



LUDWIG-  
MAXIMILIANS-  
UNIVERSITÄT  
MÜNCHEN



DEUTSCHES  
KREBSFORSCHUNGSZENTRUM  
IN DER HELMHOLTZ-GEMEINSCHAFT

# Range Verification Methods

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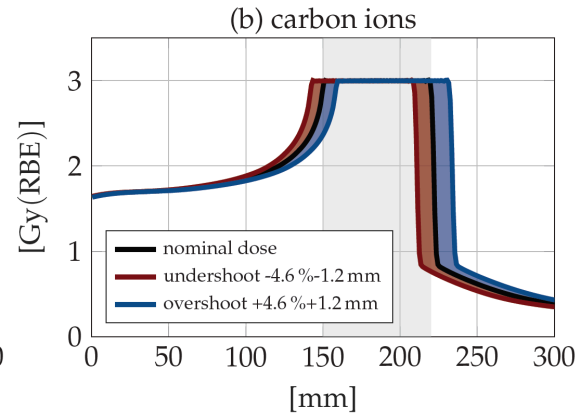
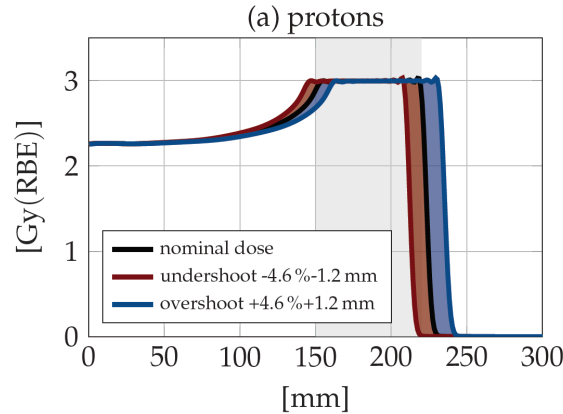
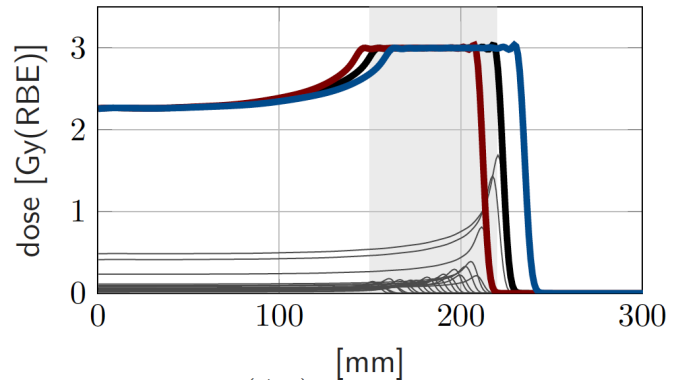
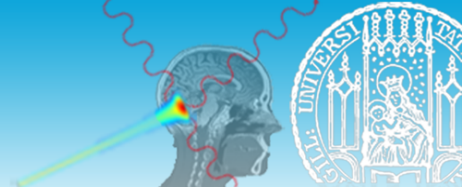
DR. HANS-PETER WIESER, LMU MUNICH

DR. NIKLAS WAHL, PROF. DR. JOAO SECO, DKFZ, HEIDELBERG



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

# Recap: Range Uncertainties



Motivation: Accurate knowledge of the exact stopping location of ions inside the patient would allow a full exploitation of their ballistic properties.

## In-vivo range or treatment verification in particle therapy

- Prompt Gamma imaging
- PET imaging
- Sonoacoustics
- Magnetic Resonance Imaging

'real time', in-beam (<ms)

delayed, in-beam and post-treatment (ms to min)

delayed, in-beam (<ms)

