Developments in microdosimetry and nanodosimetry for space and therapeutic applications

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NOTE

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5.1 Introduction

Microdosimetry has many applications both in radiation therapy and radiation protection. In radiation protection the determination of biological doses for astronauts and single event upset (SEU) rates in micro and nano electronics are important goals for world space organizations in the 21st century. Conversely, in radiation therapy a better understanding of the changes in therapeutic radiation spectra with tissues traversed will enable advances in treatment planning and possibly improved efficacy in treatment with reduced side effects. One method that can be employed in these studies is microdosimetry, especially the use of solid-state microdosimeters such as those that have been developed at the Centre for Medical Radiation Physics (CMRP) at the University of Wollongong (UoW) and which are described in Section 2.4.

The main advantage of solid-state microdosimeters for space and aircraft operation is their compact size and low voltage for operation. However, previously they have suffered the drawback of the lack of a well-defined sensitive volume (SV). This problem has been addressed using Silicon-On-Insulator (SOI) technology which results in well defined microscopically small SV's. Scaling of the mean chord length allows derivation of tissue-equivalent microdosimetric spectra. Equivalent dose and average quality factor of a radiation field can then be determined by convolution of the microdosimetric spectra with a spectra of quality coefficients [32]. The microscopically small cell size is also useful in determining SEU's in microelectronics, allowing sufficient shielding to be constructed and thus enabling extended deployments of electronic devices.

In radiation therapy, especially hadron therapy, microdosimetry provides a means for determining the dose equivalent of a wide range of therapeutic radiation fields and secondaries such as neutrons. Such abilities have been previously displayed in Section 4. SOI microdosimeters also have the added advantage of being able to be used within phantoms for measurements of changing microdosimetric spectra. This is important in hadron therapy applications as it allows the change in biological effect within a phantom
to be measured and a determination of whether this should be considered in treatment planning applications.

Previously SOI microdosimeters have undergone Monte Carlo simulation studies within homogeneous phantoms and the results compared with experimental data obtained in neutron and proton radiation fields [25, 26, 29, 30, 66, 73]. These studies have illustrated that such simulations yield useful and accurate information. However, in these cases experimental information has only been obtained for homogeneous Perspex and water phantoms. It is desirable to obtain information utilising more complex layered heterogeneous structures of biologically important materials for a number of disciplines such as radiation protection and radiation therapy. Such studies can better develop our understanding of radiation interactions within the body and the changes to the radiation spectra as it traverses biological structures. This in turn can then be utilised to more efficiently construct radiation shielding in radiation protection applications and also better consider changes in treatment radiation fields during the planning process for radiation therapy.

The aim of this work is to observe the changes in experimental microdosimetry spectra as proton radiation traverses biologically important structures such as the human head and chest. These results will be compared with simulation studies utilising the GEANT4.7.1p1 Monte Carlo toolkit [52] for validation. The experimental validation of the GEANT4 based application for heterogeneous commercial phantoms will allow for further simulation studies of the SOI microdosimeter without experimental noise limitations. These simulations will enable changes in microdosimetric parameters such as mean dose weighted lineal energy, average quality factor and dose equivalent to be observed as a function of preceding phantom material..

5.2 Experimental Method

For this study a tissue equivalent (TE) phantom was specially constructed. It consisted of 20x20x1cm³ slices of adipose, lung, brain, bone and muscle that were layered in a given order such that it could be configured to represent the structure of the human head and chest. The structure of these phantoms is outlined below and in Figure
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5-1. The compositions of these phantoms were provided by the manufacturer for simulation using GEANT4.

