Online control for Quality Assurance

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Motivations

- Range uncertainties, margin reduction…

We better trust what we see!

→Improve and secure ballistic precision

  - At the pencil beam spot basis (or few selected spots)
  - Real time
  - Range verification at mm precision (smaller than actual margins)
  - According to beam delivery mode (beam species, accelerator…)
  - Geometrical constraints (gantries, patient positionning…)
  - No reduction of patient workflow
  - Affordable cost!

- A system will not be optionnal if the efficiency is proven

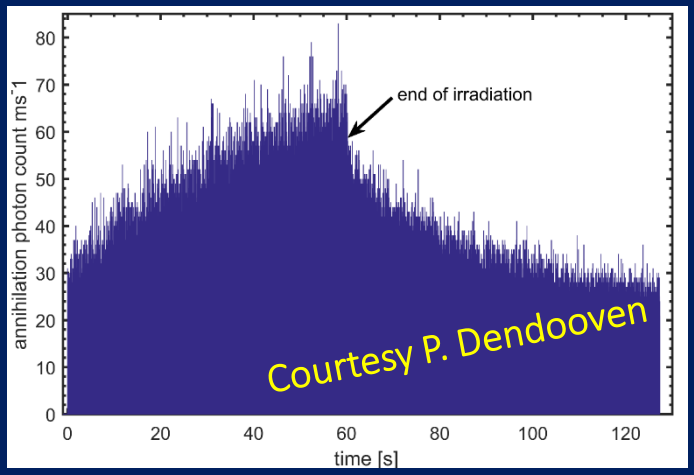
Outline

- Positron Emission Tomography
- Prompt gamma:
  - Prompt Gamma imaging
  - Non imaging modalities:
    - Prompt Gamma Spectroscopy
    - Prompt Gamma Peak Integral
    - Prompt Gamma Timing

PET ion range monitoring

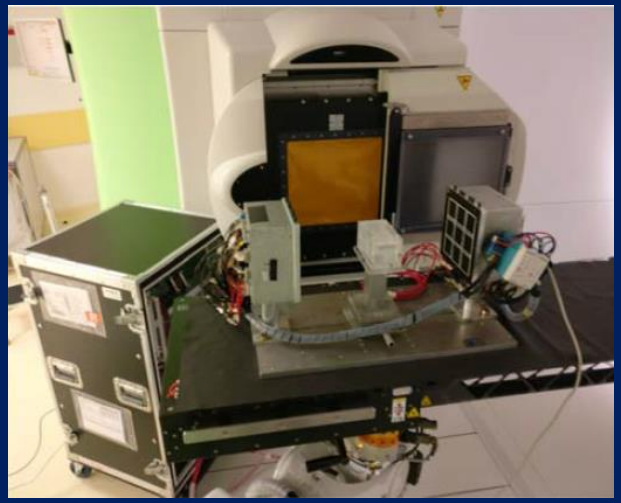
- In-room or Off-line:
  - Whole fraction verification only
- In-beam PET: acquisition between beam bunches
  Suitable at low duty cycle (eg synchro-cyclotrons)
  + short lived isotopes, eg ^{10}C
  + No washout
  - Restricted or complicated geometries

Long radioisotope lifetime ➔ no real-time



DPGA – (Clermont)

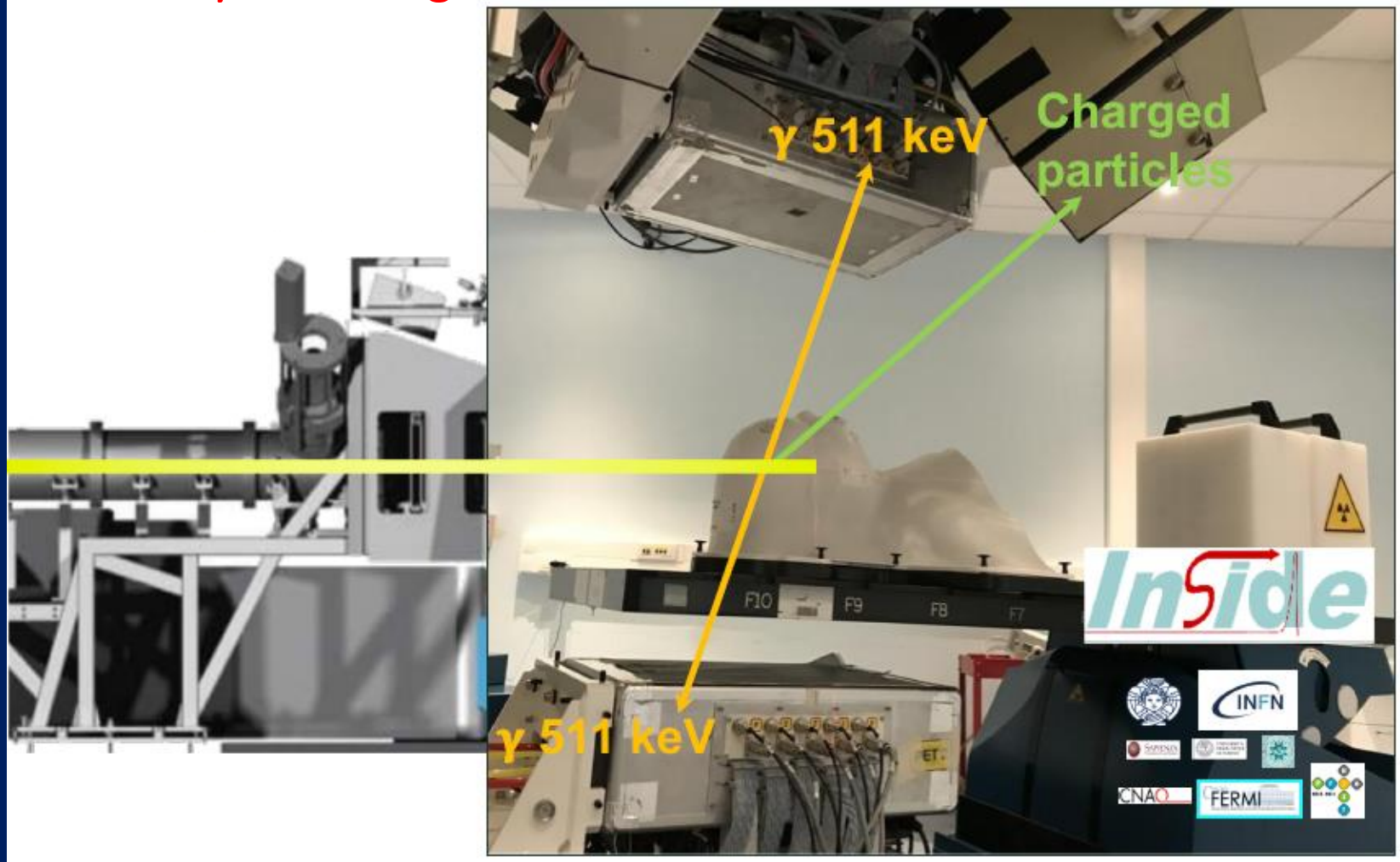
Dual ring OpenPET (NIRS)
[Yoshida IEEE TRPMS 2014]



