

Targeting cancer with proton beams: $\overline{\bm{\cup}}$ **Developments at UCL Hospital**

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Significance of radiotherapy

The Royal College of Radiologists (RCR) estimates that, of those cancer patients who are cured:

- \Rightarrow 49% are cured by surgery
- \Rightarrow 40% are cured by radiotherapy
- \Rightarrow 11% are cured by chemotherapy

Rationale for hadron beam radiotherapy

Brief history of Proton Beam Therapy

- 1946: Therapeutic use of proton beams first proposed by Robert Wilson $¹$ </sup> ¹Wilson RR. Radiological use of fast protons. *Radiology.* 1946;47:487-491
- 1954: First patient treated at the UC Lawrence Berkeley Laboratory (LBL) – Treated the pituitary gland with beams passing entirely through the brain.

- 1957: Proton radiosurgical techniques for brain tumors developed at the Gustaf-Werner Institute, Uppsala, Sweden
	- First to use range modulation
- 1961: Radiosurgery of small intercranial targets at the Harvard Cyclotron Laboratory
- 70s 80s: Physics facilities worldwide notably, the Paul Scherrer Institute (PSI) in Switzerland
- 1989: The world's first hospital-based low-energy ocular proton beam therapy facility opened at Clatterbridge Cancer Centre, UK
- 1990: The world's first hospital-based high-energy proton beam therapy facility opened at Loma Linda University Medical Center, California
- 2000s : Rapid growth in number of proton facilities internationally

Particle Therapy Statistics in 2014

Martin Jermann, MSc

Secretary of the Particle Therapy Cooperative Group Paul Scherrer Institute, Villigen, Switzerland

No. of Patients Treated (1955-2014) 160000 60 140000 50 in Clinical Operation 120000 40 100000 80000 30 **Patients** of Facilities **Facilities** ð 60000 <u>g</u> 20 40000 $\begin{array}{c} 10 \end{array}$ 20000 $\mathbf{0}$ - 32, 36, 36, 31, 31, 38, 32, 32, 32, 30, 30, 30, 30, 30, 30, **Ref.: PTCOG, 2015**

Facilities in Clinical Operation and

Personal experience in proton beam radiotherapy

2002 – 2005: 2005 – 2013:

- •First hospital-based high-energy proton therapy facility in the world.
- •First patient treated in 1990
- •18,362 patients treated by end of 2014*

- •World-leading cancer treatment and research center.
- •Proton Therapy Center opened in 2006
- •First in the USA to treat with PBS in 2008
- •5,838 patients treated by end of 2014*

OMA LINDA UNIVERSITY.

- •250 MeV synchrotron developed in collaboration with Fermi National Accelerator Laboratory
- •3 gantries (passive scattering)
- •1 fixed clinical beamline (passive scattering)
- •1 fixed ocular beamline (passive scattering)
- •1 fixed experimental beamline (passive scattering)

THE UNIVERSITY OF TEXAS

DAnderson Pancer Center

Making Cancer History®

- •250 MeV synchrotron (Hitachi PROBEAT system)
- •3 gantries (2 passive scattering + 1 pencil beam scanning)
- •1 fixed clinical beamline (passive scattering)
- •*1 fixed ocular beamline (passive scattering)*
- •*1 fixed experimental beamline (passive scattering)*

THE UNIVERSITY OF TEXAS
MDAnderson

Current Indications for NHS Patients Travelling Abroad for PBT

- **Adult**
- Base of Skull & Spinal Chordoma
- Base of Skull Chondrosarcoma
- Spinal & Paraspinal Bone and Soft Tissue Sarcomas (Non Ewing's)

• **Paediatric**

- Base of Skull & Spinal Chordoma
- Base of Skull Chondrosarcoma
- Spinal & Paraspinal 'adult type' Bone and Soft Tissue Sarcomas
- Rhabdomyosarcoma
- Orbit
- Parameningeal & Head & Neck
- Pelvis
- Ependymoma
- Ewing's Sarcoma
- Retinoblastoma
- Pelvic Sarcoma
- Optic Pathway and other selected Low Grade Glioma
- Craniopharyngioma
- Pineal Parenchymal Tumours (not Pineoblastoma)
- Esthesioneuroblastoma

What will UK service look like?

