Electric field from a proton beam in biological tissues: a potential application in proton radiotherapy

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Abstract

We computed spatio-temporal profiles of the electric field coming from a one-dimensional proton beam as it moves through five different animal tissues: muscle, lung, fat, grey matter and liver. The complex electric permittivity as a function of frequency was assumed to follow the Cole-Cole model, containing experimentally determined parameters for each tissue. The shape of the tissues was taken to be a cylinder with a radius of 10cm. The initial proton energies were chosen so as to yield the same range, i.e. depth at which the protons stop, inside all tissues. We considered two beams, both of them a square pulse, lasting 10ns and 100ns. Our results show that, for both beams, the maximal radial electric field at the outer boundary of a tissue is of the order of 150 millivolts per cm for all five tissues. Furthermore, soon after the last proton in the beam comes to a rest, the spatial profile of the radial electric field along the beam axis acquires a maximum that coincides with the proton range. The measurable magnitude of the electric field and its spatial profile lend themselves to an application in proton radiotherapy, where the proton range is an important quantity of interest.

INTRODUCTION

Proton radiotherapy offers an effective treatment of cancer with less damage to healthy tissue than conventional x-ray based treatment. This is in part due to the radically different dose profiles of these two types of particle: for x-rays, the maximum dose occurs upon the photon's entrance to the tissue; for protons, this maximum, known as Bragg peak, occurs near the end of the proton's range, where the dose falls off very rapidly (within a few millimeters). This means that, by giving the protons the correct energy, the maximum dose will be delivered to the tumor rather than a healthy tissue. However, this fortunate property of heavy ions comes at a price: the proton's range is very sensitive to changes in the tissue through which it passes [1]. Anatomical deformations, patient misalignment, and tumor shrinkage are just some of the issues causing the proton range to deviate from the desired range stipulated by the treatment plan. It is therefore imperative that a reliable way of measuring the proton range be available to clinicians, thus enabling them to keep track of the validity and effectiveness of the planned treatment.

To date, measuring the range inside a patient has not been an easy task. In this regard, the main focus has been centered on proton radiography (PR) [2–4], wherein a low intensity proton beam carrying enough energy to traverse the patient is captured in a multilayer ion chamber, allowing for a reconstruction of the Bragg peak. Though this method does provide some information about the beam's interaction with the patient's anatomy, it does not allow for accurate determination of proton range inside the patient.

Currently, the best candidate for measuring proton range within a patient is a device called the Prompt gamma camera (PGC) [5–8], which detects gamma radiation coming from the collisions between the protons in the beam and the nuclei of the tissue. It has been demonstrated that the PGC can be used to determine the range to within a few millimeters. However, one drawback of the PGC is its poor resolution near a low-density material, such as an air cavity, where the range uncertainty can be as large as the cavity itself. Another

FIG. 1. A schematic diagram of the setup. The gray block represents the medium. The red line indicates the beam, the end of which coincides with the range.

approach to detecting the Bragg peak, and thereby the range, is to measure the thermoacoustic signal resulting from energy transfer between the protons and the tissue [9–11].

In this paper we offer another way to determine the proton range: by measuring the electric field produced by the beam. To simplify our calculations, we choose a square pulse for a beam with no lateral extension. The motion of protons in the beam is described by a macroscopic model, wherein the medium through which they travel acts as a friction force, causing the protons to decelerate in a continuous fashion. From Maxwell’s equations we derive analytical expressions for the electric field in frequency space and then integrate them numerically to obtain the field’s spatio-temporal profile. The complex electric permittivity of the five tissues – muscle, lung, fat, grey matter and liver – is assumed to follow the Cole-Cole model, with the model parameters for all five tissues taken from published literature. The results of our computations reveal a correlation between the radial component of the electric field along the beam axis and the proton range for beam pulses lasting 10ns and 100ns. Coupled with the field’s magnitude of $\sim 150\text{mV/cm}$, we argue that this is a measurable effect that may be applicable in proton radiotherapy.

