Prompt-Gamma Based Range Verification in Particle Therapy: New prospects (also) for 4D?

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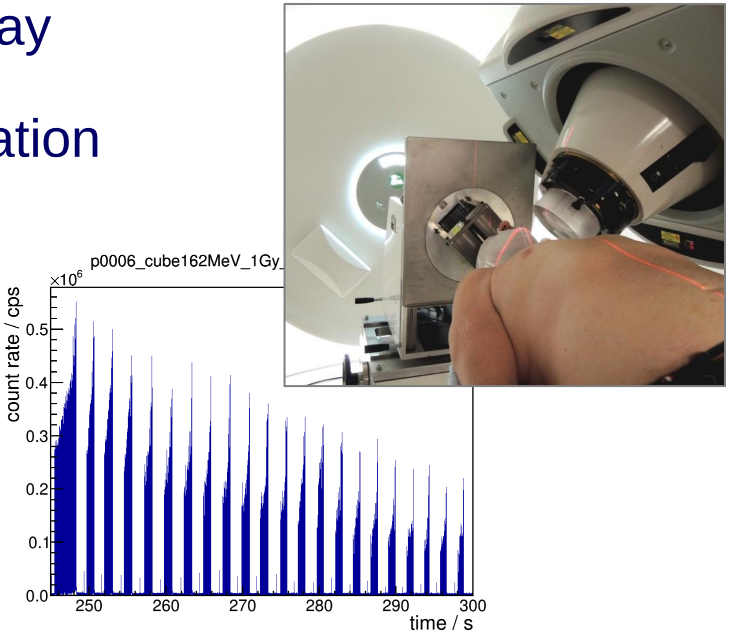
Outline

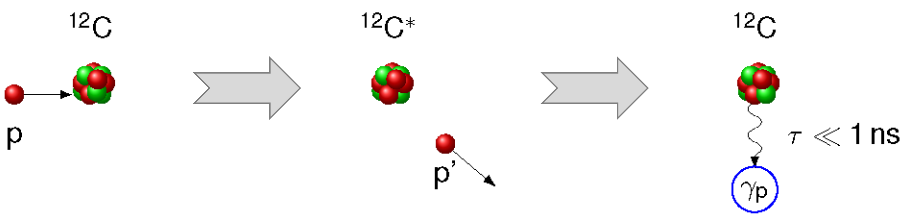
1. Origin and properties of prompt gamma rays
2. Prompt-gamma based methods of range assessment
3. Recent results obtained at OncoRay
4. Prospects for 4D treatment verification
   → PBS
5. Summary and conclusions



(Motivation covered by other talks.)

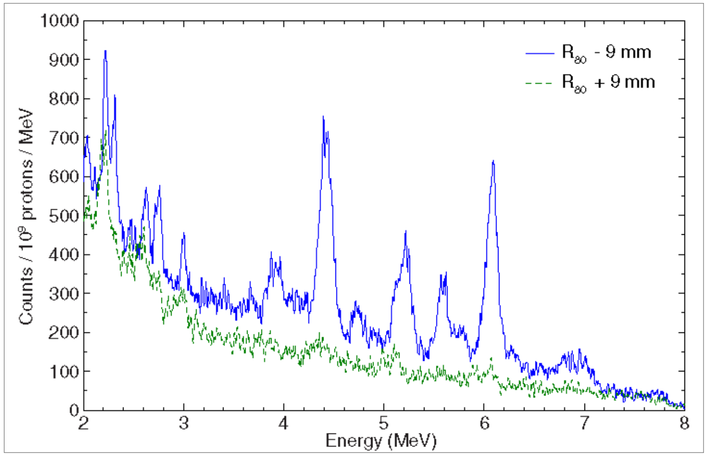
Origin and properties of prompt gamma rays

- Prompt gammas
  - Resulting from nuclear interactions of beam particles with tissue



  - Emission spectrum extends up to 7…8 MeV with prominent lines at 4.45 and 6.13 MeV
  - Emission spectrum depends on the proton energy (penetration depth)

Verburg et al., PMB 58 (2013) L37



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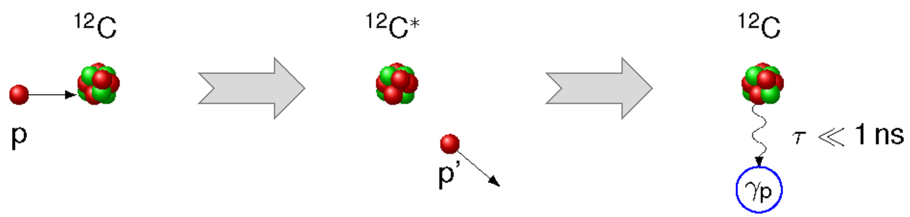

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  - Strong spatial correlation of gamma emissions with dose deposition (for 3-6 MeV gammas)

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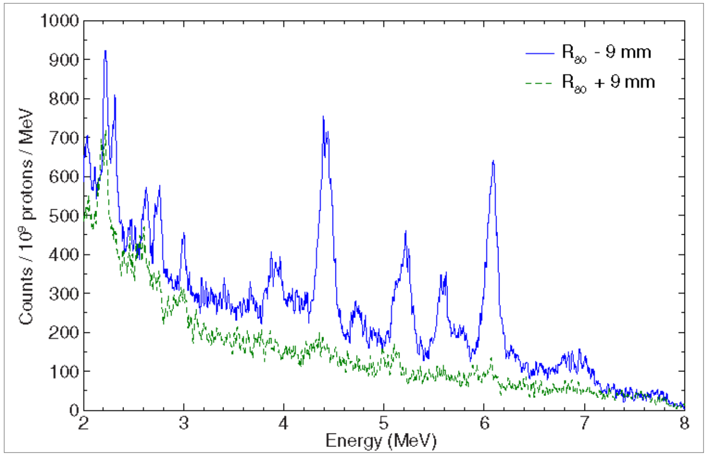

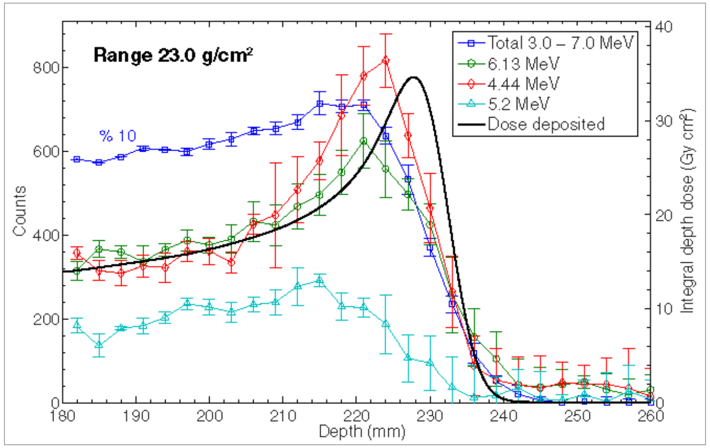

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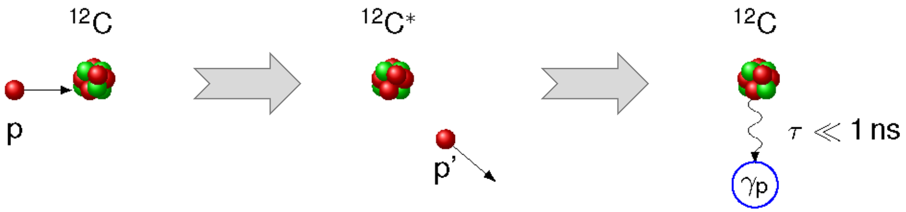

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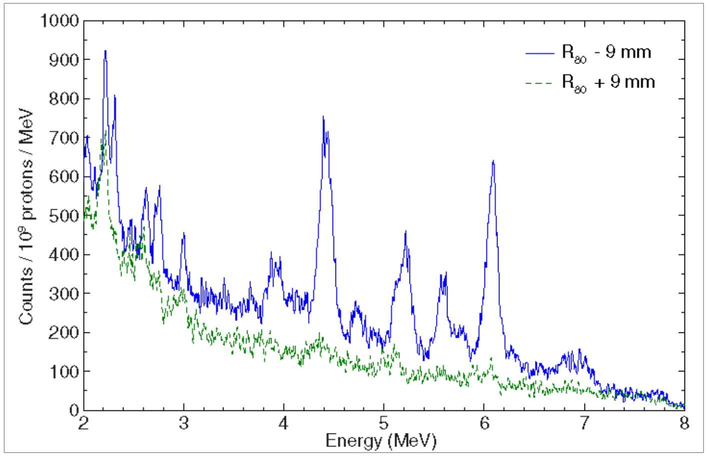

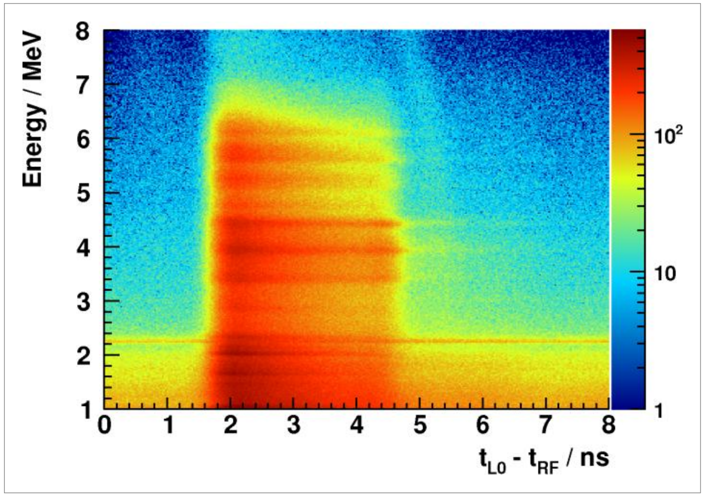

Hueso González et al., PMB60 (2015) 6247

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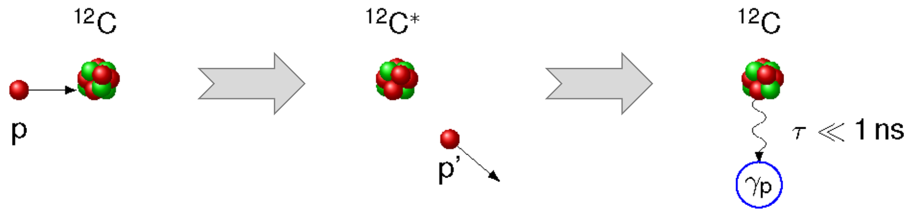

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- Options for range verification

→ Prompt gamma imaging (PGI)

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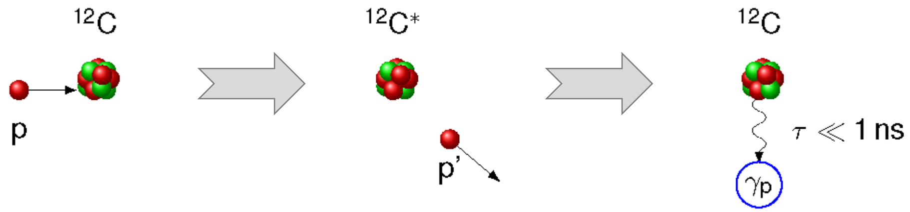

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→ Prompt gamma spectroscopy (PGS)

→ Prompt gamma imaging (PGI)

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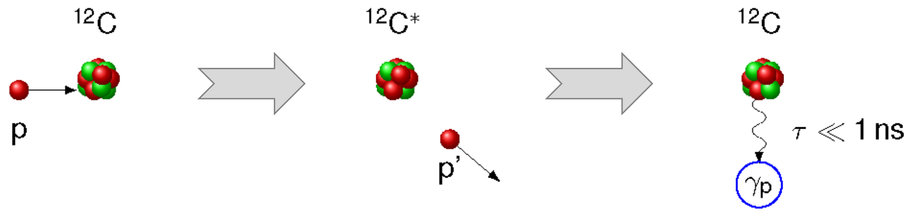

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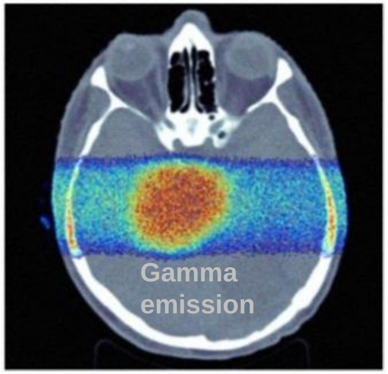
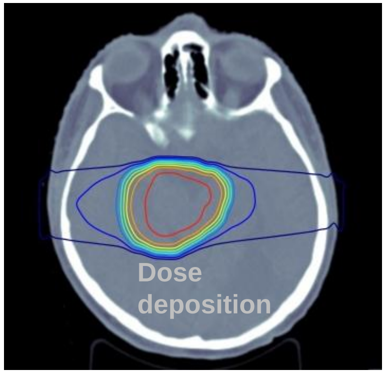
- Options for range verification

→ Prompt gamma spectroscopy (PGS)
→ Prompt gamma imaging (PGI)
→ Prompt gamma timing (PGT)

Prompt gamma imaging (PGI)

- Idea *Stichelbaut and Jongen, PTCOG 2003*
  - Emission pattern of prompt gamma rays is correlated with dose deposition
  - Imaging the prompt gamma emissions means imaging the dose deposition





