Prompt gamma based range verification - From prototyping to clinical evaluation

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Content and Goal of this Presentation

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?

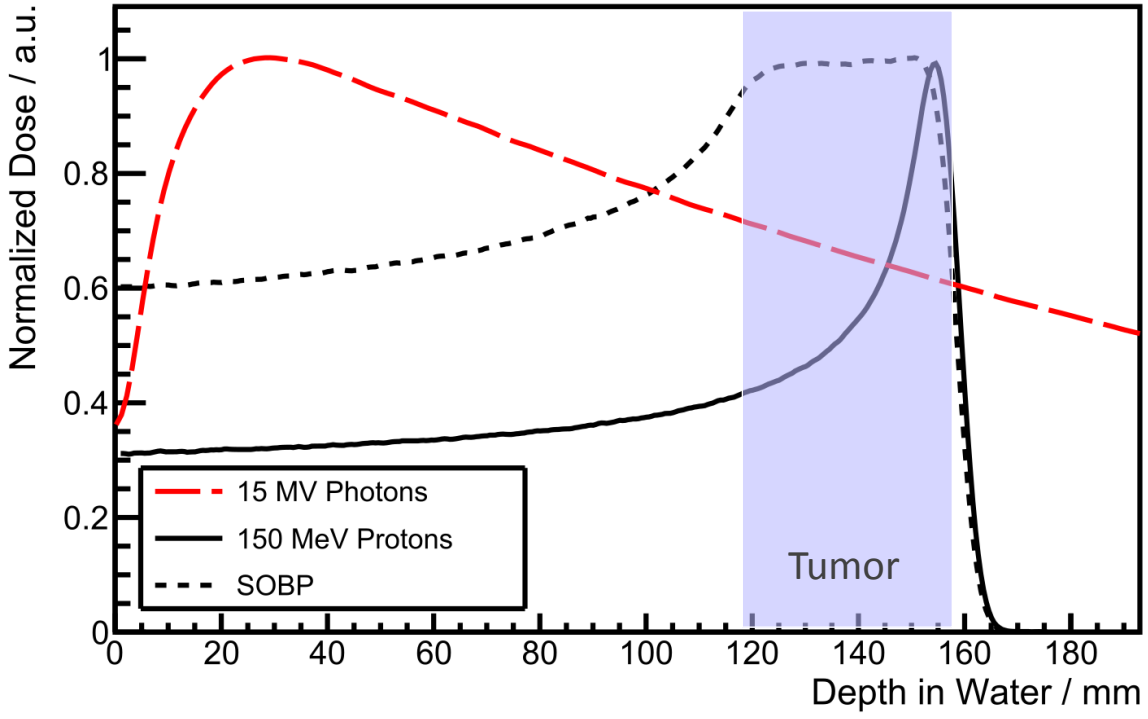
3. Research on clinical prototype within OMA project
   i. Development phases and current status of the IBA PG camera
   ii. Clinical evaluation: Detection of an anatomical change during patient treatment
   iii. What comes next?

Range Uncertainties in Proton Therapy

Radiation Therapy – Protons vs Photons

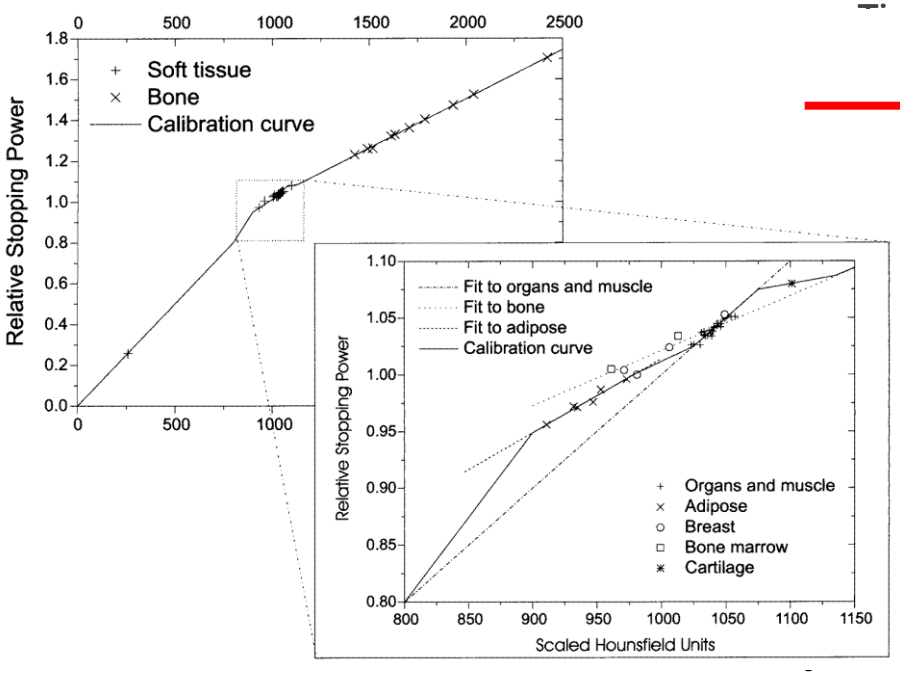
Radiation therapy is one of the cornerstones for cancer treatment

