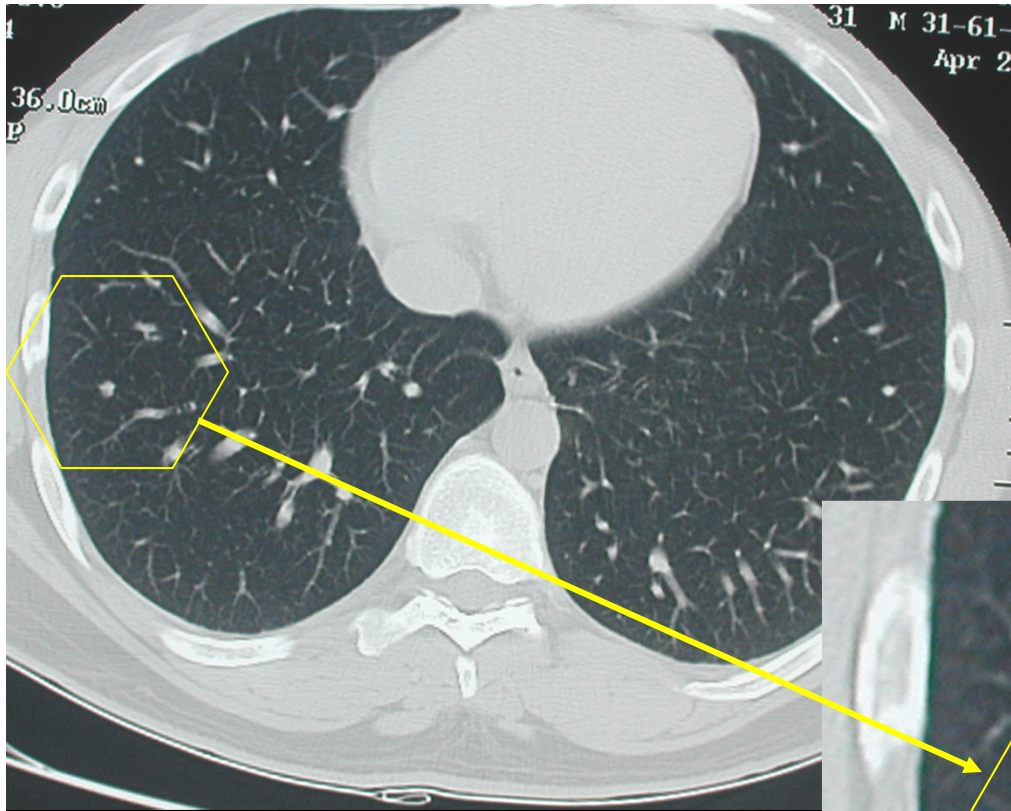


**NATIONAL  
CANCER  
INSTITUTE**

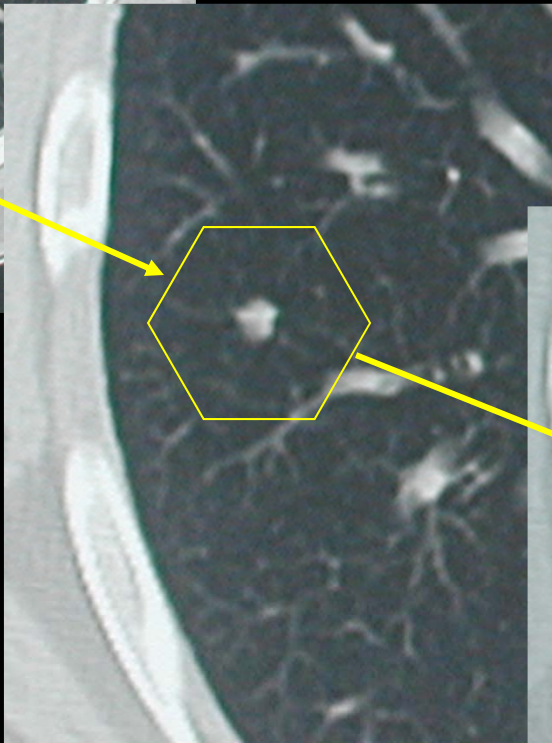


# Oncologic Imaging: Structure, Function and Molecular Biology

Peter L. Choyke, M.D.  
Molecular Imaging Program  
CCR

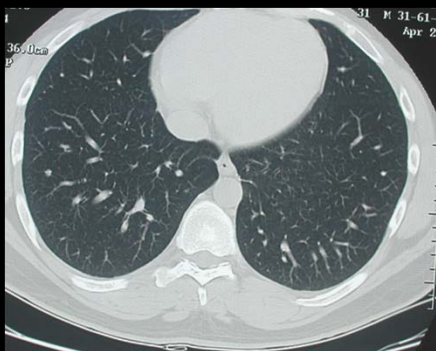


# Anatomic Imaging

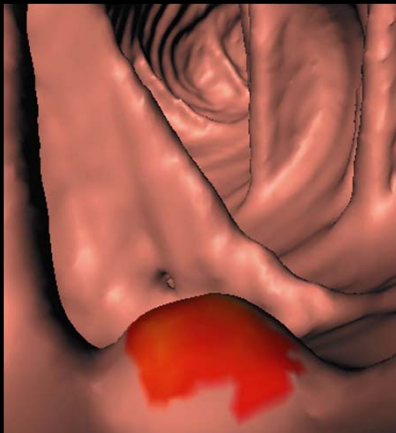


Screening for Lung Cancer  
With CT  
Detects low stage disease  
~1-2% yield

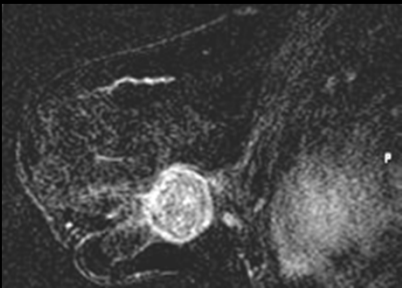
# Cancer Screening



Lung CT

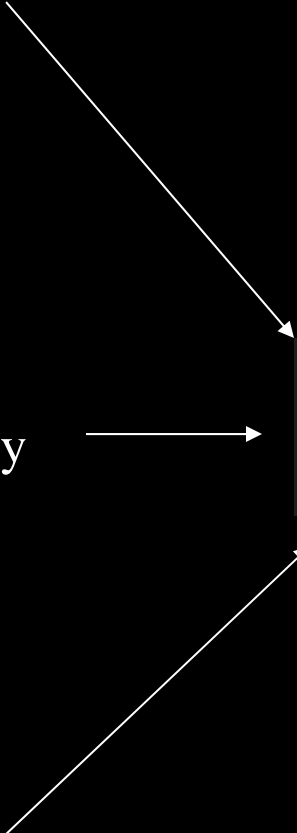
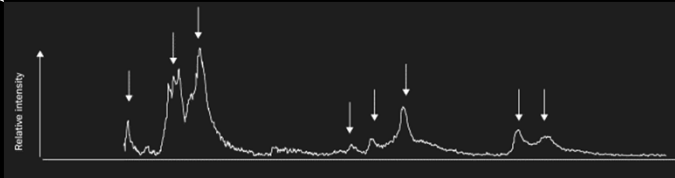


Virtual Colonography

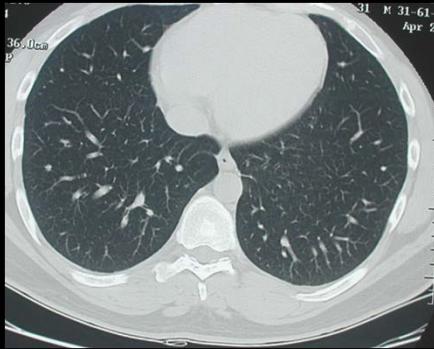


Breast MRI

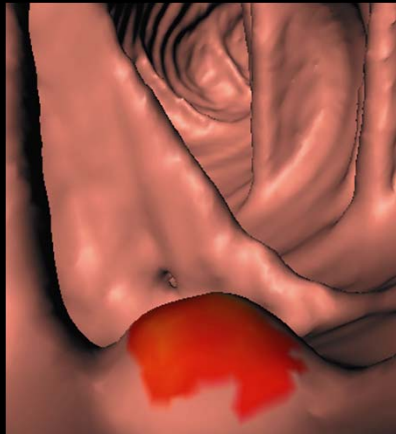
## Serum Proteomics



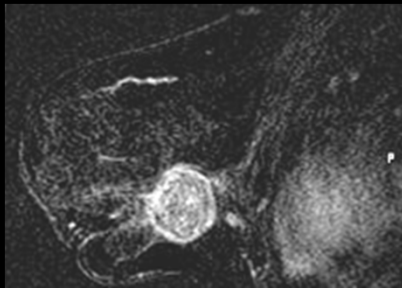
# Cancer Screening



Lung CT

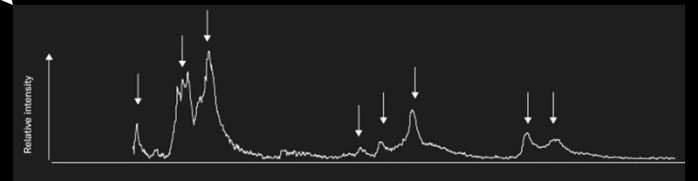


Virtual  
Colonography



Breast MRI

## Serum Proteomics



Proteomics

Imaging

Imaging

Proteomics

?



