Real-time In-Vivo Dosimetry and Range Verification

Vienna, 3 April 2019

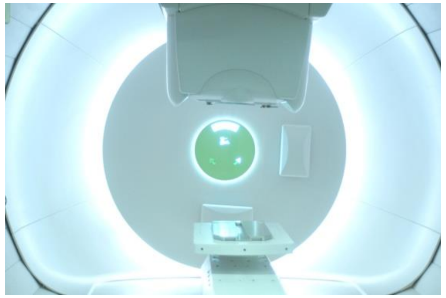
Jochen Krimmer, R&D Physicist Expert

DOSIMETRY

The IBA group

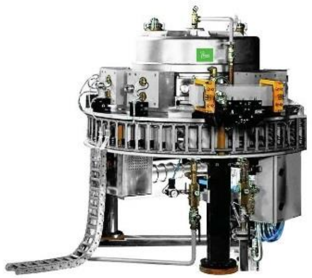
Proton Therapy

- Commercial solution with IMPT
- Compact: *Proteus®ONE*

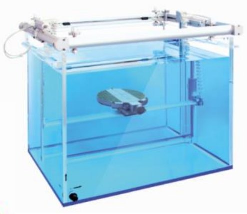


Industrial solutions

- electron accelerators
- X-ray generators
- Medical and food industry

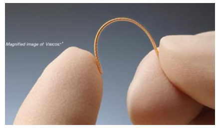


Dosimetry



- QA for standard RT
- QA for proton therapy
- Radiodiagnostics
- Fiducial markers
- Training and formation

All Connected.



Radiopharmacy

- Proton accelerators
- Isotopes for PET/SPECT
- Cyclone®70

IBA Dosimetry @ Schwarzenbruck (Nuremberg, Germany)

IBA Dosimetry Product Line

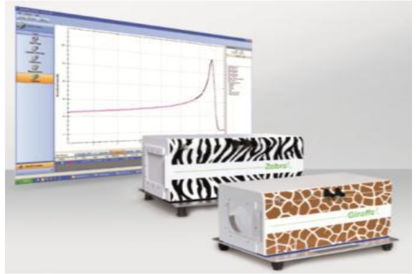
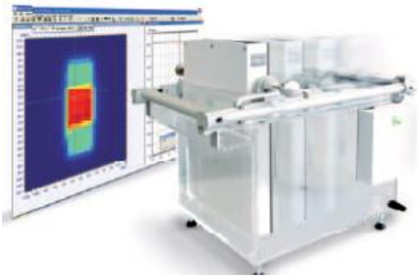
Dosimetry for RT

From LINAC commissioning to patient plan / daily QA



Dosimetry for PT

Solutions for commissioning, acceptance test and QA

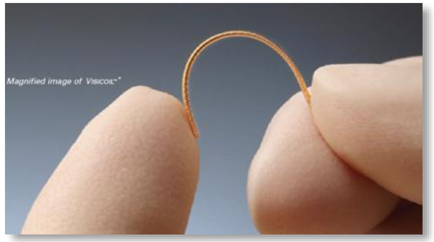




Medical imaging

Solutions for quality control in Diagnostic imaging

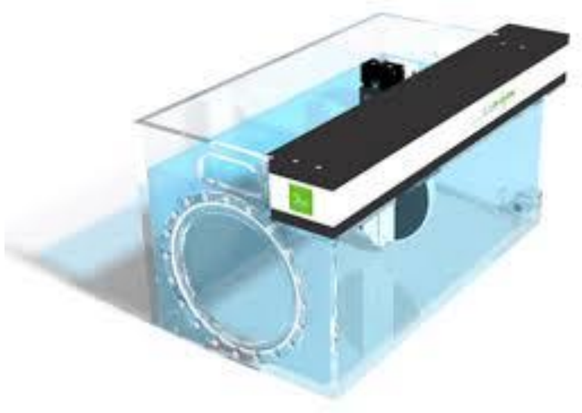
Fiducial markers

VISICOIL™
Flexible linear marker for Image guided RT

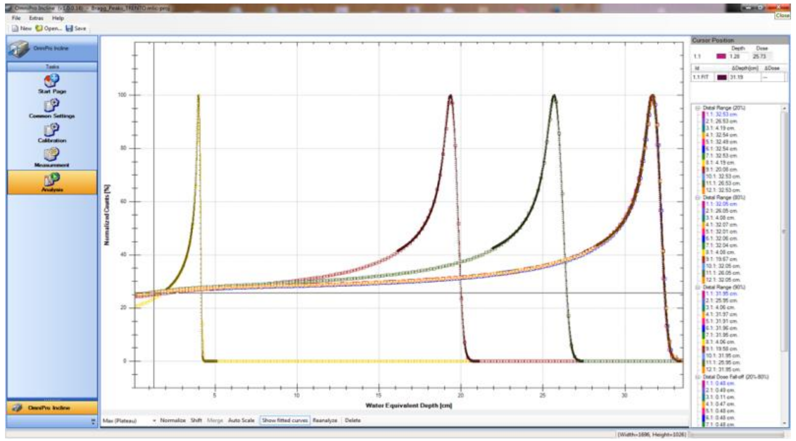


Market Survey PT QA: Commissioning, Machine QA

- 1-D water phantoms (scan of Bragg peak) :

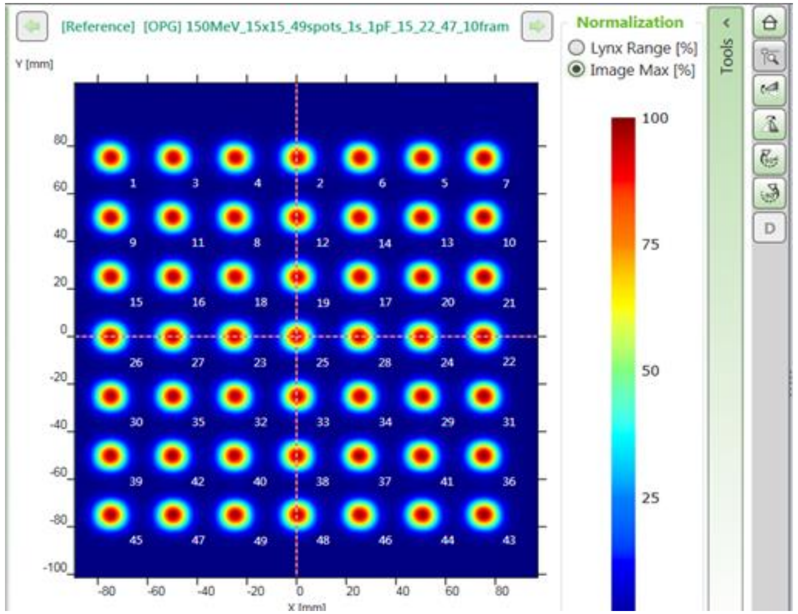


- IC Stacks for routine Machine QA:
  - 180 ICs, 2mm distance, range in a single shot

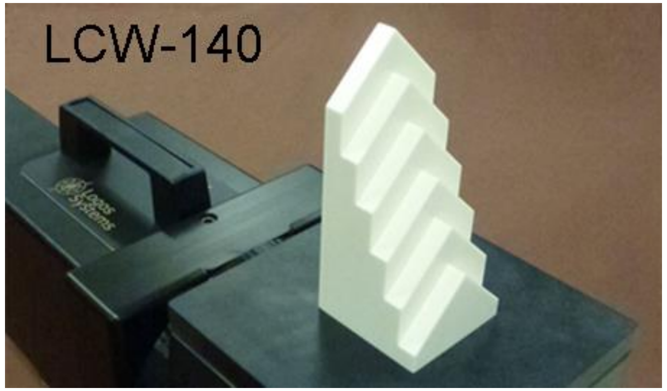


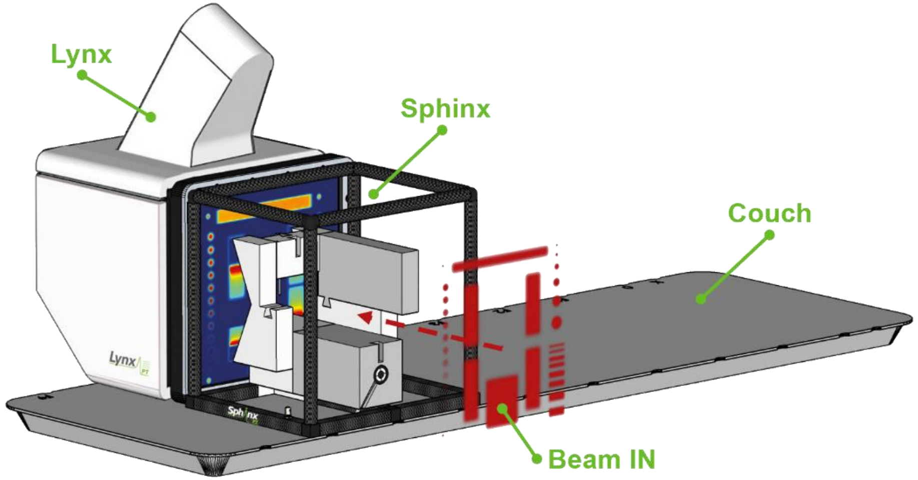
Market Survey: Commissioning, Daily QA

- Scintillator + CCD camera: Spot maps



- Absorber + 2-D detector: Daily QA

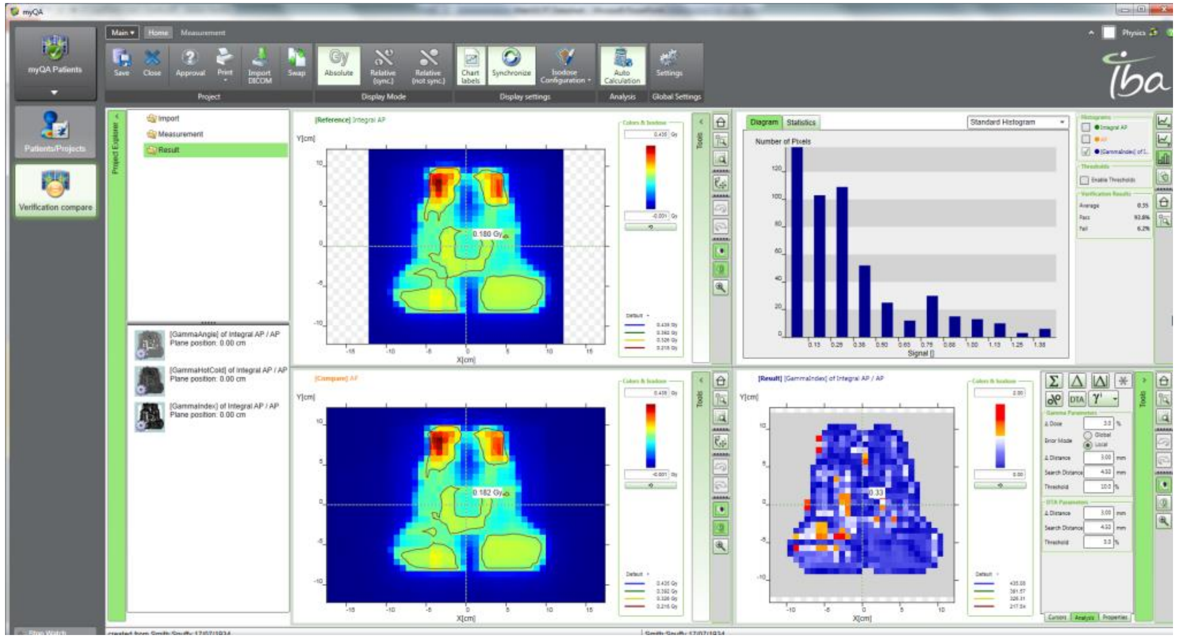




Market Survey: Pretreatment Patient QA

- 2-D arrays of ICs:
  - Calibrated for absolute dose measurements
  - Pixellated 1000 – 1500 channels, pitch 5-7 mm
  - Adaption to handle high dose rates in PT

- 2-D array in water tank: plan verification (γ-analysis)



How about Real-Time In-Vivo ?

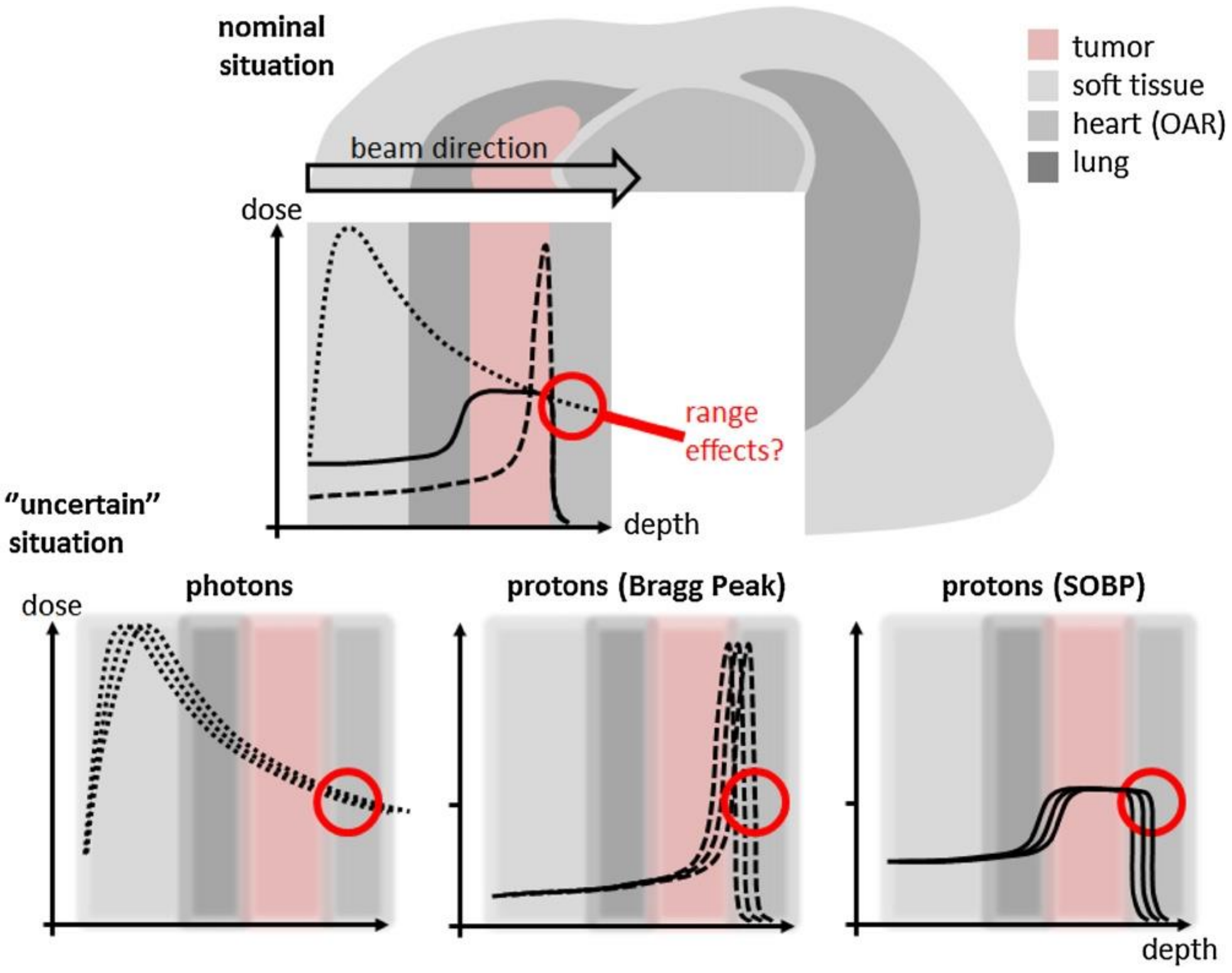
How about Real-Time In-Vivo ?