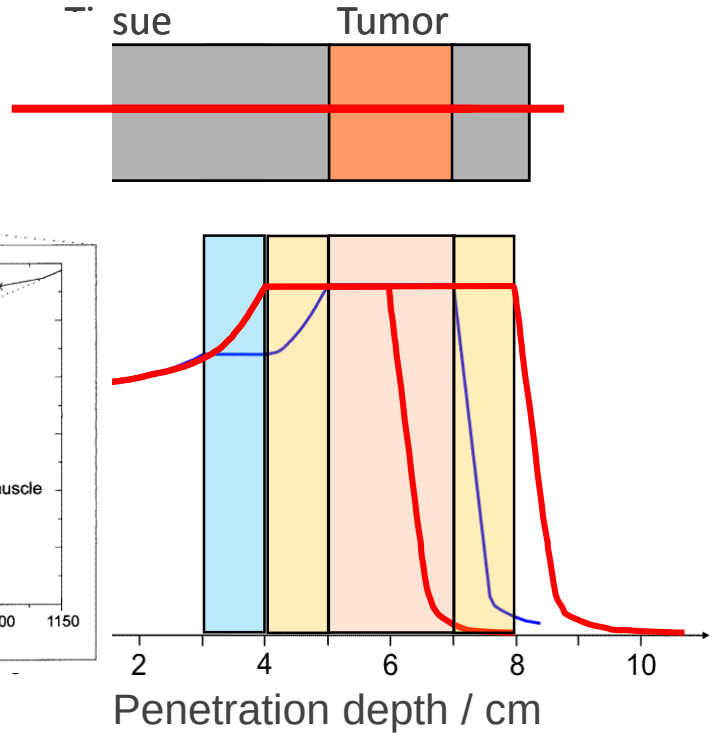
- Photons: exponential decrease of dose
- Protons: finite range and Bragg peak → spare normal tissue
- Spread-Out-Bragg-Peak (SOBP) → overlay of mono energetic proton beams



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





Schaffner and Pedroni, Phys Med Biol 43 (1998)

Reducing Range Uncertainties

Range **Predicition**
“Improve treatment planning”

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

DECT

Range probes

Proton radiography and pCT

PET

Ionoacoustics

MRI

Prompt Gamma

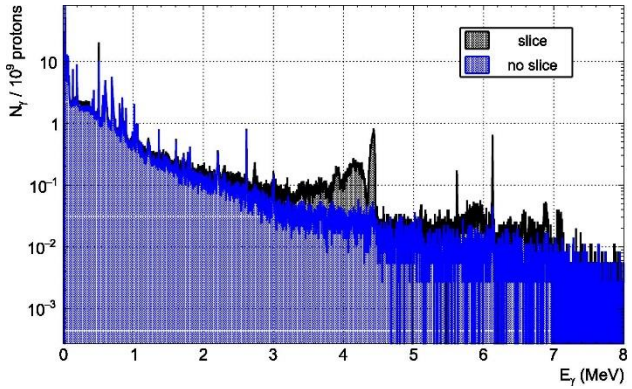
Prompt Gamma based Range Verification

Prompt Gamma Rays as Range Probe

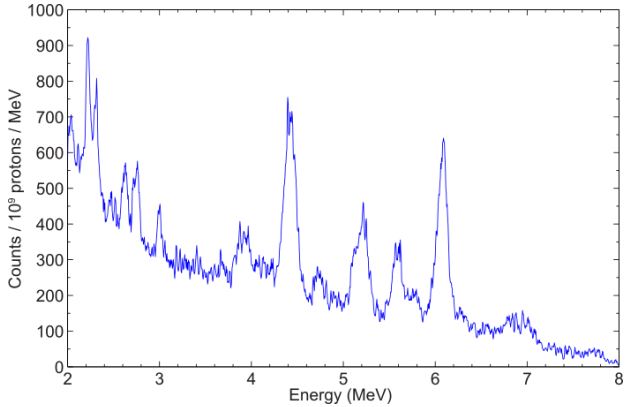
- Nuclear reactions between tissue and proton
- Excited nucleus
- Emission of prompt photons (τ << ns)
- Characteristic lines, high energies (2-7 MeV)
- Spatial correlation to dose deposition

