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The physics of Cerenkov light production during proton therapy

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Abstract
There is increasing interest in using Cerenkov emissions for quality assurance and \textit{in vivo} dosimetry in photon and electron therapy. Here, we investigate the production of Cerenkov light during proton therapy and its potential applications in proton therapy. A primary proton beam does not have sufficient energy to generate Cerenkov emissions directly, but we have demonstrated two mechanisms by which such emissions may occur indirectly: (1) a fast component from fast electrons liberated by prompt gamma (99.13\%) and neutron (0.87\%) emission; and (2) a slow component from the decay of radioactive positron emitters. The fast component is linear with dose and doxerate but carries little spatial information; the slow component is non-linear but may be localised.

The properties of the two types of emission are explored using Monte Carlo modelling in GEANT4 with some experimental verification. We propose that Cerenkov emissions could contribute to the visual sensation reported by some patients undergoing proton therapy of the eye and we discuss the feasibility of some potential applications of Cerenkov imaging in proton therapy.

Keywords: Cerenkov light, proton therapy, monte carlo, prompt gamma, dose

1. Introduction

Proton therapy is a form of radiotherapy which is rapidly increasing in importance. Around 40 new proton therapy centres are currently being built or planned worldwide (\textit{www.ptcog.ch}), many of which will use the latest type of beam delivery known as spot-scanning. This technique
was developed at the Paul Scherrer Institute in Switzerland (Lomax et al 2004) and uses a narrow proton beam which is rapidly scanned with magnets to give transverse coverage of the tumour and scanned in energy to give cover the depth required. Hence, the dose distribution is complex, 3D and varies with time. This presents challenges to quality assurance (QA) procedures and in vivo dosimetry (Thariat et al 2012). An effective QA procedure is necessary for any modern radiotherapy technique, but is arguably particularly important in proton therapy because an error in delivery can move the Bragg peak, where the dose is maximum, so that part of the tumour is missed or organs at risk might receive the maximum dose.

Current QA procedures for proton therapy are similar to those for photon radiotherapy, relying heavily on measurements with an ionisation chamber in water or a water-equivalent phantom. This gives high quality measurements at a single point in space which can be moved to give profiles. Full 3D measurements can be obtained using grids of ionisation chambers, scintillators, or gel dosimetry but all of these methods have disadvantages and none are in common use (Mijnheer et al 2013). Proton therapy does provide opportunities for in vivo dosimetry which occur as the protons interact with tissue. In particular, measuring prompt gamma emissions and positron emission tomography are being actively researched (Knopf et al 2011, Moteabbed et al 2011).

One new and potentially promising approach is the measurement of optical Cerenkov emissions both for QA and for in vivo dosimetry. These emissions was first described during conventional radiotherapy (Newman et al 2007) and electron therapy (Steidley et al 1989) and are now being actively researched as a tool of quality assurance and in vivo dosimetry in photon and electron radiotherapy (Helo et al 2014, Jarvis et al 2014).

Cerenkov radiation is emitted when a charged particle travels faster than the speed of light in the medium. For a therapeutic photon beam, Cerenkov emission occurs when electrons or positrons generated in a medium via Compton interaction or pair production have a velocity greater than the phase velocity of light in the medium. In water (refractive index $n=1.333$), this occurs when the electron energy exceeds 0.262 MeV (L’Annunziata 2007). The threshold photon energy required to produce Compton electrons which exceed the Cerenkov threshold energy (0.262 MeV) via 180° Compton scatter (in which the maximum energy is transferred to the Compton electrons) is 0.422 MeV (L’Annunziata 2007), while pair production creates electrons and positrons with energy of at least 0.511 MeV, exceeding the Cerenkov light in water. Similarly, a therapeutic electron beam will generate Cerenkov emission in water from both the primary beam and secondary electrons. However, the case is more complex for a proton beam. The threshold energy for a proton to produce Cerenkov light directly is 482 MeV in water (L’Annunziata 2007). This is greater than the maximum energy available for treatment at any centre worldwide, and much greater than the energy of the beam used in this work, which was a 60 MeV proton beam used for eye therapy at Clatterbridge Cancer Centre (Kacperek 2009).