- **Head**: 10 mm muscle, 10 mm bone, 10 mm brain (in the case of 250 MeV protons 25-50 mm Perspex is also added to simulate a greater depth in brain)

- **Chest**: 10 mm adipose, 10 mm bone, 10 mm muscle, 20 mm lung

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**Figure 5-1**: Schematic diagram of the phantom configuration as used within the experimental and theoretical portion of this work. Note the microdosimeter positions indicating the position of measurement (or simulated measurement). In the case of 250 MeV proton irradiations, 25 and 50 mm thicknesses of Perspex were also interspaced between the bone and brain layer (in the case of the head phantom) to provide additional measurement points at greater depths in brain.
A 10 \( \mu \text{m} \) thick SOI microdosimeter was used in this study. The array chosen in this experiment comprises of 4800 detector elements (40x120) with each cell having a physical size of 30x30 \( \mu \text{m}^2 \). The device was contained within a 0.9 mm thick probe holder of aluminium which would act as a Faraday cage. A 4 \( \mu \text{m} \) thick aluminium window was located immediately in front of the microdosimeter to allow for the transport of secondary particles into the SV. To enable reproducible placement of the microdosimeter probe on the central axis at tissue boundaries, it was housed within a purpose built Perspex probe holder. The probe was then placed at tissue boundaries within this phantom to ascertain the changes in microdosimetry spectra as a result of changing biological material.

The incident radiation field utilised in this study was 100 and 250 MeV protons with measurements completed on the central NASA research beam-line at Loma Linda University Medical Center (LLUMC). Experimental measurements were conducted with beam sizes of the order of 50 mm diameter at the point of entry into the phantom for 10 minutes. During this time the dead time was kept stable at 10% with a low noise threshold set on the Multi-Channel Analyser (MCA) of approximately 9 keV. Throughout the course of the experiment the device was irradiated with 0.2-0.35 cGy per spill (accelerator delivered radiation pulse of approximately 0.4 seconds duration with a total cycle time of 2.2 seconds [9]). The dose was monitored at regular intervals with a calibrated ion chamber, which has 12 \( \mu \text{m} \) Mylar entrance and exit windows, a 1.58 mm air SV thickness, and is described in [74] and Section 10.5.

### 5.3 Monte Carlo Method

The experimental setup was recreated within an application that was based on the GEANT4.7.1p1 Monte Carlo Toolkit. This included not only the SOI microdosimeter chip (as represented in Figure 5-2), but also the aluminium faraday cage, Perspex probe holder and layered phantom structure. The experimental setup in its entirety is displayed in Figure 5-3.
Figure 5-2: Schematic of the SOI microdosimeter chip as recreated within the GEANT4 based application. Note the four separate SOI microdosimetry arrays.

The SOI microdosimeter chip assembly was constructed within the GEANT4 based application from an arrangement of right angled parallelepiped volumes (RPP). Forming the body of the chip was the ceramic base layer with the dimensions of 35.4x14.6x2.0 mm$^3$ into which is formed a two stage recess with a total depth of 500 μm. Into this recess the Si substrate (279 μm thick), SiO$_2$ insulator (10 μm thick), Si SV (2, 5 or 10 μm thick depending on the device being simulated) and SiO$_2$ overlayer (1 μm thick) were defined as layered RPP volumes each with a cross sectional area of 5.5x6.5 mm$^2$. As such the Si detector was recessed into the ceramic chip with an approximate distance of 200 μm between the surface of the ceramic chip and the SiO$_2$ overlayer. Within the Si SV, four regions were defined as sensitive (i.e. energy depositions within these volumes were registered) which corresponded to the four detector arrays. The size and position of each individual array are described in [21] and were re-confirmed through microscopic analysis.
Figure 5-3: Schematic of the experimental setup as recreated within the GEANT4 based application.

The commercially available phantoms were reproduced within the simulation program according to the manufacturer’s specifications. Energy depositions within the 10 μm SOI device were scored to create a spectrum of energy deposition events for comparison with the experimental results. This comparison was used to determine the accuracy of the GEANT4 based application in simulating the response of the microdosimeter within heterogeneous commercially available TE phantoms.

The Physics processes utilised for the transport of light ions (including protons) included low energy inelastic scattering (G4preCompound model), low energy ionisation (ICRU 49) and multiple scattering models. The physics of secondary particles including photons, electrons, neutrons and nuclear secondaries was also considered and accounted for using the appropriate models, with low energy extensions for electron and photon transport used where possible. Each simulation was carried out for 2x10^7 normally incident protons transported along an evacuated beam pipe, beam exit window and across
a 3.5m air gap into the phantom and experimental probe assembly. The incident beam profile was approximated as circular with 10 mm diameter. In the case of the 250 MeV simulations, a 1.0 mm thick lead scattering foil was used to achieve a larger, more uniform field at the phantom. The advantage of completing experiments on a research beam-line was that there were minimal beam modifying structures in place which needed to be considered in the simulation. Regardless all beam-modifying devices were considered in GEANT4 simulations and were approximated using planar structures of a given thickness outlined in Table 5-1. As is the case with all Monte Carlo simulations in this study the compositions of which were defined isotopically from manufacturers specifications or from compositions sourced through NIST [35].