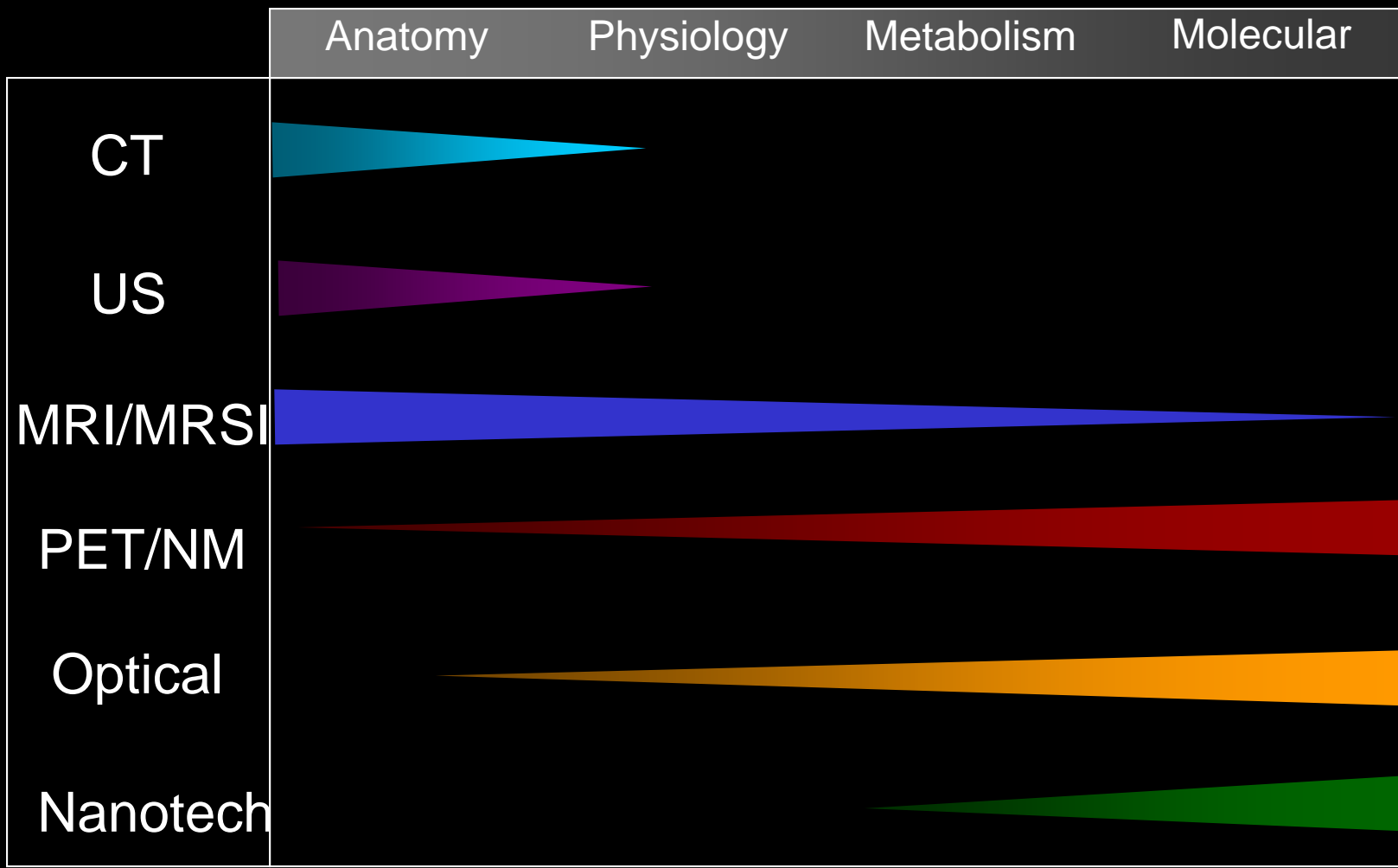
# The new challenge

Morphology

Enhancement  
Kinetics



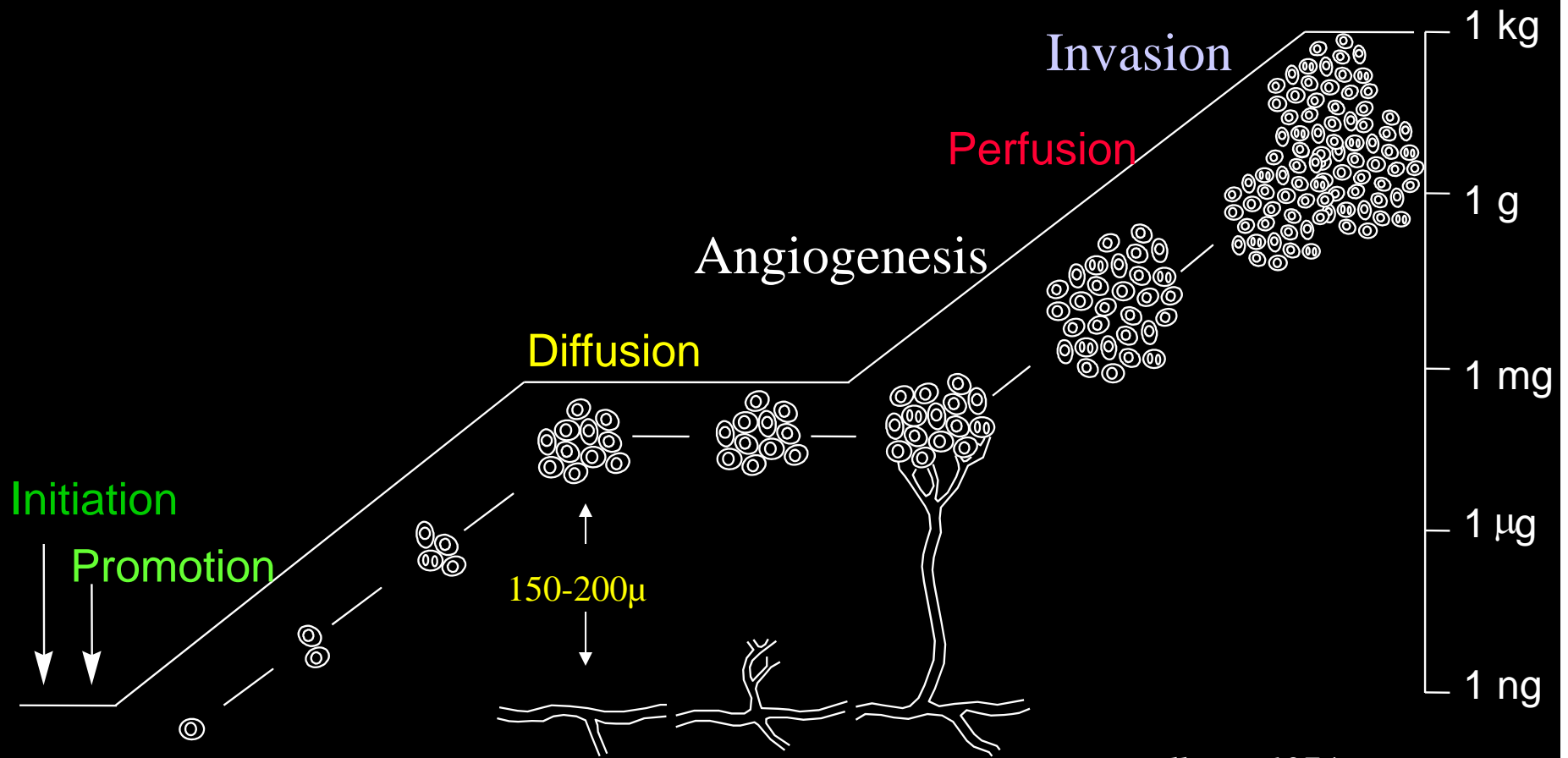
**Functional  
Imaging of  
tumors**



# Progression of Cancer

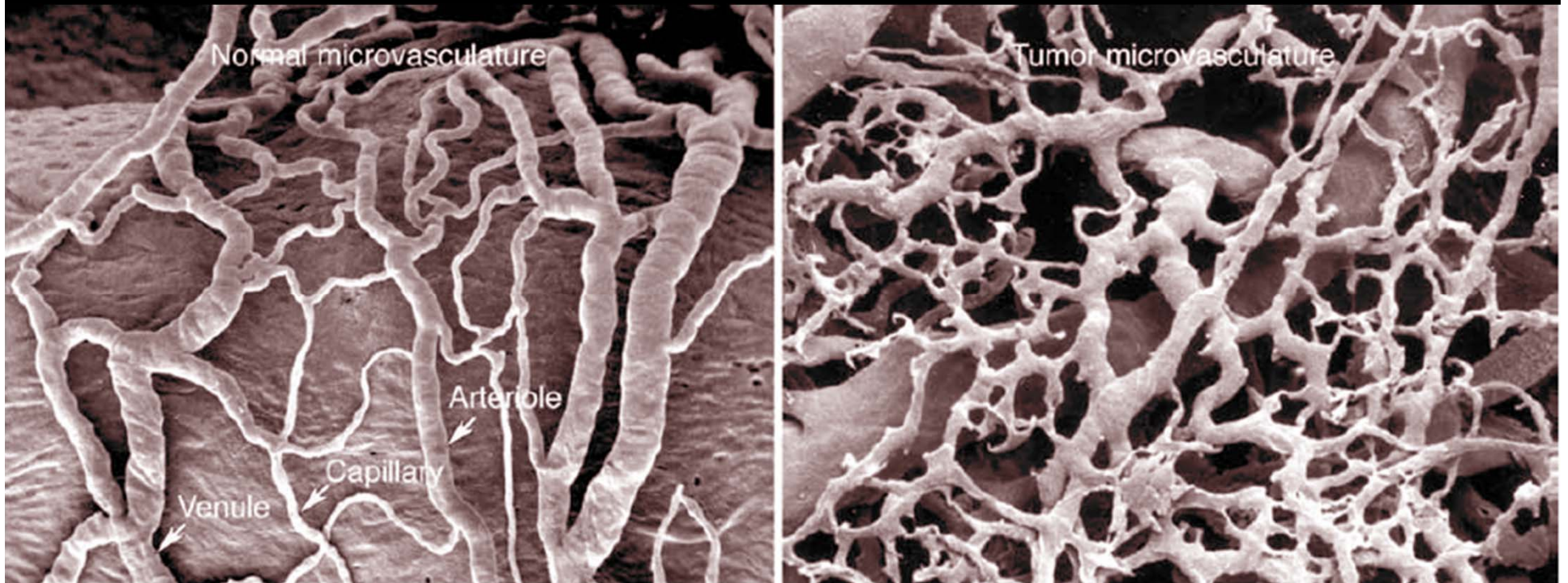
Metabolic  
Disruption

Dissemination



*J Folkman 1974*  
*IJ Fidler 2002*

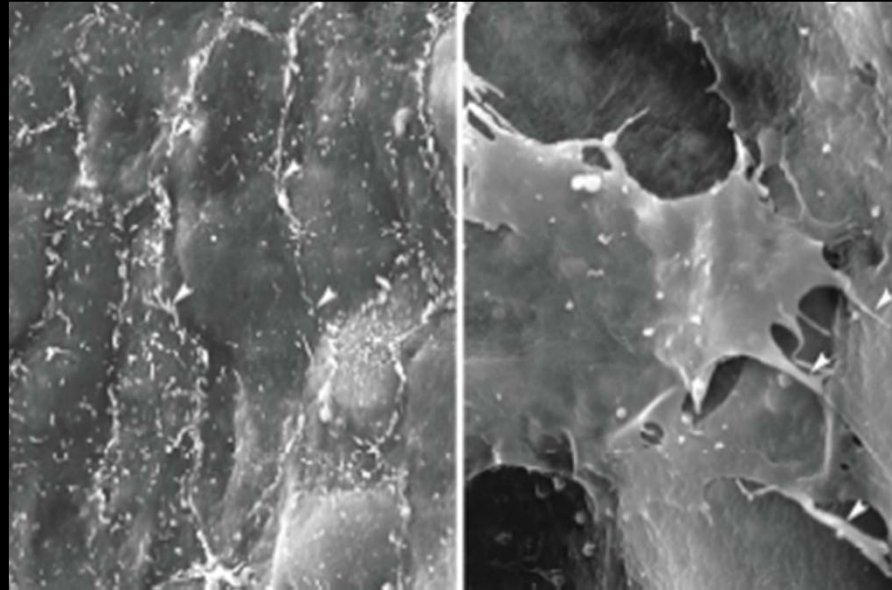
# Disorganized and Numerous





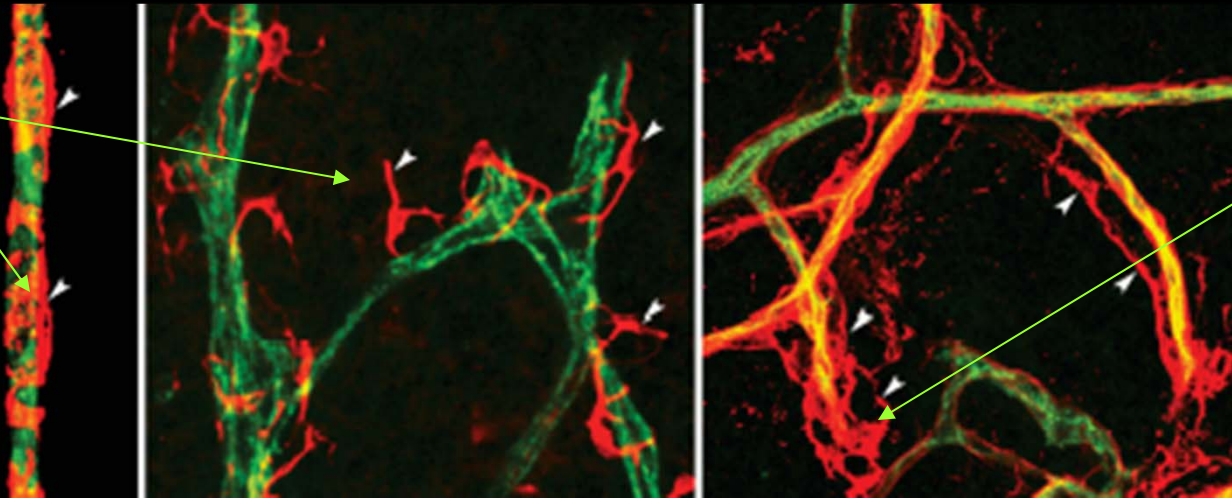
# Permeability is a Feature of Tumor Angiogenesis

