Novel Technologies in Radiotherapy: Protons and Magnetic Resonance Imaging

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UC San Diego
Disclosure

• I have no conflicts of interest to disclose.
Learning Objectives

• Understand the physics of protons beams
• Describe differences between proton & photon plans
• Summarize basic physics of MRI
• Discuss applications of MRI in radiotherapy
Question #1

• What are two methods to create a clinical proton beam?
  a) Passive scattering and active scanning
  b) Blocks, bolus and wedges
  c) Active scattering and passive scanning
  d) None of the above
Question #2

• What property of tissues makes nuclear magnetic resonance useful for imaging?
  a) Angular momentum is independent of RF energy
  b) Tissues have characteristic relaxation times
  c) RF attenuation is linearly related to tissue density
  d) None of the above
Proton Therapy

• Physics of protons
  – Dose deposition
  – Creating a proton beam

• Proton beam planning
Some Proton History

• **Cyclotron invented in 1930**

• **Suggested for medical use in 1946**

• **First patients treated in 1958**
  - In 1961, the Harvard Cyclotron Laboratory started treating intracranial lesions

• **First hospital-based system developed at the LLUMC**
  - First patient treated in 1991
  - Slater JM et al. The proton treatment center at Loma Linda University Medical Center: rational for and description of its development. *IJROBP* 1991.
# Physical Properties

<table>
<thead>
<tr>
<th>Particle</th>
<th>Symbol</th>
<th>Charge</th>
<th>Rest Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electron</td>
<td>$e^-, \beta^-$</td>
<td>$-1$</td>
<td>0.511 MeV</td>
</tr>
<tr>
<td>Positron</td>
<td>$e^+, \beta^+$</td>
<td>$+1$</td>
<td>0.511 MeV</td>
</tr>
<tr>
<td>Proton</td>
<td>$p^+, \text{ }^1H^+$</td>
<td>$+1$</td>
<td>$1836 \cdot 0.511$ MeV</td>
</tr>
<tr>
<td>Neutron</td>
<td>$n, \text{ }^0n$</td>
<td>$0$</td>
<td>$1839 \cdot 0.511$ MeV</td>
</tr>
</tbody>
</table>
Proton Interactions

- Electronic
  - Ionization
  - Excitation
Proton Interactions

• Nuclear
  I. Multiple Coulomb scattering
     Small $\theta$
  II. Elastic nuclear collision
     Large $\theta$
  III. Inelastic nuclear interaction
Ionization Density

- 10 MeV Proton
- 0.5 MeV Proton
- 1 MeV Electron
- 5 keV Electron

Linear Energy Transfer (LET)

- Energy transferred per unit track length

\[
\text{LET} = \frac{dE}{dl}
\]

- Useful as a simple way to indicate radiation quality and biological effectiveness
<table>
<thead>
<tr>
<th>Radiation</th>
<th>LET (keV/μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cobalt-60 γ-rays</td>
<td>0.2</td>
</tr>
<tr>
<td>250 keV x-rays</td>
<td>2.5</td>
</tr>
<tr>
<td>10 MeV protons</td>
<td>4.7</td>
</tr>
<tr>
<td>150 MeV protons</td>
<td>0.5</td>
</tr>
</tbody>
</table>

LET versus Depth

40 MeV

100 MeV

250 MeV

Depth (cm)
Relative Biological Effectiveness

- Equal doses of difference types of radiation do not produce equal biological effects

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

- RBE depends on
  - Dose
  - Biological system (cell type)
  - Clinical endpoint (early or late effects)

RBE for Protons

- RBE is a function of LET
  - RBE is not constant with depth
  - Must be careful at the distal end of the target and/or near critical structures

- Clinical RBE for protons $\approx 1.1$
  - 1 Gy proton dose $\approx 1.1$ Gy Cobalt dose
  - A single value might not be sufficient

1.7
1.3
1.5
160 MeV
RBE

0.9
0.9
1.1
1.7

Clinical RBE

low
high

0.6
0.2
1.0

Depth [cm]

Modulated beam

Relative dose

Source: S.M. Seltzer, NISTIIR 5221
Depth Dose


http://commons.wikimedia.org/wiki/Category:Radiation_therapy
Cobalt-60

20 MV X-rays

160 MeV Protons

Proton Beam Requirements

- Maximum energy should be about 250 MeV
- Energy should be variable starting at \( \sim 70 \) MeV
- The accelerator should be as small as possible with minimum weight
Cyclotron

Magnet

“Dees”

RF

Magnetic Field

Proton
Source

Proton Beam

\[ \vec{F}_{mag} = q \cdot (\vec{v} \times \vec{B}) \]

\[ \vec{F}_{ele} = q \cdot \vec{E} \]
Proton Beams

- Currently, two proton accelerator options based on the cyclotron
  - Cyclotron
    - Protons revolve at the same frequency regardless of energy or orbit radius
  - Synchrotron
    - The magnetic field strength and RF frequency are increased in synchrony with the increase in beam energy
Cyclotron versus Synchrotron