ELECTRIC FIELD FROM A PROTON BEAM

Moving protons interact with matter in three ways: 1) elastic proton-electron scattering; 2) elastic proton-nucleus scattering; and 3) inelastic proton-nucleus scattering. The first process is the main source of kinetic energy loss of the protons. The second process contributes

negligibly to the proton's energy loss and is mainly responsible for beam broadening. In the third process, which affects about 10 % of protons on average, the protons undergo a head-on collision with the nuclei of the tissue and are absorbed; the nuclei become unstable and emit a variety of particles, including He^3 , He^4 , α -particle, gamma ray, electron, neutron, and proton. The macroscopic net effect of all these processes is a continuous deceleration of the beam. In what follows, we consider a one-dimensional finite train of protons of a constant linear density incident on a biological tissue of cylindrical shape (see Figure (1))

For simplicity, we let the nozzle of the proton gun to be right up against the medium, i.e. at $z = 0$, and assume that the electric field for $t < 0$ is zero everywhere in the region $z > 0$. In other words, we assume that the electric field is unable to penetrate the nozzle. The equations describing the average motion of a single proton are the following:

$$\begin{aligned}\frac{dp}{dt} &= -F(K) \\ \frac{dz}{dt} &= \frac{cp}{\sqrt{(mc)^2 + p^2}},\end{aligned}\tag{1}$$

where p is the proton's momentum, z its position, c is the speed of light and m is the proton's rest mass. $F(K)$ is the force of friction, also known as stopping power (SP) and

$$K = \sqrt{(pc)^2 + (mc^2)^2} - mc^2\tag{2}$$

is the proton's kinetic energy. The form of F was derived by Bethe and Block for energies between 1 and 500 MeV [12]:

$$F = a_1 \frac{(\tilde{K} + 1)^2}{\tilde{K}(\tilde{K} + 2)} \left[\ln \tilde{K}(\tilde{K} + 2) - \frac{\tilde{K}(\tilde{K} + 2)}{(\tilde{K} + 1)^2} + a_2 \right],\tag{3}$$

where a_1 and a_2 are constants which depend on the medium and $\tilde{K} = K/mc^2$. For water, $a_1 = 0.1713$ and $a_2 = 9.47448$. For energies less than 1 MeV, F fails to represent the correct stopping power. Figure 2 shows the agreement and lack thereof between F and the measured SP in water. A low energy SP has been derived analytically; however, its form is not trivial. Since we are not attempting to solve equations (1) analytically, we let F be a linear interpolation of the data in the energy range $[0, 500]$ MeV.

FIG. 2. A) Stopping power as a function of kinetic energy. B) A plot of proton position, speed and deceleration.

In Fourier space, Maxwell's equations inside dielectrics have this form:

$$i\mathbf{k} \cdot \mathbf{D}(\omega, \mathbf{k}) = \rho_p(\omega, \mathbf{k}) \quad (4)$$

$$i\mathbf{k} \cdot \mathbf{B}(\omega, \mathbf{k}) = 0 \quad (5)$$

$$\mathbf{k} \times \mathbf{E}(\omega, \mathbf{k}) = \omega \mathbf{B}(\omega, \mathbf{k}) \quad (6)$$

$$\frac{i}{\mu} \mathbf{k} \times \mathbf{B}(\omega, \mathbf{k}) = \mathbf{J}_p(\omega, \mathbf{k}) - i\omega \mathbf{D}(\omega, \mathbf{k}), \quad (7)$$

where $\rho_p(\omega, \mathbf{k})$ and $\mathbf{J}_p(\omega, \mathbf{k})$ are the proton's charge density and current respectively, and μ is the magnetic susceptibility, which we take to be the same as for vacuum, $\mu = \mu_0$. Coupled with the relation $\mathbf{D} = \epsilon(\omega)\mathbf{E}$ and the vector identity $\mathbf{A} \times (\mathbf{B} \times \mathbf{C}) = (\mathbf{A} \cdot \mathbf{C})\mathbf{B} - (\mathbf{A} \cdot \mathbf{B})\mathbf{C}$, Eqs. (4), (6) and (7) can be combined into one equation for $\mathbf{E}(\omega, \mathbf{k})$:

$$\mathbf{E}(\omega, \mathbf{k}) = \frac{-i}{\epsilon(\omega)} \frac{\omega \mathbf{J}_p(\omega, \mathbf{k})/c(\omega)^2 - \mathbf{k} \rho_p(\omega, \mathbf{k})}{k^2 - \left(\frac{\omega}{c(\omega)}\right)^2}, \quad (8)$$

where $c(\omega) = 1/\sqrt{\mu\epsilon(\omega)}$ is the speed of light as a function of the angular frequency ω . Inside dielectric materials, the function $\epsilon(\omega)$ has a real and an imaginary component, $\epsilon(\omega) =$