SEM  
Luminal surface  
Normal blood  
vessel



Tumor vessel

Pericyte



Basement  
membrane

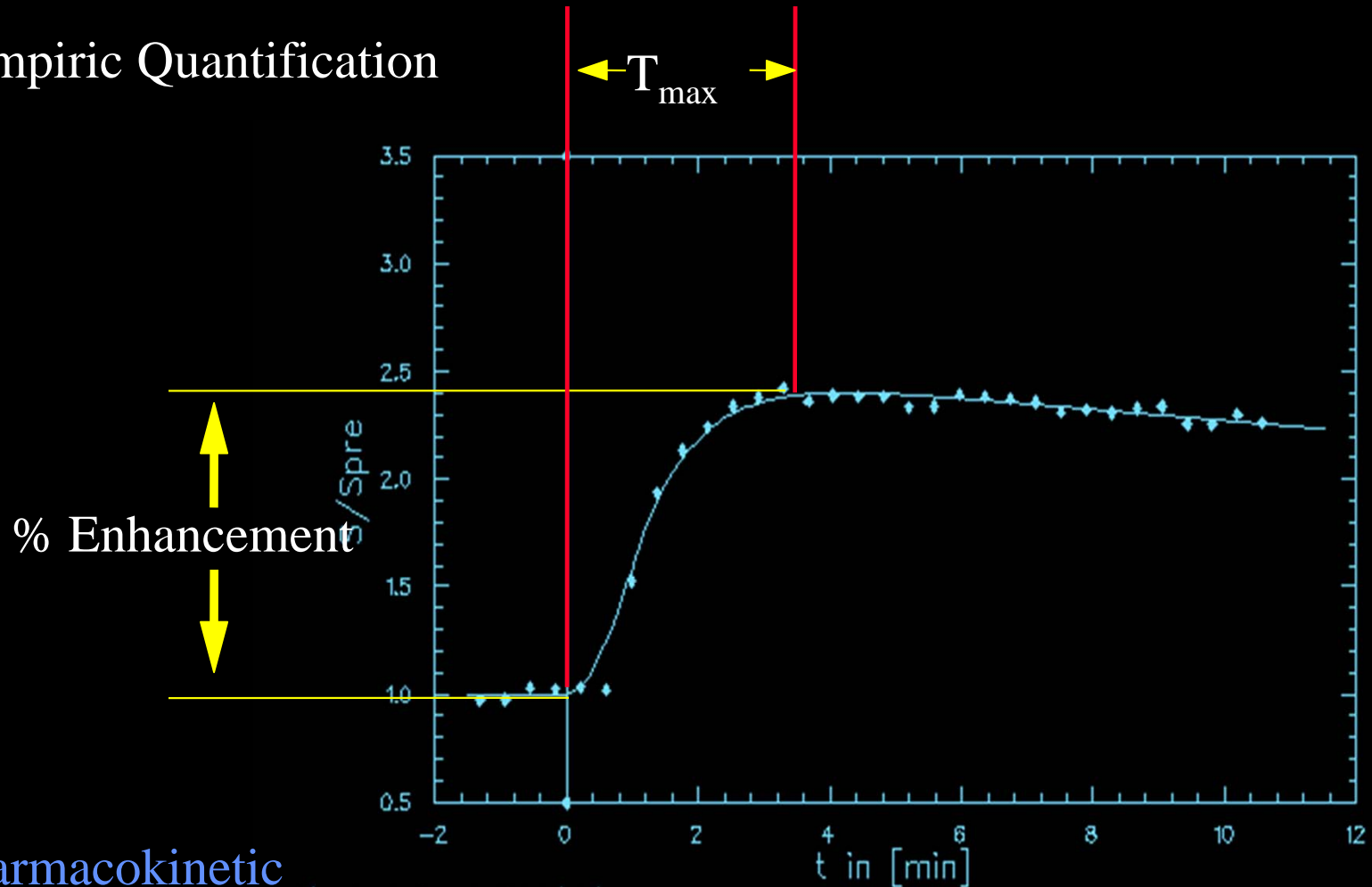
Normal

Lewis Lung Carcinoma

*Nature Med.* 9:713, 2003

# Quantification of contrast enhancement

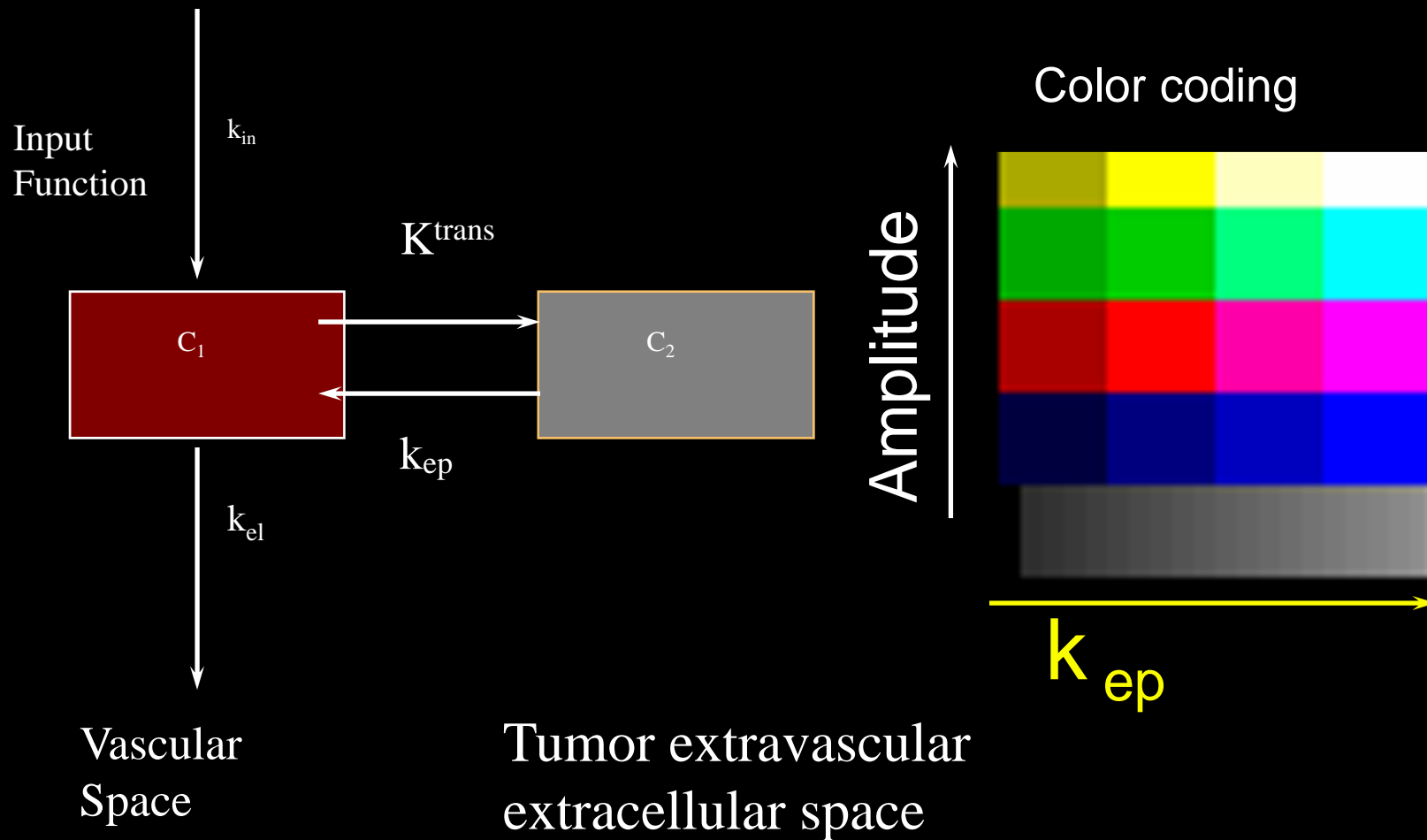
Empiric Quantification



Pharmacokinetic  
Quantification

Signalverlauf nach KM-Injektion  
Amp = 1.51 ± 0.391E-01      Max = 1.39      Chi = 0.515E-01  
K-21 = 1.10 ± 0.826E-01      T-21 = 0.630  
K-EL = 0.201E-01 ± 0.440E-02      T-El = 34.5

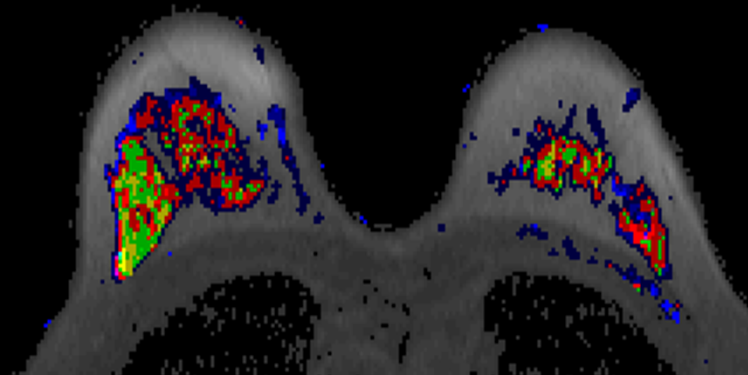
# Two compartment PK model



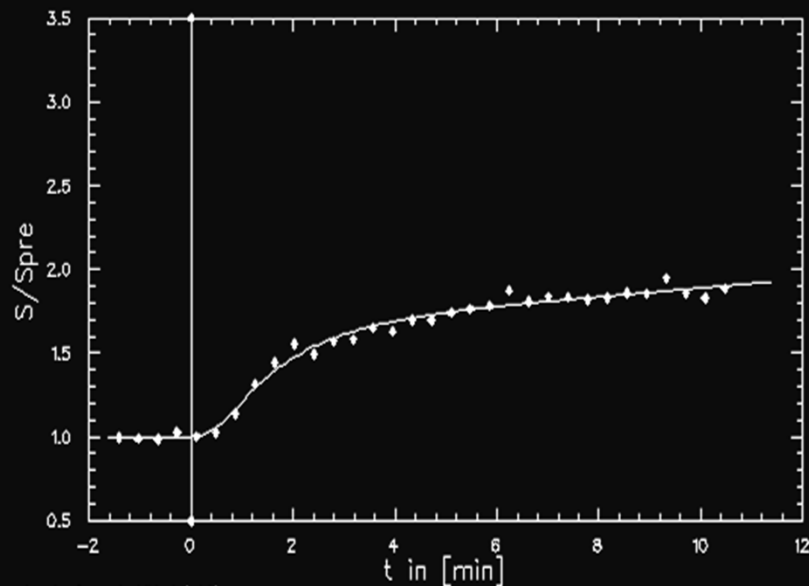


DKFZ HEIDELBERG

Schicht: 4 Pos.: -44,0



## Fibroadenoma

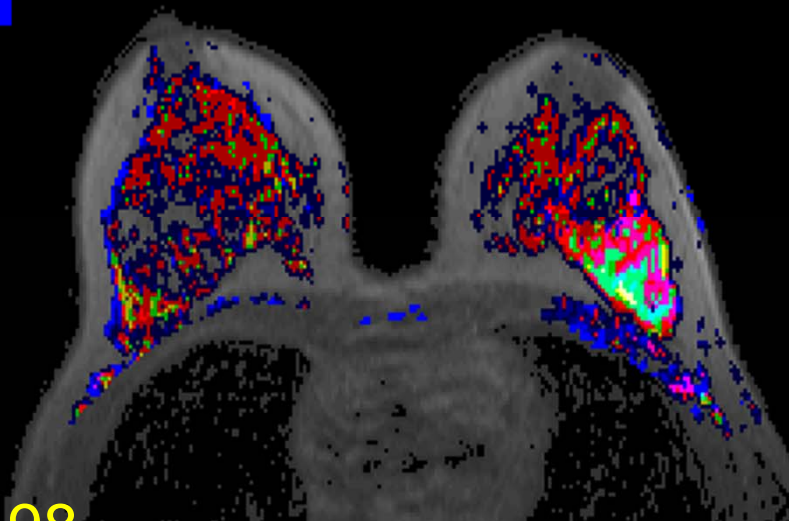


Signalverlauf nach KM-Injektion

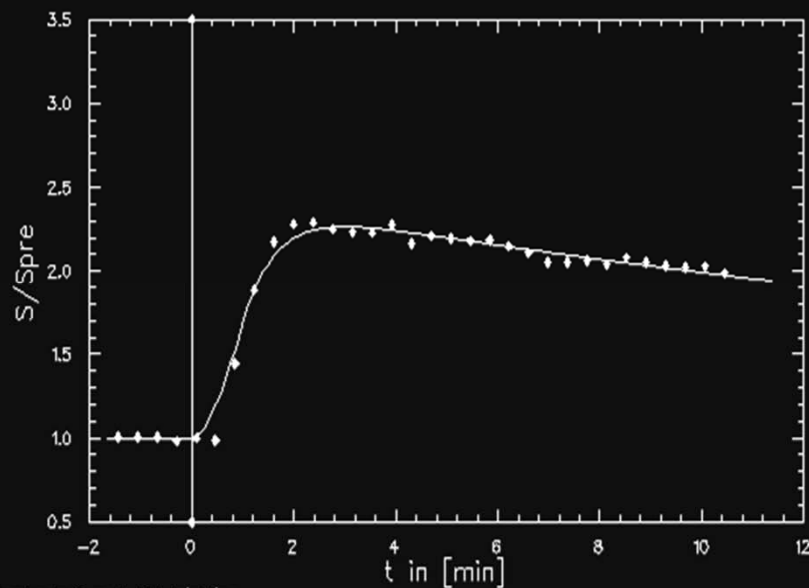


DKFZ HEIDELBERG

Schicht: 9 Pos.: -14,0



## Invasive Ductal

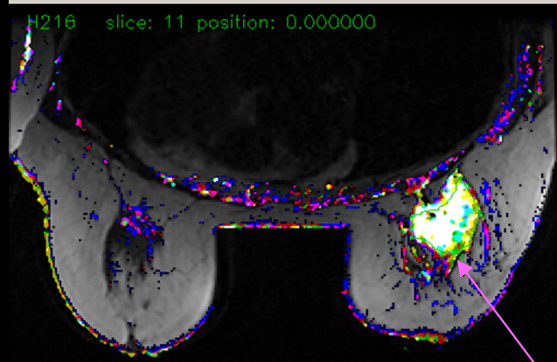
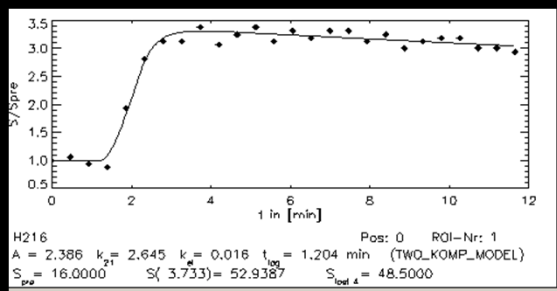


Signalverlauf nach KM-Injektion

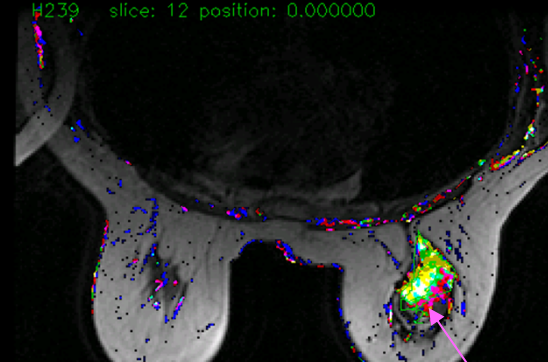
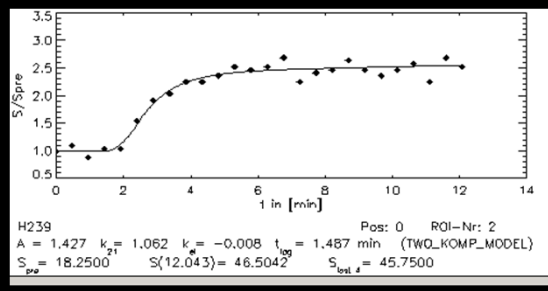
H 498



