

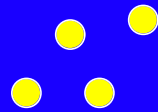
**Molecular Imaging and Therapy with  
Perfluorocarbon Nanoparticulates:  
Environmental Impact.**

**Washington University Medical School  
Saint Louis, MO**

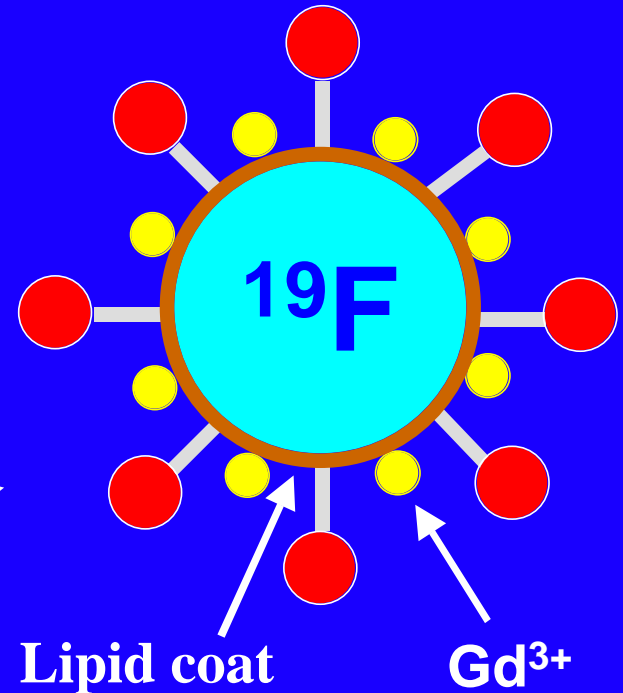
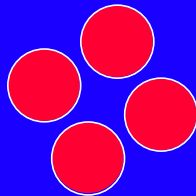
# GENERALIZED TARGETING PARADIGM

## Payloads

*Imaging agents ( $Gd^{3+}$ )*  
*Drugs*  
*Radionuclides*



*Anti-fibrin*  
*Anti-tissue factor*  
*Anti- $\alpha_v\beta_3$ -integrin*



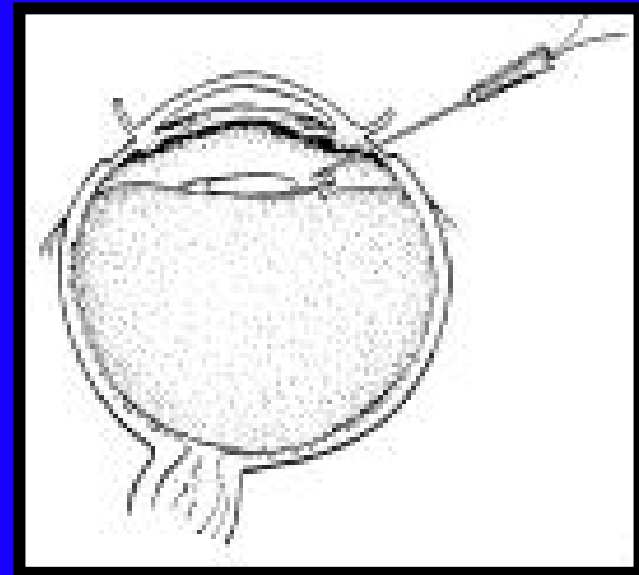
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(**MAb**, aptamers, small peptides, **peptidomimetics**, polysaccharides, etc)

