

Molecular Imaging

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Overview of Molecular Imaging (I)

- Definition 1: Molecular imaging is the in-vivo characterization and measurement of biological processes at the cellular and molecular level.

R. Weissleder & U. Mahmood, Molecular imaging, *Radiology*, 219:316-333, 2001.

- Definition 2: Molecular imaging techniques directly or indirectly monitor and record the spatiotemporal distribution of molecular or cellular processes for biochemical, biological, diagnostic, or therapeutic applications.

ML Thakur, BC Lentle, SNM; Radiological Society of North America (RSNA). Joint SNM/RSNA Molecular Imaging Summit Statement. *J. Nucl. Med* 46:11N–13N, 2005.

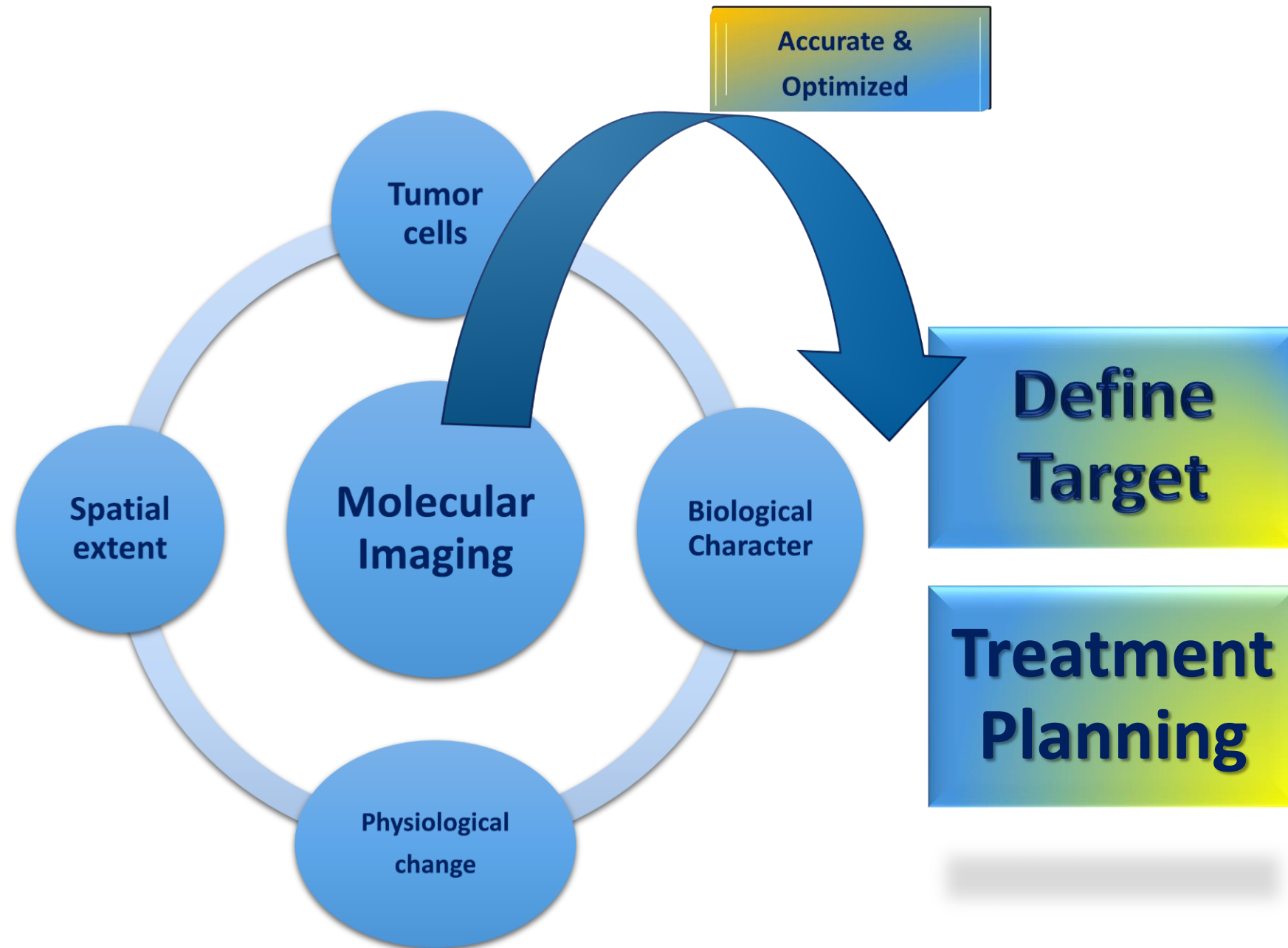
Overview of Molecular Imaging (II)

- Molecular imaging is considered as a new development of radiology. It aims to visualize processes of interest at the cellular and molecular level within living subjects, especially humans.
- Currently, medical imaging mainly focuses on morphological and anatomical changes.
- But it is often too late when these changes become detectable.
- The main driving force of molecular imaging is the radiology community.
 - Early detection
 - Direct monitoring of disease progression
 - Direct monitoring of treatment outcomes

Overview of Molecular Imaging (III)

- Molecular imaging modalities
 - PET, SPECT, CT, MRI, Ultrasound, Optical Imaging
 - These modalities are used in combination with specific molecular tracers.
- Applications
 - Cancer
 - Cardiovascular diseases
 - Neurological disease
- Research in molecular imaging started in the late 1990s.
- Most of the molecular imaging programs in the US are established after 2005.