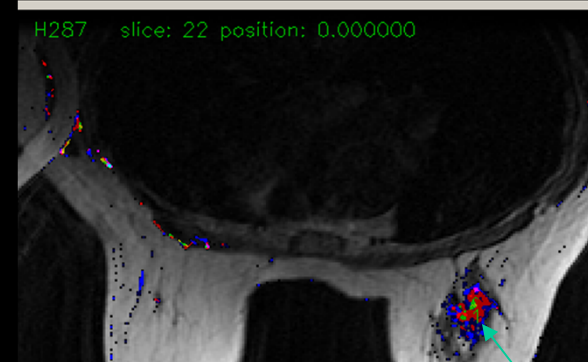
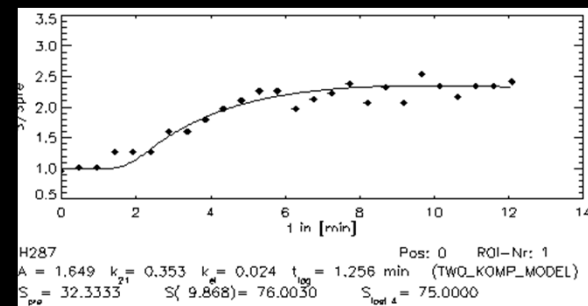
# Tumor Comparisons



Baseline



One Month

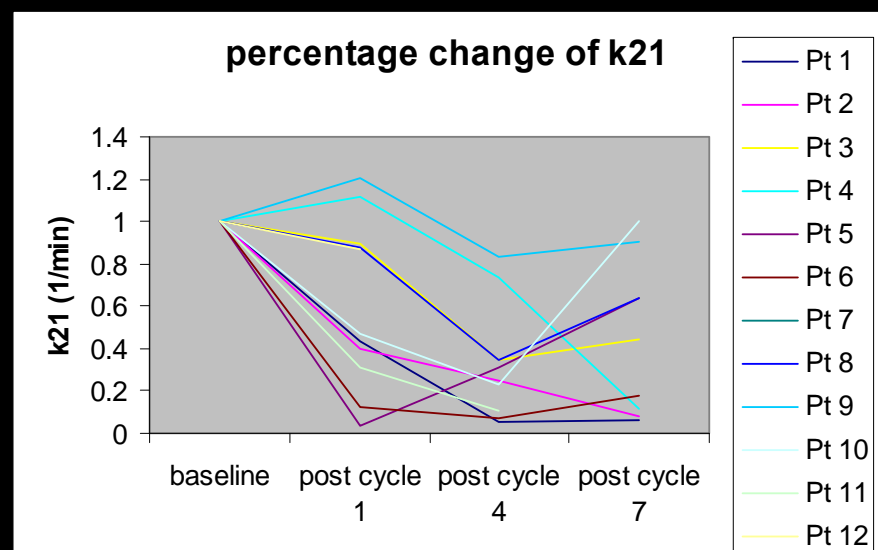
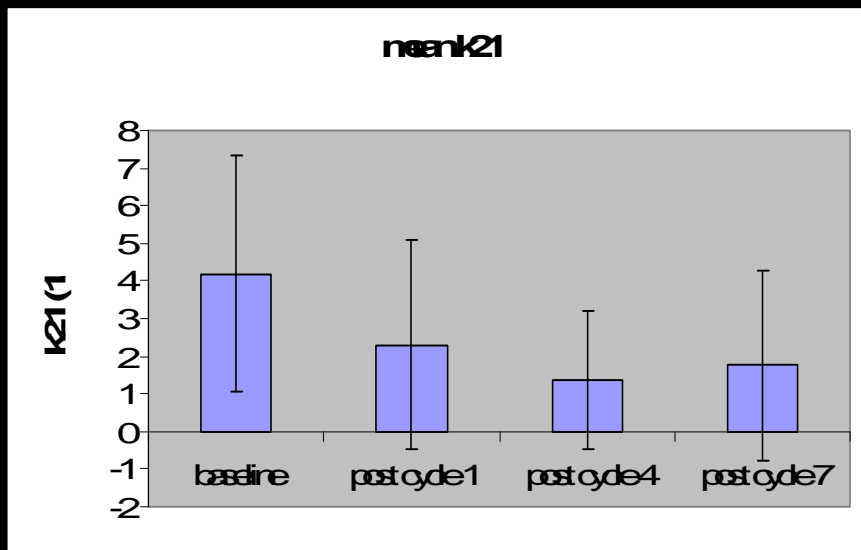
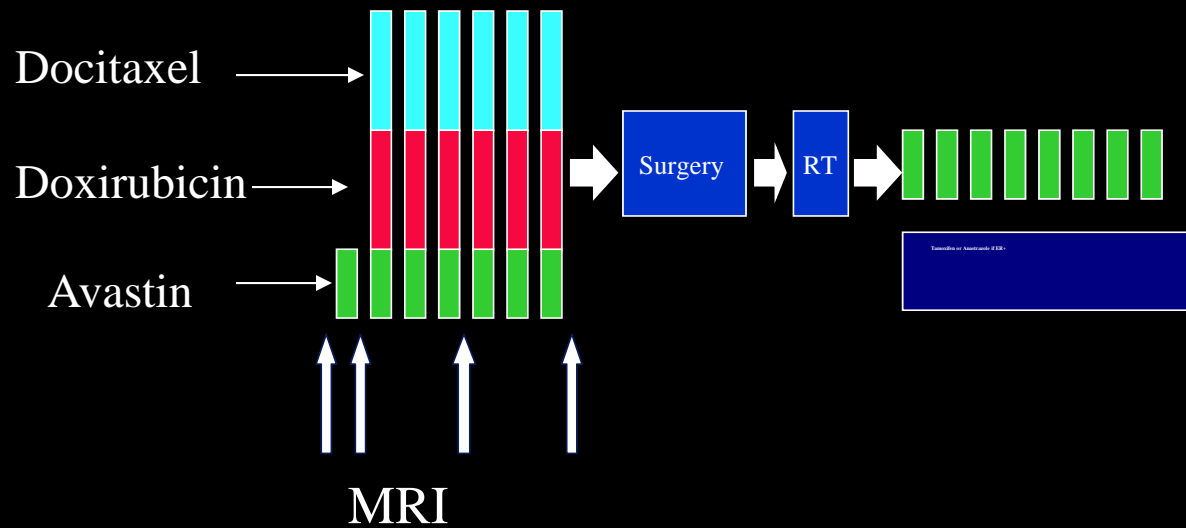


Two Months

Entire tumor

Entire tumor

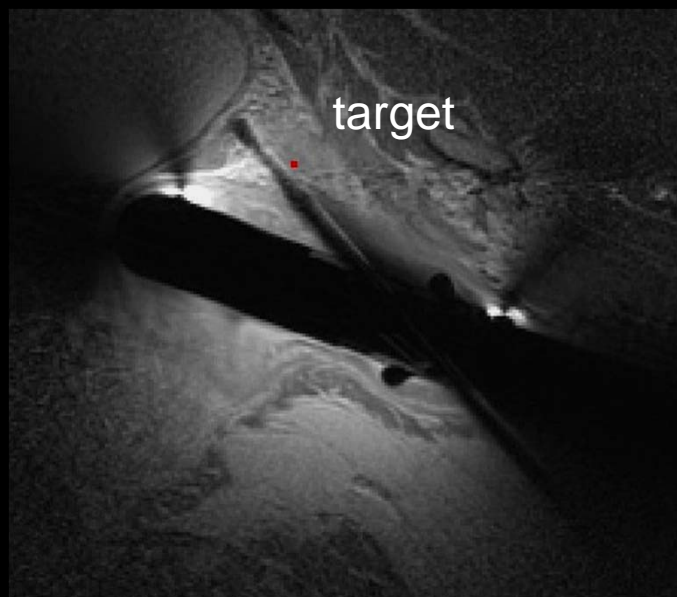
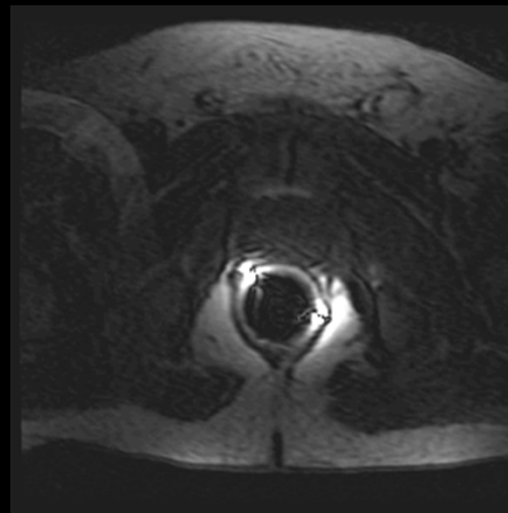
Residual enhancement



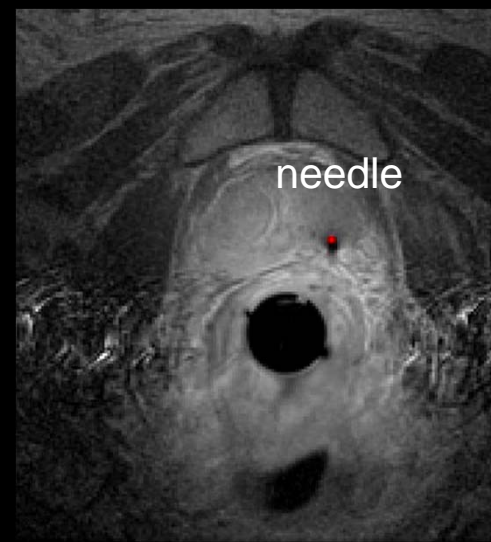
256 x 192

R

L

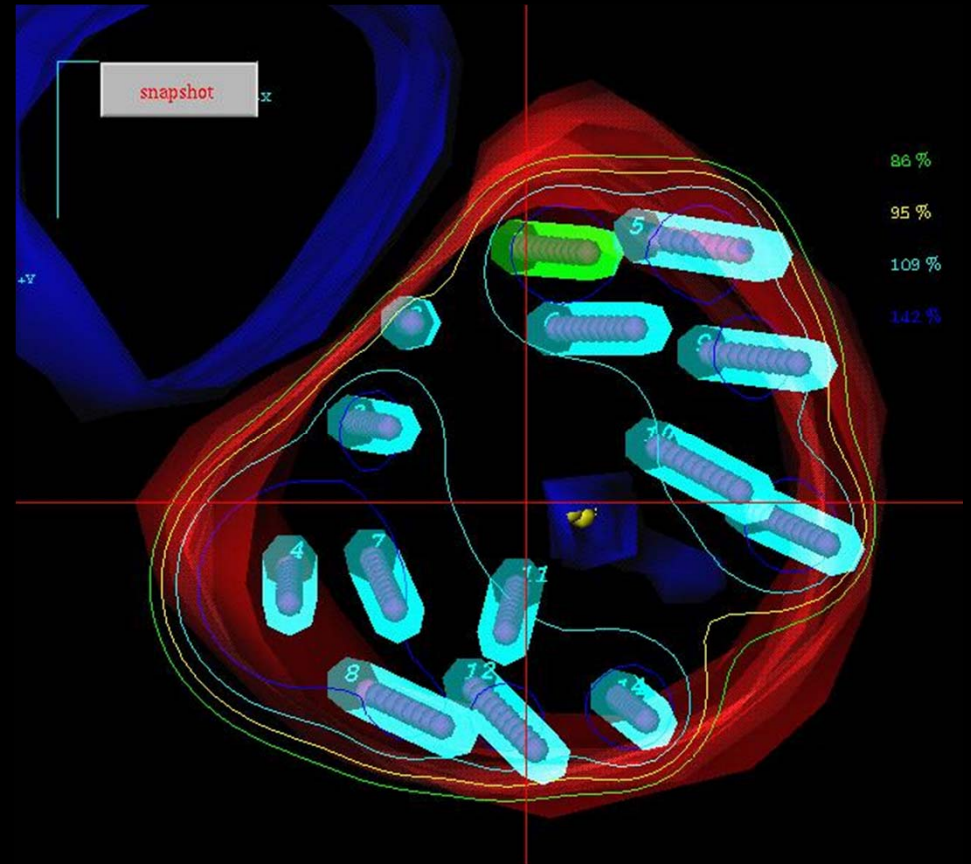
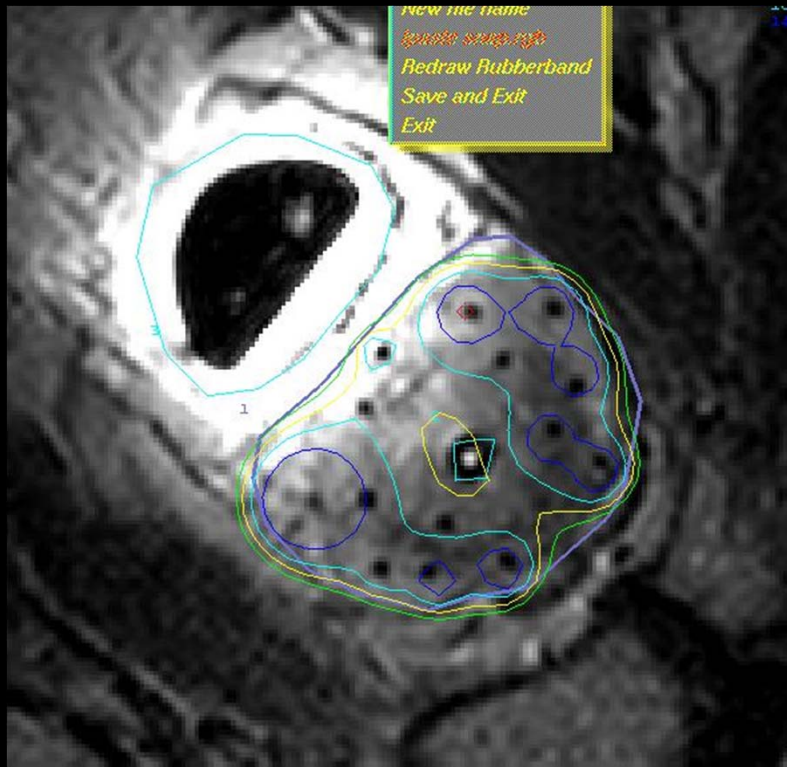