- No commercial product available so far
- First clinical tests with prototypes, only

Outline

- Motivation
- Direct range measurement
- Detection of secondary radiation
  - PET
  - Prompt gammas
  - Charged particles
- Ionoacoustics
- Conclusions

PT: Sensitivity to Range Uncertainties

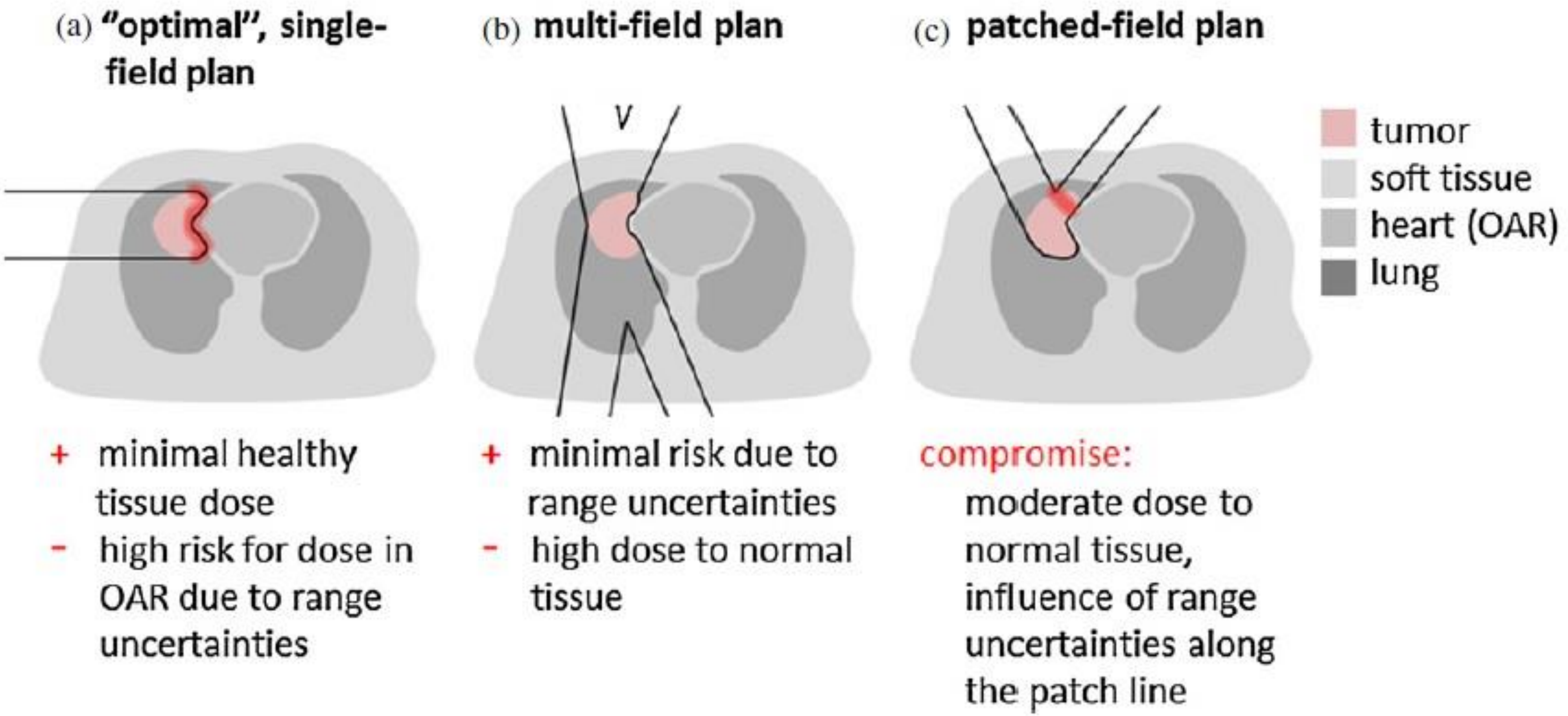


[Knopf et al. PMB 2013]

- Safety margins: (3% + 1.2 mm)
  [Paganetti et al. PMB 2012]
- Full potential of PT not yet exploited
- Head-on situations avoided
- Need for:

Real-time In-Vivo monitoring

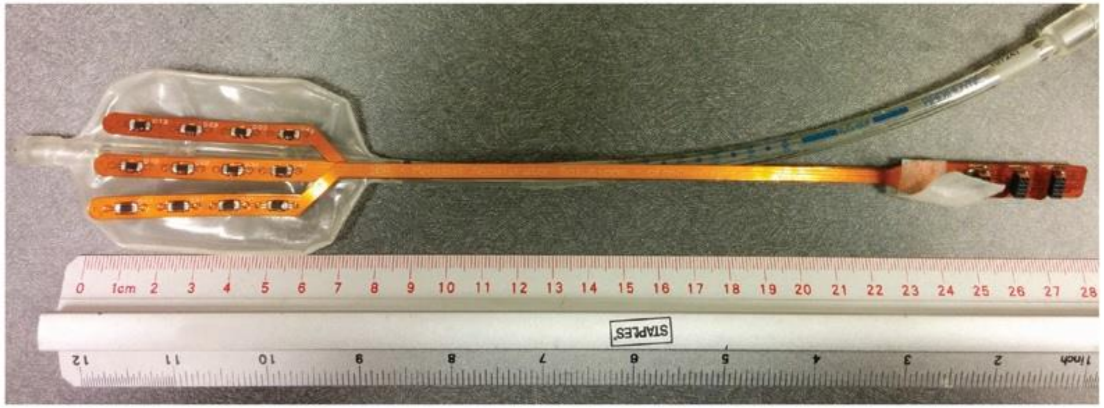
Impact on range/dose calculations

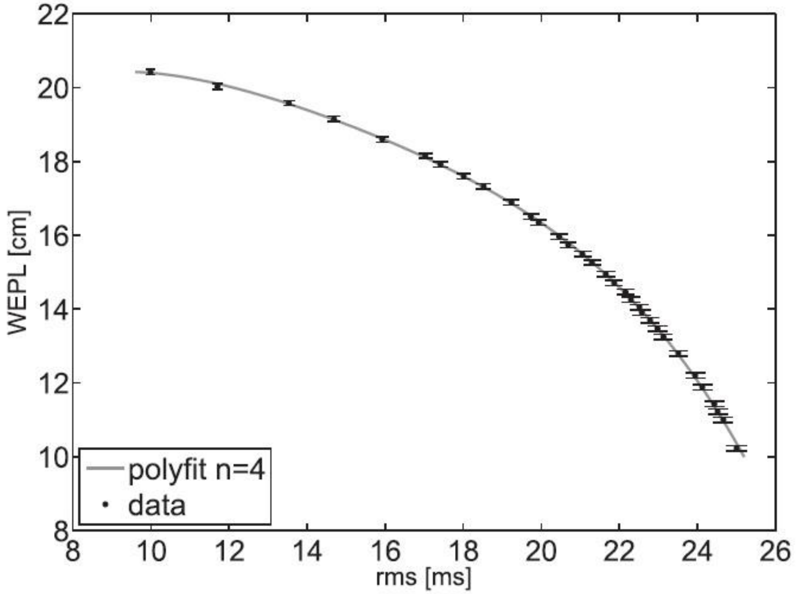


[Knopf et al. PMB 2013]

Direct Range Measurements

- Ideal: Detectors at distal edge of target volume
- Limited number of cavities in body
- Example: Prostate with anterior irradiation
- Array of diodes attached to endorectal water balloon
- Diodes: small size, no HV
- SOBP via modulator wheel
- Time resolved measurements of diodes, calibration to WEPL and dose

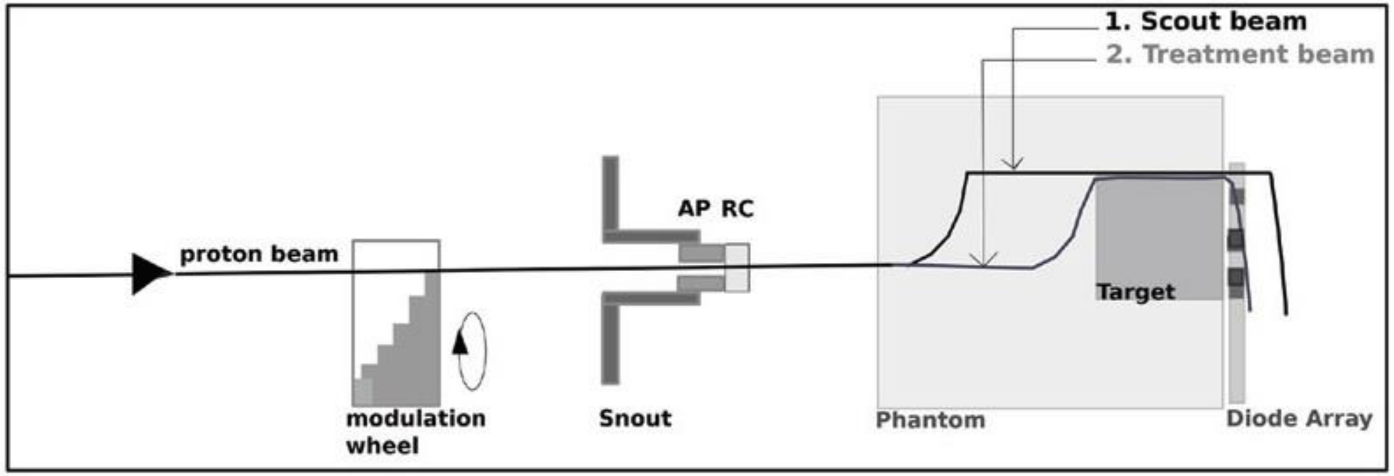


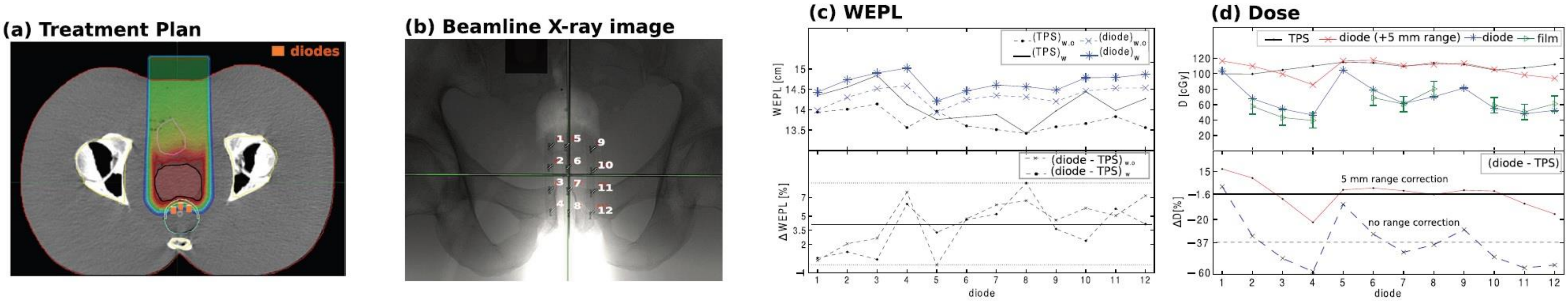


[Hoesl et al. PMB 2016]

Direct Range Measurements 2

- Scout beam (dose < 1cGy) with extended range
- Determination of actual WEPL here: in pelvis phantom
- Comparison to predicted values
- Adaption of treatment, if necessary





[Hoesl et al. PMB 2016]

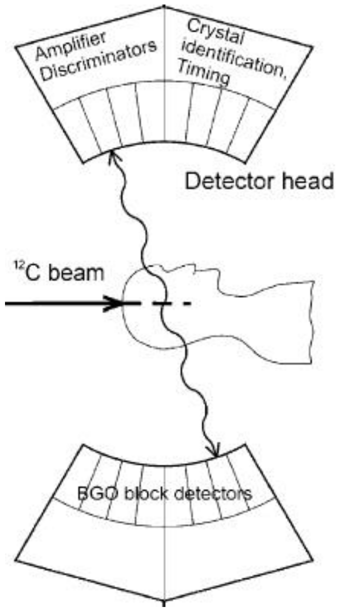
Nuclear reactions & secondary radiation

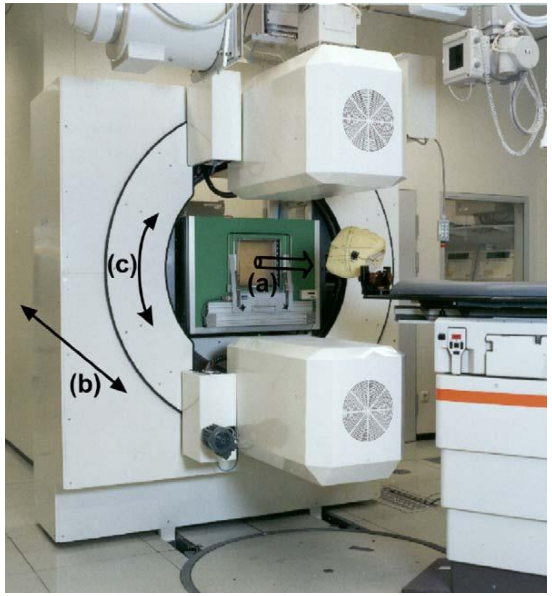
Nuclear reactions

[V. Patera et al. Eur. Phys. J. Plus 2019]

- Collision and de-excitation phase
- Creation of projectile-like and target-like fragments, e.g. ^{11}C, ^{15}O, …
  - PET monitoring
- Emission of prompt γ-rays, neutrons, light charged particles:
  - Real-time monitoring

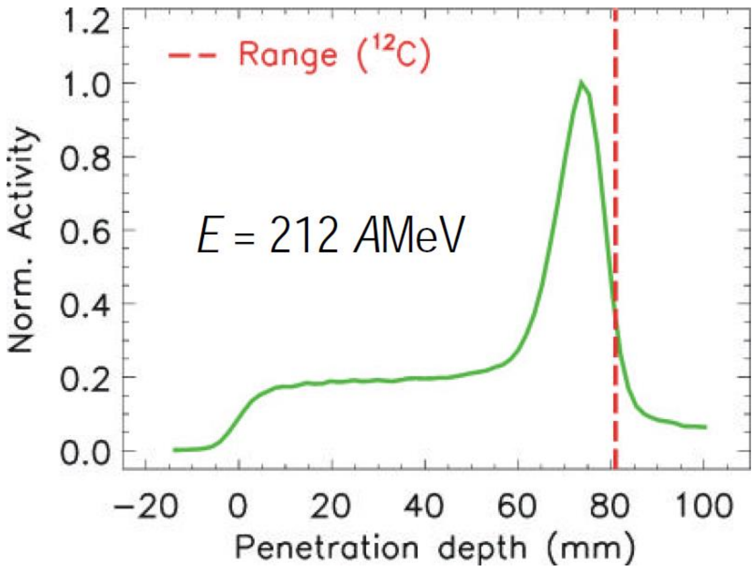
PET monitoring

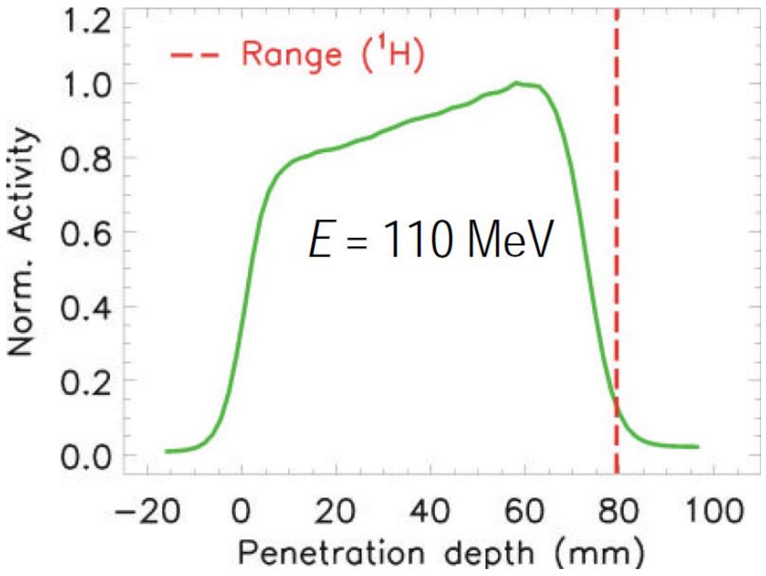




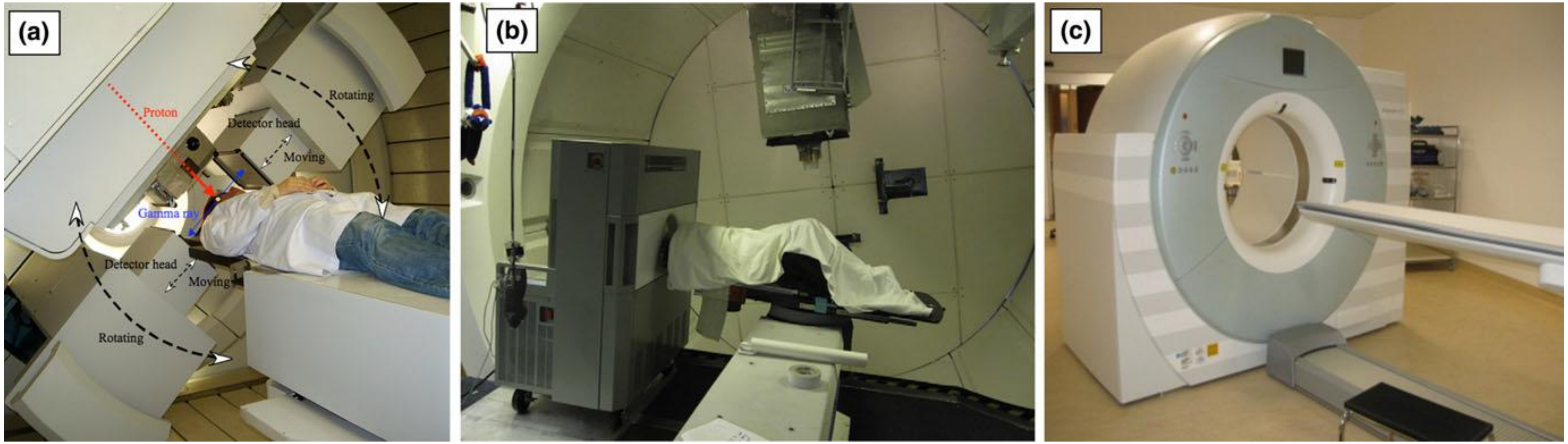
- Coincident detection of 511 keV photons
- Measurement of activity distributions
  - p-beam: target-like fragments
  - C-beam: projectile-like fragments
- Biological washout

[W. Enghardt et al. NIM A 2004]