- 2 sites selected
	- The Christie (Manchester)
	- UCLH (London)
- 2 Sites, 1 Service
	- Integrated clinically within the hospital setting
	- Integrated with existing conventional photon facilities
	- Collaboration across all areas
		- Referral
		- Protocol Development
		- Technology
		- Research
	- Due to open in 2018/2019

Why UCLH?

- Geographical access
- Viable centre size
- Integrated radiotherapy department
- High quality and recognised complex case mix
	- Largest paediatric practice in Europe

University College London Hospitals MFS **NHS Foundation Trust**

Green light for proton beam therapy centre

11 Mar 2015

The Department of Health has announced the preferred contractors for the building and supply of equipment for the proton beam therapy (PBT) service which will treat hundreds of patients each year at University College Hospital from 2018.

Green light for proton beam therapy centre Press Release Posted 11 March 2015

The Department of Health has announced the preferred contractors for the building and supply of equipment for the proton beam therapy (PBT) service which will treat hundreds of patients each year at The Christie from 2018.

VARIAN MEDICAL SYSTEMS SELECTED TO EQUIP TWO NATIONAL PROTON **THERAPY CENTERS IN ENGLAND** Mar 11, 2015

University College London Hospitals **NHS NHS Foundation Trust**

Zakrzewska P, Pitt M, **Amos RA**, D'Souza D & Ahmed T*.*

Application of building information modelling (BIM) in the design, construction, and operations management of a complex proton beam therapy facility in central London.

Proceedings of PTCOG 54. *Int J Particle Ther*. 2015;**2**(1):331-332

Operational Expectations

Facility opening times:

- 24Hour/day
- Clinical time:
	- 5 days per week
	- **14 Hours per day**
- **Quality Assurance Checks**
- **Naintenance Requirements**
- Research

Beam delivery system: Passive scattering

Beam delivery system: Pencil beam scanning

- 94 Energies: 72.5 221.8 MeV
- Range: 4.0 30.6 cm
- Adjustability: 0.1 cm
- Max field size: 30x30 cm²
- Beam size: $5 14$ mm σ (air)
- Energy absorber (*range shifter*)

Advantages of scanned beam delivery

- 1. Can "paint" any physically possible dose distribution.
- 2. Uses protons very efficiently as compared to passive scattering in which more than 50% of protons have to be "thrown away".
- 3. Generally requires no patient-specific hardware.
- 4. The neutron background is substantially reduced as a result of points (2) and (3).
- 5. Allows the implementation of IMRT with protons termed *intensity-modulated proton therapy (IMPT)*

Disadvantages of scanned beam delivery

1. The need to overcome *"interplay effects"* (Bortfeld, 2002)* induced by organ motion.

DOSIMETRIC COMPARISON OF THREE-DIMENSIONAL CONFORMAL PROTON RADIOTHERAPY, INTENSITY-MODULATED PROTON THERAPY, AND **INTENSITY-MODULATED RADIOTHERAPY FOR TREATMENT OF PEDIATRIC CRANIOPHARYNGIOMAS**

NICHOLAS S. BOEHLING, B.A.,* DAVID R. GROSSHANS, M.D., PH.D.,* JAQUES B. BLUETT, C.M.D., M.S.,[†] MATTHEW T. PALMER, C.M.D., M.B.A.,* XIAOFEI SONG, PH.D.,[†] RICHARD A. AMOS, M.Sc.,[†] NARAYAN SAHOO, PH.D.,[†] JEFFREY J. MEYER, M.D.,* ANITA MAHAJAN, M.D.,* AND SHIAO Y. WOO, M.D.*

Departments of *Radiation Oncology and [†]Radiation Physics, The University of Texas M. D. Anderson Cancer Center, Houston, TX

Int. J. Radiation Oncology Biol. Phys., Vol. 82, No. 2, pp. 643-652, 2012

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Medical Dosimetry, Vol. 35, No. 3, pp. 179-194, 2010 Copyright © 2010 American Association of Medical Dosimetrists Printed in the USA. All rights reserved 0958-3947/10/\$-see front matter

doi:10.1016/i.meddos.2009.05.004

ION STOPPING POWERS AND CT NUMBERS

MICHAEL F. MOYERS, PH.D., MILIND SARDESAI, PH.D., SEAN SUN, M.S., and DANIEL W. MILLER, PH.D.

