High Resolution Polymer Gel Dosimetry for Small and Micro Field Dosimetry, and Development of Innovative Polymer Gel Dosimeters

A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy

Submitted by
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Declaration

I certify that except where due acknowledgement has been made, the work is that of the author alone; the work has not been submitted previously, in whole or in part, to qualify for any other academic award; the content of the thesis is the result of work which has been carried out since the official commencement date of the approved research program; many editorial work, paid or unpaid, carried out by a third party is acknowledged; and ethics procedures and guidelines have been followed.

Christopher J. Wong

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<th>Meaning</th>
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<td>Aa</td>
<td>Acrylamide</td>
</tr>
<tr>
<td>AVM</td>
<td>Arteriovenous Malformations</td>
</tr>
<tr>
<td>BANANA</td>
<td>BIS, Acrylamide, Nitrous oxide, and Agarose</td>
</tr>
<tr>
<td>BANG (a.k.a. BANG-1)</td>
<td>BIS, Acrylamide, Nitrogen and Gelatine</td>
</tr>
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<td>BANG-2</td>
<td>not an acronym, refers to successor of BANG</td>
</tr>
<tr>
<td>BANG-3</td>
<td>not an acronym, refers to successor of BANG-2</td>
</tr>
<tr>
<td>BIS</td>
<td>N’ N-methylene-bis-acrylamide</td>
</tr>
<tr>
<td>CCD</td>
<td>Charged Coupled Device</td>
</tr>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>$D_{\text{max}}$</td>
<td>Depth below the surface of a sample/patient at which the maximum value of dose from a radiotherapy beam is delivered.</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic Acid</td>
</tr>
<tr>
<td>EGS4</td>
<td>Electron Gamma Shower (version 4)</td>
</tr>
<tr>
<td>EGSnrc</td>
<td>Electron Gamma Shower (National Research Council of Canada)</td>
</tr>
<tr>
<td>EPI</td>
<td>Echo Planar Imaging</td>
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<tr>
<td>FOV</td>
<td>Field of View</td>
</tr>
<tr>
<td>FSE</td>
<td>Fast Spin Echo</td>
</tr>
<tr>
<td>GDC</td>
<td>Guglielme detachable coils</td>
</tr>
<tr>
<td>GDL</td>
<td>D-(-)-Gluconic acid δ-lactone</td>
</tr>
<tr>
<td>IAC</td>
<td>Idaho Accelerator Center</td>
</tr>
<tr>
<td>IMRT</td>
<td>Intensity-Modulated Radiation Therapy</td>
</tr>
<tr>
<td>ISIS</td>
<td>Idaho State Induction Accelerator System</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear Magnetic Resonance</td>
</tr>
<tr>
<td>MAc</td>
<td>Methacrylic acid</td>
</tr>
<tr>
<td>MAG</td>
<td>Methacrylic Acid based Gel</td>
</tr>
<tr>
<td>MAGAS</td>
<td>Methacrylic Acid Gelatin with Ascorbic acid</td>
</tr>
<tr>
<td>abbreviation or acronym</td>
<td>meaning</td>
</tr>
<tr>
<td>-------------------------</td>
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</tr>
<tr>
<td>MAGAT</td>
<td>Methacrylic acid, Gelatine And Tetrakis</td>
</tr>
<tr>
<td>MLC</td>
<td>Multileaf Collimator</td>
</tr>
<tr>
<td>MMLC</td>
<td>Mini-Multileaf Collimator</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>MSME</td>
<td>Multiple Spin Multiple Echo</td>
</tr>
<tr>
<td>MU</td>
<td>Monitor Units</td>
</tr>
<tr>
<td>µ-TLD</td>
<td>Micro - Thermoluminescent Dosimeter</td>
</tr>
<tr>
<td>nMAG</td>
<td>Normoxic Methacrylic acid based Gel</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear Magnetic Resonance</td>
</tr>
<tr>
<td>nPAG</td>
<td>Normoxic Polyacrylamide Gel</td>
</tr>
<tr>
<td>PAG</td>
<td>Polyacrylamide Gel</td>
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<td>PAGAS</td>
<td>Polyacrylamide Gelatine gel with Ascorbic acid</td>
</tr>
<tr>
<td>PAGAT</td>
<td>Polyacrylamide Gel And THPC</td>
</tr>
<tr>
<td>R₁</td>
<td>spin-lattice relaxation rate</td>
</tr>
<tr>
<td>R₂</td>
<td>spin-spin relaxation rate</td>
</tr>
<tr>
<td>RF</td>
<td>radiofrequency</td>
</tr>
<tr>
<td>ROI</td>
<td>Region of Interest</td>
</tr>
<tr>
<td>SRS</td>
<td>Stereotactic Radiosurgery</td>
</tr>
<tr>
<td>SSD</td>
<td>Source-Surface Distance</td>
</tr>
<tr>
<td>T₁</td>
<td>spin-lattice relaxation time</td>
</tr>
<tr>
<td>T₂</td>
<td>spin-spin relaxation time</td>
</tr>
<tr>
<td>TE</td>
<td>Echo Time</td>
</tr>
<tr>
<td>THP</td>
<td>In this thesis, it refers to tetrakis (hydroxymethyl) phosphonium. This has also been stated to mean either bis[tetrakis(hydromethyl) phosphonium]sulfate or Tetrakis (hydroxymethyl) phosphonium chloride, depending on context in previous related literature.</td>
</tr>
<tr>
<td>THPC</td>
<td>Tetrakis (hydroxymethyl) phosphonium chloride</td>
</tr>
<tr>
<td>THPS</td>
<td>bis[tetrakis(hydroxymethyl) phosphonium]sulfate</td>
</tr>
<tr>
<td>TLD</td>
<td>Thermoluminescent Dosimeter</td>
</tr>
<tr>
<td>TR</td>
<td>Repetition Time</td>
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<tr>
<td>abbreviation or acronym</td>
<td>meaning</td>
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<td>-------------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>VIPAR</td>
<td>n-VinylPyrrolidone Argon</td>
</tr>
<tr>
<td>Vp</td>
<td>N-vinylpyrrolidone</td>
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Summary