Patients undergoing proton therapy of the eye frequently report seeing flashes of light (Khan et al 2010). Similar sensations, known as phosphenes, have been reported by about 80% of astronauts. The major contribution is thought to be direct stimulation of photoreceptors by charged cosmic rays, with Cerenkov light contributing 5–10% of the visual sensation (anticipated by the shape of the reported light flashes) and minor contributions from stimulation of the optic nerve, stimulation of the retina by secondary particles and scintillation in the lens (Sannita et al 2006, Fuglesang 2007). Similar visual sensations from x-rays have been described for over a hundred years (Röntgen 1898) and it is now well established that visual flashes occur during photon, electron, proton and heavy ion radiotherapy of the eye and brain (Steidley et al 1989, Newman et al 2007, Khan et al 2010, Schardt et al 2013). Although the conventional explanation for light sensation during photon and electron radiotherapy has been direct stimulation of
the retina, it is now accepted that there are also contributions from Cerenkov radiation (Steidley et al 1989, Newman et al 2007). However, the sensation of light during proton and heavy ion therapy has been assumed to be due to causes other than Cerenkov radiation because the primary therapeutic beam has insufficient energy to deliver Cerenkov radiation directly. These causes have been suggested to be emissions generated by interactions between protons and the beamline, production of free radicals close to the retina (Khan et al 2010), or direct stimulation of the retina (Schardt et al 2013). Indeed, (Schardt et al 2013) investigated the mechanism for flashes of light reported by patients undergoing carbon ion radiotherapy for skull base tumours. They concluded that ‘as the ion beam energy is below the Cerenkov threshold (~480MeVn⁻¹), these [light flashes] cannot be caused by Cerenkov light’, and showed that flashes were only observed when the retina was stimulated directly.

We propose that there are mechanisms by which therapeutic proton beams may produce Cerenkov emissions (figure 1), which may contribute to visual sensation. Specifically, a proton may interact with water via Coulomb interactions with electrons, via non-elastic nuclear interactions in which the proton is absorbed by a nucleus and the energy is transferred to either uncharged particles (neutrons or photons) or heavy charged particles (like deuterons and alpha particles), or by the production of radioactive isotopes which emit electrons or positrons.

A proton beam loses its energy mainly by Coulomb interactions with electrons (L’Annunziata 2007) which lead to ionisation and the liberation of secondary electrons. If these secondary electrons have energy exceeding 0.262 MeV then they will emit Cerenkov radiation. A proton beam with energy at least 120 MeV is needed in order for secondary Coulomb electrons to exceed this threshold. A 60 MeV beam, such as the one used in this work, can only produce 140 keV electrons which will not emit Cerenkov light (Jelley 1958). Recently, Glaser et al (2014) presented a simulation study of Cerenkov emission of a monoenergetic 250 MeV proton beam in a water tank and concluded that measuring Cerenkov emission in proton therapy is of little use because of the lack of Cerenkov emission from the Bragg peak, though the Cerenkov emissions from induced radioisotopes could be imaged following treatment.

During non-elastic nuclear interactions, secondary particles (charged and uncharged) are released which may lead to Cerenkov emission either directly (for charged particles) or via further ionisations (for charged or uncharged particles). If these secondary particles are gamma photons, Cerenkov light can be produced indirectly through Compton interaction and pair production. These photons are known as prompt gamma photons and may be

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**Figure 1.** Detailing the different mechanisms by which protons interact with matter and emit Cerenkov radiation.
measured directly to predict dose distribution (Park et al 2010, Kurosawa et al 2012). Fast neutrons may interact with heavy nuclei through elastic scattering or inelastic scattering, producing recoil nuclei (which may ionize the medium) or excited recoil nuclei which emit gamma rays, which may cause further ionisation and thereby Cerenkov light (Willis and Carlile 2009).

Radioactive nuclei are produced along the proton beam path due to non-elastic nuclear interactions. The nuclei which are generated are usually positron emitters. A positron travels a short distance in the medium (less than 1 mm in living tissue (Levin and Hoffman 1999)) before it annihilates with an electron and produces two or more gamma ray photons of 0.511 MeV (high enough to produce Cerenkov-producing electrons). This provides an additional mechanism for detection of dose deposition using a positron emission tomography system (Parodi et al 2007, Strååt et al 2013). In addition, positrons with energy higher than 0.262 MeV will emit Cerenkov light (Jelley 1958).

