Journal and Proceedings of the Royal Society of New South Wales, vol. 148, nos. 455 & 456, pp. 44-51.
ISSN 0035-9173/15/010044-8

3D Bridge Microdosimeter: Charge Collection Study and Application to RBE Studies in ^{12}C Radiation Therapy

Linh T. Tran[1], Dale A. Prokopovich[2], Susanna Guatelli[1], Marco Petasecca[1], Michael L.F. Lerch[1], Mark I. Reinhard[2] and Anatoly B. Rosenfeld[1]

[1]Centre for Medical Radiation Physics, School of Physics, University of Wollongong, NSW 2522, Australia
[2] Australian Nuclear Science and Technology Organisation, Lucas Heights, NSW 2234, Australia

* Corresponding author.
E-mail: tltran@uow.edu.au

Abstract

Radiotherapy using heavy ion beam such as Carbon-ion has the advantage for the treatment of deep-seated tumour over conventional radiotherapy with X-rays due to an enhanced dose deposition in the Bragg peak (BP) at the end of the ion range. The highest dose can be deposited in the tumour with much lower doses to the surrounding healthy tissue. The Relative Biological Effectiveness (RBE) of a carbon-ion radiotherapy beam greatly depends on a depth of the target volume in the body and the nuclear fragmentation process that increases close to the BP or spread out BP (SOBP) as well as neutrons. It is important to understand the RBE of the heavy ions in hadron therapy applications in order to deliver correct dose.

Microdosimetry is extremely useful technique, used for RBE study in unknown mixed radiation fields typical of hadron therapy. Conventional detectors for microdosimetry consist of tissue equivalent proportional counters (TEPC) which have advantages of a spherical sensitive volume and tissue equivalency through use of a tissue equivalent gas. However, TEPC has several limitations such as high voltage operation, large size of assembly, which reduces spatial resolution and introduces wall effects, and an inability to simulate multiple cells.

A new silicon microdosimeter with 3D sensitive volumes (SVs) has been proposed to overcome the shortcomings of the conventional TEPC. The new microdosimeter is called "bridge" microdosimeter as it has thin Si bridges between the SVs to support the Al tracks over the SVs. The charge collection study of the new device and its application for RBE determination in ^{12}C radiation therapy at the Heavy Ion Medical Accelerator in Chiba (HIMAC), Japan is presented.

This work presented the first RBE_{10} derivation in a ^{12}C ion therapeutic beam using a high spatial resolution silicon microdosimeter and demonstrated a simple and fast method for Quality Assurance in charge particle therapy.

Introduction

According to the NSW Cancer Registry Statistical Reporting, 1% of population per annum diagnosed with cancer. Approximately one third of Australians are expected to develop cancer during their lifetime with about two thirds of cancer in people aged over 65. More than 50% of all patients with localised malignant tumours are being treated with radiation (Schardt, 2010).

Conventional X-ray radiotherapy is used for treatment of many types of tumour but it has limitations as it also irradiates normal tissues surrounding the tumours especially when tumours are located in proximity to critical organs or in paediatric treatments.

Particle therapy is advantageous for the treatment of deep-seated tumours as the highest dose can be deposited in the tumour with much lower doses to the surrounding healthy tissue. The energy deposition mechanisms of ions in matter are different to photons and dominated by electronic collisions for the relevant energies of primary ion described by Bethe-Bloch formula (Bethe, 1930, Bloch, 1933). The nuclear reactions contribute substantially to the ion dose via nuclear fragments and neutrons production. Fig. 1 shows a comparison of the depth dose distribution produced by MV photons and different energies of the ^{12}C ions.

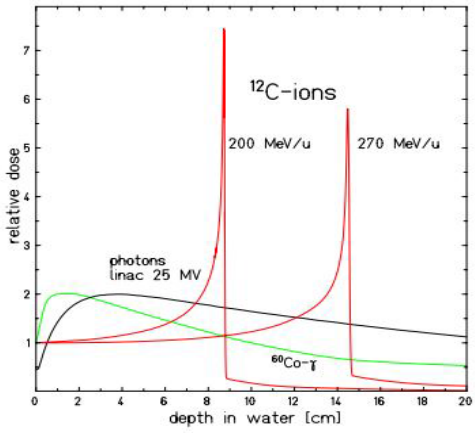

Figure 1. Depth-dose profiles of ^{60}Co γ radiation, megavolt photons, and ^{12}C ions in water (Schardt, 2010). The fragmentation tail is clearly observed downstream of the ^{12}C Bragg peak.