Fiedler and Mueller et al., 2011 IEEE NSS/MIC

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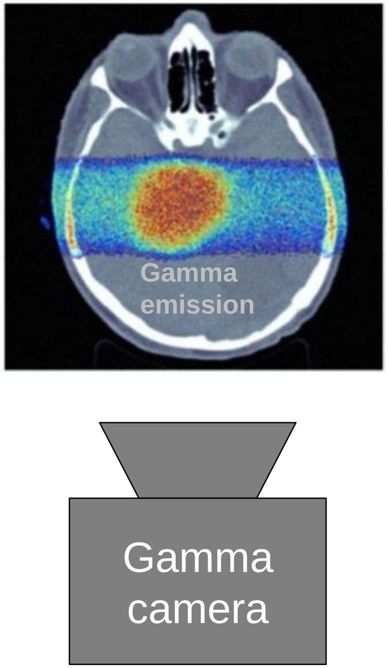

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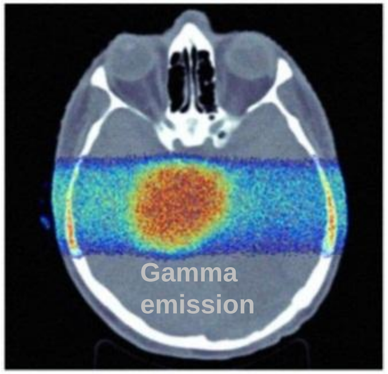

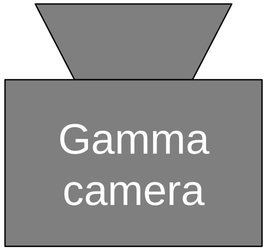

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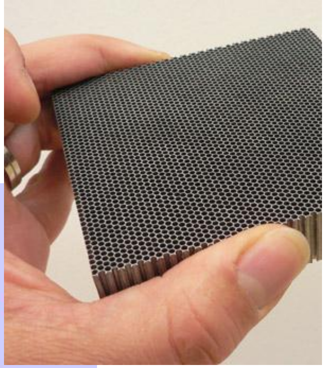

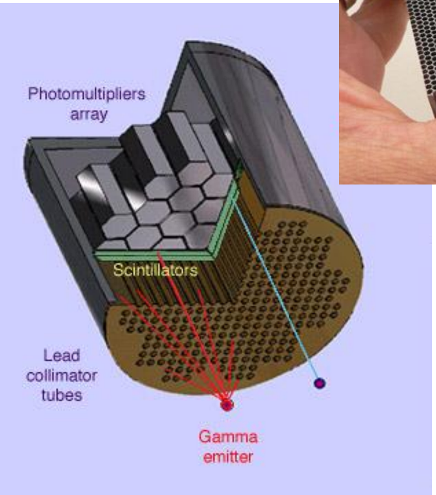

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Prompt gamma imaging (PGI)

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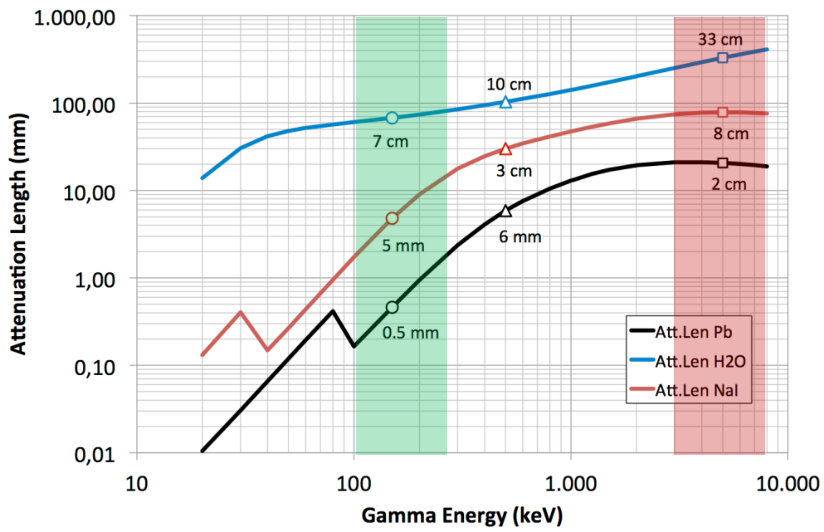

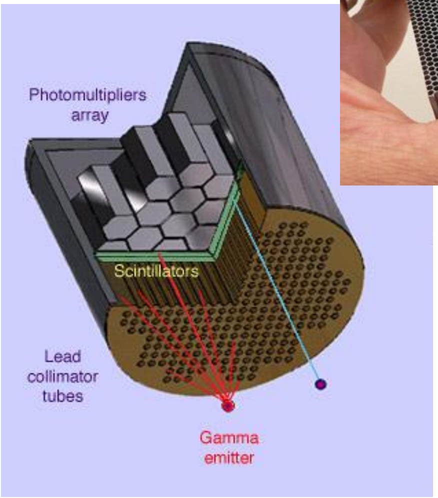

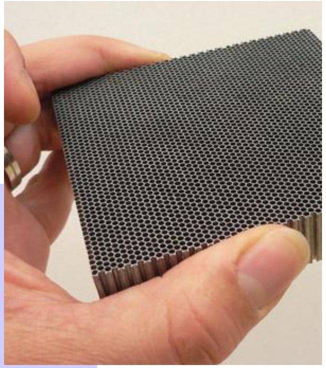

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Prompt gamma imaging (PGI)

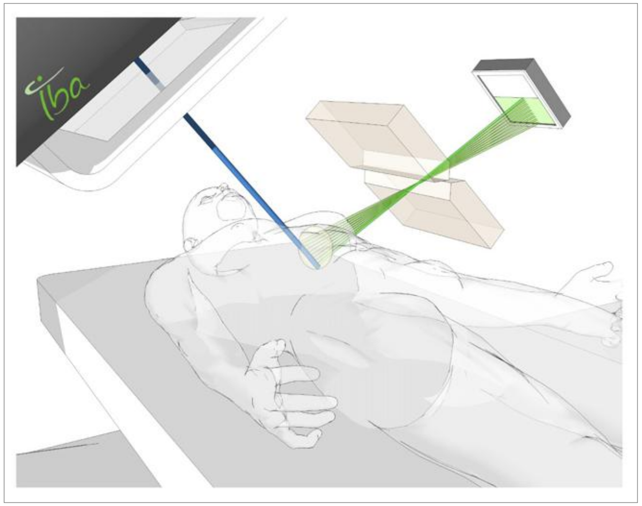
- Idea *Stichelbaut and Jongen, PTCOG 2003*
  - Emission pattern of prompt gamma rays is correlated with dose deposition
  - Imaging the prompt gamma emissions means imaging the dose deposition
- Options
  - Passively collimated systems with thick collimators
    - Knife-edge collimator
    - Multi-slat collimator
  - Electronically collimated systems
    - Compton camera
    - Compton electron tracking

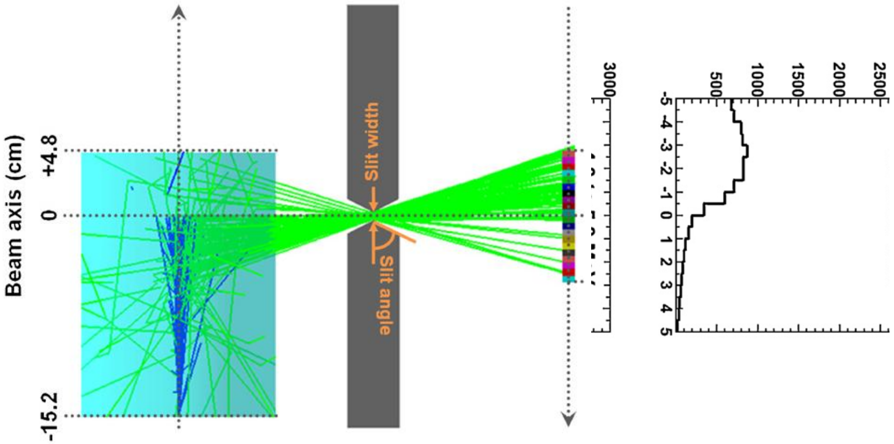
PGI with passive collimation

- Pinhole concept

2D → 1D imaging but improved efficiency

- Knife-edge collimator (IBA, …)
  - Knife-edge slit collimator + imaging detector
  - Prototype available, clinical tests performed





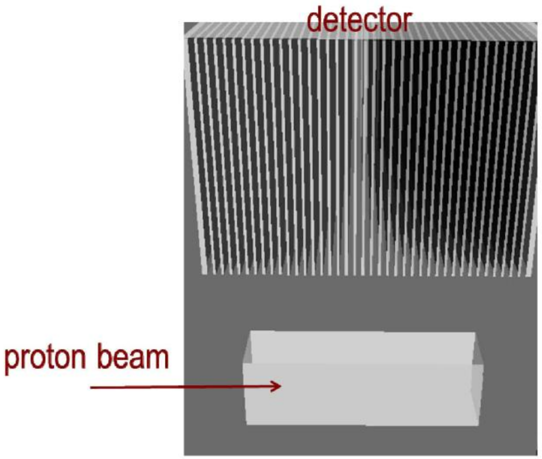
Smeets et al., PMB 57 (2012) 3371
Perali et al., PMB 59 (2014) 5849

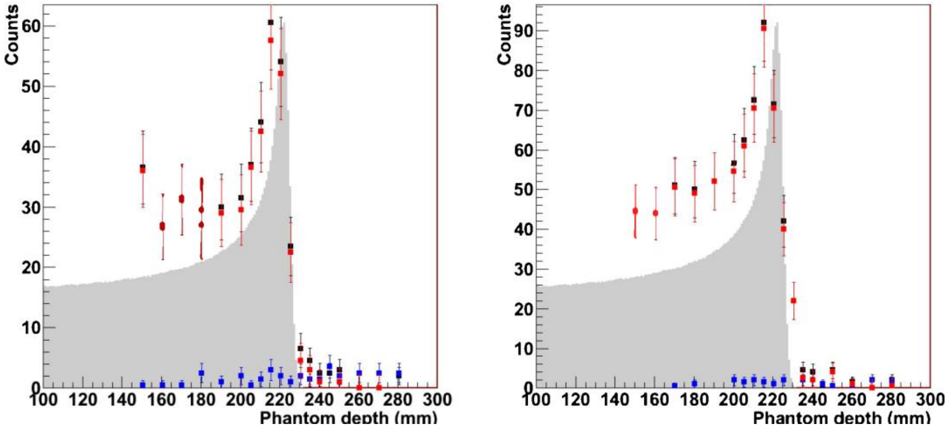
PGI with passive collimation

- Multi-hole concept

2D → 1D imaging but improved efficiency

- Multi-slat collimator (Coimbra, Delft, …)
  - Multi-slat collimator + imaging detector
  - Modeling





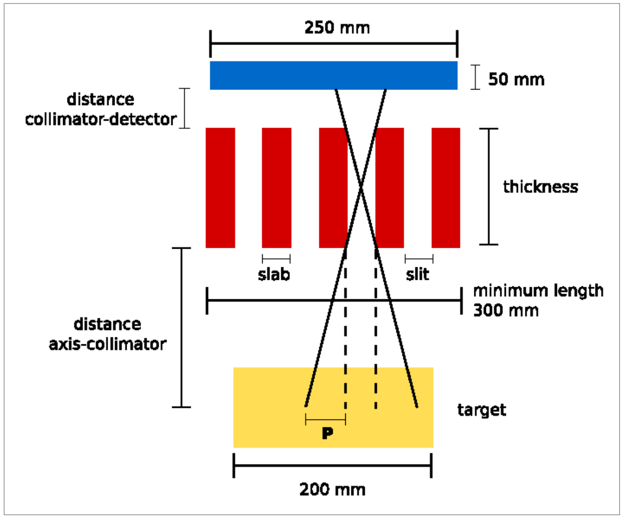
Cambraia Lopes et al., IEEE NSS/MIC 2012

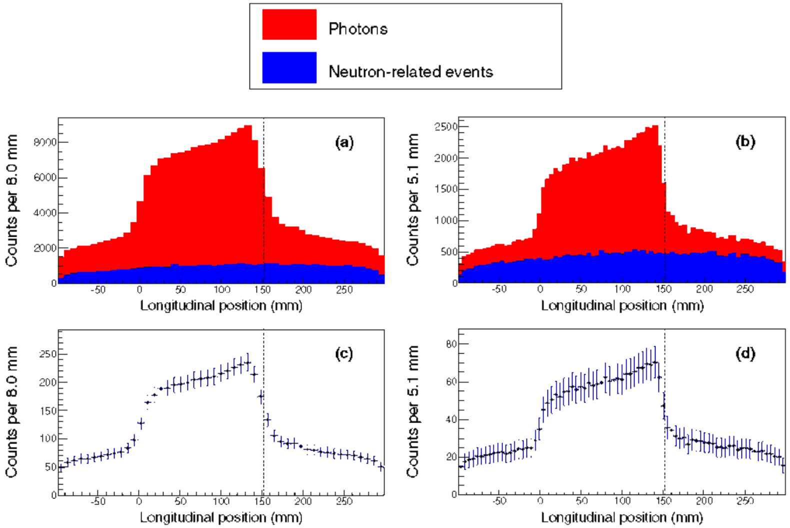
PGI with passive collimation

- Multi-hole concept

2D → 1D imaging but improved efficiency

- Multi-slat collimator (Lyon, …)
  - Multi-slat collimator + imaging detector
  - Modeling + measurements with single detector elements