# Perfluorocarbon Biomedical Applications



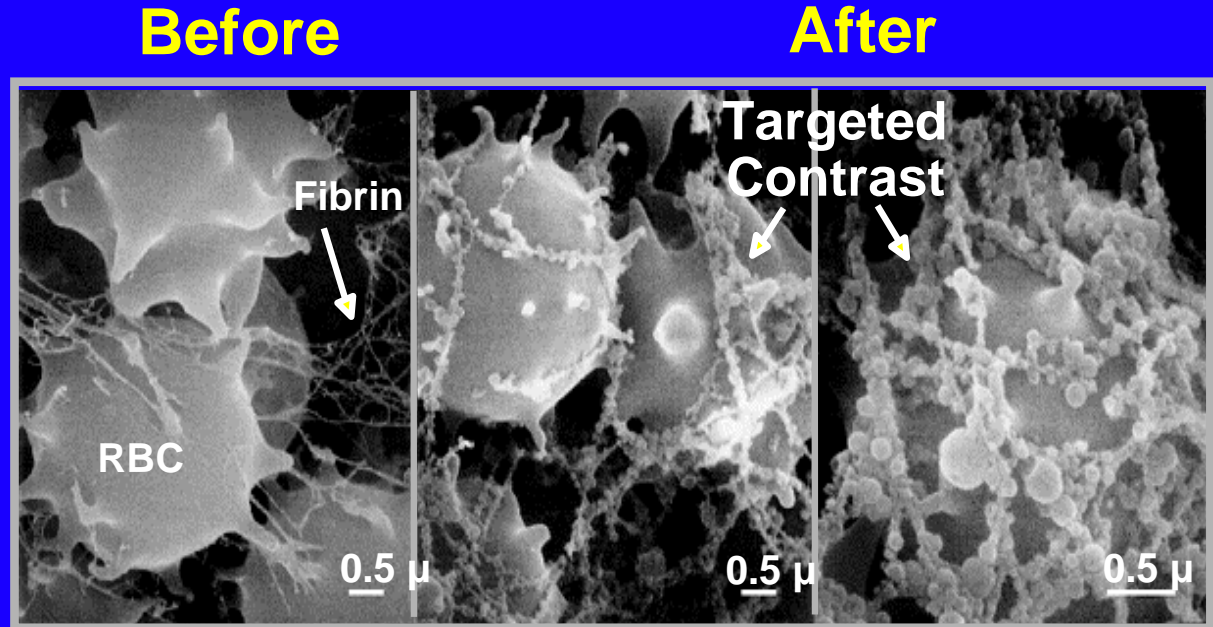
**Liquid Ventilation**



**Vitreous  
Replacement**

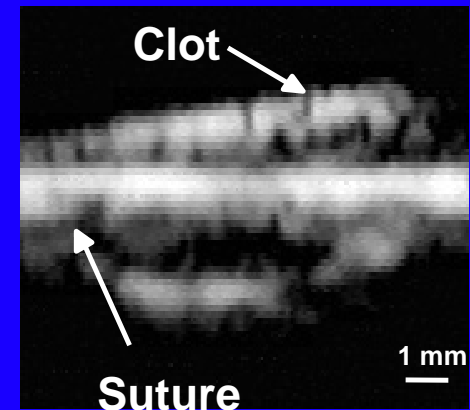
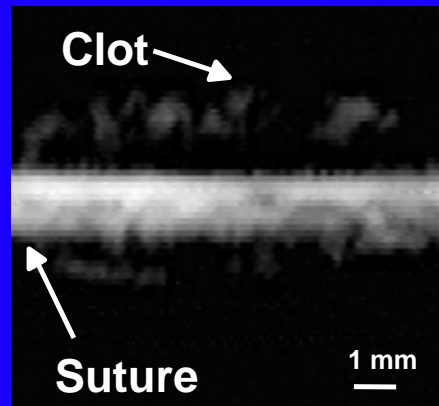
# Fibrin Imaging

Scanning EM  
clot labeled with  
fibrin targeted  
nanoparticles



## Ultrasound contrast

enhancement of fibrin  
clot in vitro using  
conventional clinical  
scanner (7.5 MHz)

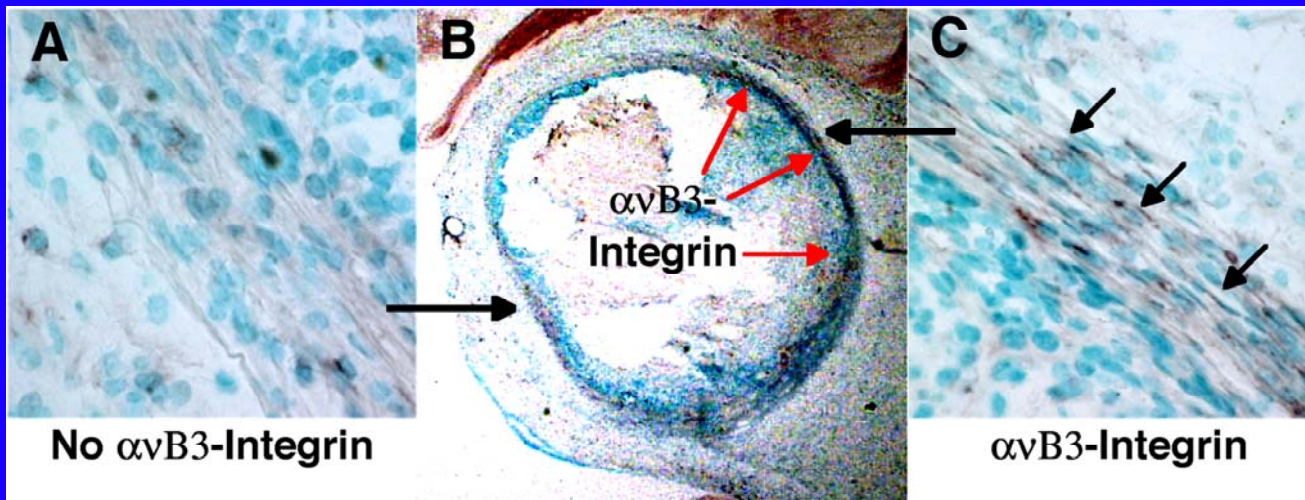
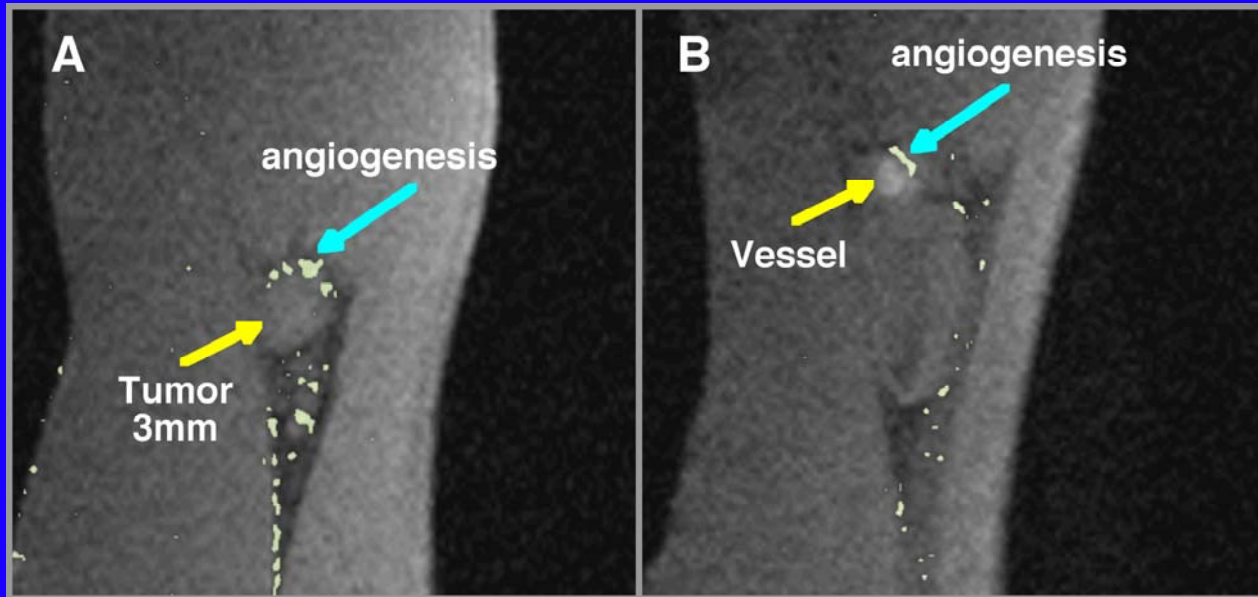