$\epsilon'(\omega) + i\epsilon''(\omega)$, the details of which will be discussed later. In real space, the density and current of a moving point charge are described by these expressions:

$$\rho_p(t, \mathbf{r}) = q\delta(x)\delta(y)\delta(z - z_p(t))\theta(t) \quad (9)$$

$$\mathbf{J}_p(t, \mathbf{r}) = qv(t)\delta(x)\delta(y)\delta(z - z_p(t))\theta(t)\hat{\mathbf{z}}, \quad (10)$$

where $z_p(t)$, the proton's position, is a solution of Eqs. (1), and $v(t) = dz_p(t)/dt$ is the proton's speed. The step function, $\theta(t)$, which is 1 for $t \geq 0$ and 0 for $t < 0$, conveys our assumption that the beam is electrically well shielded while the protons are inside the nozzle. Due to the non-trivial dependence of z_p and v on time, the Fourier transform of Eqs. (9) is also non-trivial:

$$\begin{aligned} \rho_p(\omega, \mathbf{k}) &= \frac{1}{(2\pi)^4} \int_{-\infty}^{\infty} dt d\mathbf{x} \rho_p(t, \mathbf{r}) e^{-i\omega t + i\mathbf{k} \cdot \mathbf{r}} \\ &= \frac{q}{(2\pi)^4} \int_0^{\infty} dt e^{-i\omega t + ik_z z_p(t)} \end{aligned} \quad (11)$$

$$\begin{aligned} \mathbf{J}_b(\omega, \mathbf{k}) &= \frac{1}{(2\pi)^4} \int_{-\infty}^{\infty} dt d\mathbf{x} \mathbf{J}_p(t, \mathbf{r}) e^{-i\omega t + i\mathbf{k} \cdot \mathbf{r}} \\ &= \frac{q}{(2\pi)^4} \int_0^{\infty} dt \mathbf{v}(t) e^{-i\omega t + ik_z z_p(t)}, \end{aligned} \quad (12)$$

where $\mathbf{v}(t) = v(t)\hat{\mathbf{z}}$. The electric field in real space is the inverse Fourier transform of Eq. (8), and reads

$$\mathbf{E}(t, \mathbf{r}) = -\frac{q}{(2\pi)^4} \int_{-\infty}^{\infty} d\omega \int_0^{\infty} dt' \times \left(c(\omega) \nabla + \boldsymbol{\beta}(\omega, t') \frac{\partial}{\partial t} \right) \frac{e^{i\omega(t-t')} I(\omega, t', \mathbf{r})}{c(\omega) \epsilon(\omega)}, \quad (13)$$

in which $\boldsymbol{\beta}(\omega, t') = v(t')\hat{\mathbf{z}}/c(\omega)$ and

$$I(\omega, t', \mathbf{r}) = \int_0^{\infty} k dk \int_{-\infty}^{\infty} dk_z \int_0^{2\pi} d\theta \frac{e^{-ik_z \Delta z(t') - ikr \cos \theta}}{k^2 + k_z^2 - \left(\frac{\omega}{c(\omega)} \right)^2}, \quad (14)$$

with $\Delta z(t') = z - z_p(t')$. The integration over θ yields $2\pi J_0(rk)$, which leads to

$$I(\omega, t', \mathbf{r}) = 2\pi \int_0^{\infty} k dk \int_{-\infty}^{\infty} dk_z \frac{J_0(rk) e^{-ik_z \Delta z(t')}}{k^2 + k_z^2 - \left(\frac{\omega}{c(\omega)} \right)^2}. \quad (15)$$

