MAGNETIC FOCUSED PROTON RADIOGRAPHY AND ITS IMPLICATIONS FOR PROTON BEAM GUIDANCE, ANATOMICAL ALIGNMENT AND ADAPTIVE THERAPY

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EDUCATIONAL OBJECTIVES

• UNDERSTAND THE CONCEPT OF MAGNETIC-FOCUSED PROTON RADIOGRAPHY

• UNDERSTAND HOW BEAM'S-EYE-VIEW PROTON RADIOGRAPHY CAN BE USED TO GUIDE TREATMENT

• EXPLORE THE IMPLICATIONS THAT THIS COULD HAVE FOR ADAPTIVE PROTON THERAPY
• **LANL**: 11,000 students and staff  
  • budget: $2.2B  
  • **LANSCE**: 450 students and staff  
  • estd. 1972  
  • 800 MeV proton / H⁺ linac  
  • 17 mA max current  
  • accel. rate: 1.0 MeV/m  
  • $\Delta E/E$: 0.1%  
  • emittance ($1\sigma$): 0.3 $\pi$ mm-mrad  
  • **pRad**: 20 students and staff
WHY PROTONS?

- complex geometries
- large volumes
- near sensitive tissues

Tochner Z. Rationale for Particles. PTCOG 2018.

complications of this treatment could include

- clinical nephritis
- radiation myelitis
- radiation induced liver disease
- pericarditis
- bowel obstruction / perforation

CRANIOSPINAL COMPARISON ACROSS 15 TREATMENT CENTERS

- dosimetric comparison on 14-y.o. patient
- 36.0/1.8 Gy
- dose reductions of >10 Gy to parotid, thyroid and pancreas


PBT may reduce:
- secondary maliganancies
- primary hypothyroidism
- cardiovascular events
- restrictive lung disease
- metabolic syndrome
THE BRAGG PEAK GIVES PROTONS DESIRABLE DOSE-DEPTH CHARACTERISTICS

The spread-out Bragg peak paints the tumor with dose

Bragg peak in A-150 TEP (Geant4)
PROTON TREATMENTS ARE LIMITED WITH PASSIVE SCATTERING

- large penumbra
- limited conformity
- no adaptability

• penumbra determined by FWHM of pencil beam at end of range
  • pencil beam diameter $\otimes$ scatter in the patient
• "adaptable*"
  *notice a change in daily CBCT, send patient home, re-plan, begin again the next day
NEXT STEPS IN PROTON THERAPY

- Multi-Field Optimized (MFO) is replacing Single-Field Uniform Dose (SFUD)\(^1\)
  - akin to IMPT
- The **robust treatment plan** is replacing the PTV\(^2\)
  - define acceptable uncertainties for the CTV and let TPS do the rest
  - ex.: Match cribiform plate to 2 mm, spine anterior to 3 mm, and 5 mm to spine Rt./Lt./Post.
- These advances are heavily reliant on **imaging**, such as:
  - CT-on-rails, positioned 1.5 m from Tx isocenter
  - accommodating daily changes in the immobilization device / skin folding
  - Post-Tx PET (\(^{11}\)C / \(^{15}\)O) or prompt gamma treatment verification
- Adaptive treatments?

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\(^1\)Flanz J. Technical Aspects of Beam Delivery. PTCOG 2018.
orthogonal X-ray or CBCT registers the patient. Shouldn't we use the same modality?