☹ High neutron background

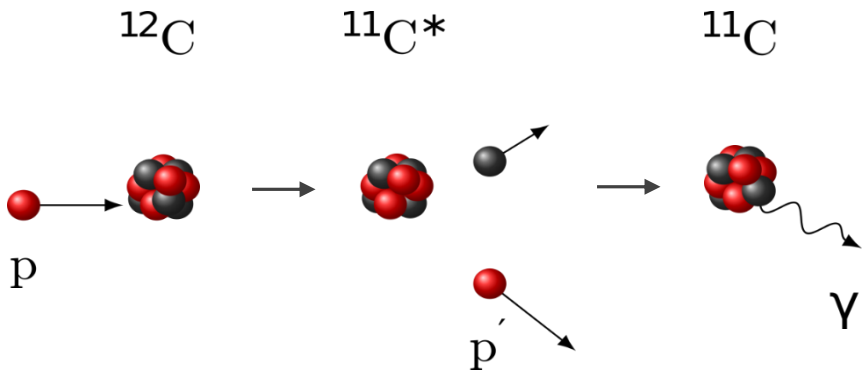
☹ High flux: 10^9 photons per second

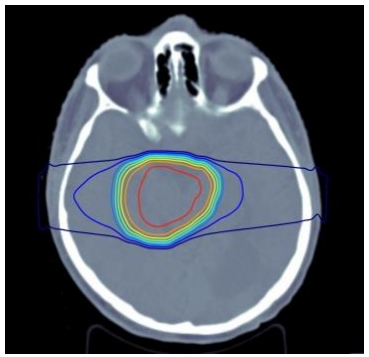


Kelleter et al., Physica Medica **34** 7, 2017

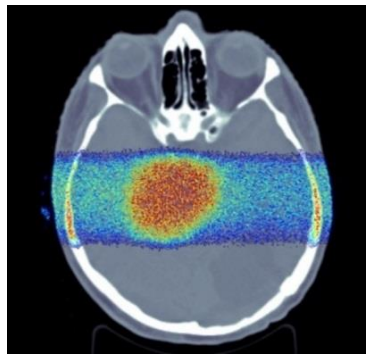


Verburg et al., PMB **58** L37, 2013





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?

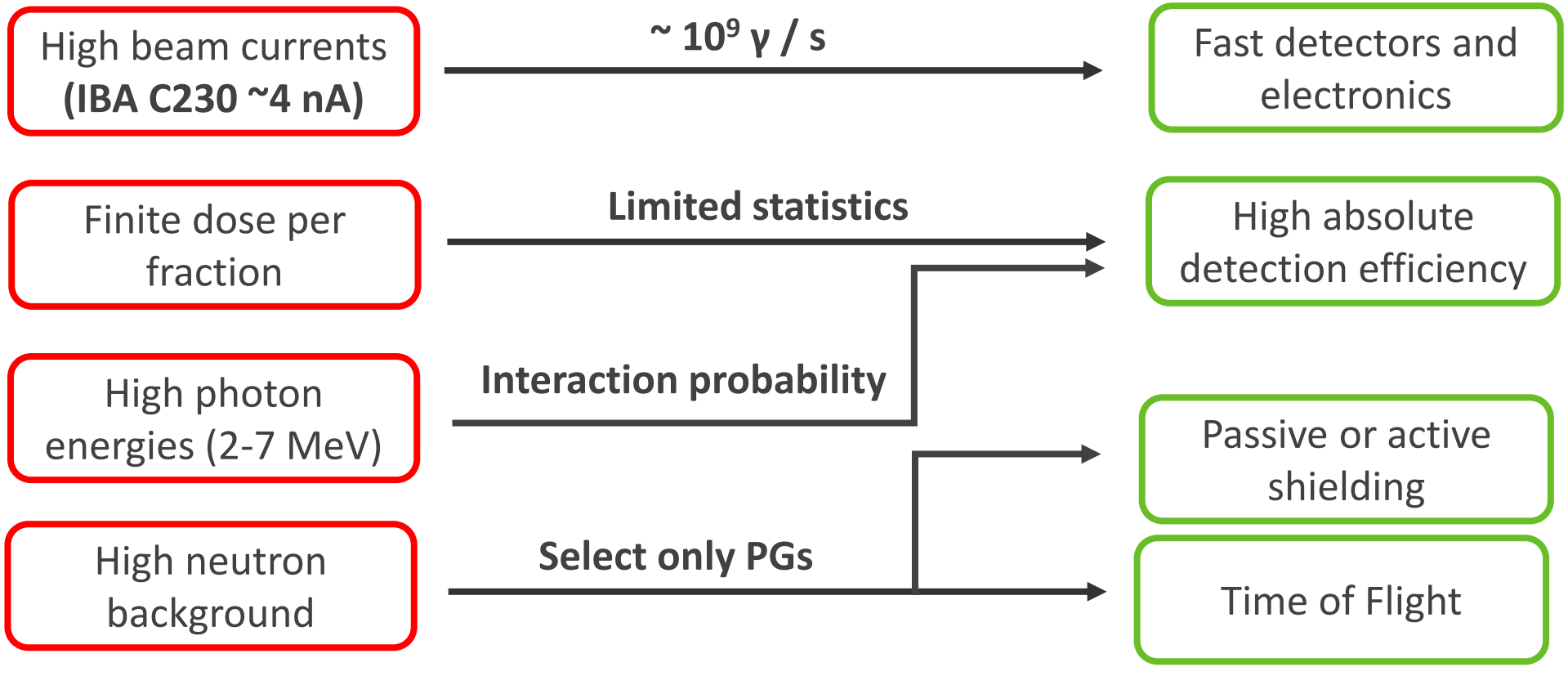
What is the aim of our study?

