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Proton beam characterization by proton-induced acoustic emission: simulation studies

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Abstract
Due to their Bragg peak, proton beams are capable of delivering a targeted dose of radiation to a narrow volume, but range uncertainties currently limit their accuracy. One promising beam characterization technique, protonacoustic range verification, measures the acoustic emission generated by the proton beam. We simulated the pressure waves generated by proton radiation passing through water. We observed that the proton-induced acoustic signal consists of two peaks, labeled $\alpha$ and $\gamma$, with two originating sources. The $\alpha$ acoustic peak is generated by the pre-Bragg peak heated region whereas the source of the $\gamma$ acoustic peak is the proton Bragg peak. The arrival time of the $\alpha$ and $\gamma$ peaks at a transducer reveals the distance from the beam propagation axis and Bragg peak center, respectively. The maximum pressure is not observed directly above the Bragg peak due to interference of the acoustic signals. Range verification based on the arrival times is shown to be more effective than determining the Bragg peak position based on pressure amplitudes. The temporal width of the $\alpha$ and $\gamma$ peaks are linearly proportional to the beam diameter and Bragg peak width, respectively. The temporal separation between compression and rarefaction peaks is proportional to the spill time width. The pressure wave expected from a spread out Bragg peak dose is characterized. The simulations also show that acoustic monitoring can verify the proton beam dose distribution and range by characterizing the Bragg peak position to within ~1 mm.

Keywords: pulsed proton beam, range verification, acoustic pulses, monitoring of dose distribution, radiation therapy

(Some figures may appear in colour only in the online journal)
1. Introduction

The main advantage of proton radiotherapy for treatment of cancer is the proton Bragg peak. Unlike photons and electrons, the finite range and the sharp dose falloff at the distal end of the proton beam’s Bragg peak increases our ability to conform the treatment dose to the tumor and spare the surrounding healthy tissues (Knopf and Lomax 2013). As a testament to its advantages, as of August 2013, the vast majority of the 43 operational particle therapy treatment facilities were proton based (see PTCOG website), and the number of proton therapy rooms is expected to increase by a factor of 3 by 2018 (Goethals and Zimmermann 2013).

However, there are uncertainties in our ability to precisely locate the proton beam Bragg peak and its distal dose gradient within the patient. Because of these uncertainties, many institutions assume a total uncertainty in the in vivo proton range of 3.5% of the calibrated range plus 1 mm. Rather than potentially missing the tumor, the treatment plan is routinely modified to include a larger-than-desirable treatment target margin, which results in a deliberate over- and undershoot of the beam into healthy tissues located in front of and beyond the tumor. This substantial increase to the margins undermines the benefits of the proton’s unique steep dose gradient, reducing the clinical potential of proton radiotherapy.

To fully exploit the advantages of the proton Bragg peak, there is a critical need to reduce proton beam range uncertainties especially at the distal edge where a sharp dose gradient exists (Knopf and Lomax 2013). One non-invasive, proposed technique is PET imaging. During proton therapy positron emitters are produced, and the photon pairs produced in the positron annihilation can be measured using a PET scanner. By comparing the actual activity measured in the patient with simulated Monte Carlo results, the proton range can be verified (Knopf et al 2009). It has been shown that 1–2 mm accuracy can be achieved in bony structure areas such as head and neck patients. However, this accuracy was not reproducible at other tumor sites (Parodi et al 2007). Another technique, prompt gamma, looks at the single emission photons produced in the body. Using a prompt gamma camera with gamma collimation it has been shown (Kurosawa et al 2012) that the prompt gamma distribution is well correlated with the proton range at clinical energies. However, this technique cannot be used for passively scattered beams. A third technique, the focus of this work, is range verification using acoustic signals, what we term ‘protoacoustics’.

Pulsed proton beams, such as those used in clinical proton therapy, create a measureable acoustic signal. As with other thermoacoustic phenomena (Tam 1986), the energy deposition of the pulsed proton beam leads to a local heating of the medium, and the local density variations create a pressure wave. Since Askaryan’s initial 1957 proposal to detect particles based on their pressure signal (Askaryan 1957), a number of groups have successfully recorded the proton-induced acoustic emission (Askariyan et al 1979, Learned 1979, Sulak et al 1979, Hunter et al 1981, Albul et al 2001, 2004, 2005, Capone and De Bonis 2006, Graf et al 2006, De Bonis 2009, Bychkov et al 2010), and the potential applications to medical physics have become apparent (Hayakawa et al 1988, 1989, Tada et al 1991, Baily 1992, Chu et al 1993, Kruglikov 1993, Hayakawa et al 1995, Terunuma et al 2007). Analytical simulations of the proton acoustic emissions have been performed assuming impulsive pulses (Terunuma et al 2007, De Bonis 2009, Bychkov et al 2010), but a systematic study of different variables is lacking.

