

US EPA ARCHIVE DOCUMENT

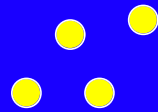
**Molecular Imaging and Therapy with
Perfluorocarbon Nanoparticulates:
Environmental Impact.**

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

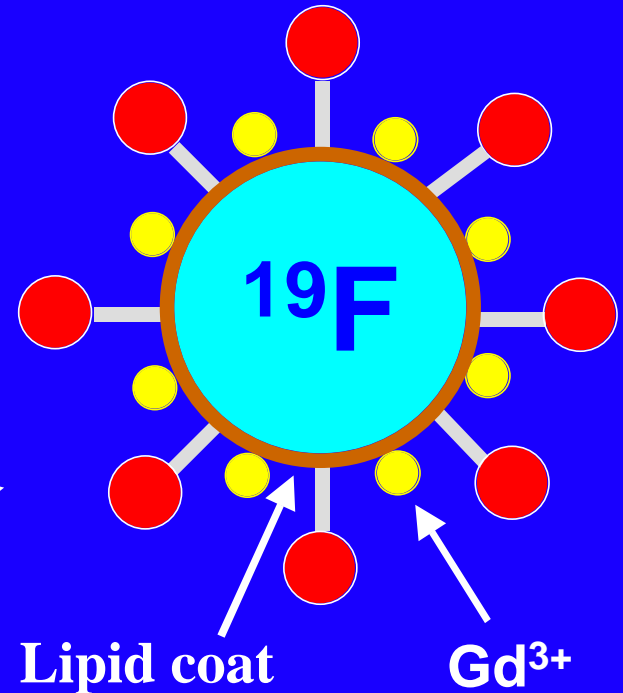
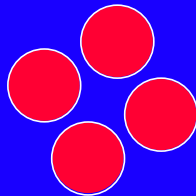
GENERALIZED TARGETING PARADIGM

Payloads

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



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

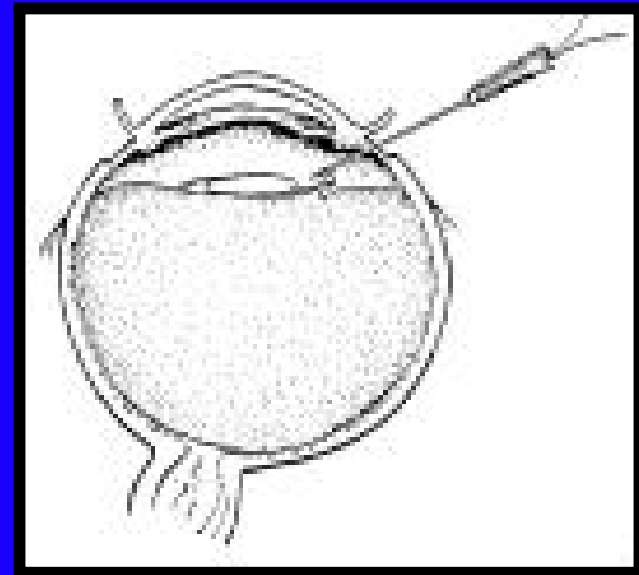


(**M**Ab, aptamers, small peptides, **peptidomimetics**, polysaccharides, etc)

