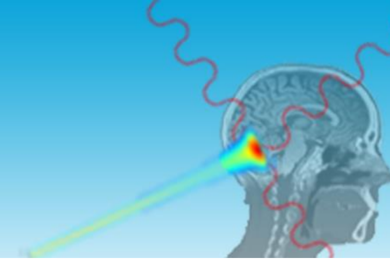
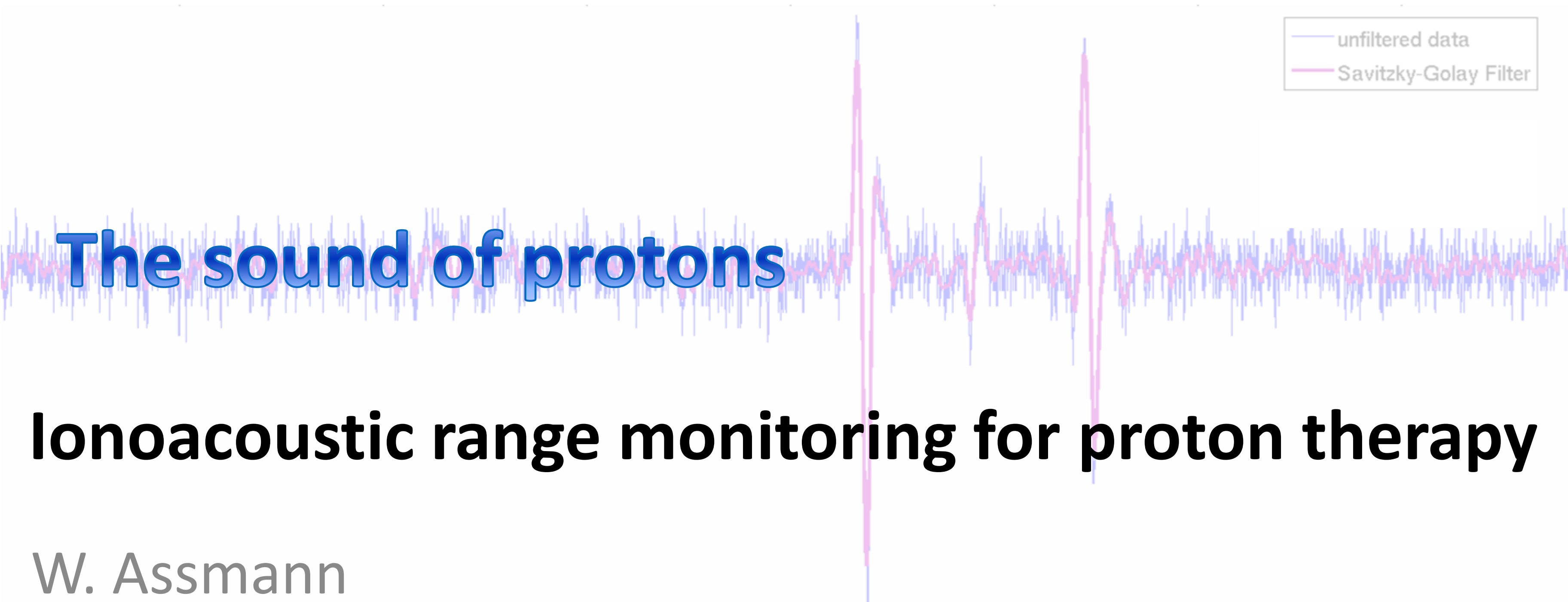




The sound of protons

Ionoacoustic range monitoring for proton therapy

W. Assmann

Faculty of Physics – Department for Medical Physics,

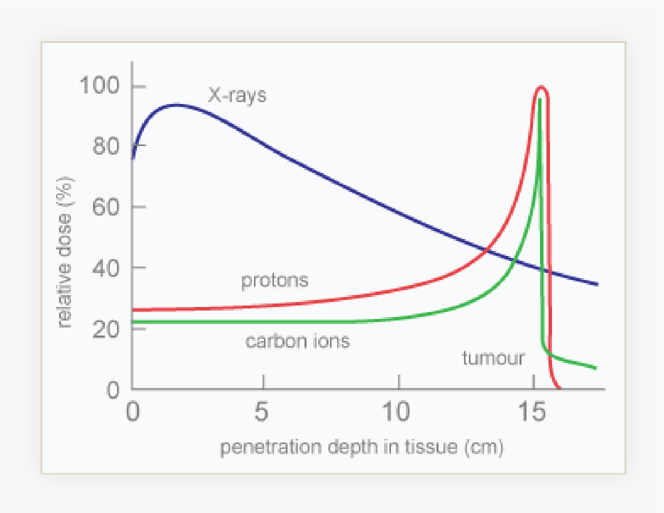
Ludwig-Maximilians-Universität München, Germany

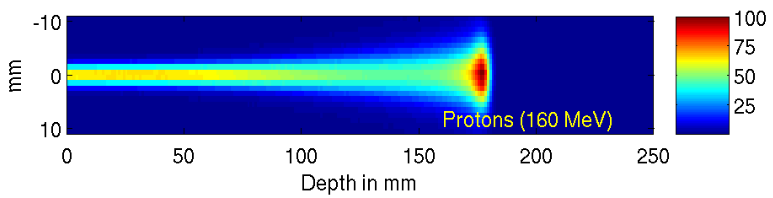
Overview

- Radiation therapy with ions: special features
- Range uncertainty: problem and present solutions
- New (old) approach: **Ionoacoustics** (thermoacoustics with ions)
- Experimental tests at 20 MeV
- Simulations with k-Wave
- First experiments around 200 MeV

Ion beam therapy

Dose distribution: photons vs. ions



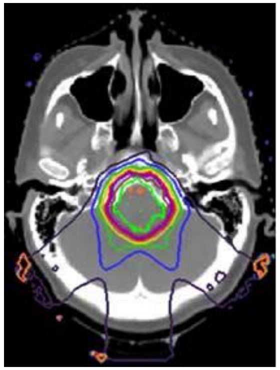


Advantages of particle therapy

- ***Finite range*** of ions
- ***Maximum*** dose deposition at end of range (***Bragg Peak, BP***)

→ highly conformal irradiation

- ***Minimum*** dose in healty tissue



Skull base tumor

Wilson, R.R., "Radiological use of fast protons", Radiology **47**, 487-91 (1946)

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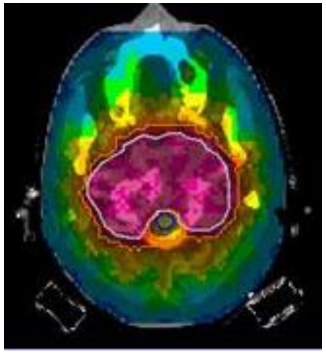
Photon vs Proton

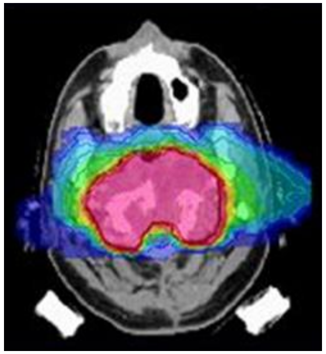
Dose delivery

photons



+ *conformal* dose distribution
  (with advanced IMRT techniques)
+ *less sensitive* to range uncertainty
- *dose bath* of healthy tissue
- *limitation* of tumor dose

protons



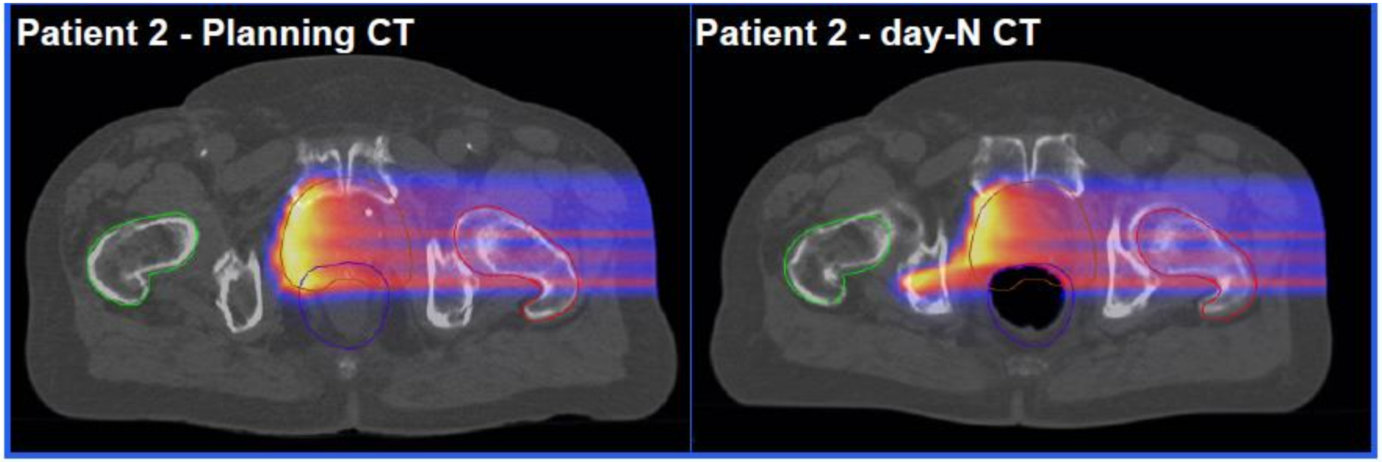
+ *maximal* dose in tumor
+ *minimal* dose in healthy tissue
- *expensive* technology
- *very sensitive* to

range uncertainty

Range uncertainty

Reasons: Calibration errors CT/HU to ion stopping power, CT artefacts, patient and tumor movement, **anatomical changes**, positioning error, …

Example: Prostate tumor - planning CT vs. situation on irradiation day-N



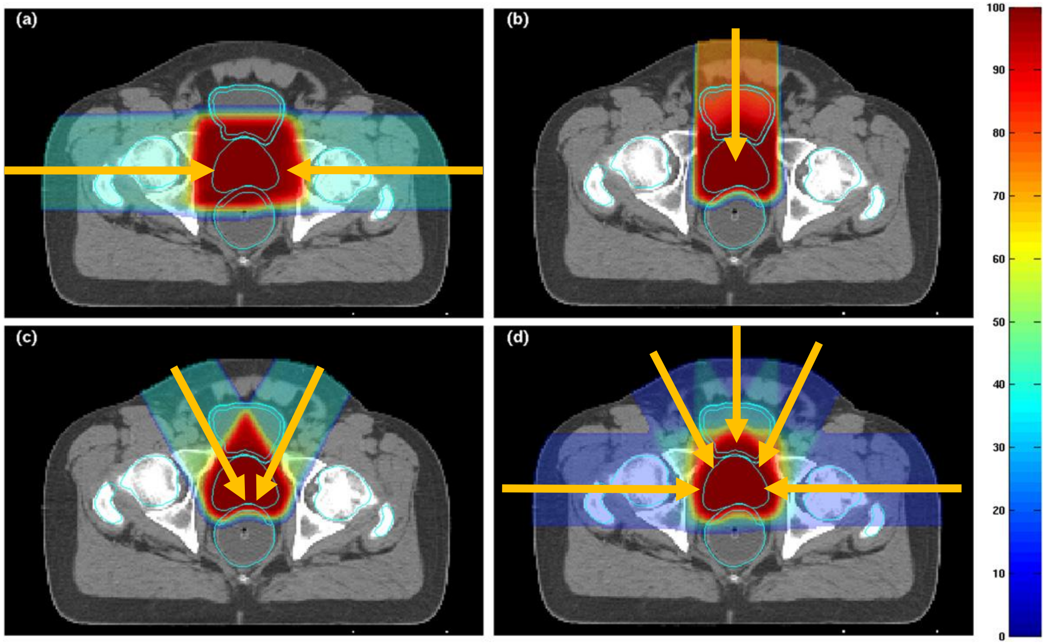
→ ***in-vivo* range verification** with ≈1 mm resolution

Range uncertainty

Example: *Prostate tumor*

at present

(a) **suboptimal lateral** dose delivery with larger dose deposition in healthy tissue (femoral heads, hip replacements!)



