A real time solid state dosimetry system for QA in synchrotron x-ray microbeam radiosurgery

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A REAL TIME SOLID STATE DOSIMETRY SYSTEM FOR QA IN SYNCHROTRON X-RAY MICROBEAM RADIOSURGERY

A Dissertation Submitted in Fulfilment of the Requirements for the Award of the Degree of Doctor of Philosophy from UNIVERSITY OF WOLLONGONG

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Centre for Medical Radiation Physics
Faculty of Engineering and Information Sciences
2017
CERTIFICATION

I, Ashley James Cullen, declare that this thesis, submitted in fulfilment of the requirements for the award of Doctor of Philosophy, in the Centre for Medical Radiation Physics, Faculty of Engineering and Information Sciences, University of Wollongong, is wholly my own work unless otherwise referenced or acknowledged. The document has not been submitted for qualifications at any other academic institution.

Ashley James Cullen
May 2017
Dedicated to the memory of John Foy Cullen
# Table of Contents

Table of Contents ........................................ iv
List of Tables .................................................. v
List of Figures/Illustrations ..................................... x
Abstract ........................................................ xi
Acknowledgements ............................................... xiii
Conferences .................................................... xiv
Publications ....................................................... xv

1 Introduction .................................................. 1
  1.1 Thesis Outline ............................................ 1
  1.2 Thesis Structure .......................................... 2
  1.3 Interactions of Radiation with Matter ..................... 4
    1.3.1 Photoelectric Effect .................................. 5
    1.3.2 Compton Scattering ................................... 6
    1.3.3 Pair Production ....................................... 6
    1.3.4 Coherent Scattering .................................. 7
  1.4 Synchrotron X-rays ....................................... 7
    1.4.1 Production of Synchrotron Radiation .................. 8
    1.4.2 European Synchrotron Radiation Facility .......... 10
  1.5 Microbeam Radiation Therapy ............................. 16
    1.5.1 Early Experiments in Spatial Fractionation .......... 17
    1.5.2 Initial Synchrotron X-ray Microbeam Experiments ... 18
    1.5.3 Animal Preclinical Trials ............................ 20
    1.5.4 Radiobiology ......................................... 22
    1.5.5 Human Prospects ..................................... 25
  1.6 Dosimetry for Microbeam Radiation Therapy ............. 27
    1.6.1 Ion Chambers ......................................... 27
    1.6.2 Radiochromic Film .................................... 28
    1.6.3 Metal-Oxide-Semiconductor Field-Effect Transistors . 29
    1.6.4 Thermoluminescent Dosimeters ....................... 30
    1.6.5 Fluorescent Nuclear Track Detectors ................. 31
    1.6.6 Optical Computed Tomography of Radiochromic Plastic . 32
    1.6.7 Optical Calorimetry ................................... 32
# TABLE OF CONTENTS

1.6.8 MRI Gel Dosimetry .................................................. 33

2 Monte Carlo Simulation ................................................. 35
   2.1 The Monte Carlo Method ........................................ 35
   2.1.1 Applied to Problems in Radiation Physics .............. 36
   2.1.2 Use in Microbeam Radiation Therapy .................. 37
   2.2 Geant4 ............................................................... 38
       2.2.1 Architecture of Geant4 ................................. 39
       2.2.2 Simulation Development ............................... 40
   2.3 The Geant4 Low Energy Electromagnetic Package .......... 41
       2.3.1 Validation of Code for Use in Radiotherapy ....... 42

3 Development of a Dosimetry System for Microbeam Radiation Therapy ................................................. 43
   3.1 Introduction ......................................................... 43
   3.2 Microstrip Detector ............................................... 44
       3.2.1 Packaging .................................................. 44
       3.2.2 Orientation ............................................... 45
   3.3 Data Acquisition Hardware ...................................... 51
       3.3.1 Preamplifier Module ..................................... 52
       3.3.2 Central Data Acquisition Unit ....................... 54
       3.3.3 Acquisition Parameters ................................. 57
       3.3.4 Detector Bias ............................................ 57
   3.4 Data Acquisition and Analysis Software .................... 58
       3.4.1 Data Loss Reduction Strategies ....................... 60
       3.4.2 Basic Data Analysis ..................................... 60
       3.4.3 Microbeam Array Peak Analysis ...................... 61
       3.4.4 Use of Acquired Data with Other Packages ........ 62
   3.5 System Characterisation ......................................... 63
       3.5.1 Slew Rate .................................................. 63
       3.5.2 Current Calibration and Linearity .................... 64
       3.5.3 Noise Performance ....................................... 66
   3.6 Modes of Operation .............................................. 66
       3.6.1 Single-Trigger Mode ..................................... 66
       3.6.2 Multi-Trigger Mode ....................................... 69

4 Energy Dependence Studies of Microstrip Detector ................................................. 71
   4.1 Characterisation with an Orthovoltage X-ray Unit ........ 72
       4.1.1 Materials and Methods .................................. 73
       4.1.2 Results .................................................... 75
   4.2 Monochromatic Synchrotron X-rays ............................ 78
       4.2.1 Materials and Methods .................................. 78
       4.2.2 Results .................................................... 79
   4.3 Energy Dependence of Hypothetical Detectors ............. 83
TABLE OF CONTENTS

4.3.1 Reduction of Epitaxial Layer .................................. 83
4.3.2 Use of Mesa Epitaxial Structures ............................... 83
4.3.3 Use of Alternative Materials ................................. 85
4.4 In-Phantom Spectral Changes .................................. 88
4.4.1 Materials and Methods .......................................... 88
4.4.2 Results and Discussion ......................................... 88

5 Charge-Collection Characterisation of the Microstrip Detector 93
5.1 Introduction .......................................................... 93
5.2 Alpha-Particle Spectroscopy ...................................... 94
5.2.1 Introduction ......................................................... 94
5.2.2 Materials and Methods ........................................... 94
5.2.3 Results .............................................................. 95
5.3 Ion-Beam-Induced Charge-Collection ............................ 97
5.3.1 Introduction ......................................................... 97
5.3.2 The ANSTO Heavy Ion Microprobe ........................... 98
5.3.3 Data Analysis ....................................................... 99
5.3.4 Materials and Methods ......................................... 100
5.3.5 Results .............................................................. 103
5.4 Synchrotron X-ray-Beam-Induced Charge-Collection .......... 106
5.4.1 Introduction ......................................................... 106
5.4.2 Materials and Methods ........................................... 107
5.4.3 Results .............................................................. 108

6 Microstrip Detector Characterisation in a Synchrotron X-ray Therapy Field 111
6.1 Pre-Irradiation Response ............................................ 111
6.2 Response versus Applied Bias .................................... 114
6.3 Effect of Guard Ring ................................................. 114
6.4 Dose Linearity ......................................................... 117
6.5 Depth Dose Response ............................................... 118
6.5.1 Comparison with Ionisation Chamber ........................ 119
6.5.2 Monte Carlo Simulation ......................................... 122
6.6 Microbeam Array Measurements .................................. 124
6.6.1 Response Versus Wiggler Gap ................................ 124
6.6.2 Peak FWHM Versus Applied Bias ............................. 128
6.7 Substrate Effects ..................................................... 129
6.7.1 Measurement in an MRT Field ................................ 129
6.7.2 Monte Carlo Simulation ......................................... 132

7 Conclusion 135
7.1 The Use of Silicon Microstrip Detectors for MRT ............. 135
7.2 Development of a Data Acquisition System for MRT .......... 136
TABLE OF CONTENTS

A  Glossary of Abbreviations  138
References  151
List of Tables

4.1 Filtration and focal source distance (FSD) for each X-ray beam of the Illawarra Cancer Care Centre Gulmay D3300 orthovoltage X-ray unit.

4.2 HVL and effective energy for each X-ray beam of the Illawarra Cancer Care Centre Gulmay D3300 orthovoltage X-ray unit.

4.3 Comparison of dosimeter and phantom material properties.
### List of Figures

1.1 Photon cross-section versus energy for each interaction in water. Data obtained from NIST XCOM Photon Cross Sections database. [14]  

1.2 Distribution of radiation emission pattern by an electron accelerated by a magnetic field with trajectory (a) (adapted from [9]) whilst travelling at a velocity of (b) 0c, (c) 0.3c, (d) 0.9c. [9] Note that the plot axes represent radiated power.  

1.3 Aerial view of the European Synchrotron Radiation Facility. [37]  

1.4 Layout of the ESRF ID17 Biomedical Beamline. [36]  

1.5 The ESRF ID17 photon spectrum for MRT (data supplied courtesy of ESRF).  

1.6 Photograph of the ESRF ID17 MRT hutch (Note: electronics on the goniometer were present only for the experiment being undertaken).  

1.7 Representation of the radiation field structure of an X-ray microbeam array measured with the X-tream system. Visible are the high dose peak regions from three microbeams, separated by valley regions of minimal dose.  

1.8 Survival curves of mice inoculated with EMT-6.5 tumour cells treated with (a) conventional radiotherapy, (b) microbeam radiation therapy. [23]  

1.9 Path of orthogonally interlaced microbeam fields on a mouse test subject. The intersection region of the two fields results in a rise in an increase in the spatial frequency of the peak regions as well as an increase in the valley dose. [16]  

1.10 Survival curves of rats bearing right frontocerebral 9L gliosarcomas receiving various MRT protocols: no irradiation (Controls), unidirectional irradiation with an entrance dose of 625 Gy (625-1), and bidirectional irradiation with an entrance dose of 312.5 and 625 Gy (312-2 and 625-2 respectively). Extracted from Laissue et al. (1998)[50]  

3.1 Diagram of microstrip detector, showing the central strip detector (connected to the central pad), the surrounding guard ring structure (connected to the left pad) and the substrate (connected right pad).
3.2 Photo of the microstrip detector as mounted on a Kapton tail. Note the detector and part of the Kapton tail are sandwiched between two slabs of PMMA for phantom measurements. The connector end of the Kapton tail is connected to the preamplifier module described below.  46
3.3 3D render of the microstrip mounted on the Kapton tail and oriented in the face-on configuration with the beam direction denoted by the arrow.  48
3.4 3D render of the microstrip mounted on the Kapton tail and oriented in the edge-on configuration with the beam direction denoted by the arrow.  49
3.5 3D render of the microstrip mounted on the Kapton tail and oriented in the end-on configuration. Note the smallest dimension of the sensitive volume is oriented with the wide axis (i.e. peak-valley direction) of the beam.  50
3.6 Photo of the X-tream data analysis hardware, consisting of: a laptop running RADplot software, the rack-mountable Central Data Acquisition Unit (CDAU) with the upper case removed and the Preamplifier module also with the upper case removed.  51
3.7 Schematic diagram of the X-tream dosimetry system. The microstrip detector is represented as a photodiode as readout by the preamplifier.  53
3.8 Schematic diagram of the firmware and main functionalities of the FPGA module; the blocks with dashed contours represent external components.  56
3.9 Screen capture of RADplot displaying acquired dosimetric data from a MRT field, and peak analysis results.  58
3.10 Screenshot of the FPGA Decoder application in the process of performing a batch decode operation with 100 × data averaging of the output.  62
3.11 (a) Calculation of a realistic slew rate expected in MRT from Monte Carlo simulation. (b) Experimental verification of the preamplifier/digital readout slew rate.  64
3.12 Counts versus measured current at various resistance values.  65
3.13 Schematic relation of the radiation beam, trigger pulse, motor motion and detector readout acquisition for the single-trigger mode.  67
3.14 Overview of the operation of single trigger mode and the interaction between the MRT control system and the X-tream data acquisition system.  68
3.15 Schematic relation of the radiation beam, trigger pulse, motor motion and detector readout acquisition for the multi-trigger mode.  69
3.16 Overview of the operation of multi-trigger mode and the interaction between the MRT control system and the X-tream data acquisition system.  70
4.1 Ratio of mass-energy absorption coefficient ratio \( \mu_{\text{en}} / \rho \) of silicon to water.  72
4.2 Computed X-ray spectra as used in Geant4 Simulations at each orthovoltage X-ray unit potential.  74
4.3 Ratio of dose to the sensitive volume of the microstrip to the dose to water in the same volume at each simulated kilovoltage energy expressed in terms of effective energy. ........................................... 76
4.4 Detector response as a function of effective energy at each orthovoltage beam quality, normalised to the response at 250 kV (115.3 keV effective energy). .......................................................... 77
4.5 Simulated dose to the sensitive volume of the microstrip detector and water in the same geometric boundary and absence of the detector. ........... 80
4.6 Experimentally measured response of ion chamber and microstrip detector to monochromatic photons, normalised to response at 80 keV photon energy. .......................................................... 80
4.7 Comparison of simulated energy dependence ratio of microstrip detector to water (black) and experimental response ratio of microstrip detector to ion chamber ratio (red) to monochromatic X-rays normalised to 80 keV photon energy. .......................................................... 81
4.8 Water equivalence dose ratio versus monochromatic photon energy for a simulation of the microstrip detector with a 6 µm and 50 µm thick epitaxial layer. .......................................................... 84
4.9 Water equivalence dose ratio versus monochromatic photon energy for a simulation of the microstrip detector constructed with a 6 µm thick mesa layer encircled by water or air. .......................................................... 86
4.10 Water equivalence dose ratio versus monochromatic photon energy for a simulation of the a hypothetical microstrip detector constructed with either a 1.5 µm or a 6 µm thick CVD epitaxial layer mounted on a 500 µm thick CVD substrate. .......................................................... 87
4.11 Variation in photon spectrum from centre of field to 1 mm out-of-field. 89
4.12 Photon spectrum as a function of depth along MRT beam axis in PMMA. Note: counts per primary particle refer to spectral counts divided by the total number of simulated primary photons. ......................... 89
4.13 Changes in photon spectrum with distance from central axis. Note the shift to softer photon energies with increasing distance from central axis, including a shift to a lower most-probable energy. ............................... 90
4.14 Changes in photon spectrum with distance from central axis, scaled to enhance the low energy range. .......................................................... 91

5.1 Schematic of the electrical configuration of the microstrip detector for alpha spectroscopy .......................................................... 95
5.2 $^{241}$Am spectral response of the microstrip detector with the guard ring both floating and grounded. .......................................................... 96
5.3 Schematic of the ANSTO microprobe beamline. [80] .......................................................... 99
5.4 Ionisation distribution in silicon calculated by TRIM-2013 [86] for 5.5 MeV $^4$He ions as a function of lateral position and depth, and as a function of depth. .......................................................... 101
LIST OF FIGURES

5.5 IBICC spatial calibration image of the copper grid shadowing the PIN photodiode. .................................................. 102
5.6 5.5 MeV $^4$He IBICC images of the microstrip detector with the guard ring floating, with the central strip biased at (a) 10 V, (b) 20 V, (c) 30 V and (d) 40 V. .................................................. 104
5.7 5.5 MeV $^4$He IBICC image of the microstrip detector with the guard ring grounded, with both guard ring and central strip biased at 50V. . 105
5.8 Synchrotron X-ray beam induced charge collection map of the microstrip detector with both central strip and guard ring biased at (a.) -10V and (b.) -40V. .................................................. 109

6.1 Integral response of virgin detector as a function of prescribed dose. Note that the current saturation level was reached on the first three measurements, with the current measurement system saturation threshold indicated. .................................................. 113
6.2 Microstrip detector response versus applied bias in expose mode in the face-on orientation. .................................................. 115
6.3 Microstrip detector peak current as a function of nominal beam height with the guard ring in the grounded and floating configuration. . 116
6.4 Integrated microstrip detector response per prescribed dose as a function of nominal beam height with the guard ring in the grounded and floating configuration. .................................................. 116
6.5 Integral response of detector as a function of prescribed dose with the corresponding linear line of best fit. .................................................. 118
6.6 Depth dose behaviour of the microstrip detector in various open-field MRT beams in a face-on orientation. .................................................. 119
6.7 Depth dose response in a 20×20 mm MRT field of the microstrip detector compared to the PTW Semiflex 31010. Both are normalised to the response at 20 mm depth. .................................................. 120
6.8 Depth dose response in a 15×15 mm MRT field of the microstrip detector compared to the PTW Semiflex 31010. Both are normalised to the response at 20 mm depth. .................................................. 121
6.9 Depth dose response in a 10×10 mm MRT field of the microstrip detector compared to the PTW Semiflex 31010. Both are normalised to the response at 20 mm depth. .................................................. 121
6.10 Percentage dose as a function of depth in PMMA for measurement and Monte Carlo simulation, normalised to measurement at 10 mm depth. . 122
6.11 Dose as a function of depth in water for the simulated microstrip detector’s sensitive volume with depth and within water of the same geometric boundaries. .................................................. 123
6.12 Ratio of microstrip sensitive volume dose versus dose to the same geometric boundaries in water as a function of depth in water. ................. 124
6.13 The microstrip detector as mounted in a PMMA phantom, with additional PMMA material placed in front to produce greater depth for radiation interactions. ........................................ 125
6.14 Microstrip detector response normalised as a function of the ID17 wiggler gap. .............................................................................................................. 126
6.15 Ratio of single microbeam to homogeneous field microstrip detector integral response as a function of the ID17 wiggler gap. .............................. 127
6.16 Full-width at half-maximum (FWHM) versus applied bias for the microstrip detector scanned laterally in an end-on orientation. ...................... 128
6.17 Schematic of the measurement set-up to determine the substrate effects for (a.) a microbeam array and (b.) the introduction of a single slit to produce a single microbeam. The detector is stepped laterally in both cases. ................................................................. 130
6.18 Scan of single and multiple microbeams with a microstrip detector in the end on orientation with detector orientation overlaid with (a) the substrate oriented to the right and (b) with the substrate orientated to the left. ............................................................. 131
6.19 Monte Carlo simulation results for a 500 × 50 µm² microbeam scanned laterally across the detector mounted in end-on orientation. ................... 133
Microbeam radiation therapy (MRT) is an experimental radiosurgical technique under investigation as a treatment for presently incurable brain lesions such as gliomas. The treatment involves the irradiation of a macroscopic target volume by delivering a very high dose to many microscopic wide sub-volumes. A very high dose rate and very low beam divergence are prerequisites for MRT, which at present necessitates the use of synchrotron radiation. The complex structure of the radiation field combined with the very high dose rate pose a challenge for conventional dosimetry. To address the dosimetric inadequacies, a complete and standalone dosimetry system was developed for MRT as part of this work. It includes the silicon microstrip detector: a high spatial resolution single strip detector, data acquisition hardware capable of remotely biasing and reading out the detector, and data acquisition software to interface with the hardware and perform analysis on received data. The system is collectively known as X-tream.

This thesis provides an introduction to MRT, the production of synchrotron X-rays and a literature review of methods of dosimetry for MRT as reported in literature. The development of the X-tream system is discussed along with an overview of its operation and initial characterisation.

Charge-collection characterisation of the microstrip detector was performed in numerous ways. Alpha spectroscopy reveals that the application of the guard ring greatly reduces the effective sensitive volume of the detector when compared to the floating configuration, but reveals no spatial information. Spatially-resolved ion beam induced charge collection (IBICC) is performed using the ANSTO Heavy Ion Microprobe to obtain spatial information about the charge collection distribution under various electrical configurations. The application of the guard ring is seen to greatly confine charge collection to the immediate vicinity of the central strip, however significant charge collection is seen near the pad region, a phenomenon not observed during MRT measurements. As the detector was not pre-irradiated prior to the investigation, it is hypothesised the combination of the metallic pad, oxide layer and silicon acts as a MOS capacitor and induces an electric field bubble in the region surrounding the pad. Subsequent exposure to radiation is then hypothesised to result in a reduction of the carrier lifetime and decrease the sensitivity of the detector. Synchrotron X-ray beam induced charge collection studies are performed on the ESRF ID17 beamline, and agree with the tight charge confinement of the guarded detector as observed for IBICC. Charge collection is not seen in the pad region, but the notable difference is that the detector has been pre-irradiated.
Energy dependence studies are performed through characterisation with a clinical orthovoltage X-ray unit and compared to Monte Carlo simulation. Both experimental and simulated results show an over-response of the detector to low energy X-rays when compared to dose to water. A more rigorous treatment is applied experimentally with monochromatic synchrotron X-rays over the range of 40 to 80 keV, which too reveal an over-response at low energy, a finding backed by Monte Carlo simulation. Hypothetical detector designs are simulated to attempt to reduce energy dependence, which include a reduced epitaxial layer thickness, a mesa structure and the use of CVD diamond. The reduced epitaxial thickness makes a minor difference, whereas the mesa structure and use of CVD diamond more dramatically reduce the low energy over-response.