Perfluorocarbon Biomedical Applications



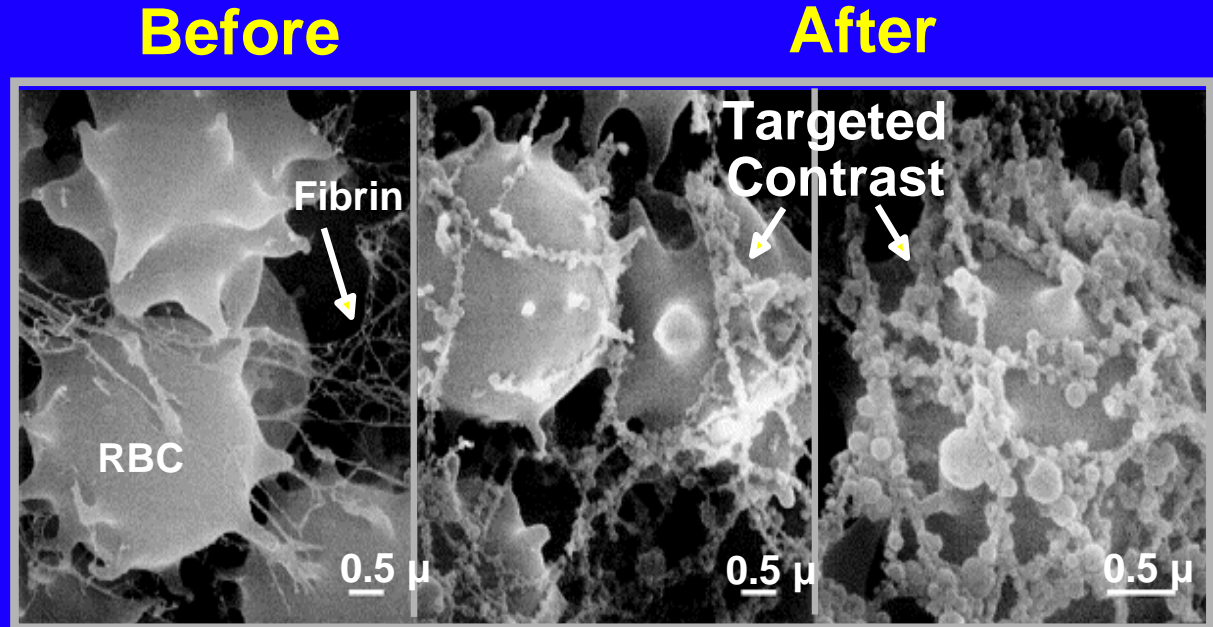
Liquid Ventilation



**Vitreous
Replacement**

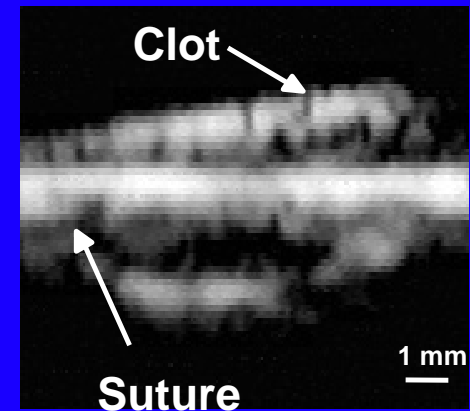
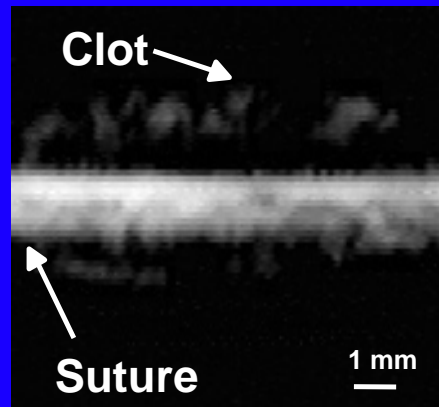
Fibrin Imaging

Scanning EM
clot labeled with
fibrin targeted
nanoparticles



Ultrasound contrast

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

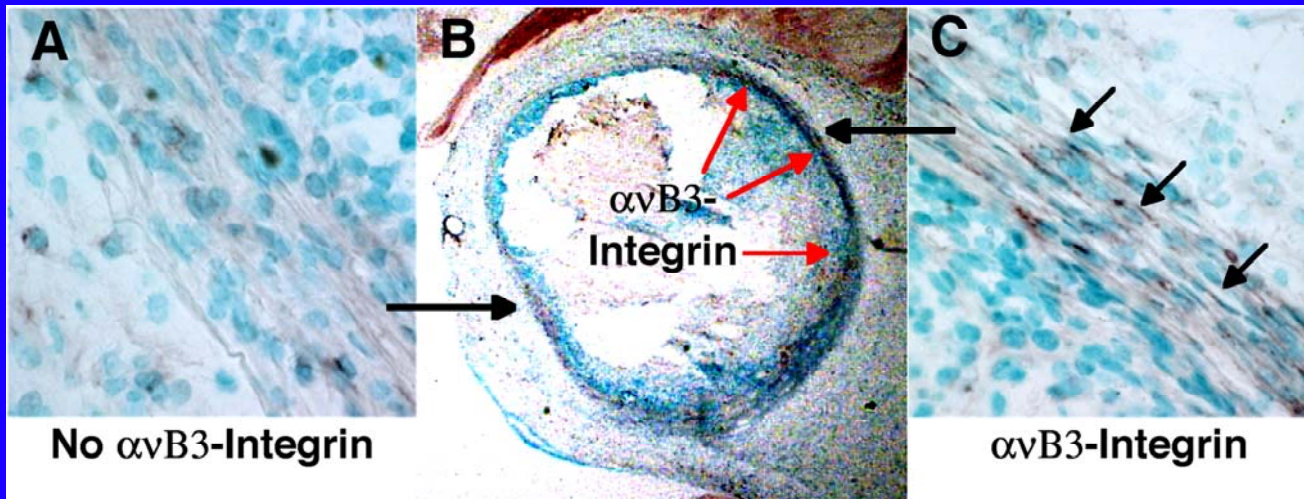
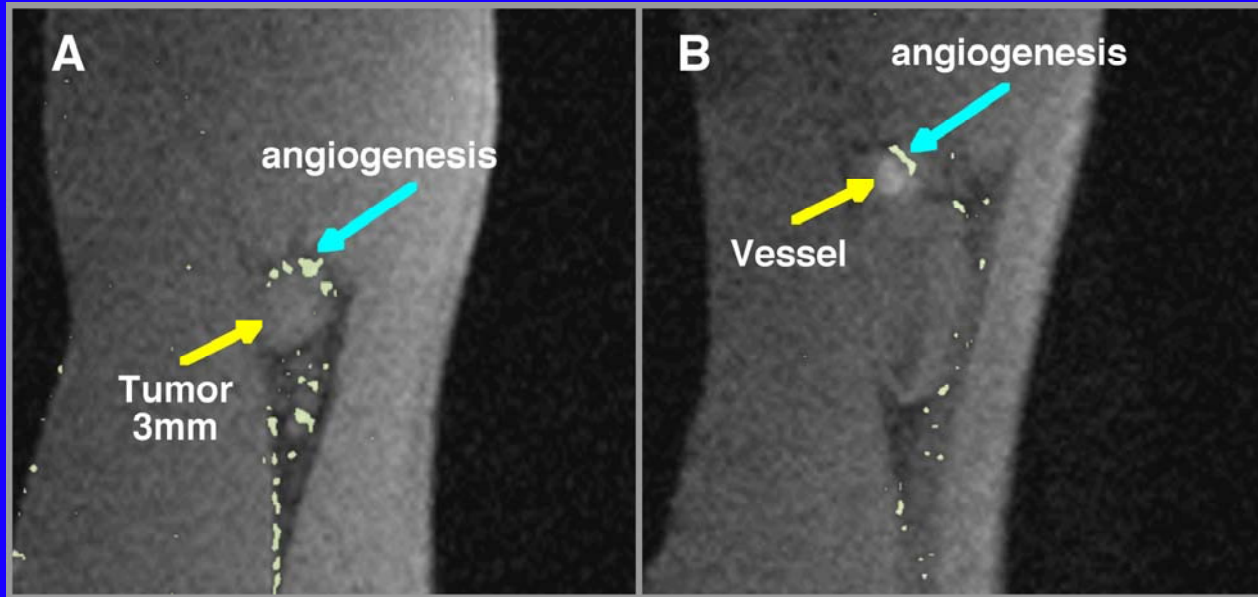