S. Tang et al., Int J Rad Oncol Biol Phys, 83(1), 408 (2012)

in the future

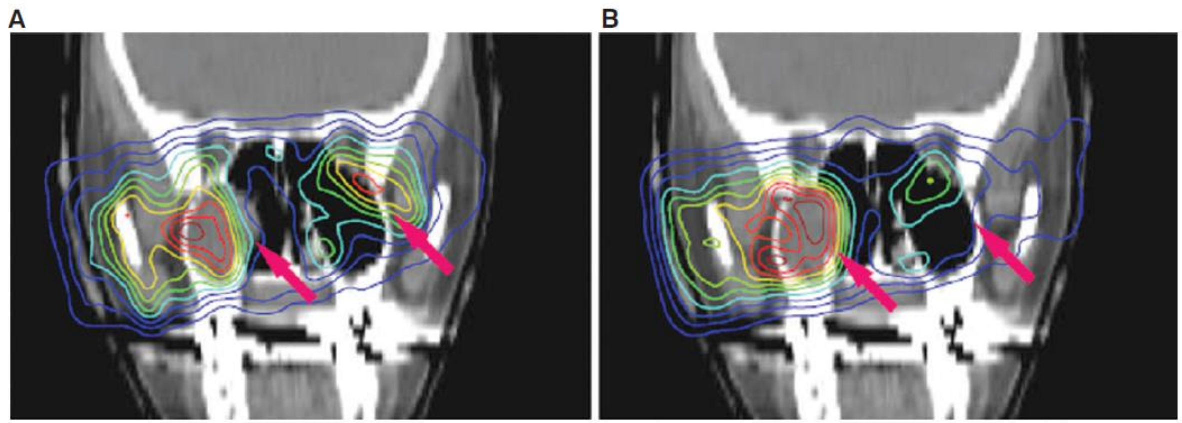
(b-c) **optimal anterior** dose delivery sparing best healthy tissue and organs-at-risk, but needs ***in-vivo* range verification** with ≤ 1 mm resolution

Range verification

Presently under development: **Nuclear Imaging Techniques**

- online PET (Positron Emission Tomography) ⟶ GSI, HIT
- Prompt gamma imaging (Compton camera) ⟶ IBA

Example:
offline
PET imaging



measurement   simulation

K. Parodi, PhD thesis, 2004

Problem:

both methods complex and indirect methods, costly and bulky equipment, 1 millimeter resolution??

Ionoacoustic effect

Stopping of ions causes **local heating** and **pressure wave**:

$$\frac{dV}{V} = -\kappa dp + \beta dT$$

$$p = \frac{\beta}{\kappa \rho C_V} D \quad *$$

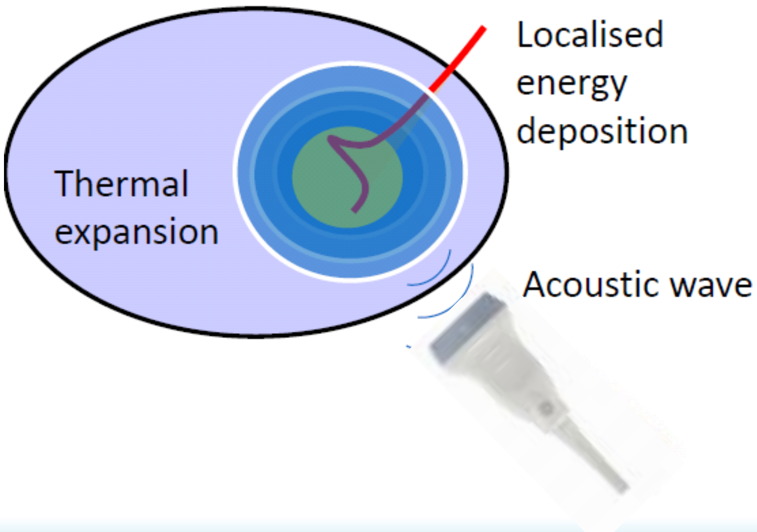
κ isothermal compression
β volume expansion coefficient
D deposited ion dose
* in thermal and stress confinement

thermal confinement:

$t_{\textit{ion pulse}} < t_{\textit{therm diffusion}}$ (here > 100 µs)

stress confinement:

$t_{\textit{ion pulse}} < t_{\textit{stress propagation}}$ (v_s ~ 1.5 mm/µs)



Ionoacoustics

General thermoacoustic equation for acoustic wave propogation :

$$\left(\nabla^2 - \frac{1}{v^2}\frac{\partial^2}{\partial t^2}\right)p(\vec{r},t) = -\frac{\beta}{\kappa {v_s}^2}\frac{\partial^2 T(\vec{r},t)}{\partial t^2}$$

in thermal confinement:

$$\rho C_v \frac{\partial T(\vec{r},t)}{\partial t} = H(\vec{r},t) \qquad \left(\nabla^2 - \frac{1}{v^2}\frac{\partial^2}{\partial t^2}\right)p(\vec{r},t) = -\frac{\beta}{C_p}\frac{\partial H(\vec{r},t)}{\partial t}$$

„Heating function“ $H(\vec{r},t) = H_s(\vec{r}) \cdot H_t(t)$ space/time uncoupled

$H_s(\vec{r})$ → Bragg curve

$H_t(t)$ → temporal pulse width

But: **1 Gy dose** → **0.25 mK ΔT** → **2 mbar Δp**

very weak effect! usable?

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New approach but old idea ...

EXPERIMENTAL STUDIES OF THE ACOUSTIC SIGNATURE OF PROTON BEAMS TRAVERSING FLUID MEDIA*

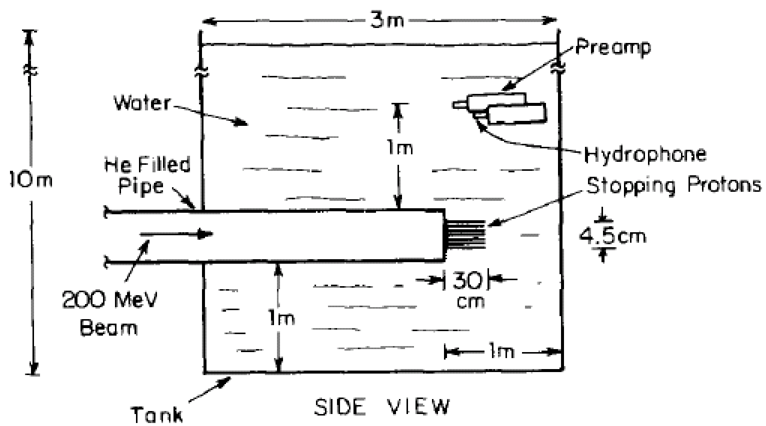
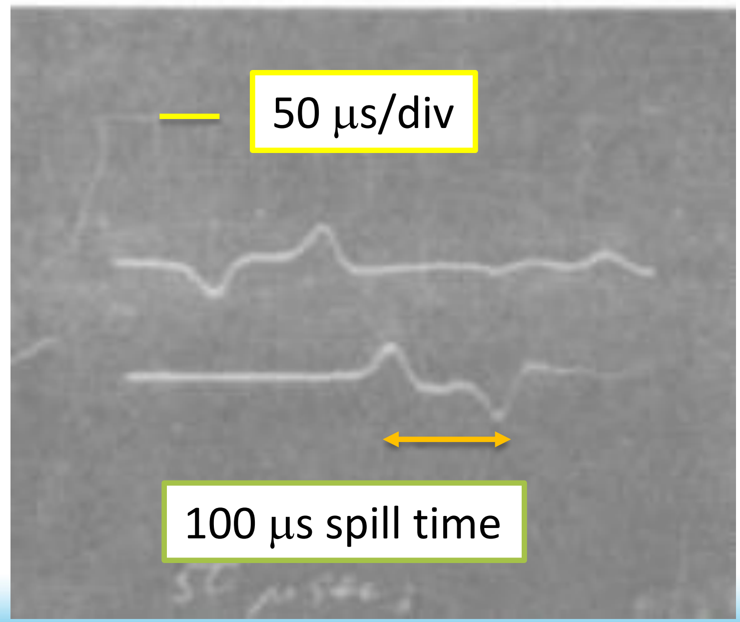


Fig. 3. Detector arrangement for the linac experiment.

Sulak et al, NIM 161 (1979), 203-217
see also:
G.A. Askariyan et al, NIM 164 (1979), 267-278

6. Conclusions

We have demonstrated that an observable acoustic signal is produced in a single transducer by charged particle depositions $\gtrsim 10^{14}$ eV in fluid media. The source of the signal is dominantly thermal expansion. Applications to beam monitoring, heavy ion experiments, high energy physics and cosmic ray physics are foreseeable.



New approach but old idea …

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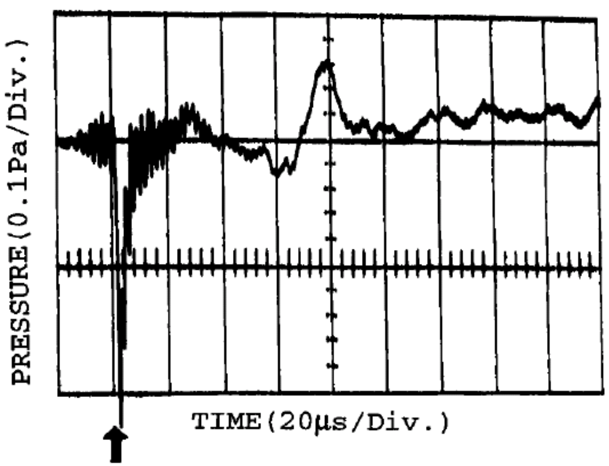
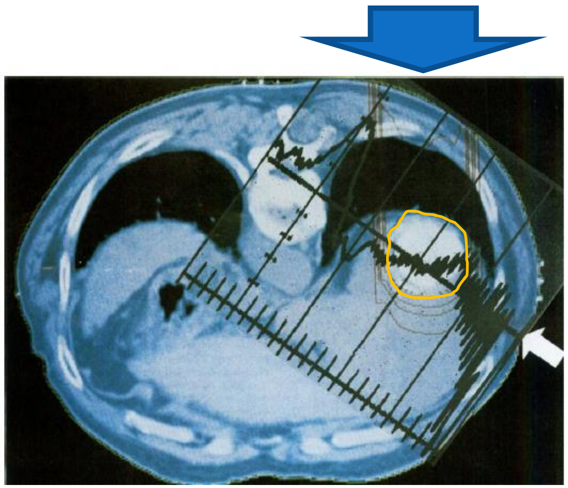
Acoustic Pulse Generated in a Patient During Treatment by Pulsed Proton Radiation Beam

Y. Hayakawa et al, Rad. Onc. Invest., 3, (1995), 42-45



proton beam



Hydrophone

Hepatic cancer treatment

(weak) US signal detected, but no progress since then…

New approach but old idea ...