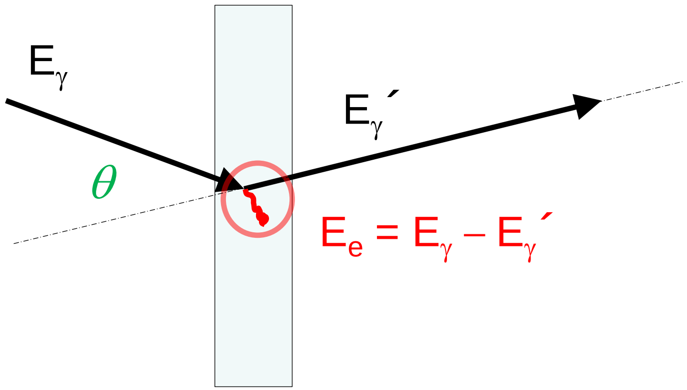
Pinto et al., PMB 59 (2014) 7653

PGI with electronic collimation

- Compton camera concept

Gamma-radiation imaging system based on the Compton effect

Everett et al., Proc. IEE 124 (1977) 995



$$\left(\frac{1-\cos\vartheta}{m_e \cdot c^2}\right) = \frac{1}{E_\gamma'} - \frac{1}{E_\gamma}$$

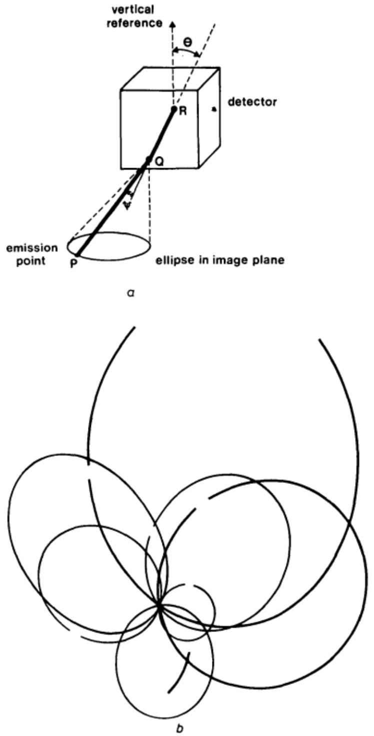
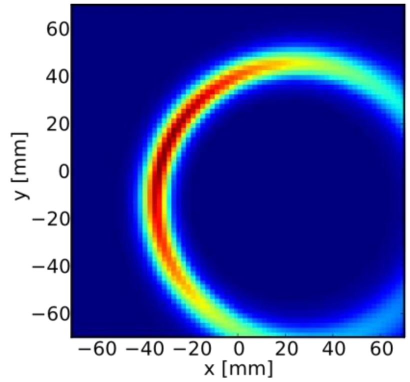


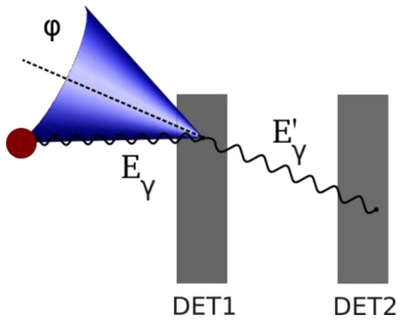
Fig. 1
Ellipses

a Generation of ellipse on image plane
b Multiple ellipses from single emission point

PGI with electronic collimation

- Compton camera concept
  - Scatter plane(s) + absorber plane
  - Measure deposited energies and interaction positions
  - Each valid event defines a cone





Courtesy of
C. Golnik and S. Schoene, 2013

PGI with electronic collimation

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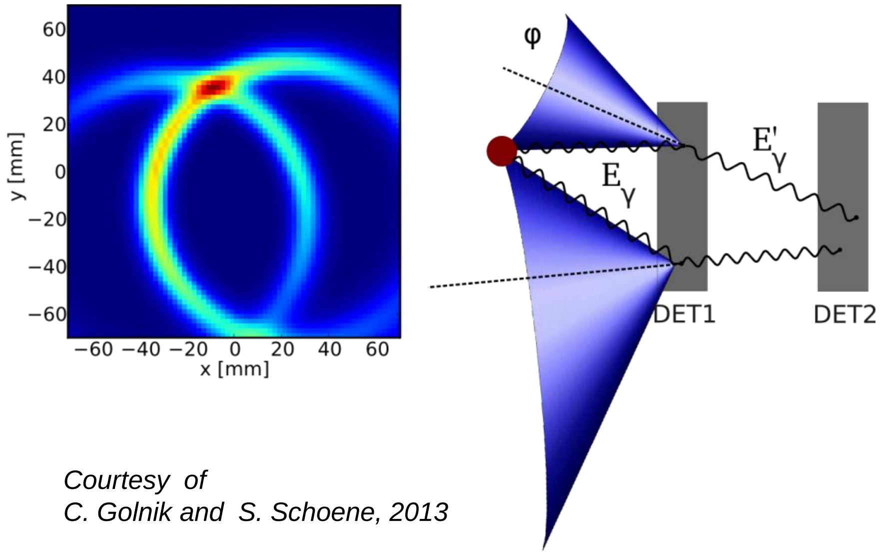
  - Superposition of many cones …



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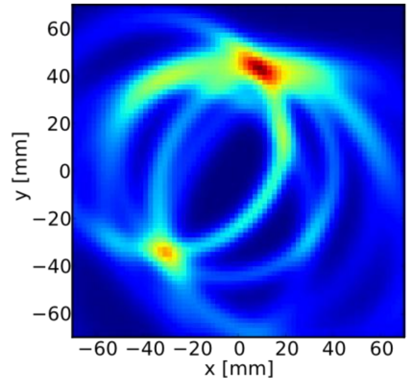

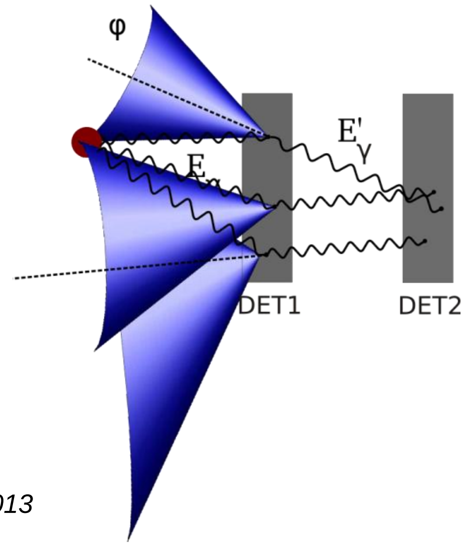

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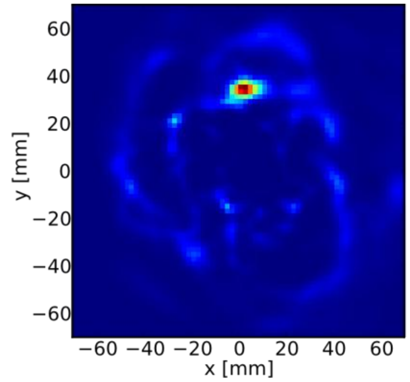
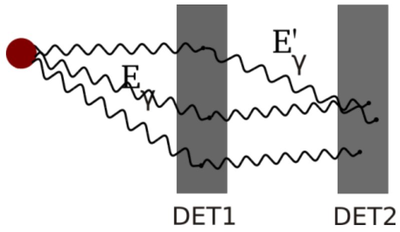
PGI with electronic collimation

- Compton camera concept
  - Scatter plane(s) + absorber plane
  - Measure deposited energies and interaction positions
  - Each valid event defines a cone
  - Superposition of many cones + image reconstruction (MLEM)
    → 3D Image of the source





Courtesy of
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PGI with electronic collimation

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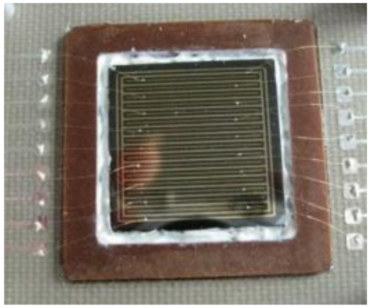
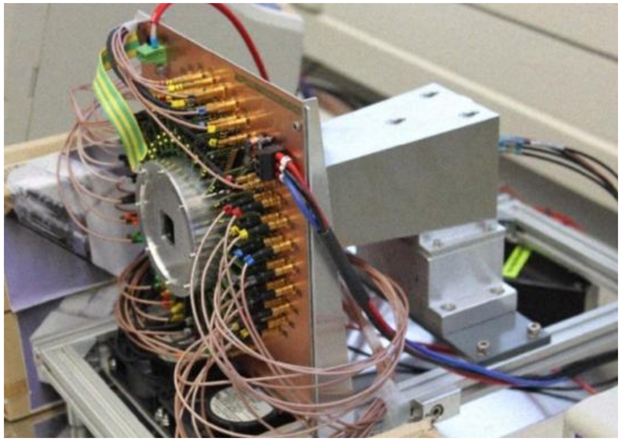
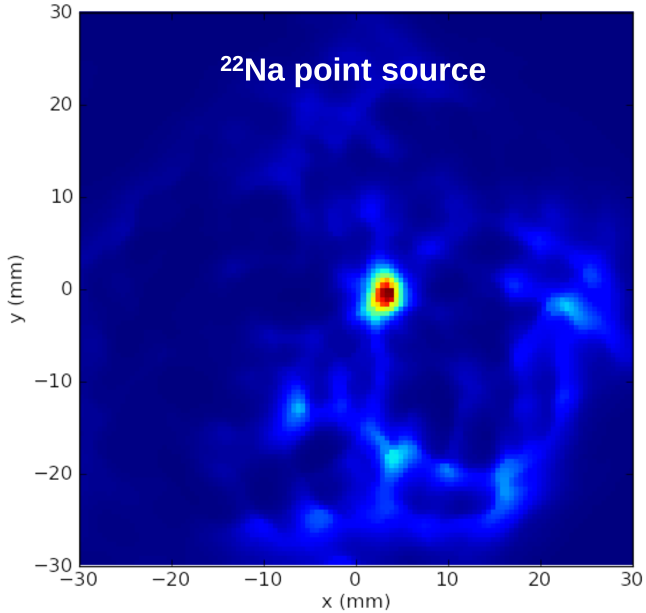
  - Dresden: CZT + segmented LSO/BGO





Kormoll et al., NIM A626-627 (2011) 113
Kormoll et al., IEEE NSS/MIC 2013



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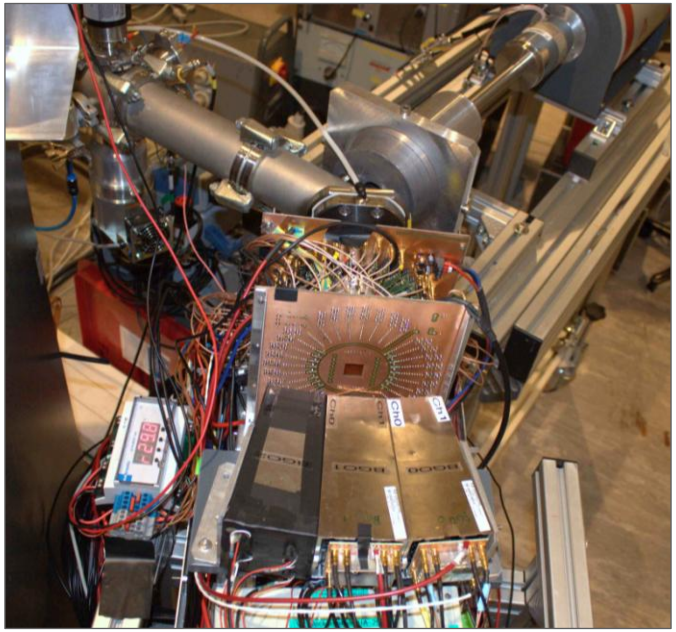
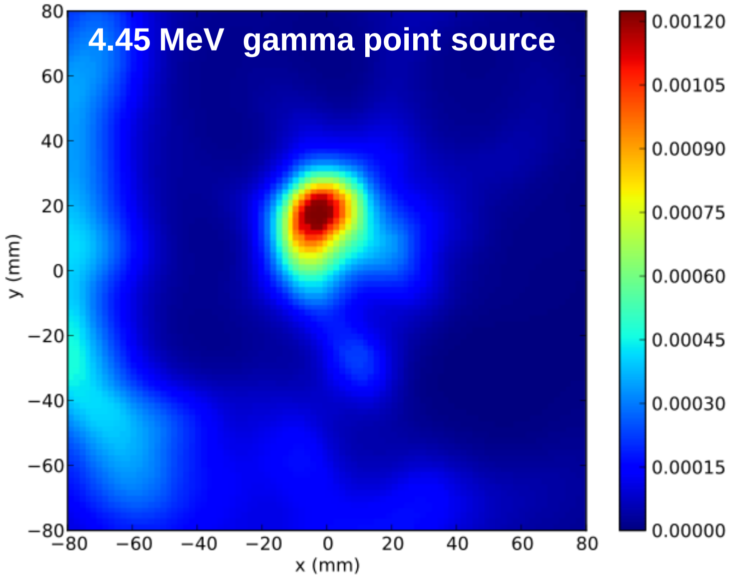