Proton Therapy, Inc., Colton, CA; Long Beach Memorial Medical Center, Long Beach, CA; City of Hope National Medical Center, Duarte, CA; and Loma Linda University Medical Center, Loma Linda, CA

IOP PUBLISHING

PHYSICS IN MEDICINE AND BIOLOGY

Phys. Med. Biol. 57 (2012) 4095-4115

doi:10.1088/0031-9155/57/13/4095

Comprehensive analysis of proton range uncertainties related to patient stopping-power-ratio estimation using the stoichiometric calibration

Ming Yang^{1,2}, X Ronald Zhu^{1,2}, Peter C Park^{1,2}, Uwe Titt^{1,2},
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Wu R, **Amos RA**, *et al.* Effect of CT truncation artifacts on proton dose calculation. (Abstract) *Med Phys* **35**, 2697 (2008)

tissue equiv. material truncated

Site-specific range uncertainties caused by dose calculation algorithms for proton therapy

J Schuemann, S Dowdell¹, C Grassberger, C H Min² and H Paganetti

Department of Radiation Oncology, Massachusetts General Hospital and Harvard Medical School, Boston, MA 02114, USA

Phys. Med. Biol. 59 (2014) 4007-4031

LAD: Left Anterior Descending artery

In vivo proton range verification: a review

Antje-Christin Knopf and Antony Lomax

Center for Proton Therapy, Paul Scherrer Institut, Villigen, Switzerland

Phys. Med. Biol. 58 (2013) R131-R160

Range probe / proton radiography

•Possible prior, during and after field delivery •pCT only possible pre- or post-delivery

Prompt gamma

•Prompt γ emission within nanoseconds •Only applicable for on-line range verification

PET

•Possible on-line, or short time after irradiation •Biological wash-out can be an issue

MRI

•Retrospective range verification as a function of tissue change.

Proton CT

⁵¹¹ keV gammas

(Existing imaging systems designed for gamma energies of a few hunded keV)

Proton Beam Range Verification using Off-site PET by Imaging Novel Proton-Activated Markers

Jongmin Cho, Geoffrey Ibbott, Matthew Kerr, Richard Amos, and Osama Mawlawi

Proceedings: 2013 IEEE Nuclear Science Symposium & Medical Imaging Conference, Seoul, Korea.

Fig. 1. Proton nuclear interaction cross sections of 63 Cu and 68 Zn in comparison with tissue endogenous elements $-$ ¹²C and ¹⁶O.

Proton Radiation Biology Considerations for Radiation Oncologists

Wendy A. Woodward, MD, PhD,* and Richard A. Amos, MSc, FIPEM^{†,‡}

*Department of Radiation Oncology, University of Texas MD Anderson Cancer Center, Houston, Texas; [†]Department of Radiotherapy Physics, University College London Hospitals NHS Foundation Trust, London, United Kingdom; and [‡]Department of Medical Physics and Biomedical Engineering, University College London, London, United Kingdom

Biological effect: Biology based planning

What is the most important metric for proton planning?

Parallel plate ion-chamber "Peakfinder" system

Multi-layer ion chamber (MLIC) 2D scintillation detector

Desirable:

• Fast and accurate 3D dosimetry for treatment plan verification and machine QA

Holy Grail:

- *In vivo* range verification and on-the-fly adaptive PBS delivery:
	- On-board image-guidance (*CBCT, MRI);*
	- Pre-treatment WEPL verification (*pCT, p-radiograph*);
	- Fast detection during treatment (*prompt gamma*);
	- Fast comparison with daily on-board imaging of anatomy;
	- Fast adjustment to spot delivery pattern;
	- Self-verification of pencil beam trajectories and energies;
	- Repeat *in vivo* verification.

PBT patient mix (2012)

Making Cancer History®

Prostate

Proton therapy **IMRT**

Image-guidance

Daily orthogonal kV x-rays taken to align anatomy with reference DRR's using 2-D matching

AP DRR

AP x-ray image

Rt Lat DRR

Rt Lat x-ray image

such as were used in the design of these plans are sufficient

to ensure target coverage in the event of rotational setup

errors of $\leq 5^{\circ}$.