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



Constraints due to practical and economical reasons

Affordable	**€ vs €€€** →	Simple and cost effective design
Easy to integrate	**Limited space** →	Low footprint
Safe and compliant with regulations	**Medical product** →	No additional risks, follow standards
Accepted by medical staff	**Benefit for patient** →	Accuracy 1-2 mm
Avoid technical overkill	**Still a prototype** →	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

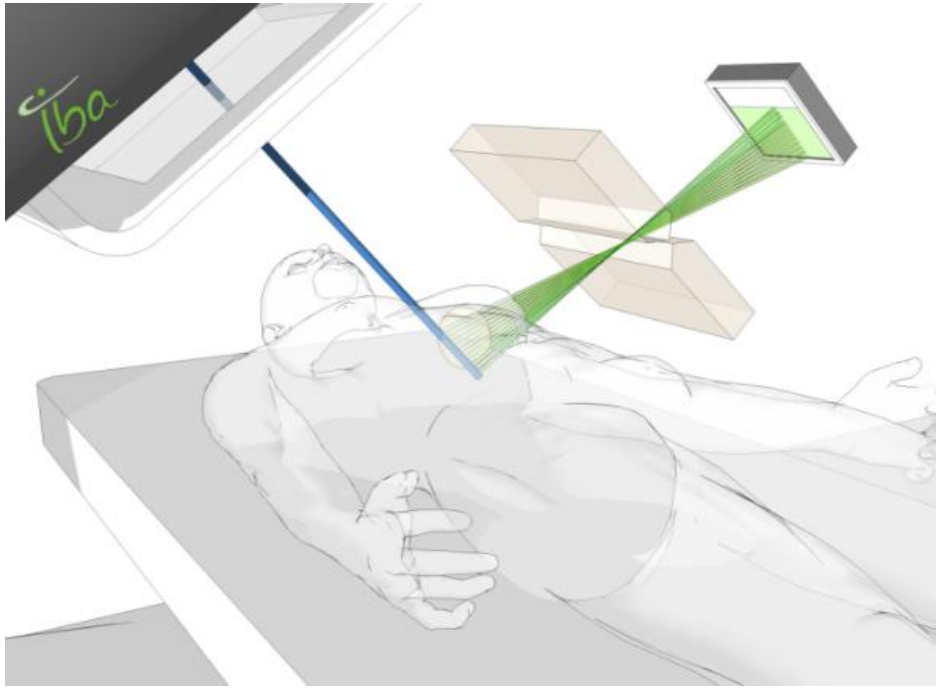
- Evaluation in real world
  - How it will be (after a lot of compromising)!
  - Test in the real world