• **Cyclotron**
  – Fixed-energy accelerator
  – Capable of high beam currents
  – Neutrons created in clinical beams

• **Synchrotron**
  – Produces proton beams of variable energies
  – Lower weight and power consumption
  – Low neutron production in clinical beams
Clinically Useful Proton Beams

• There are two main approaches

• Passive scattering systems
  – Fixed depth of penetration
  – Fixed modulation

• Active scanning systems
  – Irradiation the target using a narrow beam
  – Beam controlled in three dimensions
Passive Scattering

Active Scanning

Active (Raster) Scanning

Treatment Planning

• Acquisition of imaging data (CT, MRI)
• Conversion of CT values into stopping power
• Delineation of regions of interest
• Selection of proton beam directions
Treatment Planning

• Design of each beam

• Optimization of the plan
  – Including variable energy with each beam

• Dose calculation models
  – Broad beam (measurement)
  – Pencil beam
  – Monte Carlo
Dose Distributions

Dose Distributions

Dose Distributions

PET Treatment Verification

Remmele et al. A deconvolution approach for PET-based dose reconstruction in proton radiotherapy. PMB 2011.
Challenges in Proton Therapy

• Patient related
  – Patient setup/movements, Organ motion, Body contour, Target definition

• Biology related
  – Relative biological effectiveness (RBE)

• Physics related
  – CT number conversion, Dose calculation

• Machine related
  – Device tolerances, Beam energy
Final Comments
Magnetic Resonance Imaging

• Physics of magnetic resonance imaging
  – Nuclear magnetic resonance
  – Image creation

• Uses of MRI in radiotherapy
  – In-room systems and functional imaging
A Bit of MRI History

• Found a method to tune in on magnetic fields of spinning nuclei in 1946

• First MR image formed in 1973
  – 1973 a short paper was published in Nature entitled "Image formation by induced local interaction; examples employing magnetic resonance". The author was Paul Lauterbur, a Professor of Chemistry at the State University of New York at Stony Brook.

• The first commercial MR scanner installed in 1983
  – The Department of Diagnostic Radiology at the University of Manchester Medical School in Europe (from Picker Ltd.)
Another Use of Radiation

Wavelength (meters)
- Radio: $10^3$
- Microwave: $10^{-2}$
- Infrared: $10^{-5}$
- Visible: $.5 \times 10^{-6}$
- Ultraviolet: $10^8$
- X-ray: $10^{-10}$
- Gamma Ray: $10^{-12}$

About the size of...
- Buildings
- Humans
- Honey Bee
- Pinpoint
- Protozoans
- Molecules
- Atoms
- Atomic Nuclei

Frequency (Hz)
- MRI: $10^4$
- CT: $10^8$
- RT: $10^12$
- Pet: $10^{15}$
- Saw: $10^{16}$
- Cross: $10^{18}$
- Toc: $10^{20}$

mynasadata.larc.nasa.gov

Spring 2012 Refresher Course
April 13-15, 2012 | Westin Chicago River North | Chicago
ASTRO
Constituents of Matter

- Atoms → Nucleus + Electrons → Protons
- Charged particle’s spin
  - Angular momentum suggested by Pauli in 1924
  - A spinning charge creates a magnetic field, $\vec{B}$

Bushburg et al. The Essential Physics of Medical Imaging. 2nd Ed, 2002. Fig 14-2.
Apply External Magnetic Field

- Charged particles precess about the magnetic field
- Net magnetic moment

External magnetic field ($\vec{B}_0$) applied

Bushburg et al. The Essential Physics of Medical Imaging. 2nd Ed, 2002. Fig 14-3.
Magnetic Properties

- Processional frequency depends on field strength and type of nucleus, $\omega_0 = \gamma B_0$
  - $\gamma$ is the gyromagnetic ratio

<table>
<thead>
<tr>
<th>Nuclei</th>
<th>$\gamma/2\pi$ (MHz/T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^1$H</td>
<td>42.58</td>
</tr>
<tr>
<td>$^{23}$Na</td>
<td>11.3</td>
</tr>
<tr>
<td>$^{13}$C</td>
<td>10.7</td>
</tr>
</tbody>
</table>
$M_z$ -- Longitudinal Magnetization

Equilibrium -- more spins parallel than anti-parallel

Equal numbers of parallel and anti-parallel spins

$B_0$ -- Magnetic field

More anti-parallel spins than parallel

Resonance frequency
$42.58$ MHz / T

RF pulse ($B_1$ field)

Time of $B_1$ field increasing

Excited spins occupy anti-parallel energy levels

Bushburg et al. The Essential Physics of Medical Imaging. 2nd Ed, 2002.
$M_x(t) \propto e^{-t/T_2}$