Through numerical simulations, our work seeks to characterize the proton beam by analyzing the information content contained in the acoustic signal. The broader goal is to locate the Bragg peak from acoustic measurements and thus verify the range of protons. Our study is divided into three sections to understand the acoustic manifestations of the proton beam’s temporal pulse width (spill time, $\Theta$), beam diameter ($\sigma$), and Bragg peak width ($\psi$).
2. Methods

Pressure waves are generated by physical expansion or contraction. As an accelerated proton beam travels through water, its kinetic energy is converted into heat. As with other thermoacoustic phenomena, the heating causes a microscopic volume expansion and contraction which creates measurable sound waves. To simplify our simulation of pressure waves created by proton irradiation of water, we assume that the energy deposited by the proton beam at a position \( r \) at time \( t \), \( E \), is instantaneously \((10^{-12} \text{s})\) converted into heat, \( q \), and that this heat diffuses slower over our length scales (thermal confinement (Xu and Wang 2006)) than the timescale of our proton pulse:

\[
q (r, t) = E (r, t) \tag{1}
\]

where \( q \) and \( E \) have units of \( \text{J m}^{-3} \text{s}^{-1} \). Integration over time and volume gives the total energy contained within the pulse. Ignoring heat diffusion, the irradiated volume temperature, \( T(r, t) \), is equal to the cumulative integration of \( q \) over time divided by the density and specific heat capacity. For a step function pulse, like those used for our simulations, the temperature of the irradiated volume instantaneously increases with the leading edge of the beam, steadily increases while the beam is on, and then remains constant once the beam is off. The irradiated volume, which is on the order of \( \text{mm}^3 \), returns to the initial temperature through diffusion after milliseconds to seconds.

The heating generates a source pressure, \( p_{\text{source}} \), with units of \( \text{Pa s}^{-1} \) (Beard 2011).

\[
p_{\text{source}} (r, t) = \Gamma q (r, t) \tag{2}
\]

where \( \Gamma = \beta c^2 / C_p \) is the Grüneisen coefficient defined by the thermal expansion coefficient, \( \beta \), the speed of sound, \( c \), and the specific heat capacity at constant pressure, \( C_p \). \( p_{\text{source}} \) is proportional to both \( q \) and, equivalently, \( \partial T(r, t) / \partial t \), as is expected: a change in the temperature causes pressure. Interestingly, even though the volume does not cool on our timescales (thermal confinement), the \( p_{\text{source}} \) drops abruptly with the falling edge of our step function pulses.

Proton beams have been well-characterized, and the energy deposition, \( E(r, t) \), can be specified as the product of three functions: \( E(z) \), which describes the profile along the beam propagation, \( E(s) \), which describes the profile perpendicular to \( z \), and \( E(t) \), which defines the temporal dependence. By combining (1) and (2) and separating \( E(r, t) \), the time-dependent source pressure can be specified by three separate functions written in cylindrical coordinates \( r = s \hat{\mathbf{s}} + q \phi \hat{\mathbf{\phi}} + z \hat{\mathbf{z}} \), where bold, hatted characters are unit vectors:

\[
p_{\text{source}} (r, t) = \Gamma E(z) E(s) E(t) \tag{3}
\]

Because the proton beam is radially symmetric, there is no \( \phi \) dependence in (3).

Along the beam propagation axis, \( z \), the spatial heating profile is defined by \( E(z) \). For a proton beam with a narrow kinetic energy, the energy deposition is given by \( B(z) \), an analytical approximation of the Bethe-Block equation (Bortfeld and Schlegel 1996) that describes the energy deposition of protons passing through water.

\[
B(z) = \begin{cases} 
(R_0 - z)^{1/n-1} / n^{1/n} & z \leq R_0 \\
0 & z > R_0
\end{cases} \tag{4}
\]

with \( n = 1.77 \) and \( \lambda = 0.0022 \) for water. The \( B(z) \) is zeroed after the Bragg peak at \( R_0 \) to remove a residual tail and (4) is convolved along \( z \) with a Gaussian with a full width at half maximum (FWHM) of 2.35% of \( R_0 \) to account for range straggling (Bortfeld and Schlegel 1996, Bortfeld 1997).
Equation (4) gives the energy deposition for a pristine Bragg peak produced by a proton beam with a narrow range of kinetic energy. For treatment purposes, to deliver constant radiation to a broader volume, doses are often sequentially delivered as the sum of many \( B_i(z) \) functions weighted with a factor \( W_i \) to form a spread out Bragg peak (SOBP):

\[
E(z) = \begin{cases} 
B(z) & \text{pristine} \\
\sum_{i=1}^{50} W_i B_i(z) & \text{SOBP}
\end{cases}
\]