In order to accurately predict radiobiological effects in humans due to the radiation field of a typical cancer treatment with ions, it is important to understand how the Linear Energy Transfer (LET) of primary and secondary ions varies with depth as well as its RBE.

Microdosimetry is a method of measuring the microscopic pattern of ionizing energy deposition in a micron sized sensitive volume (SV) of similar dimensions to biological cells (Rossi, 1996). This technique is extremely useful for understanding of radiobiological properties of unknown mixed radiation fields typical of space and aviation, as well as in hadron therapy. The microdosimetric quantity used to describe the energy deposition in such a SV along a particles track is called the lineal energy deposition (*y*).

$$y = \frac{E}{\langle l \rangle} \quad (1)$$

where E is the ionizing energy deposited in a micron sized SV with an average chord length $\langle l \rangle$ from a single event. The spectrum of stochastic events $f(y)$ for all primary and secondary particles generated during an exposure of tissue to ionizing radiation can be derived from the spectrum of energy deposition events. The partial fraction of dose deposited by the charged particles within lineal energy interval $(y, y+dy)$ is $d(y)$ and is given by:

$$d(y) = \frac{yf(y)}{\overline{y_F}}, \quad (2)$$

where $\overline{y_F} = \int_0^\infty yf(y)dy$ is the frequency mean lineal energy and $d(y)$ vs. y is a microdosimetric spectra usually presented in a log scale as $yd(y)$ vs. $\log(y)$. The major microdosimetric parameter relevant to RBE and derived from microdosimetric spectra is $\overline{y_D} = \int_0^\infty yd(y)dy$, where $\overline{y_D}$ is the dose mean lineal energy. Using the microdosimetric spectra and the microdosimetric kinetic model (MKM; Kase,

2011) the RBE of the ^{12}C ion beam can be derived.

The Centre for Medical Radiation Physics (CMRP) at the University of Wollongong has initiated the concept of silicon microdosimetry to replace the current microdosimetry gold standard, the TEPC. Compared to the TEPC, the CMRP silicon microdosimeters are advantageous due to being a solid-state detector with no gas-flow ensemble, having very low operating voltages less than 10V, extremely high spatial resolution of up to 10μm and a high degree of portability and ability to simulate multiple cells (Bradley 1998, 2000). Three generations of silicon on insulator (SOI) microdosimeters have been developed, fabricated and investigated (Bradley 2000, Cornellius 2003, Ziebell 2008, Livingstone 2012). Based on previous research and development at CMRP, the feasibility of the silicon microdosimetry concept has been proven. Despite this success, a number of limitations have been observed in previous designs of SOI microdosimeter. These limitations include non-uniformity of charge collection in the SV and diffuse charge collection outside of the SV (Ziebell, 2008). In order to overcome these drawbacks, we have proposed further steps to optimize the SOI microdosimeters with the development of freestanding 3D SVs, the so called "mushroom" microdosimeter, using 3D detector technology (Tran, 2014). A Geant4 simulation study has been carried out to optimize the design and investigate the response of the "mushroom" microdosimeter in aviation neutron fields. These results have given confidence to the new microdosimeter design (Tran, 2014). However, the manufacturing process for fabricating free-standing 3D SVs on a silicon substrate is complex. As an intermediate step towards free-standing 3D SVs, an SOI microdosimeter with 3D SVs was produced by etching the silicon surrounding the SVs whilst leaving thin silicon "bridges" between the SVs to support the aluminium tracks electrically connecting SVs. The new microdosimeter is called the "bridge" microdosimeter as it has thin Si bridges connecting the SVs. The charge collection study of the new device and its application for RBE determination in ^{12}C radiation therapy is presented.

Material and Method

Design of the 3D bridge microdosimeter

The newly developed bridge microdosimeter has a large sensitive area of 4.1 x 3.6mm^2 designed for use in low dose rate environments such as those in aviation and space. The device is segmented into three sections in order to reduce the noise by minimizing the capacitance and dark current of each segment (Fig. 2a). Fig 2b shows a SEM image of an array of SVs of the 3D bridge microdosimeter where the surrounding silicon was fully etched down to 10μm depth using the deep reactive ion etching (DRIE) technique which produced a straight parallelepiped SV shape. This new technology provided well-defined geometry of micron-sized 3D SVs.