target



needle

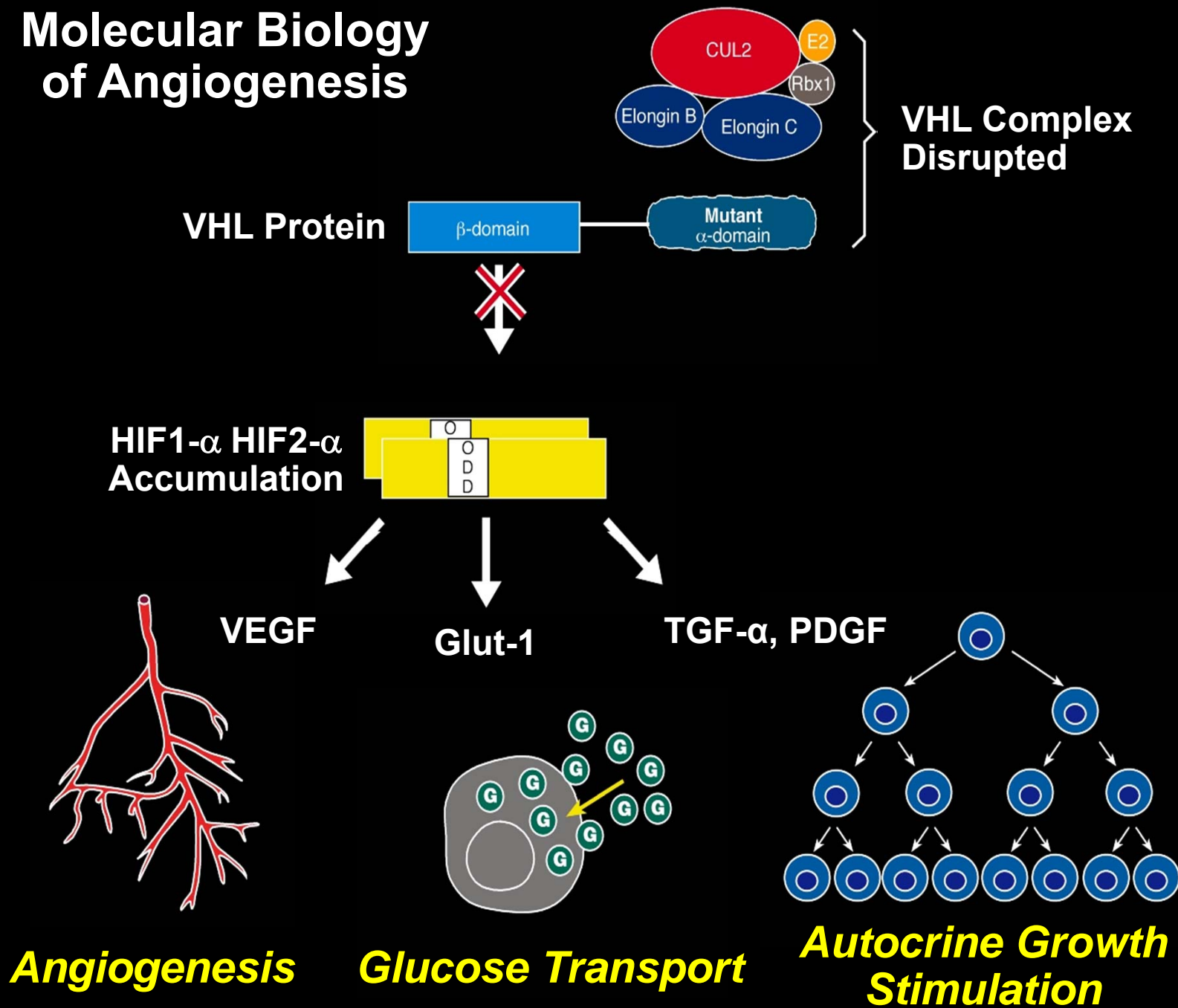
*C Menard ROB, NCI*



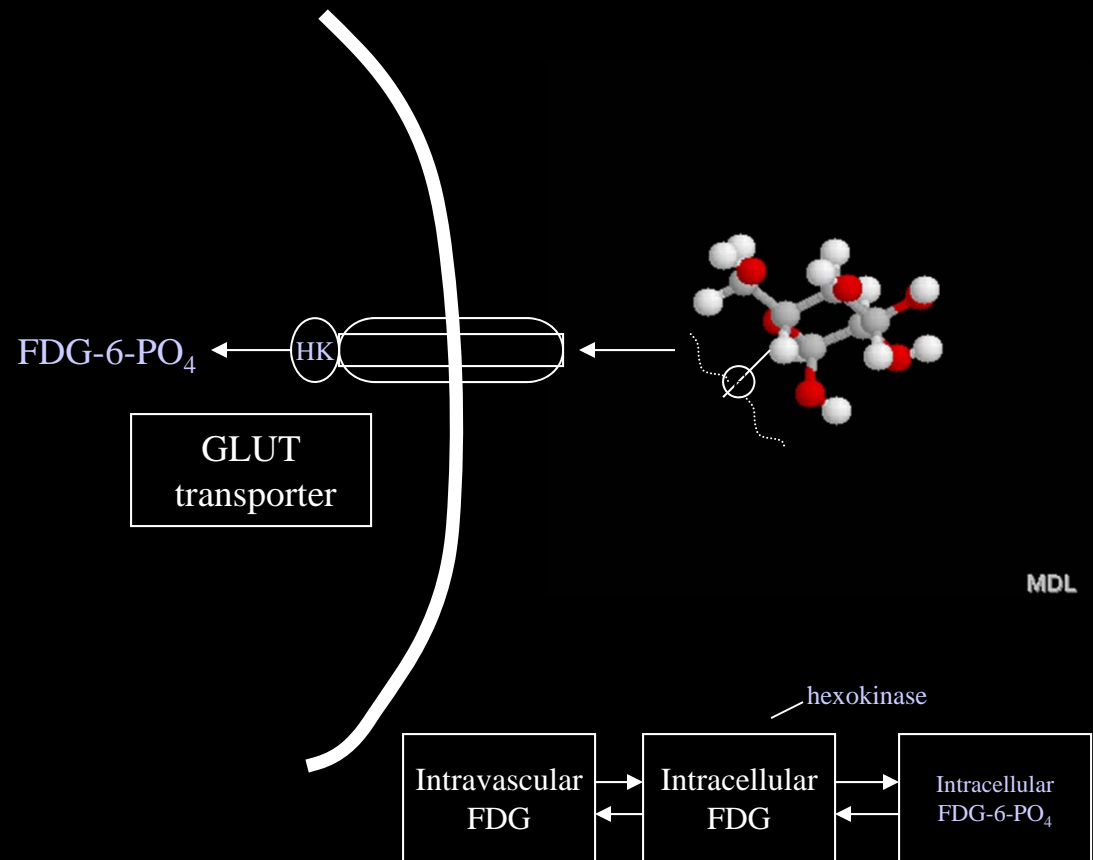
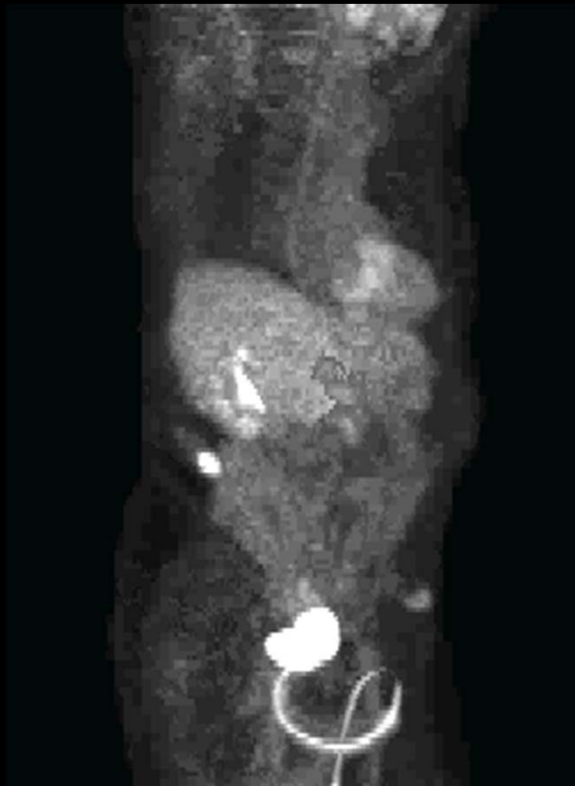
*C Menard ROB, NCI*



# Molecular Biology of Angiogenesis



# $^{18}\text{F}$ FDG PET Imaging



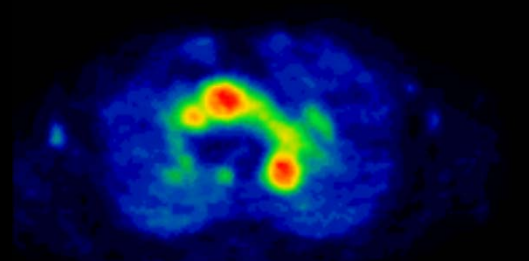
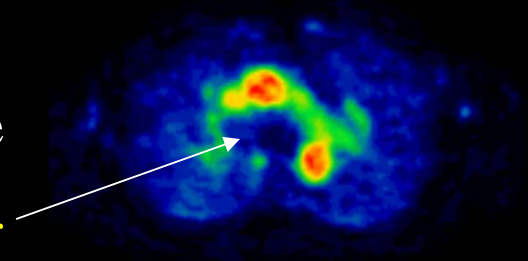
PRE

POST

Blood Volume

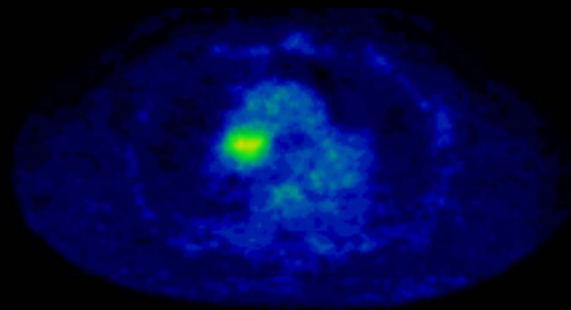
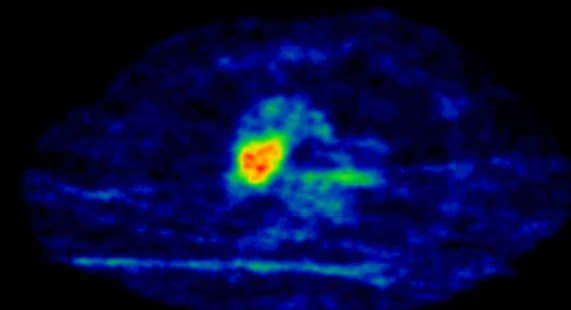
$^{11}\text{CO}$