days to weeks

*Time matters !*

# Challenge and Impact



## Challenge

How to measure a signal from the Bragg peak during treatment

→ all primary protons stop inside the patient



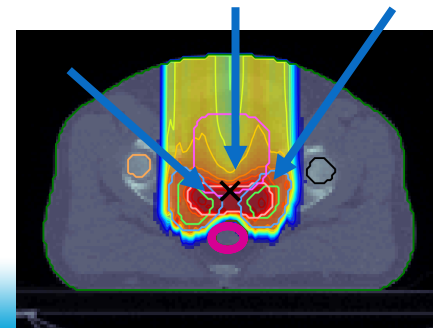
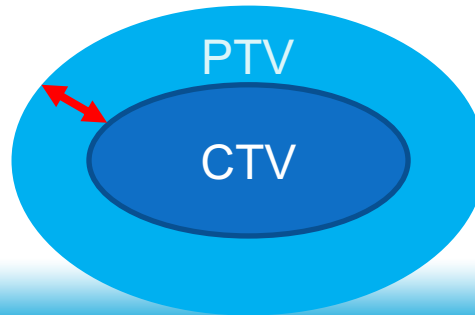
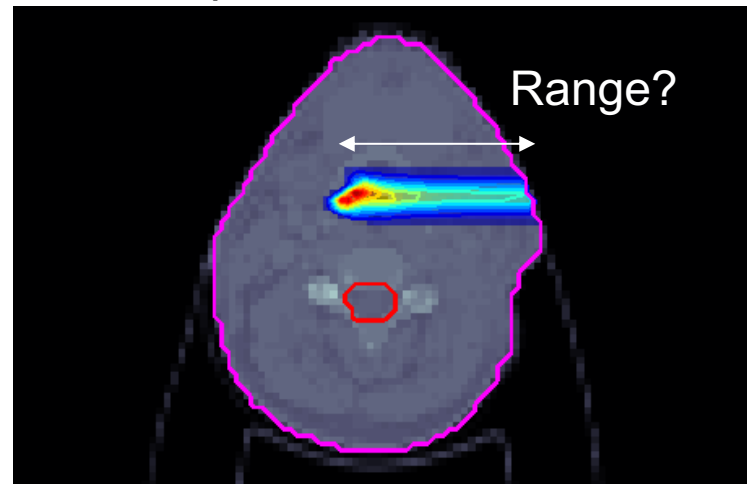
→ measure secondary signatures

→ correlate physiological changes

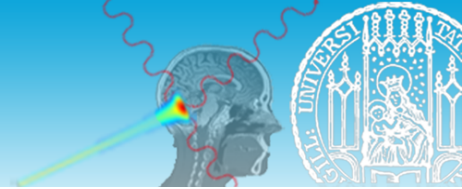
## Impact

- reduced planning margins
- new beam configuration
- adaptive treatment strategies
- improved treatment outcomes

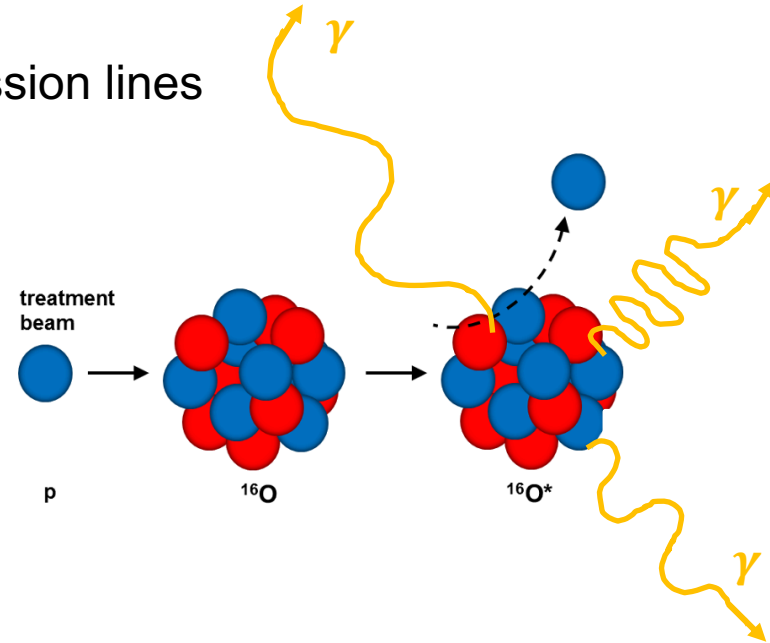
Proton pencil beam in the head



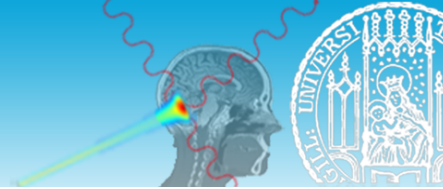
# Prompt Gamma Imaging



- energetic  $\gamma$  emission from excited target nuclei (C,O,N)
  - de-excitation  $< 1\text{ ns}$  of prompt  $\gamma$  after nuclear inelastic interaction
  - spectrum over several MeV,
  - exponentially decreasing with characteristic emission lines
  - can escape the patient, isotropic emission
- 
- spatial information (spatial location of emission is of interest - collimation system)
  - temporal information - exploit the TOF
  - exploit the photon energy  $\rightarrow$  spectroscopy



