Prompt gamma based range verification -
From prototyping to clinical evaluation

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1. Introduction
   i. Range uncertainties in proton therapy
   ii. Physics of prompt gamma rays

2. What do we have to consider for range verification in PT?
   i. What are the technical and practical constraints?

3. Research on clinical prototype within OMA project
   i. Development phases and current status of the IBA PG camera
   ii. Clinical evaluation: Detection of an anatomical change during patient treatment
   iii. What comes next?
Range Uncertainties in Proton Therapy
Radiation Therapy – Protons vs Photons

Radiation therapy is one of the cornerstones for cancer treatment

- Photons: exponential decrease of dose
- Protons: finite range and Bragg peak → spare normal tissue
- Spread-Out-Bragg-Peak (SOBP) → overlay of mono energetic proton beams
Range Uncertainties

- **Intrinsic:** conversion of **HU to SPR** (±2%)
- **Daily errors:** patient setup, tumor shrinkage, anatomical changes...
- **Safety margins to compensate uncertainties → more dose to healthy tissue**

Reducing Range Uncertainties

**Range Prediction**
“Improve treatment planning”

- DECT
- Proton radiography and pCT

**Range Verification**
“Know where the beam is”

- Range probes
- PET
- Ionoacoustics
- MRI
- Prompt Gamma
Prompt Gamma based Range Verification
Prompt Gamma Rays as Range Probe

- Nuclear reactions between tissue and proton
- Excited nucleus
- Emission of prompt photons ($\tau <<$ ns)
- Characteristic lines, high energies (2-7 MeV)
- Spatial correlation to dose deposition
- High neutron background
- High flux: $10^9$ photons per second

\[
\begin{align*}
12C & \rightarrow 11C^* & \rightarrow 11C
\end{align*}
\]

Verburg et al., PMB 58 L37, 2013

Kelleter et al., Physica Medica 34 7, 2017

Deposited dose
Fiedler et al. NSS 2011
Prompt gamma emission
Let’s build a PG range verification system

What are the technical and economical constraints?
What is the aim of our study?

1. Range verification system for clinical application

2. Accuracy well below the safety margins → 1-2 mm

3. Find the most efficient solution considering all constraints
Constraints due to clinical beam conditions and physics

- High beam currents (IBA C230 ~4 nA)
- Finite dose per fraction
- High photon energies (2-7 MeV)
- High neutron background

\[ \sim 10^9 \, \text{γ/s} \]

- Interaction probability
- Select only PGs
- Limited statistics

- Fast detectors and electronics
- High absolute detection efficiency
- Passive or active shielding
- Time of Flight
Constraints due to practical and economical reasons

- Affordable
- Easy to integrate
- Safe and compliant with regulations
- Accepted by medical staff
- Avoid technical overkill
- Simple and cost effective design
- Limited space
- Medical product
- Benefit for patient
- Still a prototype

- € vs €€€
- Low footprint
- No additional risks, follow standards
- Accuracy 1-2 mm
- Reduce technical risks first
A realistic perspective

- Initial idea and design
  - How it should be!

- Prototyping
  - How it is actually most of the time!
  - Cost and time efficient evaluation of technical risks

- Evaluation in real world
  - How it will be (after a lot of compromising)!
  - Test in the real world
IBA knife-edge slit camera

An example for passively collimated PGI
Knife-edge slit collimation – Principle

- PG emission due to proton beam → collimator to project image of the emission on detector
- Spatially resolved detector along beam path → 1D measurement (“PG profile”)
- Shift in proton range = shift in PG profile
1. Design optimization (Simulations) and first beam tests with existing detector
   - Collimator, scintillator, energy window
   - Proof-of-Concept!
2. Development of electronics, firmware, bigger prototype
   - Phantom studies
   - Detectable shifts of 1-2mm!
3. Full-scale prototype and mechanical system delivered to clinical partners
   - Let’s evaluate the system in the clinics!
PG camera – Hardware & current status

53 kg tungsten

PG camera

500 cm³ LYSO crystals

280 SiPMs

LabVIEW firmware

MatLab GUI
Do we meet the constraints?

- Fast detectors and electronics
- High absolute detection efficiency
- No additional risks, follow standards
- Accuracy 1-2 mm

- Passive or active shielding
- Reduce technical risks first
- Simple and cost effective design

- Time of Flight
- Low footprint
Prototype available – How we proceed?

Progress

Design optimization
Small prototype

Bigger prototype, electronics development

2 Full size prototypes for partners

Clinically accepted System

Patient data necessary!

2009 2011 2014

Time

2009 2011 2014

Clinically accepted System

Patient data necessary!
First patient data

1. 2015: First PG based in-vivo range verification in double scattering at OncoRay
   - Range measurement in agreement with control CTs

2. 2016: First PGI acquisition in PBS mode at UPenn
   - Range variation below safety margin
   - Spot-wise analysis possible
   - Accuracy < 2mm for ~50% of the spots
   - No deep analysis of data

3. No breakthrough of PGI yet
   - Physics vs Medicine
   - Develop new tools
   - More patient data necessary
   - Prove clinical benefit
How to prove clinical benefit?

Let’s have a look at some NEW patient data...
Lessons learned from the patient measurement

1. PGI in heterogeneous target regions possible
2. Evidence of anatomical change in PG data → more data necessary
3. New tools for data visualization → workflow has to be improved
4. More precise positioning of camera necessary (currently uncertainty of 1.2 mm – 2 σ)
5. Progress can be sometimes slow but there is progress!

So what are the next steps?
How to overcome the last barrier?

Clinical acceptance – a different world
The last percent... is the hardest one!

How do we get here?
New Features and more Patients in 2018

1. New positioning device (under the couch trolley)
   - Enabling new treatment indications (e.g. prostate, abdominal region)
   - Docked at fixed position → <1mm absolute uncertainty

2. Patient data analysis GUI
   - Improved workflow
   - Development based on experience from previous patient analysis

3. Furthermore... we need to:
   - Better understand medical needs
   - Define clinical case (when and how do we use PGI?)
   - Integrate system in clinical product?
Take home message

- PGI can **reduce range uncertainties** (based on patient measurements so far)

- **Detection of an anatomical change** using PG data

- Problem of acceptance and integration (so far no other device used in patient treatments) → **Be aware** of all constraints!

- Research in medical environment can be **challenging** but there is a **high reward** by improving patient well-being
Thank you!

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