Here, we examine potential mechanisms for optical Cerenkov emission during proton radiotherapy. We identify two different components: (1) a fast component from non-elastic nuclear interactions; and (2) a slow component from positrons and electrons emitted by radioactive decay.

We examine the properties of these two mechanisms in simulation and by measurements taken at the Douglas Cyclotron at the Clatterbridge Cancer Centre. Specifically, we compare the percentage depth dose of a 60 MeV proton beam with simulated distributions of $^1$H, $^1$C and Cerenkov emission in order to explore whether Cerenkov emissions can be used to determine the proton ranges in water. Comparisons are also made between the simulated and measured slow component of Cerenkov emission. The delivered doses are correlated to the fast and slow components with a view to determining whether they can be used for online or offline verification.

2. Method

2.1. Monte Carlo simulation

The dose deposited and the Cerenkov light distribution were modelled using a Monte Carlo simulation (GEANT4.9.6 (Agostinelli et al 2003)) of the 60 MeV clinical proton beam at the Douglas Cyclotron at the Clatterbridge Cancer Centre with realistic proton energy spectrum and beam divergence. The simulation was fine-tuned and validated by comparing the simulated proton dose distributions in water against measurements made during beam quality assurance (QA) measurements with a flat ion chamber (Classic Markus, PTW-Freiburg) which has a sensitive diameter of about 3.5 mm, and a very thin window of <0.1 mm polythene. A circular proton beam of diameter 2.5 cm and energy 60 MeV was simulated irradiating a 5 $\times$ 5 $\times$ 5 cm$^3$ water phantom with 1 mm thick Perspex walls.

A simulated spread-out Bragg peak was composed of 24 pure Bragg peaks from 60 MeV to 16 MeV in 2 MeV intervals. This approximates the range modulator wheel steps used at Clatterbridge for the experiments.

The Cerenkov light yield was scored between 400 nm and 720 nm, which corresponds to the visible range, and the range to which digital consumer CCD cameras are sensitive. The wavelength-dependent refractive index and absorption length of water were added with a spectral resolution of 25 nm (Kasarova et al 2007). The refractive index of air was assumed to be 1.0 and the absorption length of light in Perspex was assumed to be 1.0 m at all wavelengths. The refraction and reflection effects as light travels between water, Perspex and air were included in the simulation (Helo et al 2014).
To simulate the dose and Cerenkov production depth profiles, the deposited energy in the centre of the water phantom and Cerenkov light were scored within a linear array of 0.1 \times 3.5 \times 3.5 \text{mm}^3 scoring volumes. Cerenkov photons were scored in a particular volume only if they were formed in that volume; photons travelling through a volume were ignored. The scoring volume size was chosen to be similar to the size of the ionization chamber used experimentally to measure the Bragg peak.

Radioactivity introduced to the water phantom by proton-nuclear interactions was simulated. Different isotopes produced in water were identified with their percentage composition, along with the decay emission spectrum, the half-life and the average number of Cerenkov photons produced by each isotope.

The emission spectra of secondary particles were recorded at a resolution of 0.01 MeV in order to estimate the contribution of each secondary particle type to Cerenkov emission.

The number of Cerenkov photons which hit the human retina when the eye is irradiated by a circular proton beam with diameter of 1 cm and energy of 60 MeV was simulated by approximating the eyeball to a sphere of 2.5 cm diameter (Kolb et al 1995) made of water (the refractive index of water is 1.333, while the refractive index of vitreous humour is 1.336). The retina was simulated as a spherical shell covering 65% of the inside of the eyeball with thickness 0.1 mm (Kolb et al 1995). The fovea was modelled as a sphere 1.8 mm in diameter, embedded in the retina and positioned 2.5 mm away from the eye’s horizontal axis (Kolb et al 1995).

All simulations used \(10^8\) protons unless stated otherwise. In GEANT4, a cut-off value is required, below which the particle is no longer assumed to produce secondary particles. Here, a cut-off of 0.01 mm (i.e. \(~0.025\text{ MeV}\) for electrons in water) was chosen (Agostinelli et al 2003, Helo et al 2014).

2.2. Validation of Monte Carlo simulation

2.2.1. Depth dose and transverse profile. Figure 2 shows the depth dose profiles generated by Monte Carlo simulation for a pure 60 MeV Bragg peak and a spread-out Bragg peak. Both reproduced data measured with an ionization chamber and film to within 1%.

