Biomedical physics

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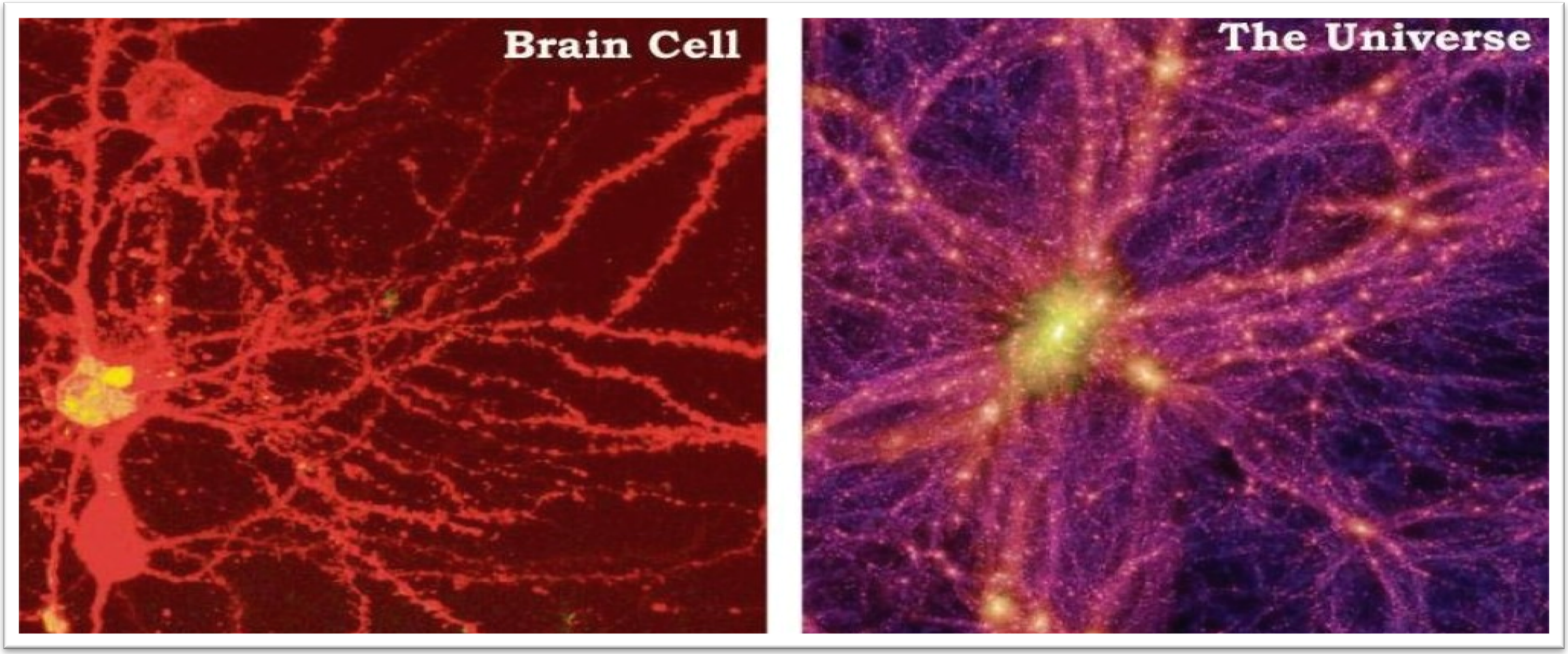
Florian Grüner



The course structure

Friday	8:30 – 10:00	Lecture	
Friday	10:15 – 11:45	Journal club / exercise	Sem. Room 3
Wed.	10:15 – 11:45	Journal club / exercise	Room 11-357

Web page:
http://www.desy.de/~garutti/LECTURES/BioMedical/Lectures_WS2019-20.htm

Journal Club:

- Begin Friday 25.10.19 for both groups (paper assignment)
- One paper / week
- Everybody read / understand / prepare a question / discuss
- During exercise hours one person introduces the paper / all discuss
- No slides required

Biomedical physics

- Fundamentals of Radiation Physics
- Medical Diagnostic Techniques
- Imaging technics (basic)
- Radiation Therapy

medical imaging

Not covered in the course (but belonging to biomedical physics):

- Advanced Imaging
- Radiation Protection and Dosimetry
- Radiobiology
- Anatomy and Physiology
- Molecular and cellular oncology

Some of the missing topics will be covered in:

66-278 Seminar on Biomedical Physics

Structure of the course

1) Introduction
2) Interaction of particles and matter } **principles / tools**
3) Therapy with proton and ion beams
4) X- ray sources
5) Sources for nuclear medicine

sources

6) Image quality } **objective**
7) X-ray imaging
8) Computed tomography
9) Planar scintigraphy
10) Emission tomography
11) Magnetic Resonance Imaging
12) Multimodal systems

imaging modalities

Medical imaging

The course will not cover ultrasound and optical imaging

Literature

Based on Prince and Links, Medical Imaging Signals and Systems and Lecture Notes by Prince. Figures are from the book.
and lectures from Yao Wang (NYU-Poly)

Additional suggested literature:

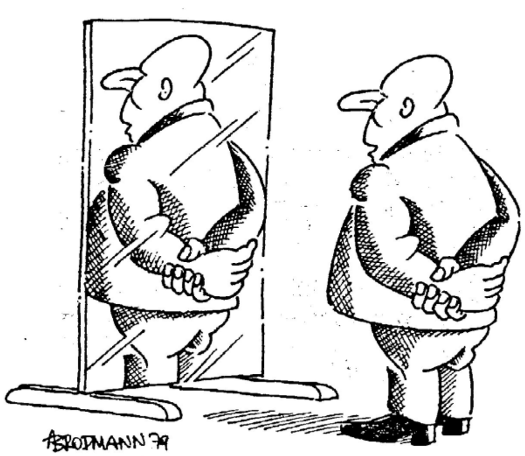
- C.Grupen and I.Buvat: Handbook of Particle Detection and Imaging;
- W.R.Leo: Techniques for Nuclear and Particle Physics Experiments, Springer;

What is the **added value** of physics for medicine?

….or why should **YOU** study **biomedical** physics?

…or why should senior physicists care about medical research?

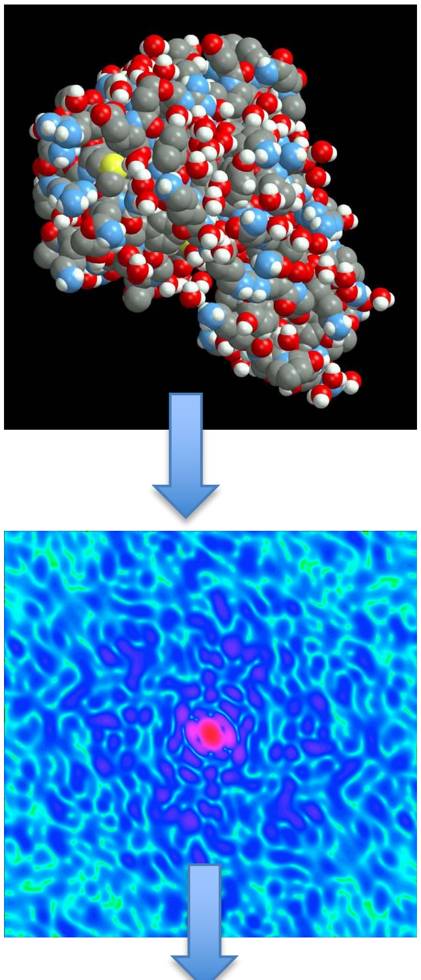
…and why care medical researchers/industry about physics???



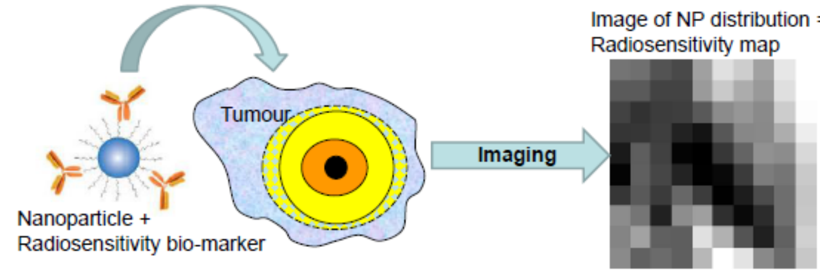
First answer….synergy!

Second answer….overcoming limits!