# Prompt Gamma Spectroscopy



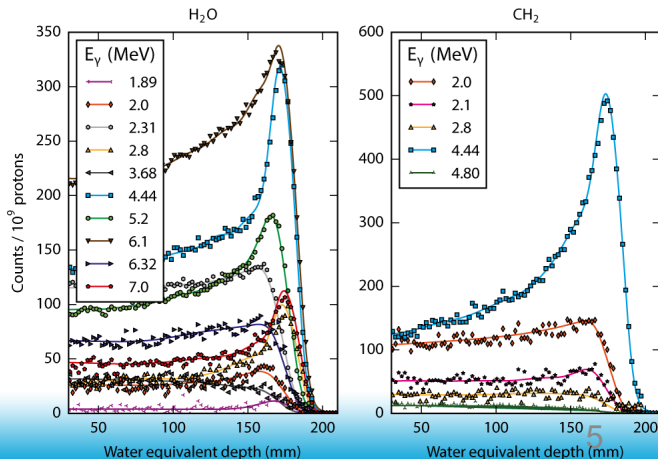
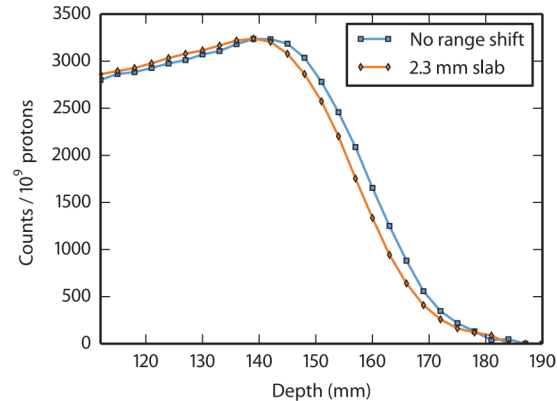
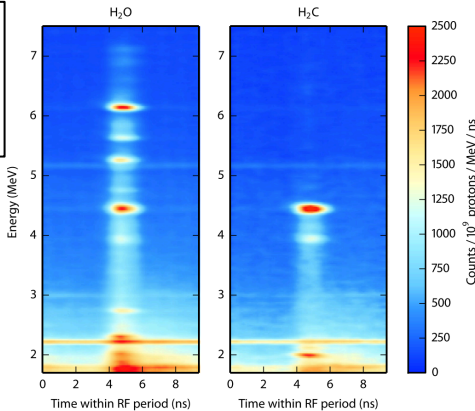
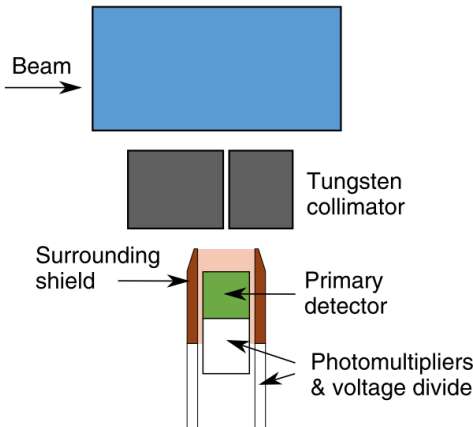
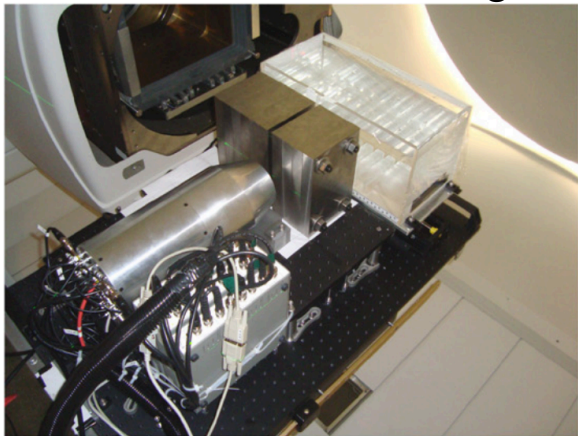
## Proton range verification through prompt gamma-ray spectroscopy