2.3. Optimization of position of photomultiplier tube

In order to optimize the measurement of the Cerenkov emissions using a photomultiplier tube (PMT), the Monte Carlo simulation was used to predict the light distribution passing through the top face of the phantom (shown as the Z-plane in figure 3(a)). The Cerenkov light distribution was found by scoring the light in the Z-plane just below the surface of the phantom. Figure 3(b) shows the Cerenkov light distribution for a 60 MeV proton beam travelling along the x-axis and the light distribution depth profile along the x-axis on the Z-plane as a function of distance. The PMT was placed at the point where the light intensity on the surface of the water tank was expected to be greatest.

2.4. Performance tests

All tests were carried out at the Douglas Cyclotron, using a maximum clinical proton energy of 60 MeV, with a 5 \times 5 \times 5 \text{cm}^3 water phantom; the distance between the collimator and the phantom face was 7.2 cm. The Cerenkov light was measured using a photomultiplier tube (H11890-210, Hamamatsu, Japan) equipped with a 2 m optical fibre, fixed 7 mm away from

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the water phantom wall, where we expect the maximum light intensity to be (figure 3). The PMT was remotely controlled from outside the beam room by a PC using a 25 m long USB cable and was placed at 90° with respect to the incident proton beam. The integration time was 1 s. All measurements were subjected to a background subtraction that was obtained in the same lighting conditions but with the beam turned off. All light sources in the room were either turned off or blocked by a black, light-tight sheet during the experiments.

Measurements were taken with a 20 × 20 mm² applicator, at a fixed dose rate of 5 Gy per minute and 60 MeV proton beam. Nominal doses between 1.7 and 25 Gy were delivered and the Cerenkov emissions were counted by summing both the detected photons when the beam was on and also by summing the detected photons for 20 s after the beam was off. (A typical dose per fraction for a treatment is 13 Gy, for choroidal melanomas.)

Figure 2. Comparison of depth dose profiles between Markus ionisation chamber measurement and Monte Carlo simulation. (a) shows a pristine Bragg peak and (b) a spread-out Bragg peak. The error-bars show the standard deviation of the simulation data.

Figure 3. (a) Simulated 2D light distribution in a 5 × 5 × 5 cm³ water phantom irradiated by a 60 MeV proton beam. Refraction and reflection at boundaries were applied. The scoring area is a mesh pixelated into 0.2 × 0.2 mm². (b) Light distribution profile across the Z-face as function of distance.
3. Results

3.1. The production of Cerenkov emission during proton therapy

3.1.1. Fast component of Cerenkov emission. Uncharged particles emitted during proton therapy (gammas and neutrons) can produce Cerenkov light indirectly by ionization of the medium (figure 1). We propose to call these light emissions the ‘fast component’ of Cerenkov production. A simulated fast component pulse following a pulse of $10^7$ protons initiated at $t = 0$ s is shown in figure 5 for a pure Bragg peak beam. The fast component of Cerenkov emissions occurs in less than 1 ns, which is the same as the time scale of prompt gamma emissions (Paganetti 2011).

Gamma emission spectrum. In order to estimate the contribution of gamma photons to the fast component of Cerenkov production, the energy spectrum of gamma emissions up to 20 MeV was simulated, as shown in figure 6 for a pure Bragg peak beam (see also Fiedler et al 2011, Polf et al 2013).

The 0.511 MeV peak from positron-electron annihilation can clearly be seen in the spectrum. The de-excitation nuclear lines of oxygen, carbon and nitrogen are also visible (4.44 MeV emission from $^{12}$C, 5.27 MeV emission from $^{15}$N and 6.13, 6.92 and 7.12 MeV emissions from $^{16}$O nuclei are highlighted). The oxygen peaks are much narrower than those from carbon and nitrogen, which is explained by Doppler broadening having more influence on emissions from the lighter carbon nuclei and nitrogen nuclei than those from oxygen (Polf et al 2013). We found that gamma contributed over 99% of the fast component of Cerenkov emission.

Neutron emissions spectrum. Similarly, the energy spectrum of neutron emissions was simulated (figure 7). This spectrum shows neutron emissions occur over all energies up to 42 MeV. We found that the neutron contribution to Cerenkov emission made up 0.9% of the fast component of Cerenkov production.

