Future directions and current challenges of proton radiotherapy.

Tony Lomax
Centre for Proton Radiotherapy, Paul Scherrer Institute, Switzerland
Overview of presentation

• New developments in treatment delivery
  • Current challenges
  • Potential solutions
  • Summary
Industrial suppliers of radiotherapy equipment

Manufacturers currently offering photon therapy equipment

Varian
Elekta
Tomotherapy
Siemens

Manufacturers currently offering particle therapy equipment

IBA*
Hitachi*
Optivus*
Varian/Accell**
Siemens**
Still River systems

* Scanning option available
** Scanning only
Laser based acceleration

- Petawatt laser beam
- Thin film target (~μm)
- Cloud of electrons stripped from target by laser
- Layer of CH or H₂O
- Protons accelerated to MeV energies in a few mm
- Very high resulting electric field

New developments in treatment delivery

Nuclear data for science and technology: Medical applications
Laser based acceleration

**Energy spectrum**

- **Maximum** proton energy reported so far is $E_p \approx 60$ MeV
- **High intensity** ($10^9$-$10^{11}$ protons) in very short pulse (~ns)
- **Very poor** (broad) energy spectrum

Laser based acceleration
Achieving mono-energetic spectrums

\[ I = 3 \times 10^{19} \text{ W/cm}^2 \]

5μm thick Ti foil

0.5μm thick PMMA dot (20x20μm)

1.2 MeV ‘mono’-energetic protons produced

Dielectric Wall Accelerators

Laser → Optical Coupling

Proton Source → Focusing

Progressively firing Blumlein transmission lines

SiC Optical Switches → Monitor → Stack of Blumleins

Thanks to Rock Mackie, UWisc/Tomotherapy Inc
Dielectric Wall Accelerators

• DWA is a multi-stage inductive accelerator under development at Lawrence Livermore National Lab.

• Acceleration gradient of 100 MV/m possible.

• 200 MeV protons in 2 meters.

• This has been demonstrated in ‘small’ examples, with lengths of 2mm!

• Beam energy, intensity and spot size variable pulse-to-pulse.
Dielectric Wall Accelerators

Proton tomotherapy

- Incorporation of DWA into a CT like treatment gantry for rotational delivery of proton therapy
- Single room facility
- Diameter ~ 5m
- Under investigation by Tomotherapy Inc. and LLNL

G Caporaso, S Hawkins LLNL
Proton Multi-leaf collimators

Particle MLC from Chiba (Japan)

• Saves changing collimators every field
• Can be used to ‘simulate’ scanning
Proton Multi-leaf collimators

Film dosimetry performed at Loma Linda using MLC and passively scattered proton beam

Shape at surface

Shape after 29cm water

Mike Moyers, Loma Linda
Proton Multi-leaf collimators
Simulated scanning using dynamic MLC’s

MLC opening

Energy 1

Energy 2

Energy 3

Energy 4

Energy 5

Energy 6

Proximal conformation
Overview of presentation

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  - Potential solutions
- Summary
Current challenges

• The neutron problem
• Range uncertainty
• Dealing with organ motion
Neutron dose during proton therapy: Is there a problem?


Neutron equivalent dose a factor 10 higher for passive protons than for IMRT?

Fig. 10. The equivalent dose outside the edge of the treatment field as a fraction of the dose at the isocenter for protons with passive modulation, for a scanning proton beam, and for 6-MV X-rays, either 4-field conformal radiation therapy (CRT), or intensity-modulated radiation therapy (IMRT). The doses are rough estimates and are likely to be highly facility dependent. The passivemodulation: proton data are from Yan et al. (19), renormalized to a 10-cm × 10-cm field and to a neutron relative biologic effectiveness (RBE) or quality factor of 10. The pencil-beam scanning proton data are from Schneider et al. (18), renormalized to a 10-cm × 10-cm field and an RBE or quality factor of 10. Both proton curves were produced by Dr. Harald Paganetti, Massachusetts General Hospital and Harvard Medical School. X-ray data are 4-field CRT and IMRT. Unpublished data for a 6-MV linear accelerator were provided by Dr. C. W. Wu, Columbia University Medical Center, New York.
Neutron dose during proton therapy: Is there a problem?

- Neutron dose equivalent from spot scanning and 15MV photons:

- Irradiation of 10 cm x 10 cm (x10cm) target to 50Gy


- Higher neutron dose in direction of beam
- Comparable neutron dose laterally
- Neutron dose very small compared to primary dose (~1000x smaller)
Current challenges: the neutron problem

Neutron dose during proton therapy: Is there a problem?