Control Thrombus Targeted Thrombus

Targeted Nanoparticles Support Enormous Paramagnetic Payloads

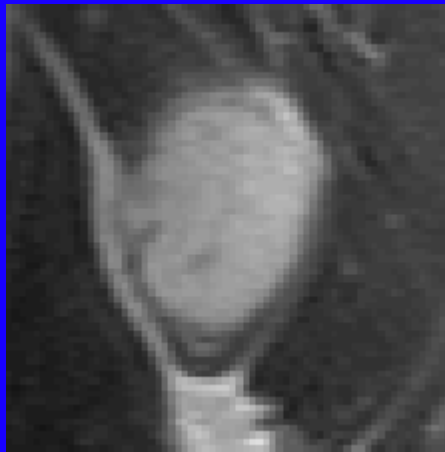
	$\alpha_v\beta_3$ -Targeted	NonTargeted
Gd³⁺ Ions / Particle	94,400	92,400
r_1 (s*mM)⁻¹ [Gd]	19.1	21.1
r_2 (s*mM)⁻¹ [Gd]	22.9	24.6
r_1 (s*mM)⁻¹ [Particle]	1,800,000	1,950,000
r_2 (s*mM)⁻¹ [Particle]	2,160,000	2,270,000

Detection of Angiogenesis in the Vx-2 Model

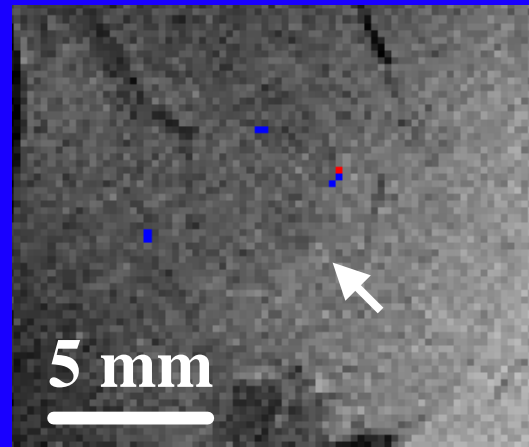


