

Molecular Imaging – Emerging Techniques and Staging of Prostate Cancer

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Non Nova. . .Sed Novae (Not New Things, but Things Done Newly)

- Molecular Imaging: defined as visualization of a unique process *in vivo*, using a specific probe and imaging modality
- Not a new field: same principle as Nuclear Medicine, but more specific
- May be viewed as a “Special Stain” for the Radiologist

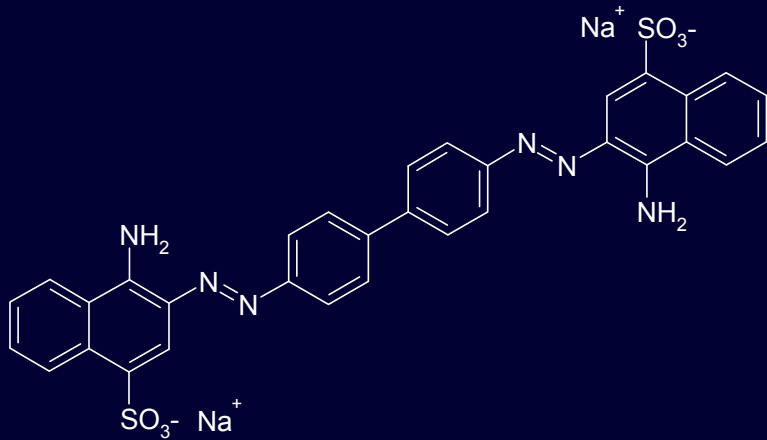
Research application: Imaging a Plaque in the Brain

- Alzheimer's disease: 4 million cases in US
- At present, no drugs to prevent or disrupt plaque formation
- Disease evaluation requires neuropathology
- *In vivo* plaque detection useful for drug development (would allow rapid detection of plaques in experimental animals)

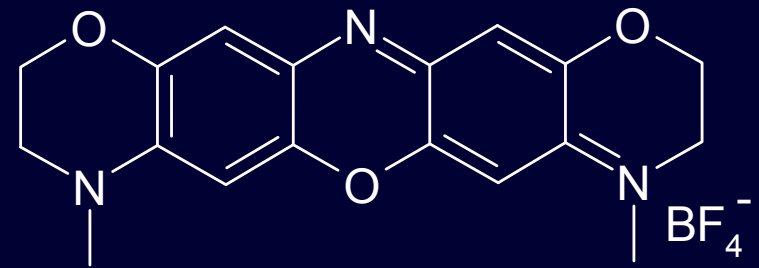
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An *In vivo* Congo Red



Congo Red



AOI-987

Modality: Optical
(Near-Infrared
Fluorescence)

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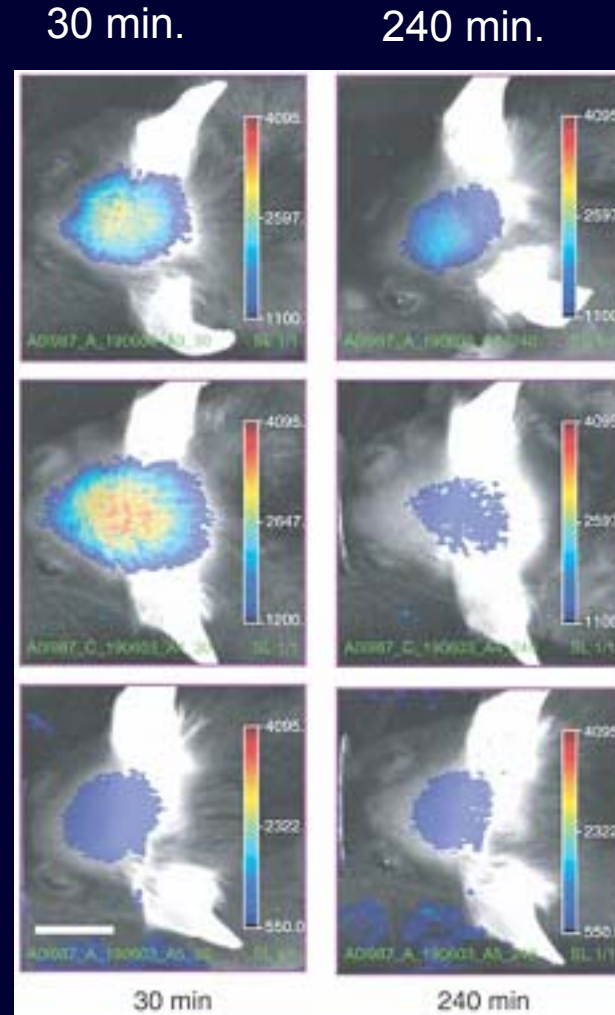
Hintersteiner *et al.*, *Nat. Biotech* **2005**, 23, 577-583