H. J. Otero et al, Molecular imaging programs in the US,
Academic Radiology, vol. 14, pp. 125-131, 2007.



Molecular Imaging Modalities and Techniques

- 5 devices for molecular imaging

- (a) PET

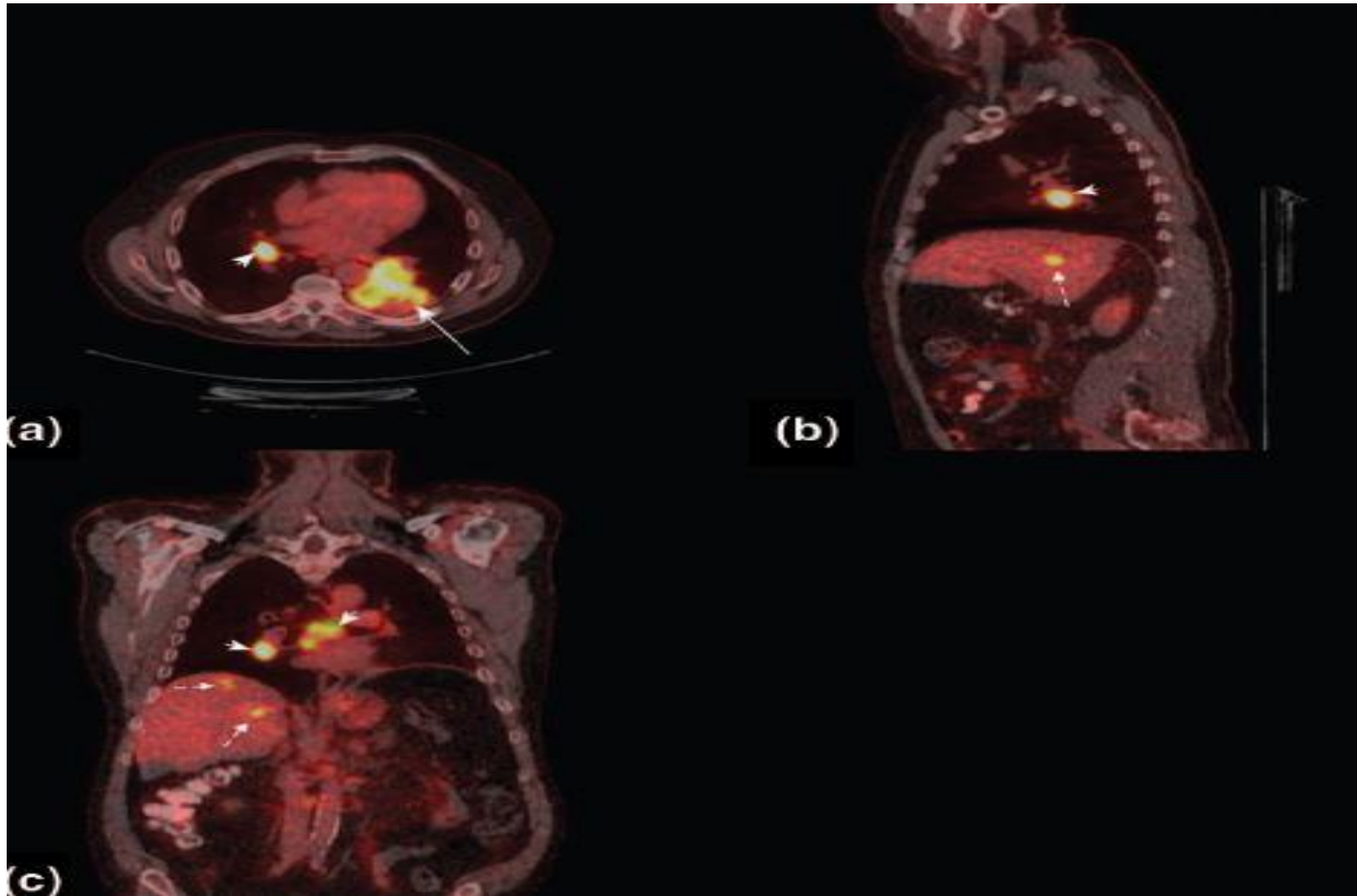
- (b) SPECT

- (c) MRI

- (d) Optical imaging

- (e) Ultrasound

A. PET – application in oncology



B. SPECT – application in oncology

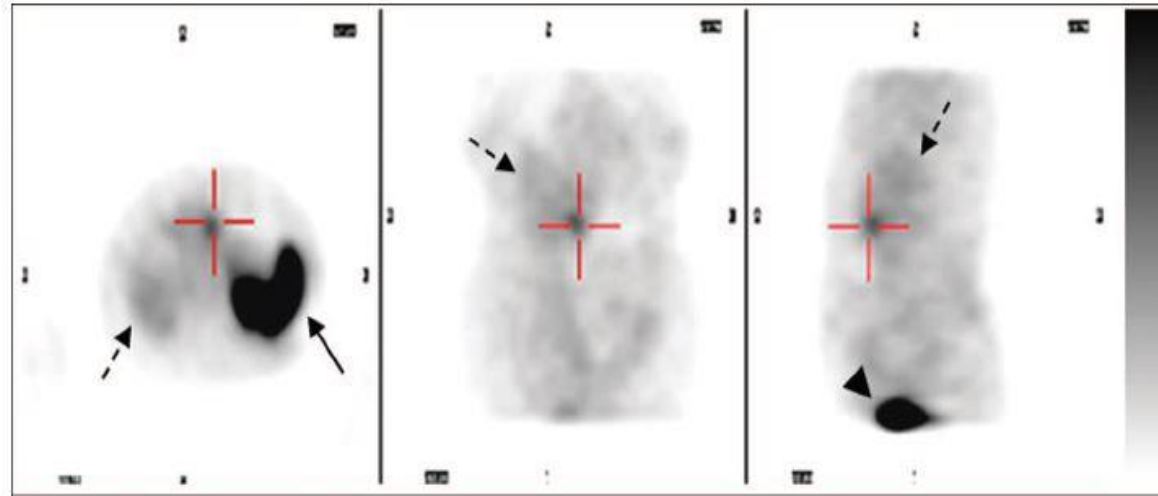


