Real-time In-Vivo Dosimetry and Range Verification

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Proton Therapy
- Commercial solution with IMPT
- Compact: Proteus® ONE

Dosimetry
- QA for standard RT
- QA for proton therapy
- Radiodiagnostics
- Fiducial markers
- Training and formation

Industrial solutions
- electron accelerators
- X-ray generators
- Medical and food industry

Radiopharmacy
- Proton accelerators
- Isotopes for PET/SPECT
- Cyclone® 70
IBA Dosimetry @ Schwarzenbruck (Nuremberg, Germany)
IBA Dosimetry Product Line

Dosimetry for RT
From LINAC commissioning to patient plan / daily QA

Dosimetry for PT
Solutions for commissioning, acceptance test and QA

Medical imaging
Solutions for quality control in Diagnostic imaging

Fiducial markers
VISICOIL™ Flexible linear marker for Image guided RT
Market Survey PT QA: Commissioning, Machine QA

- 1-D water phantoms (scan of Bragg peak):

- IC Stacks for routine Machine QA:
  - 180 ICs, 2mm distance, range in a single shot
Market Survey: Commissioning, Daily QA

- Scintillator + CCD camera: Spot maps
  - XRV-3000 Eagle

- Absorber + 2-D detector: Daily QA
  - LCW-140
Market Survey: Pretreatment Patient QA

- 2-D arrays of ICs:
  - Calibrated for absolute dose measurements
  - Pixellated 1000 – 1500 channels, pitch 5-7 mm
  - Adaption to handle high dose rates in PT

- 2-D array in water tank: plan verification ($\gamma$-analysis)
How about Real-Time In-Vivo?
How about Real-Time In-Vivo?

- No commercial product available so far
- First clinical tests with prototypes, only
Outline

- Motivation
- Direct range measurement
- Detection of secondary radiation
  - PET
  - Prompt gammas
  - Charged particles
- Ionoacoustics
- Conclusions
PT: Sensitivity to Range Uncertainties

- Safety margins: (3% + 1.2 mm) [Paganetti et al. PMB 2012]
- Full potential of PT not yet exploited
- Head-on situations avoided
- Need for: Real-time In-Vivo monitoring

[Knopf et al. PMB 2013]
Impact on range/dose calculations

(a) “optimal”, single-field plan
+ minimal healthy tissue dose
- high risk for dose in OAR due to range uncertainties

(b) multi-field plan
+ minimal risk due to range uncertainties
- high dose to normal tissue

(c) patched-field plan

compromise:
moderate dose to normal tissue,
influence of range uncertainties along the patch line

[Knopf et al. PMB 2013]
Direct Range Measurements

- Ideal: Detectors at distal edge of target volume
- Limited number of cavities in body
- Example: Prostate with anterior irradiation
- Array of diodes attached to endorectal water balloon
- Diodes: small size, no HV
- SOBP via modulator wheel
- Time resolved measurements of diodes, calibration to WEPL and dose

[Hoesl et al. PMB 2016]
Direct Range Measurements 2

- Scout beam (dose < 1cGy) with extended range
- Determination of actual WEPL here: in pelvis phantom
- Comparison to predicted values
- Adaption of treatment, if necessary

[Hoesl et al. PMB 2016]
Nuclear reactions & secondary radiation
Nuclear reactions

- Collision and de-excitation phase
- Creation of projectile-like and target-like fragments, e.g. $^{11}\text{C}$, $^{15}\text{O}$, …
  - PET monitoring
- Emission of prompt $\gamma$-rays, neutrons, light charged particles:
  - Real-time monitoring

PET monitoring

• Coincident detection of 511 keV photons
• Measurement of activity distributions
  • p-beam: target-like fragments
  • C-beam: projectile-like fragments
• Biological washout

[W. Enghardt et al. NIM A 2004]
PET monitoring 2

- Different clinical realizations:
  - a) in-beam PET
  - b) in-room PET
  - c) offline PET
- Find compromise between available hardware and clinical workflow