Shimizu S, et al. PLOS One, 9.4 e94971 (2014)

Proton therapy in the U.S. closest center: Phoenix

PBT growth
RADIOGRAPHY: A TRANSMISSIVE COMPARISON

1 cm tissue target

20 cm tissue target

150 keV $\gamma$

150 keV $\gamma$

15 MeV $p^+$

800 MeV $p^+$

FULL ABSTRACT: Energetic protons from an accelerator may be used to produce radiographs showing unusually high contrast but relatively poor spatial resolution.
1974: SCATTER PROTON RADIOGRAPHY

meanwhile, at LANSCE:

- edge detection
- thin objects
- contrast from position dependent scattering

it doesn't quite work for thick objects
PARTICLE TRACKING PROTON RADIOGRAPHY


- backprojected 100 iterations
- resolution enhanced by $\times 8$
- 1 proton at a time!
MULTIPLE COULOMB SCATTERING DOMINATES RESOLUTION

\[ \theta_o = \frac{13.6 \text{MeV}}{\beta p} \sqrt{\frac{x}{X_0}} \left[ 1 + 0.038 \ln \left( \frac{x}{X_0} \right) \right] \]


RMS width
full width half maximum=2.35 \( \theta_o \)

- \( x \): areal density (g cm\(^{-3}\))
- \( X_0 \): radiation length (cm\(^2\) g\(^{-1}\))
- \( \beta \): relativistic velocity
- \( p \): momentum
MAGNETIC FOCUSED PROTON RADIOGRAPHY

- instantaneous imaging (200 ns)
- $10^9$ protons at once
- focusing lens corrects for scatter
- resolution: 200 µm

Horizontally focusing orientation
The way that protons are transported through the magnetic lens system is described by the \textbf{R-matrix}.

Because we are only interested in position, this can reduce to 2 terms.

The magnetic lens is tuned such that $R_{12}$ is zero, effectively leaving the $R_{11}$ term: magnification.

At the Fourier plane within the lens, the inverse is true:

Here, position is exclusively a function of angle, enabling selective collimation.
SYSTEM TRANSMISSION IS CONTROLLED BY THE COLLIMATOR

\[ T_{\text{nuclear}} = e^{-\frac{x}{L}} \]

nuclear removal processes:
Beer's law

\[ T_{\text{MCS}} = 1 - e^{-\frac{-\theta^2}{2\theta^2}} \]

system removal:
• \( \Theta_o \): scattering angle (radians)
• \( x \): areal density (g cm\(^{-3}\))
• \( X_0 \): radiation length (cm\(^2\) g\(^{-1}\))
• \( \beta \): relativistic velocity
• \( p \): momentum

\[ \theta_o = \frac{13.6 \text{MeV}}{\beta p} \sqrt{\frac{x}{X_0}} \left[ 1 + 0.038 \ln \left( \frac{x}{X_0} \right) \right] \]

\[ T = e^{-\frac{x}{L}} \left( 1 - e^{-\frac{-\theta^2}{2\theta^2}} \right) \]

total estimated transmission
AT THE FOURIER PLANE: ANGLE OF SCATTER BECOMES POSITION

incident beam after object after collimator

matching identity lens

protons focusing quadrupole magnetic fields
defocusing quadrupole magnetic fields

transmission

\[ T_{MC} = 1 - e^{-\theta^2/2\sigma^2} \]
THE DETECTION PLANE: X-RAY FLAT PANELS

- our standard ultra-fast camera system is not necessary
- flat panel detectors are off-the-shelf detection planes
  - 100 µm resolution
  - 3 Hz

- results show direct detection in amorphous silicon layer
- future work will implement microcolumnar CsI to acquire imaging with less dose
Limn: To outline in clear sharp detail

Like phase-contrast radiography:
- Useful to enhance edges
- Problem for density reconstruction

Resolution proportional to energy offset

$$\sigma = \theta l_c \frac{E - E_f}{E_f}$$

780 MeV  800 MeV

Protons

tomographic limning challenge object
These are 800-MeV proton radiographs acquired at LANL:
- 200 ns flash acquisition
- $10^9$ protons / image
- 1 - 10 $\mu$Gy / image

Goals for proton radiography:
- anatomical, beam's-eye-view alignment
- increased treatment planning accuracy
CALCULATING THE WATER EQUIVALENT THICKNESS

from before:

\[ T_{\text{nuclear}} = e^{\frac{-x}{\lambda_c}} \]

this tells us that our transmission is directly a function of areal density \( (x) \), nuclear interaction length \( (\lambda_c) \) and radiation length \( (X_0) \).