The microdosimeter is based on an array of 4248 planar 30x30x10μm cubic SVs fabricated on a high resistivity n-SOI active layer of thickness 10μm and low resistivity supporting wafer. Layers of phosphorus silicate glass (PSG) and SiO_2 were deposited on top of the device. Each SV was fabricated using ion implantation to produce the square p-n junction structure (Fig. 2c). The even and odd rows of SVs are read out independently to avoid events in adjacent sensitive volumes being read as a single event in the case of oblique charged particle tracks.

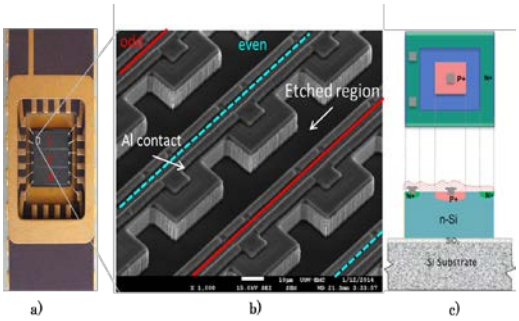

Figure 2: a) A bridge microdosimeter mounted on a Dual In Line (DIL) package, b) a SEM image of arrays of SVs, c) A top view and a cross-section of the SV of microdosimeter.

Ion Beam Induced Charge Collection (IBICC) Technique

The charge collection efficiency for the 3D mesa bridge microdosimeter was investigated using the Ion Beam Induced Charge Collection (IBICC) technique at the Australian National Tandem for Applied Research (ANTARES) heavy ion microprobe at Australian Nuclear Science and Technology Organisation (ANSTO) (Siegel, 1999). A monoenergetic beam of ions focused to a diameter of approximately 1μm was raster scanned over the surface of the microdosimeter. A 5.5MeV He^{2+} ion microbeam was used in this study. The IBICC signal corresponding to the beam position (*X,Y*) as well as the charge collection *E* for each event was processed into an event-by-event list mode file. Median energy maps showing the charge collection characteristics of the device were then created. Energy calibration of the spectroscopy chain was performed using a pulse generator which was calibrated with a 300μm thick planar silicon PIN diode with 100% Charge Collection Efficiency (CCE) exposed to the ion sources used in the IBICC experiment.

Experiment at ^{12}C ion therapy facility – Heavy Ion Medical Accelerator in Chiba (HIMAC), Japan

The 3D bridge microdosimeter was placed in various positions along the central axis of the Spread Out Bragg Peak (SOBP) of a 290MeV/u ^{12}C ion beam at the Heavy Ion Medical Accelerator in Chiba (HIMAC), Japan. A modular polymethyl methacrylate (PMMA) phantom was used to adjust the position of the Bragg peak relative to the device.

The cell survival irradiated with an absorbed dose of ionizing radiation D is described by the Linear Quadratic Model (LQM) as:

$$S = \exp(-\alpha D - \beta D^2), \tag{3}$$

The Relative Biological Effectiveness (RBE_{10}) of the ^{12}C ion beam is defined as the ratio of the absorbed dose required to achieve 10% cell survival using X-rays to that required when using the radiation of interest.

The modified MK model (Kase, 2011) relates the microdosimetric parameter – dose-mean lineal energy $\overline{y_D}$ to the LQM parameter α, for a particular radiation field. Using the LQM of the cell survival response to radiation, the RBE_{10} can be expressed as:

$$RBE_{10} = \frac{2\beta D_{10,R}}{\sqrt{\alpha^2 - 4\beta \ln(0.1) - \alpha}}, \tag{4}$$

where α, β are tissue radio-sensitivity coefficients (α in units of Gy^{-1} and β in units of Gy^{-2}). $D_{10,R}$ = 5.0Gy is the 10% survival dose for human salivary gland (HSG) tumour cells using 200 kVp X-rays.

$$\alpha = \alpha_0 + \frac{\beta}{\rho \pi r_d^2} y^*, \tag{5}$$

where α_0=0.13Gy^{-1} is a constant that represents the initial slope of the survival

fraction curve in the limit of zero LET, β=0.05Gy^{-2} is a constant independent of LET, ρ=1 g/cm^3 is the density of tissue and r_d=0.42μm is the radius of a sub-cellular domain in the MK model.

$$y^* = \frac{y_0^2 \int_0^\infty (1-\exp(-y^2/y_0^2)) f(y) dy}{\int_0^\infty y f(y) dy} \quad (6)$$

where y^* is a restricted dose-mean lineal energy which is taking into account the cell overkilling effect for lineal energy larger than y_o = 150keV/μm. The same parameter y_o was used at HIMAC in the experiments with the TEPC. The conversion factor of 0.63 was used to convert the lineal energy deposition in silicon to tissue equivalent material (Bradley, 1998).