FIG. 5. ^{111}In -Octreotide (OcteScanTM) SPECT study in a patient with suspected neuroendocrine tumor of the pancreas. Images were acquired 24 h after radiotracer administration of an activity of 200 MBq. Acquisition settings were: energy photopeaks 171 and 245 KeV; window 20% around each photopeak; angular range 3600; 120 projections; and 30 s per projection. An iterative algorithm (OSEM, 2 iterations, 10 subsets) was employed in tomographic reconstruction. Selected transverse, coronal, and sagittal slices are presented, which show abnormal focal tracer uptake at the site of the pancreatic tumor (red cross). Normal tracer accumulation in the spleen (solid arrow), the lower part of the liver (dashed arrows) and the urinary bladder (arrowhead) is also demonstrated.

C. MRI – fMRI & MRSI application

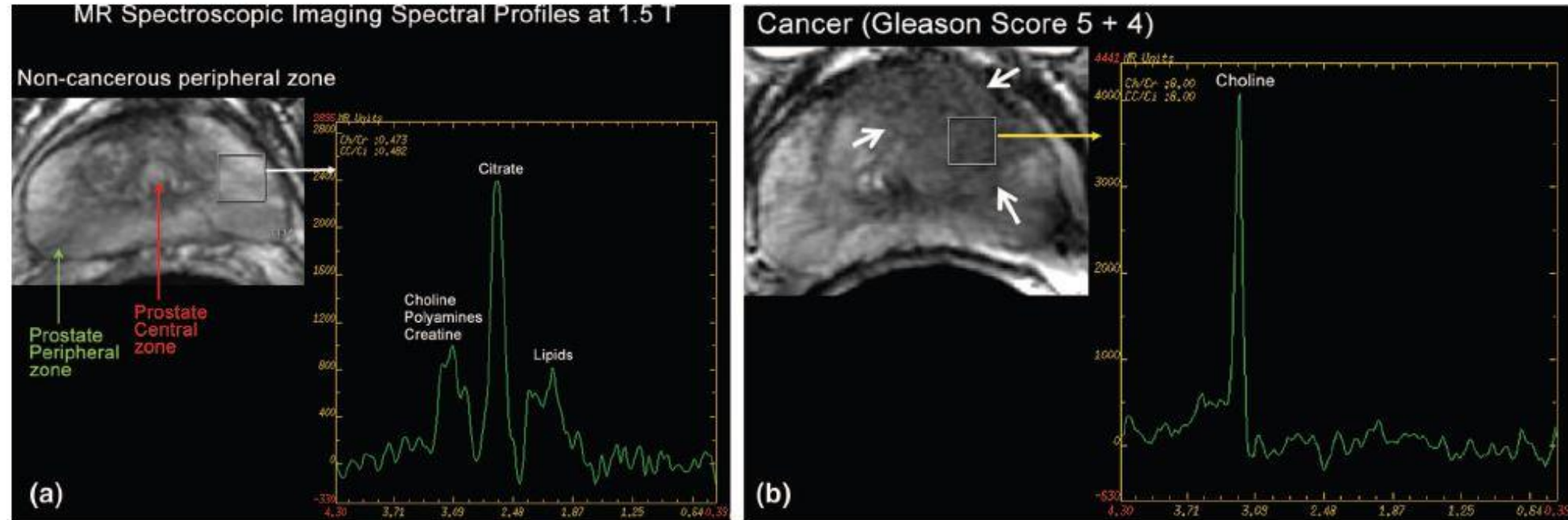
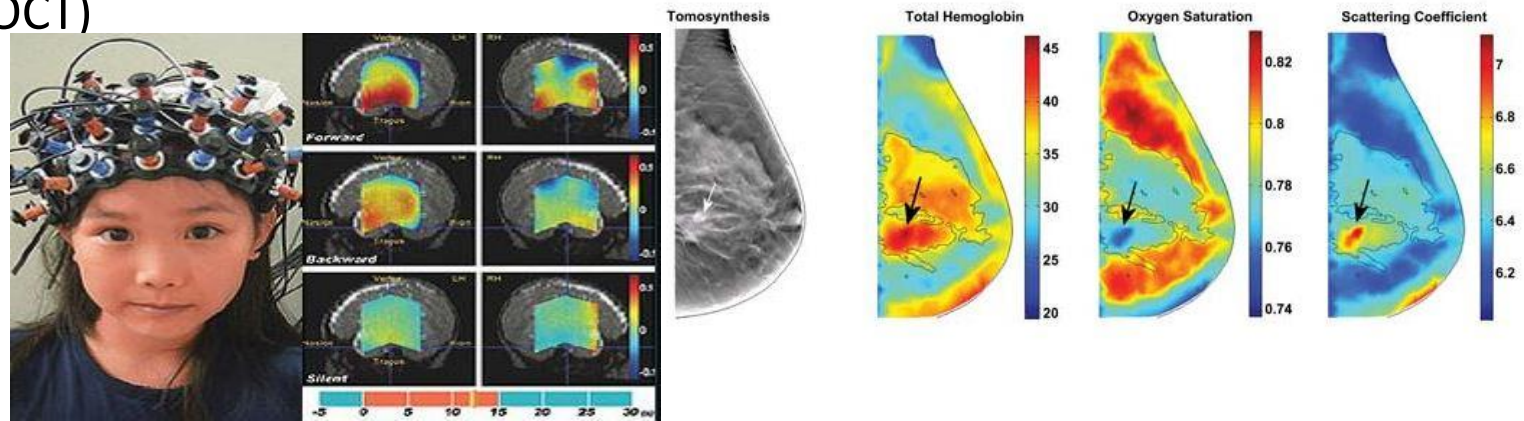
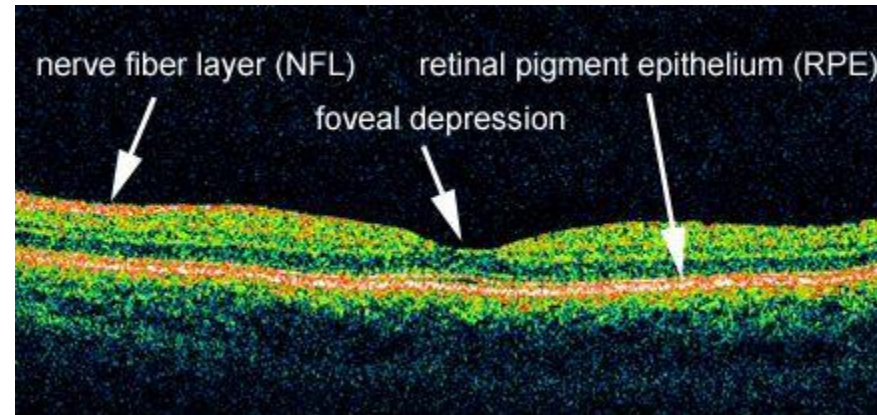
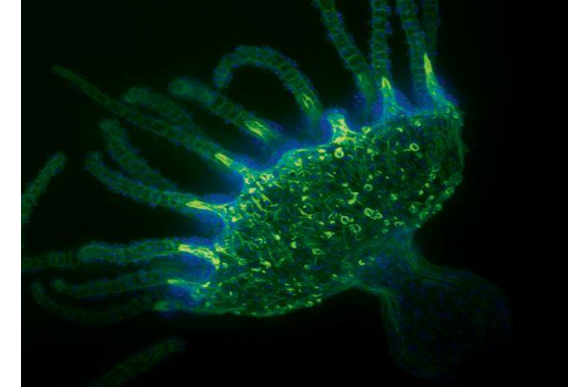