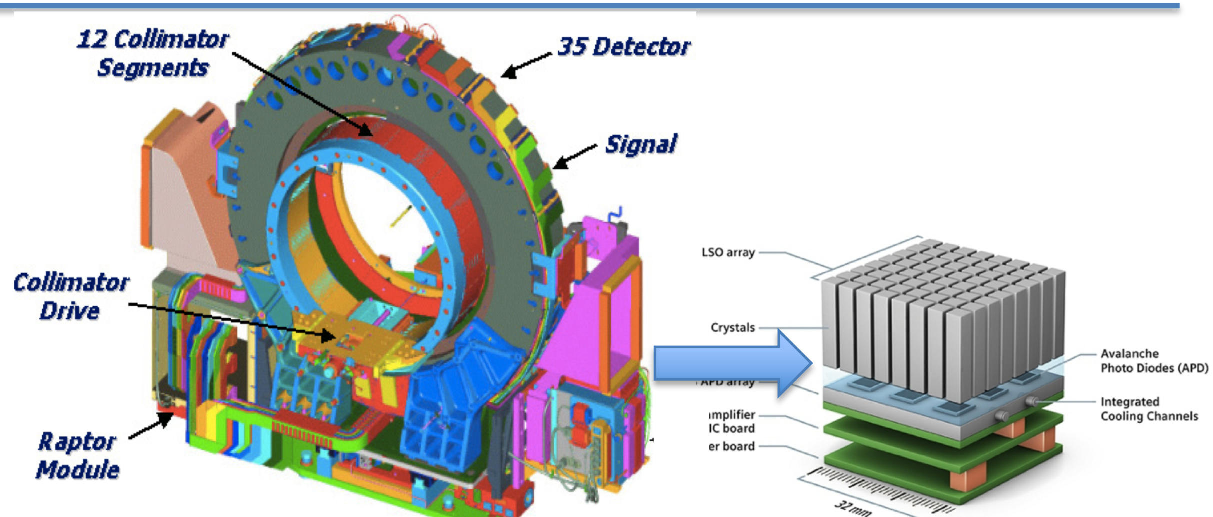
single molecule imaging



3D protein structure



imaging of diagnostic agents not possible in-vivo



CERN-sized detector reduced to patient-size

Biomedical Physics = **joint** research

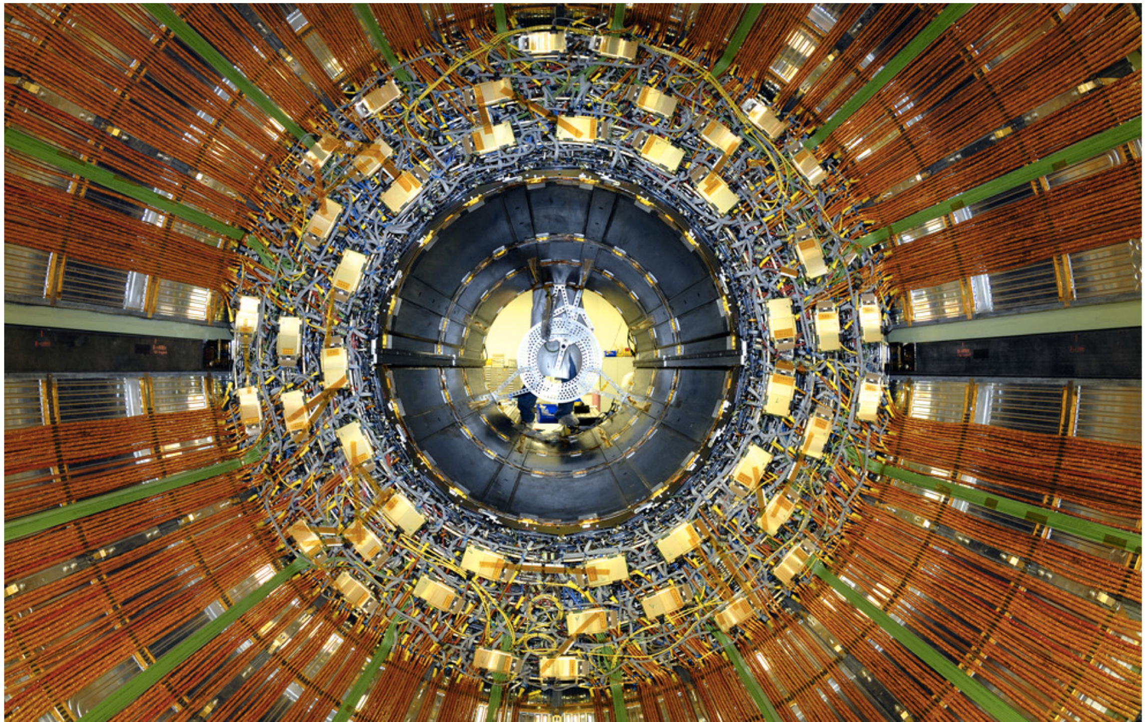
Physicists don‘t know the limits of current medical technologies

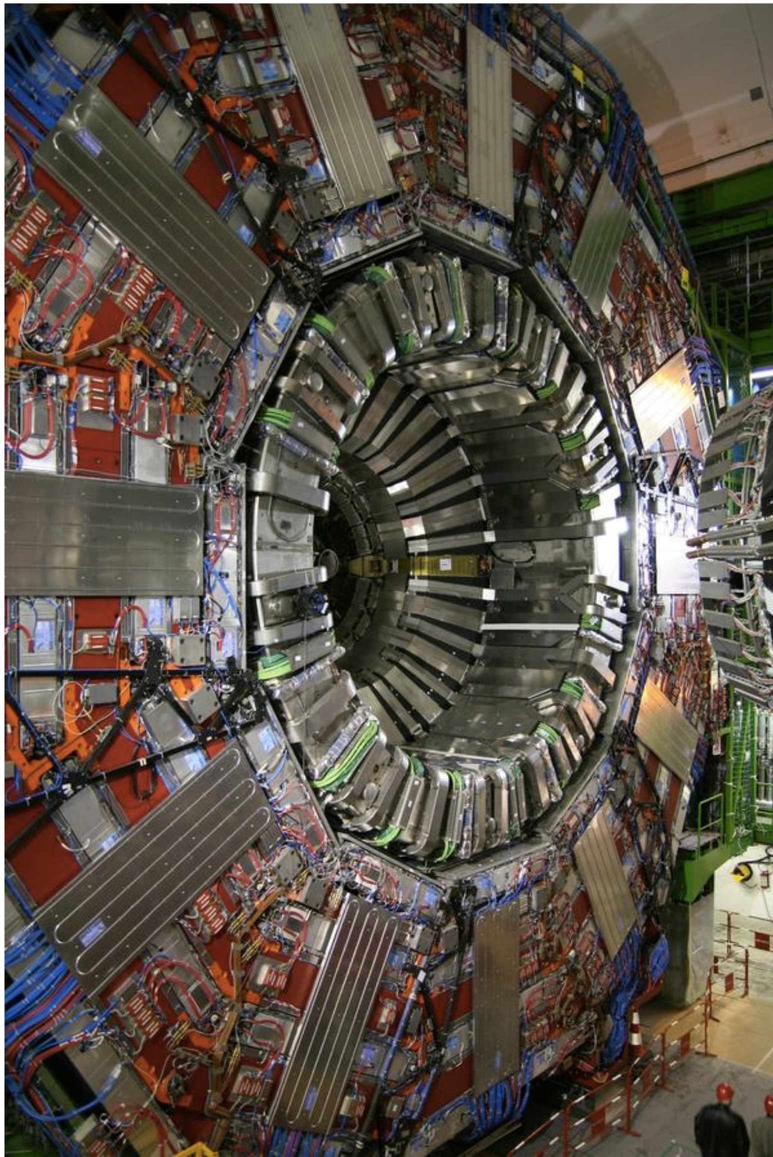
medical doctors don‘t have insight into possibilities of physics

What can HEP do for medical physics?

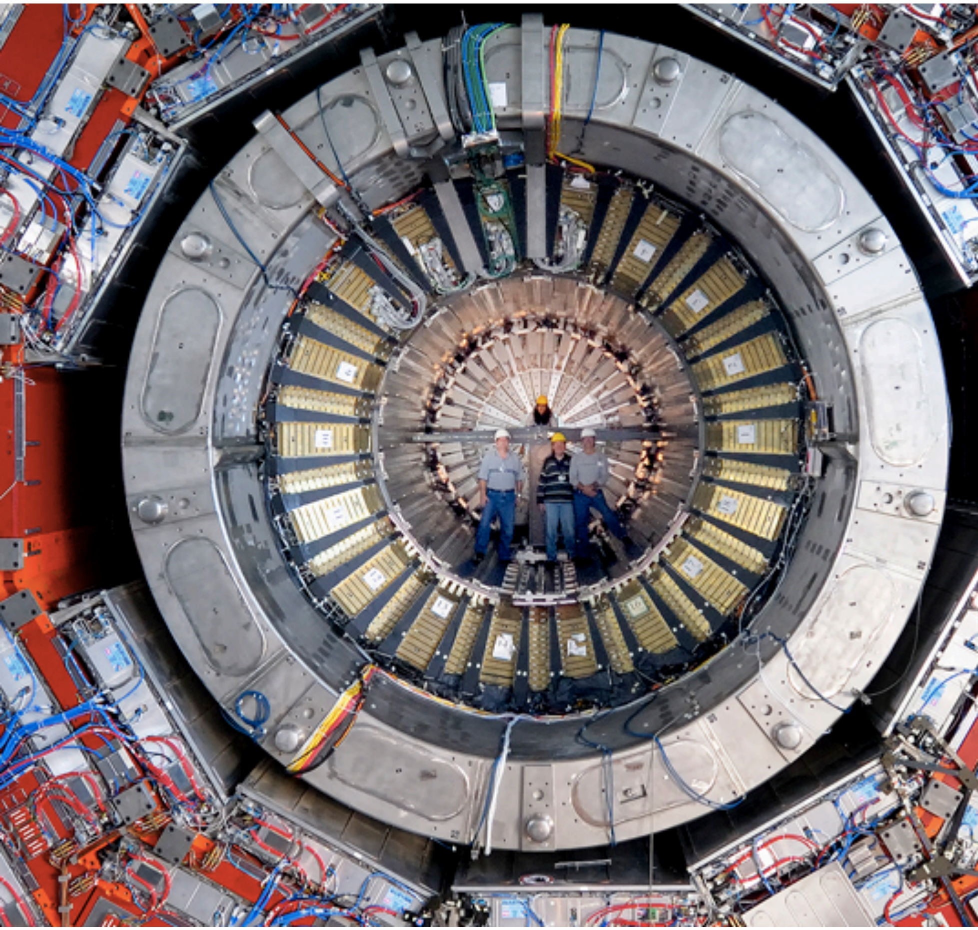
From HEP we are used to:

- Work on large complex systems
- Challenging integration conditions
- Technology frontier solution for: materials, electronics, data acquisition, data volume, processing/analysis techniques, simulation