DoPET(INFN)
Topi et al, IEEE TRPMS 2019

INSIDE BI-MODAL IN-VIVO RANGE VERIFICATION SYSTEM

Courtesy MG Bisogni



INnovative **S**olutions for **I**n-beam **D**osim**E**try in Hadrontherapy

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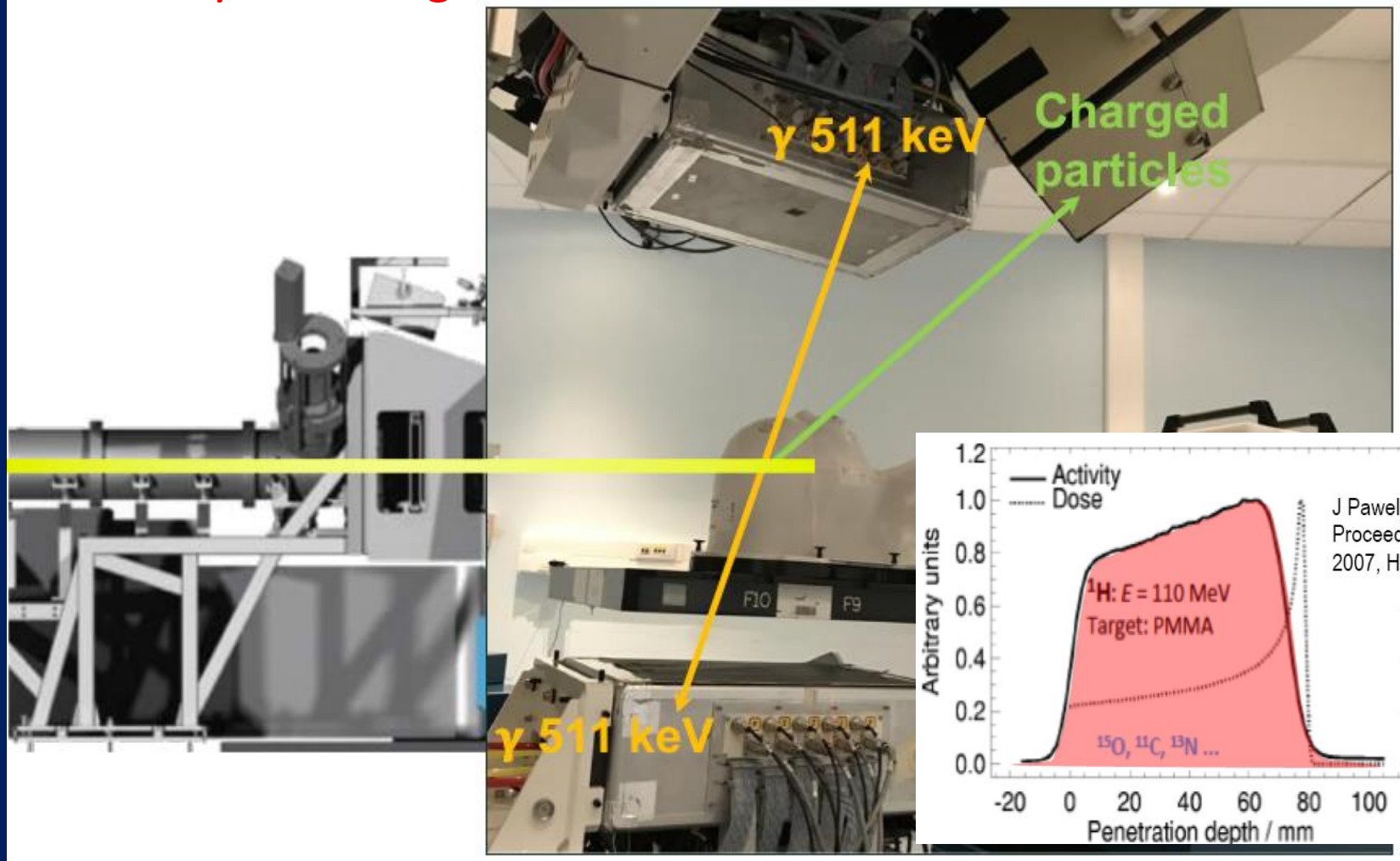

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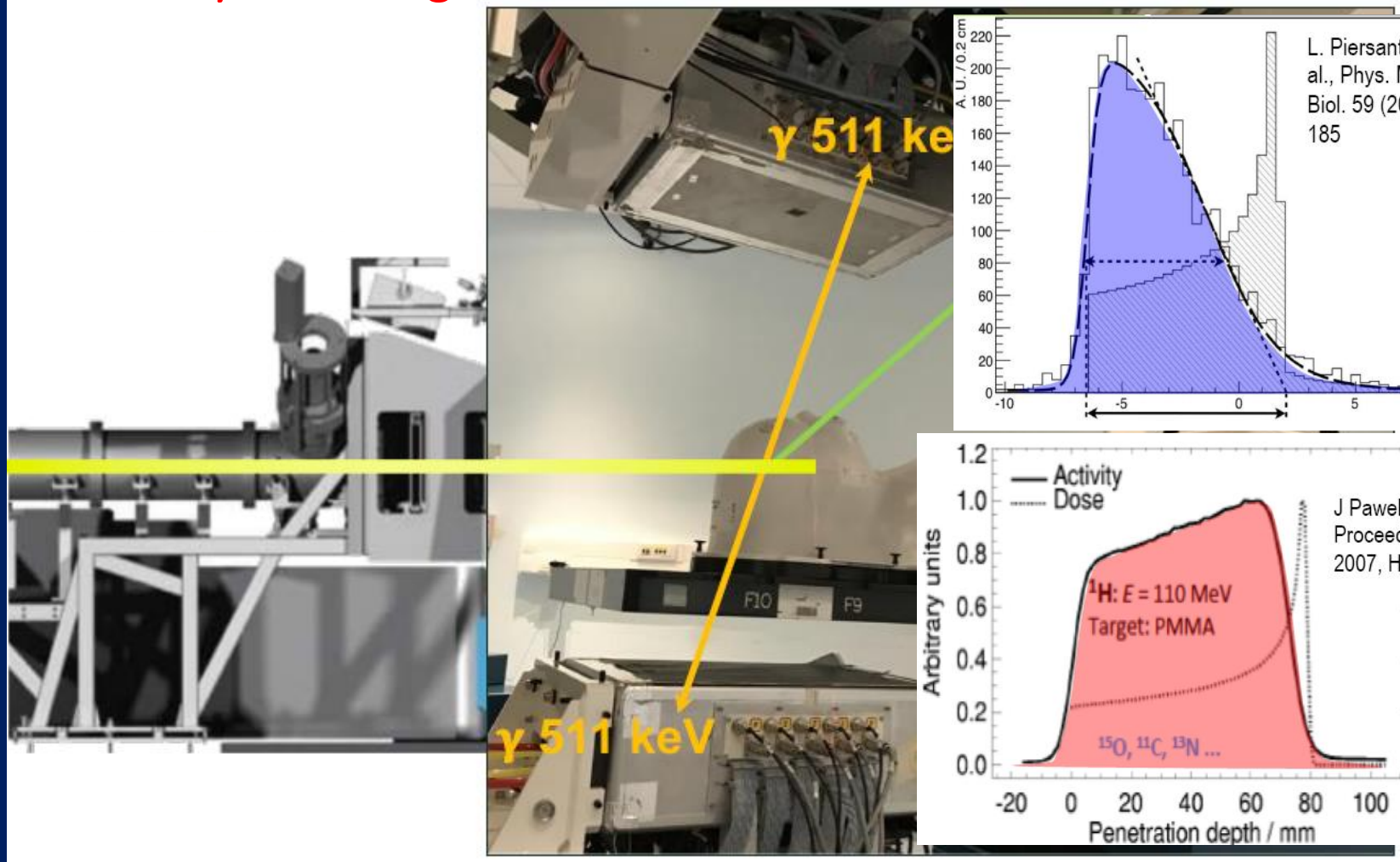

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INSIDE OBSERVATIONAL CLINICAL TRIAL

ClinicalTrials.gov
id: NCT03662373

Courtesy MG Bisogni

Cohort	40 patients treated with particle therapy (20 with protons and 20 with carbon ions)
Inclusion Criteria	• patients treated at CNAO with protons or carbon ions with horizontal beam line; • patients affected by meningioma or squamous cellular rhinopharynx carcinoma treated with proton therapy; • patients affected by Adenoid Cystic Carcinoma (ACC) or skull base (clivus) chordoma treated with carbon ion therapy; • full mechanical compatibility of the INSIDE monitoring system with all medical devices needed during the irradiation; • all emergency procedures are possible notwithstanding INSIDE system in the acquisition position; • signed written informed consent by patient.
Esclusion Criteria	• missing informed consent; • not affected by one of the selected pathologies; • failure of pre-treatment mechanical compatibility assessment; • failure of pre-treatment emergency procedures check; • medical or individual reasons.