The system is characterised in a synchrotron X-ray MRT field where it is found the detector requires pre-irradiation of the order of 20 kGy prior to use. Connecting the guard ring is found to greatly decrease detector sensitivity due to much better confinement of the charge collection volume. The system is found to have excellent linearity with prescribed dose, however depth dose measurements deviate from ionisation chamber measurements and Monte Carlo simulation of both dose to detector and dose to water. This is attributable to the energy dependence of the detector to low energy photons. With the detector oriented such that the smallest sensitive volume dimension is in the dose gradient direction, the substrate is found to result in asymmetric microbeam dose profiles. This is due to the dose enhancement of the silicon substrate relative to the phantom material on the opposite side.

The capabilities of the X-stream system are demonstrated in synchrotron X-ray MRT fields. The over response dependence of the microstrip detector to low energy photons however necessitates improvements to its energy dependence relative to water. A move to mesa-based structures and use of materials such as CVD diamond are suggested. The modularity of the X-tream system ensures that such changes of design require only minor modification to the rest of the system.

**KEYWORDS:** Microbeam Radiation Therapy, Dosimetry, Synchrotron, Monte Carlo
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Conferences

The work contained herein has been presented at the following conferences:

1. International Symposium on Radiation Physics (ISRP-11), Sept. 2009, Melbourne, Australia

2. Synchrotron Radiation Instrumentation (SRI-2009), Sept. 2009, Melbourne, Australia


4. Medical Applications of Synchrotron Radiation (MASR-2010), Feb. 2010, Melbourne, Australia (In Absence)

5. The 16th International Symposium on Solid State Dosimetry (SSD-16), Sept. 2009, Sydney, Australia

6. 2010 Australian Synchrotron User Meeting, Nov. 2009, Melbourne, Australia


8. 1st Australian Geant4 Workshop, Apr. 2010, Wollongong, Australia


Publications

The following papers were published in peer-reviewed journals whilst undertaking this work:


Chapter 1

Introduction

This thesis investigates the development, testing, implementation and improvement of a dosimetry system for synchrotron X-ray Microbeam Radiation Therapy, an experimental radiosurgical method for brain lesions.

1.1 Thesis Outline

This thesis aims to address deficiencies which currently exist in the dosimetry of synchrotron X-ray microbeam radiation therapy (MRT) fields. MRT has been used successfully in the palliation and ablation of tumours in animal studies, and it shows great promise in the treatment of paediatric neurological tumours, however for it to become a clinical reality, fast, accurate and reliable dosimetric methods must be developed. The work presented here-in is one of the many steps towards the use of MRT to treat humans.
1.2 Thesis Structure

This thesis contains 7 chapters which detail the development and characterisation of a dosimetry system for synchrotron X-ray MRT. This current introductory chapter provides an overview of radiation interactions applicable to MRT, the production of synchrotron X-rays and the European Synchrotron Radiation Facility Biomedical Beamline which was developed to amongst other capabilities, produce MRT fields. This is followed by an introduction to MRT including its origins, the development of the current technique and its application to animal preclinical trials. Whilst there are still many unknowns, an overview is provided of the radiobiology involved and human prospects for this treatment are discussed.

Chapter 2 provides an overview of Monte Carlo simulation, including Geant4, the code used for simulations presented herein. The Geant4 Low Energy Electromagnetic package is discussed along with literature detailing its experimental validation. The chapter concludes with the construction of the silicon microstrip detector within the Geant4 environment.

Chapter 3 details the development of the X-tream dosimetry system for MRT. This starts with an introduction of the design brief, which is a comprehensive system consisting of a radiation detector, hardware and software. The design of the radiation detector component, the silicon microstrip detector is described, including its physical geometry, material composition and mounting method. The detector orientations as used in MRT and used herein are defined with graphical representation. The hardware component of the data acquisition system is detailed including descriptions of the various modules, their operation and how they interrelate. An overview of the software component, RadPlot: the data acquisition and analysis software is provided with an overview of its operation. Prior to operating the system in MRT fields, the system was
characterised electrically with the results of this characterisation is presented. The two major modes of operation of the system for MRT fields are also discussed.

Synchrotron X-ray MRT makes use of a beam of relatively low energy photons when compared to megavoltage radiation therapy fields, due to the known over-response of silicon in the latter, this phenomenon is investigated in Chapter 4 for the microstrip detector. An overview of Bragg-Gray and Burlin cavity theory is presented as hypothetically applicable to the detector. The energy is experimentally characterised both with an orthovoltage X-ray unit and with monochromatic synchrotron X-rays. These results are compared with Monte Carlo simulations performed to investigate the energy dependence effects. In an attempt to improve the energy dependence, a series of hypothetical detector designs are investigated \textit{in silico} with Monte Carlo simulations. Lastly the variation of the MRT photon spectrum within a phantom is investigated to investigate its effect on the energy dependency of the microstrip detector.

Due to the high spatial resolution required of the microstrip detector for use in MRT, the spatial distribution of charge collection by the detector is investigated in Chapter 5. Firstly alpha particle spectroscopy is performed on the detector in a vacuum chamber in different electrical configurations. More sophisticated techniques are investigated through the use of ion-beam-induced charge collection studies (IBICC) involving raster scanning of helium ions across the microstrip detector and spatially resolving the resulting charge collection distribution. A similar technique is applied in an MRT field by scanning the detector across a highly collimated microbeam and determining the response as a function of detector position.

Chapter 6 investigates the response of the microstrip detector in a synchrotron X-ray therapy field. The pre-irradiation response of a virgin detector, exposed only to background radiation is first investigated, along with the response of the detector in various electrical configurations. The response of the detector to varying dose and
depth are investigated with comparison to Monte Carlo simulation. Measurements are performed in microbeam arrays, with the response of the detector to synchrotron configuration, depth and applied bias investigated. Lastly the effect of the substrate on dose enhancement is investigated due to the assymetry of the detector when oriented such as to minimise spatial resolution in the scanning direction.

Chapter 7 provides a broad overview of the summary of this work, including the development of the data acquisition system for MRT, the use of the silicon microstrip detector for MRT and future recommendations to build upon this work.

1.3 Interactions of Radiation with Matter

The interaction of radiation with matter forms the basis of all methods of radiation oncology, since the subject of this thesis involves photon beams, only photonic interactions are discussed. At therapeutic energies (several keV up to tens of MeV), photons interact in four primary ways, namely the photoelectric effect, Compton scattering, and pair production all result in the transfer of energy to other particles, however the fourth process, Rayleigh scattering does not involve such energy changes.
1.3. Interactions of Radiation with Matter

![Photon cross-section versus energy for each interaction in water. Data obtained from NIST XCOM Photon Cross Sections database.][1]

### 1.3.1 Photoelectric Effect

The photoelectric effect is the dominant process for therapeutic low energy photons, and involves the photon imparting all of its energy $h\nu$ on an atomic electron in the absorber medium. Since electrons are bound to the oppositely charged nucleus by a binding energy $E_B$, for the ejection of the electron by the incident photon this must be overcome. The energy of the ejected electron $E_{e^-}$ is thus given by:

$$E_{e^-} = h\nu - E_B$$

The ejection of the electron from an atomic shell leaves a vacancy, which may then be filled by an electron of higher potential energy, possibly resulting in the emission of a characteristic photon.
1.3.2 Compton Scattering

Compton scattering represents the dominant process at most external beam treatment energies, it involves the ejection of an electron and a scattered photon. An incident photon with energy $h\nu$, upon interaction with an electron (with rest energy $m_ec^2$) is scattered by an angle $\theta$ at a reduced energy dependent on the scattering angle. The electron is also scattered by an angle $\phi$. The energy of the scattered photon $h\nu'$ is given by:

$$h\nu' = \frac{h\nu}{1 + \frac{h\nu}{m_0c^2}(1 - \cos \theta)} \quad (1.2)$$

The angle of the Compton electron, $\phi$ is given by:

$$\cot \phi = \left(1 + \frac{h\nu}{m_0c^2}\right) \tan \frac{\theta}{2} \quad (1.3)$$

The differential cross-section $\frac{d\sigma}{d\Omega}$ for a photon interacting with a free electron at rest is given by the Klein-Nishina equation:

$$\frac{d\sigma}{d\Omega} = \frac{1}{2} \gamma_e^2 \left(\frac{h\nu'}{h\nu}\right)^2 \left(\frac{h\nu'}{h\nu} + \frac{h\nu}{h\nu'} - 1 + \cos^2 \theta\right) \quad (1.4)$$

Where $\gamma_e^2$ is the classical electron radius.

1.3.3 Pair Production

Pair production is a consequence that energy and matter are manifestations of the same entity. A photon, under the strong Coulomb field of a nucleus may be converted into a matter-antimatter pair in the form of an electron and positron. Since the rest mass of both these particles is 511 keV, it is only energetically possible at twice this energy (1.022 MeV). For photon energies exceeding the threshold, excess energy is
carried by both particles in the form of kinetic energy, that is:

\[ E_{e^-} + E_{e^+} = h\nu - 2m_0c^2 \]  

Due to the instability of antimatter in the presence of matter, the positron travels a short range before annihilating with an electron, producing a photon pair.

Pair production does not occur in MRT beams due to the photon spectrum not reaching the energy threshold of twice the electron rest mass.

### 1.3.4 Coherent Scattering

Coherent scattering is a process that occurs when a gamma photon interacts coherently with all the electrons in an absorber atom. This process does not excite nor ionise that atom, and the gamma photon retains its initial energy after the scattering event. Whilst a change in energy does not occur, a change in the direction does, which increases with decreasing photon energy. However, the effect only becomes significant at low energies below several hundred keV. [49]

### 1.4 Synchrotron X-rays

Synchrotron X-rays are generally required for microbeam radiation therapy due to the very high achievable dose rates. This permits very short treatment times which can overcome cardiosynchronous motion of neural tissues. In addition, the very low divergence possible due to the large source-to-target distance is of great benefit for a treatment where maintaining the spatial characteristics of the radiation field with depth is important.
1.4.1 Production of Synchrotron Radiation

A charged particle when accelerated in an external field emits electromagnetic radiation. At non-relativistic energies, the radiation pattern takes the form of an isotropic dipole (see Figure 1.2(b)). However at very high relativistic energies, due to the length contraction of the electric field around the particle as observed from the rest reference frame, the electric field takes the shape of a disc contracted in the direction of motion. A sudden deflection of the direction of the charged particle would require the periphery of the field to move at a velocity greater than the speed of light, an impossibility according to the laws of relativity. Therefore, the field is retarded and detaches from the particle. This results in a very short pulse in the forward direction, away from the new motion of the particle. The resultant radiation pattern is a sharp conical distribution in the forward direction as shown in Figure 1.2(d). [85][12]

Historically, synchrotron radiation was an unwanted by-product of bending charged particle beams for high energy physics experiments. In the 1950’s, the spectral characteristics of this radiation was characterised and first put to use in experiments. As demands for the use of synchrotron light for experiments increased, dedicated facilities were constructed.

At present, third generation electron synchrotron light sources are the predominant method to produce very intense radiation. The production of radiation starts with an electron gun injecting electrons into a linear accelerator, which imparts energy on the electrons through the oscillation of electric fields between electrodes of decreasing spacing along its length. The accelerated electron is then fed into the booster synchrotron for further acceleration. Electrons are injected into the storage ring once at their final energy where they circulate in an ultra-high vacuum for many hours. [12]

Electrons circulating in the storage ring will emit radiation when their direction is altered. This is achieved by using bending magnets, and to generate higher intensities:
1.4. Synchrotron X-rays

Figure 1.2: Distribution of radiation emission pattern by an electron accelerated by a magnetic field with trajectory (a) (adapted from [9]) whilst travelling at a velocity of (b) 0c, (c) 0.3c, (d) 0.9c. [9] Note that the plot axes represent radiated power.
insertion devices, consisting of wigglers and undulators. A bending magnet is simply one of many devices which force the electrons to follow an approximately circular path around the ring, modified only to have a beam port, which permits the passage of synchrotron radiation outside of the storage ring. Insertion devices are more complex and are located on straight sections of the storage ring. They consist of two stacks of alternating north and south magnets which produce a periodic magnetic field in the path of the electron, causing it to travel in a pseudo-sinusoidal path. The key difference between wigglers and undulators is the periodicity of the magnetic structure and the magnetic field intensity. Generally, the transverse motion of the electrons in undulators is non-relativistic, whilst this motion in wigglers is relativistic. [12]

RF cavities are placed in various positions along the storage to compensate the loss of energy encountered as the electrons circulate around the storage ring. A consequence of tightly confined electron bunches is that electron-electron collisions occur, resulting in a gradual loss of storage ring current. An approximately exponential decay of storage ring current occurs over time, resulting in a proportional decrease in photon production in bending magnets and insertion devices. To restore the photon brilliance to acceptable levels, a refilling of the storage ring is performed at times defined to the user in advance. This involves the careful synchronisation of accelerated electrons from the booster synchrotron being injected into electron bunches circulating the storage ring. The non-predictable intensity and stability of the beam during this period can result in spurious experimental results and so measurements are typically avoided during this period. [12]

1.4.2 European Synchrotron Radiation Facility

The European Synchrotron Radiation Facility (ESRF) is a third generation synchrotron light source, first operational in 1992. It has a storage ring 844 m in circum-
1.4. Synchrotron X-rays

Figure 1.3: Aerial view of the European Synchrotron Radiation Facility. [37]

...ference consisting of 32 bending magnets and 32 straight sections. Electrons circulate with an orbit time of 2.82 µs at an energy of 6.04 GeV. Depending on the mode of operation, the storage ring current can reach a maximum of 200 mA with a typical decay time of 50 hours in this mode. [35]

1.4.2.1 Biomedical Beamline (ID17)

The biomedical beamline is one of several “long beamlines” at the ESRF, with dedicated optics, radiotherapy and imaging hutchies. [34] The insertion device is a 1.4 T wiggler able to produce hard X-rays, necessary for medical imaging and radiation therapy. The wiggler has a critical energy of 33.5 keV, and produces a 14.3 kW of total power emission at the maximum field strength of 1.4 T. The FWHM of the photon source divergence is 3.3 × 0.1 mrad² (horizontal × vertical). [36]

Research performed with the beamline includes photon activation therapy, phase
1.4. Synchrotron X-rays

contrast imaging, radiobiology experiments and MRT. The macroscopic components of the beamline (Figure 1.4) from the source include the optics hutch, the MRT hutch, the MRT control cabin, the beam transfer tunnel, the monochromator hutch and the satellite imaging experiment hutch. [36]

The MRT and imaging hutch use the same insertion device, and as such, both cannot be used simultaneously. The MRT hutch is positioned close to the source to maximise the dose rate, whilst the imaging hutch is positioned far to achieve sufficient divergence to increase the width of the beam. For investigations involving the imaging hutch, a vacuum pipe is put in place to span the entire length of the MRT hutch to minimise beam degradation.

The properties of the beam are defined by a series of diaphragms, slit and filters located both inside the optics hutch and the upstream side of the MRT hutch. The beamline is connected to the storage ring at the front end which contains a shutter, a mechanical beam stop used to transport or block the passage of the beam along the
1.4. Synchrotron X-rays

Selection of photon beam quality can be performed through a combination of filters and a monochromator as desired. The MRT program under development uses either an unfiltered white beam of critical energy 38.1 keV or a filtered pink beam.

The determine the beam dimensions, two pairs of tungsten slits are located in vacuum before the filters. The horizontal slits determine the width of the beam for open fields or the number of microbeams for microbeam array fields, whilst the vertical slits determine the beam height.

The beam, as it exits the wiggler travels in a stainless steel vacuum pipe, through several beryllium windows, which are transparent to X-rays above 10 keV. The beam is first shaped by a fixed high-purity copper diaphragm which collimates the useful region of the beam and limits the heat load on the downstream optics. The dimensions of the aperture are 2.5×0.15 cm² (horizontal and vertical respectively), leading to a

![The ESRF ID17 photon spectrum for MRT (data supplied courtesy of ESRF).](image-url)
maximum field size of $4.1 \times 0.25 \text{ cm}^2$ at the patient position.

The beam then traverses a krypton gas filter, attenuating the beam intensity, and providing a safety measure in the event of failure. Leakage of air into the filter vessel results in an increased pressure, resulting in increased attenuation. [69] Field size at the patient is varied by altering the position on the primary slits, a quartet of four highly polished, high purity copper blocks. Water cooled filters (0.5 mm beryllium, 0.5 mm carbon, 1.25 mm aluminium, and 1 mm copper) reduce the low energy component of the spectrum to reduce the absorbed dose in the tissue and reduce the thermal load on downstream components.

The fast shutter is a beam blocking device designed to create precisely timed bursts of radiation down to $5 \pm 0.5 \text{ ms}$. It consists of two 15 mm thick tungsten carbide blades each supported by a guiding system and coupled to an actuator magnet. In the resting state, the downstream blade blocks the beam whilst the upstream blade is fully out of the beam. Upon activation, the actuator magnets are energised, resulting in both blades retracting upwards, this results in the upstream blade fully blocking the beam, with the downstream blade fully out of the beam. The retraction of the blades causes the compression of a pair of springs which accelerate the motion of the blades when the electromagnet current is cut. Upstream of the fast shutter is the photon absorber, a 40 mm thick, water cooled block of copper. The photon absorber is pneumatically actuated with a slower response than the fast shutters of approximately 1 s. [68]

To deliver a burst of radiation, the photon absorber is extended into the beam path and both shutters are energised. The beamline shutter is open and the beam is first incident upon the photon absorber, which starts to retract. After the photon absorber has fully retracted for around 1 s, the upstream blade extends, resulting in transmission of beam towards the patient. After a precisely timed pause, the downstream shutter extends, blocking the beam, followed by extension of the photon absorber to limit
heating of the blade. The sequence is finally complete with closing of the beamline shutter. [68]

The beam then transitions from vacuum to the atmosphere of the MRT hutch via a beryllium window and passes through an aluminium foil. A large area ionisation chamber is located just after the transition point to enable monitoring of the beam. A set of PMMA blocks act as photon absorbers during imaging, whilst a rotary shutter is used for some radiobiology experiments. A horizontal slit is used for beamline alignment. A set of vertical slits consist of apertures in tungsten carbide of dimensions 50, 100, 500 and 820 μm. The selected vertical slit defines the vertical beam height for MRT irradiations and collimates the transmitted beam to the central homogenous
1.5 Microbeam Radiation Therapy

Microbeam radiation therapy (MRT) is an experimental radiosurgical method under development for inoperable neurological lesions. It involves the delivery of a large, yet radiobiologically tolerable dose to a macroscopic treatment volume via the use of a quasi-parallel array of rectangular X-ray microbeams (see Figure 1.5).

High doses are delivered in the geometric boundaries of the microbeams (the peak region) separated by intermediate regions of minimal dose (the valley region) contributed to predominantly by scattering and secondary particles. The radiobiological efficacy of this treatment is dependent on the dose in the peak region being sufficiently high to ablate the tumorous tissue, whilst simultaneously maintaining a valley dose sufficiently low to minimise damage to healthy tissue. In addition to reporting the peak dose, the dosimetrically convenient peak-to-valley dose ratio (PVDR) is often used throughout the literature.

