

9. Application to Proton Therapy

9.1 Background to Proton Therapy

The use of proton beams for radiation treatment was proposed by Robert R. Wilson in 1946 [286]. Wilson referred to the ballistical aspects of the proton beam dose distribution as a rationale for the new modality. Heavy charged particles such as protons produce an energy deposition profile in tissue which is superior to profiles attainable using photon or electron irradiation. The dose distribution for a monoenergetic proton beam features a low entrance dose region followed by a slowly rising dose until the proton Bragg peak is reached, near the end of the range, where the dose rises rapidly. The beam energy is generally spread to modulate the proton range and provide a uniform high dose over the target tissue. This profile also features a moderate entrance dose and almost zero dose beyond the target [99].

In view of the excellent dose profile, proton therapy is recommended for tumors with the following characteristics [272]:

- A loco-regional evolution (thus with a low metastatic tendency)
- Cannot be totally surgically removed.
- Need high doses of radiation for cure (often more than 70 Gy)
- Lie very close to exquisitely radiosensitive organs or tissues

Particular success has been found in the treatment of uveal (or ocular) melanomas and the postoperative management of base of the skull and spinal canal malignancies. For example, Munzenrider [287] reported that enucleation (eye removal) was performed in only 57 of 1006 patients (5.7%) with uveal melanoma. Up to 1995, more than 13000 patients throughout the world had been treated with protons and almost half of them underwent treatment at the Massachusetts General Hospital in Boston [99, 272].

For patient treatment planning, knowledge of the beam RBE is vitally important. Clinical response to proton beam treatments at the Harvard Cyclotron Laboratory along with radiobiological studies led to the adoption of a universal RBE value of 1.1 for proton therapy. Studies at Loma Linda by Robertson [288] using the deactivation of V79 Chinese hamster cells *in vitro* indicated RBE values varying from 1.1 to 1.3 with

an increasing trend near the distal beam edge. Clearly, the relative biological effectiveness of the beam varies with depth. A 250 MeV proton has an initial LET of 0.4 keV/ μm . This rises sharply in the Bragg peak region reaching a maximum value of approximately 80 keV/ μm within a few microns of the end of the range. Coutrakon [155] estimated an RBE of 1.65 at the distal edge (50% of mesa dose) based on microdosimetric measurements correlated to V79 Chinese hamster cell experiments. Microdosimetric measurements, at depths where protons enter the Bragg peak region, are particularly challenging due to the high spatial resolution required.

Further justification of the need for experimental microdosimetry in proton therapy may be seen by a brief examination of the interaction of protons with matter. Protons interact with matter by continuous slowing down as a result of Coulomb collisions with electrons and nuclei, by Bremsstrahlung radiation loss, and by nuclear reactions. The Coulomb interaction with electrons is the predominant mechanism for energy loss and is typically described by the electronic stopping power or LET of the proton [284]. Radiation loss is negligible for the energies of interest in proton therapy. However, nuclear reactions have a significant effect on the proton beam characteristics. The probability that protons in the energy range of proton therapy (<250 MeV) will undergo a nuclear interaction whilst traversing 1 gm/cm² is around 1% and after 20cm 1 in 4 protons will have suffered a nuclear interaction. A NIST report by Seltzer [289] and summarized by Miller [99] describes the interactions and products. Approximately 21% of the energy lost in slowing down a 250 MeV proton beam in water is due to nonelastic nuclear reactions. This fraction drops to around 4% for a 70 MeV beam. Thus nuclear interactions affect the identity and energy distribution of the secondary particles and decrease the number of primary protons in the beam.. An important characteristic of the beam is the LET spectrum of all primary and secondary particles responsible for the radiobiological properties of beam. Thus, microdosimetric measurements in a water phantom are important in high energy proton therapy installations.

Microdosimetric studies of proton beams have been performed by several investigators [155, 288, 290-293]. Typically, a spherical proportional counter containing a low-pressure tissue equivalent gas is used to obtain the spectrum of energy deposition events [1]. The millimeter resolution required in the Bragg peak region is not achievable using such a counter which normally has a diameter of 1-2 cm. Coutrakon [155] concludes a detailed study of microdosimetry and RBE measurements at Loma Linda with the

following: "More measurements using techniques to obtain spectra with finer depth resolution on the distal edge will be useful to track lineal energy and RBE changes more precisely". Parallel plate type proportional counters have been developed [291, 292] but these are still larger than the silicon microdosimeter and not as convenient to use.

The large size of the proportional counter also creates problems with pileup effects due to simultaneous multiple events during high DC current operation or when the proton beam consists of large currents produced in nanosecond to microsecond pulses. Measurements of microdosimetric spectra using a proportional counter have been reported with count rates as low as 350 counts/sec still exhibiting pileup due to the large size of the counter [292]. Therefore, proton microdosimetry requires small microdosimeters with high spatial resolution ($<1\text{mm}$) and small collection areas along with a short collection time in the tens of nanosecond range. Furthermore, analysis of the pulse time structure of the beam current is important for correct measurements of microdosimetric spectra.

The SOI microdosimeter developed in this work offers the potential to eliminate pile-up effects and greatly improve spatial resolution due to its small size. In this chapter, experiments at two proton therapy facilities are discussed. The experiments were conducted at the Proton Medical Research Center (PMRC) at University of Tsukuba, KEK, Japan, using a 250 MeV proton beam and at the Northeastern Proton Therapy Center (NPTC), Boston using a 230 MeV proton beam. The aim of the experiments was a preliminary study of the performance of the silicon microdosimeter to confirm its capability at measuring the expected microdosimetric features. The ability of the device to minimize pileup effects and its high spatial resolution are discussed in some detail. A comparison of experimental results with computer simulations is also presented. Two different probe assemblies are used in this work corresponding to different stages in the project development.

