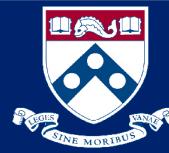




Experimental Results of Protoacoustics Capability to Verify Proton Range for CNS Cases

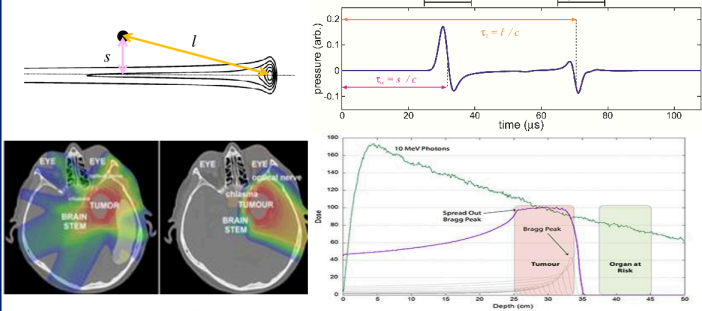


S Avery^{1*}, W Nie³, J Sohn⁴, K Jones⁵, J Eichenberger⁶, J Dorsey¹, A Kassaei¹, C Sehgal²

1. Department of Radiation Oncology, University of Pennsylvania, Philadelphia, Pennsylvania, USA
2. Department of Radiology, University of Pennsylvania, Philadelphia, Pennsylvania, USA
3. Department of Radiation Oncology, University of Nebraska, Omaha, NE
4. Department of Radiation Oncology, Emory University, Atlanta, GA,
5. Department of Radiation Oncology, Rush University Medical Center, Chicago, IL,
6. Polytec Inc., Irvine, CA

Introduction

Proton range uncertainty limits the benefits of proton therapy. Acoustic-based proton range verification, protoacoustics, is a potential *in-vivo* technique that measures the pressure waves generated by heating induced in the irradiated medium by the pulsed proton beam.



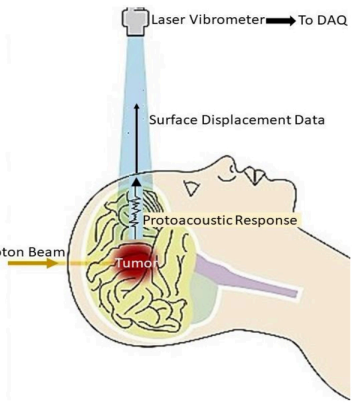
Compared to photons, which exhibit an exponential decrease in deposition with penetration depth, protons deposit a large fraction of their energy in the last few mm of their path due to their sharp distal falloff

Purpose

Due to the limitation in predicting the range of the protons with high accuracy in patients with brain tumors; radiation oncologists face the additional challenge of accounting for dose deposition in a variable and unknown volumes.

This becomes a clinically challenging issue in deep seated tumors of the Central Nervous System (CNS) where organs at risk (OARs) such as the optic nerves, optic chiasm, brainstem, pituitary, and cochlea reside.

Although proton therapy can theoretically localize dose and reduce damage to healthy tissue relative to photon irradiation methods Range uncertainties are the single most limiting factor in proton therapy.



Background

To assess the clinical application of protoacoustics at proton sources with $> 1 \mu s$ proton pulse rise times, an analytical Green's function solution was used to simulate the pressure traces generated by 150 MeV proton beams in an homogeneous water medium.

Wave equation

Green's function solution

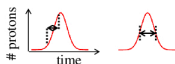
$$\nabla^2 p(\mathbf{r}, t) - \frac{1}{c^2} \frac{\partial^2 p(\mathbf{r}, t)}{\partial t^2} = -\frac{1}{c^2} \frac{\partial p_{source}(\mathbf{r}, t)}{\partial t}$$

$$p(\mathbf{r}, t) = \frac{\beta}{4\pi c_p} \iiint \frac{d^3 \mathbf{r}'}{|\mathbf{r} - \mathbf{r}'|} \left. \frac{\partial H(\mathbf{r}', t')}{\partial t'} \right|_{t' = t - |\mathbf{r} - \mathbf{r}'|/c_p}$$

