The growth of breast cancer cells expressing ERs is stimulated by estrogens, so that certain drugs blocking the estrogen effects (e.g. tamoxifen) can effectively be employed to treat cancers that usually have a better prognosis than the ER-negative cancers. On the other hand, while HER2-expressing breast cancers have a worse prognosis than the HER2-negative cancers [II-9], the HER2+ cancer cells respond well to the monoclonal antibody trastuzumab (in combination with conventional chemotherapy); such pattern has significantly improved the prognosis of these cancers [II-10]. Breast cancer cells expressing none of these receptors are called basal-like or ‘triple negative’.

## II-4. Screening and Diagnosis of Breast Cancer

Imaging plays a crucial role for breast cancer screening, for classifying and sampling non-palpable breast abnormalities, as well as for defining the extent of breast tumours, both locally, loco-regionally, and at distant sites. Evaluating response to therapy constitutes an additional important role of imaging. Therefore, imaging via different modalities represents an essential, life-long component for patients with breast cancer, from initial diagnosis throughout the evolution of the disease.

Most breast cancers are detected by physical examination or via a mammography as part of a screening programme [II-11].

### *II-4.1. X-ray mammography*

Mammography uses low-energy X-rays (usually around 30 kVp) to examine the breast and is the primary imaging modality for breast cancer screening, detection and diagnosis. The goal of a screening mammography programme is to detect small (<1 cm) tumours, typically through identification of characteristic masses and/or microcalcification (see Fig. II-2).

Mammographic screening is generally suggested to the asymptomatic 40–45-year-old female population at 2-year intervals, while the American Cancer Society and the American College of Radiology recommend yearly mammograms beginning at the age of 40 years. In case of a normal screening mammogram, the woman is simply invited to the next round of screening. Successful mammographic screening leads to cancer detection at average earlier stage and with smaller size of the lesions which in turn reduced breast cancer mortality [II-12].

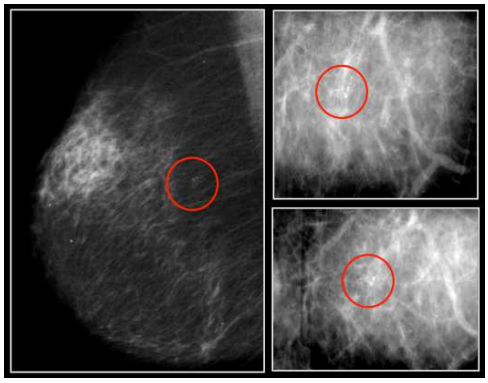

*FIG. II-2. Example of early, in-situ breast cancer detected by screening mammography in a 52-year old woman. Suspicion of cancer is raised by detecting an area with microcalcifications (indicated by red circles) in the breast; images in the right panels represent enlarged details of the same area in two different projections.*

While excisional biopsy has been for some time commonly employed to ascertain the histological nature of suspicious lesions detected during mammography, this practice has now been largely replaced by stereotactic core needle biopsy. Mammography is also used to guide placement of hook-wire needles for intraoperatively localizing non-palpable tumours (e.g. a breast cancer detected by microcalcifications); nevertheless, this procedure is now being increasingly replaced by a procedure called 'radio-guided occult lesion localization' (or ROLL) based on the intralesional injection of radiolabelled particles ($^{99m}$Tc-macroaggregates of human albumin, or $^{99m}$Tc-MAA) that do not migrate from the site of interstitial administration and on subsequent use of a hand-held gamma probe for intraoperative guidance. Moreover, mammography is used to define the extent of malignancy before definitive breast-conserving surgery as well as to monitor the breast after surgery and external beam radiation therapy.

Both ultrasound examination and magnetic resonance imaging (MRI) are important complementary modalities to X-ray mammography for diagnosing, characterizing and determining the extent of breast cancer (see Fig. II-3); while ultrasound is routinely utilized in these roles [II-13], the routine use of MRI is still limited by local logistical and availability constraints.