9.2 Experiment at PMRC-Tsukuba

The main aim of the experiment was to demonstrate the capability of the small silicon microdosimeter to perform measurements under difficult pile-up prone beam conditions for which no previous microdosimetric measurements have been performed.

9.2.1 Materials and Methods

9.2.1.1 Proton Therapy Facility at PMRC-Tsukuba

The proton therapy facility at PMRC uses the KEK 500 MeV booster synchrotron as a beam source [294]. This source was originally designed for HEP experiments and since the energy and intensity are too high for medical applications, the beam energy is degraded down to 250 MeV using carbon based degraders. Additional filters reduced this to 200 MeV for these experiments. In contrast to the NPTC facility, this synchrotron produces 50 ns pulses with an initial 2×10^9 protons per pulse. The time interval between pulses is about 1 second in parasitic beam mode and 0.05 seconds in full beam mode. Note that the protons/pulse is the same for both parasitic mode and full beam mode. The full beam mode is used for patient treatment and provides a dose rate of approximately 200 cGy/min.

The initial beam intensity is reduced by the carbon degrader followed by a collimator such that around 10^4 protons/pulse are transported to the medical beam line. Then the beam is momentum filtered and shaped for a $10 \times 10 \text{ cm}^2$ field. Thus, the beam intensity is around 4 proton/pulse/device which is much higher than at NPTC. This beam presents a difficult experimental challenge even when using the small area of the silicon based microdosimeter. Clearly, the high luminosity of this beam prevents the use of a proportional gas counter for microdosimetry due to strong pile up effects. Note that reducing the beam current does not reduce pile up effects since it usually involves a reduction in the frequency of pulses rather than the number of protons per pulse.

However, to reduce the protons per pulse one can control the momentum slit width (X) and vertical slit width (Y) which are typically set to 150 and 30 mm respectively.

9.2.1.2 Experimental Setup at PMRC-Tsukuba

This experiment was performed with "probe assembly #1" as described in section 4.3 (Note, that the improved probe assembly #2 had not been developed at this stage of the project). The $10 \text{ }\mu\text{m}$ SOI device was selected to provide the highest signal to noise ratio for the measurements. The charge collection characteristics of the device, at the selected reverse bias voltage of 10 V, were fully described in section 6.2.4.2. Under these conditions, the collection efficiency was found to be reasonably approximated by a constant value of 0.82.

Microdosimetric spectra require an estimate of the detectors mean chord length $\bar{l}$. An accurate value of $\bar{l}$ may be obtained via Monte-Carlo simulation methods which transport the protons and other charged particles through the experimental setup and determine the path length traversed through the device. However, a reasonable first order approximation assumes that the beam is largely normal to the diode surface in which case we may approximate $\bar{l} \sim 8.2\mu\text{m}$. In this paper, with an emphasis on device operation, we present all results based on the silicon mean chord length without TE correction (as discussed in section 5.5). Note also, that a direct comparison with a TE proportional counter is not performed in this study.

Since the beam is largely normal to the device, it is reasonable to use the "proton edge" for calibration, a method discussed in section 8.3.1. For a normally incident proton the maximum energy deposited, at the end of the proton range, in $9.9\mu\text{m}$ of silicon ($10\mu\text{m}$ SOI - $0.1\mu\text{m}$ LOCOS region) is 737 keV. The energy collected is then ~ 604 keV (0.82×737 keV) which corresponds to a maximum lineal energy of 73.7 keV/ μm . Thus the proton edge will occur at around 74 keV/ μm with some smoothing of the edge due to protons that are not normally incident. The spectra presented in this chapter have been calibrated to ensure the proton edge lineal energy coincides with this value. Further discussion of this spectral feature is provided in section 9.3.2.2.

The microdosimeter was placed in a $15 \times 15 \times 30\text{ cm}^3$ Lucite phantom constructed of 2.5 cm blocks. Such a construction allowed the placement of the detector at different positions along the beam line axis. To avoid pile-up and ensure a constant energy the momentum slit was fixed at $X = 3\text{ mm}$ whilst the vertical slit was varied from $Y = 30$ to 2 mm . Microdosimetric spectra at a depth of 17.5 cm were recorded at various values of vertical slit width to determine the settings required to remove pile-up effects. The acquisition time for the measurements was 600 seconds. Measurements at various depths in the Lucite phantom were then performed having found the beam setup which eliminated pile-up. The integral depth-dose was measured by a MOSFET detector.

9.2.2 Results: Microdosimetric Spectra at PMRC-Tsukuba

The depth-dose curve obtained using a MOSFET detector placed at various depths in the Lucite phantom are shown in Figure 9.1. The advantageous characteristic of a MOSFET dosimeter is the extremely small dosimetric volume ($\sim 1\mu\text{m}$) defined by the gate oxide thickness [71, 175]. High spatial resolution measurements are achievable in

the Bragg peak regions. However, the response of the MOSFET is dependent on the particle LET and angle with respect to the oxide electric field. Further investigation and comparison studies should be performed to compare the depth-dose derived from ionization chambers versus MOSFETs.