- Passive Modulation_1: Yan et al.
- Passive Modulation_2: Mesoloras et al.
- IMRT: Stovall et al. (3DCRT up-scaled by a factor of 3)
- Scanning: Schneider et al.
Neutron dose during proton therapy: Is there a problem?

Don’t forget primary dose – in this case reduced by a factor 6 for proton vs photons!
Current challenges

- The neutron problem
- Range uncertainty
- Dealing with organ motion
The advantage of protons is that they stop.

The disadvantage of protons is that we don’t always know where…

10% range error
Sources of range uncertainties

- Limitations of CT data (beam hardening, noise, resolution etc) \([\Sigma \sim 1\%]\)
- Calibration of CT to stopping power \([\Sigma \sim 1-2\%]\)
- CT artifacts \([\Sigma]\)
- Variations in proton beam energy \([\sigma (\sim 0.1\%)]\)
- Variations in patient positioning \([\sigma (\sim 1-3\text{mm})]\)
- Variations in patient anatomy \([\Sigma,\sigma]\)
The problem of CT artifacts

Rutz et al (PSI), To be submitted to IJROBP

Current challenges: range uncertainty

Future directions and current challenges for proton therapy. Tony Lomax
The problem of CT artifacts

- More advanced initial tumour at diagnosis?
- Problems in defining CTV?
- Problems in dose calculation?
- Problems in range calculations?

Rutz et al (PSI), To be submitted to IJROBP
Variations in patient anatomy

Patient set-up inaccuracies


Image courtesy of Thomas Bortfeld, MGH, Boston
Variations in patient anatomy

Patient set-up inaccuracies


Image courtesy of Thomas Bortfeld, MGH, Boston
Variations in patient anatomy

3 field IMPT plan to an 8 year old boy

During treatment, 1.5kg weight gain was observed

Note, sparing of spinal cord in middle of PTV

Max range differences:
- SC 0.8cm
- CTV 1.5cm

Francesca Albertini and Alessandra Bolsi (PSI)
Current challenges: range uncertainty

Variations in patient anatomy

Dose differences

Differences between nominal and ‘weight gain’ CT’s

Francesca Albertini and Alessandra Bolsi (PSI)
Current challenges

• The neutron problem
• Range uncertainty
• Dealing with organ motion
Current challenges: organ motion

Organ motion and range uncertainty

Exhale

Inhale

4D-CT

Engelsman et al., IJROBP 64(5):1589-1595, 2006

Images courtesy of Thomas Bortfeld, MGH, Boston

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Tony Lomax
Organ motion and the ‘interplay’ effect

A scanned beam in a static patient...

4D-CT derived from 4D-MRI

Martin von Siebenthal, Phillipe Cattin, Gabor Szekely, Tony Lomax, ETH, Zurich and PSI, Villigen

Current challenges: organ motion

Future directions and current challenges for proton therapy. Tony Lomax
Organ motion and the ‘interplay’ effect

…but real patients move.

4D-CT derived from 4D-MRI

Martin von Siebenthal, Phillipe Cattin, Gabor Szekely, Tony Lomax, ETH, Zurich and PSI, Villigen
Assume $\sigma = 0.5$ cm

For this example, dose errors of $\sim 20\%$ can result from motion (positioning) errors of 2.5 mm

Phillips et al., PMB, 37:223-234, 1992
Organ motion and the ‘interplay’ effect

Nominal (static) dose

Calculated with ‘real’ motion from 4D-MRI of volunteer

Current challenges: organ motion
Organ motion and the ‘interplay’ effect

Motion patient 1
Amplitude ~ 11mm

Motion patient 2
Amplitude ~ 8mm
Overview of presentation

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Potential solutions to …

• …range uncertainty

• …the organ motion problem
Mega-Voltage CT for artifact free imaging

kV-CT

Accuracy of range calculation due to reconstruction artifacts?

MV-CT (tomotherapy)

No artifacts and linear relationship CT units to proton stopping power

Francesca Albertini (PSI)
Mega-Voltage CT for artifact free imaging

Stopping power profiles

- kV-CT
- MV-CT

Prostheses

Francesca Albertini (PSI)

Potential solutions to range uncertainty

Nuclear data for science and technology: Medical applications

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Range adapted proton therapy
Automatic adaptation of Bragg peak ranges on a spot by spot basis depending on local change in range
Range adapted proton therapy

Automatic adaptation of Bragg peak ranges on a spot by spot basis depending on local change in range
Range adapted proton therapy

Automatic adaptation of Bragg peak ranges on a spot by spot basis depending on local change in range
Range adapted proton therapy

Potential solutions to range uncertainty

DVH

- nominal CTV
- not adapted CTV
- range adapted CTV
- nominal CE
- not adapted CE
- range adapted CE

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Tony Lomax
Robust planning techniques

Example paraspinal case

Tumour

Spinal cord

Nominal plan
10% overshoot

Robust planning techniques

3 patched, intensity modulated fields....