[G. Shakirin et al. PMB 2011]
PET: washout

- Prediction (simulation) of expected signal and comparison to measurement
- Minimization of washout: short-lived isotopes (e.g. $^{12}$N, $t_{1/2} = 11$ ms) [P. Dendooven PMB 2015]
- Measurements e.g. spill pauses of synchrotron
- First measurements at KVI: [H. Buitenhuys et al. PMB 2017]
PET: Hardware developments

- Adaption of design for beam delivery
- Single, dual ring or flat geometries possible

OpenPET @ NIRS
[T. Yamaya J. Phys. 2017]
Real-time monitoring
Prompt secondary radiation for ion range monitoring

- Simulation of protons and carbon ions on a water target (diameter 15 cm, length 20 cm)
- Vertices of particles leaving the target, energy > 1 MeV
- Correlation of vertices with ion range

[JK et al. NIM A 2017]
Prompt γ-rays

- Energy range 2-10 MeV
- Timescale < $10^{-11}$ s
- Characteristic lines from transitions in $^{12}$C or $^{16}$O
- Use for range monitoring proposed in 2003
  [Y. Jongen, F. Stichelbaut PTCOG 2003]
- Proof of concept:
  protons: [Min et al. APL 2006]
  carbon ions (using TOF): [E. Testa et al APL 2008]
- Technical realizations:
  - Mechanical collimation: knife edge, multi slit
  - Electronic collimation: Compton camera
  - no collimation: PGT, PGPI
  - Prompt gamma spectroscopy

Deposited dose

Prompt γ emission

[F. Fiedler IEEE NSS MIC 2011]
Collimated cameras: Knife-edge (IBA)

- Principle of pin-hole camera
- Prototype optimization via simulations
- Fall-off retrieval precision $\approx 1\text{mm}$ for a distal spot [J. Smeets et al. PMB 2012]

- Tests with prototype at C230 cyclotron [Perali et al. PMB 2014]
- First patient measurements [Richter et al. Radiother. Onc. 2016]
Knife-edge 2

- Software for simulation and data analysis
- Range analysis in 3D

[Richter et al., Radiother Oncol, 2016]
[Xie et al., Int J Radiat Oncol Biol Phys 2017]
[Nenoff et al., Radiother Oncol, 2017]
New hardware for prostate study

- New “under-the-couch” trolley at OncoRay for patient study on prostate treatments
- Improved workflow by mechanical docking into treatment floor
- Absolute position calibration using X-ray system and proton beam (accuracy < 0.8mm @ 2σ)
Collimated camera: Multi-slit (IPNL)

- Full ion range visible
- Collimator optimization via simulations
- Fall-off retrieval precision:
  \[ \sigma \approx 1\text{mm} @ 10^8 \text{ protons} \]
  [M. Pinto et al. PMB 2014]
Electronic Collimation: Compton Camera

- Scatter and absorber detectors: store energy and position information of interactions
- Minimum 2 interactions required
- Use Compton kinematics: reduce possible incident directions to cone
- Overlay of multiple cones: reconstruct initial vertices
- In principle 3-D information available

[Equation: \( \cos \phi_1 = 1 - m_e c^2 \left( \frac{1}{E_0(L_1, L_2 \phi_2)} - \frac{1}{E_0(L_1, L_2 \phi_2)} \right) \)]

[Cowan et al. AIP Conf. Proc 2010]

[Kim et al. PMB 2012]
Compton Camera: realizations

- Various realizations
- Monolithic scintillators: e.g. IFIC Valencia
- DSSD + scintillator: LMU Munich, IPNL Lyon
- here: CdZnTe

Reconstruction algorithms adapted to PT
- here: filtering & iteration
- 3-D information
- Limitations in beam current: random coincidences

[E. Draeger et al. PMB 2019]
No Collimation: Prompt Gamma Timing PGT

- Production of prompt gammas along proton track
- Record time-resolved emission spectra
- Use mean and width as information
- Changes in track length → changes in measured quantities on the order of ps
- Gain depends on load
- Drift of RF phase
- Corrections applied