The microdosimetric spectra obtained as a function of depth in Lucite are shown in Figure 9.2. The small peaks from 30-100 keV/ μm are due to statistical uncertainties. The general shift in the spectrum to higher lineal energies as depth increases from 14 cm to 17.5 cm is evident. The MOSFET depth-dose data indicates that at around 17.5 cm many of the protons will be approaching the end of their range. In this region, the protons have a higher LET, and therefore higher lineal energy, as they approach the Bragg peak. This behavior is in agreement with results obtained at NPTC and by Coutrakon [155] using a proportional counter.

The data obtained using the prototype assembly #1 exhibited significant environmental noise problems particularly when the beam RF was turned on. It is expected that the second prototype with its significantly improved shielding will avoid such difficulties. The lineal energy could not be obtained below 8 keV/ μm due to the high noise levels. This was the motivation for development of the low noise prototype. Despite the limited clinical utility of the incomplete spectrum, we may still verify the capability of the device in terms of high count-rate performance.

The vertical slit was adjusted down to 2 mm from the normal value of 30 mm in order to avoid pile-up. Figure 9.3 shows a comparison of microdosimetric spectrum obtained under Parasitic-Beam and Full-Beam modes at PMRC with different vertical slit widths (depth in Lucite phantom = 17.9 cm). This example shows significant pile-up effects using the Parasitic Beam despite its much lower total intensity. To avoid pile-up in either mode the beam requires a vertical slit width of 2 mm in order to reduce the number of protons/spill. The spectra of Figure 9.2 obtained at various depths used such a slit arrangement. The results indicate that the low noise prototype applied to similar beam conditions should be capable of measuring the microdosimetric spectrum down to 1.2 keV/ μm without significant pile-up complications.

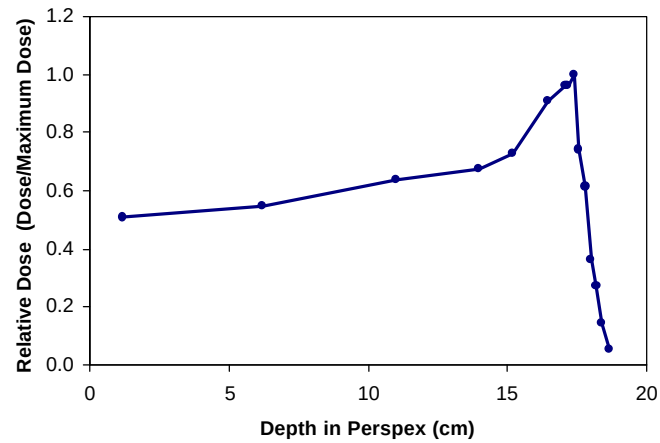


Figure 9.1: Bragg peak of 200MeV proton beam (PMRC-Tsukuba) derived by MOSFET detector in Lucite phantom. Relative dose is the dose normalized to maximum dose at depth of 17.4 cm.

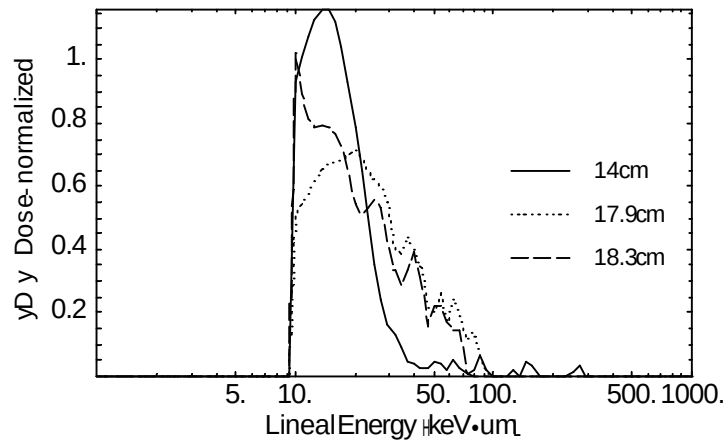


Figure 9.2: Microdosimetric spectra of 200MeV proton beam (PMRC-Tsukuba) at various depths in a Lucite phantom. Range of proton is approximately 18cm.

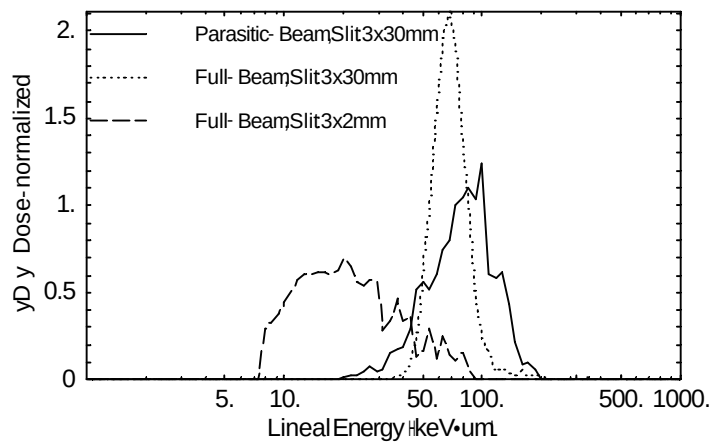


Figure 9.3: Comparison of microdosimetric spectrum obtained under Parasitic-Beam and Full-Beam modes at PMRC-Tsukuba with different vertical slit widths (depth in Lucite phantom = 17.9 cm). This example shows significant pile-up effects using the Parasitic Beam despite its much lower total intensity. To avoid pile-up in either mode the beam requires a vertical slit width of 2 mm in order to reduce the number of protons/spill.