### *II-4.2. Ultrasound*

Ultrasound (US) is routinely used in breast imaging centres as an essential complement to physical examination and mammography for the evaluation of breast masses. US not only differentiates cystic from solid masses, but also aids in discriminating benign from malignant solid masses (see Fig. II-3). Moreover, in patients with newly diagnosed breast cancer, US of the regional lymph node basins (with US-guided fine-needle aspiration of suspicious nodes) can alter the pre-therapeutic stage. US can also

be used to evaluate the treated breast and to detect and diagnose local recurrences. However, US cannot demonstrate microcalcifications, and its accuracy is highly operator-dependent. Although US can detect some non-palpable carcinomas missed by mammography, its efficacy for breast cancer screening per se remains to be proved. Because of its unique real-time capability, US has become the modality of choice for guiding percutaneous interventional procedures on breast masses, from needle biopsy to ablation.

### *II-4.3. Magnetic resonance imaging*

Magnetic resonance imaging (MRI) shows great promise for detecting mammographically occult breast cancers and for defining the extent of malignant disease (see Fig. II-3). MRI-guided needle localization and core needle biopsy techniques have been developed to complement the increased utilization of MRI for breast cancer staging [II-14]. MRI has also shown to be of value for screening in women at high risk of breast cancer, and has therefore recently been incorporated in the American Cancer Society recommendations for screening [II-15].

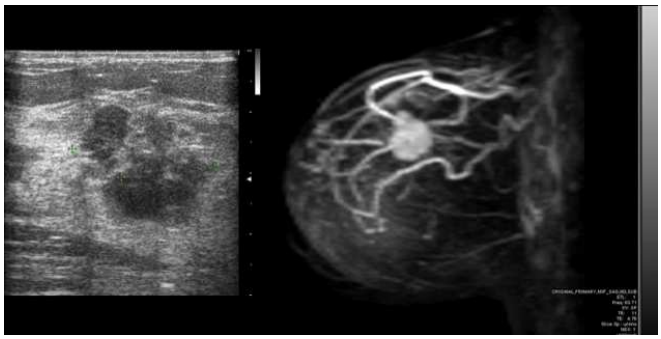

*FIG. II-3. Imaging results obtained in a 40-year old woman included in the regular screening programme for mammography show a mass with irregular margins in the upper inner quadrant of the left breast (maximum diameter 25 mm; image not available because performed in another centre). The patient was then referred for further characterization. Left panel: US imaging confirms the inhomogeneous mass with irregular margins in the left breast. Right panel: MRI with gadolinium contrast shows that the mass has ductal-type contrast enhancement, suggesting breast cancer (confirmed by needle core biopsy as infiltrating ductal carcinoma).*

### *II-4.4. Positron emission mammography*

Cancer imaging by positron emission tomography (PET) with [$^{18}$F]fluoro-2-deoxy-D-glucose ([$^{18}$F]FDG) is based on enhanced uptake of [$^{18}$F]FDG by tissues with increased metabolic demand versus their normal tissue. The large-scale diffusion of [$^{18}$F]FDG PET imaging (and especially PET/CT) for whole-body analysis in the evaluation of the majority of tumours has raised interest in its use to diagnose primary breast cancer. The primary diagnosis of breast cancer is best achieved with the use of dedicated devices for positron emission mammography (PEM). In this regard, although whole-body [$^{18}$F]FDG PET has a certain diagnostic accuracy for detecting malignant breast lesions, its sensitivity is lower than that of other standard diagnostic imaging techniques (see Fig. II-4).

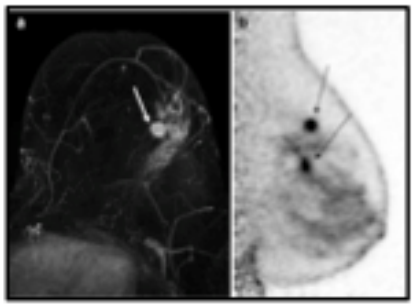

*FIG. II-4. 61-year-old woman with an area of clustered pleomorphic microcalcifications in the upper outer quadrant of the left breast which proved to be ductal carcinoma in-situ following stereotactic biopsy. US identified an additional 7-mm nodule in the same quadrant. Core sampling found this nodule to be invasive ductal carcinoma. MRI identified a 1.2-cm irregular enhancing mass (depicted by arrow) with a possible satellite lesion (left-hand image). PEM confirmed a 1.1×1.0×2.2-cm mass with a second 0.7×0.7×2.5-cm inferior mass with final pathology confirming the two cancer lesions (right-hand image), as depicted by arrows [reproduced from Schilling, K., et al., Positron emission mammography in breast cancer presurgical planning: comparisons with magnetic resonance imaging. Eur J Nucl Med Mol Imaging. 38 (2011) 23-36. The original publication is available at www.springerlink.com.]*