The last two integrals can be worked out with the help of these integral identities:

$$\begin{aligned} \int_0^{\infty} dx \frac{x J_0(x)}{x^2 + z_1} &= K_0(\sqrt{z_1}) \\ \int_{-\infty}^{\infty} dx K_0(a\sqrt{x^2 + z_2}) e^{-ibx} &= \pi \frac{e^{-i\sqrt{z_2}\sqrt{a^2 + b^2}}}{\sqrt{a^2 + b^2}}, \end{aligned} \quad (16)$$

where a and b are real numbers, and z_1 and z_2 are complex numbers. The last integral identity is valid only if $\text{Re}(z_2) \geq 0$ and $\text{Im}(z_2) \leq 0$. Substituting $z_1 = r[k_z^2 - (\omega/c(\omega))^2]$, $z_2 = (\omega/c(\omega))^2$, $a = r$ and $b = \Delta z(t')$, and applying the identities in the order they appear, yields

$$I(\omega, t', \mathbf{r}) = 2\pi^2 \frac{e^{-i\frac{\omega R(t')}{c(\omega)}}}{R(t')}, \quad (17)$$

where

$$R(t') = \sqrt{r^2 + \Delta z(t')^2}. \quad (18)$$

Carrying out the differential operation in Eq. (13), as well as the integral of Eq. (24), the frequency spectrum of the electric field along the z and r axes reveals itself to be:

$$\begin{aligned} E_z(\omega, \mathbf{r}) &= \Phi_0 \int_0^\infty dt' f_z(t', \omega, \mathbf{r}) e^{-i\omega(t' + \frac{R'}{c(\omega)})} \\ E_r(\omega, \mathbf{r}) &= \Phi_0 \int_0^\infty dt' f_r(t', \omega, \mathbf{r}) e^{-i\omega(t' + \frac{R'}{c(\omega)})} \end{aligned} \quad (19)$$

where $\Phi_0 = qN/(4\pi\epsilon_0)$ and

$$f_z(t', \omega, \mathbf{r}) = \frac{1}{2\pi\epsilon_r(\omega)} \left[\frac{\Delta z'}{R'^3} + \frac{i\omega\Delta z'}{c(\omega)R'^2} - \frac{i\omega\beta'}{c(\omega)R'} \right] \quad (20)$$

$$f_r(t', \omega, \mathbf{r}) = \frac{1}{2\pi\epsilon_r(\omega)} \left[\frac{r}{R'^3} + \frac{i\omega r}{c(\omega)R'^2} \right]. \quad (21)$$

Here $R' = R(t')$, $\Delta z' = \Delta z(t')$, $\beta' = \beta(\omega, t')$ and $\epsilon_r(\omega) = \epsilon(\omega)/\epsilon_0$ is the relative permittivity. The integral over t' must be evaluated numerically for every value of ω ; however, the integral can be split into two parts – numerical and analytical. Because the protons come to a complete stop at some time t_s , the functions $z_p(t')$ and $v(t')$, and hence the integral itself, become time independent for $t' \geq t_s$. Thus, the expressions in Eq. (19) read

$$\begin{aligned} E_z(\omega, \mathbf{r}) &= \Phi_0 \left[\int_0^{t_s} dt' f_z(t', \omega, \mathbf{r}) e^{-i\omega(t' + \frac{R'}{c(\omega)})} - \frac{i}{\omega} f_z(t_s, \omega, \mathbf{r}) e^{-i\omega(t_s + \frac{R(t_s)}{c(\omega)})} \right] \\ E_r(\omega, \mathbf{r}) &= \Phi_0 \left[\int_0^{t_s} dt' f_r(t', \omega, \mathbf{r}) e^{-i\omega(t' + \frac{R'}{c(\omega)})} - \frac{i}{\omega} f_r(t_s, \omega, \mathbf{r}) e^{-i\omega(t_s + \frac{R(t_s)}{c(\omega)})} \right]. \end{aligned} \quad (22)$$

For a beam, the electric field can be computed by invoking the principle of superposition

$$\mathbf{E}^b(\mathbf{r}, t) = \sum_{n=0}^{N-1} \mathbf{E}(\mathbf{r}, t - n\Delta z/v_0), \quad (23)$$

where Δz is the average distance between two neighboring protons before they enter the medium, v_0 is their initial velocity, and N is the total number of protons in the beam. For proton beams with high linear density, Eq. (23) can be approximated by an integral:

$$\mathbf{E}^b(t, \mathbf{r}) = \frac{N}{T} \int_0^T \mathbf{E}(t - \tau, \mathbf{r}) d\tau, \quad (24)$$

where T is the duration of the beam. The Fourier transform of Eq. (24) leads to

$$\mathbf{E}^b(\omega, \mathbf{r}) = \frac{N}{T} \frac{(e^{-i\omega T} - 1)}{-i\omega} \mathbf{E}(\omega, \mathbf{r}), \quad (25)$$