**Control Thrombus Targeted Thrombus**

# Targeted Nanoparticles Support Enormous Paramagnetic Payloads

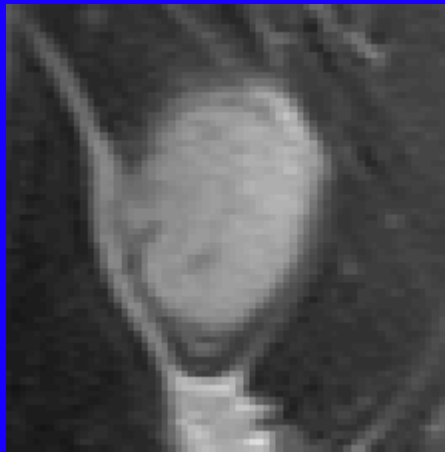
	$\alpha_v\beta_3$ -Targeted	NonTargeted
<b>Gd<sup>3+</sup> Ions / Particle</b>	<b>94,400</b>	<b>92,400</b>
<b>r<sub>1</sub> (s*mM)<sup>-1</sup> [Gd]</b>	<b>19.1</b>	<b>21.1</b>
<b>r<sub>2</sub> (s*mM)<sup>-1</sup> [Gd]</b>	<b>22.9</b>	<b>24.6</b>
<b>r<sub>1</sub> (s*mM)<sup>-1</sup> [Particle]</b>	<b>1,800,000</b>	<b>1,950,000</b>
<b>r<sub>2</sub> (s*mM)<sup>-1</sup> [Particle]</b>	<b>2,160,000</b>	<b>2,270,000</b>