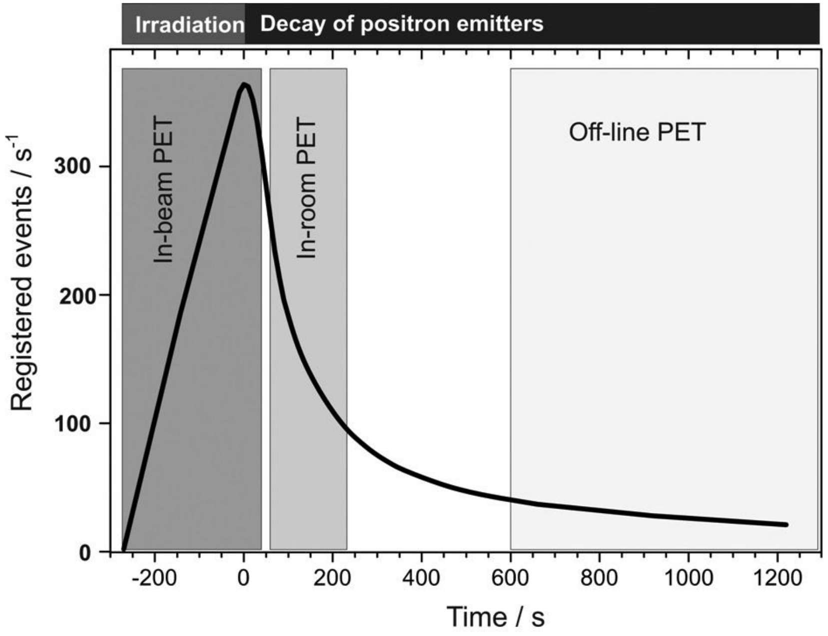




PET monitoring 2



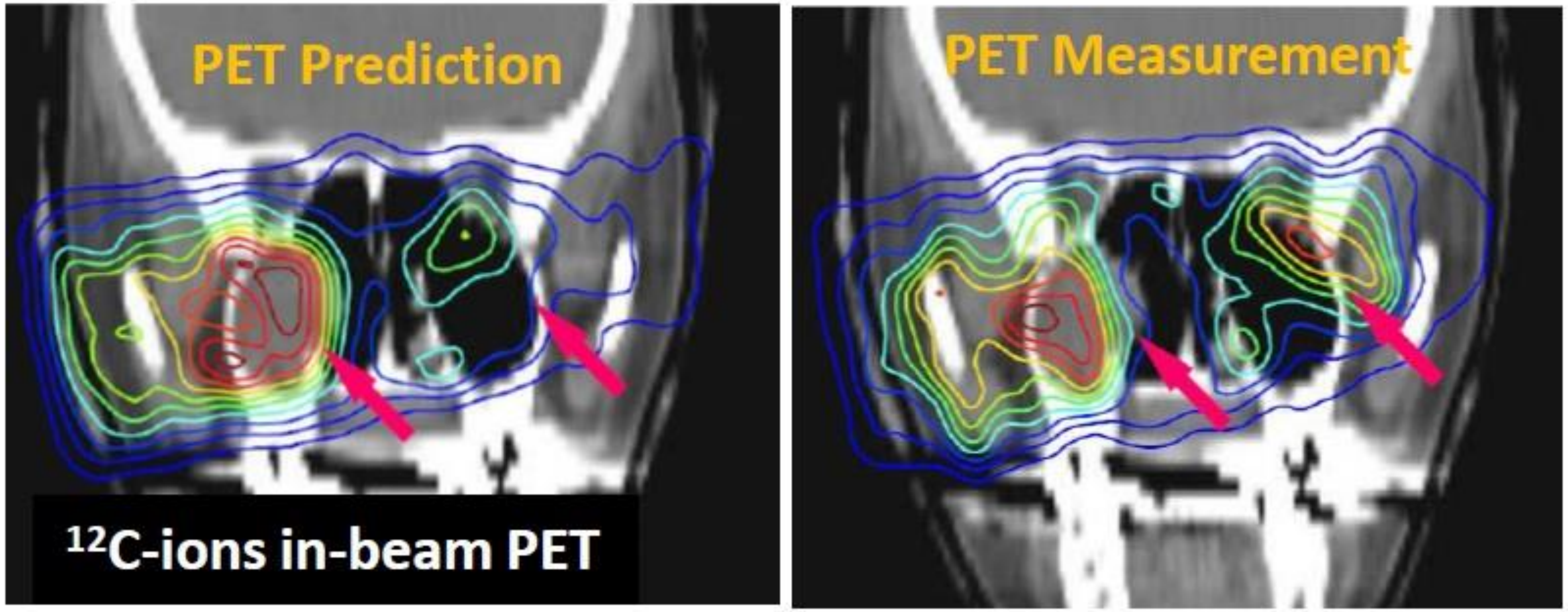
[K. Parodi et al. Med. Phys. 2018]



- Different clinical realizations:
  - a) in-beam PET
  - b) in-room PET
  - c) offline PET
- Find compromise between available hardware and clinical workflow

[G. Shakirin et al. PMB 2011]

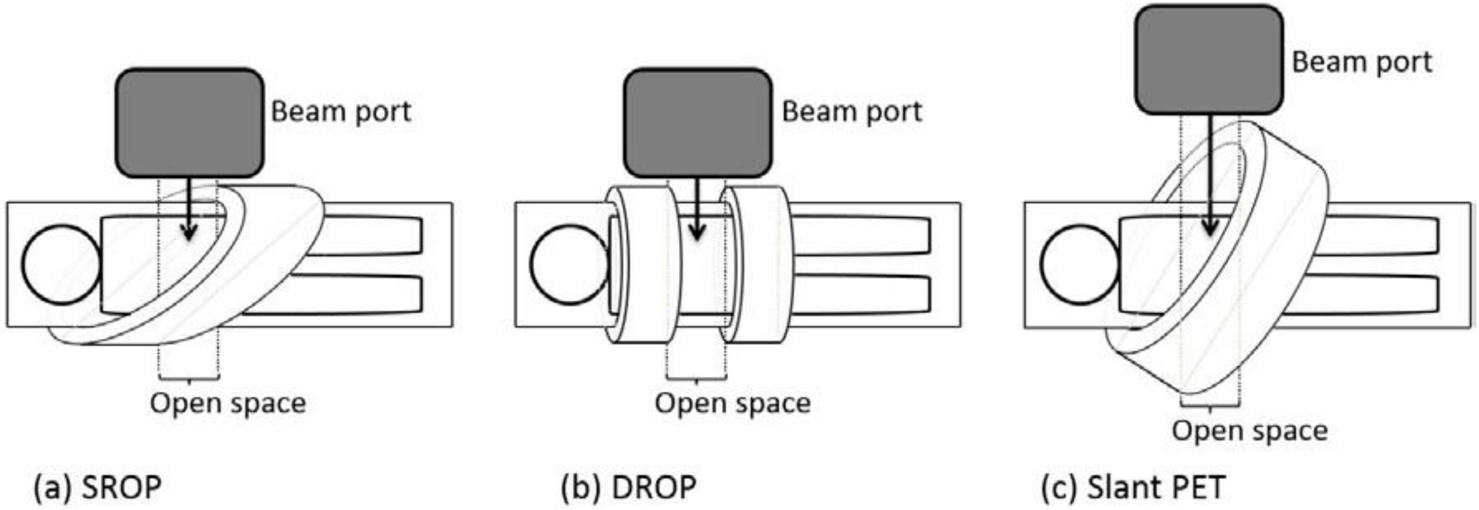
PET: washout

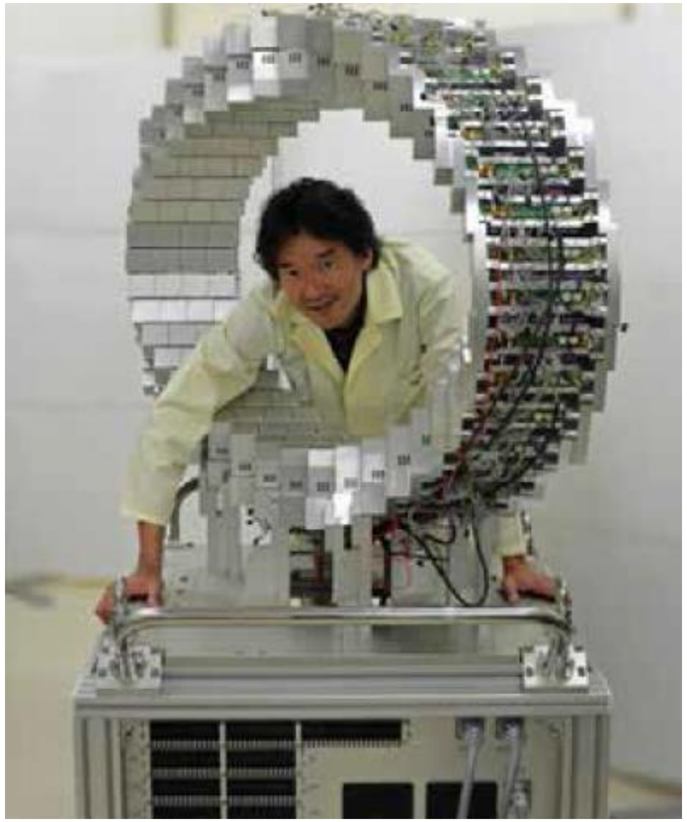


[K. Parodi et al. Rad. Onc. 2007]

- Prediction (simulation) of expected signal and comparison to measurement
- Minimization of washout: short-lived isotopes (e.g. ^{12}N, $t_{1/2}$ = 11 ms) [P. Dendooven PMB 2015]
- measurements e.g. spill pauses of synchrotron
- First measurements at KVI: [H. Buitenhuis et al. PMB 2017]

PET: Hardware developments





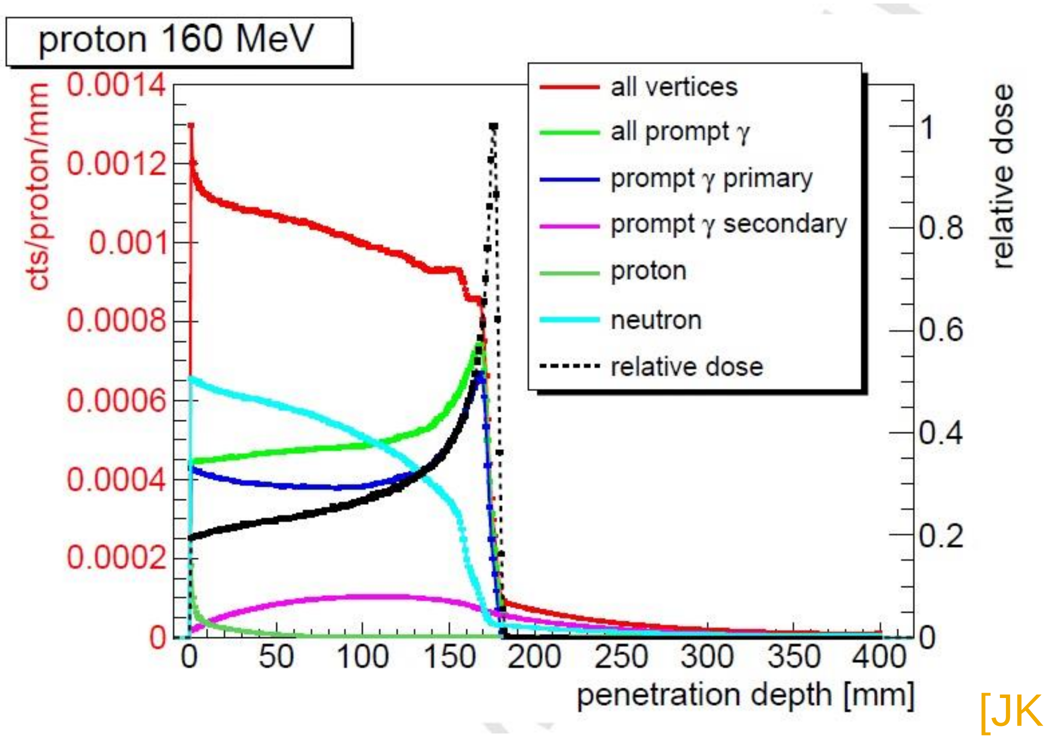
OpenPET @ NIRS
[T. Yamaya J. Phys. 2017]

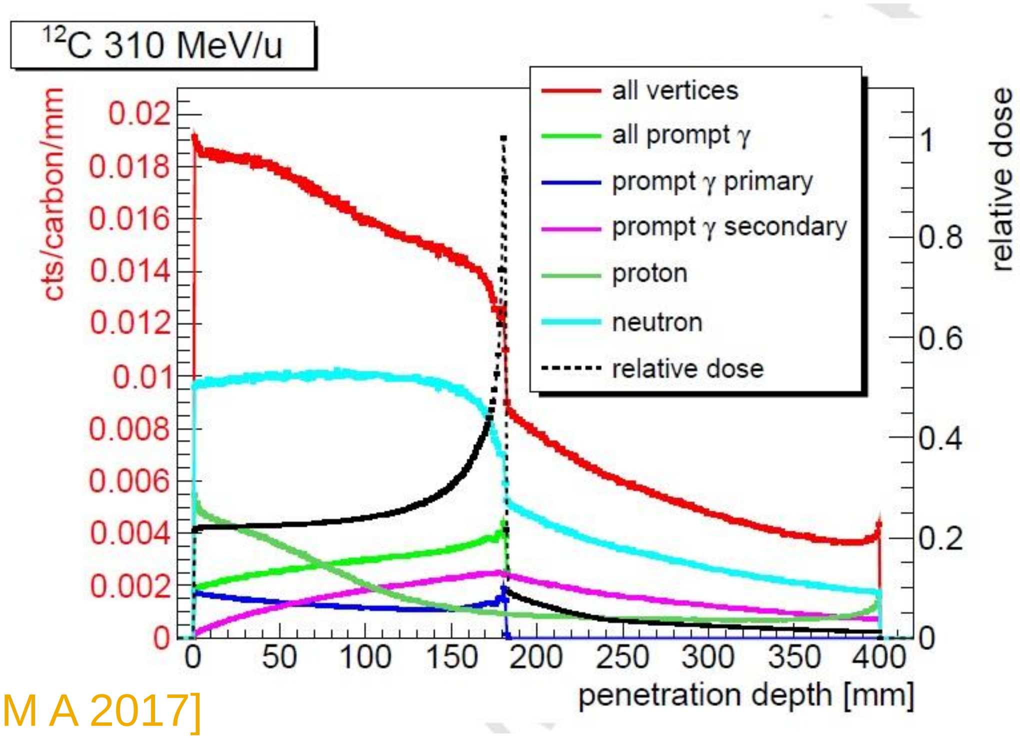
- Adaption of design for beam delivery
- Single, dual ring or flat geometries possible

INSIDE @ CNAO [Bisogni J Med Im 2016]

Real-time monitoring

Prompt secondary radiation for ion range monitoring



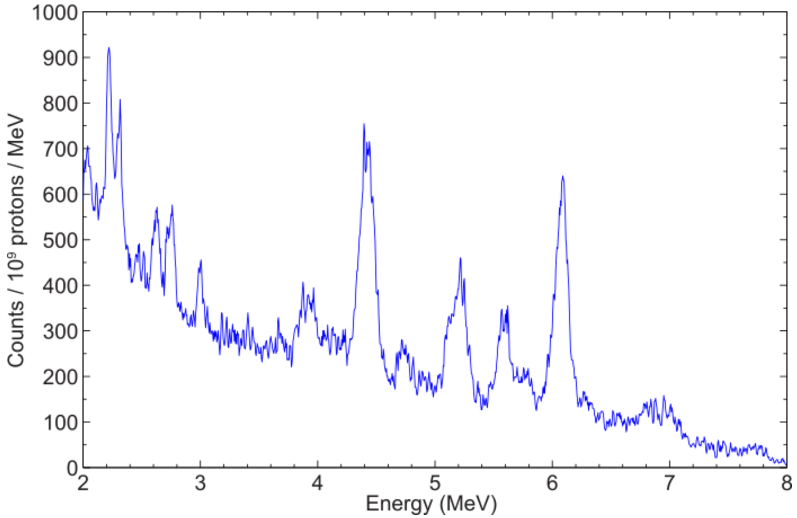


[JK et al. NIM A 2017]

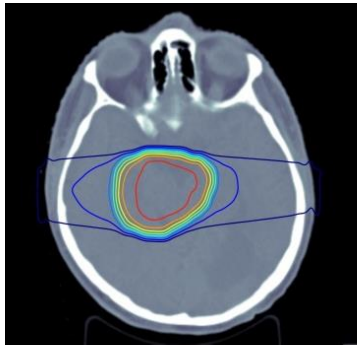
- Simulation of protons and carbon ions on a water target (diameter 15 cm, length 20 cm)
- Vertices of particles leaving the target, energy > 1 MeV
- Correlation of vertices with ion range