FIG. 6. MR ^1H spectroscopic profiles characteristic of (a) normal and (b) cancerous prostate tissue. T_2 -weighted axial images are used to identify the region of interest from which the spectra is sampled (square region) with the associated metabolic profile shown adjacent. Normal peripheral zone tissue is characterized by a high citrate and low choline concentrations as seen in (a). In contrast, the large hypo-intense mass (arrows) seen on the T_2 -weighted image in (b) shows a marked elevation of choline and no identifiable citrate peak. Metabolite locations are identified by their relative frequency shift from the water resonant frequency in units of parts per million. Metabolite peaks are measured in relative units. Images courtesy of Dr. Akira Kawashima, Department of Radiology, Mayo Clinic.

Molecular Imaging Modalities and Techniques

D. Optical Imaging – (2) Four types

1. Bioluminescence
2. Fluorescence – GFP
3. Diffuse optical tomography(DOT)
4. Optical coherence tomography(OCT)



E. Ultrasound

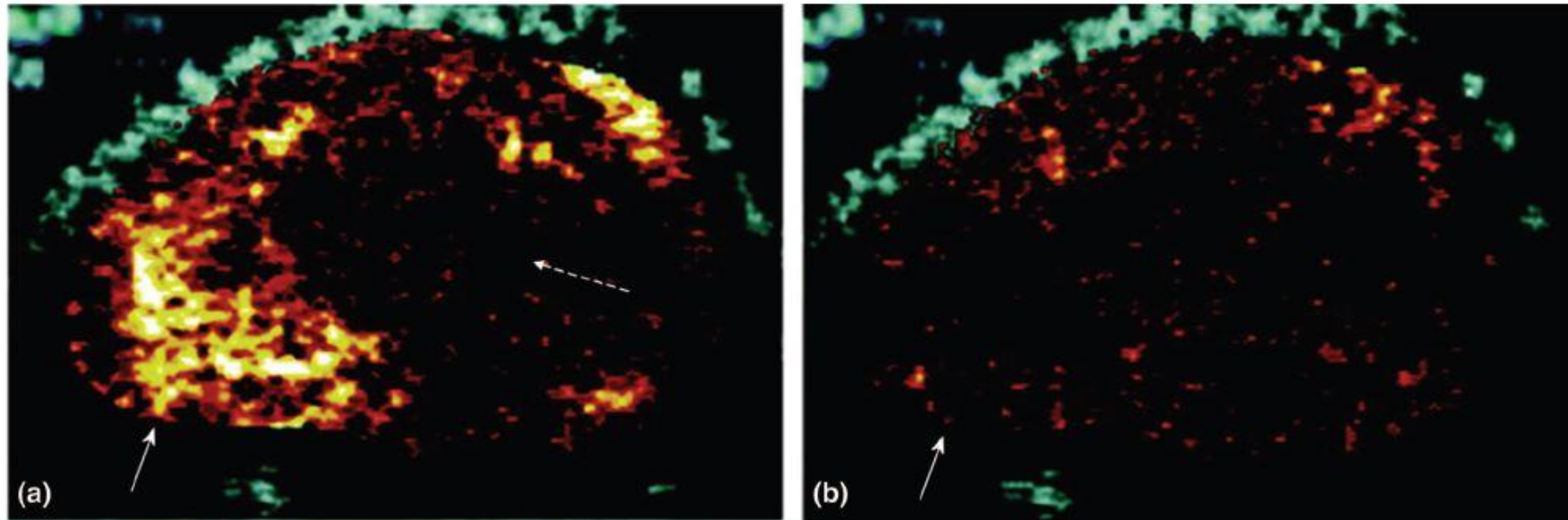
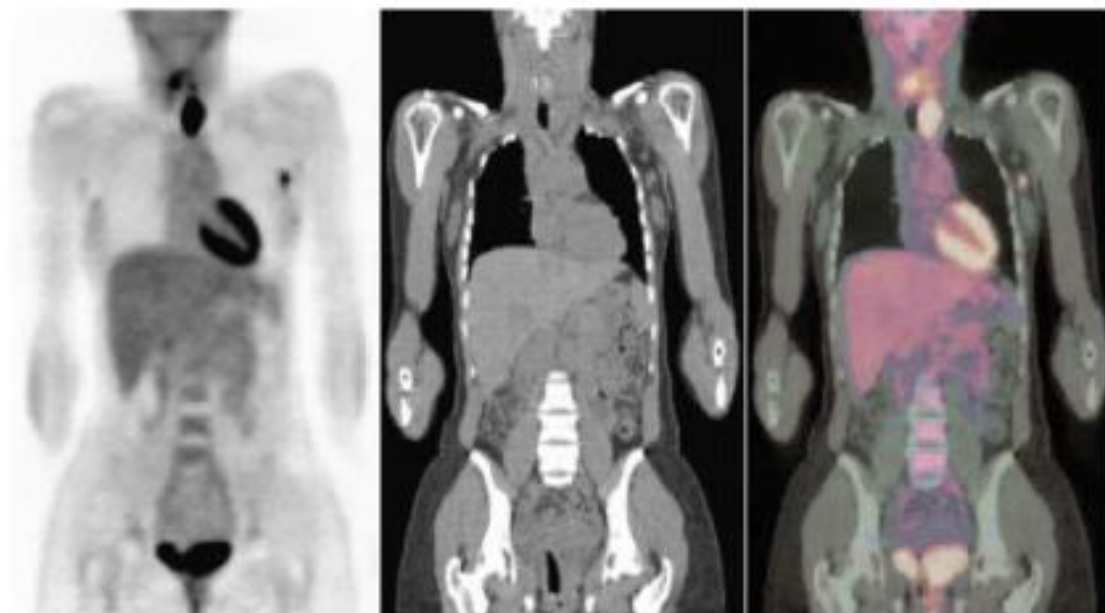


FIG. 11. Ultrasound imaging of tumor vasculature by the use of ultrasound contrast microbubbles (MB) conjugated to the tripeptide sequence arginine-arginine-leucine (RRL). Nude mice bearing PC3 human prostate cancer cell lines were imaged 120 s after injection of either MB_{RRL} or a MB control. Transverse ultrasound image depicting persistent contrast enhancement in background subtracted images after injection of MB_{RRL} [(a); white arrow], which is not seen in the control [(b); white arrow]. Noncolor coded portions are not background subtracted. The source of these images (From G. E. Weller *et al.*, "Ultrasonic imaging of tumor angiogenesis using contrast microbubbles targeted via the tumor-binding peptide arginine-arginine-leucine," *Cancer Res.* **65**, 533–539 (2005). Copyright © 2005 by American Association for Cancer Research.) states that the opacification is matching the anatomic pattern of the tumor vasculature, with a highly vascularized tumor periphery [white arrow in (a)] and a necrotic tumor core [white dashed arrow in (a)].