3Cc3

WORLD CONGRESS ON ULTRASONICS
24-27 AUGUST 1997, YOKOHAMA

ACOUSTIC DETECTION OF THERAPEUTICAL RADIATION FOR MODERN CANCER THERAPY WITH HEAVY IONS

Alexander Peiffer[1,2] and Bernd Köhler[2],
[1] Gesellschaft für Schwerionenforschung (GSI), Darmstadt, Germany
[2] Fraunhofer-Insitute for Non-Destructive Testing, Branch Lab Dresden (EADQ)
E-mail: peiffer@eadq.izfp.fhg.de, koehler@eadq.izfp.fhg.de

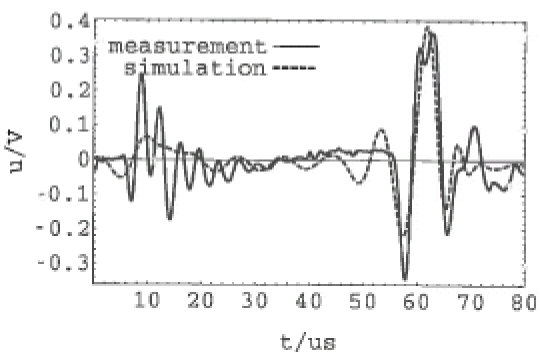


Figure 3: Simulation and measurement.

Conclusions

The possibility of measuring the beam intensity and spatial distribution of the beam track is shown for pulsed radiation. During the therapy at the GSI in Darmstadt the slow extraction mode of the SIS is used, with nearly continuous radiation intensity. Thus, the applicability of this method for on-line measurements during therapy depends on the possibility of beam modulation. If necessary modifications of the accelerator facilities are practicable, successful detection of acoustic signals during therapy is possible. Further investigations shall deal with the design of low-noise amplifiers and sensor array systems.

Time for new attempt?

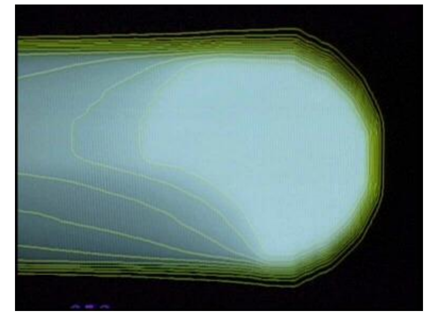
Previous irradiation technique "passive scattering"

irradiation of ***whole tumor volume*** at once

→ ***diffuse*** local dose deposition

→ ***small*** ionoacoustic signal amplitude

→ ***complex*** range information



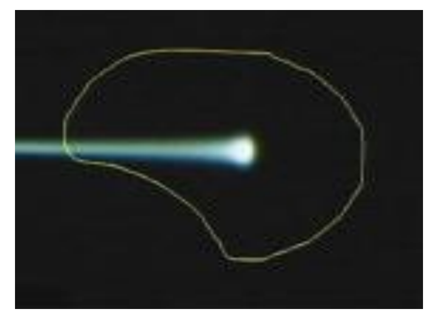
Advanced irradiation technique "active scanning"

irradiation of ***tumor volume*** by single beam spots

→ highly ***localized*** dose deposition

→ ***enhanced*** ionoacoustic signal amplitude

→ ***direct*** range information



Additionally: synchro-cyclotrons now available with ***higher*** **pulse intensity**

Test experiment

Range verification with sub-mm spatial resolution?

W. Assmann et al., Med.Phys. 42, 567 (2015)

MLL Tandem accelerator (Garching):

protons, 20 MeV

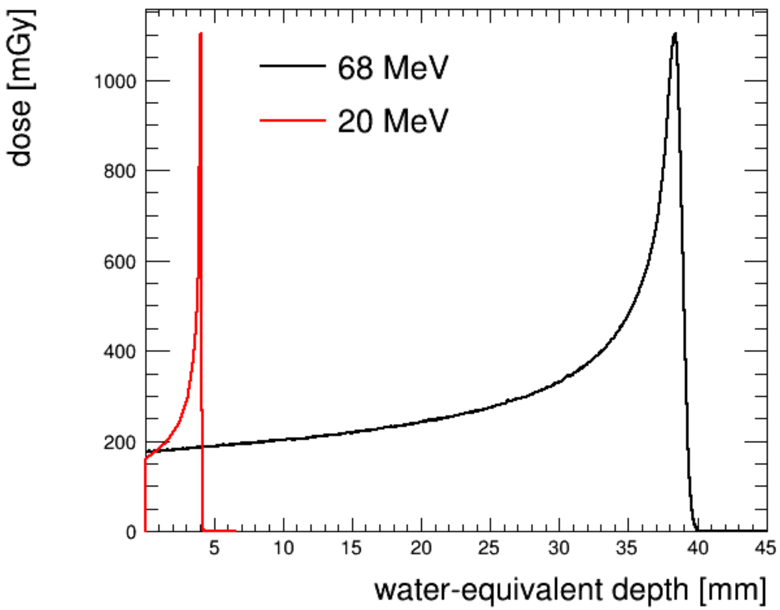
≈ 4 mm range in water

→ sharp BP (≈ 300 μm FWHM)

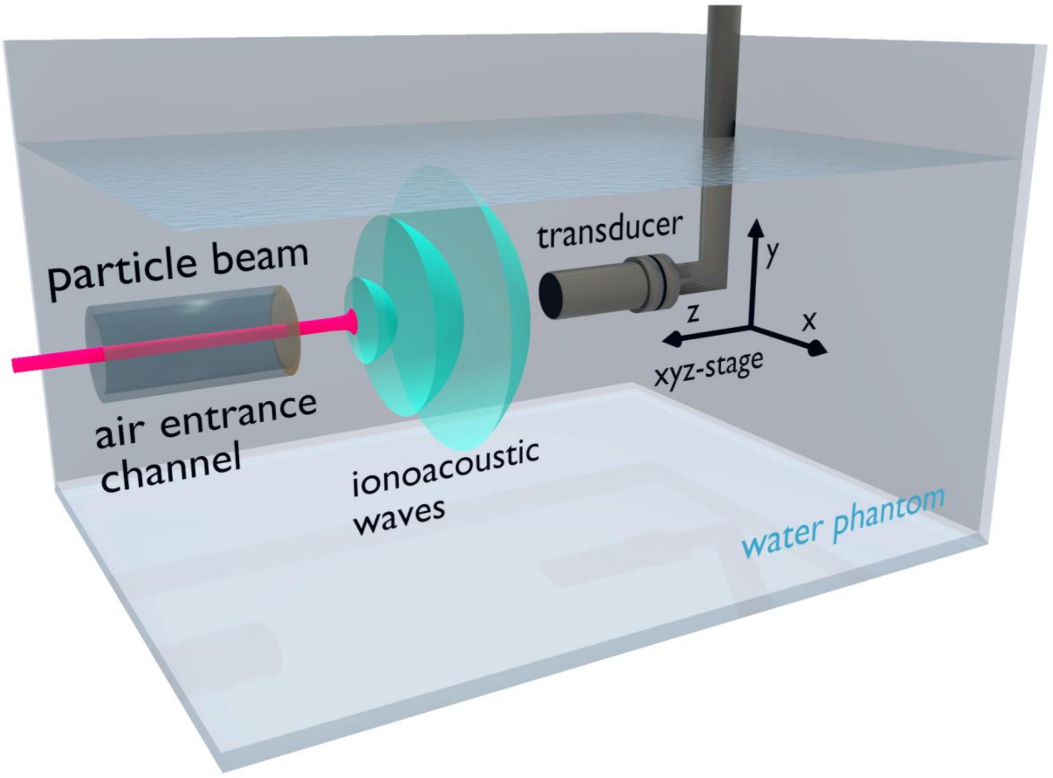
→ Pulse rise time: 3 ns
Pulse width variation: 1 ns – 1 ms
Pulse rate variation: 1 kHz - 2.5 MHz

→ ideal conditions for
ionoacoustic test experiment

MC– Simulation (Geant4)



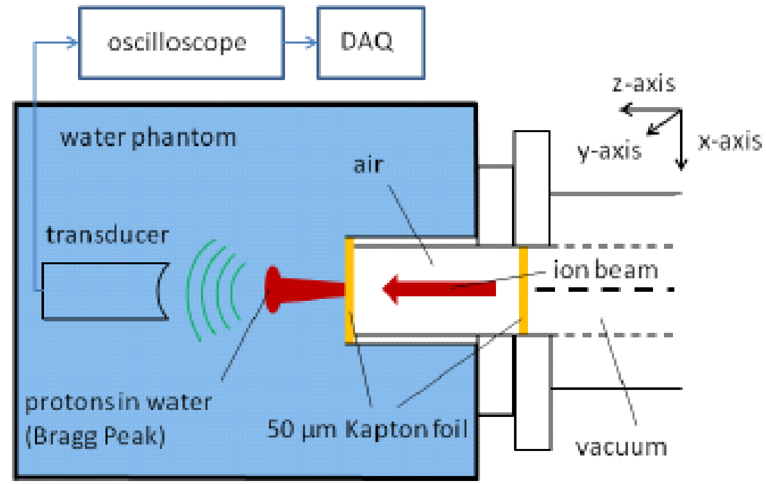
The setup

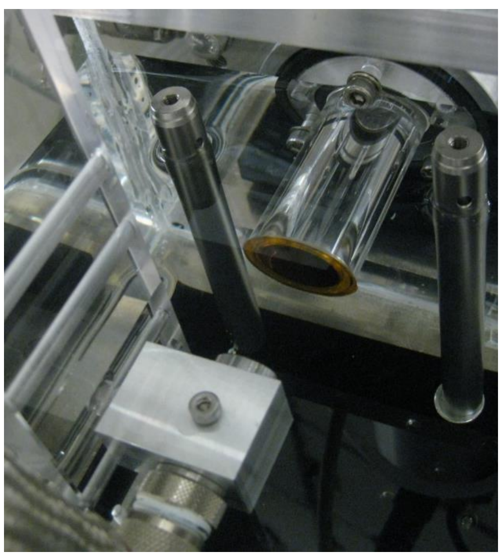

particle beam
air entrance channel
ionoacoustic waves
transducer
y
z
x
xyz-stage
water phantom

Test experiment

Experimental setup:

- Water phantom
- PZT detector, 1 – 10 MHz
  remotely controlled (scan)
- US detector array (tomography)





Model	focus	f_c [MHz]	US resolution [µm]
V-303*	spherical	1	1000
V-382*	planar	3.5	300
V-311*	spherical	10	100
array	cylindrical	5	220