Prompt γ-rays

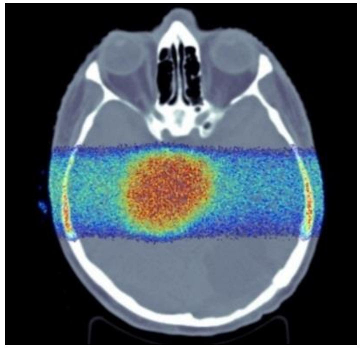
- Energy range 2-10 MeV
- Timescale < 10^{-11} s
- Characteristic lines from transitions in ^{12}C or ^{16}O
- Use for range monitoring proposed in 2003
  [Y. Jongen, F. Stichelbaut PTCOG 2003]
- Proof of concept:
  protons: [Min et al. APL 2006]
  carbon ions (using TOF): [E. Testa et al APL 2008]
- Technical realizations:
  - Mechanical collimation: knife edge, multi slit
  - *Electronic* collimation: Compton camera
  - no collimation: PGT, PGPI
  - Prompt gamma spectroscopy



[J. Verburg PMB 2011]



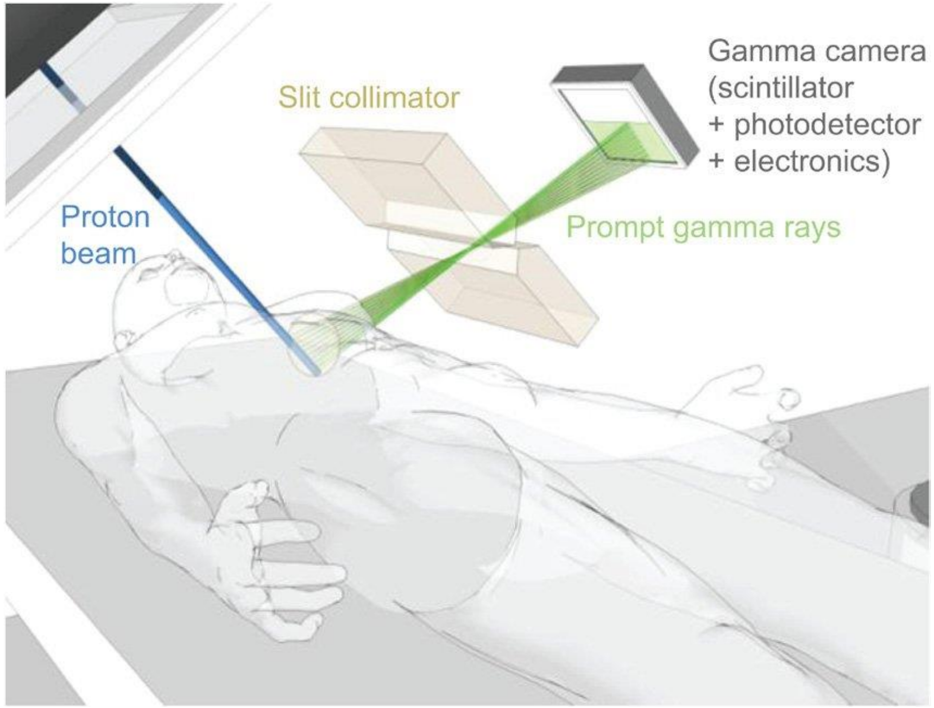
Deposited dose

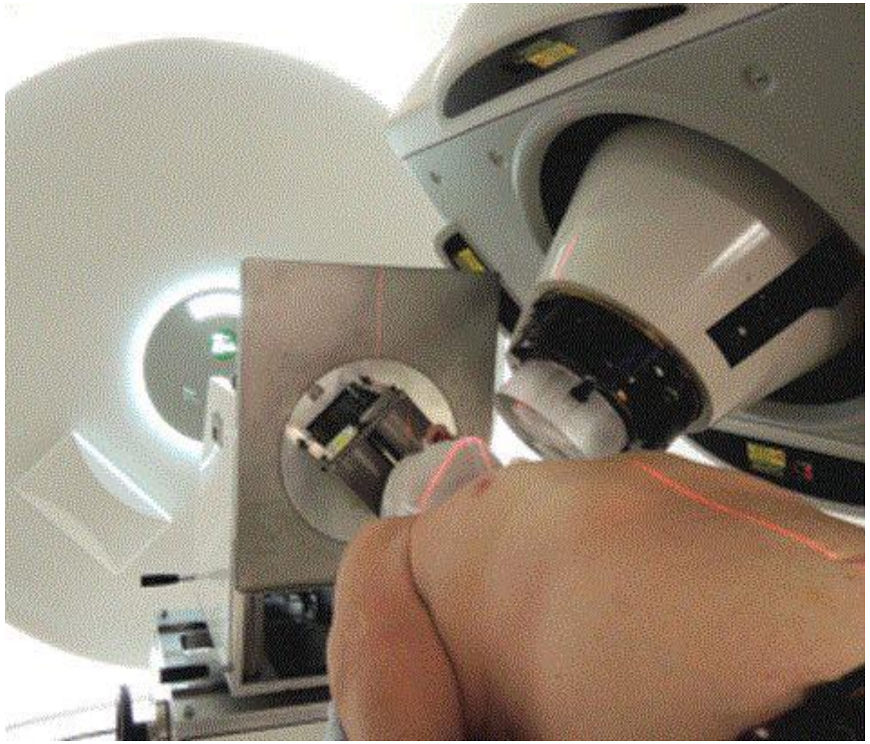


Prompt γ emission

[F. Fiedler IEEE NSS MIC 2011]

Collimated cameras: Knife-edge (IBA)

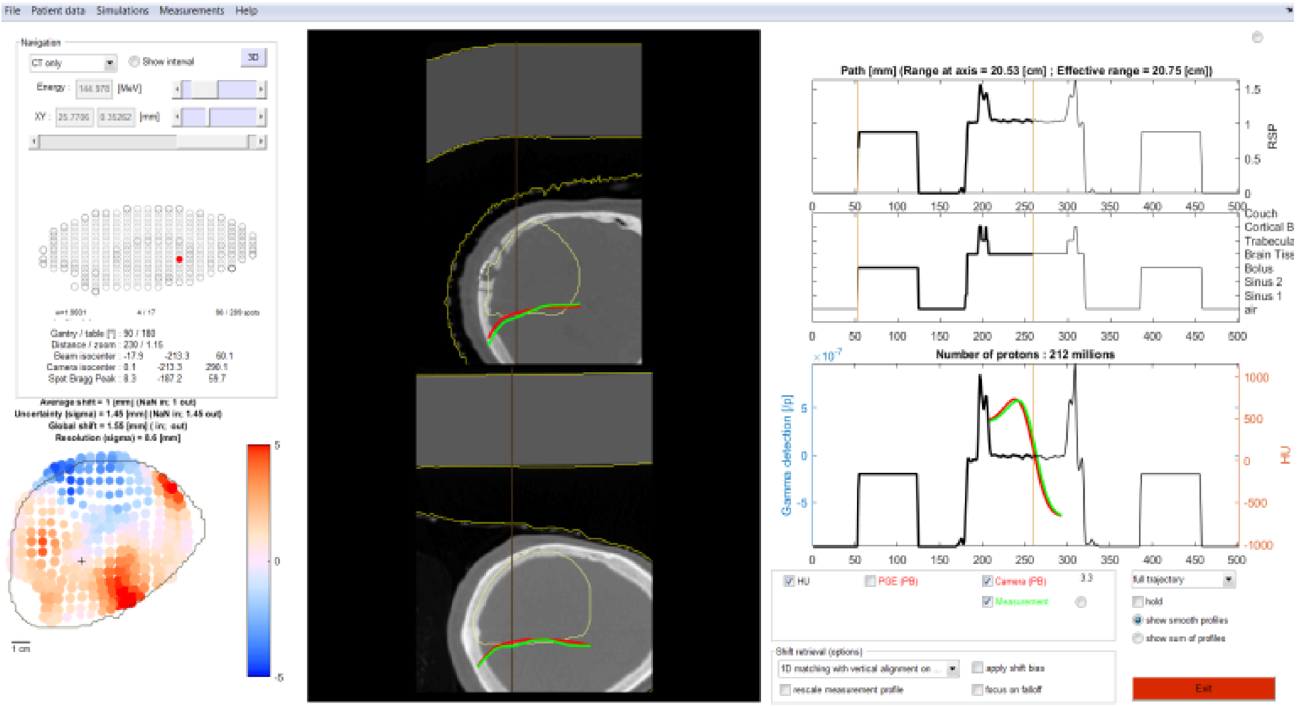




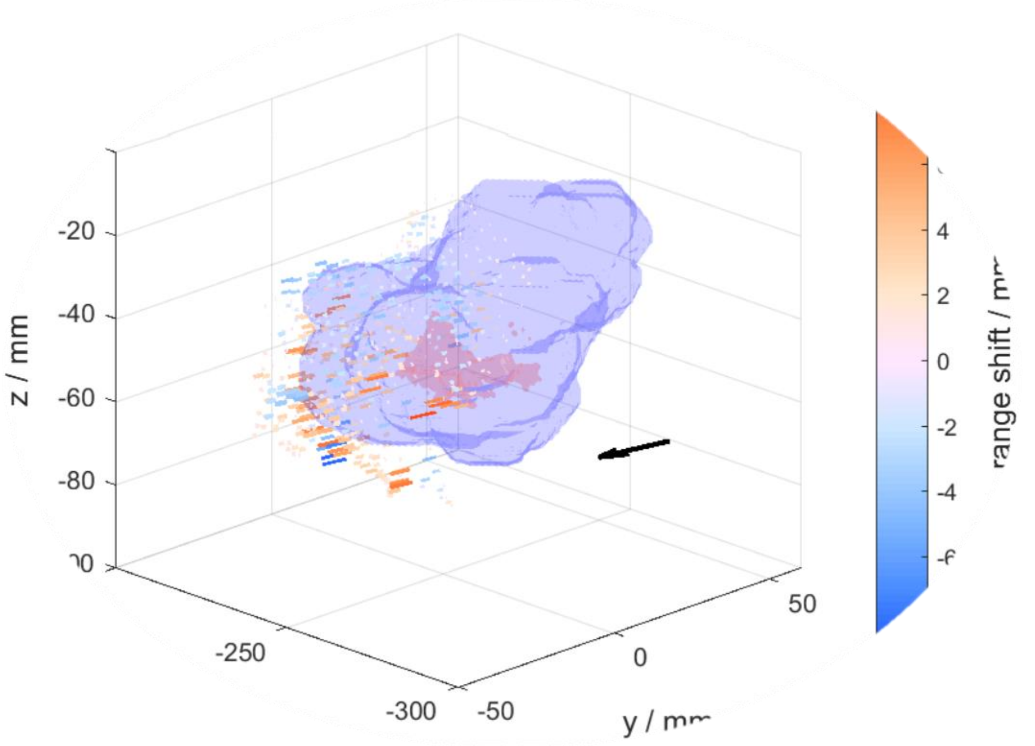
- Principle of pin-hole camera
- Prototype optimization via simulations
- fall-off retrieval precision ≈ 1mm for a distal spot
  [J. Smeets et al. PMB 2012]

- tests with prototype at C230 cyclotron [Perali et al. PMB 2014]
- First patient measurements
  [Richter et al. Radiother. Onc. 2016]

Knife-edge 2



- Software for simulation and data analysis

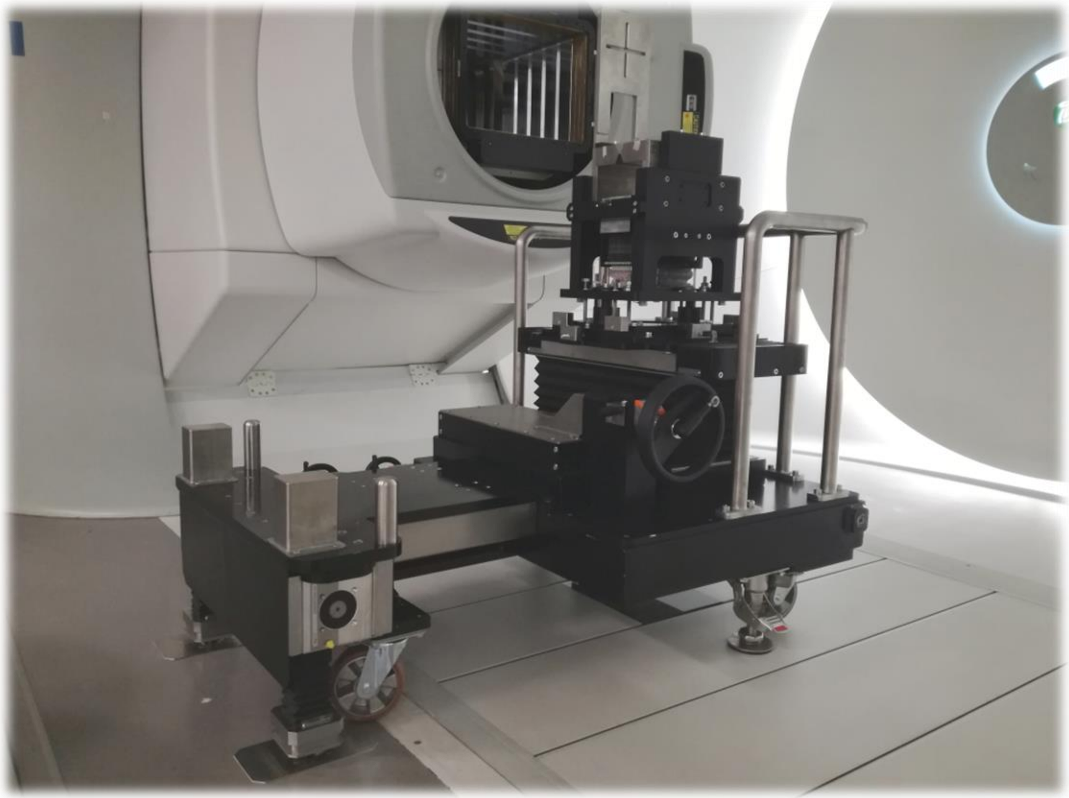


- Range analysis in 3D

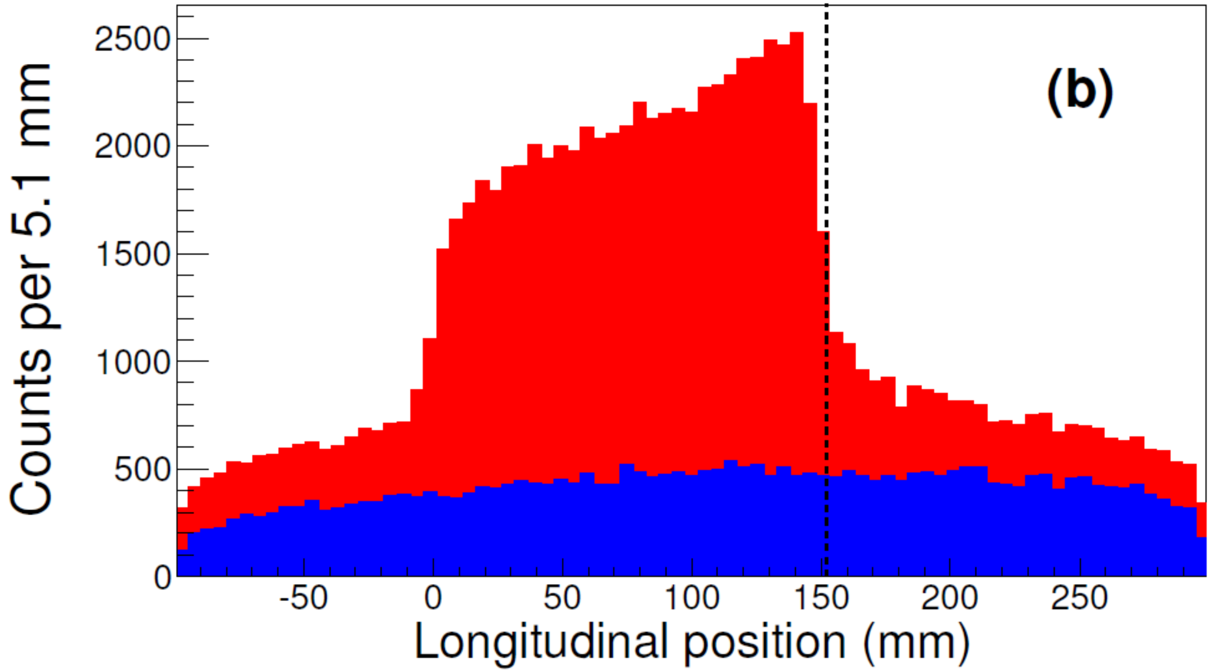
[Richter et al., Radiother Oncol, 2016]
[Xie et al., Int J Radiat Oncol Biol Phys 2017]
[Nenoff et al., Radiother Oncol, 2017]