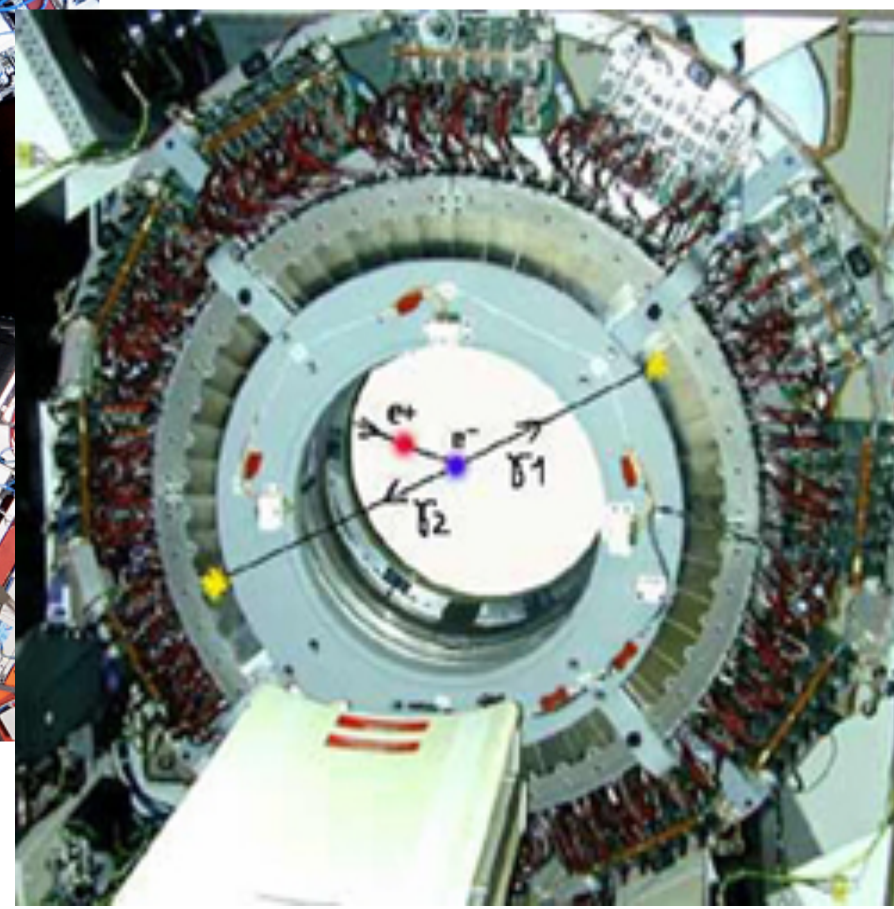




A calorimeter for HEP / PET

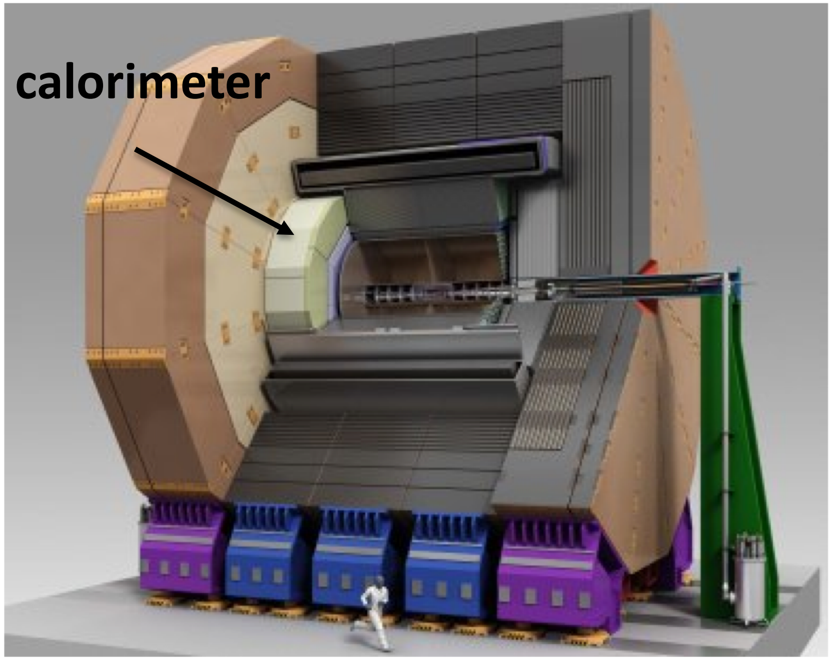


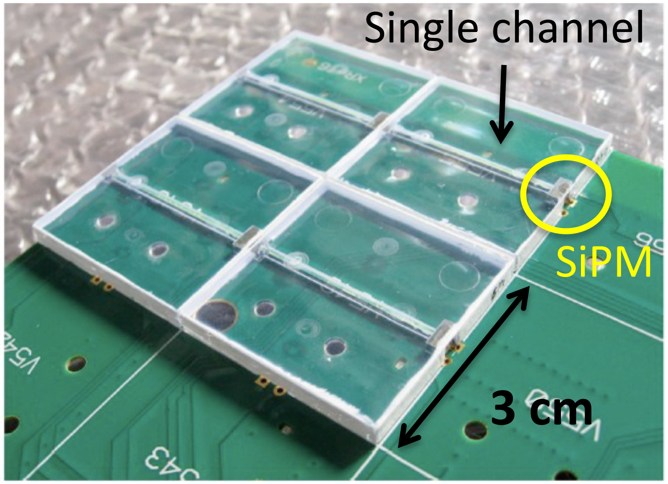
PET calorimeter system
(a laying human fits into the detector bore)



CMS calorimeter system
(the humans are not part of the experiment)

A calorimeter for HEP





Huge detector volume:

- segmented in single ch. O(10M)
- Inside ~4T magnetic coil

Single channel:

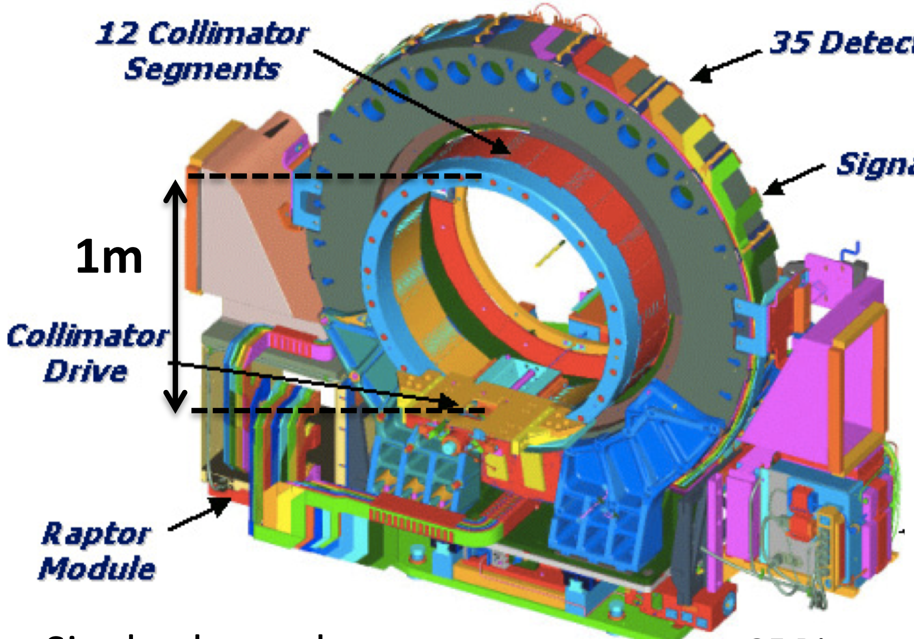
- Plastic scintillator
- Analog silicon-photomultiplier (SiPM)

Readout electronics:

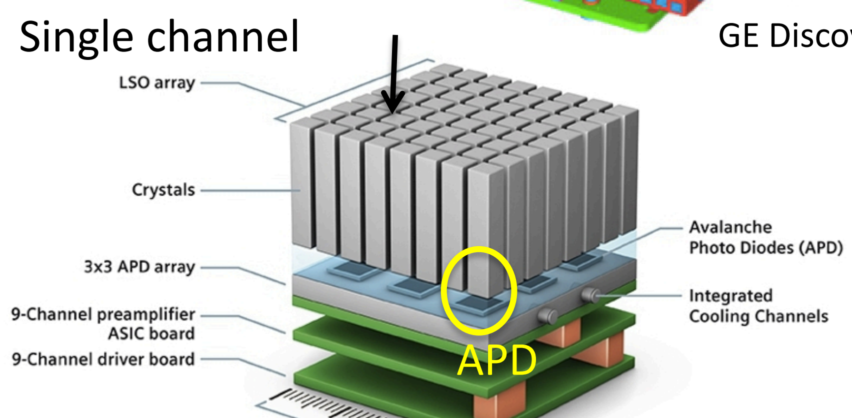
- Multi-channel r/o chip
- Energy & time measurement

Number of sellable apparatus: **1**

A calorimeter for PET



GE Discovery VCT



Siemens

Medium detector volume:

- segmented in single ch. O(100-1000)
- For PET/MRI next to ~1T coil + ~7T gradient field

Single channel:

- Inorganic scintillator (crystal)
- Currently photomultiplier tubes or Avalanche PhotoDiode

Readout electronics:

- Multi-channel r/o chip
- Energy & time measurement

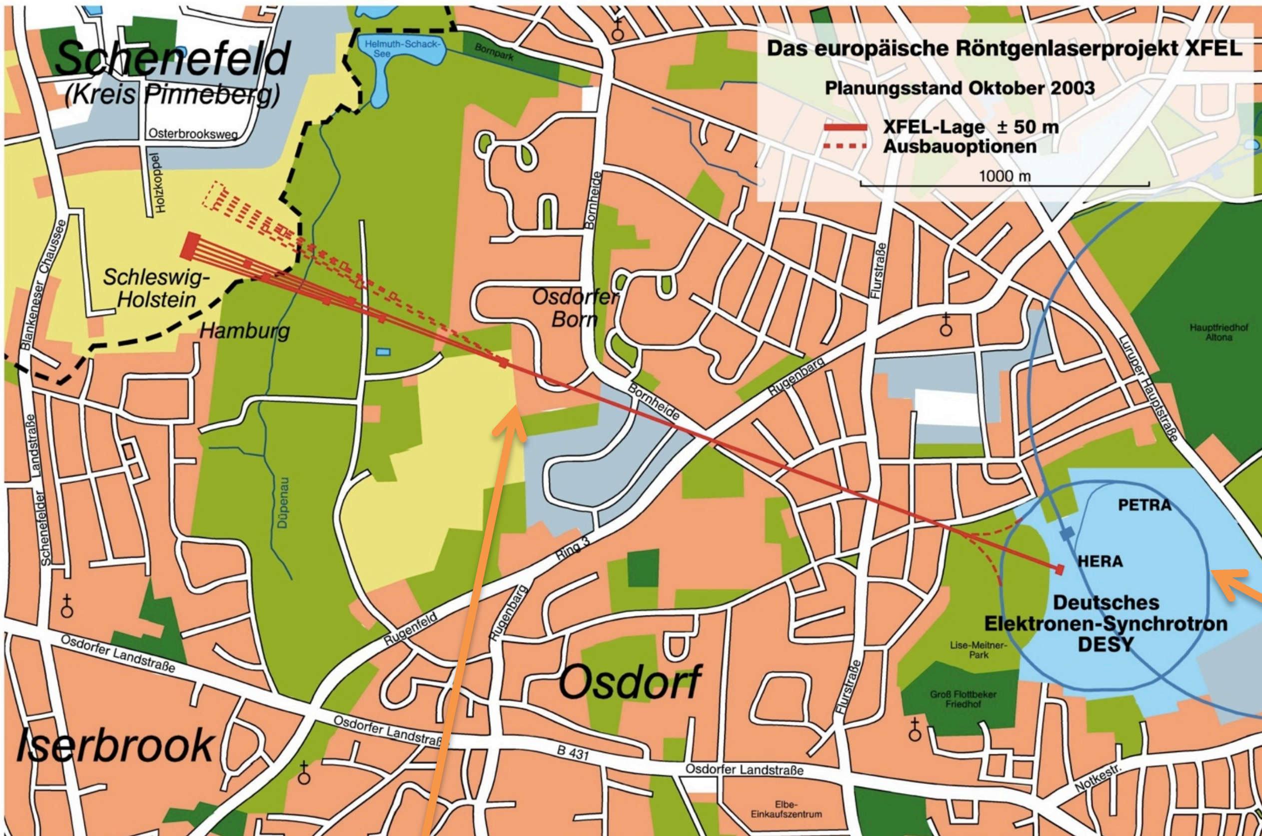
Number of sellable apparatus: **10^3-10^4**

Conventional X-ray sources

conventional/industrial X-ray tubes

- broad energy spectrum
- large divergence („ 2 pi“)
- not tunable
- large spot size, lower spatial resolution

Brilliant X-ray sources…way too large for clinical application



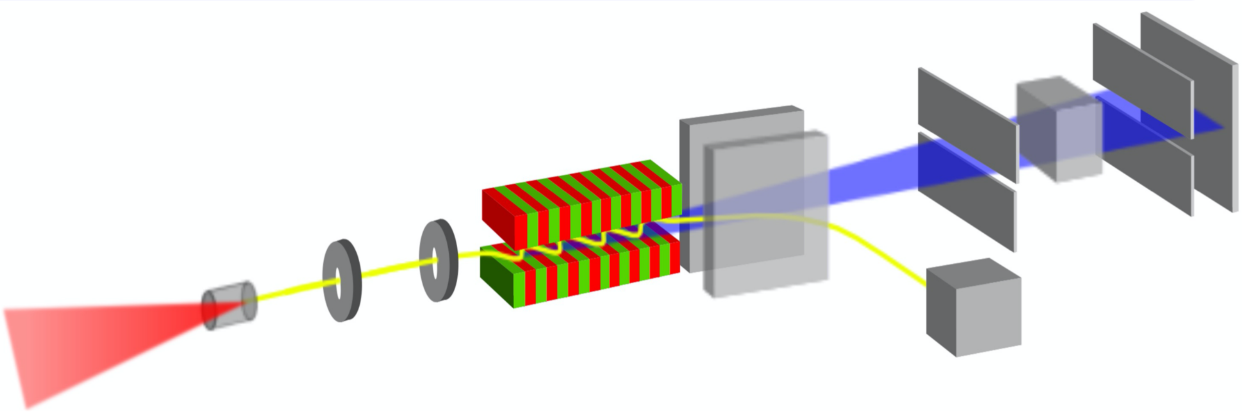
Synchrotron

XFEL

Laser-driven X-ray sources

- advantages:
  - quasi-monochromatic (few %) → high CNR/dose
  - laminar beam geometry → scatter reduction
  - low divergence → high spatial resolution
  - tunable energy

high brilliance



Diagnosis and therapy

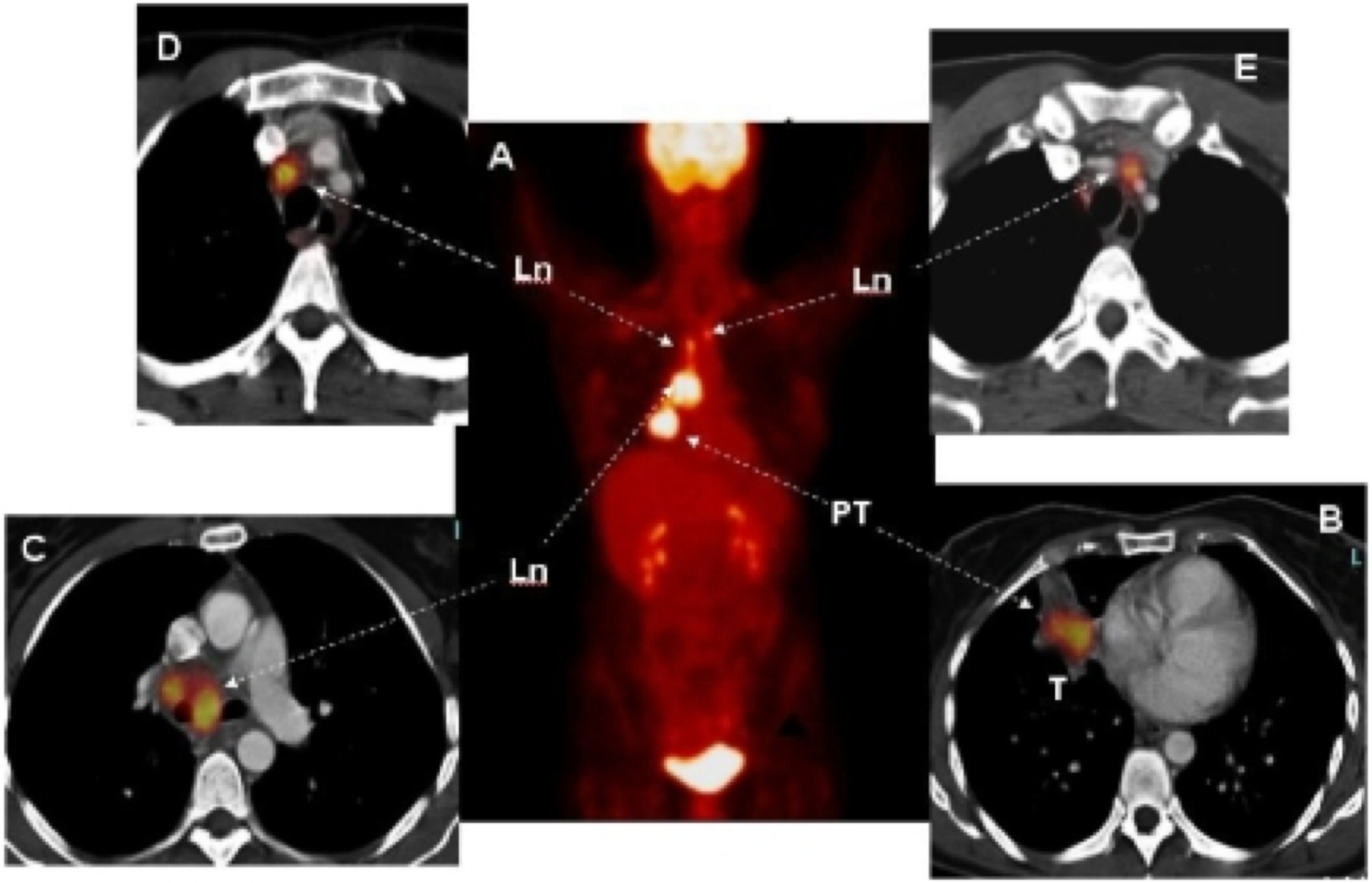
Diagnosis

Main application of medical imaging techniques in disease diagnosis, e.g.:

- cancer
- cardiovascular disease
- neurological disorders (e.g., Alzheimer’s disease)