Finally, using the Cole-Cole model of complex relative permittivity [13–15],

$$\epsilon_r = \frac{\epsilon(\omega)}{\epsilon_0} = \epsilon_s + \sum_{j=1}^n \frac{\Delta\epsilon_j}{1 + (i\omega/\omega_j)^{1-\alpha_j}} - \frac{i\sigma}{\epsilon_0\omega} \quad (26)$$

and applying the boundary conditions

$$\begin{aligned} E_r(\omega, r = R^+) &= \frac{\epsilon_+(\omega)}{\epsilon_-(\omega)} E_r(\omega, r = R^-) \\ E_z(\omega, r = R^+) &= E_z(\omega, r = R^-), \end{aligned} \quad (27)$$

where the plus and the minus refer to the outer and inner side of the boundary respectively, the electric field can now be computed for appropriate parameters ϵ_s , σ , $\Delta\epsilon_j$, ω_j and α_j whose values will be discussed in the next section.

RESULTS

For each of the five tissues, the beam energy was chosen by imposing a range of 15.6cm, which is the range in water at 150 MeV. The relation between the range in water and the range in other substances is $R_{\text{H}_2\text{O}} = S^{\text{rel}} R_s$, where R_s is the range in the given substance and S^{rel} is the stopping power of that substance relative to the stopping power of water. Combining this with the relation between $R_{\text{H}_2\text{O}}$ and the initial kinetic energy K , $R_{\text{H}_2\text{O}} = \alpha K^{1/p}$, where $\alpha = 0.0022$ and $p = 1.77$ [16], we obtain

$$K = \left(\frac{S^{\text{rel}} R}{\alpha} \right)^{1/p}. \quad (28)$$

To reach the range of 15.6cm in a tissue of choice, we multiplied $F(K)$ in Eq. (2) by S^{rel} of that tissue. The relative stopping powers for the five tissues have been experimentally

FIG. 3. Spatio-temporal contour maps of the z- and r-components of the electric field.

FIG. 4. A) Maxima of E_r starting from $t = 4$ ns. B) Temporal (upper graph) and spatial (bottom graph) profiles of E_r at $z = 15.6$ cm and $t = 20$ ns, respectively.

determined. For muscle, grey matter and liver, they are 1.032; 0.984 for fat; and 0.273 for lung.

In order to reduce the double integration over ω and t' into a single integration over ω only, we partitioned t' in the integrals of Eqs. (22) into segments of length $t_s/1000$. Then, for each value of t' , $t = [0, 20]$ ns in increments of 0.1, $z = [10, 20]$ cm in increments of 1, and $r = R^+ = 10$ cm, we integrated numerically the expressions in Eq. (22) over

TABLE I.

Parameter	Muscle	Lung(inflated)	Grey matter	Liver	Units	None
ε_s	3.91	4.44	2.32	12.7	4.52	None
Δ_1	55	14.6	2.14	32.3	36.8	None
Δ_2	663	646	19.7	1170	2550	None
ω_1	113	101.16	126.29	117.496	106.185	GHz
ω_2	4.9	20.231	53.40	14.828	7.037	MHz
α_1	0.165	0.001	0.002	0.075	0.017	None
α_2	0.387	0.181	0.259	0.315	0.219	None
σ	0.633	0.0842	0.0222	0.173	0.140	S/m

$\omega = [-60, 60]$. Plotting Eqs. (22) for different values of t' , t and z , we confirmed by visual inspection that frequencies of 60GHz and beyond are completely negligible. Due to the highly oscillatory nature of Eqs. (22), we divided the integration over ω into 120 sections, $([-60, -59], \dots, [-1, 0], [0, 1] \dots [59, 60])$, in order to reduce numerical inaccuracies. The parameters ε_s , σ , $\Delta\varepsilon_j$, ω_j and α_j , of Eq. (26) for $n = 2$ were chosen for different tissues presented in Table 1 [13].