9.3 Experiment at NPTC-Boston

9.3.1 Materials and Methods

9.3.1.1 Proton Therapy Facility at NPTC-Boston

The new proton therapy facility at NPTC utilizes a 230 MeV beam extracted from an isochronous cyclotron [295, 296]. The accelerator was built by Ion Beam Applications (IBA), Belgium and has a maximum current of 1.5 μA which is hardware limited to 300 nA in order to limit the maximum dose rate to the patient. After extraction from the cyclotron the beam passes through the Energy Selection System (ESS) designed to give a beam of any energy between 70 and 230 MeV with a user defined momentum width and emittance. The ESS uses a rapidly adjustable rotating variable thickness of graphite. Slits are provided just after the energy degrader to reduce the beam divergence to $\Delta E/E < \pm 1\%$. The facility uses a range modulator filter to create the desired spread in the proton Bragg peak. A double scattering system using a fixed scatterer and a second non-uniform thickness scatterer produce a beam with uniform intensity in the lateral profile over a $10 \times 10 \text{ cm}^2$ field size.

The NPTC cyclotron operates in continuous wave mode using a 106 MHz RF frequency. Acceleration of protons occurs within 10-15 degrees of the RF wave. The time structure of the beam is therefore semi-DC with a duty-cycle of about 10% (30deg/330deg). A typical treatment beam is 2 nA equivalent to 1.25×10^{10} protons/second. So in a single RF cycle of 9.4 ns there are 118 protons spread over 0.8 ns. For the case of a $10 \times 10 \text{ cm}^2$ field size (obtained using a double scattering method) we can expect 1.2 p/cm²/cycle. Under these conditions, a microdosimeter should have a small cross-sectional area and fast collection time.

9.3.1.2 Experimental Setup at NPTC-Boston

The improved low noise "probe assembly #2" as described in section 4.4 was used for this experiment. The 10 μm SOI device was selected to provide the highest signal to noise ratio. As discussed in section 9.2.1.2 a mean chord length of 8.2 μm is used for presentation of microdosimetry spectra.

The microdosimeter selected has an active cross-sectional area of 0.044 cm². The minimum amplifier shaping time available was 0.25 μs and the Ortec pile-up reject system was employed to eliminate pile-up signals. Note that decreasing the amplifier

shaping time further would increase noise to unacceptable levels. In order to maintain a reasonable dead-time (less than about 20%) we require less than 1 proton per $1.25\ \mu\text{s}$ striking the detector. Such a requirement may be fulfilled using a beam current of 0.25 nA in which case we expect $0.7\ \text{p}/\mu\text{s}/(\text{device area})$. In practice, higher beam currents (up to 1 nA) could be employed without excessive dead-time and distortion of the spectra due to pile-up events. The quick calculations performed above do not include losses of beam current due to scattering outside of the beam field.

The microdosimeter was placed in a Scandtronix water tank (Model RFA-300 Plus) which enabled rapid remote adjustment of the detector position. The detector position was aligned with the center of the beam and microdosimetric spectra were recorded at various distances from the beam-side wall of the tank. The depth (distance from the front wall) of the detector includes the probe overlayer materials as summarized in Table 9.1. These materials were estimated to be equivalent (in terms of stopping power) to 12mm of water. At each depth, spectra were recorded using two different gains to provide adequate dynamic range in the final merged spectrum. Initially the beam current was adjusted to ensure that the spectra were not corrupted by pile-up events. Furthermore, during measurements, the signal prior to the MCA was monitored continuously with an oscilloscope to ensure the average interval between pulses was reasonable and no pileup was present. The typical acquisition time was 600 seconds.

In addition, measurements of the depth-dose profile in the water tank were performed using a Markus ionization chamber. Measurements were made every 0.3 cm for the range 0-30 cm along the beam axis. Two measurements at each point were made using different spectroscopy amplifier gain settings (110 and 30). The results are then merged to provide a single spectrum with a higher dynamic range than the constituent spectra.

The proton beam was setup with the energy degrader in pass through position and the ESS configured to provide the full cyclotron energy of 230.5 MeV with an $\Delta E/E$ of 0.18%. The cyclotron energy is attenuated by the items identified in Table 9.2 so that the final energy (calculated using SRIM code [126]) of protons entering the water is 191.6 MeV.

Table 9.1. Probe assembly materials in front of the silicon microdosimeter and water equivalent thickness

Item	Material	Thickness (mm)	Water Equivalent Thickness (mm)
Probe Holder	Lucite	6	7.1
Shield	Al	0.4	0.8
Chip Cover	Lucite	3.5	4.1
Air on top of device	Air	0.3	0.0003
Total:			12.0

Table 9.2. Beam items in nozzle of NPTC and proton energy attenuation

Item	Material	Thickness (cm)	EnergyOut (MeV)	Energy Lost (MeV)
Cyclotron	-	-	230.5	-
Fixed scatterer	Pb	0.131	227.3	3.2
Range Modulator 1	Pb	0.4254	216.7	10.6
Range Modulator 2	C	0.0773	216.0	0.7
Beam Spread	Water Eq	3.65	199.8	16.2
Ion chambers	Water Eq	0.304	198.3	1.4
Nozzle air	Air	255	197.1	1.3
Phantom wall	Lucite	1	191.6	5.4

Water Eq: means that the effective thickness is specified in water equivalent terms. The beam spreading filter is made of lead and Lexan.