# Detection of Angiogenesis in the Vx-2 Model

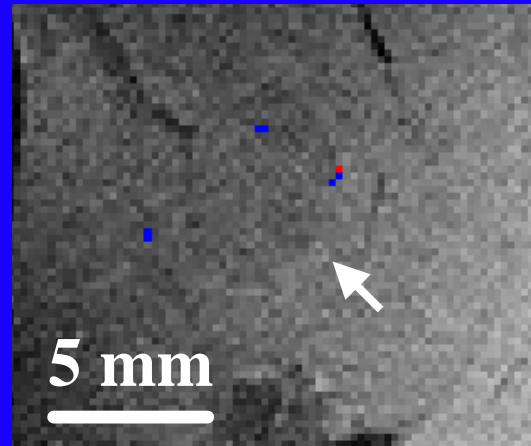


# Masses Seen By MRI Were Not Always Vx-2 Tumors

**T<sub>2</sub>-Weighted MRI**

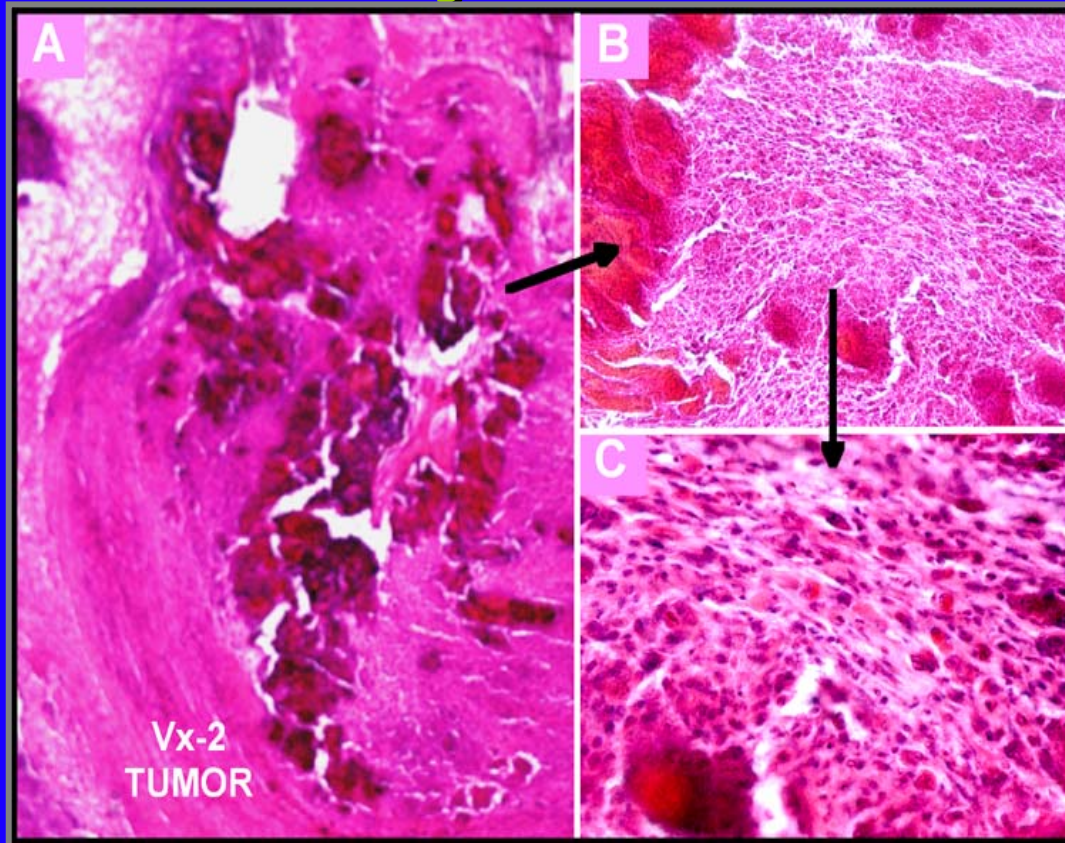


**After  
avB3-Nanoparticles**



**Histology Revealed Rejected Tumor  
Infiltrated with Inflammatory Cells**

# No Molecular Imaging of Angiogenesis for Tumors in Rejection

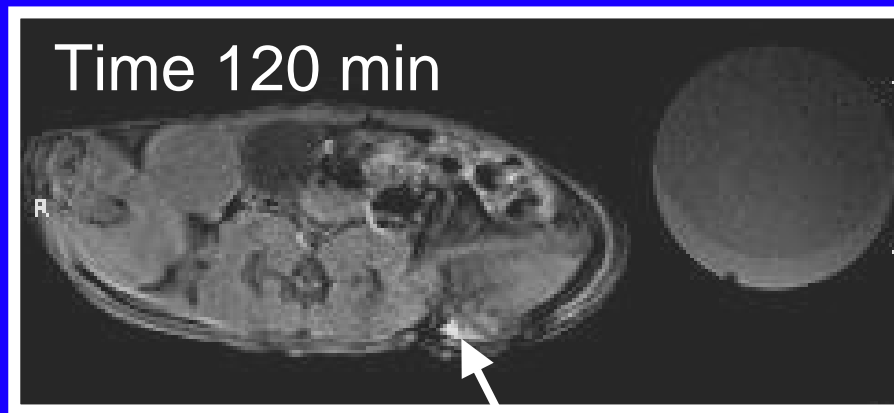
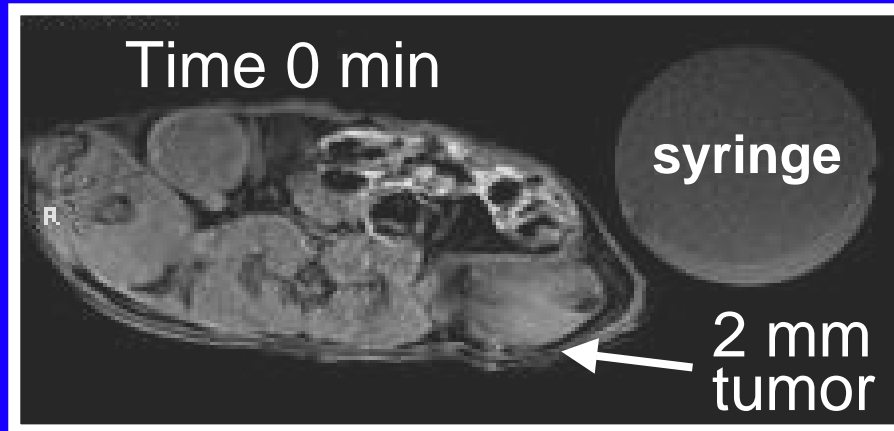