Discussion & Future Look

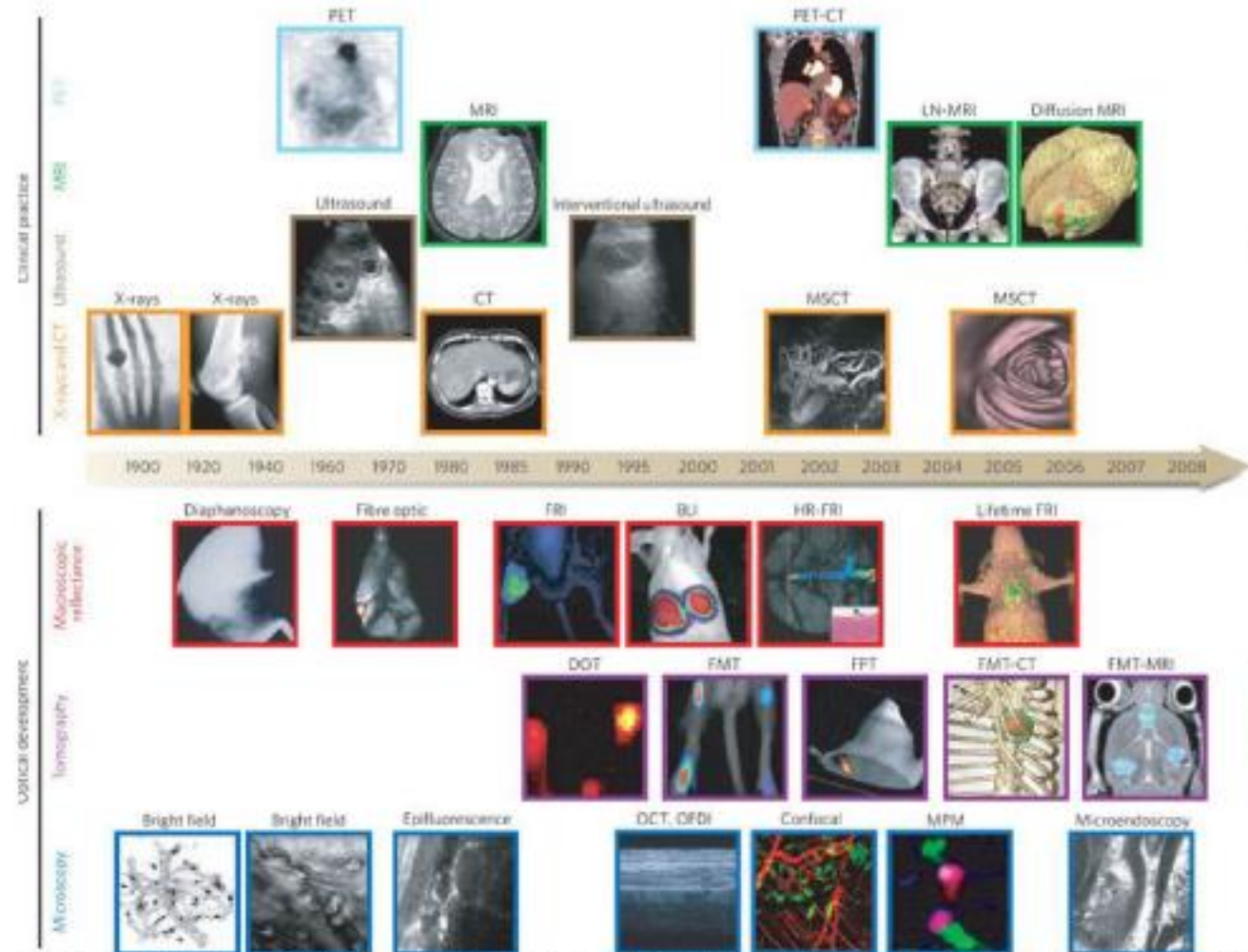
- Molecular imaging is the integration of specific molecular tagging with medical imaging modalities.
- It represents the future of medical imaging.
- A critical challenge is the development of specific molecular tags.
- Computational image analysis plays essential roles in many aspects of molecular imaging.

Molecular Imaging: an Example



http://www.medical.siemens.com/siemens/zh_TW/rg_marcom_FBAs/files/brochures/Jan_Grimm_Molecular_Imaging.pdf

Overview of Different Imaging Modalities (I)