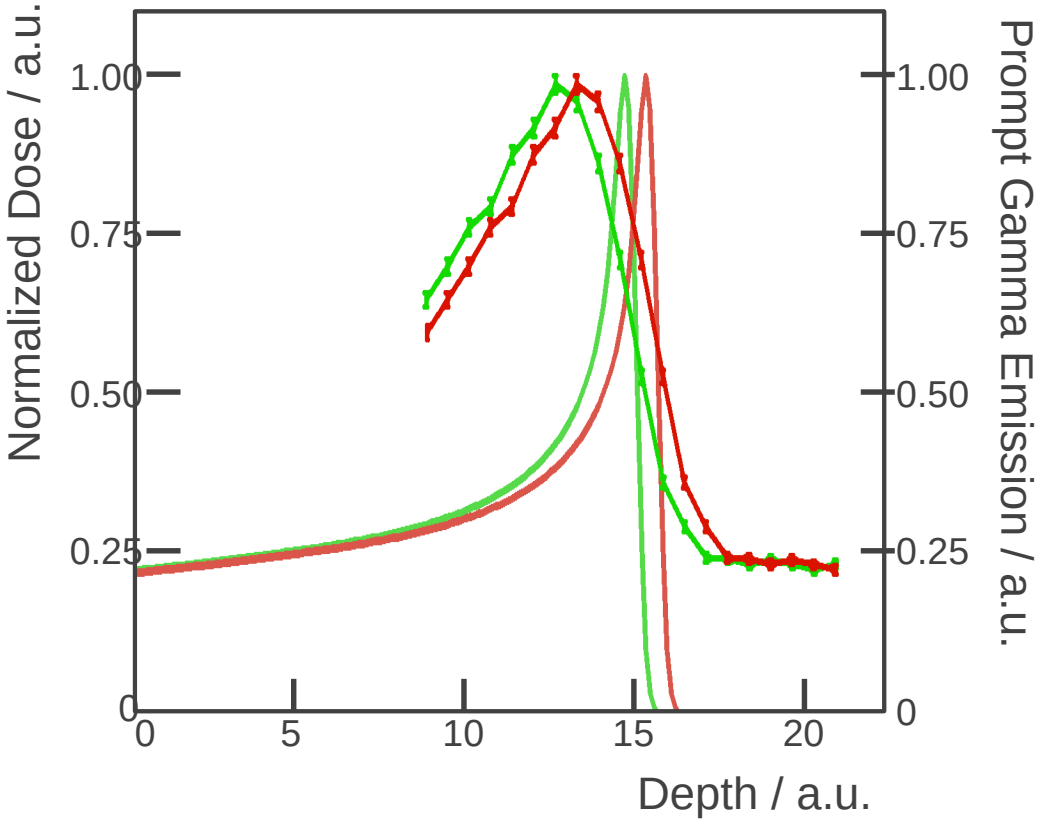
IBA knife-edge slit camera

An example for passively collimated PGI

Knife-edge slit collimation – Principle

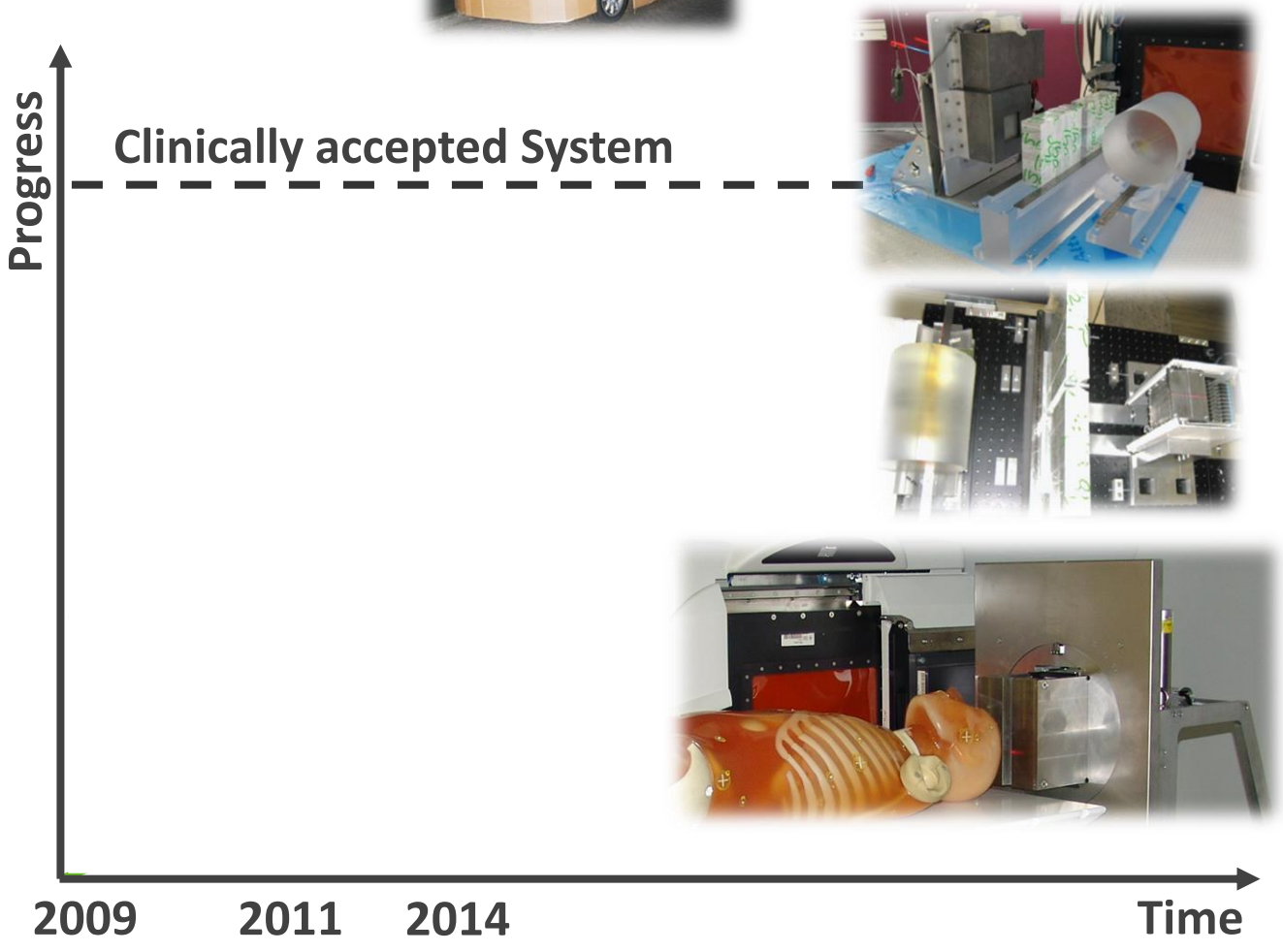
- PG emission due to proton beam → collimator to project image of the emission on detector
- Spatially resolved detector along beam path → 1D measurement ("PG profile")
- Shift in proton range = shift in PG profile





Hardware Development (Short history)

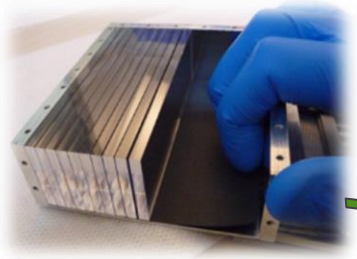
1. Design optimization (Simulations) and first beam tests with existing detector
   - Collimator, scintillator, energy window
   - Proof-of-Concept!
2. Development of electronics, firmware, bigger prototype
   - Phantom studies
   - Detectable shifts of 1-2mm!
3. Full-scale prototype and mechanical system delivered to clinical partners
   - Let's evaluate the system in the clinics!