\( p, \beta, \) and \( \Theta_c \) are fixed by the system.

\[ T_{\text{MCS}} = 1 - e^{\frac{-\theta^2}{2\sigma^2}} \]

\[ \theta = \frac{14.1\text{MeV}}{p\beta} \sqrt{\frac{x}{X_0}} \]

\[ T = e^{\frac{-x}{\lambda_c}} \left( 1 - e^{\frac{-\theta p \beta}{14.1\text{MeV} 2x}} \right) \]

→ fix some values for water:
\( \lambda_c = 57.3 \text{ g cm}^{-2} \)
\( X_0 = 36.08 \text{ g cm}^{-2} \)

→ result is an areal density calculation of the WET

→ areal density images are tomographically reconstructed for a 3D WET map that can be used for treatment planning
FROM SYSTEM TRANSMISSION TO WET

- transmission directly maps to water equivalent thickness
- more work to do: errors can be reduced with a water-equivalent step wedge calibration in FoV

- atelectasis increased the WET of the lung → under-ranging and loss of CBCT coverage
THIS ALL NEEDS TO MOUNT IN A GANTRY
THIS ALL NEEDS TO MOUNT IN A GANTRY

- rapid diffuser insert converts from treatment mode to radiographic mode
- field is 0 at quad center, allowing pencil beam transport to nozzle
• magnets can be made smaller, if superconducting
• higher energy \(\rightarrow\) higher quality radiography
• at 330 MeV, resolution is:
  • 0.5 mm through 5-cm tissue
  • 0.8 mm through 10-cm tissue
massive, energetic particles tend to resist collimation and thus the field remains with pencil beam rastering.

collimation \rightarrow 
unwanted neutron dose
TWO-STAGE COLLIMATION REJECTS PROTONS EFFICIENTLY

• MLC: 4" tungsten leaves
• 3-mrad 6" thick W collimator: 64:1 dose ratio
• 7.5-mrad 12" thick PE collimator: 120:1 dose ratio

Can this lead to real-time adaptive proton therapy?

dose map at the image location
NEXT STEPS: TREATMENT PLAN VALIDATION

- Commission eclipse with LANSCE
- Plan treatments with WET proton radiographs

Eclipse Proton Therapy T.P.S.
(e.t.a. Aug.)
NEXT STEPS: HIGHER ENERGY TREATMENTS?

- use the tightly constrained lateral spread of higher-energy protons to deliver a stereotactic dose
- how does this stack up to Bragg peak radiotherapy? The Eclipse TPS will help us answer that question.


Bending radii become large and gantries unfeasible (imaging lens up and downstream) → rotate the upright patient.

FWHM of perfect pencil beam is 5 mm for 800 MeV protons vs. 16 mm for 250 MeV, at the 250-MeV Bragg depth.

NEXT STEPS: PROTON RADIOGRAPHY OF CANCEROUS MICE

- Immuno-suppressed mice are injected with 4T1 cancer line
- Tagged with various quantities of Au or Fe nanoparticles, saline, or nothing

The realities of working at LANL:
- The mice are ready and on ice
- delayed by 6 months due to some bureaucracy
- imaging proceeds next Wednesday

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SUMMARY AND TAKE-AWAYS

- Proton therapy may help with the sparing of OARs in particular cases
- The future proposed advancements in proton therapy rely heavily on imaging
- Magnetic focused proton radiography can meet this need because it is:
  - instantaneous
  - high-resolution
  - able to provide WET data
- Daily proton-CTs can evaluate tumor shrinkage and organ motion
- Real-time, beam's-eye-view imaging can be used for:
  - anatomical alignment
  - motion gating
  - adaptive therapy
- Adaptive therapy can proceed by:
  - modulating active scanning in real time
  - collimating a stereotactic proton beam
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