...give a homogenous dose without the use of fields that abut distally against the spinal cord

Robust planning techniques

Nominal plans 10% overshoot plans

IMPT

Single field

DVH analysis

Spinal cord

Potential solutions to range uncertainty

Future directions and current challenges for proton therapy.
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Robust planning techniques

Incorporate range uncertainty into optimisation function using gaussian probability functions for range uncertainty

E.g.

\[
\min_w \quad \mathbb{E}(w) := \int \sum_{i \in PAT} \alpha_i \left[ D_i(w, \bar{\rho} + \sigma \delta) - D_i^{\text{pres}} \right]^2 P(\delta) d\delta
\]

subject to

\[ w_j \geq 0 \quad (\forall j \in PB) \]

Where \( \bar{\rho} + \sigma \delta \) assigns an uncertainty to the range of each pencil beam in the optimisation

Unkelbach et al, PMB, 52;2755-2773, 2007
Robust planning techniques

Field 1
Field 2
Field 3

Total dose

Optimised fields using ‘robust’ optimisation

Unkelbach et al, PMB, 52;2755-2773, 2007

Potential solutions to range uncertainty

Future directions and current challenges for proton therapy. Tony Lomax
Robust planning techniques

Effect of 5mm range uncertainty on robustly optimised plan

nominal range 5 mm undershoot 5 mm overshoot

Unkelbach et al, PMB, 52;2755-2773, 2007
Potential solutions to ...

• ...range uncertainty
• ...the organ motion problem
Tumour tracking

Track motion of tumour using scanning system based on some anatomical/physiological signal

+ Most conformal
+ Most efficient
- Very complex!
- Difficult QA
- Reliability of tracking signal?
Tumour tracking

Dose heterogeneity as function of tracking delay

- Nominal
- With motion

Steven van de Water, PSI
Rescanning

Repaint scanned beam many times such that statistics dictate coverage and homogeneity of dose in target (c.f. fractionation)

+ Simple method
+ Robust
- Fast scanning required
- Not very conformal
Applying the total prescribed dose in $n$ steps (each spot is applied $n$ times rather than once) provides a better homogeneity. The error is statistically decreased by $\sqrt{n}$.

Christian Hilbes, PSI
Potential solutions to organ motion

Rescanning

Analysis of Cos^4 motion with 1cm peak-to-peak amplitude

- Cylindrical target volume
- Re-scanned different times to same total dose
- Scan times calculated for realistic beam intensities and dead times between spots
- Analysis carried out for different periods of motion

Not always improving homogeneity with number of re-scans!

Marco Schwarz, Trento
The ‘synchronicity’ effect

- Very preliminary results
- A ‘real’ effect for perfectly regular breathing?
- Could well be less of an issue when breathing is more irregular
- For regular breathing, could be avoided by selecting the re-scanning period to avoid effect or varying period scan-to-scan
- Probably not a big issue in reality?

Marco Schwarz, Trento
Gating

Reduce magnitude of motion by gating delivery to small window of motion cycle

+ Simple method
- Reliability of gating signal?
- Inter/intra fraction variability of motion?
- Residual motion?
Gating

- 4D dose calculation applied to cylindrical target in presence of ‘real’ motion (4D-MRI of volunteers) in liver
- Calculations performed for static, 100, 50 and 30% duty cycles
- Gating signal taken from diaphragm wall motion (‘ideal’ gating)
- Irregularities in breathing and amplitude over duration of treatment taken into account

- Results for two volunteers
  1. $T_{av} = 4.7s, A_{av} = 10.9mm$
  2. $T_{av} = 7.1s, A_{av} = 8.3mm$
Summary.

• Proton therapy is fast moving from the research institute to the hospital

• Due to the adoption of proton therapy in a number of ‘flag-ship’ institutes in the USA, they will certainly have a higher profile in the next few years.

• Scanning and IMPT will play an ever increasing role in proton therapy, with most manufacturers offering or developing such systems

• However, proton therapy brings challenges in dosimetry, delivery accuracy and organ motion management

• There’s lot’s of interesting science still to be done….!
## Acknowledgements

Eugen Hug - Head of department and medical chief

Eros Pedroni - Head of R&D and ‘brains’ of the spot scanning project at PSI

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<thead>
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<th>R&amp;D group</th>
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<tbody>
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Thanks for your attention…