

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 positioning...)
 - No reduction of patient workflow
 - Affordable cost!
- A system will not be optionnal if the efficiency is proven

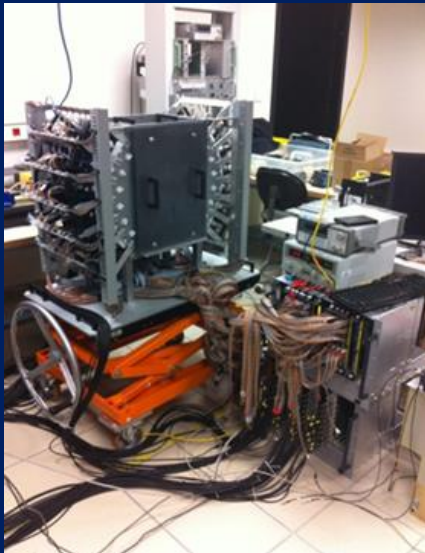
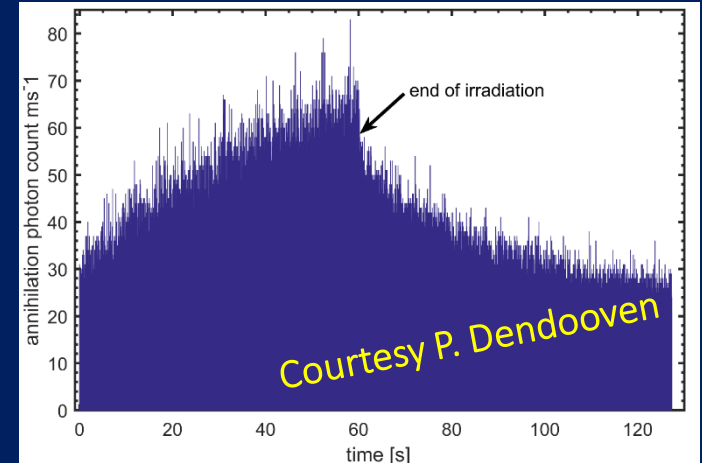
Outline

- 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

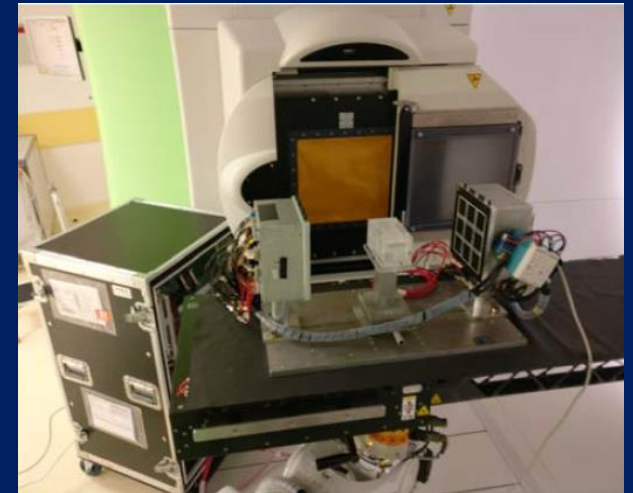
Long radioisotope lifetime → no real-time



DPGA – (Clermont)



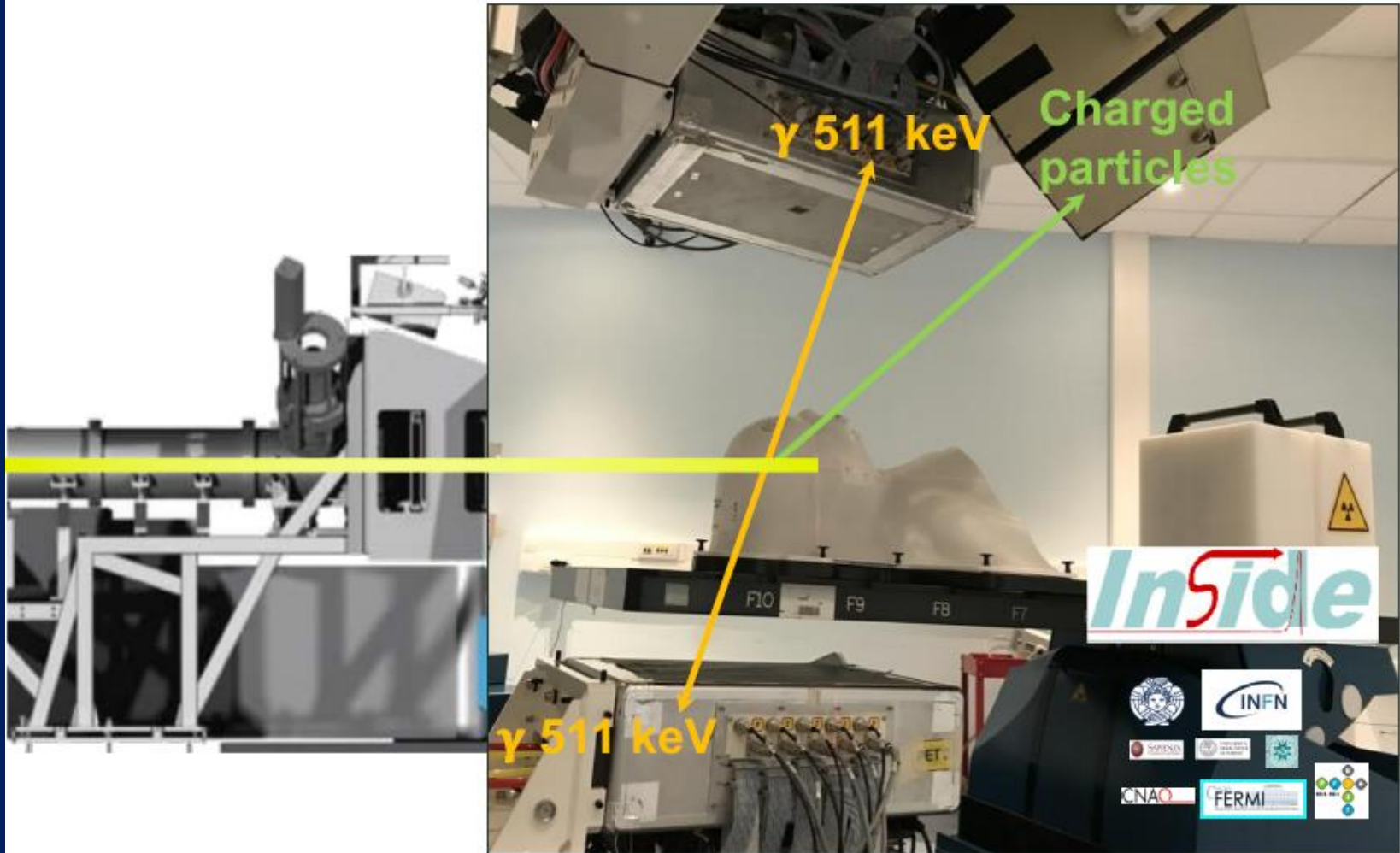
Dual ring OpenPET (NIRS)
[Yoshida IEEE TRPMS 2014]