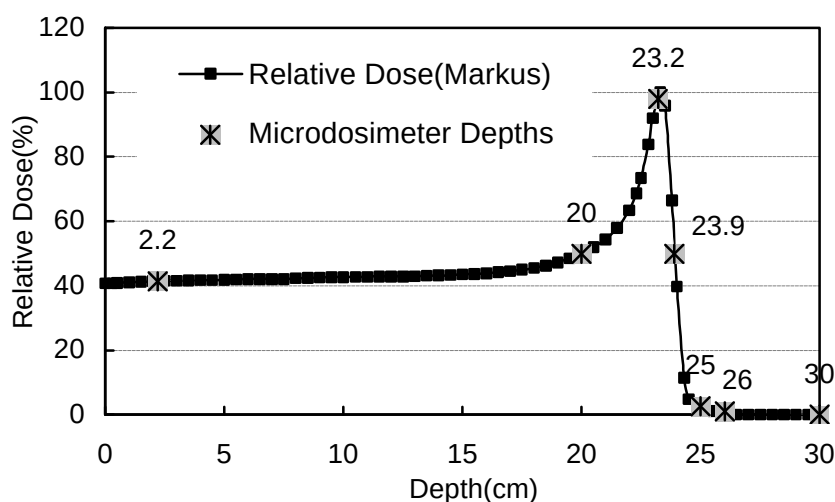


Figure 9.4: Depth-Dose curve for the NPTC 191.6 MeV proton beam in water. Relative dose is defined as Dose(Markus)/Maximum Dose(Markus). The maximum dose is at 23.2 cm and the relative dose = 1 at this point. The depths at which microdosimetric measurements are made are shown.

9.3.1.3 Simulation using SRIM and PRISM

The expected performance of the microdosimeter may be simulated using the Monte Carlo codes; SRIM (Stopping and Range of Ions in Matter) developed by Ziegler [126] and PRISM (Protons in semiconductor materials) developed by Oldfield [297]. Other

semiconductor codes such as CUPID developed by McNulty [298] may also be used for this application.

SRIM was used in the spectroscopy modeling software presented in section 6.2.1 and is capable of simulating the transport of ions through planar slabs composed of any material. SRIM results from the original work by J.P. Biersack on range algorithms [299] and the work by J.F. Ziegler on stopping theory ([184]. The program simulates elastic nuclear collision losses using the theory of Biersack [299] and inelastic atomic collisions but does not simulate inelastic nuclear collisions.

PRISM on the other hand is designed specifically for protons incident on semiconductor materials up to an energy of 450 MeV. The program models the transport of protons in a similar manner to SRIM but includes inelastic nuclear collisions between the ion and silicon target nuclei. Note that below proton energies of 8 MeV no inelastic nuclear reactions are assumed to take place and the reaction cross-section peak occurs at around 30 MeV (~650 mb). Reaction probability, residual products and energies are determined using cross-section data from a variety of sources as referenced by Oldfield [297]. For energies less than 60 MeV the work of Peterson [300] is extensively used.

The proton microdosimetry simulation was performed in three steps; the first two steps used SRIM exclusively and the last device simulation step used both SRIM and PRISM:

1. *Simulation of beam line:* The beam line as described by Table 9.2, with an initial proton energy of 230.5 MeV and an $\Delta E/E$ of 0.18%, was simulated using SRIM in order to determine the proton energy spectrum at the entrance to the water phantom. This was a crude simulation which did not consider the lateral beam spreading design since the beam spreader is a non-planer structure and thus not accurately amenable to SRIM simulation. Thus, the calculated beam energy spread ($\mu=191.6\text{MeV}$, $\sigma=1.4\text{MeV}$, $\Delta E/E=1.7\%$) underestimates the true energy spread. To compensate the derived standard deviation was doubled, somewhat arbitrarily, to 2.8 MeV, a value also found to produce a reasonable correspondence between simulated microdosimetric spectrum and experimental results.
2. *Simulation of proton transport through water phantom and pre-detector probe materials:* The entrance beam proton energy at a depth of 0 cm in the water phantom was taken to be normally distributed with a mean of 191.6 MeV (Table 9.2) and standard deviation 2.8 MeV. The particle angle of incidence was taken as zero

degrees with respect to the normal. Simulations were performed for a water depth of 2.2 cm (the nearest point to the entrance) and 23.9 cm at the distal edge of the dose distribution (50% dose point as given by Figure 9.4). The output of this simulation was a distribution of proton energies at each depth along with the direction cosines of each proton simulated.

3. *Simulation of 10 mm SOI device energy deposition and charge collection:* Both SRIM and PRISM were used for this simulation. SRIM was employed using the spectroscopic modeling environment described previously in section 6.2.1 using the proton energy and angle information derived from the previous section as input. As such, the model fairly accurately accounts for the differing device regions, varying charge collection efficiency and varying incident proton energy and angle. However, the model does not consider inelastic nuclear reactions as simulated by PRISM. Thus PRISM was run, firstly for comparison with SRIM and secondly to determine the proportion of inelastic reactions originating from the silicon. PRISM accepts RPP shaped volumes and only calculates inelastic reactions with silicon. A cubic silicon volume with side length equal to the wafer thickness of 300 μm , was modeled as shown in Figure 9.5. The width and length were selected to encompass the range of most secondary particles. This simulation volume contained the detector with dimensions of 300 $\times$ 300 $\times$ 9.9 μm where 9.9 μm is the depth of the device (calculated using 10 μm SOI - 0.1 μm LOCOS region) and the device overlayer was approximated as 1 μm of silicon. This is a relatively crude approximation to the device since the various oxide and aluminium overlayer regions were not included. However, a first order estimate of the proportion of events due to silicon inelastic interactions may be gauged. The charge collection efficiency of the device was modeled as a simple constant of 0.82 for the PRISM simulation whilst for the SRIM simulation the slightly more accurate collection efficiency function derived in section 6.2.4.2 was used. In addition, PRISM assumed normally incident protons unlike SRIM which used the previous water transport simulation results. Thus, only the proton energy and not the angular distribution was modeled in PRISM. For both models, the final spectra are presented with 20 keV of gaussian smoothing to simulate electronic noise and additional sources of variation consistent with the spectroscopy model of section 6.2.1.