Radiotherapy treatments for the treatment of cancer work under the principle that radiation inflicts damage to the DNA of cancerous cells. Ionising radiation also damages the DNA of healthy tissue, and it is therefore very important to determine the distribution of energy deposited by radiation. Techniques to measure this dose distribution are forms of dosimetry. In clinical radiotherapy techniques, the most common form of dosimetry is the ionisation chamber. Another method of dosimetry is gel dosimetry, and this is the focus of this thesis.

Polymer gel dosimeters are a phantom made of tissue equivalent materials containing monomers that polymerise in response to incident radiation. This polymerisation is dependent on the magnitude of the radiation. The polymerisation can be measured in a variety of ways, including magnetic resonance scanning, optical computed tomography, ultrasound and Raman spectroscopy. Additionally, variations on the formulation of the gel can be made, allowing specific variations of gel for different purposes.

Currently, gel dosimeters are not used on a regular basis for clinical work, and the majority of work related to them is research. This thesis describes the use of polymer gels for current radiotherapy treatment techniques, particularly for using small and micro-sized radiotherapy beams, as well as the development of new gel formulations.

Gel dosimeters have several useful advantages that make them highly desirable in radiotherapy dosimetry.

- Gels are tissue equivalent, allowing use as both a dosimeter and phantom simultaneously. Due to their chemical make-up, the distribution of energy deposited in gel is highly similar to human tissue, and gels can be shaped to model various parts of a patient’s anatomy.
- Gels permit the formation of a three-dimensional image of the incident dose distribution. The degree of polymerisation is dependent on the amount of incident radiation. By comparison, other techniques such as ionisation
chambers and radiochromic films are only capable of dose measurements at points or 2D planes.
- Gels are relatively energy independent.

Polymer gels do have several limitations. Notably, they are sensitive to oxygen, which inhibits polymerisation and thus reduces the sensitivity of the gel to radiation-induced polymerisation. Another factor is that polymer gels are not as user-friendly as other dosimetry techniques, particularly as some of the chemicals they are composed of are hazardous to humans unless special precautions are taken.

This thesis develops polymer gels and their uses into several new and innovative areas of research, with the aim of directing them towards improving their use for very small fields, and developing new applications for polymer gels. These include the development of new types of polymer gel for specific purposes, and the use of gel for the first time in several unique applications such as in microbeam radiotherapy.

In chapter 1, an introduction to the current roles of gel dosimetry is established. A more detailed explanation of the aims of this thesis is also given.

Chapter 2 explains in further detail the physical and chemical processes that underpin how gel dosimeters work, as well as some basic background on the common scanning techniques for gels used in this thesis, Magnetic Resonance Imaging and Raman Spectroscopy.

Chapter 3 describes the general method by which polymer gel dosimeters are prepared, irradiated and imaged, along with the data analysis techniques. The use of polymer gel draws on knowledge from a range of disciplines, including chemistry, physics and radiotherapy. This chapter describes how new special types of gel dosimeter were developed and applied in innovative ways for measurement of special types of radiotherapy beams, such as the high dose rate synchrotron and extremely high-dose rate injection-type accelerator.