The dedicated PEM devices have several advantages compared to whole-body PET, such as higher geometric sensitivity and spatial resolution, shorter imaging time, reduced attenuation, compression capability and small physical footprint (that allows correlation with X-ray mammography and permits PEM-guided biopsy) [II-16, II-17]. Although early studies confirm the high diagnostic accuracy of PEM, clinical data are still limited, particularly compared to the large amount of data supporting the existing breast-imaging methods

### II-5. Imaging for breast cancer staging

In patients with a known or highly suspected cancer, staging is performed to determine the extent of spread and overall burden of the disease. It includes evaluation of the affected breast, of regional lymph nodes, and of distant or systemic sites. Results of staging are stratified according to the TNM system [II-18].

Assessment of the T parameter in patients with breast cancer is commonly based on X-ray mammography, US and MRI, as described above for diagnostic characterization of suspicious tumour lesions.

Lymph node status (parameter N) is a major prognostic factor in early-stage disease and this information is of paramount importance for tailoring patient-specific treatment. In particular, the presence or absence of metastatic infiltration of the axillary lymph nodes must be considered for further treatment after surgery (adjuvant therapy). In the preoperative phase, the axillary status can be assessed by clinical examination (low sensivity/specificity), US (sensitive and inexpensive, possibly integrated with fine-needle aspiration cytology to increase specificity), and by PET/CT with [$^{18}$F]FDG (over 95% specificity, but low sensitivity for nodes <1 cm in size, and high cost). Therefore, most patients are scheduled for surgery without the axillary lymph node status having been ascertained accurately.

The traditional approach to axillary nodal staging has for several decades been represented by systematic axillary lymph node dissection. However, this procedure is frequently burdened with important immediate and long-term morbidities (such as wound infection and prolonged healing, sensory/motor nerve damage and, above all, lymphoedema of the upper limb). These drawbacks are especially important when considering that complete axillary dissection is actually necessary in only about one out of three patients with early breast cancer. In the past few years, the procedure of sentinel lymph node biopsy for predicting tumour status of the axilla has become the standard of care for breast cancer patients with a clinically negative axilla. This procedure is best performed as radio-guided biopsy of the sentinel lymph node, after lymphoscintigraphic mapping with the use of a radiocolloid agent that is injected interstitially at the tumour.

Staging for distant metastases (parameter M) as part of the initial evaluation is recommended for locally advanced breast cancer, especially for patients with advanced axillary nodal disease, because in these conditions the risk of systemic metastases is high. In these cases imaging is designed to survey the chest, abdomen, pelvis and bones; it generally includes standard chest X-ray or computed tomography (CT), abdominal ultrasound or CT, and bone scintigraphy (see Fig. II-5).

In early-stage breast cancer patients (Stage I or low-end of Stage II), systemic staging is not recommended, unless symptoms are present, since the chance of distant metastases is low and therefore the chance of false positive findings is considerably higher than the chance of true positive findings.

### *II-5.1. Radio-guided sentinel lymph node biopsy for staging*

The high morbidity of axillary lymph node dissection (see above) has stimulated the development of a less traumatic but equally accurate approach, i.e. sentinel lymph node biopsy. The term 'sentinel lymph node' indicates the first lymph node encountered by lymphatic vessels draining the primary tumour, or the first lymph node upon which a lymph vessel originating in the tumour drains directly. This definition does not always correspond to the lymph node nearest the tumour, as the route of the lymphatic vessels is often tortuous and unpredictable. There may be different lymphatic pathways draining certain tumour sites, leading to different sentinel lymph nodes (see Fig. II-6); each sentinel node should therefore be investigated for the presence of metastasis.