(5)

Here, the SOBP is the sum of 50 \( B_i(z) \) calculated at \( R_0 \)'s evenly spaced across the given SOBP width, \( \psi(z) \). Although practically the SOBP delivery is performed by incrementally (pencil beam scanning) or continuously (double-scattering) changing the amplitude and proton’s kinetic energy (and thus the \( R_0 \)), we have simulated the pressure waves produced by irradiating with a complete SOBP. Based on substituting (5) into (3), the total pressure signal induced by a SOBP is the same as the sum of the pressure waves that would be measured for individual weighted \( B_i(z) \) doses. The weighting factor is calculated using the \( W_i \) as described in the appendix (Bortfeld and Schlegel 1996) to produce a SOBP of width \( \psi \) that extends from \( z = R_0 - \psi \) to \( R_0 \).

The radial spatial dependence of the heating was calculated using a radially symmetric Gaussian profile (Bortfeld and Schlegel 1996) with FWHM of \( \sigma \):

\[
E(s) = \exp \left( -\frac{s^2}{4\ln2} \frac{1}{\sigma^2} \right)
\]

(6)

The time dependence of the proton pulse, \( E(t) \) is specified as a step function of width \( \Theta \), which is similar to simple clinical beams: the beam abruptly turns on, a brief but constant flow of protons is administered, and the beam is abruptly shut off. Due to the quantized nature of the simulation and the 1 mm grid spacing, Fourier pressure wave components with frequencies above 500 kHz were excluded, and a smoothing window was applied to remove residual oscillations that result from a sharp frequency cutoff. Due to the frequency filtering, sharp temporal and spatial features are effectively smoothed. For example, to proactively remove the unsupported frequency components, the simulation program filtered \( E(t) \) in the frequency domain before running the simulation. Thus, short \( \delta \)-function, impulsive heating pulses of 0.2, 0.8, and 2.0 \( \mu \)s widths were broadened into Gaussian-like shapes with FWHM of 1.05, 1.12, and 1.67 \( \mu \)s while longer pulses retained their step-function shapes. Given the limited frequency response of both the simulation and transducers, the pressure traces shown here generated by the Gaussian-like 1.05 \( \mu \)s wide pulse are equivalent to the signal that would be measured for a 0.2 \( \mu \)s step-function pulse by a <500 kHz transducer, which approaches a delta-function pulse. Representative \( E(z) \), \( E(s) \), and \( E(t) \) are shown in figure 1.

The acoustic response generated by proton irradiation of water was simulated using the k-Wave MATLAB toolbox (Treeby and Cox 2010). k-Wave propagates acoustic waves in time and space by solving coupled first-order partial differential equations with the k-space pseudospectral method. The wave equation solved can be expressed as:

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

(7)

where \( p(\mathbf{r}, t) \) is the pressure observed, and the driving source pressure is given by (3).

Simulations were run using a 64 \( \times \) 32 \( \times \) 256 \( (x,y,z) \) rectangular box of water with 1 mm grid spacing and \( c = 1481 \) m s\(^{-1}\), the speed of sound in water at 20 °C. The waves were
propagated linearly without loss or absorption. After specifying the spatial profile and time-dependence of the pressure-source, the \( k \)-Wave program propagated the resulting pressure waves for 108 \( \mu \)s with 0.203 \( \mu \)s time steps. Each simulation required \(~300\) s of computation to complete. The time-dependent pressure was recorded at specified transducer points, which were arranged along \( \varphi = 0 \) (in the \( xz \)-plane) as shown in figure 1. Because they should arrive distinguishably later than the original waves, we did not simulate the reflections off of tank walls nor the water surface. Reflections from the water surface undergo a sign inversion relative to the incident wave, which has been simulated previously by mirroring the negative of the source pressure across the water surface before beginning the wave propagation calculations (Terunuma et al 2007). The 1 mm grid spacing is sufficient to faithfully reproduce the sharpest spatial features of \( E(z,E(s), \sigma = 5 \) mm). Transducer positions are marked with black squares. To increase sampling above the Bragg peak, a higher density of transducers were placed around \( z = 150 \) mm \((R_0)\), which creates lines in the image. \( s \) is defined as the radial distance between a transducer and the beam propagation axis. \( l \) is defined as the distance between a transducer and the Bragg peak center.