Kormoll et al., NIM A626-627 (2011) 113
Kormoll et al., IEEE NSS/MIC 2013



PGI with electronic collimation

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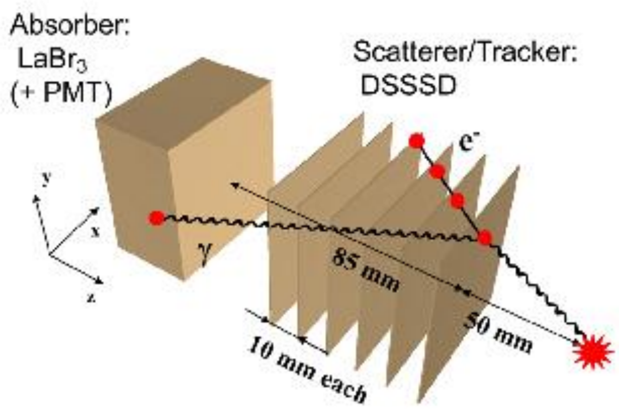
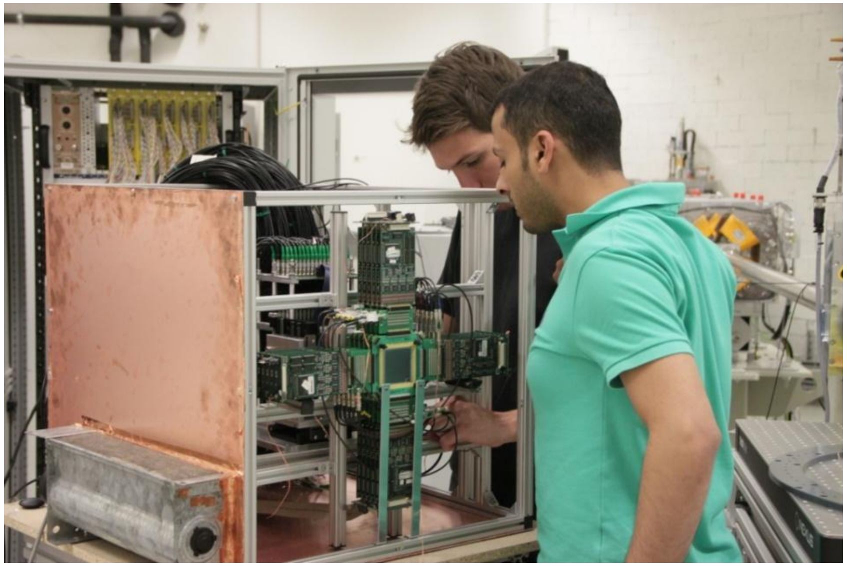
  - Dresden: CZT + segmented LSO/BGO
  - Munich: double-sided Si strip detectors + monolithic $LaBr_3$



Thirolf et al., NN 2015



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- Compton camera concepts for prompt gamma imaging: Various approaches differing in the detectors design
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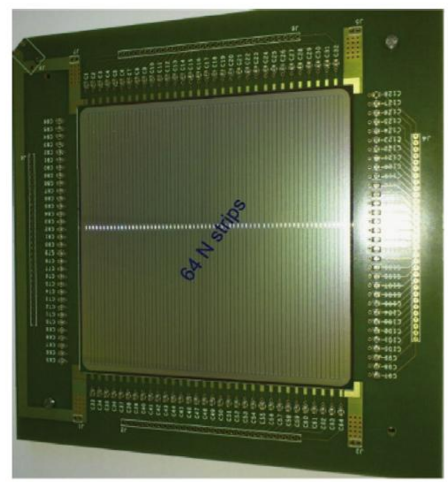

Krimmer et al., NIM A787 (2015) 98

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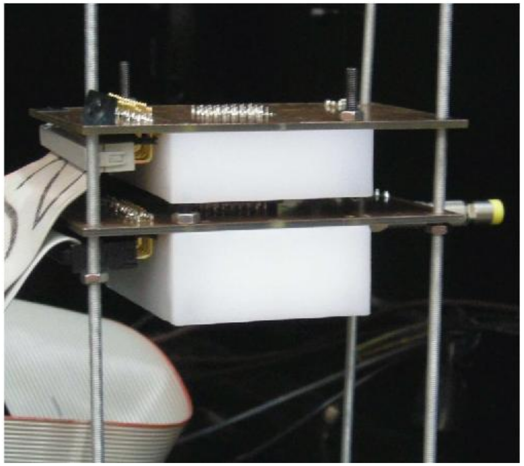

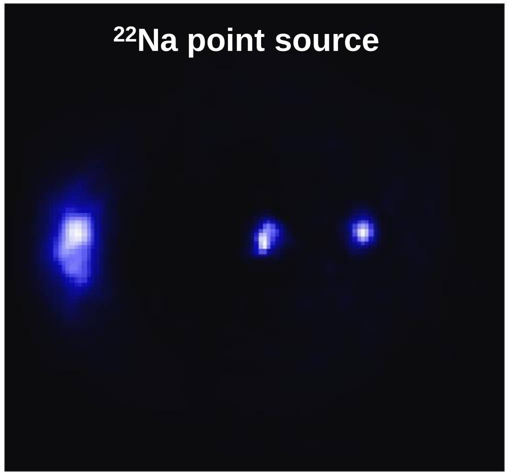

Llosa et al., NIM A718 (2013) 130

PGI with electronic collimation

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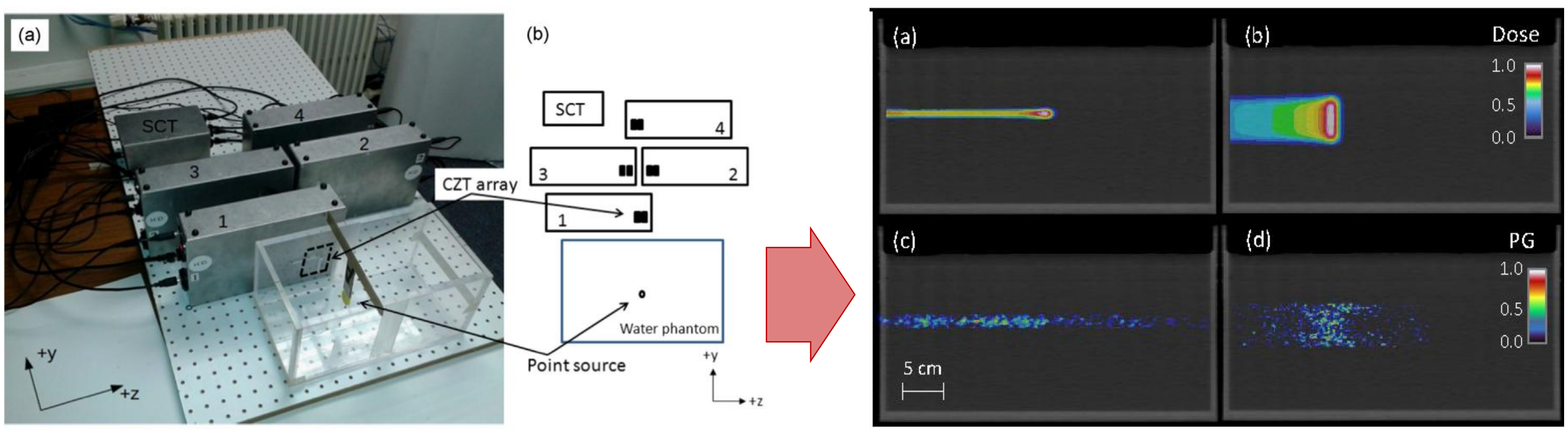
  - Munich: double-sided Si strip detectors + monolithic $LaBr_3$
  - Lyon: double-sided Si strip detectors + segmented BGO
  - Valencia: monolithic $LaBr_3$ + monolithic $LaBr_3$
  - Baltimore: multistage CZT based on POLARIS



McCleskey et al., NIM A785 (2015) 163
Polf et al., PMB 60 (2015) 7085

PGI with electronic collimation

- Compton camera concepts for prompt gamma imaging: Various approaches differing in the detectors design
- Results
  - ✓ Imaging of radioactive sources (^{22}Na)
  - ✓ Imaging of monoenergetic 4.45 MeV gamma rays
  - ~ Imaging of proton-induced prompt gamma rays at long exposures and very low beam currents
  - ✗ PGI with clinical beam currents and exposure times

Estimate		
Protons per PBS spot	up to	10^8
Scatter detector size and distance from isocenter		5×5 cm^2 25 cm
Camera efficiency *)		1.2×10^{-3}
Usable events per PBS spot	$\propto$	50
Scatter detector trigger rate **)	$\propto$	3×10^6

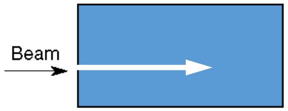
**) measured / scaled for a CZT-BGO setup; Golnik, PhD thesis, 2015 (unpublished)*

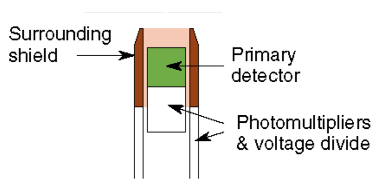
***) conservative estimate considering the minimum interaction probability of gammas in 5mm CZT*

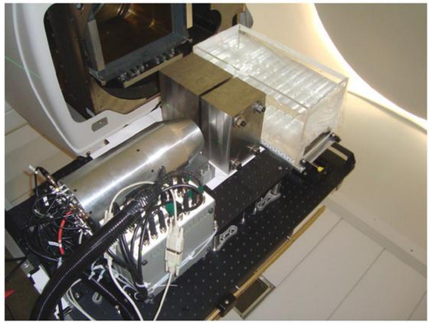
PGI with electronic collimation

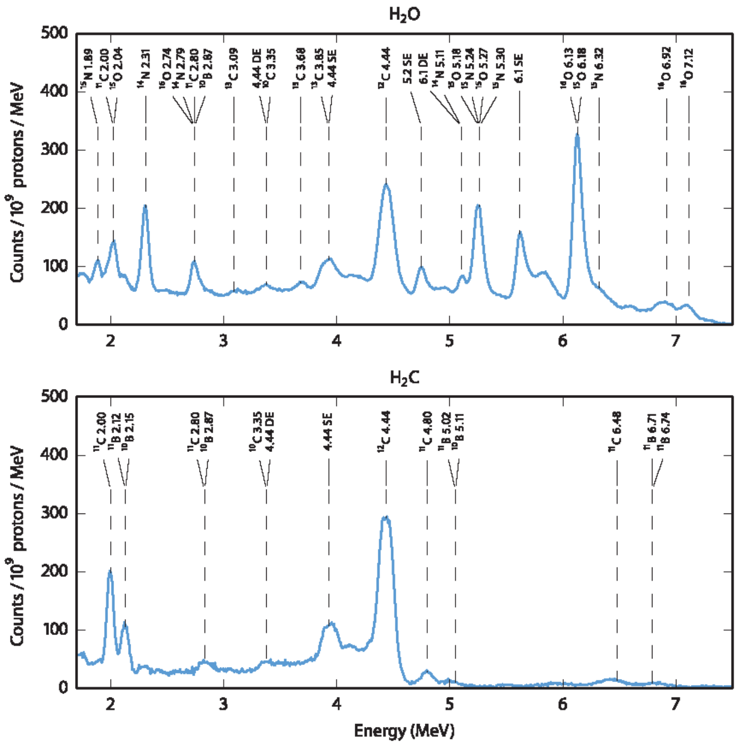
- Compton camera concepts for prompt gamma imaging:
  Various approaches differing in the detectors design
- Results
  - ✓ Imaging of radioactive sources (^{22}Na)
  - ✓ Imaging of monoenergetic 4.45 MeV gamma rays
  - ~ Imaging of proton-induced prompt gamma rays
    at long exposures and very low beam currents
  - ✗ PGI with clinical beam currents and exposure times
- Applicability basically biased by
  - Event statistics (few usable events per target volume element)
  - Detector load (limits size of detectors and camera)
  - Load asymmetry (thin scatter detectors, thick absorber detectors)
- Are there simpler/cheaper solutions?

- Idea *Verburg and Seco, PMB 59 (2014) 7089*
  - Emission spectrum of prompt gamma rays is correlated with the residual particle energy (range)
  - Spectroscopy of prompt gamma rays from a given depth discloses the residual range









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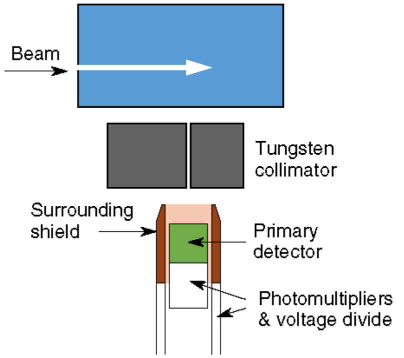

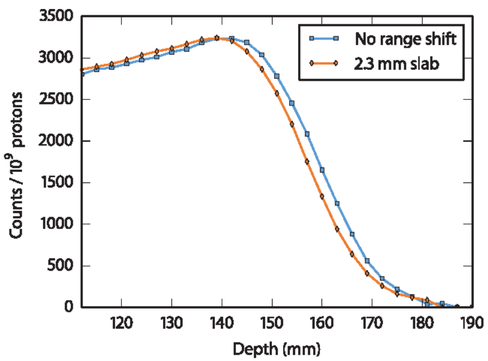

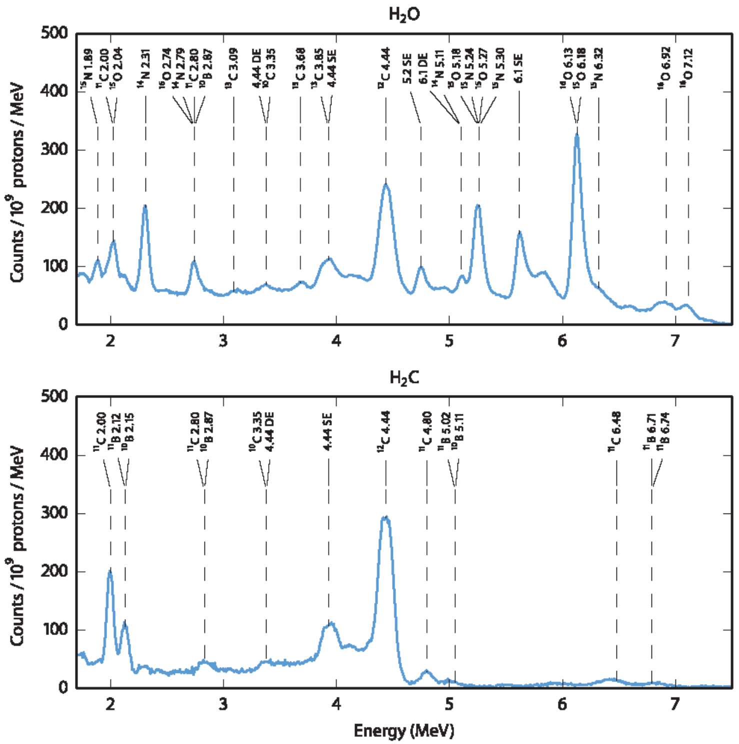

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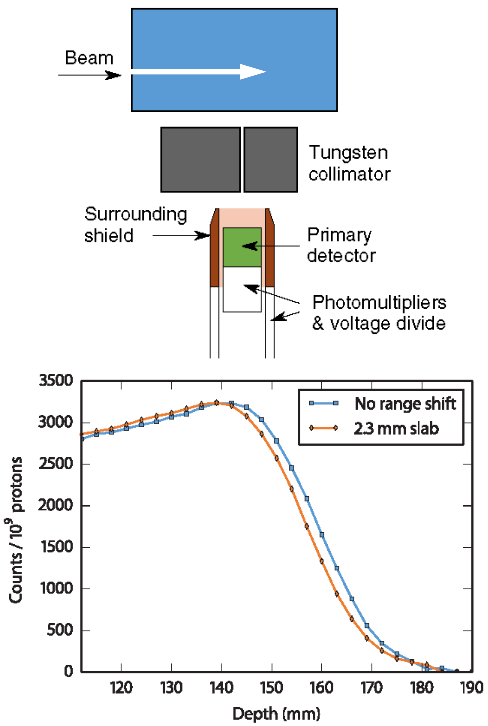