3.1.2. Slow component of Cerenkov emission. Positrons and electrons from radioactive nuclei decay may produce Cerenkov light in the medium (figure 1). The production of Cerenkov
light depends on the half-life of the radioactive decay (from a few ms to many minutes); the most abundant $\beta^+$ emitters that were found in the water phantom by Monte Carlo simulation were $^{15}$O and $^{11}$C and are shown in table 1. The most abundant radionuclide found in this work and in similar work was $^{15}$O (Vynckier et al. 1993, Beebe-Wang et al. 2003). We propose to call the optical emissions from radioactive decay the ‘slow component’ of Cerenkov production. The first 240 s of simulated and measured slow components are compared in figure 8. The calculated half-life was 114 s. This result further demonstrates that the contribution of $^{15}$O (half-life = 122.24 s) dominates over that of other radionuclides.

Positron emission spectrum. The simulated energy spectrum of positron emissions up to 3 MeV is shown in figure 9. As expected, positron emission from $^{15}$O (with maximum positron energy of 1.72 MeV) dominates the total positron emission spectrum, and the plot agrees qualitatively with that published by Tuckwell and Bezak (2007) for the decay of $^{15}$O to $^{15}$N.

3.1.3. Eyeball and retina simulation. The geometry of the eyeball simulation is shown in figure 10(a) and the light distribution in the retina is shown in figure 10(b). On average $7 \times 10^{-4}$ photons hit the retina per proton from the fast component and $6 \times 10^{-4}$ photons per proton from the slow component. $6 \times 10^{-6}$ photons per proton from the fast component and $2 \times 10^{-5}$ photons from the slow component are incident on the fovea.

Patients with eye cancer (taking uveal melanomas as an example) are given 53.1 Gy in 4 fractions, with each fraction being delivered in approximately 30 s (Kacperek 2009). The treatment therefore delivers approximately $3 \times 10^{8}$ protons per second, assuming the mass of the eyeball is 7.5 g (Suri et al. 2008). This means that the total number of photons which hit the retina is of the order of $2 \times 10^{9}$ photons per second from the fast component, which suggests that, considering the mean absorbance spectrum of the rods reported in Bowmaker and Dartnall (1980), $10^{5}$ photons per second are detected by the rods. The contribution from the slow component, on the other hand, will increase from $2 \times 10^{3}$ to $7 \times 10^{4}$ photons per second during the irradiation time as more isotopes are generated; these emissions will decrease with time following irradiation as the isotopes decay.
The human eye is capable of seeing 10–100 photons arriving within less than 100 ms when under otherwise dark conditions (Schnapf and Baylor 1987). In the treatment room, lights are usually dimmed to reduce distraction to the patient. In addition, many patients have their eyes partially closed during the treatments or their tumours may obscure the retina. Despite this, patients report seeing a light glow when the radiation is on even when their eyes are closed, indicating that Cerenkov emissions can be seen in the presence of room lights. Thus, we believe that Cerenkov emission liberated inside the eye during proton therapy is sufficiently bright that it should be visible to the patient.
Table 1. The most abundant positron emitters found in water after simulated irradiation by a 60 MeV proton beam.

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Nuclear reactions</th>
<th>Decay mode</th>
<th>Daughter</th>
<th>Half-life</th>
<th>Maximum positron energy</th>
<th>Average number of Cerenkov photons</th>
<th>Nuclides per $10^7$ protons</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{15}$O</td>
<td>$^{16}$O(p, pn)$^{15}$O$^a$</td>
<td>$\beta^+$</td>
<td>$^{15}$N</td>
<td>122.24 s</td>
<td>1.72 MeV</td>
<td>32.8</td>
<td>81,000</td>
</tr>
<tr>
<td>$^{11}$C</td>
<td>$^{16}$O(p, αn)$^{13}$C</td>
<td>$\beta^+$</td>
<td>$^{11}$B</td>
<td>20.33 min</td>
<td>0.96 MeV</td>
<td>6.9</td>
<td>23,000</td>
</tr>
</tbody>
</table>

$^a$ p + n includes deuteron (d)

Figure 8. Slow component of Cerenkov emission from experimental and simulated results. The experiment delivered 15 Gy at a high dose rate, whilst the simulation used $10^7$ protons.