Alzheimer's plaques in a mouse

APP23 + AOI-987
(Fluorescence visible at
240 min.)

Wild Type + AOI-987
(no fluorescence at
240 min.)

APP23 + Saline
(no fluorescence)



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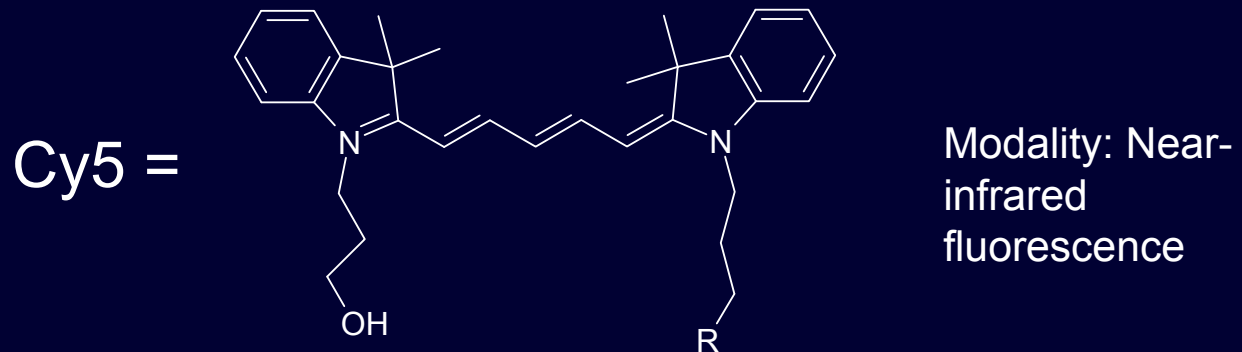
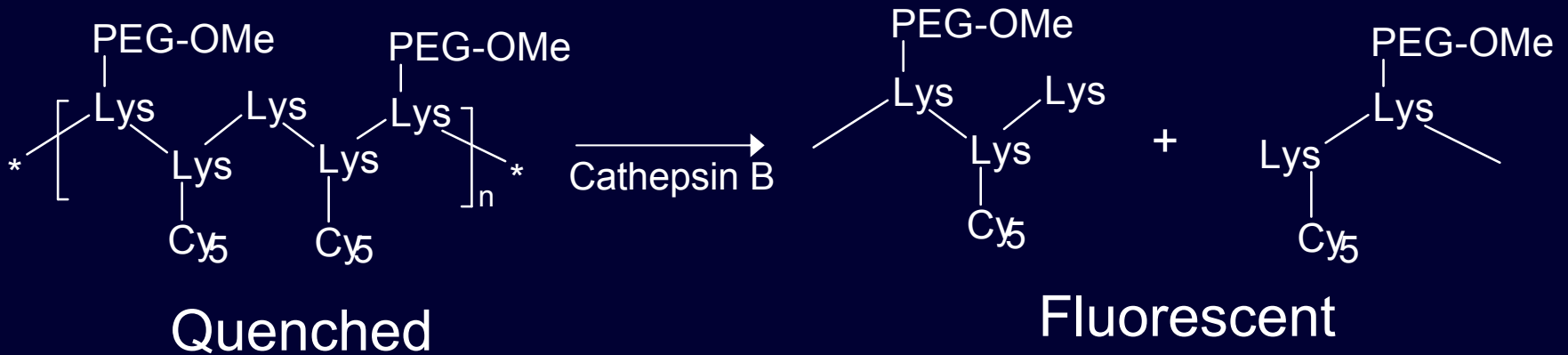
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Translational application: Imaging a Plaque in the Aorta