Joost M Verburg<sup>1,2</sup> and Joao Seco<sup>1</sup>

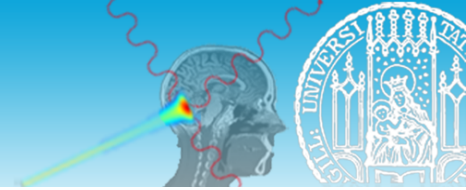
Water and  
polyethylene  
target

Measured discrete  
prompt gamma  
emissions

Reached clinical testing

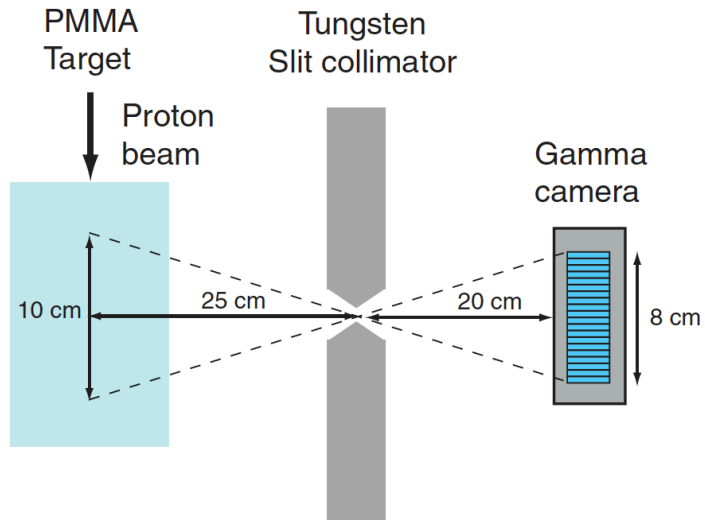


# Prompt Gamma Imaging



## Prompt gamma imaging of proton pencil beams at clinical dose rate

I Perali<sup>1,2</sup>, A Celani<sup>3</sup>, L Bombelli<sup>3</sup>, C Fiorini<sup>1,2</sup>, F Camera<sup>2,4</sup>,  
E Clementel<sup>5</sup>, S Henrotin<sup>6</sup>, G Janssens<sup>6</sup>, D Prieels<sup>6</sup>,  
F Roellinghoff<sup>6,7,8</sup>, J Smeets<sup>6</sup>, F Stichelbaut<sup>6</sup> and  
F Vander Stappen<sup>6</sup>



## 3D imaging capabilities

requires dedicated  
sensor developments

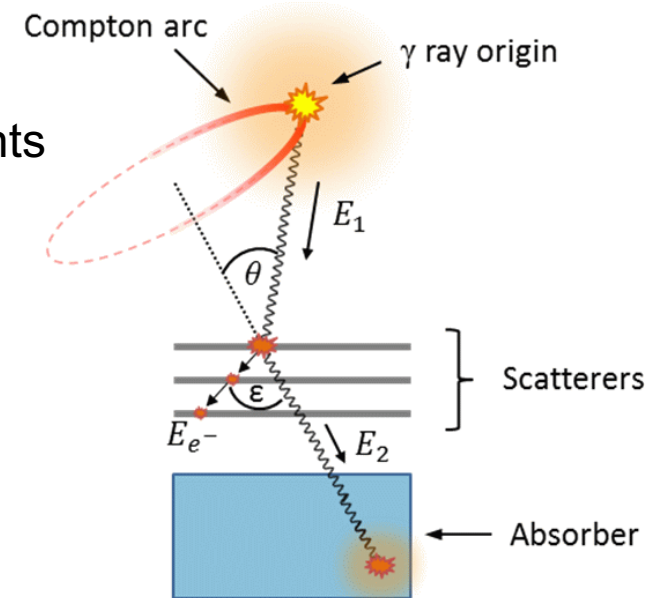
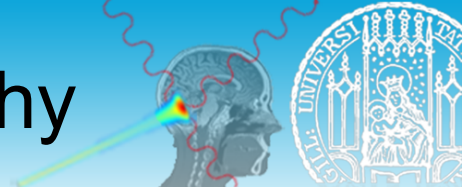
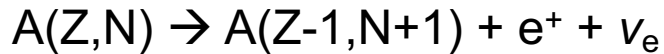


Figure adapted from  
<https://www.med.physik.uni-muenchen.de/research/range-verification/promptgamma/index.html> 6