Starts July 2019: first 20 patients, 4-6 weeks monitoring

Real-time PET for range verification

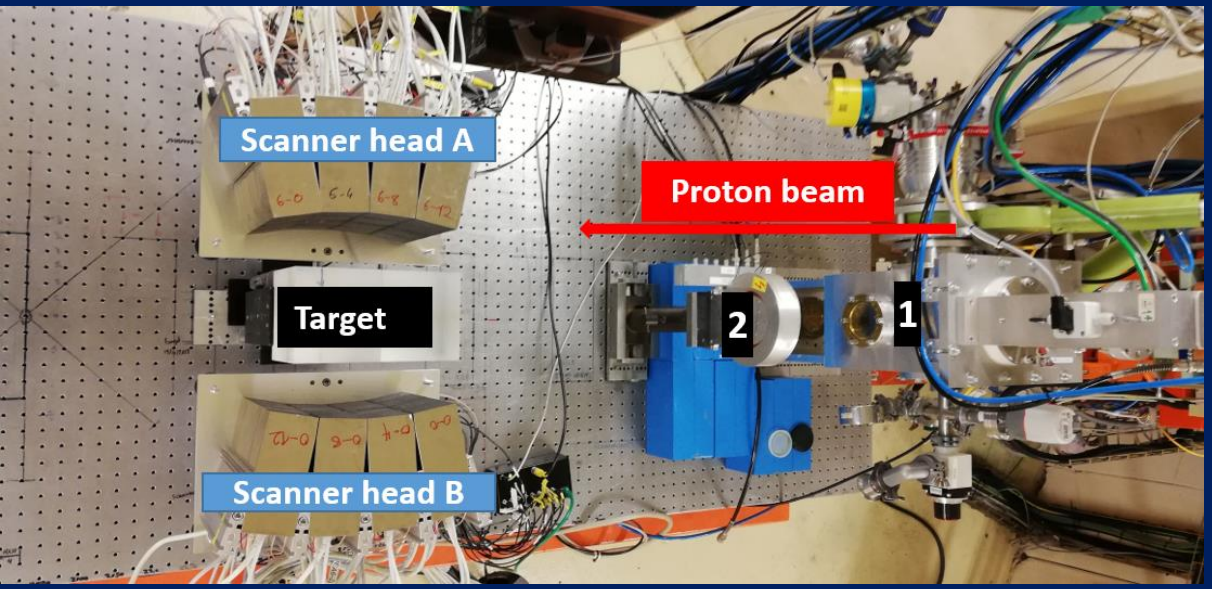
Very short-lived radioisotope:
good candidate: N-12 ($T_{1/2}$ = 11 ms)

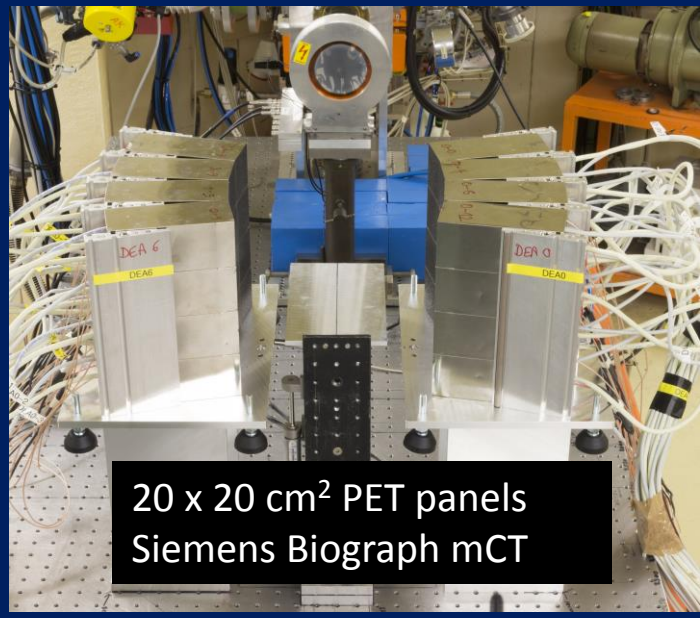
Benefits for PET imaging:

- maximum number of counts
- minimal biological washout

Courtesy P. Dendooven, S. Brandenburg, I. Ozoemelam, KVI-CART

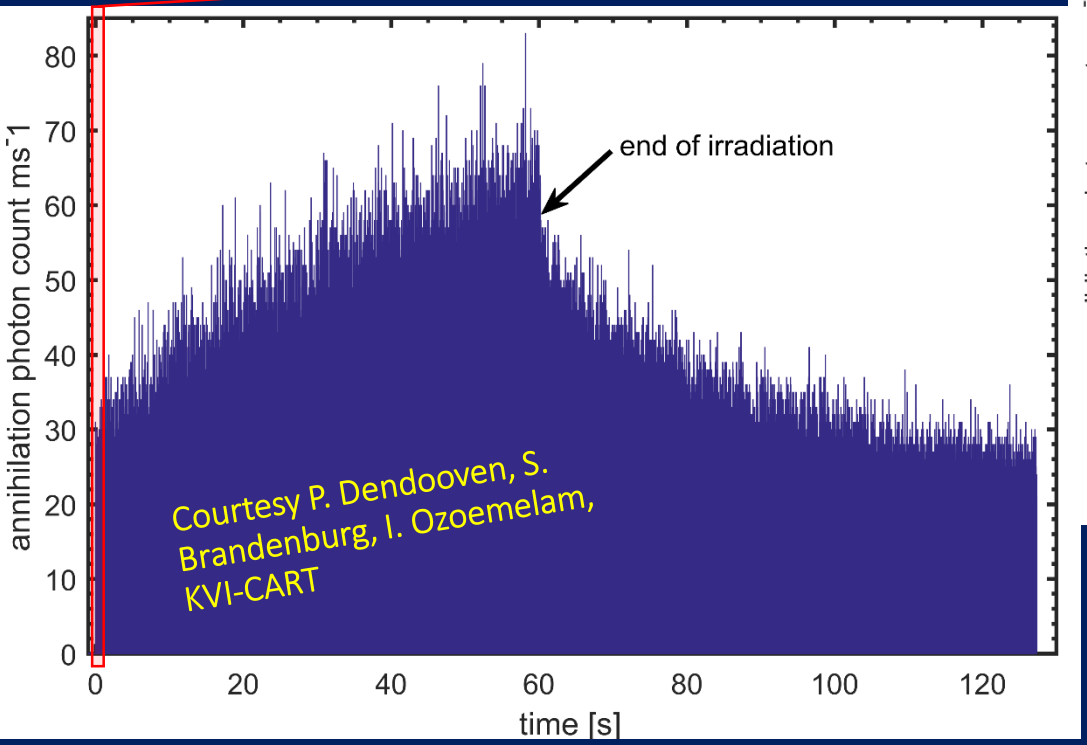
Experimental setup

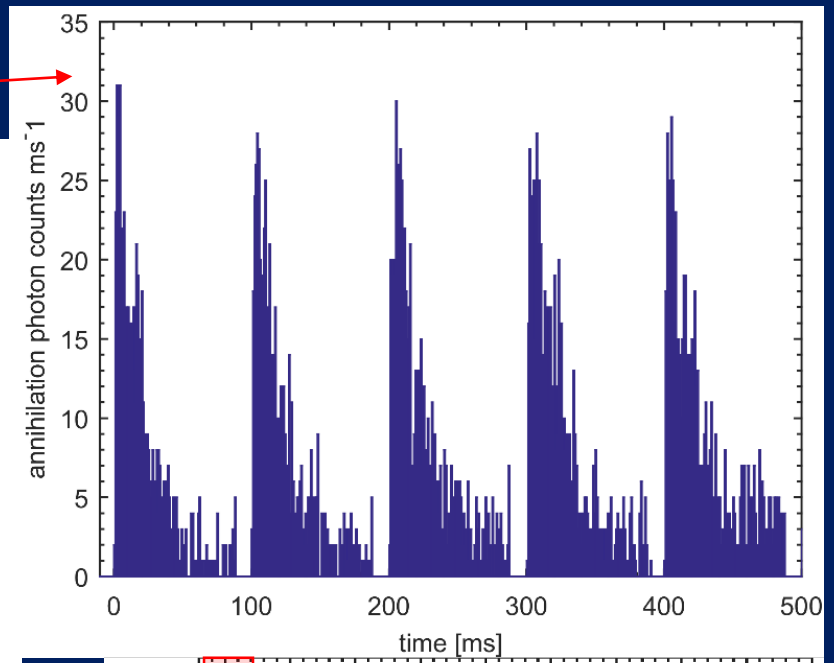


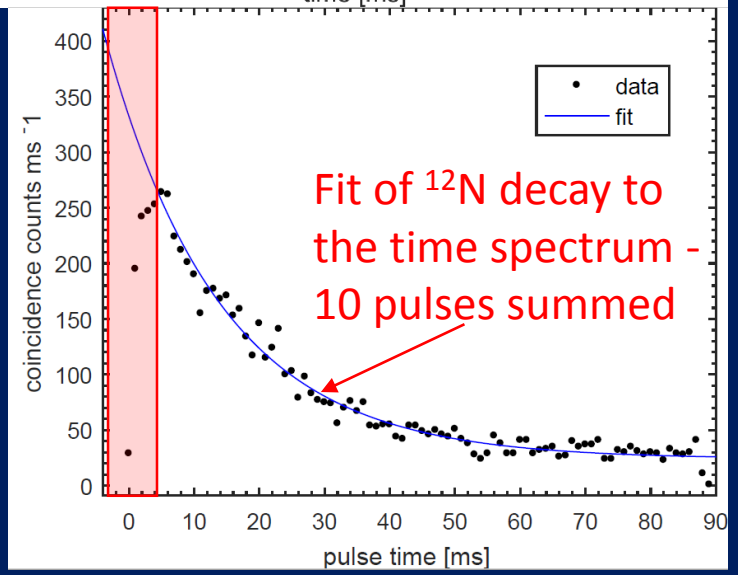


Real-time PET for range verification

Irradiation of graphite with 10^8 protons per pulse
10 ms beam-on & 90 ms beam-off



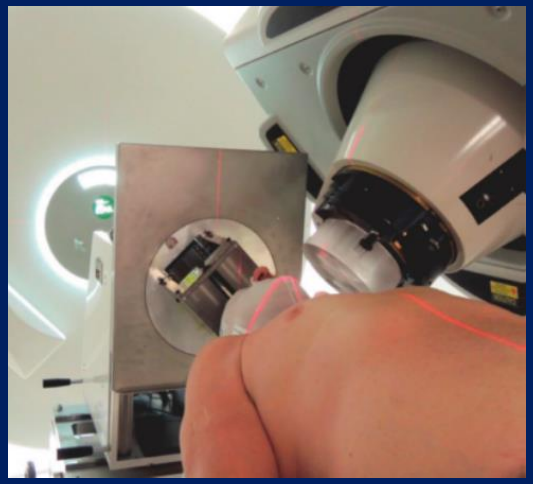




Results
~2-3 mm (1σ) range accuracy for 10^8 protons
~ 1 mm accuracy for 10^9 protons

See presentation by Sytze Brandebourg

Prompt Gamma: Clinical test of IBA knife-edge camera



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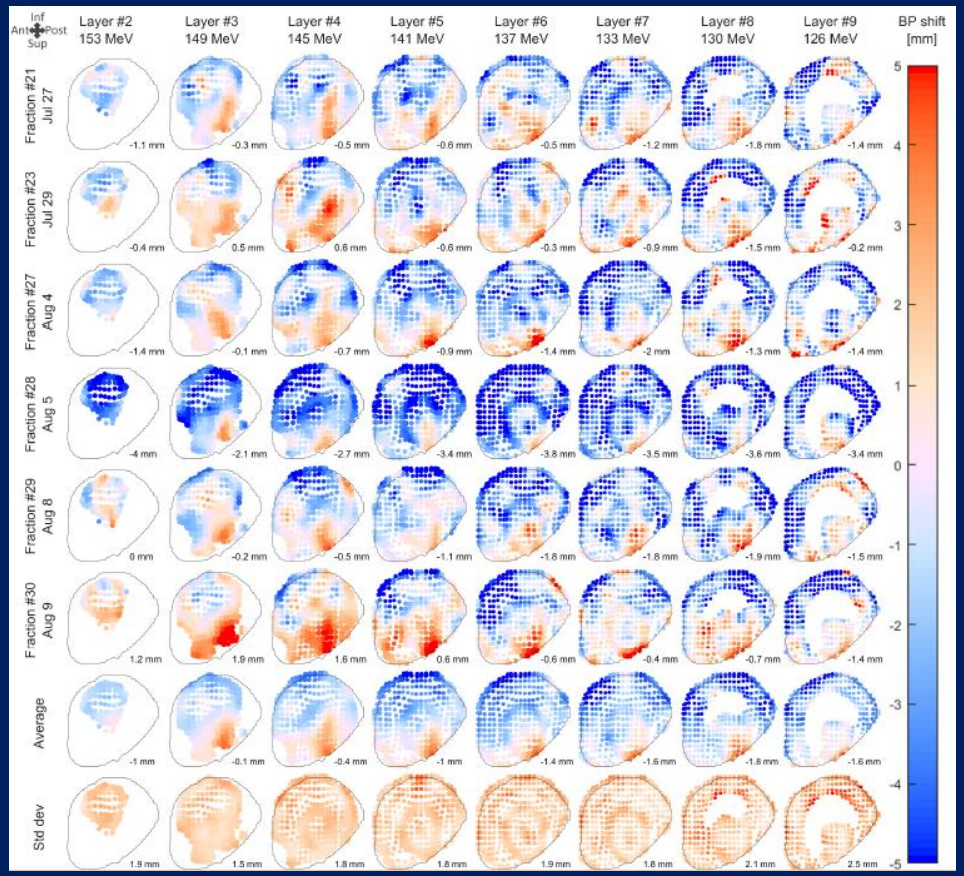