<table>
<thead>
<tr>
<th>Beam Modifying Device</th>
<th>Material</th>
<th>Thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beam Exit Window</td>
<td>titanium</td>
<td>0.025</td>
</tr>
<tr>
<td>Scattering Foil (250 MeV only)</td>
<td>Lead</td>
<td>1.0</td>
</tr>
<tr>
<td>Air</td>
<td>Air</td>
<td>3500</td>
</tr>
</tbody>
</table>

Table 5-1: Beam modifying devices considered in GEANT4 Monte Carlo simulations of the primary proton field present in the experimental case.

5.4 Result Normalisation

In comparing the simulated and experimental results for validation it is important that adequate and appropriate normalisation occurs. The experimental results were binned into 2048 channels by the MCA. An energy calibration was applied to the experimental results that in turn was derived using the method described in Section 3.6.

The simulated results were binned into 8000 bins spanning an energy range of 0-4MeV. The simulated results then had a charge collection efficiency (CCE) of 0.8 applied which has been previously determined and verified through ion beam induced charge collection studies (IBICC) [26, 27]. The simulated results were then convolved with a Gaussian of \( \sigma = 5\text{keV} \) (measured experimentally in Section 3.7) to reflect the electronic noise present in the system.
\[ f_j = \sum_{i=j-3\sigma}^{j+3\sigma} \frac{1}{\sqrt{2\pi}} f_i \exp\left(-\frac{(\varepsilon_j - \varepsilon_i)^2}{2\sigma^2}\right) \]

**Equation 5-1**: Gaussian which is convolved with simulated results to better reflect the experimental noise present in measurements. \( \varepsilon_i \) is the energy values corresponding to bin \( i \) of the frequency distribution.

Finally, both the simulated and experimental results were normalised to the total number of events present above twice the noise threshold of the experimental device. In this case the noise threshold of the experimental device was measured to be 15 keV. As such the results were normalised to total number of events higher than 30 keV.

**5.5 Microdosimetry Spectra Generation**

Once validation of the GEANT4 based application had occurred the raw simulated data was converted into microdosimetry spectra using the protocol outlined in [32] and described in Section 2.4. A mean chord length of \( <l> = 19.05 \, \mu m \) was used for these calculations. This value was calculated using Equation 2-1 based on a 30x30x10 \( \mu m^3 \) volume and a tissue equivalent scaling factor of \( \zeta=0.63 \):

The spectra produced provide the fraction of the total dose occurring from lineal energy events in the interval \( y \rightarrow y + dy \) where \( y \) is the lineal energy in keV/\( \mu m \). The mean dose weighted lineal energy (Equation 2-3) was determined from the lineal energy spectra and used as an indicator of changes to incident radiation field as a function of preceding material. The dose equivalent and average quality factor was also be used as an indicator of changes in the incident radiation field and was determined using the methods described in Section 2.5.
5.6 Validation Results and Discussion

Experimental measurements were completed on the central NASA research beam-line at LLUMC. Experimental results for all energy/phantom combinations are unobtainable below 15keV due to the noise limit of the device. This lower level noise limit is clearly evident in all the graphs displayed.

Figure 5-4: Comparative experimental and simulation results for the head phantom, when irradiated with 100 MeV protons.