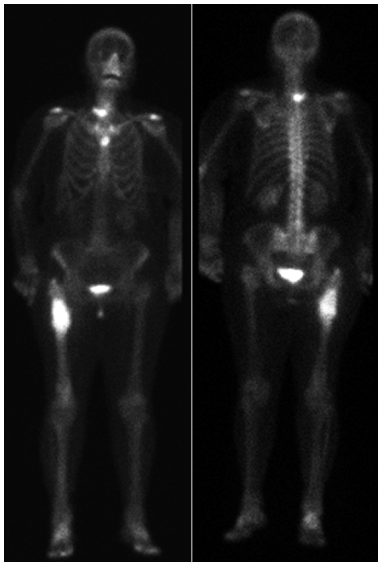

*FIG. II-5. Bone scintigraphy obtained after intravenous injection of $^{99m}$Tc-MDP in a 61-year old patient with newly diagnosed breast cancer in whom the scan was performed for preoperative staging. There are multiple areas of markedly increased uptake corresponding to previously unknown, asymptomatic metastatic lesions in the cervical spine, in the sternum, and in the upper third of the right femur. Such metastatic diffusion disqualifies the patient from curative surgery of the primary tumour.*

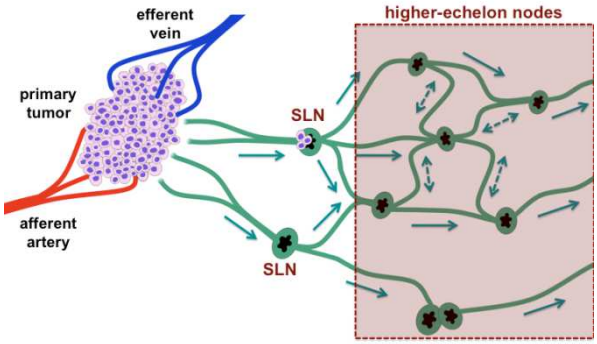


*FIG. II-6. Assuming that lymph drainage from a solid tumour proceeds in an orderly way from lower-echelon to higher-echelon nodes, the first node(s) encountered in such pathway, i.e. the sentinel node(s), is the site where tumour cells contained in the lymph are most likely to originate metastasis before involving higher-echelon lymph nodes. In any given lymphatic basin there can be more than one sentinel lymph node, as lymph drainage can occur via different channels towards the same basin. Complex interconnections occur also at higher levels, with variable directions of lymph flow at intermediate levels within the general pattern of centripetal flow.*

Typically, for sentinel lymph node mapping, a colloidal radiopharmaceutical ($^{99m}$Tc-sulphur colloid or $^{99m}$Tc-albumin nanocolloid) is injected, and sentinel nodes are identified in the preoeperative phase through lymphoscintigraphy, and in the operative phase with a gamma probe.

Interstitial administration of a small amount of radiopharmaceutical is usually performed through US-guided peritumoral injection or through intra/subdermal injection over the tumour, and/or through periareolar injection. Since lymph drains from the intra/subdermal space to the subcutaneous plexus (where lymph originating from the underlying breast parenchyma also merges), a radiocolloid injected intra/subdermally displays the same pathways of lymphatic drainage as the underlying breast gland and of cancer cells entering the lymphatic space.

Lymphoscintigraphy is an integral step for radio-guided sentinel lymph node biopsy, because it is particularly useful to identify not only axillary sentinel lymph node(s) as a guide to subsequent removal aided by intraoperative gamma probe counting, but also draining lymph nodes in other unusual lymphatic basins, especially the internal mammary chain or even infraclavicular lymph nodes. Such lymph node mapping is best performed by single photon emission computed tomography (SPECT), and especially by SPECT/CT rather than by simple planar imaging (see Fig. II-7). At the end of lymphoscintigraphy, cutaneous projection of the sentinel lymph node is marked with a dermographic pen.

In the operating theatre, the surgeon utilizes a hand-held, highly collimated probe for gamma counting (the ‘gamma probe’) to localize lymph nodes that have retained the radiocolloid, usually with very high target/background ratios (at least 10:1). These devices do not produce any scintigraphic images, but they yield both a numerical readout and an audible signal proportional to the counting rate; the latter signal, in particular, guides the surgeon to the radioactive target without distracting his/her visual attention from the surgical bed. The sentinel lymph node and any other radioactive nodes so identified are sent for intraoperative frozen-section analysis (and subsequently processed for definitive staining and histology). Analysis of sentinel lymph nodes is extremely effective and can detect the presence of macrometastasis. [II-19].