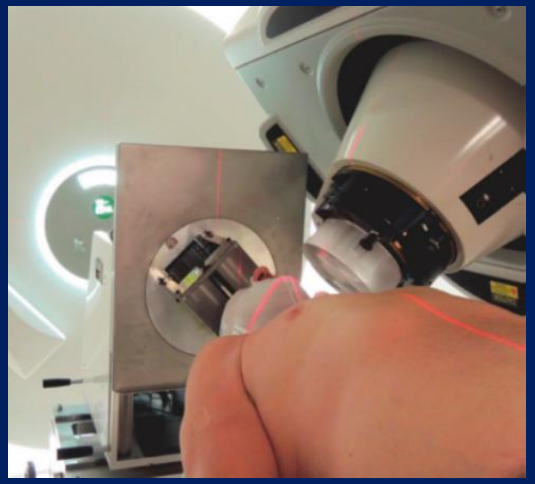

Xie et al., Int J Radiat Oncol Biol Phys 2017

Verification during 6 consecutive fractions of head treatment with PBS at Philadelphia
→ Range uncertainties < margins

Ongoing patient study with PBS at Oncoray-Dresden (Berthold et al, PTCOG 2019)

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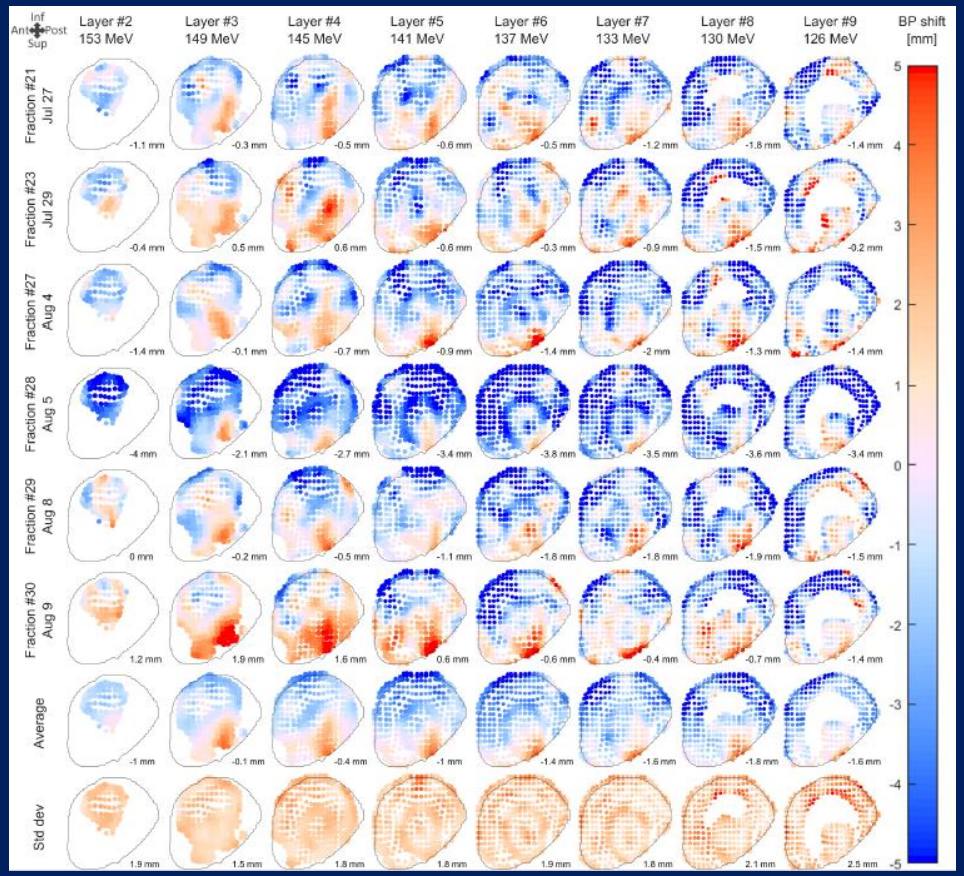

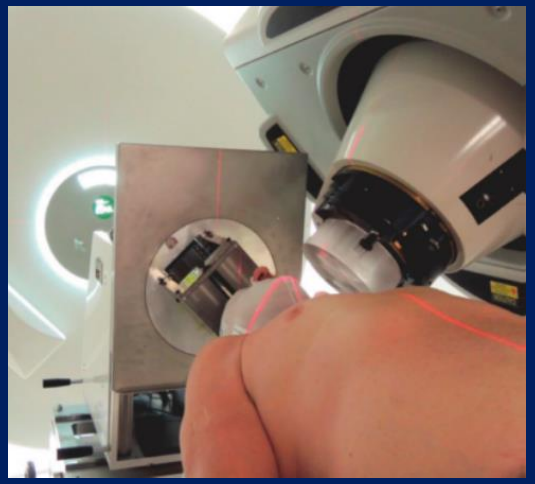

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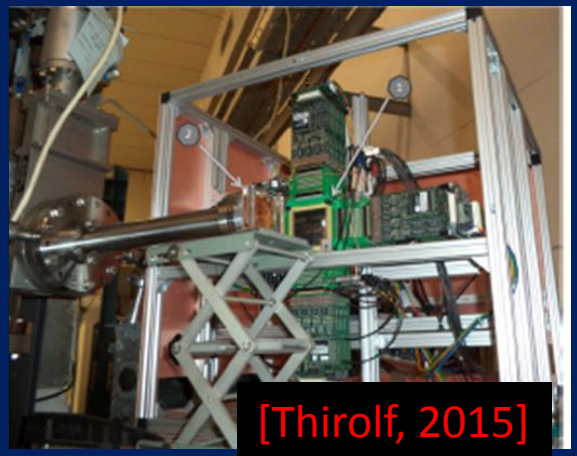
Alternative: Multi-slit collimated camera: comparable performance, larger field of view, inclusion of Time-of-Flight (CLaRyS, Delft, Korea…)

Compton cameras for hadrontherapy

Group	Scatterer	Absorber	Abs. size (mm)	Status
Valencia	LaBr3	LaBr3	30	In-beam tests
US	CdZnTe	CdZnTe	40	In-beam tests
Dresden	CdZnTe	LSO/BGO	30	tested
Munich	Si	LaBr3	50	Components tested
France CLaRyS	Si	BGO	300	In development



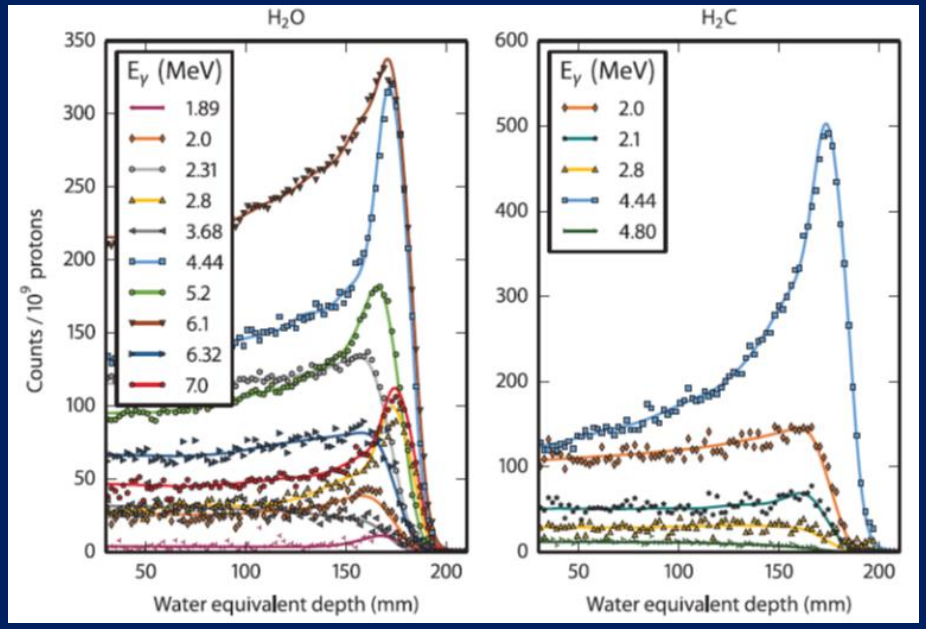
- Assets: - higher efficiency at equivalent size
  - Spatial resolution
- Issues: - High rate of random coincidences at clinical beam intensities