We computed the electric field for $T = 10\text{ns}$ and $N = 10^8$. In Figure (3) we present a density plots for the z- and r-component of the electric field. Due to the boundary conditions in Eqs. (27), the z-component of the electric field is much weaker than its r-component, which experiences a jump across the boundary. Also, the pattern in the z-t plane of the z-component does not seem to show any uniqueness near the range; whereas the maxima of the r-component approach the range as time exceeds 15ns for all five tissues, as shown in Fig. (4A). For a more accurate estimation of the maxima, we repeated all numerical computations for the depths between 15cm and 16cm in increments of 0.1cm. The top and bottom graphs of Fig. (4B) show the r-component of the electric field as a function of time at $r = 15.6\text{cm}$ and as a function of depth at $t = 20\text{ns}$, respectively. To understand the effects of the beam length on the magnitude and spatial profile of the r-component of the electric field, we also computed the temporal and spatial profiles similar to those in Fig. (4B) for $T=100\text{ns}$. Fig. () shows E_r for $T=100\text{ns}$ superimposed over E_r for $T=10\text{ns}$ between 0 and 20ns, and also E_r for $T=100\text{ns}$ with the time axis scaled up by ten.

FIG. 5. Superposition of E_r for $T = 10\text{ns}$ and E_r for $T = 100\text{ns}$ as functions of time, and E_r for $T = 100\text{ns}$ as a function of time scaled by 10.

DISCUSSION

We have computed the electric field from a proton beam traveling inside five biological tissues: muscle, lung, fat, Grey matter and liver. The z-component of the field was relatively small in magnitude and did not reveal any spatial pattern in the vicinity of the range. However, for all five tissues, the magnitude of the r-component was much larger, approximately 145mV/cm , once all the protons have come to a stop, and it exhibited a clear spatial pattern with its maximum coinciding with the range. Despite large differences in some parameter values of the Cole-Cole model, this pattern remains robust across all five tissues for beams of 10ns and 100ns .

All of our calculations have been done under the assumption that the medium in which the protons travel is continuous. This, of course, is not the case for real media. In a real

medium, the protons would be scattered at non-zero angles to the beam axis, causing the beam to broaden as it moves through the medium. Furthermore, a realistic beam will always have a lateral spread of a few millimeters. Also, the stochastic nature of these interactions would lead to a distribution of ranges: each proton would stop at a different depth. The overall range would then be the average of these depths. Since this distribution is not symmetric but skewed to the left, we decided to check its effect on the electric field by computing

$$\langle E_r \rangle_{max} = \int_{-\infty}^{\infty} P(y) E_r(d+y) dy, \quad (29)$$

$$P(y) = \frac{1}{\sqrt{2\pi}\sigma} e^{-(y-\mu)^2/2\sigma^2} \left[1 + \operatorname{erf} \left(\frac{\alpha(y-\mu)}{\sqrt{2}\sigma} \right) \right],$$

where $E_r(d+y)$ is the electric field computed earlier at $t = 20\text{ns}$. The three parameters of the skew-normal distribution μ , σ and α define its average, variance and skewness, respectively. For the average to be zero, the relation $\mu = -\sqrt{2/\pi}(\sigma\alpha/\sqrt{1+\alpha})$ must hold. We have evaluated the integral in Eq. (29) for combinations of σ and α , the former ranging from 0.1cm to 1cm in increments of 0.1, and the latter from -0.5 to -50 in increments of 0.5. The distribution of values of $\langle E_r \rangle_{max}$ had a standard deviation of 0.005cm, which is negligible. To answer the question regarding the lateral size of the beam, this will require further analysis which we have not done here. However, given how little to no effect did the longitudinal spread have on the range, we suspect that the lateral spread will exert an equally small influence on the shape of the field.

In conclusion, we have shown that a proton beam of intensity relevant in proton radiotherapy generates a growing electric field as it moves through a typical animal tissue, leveling off at approximately 150mV/cm. This is well within a measurable range. The magnitude of the field, once it reaches a plateau, is independent of the length of the beam, at least up to 100ns. This suggests that electric fields from longer beams should also be of similar magnitude. Our results suggest that measuring the electric field from a beam may be possible in a clinical setting. Furthermore, as it is possible to measure fields of far lesser magnitude, a pre-treatment range verification may be put in place, whereby a test beam of much smaller intensity is sent before the treatment beam.

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