



Ionoacoustic imaging for particle range verification

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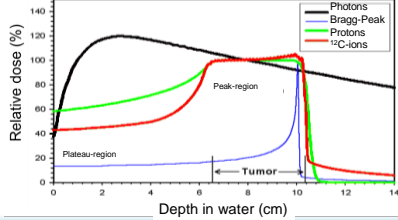
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 Advances in Experimental Medical Physics

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The physical advantages of ion beams

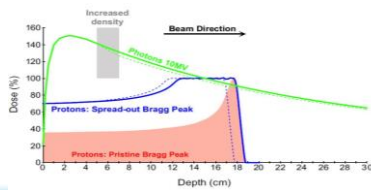
The finite range with the characteristic "Bragg-peak"





The challenges of ion beams in clinical practice

*"The advantage of protons is that they stop.
 The disadvantage of protons is that we don't always know where."*
 (Prof. Dr. AJ Lomax, Center for Proton Radiation Therapy at PSI, Villigen, Switzerland)



M. Engelsman et al, Seminars Rad. Onc. 2013

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The need of in-vivo range verification

Calibration of X-ray CT into water equivalent length and positional / anatomical uncertainties are large sources of range uncertainty, causing usage of safety margins (a) and suboptimal choice of beam angles (b)

Poll and Parodi, Phys Today 2015

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Make the invisible visible

Imaging particle beams for cancer treatment
Jeremy C. Hall and Ralph Fieser

Different emission mechanisms

Stopping of ions causes local heating and pressure wave

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

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

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

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"Ionoacoustic" range verification

The principle

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

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) acoustic signal observed for passive delivery of 50 ns pulsed p beam

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Time for a new attempt?

Passively scattered irradiation of whole tumor volume at once

- *diffuse* local dose deposition
- *small* ionoacoustic signal amplitude
- *complex* range information

Sequential tumor irradiation by pencil beam scanning

- highly *localized* dose deposition
- *enhanced* ionoacoustic signal amplitude
- *direct* range information

Trends of *higher pulse intensity* for new accelerators
like synchro-cyclotrons (6-7 μs FMHW, up to ~5pC/pulse @ 1kHz)

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Systematic studies at low beam energies

Experimental setup at the MLL Tandem accelerator

- 20 MeV protons stopped in a water phantom
- 1 – 10 MHz PZT detector, remotely controlled
- 8 ns – 4 ms beam pulse width at 3 ns rise time
- 10⁴ – 10⁸ protons per pulse

Systematic “ionoacoustic” investigations under ideal conditions

W. Assmann et al Med Phys 2015

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Range determination: Reproducibility & accuracy

Clear signal (1.6 Gy peak dose)

BP position accuracy and precision < 100 μm (= frequency independent)

Model	focus	f ₀ [MHz]
V-303*	spherical	1
V-382*	planar	3.5
V-311*	spherical	10
Array	cylindrical	5

* Immersion transducers Olympus

Geant4

	BP (mm)
10 MHz	4055 ± 20
10 MHz	4050 ± 15
3.5 MHz	4070 ± 10

W. Assmann et al Med Phys 2015; PhD S. Lehrack; MSc A. Maaß

1D Bragg peak characterization & simulation

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Simulation for point detector approximation, combining Monte Carlo (Geant4) dose deposition with K-Wave acoustic propagation

Peak to peak distance (p2p) of Bragg peak signal saturates for short pulse durations in stress confinement (i.e. $t_{on} < t_{propagation}$ [$v_s \approx 1.5 \text{ mm}/\mu\text{s}$])

Saturation value corresponds to Bragg peak width (steepest gradients)

W. Assmann et al Med Phys 2015

3D Bragg peak characterization: sonoacoustic tomography

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First test of 64-channel Transducer-Array
Developed by V. Ntziachristos for Multispectral Optoacoustic Tomography

Tomography of a pencil beam w/ w Al absorber

Kellnberger et al Sci Rep 2016

Triple-modality imaging

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First-time combination of optoacoustics, sonoacoustics and ultrasonography in a pre-clinical settings (ex-vivo mouse leg)

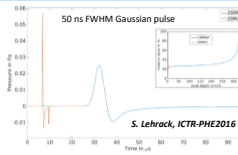
SCIENTIFIC REPORTS
OPEN Sonoacoustic tomography of the proton Bragg peak in combination with ultrasound and optoacoustic imaging

See Patch et al, TU-FG-BRB-9

Figure 3. Triple-modality imaging of a mouse leg using optoacoustics, sonoacoustics, and ultrasonography: (a) Schematic of the opto- and sonoacoustic experiment. For ultrasonography we replaced the curved array with a linear US array (picture not shown). (b) Optoacoustic reconstruction of a mouse leg positioned in the pressure beam line (scale bar represents 2 mm, star marks the medial marginal vein). (c) Ultrasonography of the mouse leg, showing medial marginal bone (scale bar represents 2 mm). (d) Cyanoide of a mouse leg with the sonoacoustic reconstruction (orange color) overlaid to the optical image, displaying the Bragg peak at the distal end of the leg with a green image slice ($z = 3.5 \text{ mm}$) (star marks the medial marginal vein).

