

MRI Contrast agents

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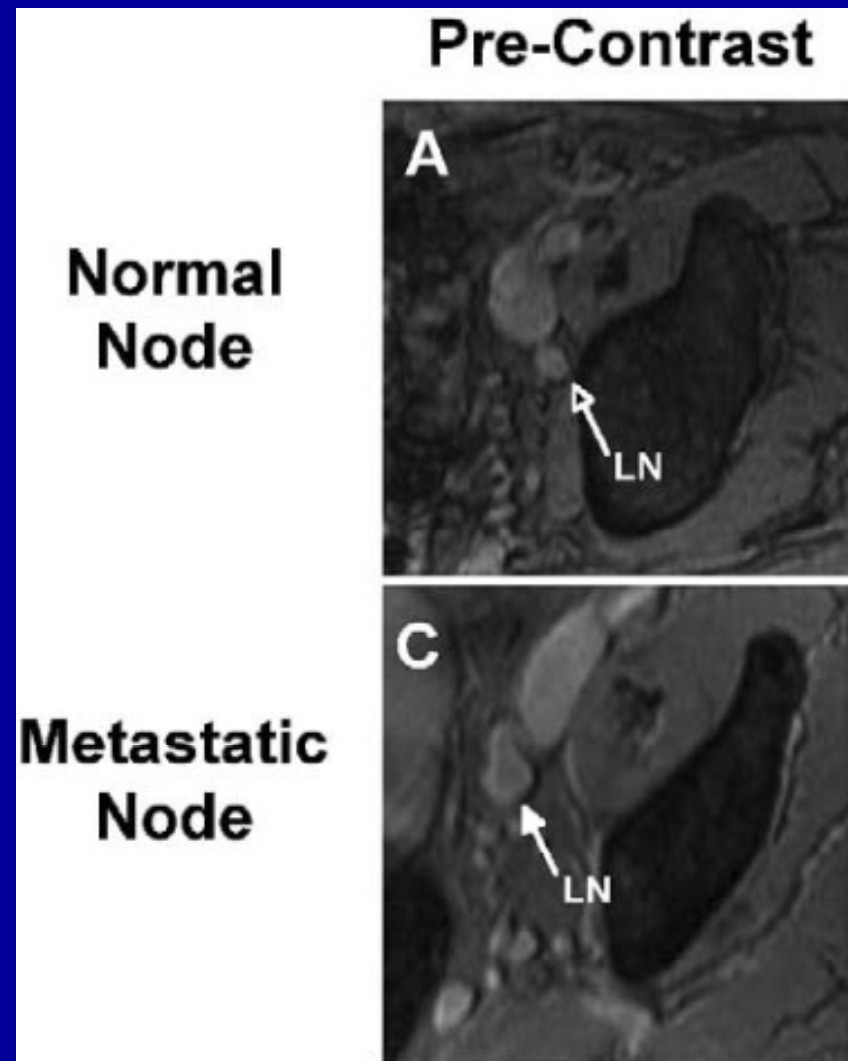
MRI

- Magnetic resonance imaging (MRI):
- A powerful non-invasive diagnostic imaging modality
- No use of ionizing radiation
- 3D reconstructed images
- High soft tissue contrast
- High spatial resolution

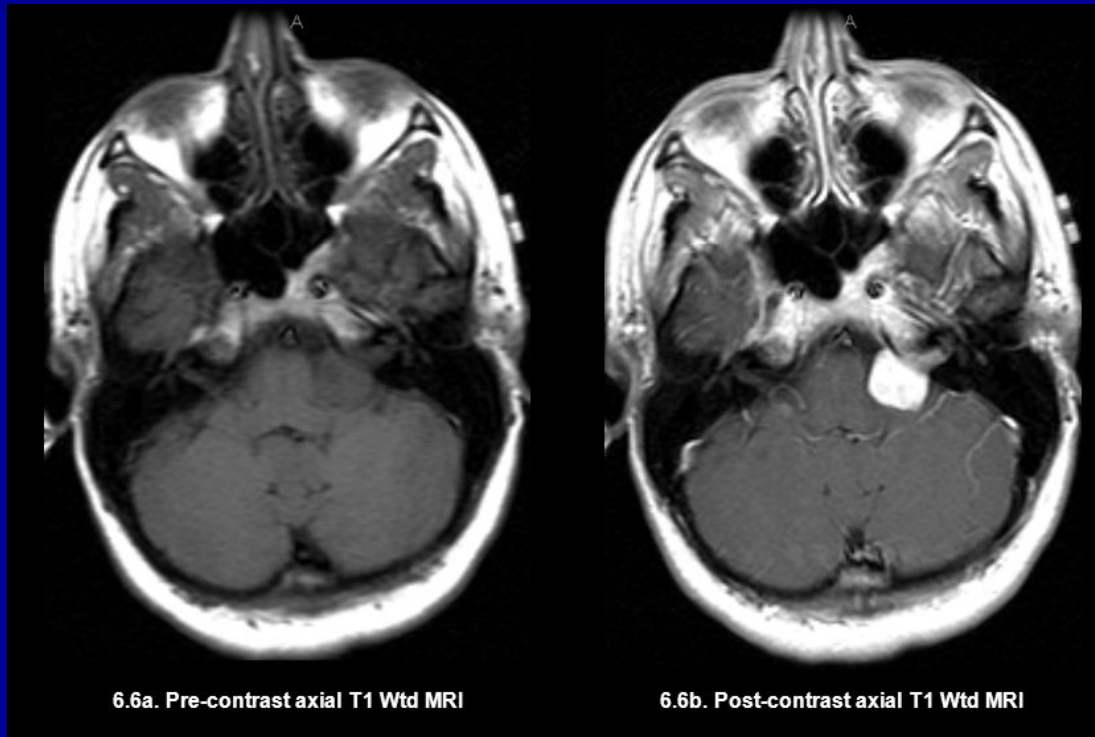
MR images contrast

- MRI contrast
- Inherent MRI contrast depends on:
- Relaxation times (T_1 and T_2)
- Proton density of the materials or tissues

MR images contrast



MRI contrast agents (CAs)



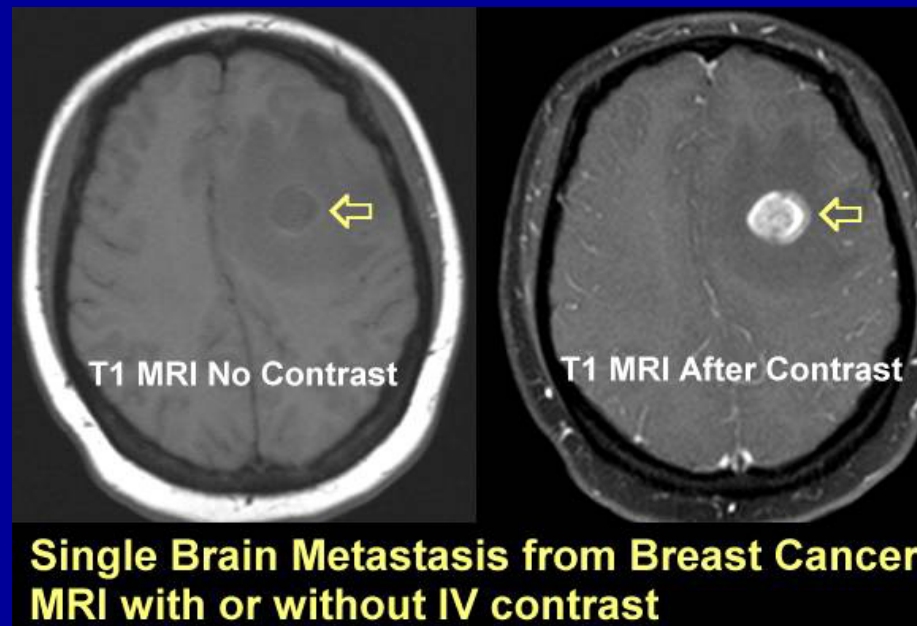
MRI contrast agents

- Paramagnetic
- Superparamagnetic
- Reduction of the proton relaxation times →
- Changes of signal intensity in the accumulated region

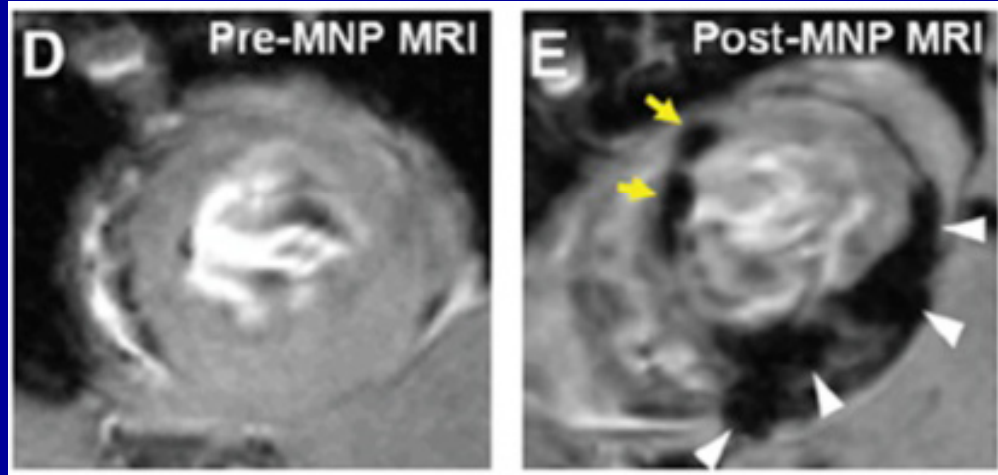
MRI Contrast agents

- Positive
- Negative

Positive contrast agents



Negative contrast agents



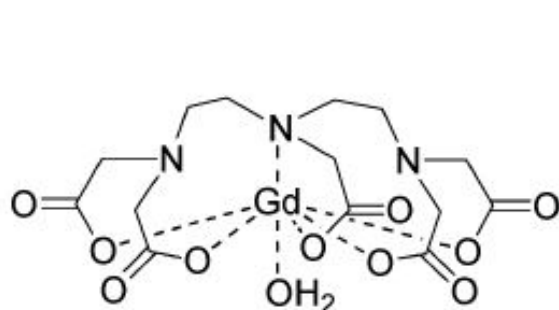
Gadolinium

- Gd:
 - Paramagnetic substance
 - Relatively large magnetic moment
 - Free Gd ions are cytotoxic and are retained in liver, spleen, and bone!
 - Attachment to a chelate

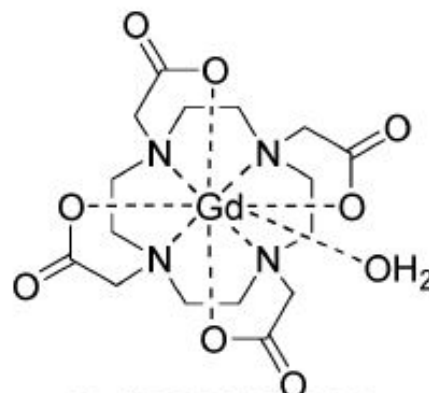
Gadolinium

- The most common chelate in use is diethylene triaminepentaacetic acid (DTPA)
- Other chelates:
 - HP-DO3A
 - DTPA-BMA
 - DOTA

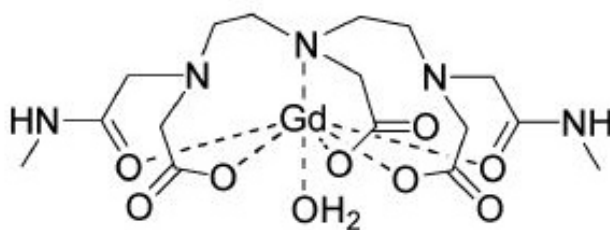
Gadolinium based commercial contrast agents



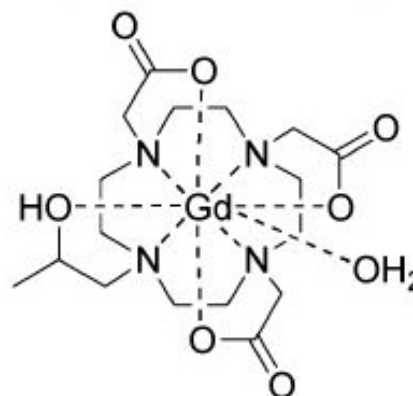
$[\text{Gd}(\text{DTPA})(\text{H}_2\text{O})]^{2-}$
(Magnevist: Berlex/Schering)



$[\text{Gd}(\text{DOTA})(\text{H}_2\text{O})]^{-}$
(Dotarem: Guerbet)



$[\text{Gd}(\text{DTPA-BMA})(\text{H}_2\text{O})]$
(Omniscan: Nycomed-Amersham)



$[\text{Gd}(\text{HP-DO3A})(\text{H}_2\text{O})]$
(Prohance: Bracco)

Figure 2. Common commercial Gd(III) contrast agents.