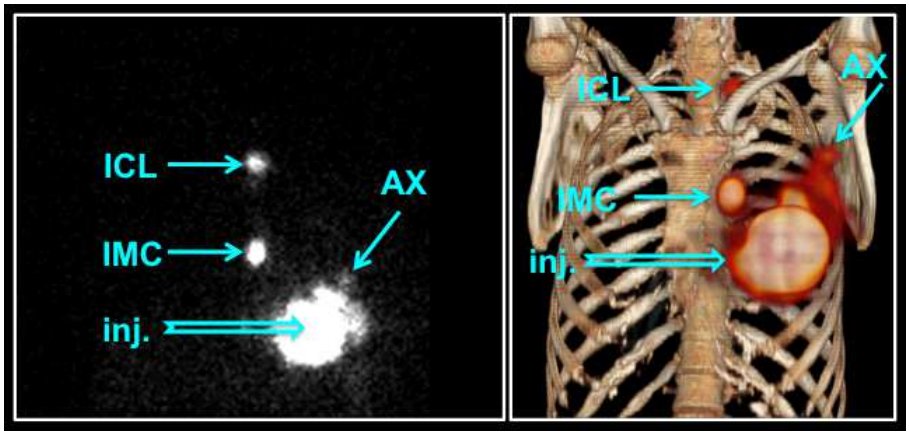


*FIG. II-7. Lymphoscintigraphic mapping obtained after peritumoral injection of 99mTc-nanocolloid in a patient with cancer of the left breast scheduled for surgery and radioguided sentinel lymph node biopsy. Planar images (left panel) show migration of the radiocolloid from the injection site to an axillary sentinel lymph node as well as to additional sentinel nodes in the internal mammary chain and in the infraclavicular space. Topographic location of such lymph nodes, that guide the surgeon for removal, are better shown by 3D volume rendering of a SPECT/CT acquisition (right panel). inj. = injection site; AX = axillary sentinel node; IMC = internal mammary chain sentinel node; ICL = infraclavicular sentinel node.*

In case of sentinel node(s) free from metastasis, the patient can be spared the full axillary dissection because the likelihood that non-sentinel lymph nodes contain metastasis is extremely low, thus making extensive dissection unnecessary. Patients whose sentinel lymph node contains metastasis usually require dissection of regional lymph nodes to determine the extent of axillary metastatic spread [II-20].

### *II-5.2. Radio-guided occult lesion localization (ROLL)*

With the widespread availability of breast cancer screening programmes, breast cancer is being increasingly detected at an earlier stage, and some of the lesions may not be palpable. Several techniques have been developed to assist the surgeon in exactly locating these small cancer foci to facilitate excision during surgery, such as percutaneous introduction of a marker (a needle or wire) during a stereotactic or US-guided biopsy. Recently, a radioguided technique based on direct intralesional injection of a radiopharmaceutical constituted by relatively large particles that do not appreciably move from the site of interstitial injection (such as $^{9m}$Tc-macroaggregates of albumin, with a size range of 10–150 μm) has been developed and largely validated. In the operating theatre, the exact location of the tumour is identified with the help of a gamma probe, which is introduced through the surgical incision and thus helps to easily localize the focal deposition of the radiopharmaceutical (and the tumour). This technique is now being increasingly performed for non-palpable breast lesions, and in several centres around the world it is now considered the routine standard procedure for such clinical condition [II-21, II-22, II-23].

## II-6. [$^{18}$F]FDG PET/CT in patients with breast cancer

### *II-6.1. Overall staging*

The introduction and diffusion of advanced cancer imaging with hybrid PET/CT equipment is having an increasing impact on the clinical management of patients with breast cancer (as well as in patients with a variety of other malignancies). In fact, this technique yields crucial information on the locoregional and whole-body burden of metabolically active disease [II-24], and therefore leads to treatment strategies tailored to the individual patient's conditions, from the phase of initial staging after diagnosis (see above) to the phase of assessing response to anti-tumour therapy [II-25].