# Positron Emission Tomography

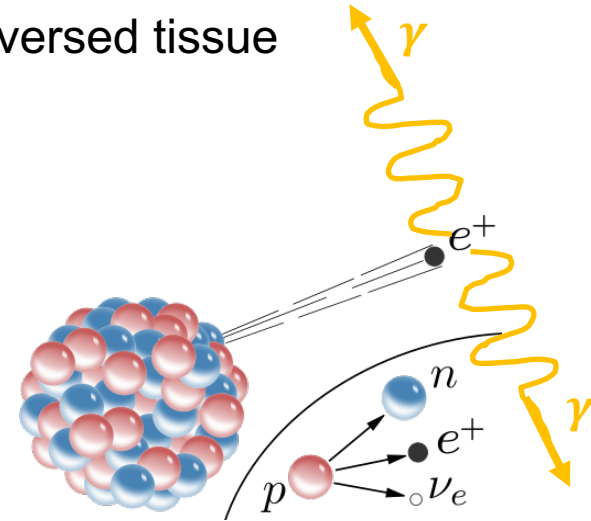


- Nuclear fragmentation reactions between ions and traversed tissue
- Radioactive  $\beta^+$  decay is induced from ion irradiation



Short lived positron emitting isotopes  $^{11}\text{C}$   $^{13}\text{N}$   $^{15}\text{O}$

Half life times **11ms** for  $^{12}\text{N}$  up to **20min** for  $^{11}\text{C}$ .



- Positron undergoes Coulomb interactions with atomic electrons until its annihilated into two photons at 511keV in opposite direction
- Detect two 511keV photons – that's the PET signal



# PET Imaging

Range verification of radioactive ion beams of  $^{11}\text{C}$  and  $^{15}\text{O}$  using in-beam PET imaging

Akram Mohammadi<sup>1,3</sup>, Hideaki Tashima<sup>1</sup>, Yuma Iwao<sup>1</sup>, Sodai Takyu<sup>1</sup>, Go Akamatsu<sup>1,6</sup>, Fumihiko Nishikido<sup>1</sup>, Eiji Yoshida<sup>1</sup>, Atsushi Kitagawa<sup>1</sup>, Katia Parodi<sup>2</sup> and Taiga Yamaya<sup>1</sup>

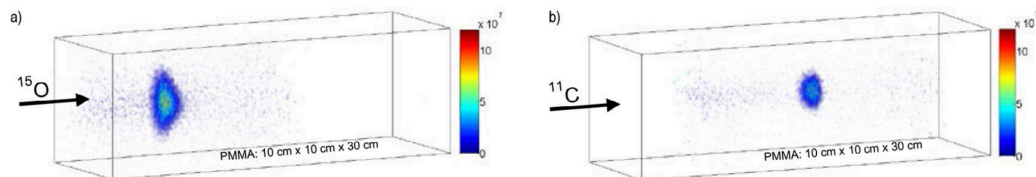
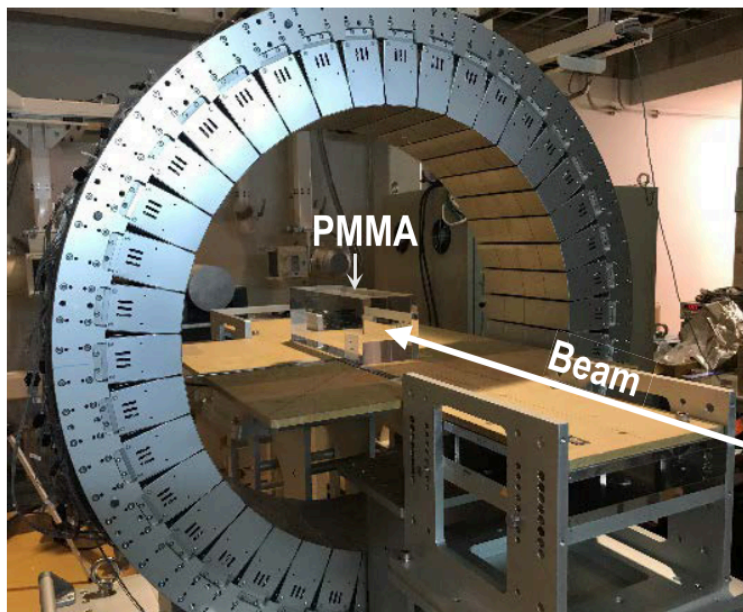


Figure 5. 3D reconstructed PET images of a PMMA phantom irradiated with the (a)  $^{15}\text{O}$  beam and (b)  $^{11}\text{C}$  beam.