Nano Gd based CAs

- Recent advances in the field of nanotechnology have lead to the synthesize ultra-small crystals (2–10 nm diameter) containing large amounts of the Gd.
- High relaxivity
- Gd_2O_3

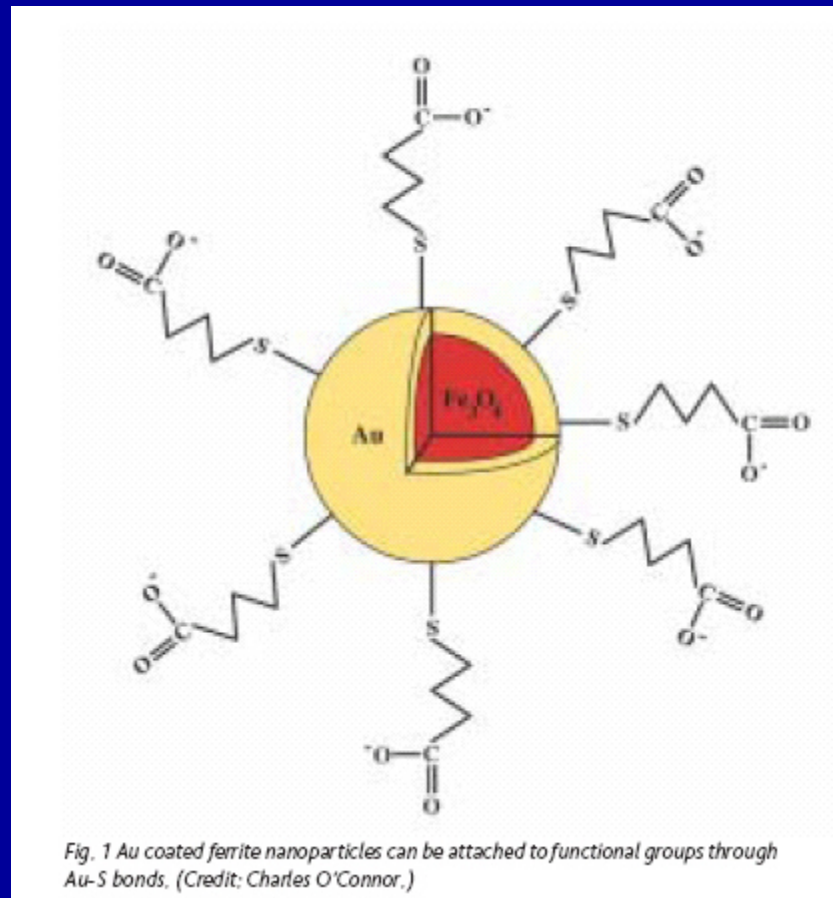
Manganese Based MR Contrast Agents

Mn properties

- A paramagnetic agent
- The second most powerful positive contrast agent for MRI after gadolinium.
- Manganese oxide

Iron oxide nanoparticles

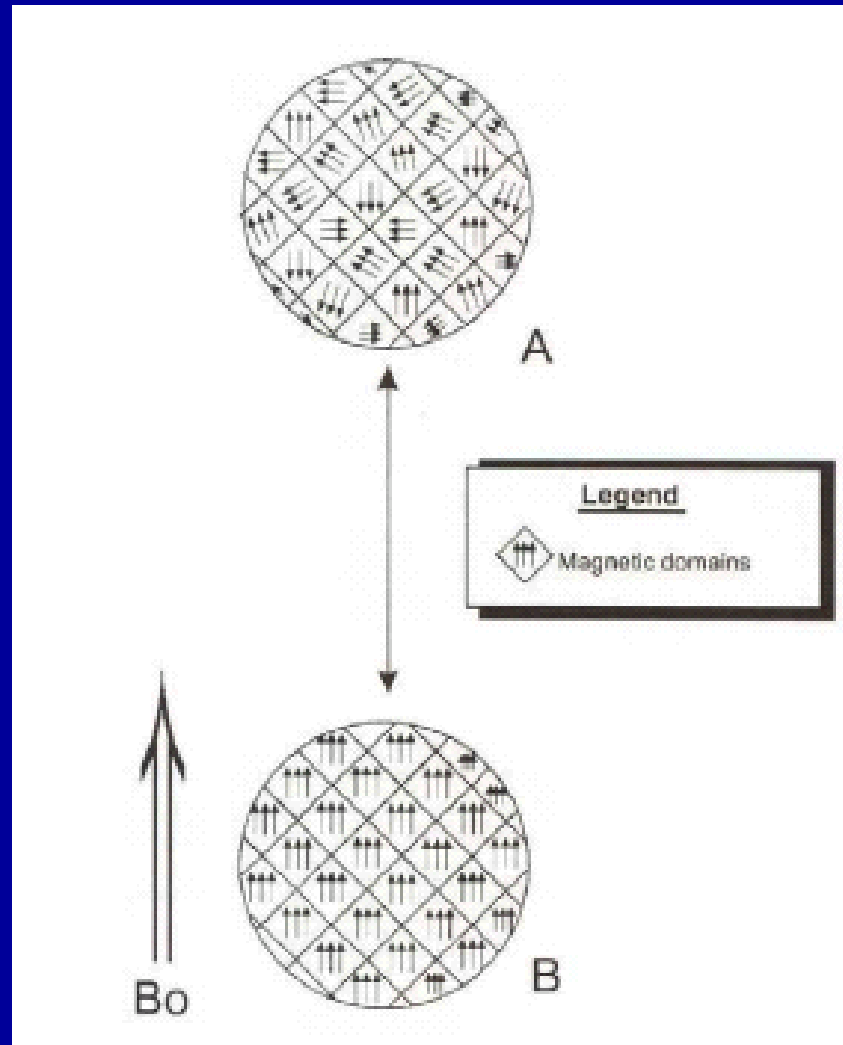
Iron oxide nanoparticles



Coating role

- Avoiding aggregation
- Chemical stability
- Reducing toxicity
- Biocompatibility

Superparamagnetism



Properties of iron oxide nanoparticles

- Superparamagnetic (SPM):
- Controlled by external magnetic fields
- High magnetic moment →
- Using with low doses in comparison with positive contrast agents

Classification

- According to the overall size of the nanoparticles:
- Diameter < 50 nm: ultrasmall superparamagnetic iron oxide (USPIO) nanoparticles
- Diameter > 50 nm: superparamagnetic iron oxide (SPIO) nanoparticles
- Diameter > 200 nm (sometimes several micrometers): large nanoparticles