New hardware for prostate study

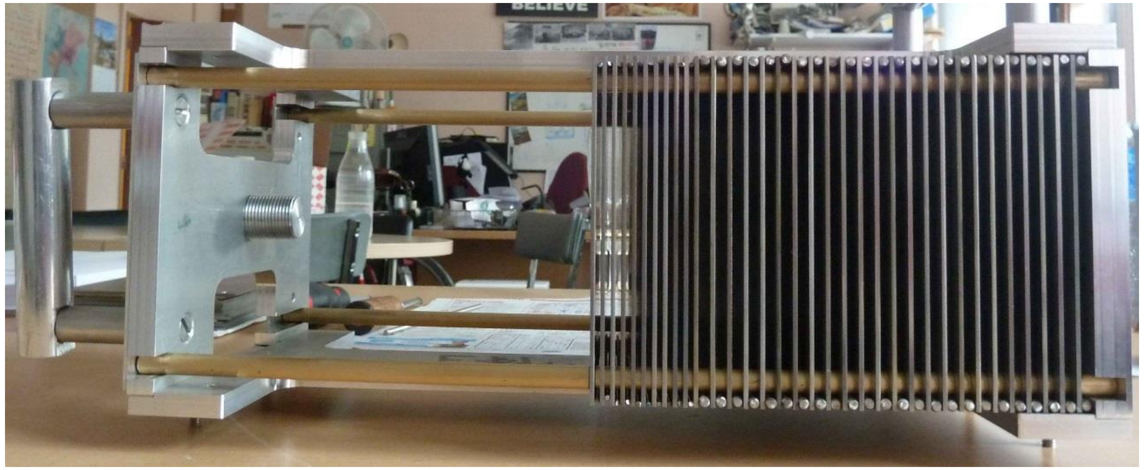
- New “under-the-couch” trolley at OncoRay for patient study on prostate treatments
- Improved workflow by mechanical docking into treatment floor
- Absolute position calibration using X-ray system and proton beam (accuracy < 0.8mm @ 2σ)

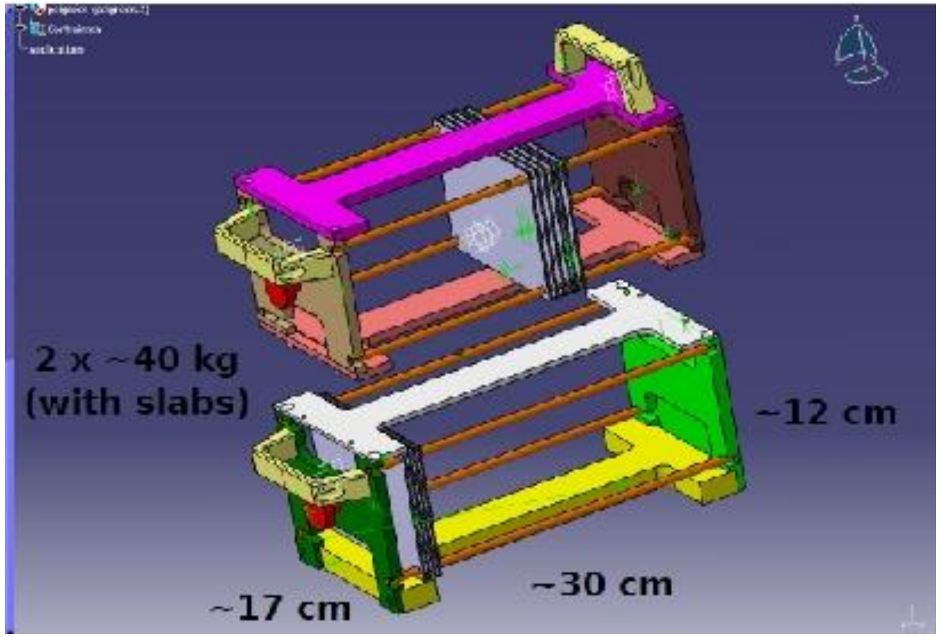


Collimated camera: Multi-slit (IPNL)

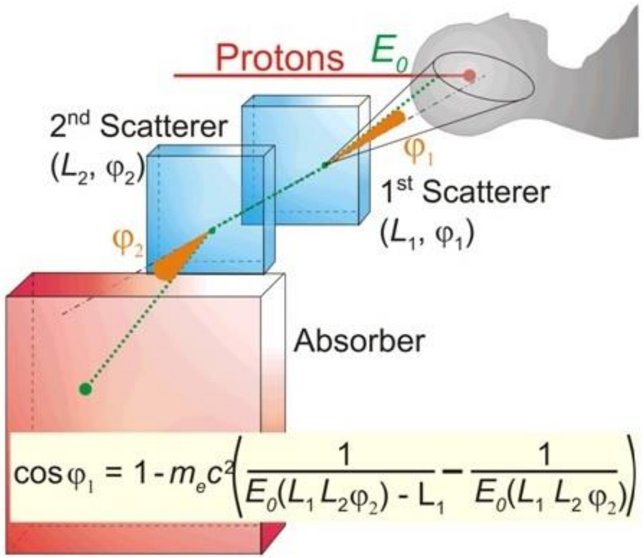


- Full ion range visible
- Collimator optimization via simulations
- fall-off retrieval precision:
  σ ≈1mm @ 10^8 protons
  [M. Pinto et al. PMB 2014]



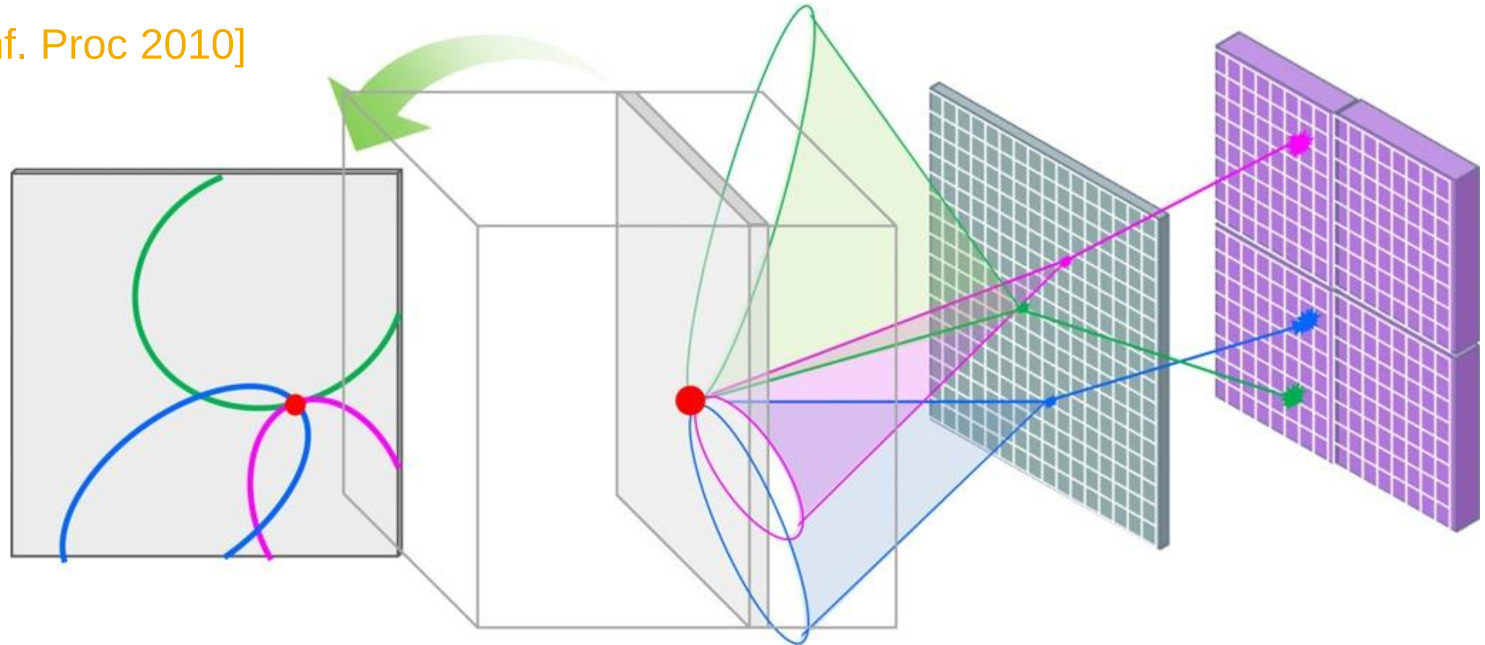


Electronic Collimation: Compton Camera



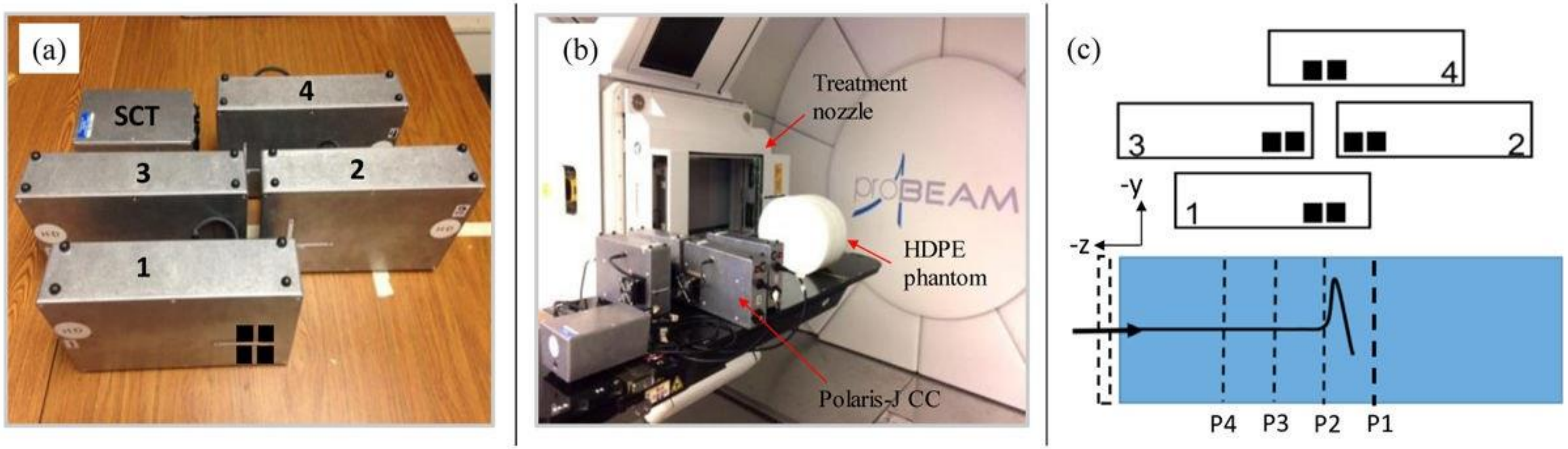
[Cowan et al. AIP Conf. Proc 2010]

- Scatter and absorber detectors: store energy and position information of interactions
- Minimum 2 interactions required
- Use Compton kinematics: reduce possible incident directions to cone
- Overlay of multiple cones: reconstruct initial vertices
- In principle 3-D information available



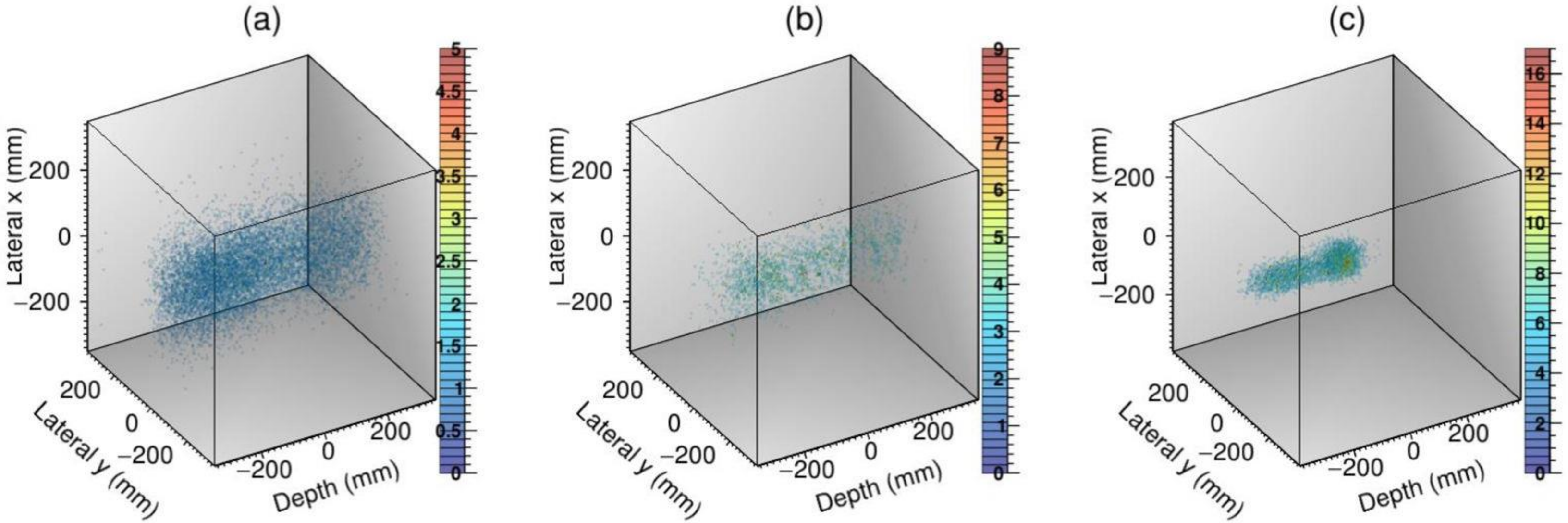
[Kim et al. PMB 2012]

Compton Camera: realizations



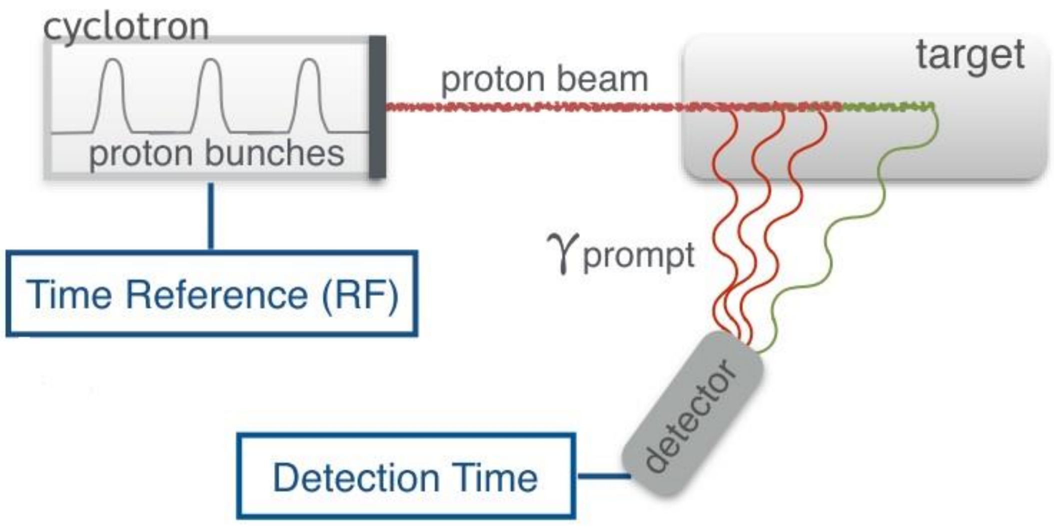
- Various realizations
- Monolithic scintillators: e.g. IFIC Valencia
- DSSD + scintillator: LMU Munich, IPNL Lyon
- here: CdZnTe

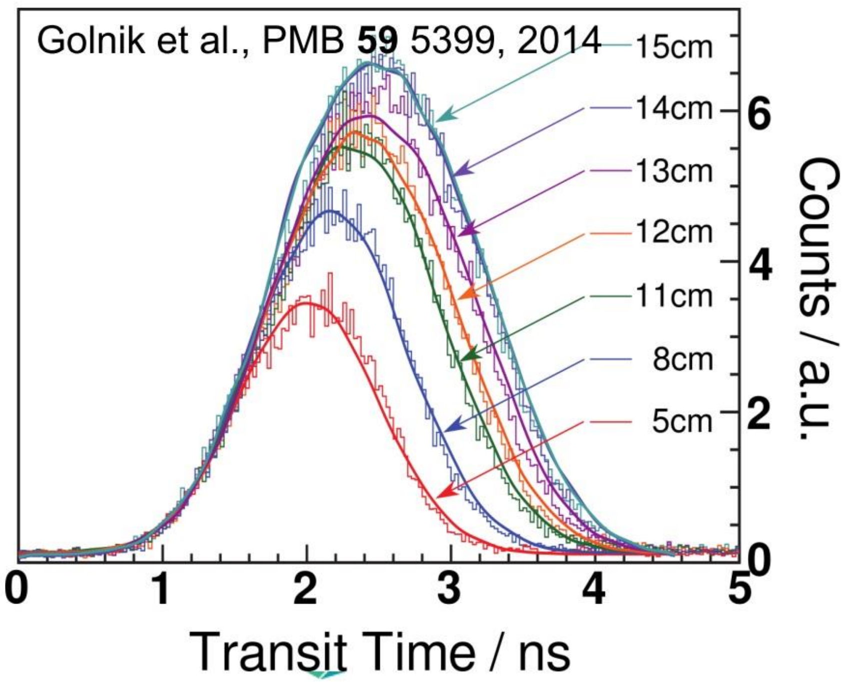
- Reconstruction algorithms adapted to PT
- here: filtering & iteration
- 3-D information
- Limitations in beam current: random coincidences

