Medical Applications of Modern Physics

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Medical Physics

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A branch of applied physics concerning the application of physics to medicine

or, in other words

The application of physics techniques to the human health
Outline of the lecture

Physics discoveries
Tools for physics applied to medicine
Medical imaging
X-ray CT
PET and PET/CT
Photon/electron radiation therapy
Hadron therapy
Outline of the lecture

Physics discoveries

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Hadron therapy
The beginnings of modern physics and of medical physics

1895
Discovery of X rays
Wilhelm C. Röntgen

1897
First treatment of tissue with X rays
Leopold Freund

J.J. Thompson

1897
“Discovery” of the electron
The beginnings of modern physics and of medical physics

Henri Becquerel (1852-1908)

1896
Discovery of natural radioactivity

1898
Discovery of polonium and radium

Thesis of Mme. Curie – 1904
\( \alpha, \beta, \gamma \) in magnetic field

Hundred years ago

Marie Curie (1867 – 1934) Pierre Curie (1859 – 1906)
First practical application of a radioisotope

- **1911**: *first practical application of a radioisotope* (as *radiotracer*) by G. de Hevesy (a young Hungarian student working with naturally radioactive materials) in Manchester.

- **1924**: de Hevesy, who had become a physician, used radioactive isotopes of lead as tracers in bone studies.
Tools for (medical) physics: the cyclotron

1930

Invention of the cyclotron

Ernest Lawrence

M. S. Livingston and E. Lawrence with the 25 inch cyclotron
The beginnings of modern physics and of medical physics

1932

Discovery of the neutron

James Chadwick (1891 – 1974)

Cyclotron + neutrons = first attempt of radiation therapy with fast neutrons at LBL (R. Stone and J. Lawrence, 1938)
The beginnings of modern physics and of medical physics

1932
Discovery of the positron

C. D. Anderson

Layer of lead
Inserted in a cloud chamber

Fast positive particle
coming from below

Slow-down particle
Historical development of radioisotopes for medicine

• **1932:** the invention of the cyclotron by E. Lawrence makes it possible to produce radioactive isotopes of a number of biologically important elements

• **1941:** first medical cyclotron installed at Washington University, St Louis, for the production of radioactive isotopes of phosphorus, iron, arsenic and sulphur

• **After WWII:** following the development of the fission process, most radioisotopes of medical interest begin to be produced in nuclear reactors

• **1951:** Cassen et al. develop the concept of the rectilinear scanner

• **1957:** the $^{99}\text{Mo}/^{99m}\text{Tc}$ generator system is developed by the Brookhaven National Laboratory

• **1958:** production of the first gamma camera by Anger, later modified to what is now known as the Anger scintillation camera, still in use today
Tools for (medical) physics: the electron linac

Sigmur Varian

William W. Hansen

Russell Varian

1939

Invention of the klystron

1950’s: development of compact linear electron accelerators by various companies

1947

first linac for electrons

4.5 MeV and 3 GHz
Tools for (medical) physics: the synchrotron

1945: E. McMillan and V.J. Veksler

discover the principle of phase stability

1 GeV electron synchrotron
Frascati - INFN - 1959

6 GeV proton synchrotron
Bevatron - Berkeley - 1954
In 1952 the “strong-focusing” method invented at BNL (USA) was chosen for the CERN PS.
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# Medical imaging

<table>
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<tr>
<th>TECHNIQUE</th>
<th>YEAR</th>
<th>ENERGY</th>
<th>PHYSICAL PROPERTY</th>
<th>IMAGING</th>
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<tr>
<td><strong>RADIOLOGY</strong></td>
<td></td>
<td><strong>X RAYS</strong></td>
<td><strong>1895</strong></td>
<td><strong>X RAYS</strong></td>
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<td><strong>ECHOGRAPHY</strong></td>
<td></td>
<td><strong>ULTRASOUND</strong></td>
<td><strong>1950</strong></td>
<td><strong>US</strong></td>
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<td><strong>NUCLEAR MEDICINE</strong></td>
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<td><strong>RADIOISOTOPE</strong></td>
<td><strong>1950</strong></td>
<td><strong>γ RAYS</strong></td>
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### Medical imaging

<table>
<thead>
<tr>
<th>TECHNIQUE</th>
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<th>PHYSICAL PROPERTY</th>
<th>IMAGING</th>
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<tr>
<td>X RAYS COMPUTERIZED TOMOGRAPHY CT</td>
<td>CT</td>
<td>1971</td>
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<td>ABSORPTION MORPHOLOGY</td>
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<tr>
<td>MAGNETIC RESONANCE IMAGING MRI</td>
<td>MRI</td>
<td>1980</td>
<td>RADIO WAVES</td>
<td>MAGNETIC RESONANCE/MORPHOLOGY/FUNCTION</td>
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<tr>
<td>POSITRON EMISSION TOMOGRAPHY PET</td>
<td>PET</td>
<td>1973</td>
<td>γ RAYS</td>
<td>RADIATION EMISSION FUNCTION</td>
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</table>
Emission versus transmission imaging