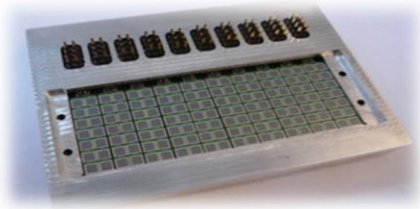
PG camera – Hardware & current status

53 kg tungsten

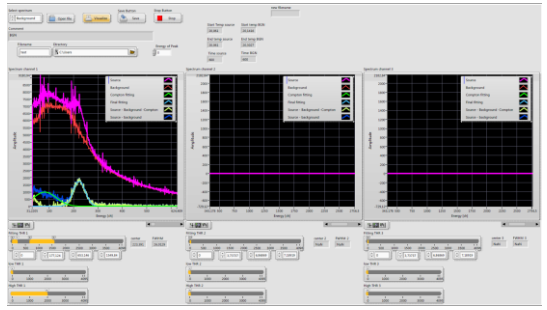
PG camera



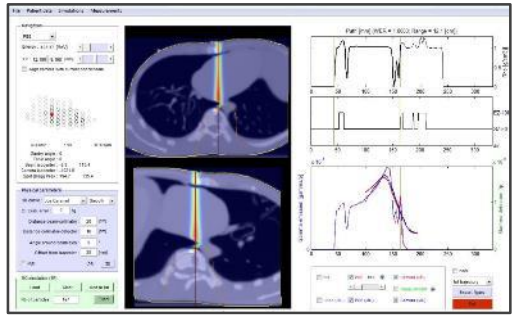
500 cm³ LYSO crystals



280 SiPMs



LabVIEW firmware



MatLab GUI

Do we meet the constraints?