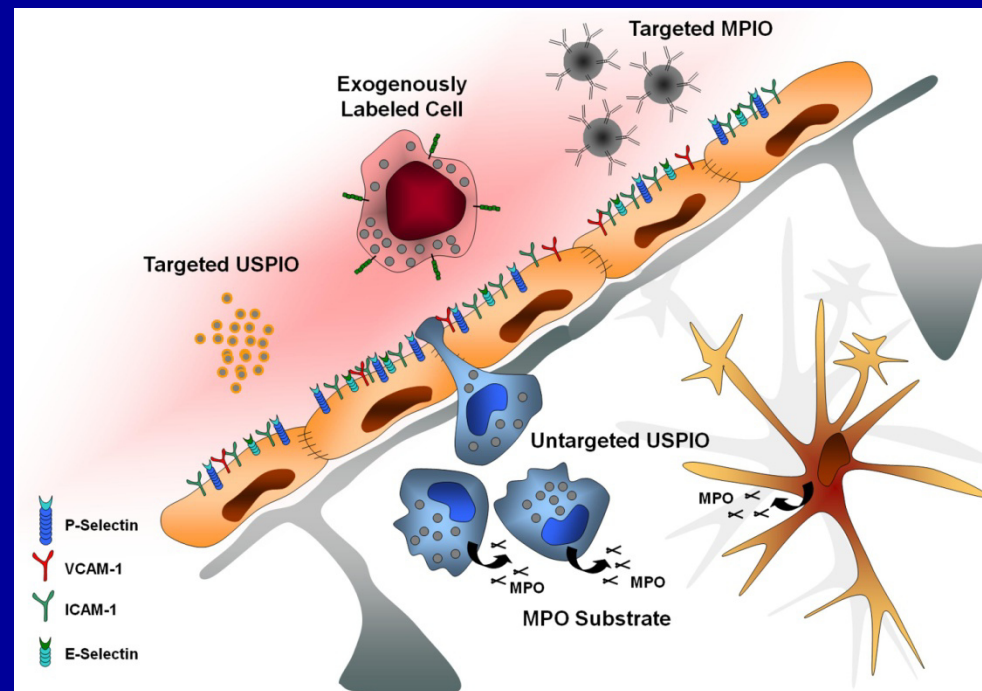
Iron oxide nanoparticles

- Reticuloendothelial system (RES)
- Targeting

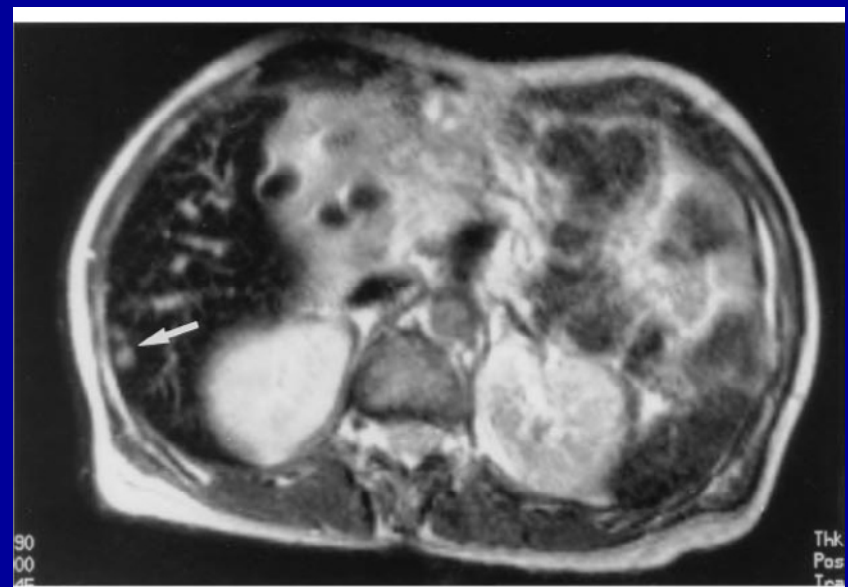
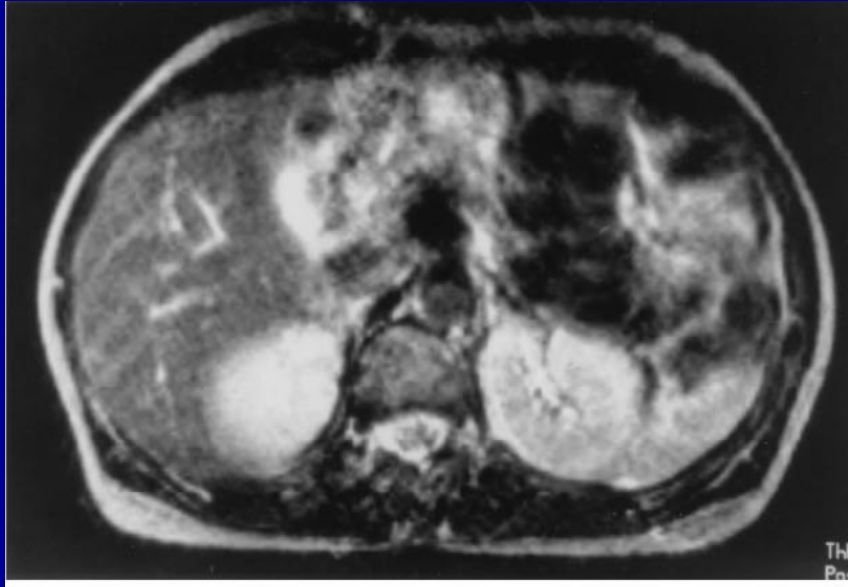
RES agents

- Iron oxide particles have been evaluated as the reticuloendothelial system (RES) agents
- Using for imaging of:
 - Liver
 - Spleen
 - lymph nodes
 - bone marrow

Half-life



Liver metastases

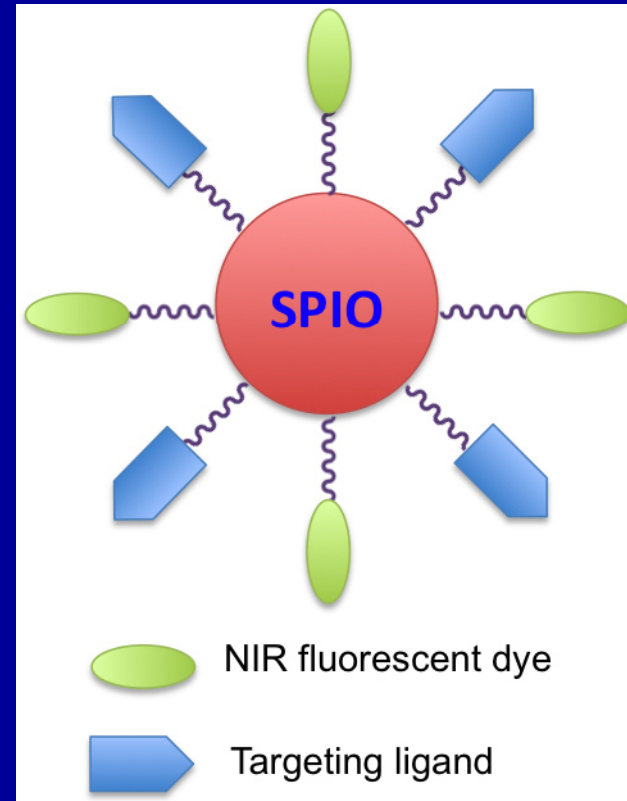
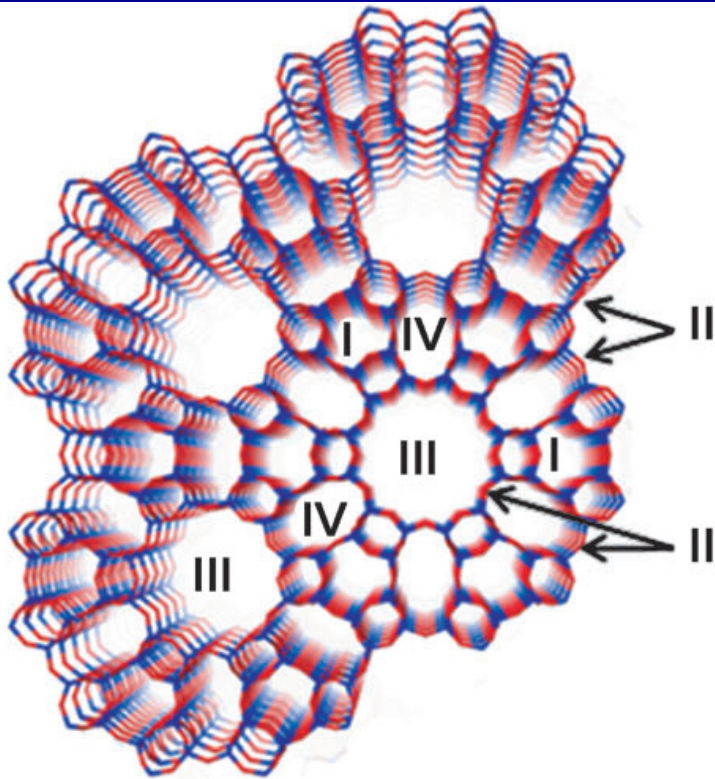


Bimodal and Multimodal agents

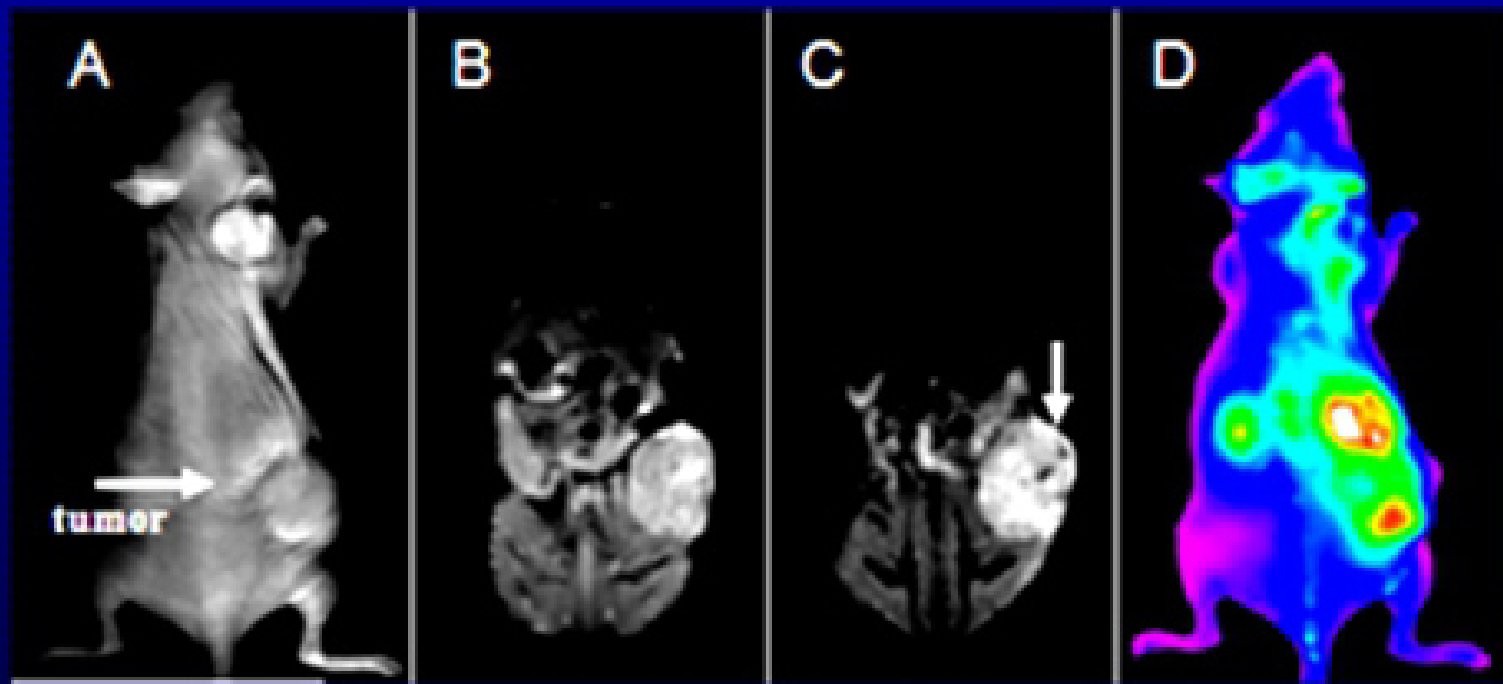
Multimodal agents

- Coordination complexes that produce MRI contrast in addition to serving as probes for other modalities are an active area of research.