DoPET (INFN)
Topi et al, IEEE TRPMS 2019⁴

INSIDE BI-MODAL IN-VIVO RANGE VERIFICATION SYSTEM

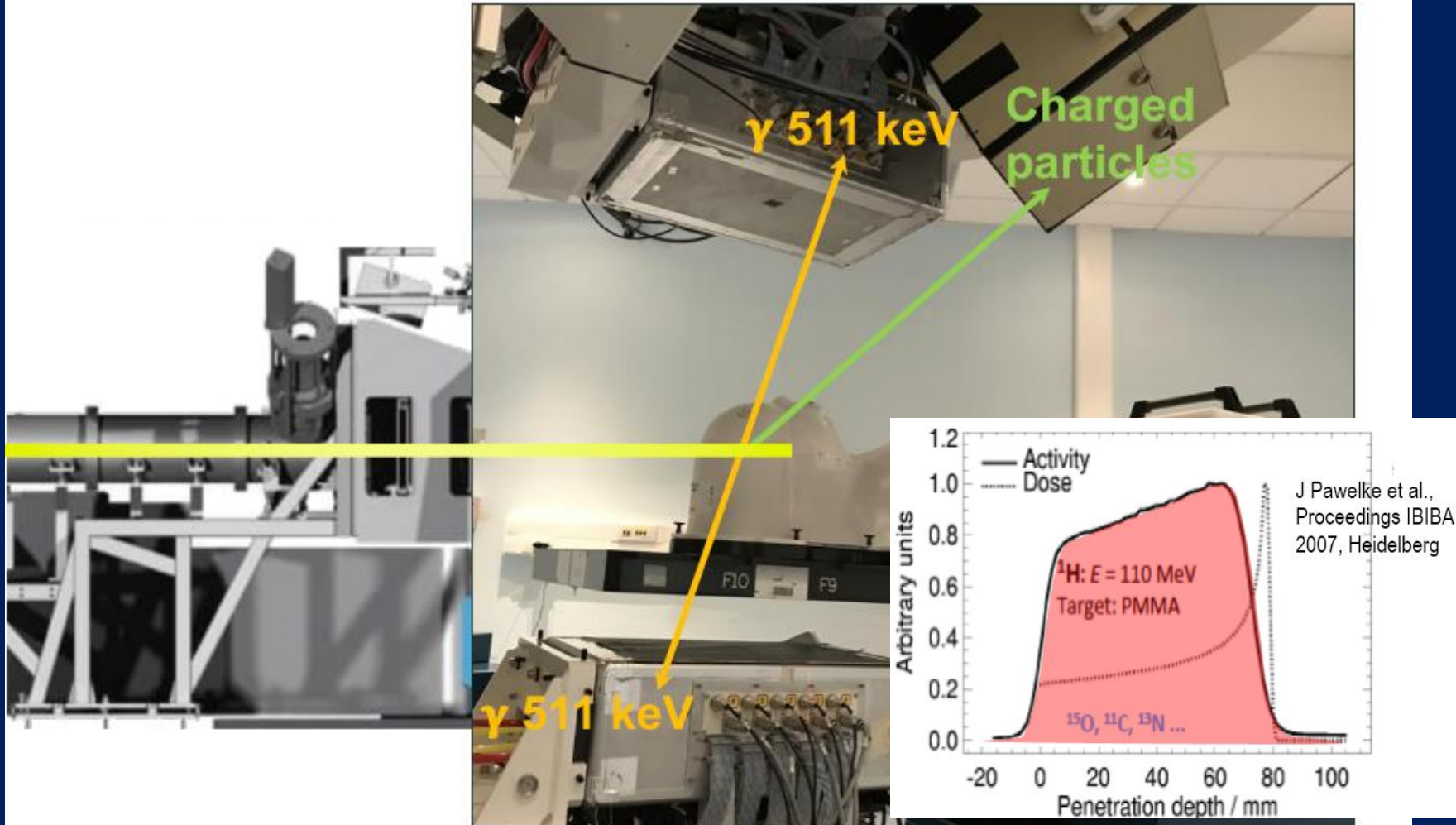
Courtesy MG Bisogni



INnovative **S**olutions for **In**-beam **DosimE**try in Hadrontherapy

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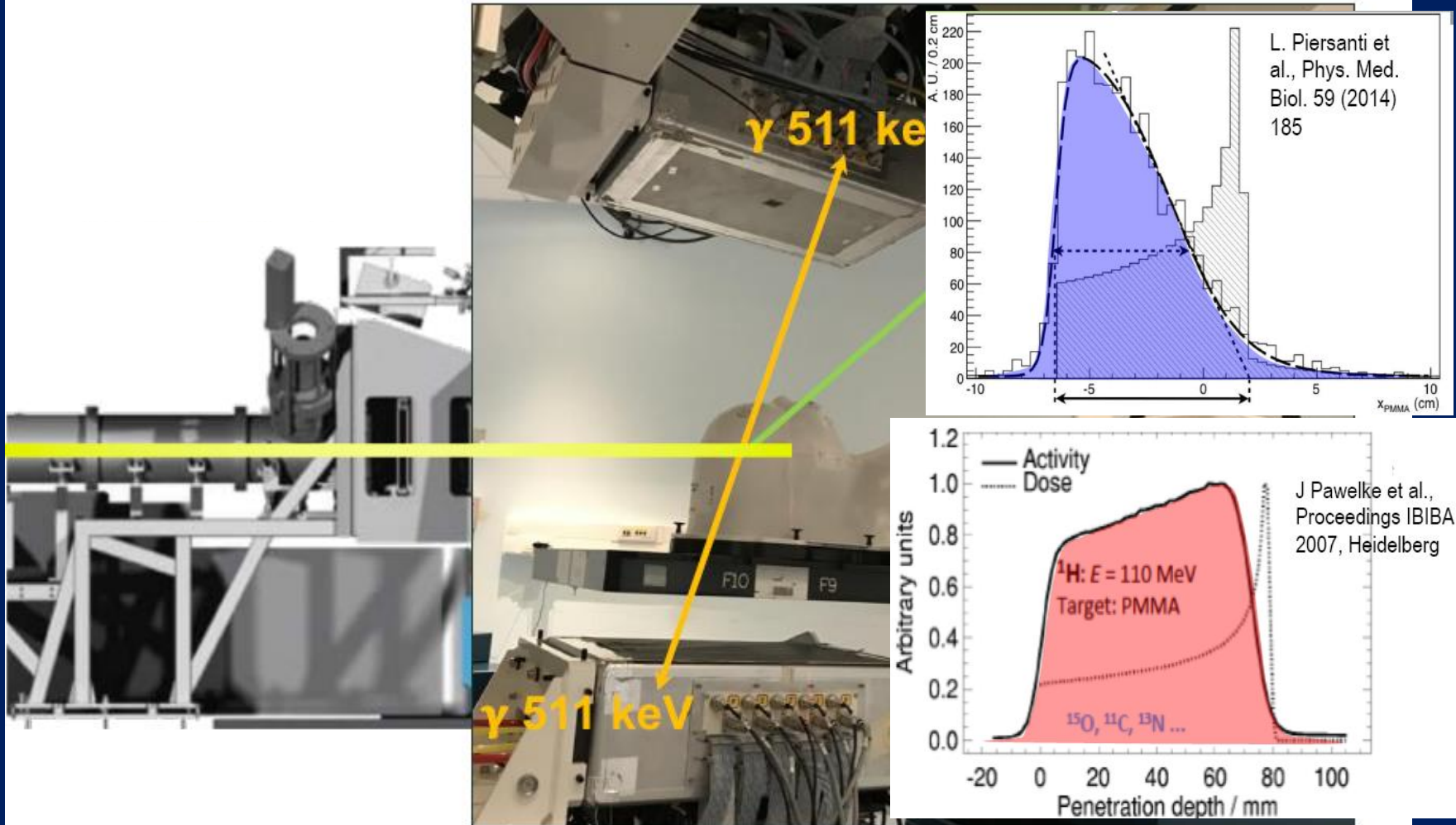
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INSIDE OBSERVATIONAL CLINICAL TRIAL