Dosimetrically it is advantageous to minimise beam divergence, which results in steeper dose gradients from the radiation field. Due to cardiosynchronous motion of
1.5. Microbeam Radiation Therapy

Figure 1.7: Representation of the radiation field structure of an X-ray microbeam array measured with the X-tream system. Visible are the high dose peak regions from three microbeams, separated by valley regions of minimal dose.

neural tissues and to prevent dose smearing, a single treatment field must be delivered in a time less than the period of a cardiac rhythm.

These strict requirements currently restrict the treatment to synchrotron X-rays facilities due to the very low beam divergence properties and very high dose rate.

1.5.1 Early Experiments in Spatial Fractionation

It is well known that temporal fractionation can improve the cumulative dose delivered to a tumour whilst minimising the impact of healthy tissues. This technique is in widespread use in contemporary external beam radiation therapy. MRT however, employs a vastly different technique: spatial fractionation; a technique utilised widely in the infancy of radiotherapy, but for the most part forgotten.

Pre-dating megavoltage radiotherapy, kilovoltage X-rays tubes were the dominant therapeutic radiation source. However, due to the superficial way in which these
relatively low energy photons deliver dose, skin burn was expected in virtually all treatments. It was discovered that if an iron grid was pressed hard against the skin, cells shielded from incident radiation would quickly heal the resulting skin burns, preventing radiation induced necrosis.

In the 1960’s, as part of an experiment to simulate the effects of cosmic radiation on astronauts, 25-µm wide 22 MeV deuteron microbeams were targeted at mice cerebral tissue. The tissue could withstand very high absorbed doses of over 3000 Gy without appreciable damage.[24][25] The range of these deuterons in tissue was only 1.5 mm, and so was of little use clinically.

At the Brookhaven National Laboratory (Upton, New York, USA) microtomography experiments were being conducted by Spanne and Slatkin on the head of a mouse.[32] A 30 µm diameter pencil beam of synchrotron X-rays was being used. With absorbed doses of fewer than 10 Gy contrast was poor, upon recounting the earlier reported tissue tolerance to such narrow beam dimensions, the doses were increased up to the order of 200 Gy. The mouse recovered from these large doses normally, and a month later, a histopathological search of the mouse’s brain failed to find any evidence of radiation-induced damage. [17]

1.5.2 Initial Synchrotron X-ray Microbeam Experiments

In 1992 Slatkin et al.[81] theorised that the use of synchrotron X-rays could be used to produce microbeams planar or cylindrical in cross section, with energies in the range of 50 to 150 keV. Experiments were performed with microbeams on murine brains, using 25 µm wide beams with 50 - 200 µm pitch. There was a histological resemblance with the earlier deuteron microbeam irradiation studies. The animals survived thousands of gray in their neural tissues without evidence of tissue necrosis. To explore the use of microbeams in a therapeutic role, 9L gliosarcoma cells were transplanted into rat
1.5. Microbeam Radiation Therapy

Figure 1.8: Survival curves of mice inoculated with EMT-6.5 tumour cells treated with (a) conventional radiotherapy, (b) microbeam radiation therapy. [23]

The use of synchrotron X-rays for MRT is advantageous in several ways. The very high dose rate (of the order of ten kilogram per second) is able to deliver a therapeutic dose in a very short amount of time, this has the benefit of minimising motion blurring of dose due to cardiosynchronous motion of central nervous system tissues. Additionally, the low divergence intrinsic to large source-to-target distances enables the complex radiation field to maintain its structure with depth. [51][82]
1.5.3 Animal Preclinical Trials

The first investigations into MRT with biological tissue occurred at the BNL in 1995. The brains of healthy rats were exposed to 20 and 37 $\mu$m wide microbeams with pitch 75 and 200 $\mu$m respectively. A single exposure of an entrance dose of 625 Gy resulted in no histopathologically evident brain damage.[82]

The first use of the technique on cancerous tissue occurred in 1998 again at the BNL when Laissue, et al.[50] investigated the effect of MRT on rats bearing right fronto-cerebral 9L gliosarcomas. Rats were treated with 25 $\mu$m wide, 1.2 cm high microbeams spaced 100 $\mu$m apart and treated either unidirectionally or bidirectionally (with the beams oriented orthogonal). The use of MRT compared to the control group resulted in a significant survival benefit, particularly for the high dose (625 Gy) protocol, with 50% of the bidirectionally irradiated group and 36% of the unidirectionally irradiated group alive 115 days post-irradiation; significantly contrasting with the control group, with 0% survival after 31 days. Histopathologically, only minor damage was observed in unidirectionally regions of tissue, with severe damage only occurring within the bidirectionally irradiated regions. These findings were significant as they showed tumour ablation could be achieved by MRT with minimal normal tissue effects.

Following these results, a series of studies were performed at BNL looking into the tissue sparing achievable with MRT and the first MRT preclinical studies were commenced at the ESRF[51].

Laissue et al. [52] investigated the effect of 20-30 $\mu$m wide microbeams spaced 210 $\mu$m on healthy weanling cerebella. Entrance doses were 150, 300, 425, and 600 Gy. Over a period of 57 to 66 weeks, the weanlings were observed to be developmentally, behaviourally, neurologically and radiologically normal as observed by experienced farmers and veterinary scientists unaware which piglets were irradiated or sham-irradiated. This work was significant in that for the first time behavioural and
neurological function were assessed as part of a study into MRT and were found to be unaffected up to large peak doses.

Dilmanian et al. [26] investigated the effect of varying beam spacing and radiation dose with tumour control and normal tissue effects. Rats bearing 9L gliosarcomas were exposed laterally to a single microbeam 27 \( \mu \text{m} \) wide by 3.8 mm high in a stepwise manner to produce an array with 50, 75, or 100 \( \mu \text{m} \) pitch spacing, and with 150, 250, 300, or 500 Gy entrance doses. An important finding of this work was that the sparing effect appeared to depend primarily on the valley dose, with little dependence on the peak dose (within limits). The brain sparing effect vanished as measured by the appearance of white matter necrosis when the valley dose approached the normal tissue tolerances to broadbeam radiation.

A study by Serduc et al. [76] investigated the effects of 25, 50, and 75 \( \mu \text{m} \) wide microbeams all spaced 211 \( \mu \text{m} \) apart on 9L gliosarcoma-bearing rats. For each configuration, peak entrance doses were calculated to produce identical valley doses of 18 Gy per array at the centre of the tumour. Rats were sacrificed at 2, 7 and 14 days post irradiation to histopathologically assess the extent of tumour necrosis, and the presence of proliferating tumour cells and vessels. The findings showed that the 50 \( \mu \text{m} \) wide microbeams lead to both the best median survival time and resulted in the best compromise between tumour control and normal brain toxicity.

Brauer-Krisch et al. [16] proposed the technique of field interlacing to optimise the target valley dose in a MRT treatment. It was proposed that instead of a single incident microbeam field, two fields can be orthogonally cross-fired into the target volume such that they are non-intersecting and mutually equispaced. This results in a doubling of the spatial frequency of peak and valley regions in the target volume, and a rise in the valley dose due to the increased scatter contributions. It additionally permits better tissue sparing through the reduction of valley dose to healthy tissue in
1.5. Microbeam Radiation Therapy

Figure 1.9: Path of orthogonally interlaced microbeam fields on a mouse test subject. The intersection region of the two fields results in a rise in an increase in the spatial frequency of the peak regions as well as an increase in the valley dose.\[16\]

the entry- and exit-dose regions. \[16\] \[28\]

This technique effectively produces a broadbeam dose distribution in the overlap region. An interlacing investigation by Dilamnian et al. observed significant tissue damage in overlap region in the brain when doses of 120 and 150 Gy were delivered, but no apparent damage elsewhere. \[27\] However one disadvantage of this technique is that it does not provide a conformal distribution of dose in the high-dose interlaced region. A rectangular prism of high dose is generated, potentially causing unacceptable normal tissue damage in the periphery of the tumour.

1.5.4 Radiobiology

The act of spatially fractionating the dose to the patient is unconventional, where the goal of conventional radiotherapy is delivering a sufficiently high, but uniform dose to the tumour, whilst minimising dose to normal tissues. \[45\]\[46\] As such, most radiobiological knowledge as applied to current clinical practice is not transferrable to the highly spatially fractionated treatment fields of MRT. The radiobiology of MRT is largely still poorly understood, with more research required into both its efficacy on tumours and its sparing of normal tissues.

In high dose conventional radiotherapy such as stereotactic-based treatments, the
1.5. Microbeam Radiation Therapy

Figure 1.10: Survival curves of rats bearing right frontocerebral 9L gliosarcomas receiving various MRT protocols: no irradiation (Controls), unidirectional irradiation with an entrance dose of 625 Gy (625-1), and bidirectional irradiation with an entrance dose of 312.5 and 625 Gy (312-2 and 625-2 respectively). Extracted from Laisseu et al. (1998)[50]

damage to vasculature has been shown to be the main mechanism of tumour ablation. Park et al.[61] showed MRT is able to delay tumour growth and result in a significant reduction in blood vessel density. The results suggest that tumour vascular damage induced by MRT at potentially clinically acceptable peak entrance doses may provoke vascular normalisation and through the use of angiogenesis targeting agents, be used to improve tumour control.[61] The microvasculature of normal tissues irradiated with MRT was found to regenerate from the surviving cells in the unirradiated valley regions, however this effect is not observed within tumours. Distinctive strips of radiation damage are observed in neural cells of the cerebellum treated with microbeams, however this same damage is not observed in skin or tumours using conventional histological methods. [52]

Crosbie et al.[23] delivered MRT to inoculated EMT-6.5 tumour cells and normal mouse skin tissues and investigated the effects with immunohistochemical detection of γ-H2AX. An unexpected finding was that within 24 hours of the delivery of MRT, that
peak and valley irradiated zones were indistinguishable in tumours due to extensive cell migration between the zones. This same phenomenon was not observed within normal skin, which appeared to undergo a coordinated repair response. [23]

1.5.4.1 The Bystander Effect

The bystander effect is a phenomenon whereby unirradiated cells exhibit the same effect of irradiated cells due to chemical signals received from nearby irradiated cells. [59] This effect was first observed by Nagasawa et al. [59] who irradiated Chinese hamster ovary cells in the G1 cell cycle with alpha particles. A significant increase in the frequency of sister chromatid exchanges (SCE) occurred at doses as low as 0.31 mGy. 30% of cells showed an increase in SCE at this dose, despite less than 1% of cells being traversed by an alpha particle. The authors found a dose of approximately 2.0 Gy was required to elicit the same increase in SCE using X-rays with dose uniformity.

Sawant et al.[72] irradiated the nuclei of C3H 10T1/2 cells with precise numbers of alpha particles ranging from 0-8 per nuclei. Either 10% of cells on a dish or all cells on a dish were irradiated with the same number of alpha particles per nuclei. They found that more cells were inactivated than were actually irradiated and that when 10% of cells on a dish were exposed to alpha particles, the frequency of transformation is not less than when every cell on the dish is exposed to the same number of alpha particles.[72]

An investigation by Azzam et al.[8] was performed into the signalling mechanism involved by cells genetically compromised in their ability to perform gap junction intracellular communication. After irradiation of 1% of cells in the population, they found the stress-inducible p21(Waf1) protein present in non-irradiated gap junction-competent cells only, and in numbers far exceeding the fraction of cells irradiated.

Gerashchenko et al.[42] used a flow cytometric approach to study the proliferation of bystander cells co-cultured with irradiated cells. Confluent monolayers of rat liver
epithelial cells were irradiated with gamma rays at doses over the range of 0.5-20 Gy. Unirradiated cells were mixed with those that were irradiated at a 1:1 ratio and cultured together for 24 hours, which was followed by a flow cytometry study of their proliferation. The unirradiated cells were first stained with a lipophilic fluorescent dye to discriminate the two cell populations. They found that the unirradiated cells in the presence of cells irradiated with doses above 0.5 Gy showed an enhanced cell growth by 14-17%. [42]

These studies support the hypothesis that the bystander effect involves the secretion of chemical factors from irradiated cells. These chemical factors then propagate up to several millimetres through the intracellular medium and elicit a response in nearby unirradiated or minimally irradiated cells. [58] The probability of triggering the bystander effect appears to be proportional to dose until a saturation threshold is reached, where the signalling effect plateaus. [73] At higher doses however, radiation-hit induced cellular damage becomes the dominant effect responsible for cell death.

Morthersill and Seymour [57] have shown that bystander signalling is dependent on the cell type, which show that the efficacy of MRT may be dependent on both the type of tumour cells targeted as well as irradiated normal cells. Dilmanian et al. [29] suggests that the apparent tissue sparing efficacy of MRT in CNS targets is due to the beneficial bystander effect.

Whilst there are still many unknowns, due to the very steep dose gradients in MRT ranging from tumour ablative, to tissue tolerant doses, it is expected that the bystander effect plays a significant role in the apparent efficacy of the treatment.

### 1.5.5 Human Prospects

Radiation therapy is the most effective adjunctive treatment to neurosurgery for central nervous system tumours in children. However, the side-effects of radiation therapy
can be quite considerable.\[48\] The risks of dysfunctional development of a child’s central nervous system from irradiation are so severe that it is common for oncologists to prolong the onset of chemotherapy in order to postpone or avoid radiation therapy treatments. This strategy, whilst required for conventional therapy, has the potentially to negatively influence the survival outcome of a patient treated in this manner.\[53\]

Whilst the majority of effort in the field of MRT research is directed at cancerous pathologies, other diseases may benefit from its unique tissue sparing capabilities. Epilepsy is a condition that may be treated effectively using interlaced MRT. Epileptic seizures typically arise from restricted brain volumes that can often be identified by non-invasive methods, however surgical resection, the typical and highly effective standard of care cannot always be performed. The use of conventional stereotactic radiosurgery to ablate epileptic foci has shown some efficacy, however the lateral dose fall-off is often insufficient to deliver adequate target doses in the vicinity of sensitive normal tissues structures. \[41\]\[64\]

Pouyatos et al.\[64\] investigated the ability of synchrotron interlaced MRT to suppress seizures in genetic absence epilepsy rats (GAERS rat model). The region of involvement in GAERS rats was targeted, the somatosensory cortex (bilaterally), as were two structures involved in propagation: the motor cortex and the ventrolateral thalamic nuclei. Correct targeting was verified by T1-weighted magnetic resonance imaging two weeks post-irradiation, with general behaviour analysed by standard tests to detect possible side effects. During the 4 month period after irradiation, seizures in freely moving animals were monitored from depth electrodes implanted in the three target regions. The mechanisms behind anti epileptic effects were investigated by performing \textit{in vivo} intracellular recordings of individual irradiated neurons of the somatosensory cortex.

Interlaced MRT was able to modify the epileptogenic cortex and disable the ability
to initiate seizures by preventing wide-scale synchronisation among the irradiated neuronal networks. [64] The study provides preliminary evidence for the potential efficacy of MRT as a treatment for epilepsy in humans.

### 1.6 Dosimetry for Microbeam Radiation Therapy

The ability to perform accurate dosimetry for MRT is a necessary precursor to its use in human clinical trials. However, dosimetry for this modality is not without insignificant challenges, namely the very high dose rate (of the order of tens of kilogram per second), which requires a rather insensitive detector to ensure the dynamic range is of use. A further challenge is the very fast treatment time (tens of milliseconds), for which the response of the detector system must be appropriately fast. Perhaps the biggest demand is the ability to measuring the radiobiologically crucial structure of the radiation field, all whilst possessing all other necessary attributes.

#### 1.6.1 Ion Chambers

Ion chambers are used at present to provide dosimetric information about MRT fields. These detectors are essentially a gas cavity surrounded by electrode plates, which are biased to a set potential. When ionising radiation interacts with the gaseous medium, it knocks electrons from gas molecules, producing an ion-pair consisting of a negatively charged free electron and a positively charged hole.

In the presence of an applied electric field, the drift of the electron and hole results in an electric current. However, recombination of charge carriers will occur, the applied potential must be such that recombinant effects are negligible. If this condition is satisfied, the produced current is an accurate measure of the rate at which ion-pairs are produced in the chamber volume. By measuring the integral current with an ammeter and with various calibration factors applied, a value of dose rate can be
1.6. Dosimetry for Microbeam Radiation Therapy

obtained.

As MRT fields generally employ very high dose rates, one difficulty in the use of ion chambers is accurately determining the recombination correction factor. Fournier et al. [39] investigated the use of the two-voltage method, a cross-calibration method using alanine dosimeters and a storage ring current ramping method. The latter involves quantifying the decrease in ionisation chamber response while the increasing the storage ring current, with the decrease attributable to the lack of ion recombination correction. This storage ring current based method was found to be the most appropriate method.

Ion chambers are particularly suited as transmission detectors, where the thin chamber walls of such detectors minimally perturb the beam. Large area transmission ion chambers installed on the ESRF ID17 MRT beamline both upstream and downstream of the treatment subject location. These however provide only information on the overall intensity of the beam, not its microscopic structure. Ion chambers designed for point-based measurement are employed in MRT dosimetry, however their large size relative to microbeams prevents their use for purposes other than measuring relatively homogenous open fields.

1.6.2 Radiochromic Film

Radiochromic film is a solid-state dosimeter which upon absorption of ionising radiation, changes chemical structure and undergoes a change in colour. The significance of this attribute over existing film dosimetry is that radiochromic film is self-developing, that is it does not require post-irradiation chemical processing. Radiochromic film is well characterised and in widespread use as a high resolution dosimeter for use in conventional external beam radiation therapy. [38] [20]

Radiochromic films designed for conventional radiation therapy are unsuitable for
use in MRT as their upper sensitivity limit is well below doses commonly encountered. At present, only Gafchromic™ HD-810 and HD-V2 films (both from Ashland, USA) have an appropriate dynamic range of sensitivity for MRT.

The use of these radiochromic films for MRT dosimetry has been well characterised[22]. Whilst radiochromic film intrinsically permits high spatial resolution dosimetry, the determination of the measured distribution of dose is an offline process, requiring the digitisation of optical densities and the application of sensitometric calibration curves. One limitation of using film for MRT dosimetry is that, the difference in dose between the peak and valley regions exceeds the dynamic range of HDR radiochromic film. This necessitates two separate irradiations to occur, one low dose irradiation to provide peak information, with the underexposure of the valley region; and a second high-dose rate irradiation to provide valley information at the expense of the peak region being saturated. The requirement to use multiple films to measure the dose distribution of an MRT field results in positional uncertainty between measurements, as well as uncertainty associated with dose co-registration.

1.6.3 Metal-Oxide-Semiconductor Field-Effect Transistors

Metal-oxide-semiconductor field-effect transistors (MOSFET) dosimeters are solid state devices able to provide dose information at a point with high spatial resolution. MOSFET dosimeters consist of a doped substrate of silicon, overlaid with a silicon dioxide layer, in turn overlaid with a metal electrical contact. At either side of the oxide layer, are two regions of the substrate heavily oppositely doped as compared to the substrate, these are the source and drain.

Due to silicon dioxide being a dielectric material, this makes the MOSFET act like a capacitor, with the substrate-oxide interface a semiconductor device. When ionising radiation is incident on the oxide layer, electron-hole pairs are formed. Holes
are forced towards the substrate-oxide interface where they are trapped, producing a sheet of charge. The drain-source current is very sensitive to the charge sheet, and so a small adjustment to the gate voltage is required to keep the current constant. By determining this voltage, dose can be measured. The sensitivity of this quantity makes MOSFETs a particularly sensitive detector to small changes in dose.

The very small size of the sensitive volume makes MOSFET detectors well suited to high spatial resolution dosimetry applications, and indeed their use in MRT been explored. Very high spatial resolution is achievable with the detector oriented in the edge-on orientation, with the oxide film oriented such that its smallest direction is along the peak-valley axis. One issue with MOSFETs however is their lack of radiation hardness to the extreme doses encountered in MRT, an issue that results in an impractically short detector life.