To assess the clinical application of protoacoustics to inhomogeneous materials, the acoustic signals generated in heterogeneous tissue were numerically simulated based on a CT image. The CT image was used to calculate the dose deposition for a single pencil beam. The dose deposition was then used to seed the initial pressure in a numerical acoustic simulation in which the acoustic parameters, including the Grüneisen parameter that relates dose to source pressure, were also determined from the CT. The k-Wave matlab toolbox was used to propagate the pressure waves through the inhomogeneous material.

Clinical proton pulses

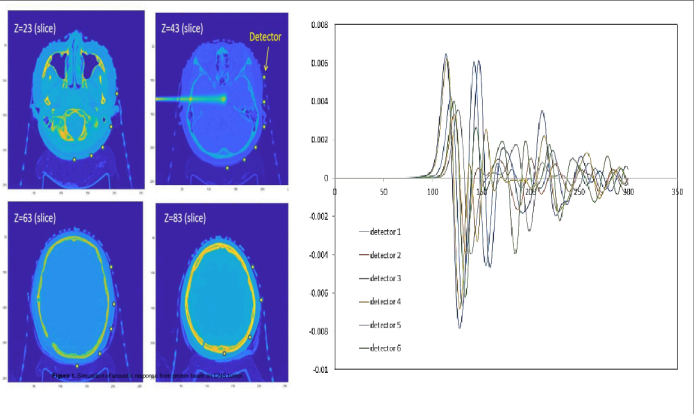
Previously reported simulations and experiments have employed proton pulses with rise time of $< 1 \mu s$. Current clinical proton sources generate protons with longer rise times.



| Research | Rise Time | FWHM |
|--|-------------|-------------------|
| Simulation | $< 1 \mu s$ | $< 40 \mu s$ |
| Experiments | | |
| Synchrotron (few bunches) (ITEP: Sokolov; Tsukuba: Hayakawa) | $< 50 ns$ | 50-70 ns |
| Tandem Accelerator (TU Munich: Parodi) | $< 57 ns$ | 57 ns – 1 μs |
| Isochronous Cyclotron (Harvard: Learned; Uppsala: Stegmann) | ? | $> 50 \mu s$ |
| Clinical | Rise Time | FWHM |
| Isochronous Cyclotron | 50 μs | $> 1 ms$ |
| modified | 20 μs | 20 μs |
| Synchrotron | 200 μs | 200 ms |
| Synchrocyclotron | $< 7 \mu s$ | 7 μs |

Methods

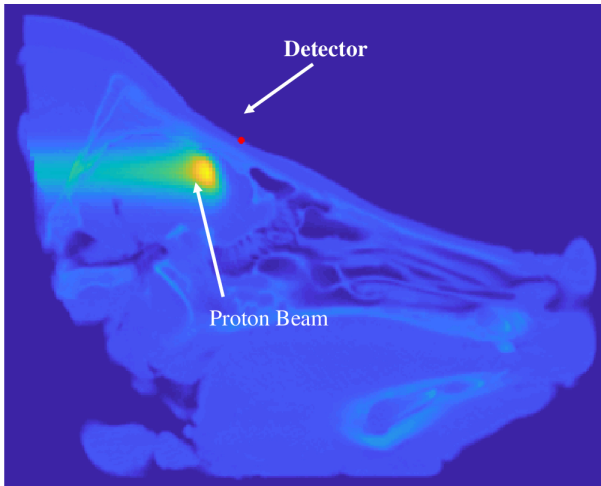
Simulation Acoustic response from proton beam on CNS tumor



Treatment Planning CT study and proton plan for hog head.