ClinicalTrials.gov

id: **NCT03662373**

Courtesy MG Bisogni

Cohort	40 patients treated with particle therapy (20 with protons and 20 with carbon ions)
Inclusion Criteria	<ul style="list-style-type: none">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.
Exclusion Criteria	<ul style="list-style-type: none">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

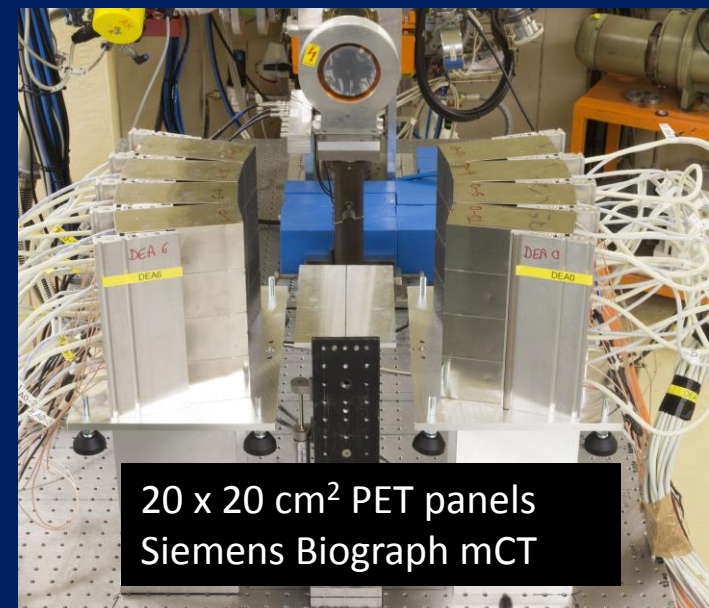
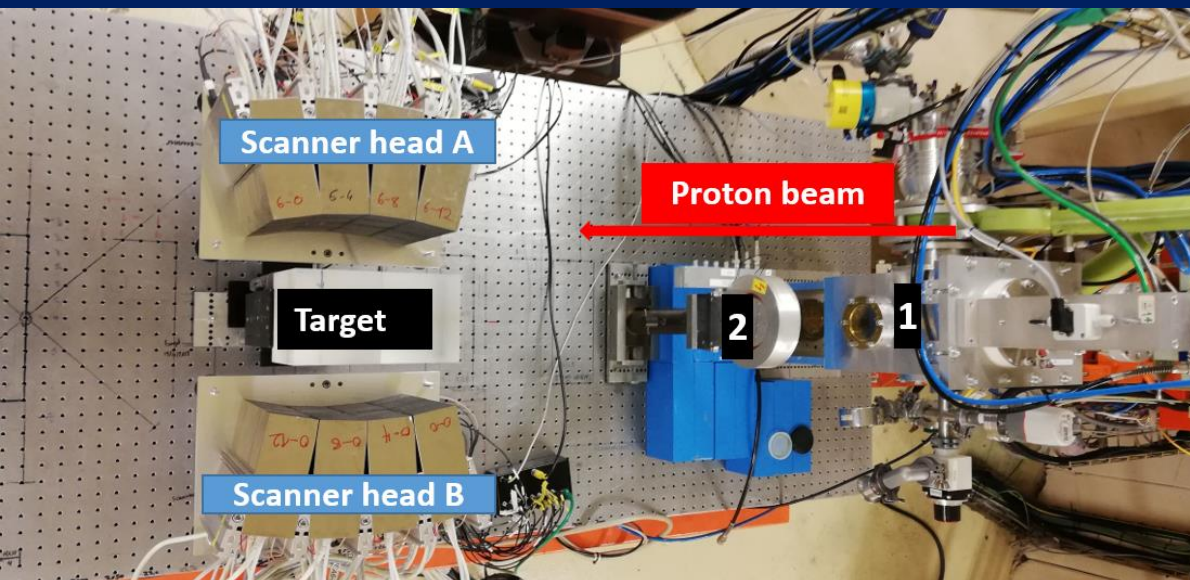
Very short-lived radioisotope:
good candidate: N-12 ($T_{1/2} = 11$ ms)

Benefits for PET imaging:

- maximum number of counts
- minimal biological washout

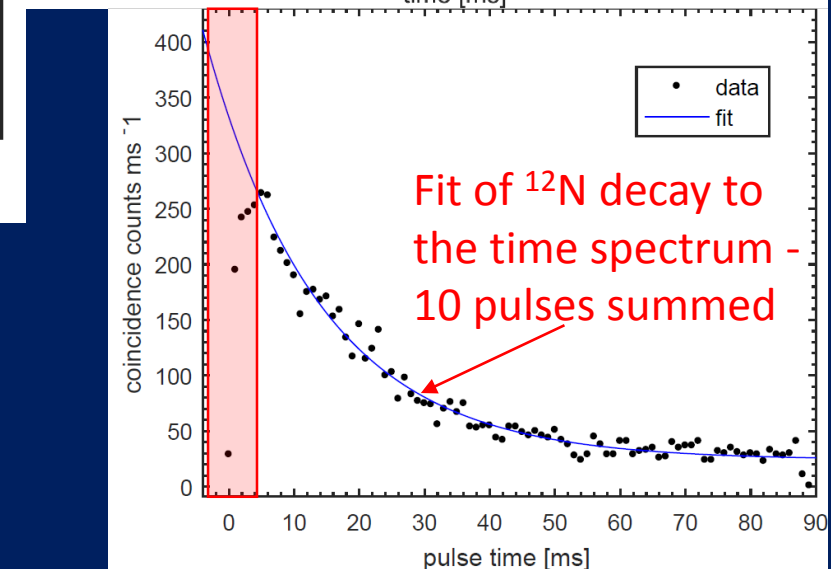
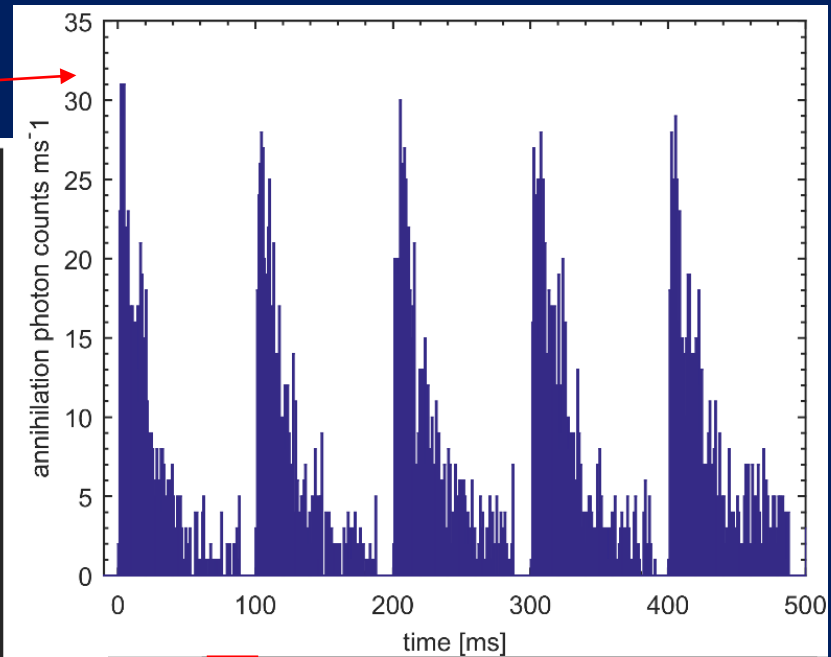
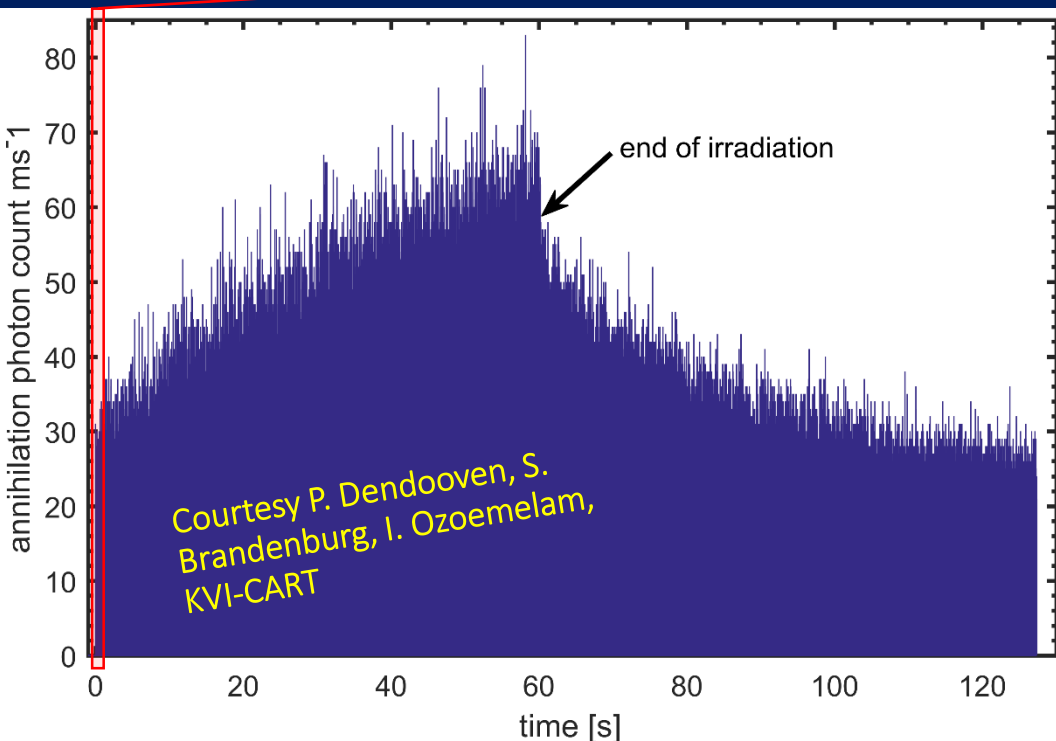
*Courtesy P. Dendooven,
S. Brandenburg, I.
Ozoemelum, KVI-CART*