  [Ortega PMB 2015], [Rohling PMB 2017], [Fontana IEEE TRPMS 2019] (Lyon)
  - Reconstruction time

Prompt Gamma Spectroscopy

- Idea (Verburg et al, PMB 2014):
  - Individual PG lines depend on
    - proton energy
    - target composition
  - High resolution spectroscopy using TOF at given position
    - Collimation
    - synchronization HF cyclotron

➔ Range and tissue composition



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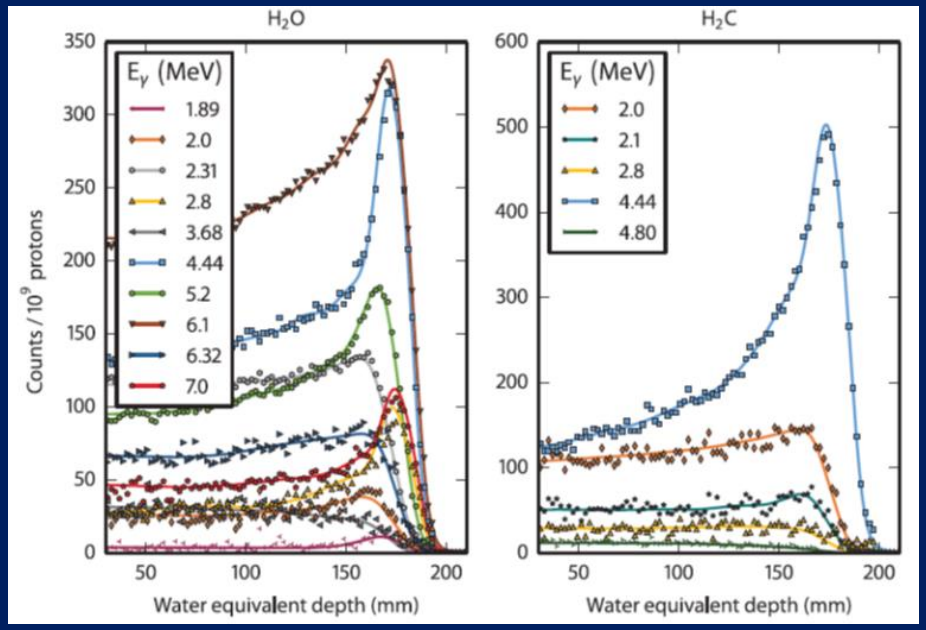
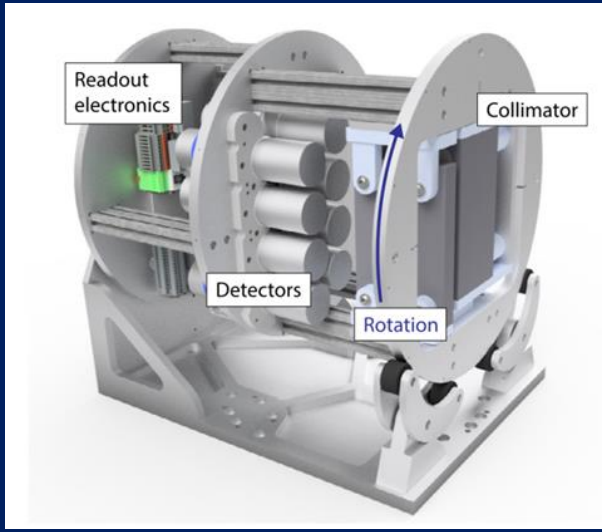
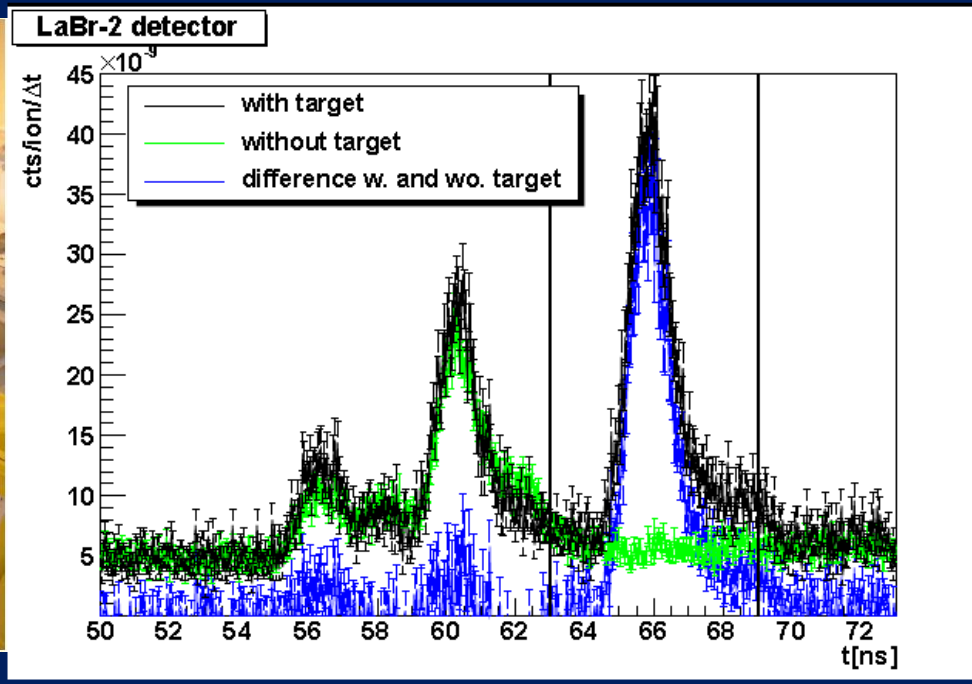




- Prototype (Hueso Gonzáles et al, PMB 2018):
  - Tested at MGH with clinical beams and realistic treatment plans with PBS
  - Ready for clinical tests at MGH (Verburg, PTCOG 2019)
- Extension to He, Li… ions by Seco et al. at HIT synchrotron (beam hodoscope)

Prompt Gamma Peak Integral

- **Basic idea:** measure PG issued from the patient (with TOF) with a few detectors around the patient
  - Related to the energy deposited and to the material
  - No severe requirements on TOF precision and energy resolution



Measurements at Essen, HIT, GANIL, CAL, Arronax
Protons and carbon

[J. Krimmer, APL 2017]