Bimodal MR/optical imaging



Bimodal MR/optical imaging for breast cancer imaging

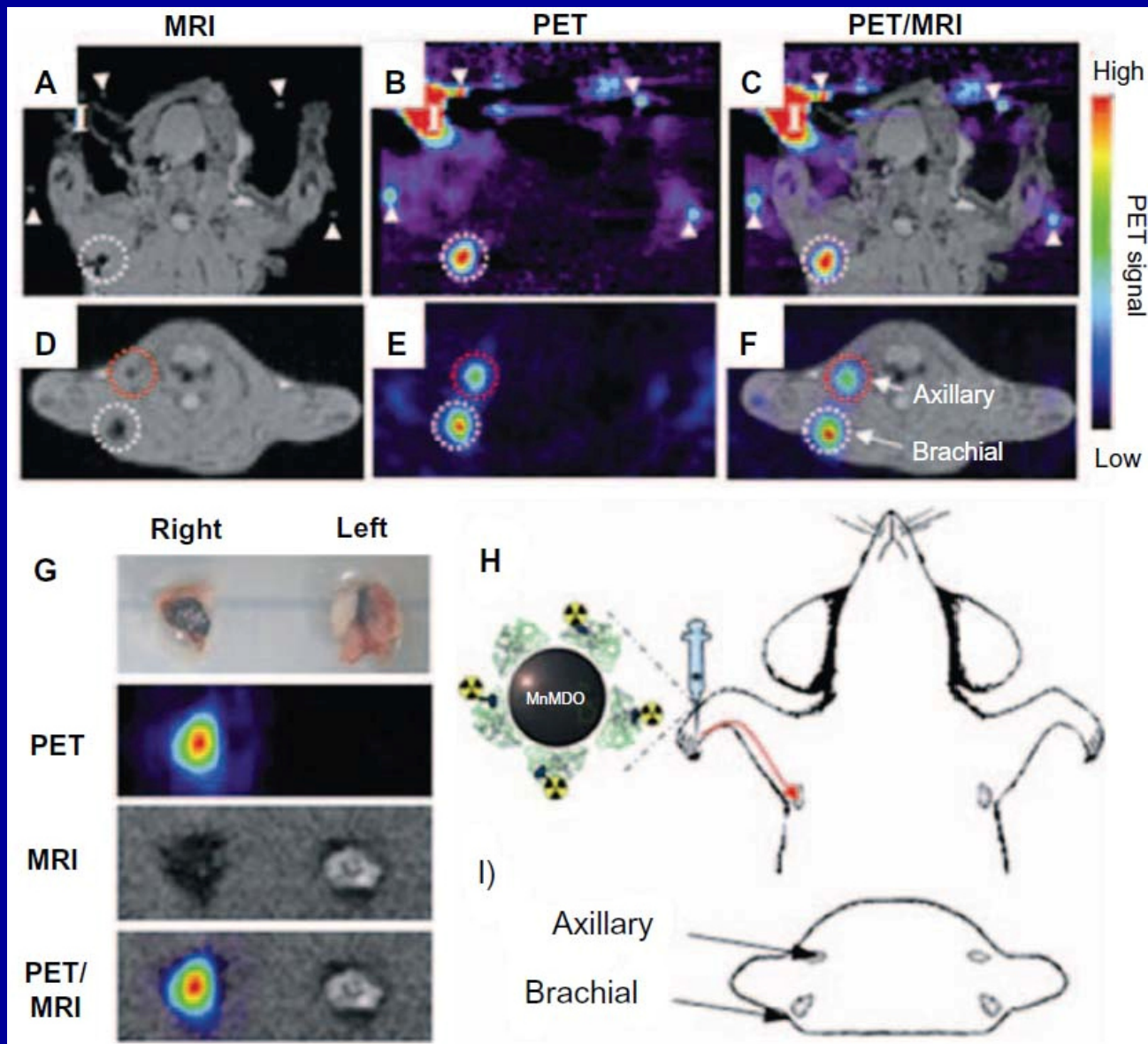


Pre contrast

ATF-IO contrast
enhanced

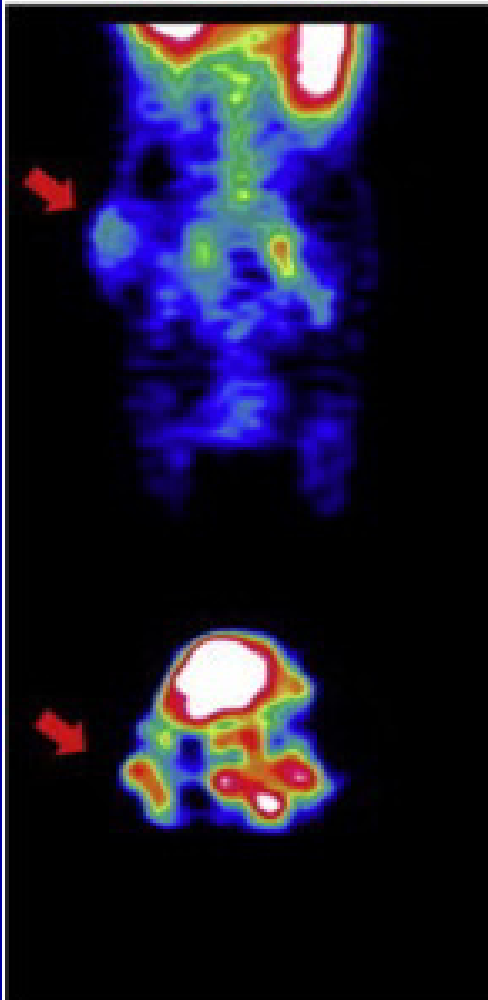
NIR imaging
Cy5.5-ATF-IO

PET/MRI

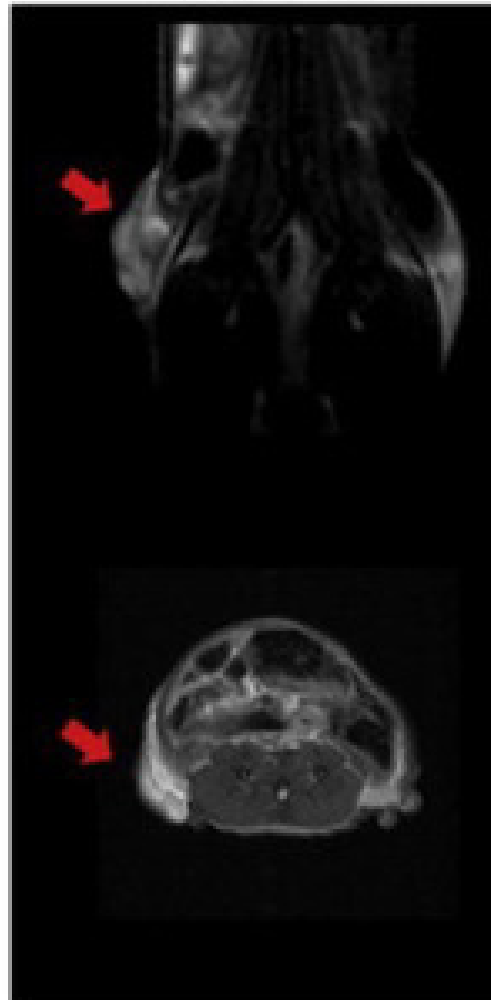


PET/MRI

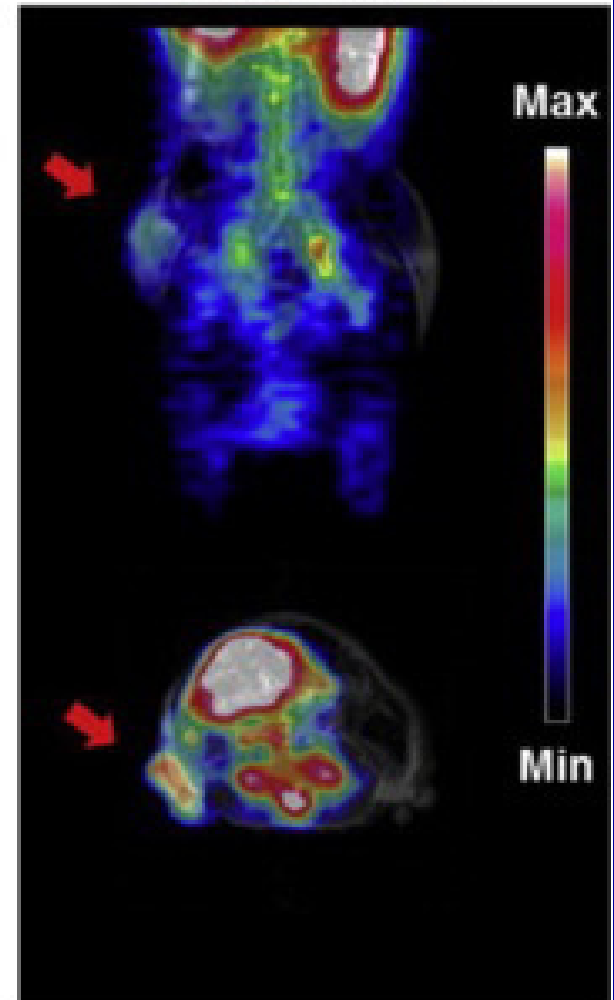
PET image



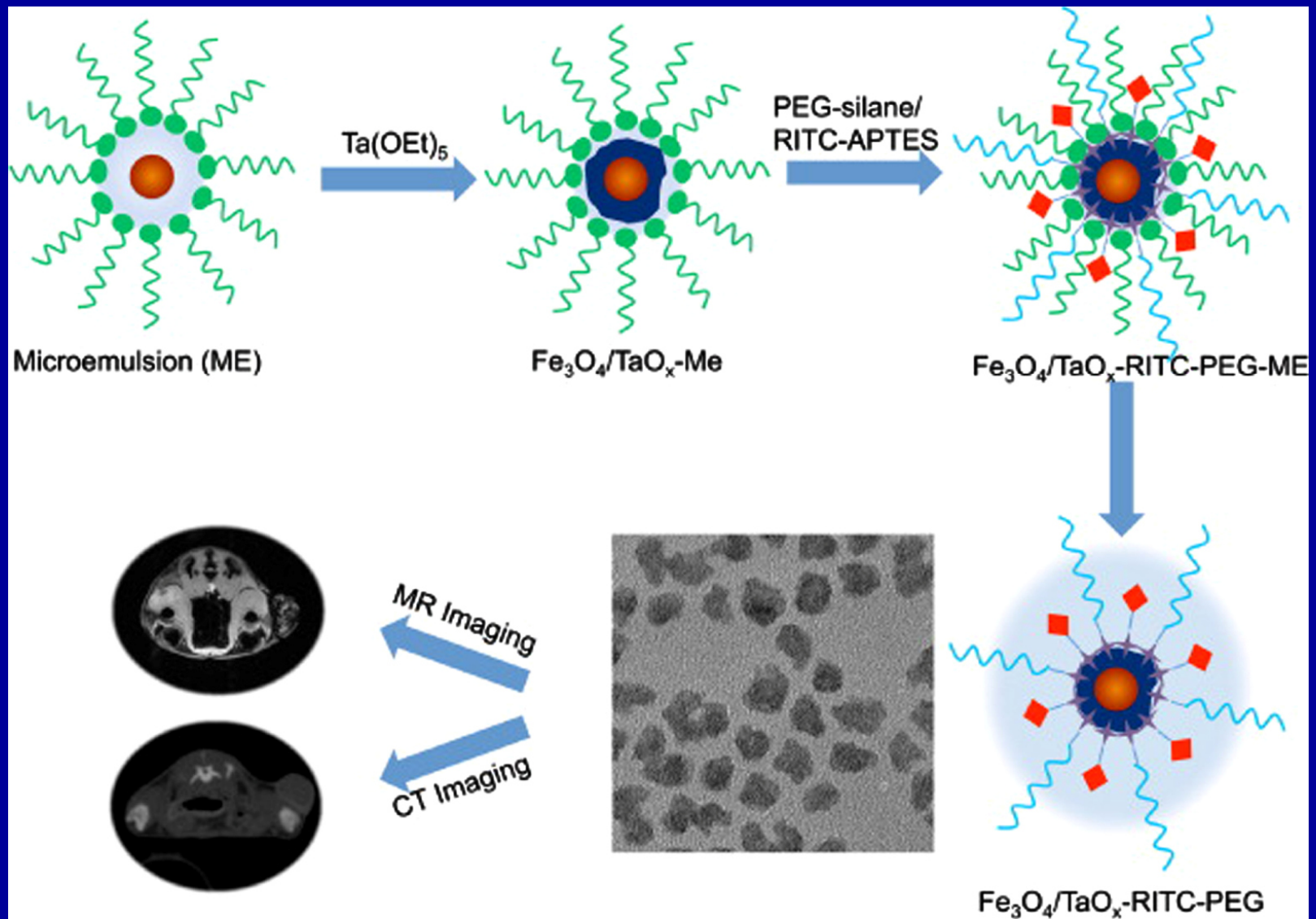
MR image