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

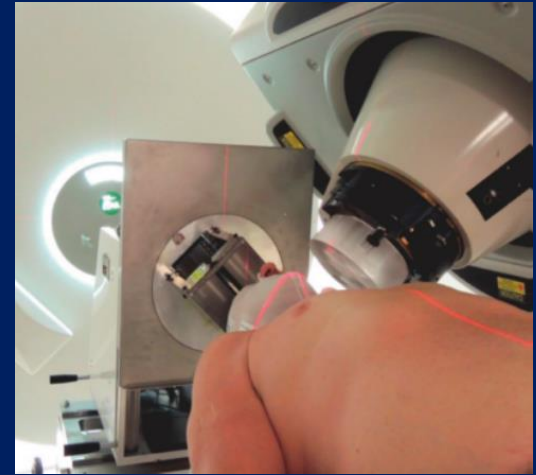


Results

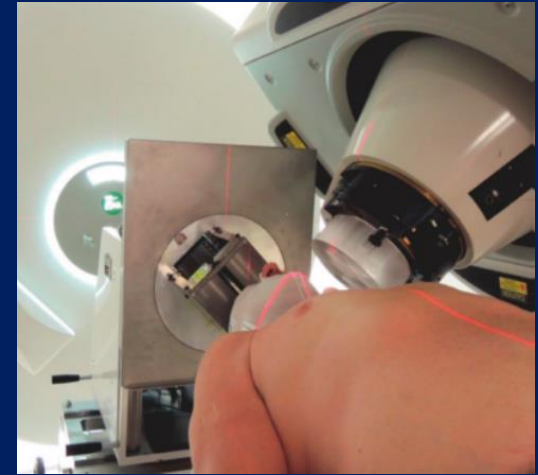
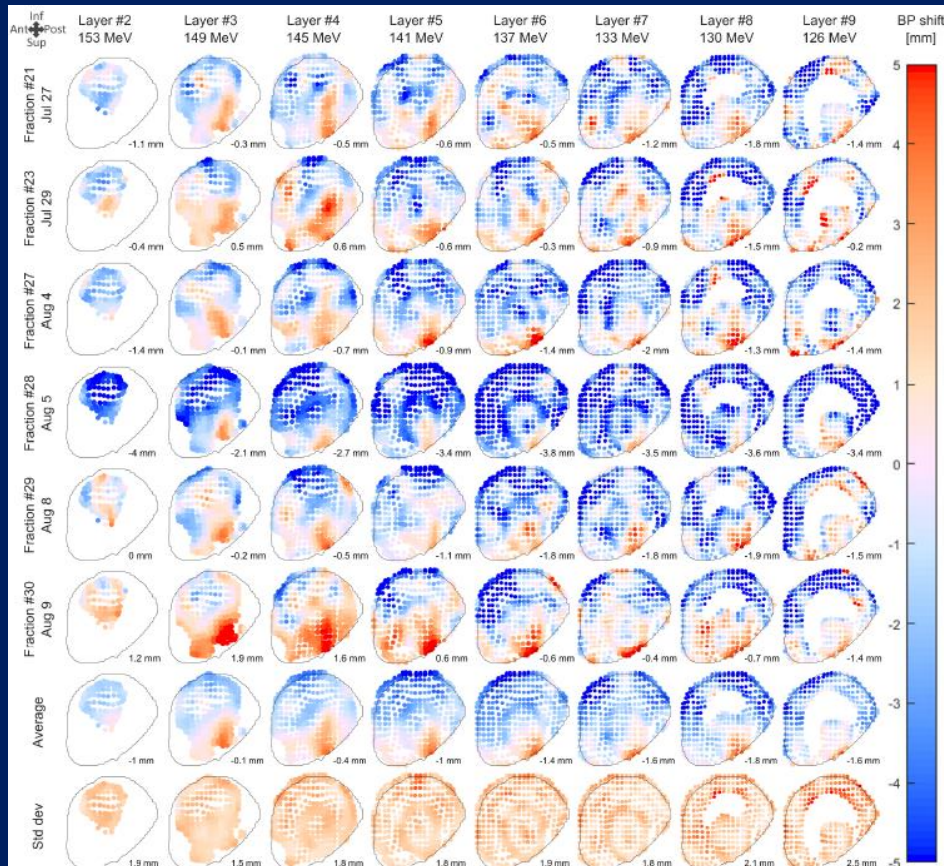
$\sim 2\text{-}3$ mm (1σ) range accuracy for 10^8 protons
 ~ 1 mm accuracy for 10^9 protons

See presentation by Sytze Brandebourg

Prompt Gamma: Clinical test of IBA knife-edge camera



Prompt Gamma: Clinical test of IBA knife-edge camera

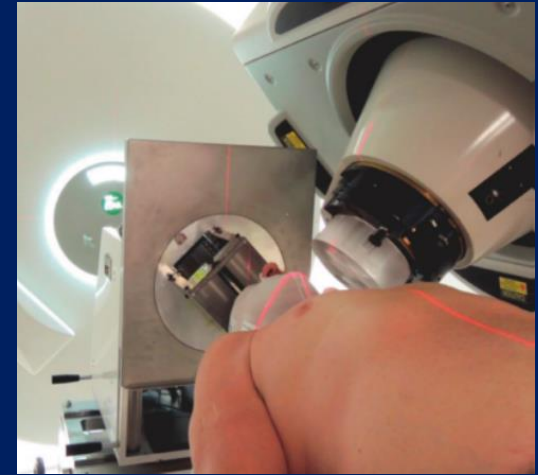
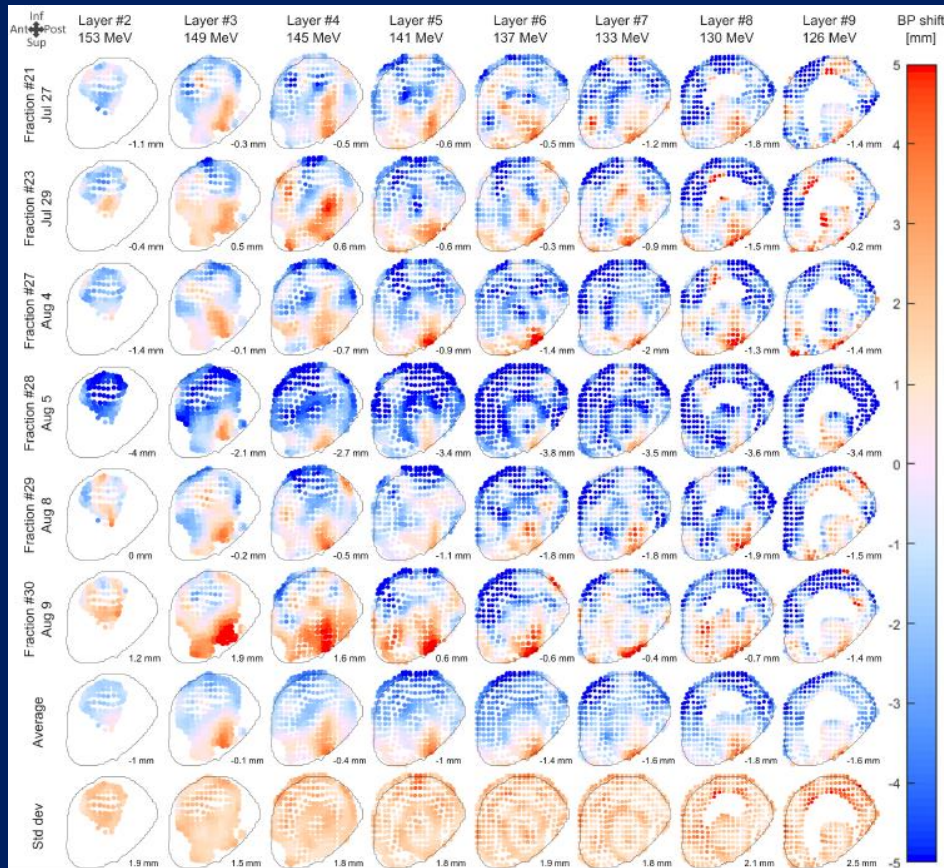


Xie et al., Int J Radiat Oncol Biol Phys 2017

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)

Prompt Gamma: Clinical test of IBA knife-edge camera



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

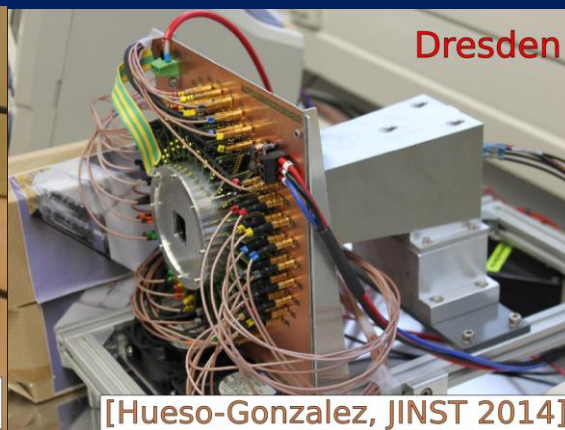
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Alternative: Multi-slit collimated camera: comparable performance, larger field of view, inclusion of Time-of-Flight (CLaRyS, Delft, Korea...)