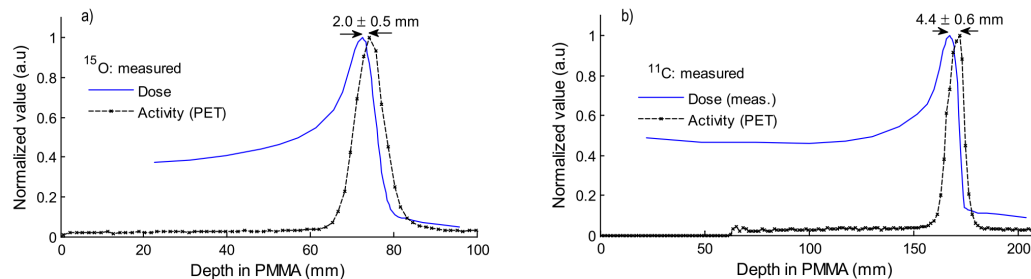
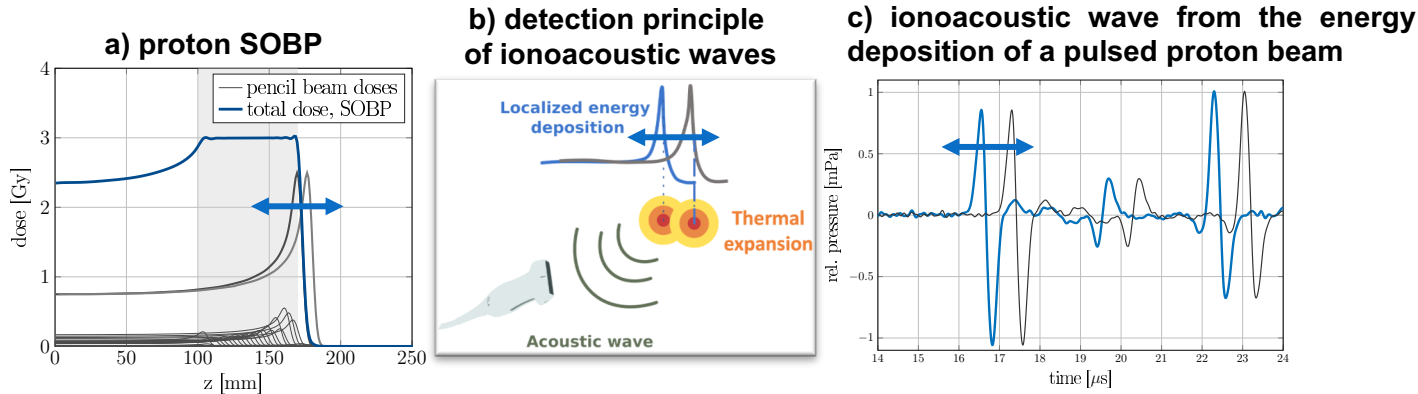


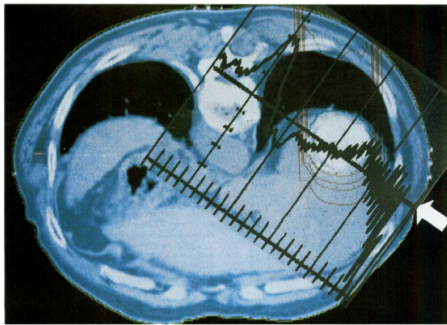
Figure 6. Comparison of the difference between the Bragg peak position and the PET peak position in mm for (a)  $^{15}\text{O}$  and (b)  $^{11}\text{C}$  ion beams. The results were obtained from the measurements.



# Ionoacoustics



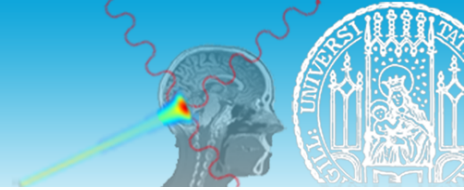
**1995, Hayakawa et al, Acoustic Pulse Generated in a Patient During Treatment by Pulsed Proton Radiation Beam**



*"These results suggest the feasibility of **non-invasive monitoring of proton dose distributions** in patients by sensing acoustic pulses generated during irradiation by a pulsed proton radiation beam."*