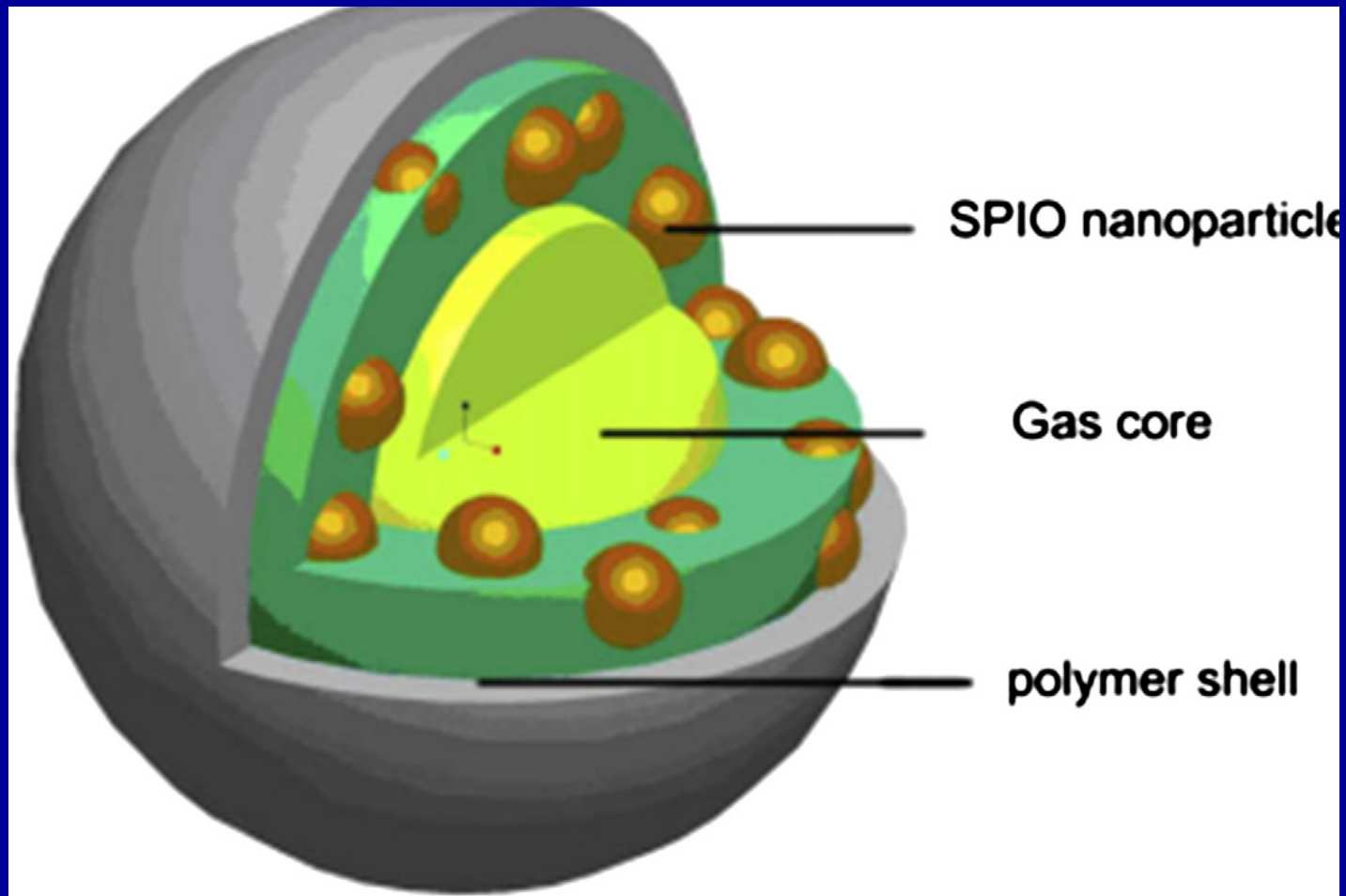
PET/MRI image



MRI/CT



MRI/Ultrasound



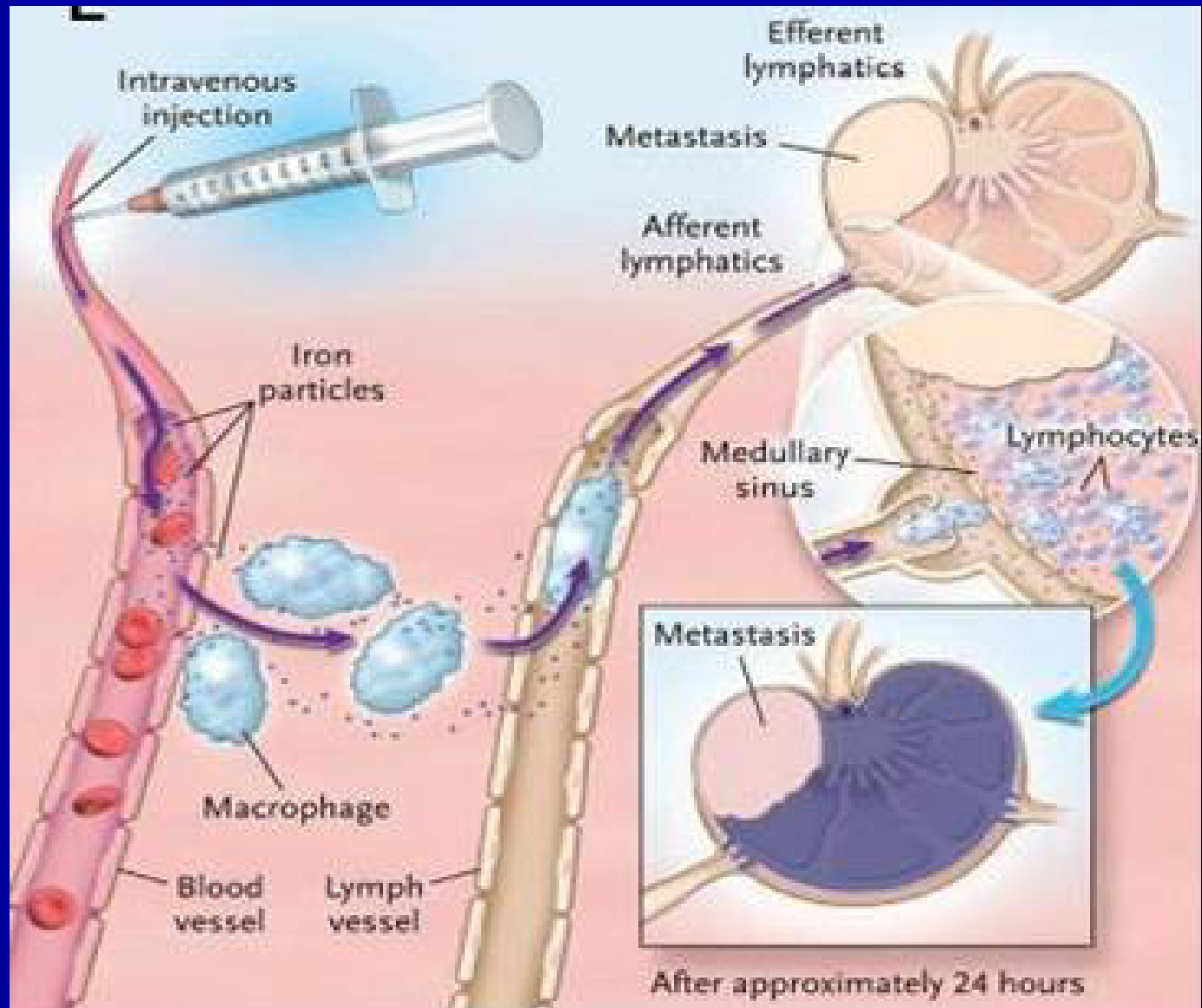
Nanoparticles applications

Cancer detection

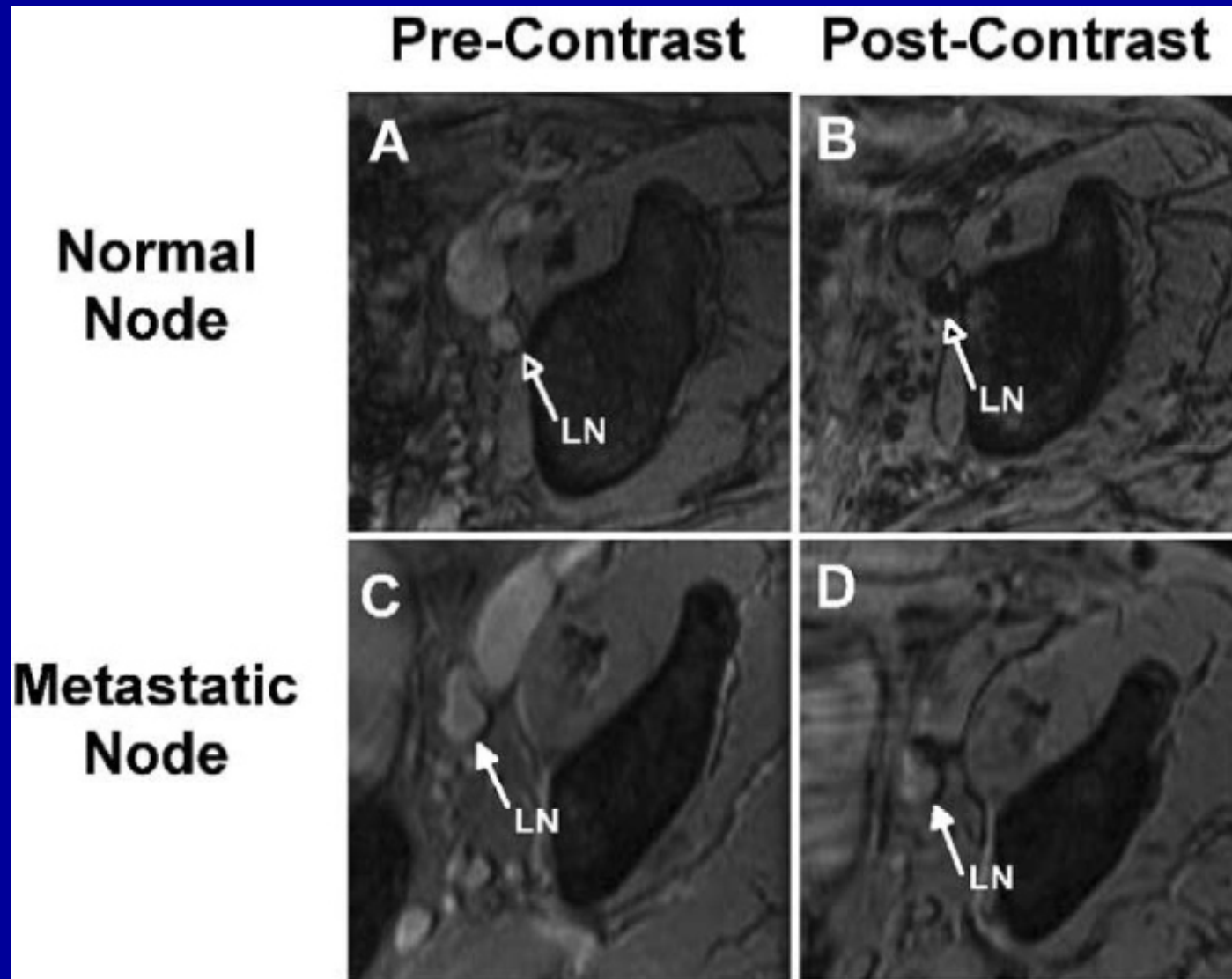
Cancer detection

- A typical clinical application of USPIOs is lymph-node imaging.
- The detection of lymph nodes is critical for:
- Accurate tumor staging
- The subsequent therapeutic planning