External versus internal radiation sources

Transmission

Emission
X-ray image versus CT scan

A conventional X-ray image is basically a shadow: you shine a “light” on one side of the body, and a piece of film on the other side registers the silhouette of the bones (to be more precise, organs and tissues of different densities show up differently on the radiographic film).

Shadows give an incomplete picture of an object's shape.

Look at the wall, not at the person. If there's a lamp in front of the person, you see the silhouette holding the banana, but not the pineapple as the shadow of the torso blocks the pineapple. If the lamp is to the left, you see the outline of the pineapple, but not the banana.
Computed tomography

- The X-rays source rotates around the longitudinal axis of the body: it moves 360° around the patient, scanning from hundreds of different angles.

- Opposite to the x-ray source, a series of detectors measure the radiation emerging from the body.

- Each rotation scans a different body slice.

- The couch moves to scan the next slice.

- A computer analyses the data and reconstructs the 3D image through mathematical algorithms.
Volumetric CT

< 0.4 sec/rotation
Organ in a sec (17 cm/sec)
Whole body < 10 sec
Cardiac CT

DYNAMIC CT ACQUISITION

PHASES OF A CARDIAC CYCLE

FUNCTIONAL PARAMETERS

- EJECTION FRACTION
- CARDIAC OUTPUT
- REGIONAL WALL MOTION
- ...

VOLUME RENDERED IMAGE OF HEART AND VESSELS
Production of radionuclides for medical imaging and therapy

All radionuclides commonly administered to patients in nuclear medicine are *artificially* produced

Three production routes:

- **(n, γ) reactions** *(nuclear reactor)*: the resulting nuclide has the same chemical properties as those of the target nuclide
- **Fission** *(nuclear reactor)* followed by separation
- **Charged particle induced reaction** *(cyclotron)*: the resulting nucleus is usually that of a different element
Positron Emission Tomography (PET)

**ISOTOPES** | **Half-Life** | **Remarks**
--- | --- | ---
11-C | 20.4 min | "natural"
13-N | 10.0 min | "natural"
15-O | 2.0 min | "natural"
18-F | 109.8 min | "pseudo-natural"

Cyclotron

Radiochemistry

PET camera

Detector Array

γ - radiation

Positron

Radioactive tracer

High-school teachers 2018

M. Silari – Medical Physics
Positron Emission Tomography (PET)

Coverage: 
~ 15-20 cm

Spatial Resolution: 
~ 5 mm

Scan time to cover an entire organ: 
~ 5 min

Contrast Resolution: 
depends on the radiotracer
PET functional receptor imaging

Normal Subject

Parkinson’s disease

$^{[11}C] \text{FE-CIT}$

Courtesy HSR MILANO
PET coverage and axial sampling

**FIRST GENERATION PET**

1 SLICE – 2 cm

**CURRENT GENERATION PET**

> 40 SLICES – 6 mm
Axial FOV: 15 – 20 cm
PET: total body studies

TRANSAXIAL IMAGES

CORONAL

SAGITTAL
PET/CT scanner
PET/CT scanner

CT  PET

Courtesy HSR MILANO
PET/CT scanner

Courtesy HSR MILANO

High-school teachers 2018

M. Silari – Medical Physics
18F-FDG PET/CT

Courtesy HSR MILANO
A look into the future: whole-body PET
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Three classes of medical accelerators

Electron linacs for conventional radiation therapy, including advanced modalities:

- Cyberknife
- IntraOperative RT (IORT)
- Intensity Modulated RT

Low-energy cyclotrons for production of radionuclides for medical diagnostics

Medium-energy cyclotrons and synchrotrons for hadron therapy with protons (250 MeV) or light ion beams (400 MeV/u $^{12}$C-ions)
Availability of radiation therapy worldwide

Number of radiation therapy machines per million people
Treatment planning and dose delivery to tumour volume
Tumour control and therapeutic window

![Graph showing tumor control and therapeutic window](image)

- **Tumour control**
- **Therapeutic advantage**
- **Complications**
- **Tumour control w/o complications**

<table>
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<tr>
<th>Probability (%)</th>
<th>Dose</th>
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<tr>
<td>100</td>
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<td>90</td>
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<td>10</td>
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</tr>
<tr>
<td>0</td>
<td>100</td>
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X-rays in radiation therapy: medical electron linacs