Figure 5-4 shows a comparison between simulated and experimental results for 100 MeV protons within the head phantom. A discontinuity is observed in the simulated case at approximately 140 keV. The simulated case has a sharp drop before continuing parallel to the experimental trend at higher energy values. This is observed for all 100 MeV simulations, yet no discontinuity is observed for 250 MeV incident protons. Possible explanations for the discontinuity are:

a) A discontinuity in the physics models for lower proton energies regarding nuclear reactions. However, as the same models are used for the higher energy simulations with no discontinuity observed this seems unlikely.
b) The range cut in electron transport preventing low energy electrons for depositing energy in the device. However, as the same cut is used for the higher energy simulations with no discontinuity observed this seems unlikely.

c) An overestimation in the device overlayer in the simulated case. The simulated overlayer was constructed within the GEANT4 simulation to be a uniform layer of SiO₂ with a 1μm thickness. In actual fact it may have regions of varying thickness and possibly composition. Also, the aluminium contacts were not constructed within the simulation which could lead to errors in particle transport into the SV. Such errors could cause low energy protons to be prevented in reaching the SV. This would be seen causing a greater impact on 100 MeV results as nuclear secondaries (including recoil protons) produced would have a lower energy, which could be affected to a greater degree by inaccurate overlayer simulation.

Figure 5-5: Comparative experimental and simulation results for the head phantom, when irradiated with 250MeV protons.
Figure 5-5 and Figure 5-6 show the comparison between experimental and simulated spectra for 250 MeV protons incident on the head and chest phantom, respectively. The agreement between the simulated and experimental cases is best in the region of 15-80 keV with almost no discrepancy. In the region of 80-500 keV there is some discrepancy between the simulated and experimental data, which can be as large as a factor of 2-3. This difference was most likely caused by an oversimplification in simulation of the device overlayer as for high linear energy transfer (LET)/low range secondaries an incorrectly simulated overlayer could result in error in their transport and hence energy deposition within the SV.

It is also important to note that this difference is most pronounced for the first 10 mm layer of each phantom structure. This amplification in discrepancy is most likely caused by an underestimation of the beam divergence as it travels along the beam pipe towards the experimental set-up. In the simulation, the beam was approximated as circular in profile travelling normally down an evacuated beam pipe, however, this may not be the case in practice. Such discrepancies are only observed in the first 10 mm of the phantom, as small initial beam divergence errors are nullified at depth within the phantom due to internal scatter of the incident protons. Despite this discrepancy the trend of the experimental results are well represented by the simulation for all phantom material configurations.

In the case of the head phantom for 250MeV incident protons a 25 mm thick Perspex slab was used to simulate a greater depth within the brain. However, in this case the brain slab was re-orientated to remain the last layer of the phantom immediately before the microdosimeter probe assembly. This would ensure that any short range secondaries produced by the brain phantom were transported and detected by the device, not attenuated by Perspex.
Figure 5-6: Comparative experimental and simulation results for the chest phantom, when irradiated with 250MeV protons.

5.7 Microdosimetry Results and Discussion

Although some discrepancy was observed between the simulated and experimental cases for higher energy deposition events, the experimental trend/response of the microdosimeter (a complex radiation metrology device) was well reflected in the simulation. The advantage which the simulation provides over the experimental device is that it is possible to simulate a device with no electronic noise and no lower level noise threshold, which may provide a better understanding of the radiation field at a given point.

The simulated results with no noise convolution or charge collection applied were converted into dose weighted lineal energy spectra according to the protocol outlined in [32, 33] and Section 2.5. Due to small variations in microdosimetry spectra as a function of phantom material upstream of the measurement position, the mean dose weighted
lineal energy, dose equivalent and average quality factor were used to discern changes in radiation field. Such measurement parameters provide information not only on changes in radiation field composition, but also possible variations in the radiobiological effect (RBE) for different regions in the heterogeneous phantom. These results are presented in Table 5-2 and Table 5-3 for the case of 250MeV protons irradiating the head and chest phantom. The advantage of using 250MeV protons for this study is that all simulated measurement positions took place within the plateau region, before the Bragg Peak. As such the changes in lineal energy are mostly caused by the changing phantom material rather than the slowing of the proton in the Bragg peak region.