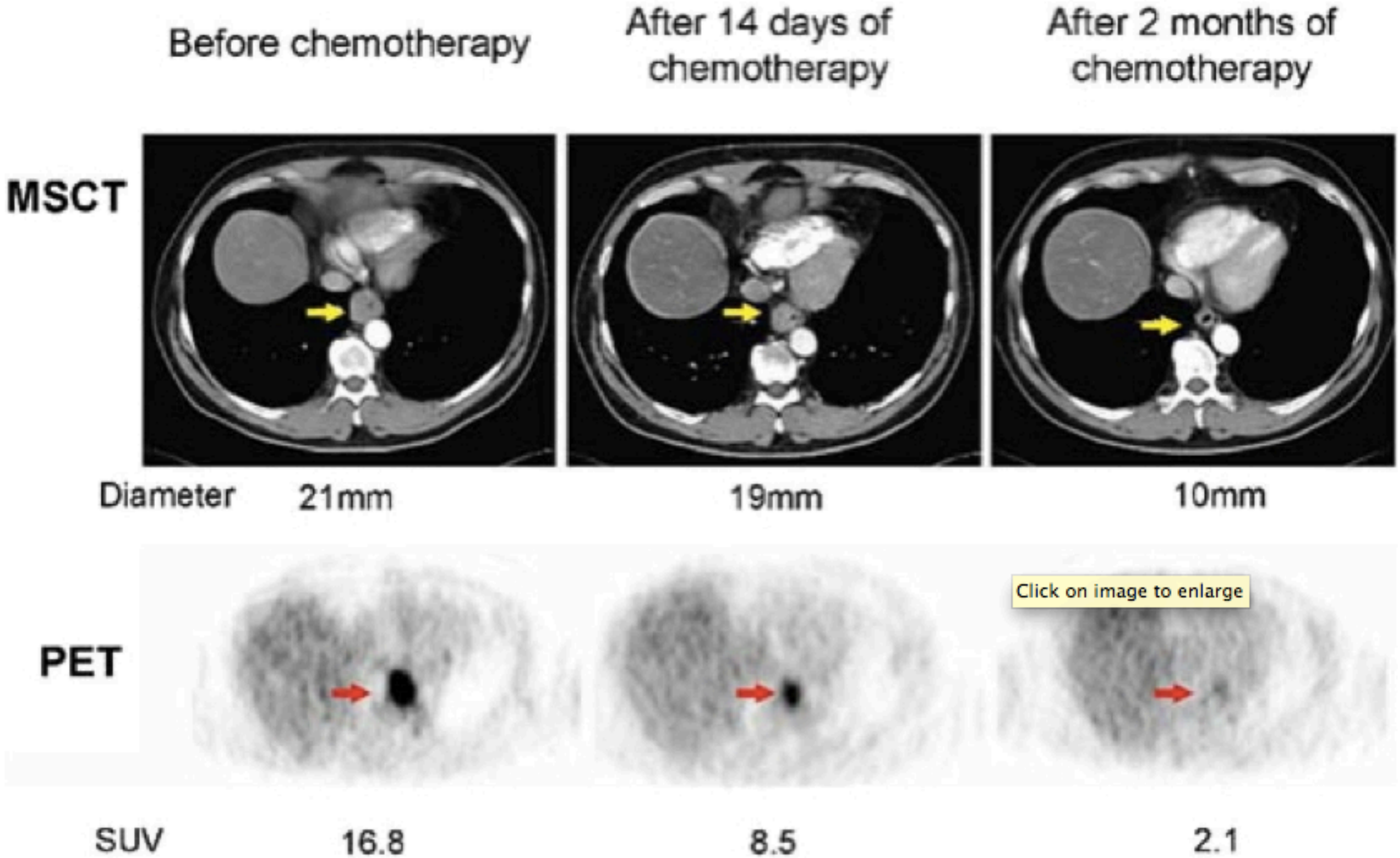
and in drug development (small animal imaging with microPET or microSPECT, microCT, microMRI, bioluminescence and fluorescence imaging systems)

Next three slides are from: Nuclear Medicine Imaging in Diagnosis and Treatment
Advancing Nuclear Medicine Through Innovation.
National Research Council (US) and Institute of Medicine (US) Committee on State of the Science of Nuclear Medicine.
Washington (DC): National Academies Press (US); 2007.



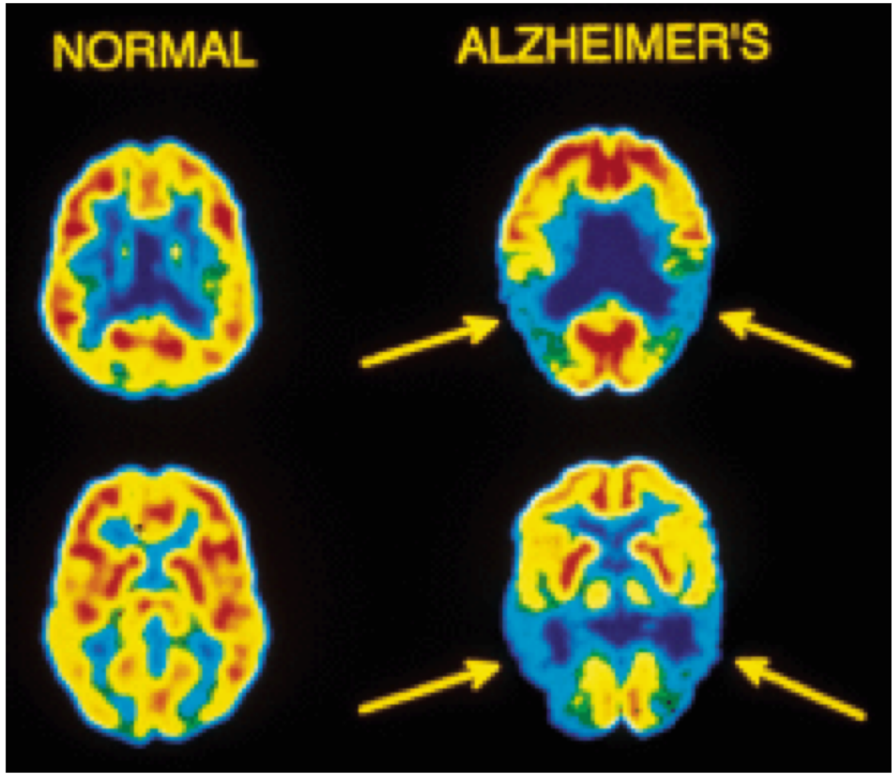
Staging of lung cancer with FDG and PET/CT. The whole-body image (Panel A) shows normal FDG uptake in the brain and the urinary bladder. In addition, several regions of intensely increased FDG uptake are seen in the chest. On the cross-sectional images of chest (Panels B through E), the primary tumor (PT, Panel B) is seen in the right lung (Ln) (arrow) with several malignant lymph nodes on the same side. There are additional malignant lymph nodes on the opposite side of the patient's chest (Panel E, arrows).

SOURCE: Courtesy of Wolfgang Weber, University of California at Los Angeles (UCLA).



Monitoring the effects of chemotherapy on tumor volume and glucose uptake with serial multislice computed tomography (MSCT) and PET imaging in a patient with cancer of the esophagus. The large tumor seen on the MSCT image (yellow arrow) is associated with intense FDG uptake on the pre-treatment PET image (red arrow). At 2 weeks, the tumor volume decreased only mildly (decrease in diameter from 21 mm to 19 mm), while the FDG uptake declined by about 50 percent (reflected by the decrease in the standardized uptake value of FDG from 16.8 to 8.5). At 2 months, the tumor volume has strikingly decreased and the FDG uptake is only faintly visible.

SOURCE: Reprinted by permission of the Society of Nuclear Medicine from Wieder et al. 2005.



DFG- PET brain images in a normal volunteer (left panel) and in a patient with Alzheimer's disease (right panel). Tomographic slices through the brain at the level of inferior parietal/superior temporal cortex are shown. The color displayed in each part of the brain reflects the concentration of FDG corresponding to the metabolic activity of the neurons in that region. Red, orange, and yellow areas are (in decreasing order) the most active, while green, blue, and violet areas are progressively less active. Note that in neurologically healthy individuals, the entire cerebral cortex has a moderately high level of metabolism. In the patient with Alzheimer's disease, the arrows indicate areas of diminished metabolic activity in the patient's parietotemporal cortex, a region important for processing of language and associative memories.
SOURCE: Courtesy of Daniel Silverman, UCLA.

Radiotherapy

After diagnosis some diseases like hyperthyroidism, cancer, blood disorders, etc… can be treated using radiotherapy.

Three main methods:

- Unsealed source radiotherapy
- Brachytherapy (sealed source therapy) ➔
- External beam: x-rays, electrons, p, n, heavy ions

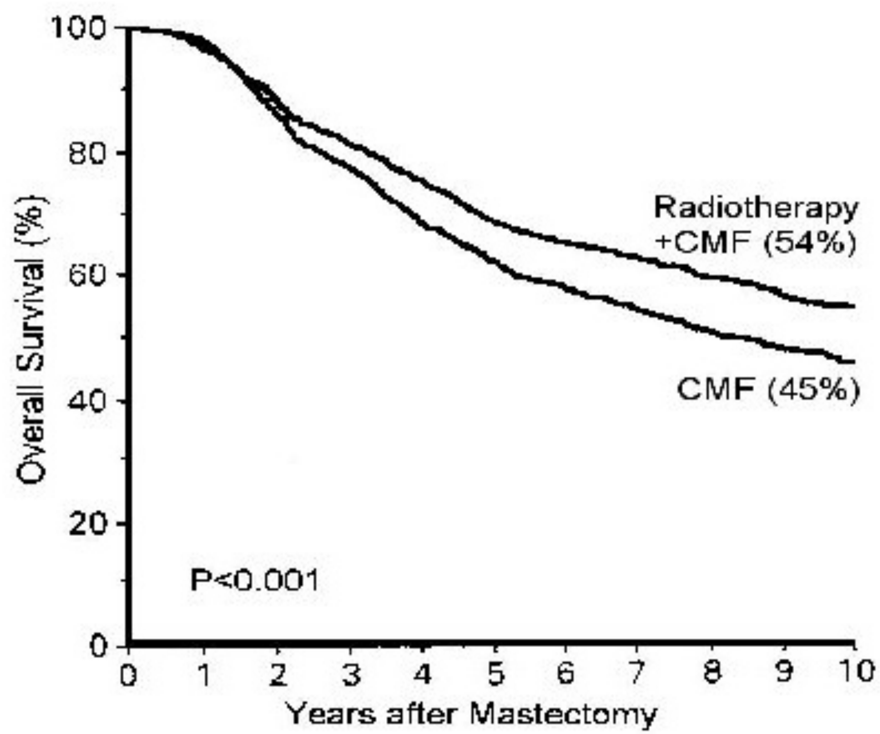
- Stages in the radiotherapy process:
  QA, imaging, planning, simulation,
  treatment, verification, modelling outcome

Physics, engineering, imaging, technology based

"seeds" - small radioactive rods implanted directly into the tumor.