Results and Discussions

Charge Collection Studies

The response of the 3D bridge microdosimeter was investigated using 5.5 MeV high LET He^{2+} ions. Fig. 3 shows MCA (Multi-channel analyser) spectra and median energy maps obtained from odd and even arrays of the 3D bridge microdosimeter.

The microbeam was scanned across the microdosimeter using a scanning area of 0.3mm x 0.3mm. The microdosimeter was biased at –10 V. At –10 V the peak of the deposited energy distribution in the 10μm bridge microdosimeter is approximately 1350keV which is close to expected value of 1480keV from 5.5MeV He^{2+} in 10μm silicon and 1μm SiO_2 over-layer, calculated by SRIM 2008 (Ziegler, 2008). Compared to previous generations of SOI microdosimeters, low energy events no longer exist in the 3D bridge microdosimeter because of excellent etching technique, removing silicon surrounding the SVs.

Fig. 3b shows full charge collection in the SVs and slightly less than 100% charge collection efficiency in the bridge region due to diffused charge collection.

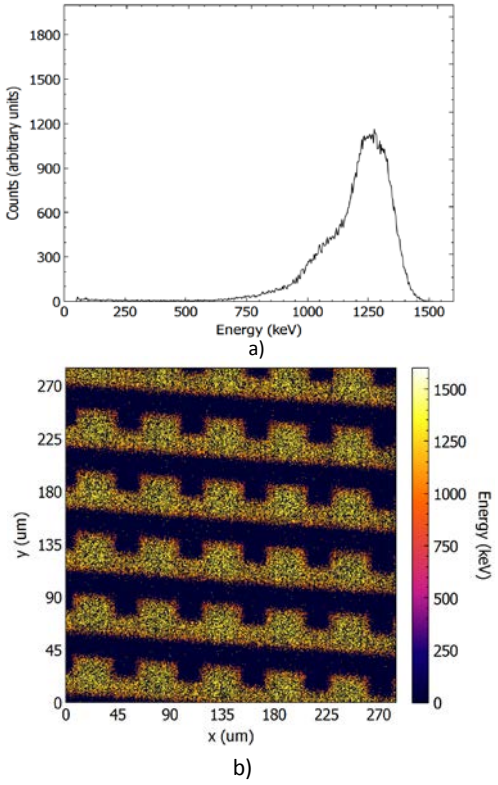

Figure 3. Response of 3D bridge microdosimeter to 5.5MeV He^{2+} ions biased at –10V. (a) Energy spectrum and (b) median energy 2D map.

Experiment at ^{12}C heavy ion facility in Chiba, Japan

Derived RBE_{10} values based on the MK model and 3D bridge microdosimetric spectra in response to 290MeV/u carbon-ions is presented in Fig. 4. The RBE_{10} values match very well with those obtained from the TEPC measurements. Due to the high spatial resolution of the microdosimeter, a more detailed RBE_{10} distribution was obtained at the end of the SOBP compared to the TEPC. The maximum derived RBE_{10} found using

the bridge microdosimeter was 2.56 that is higher than the one of 2.35 obtained with the TEPC due to high spatial resolution of the SOI microdosimeter which was able to measure at the end of the SOBP with 0.5 mm resolution. In general, the obtained RBE_{10} values were found to be in good agreement with values obtained using a TEPC, with an exception immediately downstream of the SOBP in the fragmentation region. This is due to two facts: i) The TEPC measurements being carried out in water which lacks the C atoms in PMMA; ii) the spatial resolution of the TEPC is not good enough to measure separately the distal part of the SOBP. This region is determined by low energy ^{12}C ions with high LET and the fragmentation region with the LET dropping fast below 150keV/µm. This leads to an effective increase in RBE_{10} where the chosen parameter of the overkilling effect is y_0 = 150 keV/µm (equation 6). It should be noted that the bridge microdosimeter measurements were done in a PMMA phantom while the TEPC measurements were carried out in water, hence range scaling has been used to match the results.