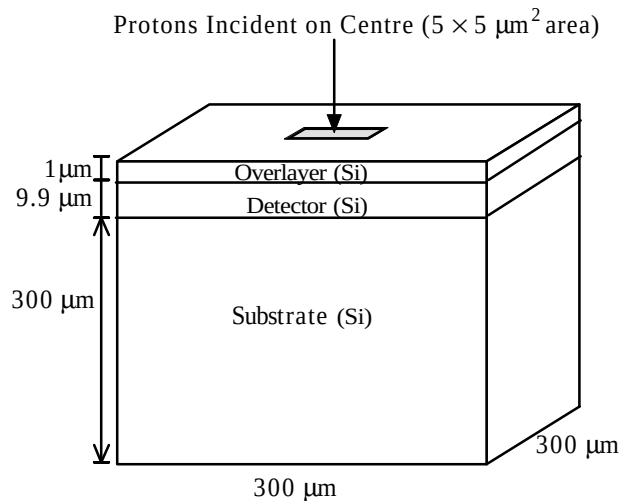


Figure 9.5. Geometry used for PRISM simulation of 10 μm SOI microdosimeter

9.3.2 Results

9.3.2.1 Microdosimetric Spectra at NPTC-Boston

The microdosimetric spectra obtained as a function of depth at NPTC are shown in Figure 9.6. One first notes the significantly improved noise performance of the low noise prototype in comparison to measurements made at PMRC. Measurements were obtained down to the noise level of about 1.2 keV/ μm (Silicon). The depth-dose curve obtained using the Markus chamber and the microdosimeter measurement positions are shown in Figure 9.4. At depths less than 20cm, the large dose contribution from low lineal energy events is due to significant high energy proton and gamma contributions which both have an LET below 2 keV/ μm . As we approach the Bragg peak, the LET of the protons rises as seen by the increase in the mean lineal energy and the shift of the spectra to higher lineal energies at depths between 20-26 cm. These effects were also observed using a proportional counter at the Loma Linda proton beam by Coutrakon [155] This shift is not due to pileup effects since, firstly, the signal was continuously monitored with an oscilloscope and, secondly, the count rate is lower at higher depths due to beam spreading.

Note the step decline in the microdosimetric spectra at around the maximum lineal energy of protons of 74 keV/ μm . Dose contributions are evident at lineal energies above the maximum proton LET due to nuclear reaction products such as alpha particles and heavy ion recoils. However, the relative number of such events is much smaller than the proton events hence the step change above the maximum proton LET. Scattered

protons, which are not normally incident on the device, also contribute to the microdosimetric spectrum at lineal energies above $74 \text{ keV}/\mu\text{m}$.

As we exceed the maximum range of the protons, the higher lineal energy components contribute a relatively higher proportion of dose. At 30 cm, well past the primary proton range, the spectrum is comprised totally of neutron reaction products including recoil protons, alpha particles and heavy ion recoils. The neutron reaction products tend to have a large proportion of dose at higher lineal energies. The maximum lineal energy measured of around $700\text{--}800 \text{ keV}/\mu\text{m}$ was limited by saturation of the multi-channel analyzer at the selected gain. An additional measurement using a lower gain and over a longer measurement time is required to obtain the small number of counts at lineal energies above the current maximum. These results will be further discussed in the next section comparing selected spectra with simulation.

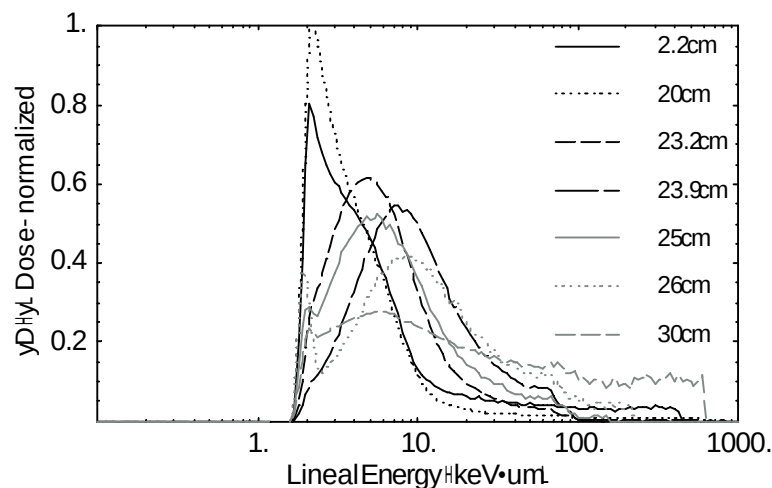


Figure 9.6: Microdosimetric spectra of 191.6 MeV proton beam at various depths in a water phantom. Range of proton is approximately 23.7 cm.