Chapter 4 reports the results of gel dosimeters to measure the dose distribution of radiotherapy beams from a clinical linac. Radiotherapy techniques tighten the size of
the field and conform it as much as possible the target, so accurate measurements of the dose distribution are required. In this work, radiotherapy beams are collimated down to sub-centimetre field sizes, down to $3 \times 3$ mm$^2$, and the dose distributions measured using polymer gels. Comparison measurements using radiochromic film and micro-thermoluminescent diodes are also made. Improvements to the resolution are also achieved by employing specialised high-strength (7 T) micro-imaging MRI scanners.

Chapter 5 investigates the use of polymer gels for the measurement of synchrotron generated microbeams. These beams have a nominal width in the micrometre range, and have demonstrated promising results for future radiotherapy techniques. However, the beam dimensions make dose distribution measurements a challenging task. Polymer gels were explored as a possible dosimeter for these beams. An important factor was the use of oxygen to create a new type of gel. Oxygen was deliberately introduced to reduce the rate of polymerisation, as the dose rate of a synchrotron will quickly saturate a standard gel dosimeter. Raman spectroscopy was used to measure the dose distribution, as it is one of the few imaging techniques with the required micrometre resolution.

Chapter 6 examines the dose artefacts induced in a gel phantom by a metallic inhomogeneity. Patients undergoing treatment for aneurysms may have an aneurysm clip placed in their brain. Later radiotherapy treatments that take place around this clip will have an altered dose distribution, so the influence of this artefact was measured by use of a gel dosimeter phantom with a clip.

Chapter 7 examines several aspects of gel dosimetry developed during the course of this thesis. These include the use of polymer gels phantoms to potentially measure the production of secondary neutrons induced by high energy radiotherapy beams. A new special type of polymer gel was developed, with the aim of creating a gel that would remain clear when irradiated. Such a clear-type gel has potential for overcoming the inability of Raman spectroscopy to make measurements below the surface of the gel. Also, a preliminary measurement made using special high-resistance gels for an injection type linear accelerator. These types of linacs are capable of extremely high
dose rates, making dosimetry difficult. Finally, a first measurement of a high energy (230 MeV) proton beam using a polymer gel is reported.
1. INTRODUCTION, LITERATURE REVIEW AND AIMS
1.1. Introduction

Radiation therapy (or radiotherapy) is the use of ionising radiation in the treatment of cancer. Ionising radiation is specifically targeted towards the site of the cancerous cells, with the aim of causing DNA damage to malignant tissue. Simultaneously, it is important to minimise the damage to healthy organs surrounding the treatment area. This has lead to the development of more complex radiation therapy treatments such as brachytherapy, intensity modulated radiotherapy (IMRT) and stereotactic radiosurgery (SRS). As such radiotherapy techniques develop to allow more accurate targeting of cancerous regions while sparing surrounding healthy tissue, the collimation of external radiotherapy beams used in these techniques will become tighter and more precise.

Dosimetry is the technique of quantifying the amount of energy deposited by radiation. With all methods of radiation therapy, it is important to determine ahead of time the dose distribution of ionising radiation within the patient. Gel dosimeters are a class of radiation dosimeters that act as 3-dimensional, tissue-equivalent materials [1, 2] that change in chemical structure in proportion to the level of irradiation they receive. This change in response to radiation is localised to the region irradiated. Hence, gel dosimeters act as a method of recording the extent to which energy from radiation has been deposited throughout the volume.

There are a wide variety of methods available to measure and quantify the polymerisation of dosimetric gel, allowing the degree and distribution of the incident radiation to be determined. The majority of these imaging techniques are non-invasive and allow the possibility of using multiple imaging techniques to cross-check a single sample. These imaging techniques include Magnetic Resonance Imaging (MRI) [3-6], optical and x-ray computed tomography (CT) [7-12], Raman Spectroscopy [13, 14] and Ultrasound [15, 16].

Gel dosimeters have several desirable properties for use in radiotherapy dosimetry. Most notably, they are a three-dimensional dosimetry modality [2, 17-19] in contrast
to other methods which are either only point measurements (ionisation chambers, µ-TLDs) or two dimensional sheets (film being the most common example of this type). Polymer gels have been reported as being energy independent for photons at low energies (less than approximately 8 MV), with only a slight energy dependence at higher energies [2, 18, 20, 21]. It is important to recognise however that there exist various types of gel dosimeters, and as such the energy dependence of various gel dosimeters should not be generalised. A dependence on electron beam energy in the radiation dose response of some types of polymer gels has also been observed [21].