DOSIMETRIC CHANGES RESULTING FROM PATIENT ROTATIONAL SETUP ERRORS IN PROTON THERAPY PROSTATE PLANS

SAMIR V. SEJPAL, M.D., M.P.H.,* RICHARD A. AMOS, M.S.,* JAQUES B. BLUETT, M.S.,* LAWRENCE B. LEVY, M.S.,* RAJAT J. KUDCHADKER, PH.D.,* JENNIFER JOHNSON, M.S.,* SEUNGTAEK CHOI, M.D.,* AND ANDREW K. LEE, M.D., M.P.H.*

* Division of Radiation Oncology, University of Texas M. D. Anderson Cancer Center, Houston, TX

Int. J. Radiation Oncology Biol. Phys., Vol. 75, No. 1, pp. 40-48, 2009

SPOT SCANNING PROTON BEAM THERAPY FOR PROSTATE CANCER: TREATMENT PLANNING TECHNIQUE AND ANALYSIS OF CONSEQUENCES OF ROTATIONAL AND **TRANSLATIONAL ALIGNMENT ERRORS**

JEFF MEYER, M.D.,* JAQUES BLUETT, M.S.,* RICHARD AMOS, M.S.,* LARRY LEVY, M.S.,* SEUNGTAEK CHOI, M.D.,* QUYNH-NHU NGUYEN, M.D.,* X. RON ZHU, PH.D.,* MICHAEL GILLIN, PH.D.,* AND ANDREW LEE, M.D., M.P.H.*

From the *University of Texas-M.D. Anderson Cancer Center, Houston, TX

Int. J. Radiation Oncology Biol. Phys., Vol. 78, No. 2, pp. 428-434, 2010

Standardized treatment planning methodology for passively scattered proton craniospinal irradiation

Annelise Giebeler^{1,24}, Wayne D Newhauser^{1,2,5}, Richard A Amos^{1,2}, Anita Mahajan³, Kenneth Homann^{1,2} and Rebecca M Howell^{1,2*}

Giebeler et al. Radiation Oncology 2013, 8:32 http://www.ro-journal.com/content/8/1/32

Comparison of Discrete Spot Scanning and Passive Scattering Craniospinal Proton Irradiation

J Stoker*, R Amos, Y Li, W Liu, P Park, N Sahoo, X Zhang, X Zhu, M Gillin, MD Anderson Cancer Center, **Houston, TX**

Conclusion:

This work demonstrates the potential for improved robustness of proton craniospinal irradiations using a DSS delivery method, as well as significant decreases in clinic expenses. The use of apertures to define the sagittal plane field edge for DSS delivery improves the dose to target.

Head & Neck

Spot-scanning beam proton therapy vs intensity-modulated radiation therapy for ipsilateral head and neck malignancies: A treatment planning comparison

Shravan Kandula, M.D.,* Xiaorong Zhu, Ph.D.,† Adam S. Garden, M.D.,* Michael Gillin, Ph.D.,† David I. Rosenthal, M.D.,* Kie-Kian Ang, M.D., Ph.D.,* Radhe Mohan, Ph.D.,[†] Mayankkumar V. Amin, C.M.D.,* John A. Garcia, C.M.D.,* Richard Wu, Ph.D.,[†] Narayan Sahoo, Ph.D.,[†] and Steven J. Frank, M.D.*

*Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; and [†]Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, Houston, TX

Medical Dosimetry 38 (2013) 390-394

IMPT H&N - Example

Post-irradiation photography!

Cone-Beam Computed Tomography and Deformable Registration-Based "Dose of the Day" Calculations for Adaptive **Proton Therapy**

Catarina Veiga, MSc¹; Jailan Alshaikhi, MSc^{1,2}; Richard Amos, MSc²; Ana Mónica Lourenço, MSc^{1,3}; Marc Modat, PhD⁴; Sebastien Ourselin, PhD⁴; Gary Royle, PhD¹; Jamie R. McClelland, PhD⁴

Figure 3. Dose color wash overlayed on the replan CT (top row) and difference in dose between replan CT and deformed CT (bottom row) for (A) the IMRT plan, (B) the $IMPT_{3B}$ plan, (C) the SFUD_{3B} plan, and (D) the IMPT_{5B} plan for one of the patients included in this study. The horizontal purple lines indicate the length of the CBCT FoV. Abbreviations: CBCT, cone-beam computed tomography; CT, computed tomography; FoV, field of view; IMPT, intensitymodulated radiation therapy; IMRT, intensity-modulated radiation therapy; SFUD, single-field uniform dose.