![Figure 1](image)

**Figure 1.** (a) A cascade plot of the energy deposition profile along \( z \), \( E(z) \), given in (4) and (5). \( R_0 = 15 \) cm. A pristine Bragg peak, \( B(z) \) is shown with a dashed line. \( \psi \), the SOBP width, varies from 30 (top) to 1 mm (bottom), as described in table 1. (b) The radial Gaussian profile of the proton beam, \( E(s) \), given in (6). The \( E(s) \) with diameter of \( \sigma = 5 \) mm is shown with a dashed line. Each peak corresponds to the radial profile for a different \( \sigma \) ranging from 2 to 10 mm, as described in table 1. (c) A cascade plot of the time-dependence of the proton beam, \( E(t) \). Each trace corresponds to a different spill time, \( \Theta \), ranging from 1.05 (bottom) to 40.5 \( \mu \)s (top), as given in table 1. (d) The spatial beam profile along the \( x \) and \( z \) axes (pristine \( E(z) \), \( \sigma = 5 \) mm). Transducer positions are marked with black squares. To increase sampling above the Bragg peak, a higher density of transducers were placed around \( z = 150 \) mm \((R_0)\), which creates lines in the image. \( s \) is defined as the radial distance between a transducer and the beam propagation axis. \( l \) is defined as the distance between a transducer and the Bragg peak center.

To determine the dependence on (i) spill time, (ii) beam diameter, and (iii) Bragg peak width, three sets of simulations were run with the values tabulated in table 1, where the SOBPs for (iii) start at \( z = R_0 - \psi \) and extend to \( z = R_0 \). The values were chosen to reflect typical conditions keeping in mind the computationally limited size of our simulation volume.
3. Results

A characteristic set of pressure traces is shown in figure 2. These traces were recorded on an array of transducers equally spaced along z at constant radial distance s. Each trace shows at most two sets of peaks, which have been labeled α and γ following after (Albul et al 2004). Each set of peaks is composed of a characteristic bi-polar waveform which precedes a negative rarefaction feature. Based on its arrival at constant time as a function of the transducer z position and because it merges with γ in the region where z > R₀, the α feature results from the ‘cylindrical’, flat pre-Bragg peak portion of the E(z) heating region. Based on the z-dependence of its arrival time, the γ feature results from the Bragg peak. The single set of peaks observed at z > R₀ is due to overlap of the α and γ waves, and because of its behavior, we refer to it as γ as well. In figure 3, plotting the arrival time of the center of the bi-polar pulse versus the transducer’s l and s distances (defined in figure 1) for α and γ shows that these features arrive at a time determined by the radial distance s (for α) or Bragg peak distance l (for γ).

Based on these observations (see appendix for further details), the pressure source can be thought of intuitively as a combination of a cylinder (the pre-Bragg peak portion) and a higher amplitude disc (the Bragg peak) (Albul et al 2005). The maximum pressure measured along a row of constant-s transducers is shown in figure 4. Interestingly, the maximum pressure is not observed directly above the Bragg peak because of amplitude generated by the pre-Bragg ‘cylinder’ heating (Albul et al 2005). As the transducer row is moved further from the beam axis (larger s), the maximum pressure z-position moves farther from R₀.

The effect of changing the spill time was simulated by varying the pulse widths of the source pressure (see (2) and (3)). Increasing the spill time increases the time delay, τp-to-p, between the compression and rarefaction peaks, as is shown in figure 5. The generated pressure waves are proportional to the 1st derivative of the source pressure (Diebold et al 1991). For step function pulses, the leading edge (heating and expansion) generates the compression peak while the falling edge (contraction) generates the rarefaction peak. When the pulse width is long, the compression and rarefaction peaks are well separated. As the spill time decreases, the features overlap and interfere. These two regimes are observed in both the peak-to-peak time shown in figure 5(b) and the FWHM of the compression(rarefaction) α(γ) peak shown in figure 5(c). Above Θ = 10 µs, the peak-to-peak time is equal to the spill time, while the τFWHM is constant at 4.9 µs and 4.6 µs for the α and γ features, respectively. The τFWHM is determined by the spatial characteristics of the beam. Below Θ = 10 µs, the compression and rarefaction peaks interfere, which results in both decreased τp-to-p and τFWHM.