The formulation of a polymer gel can be altered and made suitable for a specific application. For instance, most polymer gels change from clear to white when polymerised (an example is shown in Figure 1), allowing techniques such as optical CT which operate based on the attenuation of light to be used [7, 10, 11, 22-25]. However, when using Raman Spectroscopy as a measurement method, this colour change alters the magnitude of the signal, limiting the usefulness of the gel dosimeter for anything other than surface measurements [14]. A change in the formulation can be made such that the polymer gel remains clear when irradiated. It can no longer be scanned by optical CT, but measurements at depths below the surface are possible when using Raman Spectroscopy, allowing for the possibility of three-dimensional measurements of the dose distribution.

Figure 1 An image of polymer gels. The 3rd gel from the left is unirradiated and is therefore clear, the other gels have been irradiated to various degrees. The intensity of colour change is dependent on the level of radiation, and only occurs in those parts of the gel that have been irradiated.
Gel dosimeters are a tissue equivalent material. That is, they are made up from elements with approximately the same density and atomic composition as tissue. As a result, the distribution of radiotherapy beams as they are scattered and attenuated by the gel dosimeter will be the same compared to human tissue. This allows polymer gels to act as a phantom for dose distribution measurements, and the entire phantom can be examined through methods such as MRI for a full 3-dimensional map of the dose distribution.

Polymer gels are not without limitations, and there has been much work undertaken to overcome these problems. One notable hurdle was role of oxygen exposure in desensitising the polymer gel to radiation. This made the gel solution preparation process awkward and difficult. The development of normoxic polymer gels that could be prepared in a normal oxygen environment was a step that greatly sped up and simplified the process of making polymer gels [26]. Another major problem associated with polymer gel dosimetry is the toxicity of the materials that make up the gel solution. Acrylamide and N’ N-methylene-bis-acrylamide are the common monomers used in polymer gels and both are known to be toxic chemicals ([3, 26-30]. Efforts to overcome these toxicity problems involve replacing these chemicals with safer alternatives such as sodium methacrylate and N-isopropylacrylamide [27, 31].

This thesis is aimed at examining polymer gel dosimeters for use in radiotherapy treatments that are characterised by small field size beams and microbeam radiations, techniques which are becoming more important with the advent of more precise treatment planning systems. This thesis also examines the use of polymer gels in applied situations of determining the dose enhancement due to metallic artefacts and the generation of neutrons in a target exposed to high-energy radiation, factors that generally are not accounted for in treatment planning. Finally, this thesis will examine the use of polymer gels in the use of two new types of beam, one from the Idaho State Induction Accelerator System\(^1\) (ISIS) which provides an extremely high dose rate, and as a measurement technique for a high energy (230 MeV) proton beam.

---

\(^1\) The Idaho Accelerator Center, ISIS webpage is located at: http://iac.isu.edu/isis/isis.html
1.2. Chronological developments of gel dosimetry

The idea of using a gel that can change structure in response to radiation has been discussed since the 1950’s however it was not until the 1980’s that significant developments in this field came to pass, making them suitable as dosimeters as they are currently used.

It was proposed by Day and Stein [32] that an aqueous solution targeted with ionising radiation would produce hydrogen and hydroxyl radicals. Acceptors (such as benzene) react with these radicals, and the products of these interactions used as a measure of radiation dose. The aqueous solution (the medium used to measure dose) has the benefit of being much more akin to tissue in terms of its radiation properties than the then currently used methods of radiation dose measurement in air.

Later, Day and Stein [33] raised the possibility of using a semi-solid material instead of an aqueous solution to mimic the properties of tissue. This would allow the radiation dose to be measured as a three-dimensional distribution, as opposed to the aqueous solution in which only an average dose over the size of the volume could be obtained. To create this system, they used gels that changed colour in proportion to the level of radiation absorbed. Based on earlier work, they proposed that the water molecules reacted under radiation as in equation (1).

\[ H_2O \rightarrow H_2O^\cdot + e \]  

(1)

Thus leading to the electron being available for various competing reactions listed in equations (2), (3) and (4).

\[ H_2O + e \rightarrow H_2O^- \]  

(2)

\[ O_2 + e \rightarrow O_2^- \]  

(3)
It was noted that oxygen inhibits this change listed in equation (4) if present in the solution. Oxygen consumes radicals that would otherwise be available for reaction with the dye.

Andrews, Murphy, and LeBrun [34] were able to perform depth-dose measurements on x-rays and electrons using a chloral hydrate-agar gel. The gel changes colour with irradiation, allowing the dose to be measured via light spectral absorption. A limitation of this method of measurement was the poor spatial resolution of the medium used at the time. The dose can also be measured by detecting the changes in pH levels or the electrical resistance of the gel.

