Advances in ion imaging and range verification
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Conflict of Interest
Research collaboration and two license agreements with RaySearch Laboratories AB

Challenges in clinical practice
- Increased sensitivity to uncertainties in beam delivery
- Anatomical changes (inter- and intra-fractions)
- Tissue stopping power (relative to water, SPR)

In-vivo verification and adaptation?
Enhanced in-room (ideally at isocenter) imaging with SPR information

- On-board scatter-corrected CBCT
- On-rails (DECT)
- Ion radiography/tomography
- Magnetic Resonance Imaging

More demanding than solutions in clinical use for photon therapy

• On-board scatter-corrected CBCT
• On rails (DECT)
• Ion radiography/tomography
• Magnetic Resonance Imaging

Landry …Parodi MP 2015

Scatter-corrected CBCT

- Fast (< 10 s) scatter correction possible with deep learning
- Promising results for both correction methods at projection level (< 10 ms / projection) and image level
- Space for improvement for more reliable dose calculation in ion beam therapy (e.g., connected to beam records)
- Similar results for synthetic CT generation from MRI
- However, SPR information not yet incorporated (enhancement with DE, pRAD, direct SPR conversion?)

See talk H. Bouchard

Ion transmission imaging

• Direct (integral) SPR determination for patient-specific refinement of planning information
  (Schneider et al, Med Phys 2005, Schulte et al TANS 2012)
• Daily, low-dose image guidance for patient positioning (Cassella et al JACMP 2019)

Comparison of simulated (realistic) proton CT vs experimental DECT and SECT

Reduced errors (RMSE) for pCT (~0.1-0.2%) vs DECT (~0.5-0.9%) and SECT (~1.6-2.7%)

DeJongh et al SU-I330 GE PD F6 5 and discussion about optimisation

Several detector concepts under investigation worldwide and discussion about optimisation

Krah et al PMB 2019
Proton imaging promises better than 1% SPR accuracy at dose ≤ 1\text{-}2 mGy.

Competitive performance of proton CT prototype vs dual-source DECT (MAPE of 0.55\% vs 0.67\% at ~20 reduced dose).


Competitive performance of proton CT prototype vs dual-source DECT (MAPE of 0.55\% vs 0.67\% at ~20 reduced dose).

Dedes, …, Schulte, Landry, Parodi, PMB, in press

DECT proton CT

Experiment (head phantom)

Dedes et al SU-F-221AB-5

MC simulation of an ideal detector for proton, helium and carbon ion CT

Comparably better range accuracy than X-ray CT regardless of ion species

Reduced RBE for ion CT compared to imaging X-rays (according to RMF model*).

*Carlson et al., Radiation Research 2008

Fluence-modulated proton CT (FMpCT)

FMpCT achieves arbitrary image noise targets

Local reduction of imaging dose

Frequent dose verification within region of good image quality

Iterative optimization based on variance reconstruction and a Monte Carlo patient model

Dickmann et al. WE-08-SANZ-22
Make the invisible visible

Different emission mechanisms

\[ \text{Different emission mechanisms:}
\begin{align*}
\text{Photoneutron:} & \quad \text{Photoneutron scattering process}\nonumber \\
\text{Proton-scattered:} & \quad \text{Proton-scattered process}\nonumber \\
\text{Fast:} & \quad \text{Fast process}\nonumber \\
\text{Plasma:} & \quad \text{Plasma process}\nonumber \\
\text{Other:} & \quad \text{Other processes}\nonumber 
\end{align*} \]

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Investigation of high sensitivity and broadband detection systems

- Low pressure amplitudes challenging to detect (mPa vs. kPa/MPa for US imaging)
- Improvement of the signal-to-noise ratio to reduce the detection threshold (minimal dose)
- Broadband sensors: independent of the beam energy and sensor position w.r.t to the Bragg peak

Co-development of CMUT* sensors

- Collaboration with ACULAB
  Dr. Savoia - University of Roma Tre, Italy
- Dedicated CMUT design and front-end electronics
- Optimization of the sensor geometry based on a k-Wave simulation platform