* immersion transducers (Videoscan) Olympus

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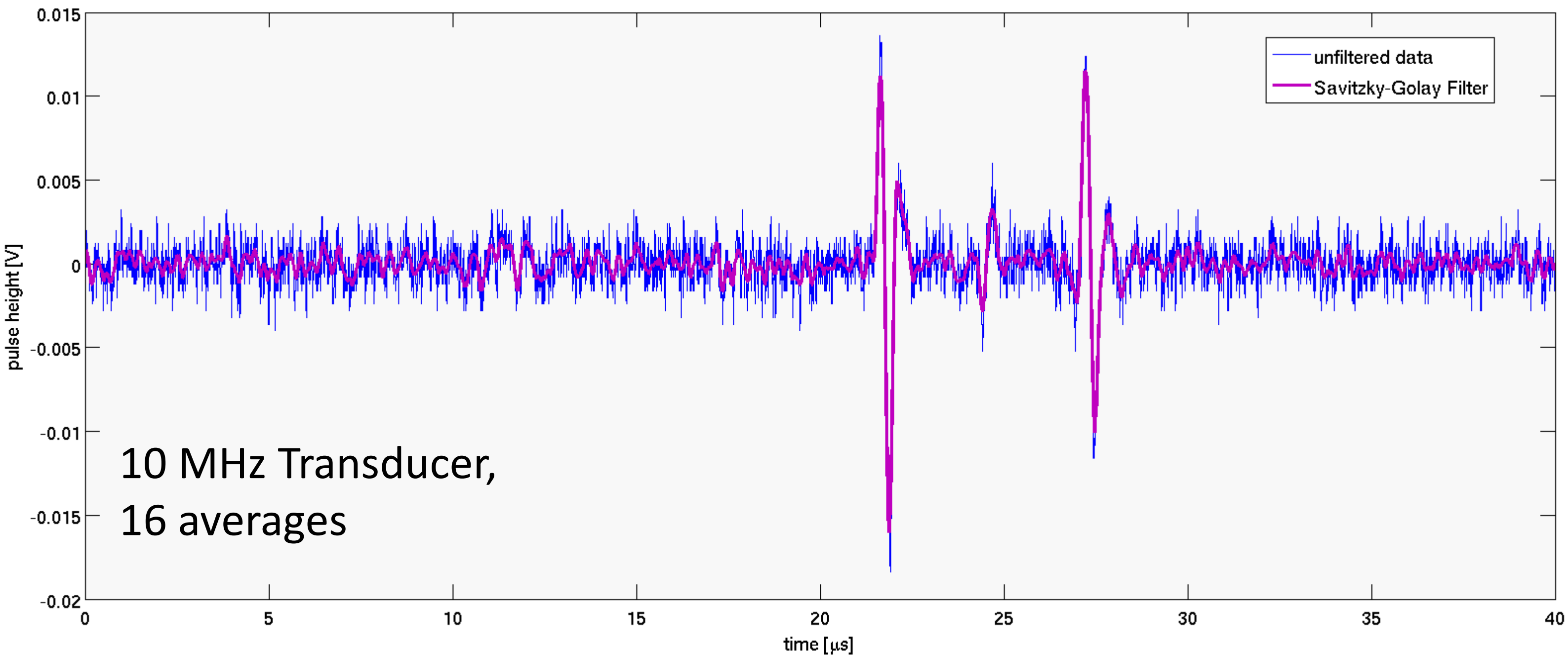
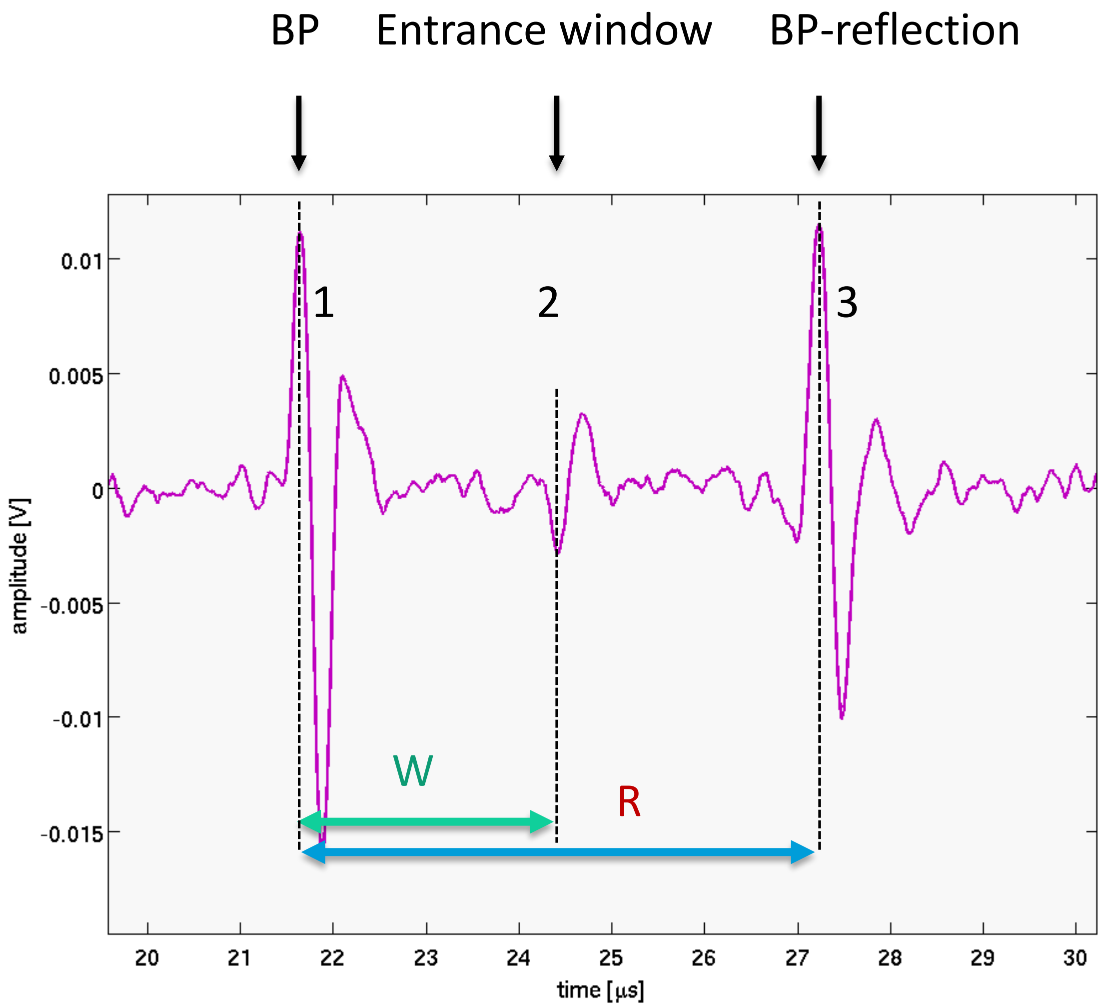
The sound of protons

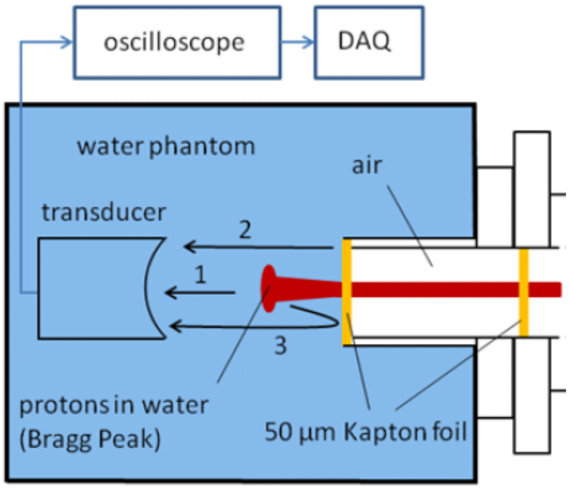


20 MeV protons, 280 ns pulse width, 63 dB amplifier

$2 \cdot 10^6$ p per pulse → $4 \cdot 10^{13}$ eV total energy deposition (ca 2 Gy)

Ionoacoustic signal

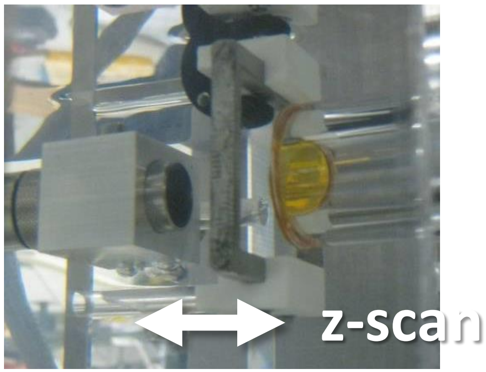




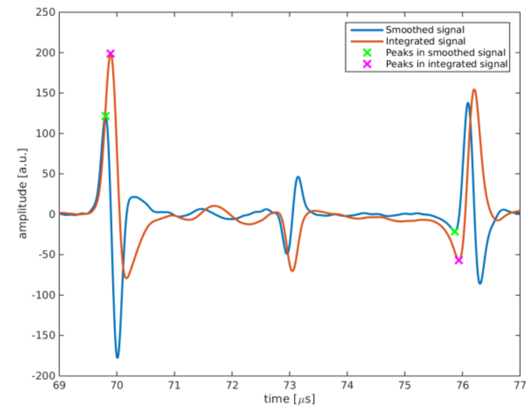
1 Bragg Peak (BP)
2 Entrance window (W)
3 Reflection (R)

Speed of sound:
1520 m/s (H_2O, 35 ^oC)
or **1.52 mm/µs**

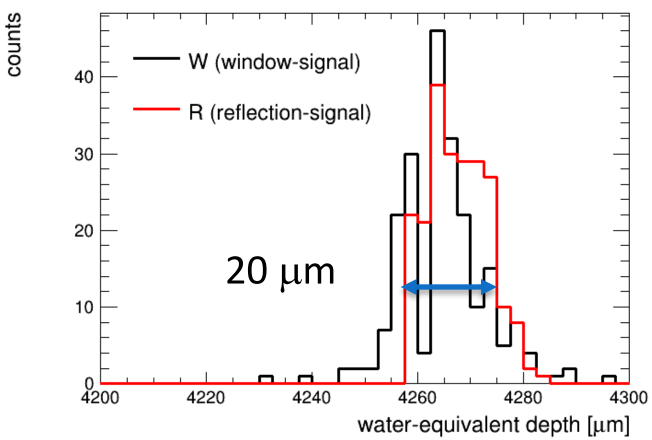
Reproducibility & resolution



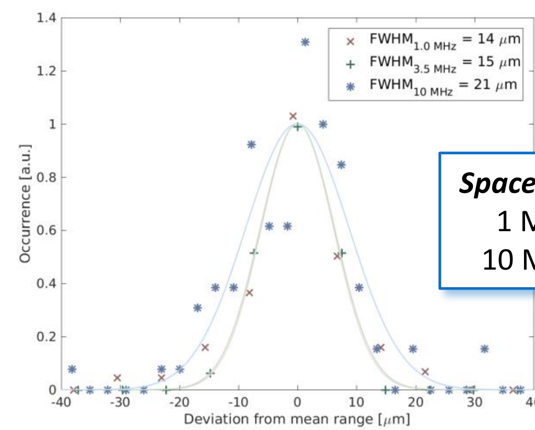
Repetition in 200 um steps



Signal integration



Reproducibility of BP position (10 MHz)



Space resolution in US:
1 MHz: 1.0 mm
10 MHz: 0.10 mm

Frequency dependence

Bragg peak position

Vacuum window	Kapton	Titanium	Titanium
Proton energy [MeV]	**20**	**20**	**21**
Geant4 simulation [μm]	4040 +- 30	4070 +- 30	4450 +- 30
Experiment [μm] Bragg peak – foil Bragg peak – reflection	 3990 +- 40 4020 +- 20	 4090 +- 40 4060 +- 20	 4490 +- 40 4460 +- 20
Difference simulation – exp [μm]	**-50** **-20**	**+20** **-10**	**+40** **+10**