T2 Dephasing

$M_z(t) = M_0(t) \cdot \left(1 - e^{-t/T_1}\right)$

T1 Relaxation
T1 and T2

• T1, longitudinal relaxation time
  – Restoration of the precession of the nuclei in the static B field

• T2, transverse relaxation time
  – Following the RF excitation, the free induction signal vanishes because the transverse component of the magnetization decays

• T1 and T2 are tissue specific
  – Distinguishing characteristic of tissues that makes nuclear magnetic resonance useful for imaging
Bloch and Purcell

- Detecting energy changes
- All modern MRI signals work on these principles

Magnetic Fields

- **Units of magnetic field strength**
  - Tesla (SI units); \((\text{newton} \cdot \text{second}) / (\text{coulomb} \cdot \text{meter})\)
  - Gauss (cgs units); 1 tesla = 10,000 gauss

<table>
<thead>
<tr>
<th>Item</th>
<th>Magnetic field strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Earth’s magnetic field**</td>
<td>0.000025 – 0.000065 T</td>
</tr>
<tr>
<td>Hair dryer, Electric shaver*</td>
<td>0.000065 T</td>
</tr>
<tr>
<td>Really strong refrigerator magnet**</td>
<td>0.01 T</td>
</tr>
<tr>
<td>Typical clinical MRI</td>
<td>0.5 – 3.0 T</td>
</tr>
</tbody>
</table>

**http://www.magnet.fsu.edu/education/tutorials/magnetminute/tesla-transcript.html
Pulse Sequences

• Spin Echo

  - First tip by 180°, then let decay (longitudinally) for TI (~300ms)
  - Then add on a standard spin echo (90° + 180°)
  - Can repeat for several TI’s.
  - Images are heavily T1-weighted

• Inversion recovery

Slide Courtesy Shantanu Sinha, PhD, UC San Diego
## Typical T1 and T2 Values

<table>
<thead>
<tr>
<th>Tissue</th>
<th>T1 for 0.5 T (msec)</th>
<th>T1 for 1.5 T (msec)</th>
<th>T2 (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat</td>
<td>210</td>
<td>260</td>
<td>80</td>
</tr>
<tr>
<td>Muscle</td>
<td>550</td>
<td>870</td>
<td>45</td>
</tr>
<tr>
<td>White matter</td>
<td>500</td>
<td>780</td>
<td>90</td>
</tr>
<tr>
<td>Gray matter</td>
<td>650</td>
<td>900</td>
<td>100</td>
</tr>
<tr>
<td>CSF</td>
<td>1800</td>
<td>2400</td>
<td>160</td>
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![Image of MRI scans](image-url)
T1 Weighted

Image Contrast

T2 Weighted Image Contrast

Bushburg et al. The Essential Physics of Medical Imaging. 2nd Ed, 2002. Fig 14-23.
Proton Density Weighted Image Contrast
FLAIR

Inversion Time (TI)  TE/2  TE/2

180°  90°  180°
An image of N x N pixels requires N independent projections, each defined by N points.

MR image reconstruction by back projection of the MR frequency domain signal is equivalent to using the CT attenuation profiles to create a CT image.
Both vials resonate at:

\[ \omega_0 = \gamma B_0 \]

Vials resonate at:

\[ \omega(x) = \omega_0 \gamma \left( \frac{\delta \bar{B}}{\delta x} \right)_x \]

Image Construction

• To make a “slice” (i.e., constrain z), make the RF excitation itself spatially-selective.

\[ B > B_0 \]
\[ B = B_0 \]
\[ B < B_0 \]
\[ \omega > \omega_0 \]
\[ \omega = \omega_0 \]
\[ \omega < \omega_0 \]
\[ \omega_0 = \gamma B_0 \]
Slice Thickness

Signal is proportional to the number of protons per voxel. As slice thickness increases, the number of protons increases linearly with slice thickness. Partial volume effects also increase with slice thickness. Thinner slices are always preferred since they offer better resolution but are limited by SNR and gradients.
Enhanced Contrast

Gadolinium T1 contrast enhancement by IV injection of exogenous contrast agent.

Slide Courtesy Shantanu Sinha, PhD, UC San Diego
Contrast From Flow

MR Angiography utilizes inherent differences in contrast between flowing (blood) spins and stationary tissue.

Time-of-Flight MRA for visualization of vasculature.

Slide Courtesy Shantanu Sinha, PhD, UC San Diego
MRSI

- MR spectroscopy and MR imaging methods
  - Produce a spectrum identifying different chemical compounds (metabolites) in various tissues

- Metabolite ratios differentiate between active tumor, normal tissue, and necrosis

In-Room MR Technologies

Courtesy of Viewray, Inc.

In-Room MR Technologies


Question #1

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