R. Weissleder, MJ Pittet, Imaging in the era of molecular oncology, *Nature*. 2008 Apr 3;452(7187):580-9.

Applications (I): Cancer Detection in Mouse

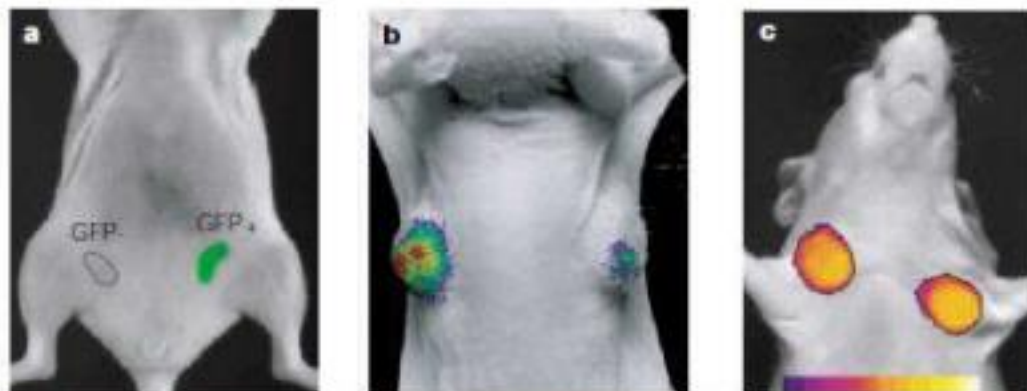
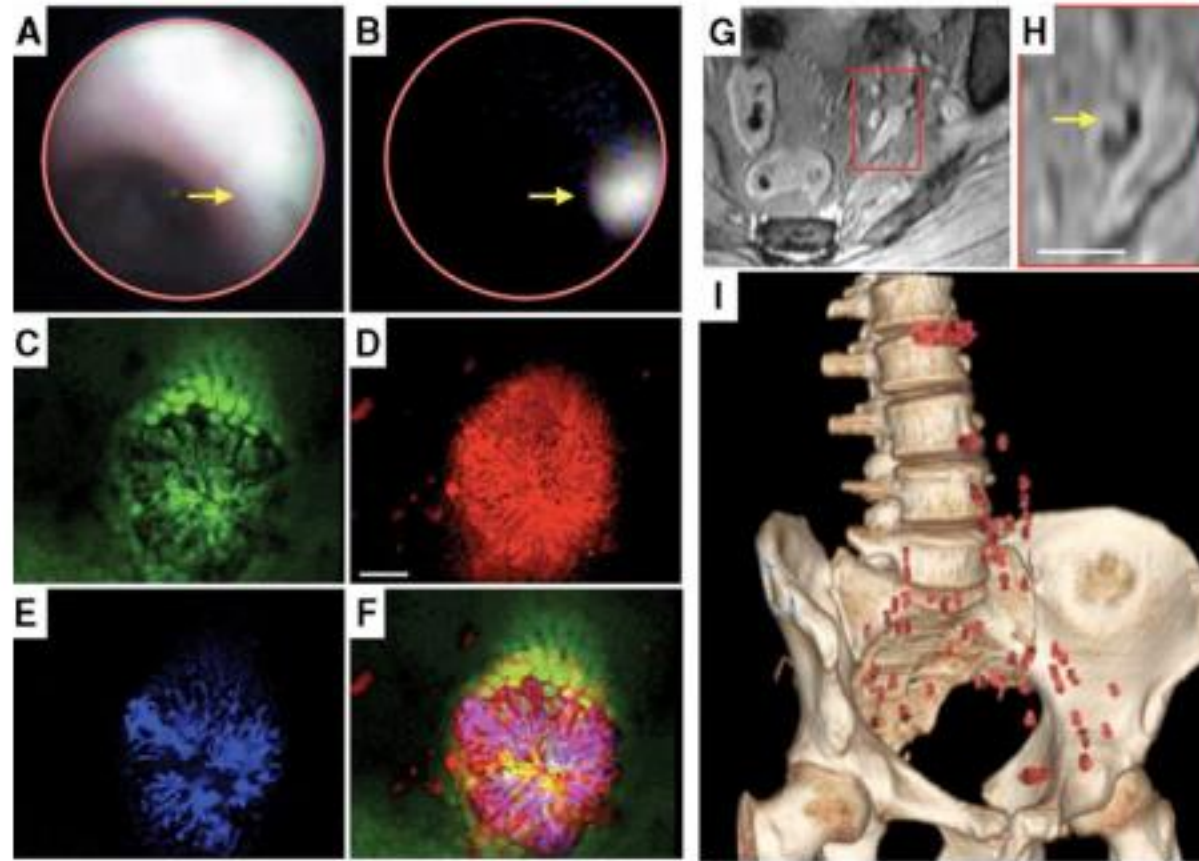


Figure 2 | **Optical imaging.** Fluorescent and bioluminescent signals emanating from superficial structures such as surface-implanted tumours can be imaged with sensitive charge-coupled device cameras. **a** | Fluorescence imaging in the visible light range (400–600 nm) can be used to detect green fluorescent protein (GFP) expressed by the right, but not by the left, tumour. **b** | Bilateral chest tumours expressing transgenic luciferase and imaged with a photon-counting camera after intraperitoneal injection of luciferin. The tumour on the left expresses higher levels of luciferase, indicated by areas of red, yellow and green colouration, than the tumour on the right. **c** | Near-infrared (NIR) fluorescence imaging (700–900 nm) can be used to image deeper tumours than can fluorescence imaging in the visible light range⁵³. This example shows matrix metalloproteinase 2 (MMP-2) enzyme levels in bilaterally implanted breast tumours using an NIR fluorescence probe coupled to an MMP-2 substrate⁵⁴. (Image in **a** courtesy of U. Mahmood, MGH CMIR, Boston, USA; image in **b** courtesy of Y. Saeki and V. Ntziachristos, MGH CMIR, Boston, USA.)