The idea of combining gels with polymerisation of monomer was raised by Hoecker and Watkins [35]. As a measurement of radiation dose, they investigated the degree to which a liquid monomer solution became solid through polymerisation due to radiation. They also compared the amount of radiation absorbed by the gel with muscle, as a test of its tissue equivalence, and found them to be quite similar. Hoecker et al. [35] also found that the process of polymerisation was effectively limited to a short time after irradiation. They also found that the minimum dose required to induce a solidifying polymerisation could be controlled by the addition of a quantity of scavenger which would then consume a portion of radicals in the gel.

A class of dosimeters called Fricke solutions contain Fe$^{2+}$ ions (in a ferrous ammonium sulphate solution) which convert to Fe$^{3+}$, a process initiated by the absorption of ionising radiation. The degree of conversion of Fe$^{2+}$ ions to Fe$^{3+}$ can then be measured using nuclear magnetic resonance (NMR) techniques, as Fe$^{2+}$ and Fe$^{3+}$ both alter the relaxation times of protons in water, a process that was developed by Gore, Kang and Schulz [36]. These Fricke solutions were then improved by placing the ions into a gel solution so that the final result became solid [37], so that the degree of ionisation was related to the local incident dose.
A major limitation associated with Fricke gels was the occurrence of diffusion of ferric ions through the solution over time. This meant that imaging of Fricke gels must be done quite quickly after irradiation in order to prevent the blurring of images [38-42]. To overcome this limitation, a gel dosimeter in which the irradiated region remains more or less fixed is desirable and this lead to experimentation with various gelling agents in the gel solution to reduce the effects of diffusion [40, 41].

Another problem associated with the use of Fricke gels is their high electrical conductivity. This causes signal attenuation during MRI scanning, making accurate measurements difficult [4]. Polymer gels do not suffer this problem as they do not attenuate the RF field of the MRI scanner to such a degree.

A significant advancement in gel dosimetry was the introduction of gels based on the polymerisation of monomers. The first of these focused on the polymerisation of acrylamide and bis-acrylamide, developed by Maryanski, Gore, Kennan and Schulz [1]. As this gel was comprised of BIS, Acrylamide, Nitrous oxide and Agarose, it was given the acronym BANANA. BANANA gels did not have the diffusion problems that Fricke gels suffered, as they worked on the basis of monomer polymerising when exposed to free radicals generated by water exposed to radiation.

In 1994, BANG gel, which is a basis of the gel used in this work, was developed by Maryanski, Schulz, Ibbott, Gatenby, Xie, Horton and Gore [3]. BANG is an acronym for BIS Acrylamide Nitrogen Gelatin, the components of the gel in addition to water on which it is based. The term BANG is trademarked and a patent was acquired for this gel type [43].

The basic formulation of polymer gels (including those used in this thesis) generally uses the work of Maryanski as a starting point. Monomers such as acrylamide and BIS are mixed into a solution, which also contains also gelatine (or another gelling agent) in order to ensure that the solution is solid. The solution is also degassed with nitrogen or argon before the addition of the chemicals to ensure that oxygen that is dissolved in the solution is removed. This work is done inside a glove box or other sealed environment. The presence of oxygen is a major inhibitor to the sensitivity of gels, so its removal is an important step in maximising the sensitivity of a polymer gel.
Several other gel formulations were developed (as listed in Table 1) to further understand and improve the properties of gels.

These developments include:

- the extent to which oxygen diffusion throughout the gel causes an inhibition of polymerisation [44].
- the influence that the magnitude of cross-linking during polymerisation has on the gel’s magnetic properties [45].
- the ways of reducing the toxicity of a polymer gel [27, 31].
- the influence of temperature while MRI scanning [46].

An important development in gels was the introduction of anti-oxidants. It was well established that the presence of oxygen within gel acted as an inhibitor to polymerisation, reducing their sensitivity [3, 4, 20, 26, 44, 47-49]. An anti-oxidant added to the gel formula during preparation would ideally consume free oxygen within the gel. This reduced the complexity of preparation as gels no longer needed to be degassed [26], there are known as normoxic gels. A list of such normoxic gels are presented in Table 1.

In conjunction with improvements in gel design, there have been improvements in many of the techniques that surround gel dosimetry. The scanning process was initially performed using MRI. This is still a popular method of scanning, with several works published in reporting on the properties, potential artefacts and results of possible MRI sequences [5, 6, 50-54]. Another scanning method of interest is Raman Spectroscopy. Raman Spectroscopy uses the inelastic scattering of light from the bonds within chemicals as a method of identification. Raman Spectroscopy allows for the direct measurement of the chemical makeup of the gel dosimeter, revealing details behind the process of polymerisation [13, 14, 55-57]. This type of scanning is notable for potentially having a very high spatial resolution in comparison of other scanning techniques, on the order of 1 µm [14]. In comparison, a typical clinical MRI scanner (1.5 T) has resolution in order of 1 mm.
Aside from MRI and Raman Spectroscopy, there have been several other methods by which the dose distribution within gel dosimeters has been measured. These include:

- Optical scanning and optical computed tomography [7, 10, 11, 22-25].
- X-ray computed tomography [8, 9, 12, 58, 59].
- Ultrasound [15, 16, 60-62].