Prompt-Gamma Timing

- Principle

  Golnik et al., PMB 59 (2014) 5399

- Detection system

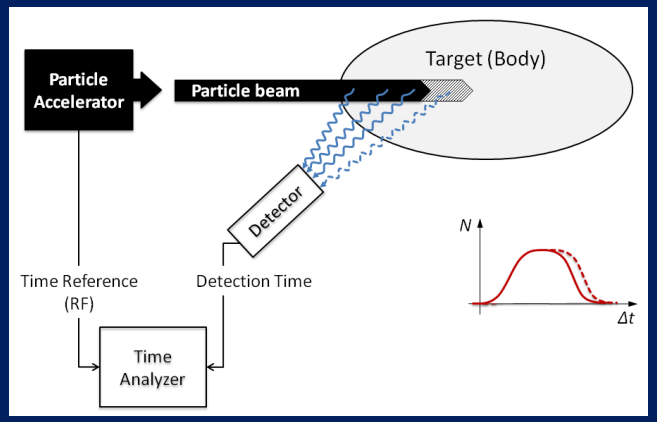
  Pausch et al., IEEE TNS 63 (2016) 664

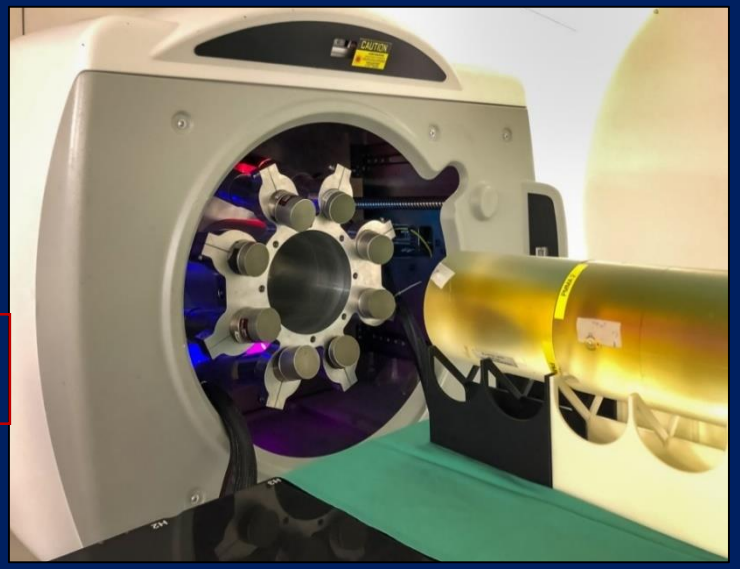
- Remaining problems

  Werner et al., PMB 64 (2019) 105023

  - Instabilities of the time reference caused by accelerator effects
  - Integration of proton bunch monitoring in the medical beamline
  - Integrating PGT spectrum prediction in IBA's RV software used for PGI

Translation to clinical application is on the way.



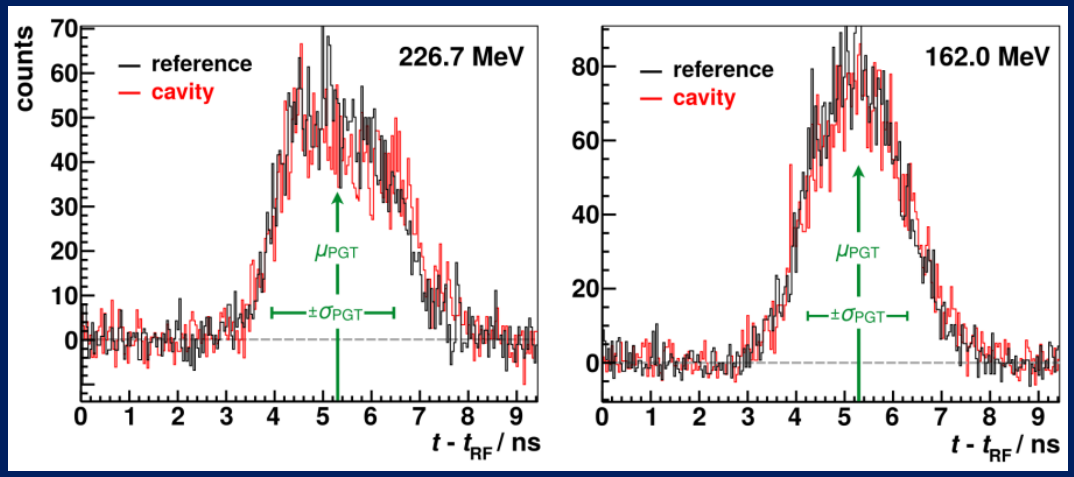


Courtesy G. Pausch, ONCORAY-Dresden

Ultra-fast timing with single proton

20 mm air cavity in PMMA
~ 1 ns bunch resolution
(Werner et al, PMB 2019)

- Best precision achievable = Pulse width (~1 ns)



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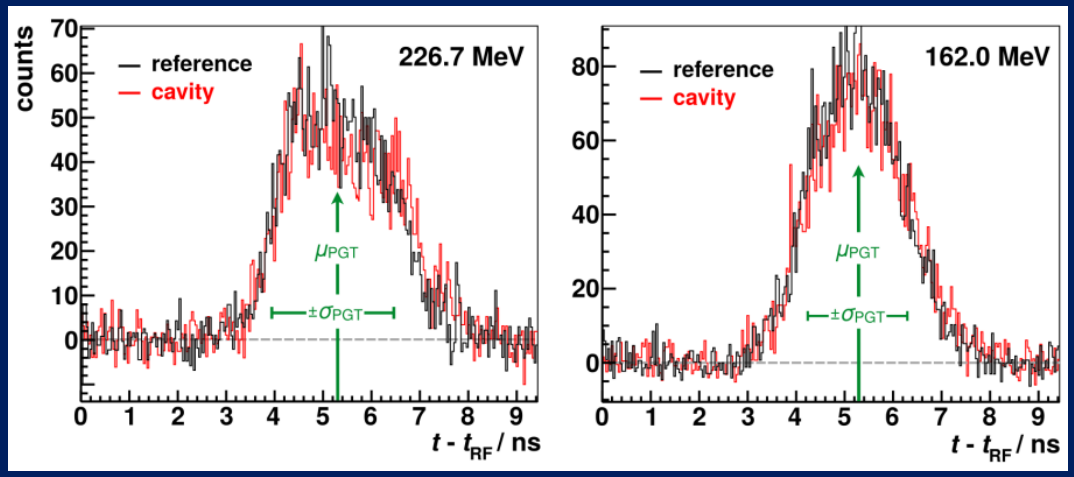
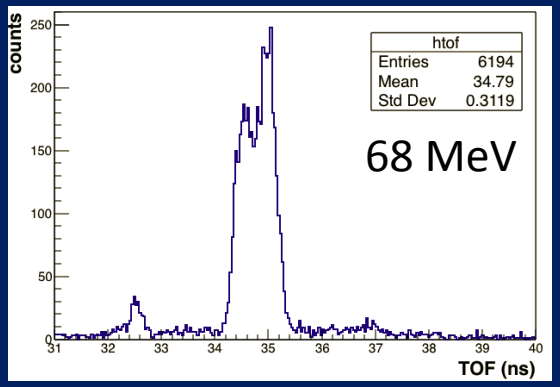


25 mm air cavity in PMMA
Single proton identification
with diamond detector in beam
(Marcatili et al, submitted APL)



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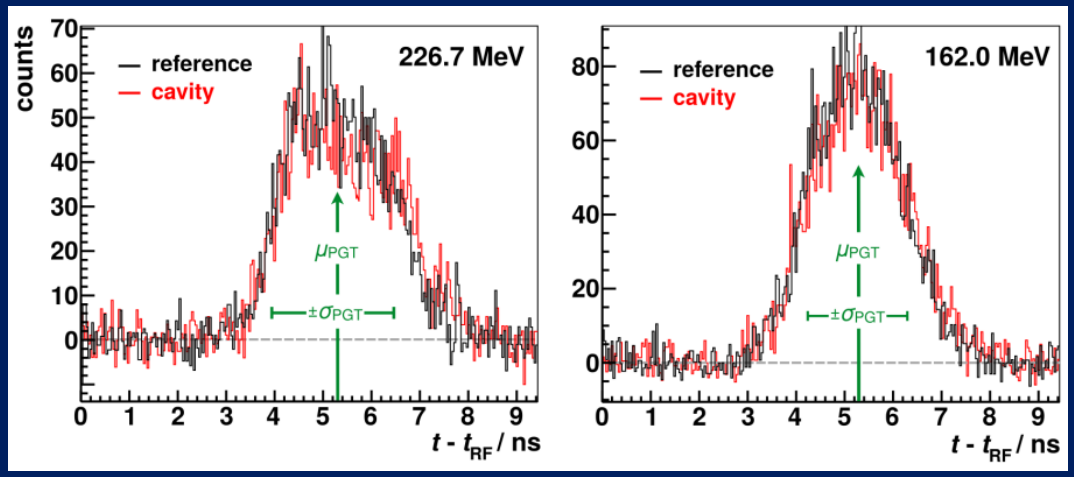