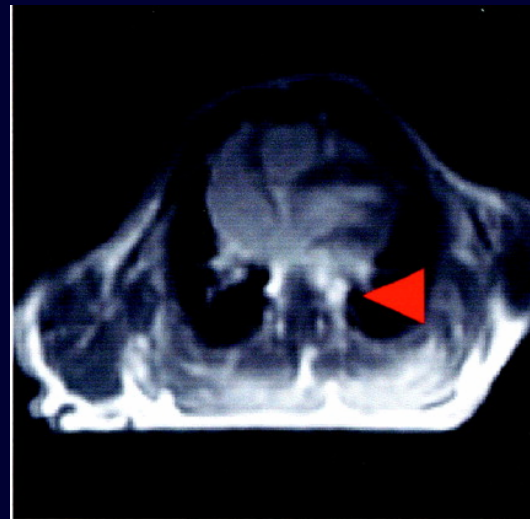
- Coronary Artery Disease: ~500,000 deaths/year
- Conventional imaging assesses calcification and degree of stenosis – but not risk of plaque rupture
- Vulnerable plaque cannot be imaged at present – but has high levels of inflammatory cell and protease activity that might be imaged

An active probe for Cathepsin B

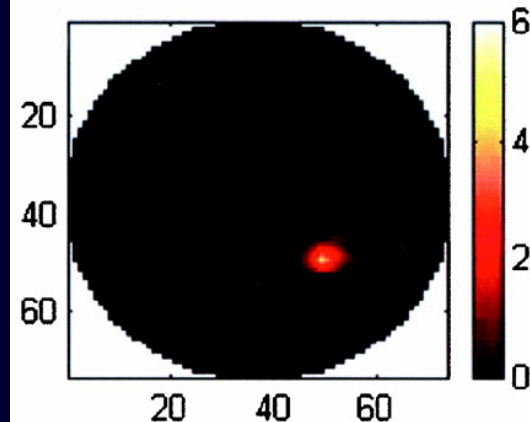


Cathepsin B activity – *in vivo*

MRI



Fluorescence-mediated tomography-shows active
Cathepsin B



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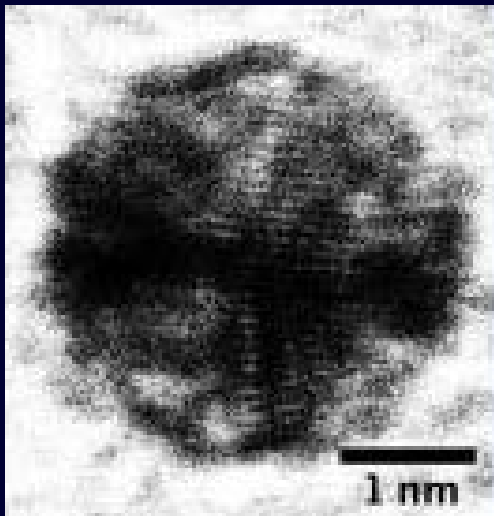
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Chen *et al.*, *Circulation* **2002**, 105, 2766-2771

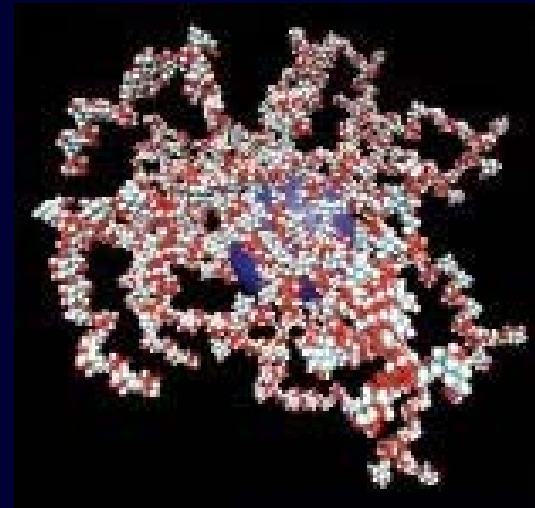
Lymph Node Imaging for Prostate Cancer

- ~200,000 diagnoses/year; ~30,000 deaths
- Two principal avenues of therapy based on metastases
 - Local: Radical prostatectomy, radiotherapy, or watchful waiting
 - Locally advanced/metastatic: Androgen-deprivation therapy and radiation
- Current methods to detect metastases limited by node size