Similar results were observed and interpreted previously (Sulak et al 1979). Inspection of figure 5(a) shows that at long spill times the α pressure does not return to zero (marked with

<table>
<thead>
<tr>
<th>Set</th>
<th>R₀ (cm)</th>
<th>σ (mm)</th>
<th>Θ (µs)</th>
<th>Ψ (mm)</th>
</tr>
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<tbody>
<tr>
<td>i</td>
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<td>5</td>
<td>1.05, 1.12, 1.67, 3.04, 4.05, 5.06, 6.08, 12.2, 20.3, 26.3, 32.4, 40.5</td>
<td>Pristine</td>
</tr>
<tr>
<td>ii</td>
<td>15</td>
<td>2, 3, 4, 5, 6, 7, 8, 9, 10</td>
<td>1.05, 20.3</td>
<td>Pristine</td>
</tr>
<tr>
<td>iii</td>
<td>15</td>
<td>5</td>
<td>1.05, 20.3, 40.5</td>
<td>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30</td>
</tr>
</tbody>
</table>

Table 1. Variables used for simulations. R₀: maximum z-position of the Bragg peak; σ: radial FWHM; Θ: spill time; Ψ: SOBP width.
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The diameter FWHM of the pressure source, $\sigma$, was varied from 2 to 10 mm. As is shown in figure 6, as the diameter is increased, the $\tau_{\text{FWHM}}$ of the $\alpha$ compression peak and $\gamma$ rarefaction peak increase linearly, although the $\tau_{\text{FWHM}}$ is more strongly affected. This trend is observed at both tested spill times, although the slopes of the lines mapping diameter to $\tau_{\text{FWHM}}$ changes from $1/1.807$ to $1/1.103\, \mu\text{m}^{-1}$ ($\alpha$) and from $1/6.147$ to $1/3.684\, \mu\text{m}^{-1}$ ($\gamma$) as the spill time increase from 0.2 to 20.3 $\mu\text{s}$. The observed pressure wave can be thought of as the constructive dotted line) immediately following the initial compression(rarefaction) maxima(minima). This behavior is not observed for the $\gamma$ peaks, suggesting that it is due to the spatial shape of the heated region; at the transducer, the initially observed high amplitude pressure is from the closest portion of the pre-Bragg peak cylinder while the tail offset is from heated volume that is further away.

The $\tau_{\text{FWHM}}$, $\tau_{\text{center}}$, and $\tau_{\text{p-to-p}}$ are calculated for both the $\alpha$ and $\gamma$ feature.
Figure 3. The $\tau_{\text{center}}$ is calculated for transducers found in the pre-Bragg peak region where the $\alpha$ and $\gamma$ features are well separated ($0.1R_0 < z < 0.8R_0$), and in the post-Bragg peak region ($z > 1.1R_0$). The $\tau_{\text{center}}$ is plotted versus the distance $s$ and $l$. The fit lines show that $\tau_{\text{center}}^\alpha = s/c$ and $\tau_{\text{center}}^\gamma = l/c$ ($c = 1.481 \text{ mm} \mu\text{s}^{-1}$).

Figure 4. (a) The maximum pressure measured at a line of transducers positioned at $s = 35 \text{ mm}$. The $z$ transducer position with the highest recorded pressure is offset from the maximum of $E(z)$ (the Bragg peak at $R_0$) by $\Delta z_{\text{max}}$. (b) Offset between Bragg peak maximum and the $z$-position of maximum pressure ($\Delta z_{\text{max}}$) is plotted versus $s$. The $z$-axis has 1 mm increments, which limits the resolution of $\Delta z_{\text{max}}$.

Figure 5. (a) A cascade plot where each trace shows the pressure measured at transducer $(35, 80 \text{ mm})$ for simulations run with different spill times ($\Theta = 1.05 \mu\text{s}$ at top through $\Theta = 40.5 \mu\text{s}$ at bottom). A gray dashed line is added to track the $\gamma$ compression and rarefaction peaks. (b) $\tau_{\text{p-to-p}}$ is plotted versus spill time ($\Theta$). The deviation at $\Theta = 20.3 \mu\text{s}$ is due to overlap of the $\alpha$ rarefaction and $\gamma$ compression peaks. A diagonal line ($\tau_{\text{p-to-p}} = \text{spill time}$) is plotted for reference. (c) $\tau_{\text{FWHM}}$ is plotted versus spill time ($\Theta$).
interference of microscopic pressure waves generated by microscopic volumes. Thus, increasing the overall size of the heated region by increasing the diameter will increase the width of the observed pressure wave.