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



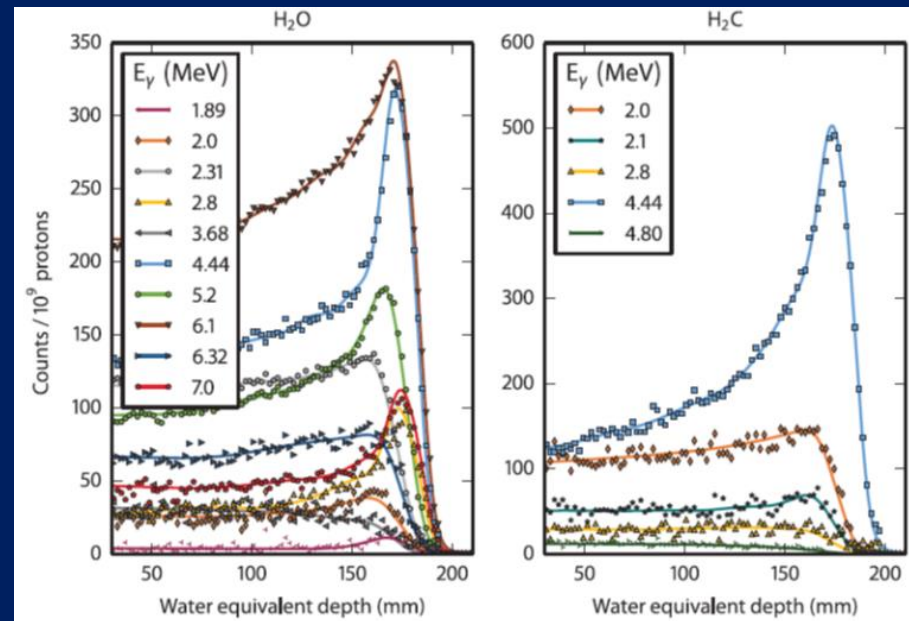
- Assets: - higher efficiency at equivalent size
- Spatial resolution
- Issues: - High rate of random coincidences at clinical beam intensities

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

- Reconstruction time

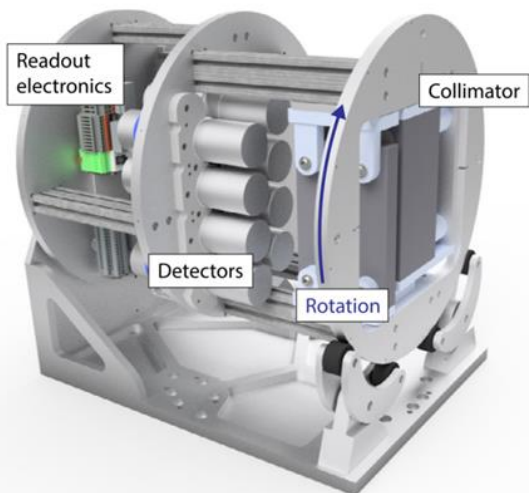
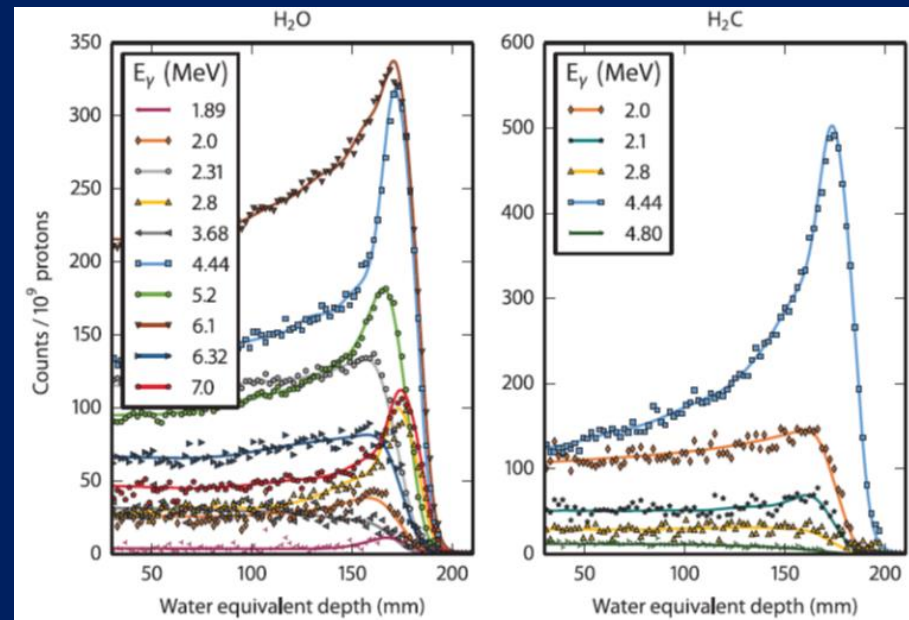
Prompt Gamma Spectroscopy

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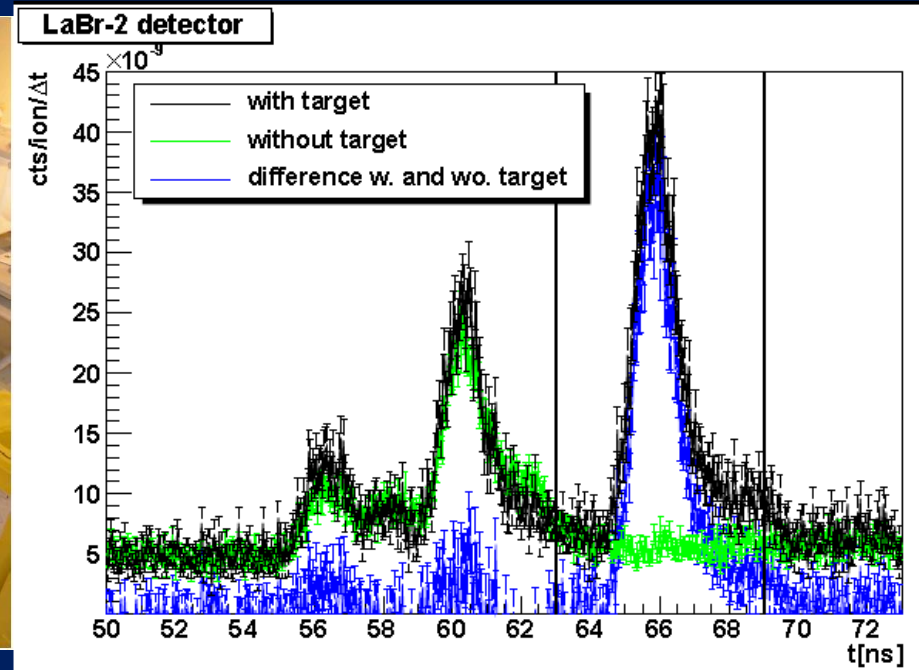
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- Prototype (Hueso González et al, PMB 2018):
 - Tested at MGH with clinical beams and realistic treatment plans with PBS
 - Ready for clinical tests at MGH (Verburg, PTCOG 2019)
- Extension to He, Li... ions by Seco et al. at HIT synchrotron (beam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