Masses Seen By MRI Were Not Always Vx-2 Tumors

T₂-Weighted MRI

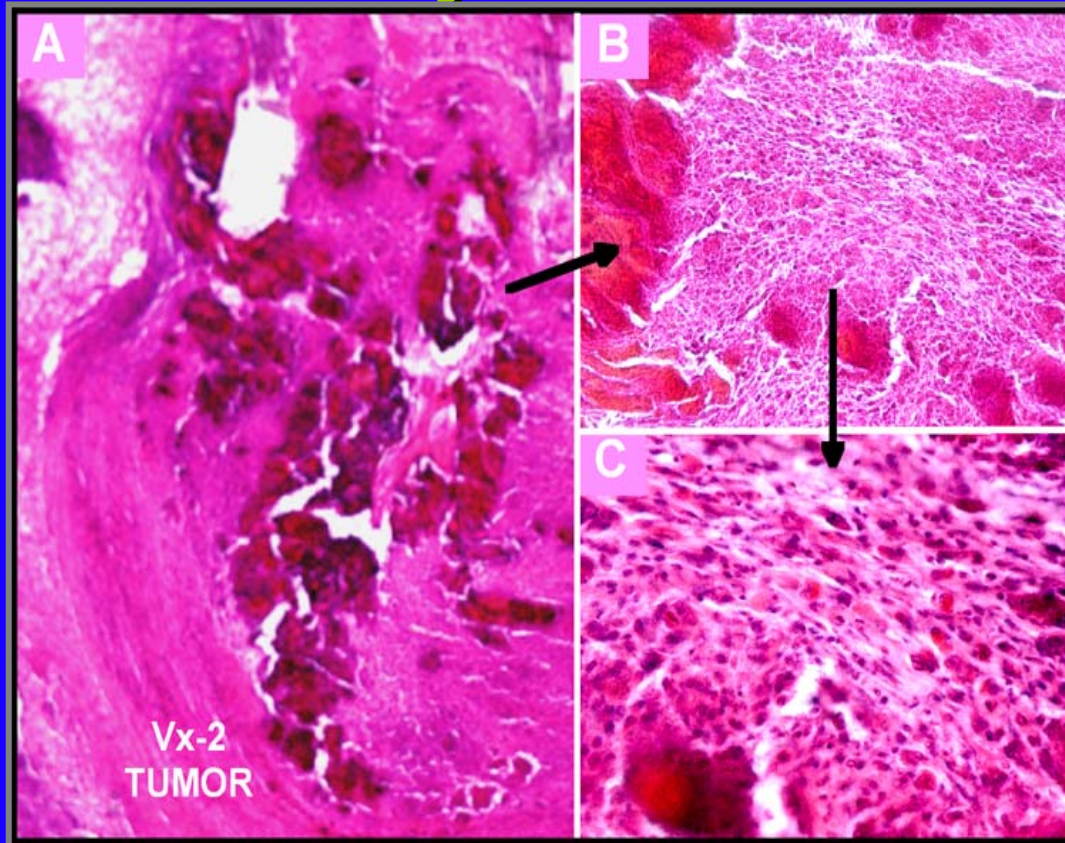


After
avB3-Nanoparticles



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

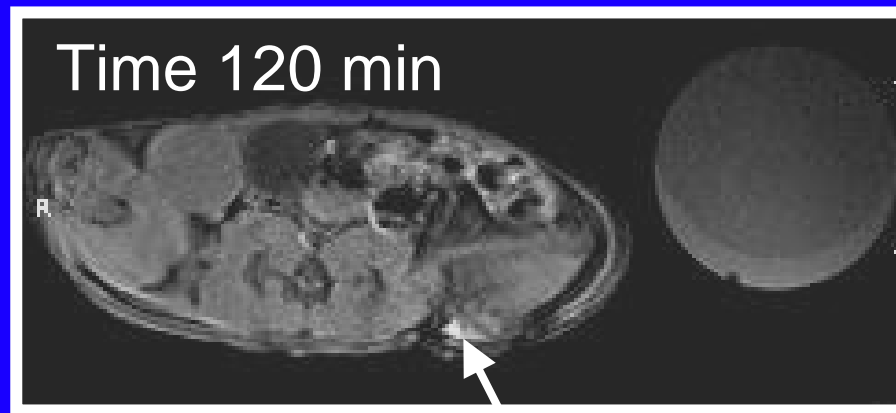
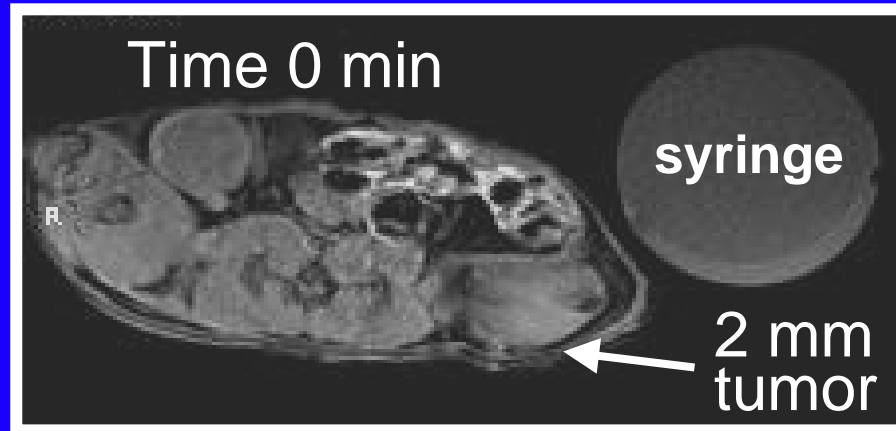
No Molecular Imaging of Angiogenesis for Tumors in Rejection



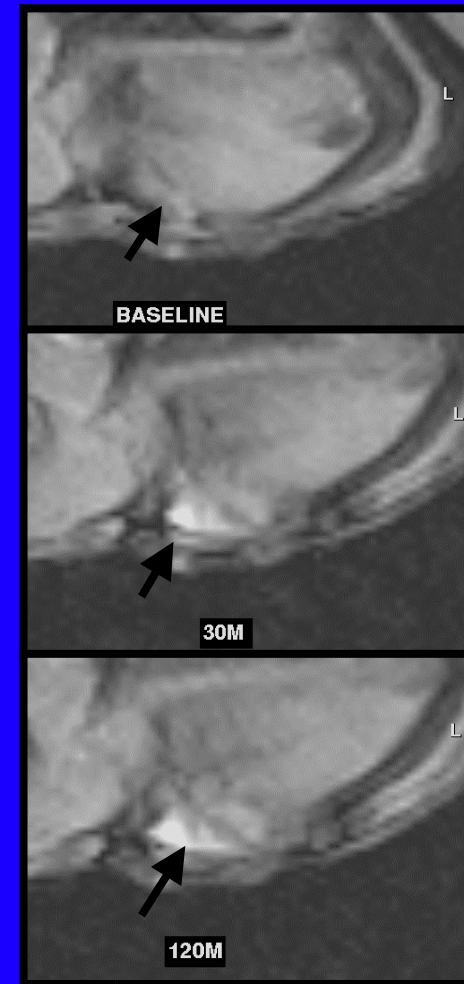
**Histology Revealed Rejected Tumor
Infiltrated with Inflammatory Cells**