The dependence on diameter is consistent with our previous observation: the $\alpha$ peak is generated by the pre-Bragg peak heated cylinder while the $\gamma$ peak results from the Bragg peak disc. As the diameter of the cylinder is increased, the $\tau_{\text{FWHM}}$ of the $\alpha$ and $\gamma$ compression and rarefaction peaks increase. At the monitored transducer, however, the $\alpha$ peaks are more affected (larger slope in figure 6) than the $\gamma$ peaks. We expect the slope relating $\tau_{\text{FWHM}}$ to the radial FWHM, $\sigma$, to depend on the projection of the diameter (along the $\hat{s}$ direction) onto the propagation direction of the $\alpha$ ($\hat{s}$ direction) and $\gamma$ ($\hat{l}$ direction) pressure waves.

The effect of changing the Bragg peak width was determined by simulating the pressure waves generated by SOBP of widths that vary from 1 to 30 mm. The resulting pressure waves are shown in figure 7. Consistent with our assignments, the time dependence and shape of the $\alpha$ peaks are unaffected by increasing the SOBP width. The $\gamma$ peaks, however, show a drastic change with $\psi$. As the width is increased, the compression $\gamma$ peak (marked with a *) is washed out due to destructive interference while the width of the rarefaction $\gamma$ peak increases. To quantify the changes, the 1st derivative of the pressure waves were calculated, and a Gaussian was fit to the rarefaction $\gamma$ peak. The width of the fit Gaussian, 1st derivative $\tau_{\text{FWHM}}$, increases monotonically with $\psi$ (figure 7(b)), but beyond $\psi = 10$ mm, the $\tau_{\text{FWHM}}$ plateaus. No metrics were found that consistently and quantitatively correlate with the SOBP width.

4. Discussion

The characteristic proton beam energy deposition profile can be thought of as the linear combination of two geometrical shapes: a pre-Bragg peak cylinder that generates the $\alpha$ pressure wave and a high-amplitude Bragg peak disc that generates the $\gamma$ pressure wave.

Acoustic measurements can characterize many aspects of a proton beam passing through water. Most important, without having to run simulations to map dependencies, the distances separating the transducer from the beam axis ($s$) and Bragg peak center ($l$) can be determined directly from the arrival times ($\tau_{\text{center}}$) of the $\alpha$ and $\gamma$ peaks, respectively. This allows for range verification of clinical proton irradiation sources. To quantify the error in these measurements, $s$ and $l$ were calculated from $\tau_{\text{center}} \times c = s_{\text{calc}}$ and $\tau_{\text{center}} \times c = l_{\text{calc}}$, and the actual values were subtracted for the simulation with $\Theta = 1.05 \mu s$. The errors are shown as a histogram in figure 8. The $s_{\text{calc}}$ consistently overshoots $s_{\text{act}}$ by ~1 mm. This may be due to asymmetry in
the $\alpha$ compression and rarefaction peaks or the quantized nature of our simulated water volume. The $l_{\text{calc}}$ from the pre-Bragg and post-Bragg peak region is within $\pm 0.5$ mm and $\pm 1$ mm, respectively, although the error is slightly dependent on the magnitude of $l$. A previous experimental study calculated a $\sim 3$ mm error in Bragg peak position based on the post-Bragg arrival time (Tada et al 1991).

Based on these small errors, which will likely become larger with the introduction of experimental laboratory noise, acoustic measurements should be taken at more than one position either by moving a single transducer or employing an array of transducers. To clearly separate the $\alpha$ and $\gamma$ peaks, some transducers should be placed in the pre-Bragg peak region. To average out errors in calculating $s$, transducers should be placed at different $\phi$ positions. To average out errors in calculating $l$, transducers should also be placed in the post-Bragg peak region. Although our simulations were done with small beam sizes, the error here in determining the Bragg peak position for a pristine beam is on the order of 1 mm. This error is similar

Figure 7. (a) A cascade plot of the pressure waves measured for SOBP of width $\psi$ (ranging from 1 to 30 mm as described in table 1). The pressure amplitude is magnified by x5 after the $\alpha$ peaks. The * indicates the $\gamma$ compression peak. (b) The $\tau_{\text{FWHM}}$ of the 1st derivative of the $\gamma$ rarefaction pressure peak, $dp/dt$ (shown in the box in a).

Figure 8. A transducer’s distance from the beam propagation axis ($s$) and Bragg peak ($l$) can be calculated from $r_{\text{center}} \times c = s_{\text{calc}}$, and $r_{\text{center}} \times c = l_{\text{calc}}$. Here, the error in these measurements ($\delta_s = s_{\text{act.}} - s_{\text{calc.}}$) is shown as a histogram of values. (a) $\delta_s$ (from $\alpha$ peaks), (b) $\delta_l$ ($\gamma$ peaks in pre-Bragg region), and (c) $\delta_l$ ($\gamma$ peaks in post-Bragg region) are shown for $\Theta = 1.05 \mu s$. 