Fast detectors and electronics

Passive or active shielding

High absolute detection efficiency

Reduce technical risks first

No additional risks, follow standards

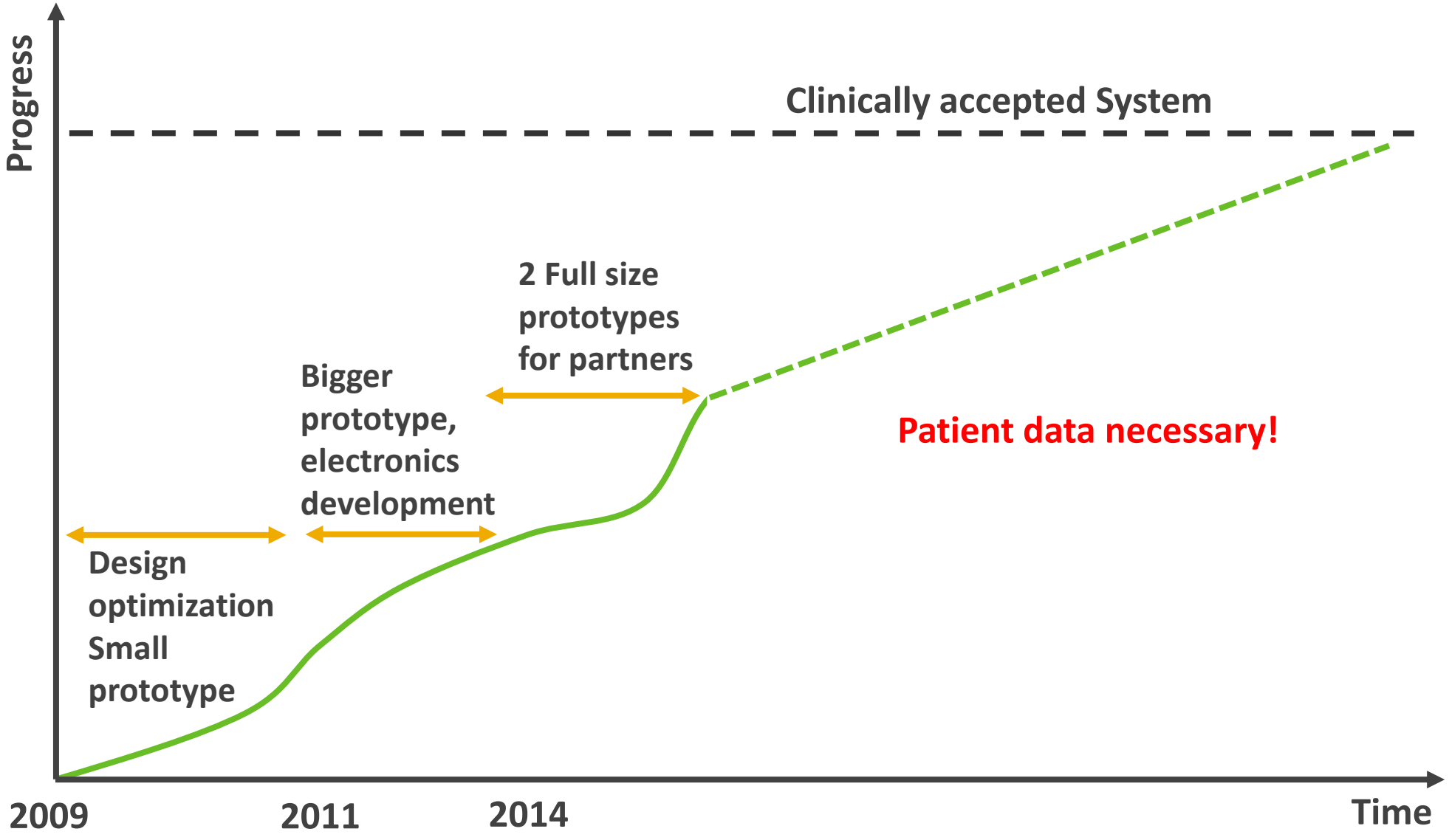
Simple and cost effective design

Accuracy 1-2 mm

Time of Flight

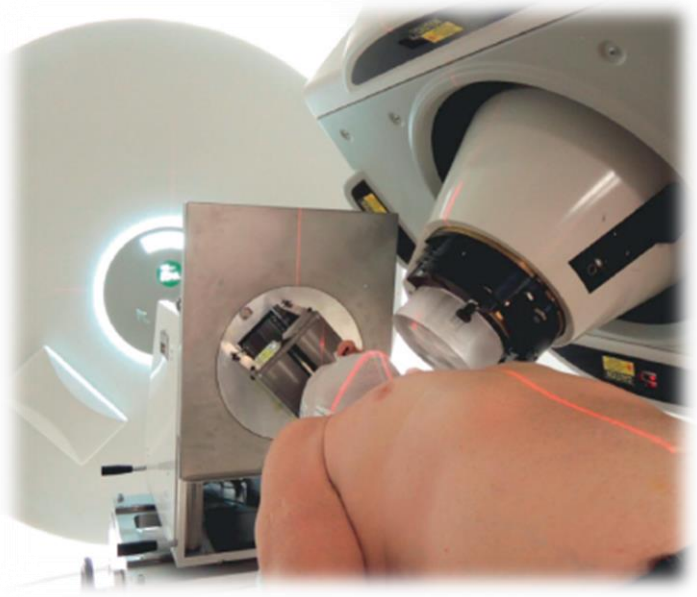
Low footprint

Prototype available – How we proceed?



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



WORLD'S FIRST SPOT-BY-SPOT IN-VIVO RANGE VERIFICATION IN PROTON THERAPY

Proton therapy / Jul 14 2016 - 11:45am

IBA's new imaging technology successfully applied for clinical evaluation in PBS

Philadelphia, PA, USA, July 14, 2016 – Today, IBA (Ion Beam Applications S.A.), the world's leading provider of proton therapy solutions for the treatment of cancer, announces that the clinical team at Penn Medicine, Philadelphia has successfully deployed IBA's Prompt Gamma Camera during patient treatment in Pencil Beam Scanning (PBS) mode, marking a milestone achievement for this new technology.

Since June 30 2016 the Prompt Gamma Camera has been operated by IBA's longtime customer and research partner, the Penn Medicine team at the Roberts Proton Therapy Center in Philadelphia, Pennsylvania, in several fractions of proton therapy delivered to treat a patient with a brain tumor.

This world first clinical application in PBS mode showcases the unique capacity of our new technology; specifically that it provides in vivo feedback on the proton beam penetration depth within the patient on an individual spot basis; thus allowing unprecedented quality control of the target volume coverage.

How to prove clinical benefit?