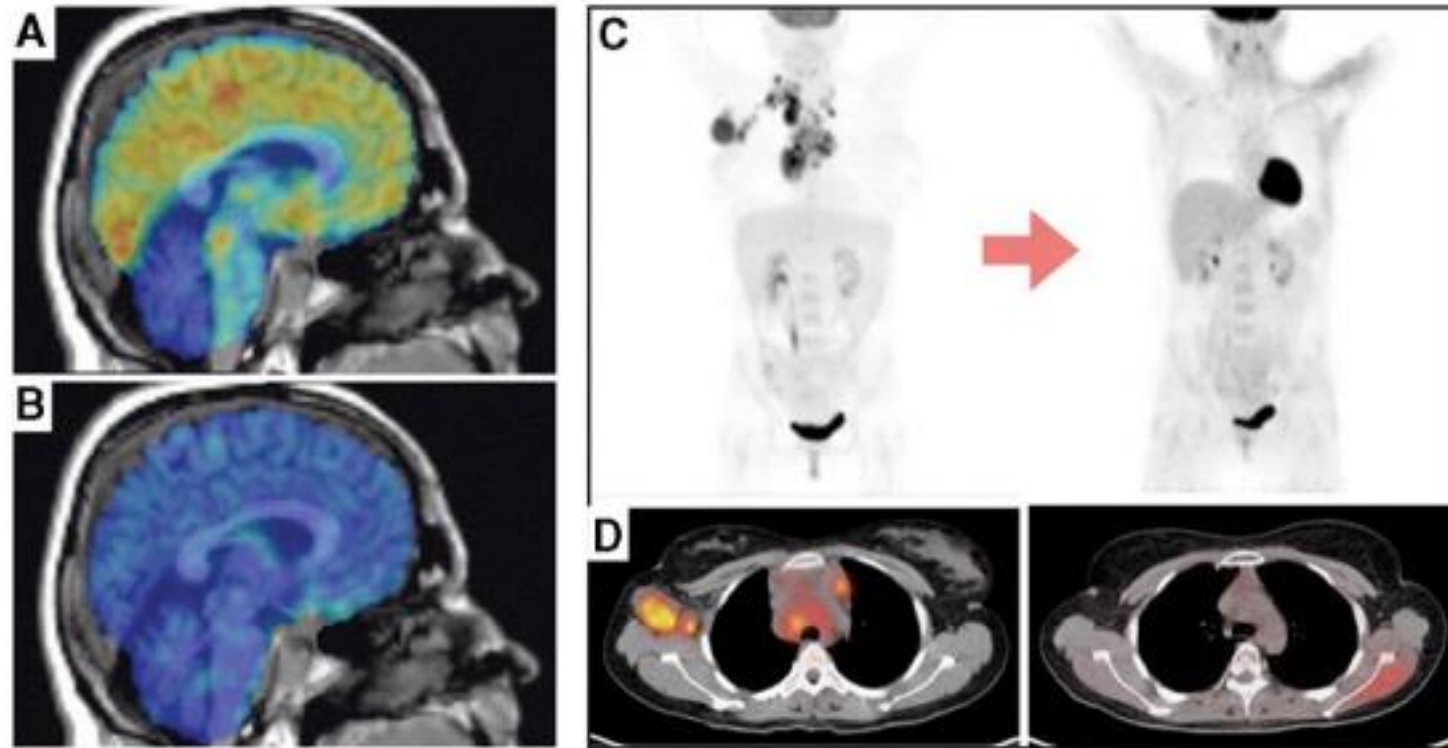
R. Weissleder, Scaling down imaging: molecular mapping of cancer in mice, *Nature Review Cancer*. 2002 2: 1-8.

Applications (II): Cancer Detection in Human



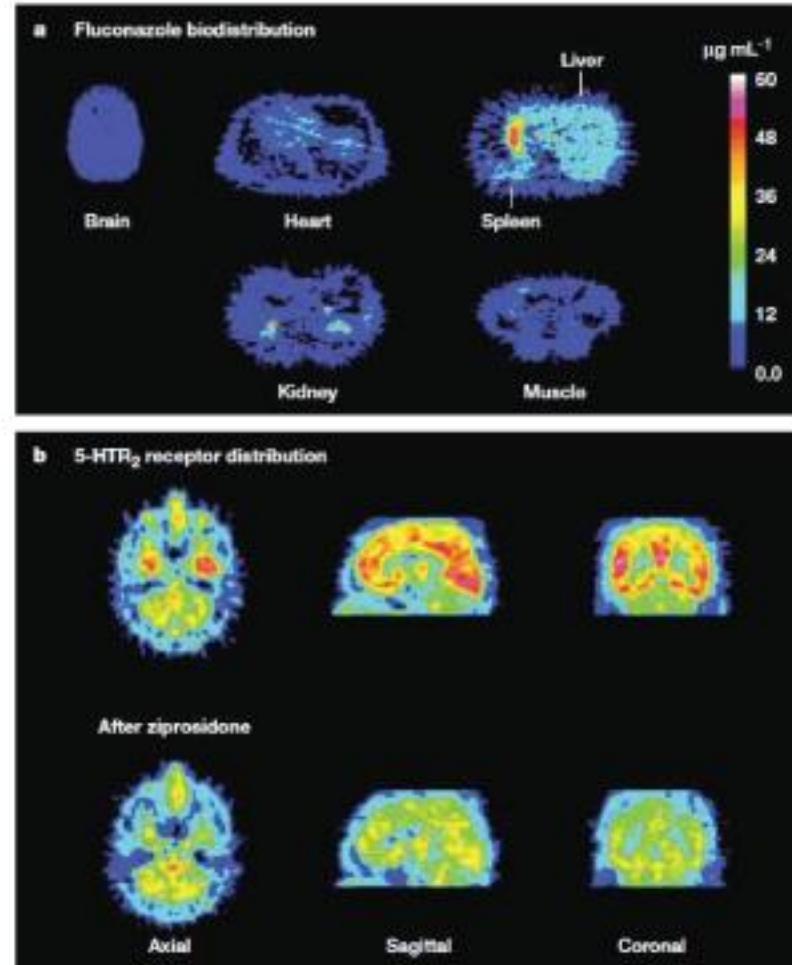
R. Weissleder, Molecular imaging in Cancer, *Science*. 2006 312:1168-1171.

Applications (III): Drug Treatment Monitoring



R. Weissleder, Molecular imaging in Cancer, *Science*. 2006 312:1168-1171.

Application (IV): Drug Development



R. Weissleder, Molecular imaging in drug discovery & development, *Nature Review Drug Discovery*. 2003 2: 123-131.