Uncertainty of Geant4 simulation: beam path geometry
mean excitation energy

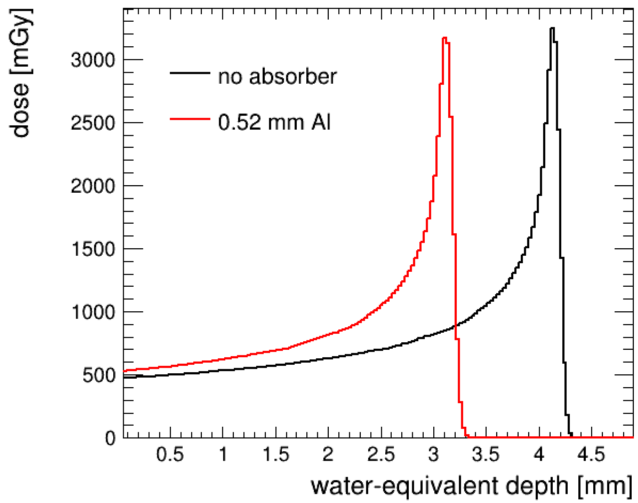
Range shift accuracy

	Range
no absorber	
Geant4 [μm]	4060
Measurement [μm]	4040 +- 30
0.52 mm Al	
Geant4 [μm]	3000
Measurement [μm]	3020 +- 30

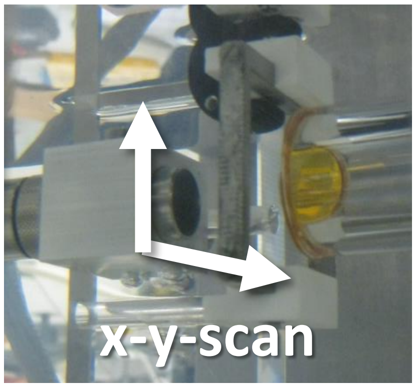
Range shift with Al absorber:

Δ_{Geant4}: 1060 μm

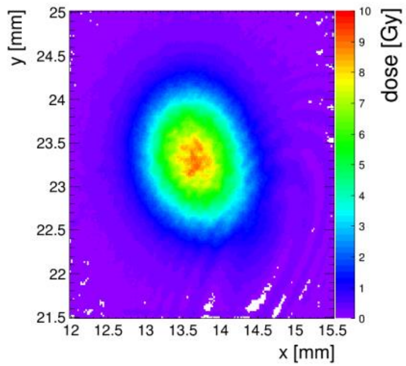
Δ_{meas}: 1020 μm



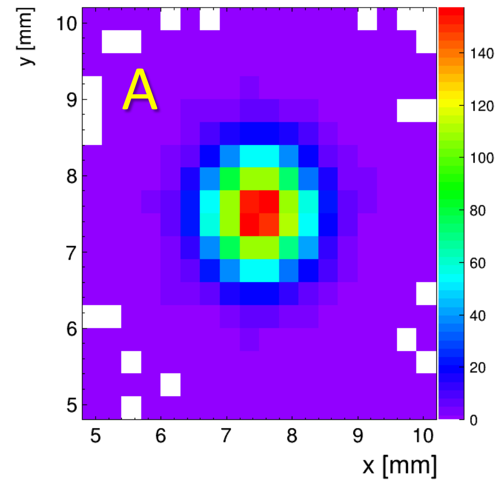
2D Bragg peak image

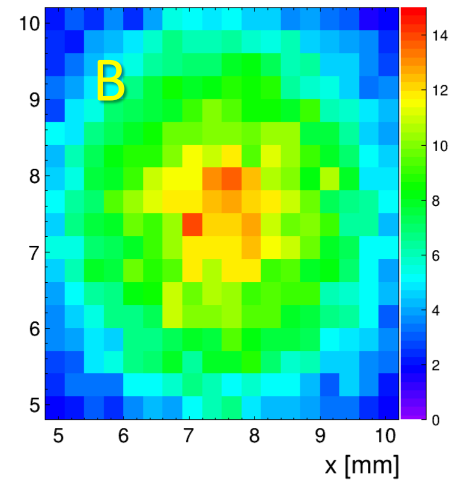


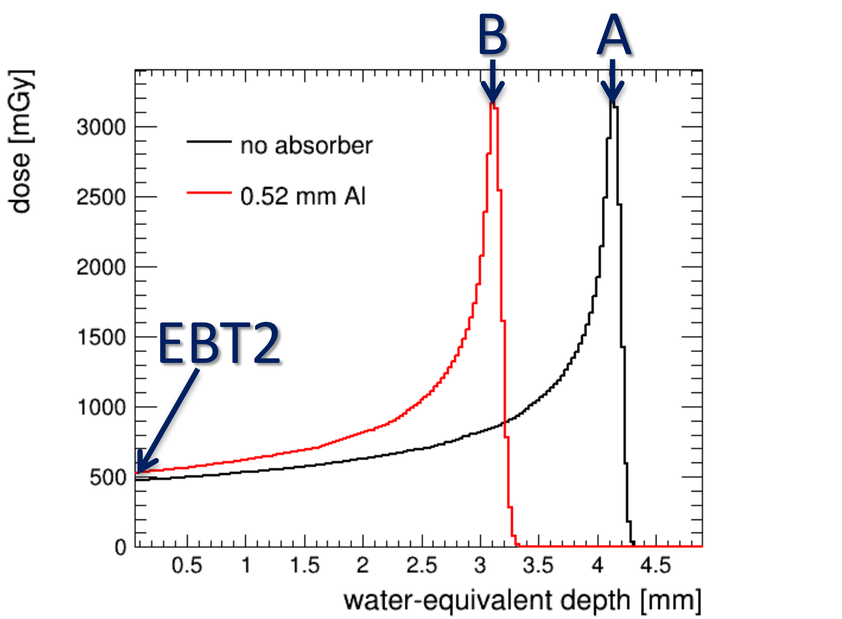
EBT2 film



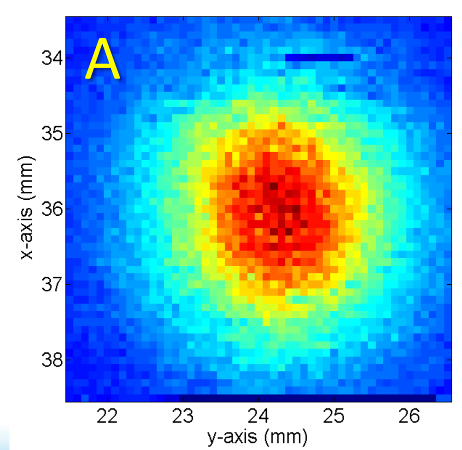
MC-simulation, *Geant4*



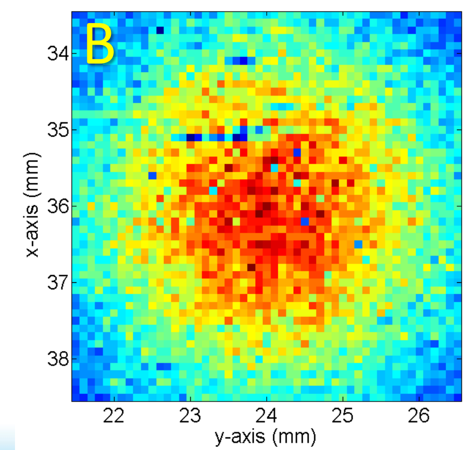




Measurement, 10 MHz Transducer



no absorber

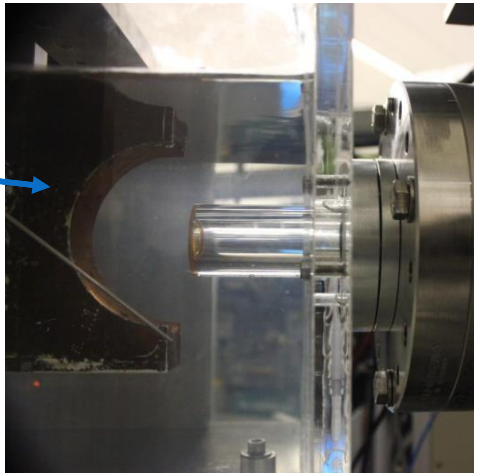


Al absorber

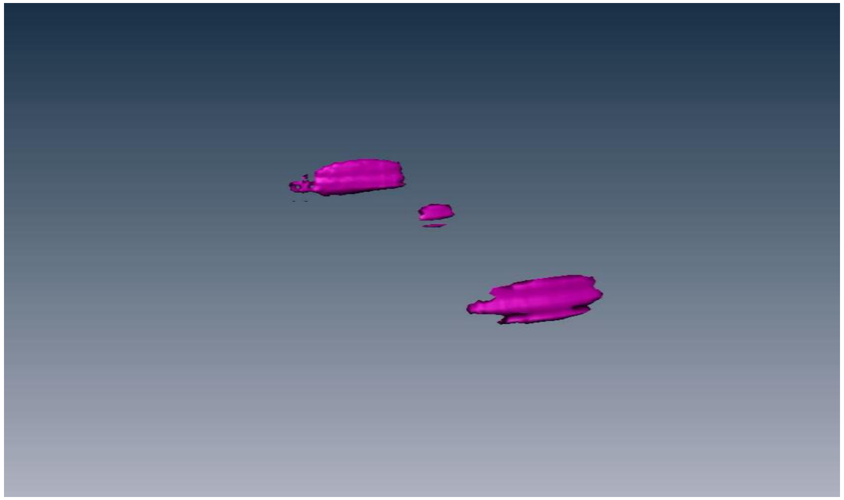
Tomography

Real-time tomography with

64-channel transducer-array



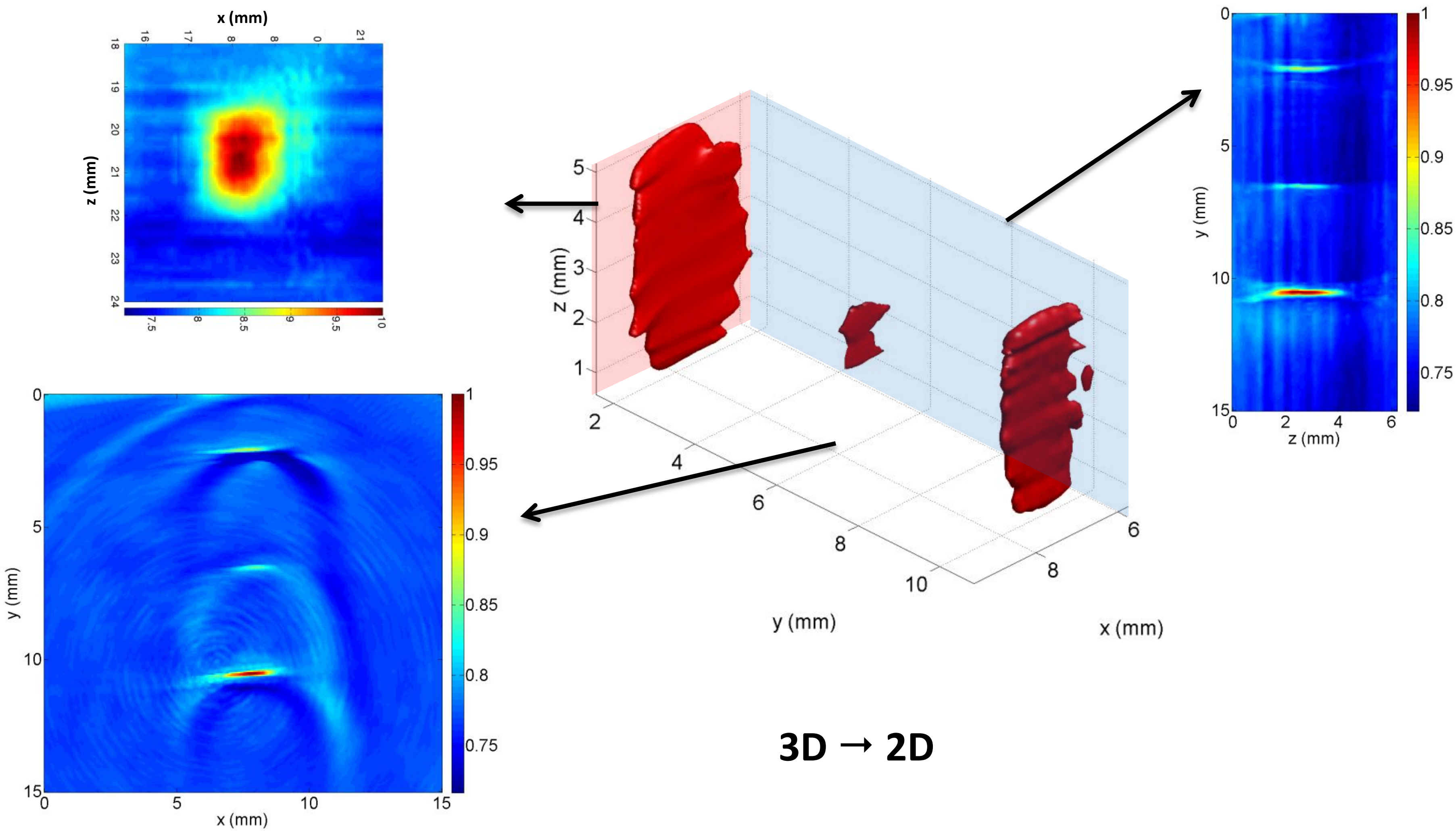
US detector setup



3-dim reconstruction of US waves

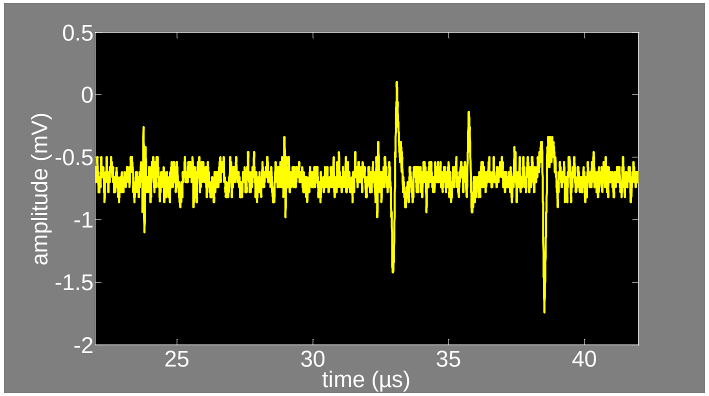
S. Kellnberger et al., to be published

Image reconstruction

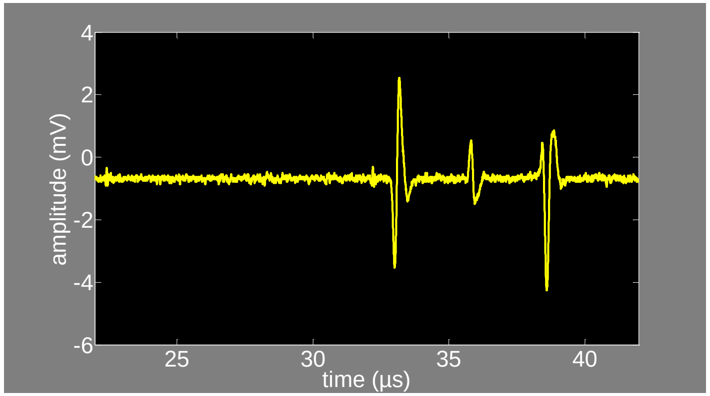


3D → 2D

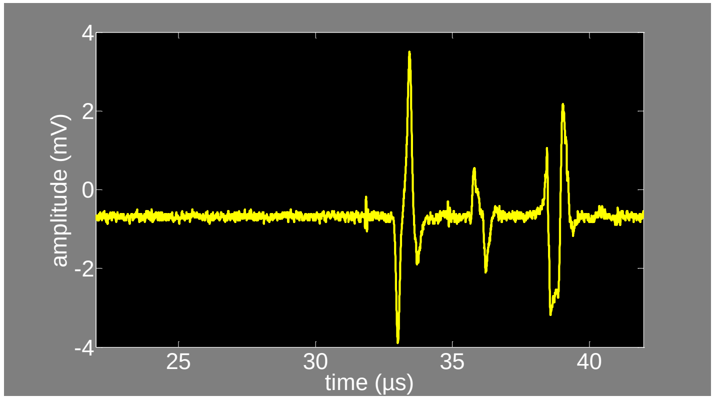
Pulse length variation



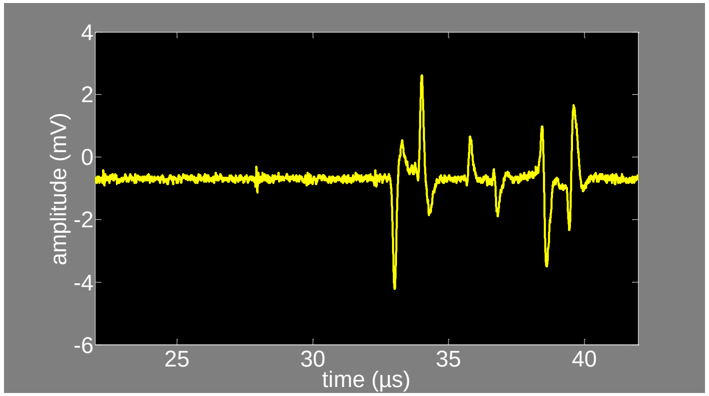
50 ns



200 ns



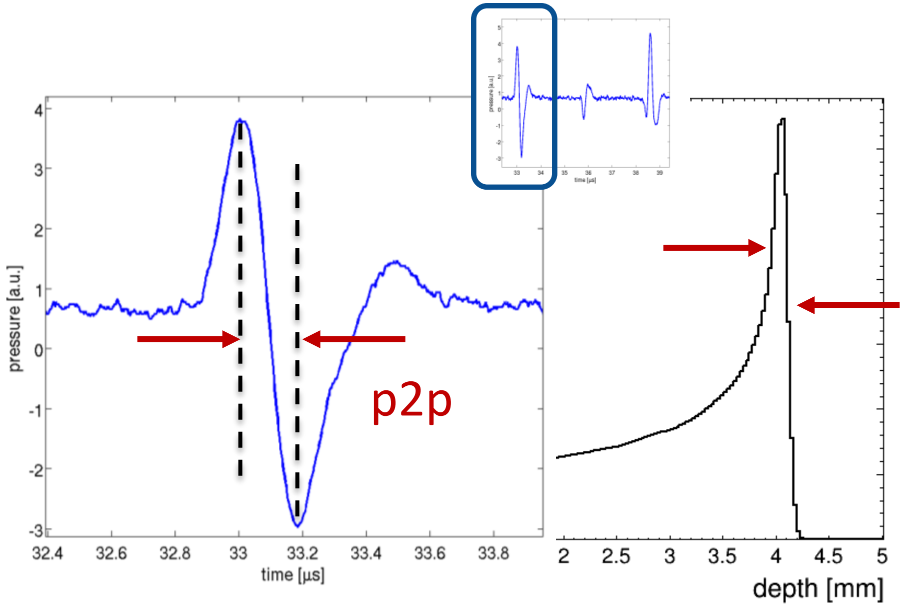
500 ns



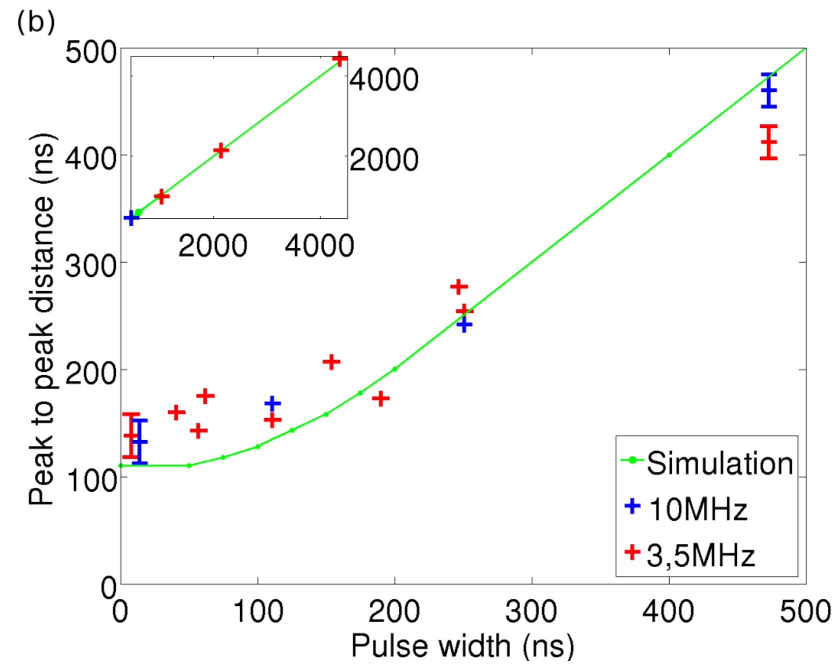
1000 ns

Note: inverting preamp

Bragg peak width



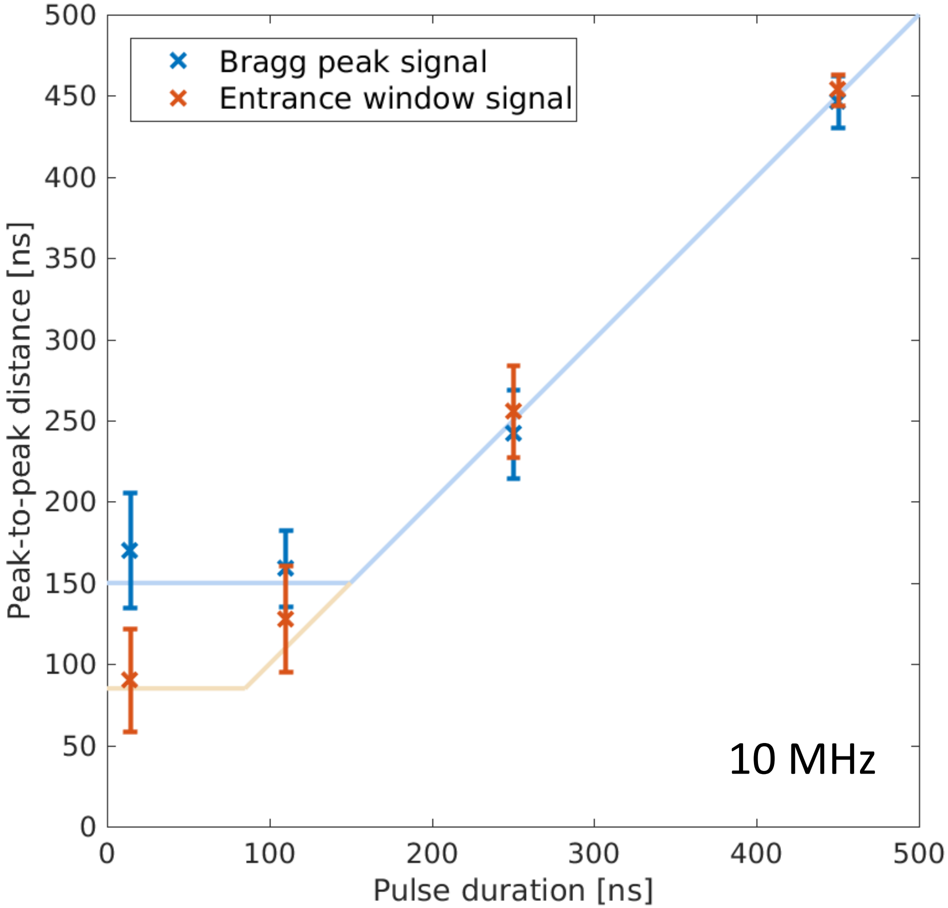
Point detector approximation

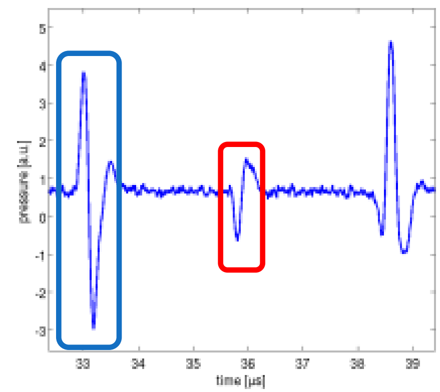


peak to peak distance (p2p) of Bragg peak signal saturates for short pulse durations (i.e. in ***stress confinement***)