<table>
<thead>
<tr>
<th>Measurement Position</th>
<th>$\bar{Y}_d$ (keV/µm)</th>
<th>Dose Equivalent (mSv)</th>
<th>Average Quality Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phantom Surface</td>
<td>4.06</td>
<td>0.53</td>
<td>1.17</td>
</tr>
<tr>
<td>Muscle/Bone Interface</td>
<td>4.75</td>
<td>0.63</td>
<td>1.32</td>
</tr>
<tr>
<td>Bone/Brain Interface</td>
<td>5.85</td>
<td>0.80</td>
<td>1.58</td>
</tr>
<tr>
<td>10mm Depth Brain</td>
<td>5.65</td>
<td>0.75</td>
<td>1.51</td>
</tr>
<tr>
<td>35mm Depth Brain</td>
<td>4.46</td>
<td>0.61</td>
<td>1.25</td>
</tr>
<tr>
<td>60mm Depth Brain</td>
<td>4.79</td>
<td>0.63</td>
<td>1.31</td>
</tr>
</tbody>
</table>

Table 5-2: Mean dose weighted lineal energy values for simulated measurement positions within the head phantom when irradiated with 250MeV protons. Presented also is the corresponding dose equivalent measurement and average quality factor that was determined from the simulated response of the SOI microdosimeter.

In the case of the head phantom it is clear that there is a variation in the mean dose weighted lineal energy as a result of the preceding TE material. Measurements immediately behind the bone boundary result in an increase in mean dose weighted lineal energy of approximately 44%. An elevated value is also recorded at 10 mm depth within brain before returning to more stable values at greater depths within the TE brain phantom as simulated by additional layers of Perspex. The dose equivalent (for $2\times10^7$ incident protons) and average quality factor also exhibit elevated values past the bone layer which is clearly evident in Figure 5-7. Immediately after the bone layer, the dose equivalent increases by a factor of approximately 50% while the average quality factor shows a similar increase of 35%. The dose equivalent and average quality factor
decrease to more stable values after traversing 35 mm of brain material. This would indicate that high LET low range secondaries are produced within the bone layer in turn increasing the mean dose weighted lineal energy, dose equivalent and average quality factor in the region immediately behind the bone boundary.

![Graph](image)

**Figure 5-7:** Graph of the variation in dose equivalent and average quality factor as a function of position within the head phantom.

It is clear from Table 5-2 and Figure 5-7 that the radiation quality has changed as a result of traversing a bone layer in the head phantom. The change in beam quality from the surface provides further information on the change in biological effectiveness as a function of preceding phantom material. In the case of the head phantom the dose equivalent increases by 50% after the proton beam traverses the bone layer. However, as current treatment planning relies on analytical simulation techniques and absorbed dose as the measurement parameter, such variations may not be considered and could have an adverse impact on sensitive normal structures in this region.
<table>
<thead>
<tr>
<th>Measurement Position</th>
<th>$\bar{\gamma}_d$ (keV/μm)</th>
<th>Dose Equivalent (mSv)</th>
<th>Average Quality Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phantom Surface</td>
<td>4.05926</td>
<td>0.53</td>
<td>1.17</td>
</tr>
<tr>
<td>Adipose/Bone Interface</td>
<td>5.08208</td>
<td>0.69</td>
<td>1.44</td>
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<td>Bone/Muscle Interface</td>
<td>5.70244</td>
<td>0.72</td>
<td>1.45</td>
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<tr>
<td>Muscle/Lung Interface</td>
<td>5.79357</td>
<td>0.78</td>
<td>1.57</td>
</tr>
<tr>
<td>20mm Depth Lung</td>
<td>5.38776</td>
<td>0.63</td>
<td>1.36</td>
</tr>
</tbody>
</table>

Table 5-3: Mean dose weighted lineal energy values for simulated measurement positions within the chest phantom when irradiated with 250MeV protons. Presented also is the corresponding dose equivalent measurement and average quality factor that was determined from the simulated response of the SOI microdosimeter.