First proof-of-concept at 20 MeV compared to conventional (PZT) transducers

PET range verification: The clinical implementations

Feasibility to detect inter-fractional changes (anatomy, positioning) despite low SNR, biological washout and suboptimal instrumentation

New dedicated detector concepts under development worldwide

PET range verification: Next-generation instrumentation

- Clinical evaluation ongoing with protons and soon also 12C ions
- Testing 12C ion dose reconstruction algorithm

Measurement Simulation PET range verification: Next generation instrumentation

- Testing 12C ion dose reconstruction algorithm
Fast (sub-ns) emission eliminates issue of biological washout. Signal fall-off is closely correlated to Bragg peak position due to lower cross section thresholds than for PET. Dedicated developments for directional detection of high energy PGs (~2-7 MeV) embedded in huge neutron background.

Prototype 1D PG camera with slit collimators

Xie et al IJROBP 2017, Courtesy Kevin Teo, UPENN

First clinical implementation

First clinical study with PBS reported proton range shift retrieval accuracy of 2mm in brain with spot aggregation. Recent results for brain patient with more heterogeneities in PTV and re-planning after control CT showed ability to detect shifts, despite complex signal from range mixing.

Shifts averaged over inside (left) and outside (right) of the anatomical change region.

Anatomical change region

Xie et al IJROBP 2017, Courtesy Kevin Teo, UPENN

Prompt gamma (PG) range verification

Future clinical implementations

Prompt gamma spectroscopy

– Exploits PG energy information
– Custom-made collimated prototype
  close to start pilot clinical study @ MGH

Verburg et al, PMB 2013; van der Schee et al, PMB 2018

Prompt gamma timing

– Exploits timing information, overcoming collimation
– Custom-made prototype under development for future clinical translation @ Oncoray Dresden

Panthi et al MO-I345-GePD-F6-5

Prompt gamma spectroscopy

– Exploits PG energy information
– Commercial prototype under further development for future clinical translation @ Maryland

Golnik et al PMB 2014; Compton camera imaging

– Exploits Compton kinematics, overcoming collimation
– Commercial prototype under further development for future clinical translation @ Maryland

Draeger... Polf, PMB 2018
**Next-generation of hybrid detectors**

Comparison of different detector technologies & geometries in collaboration with NIRS toward „Whole Gamma Imaging“

**Integration in clinical workflow**

Analytical PET calculation & ongoing integration of prompt gamma in a research version of Treatment Planning System “RayStation”

**Toward a new treatment planning strategy**

Range retrieval accuracy and precision crucially depend on PB statistics and PG-dose correlation
Conclusion & Outlook

Several techniques under investigation and development to enable
- Improved anatomy & SPR characterization prior to treatment
- In-vivo range verification during treatment

...yet still a lot to do to fully exploit Bragg Peak clinically

Thank you

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Penn Medicine
Penn Radiation Oncology

Collaborations
- C. Belka, G. Landry, C. Kurz, F. Kamp et al, LMU University Hospital
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- T. Yamaya, NIRS
- S. Rit, CREATIS
- D. Hansen, Aarhus University Hospital
- B. Raaymakers et al, Utrecht Medical Center
- M. Vidal, J. Herault, CAL
- E. Traneus, R. Nilsson, RaySearch
- U. Weber, C. Trautmann, M. Durante, GSI
Clinical results of ibPET@GSI

Indirect estimation of $^{12}$C dose deviation from in-beam PET

Original CT - Modified CT

CT after PET findings

Prompt gamma-based range measurement

Absolute range determination with 1 mm precision (<5%) at clinical doses has shown possible in phantom and almost in reach for clinical cases (for pencil beams of sufficient statistics)

Absolute range determination with 1 mm precision (2σ) at clinical doses has shown possible in phantom and almost in reach for clinical cases (for pencil beams of sufficient statistics)

On-board 3D imaging for dose adaptation

Dose calculation requires CBCT intensity correction and updated contours

- Comparison of contours for prostate cases:
  - Low CBCT contrast & strong anatomical changes 
  - Limited DIR accuracy