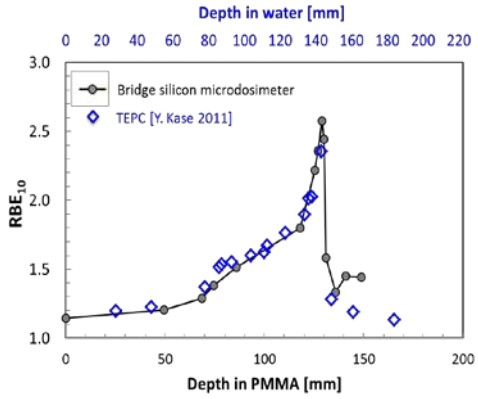

Figure 4. Derived RBE_{10} along the central axis of the SOBP of ^{12}C ion beam, obtained by SOI bridge microdosimeter and TEPC at NIRS.

Conclusions

The CMRP 3D bridge microdosimeter was investigated in detail using 5.5 MeV He^{2+} microbeams. The etching of silicon surrounding the SVs has shown to remove all low energy artefacts in comparison with planar SOI microdosimeters.

This work presented the first RBE_{10} derivation in a ^{12}C ion therapeutic beam using a high spatial resolution SOI microdosimeter. The obtained RBE_{10} values were found to be in good agreement with values obtained using a TEPC, with an exception at the distal part of the SOBP. This is due to TEPC measurements being carried out in water which lacks the C atoms in PMMA and a lack of high spatial resolution in the TEPC.

The development of extremely high spatial resolution SOI microdosimeter is very important for better understanding of radiobiological dose in heavy ion therapy as well as aspects of physics of ions such as the fragmentation process and deposition of energy at the end of the BP.

This current bridge SOI microdosimeter is an intermediate step towards a fully 3D microdosimeter with free-standing 3D SVs microdosimeter.

Future Work

The proposed 3D SVs microdosimeter ("mushroom" microdosimeter) is currently being fabricated at SINTEF MiNaLab. The design of this 3D microdosimeter was proposed by CMRP, and it has 3D cylindrical SVs to provide a well-defined sensitive region. Fig 5 shows the proposed fully 3D microdosimeter. It is fabricated on SOI material with a buried oxide layer that isolates the microdosimeter's SV from the support wafer. An array of n^+ electrodes and surrounding ring p^+ electrodes are produced using DRIE, followed by polysilicon

deposition and doping. The proposed microdosimeter is also important for characterization of RBE in neutron fields of aviation, space and accelerators radiation environment for radiation protection. To improve the tissue equivalency of the new microdosimeter, the support handle wafer will be removed and filled with a tissue equivalent material such as polymethyl methacrylate (PMMA).

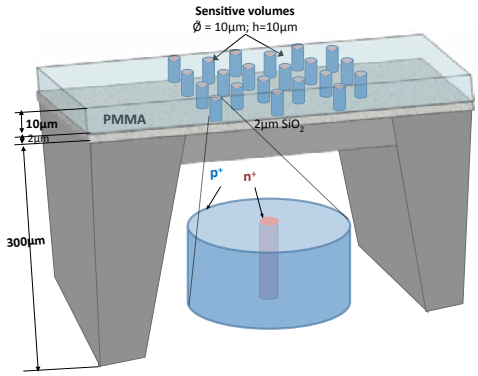

Figure 5. Proposed design of a fully 3D "mushroom" microdosimeter.

Future work will also be focused on comparing the experimental response of the 3D bridge and 3D mushroom microdosimeters in a ^{12}C ion therapy beam with Geant4 simulations.

Acknowledgements

The authors would like to acknowledge the support of the Accelerator Operation Team, Institute of Environmental Research, Australian Nuclear Science and Technology Organization (ANSTO) for IBICC experiments and Professor E. Pereloma and her team at the Australian Institute for Innovative Materials (AIIM), University of Wollongong for Scanning Electron Microscopy images. Special thanks to Dr. V. Perevertaylo of SPA-BIT (Ukraine) microelectronic foundry for fabrication of CMRP designed bridge microdosimeter chips. The authors also wish to thank Prof. N. Matsufuji of NIRS (Japan) for his support during the experiments at the ^{12}C heavy ion therapy facility.

References

Bethe, H. (1930) "Theory of the Passage of Fast Corpuscular Rays Through Matter" Ann. Phys., 397, 325-400.

Bloch F. (1933) "Bremsvermogen von Atomen mit mehreren Elektronen", Z. Phys., 81, 363-376.

Bradley, P.D., Rosenfeld, A.B., Lee, K.K. Jamieson, D.N., Heiser, G. and Satoh, S. (1998) "Charge collection and radiation hardness of a SOI microdosimeter for medical and space applications," *IEEE Trans. Nucl. Sci.*, vol. 45, no. 6, pp. 2700–2010.