1.6.4 Thermoluminescent Dosimeters

Thermoluminescent dosimeters (TLDs) are a solid-state detector, consisting of a phosphor such as lithium fluoride or calcium fluoride in a crystalline structure. The material contains small amounts of activators which enable it to act as a thermoluminescent material, and are often present in only trace quantities. The activators provide two kinds of centres: traps for the electrons and holes, which capture and hold charge carriers in a potential well for a useful amount of time, and luminescent centres, which are located at either electron or hole traps, and emit light when charge carriers are able to recombine with this centre. Irradiation of TLD detectors results in electron and holes being trapped in trapping centres. They are later liberated by the application of thermal energy through precisely controlled heating, whilst luminescent centres release visible light which is read out by an optical detector and amplification system. A proportionality relationship exists between luminescence and absorbed dose.
1.6. Dosimetry for Microbeam Radiation Therapy

For MRT, a 2-dimensional thermoluminescent dosimetry system has been used consisting of LiF:Mg,Cu,P foils and a TLD reader equipped with a CCD camera, with a large size 72 mm planchete heater developed to perform high resolution dosimetry. TLDs were irradiated at the ESRF, Grenoble, France to microbeams fields with varying microbeam width and pitch. [66]

1.6.5 Fluorescent Nuclear Track Detectors

Fluorescent nuclear track detectors (FNTD) are a novel passive integrating detector sensitive to high-LET radiation. The detectors consist of a Al$_2$O$_3$:C,Mg crystal developed by Landauer, Inc. which is reusable by annealing of the detector. As radiation ionises along its track, it leads to ionisation of the Al$_2$O$_3$ crystal, resulting in the production of electron-hole pairs. The electrons become trapped in the aggregate oxygen vacancy defects in the Al$_2$O$_3$:C,Mg, resulting in the radiochromic transformation of fluorescent colour centres. Subsequent analysis using a confocal fluorescent laser scanning microscope results in the colour centres to fluoresce when the laser beam passes over them. The fluorescence in a localised region is increased in proportion to the ionisation that has occurred. Since the confocal imaging system enables the measurement of ionisation-induced fluorescence, it is possible to produce a 3-dimensional map of dose distributions.[3]

FNTD detectors have been applied to dosimetry of MRT fields by Bartz et al. [10] Irradiations were performed at the ESRF, Grenoble, France, with the detectors irradiated with doses from 3 - 100 Gy. Acrylic absorbers were placed in front of the detector ranging from 1 - 31 mm to mimic radiation interaction in tissue and with microbeams with width 50 µm and pitch varying from 100 - 400 µm. Detector readout was performed through the use of a custom-developed confocal laser scanning fluorescence microscope and read at a depth of 3.5 µm below the detector surface.
MRT radiotherapy fields were read with high spatial resolution, however due to the preliminary nature of the investigation, detectors were not individually calibrated by background fluorescence and sensitivity.

### 1.6.6 Optical Computed Tomography of Radiochromic Plastic

Optical Computed Tomography (CT) is a technique operating on the same fundamental principles as radiographic CT scans. Many 2-dimensional images are obtained, and reconstructed into a 3-dimensional image using tomographic algorithms. PRESAGE™ is a radiochromic plastic which operates in the same way as 2-dimensional film and is read out using an optical CT scanner.

Dosimetry is able to be performed in the dose range of tens to hundreds of Gy, and with spatial resolutions of 20 \( \mu m \), with 50 \( \mu m \) microbeams easily discerned. Preliminary investigations reveal little energy dependence of the PRESAGE™ material, however there is drifts in measured response of the order of a few percent per day. [31] [67]

### 1.6.7 Optical Calorimetry

Optical calorimetry is based on the principle that almost all imparted radiation on an absorbing medium is converted to heat. Immediately after irradiation of a transparent medium, the temperature rise and spatial distribution of temperature can be directly related to the dose distribution within the medium. As the refractive index of the transparent medium is dependent on temperature, localised changes in the refractive index are representative of dose.[2] The change of refractive index is approximately proportional to temperature, and over the range of 0 - 30 °C can be considered linear. [1]
The temperature distribution representative of the dose distribution will only remain for a very short amount of time (several milliseconds), before thermal dissipation effects results redistribute temperature spatially. This phenomenon requires that not only must the readout time be very short, but the irradiation time must be as well. [2]

The reference image topography method proposed by Ackerly et al. [2] for MRT involves the use of a backlit speckled patter on one side of a transparent waterbath, with a CCD array coupled with a macro lens forming a camera on the other side. The camera is focused on the speckle pattern, and a series of reference images taken. As a proof of principle, a heated wire was placed in the waterbath, and the resulting thermal distributions imaged by the system, with temperature variations determined from the inferred refractive index changes. The technique has been further applied by Cavan et al.[19] who was able to determine high dose-rate brachytherapy dose distributions using this technique.

1.6.8 MRI Gel Dosimetry

Gel dosimetry is a technique where the properties of a gel substance are changed in response to absorbed ionising radiation. Fricke gel is a well-researched method, which contains an agarose gel containing ferrous(II)sulphate. Upon irradiation, a set of chain redox reactions result in the oxidation of ferrous ions, which results in a change of the nuclear magnetic spin-lattice relaxation time, $T_1$. [56] However, the biggest disadvantage of this method for high spatial resolution is that diffusion of ferric and ferrous ions occurs, which results in blurring and a loss of spatial resolution. BANG gel was developed to address this issue, and is a gelatin gel in which monomers are dissolved. Upon exposure to ionising radiation, co-monomers polymerise to cross-linked polyacrylamide, which results in a change in the localised nuclear magnetic
spin-spin relaxation time, $T_2$.\cite{56}

Dilmanian et al.\cite{30} applied BANG gel dosimetry towards MRT with the construction of a homogeneous BANG-gel-filled acrylic phantom and a anthropomorphic head phantom using a human skull. Complex dose distributions were able to be studied, such as interlacing, in 3 dimensions with the use of a clinical MRI machine. However, irradiations were performed at the National Synchrotron Light Source, Upton, USA using 680-\(\mu\)m -wide microbeams, spaced 670 \(\mu\)m apart. Measurements were ultimately limited by the spatial resolution of the MRI machine, which was 440 \(\mu\)m , with a pixel size of 84 \(\mu\)m .\cite{30} Currently, pre-clinical MRT animal experiments at the ESRF are performed with 50-\(\mu\)m -wide microbeams, spaced 350 \(\mu\)m apart, parameters which at present exceed the spatial resolution of this system.
Chapter 2

Monte Carlo Simulation

2.1 The Monte Carlo Method

The Monte Carlo method provides a numerical solution to problems that can be described as a temporal evolution of objects interacting with other objects based on object-object interaction relationships. The rules of these interactions are processed randomly and repeatedly until the numerical results converge to means, moments and variances of useful significance. The Monte Carlo method can be epitomised as the solution to a macroscopic system through the simulation of its microscopic interactions.[74]

The true power of this technique becomes apparent when determining the result of a large series of processes occurring, with each dependent on the outcome of the former process. However, a disadvantage over pure analytical methods is that the result is subject to the laws of chance, and as such, it is important to know the uncertainty in any such determination.[33]

The probability of an occurrence $p$, which is observed $k$ times in $n$ simulated itera-
2.1. The Monte Carlo Method

The Monte Carlo Method approximates a probability by:

\[ p \approx \frac{k}{n} \tag{2.1} \]

in the limit as \( n \) tends to infinity, the probability becomes an equality:

\[ \lim_{n \to \infty} p = \frac{k}{n} \tag{2.2} \]

For finite iterations, the uncertainty is reduced by having larger iterations of simulated quantities. [54] The technique itself does not necessitate the use of a computer, but complex determinations, such as those used for problems in radiation physics make the use of a computer a practical requirement.

2.1.1 Applied to Problems in Radiation Physics

The earliest recorded use of the Monte Carlo method applied to radiation physics occurred at Los Alamos Scientific Laboratory, where physicists were investigating radiation shielding and the depth to which neutrons would penetrate various materials. The investigators had most of the data necessary to solve the problem, including the mean free path, and the energy given off in an interaction, however the problem was not readily solved using deterministic methods. Stanislaw Ulam proposed the use of random number generation and sampling probability distributions. Monte Carlo methods were used extensively during the post-war stages of the Manhattan Project despite computing power being greatly limited at the time. In the 1950s, Monte Carlo simulations performed an important part of the early work on the development of the hydrogen bomb.

For medical physics purposes, the Monte Carlo method provides numerical solutions that can be described as a temporal evolution of quantum particles in their
surroundings. The rules of radiation interaction, whether theoretical, empirical, or a hybrid are processed randomly and repeatedly until a convergence of numerical results to estimated means, moments and their variances occurs. [75]

2.1.2 Use in Microbeam Radiation Therapy

Investigating dosimetric quantities in MRT are particularly troublesome, the very high photon luminance makes spectroscopic measurements impossible using conventional means, and access to synchrotron facilities have high demand, but limited beam time. [78] The use of Monte Carlo simulations not only enables investigations to be carried out without access to a synchrotron, but also enables the researcher to perform the physically impossible; for instance, disabling a particular physical interaction or determining theoretical detector response assuming perfect charge collection characteristics throughout an entire defined sub-volume.

Siegblahn et al. [77] used the PENELOPE code to investigate build-up dose and lateral dose profiles of microbeams for comparison with experimental microdosimetry, radiochromic films and MOSFET detectors. Siegbahn et al. (2006) The dependence of the PVDR on microbeam width and spacing, and X-ray energy were investigated using PENELOPE by Siegbhan et al. [78]

Nettelbeck et al. [60] investigated the influence on dose distribution of modelling a full array of microbeams versus modelling a single microbeam and performing superposition methods. The single array method resulted in discrepancies of up to $5 \mu m$ in the FWHM of microbeam profiles across the array, leading to minor PVDR variations. However, this work modelled a two-stage multislit collimator (MSC) in use at the ESRF in which one stage translated to produce variable microbeam widths. The current MSC in use is at the ESRF and for forthcoming animal clinical trails consists of a single stage and should have much negligible divergent positional dependence.
2.2. Geant4

The influence of the partial linear polarisation of the MRT beam on dose deposition was investigated by Spiga et al. [84] using Geant4 and multiple polarisation libraries. This work found that accounting for polarisation results in dose profiles that are more round, and that the effect is more dominant for the lower energy components of the MRT beam. However, discrepancies in depth dose profile results across libraries raised questions over their reliability.

Prezado et al. [65] performed an assessment of scatter factors, relating the absolute dose measured in reference conditions (a $2 \times 2$ cm$^2$ field at a depth of 2 cm in water) to the peak doses. Monte Carlo simulations were performed using PENELOPE and GEANT4 to provide intercomparsion and compared with experimental data in the form of high dose radiochromic film and a large diameter plane-parallel chamber. Good agreement was found between both Monte Carlo codes and the experimental results.

More recently, Monte Carlo methods have been investigated for use in MRT treatment planning. [55] Most recently, Bartzsch et al. [11] characterised the ESRF ID17 MRT source with respect to its phase space and photon polarisation. These results simplify the phase space model for dose calculations and lay the foundation for dose calculation for the first clinical pet trials. This study also showed that the influence of polarisation is of minor importance to the peak and valley doses inside the microbeam field, with the major effect out-of-field.

2.2 Geant4

Geant4 is a Monte Carlo based toolkit for the simulation of particle transport through matter. Development started in 1993, where groups from CERN and KEK sought to utilise modern computing technologies such as an object oriented methodology to improve upon the predecessor, GEANT3. [71] It was developed for the simulation of
2.2. Geant4

high-energy physics processes, but since has been expanded to lower energies relevant for medical physics.

2.2.1 Architecture of Geant4

2.2.1.1 Events and Runs

Events in Geant4 are the main unit of simulation. They start with the tracking of a primary particle and terminate with the completion of tracking the primary and all secondaries produced through interactions. A Run in Geant4 is the simulation of a specified number of primary particles. The run is the main unit of simulation and represents an entire simulation in a given configuration.

2.2.1.2 Geometry, Materials and Detector

Geant4 has the concepts of logical and physical volumes. A logical volume is a geometric element of a specific shape, material and density. The shape of a logical volume is defined as a separate entity known as a solid. Simple geometric shapes are predefined and only geometric parameters need to be defined, however much more complicated solids can be defined by bounding surfaces. Additionally, solids can be produced by geometric Boolean operations including union, intersection and subtraction.

A physical volume is an instance of a logical volume with physical placement within a specified mother volume. In many detector designs, sensitive volumes may be identical in geometric shape and material composition, so Geant4 provides the ability to duplicate logical volumes in the form of replicas with parametrised placement.

2.2.1.3 Tracking and Stepping

Geant4 treats the tracking of particles in a generic way, independent of particle attributes and physics processes. Each particle is moved step-by-step in a manner such
that tolerances achieve a balance between optimisation of simulation execution time.
All physics processes associated with a particle propose a step, which for a particle
in motion is a length, and at rest is a time. The step length is chosen such that the
smallest of either: the maximum allowed step specified by the user, or the step pro-
posed by all processes attached to the particle, including geometrical limits such as
geometric boundaries.

Physics processes may be represented by the actions handled by the tracking in
three stages: at rest, along step and post step. At rest is used by processes such as decay
at rest, along step implements behaviour such as energy losses or secondary particle
production which happens continuously along the step, and post step is invoked at the
end of the step. Along step actions take place in a cumulative fashion, whilst others
occur exclusively. [71]

2.2.1.4 Physics

Geant4 provides a highly customisable environment for defining physical models which
govern radiation transport in a simulation. A plethora of electromagnetic and hadronic
physics models exist for use in Geant4 simulations, it is up to the user to select the
most appropriate models for their particular application. The primary electromagnetic
models for Geant4 version 9.2 are the standard and the low energy electromagnetic
physics packages. As the low energy package was used for investigations as part of
this work, it is described in more detail in Section 2.3.

2.2.2 Simulation Development

Geant4 provides an abstract interface for eight user classes from which a simulation is
constructed. Of the eight, three are mandatory to implement in a simulation:

- G4VUserDetectorConstruction - used for defining the geometry of the simulated
world and all materials contained within it. Also, volumes may be defined as sensitive volumes, and visualisation attributes may be defined.

- G4VUserPhysicsList - for defining all particles used in a simulation, the physical processes and parameters pertaining to the cutting of detectors

- G4VUserPrimaryGeneratorAction - for generating primary particles with position and energy attributes

Additionally, the remaining 5 user classes can be optionally activated to modify the default Geant4 behaviour:

- G4UserRunAction - for actions at the beginning and end of every run

- G4UserEventAction - for actions at the beginning and end of every event

- G4UserStackingAction - for the customisation of access to track stacks.

- G4UserTrackingAction - for actions occurring at the start and end of every track

- G4UserSteppingAction - for customising the behaviour at every step

2.3 The Geant4 Low Energy Electromagnetic Package

The Geant4 Low Energy electromagnetic package provides radiation transport models down to an energy of 250 eV with good accuracy and up to an energy of 100 GeV. All processes are based on theoretical models and on exploitation of evaluated data. The processes involve two distinct phases: the calculation and use of total cross sections and the generation of the final state. The set of processes is based on detailed models of the shell structure of the atom and precise angular distributions. [5] It was developed in
such a way as to be complementary to the Geant4 Standard electromagnetic package, however for the sake of simplicity and due to its coverage of the entire energy range encountered in MRT, it has been used for all Geant4 simulations the subject of this work.

Calculation of interaction cross sections is performed through logarithmic interpolation of data libraries. Compton (incoherent) scattering photon energies are determined from the Klein-Nishina formula, whilst the angular distributions of the scattered photon and recoil electrons are obtained from the EPDL97 data library. Rayleigh (coherent) scattering angular distributions are sampled from the Rayleigh formula and include the Hubbel form factor from EPDL97. Bremsstrahlung is determined using parameterisation from the EEDL data with 16 parameters for each atom, whilst ionisation is determined using parameterisation based on 5 parameters for each shell.

2.3.1 Validation of Code for Use in Radiotherapy

The use of the Geant4 Low Energy electromagnetic package has been well validated against published reference data. Comparisons of the photon and electron models have been made against the NIST-XCOM Photon Cross-Section Database [4] with excellent agreement with reference data.
Chapter 3

Development of a Dosimetry System for Microbeam Radiation Therapy

3.1 Introduction

The efficient use of synchrotron beamtime for MRT requires relative fast quality assurance along with the necessary high spatial resolution required for a treatment where efficacy and safety are highly reliant on the spatial distribution of dose. A standalone MRT dosimetry solution was developed at the Centre for Medical Radiation Physics (CMRP) at the University of Wollongong. The system was designed from inception to be highly modular, permitting easy upgrading as features are added or components improve.

The system comprises three main components:

- Microstrip detector: a single channel, very high spatial resolution dosimeter
3.2 Microstrip Detector

- Data acquisition hardware: to set electrical parameters, readout dosimeter response and interface with software

- RadPlot: a data acquisition and analysis software package

The data acquisition hardware components of the system were developed by M. Petasecca and I. Fudulli of the University of Wollongong, with details included for completeness. The data acquisition and analysis software was developed by the author to interface with the data acquisition hardware and provide post-acquisition analysis functions.

3.2 Microstrip Detector

The silicon microstrip detector was developed to provide very high resolution dosimetry for microbeam radiation therapy, when scanned through the beam with external mechanical means. The detector consists of a single 10 µm wide silicon diode fabricated on a 100 Ω·cm p-type 50 µm thick epitaxial substrate of dimensions 1.5 × 1.0 mm² (see Figure 3.1). This epitaxial layer is grown on a 370 µm thick p-type 0.0001 Ω·cm silicon substrate. The silicon diode is surrounded by a n⁺ guard ring which limits the extent of the sensitive volume. The detector can be used in either a passive or biased mode of up to 200 V.

3.2.1 Packaging

Dose enhancement due to the surrounding packaging has been minimised by mounting using drop-in technology patented by the CMRP. This packaging consists of the detector being mounted on a flexible kapton probe of dimensions 600 µm thick, 10 mm wide and 300 mm long (see Figure 3.2). The detector chip is attached to the probe by a flexible carrier consisting of a thin polyamide supporting substrate with a
3.2. Microstrip Detector

![Diagram of microstrip detector](image)

Figure 3.1: Diagram of microstrip detector, showing the central strip detector (connected to the central pad), the surrounding guard ring structure (connected to the left pad) and the substrate (connected right pad).

chemically deposited aluminium layer which is tab-bonded to the detector chip’s pads and to the probe’s tracks. The packaging design enables great flexibility in the use of the detector in various configurations such as embedding within machined PMMA or mounting on a linear stage of a water tank.

3.2.2 Orientation

The orientation of the microstrip detector has an impact on both the spatial resolution and the detector response. Three main orientations have been defined for the purpose of this work, namely: face-on, edge-on, and end-on; all referring to the orientation of the detector’s sensitive volume with respect to the radiation field.
3.2. Microstrip Detector

Figure 3.2: Photo of the microstrip detector as mounted on a Kapton tail. Note the detector and part of the Kapton tail are sandwiched between two slabs of PMMA for phantom measurements. The connector end of the Kapton tail is connected to the preamplifier module described below.
3.2.2.1  Face-on

The face-on orientation (Figure 3.3) results in the surface of the central strip oriented normal to the incident radiation field. This configuration results in an effectively symmetric detector structure, negating asymmetric substrate dose enhancement effects later discussed, however it also results in the poorest spatial resolution.

3.2.2.2  Edge-on

Orienting the detector in edge-on orientation (Figure 3.4) results in alignment of the long side edge of the central strip sensitive volume normal to the radiation field. This provides greater spatial resolution than the face-on orientation, with less response sensitivity to angular misalignment. However, for the majority of beam heights employed in MRT, the vertical dimensions of the sensitive volume is larger than the radiation beam.