50 ns pulse width, hepatic cancer patient, **passively scattered beam**

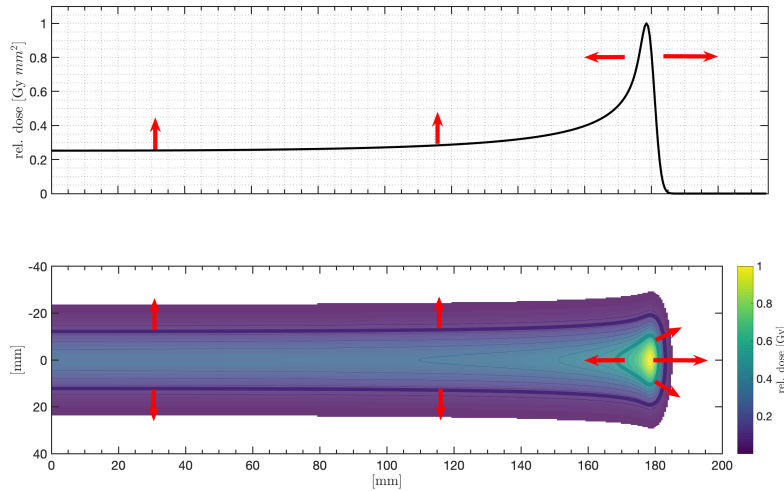
# Ionoacoustics



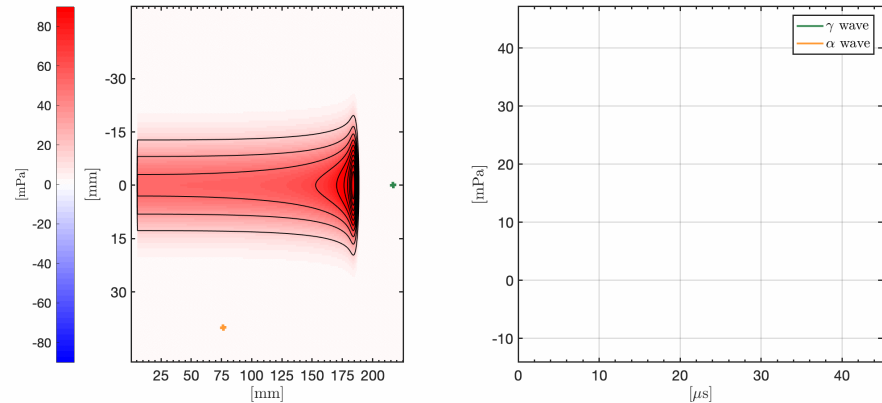
Stopping of ions  $\rightarrow$  local heating  $\rightarrow$  thermal expansion  $\rightarrow$  pressure wave

Cylindrical waves from the entrance

Spherical wave from the Bragg Peak

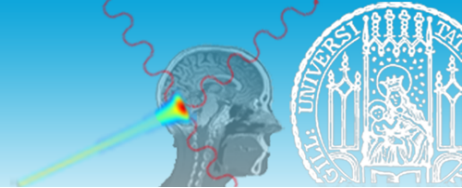


## Simulation of wave propagation



Pressure wave is weak and typically below 200kHz

# MR imaging



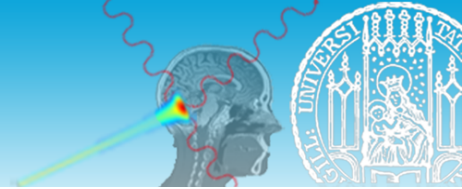
- MR offers good soft-tissue contrast
- detect physiological changes that correlate with beam range
- post-treatment verification using T1 weighted MRI scans
- In vivo proton range verification on spine could be demonstrated

Latest developments from Oncoray in Dresden:

**PARTICLE THERAPY | RESEARCH UPDATE**

Online MR imaging verifies proton beam range

# Conclusion



- Non-invasively measuring the proton range online and in-vivo is challenging
- Secondary signals are correlated with the Bragg peak location
  - prompt  $\gamma$
  - Position emission tomography (PET)
  - Ion-acoustic
- MR imaging might be an alternative solution

# Thank you !

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*This material was prepared and presented within the HITRIplus Heavy Ion Therapy MasterClass school,  
and it is intended for educational purposes to facilitate students;  
people interested to use any of the material for any other purposes  
(such as other lectures, courses etc.) are requested to please contact the authors  
Hans-Peter Wieser [h.wieser@lmu.de](mailto:h.wieser@lmu.de)*



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