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

Mouse Imaging @ 1.5T

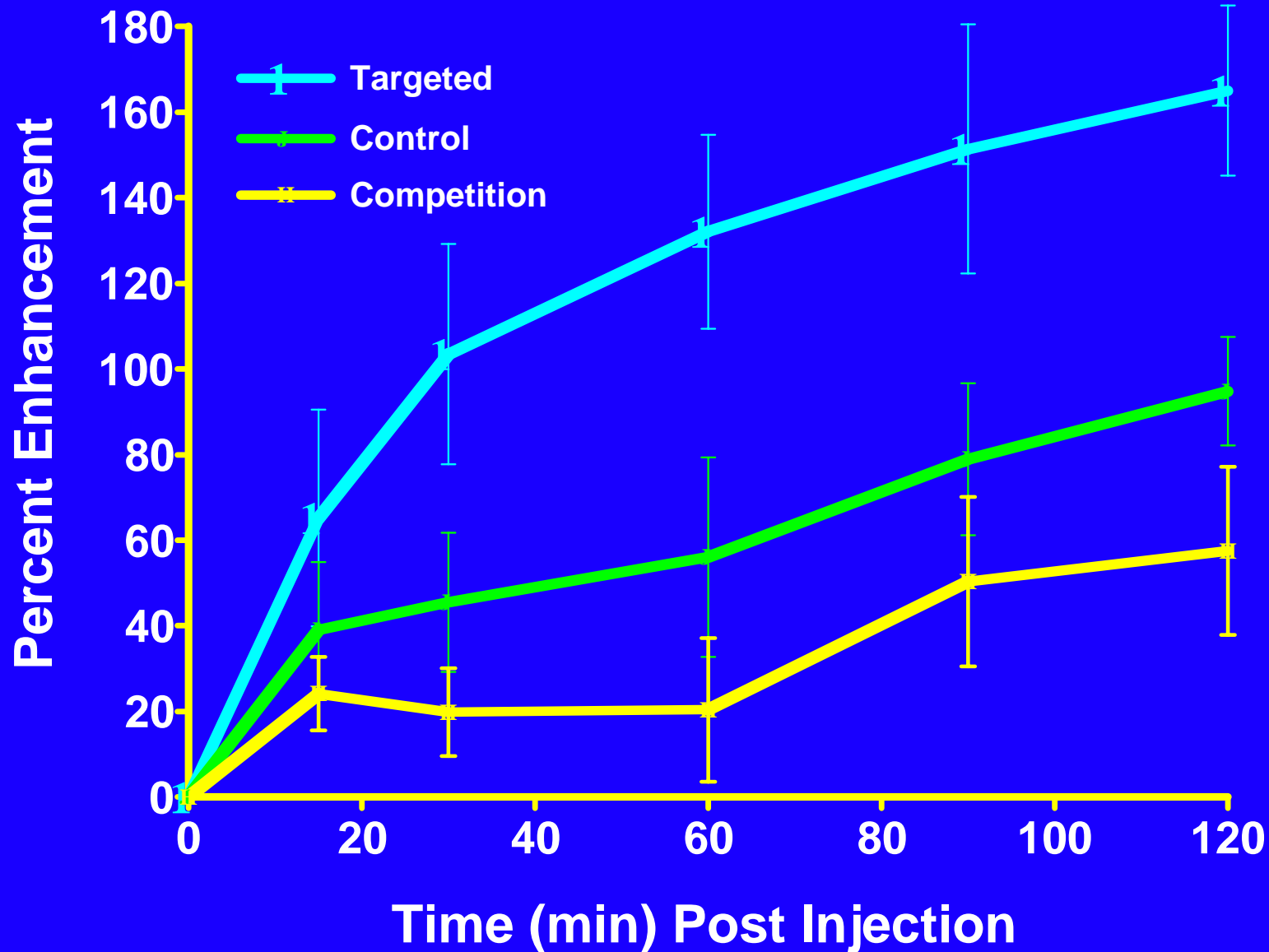


Angiogenesis around
2 mm melanoma tumor

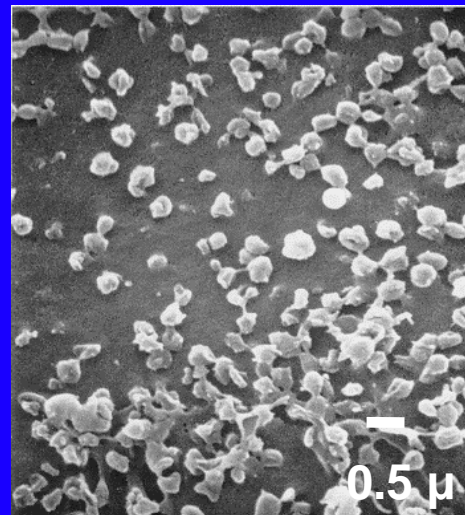
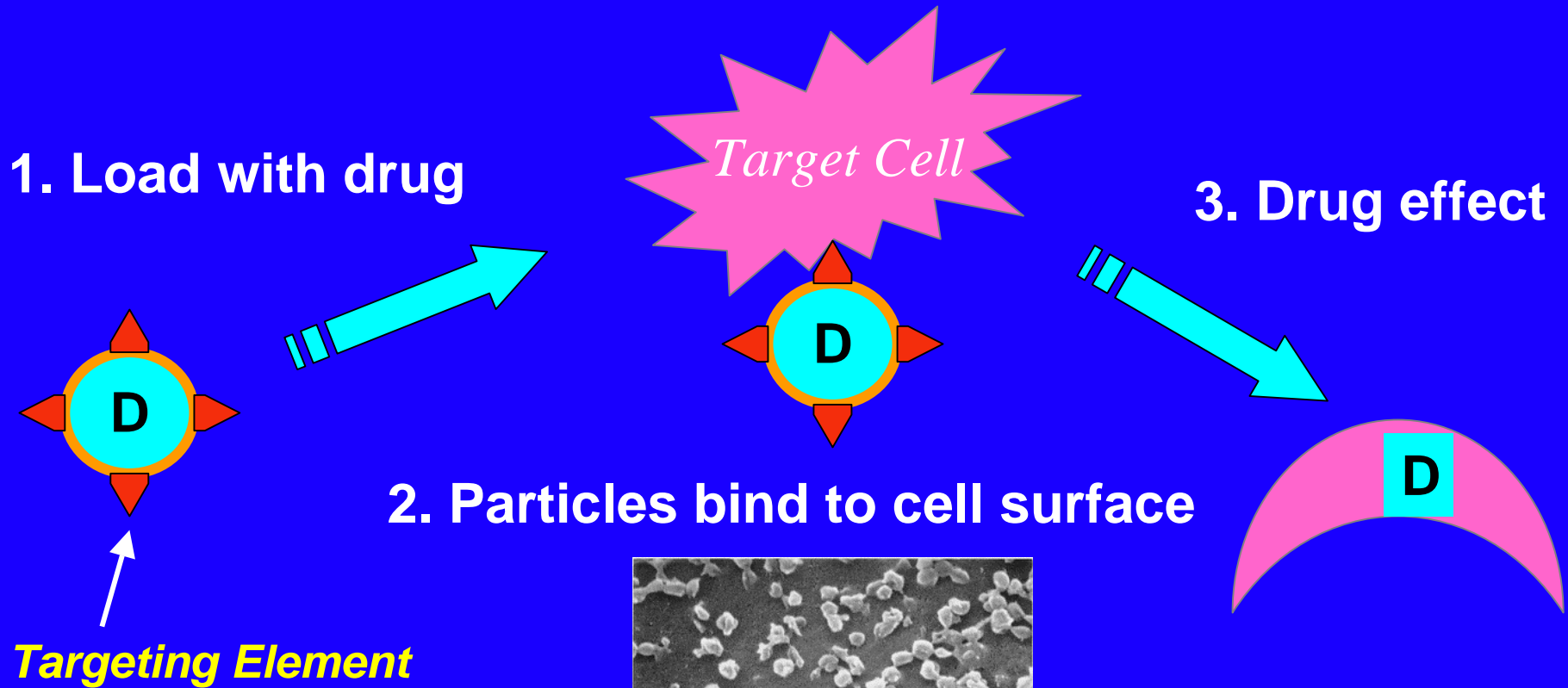