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From 20MeV to clinical energies



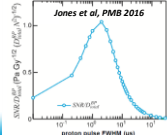
50 ns FWHM Gaussian pulse
S. Lehrack, ICTR-PHE2016

Challenges

- Decreased signal for same proton pulse due to increased Bragg peak width
- Decreased ionoacoustic frequencies = 200 kHz
- Soft tissue attenuation (50x water, but low US frequencies)
- Tissue inhomogeneity and patient noise

But
Optimum expected around few μs pulse
(still in stress confinement due to broader Bragg peaks)

Synchro-cyclotrons offer ideal scenario for ionoacoustics



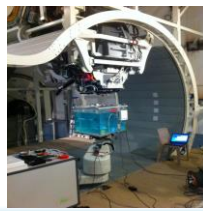
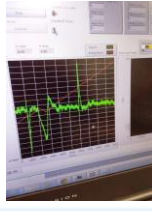
Jones et al, PMB 2016



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Tests at clinical energies: Synchro-cyclotron

ionoacoustic experiment at the IBA 230 MeV synchro-cyclotron (Nice, France)
(6-7 μs FMHW, ~5pC/pulse @ 1kHz)

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Note:
1024 averages

S. Lehrack et al, presented at ICTR-PHE 2016

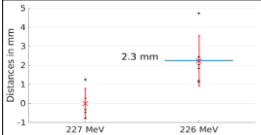
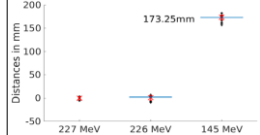


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Tests at clinical energies: Synchro-cyclotron

Energy (range) variation

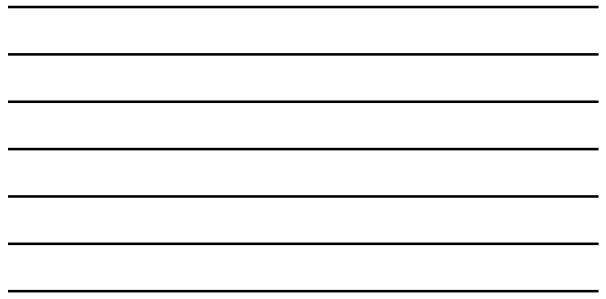
$\Delta E = 1$ MeV — Geant4 simulation — $\Delta E = 81$ MeV

Promising mm-accuracy but reproducibility issues to due setup shortcomings

New experimental run on July 25-26 2016 (data analysis in progress)

S. Lehrack et al, presented at ICTR-PHE 2016



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Tests at clinical energies: artificially pulsed cyclotron

Artificially pulsed cyclotron (19 μ s and 790 nA max current)

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Medical Physics

Experimental observation of acoustic emissions generated by a pulsed proton beam from a hospital-based clinical cyclotron.

Walter C. Assmann, Tobias Stapp, Christian R. Bahr, Silke Janzow, Peter A. Lee, Daniel Pflanz, Timothy D. Solberg, Chandra M. Sengul, and Dieter Acker

Courtesy of K. Jones, UPenn

Jones et al, Med Phys 2015

See Jones et al, SU-C-207A-4

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Conclusion & outlook

- Renewed interest in ionoacoustics, favoured by modern pencil beam scanning
- Promising results achieved at pre-clinical experimental sites as well as clinical synchro-cyclotrons and artificially pulsed isochronous cyclotrons
- Main remaining challenges are detector sensitivity and tissue heterogeneities

Envisioned clinical application will combine ionoacoustics with ultrasonography for real-time range verification (e.g., liver, prostate, breast)

Transrectal ultrasonography of prostate tumor tissue

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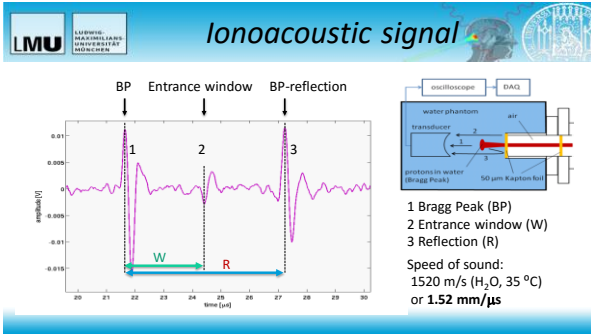
Stephan Kellnberger IBMI/TUM

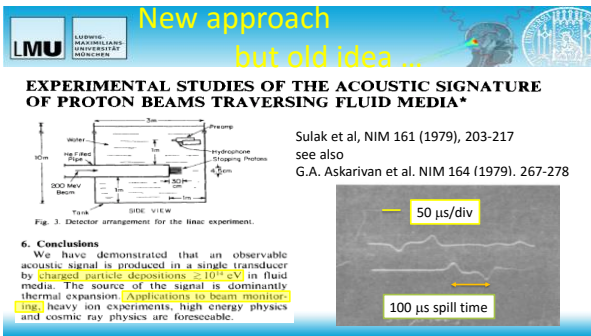
Sebastian Lehrack LMU

MLL

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...and thank you all for your attention!





Time resolved properties of acoustic pulses generated in water and in soft tissue by pulsed proton beam irradiation—A possibility of doses distribution monitoring in proton radiation therapy

J. Tada et al, Med. Phys., 18, (1991), 1100-1104

A review of the processes by which ultrasound is generated through the interaction of ionizing radiation and irradiated materials:
Some possible applications

N. Bailly, Med. Phys., 19, (1992), 525-532

- US amplitude proportional to energy deposition
 - Dose verification
- Determination of beam position

Range verification with sub-mm spatial resolution?