Let’s have a look at some **NEW** patient data…

Lessons learned from the patient measurement

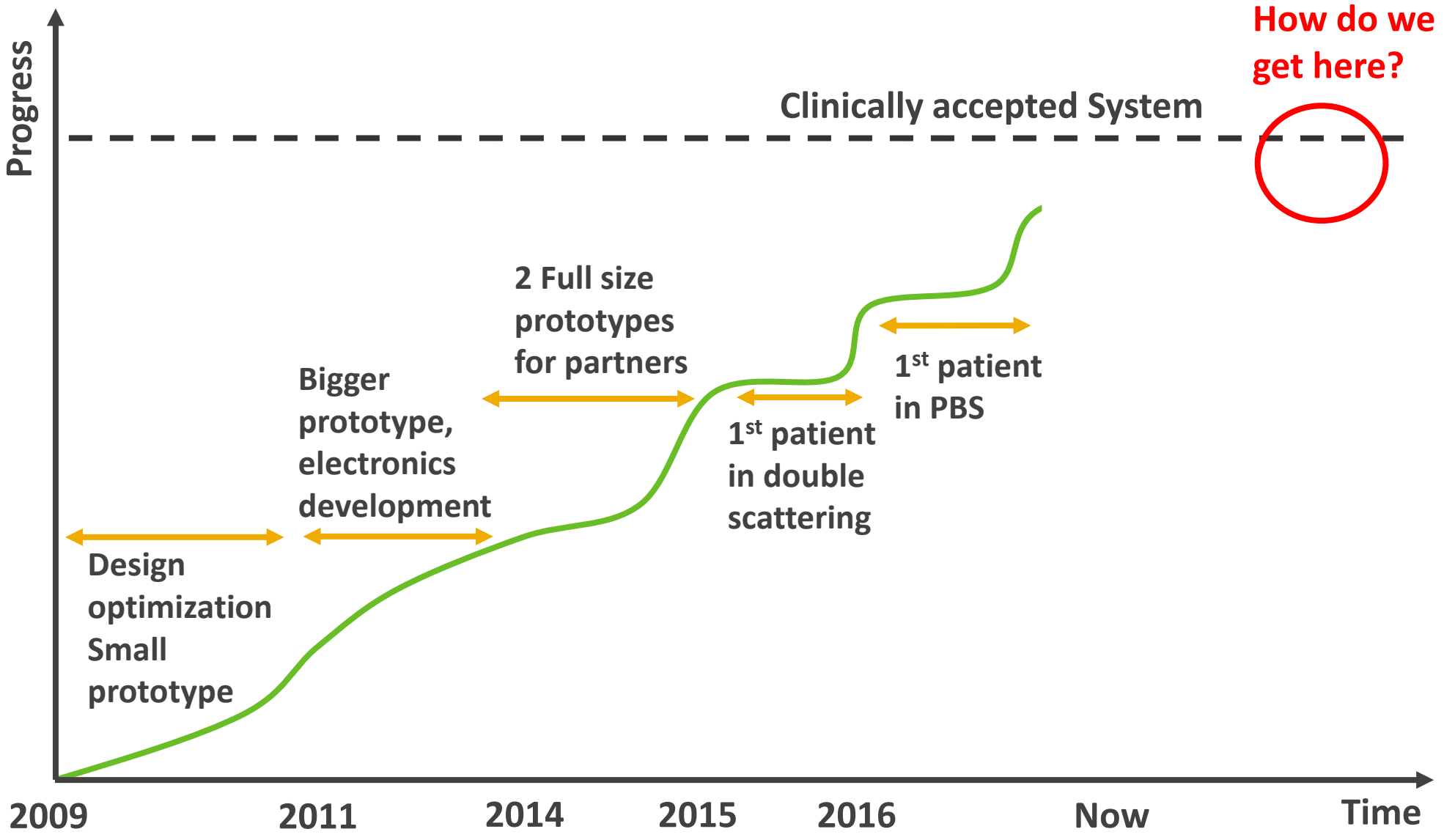
1. PGI in heterogeneous target regions possible
2. Evidence of anatomical change in PG data → more data necessary
3. New tools for data visualization → workflow has to be improved
4. More precise positioning of camera necessary (currently uncertainty of 1.2 mm – 2 σ)
5. Progress can be sometimes slow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

So what are the next steps?

How to overcome the last barrier?

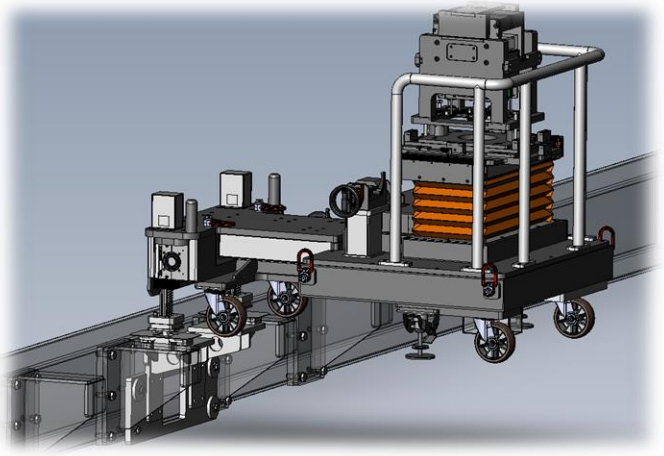
Clinical acceptance – a different world

The last percent... is the hardest one!

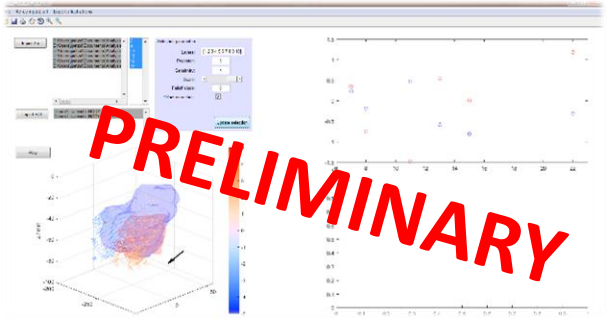


New Features and more Patients in 2018

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!

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Sklodowska-Curie grant agreement No 675265, OMA – Optimization of Medical Accelerators.