9.3.2.2 Comparison with Simulation

The energy spectrum of protons incident on the detector when placed at a depth of 23.9 cm is shown in Figure 9.7. The SRIM calculation also estimates that 48.5% of protons are stopped completely in the water; a value that coincides with the 50% maximum dose observed at a depth of 23.9 cm as shown in Figure 9.4. The energy spectrum has a large relative variance resulting in a wide variation in proton LET(Si) of between 135 (at 70 keV) and $2.5 \text{ keV}/\mu\text{m}$ (at 45 MeV).

Using this energy spectrum, the expected microdosimetric spectrum was simulated and compared with the experimental spectrum as shown in Figure 9.9. Overall, the match between experimental spectrum and simulation results is quite good. The peak in lineal energy at $7.5 \text{ keV}/\mu\text{m}$ was well matched and the proton edge at $73 \text{ keV}/\mu\text{m}$ roughly coincides between the spectra. At lower lineal energies, the simulations do not produce as much spectral spread as the experimental spectrum due to the various simplifying approximations used in the simulations such as simple geometrical models. In addition, the shape of the spectra around the proton edge differs in all three cases.

The proton edge for the experimental data is spread from about 65 to $100 \text{ keV}/\mu\text{m}$ due to a variation in the angle of incidence of the protons increasing the chord length and hence energy of these events. Such a spread is not as evident in the simulations due to inadequate modeling of the proton angular distribution. The SRIM simulation is slightly better (greater proton edge spreading) than PRISM since angle information from the previous water transport simulation was employed in SRIM whilst PRISM assumes normally incident protons. The calculated probability distribution of proton angle is shown in Figure 9.8. The SRIM water transport simulation assumes normally incident protons at a water depth of 0 cm which is a crude approximation that results in an inadequate spread in the angles incident on the device. Improved modeling would require an accurate simulation of the beam line scattering particularly the lateral spreading filters.

The experimental spectrum and simulations were also compared at 2.2 cm water depth as shown in Figure 9.10. The main point derived from this comparison is that the experimental spectrum does not have a sufficiently low noise cutoff to adequately record the spectrum. The spectrum is missing below around $2 \text{ keV}/\mu\text{m}$ which severely affects the normalization process. Note, that the peak from $2\text{-}2.5 \text{ keV}/\mu\text{m}$ is anomalous and was traced to a known hardware design fault in the Amptek Pocket MCA-8000. The fault only occurs at high sub-lower level discriminator count rates encountered at depths of 2.2 and 20 cm. In summary, the silicon microdosimeter probe assembly requires at least a factor of two improvement in noise performance in order to correctly measure spectra at depths less than about 20 cm. This is not a significant deficiency since the microdosimetric characteristics of the beam are not as clinically important at these depths.

The PRISM simulation enabled a calculation of the proportion of events that are due to inelastic nuclear reactions between protons and silicon in the device. It is desirable to have this proportion as low as possible since such events affect the tissue equivalence of the device operation as discussed in section 5.5.3. Of the 10000 protons transmitted through the device only 3 of the energy deposition events were due to inelastic nuclear events (all $\text{Si}^{28}(\text{p,p})\text{Si}^{28}$ reactions). These events deposited relatively small energies from secondary proton products intercepting the sensitive volume. The energies were 56.9, 45.5 and 69.2 keV, yielding collected lineal energies of 5.7, 4.6 and 6.9 keV/ μm , respectively. Prism provides a facility to increase the probability of such reactions and it was determined that only 0.043 $\pm$ 0.004% of all events are due to inelastic reactions at 23.9 cm. At the lower simulated depth of 2.2 cm the proportion is even lower, 0.03 $\pm$ 0.003%, due to the decreased inelastic cross-section at higher proton energies. Thus, the proportion of inelastic nuclear interaction events with silicon is negligible up to depths of around 25 cm and thus, the silicon microdosimeter with appropriate geometrical scaling may be considered tissue equivalent. At greater depths, neutron events begin to dominate the microdosimetric spectrum as discussed in the previous section. The tissue equivalence of neutron interactions was discussed in sections 5.5 and 8.3.3. Such interactions were not modeled in this simulation and future work is suggested.

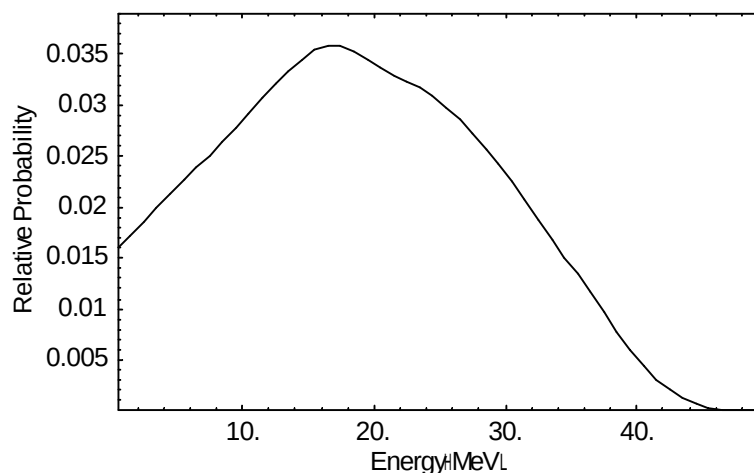


Figure 9.7. Proton energy spectrum following the transport using SRIM of 191.6 MeV protons (normal distribution with $\mu=191.6$ MeV, $\sigma=2.8$ MeV) through 23.9 cm of water. Note also that 48.5% of protons are stopped completely in the water (i.e. $E=0$).