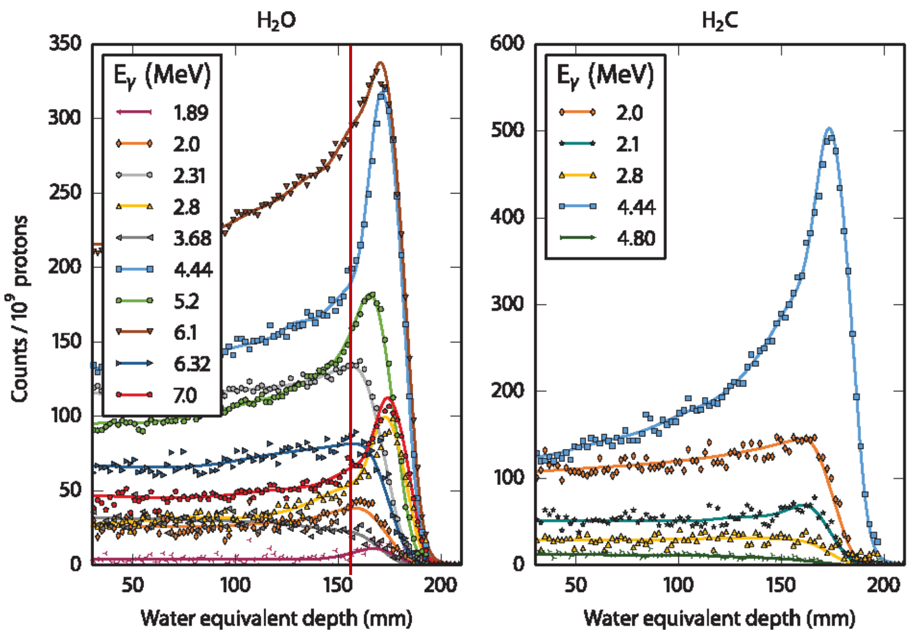

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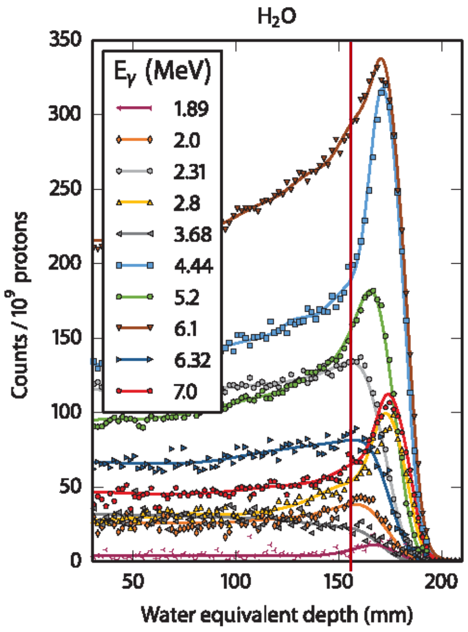
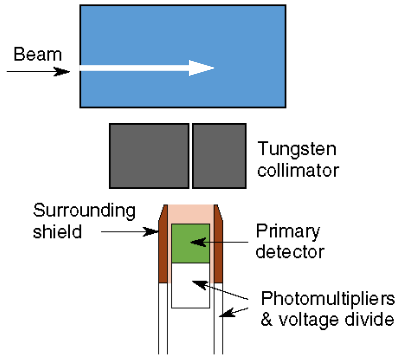
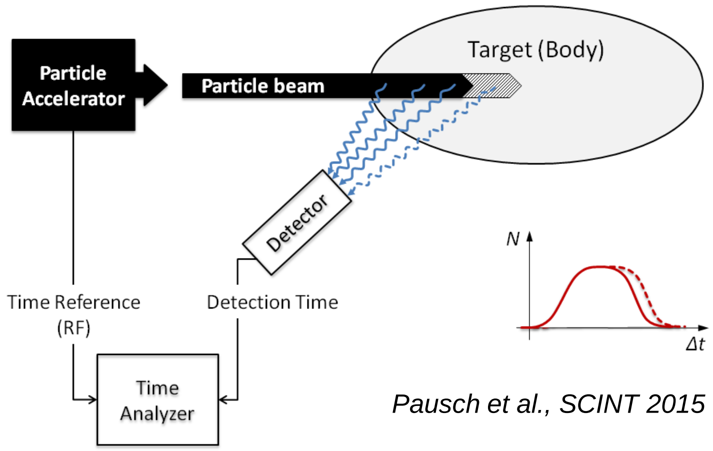
  - Spectroscopy of prompt gamma rays from a given depth discloses the residual range
- Procedure
  - Focus a collimated spectroscopic detector on the last few millimeters of beam range
  - Measure distinct line intensity ratios
- Challenge
  - Achievable statistics
    - → to be combined with multi-slat concept?





Prompt gamma timing (PGT)

- Idea *Golnik et al., PMB 59 (2014) 5399*
  - Emission time of prompt gamma rays is correlated with the stopping time of particles in tissue and thus with the stopping distance (range)
  - Timing spectroscopy of prompt gamma rays discloses the particle range



Pausch et al., SCINT 2015

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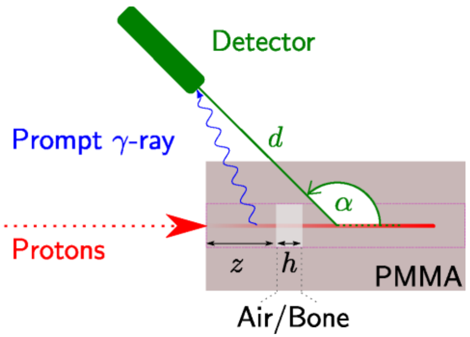

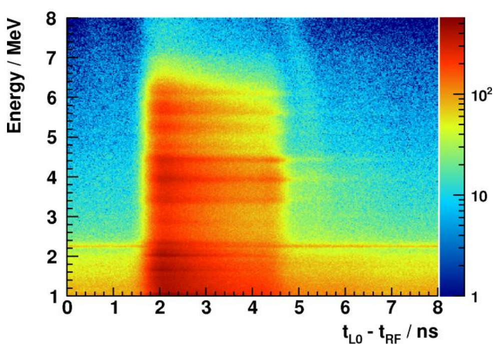

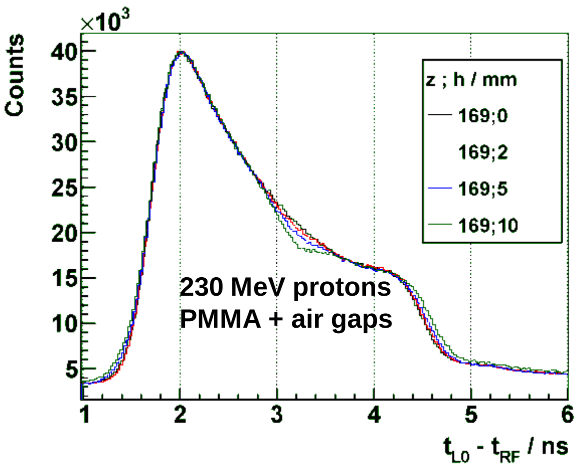

Hueso González et al., PMB 60 (2015) 6247

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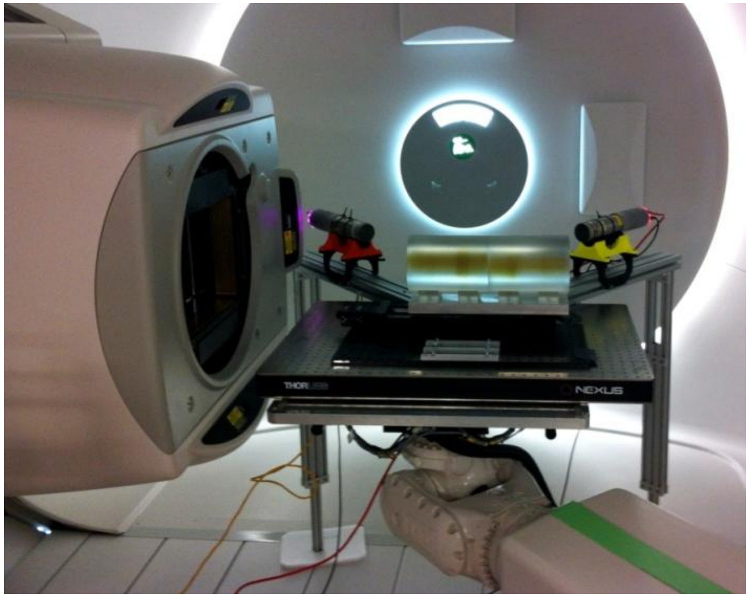
  - Timing spectroscopy of prompt gamma rays discloses the particle range
- Procedure
  - Put timing detectors close to the target
  - Measure timing spectra
- Advantage and challenge
  - Uncollimated detector
  - Statistics only limited by tolerable detector load and DACQ throughput

    → Fast energy and timing spectroscopy at about 1 Mcps throughput rates and up to 10 Mcps detector load

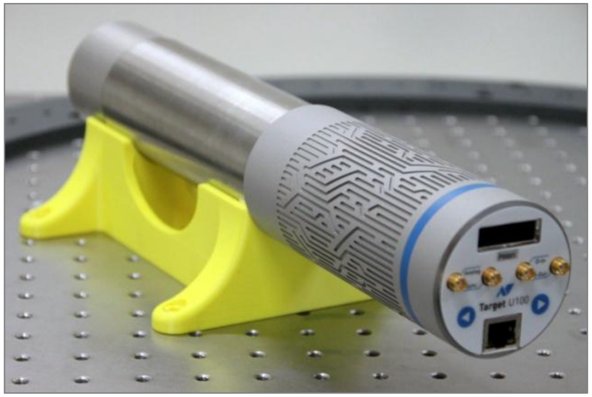
Pausch et al.,
paper accepted for publication in IEEE TNS, 2015



State of the art in PGT

- PGT hardware *Pausch et al., paper accepted for publication in IEEE TNS, 2015*
  - Detection of ≤ 5 mm range deviations in single pencil beam spots
  - Maximum throughput to collect the statistics needed with few (2-4) detectors

Target U100 - Parameters and Features	
Features	Fast timing and energy spectrometer List mode and spectrum (1D, 2D) output 14-pin plug-on PMT connector Ethernet featuring POE
Timing resolution	< 200 ps (FWHM) with $CeBr_3$ detector
Dynamic range	> 1:1.000 (10 keV … 10 MeV)
Throughput	up to ~1 Mcps (spectroscopy, list mode)



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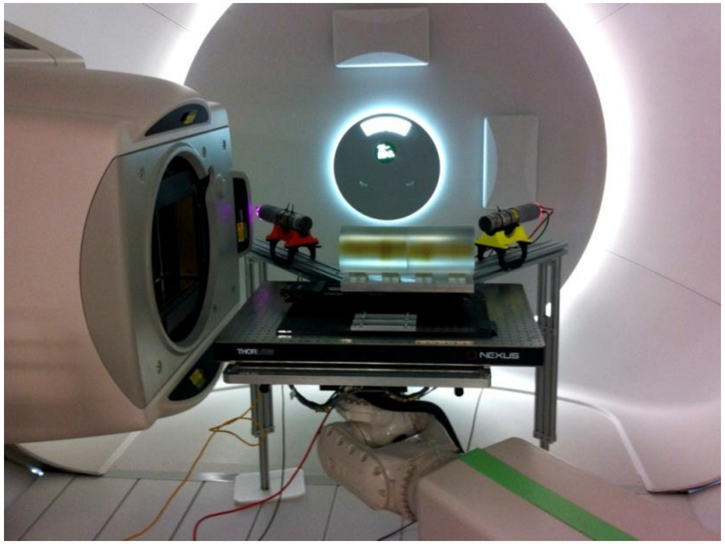