Superparamagnetic Iron Nanoparticles – a marker for the lymph system



Electron Micrograph



Model of Nanoparticle coated with 10 kDa dextran

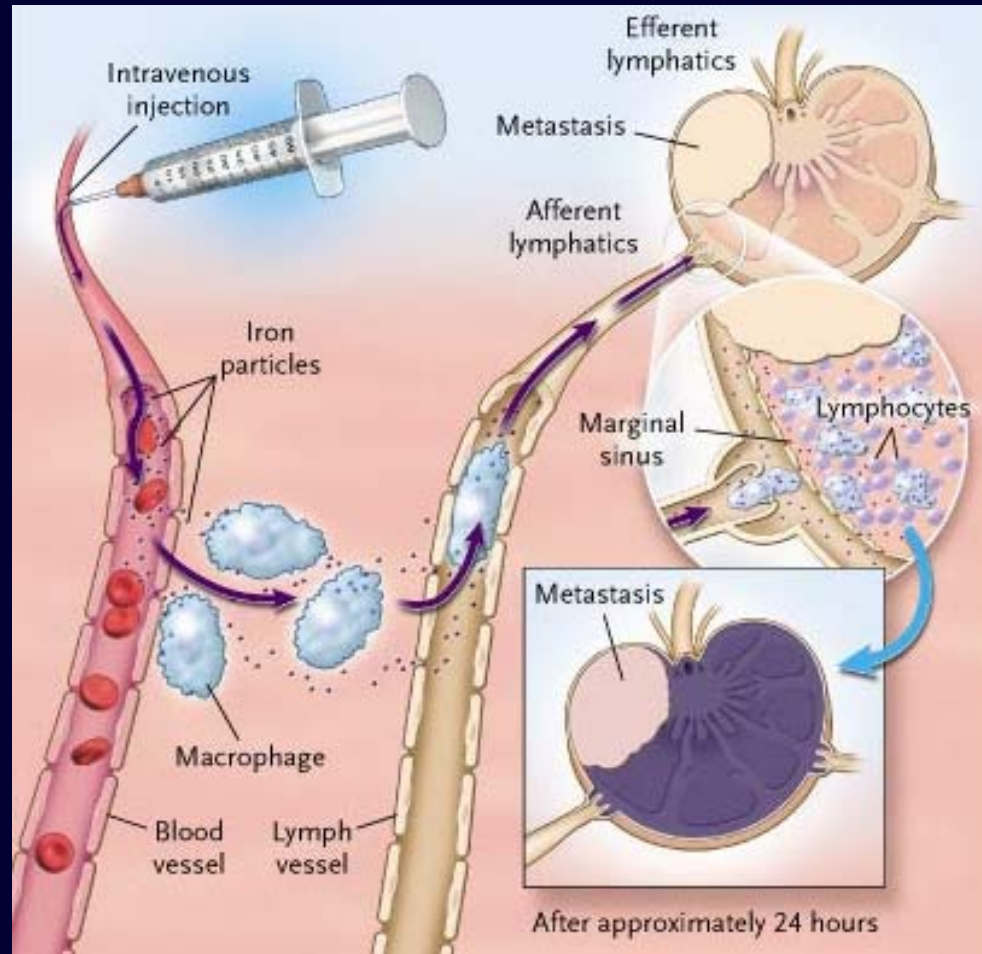
Modality: MRI (lymphatics have low signal 24 hrs. post injection with nanoparticles)

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Harisinghani *et al.*, *NEJM* **2003**, 348, 2491-2499¹⁰