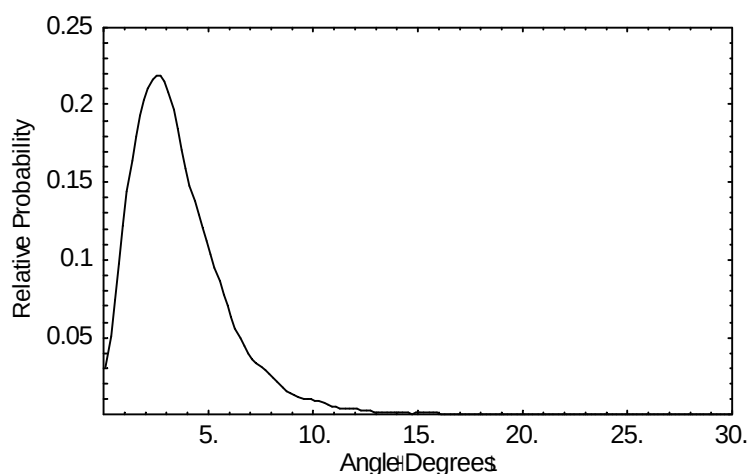


Figure 9.8. Probability distribution of proton angle of incidence with respect to the device normal. Calculated using SRIM transport of 191.6 MeV protons (normal distribution with $\mu=191.6$ MeV, $\sigma=2.8$ MeV) through 23.9 cm of water

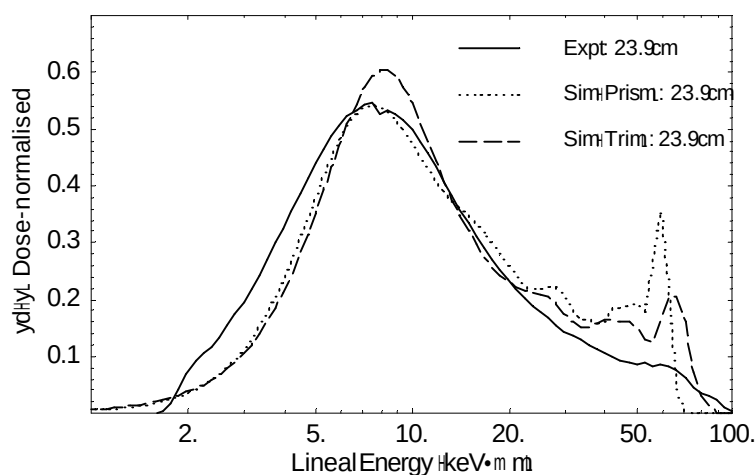


Figure 9.9. Experimental silicon microdosimeter spectrum at 23.9 cm in water phantom at NPTC compared to Monte-Carlo simulation results using PRISM and SRIM.

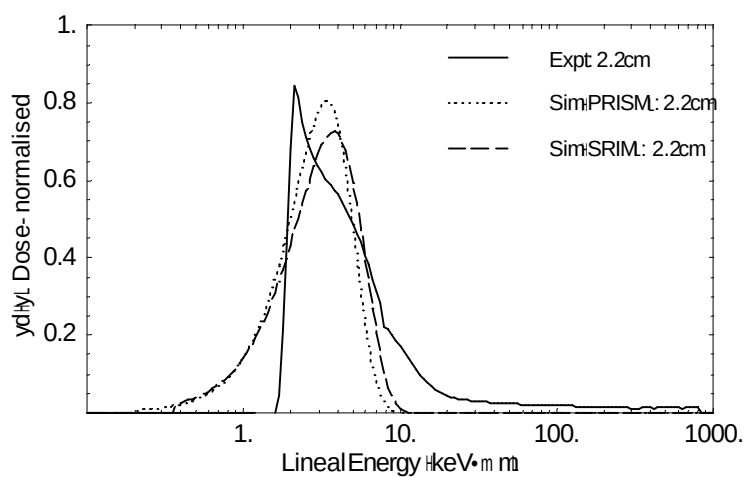


Figure 9.10. Experimental silicon microdosimeter spectrum at 2.2 cm in water phantom at NPTC compared to Monte-Carlo simulation results using PRISM and SRIM.

9.4 Summary of Proton Therapy Applications

These measurements provide valuable information for radiobiological studies of the varying effectiveness of the beam as a function of depth. Testing at the recently constructed NPTC facility in Boston demonstrated the capability of the device at recording lineal energy spectra with high spatial resolution. The spectra were consistent with simulations performed using SRIM and PRISM and qualitative expectations based on previous proportional counter measurements in protons beams and an understanding of the beam characteristics. Future work may be directed towards the analysis of beam relative biological effectiveness such as performed at Loma Linda by Coutrakon [155] at a higher spatial resolution than previously attempted.

In general, pile up and perturbation effects were avoided due to the small area (0.04 cm^2) of the total pixel array. Pileup did occur for experiments at PMRC when the vertical momentum slit width was greater than 2 mm. Under these conditions, an even smaller area detector is required. Note that the area requirements are still well within the design capability of silicon technology. The detector was coupled to a radiation-hard charge sensitive amplifier with the probe assembly capable of measuring an LET down to $1.2 \text{ keV}/\mu\text{m}$ (Silicon). The device offers much improved spatial resolution compared with a proportional gas counter particularly in the critical high dose region around the proton Bragg peak.

We have demonstrated a new approach to microdosimetry in radiation oncology using a silicon SOI p-n junction array applied to proton therapy beams. Low noise, small size and good radiation hardness facilitate the application of this device in radiation oncology.