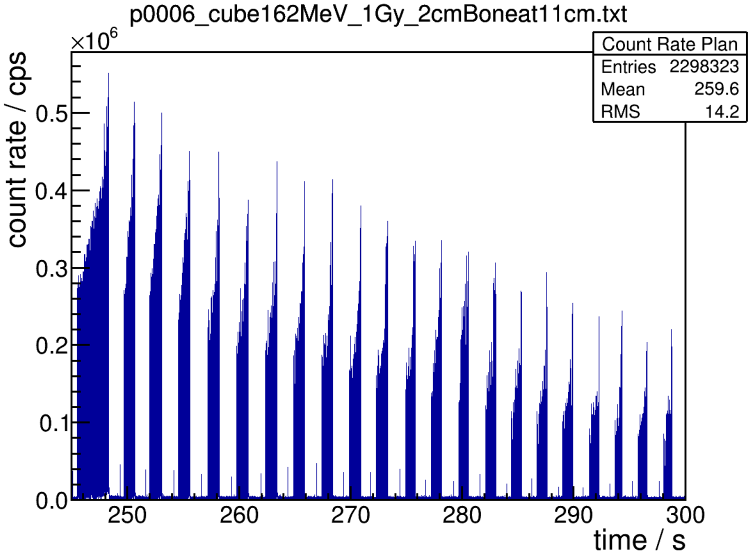

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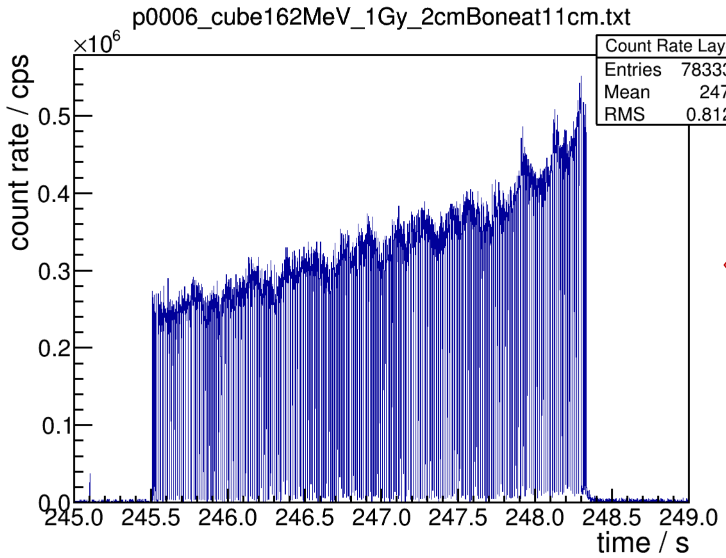

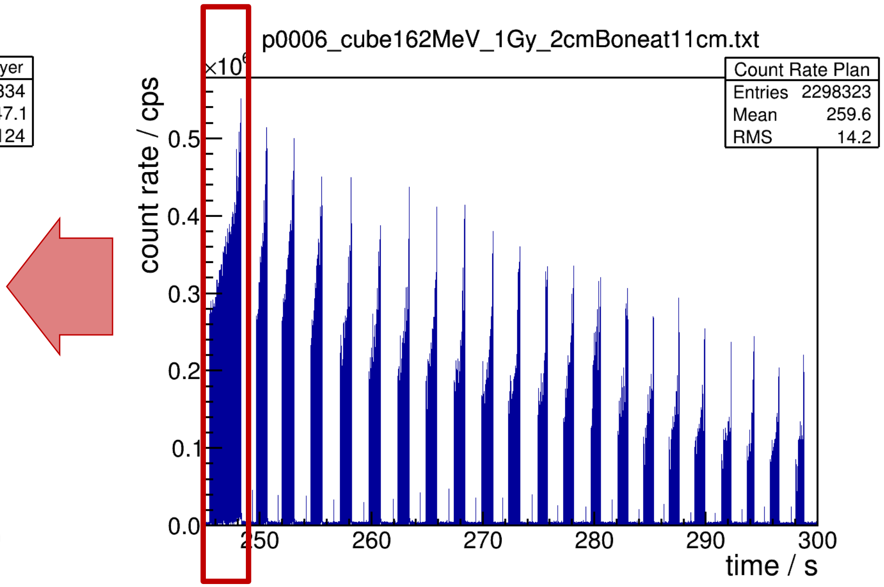

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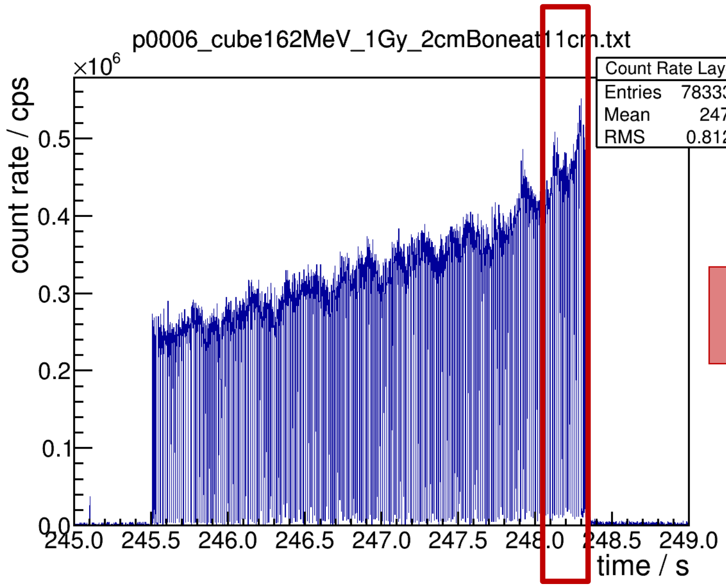

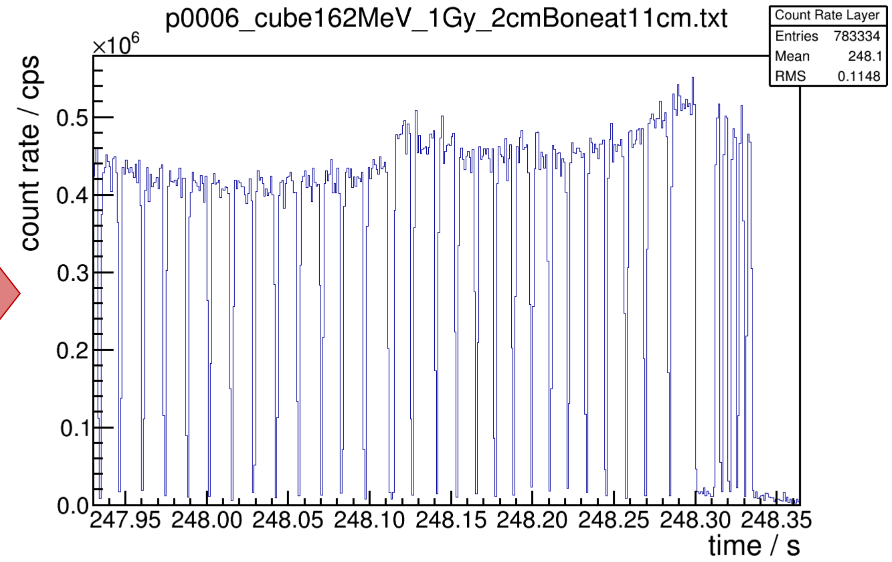

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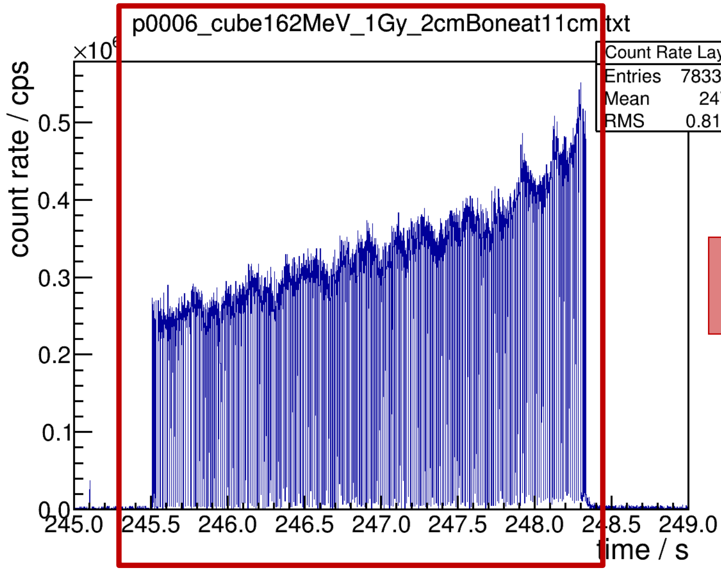

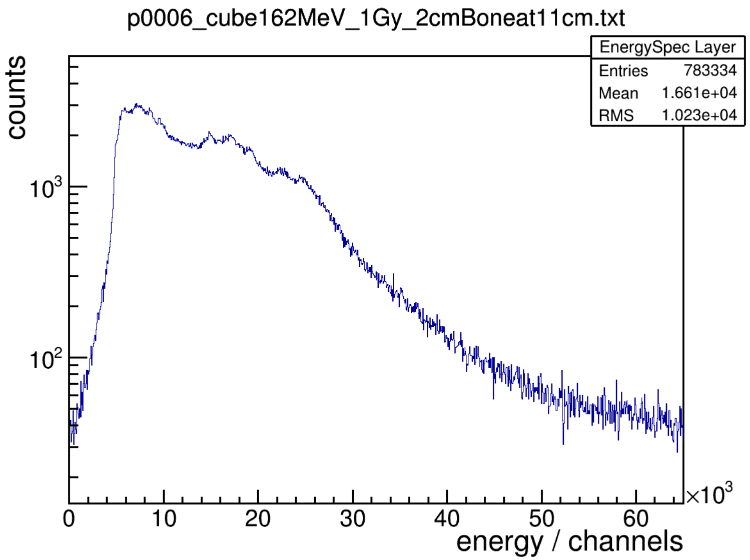

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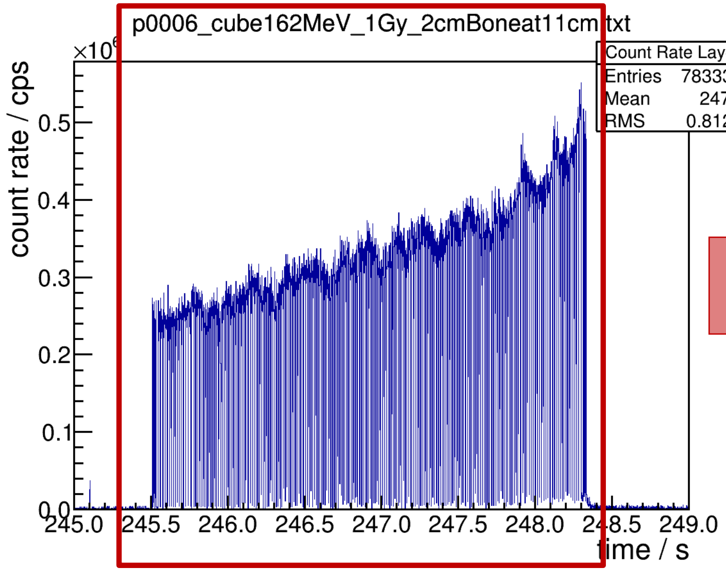

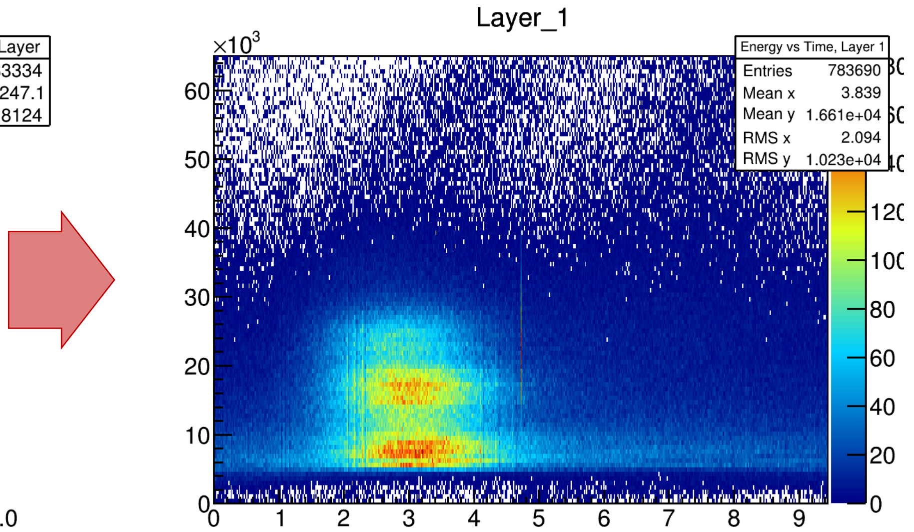

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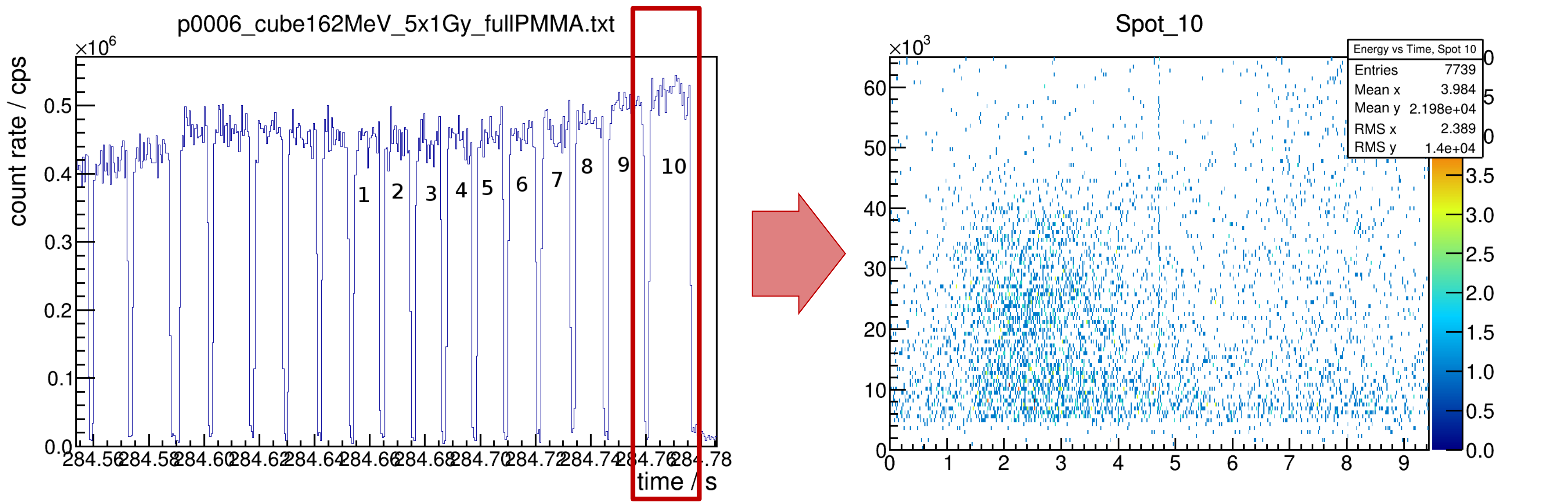