MR Lymphography



MR images of normal and metastatic lymph nodes

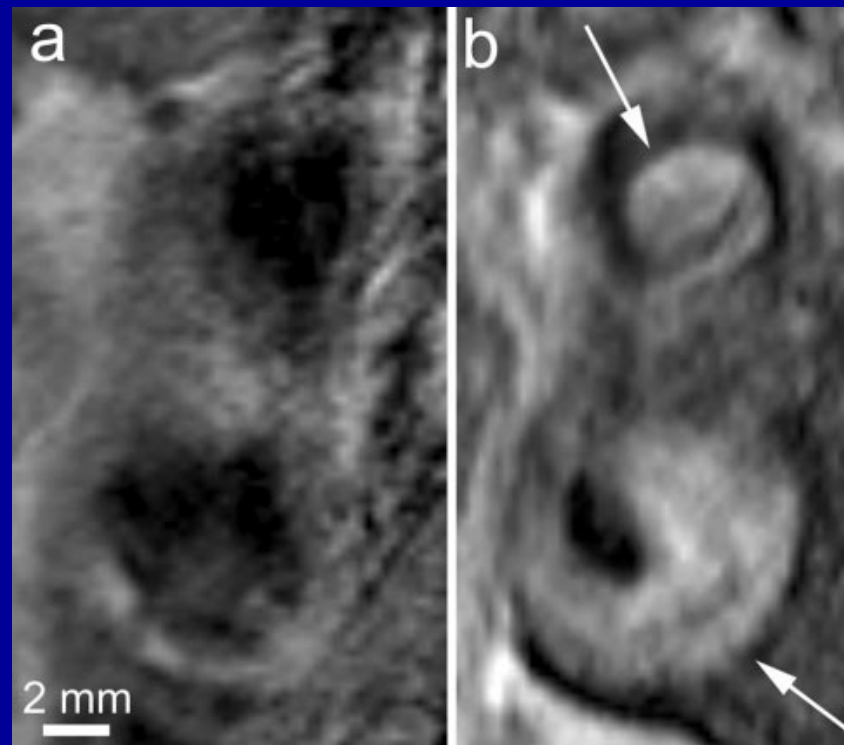


Inflammation/Infection

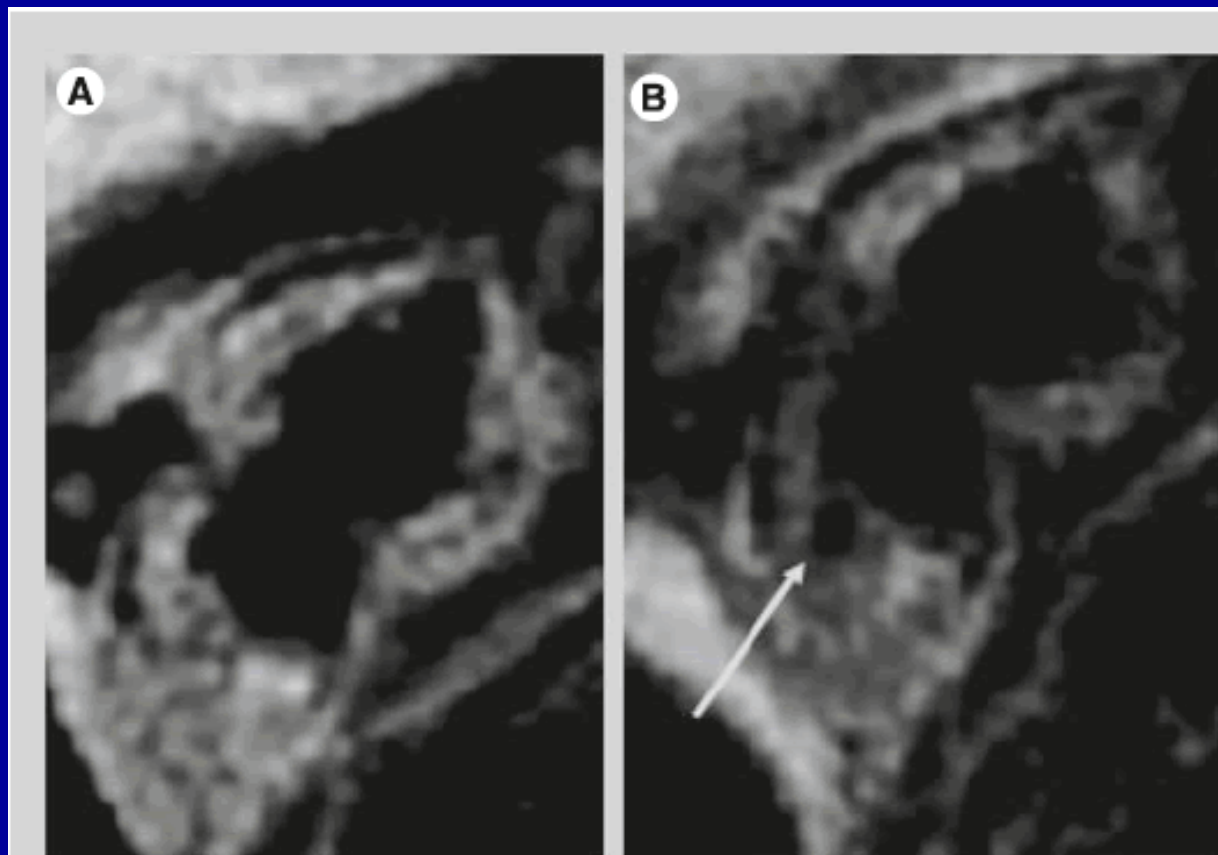
Inflammation

- Phagocytosis by macrophages of injected SPIONs results in hypointensity of macrophage-infiltrated tissues in contrast-enhanced MR images.

Detection of atherosclerotic plaques



USPIO imaging in carotid artery plaque



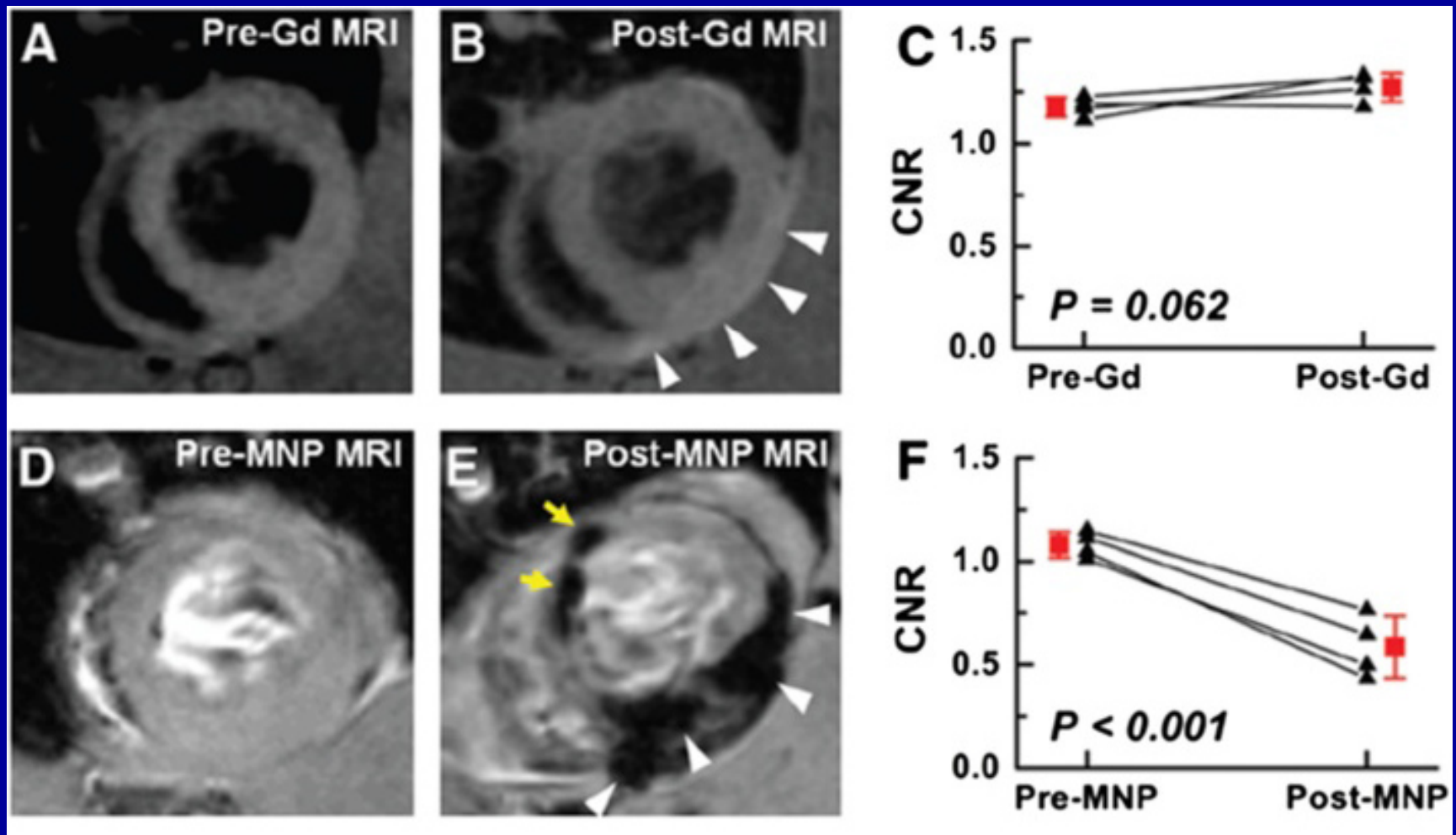
SPIOs applications in patients

- Both **coronary and carotid plaques** that take up SPIOs are more prone to **rupture**
- **Abdominal aneurysms** with increased SPIO uptake are more likely to **grow**

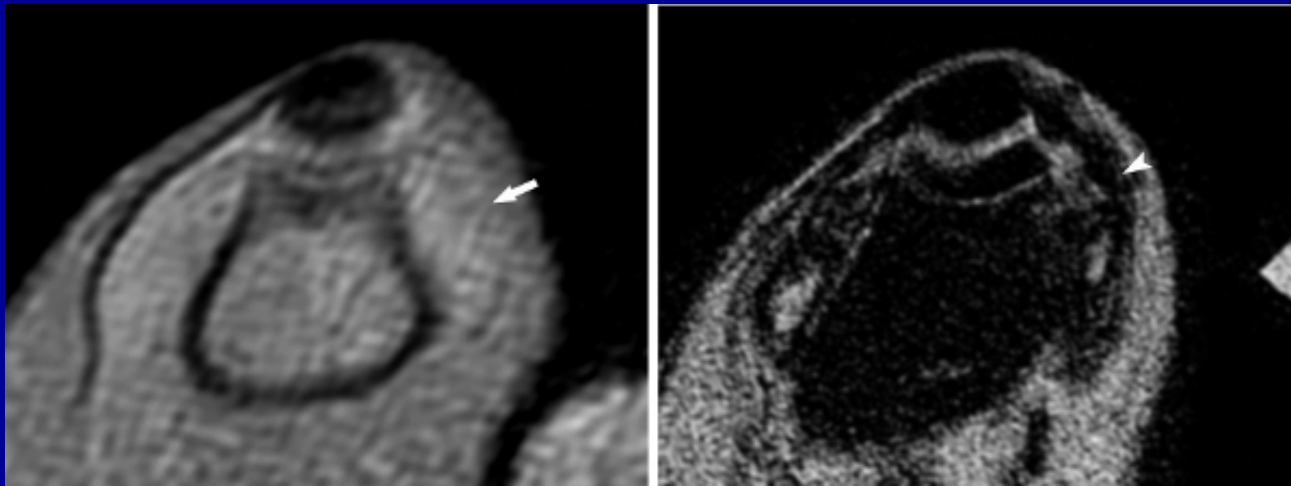
Inflammation

- **SPIOs in Cardiovascular magnetic resonance (CMR):**
- Assessment of **myocardial infarction** and **myocarditis**.