Time course

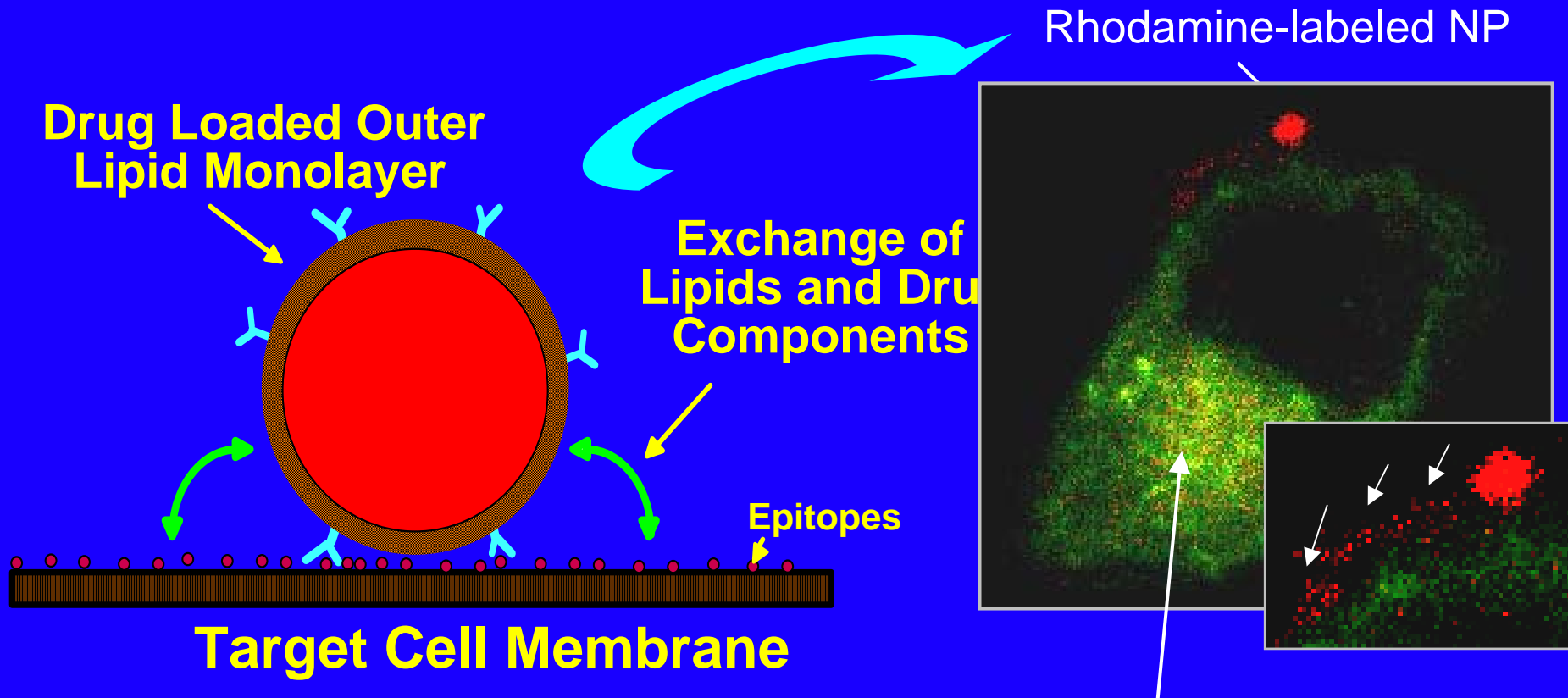
Time course of MRI Contrast Enhancement



Site-Targeted Drug Delivery



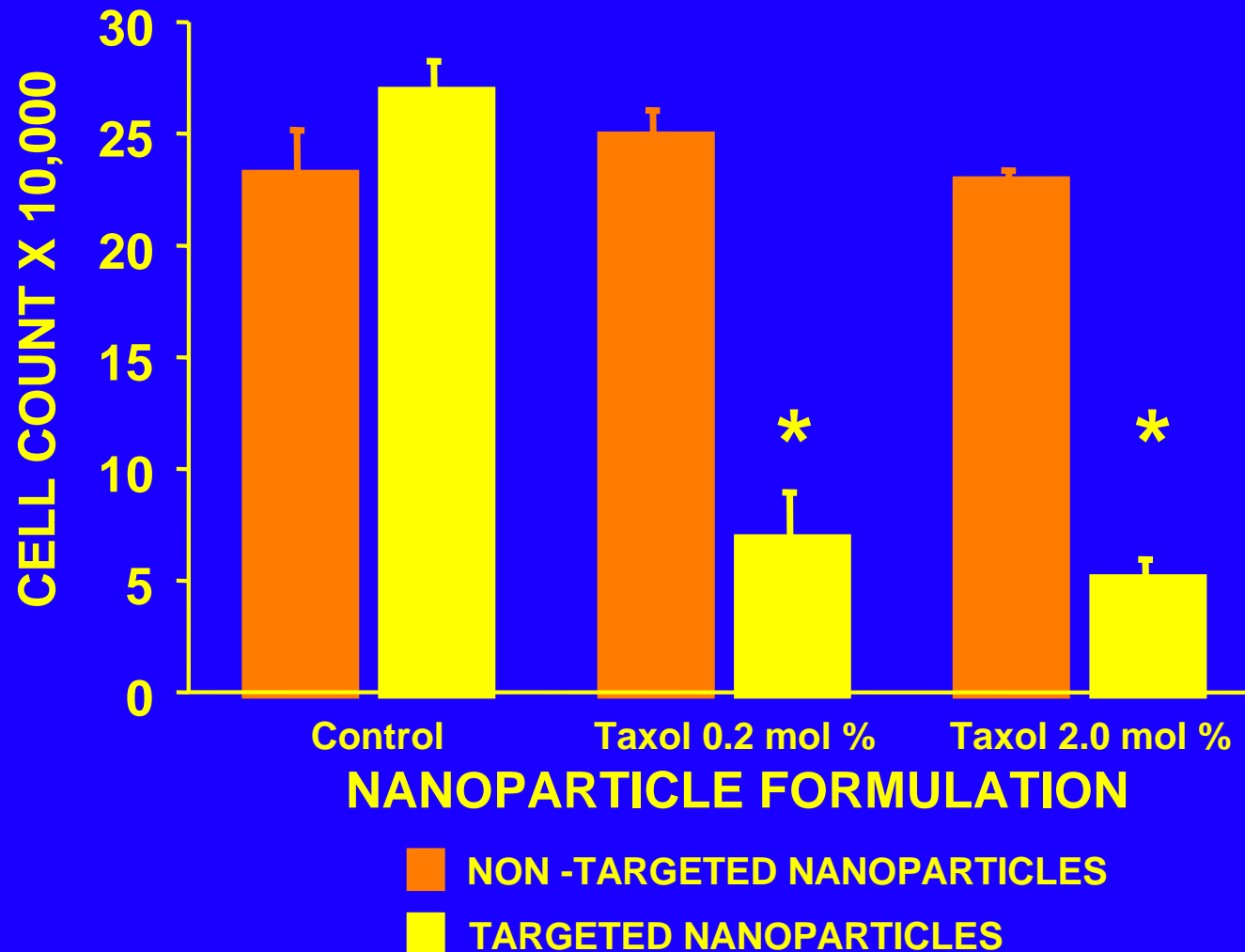
Novel Mechanisms Of Drug Delivery: “Contact Facilitated Drug Delivery*”