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if not better than errors observed for the alternative range verification methods, PET imaging and prompt gamma. Acoustic range measurement has the advantage of reporting on other beam characteristics, and it may be simpler and faster.

Interestingly, our simulations show that determining the Bragg peak position based on the arrival times \( \tau_{\text{center}} \) of the \( \alpha \) and \( \gamma \) pressure waves is more reliable than measuring the maximum pressure at different \( z \)-positions (figure 4), as has been attempted before (Sulak et al 1979, Albul et al 2005) because the maximum pressure method requires calibration to account for the >5 mm mismatch. This is because the pre-Bragg cylinder \( \alpha \) peaks’ intensity constrictively interferes with the \( \gamma \) pressure waves to skew the \( z \)-position of maximum pressure towards \( z < R_0 \).

Other information, such as the radial width of the beam (\( \sigma \)), the spill time (\( \Theta \)), and the width of the Bragg peak (\( \psi \)) can also be determined from the acoustic pressure wave signal. The width (\( \tau_{\text{FWHM}} \)) of the \( \alpha \) compression peak and the \( \gamma \) rarefaction peak scale linearly with the diameter of the beam while the time separation between compression peak and rarefaction trough (\( \tau_{\text{p-to-p}} \)) scales linearly (when \( \Theta \) is large enough) with the spill time. This information is useful, but the scaling constants that relate the observables to beam characteristics must be determined for specific systems. For example, determining how \( \tau_{\text{FWHM}} \) scales with \( \sigma \) requires mapping either through experiment or simulations customized for the specific experimental variables.

The SOBP simulations were of particular interest. In the clinic, the SOBP dose is produced by sequentially administering pristine Bragg peak beams with \( R_0 \)’s varied by adjusting the kinetic energy of the protons and amplitudes varied by changing the number of protons emitted. At the end of the dose, the sum of the incremental doses produces the desired SOBP energy deposition profile. If one can separately measure the acoustic pressure generated by each pristine Bragg peak dose, then one can characterize each beam deposition separately. If, however, the synchronization is difficult, one can also average together the signal from the individual depositions. The simulations performed here show what the sum of the individual pressure waves will look like, which is equivalent to the pressure wave produced if a SOBP was deposited at once with a well defined spill time (\( \Theta \)). Unfortunately, beyond a SOBP width (\( \psi \)) of \( \approx 10 \text{ mm} \), the \( \gamma \) peaks are washed out due to destructive interference and beam characterization becomes difficult.

The quantized nature of our water box elements and the computation limitations on our dimensions intrinsically limited our frequency spectrum to less than 500 kHz. Because the time width of the pressure waves is related to the geometrical size of our system (the expected signal frequency is approximately the speed of sound divided by the diameter of the beam (Baily 1992)), the necessary frequency response of an appropriate transducer is also tied to the geometry of the beam. If finer spatial resolution is needed, a higher frequency transducer is necessary (Xu and Wang 2006).

One important aspect that the present simulations did not include is the treatment of pressure amplitude. Because the actual expected amplitude is affected by numerous variables such as beam energy, beam diameter, water temperature, transducer position, transducer sensitivity, and spill time, we did not consider the amplitude. Rather, we assumed the system has a linear response and focused on the functional form and relative intensities to assess the information content of the acoustic signals. As a simple calculation of the expected pressure amplitude, 1 cGy dose delivered in 1 \( \mu \text{s} \) will (dividing by \( C_p \)) create a 2.4 \( \mu \text{K} \) temperature change and a corresponding (multiplying by \( \rho \beta c^2 \) and dividing by the pulse length, where \( \rho \) is the density) \( p_{\text{source}} \) of \( 1.4 \times 10^6 \text{Pa s}^{-1} \). Based on preliminary simulations, this generates an observed pressure on the order of \( 5 \times 10^{-2} \text{Pa} \), which is a factor of 10 lower than the 50 Pa/Gy previously reported (Tada et al 1991). Although the expected signal is small relative to

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standard ultrasound levels, averaging the protoacoustic signal measured with low noise, amplified transducers has made experimental observation with clinical doses possible (Tada et al 1991).