tumor



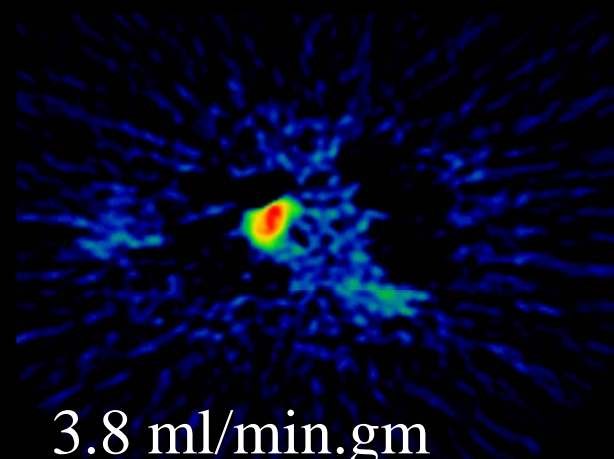
Glucose  
Metabolism

$^{18}\text{FDG}$

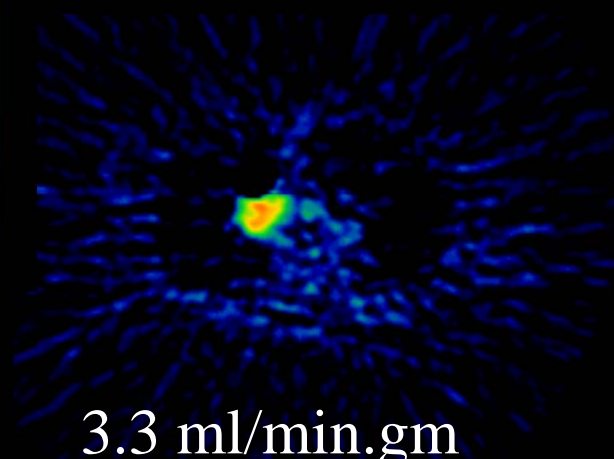


Blood Flow

$\text{H}_2^{15}\text{O}$



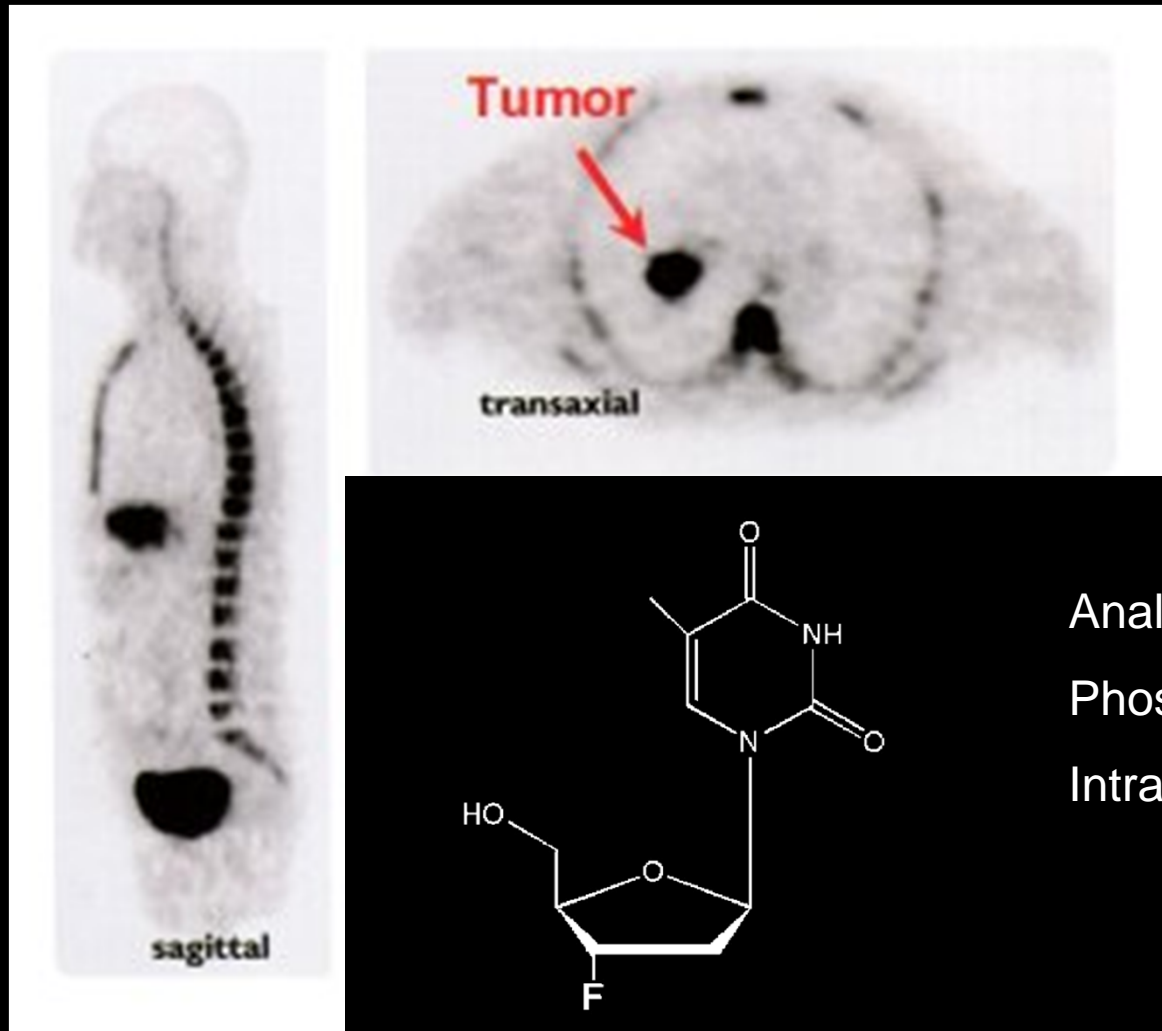
3.8 ml/min.gm



3.3 ml/min.gm



# $^{18}\text{F}$ -Fluoro L-Thymidine



Analog of AZT

Phosphorylated by TK

Intracellular Trapping

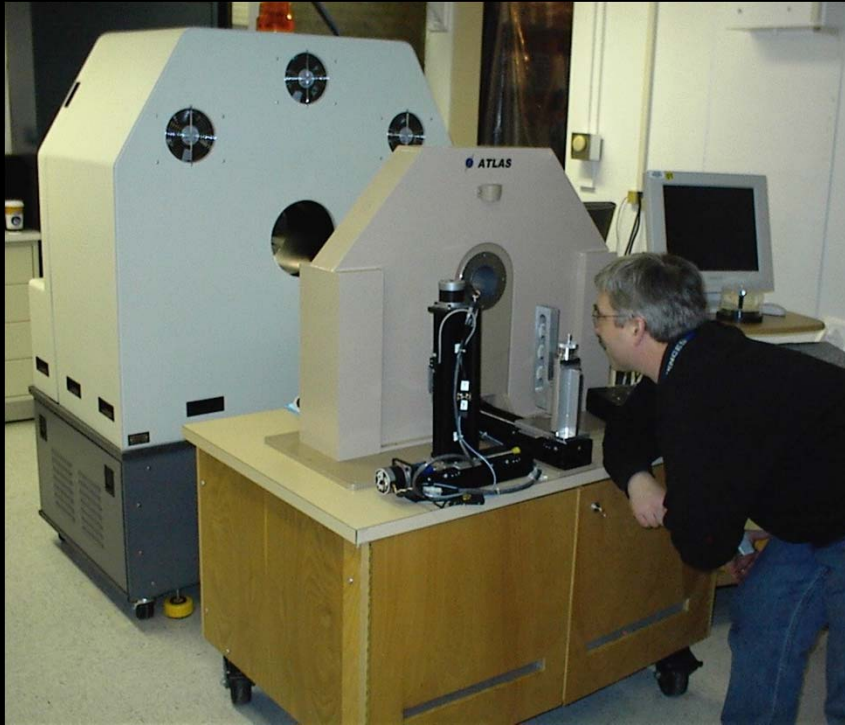
FLT



# DCIDE PET Agents (NCI IND)

- $^{64}\text{Cu}$  ATSM Hypoxia Imaging
- $^{18}\text{F}$ ACBC Amino acid trapping
- $^{18}\text{F}$  RGD Integrin receptor
- $^{11}\text{C}$  Acetate Lung, prostate, brain cancer
- $^{18}\text{F}$ Ch Choline analog
- $^{18}\text{F}$ FLT L-Thymidine, proliferation
- $^{18}\text{F}$ MISO Hypoxia Imaging