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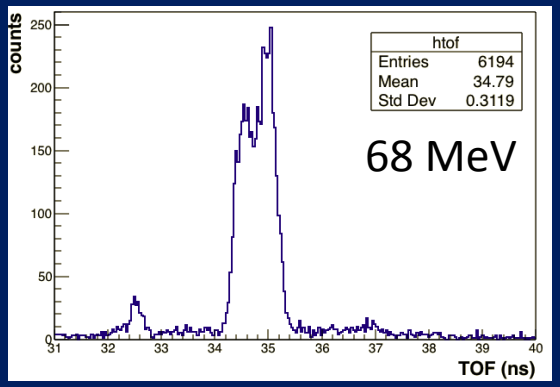

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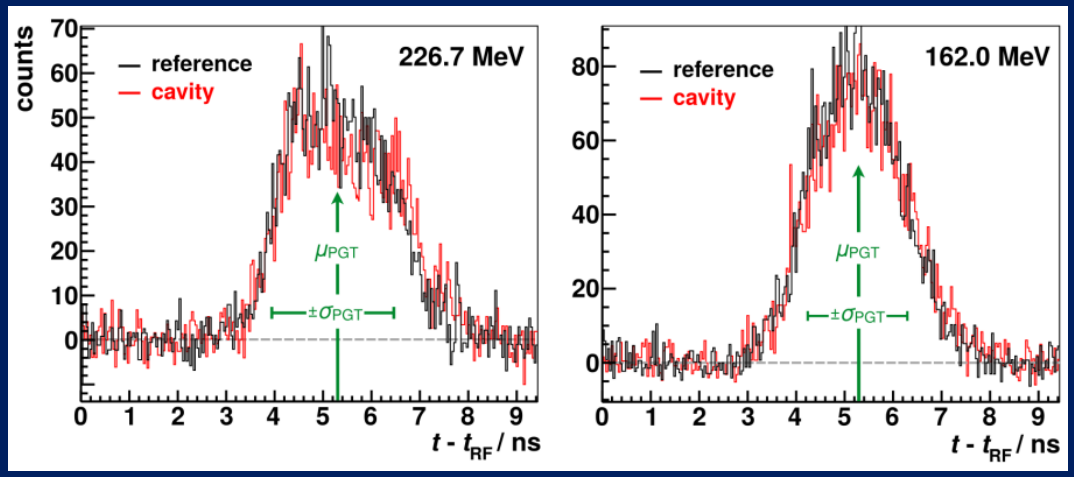

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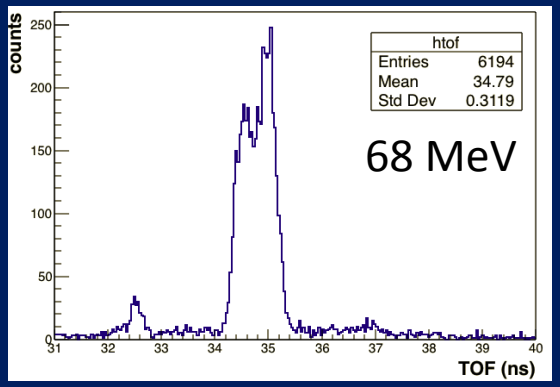

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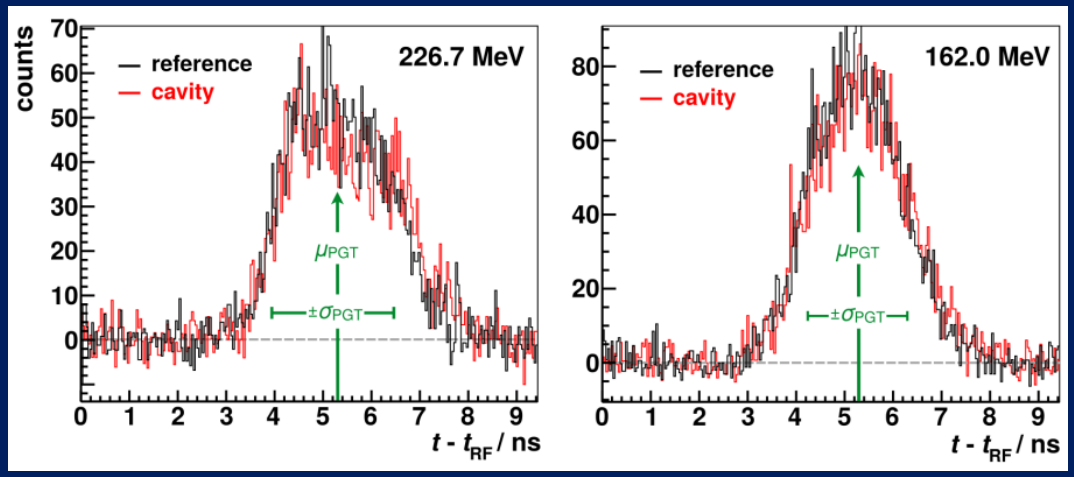

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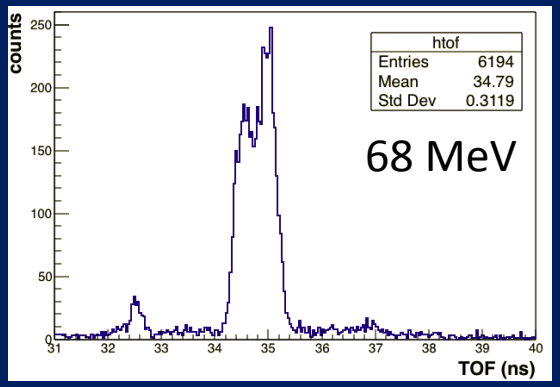

- 100 ps timing resolution achieved with diamond beam hodoscope and fast scintillator (see Sébastien Curtoni poster)
- Beam reduction to 1 proton/bunch (a few seconds irradiation time increase for few bunches)
- Reconstruction simplified in Compton Imaging (Livingstone et al PTCOG 2019)

Conclusion

- 15-20 years of developments for range verification
  - → Clinical tests with PET and PG
  - →PET and PG predictions are included in treatment plans
    - Kroniger et al., Med Phys 2015: analytical
    - Tian et al., PMB 2018: MC planning: a few spots ‘’boosted’’
  - → Next generation devices appear (PGS, PGT, PGPI, …)
  - → Other promising modalities (Ionoacoustic, Bremsstrahlung, MRI…) + planning imaging (DECT, pCT)

- Strong dependence of the beam temporal structure on the range verification modality

  (see paper by G. Pausch et al, NIMA 2019, in press)
  - PG will be challenging at higher intensities (Synchro-cyclotron, Flash)
  - High performance with reduced intensity

  → Enable one or few spots in 10-30 s at the beginning of a fraction for verification?

Thanks and Acknowledgements

- G. Bisogni, G. Pausch, P. Dendooven for providing inputs
- CLaRyS collaboration (IPN Lyon, CPPM Marseille, LPSC Grenoble, CREATIS Lyon)

- LabEx PRIMES and Plan Cancer (INCa)