Varian Clinac 1800

- Energy: 6-25 MeV
- Dual e⁻/γ beams

Multi-leaf collimator

e⁻ + target → X-rays
Intra-Operative Radiation Therapy (IORT)

• Small electron linac
• Energy 6 – 12 MeV
• Treatment with electrons only
• Single irradiation
• Three models of linac produced by three manufacturers (two in Italy)
CyberKnife (CK) Robotic Surgery System

6 MV Linac mounted on a robotic arm

- Non-Isocentric
- Average dose delivered per session is 12.5 Gy
- 6 sessions/day
- Dose rate @ 80 cm = 400 cGy/min

http://www.accuray.com/Products/Cyberknife/index.aspx
An example of intensity modulated treatment planning with photons. Through the addition of 9 fields it is possible to construct a highly conformal dose distribution with good dose sparing in the region of the brain stem (courtesy of T. Lomax, PSI).

E. Pedroni, Europhysics News (2000) Vol. 31 No. 6

Yet X-rays have a comparatively poor energy deposition as compared to protons and carbon ions.
Helical tomotherapy

www.tomotherapy.com

• Integrated CT guidance
  • Integrated CT scanner allowing efficient 3D CT imaging for ensuring the accuracy of treatment
• A binary multi-leaf collimator (MLC) for beam shaping and modulation
• A ring gantry design enabling TomoHelical delivery
  • As the ring gantry rotates in simultaneous motion to the couch, helical fan-beam IMRT is continuously delivered from all angles around the patient
• Very large volumes can be treated in a single set-up
MRI-guided radiation therapy

Dedicated sequences for MRI guided radiotherapy treatments

1) 1.5 T MRI
2) 6 MV accelerator
3) Split gradient coil
4) Superconducting coils
5) Low magnetic field toroid
Hadrontherapy: n, p and C-ion beams

- carbon ion = 6 protons + 6 neutrons
- Proton or neutron
- electron “e”
- “hadrons” are made of quarks
- quark “u” or “d”
Proton radiation therapy

![Proton radiation therapy diagram](image)

**Fig 2 and Fig 3:** Prostate Cancer Treatment from the front and sides.

**Fig 4, Fig 5, Fig 6, and Fig 7:** Prostate cancer treatment from the sides, X-Ray vs Proton Side effects, and Treating Prostate cancer.
Treatment planning

- **Ion beam therapy is more conformal than photon beam RT**
- **Sharper dose fall off**
- **Range of ions much more influenced by tissue heterogeneities than photon beams with direct impact on TCP and NTCP**
- **Image guidance is necessary for ion beam therapy**
Radiobiological effectiveness (RBE)

\[
\text{RBE} = \frac{D_{\text{x-ray}}}{D_{\text{particle}}}
\]
Hadrontherapy

200 MeV protons

4800 MeV carbon ions

charged hadron beam that loses energy in matter

tumour target

27 cm
Hadrontherapy in Europe and worldwide

Particle Therapy Facilities worldwide

CERN Courier Jan/Feb 2018
Proton radiation therapy

IBA

Accel-Varian

Loma Linda (built by FNAL)

Hitachi
Isocentric gantry

A gantry is a massive structure that allows directing the beam to the tumour from any direction. It carries:

- the final section of the beam line
- the beam spreading ‘nozzle’
- the proton ‘snout’ which carries the aperture and range compensator
National Centre for Oncological Hadrontherapy, CNAO, Pavia, Italy
Ion sources

LEBT components

Courtesy S. Rossi, CNAO

Injector linac

Quadrupole magnets

RF cavity

Dipole magnets
National Centre for Oncological Hadrontherapy, CNAO, Pavia, Italy
The future of hadrontherapy: single room facilities?

IBA Proteus Nano

Mevion Medical Systems
A look into the future: flash irradiation

• New accelerator-based technology being developed by the Department of Energy's SLAC National Accelerator Laboratory and Stanford University

• Irradiation time reduced from minutes to under a second
• Tumour position “frozen”
• Technology for X-rays and protons
• Need accelerator structures that are hundreds of times more powerful than today's technology

• PHASER: flash delivery system for X-rays
• PHASER version for protons

• In mice healthy cells suffer less damage when radiation dose is applied very quickly, with same tumour-killing effect

• Make radiation therapy more accessible for patients worldwide

A look into the future: CERN’s compact gantry

Gantry + Toroid = GaToroid \rightarrow GaTo

L. Bottura, E. Falcini et al, TE-MSC
Acknowledgements

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