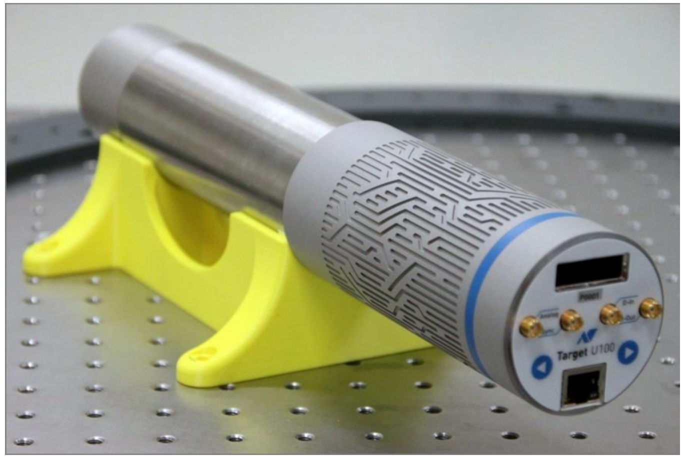


[E. Draeger et al. PMB 2019]

No Collimation: Prompt Gamma Timing PGT

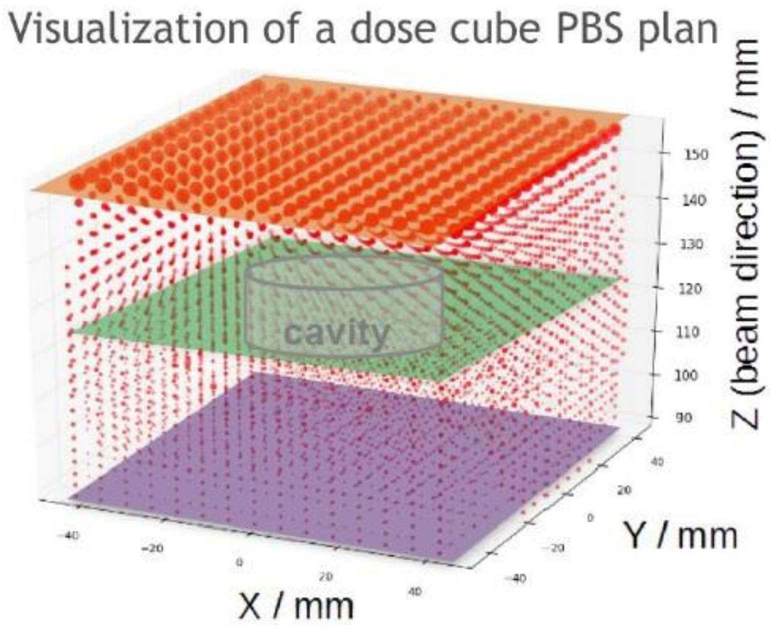


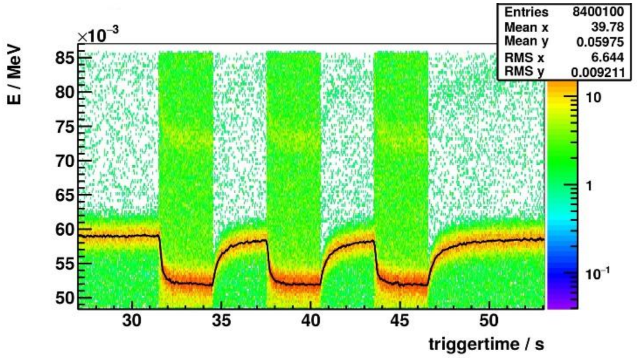


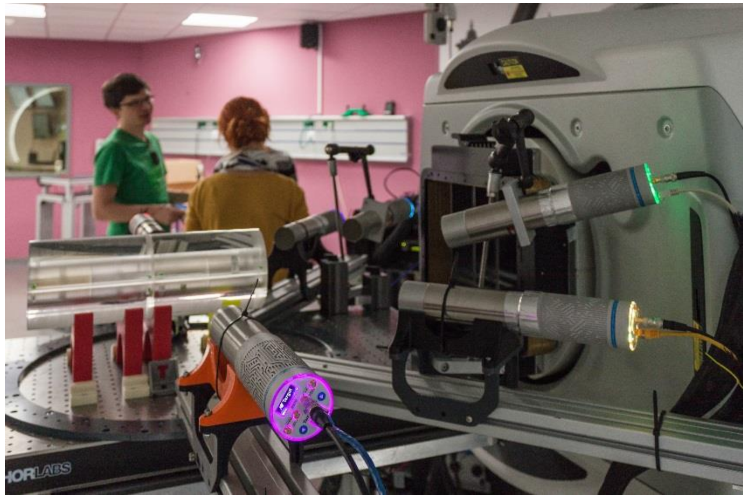


- Production of prompt gammas along proton track
- Record time-resolved emission spectra
- Use mean and width as information
- Changes in track length → changes in measured quantities on the order of ps

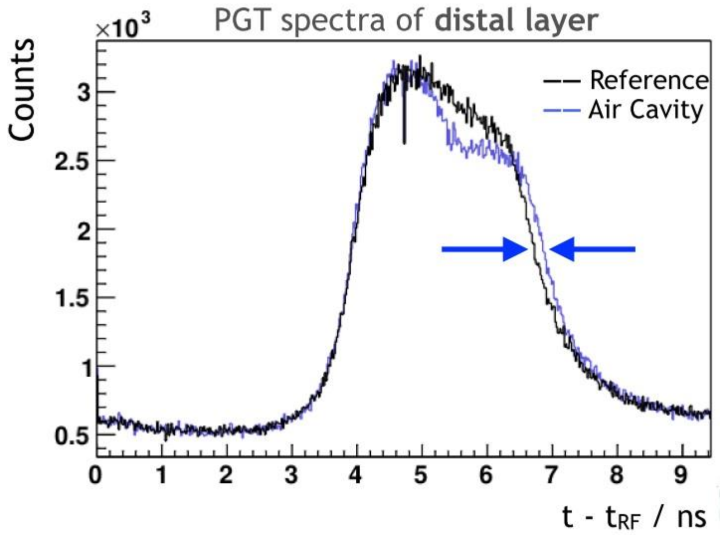
PGT: Towards Clinical application



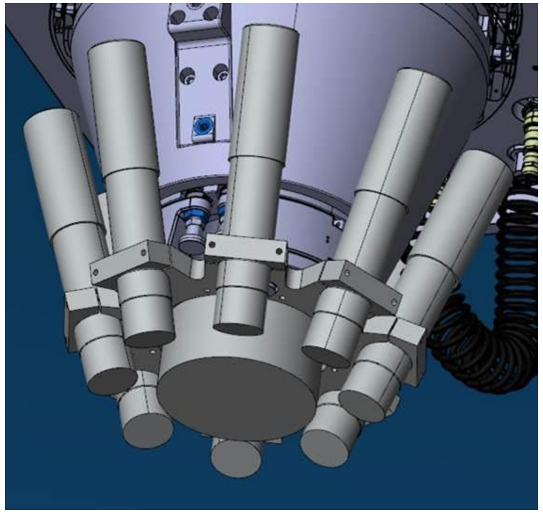




- Gain depends on load
- Drift of RF phase
- Corrections applied



- Use information from multiple detectors
- Visualize effect of air cavity
- New prototype: integrated in nozzle

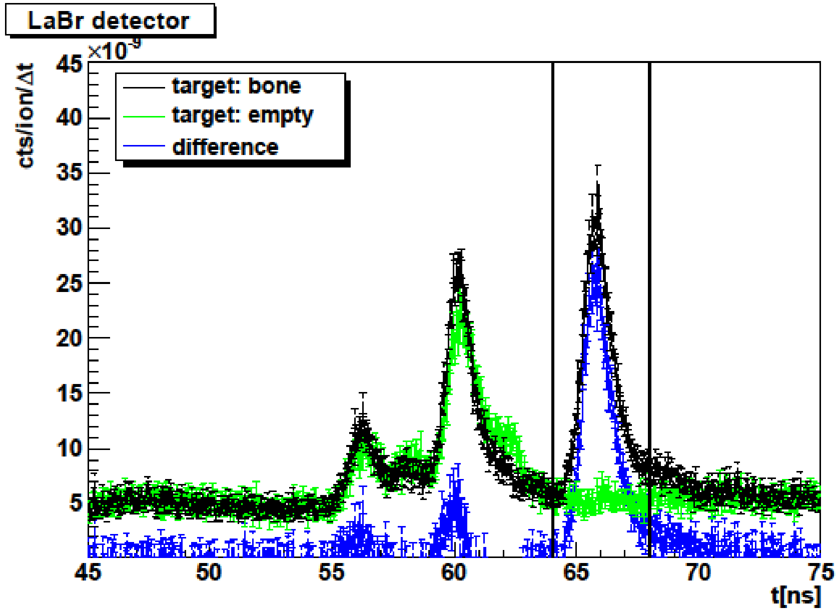


[T. Werner MEDINET mid-term Meeting 2018]

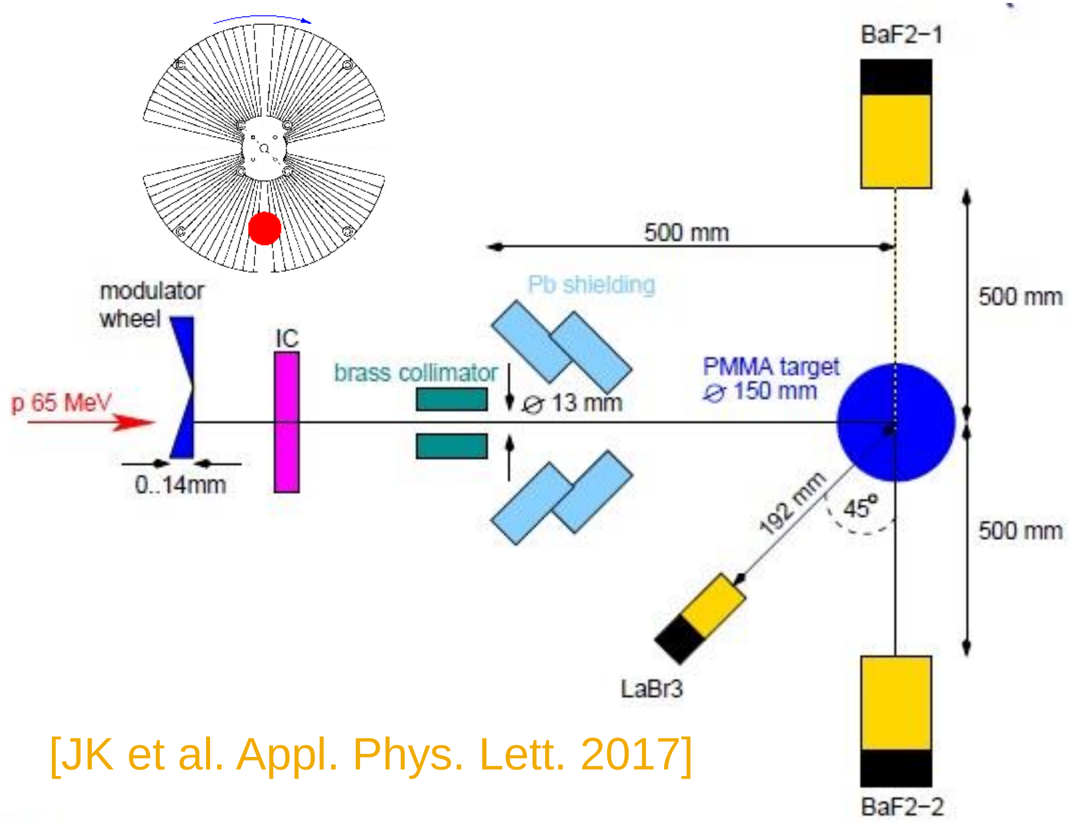
Prompt Gamma Peak Integral PGPI

- Detect prompt gamma rays produced in target (patient)
- Use TOF for event selection (nozzle – target)
- Integral depends on absorbed energy (range) as well as on material

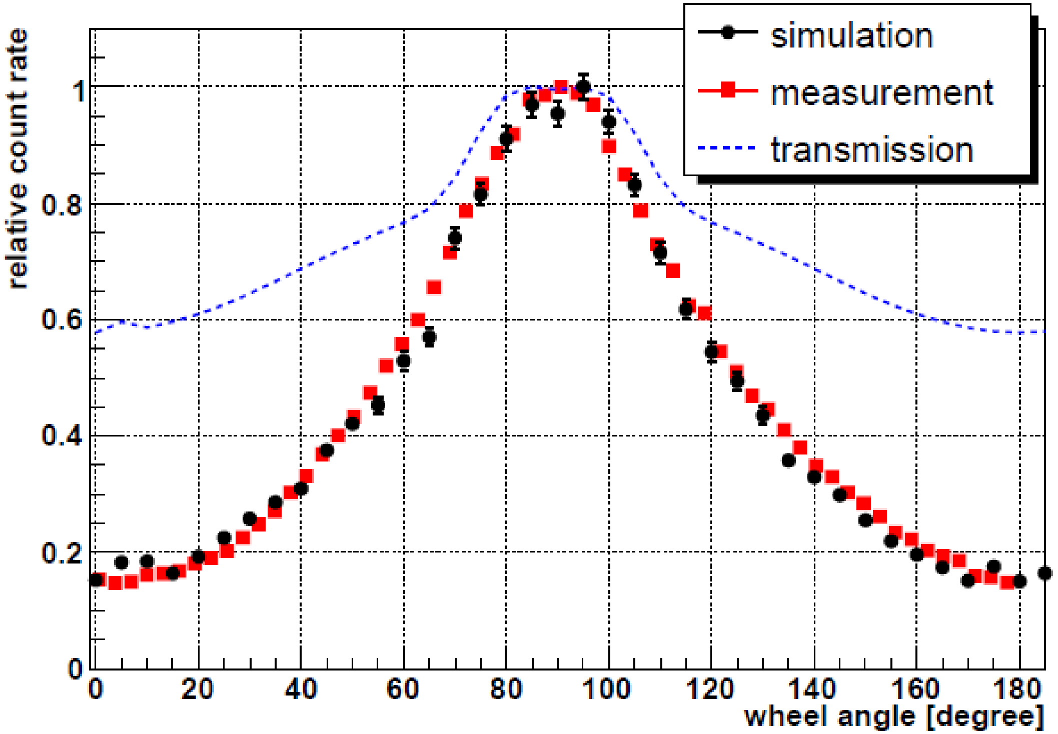
- Test measurement at CAL in Nice
- 65 MeV protons (cyclotron)
- Scintillation detectors: NaI, $LaBr_3$, BaF_2

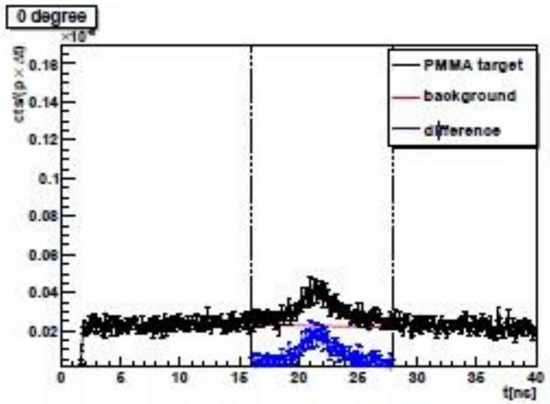


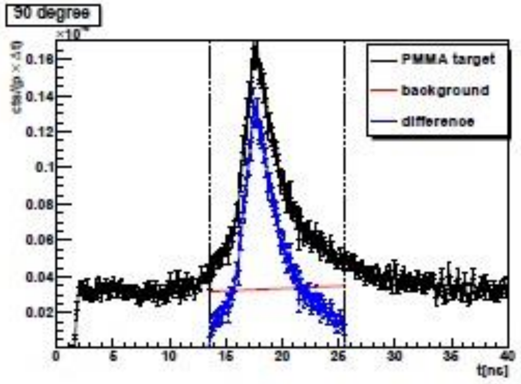
PGPI: Test with modulator wheel



[JK et al. Appl. Phys. Lett. 2017]

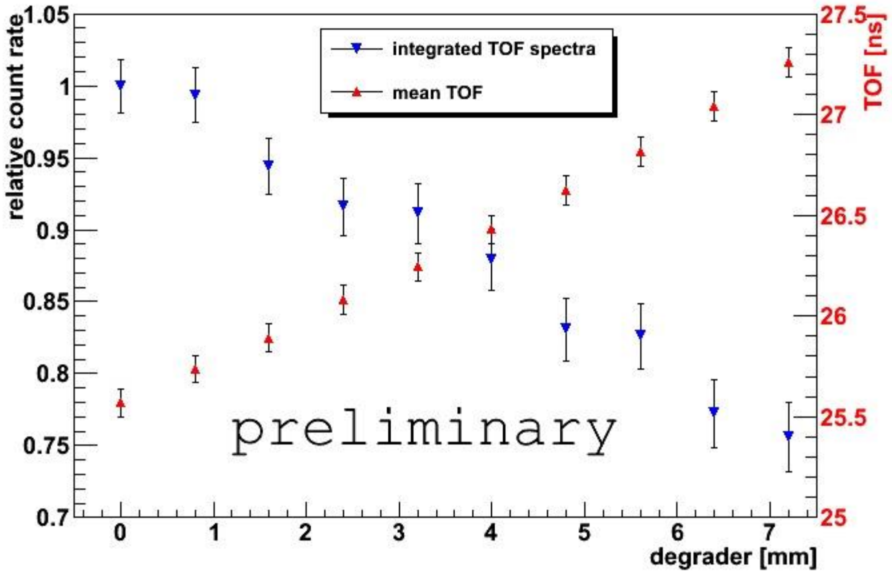






- Relative count rate as a function of wheel angle
- Reduction by more than factor five:
  - Scattering in wheel: protons not passing collimator any more
  - Reduction of proton range in target
- Data well described by simulations