→ saturation value corresponds to **Bragg peak width** (steepest gradients)

Entrance window width





critical dimension l_c and stress confinement time t_s

- Bragg peak:
  l_c = 230 µm, t_s = 150 ns
- entrance window:
  l_c = 50 µm, t_s = 30 ns

→ detector frequency and size limited

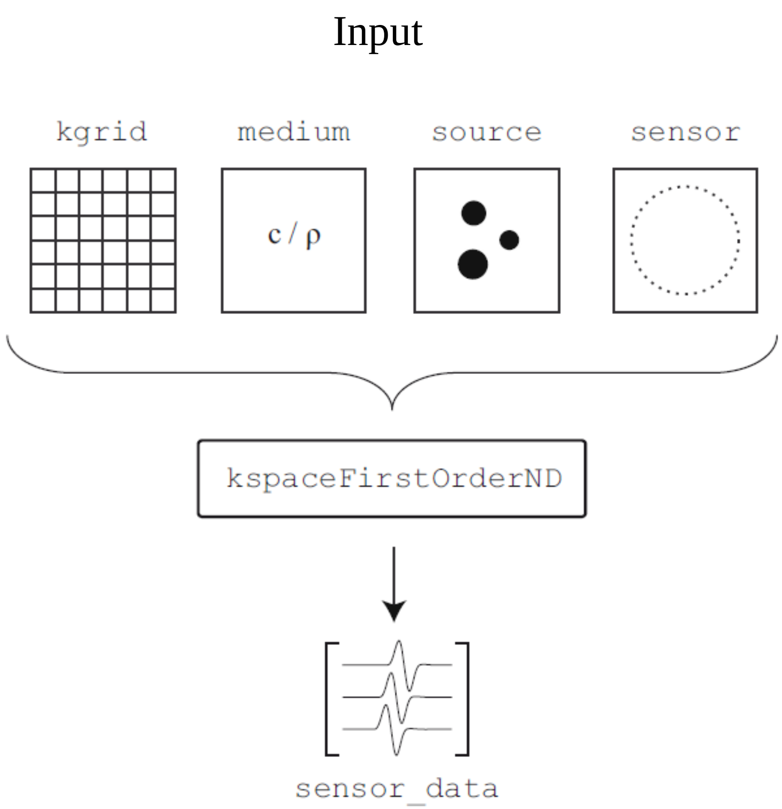
Acoustic simulations

k-Wave program

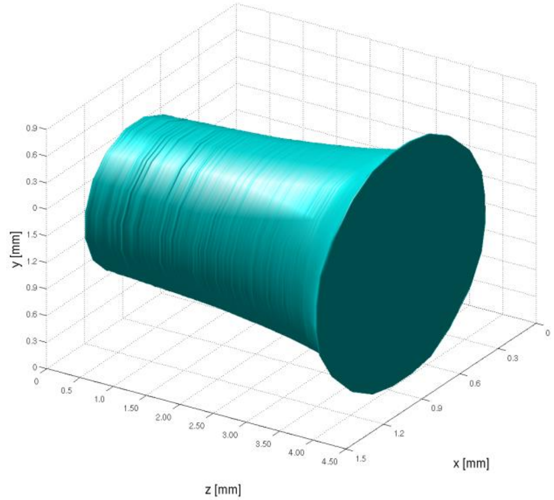
B.E. Treeby, B.T. Cox, J Biomed Opt 15 (2010)

- Matlab toolbox for ***time-domain modelling*** of acoustic wave propagation

- Solving of the coupled first order acoustic wave equation by ***k-space pseudospectral method***



k-Wave input

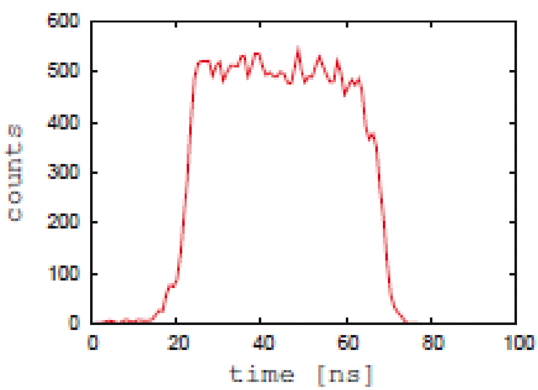


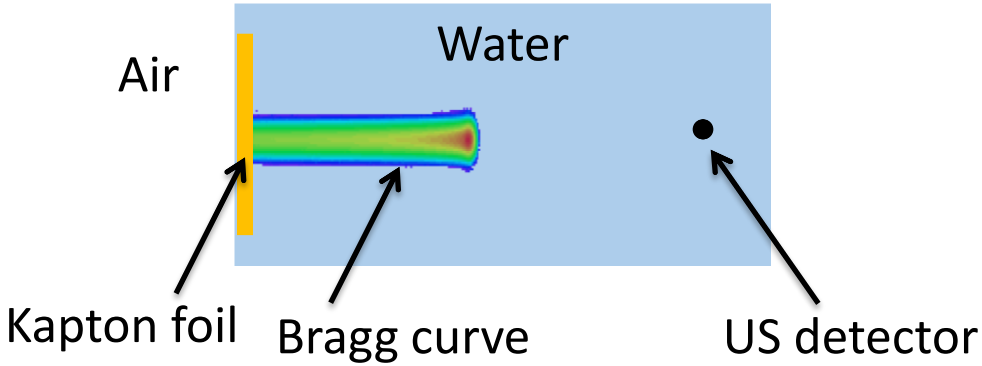
Source term:

- *Geant4* dose distribution
- Proton pulse time profile

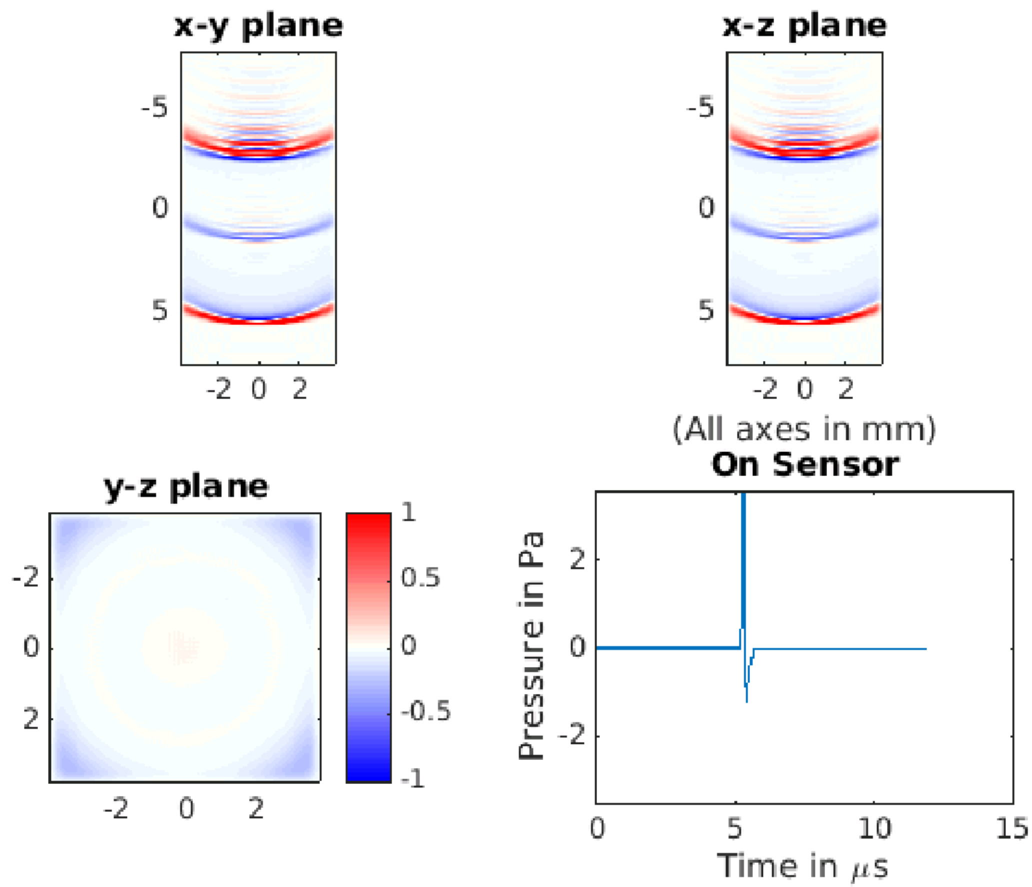
Grid size:

- Space: 30 – 60 µm
- Time: 10 ns

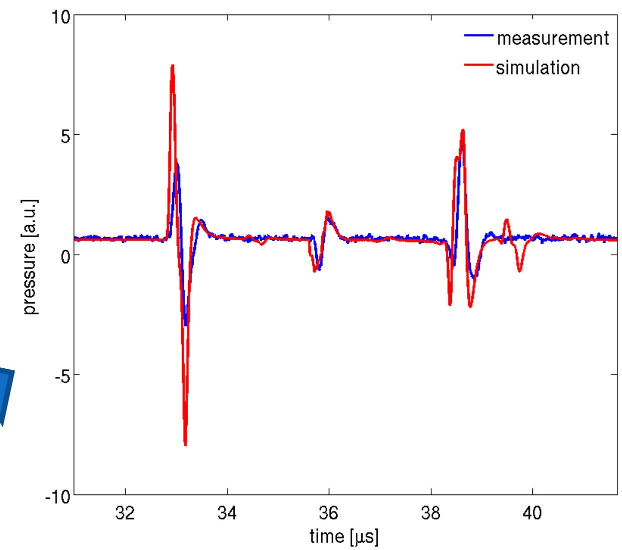




Example



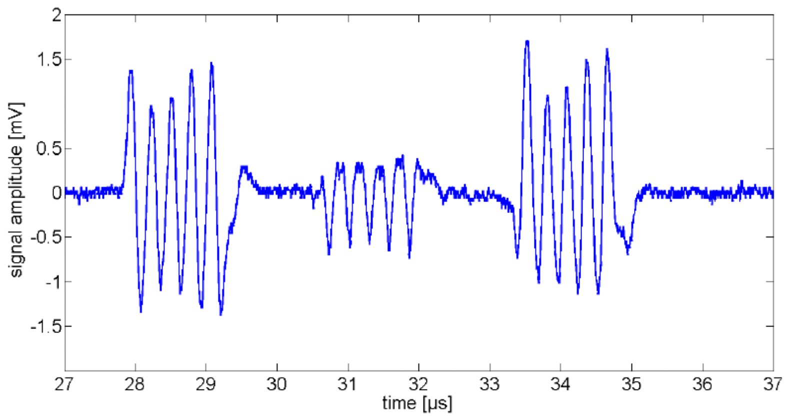
simulation vs exp



Conclusion from 20 MeV test experiments

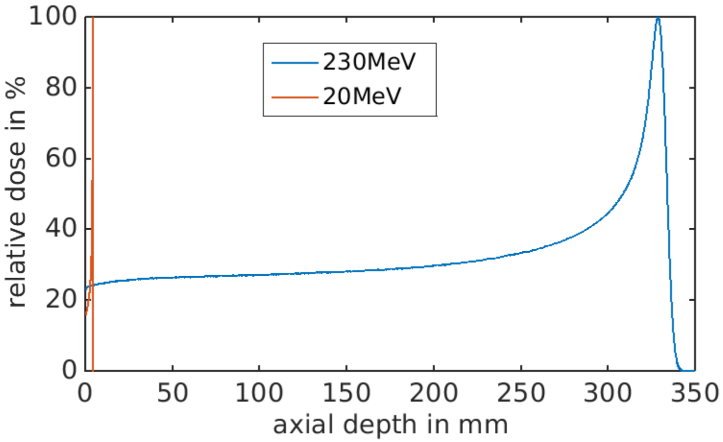
Proof-of-Principle:

- **submillimeter** range accuracy
- frequency independent
- lowest detectable signal:
  10^4 p per pulse → 10^{12} eV
  (corresponding to 0.1 Gy)
- beam modulation demonstrated
  → lock-in technique to improve SNR



1 µsec pulse with 3.5 MHz modulation

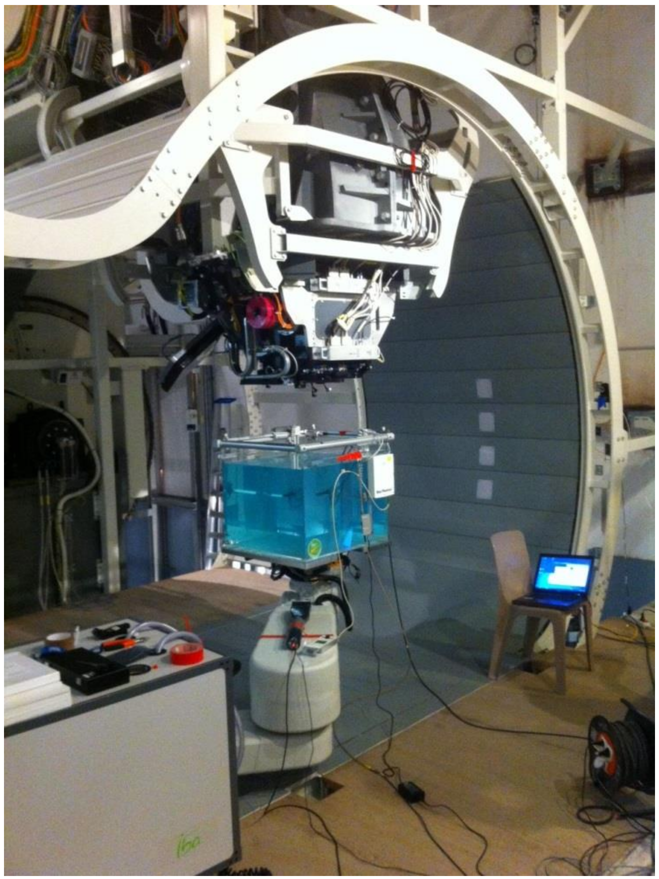
Clinical Application:

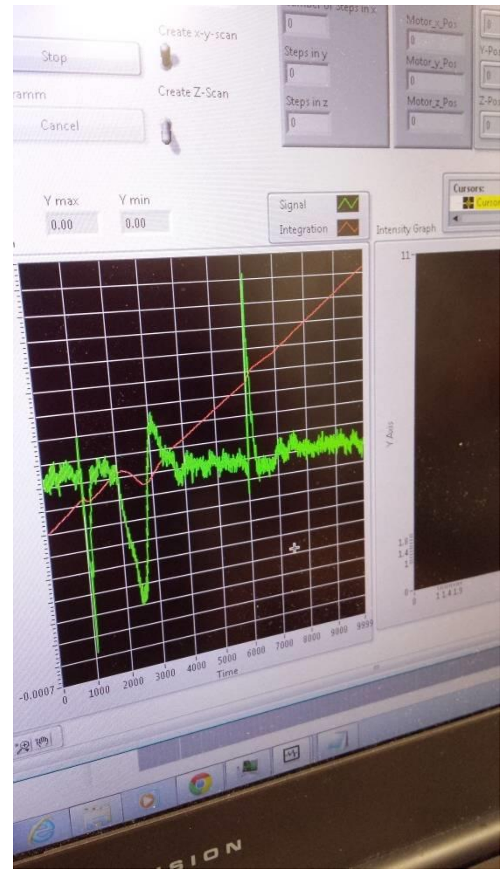


- Bragg peak width at clinical energies of 120 – 230 MeV: **5 - 20 mm**
- ionoacoustic frequencies ≈ **200 kHz**
- soft tissue attenuation
  (50x water, but 200 kHz!)
- tissue inhomogeneity and patient noise
- position resolution at 200 kHz??

First test at clinical energies

Ionoacoustic experiment at the IBA 230 MeV synchro-cyclotron (Nice, France)



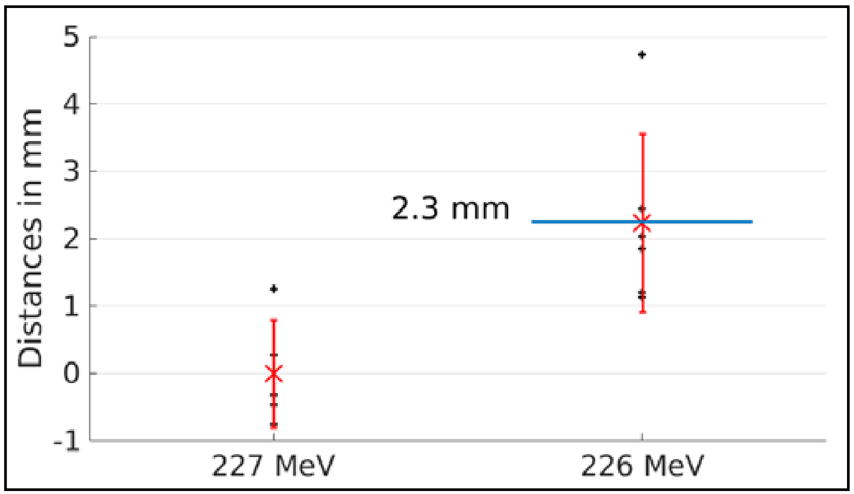


Note:
1024 averages

Preliminary results...

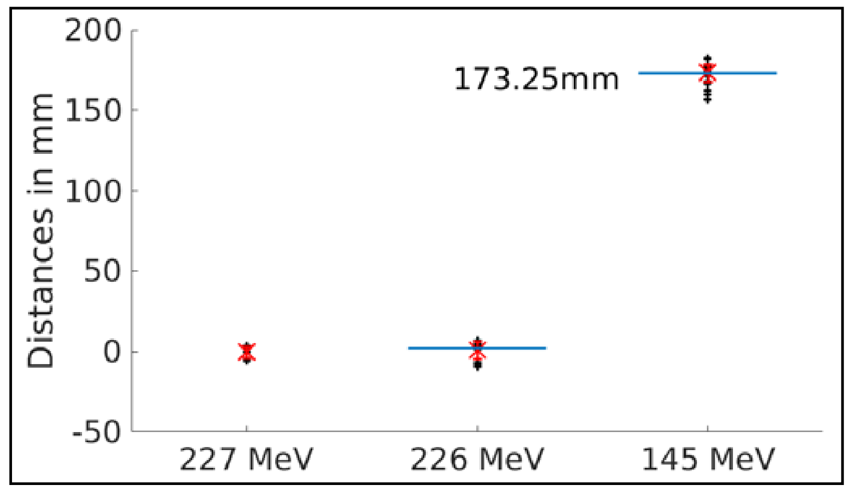
Energy (range) variation

ΔE = 1 MeV



Geant4 simulation

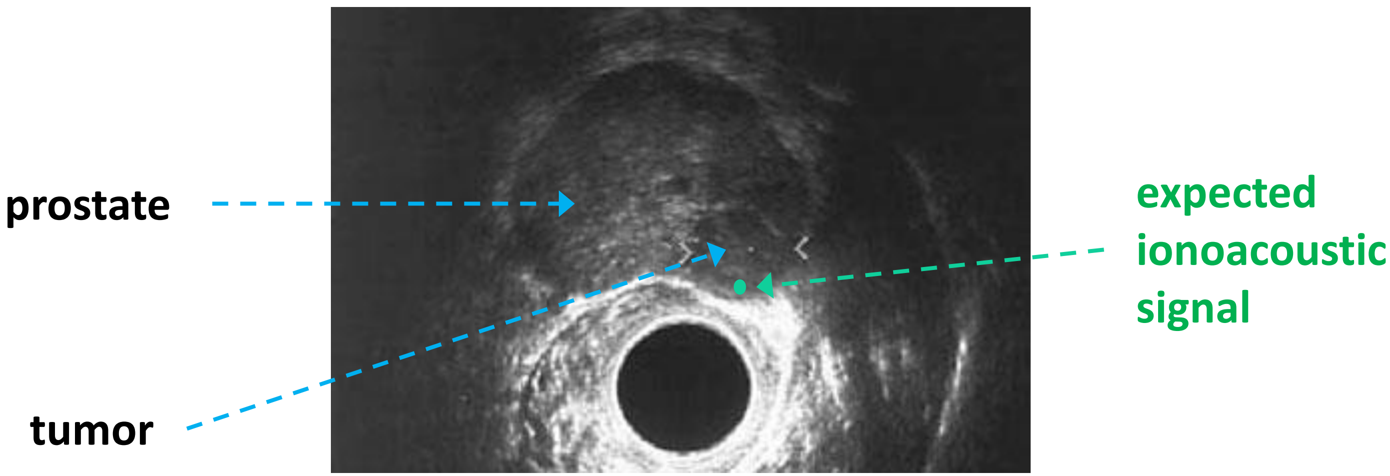
ΔE = 81 MeV



See also: K.C. Jones at al., *Experimental observation of acoustic emissions generated by a pulsed proton beam from a hospital-based clinical cyclotron,* Med Phys **42** (2015) 7090.

Grand goal

Corregistration of ultrasound imaging with ionoacoustic Bragg peak signal!?



Transrectal ultrasonography of prostate tumor tissue

Main problem: ionoacoustic signal to noise ratio

Thanks to .....

IBMI, Helmholtz-Zentrum München

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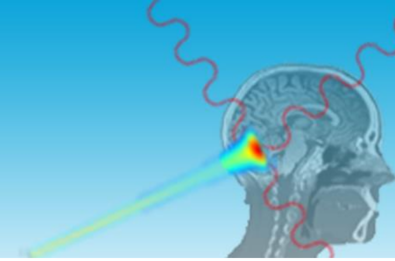
IBA, Ion Beam Applications SA, Belgium

F. Vander Stappen, D. Bertrand, D. Prieels

→ **Recent review:** K. Parodi and W. Assmann, Mod Phys Lett A 30, 17 (2015) 1540025

Finally…



Thank you for your attention