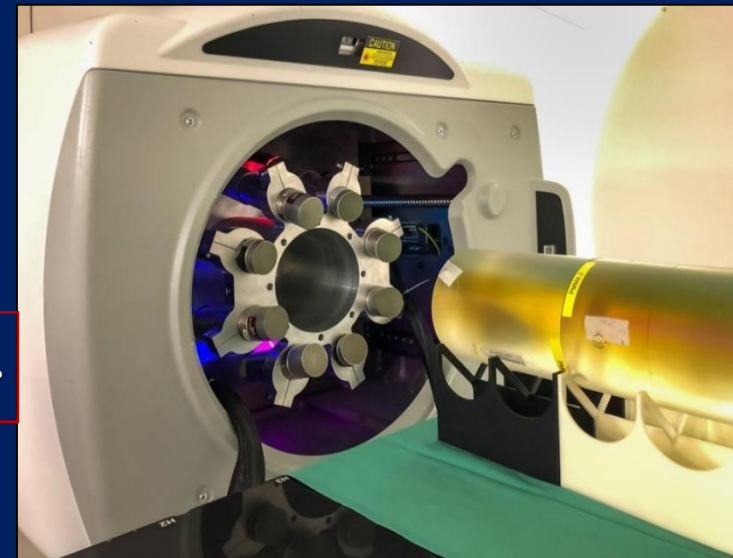
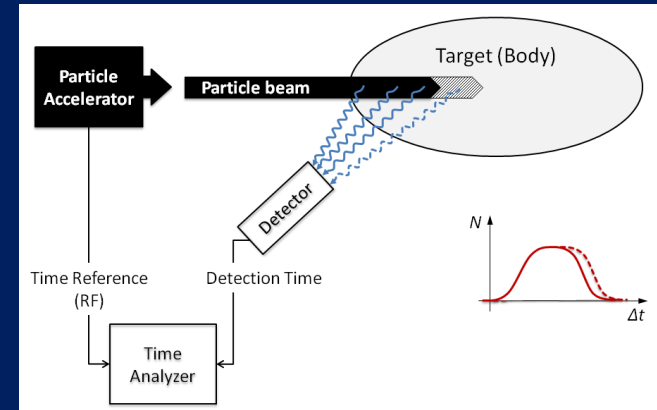
- Remaining problems

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.

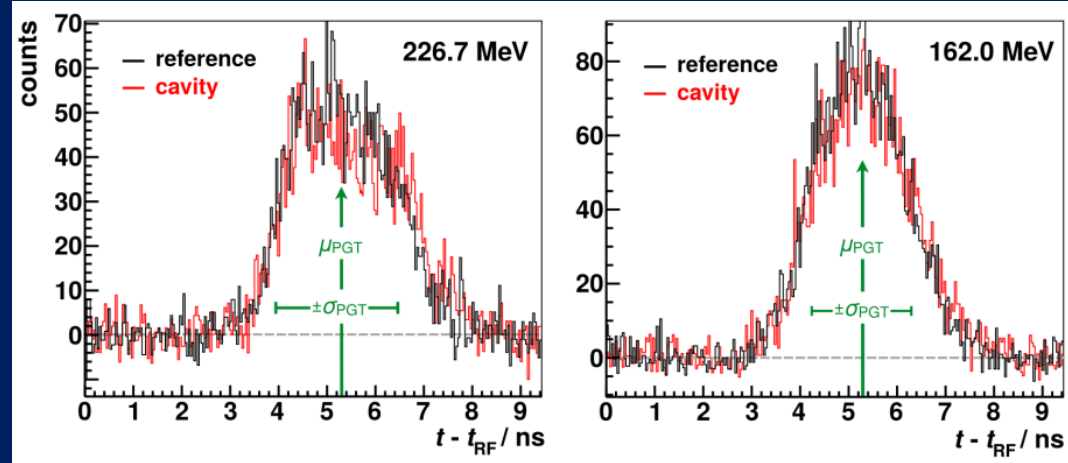
Courtesy G. Pausch, ONCORAY-Dresden



Ultra-fast timing with single proton

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

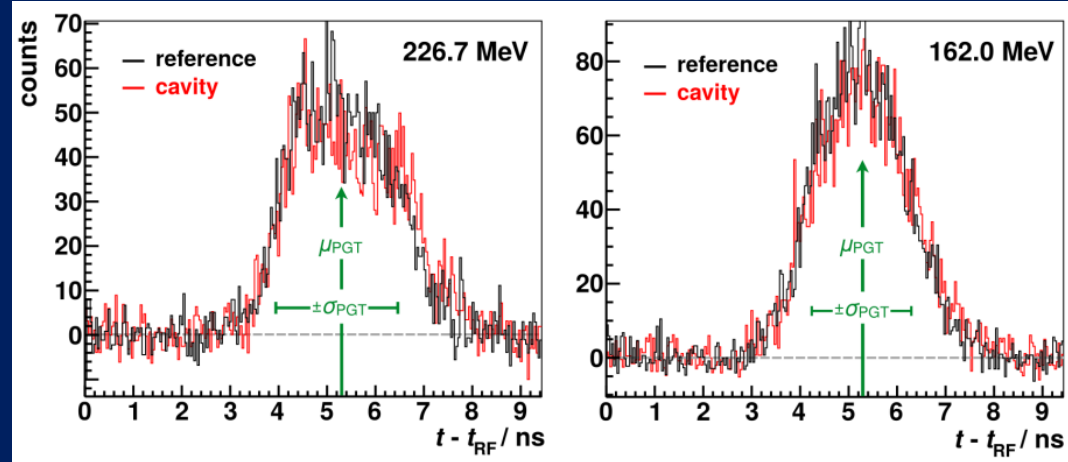
- Best precision achievable
= Pulse width (~1 ns)