Inflammatory lesion in rat left ventricular wall with Gd and SPION



Septic arthritis



Tumor-associated macrophages (TAMs)

- Non-invasive imaging of TAMs using SPION:
 - 1) Staging the inflammatory microenvironment of primary and metastatic tumors
 - 2) Monitoring the treatment response of cancer patients treated with radiation and immunotherapy.

Other USPIO applications

- As positive contrast agent:
- MR angiography
- Perfusion imaging of brain, myocardium and kidney
- Tumor vascular imaging

Cancer therapy

Hyperthermia

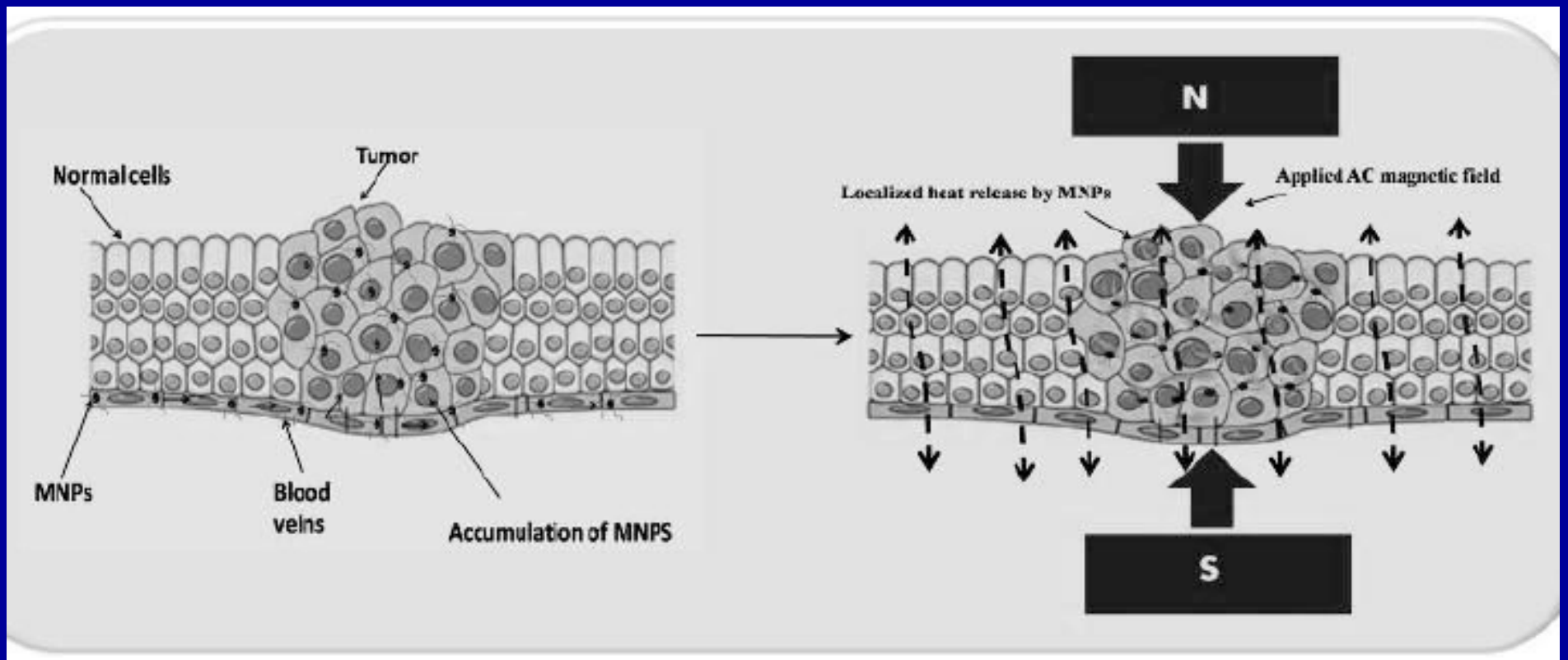
Hyperthermia

- Hyperthermia therapy is a type of treatment in which body tissue is exposed to high temperatures to:
 - 1) damage and kill cancer cells
 - 2) make cancer cells more sensitive to the effects of radiation and certain anticancer drugs.
- Temperature level: 41- 45 C

Hyperthermia

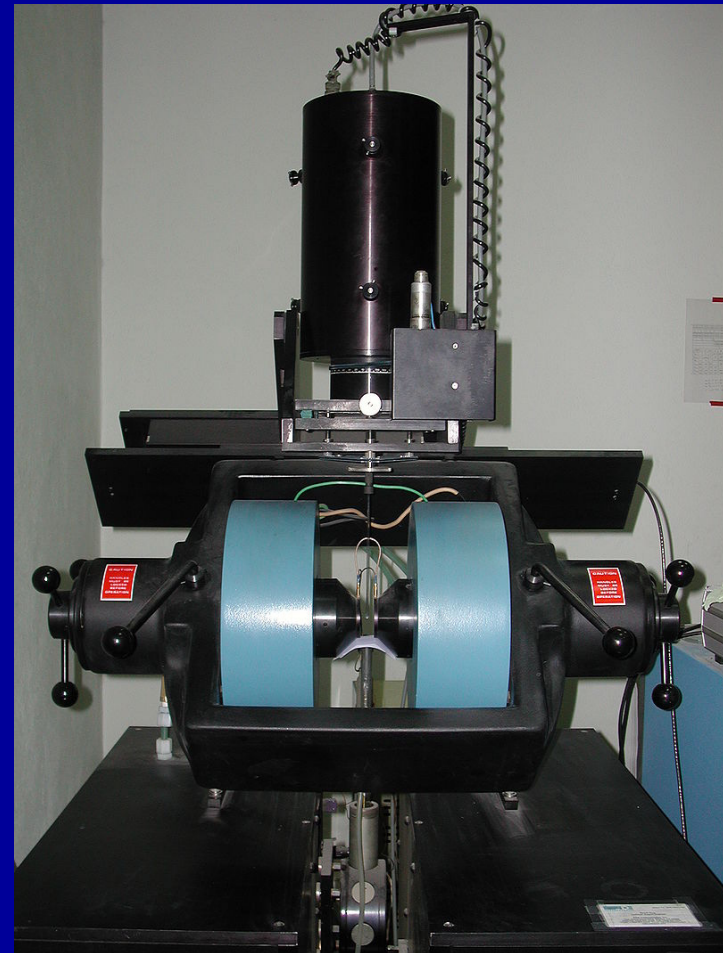
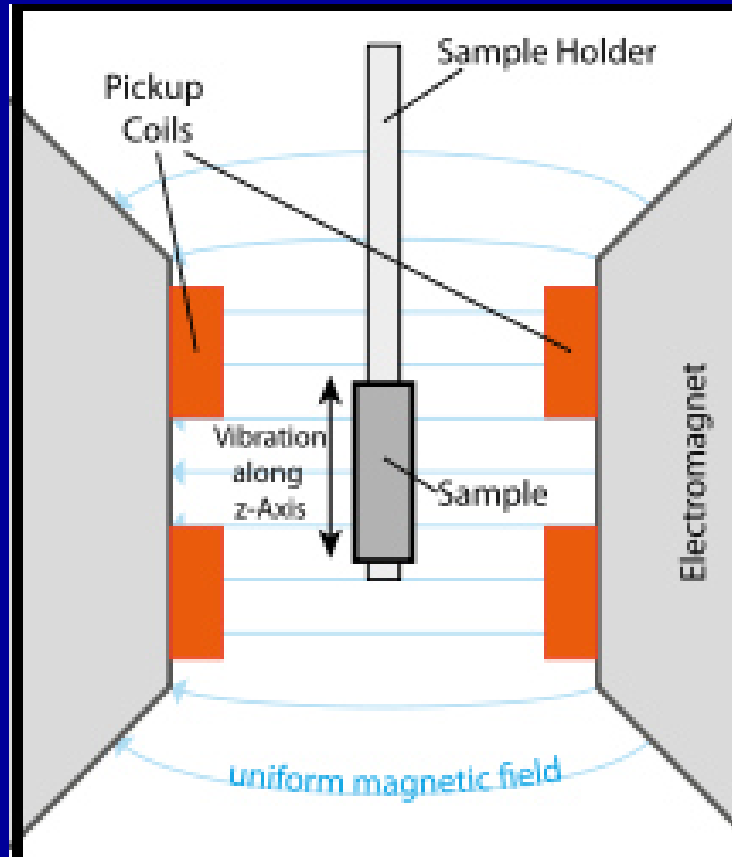
- External hyperthermia:
- The heat is applied from outside the body using various means such as microwaves, radiofrequencies, ultrasound etc.
- Internal hyperthermia:
- Certain foreign substances are inserted inside the body to act as sources of heat.