# PET Imaging



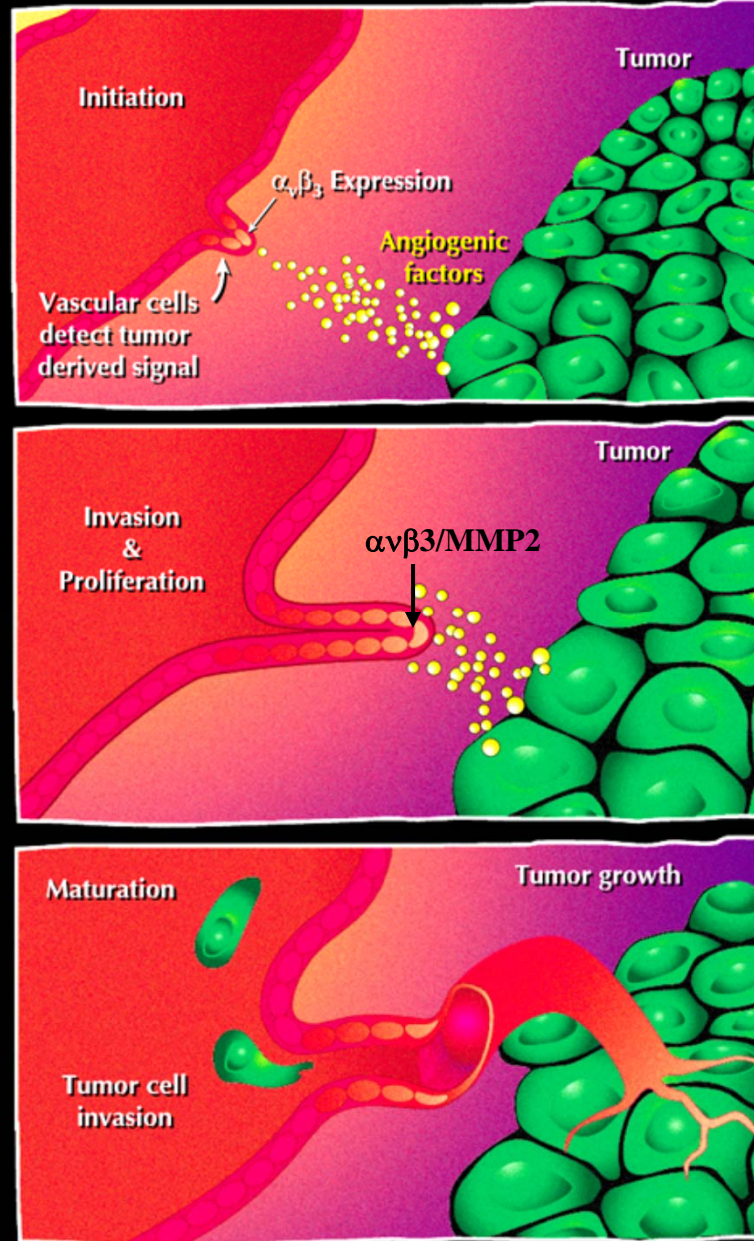
“micro” PET-CT



“macro” PET-CT

# Molecular Targeting

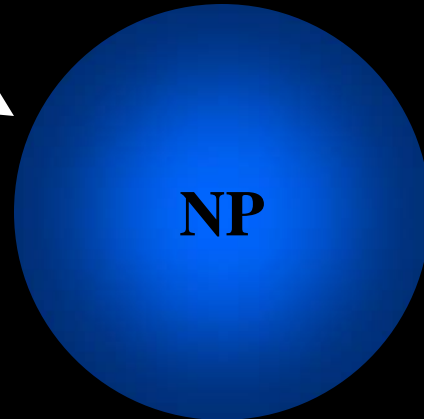
## Steps in Tumor-Induced Angiogenesis



# Goal: Early detection and treatment

**Target**

Peptide  
scFv MAb  
Growth factor  
Nutrient



**NP**

**Diagnostic**

Gd(MRI)  
<sup>111</sup>In (SPECT)  
<sup>18</sup>F (PET)  
Optical



Cytokine  
Chemokine  
Toxin



Gene  
Rx

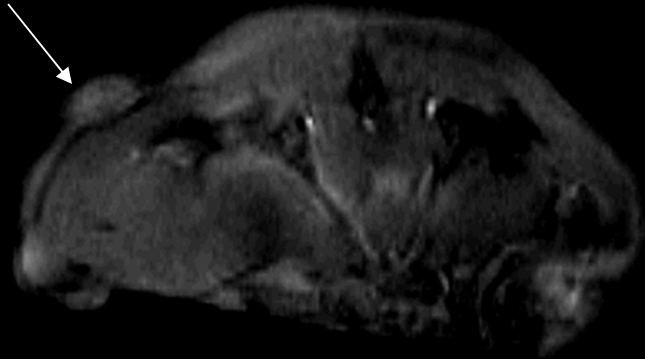


Doxorubicin  
Taxane

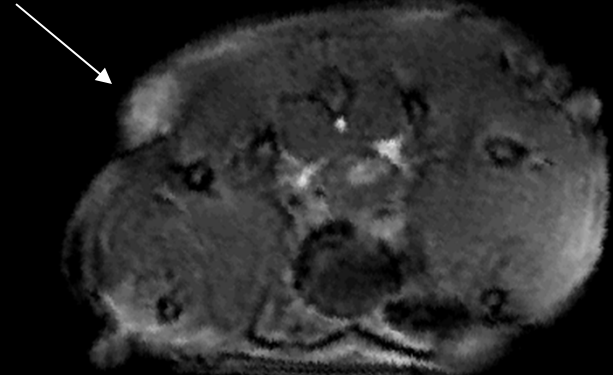


**Therapeutic**

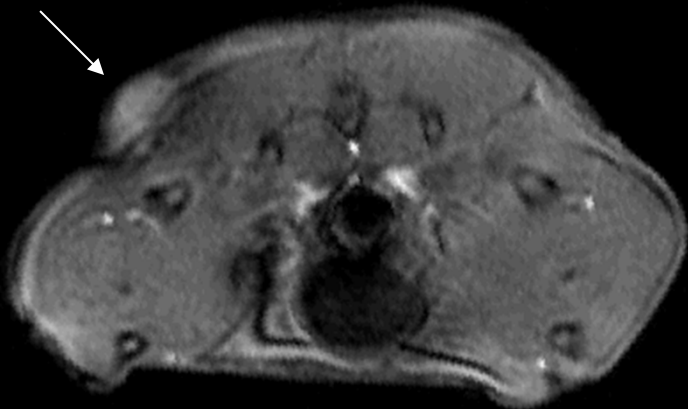




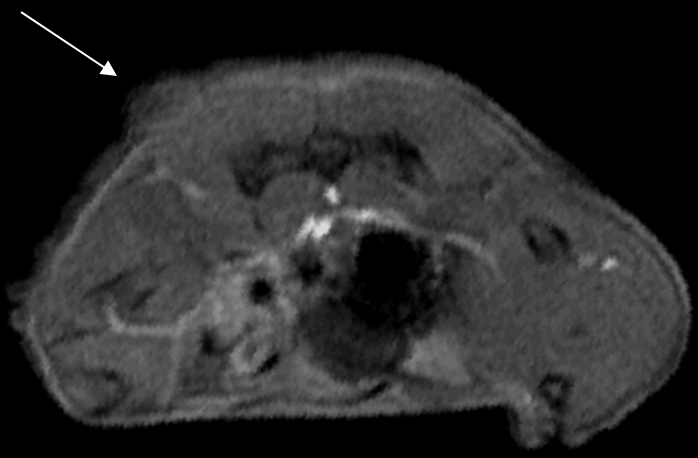
Baseline



2 hrs

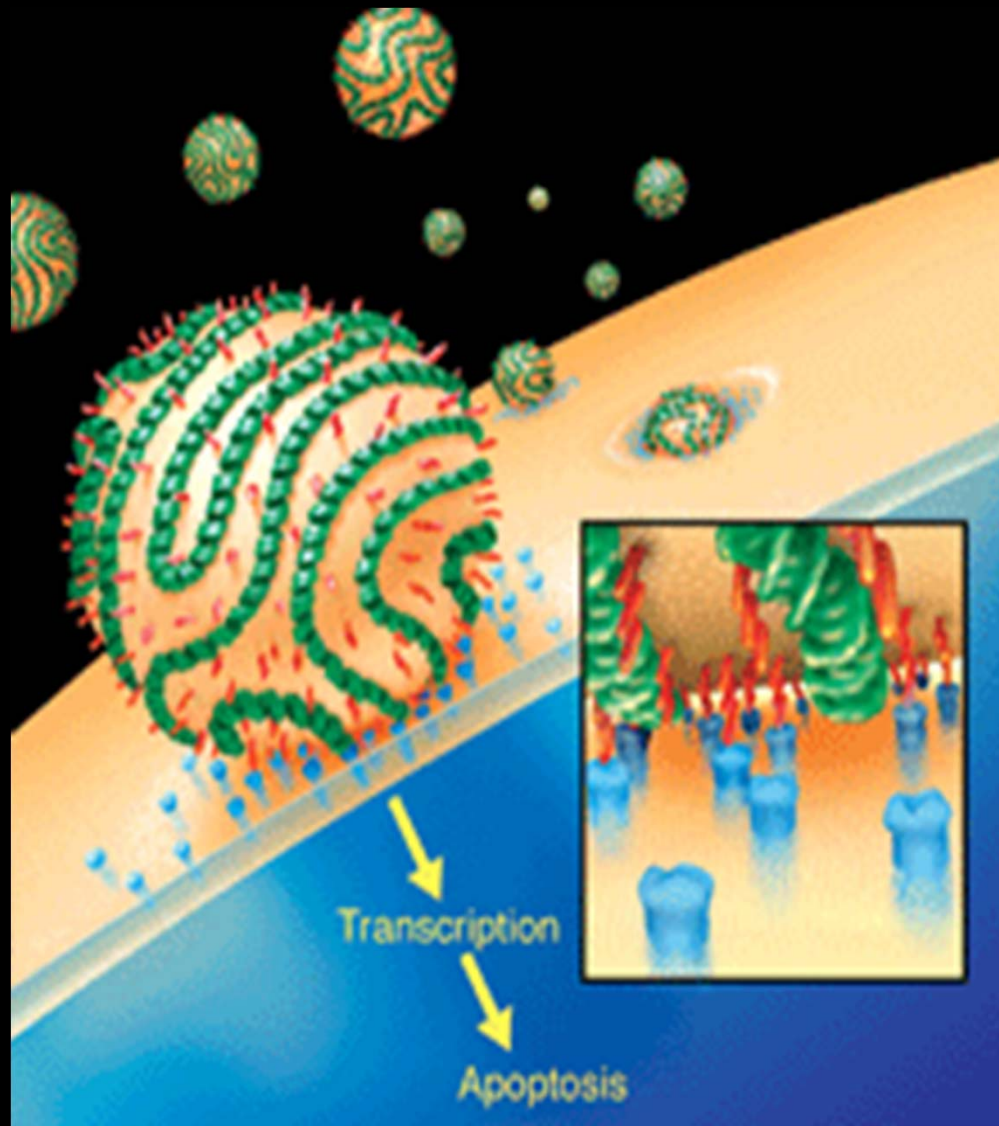


4 hrs

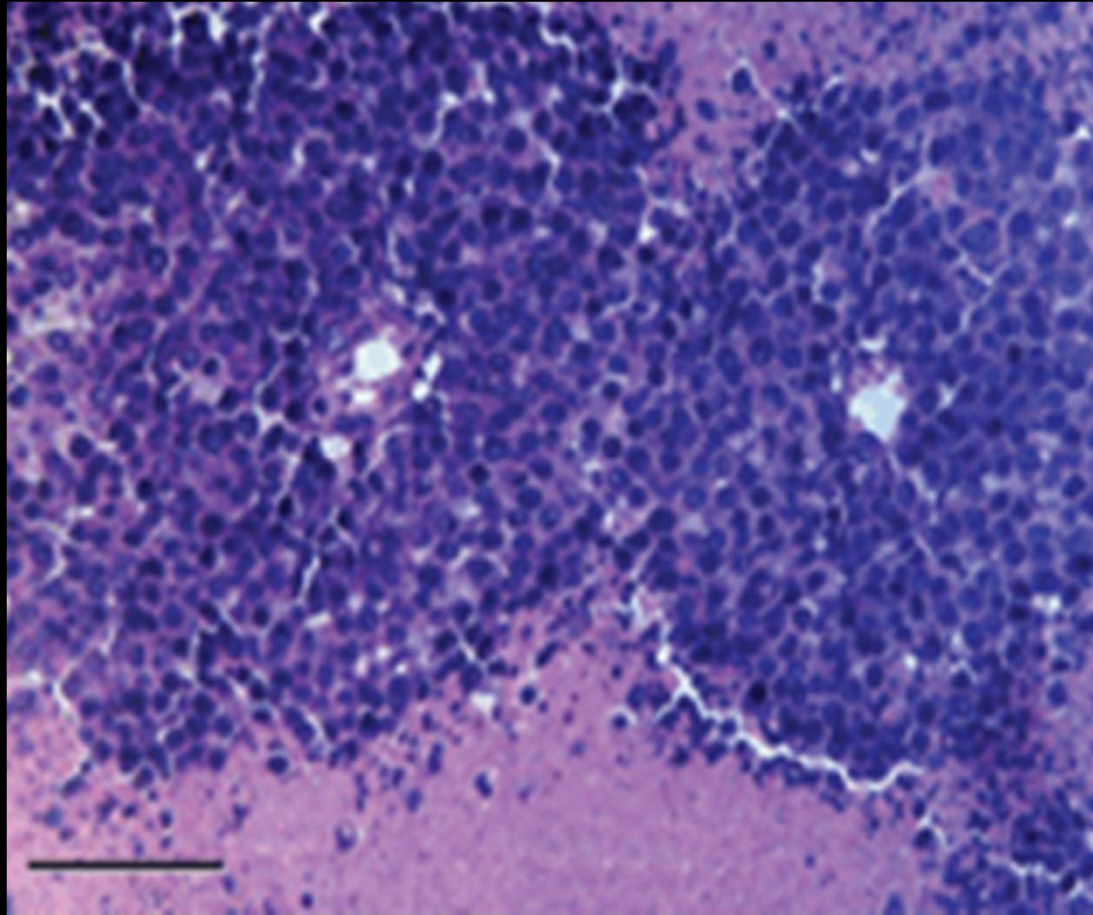


6 hrs

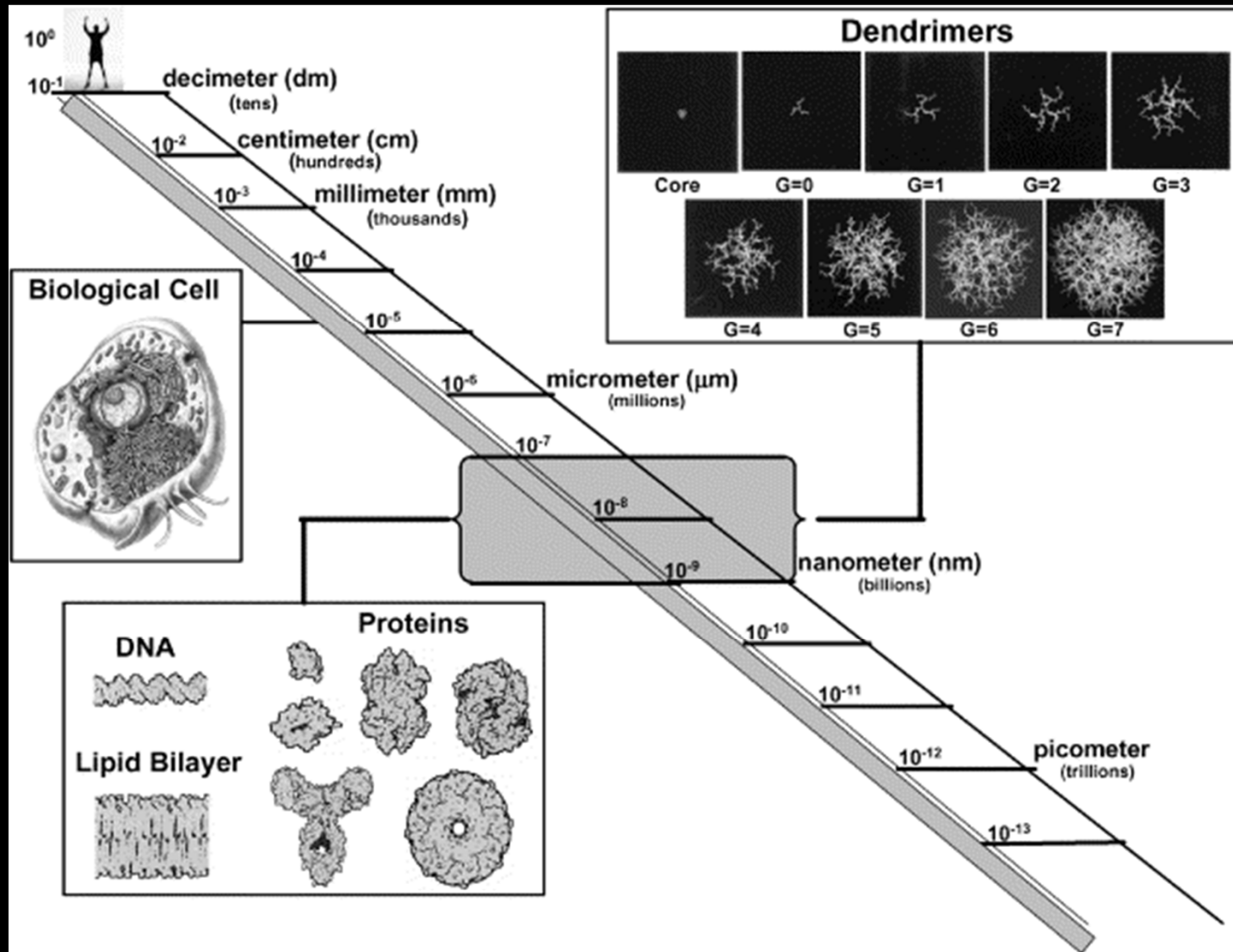
Targeted NP with Gd DOTA, M21 tumor flank