Simulation of the microdosimetry spectra within the chest phantom (see Table 5-3 and Figure 5-8) reveals the same trends as is seen as in the head phantom. Immediately after the bone layer there is an increase in mean dose weighted lineal energy of 42% which continues to greater depth within the phantom. In this instance the elevated mean dose weighted lineal energy values traverse into the lung phantom which is an indication of higher LET secondaries being able to travel to greater depths within the lower density lung material. As in the head phantom the elevated dose equivalent and average quality factor occurs past the bone layer with increases of 34% in both parameters when compared with values measured at the surface. This further supports the trend of increasing biological effectiveness of therapeutic proton radiation as a direct result of traversing a hard boundary such as bone.
Another interesting trend observed in these results occurs in both phantoms after only 10 mm of material. In the case of the head phantom muscle is the most anterior (i.e. closest to the incident radiation) phantom layer, while in the case of the chest phantom this material is adipose. The differing composition of these two layers results in a clear variation in not only in the mean dose weighted lineal energy but also the dose equivalent and average quality factor. As the main variation of composition in these commercially available TE phantoms is that adipose contains approximately 5% more carbon, it could be concluded that these increased levels of carbon produced increased levels of inelastic and elastic scatter resulting in an increased dose weighted mean lineal energy, quality factor and dose equivalent.

5.8 Overall Conclusions & Recommendations

This study has highlighted the ability of GEANT4 in simulating therapeutic proton radiation. In this work the response of a relatively complex radiation detection structure was simulated with acceptable accuracy considering the complex nature of the incident beam, and heterogeneous phantom structure. Some discrepancies were observed which can be reduced through further improvements to the simulation program. In this case improvements could include:
- A better estimation of the initial beam size and divergence in both the vertical and lateral direction. In this instance the initial beam was approximated as a circular beam with 10 mm diameter and zero divergence. Such an approximation has lead to some level of error in surface measurements, however discrepancies were removed through in-phantom scattering for measurements at depth.

- A more complex model of the SOI microdosimeter including a more complex simulation of the device overlayer and contact structure.

- Testing with improved physics models released with the GEANT4.8.1 toolkit. Such physics models may explain the differences observed at 100MeV [75].

From the simulated response of the microdosimeter within commercially available TE phantoms it is clear that the quality of the proton radiation varies in different tissue substances. This has been established through the comparison of mean dose weighted lineal energy, dose equivalent and average quality factor obtained through the simulated response of an SOI microdosimeter situated at tissue boundaries within a head and chest phantom. Such variations in radiation quality were most prevalent immediately past the bone layer. In the head phantom this is evident with increases in mean dose weighted lineal energy of 44%, dose equivalent of 50% and average quality factor of 35%. These trends are also reflected in the chest phantom with increases in mean dose weighted lineal energy of 42%, dose equivalent and average quality factor of 34%. As all simulated responses were completed within the plateau region of the 250 MeV Bragg peak, changes in these parameters are most likely caused by changes in the proceeding phantom material and hence the spectra of secondary particles produced when the primary proton field traverses these materials.

While the biological effects of small variations in radiation quality and dose equivalent are unclear, it would be advisable that they be considered over the entire course of treatment as the summation of these effects may become clinically relevant. Such changes in radiation quality are not accounted for in current treatment planning systems which rely on analytical simulation techniques and the macroscopic quantity of absorbed dose as a planning parameter. Future advances in treatment planning may
utilise Monte Carlo methods, microdosimetry and dose equivalent as their basis to accurately plan for changes in radiation field composition.

To better understand the effect produced by actual tissue materials, simulation studies should be initiated using homogeneous phantoms of commercially available TE materials, ICRP/ICRU TE material compositions and water scaled to the physical and electron density of the TE material being simulated (typically done in treatment planning). In such simulations it is important to consider the changes in depth dose profile, lateral profile and microdosimetry spectra. Such simulations will illustrate how well commercially available TE materials and water scaled to the physical and electron density of the TE material reflect actual tissue compositions in proton therapy.

To compliment such simulations in a homogeneous phantom material, heterogeneous studies should also be completed. In this instance phantoms such as the ones presented in this section or anthropomorphic phantoms [76] should be recreated within the simulation program using commercially available TE materials, ICRP/ICRU TE material compositions and water scaled to the physical and electron density of the TE material being simulated. Again the response of the SOI microdosimeter should be simulated with mean dose weighted lineal energy, dose equivalent and average quality factor used to determine any change in the radiation quality as a function of preceding phantom material. Such simulations will again provide information on the effect of tissue boundary on therapeutic proton radiation spectra, but will also illustrate how accurately commercially available TE materials and water scaled to the electron/physical density to represent tissue, reflect actual tissue in the transport of proton radiation.