Benefits of Radiotherapy

- Breast Cancer
- Mastectomy
- Compare surgery and chemotherapy (CMF) with and without radiotherapy
- 10 year survival improved by 10%



What is medical imaging?

Every non-invasive technique that allows to look inside the human body.

Invasive techniques	surgery, endoscopy
Non-invasive techniques	magnetic resonance imaging, ultrasound projection radiography, computed tomography, nuclear medicine ➔ **but exposure to radiation**

In addition see things that are not visible to the eye (blood flow, organ metabolism, receptor binding)

Different techniques (modalities) allow to look inside the human body in different ways (looking at different signals)

Signals and Modalities

Signal	Modality	Property imaged
X-ray transmission through the body	projection radiography or CT	attenuation coefficient to X-ray
Gamma-ray emission from within the body	Planar scintigraphy or emission tomography	Distribution of induced radio sources
Nuclear magnetic resonance induction	Magnetic resonance imaging	Hydrogen proton density, spin precession in large magnetic field
Ultrasound echoes	Ultrasound imaging	Sound reflectivity

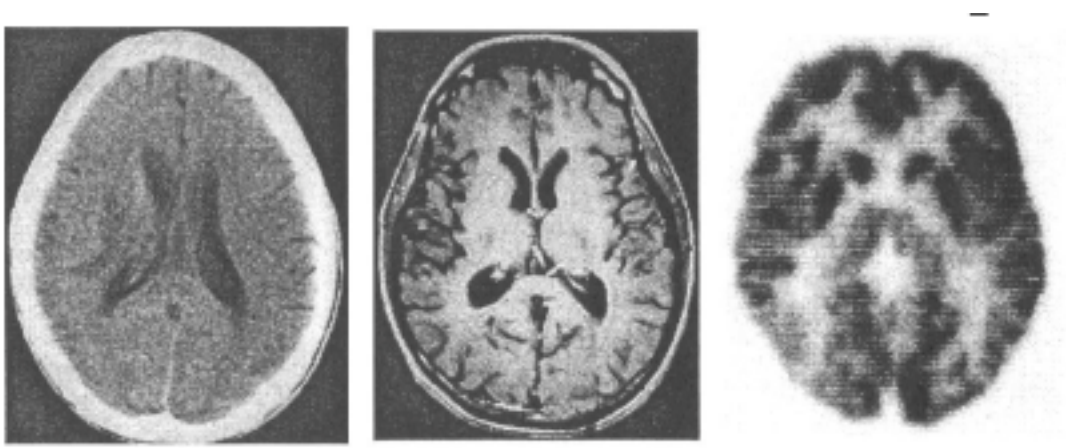
Anatomical vs. Functional imaging

Some modalities are very good at depicting anatomical structures (bones):

- X-ray and CT
- MRI

Some modalities are less good with anatomical structure but reflect the functional status (blood flow, oxygenation, etc…)

- Ultrasound
- PET, functional MRI



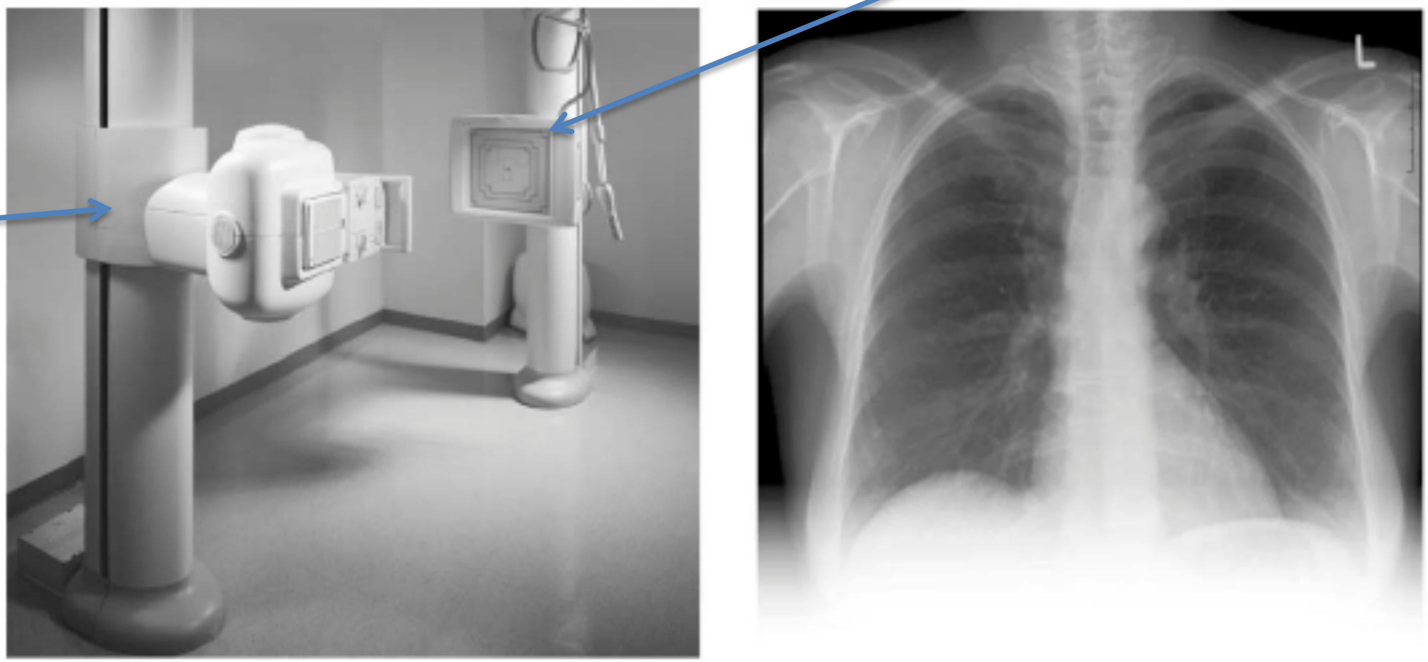
(a) CT (b) MRI (c) PET

Projection radiography

Scintillator screen and detector (film, camera, solid-state)

X-ray tube

cone beam



(a) (b)

Figure 1.1

Medical Imaging Signals and Systems, by Jerry L. Prince and Jonathan Links.
ISBN 0-13-065353-5.

Projection radiography

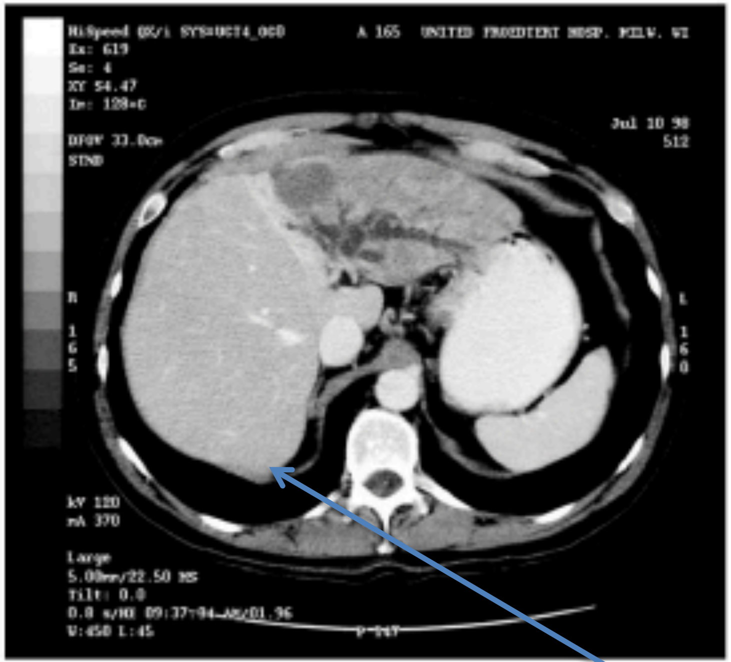
• Year discovered:	1895 (Röntgen, NP 1905)
• Form of radiation: radiation	X-rays = electromagnetic (photons)
• Energy / wavelength of radiation:	0.1 – 100 keV / 10 – 0.01 nm (ionizing)
• Imaging principle:	X-rays penetrate tissue and create "shadowgram" of differences in density.
• Imaging volume:	Whole body
• Resolution:	Very high (sub-mm)
• Applications:	Mammography, lung diseases, orthopedics, dentistry, cardiovascular,

From Graber, Lecture Note for Biomedical Imaging, SUNY

Computed tomography

X-ray in a 2-D "fan beam" rotated around the subject
The image of one cross-section is computed from all projections (digital)
Whole body scan in less than one minute

(a)



(b)