**Histology Revealed Rejected Tumor  
Infiltrated with Inflammatory Cells**

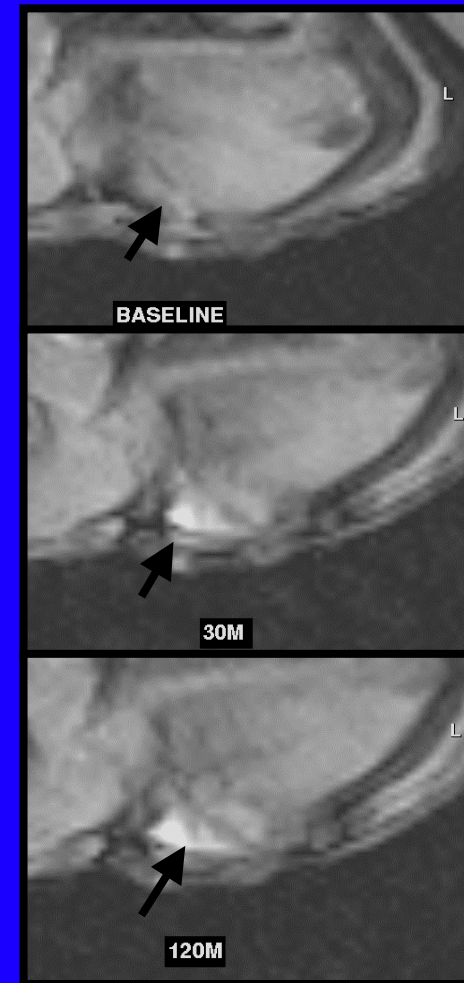


# Melanoma Angiogenesis: Detection With $\alpha_v\beta_3$ Integrin-Targeted Paramagnetic Nanoparticles

## Mouse Imaging @ 1.5T

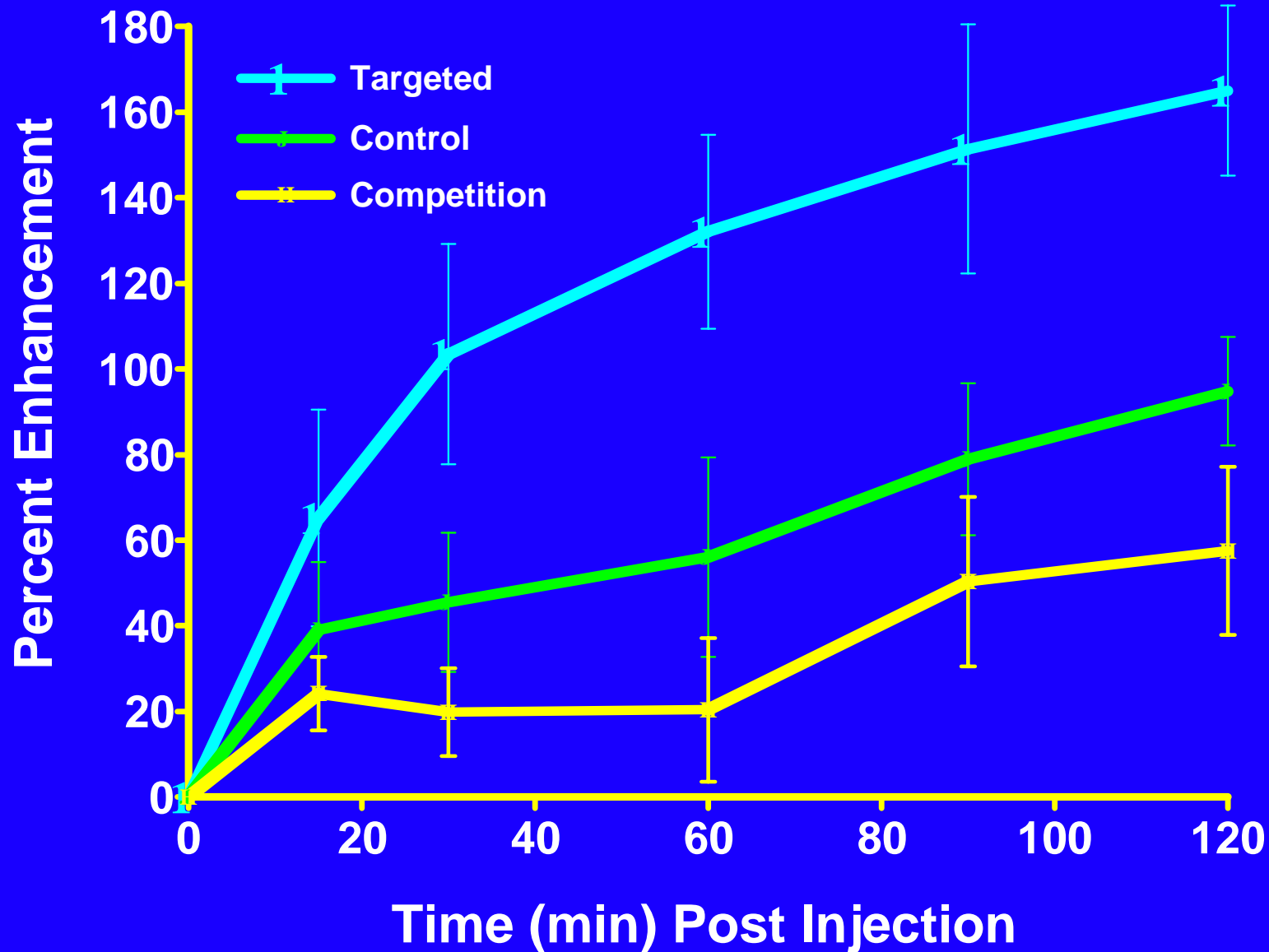


Angiogenesis around  
2 mm melanoma tumor

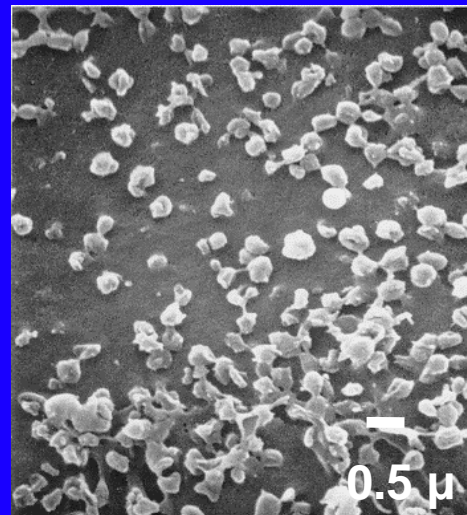
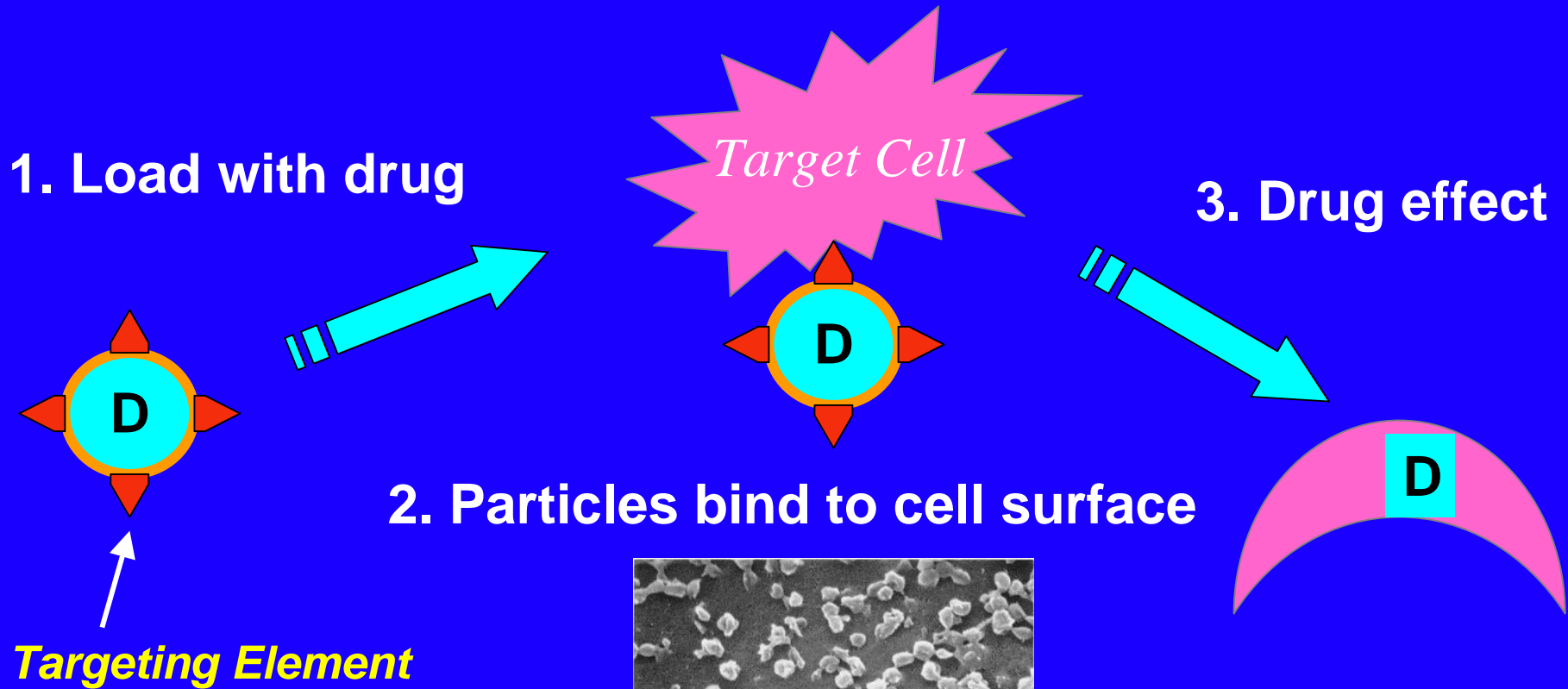