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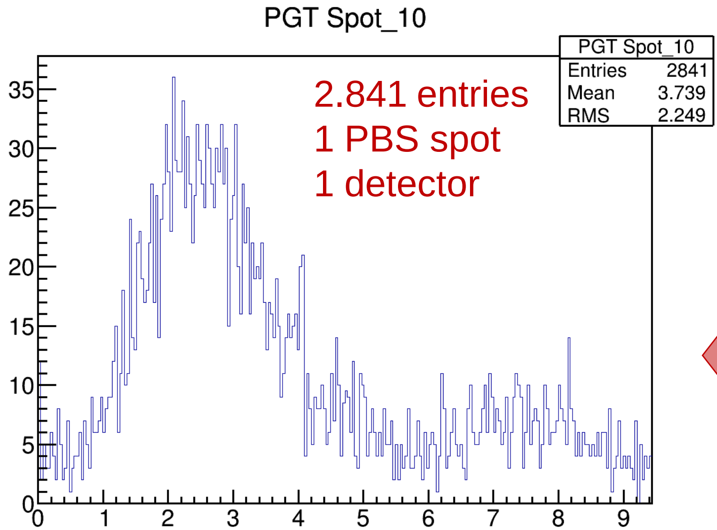
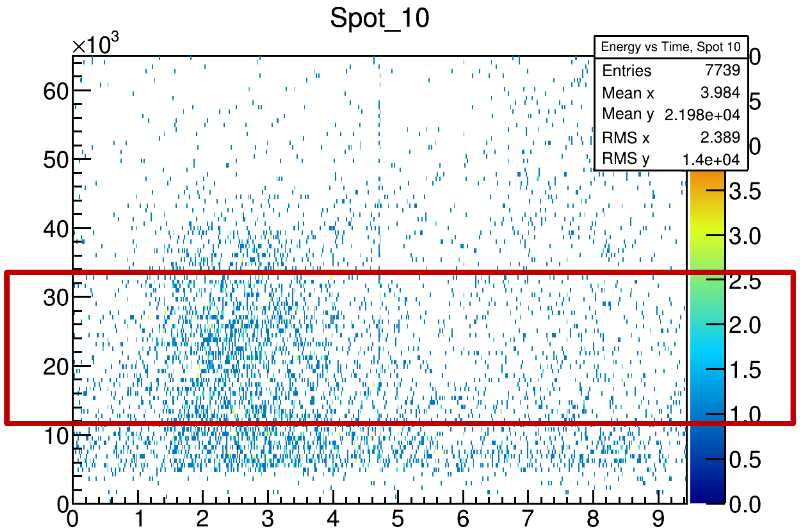
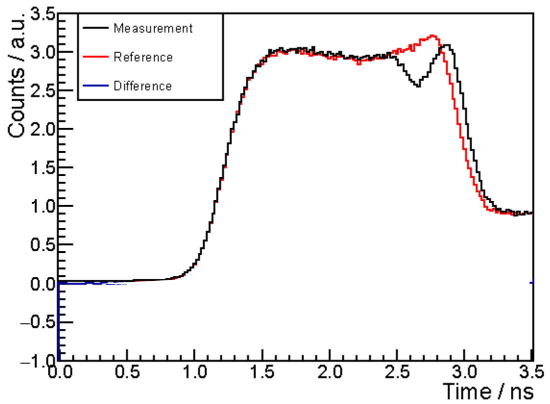


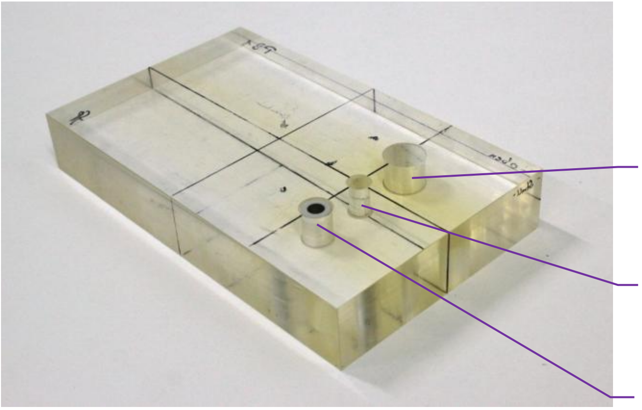


  - This is in accordance with our estimates and design goals.

State of the art in PGT

- Prompt gamma timing *Petzoldt et al., submitted to PMB, 2015*
  - Proton beam scanning of a structured PMMA target at OncoRay to explore imaging capabilities of PGT
  - PGT spectra measured and corrected for RF-bunch phase shifts, target absorption, and solid angle variation





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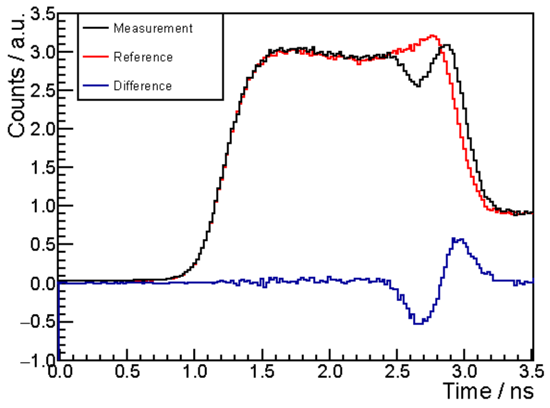

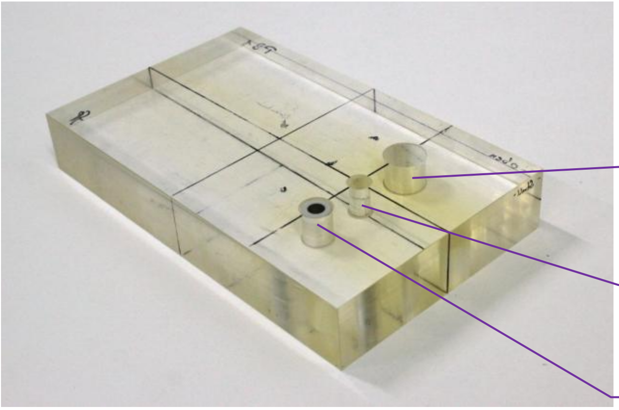

∅ 19mm (large) cavity

∅ 9mm (small) cavity

∅ 13mm filled cavity („marrowbone“)

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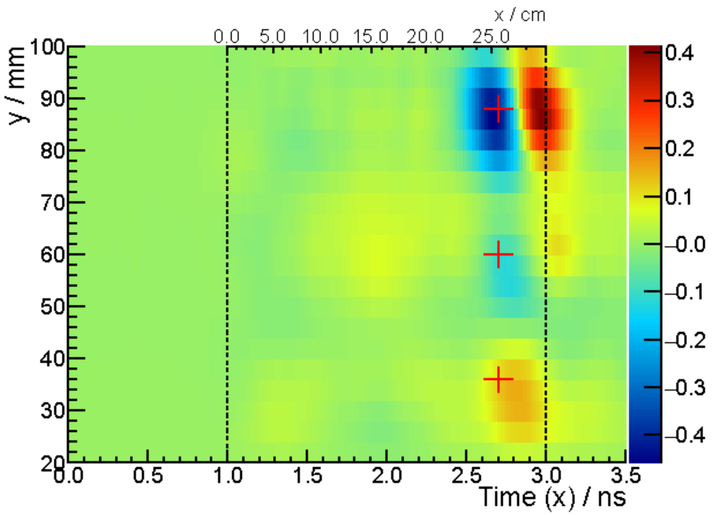

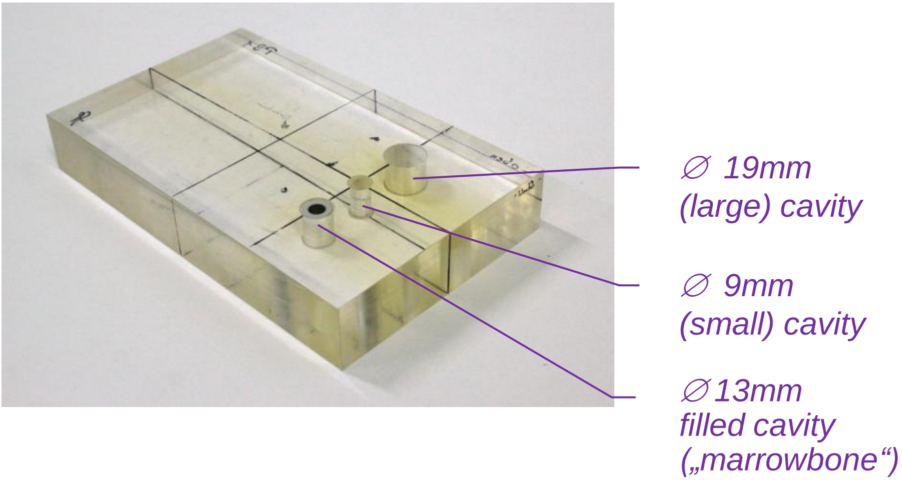

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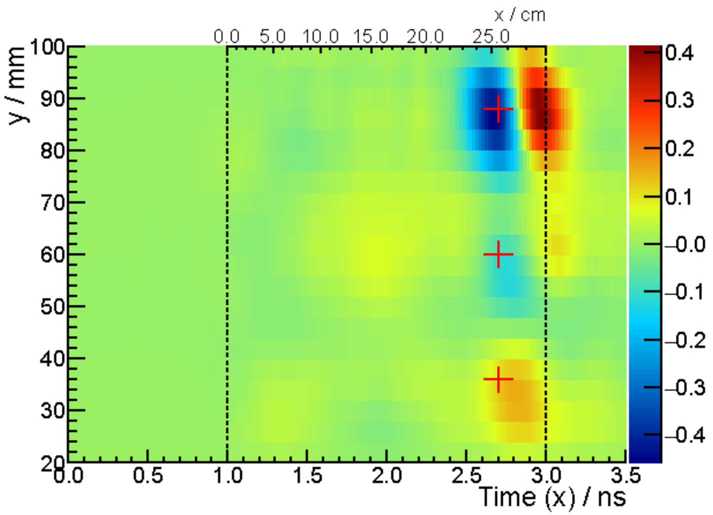


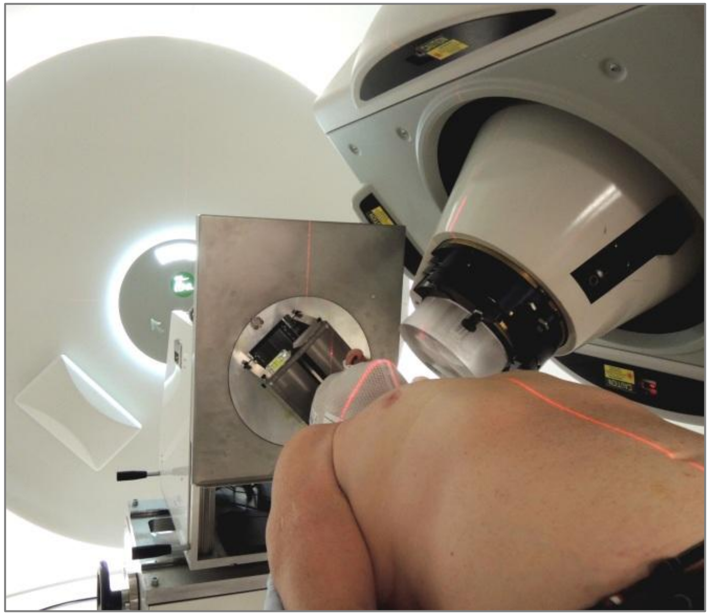
First prompt-gamma based image of target inhomogeneities and resulting proton beam overranges ever made!