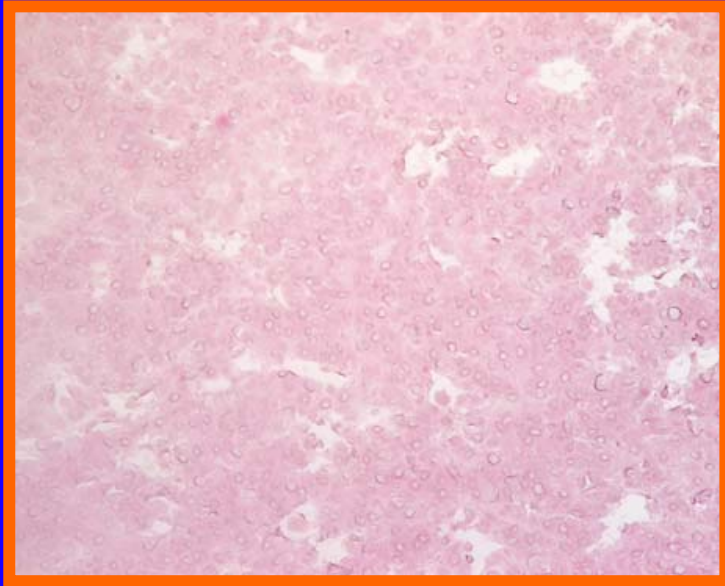
*Lanza GM, Wickline SA et al: Targeted antiproliferative drug delivery to vascular smooth muscle cells with magnetic resonance imaging nanoparticle contrast agent: implications for rational therapy of restenosis. *Circulation* 2002; 106:2842-2847

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

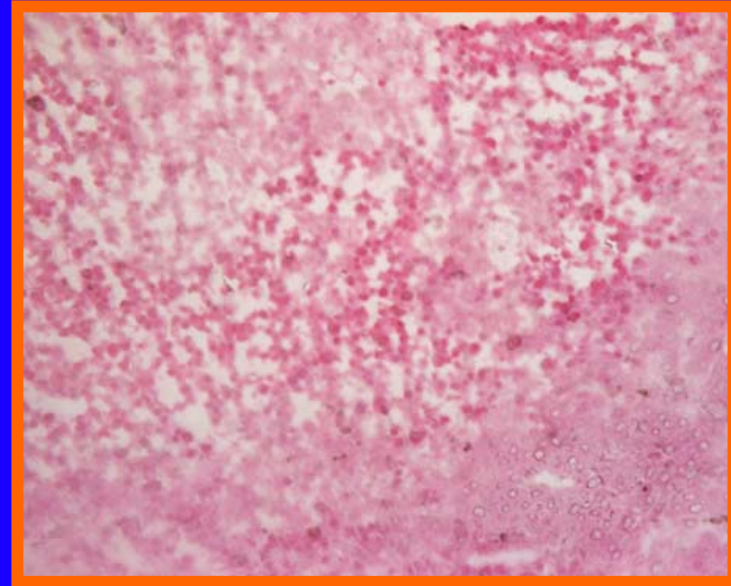
Antiproliferative Effects of Free versus Tissue Factor - Targeted Paclitaxel Nanoparticles on Vascular Smooth Muscle Cells



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

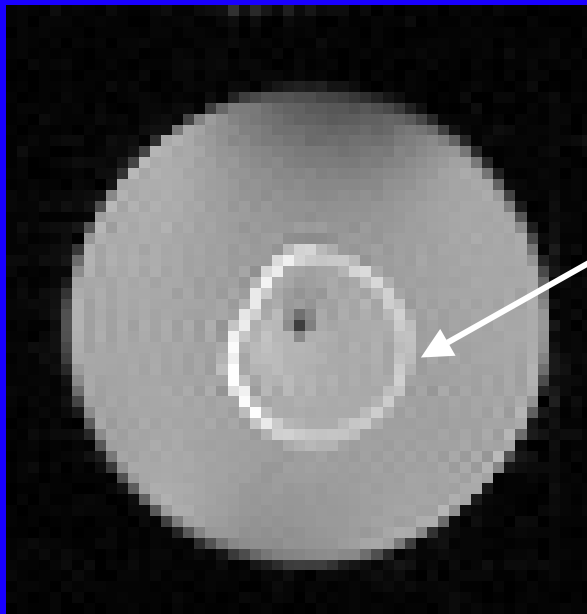


Control
3/3



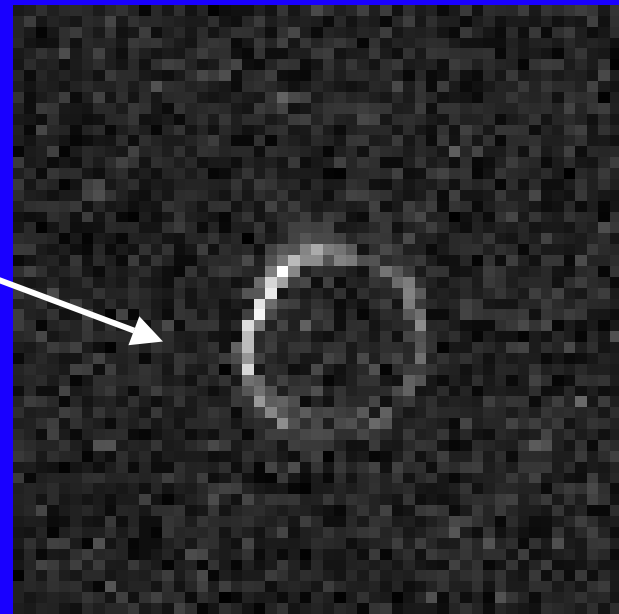
$\alpha_v\beta_3$ -DXR-NP
(4/4)