3.2.2.3  End-on

The end-on configuration (Figure 3.5) results in the smallest cross-section of the central strip sensitive volume being oriented normal to the radiation field. This results in the greatest spatial resolution, but is also the most sensitive to angular misalignment, as a 1° lateral misalignment will result in a 14 µm broadening of the beam’s-eye cross-section.
3.2. Microstrip Detector

Figure 3.3: 3D render of the microstrip mounted on the Kapton tail and oriented in the face-on configuration with the beam direction denoted by the arrow.

Figure 3.3: 3D render of the microstrip mounted on the Kapton tail and oriented in the face-on configuration with the beam direction denoted by the arrow.
Figure 3.4: 3D render of the microstrip mounted on the Kapton tail and oriented in the edge-on configuration with the beam direction denoted by the arrow.
Figure 3.5: 3D render of the microstrip mounted on the Kapton tail and oriented in the end-on configuration. Note the smallest dimension of the sensitive volume is oriented with the wide axis (i.e. peak-valley direction) of the beam.
3.3 Data Acquisition Hardware

The X-tream system is based around a Field-Programmable Gated Array (FPGA), an integrated circuit configurable post-manufacture. The hardware is comprised of two discrete modules, the Preamplifier Module and the Central Data Acquisition Unit.

The Central Data Acquisition Unit (CDAU), the main hardware component, applies a specified bias to the detector, amplifies the radiation-induced current in the detector’s sensitive volume, and samples this signal at a high repetition rate. [62] The data acquisition hardware has been developed to be a complete standalone solution when coupled to a Windows-based computer running RadPlot, the GUI-based data acquisition and analysis system (see Section 3.4) over a USB2.0 link. The hardware is entirely controlled by this custom software, however the unit does contain some...
manual hardware override functionality, primarily for diagnostic purposes.

The CDAU is designed to be mounted outside of the treatment room to minimise the effects of radiation damage on its components, whilst the preamplifier module is located in close proximity to the radiation detector to minimise the impact of noise. The CDAU and preamplifier module are connected by a long twisted pair shielded cable which enters the treatment room through a cable port.

### 3.3.1 Preamplifier Module

The very high ratio of the dose rate in the peak and valley regions of a radiation field in MRT has largely driven the development of the preamplifier module. Since the PVDR at the surface of a 20-mm-wide microbeam field as predicted by Monte Carlo simulation is several thousand, the minimum dynamic range for the dosimeter is necessarily in the order of $10^4$.

Furthermore, the capacitance of the detector as mounted in the kapton probe has an effect on this dynamic range. At an applied bias of 50 V, the capacitance of the probe has been measured as 7 pF. In spite of this significant capacitance at the input of the preamplifier, a dynamic range of greater than $10^4$ must be maintained. As the system is, by design, to be used for accurate dosimetry, linearity must be maintained over the full dynamic range whilst exhibiting wide bandwidth to correctly measure the input signal variation from the detector probe. A logarithmic amplifier would satisfy the dynamic range requirement; however, the temperature dependence of the preamplifier characteristics would significantly affect the linearity of the response.

The photocurrent induced in the detector due to the interaction of a given X-ray beam is in principle, directly proportional to the dose rate. Therefore, the desired input signal dynamic range is of the same order of magnitude as the expected dose rate. A preamplifier architecture which best satisfies this requirement is a transimpedance
3.3. Data Acquisition Hardware

Figure 3.7: Schematic diagram of the X-tream dosimetry system. The microstrip detector is represented as a photodiode as readout by the preamplifier. [62]
amplifier with a gain of approximately $10^5$. The input stage impedance must match the probe capacitance whilst minimising input leakage current so as to reduce the output offset of the preamplifier. The solution employed is based on a commercial JFET input stage operational amplifier with cascade-compensated architecture (AD795, National Semiconductor, USA).

As the preamplifier is relatively radiation hard, whilst the CDAU is not, the preamplifier module was designed such that it could be connected to the CDAU by a long cable. This permits placement of the preamplifier module in the high radiation level environment of the MRT hutch, whilst placing the CDAU in an external electronics rack, protecting the integrated circuits from radiation damage. Noise rejection and analog signal integrity is achieved through the use of a differential amplifier driver and receiver pair (EL5172 and EL5072 respectively from Intersil, USA).

### 3.3.2 Central Data Acquisition Unit

As there is typically a significant distance between a synchrotron beam hutch and the control room, remote control of the dosimetry system is essential. The CDAU controls the acquisition of the differential signal generated by the preamplifier module, the offset adjustment, the digital conversion of the signal, the high voltage bias of the detector and the regulated bias for all the electronic components.

The core of the CDAU is a Field Programmable Gate Array (FPGA), a Spartan-3 (Xilinx, USA) equipped with a CY68013 USB microcontroller (Cypress, USA) for implementation of the USB 2.0 interface. The system also has a Cypress PLL PLL (CY22150), which provides clock synchronisation of the I/O buses and generation of internal blocks. The firmware which operates the FPGA was designed in the descriptive language Verilog.

The digital clock manager (DCM) is fed by the main clock from the PLL at 140
3.3. Data Acquisition Hardware

MHz, generating all time bases of the CDAU. The primary task to the DCM is the synchronisation of the FIFO blocks, which have input at 20 MHz and an output bit stream at 48 MHz. Each word stored in the FIFO is comprised of a 16 bit header followed by 16 bit ADC data. The ADC data is sampled at a rate of 1 MHz, with the integer values corresponding proportionally to the amplitude of the current. The **START** signal from the USB interface produces the activation of the state machine, which controls the ADC for the acquisition of the current signal from the detector. It also enables the acquisition chain and the FIFOs through the DCM.

Two asynchronous modules control the high voltage bias of the detector by a DAC to set the value of the switching regulator and by an ADC to check if the applied value is correct. Upon user verification that the correct bias has been produced, it may be applied safely to the detector. All controls and read-outs for this system are implemented in the graphical interface (RadPlot).

The **AvrgModule**, is a firmware module controlled directly by the software interface which calculates in real time, the average of either 2, 4, 8, or 16 samples, thereby reducing the file size of large acquisitions. Averaged data are then transferred to the FIFO block for temporary storage. The data storage strategy employed is based on the use of a FIFO arranged by a dual-layer stack memory, with the first layer of 1k words (16 bit per word) which stores a pair (header and data) for each clock cycle at 20 MHz. The second layer is comprised of 16k words and is enabled only when the first FIFO stack is filled by three words. Header/data pairs are then transferred at 20 MHz from the first layer to the second and a **DATA READY** flag is sent to the USB interface.

Upon receipt of the **DATA READY** flag, the software generates a **DATA TRANSFER** command, which starts the transfer of the data from the second layer to the computer at 48 MHz through the USB link. This strategy is necessary since there exists a latency
3.3. Data Acquisition Hardware

Figure 3.8: Schematic diagram of the firmware and main functionalities of the FPGA module; the blocks with dashed contours represent external components. [62]
time between the \texttt{DATA\_READY} being generated by the FIFO and the \texttt{DATA\_TRANSFER} command being generated by the interface of about 3 ms. At a data acquisition rate of 1 MHz, corresponding to the transfer of 6000 words to the FIFO, this has to be compensated by a memory buffer size of at least 6k words. The Xilinx Spartan-3 supports the use of 17 blocks of RAM to build a FIFO, and the 1+16 block strategy acts to maximise the buffer size allocable, whilst avoiding data loses during handshaking of the USB link. The USB link transfers the FIFO contents to the computer in blocks of 1064 bytes, with the number of blocks transferred by using a user-defined fixed virtual data buffer. The CDAU contains a trigger module to manage external asynchronous triggers; a feature particularly useful when the acquisition is to be synchronised with the Synchrotron Control System based on spec (Certified Scientific Software[83]).

### 3.3.3 Acquisition Parameters

Acquisition parameters can be set from the CDAU and send to the FPGA via USB to the command module. Acquisition parameters such as the delay time, the time of the acquisition and hardware averaging can be set.

### 3.3.4 Detector Bias

Biasing of the detector can be configured such as to be floating, positive or negative. Dedicated EMCO high voltage power supplies are controlled by the FPGA under computer control. A separate power supply produces either positive or negative voltage, with the active supply selected by a FPGA-controlled relay. An ADC measures the voltage between this relay and ground, providing feedback to the FPGA and software of the measured voltage, providing confirmation that the requested voltage has in fact been set. The set bias can be selectively applied or removed to the detector by FPGA control of a further relay, enabling a voltage to be set and verified as stable prior to
Figure 3.9: Screen capture of RADplot displaying acquired dosimetric data from a MRT field, and peak analysis results.

3.4 Data Acquisition and Analysis Software

A data acquisition and analysis program (see Figure 3.9) was written in C++ using the Qt widget toolkits to interface with hardware to perform acquisitions and produce subsequent analysis functionality. The data acquisition parameters are separated into single trigger and a multi-trigger modes. The single trigger mode is used for the acquisition of continuous-motion scans, such as lateral scans across the microbeam radiation field array. A single TTL trigger pulse starts the acquisition, which continues until the user-specified acquisition time is reached.

The multi-trigger mode is used for discrete step-wise scanning across the radiation field, a trigger starts the acquisition of points at every position along the scan until
either the user ends the acquisition or a time-out duration is reached.

The acquisition parameters and file creation information are encoded in a binary header at the start of every acquisition file. Recorded parameters include:

- Trigger mode (single or multi-trigger)
- Trigger method (internal or external trigger)
- Acquisition time (in ms)
- Set delay (in $\mu$s)
- Buffer size (in bytes)
- Hardware averaging factor
- Bias status (bias on or off)
- Bias polarity (positive or negative)
- Set bias (in V)
- Measured bias (in V)
- Year, month and day of acquisition file creation
- Day, minute and second of acquisition file creation

The header structure has been devised with additional unused fields reserved for synchrotron data (such as storage ring current, scan type, motor speed, etc.) which can be utilised with future interfacing of RADplot to the MRT control computers.
3.4.1 Data Loss Reduction Strategies

Multithreading is employed to separate the graphical user interface and data acquisition functionalities into two separate threads. The data acquisition thread is coded so as to have the highest priority, taking precedence over any other application functionality. This greatly reduces the probability of data loss through excessive communication latency, with checks in place to ensure the user is notified should this occur. From the specified acquisition time, the sampling frequency and the hardware averaging factor, RADplot calculates the expected number of data points for any given acquisition, during post-acquisition pre-processing of the acquired data, a count of the number of points in the file is made. If a discrepancy is present, the user is notified immediately by a message box and on any occasion the acquisition file is opened at a later date.

3.4.2 Basic Data Analysis

The software provides the ability to perform statistical operations on acquired data, giving the average and standard deviation of an acquisition. A subset of an acquisition can be selected as a region of interest to perform selective analysis including the mean, the standard deviation and the standard deviation with various levels of software averaging (10×, 100× and 1000×).

To determine the integral response of the detector due to part or all of an irradiation, integral analysis can be performed. A baseline region is defined by the user for the purpose of leakage current subtraction, and the limits defined for the region of integration. The position of the baseline and integral regions of interest are displayed, along with the mean baseline and computed integral with uncertainty.
3.4.3 Microbeam Array Peak Analysis

More advanced analysis functionality exists in the form of peak analysis. Radplot automatically locating peaks given search parameters specific to the configuration of the detector and beamline components. Since noise may produce spurious results for this function, features such as data reduction and window smoothed averaging are incorporated as options for use with this feature. The peak analysis module is able to determine:

- Peak amplitude by peak number
- Peak amplitude histogram
- Valley amplitude by valley number
- Valley amplitude histogram
- Full-width at half-maximum (FWHM) by peak number
- Symmetry of half-widths at half-maximum (HWHM) by peak number
- Peak-to-valley dose ratio (PVDR) per peak pairs and associated valley
- Histogram of PVDR per peak pair and associated valley

All computed results are immediately output graphically in a results window and are output to a text log file in the same directory as the acquisition file. The instant output of these results greatly simplifies the analysis of microbeam irradiations, negating the need for dedicated offline analysis software and giving immediate feedback to the system operator. The use of these analysis tools may also simplify initial detector set up as a detector misalignment may manifest as a gradient in the peak amplitude or a heavily weighted asymmetry. Ultimately, the ability to perform fast and accurate quality assurance is greatly enhanced with these tools.
3.4. Use of Acquired Data with Other Packages

To enable the use of other software packages, a separate stand-alone decoding application (see Figure 3.10) was written which converts the binary-formatted data into an ASCII format able to be read by virtually all third-party data analysis packages. This application was particularly useful during the testing stages of the whole data acquisition system to verify results, but it also expands analysis operations beyond what is included in RADplot. The ability to perform data reduction averaging on acquired files is able to enhance the signal-to-noise ratio of data, at the expense of temporal resolution. Decoding and averaging, whilst computationally more intense than simple decoding, is actually a faster operation since disk-write access is the slowest operation on modern computers. To improve disk read and write performance, buffers are employed to store data in random access memory, and are only written to disk once...
full, producing significant speed improvements on the large files which are produced at acquisition rates of up to 1.6 MHz.

3.5 System Characterisation

3.5.1 Slew Rate

Real-time measurements in MRT are typically performed in two ways: continuous translation of the detector with continuous current sampling or step-wise translation and with synchronous current sampling at each point. The accuracy of the system, particularly in the continuous translation method results in steep temporal dose gradients. The slew rate of the system if not sufficiently high will degrade the accuracy of dosimetric measurements. The slew rate of a preamplifier is measured in units of $V/\mu s$, and is defined as the maximum rate of variation of the output voltage:

$$SR_{th} = \left| \frac{dV_{out}}{dt} \right|_{\text{max}}$$  \hspace{1cm} (3.1)

Limitations of the slew rate can distort the shape of a measured output signal as a function of time. Given that one of the main parameters in the characterisation of the radiation field of MRT is the X-ray microbeam profile, it is important that the shape of measured profiles are not appreciably distorted. During measurement, the microstrip detector is moved at a constant speed (typically 1 mm·s$^{-1}$) through the radiation field with a dose gradient of approximately 1000 Gy·s$^{-1}$·µm$^{-1}$, so the design of the preamplifier is crucial to ensure that the slew rate produces minimal distortion in the measurement of microbeam profiles.

Calculation of the theoretical slew rate is performed which for MRT involves the assumption of a constant linear translation, $v_{tr}$, of the detector at 1 mm·s$^{-1}$, a sampling
3.5. System Characterisation

Figure 3.11: (a) Calculation of a realistic slew rate expected in MRT from Monte Carlo simulation. (b) Experimental verification of the preamplifier/digital readout slew rate. [62]

Time of 1 $\mu$s (a sampling rate of 1 MHz). For this calculation, a microbeam peak was assumed to be 4.096 V (the maximum measurable voltage by the system). The resulting dose distribution of a Monte Carlo simulation of a 52 $\mu$m wide microbeam at 10 mm depth in water is shown in Figure 3.11(a), and the derivative $dD/dx$ calculated. The theoretical slew rate required corresponding to these conditions becomes:

\[
SR_{th} = \left| \frac{dV_{out}}{dt} \right|_{\text{max}} = \frac{V_{\text{max}}}{D_{\text{max}}} \left| \frac{dD}{dt} \right|_{\text{max}} = \frac{V_{\text{max}} v_{\text{lin}}}{D_{\text{max}}} \left| \frac{dD}{dx} \right|_{\text{max}} = 1.4 \text{mV} \cdot \mu\text{s}
\]

3.5.2 Current Calibration and Linearity

To calibrate the counts of the system into the more relevant quantity of current, a calibration was performed. A resistor was connected in across the detector input of
the pre-amplifier box, with an ammeter connected in series to measure current. An acquisition was taken, whilst current was measured by determining the mean with uncertainty for 10 measurements during this period. Bias was applied at a level of -1.2 V, causing a current to flow in direct proportionality to the resistance. The value of the resistor was varied to generate multiple data points, and enable the fitting of a line of best fit.

Whilst there is an offset present due to the offset of the pre-amplifier input level, this has no impact on the calibration with other offset values, since the baseline of each measurement is subtracted from acquired data prior to further analysis. The slope of the line of best fit gives the inverse calibration factor of current per count. This is 588 ± 16 pA/count.
3.5.3 Noise Performance

When a continuous signal is sampled at a constant sampling rate, aliasing may occur. For a sampling frequency of $f_s$, all noise components above the Nyquist frequency of $f_s/2$ will cause aliasing when digitised by an unfiltered ADC. A shaper filter has been used to cut the bandwidth of the input signal to the ADC to less than the Nyquist frequency of 500 kHz.

3.6 Modes of Operation

3.6.1 Single-Trigger Mode

Single-trigger mode is the primary mode of operation of the dosimetry system and will acquire data at a rate of up to 1.6 MHz. This mode is selected via the Single Trigger tab in the RadPlot GUI. The user must first upload the firmware to the FPGA via the USB link by clicking the Upload Firmware button. Acquisition parameters such as delay time, acquisition time and hardware averaging factor are selected prior to acquisition. These parameters are written to the FPGA each time an acquisition is started.

If the internal trigger has been selected, the FPGA will internally generate a trigger which will start the acquisition as soon as the FPGA is ready. Selecting the external trigger will wait for the positive edge of a TTL pulse being detected on the CDAU trigger input which will commence the acquisition. The acquisition will terminate once the acquisition time has been reached as measured by the FPGA clock.
3.6. Modes of Operation

Figure 3.13: Schematic relation of the radiation beam, trigger pulse, motor motion and detector readout acquisition for the single-trigger mode.
3.6. Modes of Operation

Operator Commanded
Irradiate Scan
Open Safety
Shutter
Accelerate Motor
to Constant
Delivery Velocity
Open Fast Shutter
Close Safety
Shutter

MRT Control System

RadPlot
RadPlot
CloseFast Shutter
Initial Position Reached

Acquisition Time Not Reached
FinalPosition Reached

Start Acquisition
Clicked
Trigger Detected
Acquire Readings
Write to FPGA Buffer
Read FPGA Buffer
Update Memory
Stop Acquisition Clicked
by User
Write Acquisition to
Disk

Figure 3.14: Overview of the operation of single trigger mode and the interaction between the MRT control system and the X-tream data acquisition system.
3.6.2 Multi-Trigger Mode

Multi-trigger mode was developed to enable correlation of known discrete detector step sizes with measured response. The primary intended purpose for operating the system in this mode is for alignment of the detector to the radiation field. Selection of this mode is via a dedicated tab in the RadPlot GUI. Custom firmware for operating this system must then be uploaded to the FPGA via the USB link by clicking the *Upload Firmware* button. The system performs a communication test with the FPGA, and notifies the operator if there are any issues.

![Diagram](image)

**Figure 3.15:** Schematic relation of the radiation beam, trigger pulse, motor motion and detector readout acquisition for the multi-trigger mode.

The system is triggered to make an acquisition by a positive TTL pulse edge on the CDAU trigger input. Eight points are acquired by the system and transmitted via USB to RadPlot, where the average of the points is taken and plotted instantaneously. The system awaits the next TTL pulse and will repeat until the user terminates the acquisition by clicking the *Stop* button in the GUI.
3.6. Modes of Operation

Figure 3.16: Overview of the operation of multi-trigger mode and the interaction between the MRT control system and the X-tream data acquisition system.
Chapter 4

Energy Dependence Studies of Microstrip Detector

There exists a well-known over response of silicon as compared to water at low energies. This is caused by the increased photoelectric cross section for silicon relative to water, which results in an increased mass energy-absorption coefficient ratio for photon energies of less than 100 keV (see Figure 4.1). As the photon energy spectrum as employed for MRT at the ESRF has a most probable energy of 83 keV and a mean energy of 107 keV, [77] characterising the energy dependence of the microstrip detector is crucial over this energy range.