Gel dosimetry is not yet a mainstream clinical technique, but they have been applied in certain situations, such as the measurement of IMRT [63, 64] and the verification of patient dose before treatment [65]. Investigations have also been made into using gel dosimeters to measure the dose enhancement due to iodine contrast agents [66, 67], and applying polymer gels to measure the dose enhancement through boron neutron capture therapy [68].

Table 1 lists several types of polymerising gels that have been investigated in literature previously as well as their components².

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² In literature, the acronym THP has been used previously to refer to:
- tetrakis(hydroxymethyl)phosphonium (eg. [75])
- bis[tetrakis(hydromethyl)phophonium]sulphate (eg. [80])
- Tetrakis (hydroxymethyl) phosphonium chloride (eg. [78])

In this thesis, Tetrakis (hydroxymethyl) phosphonium chloride was used in the preparation of normoxic gels and will be referred to as THPC. Bis[tetrakis(hydroxymethyl) phosphonium]sulfate will be referred to as THPS and tetrakis(hydroxymethyl)phosphonium referred to simply as THP, however neither of these compounds were used in this work.
Table 1 List of some polymerising gel types. All gels contain water as a majority component.
Note that Aa = acrylamide, BIS = N’ N-methylene-bis-acrylamide, MAc = Methacrylic acid

<table>
<thead>
<tr>
<th>name</th>
<th>name basis</th>
<th>components</th>
<th>normoxic?</th>
<th>notes</th>
<th>references using this gel</th>
</tr>
</thead>
<tbody>
<tr>
<td>BANANA</td>
<td>BIS, acrylamide, nitrous oxide, and agarose</td>
<td>Aa, BIS, agarose</td>
<td>No</td>
<td>Nitrous oxide gas used to displace dissolved oxygen</td>
<td>[1]</td>
</tr>
<tr>
<td>BANG / BANG-1</td>
<td>BIS, acrylamide, nitrogen and gelatine</td>
<td>Aa, BIS, gelatine</td>
<td>No</td>
<td></td>
<td>[3, 20, 69-71]</td>
</tr>
<tr>
<td>BANG-2</td>
<td>Named as successor to BANG-1</td>
<td>acrylic acid, BIS, sodium hydroxide, gelatine</td>
<td>No</td>
<td></td>
<td>[4, 21, 72]</td>
</tr>
<tr>
<td>BANG-3</td>
<td>Named as successor to BANG-2</td>
<td>MAc, gelatine</td>
<td>No</td>
<td></td>
<td>[54, 73]</td>
</tr>
<tr>
<td>unnamed</td>
<td></td>
<td>Na methacrylate, BIS, gelatine</td>
<td>No</td>
<td></td>
<td>[27]</td>
</tr>
<tr>
<td>VIPAR</td>
<td>N-vinylpyrrolidone argon</td>
<td>N-vinylpyrrolidone, BIS, Gelatine</td>
<td>No</td>
<td></td>
<td>[74]</td>
</tr>
<tr>
<td>PAG</td>
<td>Polyacrylamide gel</td>
<td>Primarily acrylamide (or variant) as the monomer, + various others components</td>
<td>No</td>
<td>General term, which includes any gel based on the polymerisation of acrylamide as the main measure of dose</td>
<td>[45]</td>
</tr>
<tr>
<td>MAGIC</td>
<td>Methacrylic and ascorbic acid in gelatine initiated by copper</td>
<td>MAc, gelatine, hydroquinone, copper sulphate, ascorbic acid</td>
<td>Yes</td>
<td></td>
<td>[26, 63, 75, 76]</td>
</tr>
<tr>
<td>MAGAS</td>
<td>Methacrylic acid gelatine with ascorbic acid</td>
<td>MAc, gelatine, ascorbic acid</td>
<td>Yes</td>
<td></td>
<td>[76, 77]</td>
</tr>
</tbody>
</table>
1.2.1. Comparison of gel dosimeters with other methods of dosimetry

There exist several types of well established dosimeters for measuring dose distributions from radiotherapy beams. The most commonly used of these methods is the ionisation chamber. Other methods include radiochromic films and thermoluminescent dosimeters. In addition, Monte Carlo simulations are used to predict and model the distribution of radiation throughout a patient or target phantom.