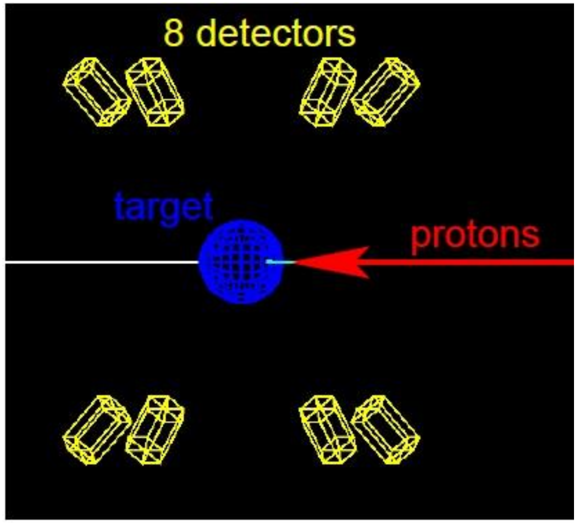
PGPI: Perspectives

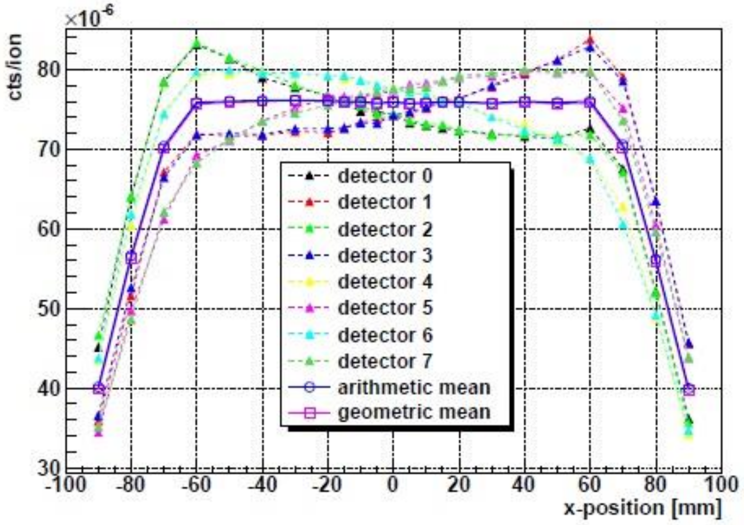


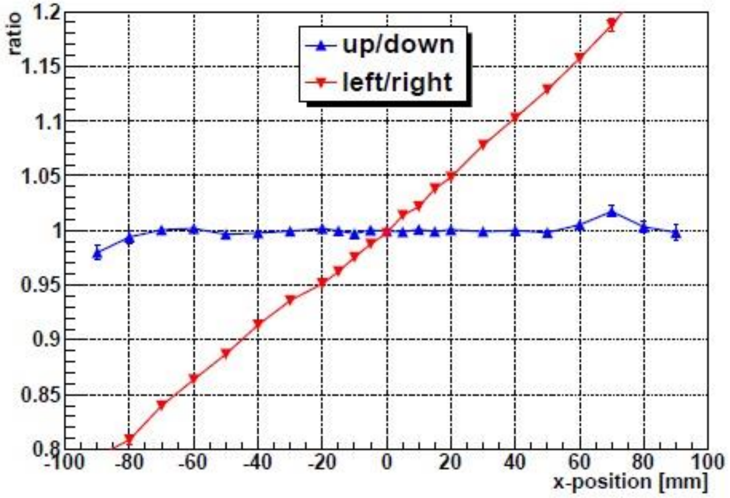
- 10^8 protons (65 MeV) on PMMA target
- Change range via degraders
  3 mm can be detected at given statistics

- Simulation: 8 detectors
- Horizontal displacement of target
- Combine information from detector groups: correlation with displacement

[JK et al. IEEE NSS MIC 2016]

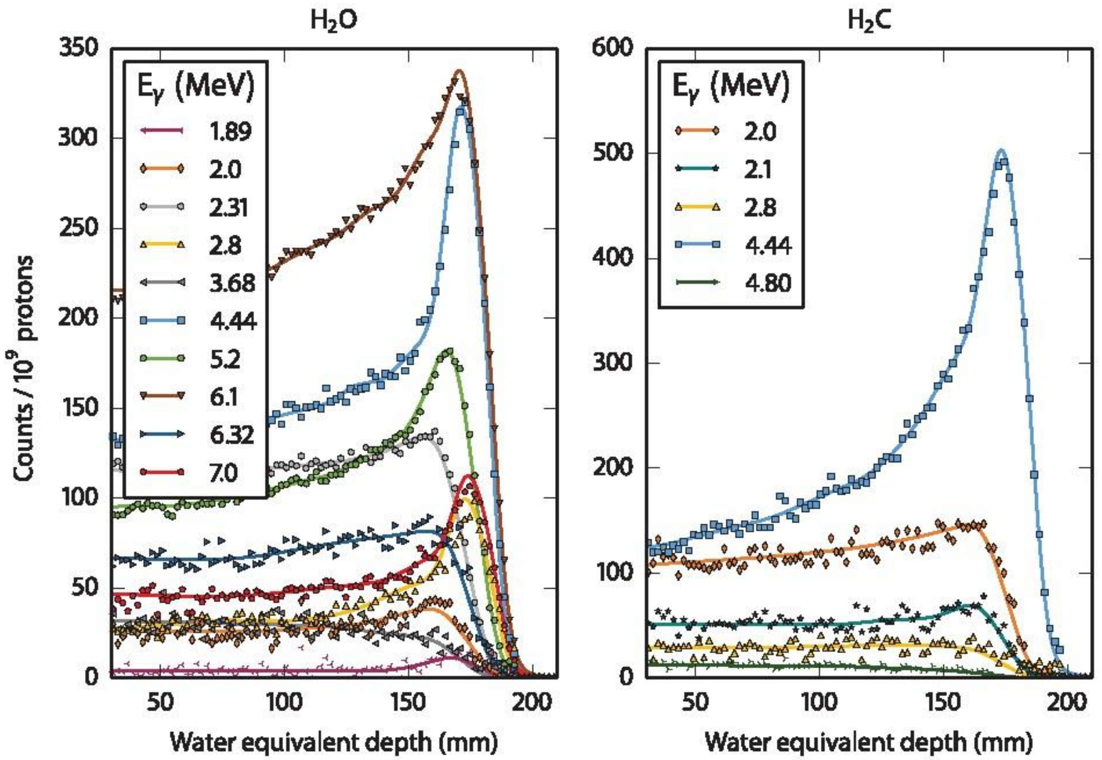


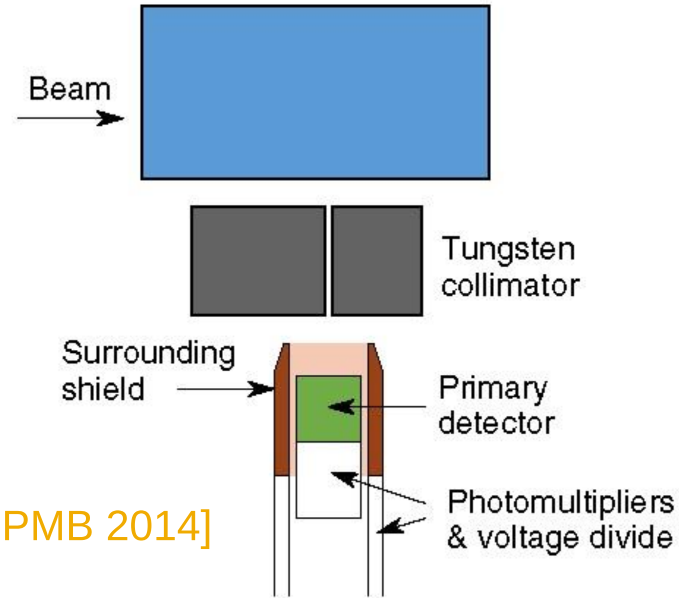




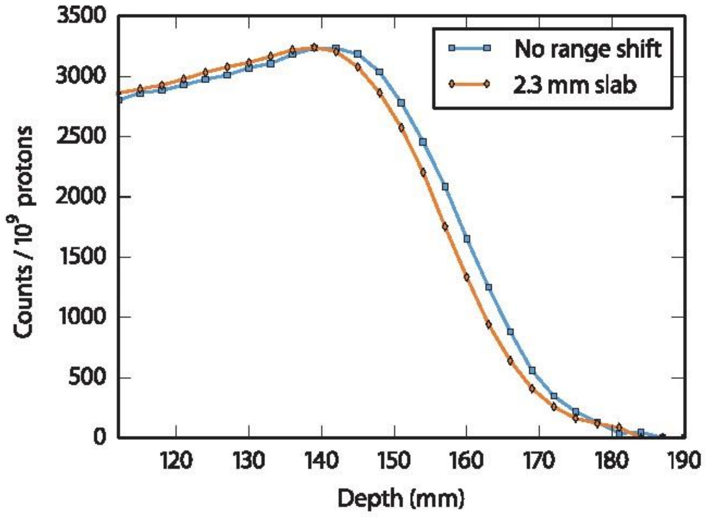
Prompt Gamma Spectroscopy PGS

- Idea: Emission spectrum of prompt gamma rays is correlated with range
- Emission spectrum registered at a given depth gives a measure of the residual range

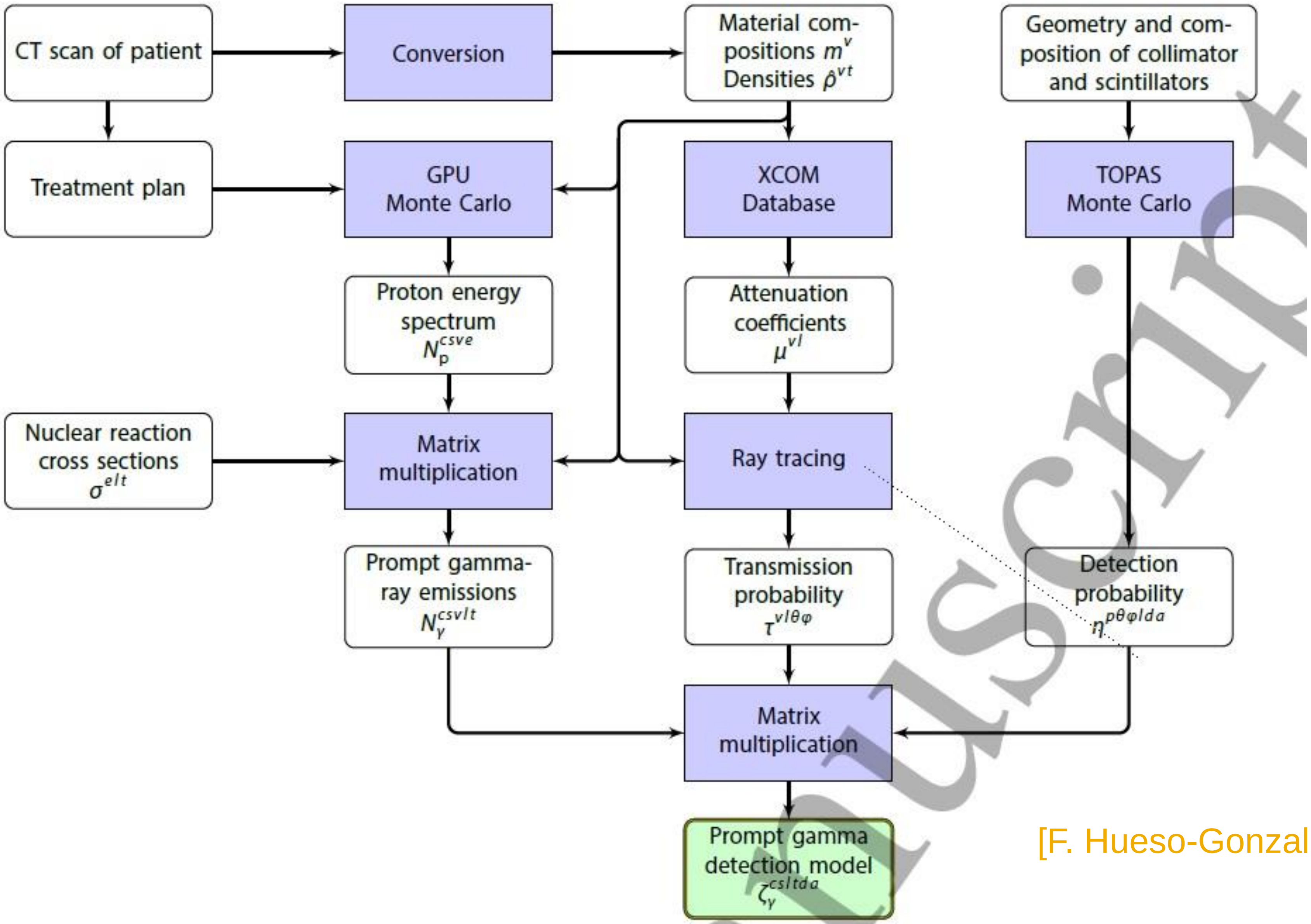




[J. Verburg et al. PMB 2014]

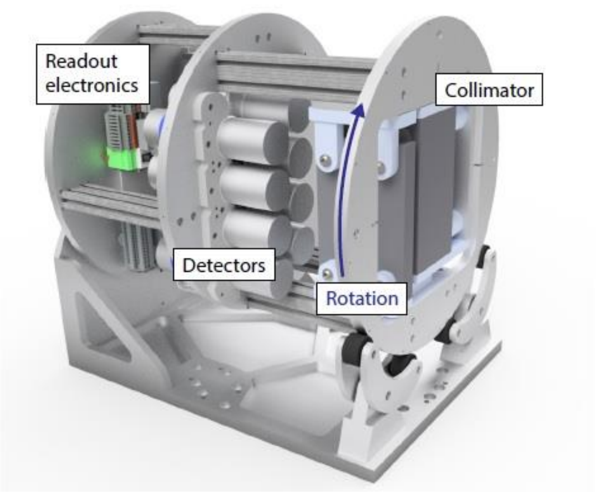


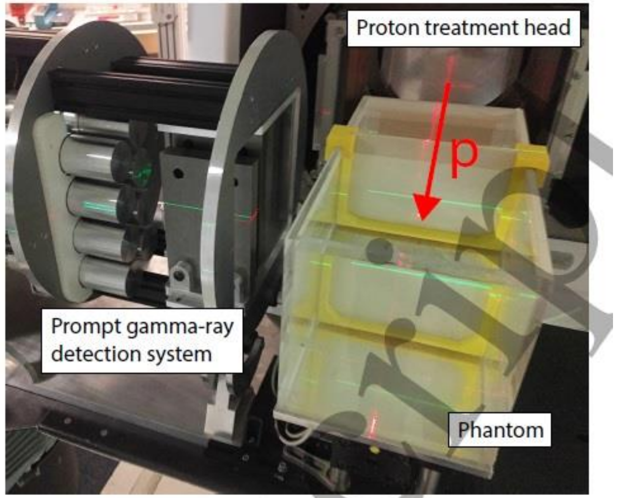
PGS: Workflow



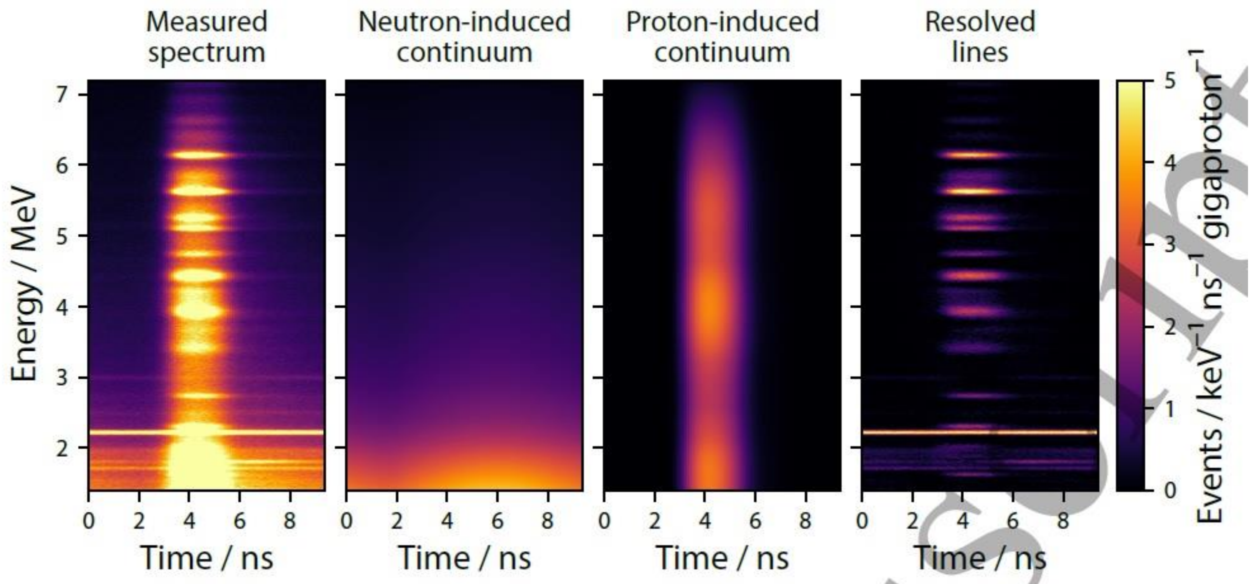
[F. Hueso-Gonzalez et al. PMB 2018]