Figure 9. The simulated spectrum of secondary positron emissions. The error bars (illustrating the typical standard deviation) are smaller than the point size in some points of the curve.
3.2. Investigation of the possible application of measuring or imaging Cerenkov emission during proton therapy

3.2.1. Spatial distribution of Cerenkov production.

*Fast component.* The spatial relation between the Bragg peak and the fast component of Cerenkov production for a 60 MeV proton beam was investigated by scoring the deposited energy and the fast component of Cerenkov light which was generated in the same volume (figure 11). The spatial information available in the fast component signal is limited as it depends on gamma photons, which may interact far from their point of origin. The depth dose curve from fast Cerenkov emissions (figure 11), therefore, bears little relation to the Bragg peak.
Slow component. The relation between the Bragg peak and the Cerenkov production profile for a 60 MeV proton beam was investigated by scoring the deposited energy and the slow component of Cerenkov light which was generated in the same volume (figure 12). The depth distribution of induced $^{15}$O and $^{11}$C nuclides are shown in the same figure where the $^{11}$C curve is normalized to the $^{15}$O curve. The Cerenkov production profile agrees closely with the production profile of $^{15}$O, once again demonstrating that the dominant isotope is $^{15}$O. This suggests that this work can benefit from the extensive work done on PET imaging during proton therapy (Paganetti 2011), as described in the discussion.

The contribution of $^{15}$O to the slow component of Cerenkov production is greater than that of $^{11}$C largely because the number of $^{15}$O nuclides produced is 3.5 times greater than the number of $^{11}$C nuclides (table 1). In addition, the energy spectrum of $^{15}$O decay extends to 1.72 MeV, while the spectrum of $^{11}$C does not exceed 0.96 MeV, so positrons emitted by $^{15}$O will travel faster and deeper in the medium and therefore produce more Cerenkov emission.

3.2.2. Linearity between Cerenkov measurements and dose or dose rate.

Fast component. The linearity of the fast component to dose was modelled by delivering different doses to the water phantom and measuring the emitted Cerenkov light. As the measurements would take place during the irradiation time, the measured signal is a combination of the fast component and the slow component (described in section 3.1.2). Figure 13 shows the dose linearity of the fast and the slow component of Cerenkov emission during the irradiation time, using a 60 MeV proton beam. Simulation showed that the contribution of the slow component in the detected signal varies between 0 and 27% depending on the time required to deliver a given dose. This will introduce non-linearity to the measured signal.

Slow component. The linearity of the slow component was examined in simulation by delivering different doses to the water phantom and measuring the emitted Cerenkov light after the beam has been switched off. Figure 14 shows the linearity of the slow component of Cerenkov measurements with dose, using a 60 MeV proton beam. The slow component is non-linear with dose. This is due to the extended time required to deliver a given dose, meaning that any radionuclides which are generated during beam delivery will have begun to decay by the end of the irradiation time, reducing the measured count rate from higher doses (and therefore

Figure 12. Comparison between simulated Bragg peak, simulated Cerenkov production profile, $^{15}$O depth profile and $^{11}$C depth profile in a water phantom for a 60 MeV proton beam.
longer delivery times). The good agreement between experiment and simulation supports the suggestion that the non-linearity is due to decay rather than other potential mechanisms, which are not included in the model such as molecular diffusion.

4. Discussion

4.1. Cerenkov emissions as a contribution to visual sensation

This work was initially motivated by the observation that patients undergoing proton therapy of the eye report seeing visual flashes. The most common mechanism proposed for this is
direct stimulation of the retina because the energy of the primary therapeutic beam is too low to elicit Cerenkov radiation directly, as discussed in the Introduction. We have proposed two mechanisms by which Cerenkov radiation could be produced, even when the energy of the primary protons is less than the threshold energy required for direct Cerenkov production. We suggest that Cerenkov emission provides a potential mechanism for the visual sensation during eye proton therapy, in addition to contributions from direct stimulation.