For our simulations, we assumed that the deposited energy was instantaneously converted to heat, we ignored heat diffusion, and we assumed the pressure waves propagated linearly without loss. These approximations appear to be valid. Ionization energy is converted into heat on the $10^{-12}$ s timescale (Gauduel et al 1990), which is 5 orders of magnitude faster than our simulation time step. For heat diffusion considerations, the 1 mm grid spacing of our simulations defines our minimum length scale of interest, $L_p$. The timescale of heat diffusion, $\tau_{th}$, for $L_p = 1$ mm is $1.8$ s, according to $\tau_{th} \sim L_p^2/4D_T$, where $D_T$ is the thermal diffusivity of the sample (water) (McKenzie 1990). For our simulation, $\tau_{th}$ is much greater than $\Theta$, our pulse width, which satisfies thermal confinement and validates ignoring heat diffusion. At long times, heat diffusion will cause a change in the temperature and a resulting pressure wave, but the amplitude will be small due to the slow change. Thermal diffusion will become relevant for a simulation with a $40\mu$s pulse once the grid spacing is reduced to $\sim 5\mu$m. Nonlinear propagation effects are expected for large pressure amplitudes propagating over long distances (Muir and Carstensen 1980). For our simulations, given the small amplitude expected (<1 Pa) and the short distance (<4 cm) between the beam axis and the transducer element, we maintain that the linear propagation assumption is valid. Experimentally measured protoacoustic waves retain their bipolar shape and do not exhibit sawtooth peak distortions, which suggests linear propagation (Learned 1979, Albul et al 2004). Even if nonlinear distortions of the pressure waves were to occur, we assume that they would affect the wave shape with a minimal affect on the arrival time. In this study we assumed lossless acoustic propagation. Consideration of the attenuation will reduce the amplitude of the pressure waves, without affecting the arrival time or peak width.

Aside from detecting low pressure amplitudes, density differences in heterogeneous tissue and background noise present further challenges to adapting protoacoustic measurements for in vivo range verification. Tissue heterogeneity will result in acoustic reflection, absorption, refraction, and changes in $c$, all of which will affect the arrival time measurements, potentially distort the pressure wave shape, and add error to the range verification. Triangulating the beam position through transducer measurements at different $\phi$ values will reduce this error. a priori CT, MRI, and/or ultrasound information of the patient-specific tissue structure may also aid in correcting for error. Further simulations and experiments with explicit tissue heterogeneity will help to reveal the complications. Background noise, from the heartbeat for example, if detected, can be averaged out by firing the proton beam at a different repetition rate or during rest periods. Ultimately, the same challenges that face ultrasound and photoacoustic techniques will also complicate protoacoustic range verification, but similar solutions may be applied.

5. Conclusion

Our simulations show that protoacoustic measurements are a powerful tool for proton beam range verification and characterization. The rich information content, relatively low instrumental cost, and predicted ease of use make the proposed range verification method an attractive option for clinical therapeutic quality assurance applications. Further advances in sensitivity and practical engineering may even allow for real-time monitoring of dose distribution by measuring the acoustic waves generated in tissue.
Appendix A: SOBP weighting factor

From (5), for a SOBP that extends from \( d_a = R_0 - \psi \) to \( d_b = R_0 \), pristine Bragg peaks \( B_i(z) \) with maxima at \( R_i \) were summed with a weighting factor, \( W_i \), given by:

\[
W_i(R) = \begin{cases} \frac{n^2 x^{1/n} \sin(\pi / n)}{\pi(n-1)} \left( \frac{\Delta}{2} \right)^{1-1/n} : R = d_b \\ \frac{n^2 x^{1/n} \sin(\pi / n)}{\pi(n-1)} \left[ (d_b - R + \frac{\Delta}{2})^{1-1/n} - (d_b - R - \frac{\Delta}{2})^{1-1/n} \right] : R = d_b - \Delta, d_b - 2\Delta, ... , d_a \end{cases}
\]

(A.1)

where \( \Delta \) is the spacing between \( R_i \) (Bortfeld and Schlegel 1996). We summed over 50 \( B_i(z) \), so \( \Delta = \psi / 49 \).

Appendix B: origin of \( \alpha \) and \( \gamma \) waves

To verify our observation that the \( \alpha \) and \( \gamma \) peaks can be attributed to the pre-Bragg peak ‘cylinder’ and Bragg peak ‘disc’ portion of the proton beam’s deposition profile, we ran two other simulations with modified energy depositions corresponding to a cylinder and a disc. All other details of the simulation, including the Gaussian radial profile, \( E(s) \), were kept the same.
The resulting pressure waves are shown in figure B1. As expected, the cylinder deposition produces the $\alpha$ peak while the disc deposition produces the $\gamma$ peak.

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