Before gel dosimetry can be accepted into a clinical environment as a standard dosimeter, it needs to be validated by comparing it against these other more established techniques. In this thesis, ionisation chambers, radiochromic films and TLDs were employed as a comparison to gel dosimetry measurements.
1.2.1.1. Ionisation chambers

The most commonly used method of dosimetry measurement is using ionisation chambers. An ionisation chamber consists of a small volume of air between two electrodes (cathode and anode) with a potential difference applied across them. Ionising radiation will create ion pairs within this air. These ions are then attracted to the electrodes, generating a current proportional to the incident radiation. The ionisation chamber has a shell designed to be equivalent to air for photon attenuation, and the thickness of the shell equivalent to the maximum range of produced secondary electrons. An image of an ionisation chamber is shown in Figure 2.

However, while ionisation chambers are well established and work well for beams that are collimated to large field sizes, ionisation chambers have difficulties in measurements of small beams, where the irradiated field size becomes comparable to the maximum electron range [82-85]. When the size of the ionisation chamber is relatively large in comparison to the size of the irradiated field, problems in measurement arise.

Of these, the most notable are firstly the dose-averaging effect which arises from the physical scale compared to the field and averaging of the dose in a pre-determined size volume [84, 86]. In such cases, there will be a significant variation of the dose over the volume that the ionisation chamber occupies. The net result of this is an overestimation of the dose in the penumbra regions and an underestimation of dose in the central regions. A further problem is associated with using ionisation chambers to measure small radiation fields is the failure to achieve electronic equilibrium within the ionisation chamber [86, 87]. As a result, the influence of secondary electrons created by the photon beam with in region of the ionisation chamber will not match the situation in the absence of the chamber, and a false impression of the dose distribution is obtained. These problems necessitate the use of alternative method to measure small field size beams and highly collimated microbeams.
1.2.1.2. Radiochromic films

Radiochromic films are a type of film used in radiotherapy as a dosimeter. When exposed to radiation, they change colour in proportion to the incident dose. In contrast to earlier types of films, radiochromic films do not require wet chemical processing, as they are self-developing and change colour automatically in response to radiation [88, 89]. Certain types of light, such as sunlight and other UV sources, may still have adverse effects on the film however, if the film is exposed for extended periods of time [90]. Radiochromic film is also relatively energy independent, dose-rate independent and it is considered to have a high intrinsic resolution (estimated at >1200 line/mm [91].

In this work, radiochromic film (type MD-55, ISP Technologies Inc. Dosimetry Media, Figure 3) was used as a comparison method to gel dosimetry for measuring the dose distribution of small fields produced by a multi-leaf collimator (field sizes between $18 \times 18 \text{ mm}^2$ and $3 \times 3 \text{ mm}^2$).
1.2.1.3 Thermoluminescent dosimeters

Thermoluminescent dosimeters (TLD) are crystals that can be used as a dosimeter for radiotherapy beams. The electrons excited by radiation in TLDs will become trapped in a higher energy state due to intentional impurities in the crystal. Heating the crystal will cause these electrons to fall back to their ground state and emit light in proportion to the incident radiation, permitting them to be used as a method of dosimetry [92]. By placing several of these crystals within an irradiated region, a measurement of the dose distribution over the volume of the TLD can be obtained on a point-by-point basis. However, the size of a TLD poses a limitation on its accuracy in situations where the dose can vary quickly between regions which are only separated by short distances.

In this thesis, micro-sized TLDs (type Harshaw TLD-100, made from Lithium Fluoride, Figure 4) of the $1 \times 1 \times 1 \text{ mm}^3$ were one of the methods used to examine the dose distribution of small field sizes (4 mm circular diameter and $3 \times 3 \text{ mm}$ collimated field) to provide a comparison measurement against gel dosimeters.
1.2.1.4. Monte Carlo simulations

Monte Carlo simulations refer to the use of computer modelling techniques to model the overall statistical outcome of a situation by individually simulating each individual aspect of that system. More specifically, in radiation therapy, it refers to using a computer simulate and track each individual particle (such as photons or electrons) as they travel through a system, such as a linear accelerator head or patient.

The direction, energy and interaction of each particle is calculated and recorded individually, and from this overall statistical outcomes such as the energy deposited in certain geometric regions can be determined. The number of incident particles simulated is typically in the millions or even billions, possible due to the processing power of modern computers, and each of these is capable of generating numerous scatter particles which are also simulated. There are several programs available for modelling radiotherapy beams made from photons, electrons and protons.
In this thesis, the program Electron Gamma Shower (EGSnrc) (developed by the National Research Council of Canada) was employed to simulate the interaction of radiotherapy particles and target materials such as water, tissue or polymer gels. EGSnrc is a Monte Carlo program for simulating particles at radiation therapy energies and is available under a GNU General Public Licence for academic use. EGSnrc can determine the distribution of energy deposited within a pre-defined volume based on calculations of the probability of interaction for each particle type within a material of known composition, and uses a pseudo-random number generator to randomise the results of individual particles.