Slice of the liver
(1 sec data taking)

Figure 1.2

Computed tomography

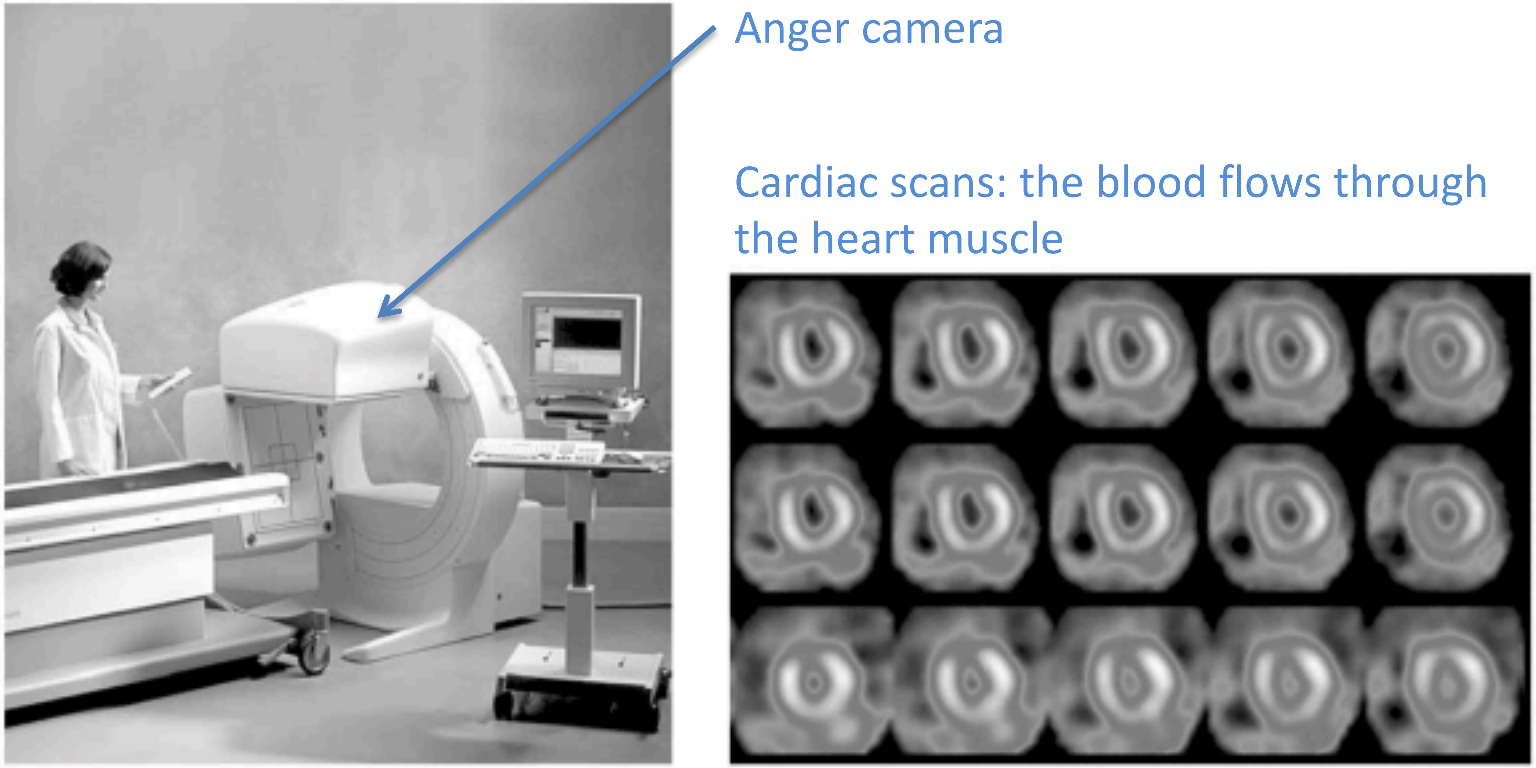
• Year discovered:	1972 (Hounsfield, NP 1979)
• Form of radiation:	X-rays
• Energy / wavelength of radiation:	10 – 100 keV / 0.1 – 0.01 nm (ionizing)
• Imaging principle:	X-ray images are taken under many angles from which tomographic ("sliced") views are computed
• Imaging volume:	Whole body
• Resolution:	High (mm)
• Applications:	Soft tissue imaging (brain, cardiovascular, GI)

From Graber, Lecture Note for Biomedical Imaging, SUNY

SPECT

Anger camera

Cardiac scans: the blood flows through the heart muscle



(a) (b)

Figure 1.3

Medical Imaging Signals and Systems, by Jerry L. Prince and Jonathan Links.
ISBN 0-13-065353-5.

Nuclear medicine

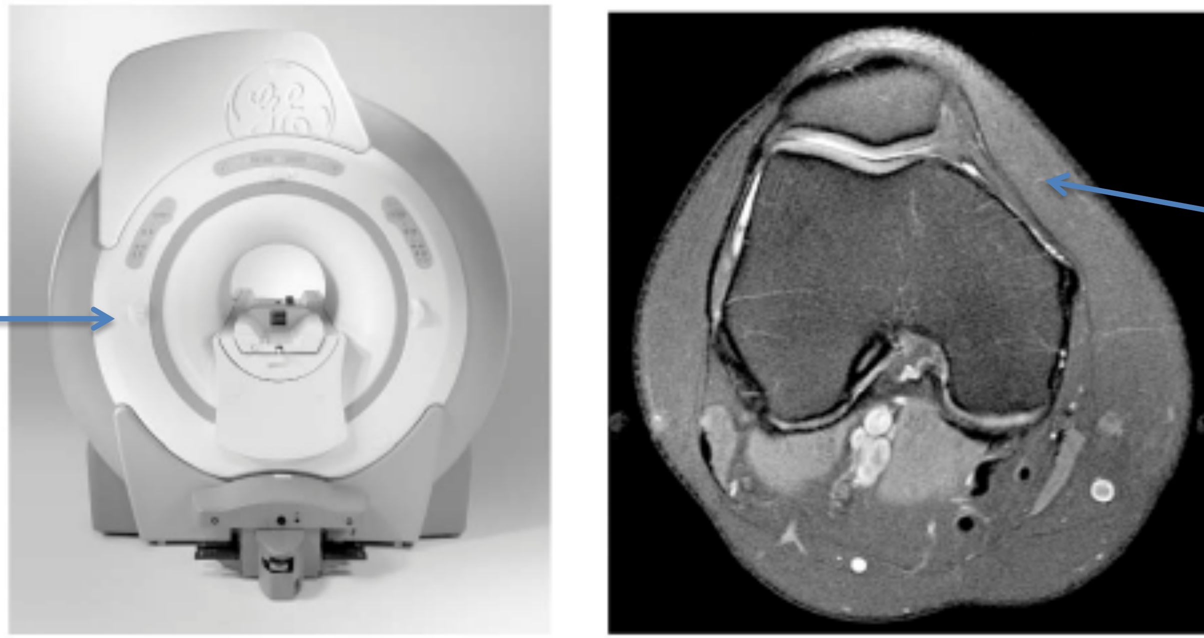
- Year discovered: 1953 (PET), 1963 (SPECT)
- Form of radiation: Gamma rays
- Energy / wavelength of radiation: > 100 keV / < 0.01 nm (ionizing)
- Imaging principle: Accumulation or "washout" of radioactive isotopes in the body are imaged with x-ray cameras.
- Imaging volume: Whole body
- Resolution: Medium – Low (mm - cm)
- Applications: Functional imaging (cancer detection, metabolic processes, myocardial infarction)

From Graber, Lecture Note for Biomedical Imaging, SUNY

Magnetic resonance imaging

In a magnetic field protons (H) align themselves along the field lines
An additional gradient field can locally disturb the alignment
To reestablish the alignment protons precess and generate detectable EM-waves

2 Tesla super-conductive magnet



Human knee

(a) (b)

Figure 1.5

Medical Imaging Signals and Systems, by Jerry L. Prince and Jonathan Links.
ISBN 0-13-065353-5.

Magnetic resonance imaging

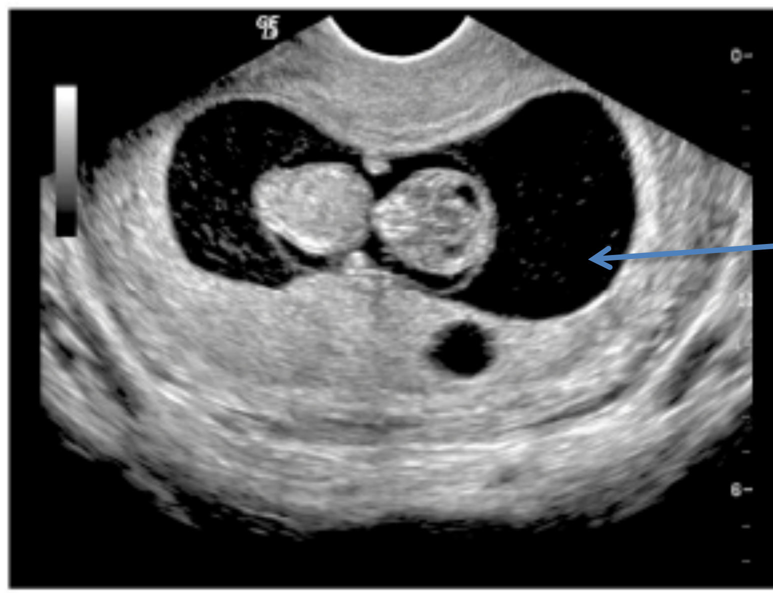
- Year discovered: 1945 ([NMR] Bloch, NP 1952)
  1973 (Lauterbur, NP 2003)
  1977 (Mansfield, NP 2003)
  1971 (Damadian, SUNY DMS)
- Form of radiation: Radio frequency (RF) (non-ionizing)
- Energy / wavelength of radiation: 10 – 100 MHz / 30 – 3 m (~10-7 eV)
- Imaging principle: and response: Proton spin flips are induced, the RF emitted by their (echo) is detected.
- Imaging volume: Whole body
- Resolution: High (mm)
- Applications: Soft tissue, functional imaging