Besides its use for initial staging of the axilla (see above), [$^{18}$F]FGD PET/CT is now being recommended for systemic staging in patients with locally advanced breast cancer, i.e. either a primary tumour larger than 5 cm, and/or skin or chest wall tumoral involvement, fixed axillary nodes, positive supraclavicular/infraclavicular and/or internal mammary chain lymph nodes, and inflammatory cancer (see Fig. II-8). Currently, the standard curative approach with these patients consists of neoadjuvant chemotherapy followed by surgery with axillary nodal dissection and external beam radiation therapy.

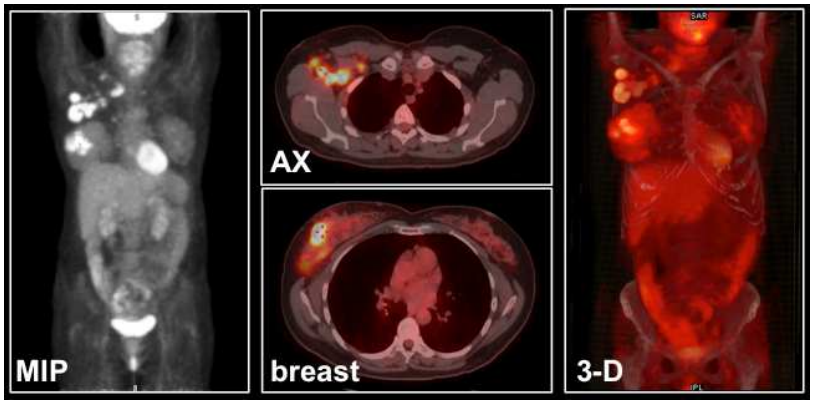


*FIG. II-8. Example of [$^{18}$F]FDG PET/CT in a 58-year old patient with locally advanced cancer of the right breast. The maximum-intensity-projection image in the left panel (MIP) and the 3-D volume rendering in the right panel (3-D) show overall tumour involvement as areas with markedly increased [$^{18}$F]FDG uptake in the breast and in lymph nodes of the axilla, but also extending to infraclavicular nodes (and possibly to internal mammary chain nodes). Selected fused transaxial PET/CT sections at different levels (breast in lower, axilla in upper middle panels) demonstrate in greater detail the anatomo-topographic correlations of the primary tumour and of its lymph node metastases.*

However, some of these patients may have occult distant metastases, and therefore aggressive therapies with curative intent may not be indicated. The presence of distant metastases is also an important prognostic factor in patients with newly diagnosed early breast cancer, and the extent of metastatic disease affects the therapeutic options. [$^{18}$F]FDG PET/CT is reported to be highly sensitive and specific for detecting additional sites of loco-regional lymph nodal spread and/or distant metastases not detected by standard imaging, thus changing staging in up to 25% of the cases. On the other hand, MRI is the method of choice for detecting brain metastasis. Therefore, [$^{18}$F]FDG PET/CT

should complement conventional staging procedures and should not be considered as a total replacement for either bone scintigraphy or diagnostic CT [II-26].

### *II-6.2. Assessment of the efficacy of anti-tumour therapy*

[$^{18}$F]FDG PET/CT has been shown to be particularly useful for restaging breast cancer both in patients with rising tumour markers and negative/equivocal findings at conventional imaging, and for evaluating response to therapy [II-27]. In fact, there is increasing clinical evidence for breast cancer and other tumours that post-treatment [$^{18}$F]FDG PET/CT is the most accurate procedure for assessing response to therapy, both in the neoadjuvant setting and in case of tumour recurrence after primary treatment. The concept of using [$^{18}$F]FDG PET/CT for predicting a therapeutic response is based on an early decrease in glucose metabolism (instead of changes in size, that generally occur later when evaluated by other conventional imaging modalities); such reduction in glucose consumption is closely correlated with the efficacy of therapy. In particular, [$^{18}$F]FDG PET/CT has been shown capable of discriminating patients as responders from non-responders earlier than CT and/or MRI [II-28].