The author performed all Monte Carlo simulations presented in this chapter and subsequent analysis and discussion. Orthovoltage X-ray irradiations were performed by the author with assistance from Dr. Martin Carolan with operating the X-ray unit. Monochromatic synchrotron X-ray experiments were performed by the author with assistance from Dr. Marco Petasecca and Assoc. Prof. Michael Lerch in performing the detector irradiations. All experimental analysis and discussion presented in this chapter are the sole work of the author.
4.1 Characterisation with an Orthovoltage X-ray Unit

Whilst the use of linear accelerators is the predominant modality for external beam radiotherapy due to the beam’s high penetration and dose rate, orthovoltage X-ray units are still in use to treat superficial lesions. The lower photon energies are of a similar range to those employed in synchrotron MRT, and so provide a readily accessible way to characterise the energy dependence of the detector, by varying the X-ray tube potential, $kV_p$. 

![Graph showing ratio of mass-energy absorption coefficient ratio $\mu_e/\rho$ of silicon to water.](image)
Table 4.1: Filtration and focal source distance (FSD) for each X-ray beam of the Illawarra Cancer Care Centre Gulmay D3300 orthovoltage X-ray unit.

<table>
<thead>
<tr>
<th>Energy (kV)</th>
<th>Filtration</th>
<th>FSD (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>1.65 mm Al</td>
<td>30</td>
</tr>
<tr>
<td>75</td>
<td>2.40 mm Al</td>
<td>30</td>
</tr>
<tr>
<td>100</td>
<td>3.10 mm Al</td>
<td>30</td>
</tr>
<tr>
<td>125</td>
<td>0.1 mm Cu + 2.5 mm Al</td>
<td>30</td>
</tr>
<tr>
<td>150</td>
<td>0.35 mm Cu + 1.5 mm Al</td>
<td>30</td>
</tr>
<tr>
<td>200</td>
<td>0.9 mm Cu + 1.0 mm Al</td>
<td>50</td>
</tr>
<tr>
<td>250</td>
<td>0.3 mm Sn + 0.5 mm Cu + 1.5 mm Al</td>
<td>50</td>
</tr>
</tbody>
</table>

Table 4.2: HVL and effective energy for each X-ray beam of the Illawarra Cancer Care Centre Gulmay D3300 orthovoltage X-ray unit.

<table>
<thead>
<tr>
<th>Energy (kV)</th>
<th>HVL (mm Al)</th>
<th>Effective Energy (keV)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>1.40</td>
<td>23.0</td>
</tr>
<tr>
<td>75</td>
<td>2.48</td>
<td>30.9</td>
</tr>
<tr>
<td>100</td>
<td>3.72</td>
<td>36.4</td>
</tr>
<tr>
<td>125</td>
<td>6.40</td>
<td>47.7</td>
</tr>
<tr>
<td>150</td>
<td>0.29</td>
<td>65.5</td>
</tr>
<tr>
<td>200</td>
<td>1.35</td>
<td>90.0</td>
</tr>
<tr>
<td>250</td>
<td>2.24</td>
<td>115.3</td>
</tr>
</tbody>
</table>

### 4.1.1 Materials and Methods

The X-ray source used was a Gulmay D3300 orthovoltage X-ray unit located at the Illawarra Cancer Care Centre in Wollongong. This machine can operate at tube potentials of 50, 75, 100, 125, 150, 200 and 250 kV, with appropriate filtration materials at each energy. The filtration parameters for each X-ray beam, and focal source distance (FSD) are listed in Table 4.1. In addition to these filters, the beam passes through a 3 mm beryllium window. The corresponding beam qualities (half-value layer) and effective energy for each beam are tabulated in Table 4.2.

Complementary Monte Carlo simulations were produced using Geant4 version 9.3 and The X-ray spectrum for each energy (Figure 4.1.1) were calculated using

¹Effective energies were calculated by determining the photon energy attenuated by a factor of two at each nominal HVL. The data was determined for aluminium and copper using the NIST X-ray mass attenuation coefficients.[44]
Figure 4.2: Computed X-ray spectra as used in Geant4 Simulations at each orthovoltage X-ray unit potential.
4.1. Characterisation with an Orthovoltage X-ray Unit

SpekCalc[40][63], a software package for calculating the X-ray spectra produced from tungsten targets and attenuated by filters. Complementary Monte Carlo simulations were produced using Geant4 version 9.3, simulating a point source at the FSD for each beam. Since SpekCalc outputs photon flux at a distance of 1 m from the source, the inverse square law of $I = \frac{I_0}{r^2}$ was applied to determine the photon flux.

The X-ray source was modelled isotropically, using angular boundaries replicating the surface field produced by the PMMA applicator. The microstrip detector was modelled as being placed on the surface of a 10 mm thick piece of $30 \times 30$ cm$^2$ solid to replicate the solid water used for the experimental irradiation.

Due to the dose rate being much lower by an order of 1000, a high preamplifier gain was used to enhance the signal. Whilst this results in a greatly decreased temporal resolution, the much improved signal to noise ratio is of much greater importance since the only quantity of interest is the energy dependence of the integrated response signal.

4.1.2 Results

An over response of the detector at low energies is observed experimentally in Figure 4.4. The results of the Monte Carlo simulations represent the ratio of dose to the sensitive volume of the detector, embedded in water, to that of water in the same sensitive volume (Figure 4.3). The spectra were approximated by SpekCalc, taking into account only the target configuration and filtration. The effects of the monitor chamber and the collimation system on the beam were not modelled, with any electron contamination of the beam neglected. The isotropic (over the angle of acceptance of the applicator) modelling of the beam also did not take into account spectral changes over the beam profile. Whilst it may be possible to improve the modelling of the kilovoltage beams, it would not be of insignificant effort, yet would add little to this
4.1. Characterisation with an Orthovoltage X-ray Unit

Figure 4.3: Ratio of dose to the sensitive volume of the microstrip to the dose to water in the same volume at each simulated kilovoltage energy expressed in terms of effective energy.
4.1. Characterisation with an Orthovoltage X-ray Unit

Figure 4.4: Detector response as a function of effective energy at each orthovoltage beam quality, normalised to the response at 250 kV (115.3 keV effective energy).
4.2 Monochromatic Synchrotron X-rays

Due to the comparatively very weak interaction of X-ray photons with matter, producing a monochromatic X-ray beam from a continuous spectrum of radiation is a very inefficient process. The production of monochromatic X-rays is thus typically done at synchrotron facilities, primarily due to the very high flux able to be produced. At the ESRF ID17 Bio-medical Beamline, photon-activation radiation therapy is performed in addition to MRT. This treatment involves injecting a cis-platinum containing compound bound to a biological compound metabolised by the body. Photons are produced with a very narrow energy range corresponding to the K-edge photoelectric absorption energy, causing a high proportion of absorption to occur. Whilst not directly applicable to MRT, the monochromator is installed on the same beamline, so its use in energy dependence experiments was relatively straightforward.

4.2.1 Materials and Methods

In an optics hutch, upstream of beam aperture slits, the monochromator was used to produce monochromatic photons of the range 40 - 80 keV in 10 keV steps. Whilst a larger range would have been preferable, the monochromator was constructed for a specific role in imaging and photon activation therapy and so irradiations were restricted to this range.

The microstrip detector was placed in a face-on configuration at a depth of 0.5 cm, located centrally in a $10 \times 10 \times 10$ cm$^3$ PMMA phantom. The detector was irradiated at each energy and the detector was removed and replaced with a PTW Semiflex 31010 small field ionisation chamber calibrated to dose to water at the same position in order to provide reference data, and also irradiated at the same photon energies.
Hill et al. [43] investigated the depth dose response of many chambers including the Semiflex 31010 in various clinical kilovoltage beams. They found that the Semiflex 31010 appeared to exhibit a minimal energy dependence over the range of investigated beam qualities (50 to 280 kVp).

Geant4 simulations were produced to replicate irradiation conditions to determine raw energy deposition in the absence of any charge-collection effects. The detector was constructed virtually and placed in a PMMA phantom with the same dimensions of that used experimentally. $10^9$ photons were fired centrally upon the detector in a homogeneous rectangular beam of dimensions $100 \, \mu m \times 820 \, \mu m$. Due to the flexibility of Monte Carlo simulation in particular, no restriction on monochromatic energy, a much broader energy range of 20 - 150 keV in 10 keV steps was simulated. To provide dose-to-water measurements, complementary simulations were performed with the detector was entirely replaced with water, and dose deposition recorded in the same geometric boundaries as the sensitive volume of the detector.

### 4.2.2 Results

Note that the results in Figure 4.5 and 4.6 are not directly comparable due to relative differences in the photon fluence. For the Monte Carlo simulation, an exact number ($10^9$ histories) of primary photons are simulated for each data point. Whilst for the experimental results, the fluence at each energy is dependent on the configuration of the insertion device, filtration through the beam line, and on energy-dependent monochromator efficiency. The ratio of the dose to silicon in the sensitive volume to dose to water of the Monte Carlo simulation is however comparable in quantity to the experimentally obtained results (i.e. detector response to ionisation chamber response, assuming minimal energy dependence of the ionisation chamber).

The experimental results in Figure 4.7 show a significant over response of the mi-
4.2. Monochromatic Synchrotron X-rays

Figure 4.5: Simulated dose to the sensitive volume of the microstrip detector and water in the same geometric boundary and absence of the detector.

Figure 4.6: Experimentally measured response of ion chamber and microstrip detector to monochromatic photons, normalised to response at 80 keV photon energy.
4.2. Monochromatic Synchrotron X-rays

Figure 4.7: Comparison of simulated energy dependence ratio of microstrip detector to water (black) and experimental response ratio of microstrip detector to ion chamber ratio (red) to monochromatic X-rays normalised to 80 keV photon energy.

crostrip detector to decreasing photon energy when compared directly to the ionisation chamber results. These results agree with Monte Carlo simulations normalised to the response at 80 keV. A greater energy range would have been ideal to characterise the response of the detector experimentally over the range of photon energies encountered in MRT, however this was limited by the range of the monochromator.

4.2.2.1 Application of Bragg-Gray Cavity Theory

If a small sub-volume within an irradiated medium is so small, that its presence does not perturb an incident charged particle field, this may be referred to as the Bragg-Gray relation [7]

\[
\frac{D_w}{D_s} = \frac{m \bar{S}_w}{m \bar{S}_s} = \bar{S}_w
\]  

(4.1)
which may be rearranged for $D_w$, the dose to water:

$$D_w = D_s \bar{S}_w^w$$  \hspace{1cm} (4.2)

If the ratio the mean stopping powers, $\bar{S}_w^w$ is known, it is possible to find the dose to water, $D_w$ by multiplication of the readout dose by this factor.

The mass stopping power, well characterised for single electron energies, becomes rather problematic when considering a polychromatic beam such as that employed in MRT. The parameter is dependent on the secondary charged particle spectrum, which may vary in an irradiated medium as the primary photon spectrum hardens with depth.

### 4.2.2.2 Burlin Cavity Theory

Since Bragg-Gray Cavity theory is inadequate to explain the Monte Carlo and experimental results, another theory explaining the mode of dose deposition within the sensitive volume should be employed. Burlin cavity theory was developed to provide an explanation for the intermediate region between small cavities of Bragg-Gray and of large volumes. [18] The Burlin cavity equation may be written as:

$$\frac{D_{\text{vol}}}{D_{\text{med}}} = d \bar{S}_{\text{vol}} S_{\text{med}} + (1 - d) \left( \frac{\bar{\mu}}{\rho} \right)_{\text{med}}$$  \hspace{1cm} (4.3)

The value of $d$ determines which regime the cavity size is most similar to, with values approaching unity for small cavities and zero for large cavities.

The results for the microstrip detector exhibit a trend following the photon mass-energy absorption coefficient. Burlin $d$ values approach 1, thus the detector may be viewed as a ‘large detector’, and does not exhibit Bragg-Gray Cavity behaviour. Due to this, scaling based on material electron stopping power ratios cannot be used, and
instead photon interaction quantities used to determine dose equivalence. This infers that the deposition of energy is not largely contributed by *crossers*, but rather by *starters* and *stoppers*.

### 4.3 Energy Dependence of Hypothetical Detectors

The silicon microstrip detector exhibits strong low energy over response both experimentally and in Monte Carlo simulation (see Sections 4.1 and 4.2). To investigate strategies to reduce this energy dependence, the ability of Monte Carlo simulation to explore the response of hypothetical detector designs not yet in existence is exploited in this section.

#### 4.3.1 Reduction of Epitaxial Layer

The effect that the epitaxial layer thickness of the microstrip detector has on energy dependence is investigated through Monte Carlo simulation by shrinking the epitaxial layer thickness from 50 µm to 6 µm. The Monte Carlo simulations of Section 4.2 are repeated identically, but with the reduced epitaxial layer thickness. Complementary simulations are also performed with the detector replaced entirely with water and with the correspondingly reduced sensitive volume in order to normalise to dose to water.

A reduction in the low energy dependence of the detector design is observed in Figure 4.8 for low energy monochromatic photon beams, however significant over response still occurs.

#### 4.3.2 Use of Mesa Epitaxial Structures

The hypothesis that the reduction in the epitaxial layer can reduce the energy dependence of the detector was further investigated through the use of a mesa epitaxial
Figure 4.8: Water equivalence dose ratio versus monochromatic photon energy for a simulation of the microstrip detector with a 6 \( \mu \text{m} \) and 50 \( \mu \text{m} \) thick epitaxial layer.
4.3. Energy Dependence of Hypothetical Detectors

Table 4.3: Comparison of dosimeter and phantom material properties.

<table>
<thead>
<tr>
<th>Material</th>
<th>Physical Density (g·cm(^{-3}))</th>
<th>Atomic Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>1.00 [13]</td>
<td>7.42 (Effective)(^1)</td>
</tr>
<tr>
<td>PMMA</td>
<td>1.19 [13]</td>
<td>5.17 (Effective)(^1)</td>
</tr>
<tr>
<td>Silicon</td>
<td>2.33 [13]</td>
<td>14</td>
</tr>
</tbody>
</table>

structure. That is, the sensitive epitaxial layer consists only of the sensitive volume, with all surrounding structures, including the guard ring absent. Two very similar detector geometries were produced, one in which the mesa layer, consisting of a 500 µm \(\times\) 10 µm strip of thickness 6 µm surrounded by air, and another by water. The Monte Carlo simulations of Section 4.2 were repeated with these new detector geometries. These simulations are a gross simplification in that full charge collection efficiency is assumed within the mesa layer, neglecting effects of the abrupt edge on electric field distributions.

The results in Figure 4.9 show excellent water equivalence with the mesa structure surrounded by water, but a significant low energy over-response with the mesa structure surrounded by air.

4.3.3 Use of Alternative Materials

The strategy employed in Section 4.3.1 to optimise the detector geometrically to reduce the energy dependence does have an effect on the low energy over response, however the result is still far from ideal. To further improve the energy dependence, the use of more tissue equivalent materials are investigated. One proposal is the use of chemical vapour deposition (CVD) diamond as either the substrate material or as the entire detector. Whilst CVD diamond has a greater density than water (3.515 g·cm\(^{-3}\)) due to its tightly packed lattice structure, the atomic number is much closer to water and PMMA than silicon as tabulated below.
4.3. Energy Dependence of Hypothetical Detectors

Figure 4.9: Water equivalence dose ratio versus monochromatic photon energy for a simulation of the microstrip detector constructed with a 6 \( \mu \text{m} \) thick mesa layer encircled by water or air.
4.3. Energy Dependence of Hypothetical Detectors

![Graph showing energy dependence of hypothetical detectors](image)

Figure 4.10: Water equivalence dose ratio versus monochromatic photon energy for a simulation of the a hypothetical microstrip detector constructed with either a 1.5 \( \mu m \) or a 6 \( \mu m \) thick CVD epitaxial layer mounted on a 500 \( \mu m \) thick CVD substrate.

The energy dependence of two hypothetical diamond detectors is investigated through Monte Carlo simulation. One design has a 6 \( \mu m \) thick sensitive volume layer constructed out of CVD diamond, on a 500 \( \mu m \) thick CVD diamond substrate. The second design differs only with a 1.5 \( \mu m \) thick sensitive volume. The energy dependence simulation is performed with each detector and an entirely water surrogate to determine water dose equivalency to the same sensitive volume.

The results in Figure 4.10 show that both designs exhibit significantly better energy dependence over the range of monochromatic photon energies when compared to the silicon microstrip detector.
4.4 In-Phantom Spectral Changes

It has been shown that the detector exhibits a strong energy dependence at low energies (see Sections 4.1.2 and 4.2.2) which is of importance within a phantom where the spectrum changes with position. Due to the flux of a synchrotron photon beam and the required event collection rate, conventional spectroscopic measurements are rendered useless, leaving only methods such as powder diffraction as viable experimental methods to observe spectrum. Since such methods are unable to measure in-phantom measurements and are inherently overly complex, Geant4 simulations are employed to determine the spectrum.

4.4.1 Materials and Methods

A pencil beam is modelled entering a $10 \times 10 \times 10$ mm$^3$ PMMA phantom. Photons entering a $1 \times 1 \times 1$ mm$^3$ sub-volume placed at various depths are binned by energy, producing a spectrum at each sub-volume location. This is performed for various depths along the depth of the beam.

4.4.2 Results and Discussion

The photon spectrum softens with distance off-axis; this is due to degradation of mean photon energy, the probability of a photon being Compton scattered several times increases with distance from central axis. This has implications for dosimetry with the microstrip detector as the ratio of dose deposition in silicon to water increases significantly below photon energies of 100 keV. The count of photons out-of-field in the 20-35 keV energy range does not diminish with distance from the central axis up to the relatively large distance of 20 mm. It is in this photon energy range that the over-response of silicon is greatest due to the much increased photoelectric absorption
4.4. In-Phantom Spectral Changes

Figure 4.11: Variation in photon spectrum from centre of field to 1 mm out-of-field.

Figure 4.12: Photon spectrum as a function of depth along MRT beam axis in PMMA. Note: counts per primary particle refer to spectral counts divided by the total number of simulated primary photons.
4.4. In-Phantom Spectral Changes

Figure 4.13: Changes in photon spectrum with distance from central axis. Note the shift to softer photon energies with increasing distance from central axis, including a shift to a lower most-probable energy.
4.4. In-Phantom Spectral Changes

Figure 4.14: Changes in photon spectrum with distance from central axis, scaled to enhance the low energy range.
cross section.

These results show that it is clear that a more phantom-equivalent dosimeter is needed as a low energy photon wash is present distal to the central axis of an incident MRT beam. The simulated results of Section 4.3.3 show excellent energy dependence over the range of photon spectral components encountered in this in-phantom spectral study, suggesting CVD diamond as an ideal dosimeter material for MRT dosimetry.
Chapter 5

Charge-Collection Characterisation of the Microstrip Detector

5.1 Introduction

This chapter investigates the use of charge-collection techniques to characterise the response of the microstrip to incident radiation. Firstly, the spectroscopic response of the detector with and without the guard ring electrically connected is investigated through the use of alpha-particle spectroscopy.

A far more advanced technique is also used in the form of ion-beam-induced charge-collection spectroscopy, enabling spatially-resolved charge-collection to be investigated. This technique involves the use of an accelerated ion beam of a precise energy which is magnetically raster-scanned across the detector, and the spectroscopic response of an event is coupled to the position of the ion beam at the time of interaction.

Finally, the ESRF ID17 MRT beamline is used to perform a spatially-registered response of the detector to narrowly collimated X-rays with the therapeutic spectrum used for MRT preclinical studies.
The author performed all alpha-particle spectroscopy measurements independently. Ion-beam-induced charge-collection (IBICC) studies were performed with the assistance from Anthony Espinoza in preparing the samples, while expertise in operating the ANTARES accelerator was provided by Dr. Dale Prokopovic and Dr. Reiner Siegele. X-ray-beam-induced charge-collection experiments were performed by the author with assistance from Dr. Marco Petasecca and Assoc. Prof. Michael Lerch in irradiating the detector samples. All analysis and discussion presented in this chapter is solely the work of the author.