From Graber, Lecture Note for Biomedical Imaging, SUNY

Ultrasound imaging

- High frequency sound are emitted into the imaged body, time and strength of the returned sound pulses are measured
- Comparative inexpensive and completely non-invasive
- Image quality is relatively poor

(a)



11-weeks-old human embryo

(b)

Ultrasound imaging

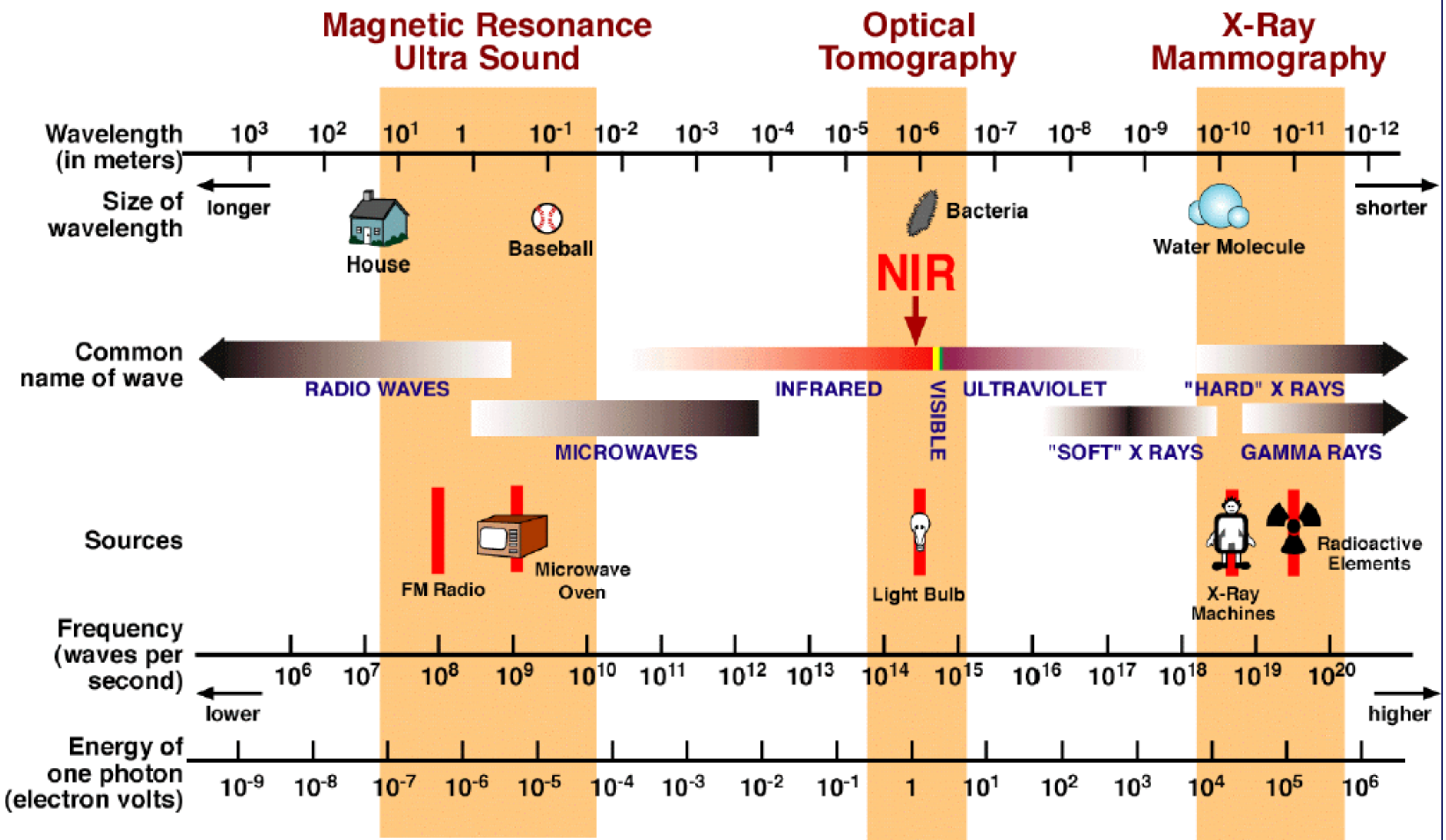
• Year discovered:	1952 (clinical: 1962)
• Form of radiation:	Sound waves (non-ionizing) ***NOT*** EM radiation!
• Frequency / wavelength of radiation:	1 – 10 MHz / 1 – 0.1 mm
• Imaging principle:	Echoes from discontinuities in tissue density/speed of sound
are	registered.
• Imaging volume:	< 20 cm
• Resolution:	High (mm)
• Applications:	Soft tissue, blood flow
(Doppler)	

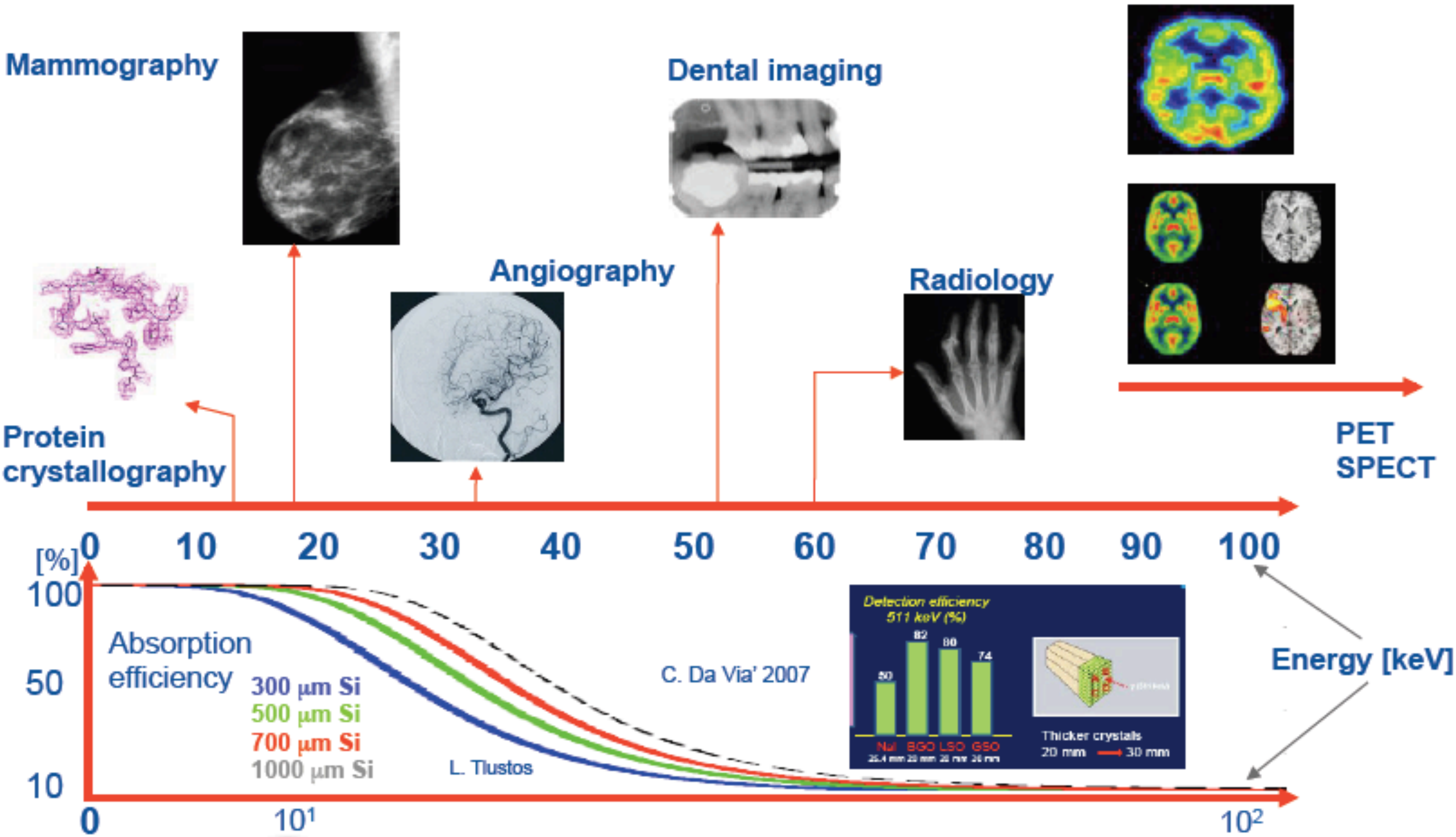
From Graber, Lecture Note for Biomedical Imaging, SUNY

Electromagnetic waves used in medical imaging

larger than 1 Å high attenuation from the body,

shorter than 10^{-2} Å = too high energy (>1MeV) for direct detection




Mammography
Dental imaging
Angiography
Radiology
Protein crystallography
PET
SPECT
0 10 20 30 40 50 60 70 80 90 100
[%]
100
50
10
0
Absorption efficiency
300 μm Si
500 μm Si
700 μm Si
1000 μm Si
L. Tlustos
C. Da Via' 2007
Detection efficiency 511 keV (%)
50 82 80 74
NaI BGO LSO GSO
Thicker crystals
20 mm → 30 mm
10^1
10^2
Energy [keV]