During the course of their disease, about 30% to 85% of patients with recurring and/or metastatic breast cancer develop bone metastases, mostly to the spine and pelvis, followed by ribs, skull and femur. Although bone scanning with $^{99m}$Tc-labelled phosphonates is the most commonly used method for staging bone metastases, the high sensitivity of this technique is counter-balanced by low specificity, since false positive findings can be due to trauma, degenerative changes, and other benign conditions; on the other hand, false negatives can occur in the presence of metastases with predominantly osteolytic patterns and low bone turnover. The availability of a bone-seeking PET agent such as $^{18}$F-fluoride (that accumulates by chemio-adsorption at sites of increased bone turnover) has increased the potential clinical applications of PET/CT imaging also for evaluating bone involvement, e.g. by metastasis. This imaging technique is much more sensitive (and also more specific) than conventional bone scintigraphy with $^{99m}$Tc-labelled bone-seeking agents. Nevertheless, several cost and availability issues must be adequately addressed before this imaging technique can be recommended for patients with breast cancer, especially considering that bone metastases from this tumour tend to be osteolytic or intramedullary and are therefore likely to be better detected by [$^{18}$F]FDG PET/CT than are osteoblastic lesions [II-29, II-30].

## II-7. Challenges and possible responses

All the diagnostic and therapeutic strategies outlined above presuppose nationwide availability of both state-of-the-art diagnostic imaging equipment and implementation of adequate screening programmes and of procedural guidelines for treatment of breast cancer patients, be it single modality or multiple modality therapies. However, this is most often not the case. In particular, while in developed countries with high standards of care the current economic constraints raise issues concerning optimization of procedures and resources, in developing countries more basic issues frequently arise, such as the availability of adequate equipment, logistics, the availability of trained human resources, the existence of a national health care service, and access to health facilities. For instance, the reduced availability of PET/CT (labour-intensive equipment that is relatively expensive in terms of acquisition, setup, daily operation, and well-trained technical and medical personnel) limits the impact of this procedure which is potentially cost-saving if employed systematically according to well-established clinical guidelines.

A paradigm of this situation is represented by radio-guided sentinel lymph node biopsies, the clinical impact of which is most beneficial for those patients with early rather than advanced breast cancer. Various determinants (from socioeconomic and geographic in terms of accessibility to medical centres

with oncological services, to cultural with patients resorting to traditional healers) result in a higher fraction of women with more advanced breast cancers in developing than in developed countries. Therefore, making sentinel lymph node biopsy the standard care in developing countries as it is in developed countries [II-31] actually entails a more comprehensive programme, from implementation of nationwide screening for breast cancer to optimizing access to specialized oncological services. On the other hand, these perspectives should stimulate the implementation of associated training programmes, quality assurance, and validation programmes that would eventually result in overall improvements in the general quality of health care.

## II-8. Summary

Although the incidence of breast cancer (expressed as age-standardized rate) is almost three-fold higher in developed than in developing parts of the world, this is the most common female cancer in both developed and developing countries. On the other hand, mortality is growing especially in those regions of the world without early detection programmes. Age, family history and genetics, late first pregnancy, and obesity are well-established risk factors for breast cancer. Imaging plays a crucial role for breast cancer screening, for classifying and for defining the extent of breast tumours locally, loco-regionally, and at distant sites.

Most breast cancers are detected by X-ray mammography, usually as part of nationwide screening programmes. Ultrasound (US) examination is routinely used as an essential complement to physical examination and mammography in the evaluation of suspicious/equivocal breast masses; US has also become the modality of choice for guiding percutaneous interventional procedures on breast masses, from needle core biopsy to ablation. Magnetic resonance imaging (MRI) with a contrast agent has an important role for identifying mammographically equivocal breast masses as malignant or benign, as well as for defining the local extent of malignant disease.

Besides radiological imaging (mammography, US, MRI), nuclear medicine imaging techniques are playing an increasingly complementary role in the diagnostic characterization of breast lesions, especially when breast-dedicated devices are employed, both for conventional scintimammography and above all for positron emission tomography (PET). Radionuclide procedures play crucial roles for radio-guided surgery in patients with breast cancer, either as radio-guided occult lesion localization (ROLL) or as radio-guided sentinel lymph node biopsy in the phase of primary treatment. Whole-body PET is also of paramount importance for systemic staging, for restaging after neoadjuvant therapy of locally advanced breast cancer, and for assessing the efficacy of anti-tumour therapy.

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