- Use information from multiple detectors
- Visualize effect of air cavity
- New prototype: integrated in nozzle

[31. T. Werner MEDINET mid-term Meeting 2018]
Prompt Gamma Peak Integral (PGPI)

- Detect prompt gamma rays produced in target (patient)
- Use TOF for event selection (nozzle – target)
- Integral depends on absorbed energy (range) as well as on material

- Test measurement at CAL in Nice
- 65 MeV protons (cyclotron)
- Scintillation detectors: NaI, LaBr$_3$, BaF$_2$
PGPI: Test with modulator wheel

- Relative count rate as a function of wheel angle
- Reduction by more than factor five:
  - Scattering in wheel: protons not passing collimator any more
  - Reduction of proton range in target
- Data well described by simulations

PGPI: Perspectives

- $10^8$ protons (65 MeV) on PMMA target
- Change range via degraders
  3 mm can be detected at given statistics
- Simulation: 8 detectors
- Horizontal displacement of target
- Combine information from detector groups:
  correlation with displacement

[JK et al. IEEE NSS MIC 2016]
Prompt Gamma Spectroscopy PGS

- Idea: Emission spectrum of prompt gamma rays is correlated with range
- Emission spectrum registered at a given depth gives a measure of the residual range

[J. Verburg et al. PMB 2014]
PGS: Workflow

CT scan of patient → Conversion → Material compositions $m^y$ and Densities $\rho^y$ → Geometry and composition of collimator and scintillators

Treatment plan → GPU Monte Carlo → Proton energy spectrum $N_0^{\text{pro}}$ → TOPAS Monte Carlo

Nuclear reaction cross sections $\sigma^{\text{crit}}$ → Matrix multiplication → Ray tracing → Detection probability $\eta_{\text{det}}$

Matrix multiplication → Prompt gamma-ray emissions $N_{t\text{g-ray}}^{\text{crit}}$ → Transmission probability $t_{\text{trans}}$

Transmission probability $t_{\text{trans}}$ → Prompt gamma detection model $\eta_{\text{det}}$

[F. Hueso-Gonzalez et al. PMB 2018]
• Clinical size prototype
• Delivery of 0.9 Gy in 5x10x10cm³
• PBS at 2nA

• Energy vs TOF, identification of spectral lines
• Determination of proton range for each spot with a precision of 1.1 mm

[F. Hueso-Gonzalez et al. PMB 2018]
Interaction Vertex Imaging IVI
IVI: Simulations

- Head-like phantom
- Tracking of secondary protons
- Variation of incident ion energy
- Fit of error-function: inflection point
- Correlation of IPP with ion range

[P. Henriquet et al. PMB 2012]
IVI: measurements

- CMOS detectors: MIMOSA 26 (IPHC Strasbourg)
- Measurements at HIT
- Variation of carbon energy
- Vertex distributions

[V. Reithinger PTCOG 2013]
Ionoacoustics
Ionoacoustics: History

Ionoacoustic Characterization of the Bragg Peak (1979)

Acoustic radiation from idealized cylindrical energy deposition

Typical signals from the hydrophones

Ionoacoustics: Today

- Detection of ionoacoustic waves via transducer
- Range information via transit-time millimetric precision
- Well adapted to pulsed beam deliveries
- S2C2 1kHz rate, 8µs pulse width

[W. Assmann et al. PMB 2015]
[S. Lehrack et al. PMB 2017]
[S. Kellnberger et al. Nature SREP 2016]
Conclusions

- **Status:**
  - No commercial product for “Real-time In-Vivo Dosimetry and Range Measurements”
  - PET: clinically used, but not (yet) real-time
  - First clinical tests with prototypes for detection of secondary radiation
  - Focus on range verification, goal: reduction of safety margins

- **Outlook:**
  - Micro/nano-dosimetry (not covered in this presentation)
  - Methods based on detection of secondary radiation:
    - Integration in clinical workflow
Thank you very much for your attention!