4.2. Evidence for Cerenkov emission

Even if we accept that some part of the visual sensation is indeed caused by visible light in addition to any contributions from direct simulation, there are other mechanisms by which such light may be generated such as radioluminescence of air or water (Tarasov et al 2007) or scintillation from the walls of the Perspex tank or the optical fibre material (Beddar et al 1992). These other mechanisms, however, occur within timescales of a few nanoseconds, the same timescale as the fast Cerenkov component. We therefore cannot yet conclusively exclude the possibility of these other mechanisms occurring, but as figure 8 demonstrates, there is light emission for a number of minutes after the end of irradiation. We believe that this must be the slow component of Cerenkov emission. The half-life was 114 s, which is similar to the half-life of $^{15}$O, which can be imaged by PET following proton therapy.

4.3. Applications of the fast Cerenkov signal

The interactions which lead to the fast signal are the same as those which lead to prompt gamma emission. Prompt gamma measurements have been proposed for imaging the dose distribution (Bom et al 2012) and range verification (Moteabbed et al 2011) in real time, but have yet to reach routine clinical practice because the complex interactions lead to uncertainties in yield and because of the difficulty of detecting high-energy gamma photons (Paganetti 2011).

The Cerenkov fast signal occurs during irradiation; it is linear with dose and dose-rate but measuring it separately would be challenging as it is mixed with the slow component; the fast component provides little spatial resolution as the interactions occur along the paths of the prompt gamma photons. It will also have limited range in tissue as the optical photons are scattered and absorbed, and it will suffer from the same yield uncertainties as prompt gamma emissions. It is unlikely that measuring the fast component will provide useful information during proton therapy.

4.4. Applications of the slow Cerenkov signal

The slow Cerenkov signal is generated by the emission of positrons. PET imaging of these same positron-emitting isotopes is currently being developed as a tool for post-verification treatment (Beebe-Wang et al 2003). However, there are disadvantages in using PET in proton therapy, most of them related to time in moving the patient to the PET room, the biological washout, and cost (Zhu et al 2011). Imaging the Cerenkov emission following the introduction of positron-emitting isotopes is being developed in Cerenkov luminescence tomography of small animals (Li et al 2010).

The slow Cerenkov signal is non-linear with dose and dose-rate (as is the PET signal), but can provide better spatial resolution than the fast signal. As before, however, optical photons will be heavily scattered and absorbed by tissue, so this technique will be largely restricted to a method of measuring the distribution of dose or fluence across the surface of the patient.
Very recently, such an approach has been shown to be feasible in photon therapy (Jarvis et al 2014). A potential clinical application specific to proton therapy is in-vivo imaging of the slow component of Cerenkov production in the human eye for treatment verification, where penetration is low and the tissue is transparent.

Range measurements are essential in proton therapy and are currently performed for QA by scanning the water phantom with an ionization chamber. We propose that measuring the slow component of Cerenkov production from a water tank from mainly $^{15}$O emissions, using a camera or bundle of optical fibres, could allow the Bragg peak range to be predicted by taking advantage of the relation between radioactivity and range. This would be directly analogous to using PET imaging, but could be carried out routinely in the treatment room. A similar approach has been taken in photon radiotherapy where the Cerenkov light has been imaged directly (Glaser et al 2013b), and also indirectly by using the Cerenkov emissions to stimulate fluorescence (Glaser et al 2013a). Even though Cerenkov images are not expected to reproduce the depth dose of the proton beam, this method could be used to quickly monitor any changes in the beam depth in a water phantom.

Finally, measuring Cerenkov emissions in tissue during radiation therapy has been proposed as a method for measuring haemoglobin oxygen saturation in superficial tumours by exploiting the differential absorption of the Cerenkov light as a function of wavelength, using techniques pioneered in near infrared spectroscopy (Axelsson et al 2012). The role of tissue oxygenation in radiotherapy effectiveness is well known.

5. Conclusion

Cerenkov imaging is currently being actively researched as a tool for QA and in vivo dosimetry in photon and electron therapy. We have, for the first time, proposed a mechanism for Cerenkov emission during proton therapy even though the energy of the primary proton beam is below the threshold for direct Cerenkov emission. We have confirmed this by measuring the resulting optical emissions which continue to be released after irradiation has ceased.

We believe that the recent interest in Cerenkov imaging in photon and electron radiotherapy can also be applied to proton radiotherapy, particularly as a tool for QA and in vivo surface dosimetry. Furthermore, we have shown that the possibility that Cerenkov emissions contribute to the visual sensation cannot be excluded.

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