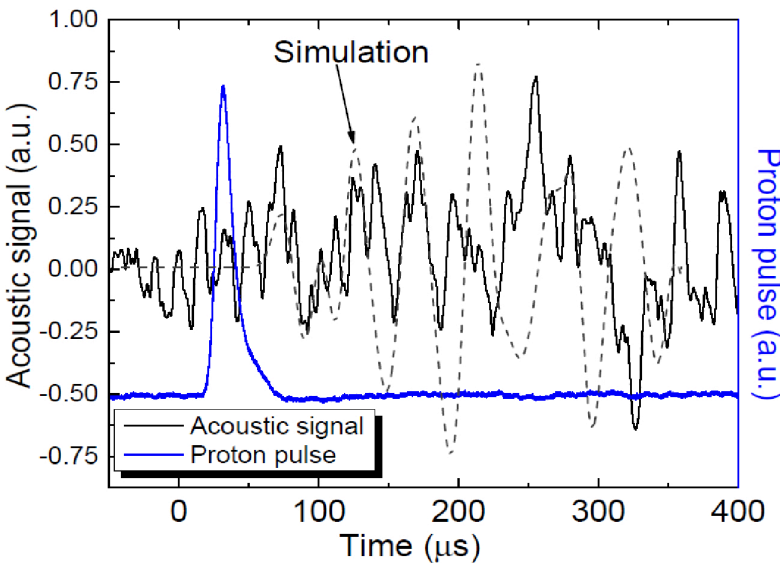
Simulation Acoustic response from proton beam on hog head.



Clinical Measurements



Accelerometers were attached on the hog head on the distal side of the proton beam. The detected acoustic signal was overlapped with proton pulse and simulation, in which the acoustic TOF agrees with the distances between BP and detector calculated in TPS.



Results of our preliminary data on a hog head characterizing the effects of heterogeneity. Although sites classically inaccessible to ultrasound imaging, such as the brain and the head and neck, will be simulated and are amenable to protoacoustic range verification because the penetration of protoacoustic pressure waves (frequency $< 50 kHz$) through skull and bones is expected to be higher than $> 1 MHz$ ultrasound waves.

Conclusions

Relative to conventional x-ray therapy, proton therapy is advantageous because protons have a limited range, called the Bragg peak (BP), which spares distal tissues. Due to range uncertainty, treatment plans do not take full advantage of the proton's sparing capabilities. A critical need exists to verify the proton range which becomes a clinically challenging issue in deep seated tumors of the Central Nervous System (CNS), especially in children, where organs at risk (OARs) such as the optic nerves, optic chiasm, brainstem, pituitary, and cochlea reside. Protoacoustic range-verification will provide a simple and inexpensive method for real-time, in vivo patient monitoring during proton irradiation with greater confidence in the proton range.

References

1. B. E. Treeby and B. T. Cox, "k-Wave: MATLAB Toolbox for the Simulation and Reconstruction of Photoacoustic Wave Fields," J. Biomed. Opt. **15**, 021314 (2010).
2. K. C. Jones, A. Witzum, C. M. Sehgal and S. Avery, "Proton beam characterization by proton-induced acoustic emission: simulation studies," Physics in Medicine and Biology **59**, 6549 (2014).
3. P. Hasgall, E. Neufeld, M. Gosselin, K. A. and N. Kuster, "IT'IS Database for thermal and electromagnetic parameters of biological tissues," Vol. 2014, (2014).
4. F. Duck, *Physical Properties of Tissues: A Comprehensive Reference Book*. (Academic Press Limited, London, 1990).
5. T. D. Mast, "Empirical relationships between acoustic parameters in human soft tissues," Acoustics Research Letters Online **1**, 37-42 (2000).
6. Nie L, Cai X, Maslov KI, Garcia-Urbe A, Anastasio MA, Wang LV: Photoacoustic tomography through a whole adult human skull with a photon recycler. In: 2012. SPIE: 3.
7. Jennifer Vogel, Ruben Carmona, Christopher G Ainsley, Robert A Lustig: The Promise of Proton Therapy for Central Nervous System Malignancies, Neurosurgery, Volume 84, Issue 5, May 2019, Pages 1000–1010