Bradley, P.D. and Rosenfeld, A.B. (1998) "Tissue equivalence correction for silicon microdosimetry detectors in boron neutron capture therapy," *Medical Physics*, vol. 25, no. 11, pp. 2220–2225.

Bradley, P. (2000) "The development of a novel silicon microdosimeter for High LET radiation therapy," Ph.D. Thesis, University of Wollongong, Wollongong, Australia.

Cornelius, I.M., Rosenfeld, A.B., Seigele, R., and Cohen, D. (2003) "LET dependence of the charge collection efficiency of silicon microdosimeters," *IEEE Trans. Nucl. Sci.,* vol. 50, no. 6, pp. 2373–2379.

ICRU, (1983) "Microdosimetry," *ICRU Report 36*.

Kase, Y., Kanai, T. Sakama, M., Tameshige, Y., Himukai, T., Nose, H., Matsufuji, N. (2011) "Microdosimetric Approach to NIRS-defined Biological Dose Measurement for Carbon-ion Treatment

Beam," *Journal of Radiation Research*; ISSN: 0449-3060; vol. 52, no.1, pp. 59–68.

Lim, W.H., Ziebell, A.L., Cornelius, I., Reinhard, M.I., Prokopovich, D.A., Dzurak, A.S., Rosenfeld, A.B. (2009) "Cylindrical silicon–on-insulator microdosimeter: Design, fabrication and TCAD modelling," *IEEE Trans. Nucl. Sci.*, vol. 56, no. 2, pp. 424–428.

Livingstone, J., Prokopovich, D.A., Lerch, M. L.F., Reinhard, M.I., Petasecca, M. and Rosenfeld, A.B. (2012) "Large Area Silicon Microdosimeter for Dosimetry in High LET Space Radiation Fields: Charge Collection Study," *IEEE Trans. Nucl. Sci.,* vol. 59, no. 6, pp. 3126–3132.

NSW Cancer Registry Statistical Reporting, www.statistics.cancerinstitute.org.au

Rossi and Zaider M. (1996) "Microdosimetry and its Applications," London: *Springer*.

Schardt, D., Elsässer, T., Schulz-Ertner, D. (2010) "Heavy-ion tumor therapy: Physical and radiobiological benefits" Reviews of Modern Physics, vol. 82, Issue 1, pp. 383-425.

Siegele, R., Cohen, D., and Dytlewski, N. (1999) "The ANSTO high energy heavy ion microprobe," *Nucl. Instrum. Meth. Phys. Res. B*, vol. 158, pp. 31–38.

Tran, L.T., Prokopovich, D.A., Petasecca, M., Lerch, M.L.F., Kok, A., Summanwar, A., Da Via, C., Reinhard, M.I., Schjølberg-Henriksen, K. and Rosenfeld, A.B. (2014) "3D Radiation Detectors: Charge Collection Characterisation and Applicability of Technology for Microdosimetry," *IEEE Trans. Nucl. Sci.,* vol. 61, no 4, pp. 1537–1543.

Tran, L.T., Guatelli, S. Prokopovich, D.A., Petasecca, M., Lerch, Reinhard, M. ., Ziegler, J.F.M. and Rosenfeld A.B. (2014) "A Novel Silicon Microdosimeter using 3D Sensitive Volume: Modelling the Response in Neutron Field Typical of Aviation," *IEEE Trans. Nucl. Sci.,* vol. 61, no. 4, pp. 1552–1557.

Ziebell, A.L., Lim, W.H., Reinhard, M.I., Cornelius, I., Prokopovich, D., Siegele, A., R., Dzurak, A.S. and Rosenfeld, A.B. (2008) "A cylindrical silicon-on-insulator microdosimeter: Charge collection characteristics," *IEEE Trans. Nucl. Sci.,* vol. 55, no. 6, pp. 3414–3420.

Ziegler, J.F., Biersack, J.P. and Ziegler, M.D. (2008) "SRIM – The Stopping and Range of Ions in Matter", *Ion Implantation Press*, Available: http://www.srim.org.

Linh Tran is a PhD candidate at the University of Wollongong. She was the recipient of the Jak Kelly Award of the RSNSW and the Australian Institute of Physics in 2014, awarded to the best PhD student talk given at a joint meeting of the two societies.

Received: 22, March 2015 *Accepted: 1, June 2015*