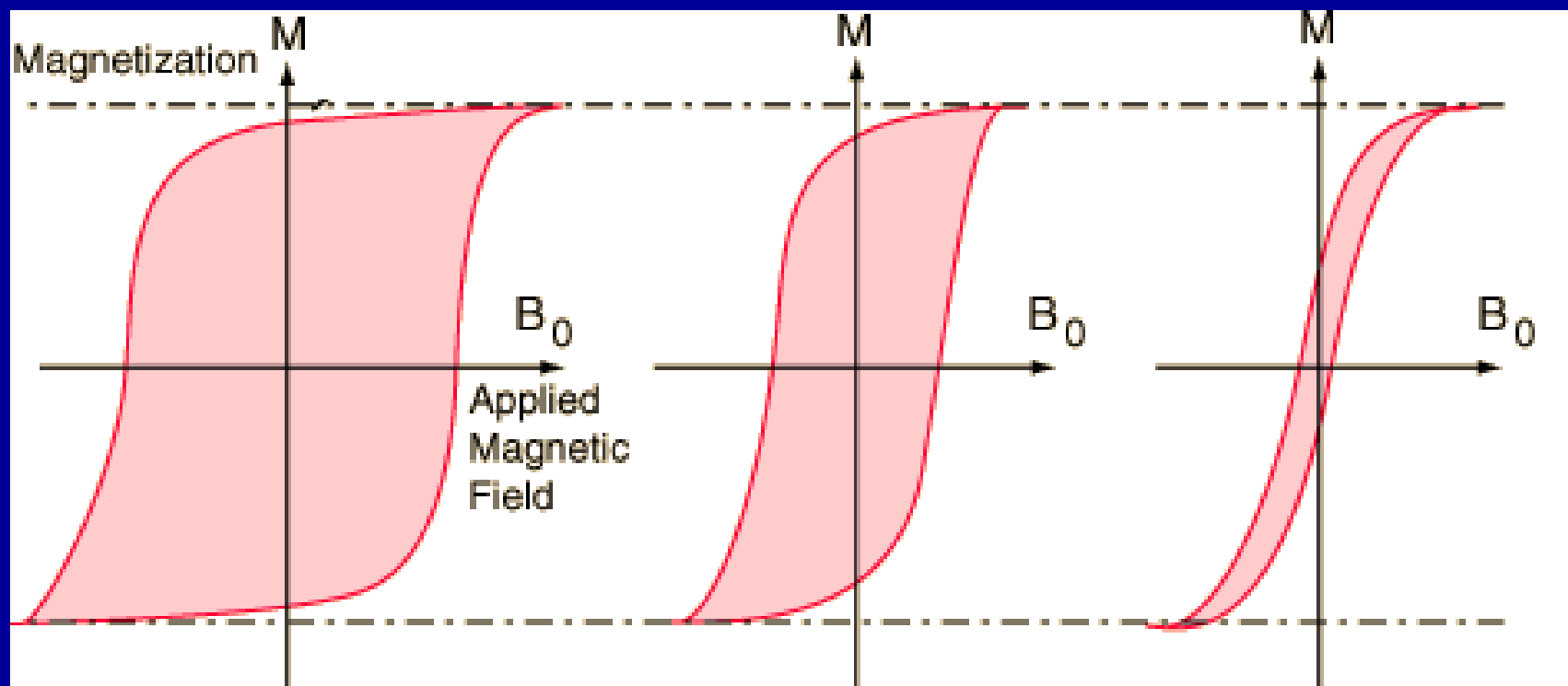
Hyperthermia



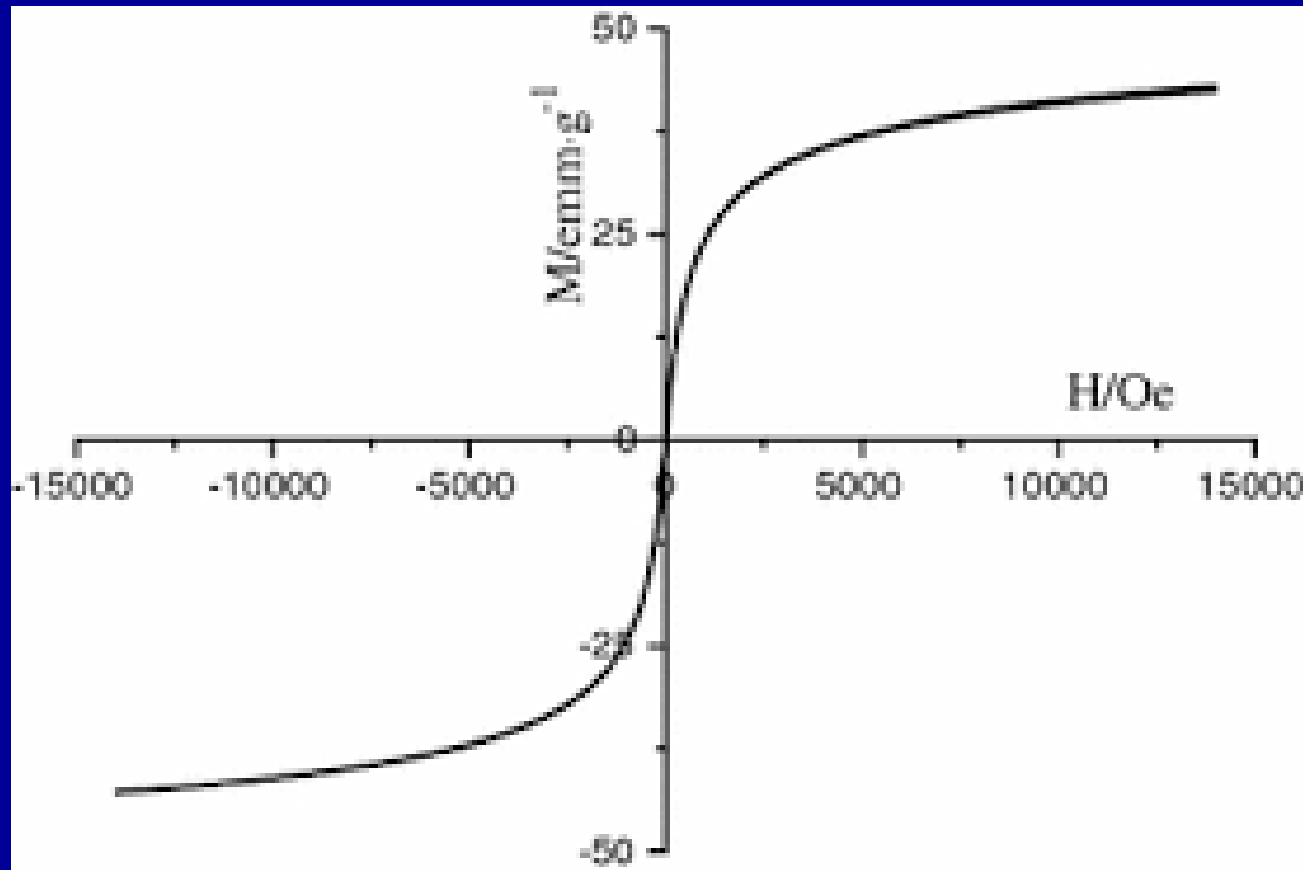
Magnetometry

Vibrating sample magnetometer (VSM)



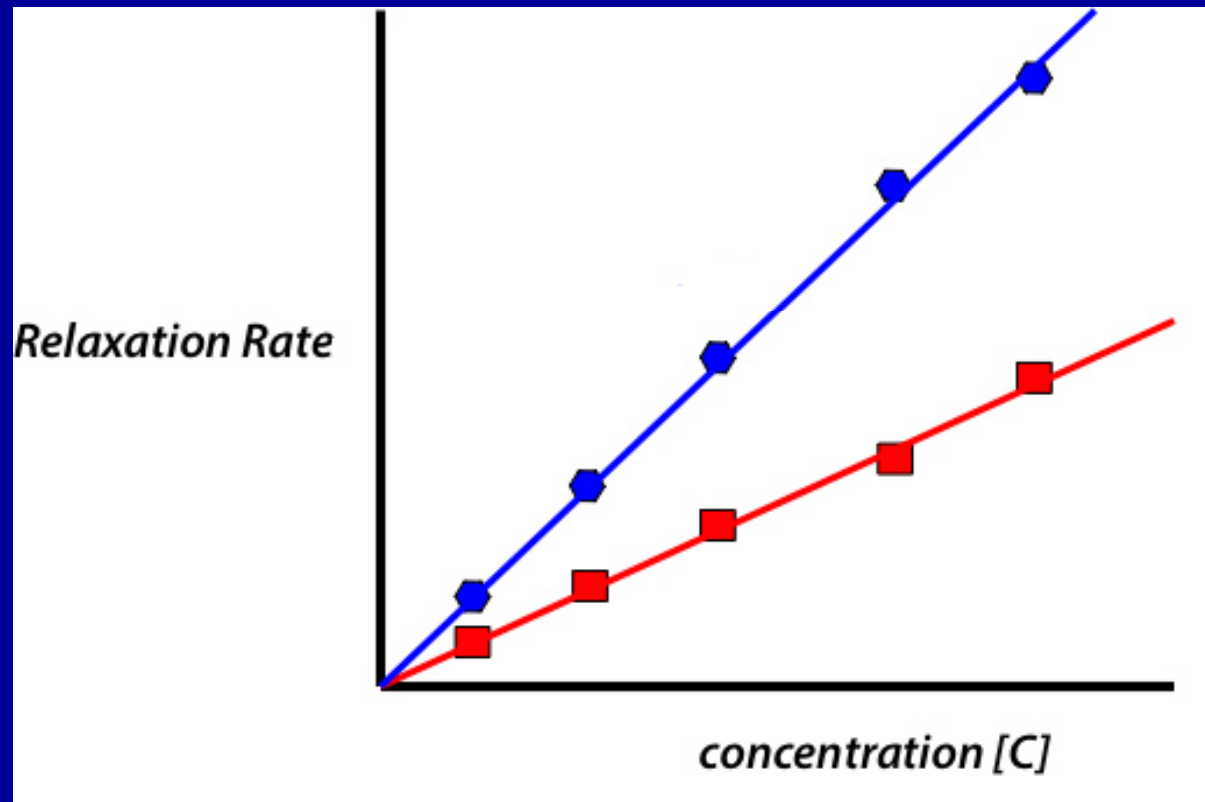


Superparamagnetic contrast agent magnetization curve

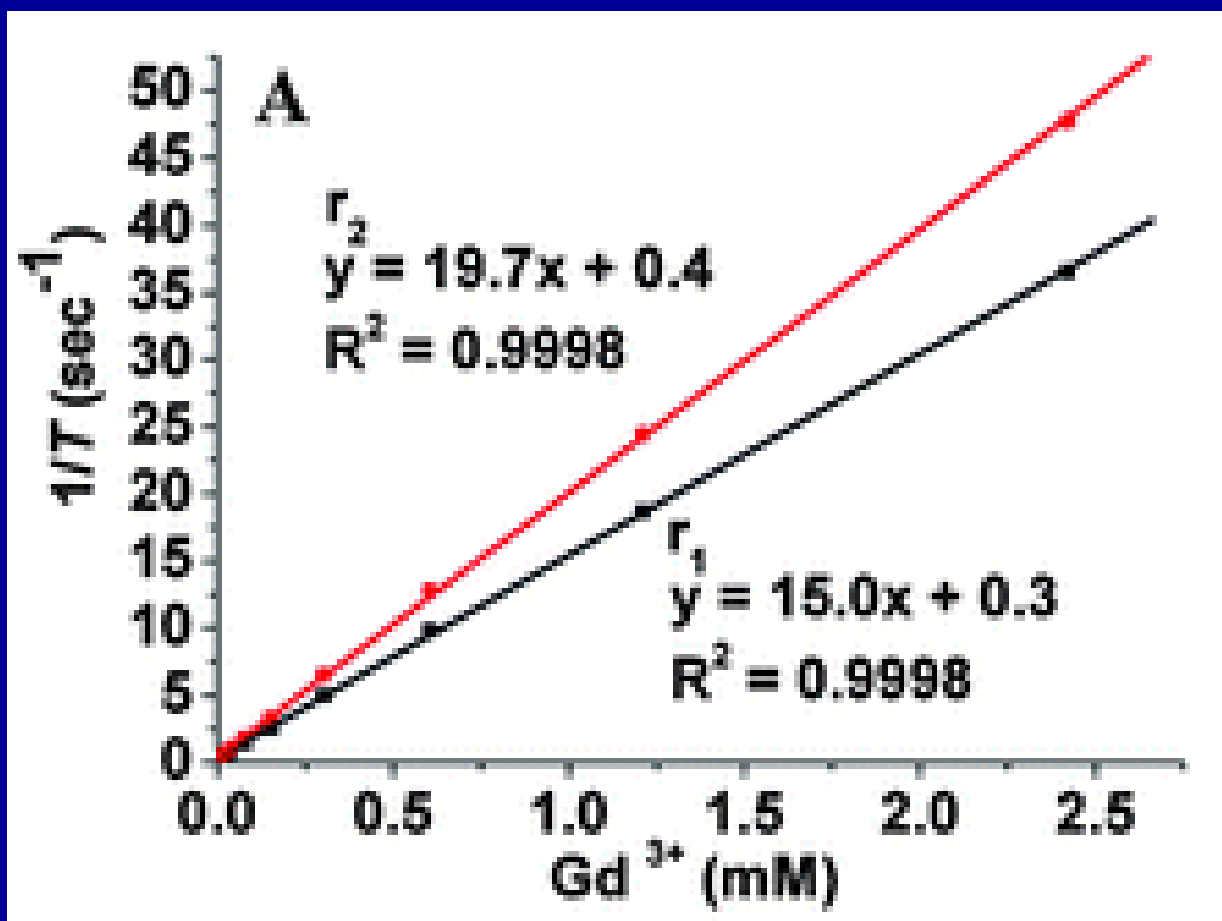


Relaxivity

Relaxivity



Relaxivity



Relaxivity