Time course

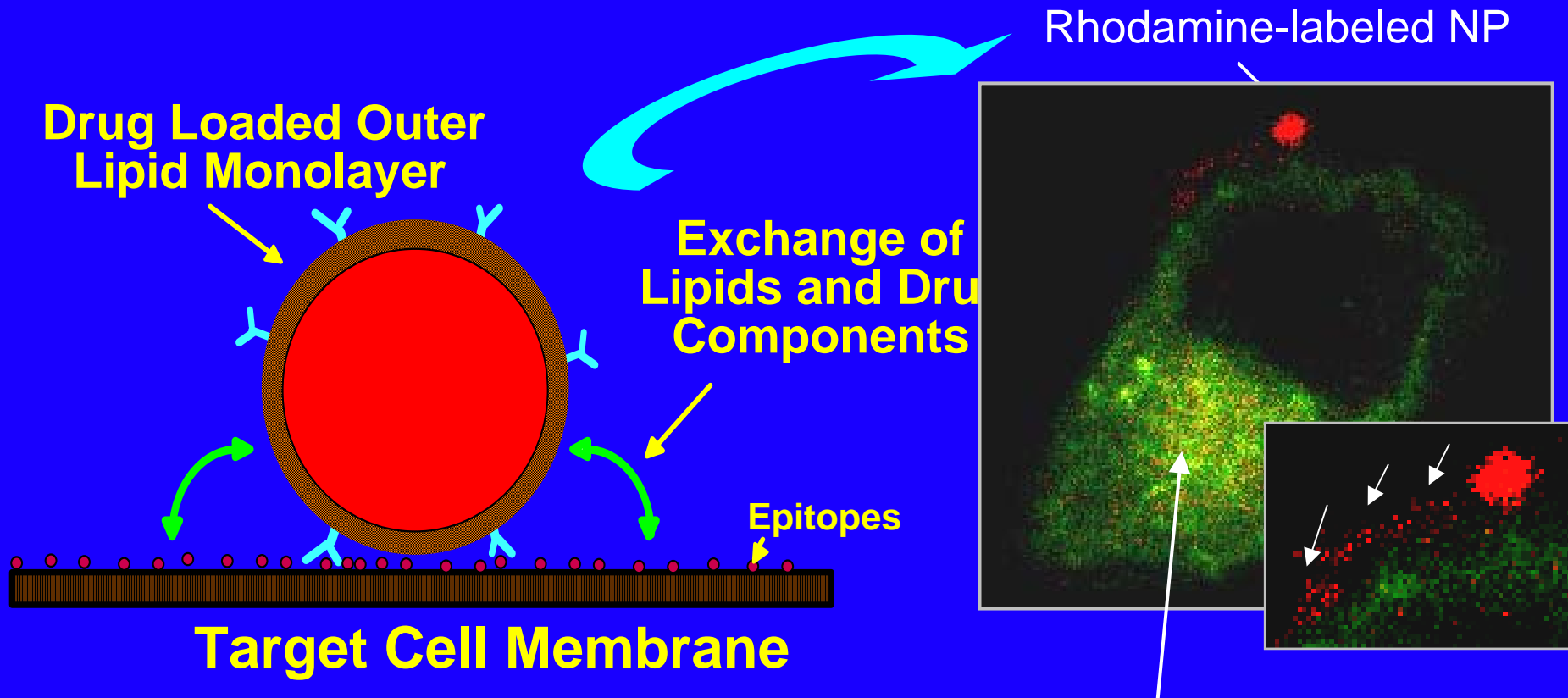
# Time course of MRI Contrast Enhancement



# Site-Targeted Drug Delivery



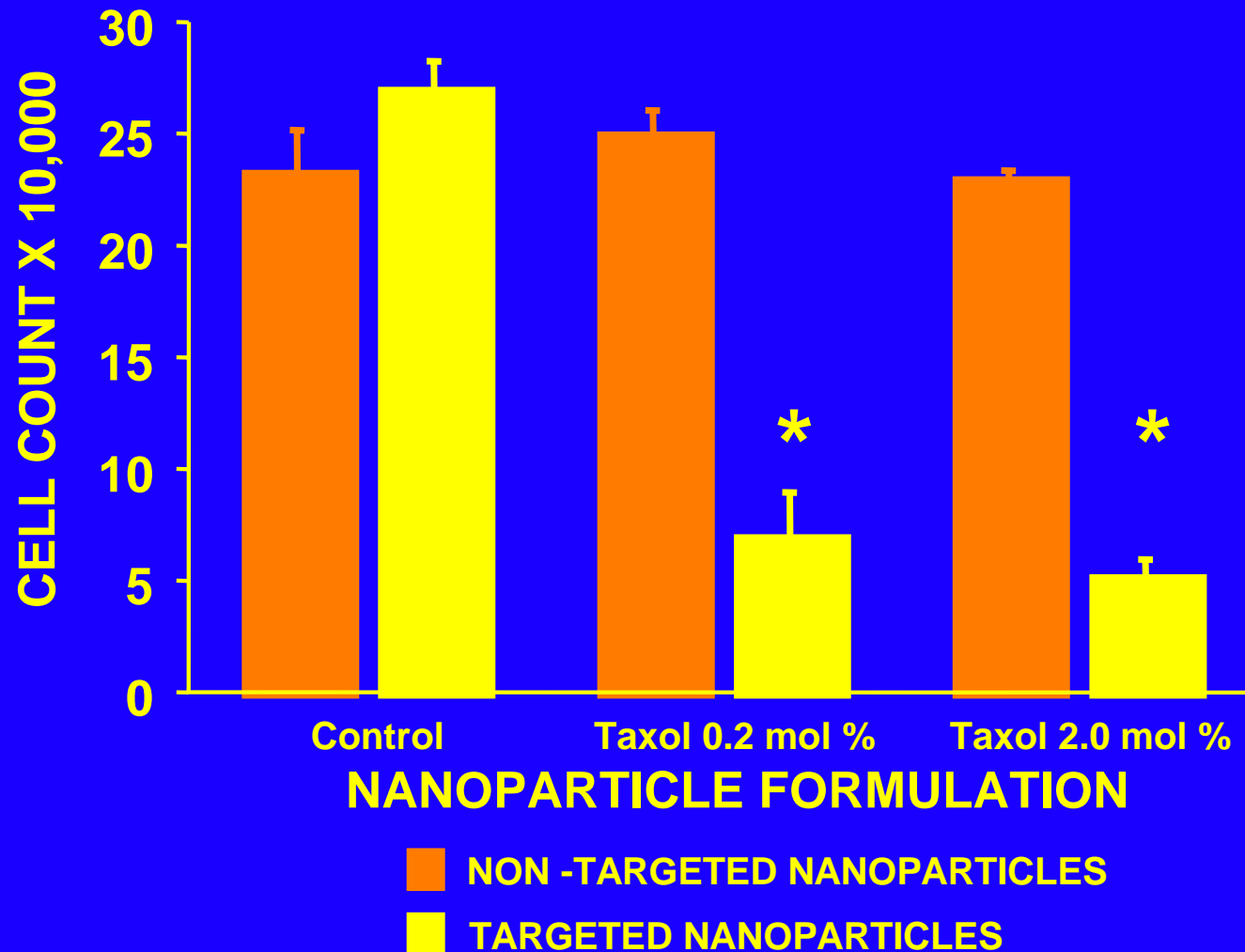
# Novel Mechanisms Of Drug Delivery: “Contact Facilitated Drug Delivery\*”