Thoracic

Obtain 4D-CT data

Avg, MIP, and breathing phase data sets transferred to Eclipse TPS, and all registered to the Avg. CT.

MedTec: Knee-and-Feet Lok™

Dose calculated on Avg CT

Verification plans are calculated on at least T_0 and T_{50} , using original compensator and aperture designs, to evaluate coverage in extreme phases

 T_0 (end inspiration phase)

 T_{50} (end expiration phase)

Fig.2 Comparison of dose distribution from single RAO field before and after tumor shrinkage as detected during third week of treatment. (This patient experienced the most dramatic tumor shrinkage).

Fig.3 Comparison of total dose distribution before and after tumor shrinkage. (Same patient as $Fig. 2)$

Amos R, *et al.* Variation in dose distribution with tumor shrinkage for proton therapy of lung cancer. Proceedings of PTCOG 46, Zibo, Shandong, China, 2007

ARTICLE IN PRESS

International Journal of Radiation Oncology $\frac{1}{2}$ biology \bullet physics

Summary

Intensity modulated proton therapy (IMPT) can offer improved dose conformality but also has increased uncertainties, particularly when used to treat moving targets. We report here our preliminary experience with the clinical implementation of **IMPT** for thoracic cancer and describe clinical indications, motion analysis and management, plan optimization and robustness analysis, and quality assurance. Our data indicate that **IMPT** treatment for thoracic cancer with tumor motion \leq 5 mm is safe with use of the approach developed at our institution.

Clinical Implementation of Intensity Modulated Proton Therapy for Thoracic Malignancies

Joe Y. Chang, MD, PhD,* Heng Li, PhD, † X. Ronald Zhu, PhD, † Zhongxing Liao, MD,* Lina Zhao, MD,* Amy Liu, MS,¹ Yupeng Li, PhD, †,‡ Narayan Sahoo, PhD, † Falk Poenisch, PhD, † Daniel R. Gomez, MD,* Richard Wu, MS, † Michael Gillin, PhD, † and Xiaodong Zhang, PhD^{\dagger}

*Department of Radiation Oncology and [†]Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, Houston, Texas; and ‡ Applied Research, Varian Medical Systems, Palo Alto, California

Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer

Sarah C. Darby, Ph.D., Marianne Ewertz, D.M.Sc., Paul McGale, Ph.D., Anna M. Bennet, Ph.D., Ulla Blom-Goldman, M.D., Dorthe Brønnum, R.N., Candace Correa, M.D., David Cutter, F.R.C.R., Giovanna Gagliardi, Ph.D., Bruna Gigante, Ph.D., Maj-Britt Jensen, M.Sc., Andrew Nisbet, Ph.D., Richard Peto, F.R.S., Kazem Rahimi, D.M., Carolyn Taylor, D.Phil., and Per Hall, Ph.D.

CONCLUSIONS

Exposure of the heart to ionizing radiation during radiotherapy for breast cancer increases the subsequent rate of ischemic heart disease. The increase is proportional to the mean dose to the heart, begins within a few years after exposure, and continues for at least 20 years. Women with preexisting cardiac risk factors have greater absolute increases in risk from radiotherapy than other women. (Funded by Cancer Research UK and others.)

Howell R, **Amos R**, Kanke J, *et al.*

Predicted risk of cardiac effects with modern cardiac-sparing radiation therapy techniques

Proceedings of PTCOG 53. *Int J Particle Ther*. 2014;**1**(2):617-618

Proton Physics Research & Implementation Group

http://www.pprig.co.uk/pprig/

ucli

National Physical Laboratory http://www.npl.co.uk

**University College London
Hospitals**

http://www.uclh.nhs.uk

NHS Foundation Trust

The Christie **NHS**

The Clatterbridge Cancer Centre http://www.clatterbridgecc.org.uk/

University Hospital **NHS** Birmingham **NHS Foundation Trust**

University Hospitals Birmingham

http://www.uhb.nhs.uk/

The St James's Institute of Oncology

http://www.leedsth.nhs.uk/patients-and-visitors/ourhospitals/st-james-university-hospital

University College London http://www.ucl.ac.uk/

UNIVERSITY OF University of Surrey http://www.surrey.ac.uk/

The University of Manchester http://www.manchester.ac.uk/

The University of Manchester

UCL Proton Therapy Research Group

5,000 mile commute!

Thank you!

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