5.2 Alpha-Particle Spectroscopy

5.2.1 Introduction

Alpha-particle spectroscopy involves the use of an alpha-emitting radioactive source to characterise the spectroscopic response of a detector. Due to the short range of alpha particles owing to their intrinsically high linear energy transfer, full energy deposition occurs over a range of tens-of-microns. This property makes them ideal to characterise silicon detectors of planar construction, as depletion regions exist close to the surface. For $^{241}$Am, the range is approximately $28 \ \mu$m, resulting in complete energy deposition in the 50-$\mu$m-thick epitaxial layer. The short range of alpha particles also results in significant degradation of energy as the particles traverse air, generally alpha-particle spectroscopy is performed in-vacuum to overcome this effect.

5.2.2 Materials and Methods

To observe the effect of the variation in the change of the depletion region of the central strip, alpha spectroscopy was performed on the microstrip detector in a vacuum chamber. An $^{241}$Am spectroscopic source was placed directly above the detector.
The central strip and guard ring were each connected to Amptek A250 preamplifiers mounted on Amptek PC250 test boards (see Figure 5.1), whilst only the central strip was to be spectroscopically analysed, this step was performed to ensure they both shared the same virtual ground. Air was evacuated from the chamber to high vacuum levels through the use of a dual-stage piston/turbo-molecular pump to reduce the atmospheric energy degradation of the alpha particles to negligible levels.

### 5.2.3 Results

An energy spectrum (Figure 5.2) was obtained with the guard ring floating and again with the guard ring grounded. An energy calibration was not performed as the microstrip detector is not a spectroscopic detector.
Figure 5.2: $^{241}$Am spectral response of the microstrip detector with the guard ring both floating and grounded.
5.3. Ion-Beam-Induced Charge-Collection

A significant reduction of the total collected energy occurs with the guard ring grounded. Physically this manifests as confinement of the depletion region of the central strip due to the potential applied across the guard ring. The effect of the guard ring when biased results in a separate concentric depletion region concentric to the central strip depletion region. Charge collection due to the guard ring structure encroaches into the un-guarded depletion region of the central strip, resulting in a reduction of the central strip collection volume.

The spectral shape also changes significantly, demonstrating that the alpha particles are for the most part attenuated in energy prior to depositing energy in the sensitive volume of the detector. This manifests in the alpha particles, with the guard ring grounded, now being restricted to traversing the aluminium overlaying the central microstrip prior to depositing charge in the central strip depletion region. With the guard ring floating, they are able to deposit energy in the gap between the aluminium overlaying the central microstrip and guard ring region, crossing only the passivation region (see Figure 3.1). This too is true for the region surrounding the bonding pads, as confirmed in Section 5.3.

5.3 Ion-Beam-Induced Charge-Collection

5.3.1 Introduction

Ion-beam-induced charge-collection (IBICC) studies are a method of spatially resolved ion beam spectroscopy. An ion beam is raster scanned over a device sensitive to radiation, and the electrical response is correlated to position of the beam at the time. From this, the electrical response of a radiation detector to induced charge at a given location near the surface can be deduced from the results. [21]
5.3.2 The ANSTO Heavy Ion Microprobe

The heavy ion microprobe is situated on a beamline at the ANTARES dual-stage van de Graaff accelerator at ANSTO in Sydney, Australia. It is capable of using particles ranging from light ions such as protons and helium ions, to heavy ions such as bromine and iodine with reasonable intensity.

Ions are accelerated to keV energies and electrostatic steering plates are used to focus and steer the beam to the low energy flange of the van de Graaff accelerator. The accelerator of the ion beam to MeV energies occurs in two stages: negative ions are attracted to the positively charged terminal and passed through a stripping gad, removing electrons; the now positively charged ion beam is repelled from the like-charged terminal. The energy of the beam exiting the high-energy flange of the accelerator is dependent on the charge of the ion produced by the source and the electron stripping at the accelerator centre. The current on a 30° analysing magnet is precisely set to select the energy and ion species of the desired beam, and deflect it to the microprobe beamline, with unwanted energies and ions excluded.

A set of pre-slits and a set of adjustable four-jaw apertures are used to limit the beam current, the roughly collimated beam is finely shaped by the object slits, a set of highly-polished stainless steel cylinders. A Faraday cup and beam viewer are located immediately after the object slits to optimise and align the beam as it exits the slits. A beam profile monitor, a Faraday cup and another beam viewer enable further fine-tuning of the beam.

An Oxford Microbeams magnetic quadrupole triplet raster scans the ion beam under the control of computer software. The final stage of the microprobe, the target chamber is an octagonal stainless steel vacuum chamber, 165 mm in internal diameter. 2 ports are located on each face, facilitating the attachment of electrical feed-throughs, gauges and detectors. A CCD camera enables the alignment of the target in order to
For all IBICC studies, the target is a device which responds electrically to an impinging beam of ions, producing a pulse which is amplified in the first stage by an Amptek A250 charge sensitive pre-amplifier, further amplified and shaped by a AMF research amplifier, before being fed into a ADC for pulse-height digitisation. The position of the beam is made possible by reading the current on the magnets at the moment of the event. This enables coregistration of the energy deposition event with the spatial location of the beam which resulted in its occurrence. If an electronic noise event occurs, it will be binned accordingly with the beam position at its occurrence, this necessitates setting the lower-level discriminator on the ADC to a sufficiently high enough value to exclude this noise, whilst not discriminating true events.

The results from the study are recorded in a list-mode file format, this produces large files, but results in no loss of information acquired during the study. The file contains a sequentially numbered event ID, the $x$ and $y$ coordinates of the beam, and the uncalibrated energy of the event.

### 5.3.3 Data Analysis

In order to assess the results, the list-mode output from the microprobe data acquisition system has to be converted into a more useful format. Whilst converting data
5.3. Ion-Beam-Induced Charge-Collection

into mean energy maps results in acceptable images, the production of median energy maps is more resilient to electronic noise recorded during acquisition.

To do this, data is first converted into an ASCII text file which has the form:

Event Number  Ch.1 Energy  Ch.2 Energy  x-Position  y-Position

which is then imported into MATLAB as an array. Custom scripts were written which process this data into median energy maps and perform necessary calibrations.

To calibrate results for energy, a Hamamatsu PIN photodiode was biased to full depletion and the ion beam is scanned across its surface. Full charge collection is assumed and a precision pulse generator was calibrated to this energy. An acquisition of various pulser energies were obtained and used prior to analysis to determine an energy calibration factor.

Spatial calibrations are produced by means of a copper square grid of pitch 25 µm mounted on the same test strip as the detector sample. A PIN photodiode placed downstream of the copper grid performs transmission measurements whilst the ion beam is scanned and the output is recorded by the data acquisition system. The production of median energy maps from this data produces an image by which the horizontal and vertical dimensions are known, enabling a calibration factor to be determined for the scan size used. User-specified changes to the scan size scale linearly with setting, permitting the application of the calibration factor to all obtained data from the experimental set-up.

5.3.4 Materials and Methods

The microstrip detector was mounted on a machined aluminium plate, purpose built for the mounting of samples in the heavy ion microprobe vacuum chamber along with a copper grid and Hamamatsu PIN photodiode for the spatial calibration. An Amptek A250 charge sensitive preamplifier mounted on a PC250 test board was connected to
5.3. Ion-Beam-Induced Charge-Collection

![Image](a)

![Image](b)

Figure 5.4: Ionisation distribution in silicon calculated by TRIM-2013\[86\] for 5.5 MeV $^4$He ions as a function of lateral position and depth, and as a function of depth.

the PIN diode in a DC-coupled mode. 5.5 MeV $^4$He(2-) ions were utilised for the IBICC characterisation. The scaling of the scan field was set to a region sufficient to for the investigation by setting the gain on the scanning magnet amplifiers.

5.3.4.1 Spatial Calibration

To spatially calibrate the results, an acquisition of charge collection distribution was obtained with the PIN diode whilst shadowed by the copper grid (see Figure 5.5).

A calibration factor was determined by comparing pixel distances to known dimensions. As the grid was slightly rotated, pixel distances were taken as the diagonals parallel to the grid axes.

5.3.4.2 Energy Calibration

To convert from the microprobe energy channel number, a calibrated spectroscopic pulser was used. This pulser was first calibrated in a vacuum chamber using a PIN photodiode coupled to the same preamplifier and amplifier used for the IBICC acqui-
Figure 5.5: IBICC spatial calibration image of the copper grid shadowing the PIN photodiode.

sitions. An $^{241}$Am spectroscopic source was used to acquire a spectrum, with a linear fit of known peak energies to MCA channel number. The equation of this line gives the calibration factor for the spectroscopic electronics, which was then used to calibrate the energy axis of the MCA acquisition software. The spectroscopic pulser was used to inject pulses of variable amplitude, with the calibration dial varied to obtain a direction correlation between the pulse height dial setting and energy.

As the MCA utilised for IBICC is integrated into the microprobe electronics rack, it must be calibrated separately to the MCA used for the pulser calibration. An IBICC scan was started, however a Faraday cup was inserted into the beam to act as a beam block. Whilst the microprobe will acquire a spatially resolved image of where the beam would have been during pulser charge injection, only the spectrum of the charge collection is of interest to calibration. The channel analyser number corresponding to each pulser peak is determined and correlated with the pulser energy calibration. A linear equation of a line is fit to these points, resulting in the energy calibration factor
for all subsequent energy factors.

5.3.5 Results

With the guard ring floating (Figure 5.6), charge collection by the central strip is confined to the region just distal to the guard ring. This is due to the presence of the p-spray region, which encircles the guard ring, ensuring the depletion region is still confined even in the absence of an active guard ring. Whilst the effect of the floating guard ring results in broadening of the charge collection region surrounding the central strip, significant charge collection occurs near the pads.

By grounding the guard ring (Figure 5.7), the electrical configuration of the experiment results in equipotential of both the central strip and guard ring with respect to the substrate. The action of the guard ring around the central detector is to greatly confine charge collection to the central detector by compressing its electric field distribution. Charge deposited in the vicinity of the guard ring is collected by it and converted into current through the bias circuitry. The most significant difference with the active guard ring in the IBICC results is the confinement of charge collection in the pad region to only the central strip pad and the immediate vicinity. The encirclement of the guard ring about this pad ensures that charge deposited outside the central strip pad, but within the region encircled by the p-spray is not collected by the central strip, but converted into current in the guard ring bias circuitry.

The apparent charge collection in the pad region of the device is an interesting result, and one not observed experimentally in MRT irradiations. Of particular note is that a virgin detector was used for this IBICC study, but such detectors cannot be used for MRT. Significant over-response is observed with a virgin detector in an MRT beam until sufficient pre-irradiation has occurred (see Section 6.1).

It is theorised that at the interface of the pad with the epitaxial layer, a charge
Figure 5.6: 5.5 MeV $^4$He IBICC images of the microstrip detector with the guard ring floating, with the central strip biased at (a) 10 V, (b) 20 V, (c) 30 V and (d) 40 V.
Figure 5.7: 5.5 MeV $^4$He IBICC image of the microstrip detector with the guard ring grounded, with both guard ring and central strip biased at 50V.
collection layer exists. This charge collection channel closes once the production of a space charge layer in this location inhibits the mechanism.

The combination of the metallic pad, oxide layer and silicon acts as a MOS capacitor. When bias is applied to the detector, the pad has a negative potential with respect to the p+ region. This results in an electric field "bubble" in the silicon below and surrounding the pad. This results in an extension of the charge sensitive volume from the central detector towards and around the pad. With exposure to radiation, point defects are produced in this region and indeed throughout the detector primarily in the form of lattice defects, acting as recombination centres for radiation-induced charge. The net effect is a reduction in the carrier lifetime, $\tau$, resulting in decreased sensitivity of the detector at a given applied bias due to the increased recombination.

5.4 Synchrotron X-ray-Beam-Induced Charge-Collection

5.4.1 Introduction

Characterising a detector such as the microstrip detector using an ion beam reveals information about charge collection properties, but due to the superficial range of the ions employed, only at the surface being irradiated. To the MRT X-ray field however, the detector is relatively insensitive to photons, and so ionisation will occur throughout the detector. Thus to provide more relevant charge collection information, a small X-ray field is needed. While there exists at several synchrotron facilities, the ability to produce X-ray beams of the order of a micron in diameter, this is of a far lower energy than employed in MRT. For equivalence purposes, the MRT X-ray beam is collimated down to the smallest reliable beam size.
5.4.2 Materials and Methods

This experiment was performed using the MRT X-ray beam at the ID17 Bio-medical Beamline at the ESRF, Grenoble, France. The beam was firstly collimated with the fixed vertical slits to the smallest vertical height of 50 \(\mu\text{m}\). In the horizontal direction, however the beam can be collimated down to a size of 5 \(\mu\text{m}\), using the upstream moveable tungsten slits. The detector was mounted in a face-on orientation, with the smallest dimension of the sensitive volume aligned with the smallest dimension of the beam. Irradiations are performed with the detector at various vertical positions and scanned in the horizontal dimension.

Horizontal position of the detector relative to the beam can be determined by correlating the known sample number, with acquisition frequency and horizontal scanning motor speed. Vertical position is obtained by the discrete stepping of the scanning apparatus.

The time-delay between the trigger signal from the control computer, and the subsequent scanning of the goniometer motor and opening of the beam shutter is somewhat variable. This necessitates calibration of position relative to the peak of the acquired data, a process whose validity is confirmed by IBICC measurements as in Section 5.3.4 to within the spatial resolution of that technique. Measured data are then corrected by a relevant offset factor such that the centroid as determined by the FWHM is the centre of each acquisition.

Results are then calibrated using motor speed to give spatial position and recorded storage ring current to normalise results such that they are in units of instantaneous current per mA of storage ring current. Resampling of results is performed in the horizontal direction to increase the signal to noise ratio at the expense of spatial resolution. This is achievable with minimal impact to results since points in this axis are acquired at a rate of 1 MHz.
Finally, the corrected 1-dimensional charge collection scans are composed into a 2-dimensional XBICC map as a function of position. Due to the dimensions of the beam being much smaller in the horizontal direction compared to that of the vertical (5 μm versus 50 μm respectively) and due to continuous scanning (with a 1 MHz sampling rate) in the direction compared to discrete steps, the reconstructed X-ray charge collection map has much better spatial resolution in the horizontal direction.

5.4.3 Results

The reconstructed XBICC charge collection maps (Figure 5.8) show a high degree of conformity about the central strip region. Negligible charge collection exists for regions outside this area, with the primary contributory source due to scatter into the sensitive volume, not extra cameral signal. Note that the jagged appearance of the XBICC images is due to the variable latency between the trigger pulse and the opening of the fast shutter.

Slight broadening of the charge collection profile about the electrical contact is observed, which is consistent with the IBICC results in Section 5.3.5. For the XBICC results however, the effect appears much less pronounced, this is consistent with the theory that the effect is due to MOS capacitance (see Section 5.3.5), which decreases with increasing radiation damage and a decrease in the charge carrier lifetime.

The application of a greater bias from -10V to -40V results in tighter confinement of the sensitive volume. This is due to the greater electric field density ensuring the guard ring is more effective at removing charge deposited in the vicinity of the central microstrip. The greater electric field density also leads to greater charge collection efficiency in the centre of the microstrip.

The resolution of this technique is lower than that of IBICC owing due to the weakly interacting nature of photons and their ability to readily scatter. However,
5.4. Synchrotron X-ray-Beam-Induced Charge-Collection

Figure 5.8: Synchrotron X-ray beam induced charge collection map of the microstrip detector with both central strip and guard ring biased at (a.) -10V and (b.) -40V.
energy deposition will be to a first approximation, constant over the depth of the entire microstrip detector, compared to total energy deposition over tens-of-microns for light ions used for IBICC techniques.
Chapter 6

Microstrip Detector
Characterisation in a Synchrotron X-ray Therapy Field

This chapter details the characterisation of the microstrip detector in a synchrotron X-ray therapy field, as per the intended use of the X-tream system. The author performed all experiments detailed in this chapter with assistance from Dr. Marco Petasecca and Assoc. Prof. Michael Lerch in irradiating the detector samples. Monte Carlo simulations presented in this chapter were performed in entirely by the author. All analysis and discussion are the sole work of the author.

6.1 Pre-Irradiation Response

The sensitivity of semiconductor detectors changes over time with exposure to radiation. This dynamic behaviour is a result of radiation induced damage which can be classified into two categories of bulk and surface effects. Surface effects result in an
6.1. Pre-Irradiation Response

increase in leakage current and a loss of detector energy resolution. For detectors such as the silicon microstrip detector with oxide passivation layers, the surface effects are related to the ionisation created within the oxide and its trapping at interfaces. [49]

Bulk effects arise from the displacement of an atom of semiconductor material from its lattice site. The defects become recombination centres for the minority charge carriers, resulting in a reduction of the minority carrier lifetime and the sensitivity of the detector. X-rays and electrons in the energy range encountered in MRT cause only point defects, localised sites of defects, contrasting the cluster defects created by heavy charged particles. A steep reduction of detector response occurs initially, however the rate substantially stabilises at a point after the induction of sufficient defects. [49]

For commercial radiotherapy diodes, and indeed the microstrip detector, it is necessary to pre-irradiate the detector before it can be used for dosimetric purposes. A detector which had not been exposed to any ionising radiation except natural background radiation was used for this purpose. The detector was placed at the surface of a PMMA phantom and measurements were performed with the X-tream data acquisition system for fourteen successive irradiations of 780 Gy prescribed to the surface of water. The peak measured current was determined for each measurement with background current subtraction performed. The resulting pre-irradiation response curve is shown in Figure 6.1.

Measurement system saturation occurred for the first three measurements, however from the fourth and subsequent irradiations (a cumulative prescribed dose of 3.12 kGy and greater) peak currents were below measurement system saturation. Increasing cumulative dose resulted in a steep but declining gradient as further recombination centres were generated, and minority charge carrier lifetime stabilised.

As the results were analysed retrospectively, additional data on pre-irradiation response is not available, however the trend of decreasing variability in response with
Figure 6.1: Integral response of virgin detector as a function of prescribed dose. Note that the current saturation level was reached on the first three measurements, with the current measurement system saturation threshold indicated.
cumulative dose is expected to continue. An absorbed dose of 20 kGy as delivered to commercial p-type diodes prior to customer delivery is expected to be sufficient to reduce pre-irradiation over-sensitivity to negligible levels.

6.2 Response versus Applied Bias

To investigate the response of the microstrip detector to increased bias voltage in a synchrotron beam, a homogenous field of dimensions 800 µm wide by 500 µm high was used. The detector was irradiated in irradiate mode, where the fast beam shutter system delivers a precisely timed burst of radiation to a static object.

Three seconds of radiation was delivered with the detector in face on orientation, at zero applied bias to both central strip and guard ring, with the integral detector response determined and normalised against storage ring current. The detector response as a function of bias was determined by performing further measurements at various applied bias voltages, with the resulting response shown in Figure 6.2.

At an initial applied bias of 0 V, the effect of increasing bias initially results in a drop in response. This is due to the ineffectiveness of the guard ring structure with no applied bias, which results in an increased charge collection volume relative to when bias is applied. With an increase in the magnitude of the applied bias, the response per beam current then increases due to an increase in charge collection efficiency within the central strip of the microstrip detector.

6.3 Effect of Guard Ring

The central strip of the detector is surrounded by a guard ring structure to confine charge collection to a small, well defined sensitive volume. The effect of the guard ring on detector response was investigated by placing the microstrip detector in a face-
6.3. Effect of Guard Ring

Figure 6.2: Microstrip detector response versus applied bias in expose mode in the face-on orientation.

on orientation, grounding the guard ring and performing irradiations with several prescribed doses in expose mode. Measurements were performed at prescribed doses of 60, 100, 600 and 780 Gy, resulting in nominal scanned field heights of 60, 100, 600 and 800 µm respectively. The measurements were then repeated with the guard ring floating, by electrically disconnecting it at the preamplifier box.