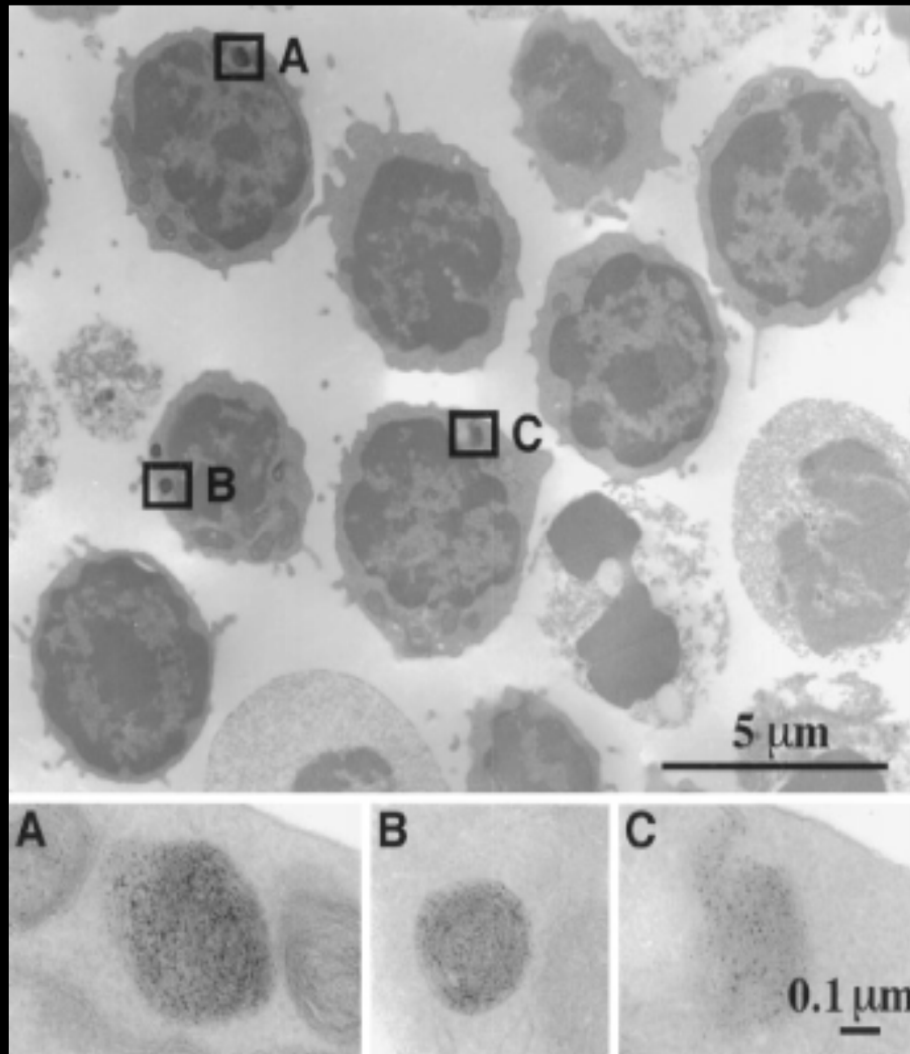
*Hood et al. Science 2002*



*Hood et al. Science 2002*



# The Fate of Dendrimer-Avidin post-Endocytosis

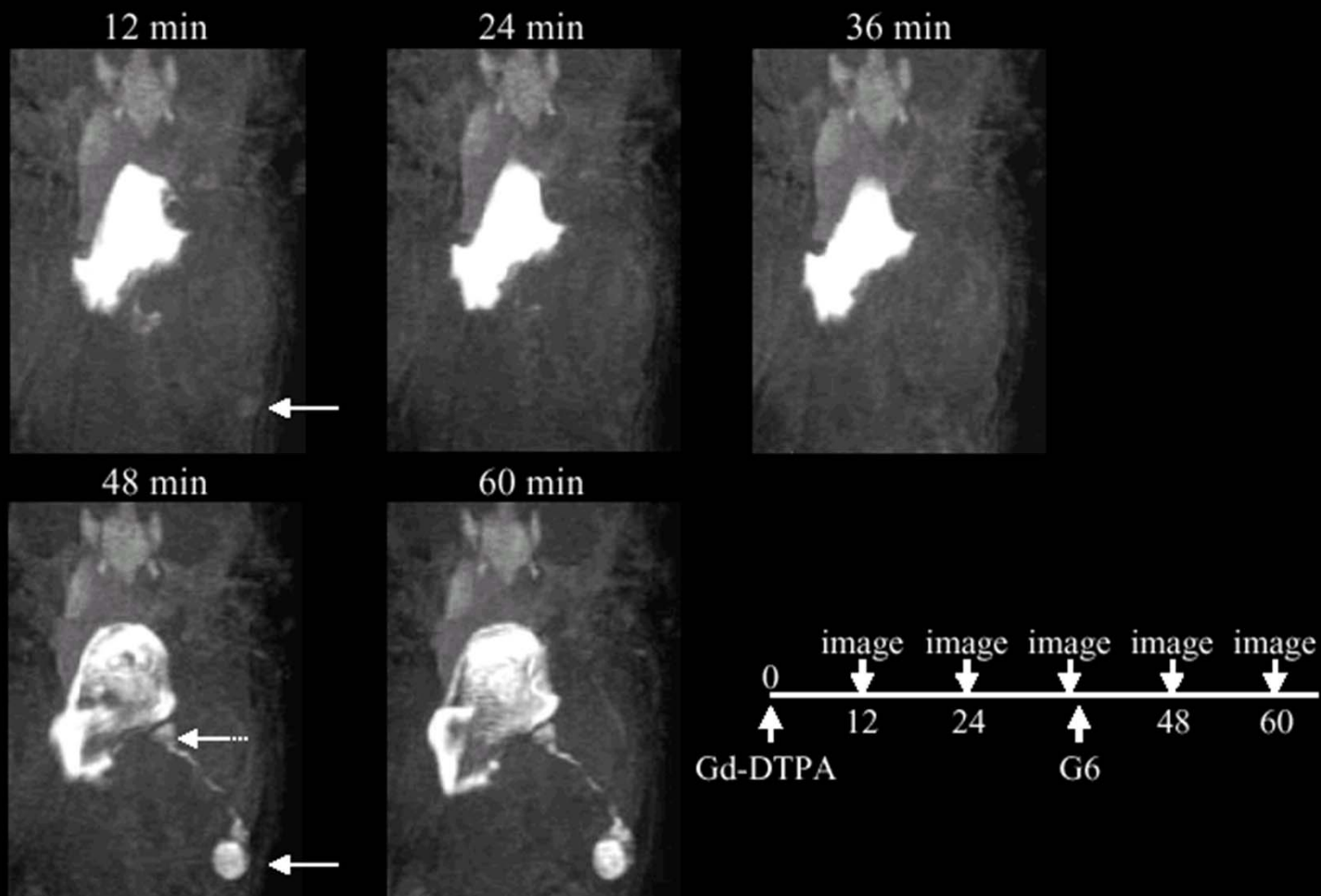


The macromolecules, which go into the cell by endocytosis, accumulated in a single or two fused endosomes of Shin tumor cells. Properties depend on:

- Size
- Charge
- Lipophilicity
- Stability



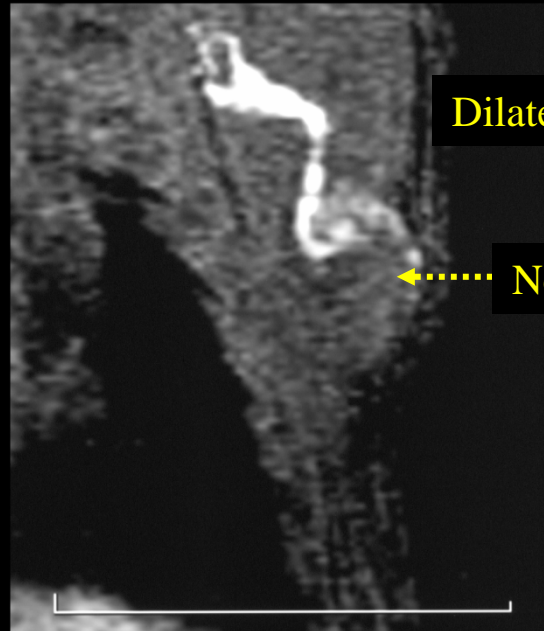
# G6 Dendrimer Sentinel Node



No metastasis

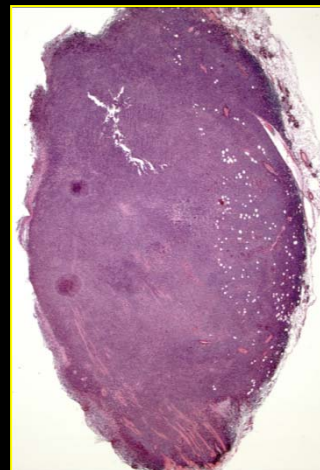
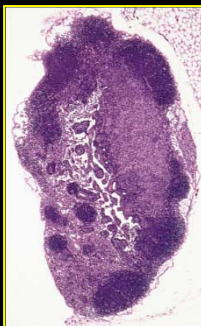


With metastasis of PT-18

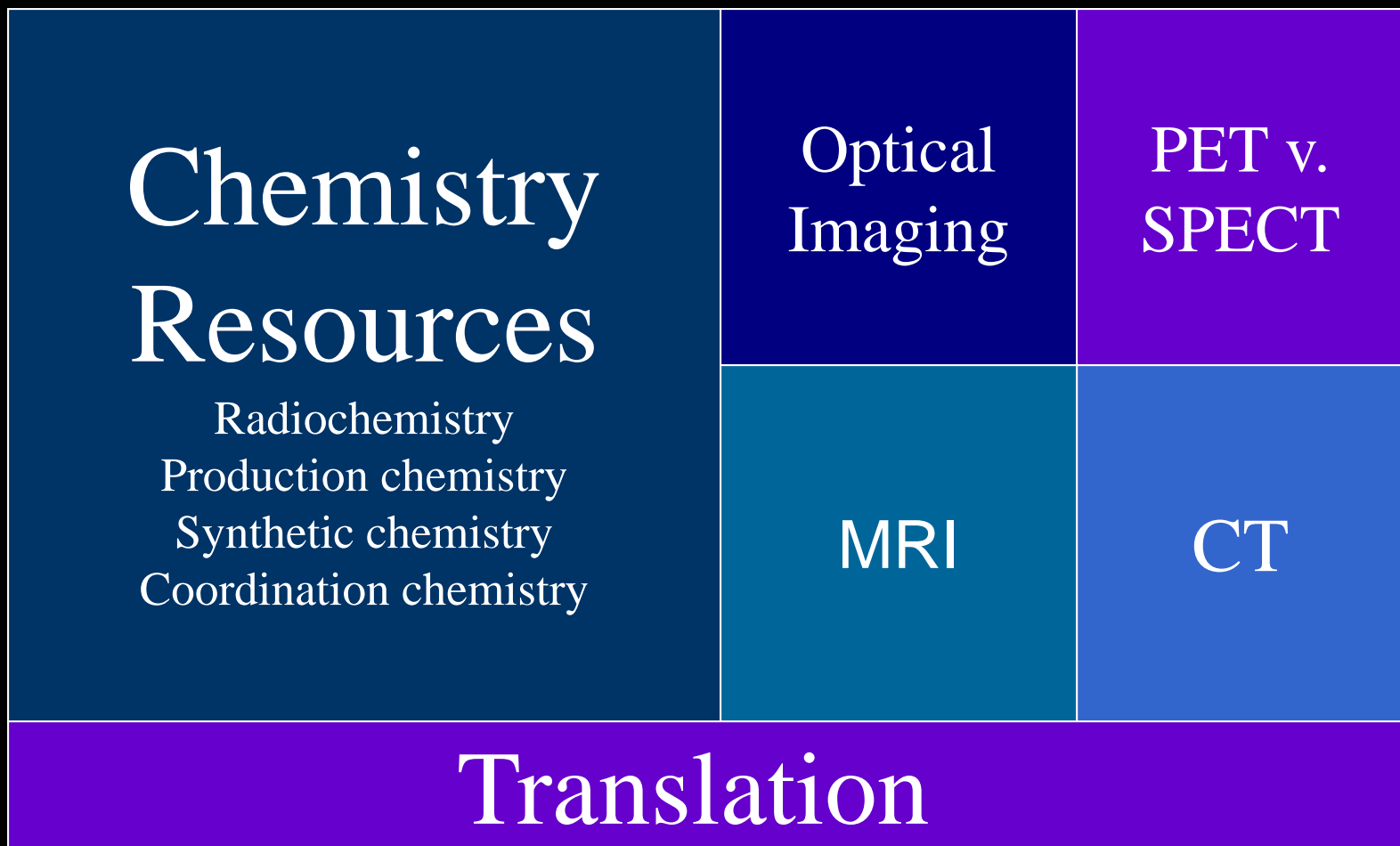


Dilated lymphatic vessel

←..... No filling of the contrast agent



# Molecular Imaging Program



Micro CT



MicroSPECT/CT



MRI



# Animal Imaging



Ultrasound

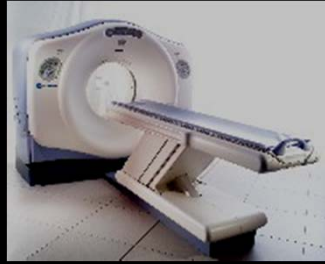


MicroPET



Optical

CT



SPECT/CT



MRI



Fusion Imaging

Human Imaging



Optical



PET CT



Ultrasound



# Acknowledgements

Steve Libutti MD

Jim Yang MD

Sandy Swain MD

Suparna Wedem MD

Cynthia Menard MD

Rob Susil Ph.D.

Norm Coleman MD, Ph.D

Martin Brechbiel Ph.D,

Hisataka Kobayashi, MD, Ph.D.

Garry Choy BS

Reyes Eulate MD

Justin McKellop BS

Cesar Castro BS

Nick Costouros MD

King Li MD, MBA

Mark Bednarski MD, Ph.D.

Cathy Chow MD

David Thomasson Ph.D

Jack Yao Ph.D.

Andrew Dwyer M.D.

Steve Bacharach Ph.D.

Jorge Carrasquillo MD

Mike Green MS

Michael Knopp (OSU) M.D. Ph.D.

Philips Medical Systems

General Electric Medical Systems

Alnis Corp.

Targesome Corp