PGS: Performance





- Clinical size prototype
- Delivery of 0.9 Gy in 5x10x10cm^3
- PBS at 2nA



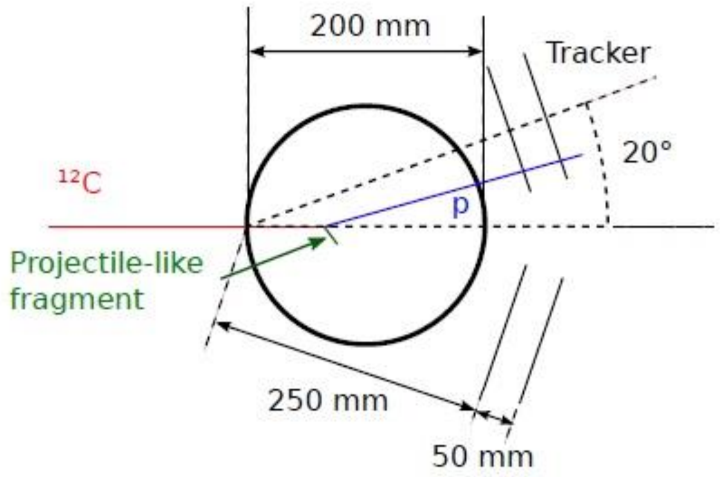
- Energy vs TOF,
  identification of spectral lines

- Determination of proton range for each spot with a precision of 1.1 mm

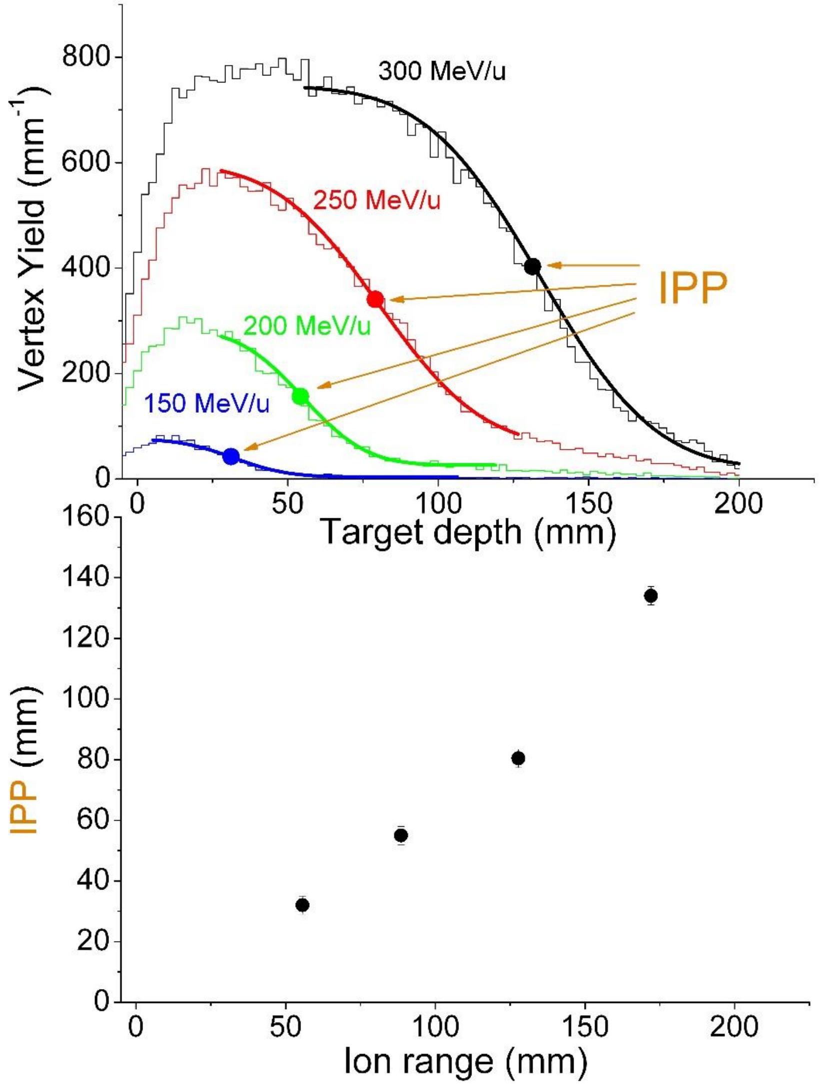
[F. Hueso-Gonzalez et al. PMB 2018]

Interaction Vertex Imaging IVI

IVI: Simulations

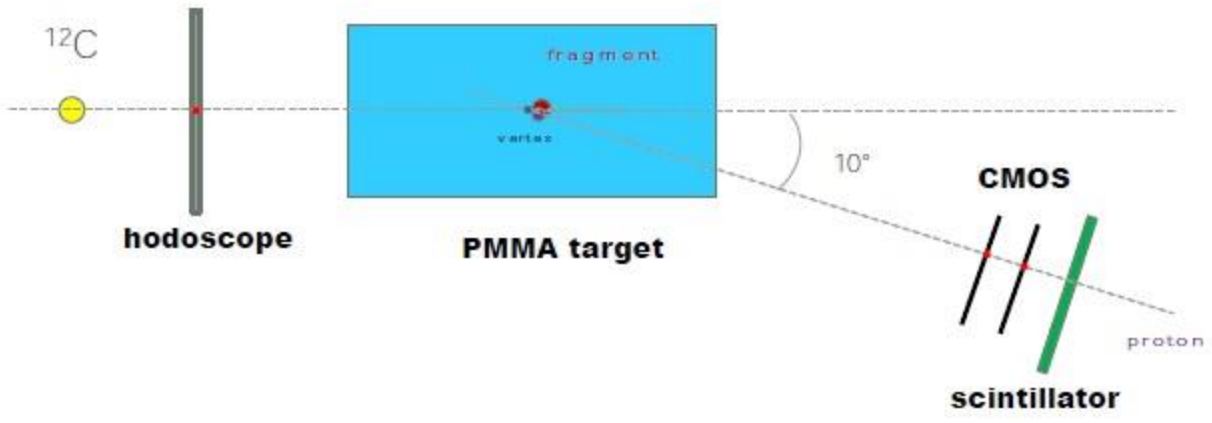


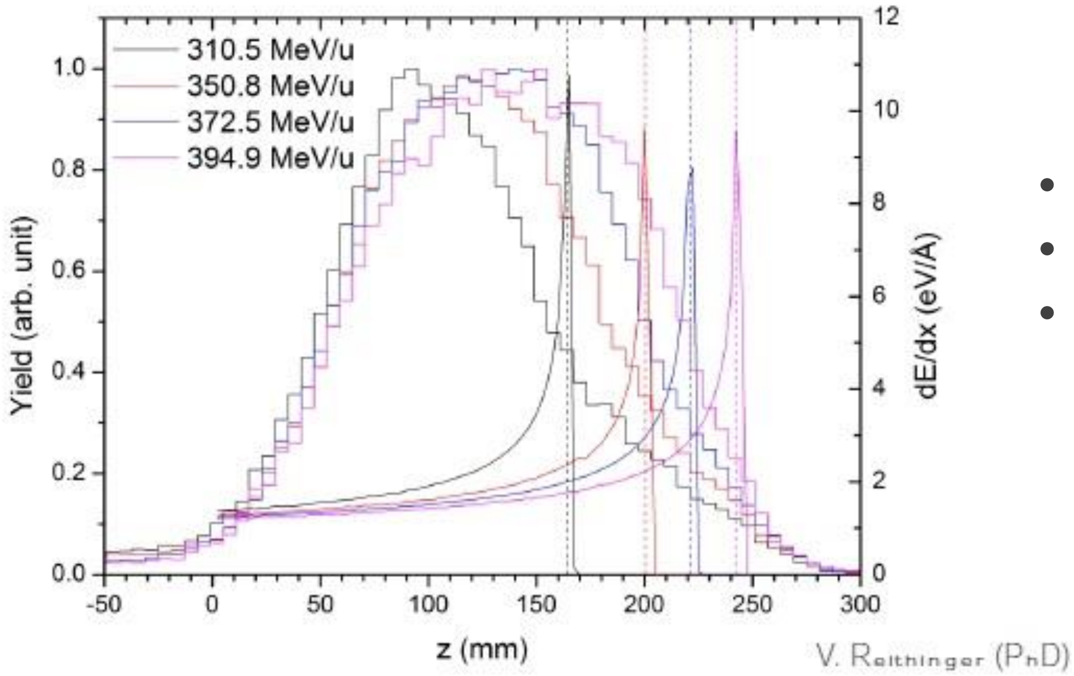
- Head-like phantom
- Tracking of secondary protons
- Variation of incident ion energy
- Fit of error-function: inflection point
- Correlation of IPP with ion range



[P. Henriquet et al. PMB 2012]

IVI: measurements





- CMOS detectors:
  MIMOSA 26 (IPHC Strasburg)

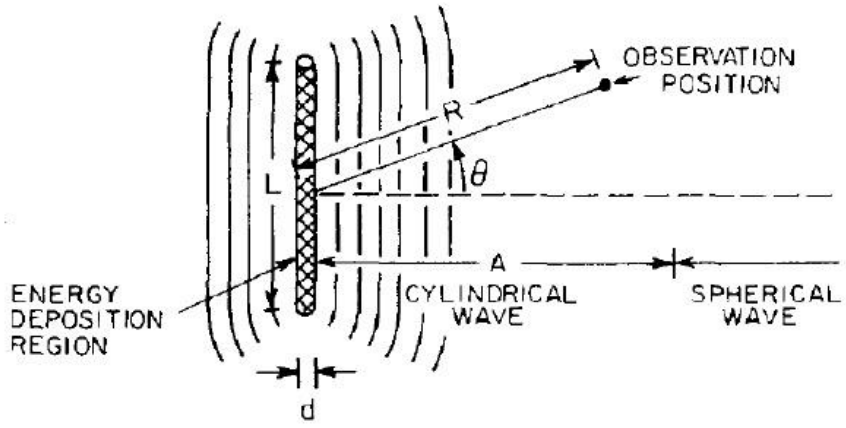
- Measurements at HIT
- Variation of carbon energy
- Vertex distributions

[V. Reithinger PTCOG 2013]

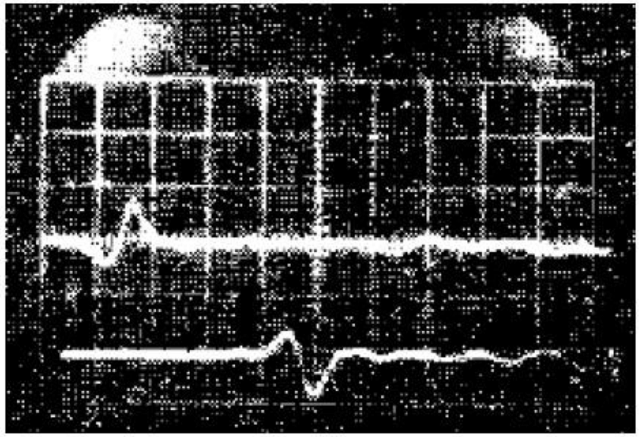
Ionoacoustics

Ionoacoustics: History

Ionoacoustic Characterization of the Bragg Peak (1979)



Acoustic radiation from idealized cylindrical energy deposition

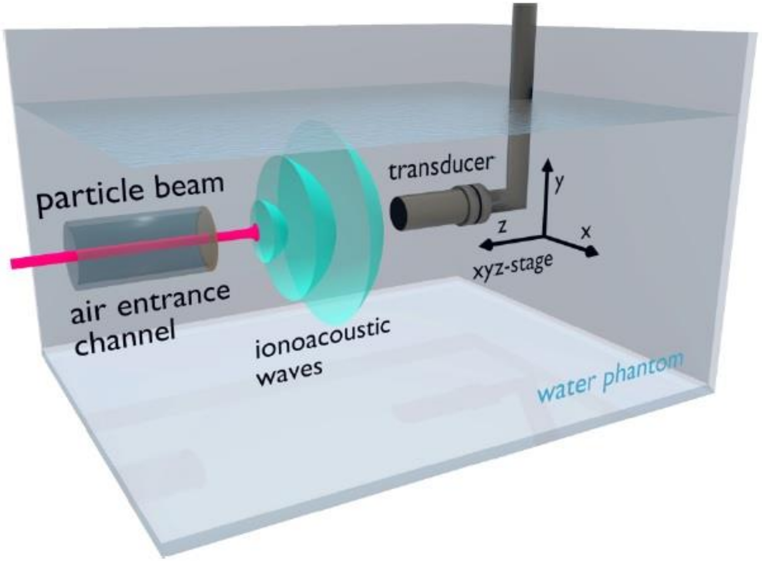


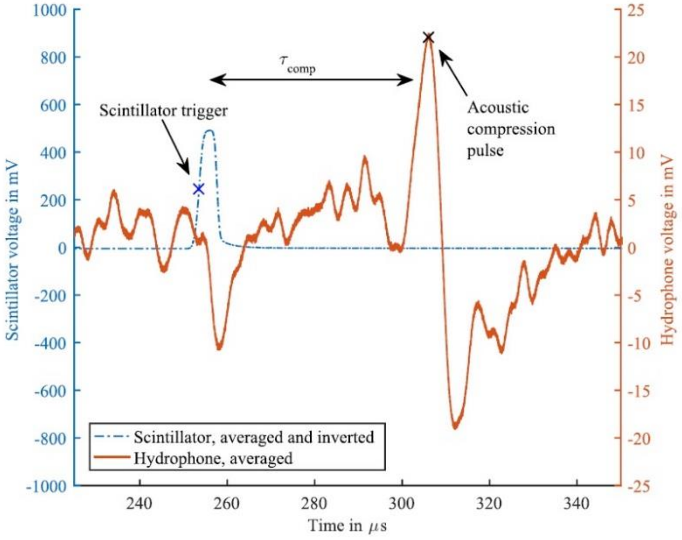
Typical signals from the hydrophones

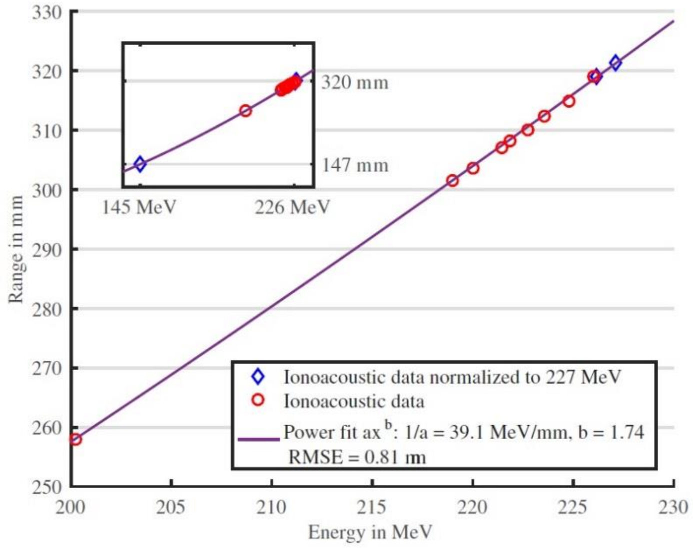
Sulak, L., et al. "Experimental studies of the acoustic signature of proton beams traversing fluid media." *Nuclear Instruments and Methods* 161.2 (1979): 203-217.

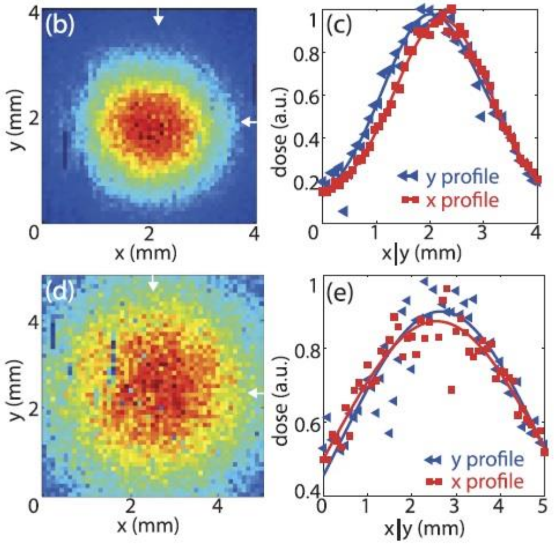
ELSEVIER

Ionoacoustics: Today









- Detection of ionoacoustic waves via transducer
- Range information via transit-time millimetric precision
- Well adapted to pulsed beam deliveries
- S2C2 1kHz rate, 8µs pulse width

[W. Assmann et al. PMB 2015]

[S. Lehrack et al. PMB 2017]

[S. Kellnberger et al. Nature SREP 2016]

Conclusions

- Status:
  - No commercial product for
    "Real-time In-Vivo Dosimetry and Range Measurements"
  - PET: clinically used, but not (yet) real-time
  - First clinical tests with prototypes for detection of secondary radiation
  - Focus on range verification, goal: reduction of safety margins
- Outlook:
  - Micro/nano-dosimetry (not covered in this presentation)
  - Methods based on detection of secondary radiation:
    - Integration in clinical workflow

Thank you very much for your attention !