The peak current of the detector during each irradiation was determined by finding the dark current-corrected peak current after smoothing to reduce the impact of noise (Figure 6.3). Additionally, the integral response was determined by integrating the dark current-corrected measured current over the duration of the irradiation (Figure 6.4).

Grounding of the guard ring causes confinement of charge collection to a small region surrounding the central strip. This confinement results in a large decrease in the sensitivity of the microstrip detector as observed for numerous beam configurations.
6.3. Effect of Guard Ring

Figure 6.3: Microstrip detector peak current as a function of nominal beam height with the guard ring in the grounded and floating configuration.

Figure 6.4: Integrated microstrip detector response per prescribed dose as a function of nominal beam height with the guard ring in the grounded and floating configuration.
6.4 Dose Linearity

Due to the very high beam intensity of MRT radiation fields, this sensitivity reduction does not present an issue in terms of the signal to noise ratio.

6.4 Dose Linearity

One of the many ideal characteristics of any radiation dosimeter is a linear response to radiation dose deposition. To determine the detector linearity, the microstrip detector was placed at the surface of a PMMA phantom. A range of prescribed dose quantities were delivered using the GUI-based control system at the ESRF ID17 biomedical beamline.

The delivery of a prescribed dose is produced by the controlled timing of the fast-shutter system and the vertical stage of the goniometer. The combination of these two systems produce a precisely timed burst of radiation, with a linear translation through the radiation field. The irradiated object is accelerated to the velocity required to deliver the dose rate in a way that this velocity is achieved prior to exposure to the beam. A constant velocity during beam-on results in a constant dose rate delivered per unit area in the primary beam for a sufficiently large homogeneous object. The dosimetric accuracy of the system has been well characterised by the staff at the ESRF.

The response of the microstrip detector was measured by the X-tream data acquisition system, with the total response determined by integrating the detector response curve with dark current accounted by subtracting the signal level with the beam off.

Dose linearity over the range of prescribed doses was observed as shown in Figure 6.5, when compared to a linear line of best fit, which has a coefficient of determination of 0.99982. The X-tream system has an excellent linearity response to delivered dose, an important characteristic for MRT.
6.5 Depth Dose Response

Measurements of the depth dose response were made in irradiate mode with a 100 µm high homogeneous beam, with the microstrip detector at depths of 5 to 60 mm in a watertank. The horizontal width of the beam was set with the horizontal collimators, and the vertical height achieved through vertical scanning of the water tank. Figure 6.6 shows the results of the response per ring current over a range of depths, field sizes and vertical scanning speeds.
6.5. Depth Dose Response

The air-filled ionisation chamber is the gold standard in ionising radiation dosimetry, making it the ideal comparison dosimeter. A series of measurements were performed with the Semiflex 31010 (PTW, Germany) cylindrical ionisation chamber to compare to the relative response of the microstrip detector and X-tream readout system. This chamber contains an 0.125 cm$^3$ sensitive volume, and has a nominal useful energy range for 30 kV to 50 MV photons. Whilst the manufacturer recommends the use of the chamber in fields larger than 30×30 mm for megavoltage fields, the short range of the secondary electrons produced by the MRT photon spectrum validate its use for this purpose.

The ionisation chamber was placed at effective depths in water of 5, 15, 20, 40 and 60 mm. As for 6.5, a 100 μm high homogeneous beam was delivered to the detector,

Figure 6.6: Depth dose behaviour of the microstrip detector in various open-field MRT beams in a face-on orientation.

6.5.1 Comparison with Ionisation Chamber

The air-filled ionisation chamber is the gold standard in ionising radiation dosimetry, making it the ideal comparison dosimeter. A series of measurements were performed with the Semiflex 31010 (PTW, Germany) cylindrical ionisation chamber to compare to the relative response of the microstrip detector and X-tream readout system. This chamber contains an 0.125 cm$^3$ sensitive volume, and has a nominal useful energy range for 30 kV to 50 MV photons. Whilst the manufacturer recommends the use of the chamber in fields larger than 30×30 mm for megavoltage fields, the short range of the secondary electrons produced by the MRT photon spectrum validate its use for this purpose.

The ionisation chamber was placed at effective depths in water of 5, 15, 20, 40 and 60 mm. As for 6.5, a 100 μm high homogeneous beam was delivered to the detector,
6.5. Depth Dose Response

Figure 6.7: Depth dose response in a 20×20 mm MRT field of the microstrip detector compared to the PTW Semiflex 31010. Both are normalised to the response at 20 mm depth.

but with field sizes of 10×10, 15×15 and 20×20 mm delivered in irradiate mode with a vertical motor speed of 100 mm·s$^{-1}$. For all measurements, the reading was corrected for storage ring current.

The results were normalised to the response at 20 mm depth, and compared to the microstrip detector response under the same beam delivery conditions as presented in Figures 6.7, 6.8 and 6.9.

Relative to the ionisation chamber, the microstrip detector shows over-response at shallow depths, with the trend agreeing better at depth. This behaviour can be attributed to the hardening of the beam with depth. With a reduced low energy photon component in the beam, the photoelectric effect becomes less dominant of an interaction process in the silicon. With the Compton effect more dominant, the detector becomes more tissue equivalent. However, due to the sensitive volume of the ionisation chamber being significantly larger than that of the microstrip detector, only a general trend may be inferred from these results.
6.5. Depth Dose Response

Figure 6.8: Depth dose response in a 15×15 mm MRT field of the microstrip detector compared to the PTW Semiflex 31010. Both are normalised to the response at 20 mm depth.

Figure 6.9: Depth dose response in a 10×10 mm MRT field of the microstrip detector compared to the PTW Semiflex 31010. Both are normalised to the response at 20 mm depth.
6.5. Depth Dose Response

Figure 6.10: Percentage dose as a function of depth in PMMA for measurement and Monte Carlo simulation, normalised to measurement at 10 mm depth.

6.5.2 Monte Carlo Simulation

A series of simulations designed to be complementary to the experimental results of Section 6.5.1 were developed. These simulations seek to overcome the significant sensitive volume variability, and compare dose to the sensitive volume of the microstrip detector to dose to water in its absence, but in the same geometric boundaries.

The first stage of the simulation was developed with the microstrip detector in a face-on configuration within a water phantom. A homogeneous rectangular beam of dimensions 10×10 mm was set incident on the phantom surface and dose scored within the detector’s sensitive volume. The detector was stepped through various depths in the range of 1 to 80 mm from the phantom surface. To benchmark the simulation, the results of this simulation were first compared to experimentally obtained results as shown in Figure 6.10.
Figure 6.11: Dose as a function of depth in water for the simulated microstrip detector’s sensitive volume with depth and within water of the same geometric boundaries.

Excellent agreement with the first stage of the simulation was obtained with the limited number of data points obtained experimentally. The second stage of the simulation mirrored the first, except the detector was replaced entirely with water, and with dose scored to the exact same geometric boundaries of that of the replaced detector’s sensitive volume (Figure 6.11). The ratio of the dose to the detector and dose to water under the same set up conditions was compared at each point to determine the water equivalence dose ratio (Figure 6.12).

The results show an over-response of the microstrip detector relative to water at shallow depths, which decreases with depth. This agrees with the experimentally obtained results of 6.5.1, but notably does not suffer from the effects of the large difference in sensitive volume.
6.6 Microbeam Array Measurements

6.6.1 Response Versus Wiggler Gap

The wiggler gap on the ID17 can be physically varied to alter the properties of the emitted photons. Opening the gap has the effect of reducing the magnetic field strength along electron trajectory of the insertion device, which results in a reduced dose rate and a softer photon spectrum. The impact of various wiggler gaps on the microstrip detector response was investigated experimentally.

The microstrip detector was placed in a 20×20×20 cm PMMA phantom in a face-on orientation with 2 cm of PMMA placed on the entrance surface for build-up. The detector was biased to a voltage of -51.2 V as measured by the RadPlot software readout. The multislit collimator (MSC) was introduced into the beam and the detector dosimetrically centred on the central peak. The wiggler gap was initially set at 24.8
Figure 6.13: The microstrip detector as mounted in a PMMA phantom, with additional PMMA material placed in front to produce greater depth for radiation interactions.
mm, and a static exposure of the detector performed with simultaneous readout. This was repeated for a range of wiggler gaps up to 70 mm. The process was then repeated with the MSC retracted from the beam to produce an open field. The response was integrated with dark current correction and corrected by dividing by the storage ring current (Figure 6.14). Normalisation was performed across both result sets by normalising to the corrected open-field response at a wiggler gap of 24.8 mm (Figure 6.15).

The X-ray spectrum varies as a function of wiggler gap, being hardest at the smallest gap, but also producing the greatest intensity. At the smallest gap (24.8 mm), the increased beam intensity greatly dominates over any spectral effects and the low energy over response of silicon. Due to the inability to easily deconvolve these beam properties, conclusions can only be drawn on results at each wiggler gap with and without the MSC present.
Figure 6.15: Ratio of single microbeam to homogeneous field microstrip detector integral response as a function of the ID17 wiggler gap.

Figure 6.15 reveals that for small wiggler gaps (24.8 to 40 mm), increasing the wiggler gap results in a decreased response ratio. A decrease in wiggler gap results in a higher response ratio, presumably due to slightly less relative lateral scatter and backscatter due to the higher average photon energy. The effect of reducing the beam size has increasingly less of an impact as the beam hardens. However, for wiggler gaps greater than 50 mm, the trend reverses and the response ratio increases with increasing wiggler gap. As the gap broadens, the average photon energy decreases, resulting in the photoelectric effect becoming more dominant relative to Compton scattering. With Compton scattering reduced, the influence of the open field in reducing the response ratio due to scattering into the sensitive volume is reduced and the response ratio increases.
6.6. Microbeam Array Measurements

6.6.2 Peak FWHM Versus Applied Bias

Previous results show the effect of applied bias on both detector sensitivity (Section 6.2) and the spatial distribution of charge collection efficiency (Sections 5.3 and 5.4). As the microstrip detector has been developed to resolve complex dose distributions, the impact of the detector bias on the peak full-width at half-maximums is investigated.

A 500 µm high by 10 mm wide array of microbeams (consisting of 24 microbeams) beam was delivered to the microstrip detector. The detector was scanned laterally through the field in an end-on orientation to minimise the dimension of the sensitive volume in the peak-valley direction. The FWHM was determined for peak 12 for a range of applied bias voltages with the guard ring grounded, with the results in Figure 6.16

The FWHM of the measured microbeam decreases in size with increasing applied
6.7 Substrate Effects

In order to achieve the highest possible spatial resolution with the microstrip detector, it is necessary to place it in an *end-on* configuration, that is with the thinnest dimension of the sensitive volume aligned in the peak-valley axis. A consequence of this configuration is that it results in asymmetry of the detector in the peak-valley direction, whereby the detector substrate is located on a single side of the sensitive volume in the scanning direction. The effect of this is readily apparent in microbeam array measurements, with broadening of the shoulder of peaks on the side of the substrate, and tight fall-off on the opposing side.

Physically, this effect manifests as dose-enhancement caused by increasing radiation interaction in the substrate as opposed to PMMA on the epitaxial side due to the higher atomic number of silicon relative to PMMA. This results in an increased proportion of backscatter resulting in dose deposition in the sensitive volume. Despite this phenomenon, it is highly desirable to operate in this configuration which although results in some distortion of measured profiles, results in much better spatial resolution than *edge-on* or *face-on* configurations. As such it is necessary to characterise the effect on measured profiles.

6.7.1 Measurement in an MRT Field

The effect of the silicon substrate on the measured microbeam profile was investigated by introducing a 0.1 mm wide single slit collimator upstream of the MSC positioned to produce a single microbeam (see Figure 6.17). A lateral scan of the microstrip detector
6.7. Substrate Effects

Figure 6.17: Schematic of the measurement set-up to determine the substrate effects for (a.) a microbeam array and (b.) the introduction of a single slit to produce a single microbeam. The detector is stepped laterally in both cases.

was performed using a Keithley DMM recording dose as a function of position. The use of external readout circuitry was performed to entirely eliminate the data acquisition system as a source of potential influence. The detector was stepped incrementally laterally with respect the beam, with the readout of the induced current measured at each position. The measurement was then repeated with the slit removed to determine response to a complete microbeam array.

The orientation of the microstrip detector was reversed by flipping the sensitive volume and substrate to opposite sides of the scanning direction whilst maintaining the end-on configuration (see Figure 6.18). Measurements were then performed both with and without the single slit collimator to determine the response of the detector in the new orientation.
6.7. Substrate Effects

Figure 6.18: Scan of single and multiple microbeams with a microstrip detector in the end on orientation with detector orientation overlaid with (a) the substrate oriented to the right and (b) with the substrate orientated to the left.
6.7. Substrate Effects

The effect of the substrate is clearly evident in the dose of the tail region for a single microbeam, where there is a relative over-response of the detector when positioned on one side of the peak to the other. This characteristic alternates to the opposite side of the peak when the detector orientation is flipped, showing that this is independent of detector alignment effects and radiation field, and is a result of the detector orientation. Another effect which is present in both single microbeam and microbeam array fields is the apparent peak asymmetry. This effect too, alternates side with reversal of the physical detector orientation, showing it to be a dose enhancement effect of the substrate.

6.7.2 Monte Carlo Simulation

To observe the effect independent of beam alignment and dose distribution, a Monte Carlo simulation was performed with the detector aligned in an end-on configuration in a PMMA phantom at a depth of 5 mm. A radiation field was simulated as being a single $50 \times 500 \, \mu m$ homogeneous field of radiation, with a photon spectra replicating that of the MRT beam. Initially a simulation was performed with the radiation field centralised over the sensitive volume, but then repeated with the detector stepped laterally in $5 \, \mu m$ increments in both directions. Dose was scored only in the volume of the sensitive strip volume, with dose per primary photon recorded at each position, with the results in Figure 6.19.

The simulation results display the very same characteristics of the experimental results, with the asymmetry in the dose fall-off region most significant. In a block of PMMA, dose to this region is almost solely contributed to by radiation scattered within the phantom. Due to the asymmetric structure of the detector in end-on orientation, with the detector’s sensitive volume positioned just beyond the peak, and the substrate in the peak region, the proportion of scattered radiation reaching the sensitive volume
Figure 6.19: Monte Carlo simulation results for a 500 $\times$ 50 $\mu$m$^2$ microbeam scanned laterally across the detector mounted in end-on orientation.
is increased relative to the contribution for the symmetric opposite position. When the detector is positioned such that the substrate is just beyond the beam edge, a situation which occurs at a position of 398 μm for the Monte Carlo situation, there is a sharp decline in the dose per primary photon. This is due to photons in the peak region now interacting within PMMA, resulting in less lateral scatter reaching the detector volume.
Chapter 7

Conclusion

The aim of this work was the development and characterisation of a dosimetry system for synchrotron X-ray microbeam radiation therapy. This was realised with the development of the X-tream dosimetry system comprising a silicon microstrip detector, data acquisition hardware, and data acquisition and analysis software. The system was characterised in terms of electrical performance, energy dependence and spatially-resolved charge collection studies. Furthermore, the system was able to successfully perform dosimetric measurements in a synchrotron X-ray MRT field, where the system was further characterised.

7.1 The Use of Silicon Microstrip Detectors for MRT

The silicon microstrip detector has been demonstrated to provide high spatial resolution dosimetry for MRT. However, one major disadvantage in its use is the low energy over-response intrinsic to silicon detectors with respect to water for photon energies of less than 100 keV. This is due to an increase in the photoelectric interaction cross-
section due to the higher atomic number of silicon. This also leads to an asymmetric response of the detector scanned through an MRT field in the *end on* orientation compared to the response with the detector flipped.

Changing all or part of the silicon to a more tissue-equivalent material would lead to an improved energy response. One proposal is to use CVD diamond as either the substrate material or for the entire detector as investigated in Section 4.3.3. These results show the use of this material has the potential to greatly improve the energy response of the detector over the energy range of relevance to MRT. However, whilst it is predicted detectors constructed out of this material and geometrically similar to the silicon microstrip detector will also exhibit high spatial resolution, this would have to be investigated more rigorously. Such an investigation would involve experimentally verifying the energy dependence, performing spatially resolved charge collection studies and ultimately characterising the detector in an MRT radiation field; ultimately requiring physical fabrication of these detectors, an exercise well beyond the scope of this work.

### 7.2 Development of a Data Acquisition System for MRT

X-tream, a highly versatile, integrated software and hardware data acquisition system was developed as a dosimetry solution for MRT. The system was able to be controlled remotely from the beamline control room without the need to physically alter parameters. Data was able to be reliably acquired at a very high temporal resolution (up to 1.6 MHz), which combined with linear scanning or stepping of a dosimeter with a very small sensitive volume, results the acquisition of data with a very high spatial resolution. The development of the *single trigger* mode was developed for perform-
ing dosimetric scans immediately after an irradiation has been commanded from the MRT control console, whilst multi-trigger mode was developed for detector alignment purposes, enabling precise positioning of the detector based on its response at known discrete positioning step sizes.

The modular design of the data acquisition system, in particular the separation of the preamplifier module from the central data acquisition unit (CDAU) ensures that any change in detector type at most will require a specifically optimised preamplifier module. By ensuring that only this one module needs to be optimised for the altered dynamic range and capacitance of the detector type, enables the one data acquisition system to be used with many types of detectors and future proofs the system.

The RADplot data acquisition and analysis software enables both basic analytical functions and MRT-specific analysis to be performed on newly acquired or previously saved acquisitions. The development of a decoding application also permits the use of acquired data with any third-party data analysis software package, expanding the capabilities beyond those incorporated into RADplot.

The system is now installed and in use at several synchrotrons around the world for performing high spatial resolution dosimetry and research. Whilst the radiation detectors are likely to change, the flexibility and modularity of the system will enable the use of the continued system with future detectors with minimal changes.
# Appendix A

## Glossary of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>ADC</td>
<td>Analog-to-Digital Converter</td>
</tr>
<tr>
<td>ANSTO</td>
<td>Australian Nuclear Science &amp; Technology Organisation</td>
</tr>
<tr>
<td>ANTARES</td>
<td>Australian National TAndem RESearch (Accelerator)</td>
</tr>
<tr>
<td>ASCII</td>
<td>American Standard Code for Information Interchange</td>
</tr>
<tr>
<td>CDAU</td>
<td>Central Data Acquisition Unit</td>
</tr>
<tr>
<td>CVD</td>
<td>Chemical Vapour Deposition</td>
</tr>
<tr>
<td>DAC</td>
<td>Digital-to-Analog Converter</td>
</tr>
<tr>
<td>ESRF</td>
<td>European Synchrotron Radiation Facility</td>
</tr>
<tr>
<td>FNTD</td>
<td>Fluorescent Nuclear Track Detector</td>
</tr>
<tr>
<td>FPGA</td>
<td>Field-Programmable Gated Array</td>
</tr>
<tr>
<td>FWHM</td>
<td>Full-Width at Half-Maximum</td>
</tr>
<tr>
<td>GUI</td>
<td>Graphical User Interface</td>
</tr>
<tr>
<td>IBICC</td>
<td>Ion-Beam-Induced Charge-Collection</td>
</tr>
<tr>
<td>ID17</td>
<td>Insertion Device 17 (ESRF Biomedical Beamline)</td>
</tr>
<tr>
<td>MOSFET</td>
<td>Metal-Oxide-Semiconductor Field-Effect Transistor</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>MRT</td>
<td>Microbeam Radiation Therapy</td>
</tr>
<tr>
<td>PMMA</td>
<td>Polyethyl Methacrylate</td>
</tr>
<tr>
<td>TLD</td>
<td>Thermoluminescent Dosimeter</td>
</tr>
<tr>
<td>TTL</td>
<td>Transistor-Transistor Logic</td>
</tr>
<tr>
<td>USB</td>
<td>Universal Serial Bus</td>
</tr>
<tr>
<td>XBICC</td>
<td>X-ray-Beam-Induced Charge-Collection</td>
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