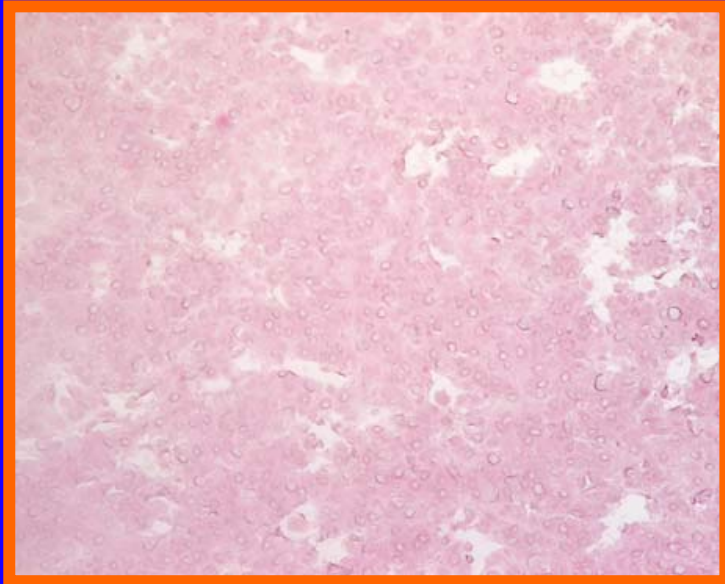
\*Lanza GM, Wickline SA et al: Targeted antiproliferative drug delivery to vascular smooth muscle cells with magnetic resonance imaging nanoparticle contrast agent: implications for rational therapy of restenosis. *Circulation* 2002; 106:2842-2847

GFP-linked endocytotic markers rab5 and rab7 in transfected C32 melanoma cells

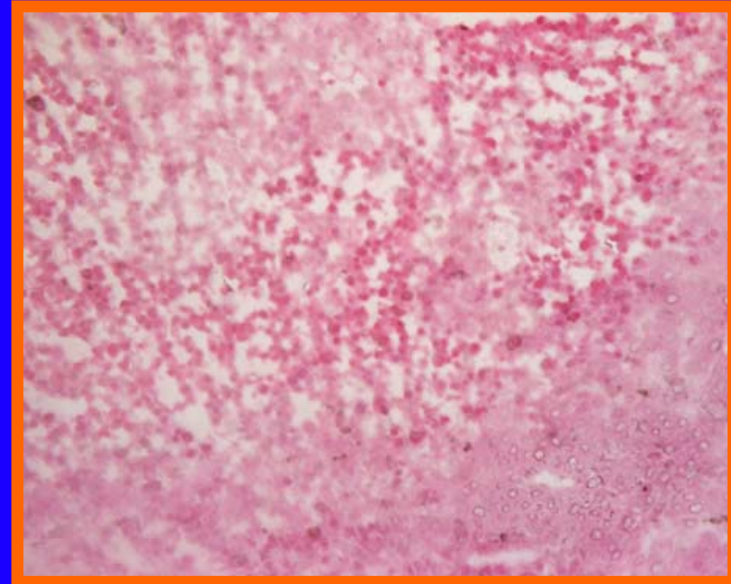
# Antiproliferative Effects of Free versus Tissue Factor - Targeted Paclitaxel Nanoparticles on Vascular Smooth Muscle Cells