Not a clinical scenario:
High dose, maximum beam energy, long exposure (minutes per "spot")

First clinical application of PGI

- OncoRay has operated / tested the IBA slit camera prototype since Sept 2014
- First clinical application in Aug 2015
  - H&N patient, DS, 3 fields, proton boost
  - Inter-fractional treatment verification

Barczyk, Priegnitz et al., submitted to PMB, 2015
Richter et al., submitted to Radiother Oncol, 2015



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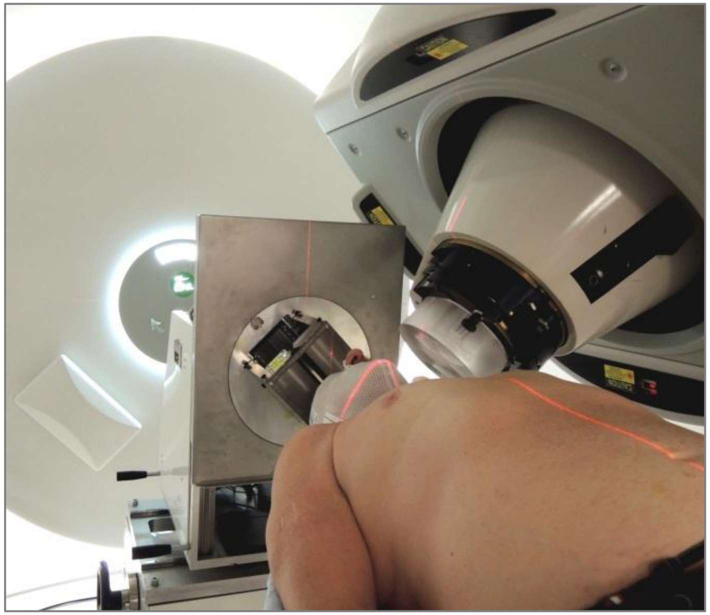
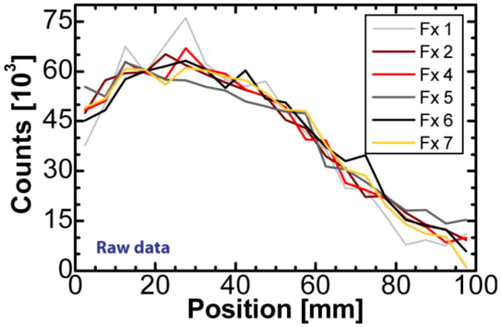
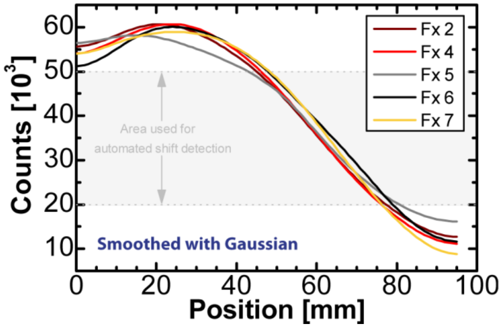


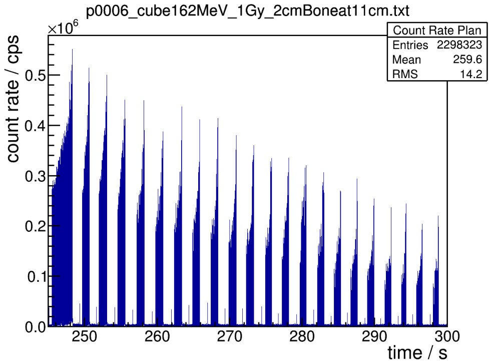


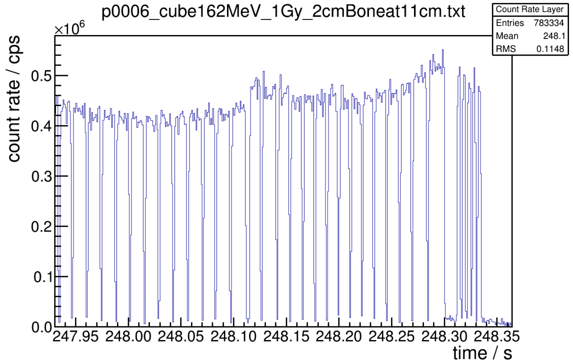


ΔR= [-2.0 mm,1.3 mm]
consistent with control-CT based dose-recalculation

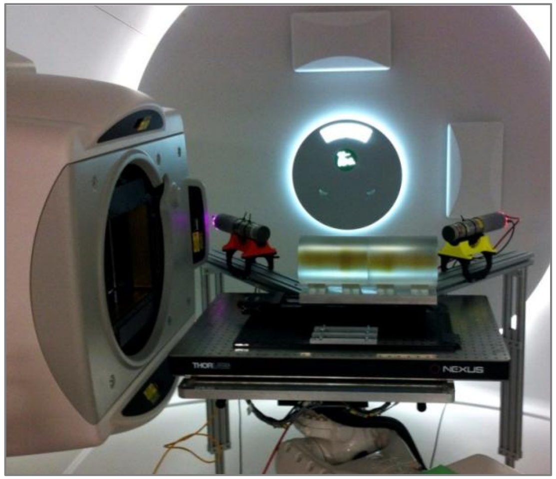
Prospects for 4D treatment verification

1. All PG methods could provide accurate beam timing information





Petzoldt et al., unpublished data

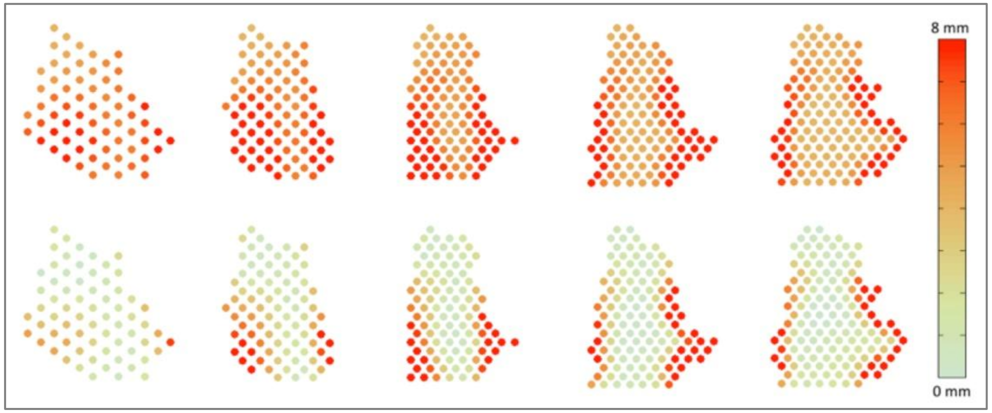


- Each PBS spot can be exactly allocated in time
- If synchronized with motion monitoring, this provides the exact motion phase of spot delivery
- If 4D CT and motion model are available, this allows calculating the 3D dose deposition for each individual PBS spot after the treatment (supposed that the lateral spot positions of the full sequence are known)

Prospects for 4D treatment verification

1. All PG methods could provide accurate beam timing information
   → Post-treatment 3D dose evaluation

2. Some methods could provide range verification per PBS spot
   – IBA slit camera (sensitivity study to setup errors in a realistic PBS plan):



Janssens et al., accepted for publication in Radiother Oncol, 2015

   – PGT (estimates supposing 4 of the existing hardware units):
     $\Delta R \leq 5$ mm for PBS spots with $\geq 10^8$ protons
   – This allows verifying the 3D dose deposition for each individual PBS spot

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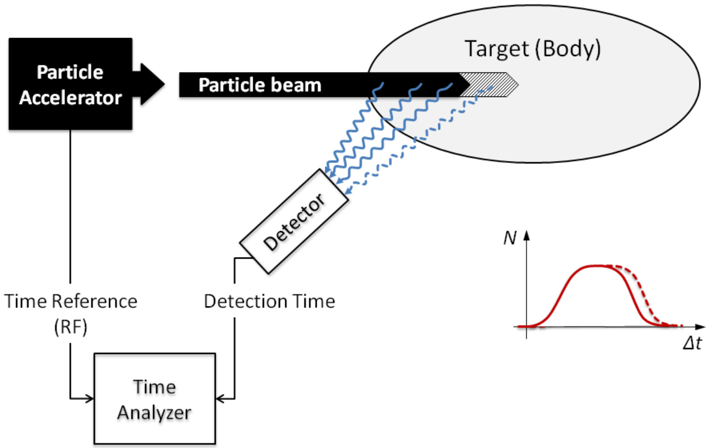
   - PGT spectrum comprises
     - Proton stopping time
     - Prompt gamma TOF



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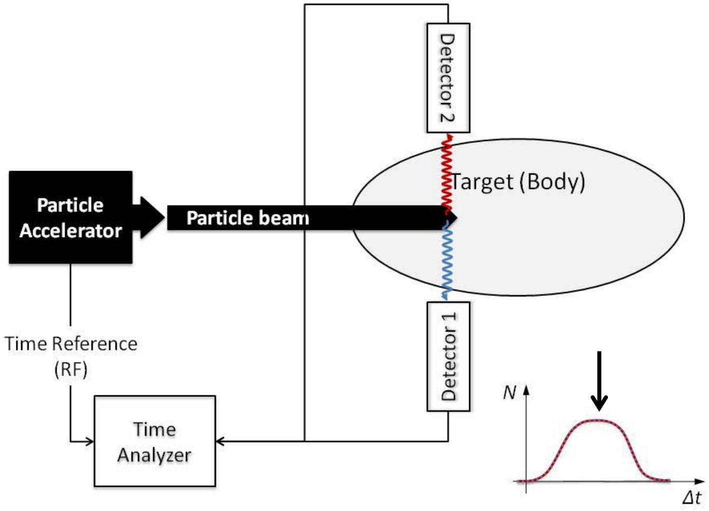

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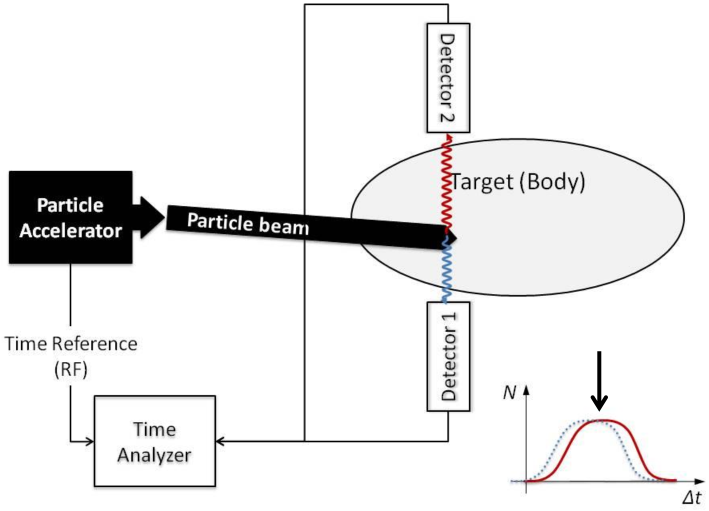

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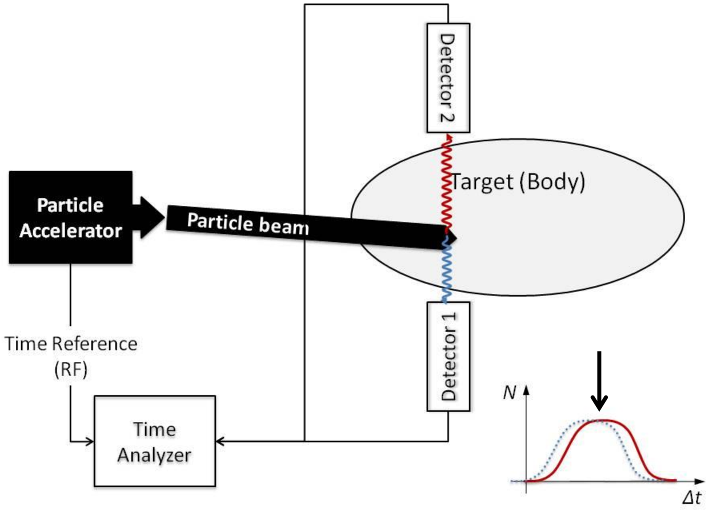
3. PGT could provide beam position information per PBS spot
   - PGT spectrum comprises
     - Proton stopping time
     - Prompt gamma TOF
   - Use of multiple (at least 4) PGT detection units
     - Improved statistics per spot
     - TOF component discloses beam position



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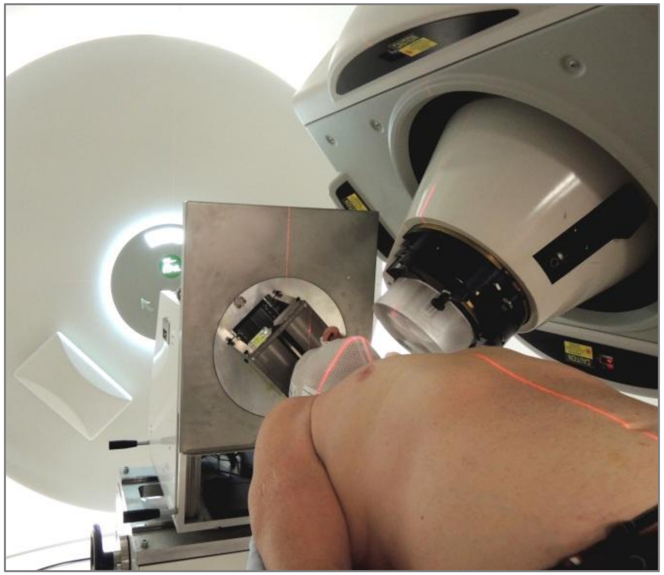
   → Post-treatment 3D dose verification
3. PGT could provide beam position information per PBS spot
   → Post-treatment 3D dose verification

Summary and conclusions

- Prompt gamma rays (PG) are appropriate probes for range assessment in PT.
- So far, none of the electronically collimated PG imaging (PGI) systems under development could demonstrate imaging under treatment conditions. “Simpler” approaches seem more promising.
- So far, the passively collimated IBA knife-edge slit camera is the only PGI system with proven clinical applicability.
- PG timing (PGT) and spectroscopy (PGS) are promising, inexpensive alternatives to PGI. Clinical tests are in sight.
- PG measurements, combined with 4D CT and motion monitoring, could provide data for 3D dose re-calculation after treatments.



- PGI and PGT could even provide range verification for (strong) PBS spots.
- OncoRay is on the way to translating PGI and PGT into clinical practice.

Thank you for your attention.