Proton and Fluorine Imaging



Proton Imaging

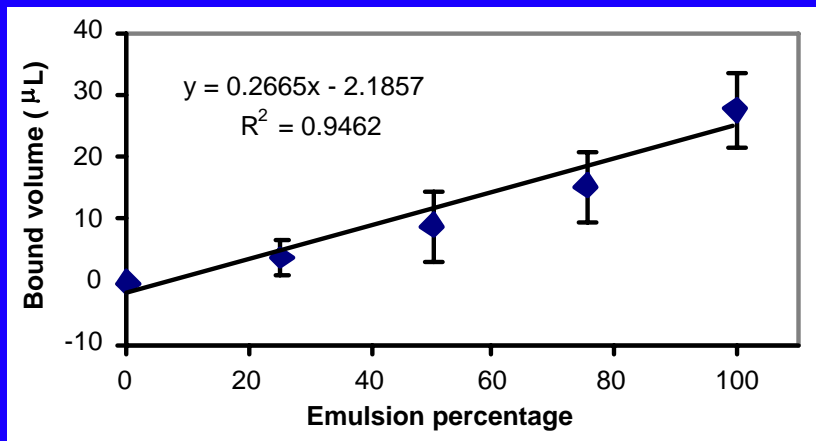
Clot



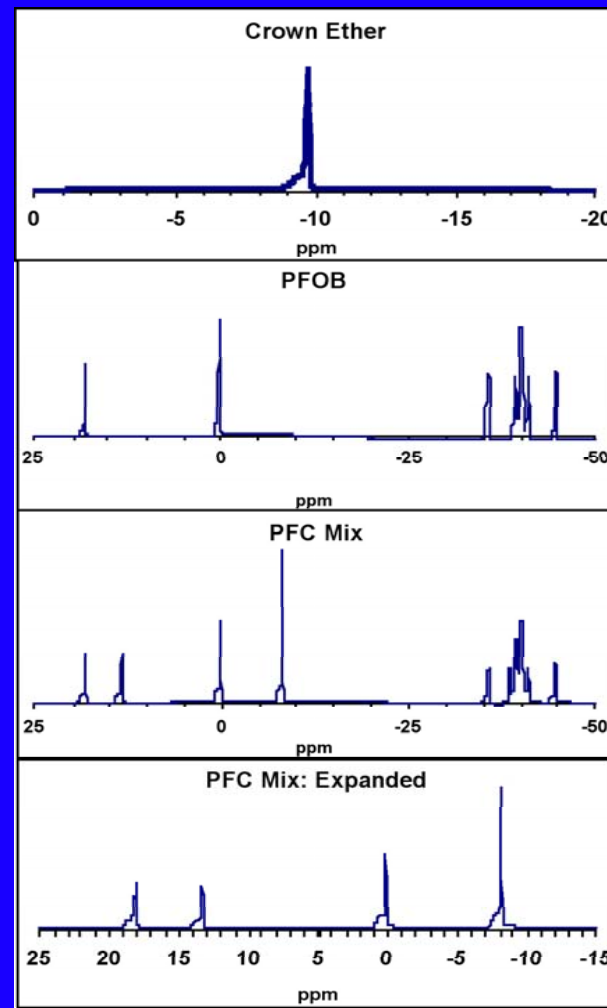
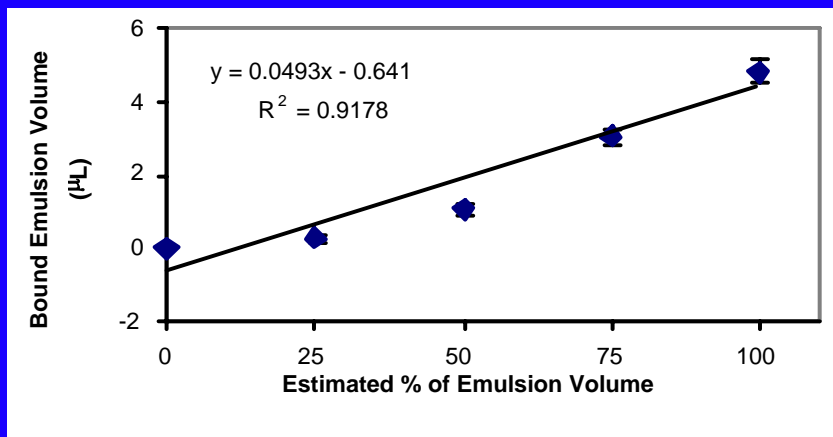
Fluorine Imaging

Dosimetry of Targeted Nanoparticle Levels

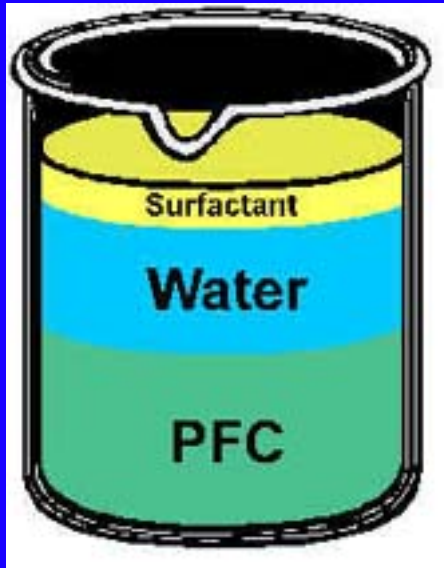
15:5 Crown-Ether



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.

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