# Rejection of Mouse Melanoma 7d following $\alpha_v\beta_3$ -Targeted, DXR, Paramagnetic Nanoparticles

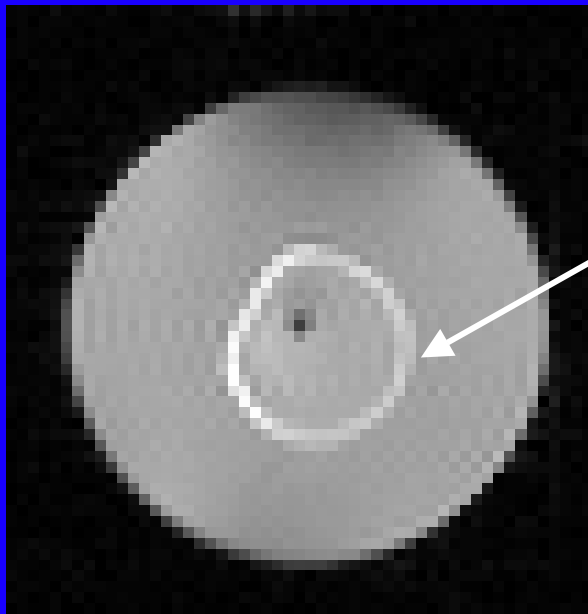


**Control**  
**3/3**

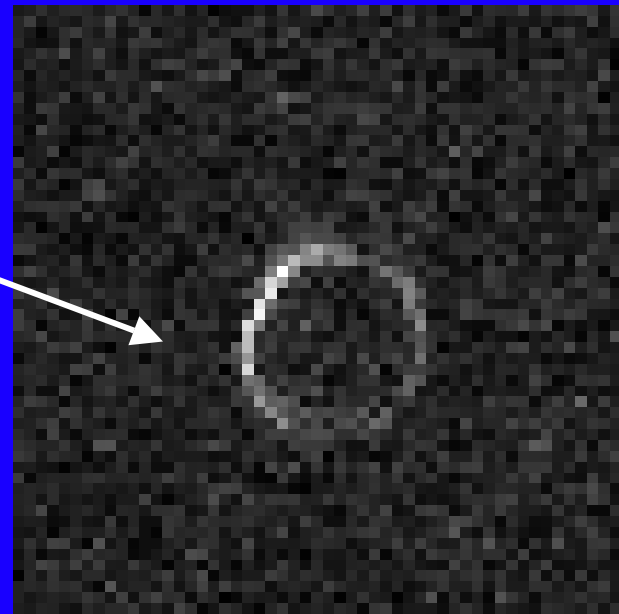


**$\alpha_v\beta_3$ -DXR-NP**  
**(4/4)**

# Proton and Fluorine Imaging



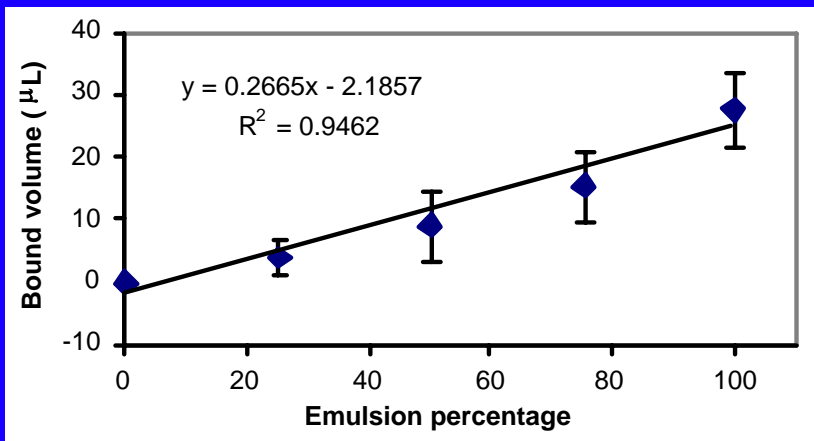
Proton Imaging



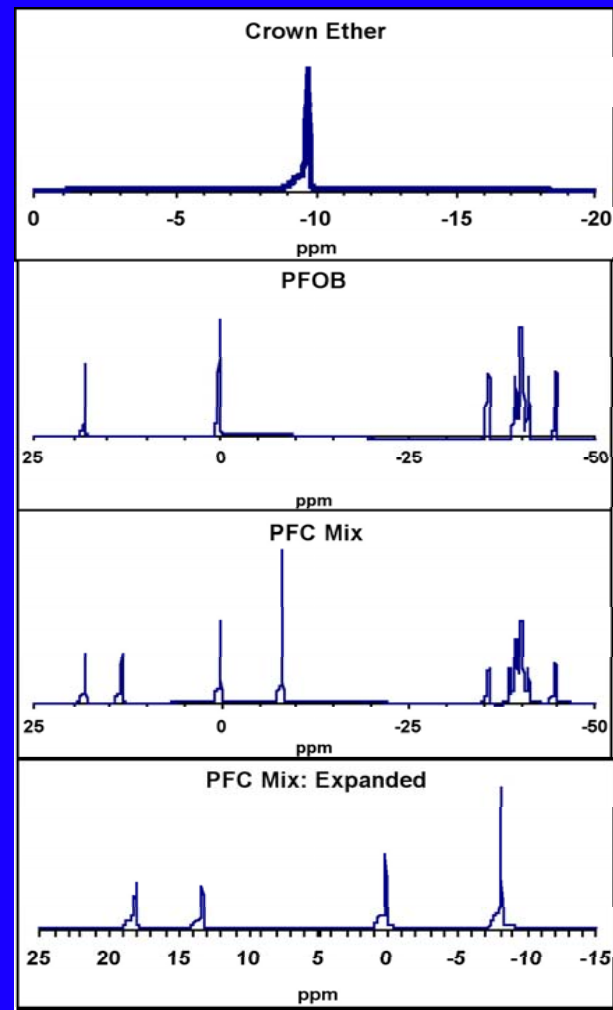
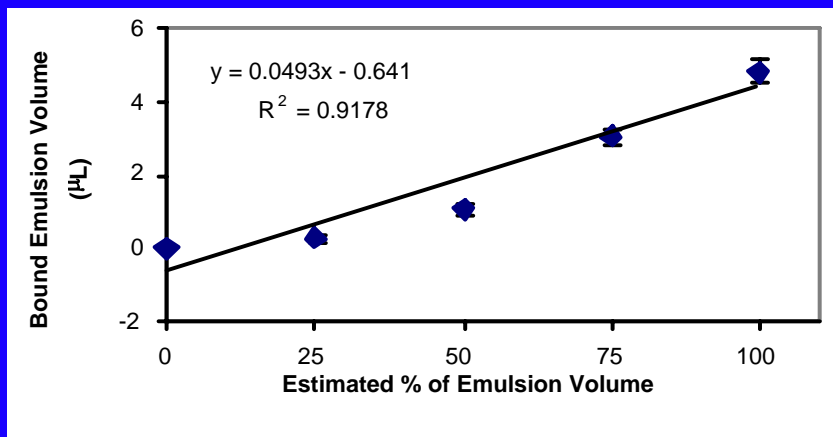
Fluorine Imaging

# Dosimetry of Targeted Nanoparticle Levels

## 15:5 Crown-Ether

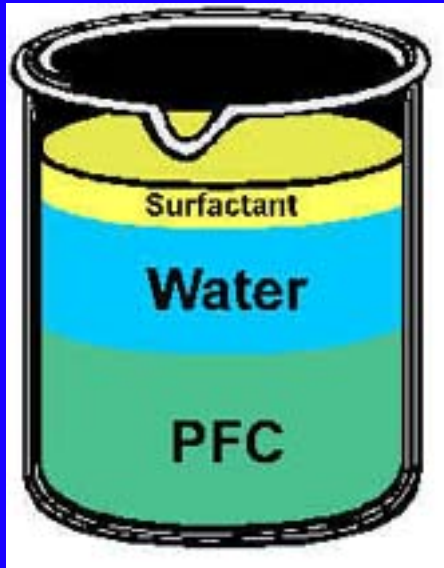


## PFOB





# Typical Pharmaceutical Emulsification Process



**Alliance Pharmaceutical  
Oxygent Production**



**President Bush:** reduce the greenhouse gas intensity of the U.S. economy by 18% over the next ten years.

**Perfluorocarbons have 10,000 times the global warming impact of carbon dioxide**

**Major PFC applications:**

- **electronic insulators**
- **aluminum smelting**
- **refrigerants**
- **subsurface barrier testing**

## **EPA suggested four options for its formal definition of "leak rate." :**

- "annualizing" method.
- "rolling-average" method
- the higher calculated leak rate.
- consistent method

**Non-VOC with no significant participation in ozone formation in ambient air.**

# WU Personnel



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