Imaging the Lymphatic System

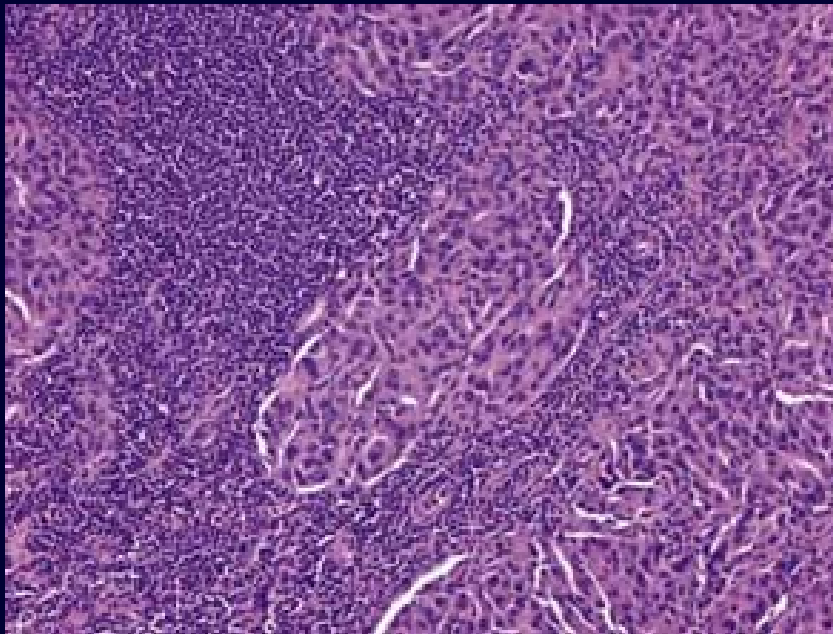


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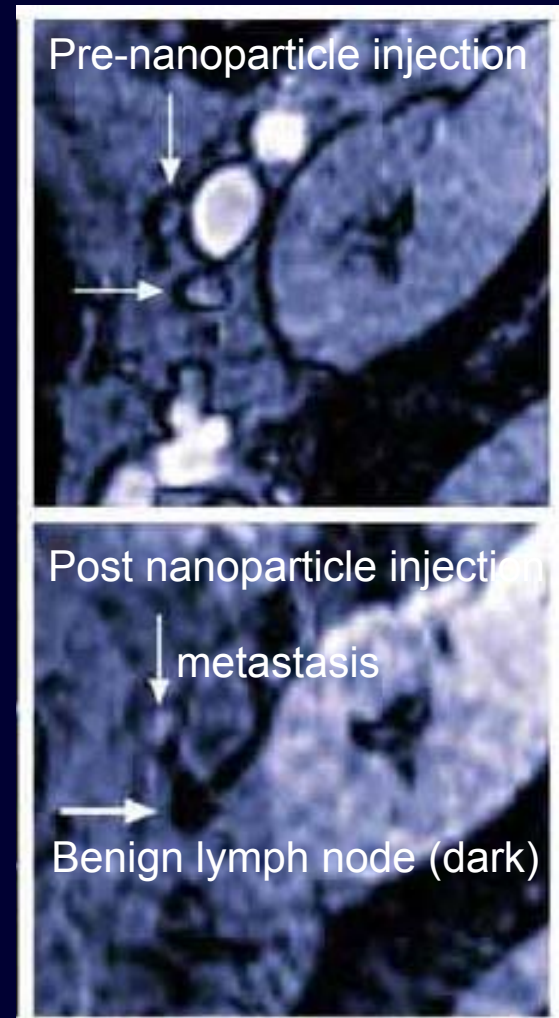
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Metastases Visualized *in vivo*



Pathology post-excision



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Harisinghani *et al.*, *NEJM* **2003**, 348, 2491-2499¹²

Lymph Node Metastasis Detection

All sizes	MRI	MRI+Probe
Sensitivity	35.4	90.5*
Specificity	90.4	97.8
5-10 mm		
Sensitivity	28.5	96.4*
Specificity	87.2	99.3
<5 mm		
Sensitivity	0	41.1
Specificity	100	98.1

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*P<0.001

Harisinghani *et al.*, *NEJM* 2003, 348, 2491-2499¹³

Conclusions

- Molecular imaging of specific biological processes enhances the diagnostic power of radiology
- At a basic research level, molecular imaging is useful for observing molecular events in living organisms and for evaluation of therapeutics
- The clinical applications of molecular imaging include earlier detection and more effective intervention and treatment

References

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