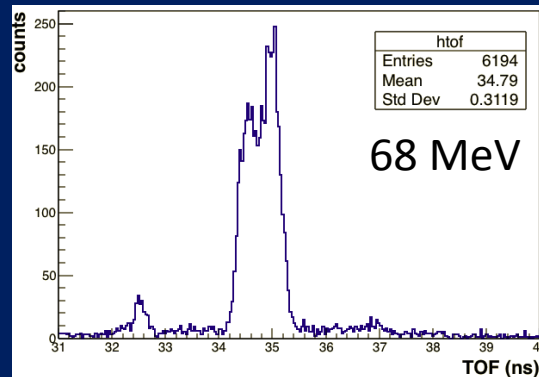
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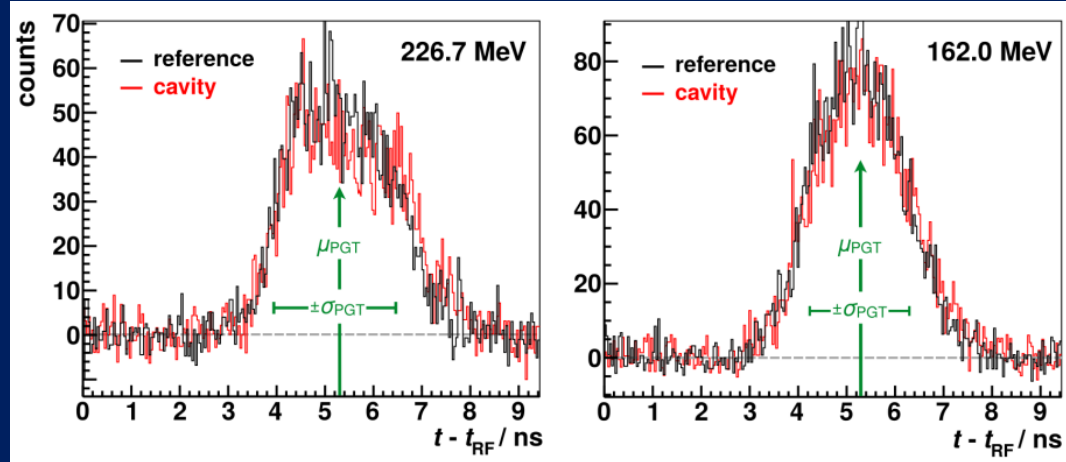
25 mm air cavity in PMMA
Single proton identification
with diamond detector in beam
(Marcatili et al, submitted APL)



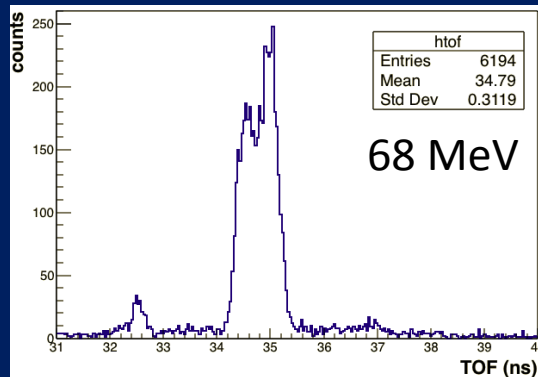
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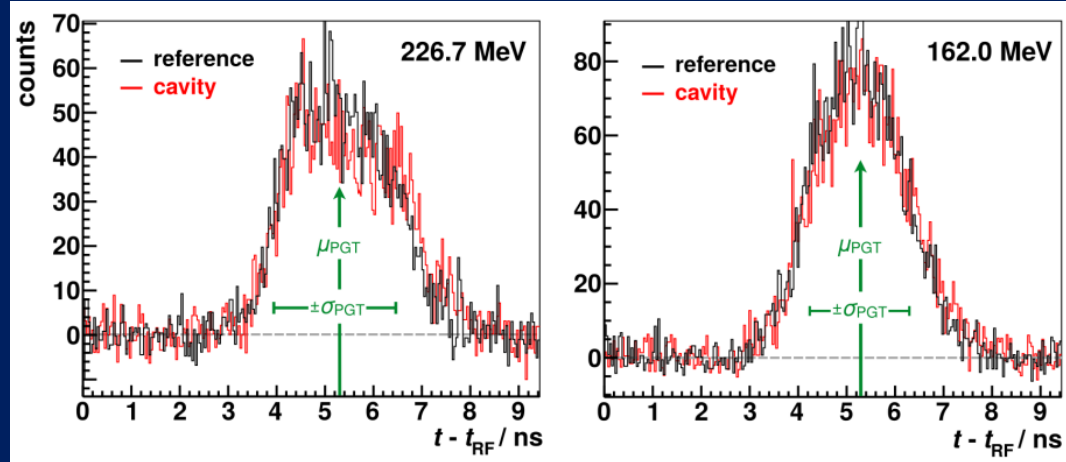


- 100 ps timing resolution achieved with diamond beam hodoscope and fast scintillator (see Sébastien Curtoni poster)

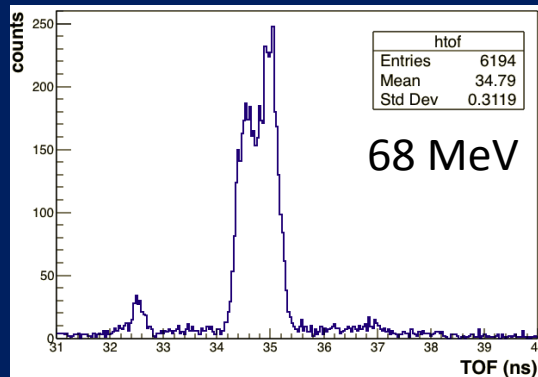
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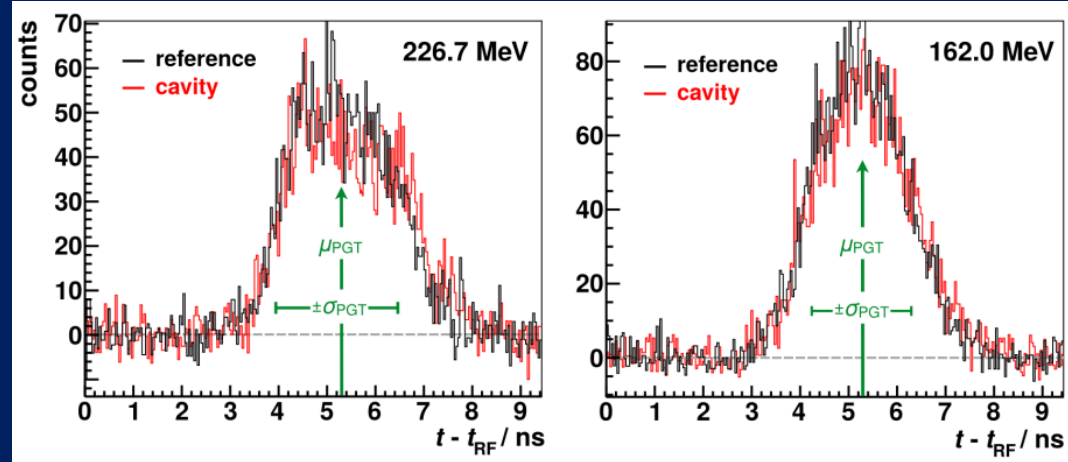


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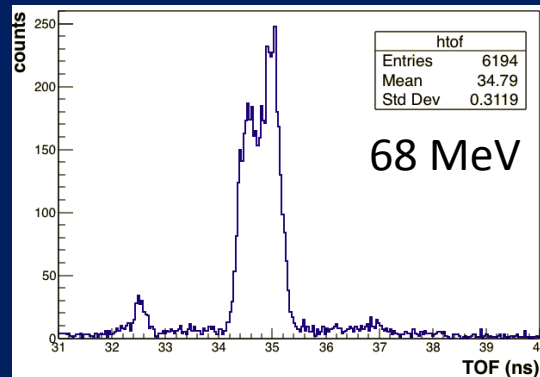
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- Reconstruction simplified in Compton Imaging (Livingstone et al PTCOG 2019)

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)