The program BEAMnrc is a specialised component of EGSnrc that allows the quick development of linear accelerator geometries. In this work, BEAMnrc was used to simulate the head of a Varian 600C linac irradiating various field size beams unto gel dosimeter and water phantoms for the purpose of confirming out results.

1.3. Thesis’s aims

This thesis develops new types of gel dosimetry to measure and verify the dose distribution of small and micro-sized radiation fields, areas that are currently becoming very important in radiotherapy. The gel dosimeter’s ability to act as both a dosimeter and phantom was used in practical situations such as use in treatment planning around inhomogeneities and for the measurement of secondary radiations. They were also employed to investigate special types of radiotherapy beams for the first time. New types of gel dosimeters were developed in order to achieve these aims. These aims include:

- Using gel dosimeters to determine the dose distribution in small field size radiotherapy beams, down to $3 \times 3 \text{ mm}^2$, sizes which are difficult to measure with conventional techniques such as ionisation chambers [93, [94]. Gel dosimetry scanned using special high-spatial resolution 7 T MRI imaging to obtain dose profiles for these field sizes with sufficient measuring points to compile a full profile, and the results are compared with those obtained from
measurements using other dosimeters such as ionisation diodes, radiochromic film and micro-thermoluminescent diodes.

- The spatial resolution of gel dosimeters was then examined at another step higher in resolution, to the scale on the micrometers level. Polymer gel dosimeters were used to measure the dose distribution in microbeam radiotherapy beams. The geometry of microbeam radiotherapy makes dosimetry inherently difficult. A high resistance gel dosimeter was developed in order to determine the dose distribution of microbeam radiotherapy beams which are characterised by high dose rates. Raman Spectroscopy was used to demonstrate for the first time the spatial measurements of the dose distribution on the micrometre scale.

- The development of a polymer gel that remains clear when irradiated (compared with typical polymer gels which change colour when irradiated). Currently, Raman Spectroscopy is a technique for gel dosimeter measurements; however measurements are limited to surface regions due to the light scattering of polymerised gel dosimeters. In this thesis, work was undertaken to develop a gel that remains clear when irradiated. This would allow future Raman Spectroscopy measurements to be made below the surface of the gel dosimeter.

- An application of polymer gels as a dosimeter and phantom to determine the dose enhancement in IMRT treatments when a metallic implant is in the target as an inhomogeneity.

- The estimation of the effect that photoneutrons produced from high energy (>15 MV) radiotherapy beams using gel dosimeters. The neutrons produced in these high energy beams are typically not accounted during dose estimations, and in this work, gel dosimeters were used to attempt to quantify any difference in dose deposited, as well as a phantom from which gamma rays signifying the presence of photoneutron were detected.
Using modified high resistance gel dosimeters, made suitable for measuring extremely high doses, for the characterisation of capacitor-style linear accelerations for the first time. These types of linear accelerators are characterised by their ability to deliver extremely high dose rates beams, and the possibility of using gel dosimetry as a dosimeter was examined.

In this thesis the application of the gel dosimeters was extended to include the dosimetry of high energy protons for the first time. In this thesis, polymer gels were examined to determine their response for the first time from a high energy (230 MeV) proton beam at the National Cancer Centre in South Korea.

1.3.1. Dosimetry of sub-centimetre radiotherapy fields

Radiation Therapy techniques are continuously being refined to enhance the delivered dose to the target while reducing dose to surrounding tissues, particularly in relation to the application and use of smaller and more tightly collimated radiotherapy beam field sizes [93, 94]. This allows the delivery of radiotherapy treatments that more accurately conform to the target region while sparing surrounding and close by healthy tissues from unnecessary irradiation.

Gas ionisation chambers, currently the primary method of dosimetry for radiotherapy beams, are inadequate for the measurement of field sizes with dimensions in the sub-centimetre range. The relatively large size of these ionisation chambers [85] (minimum in the range of 10 mm$^3$) in comparison to the sub-centimetre radiotherapy beams causes volume averaging in dose measurements [85, 87, 95-97] and the lack of charge equilibrium in such conditions [85, 96]. Thus, ionisation chambers are not a reliable method of dosimetry for such small field size radiotherapy beams. Similarly, thermoluminescent dosimeters are also too large for field sizes of just a few millimetres. Radiographic films do have the resolution needed, but unlike gel dosimeters do not have the potential to measure the distribution in three dimensions, an important factor in radiotherapy beams that have large changes in deposited dose over small volumes and they are not tissue equivalent like gel dosimeters, therefore necessitating tedious corrections.
Hence, alternative methods need to be employed when examining small field dosimetry. Gel dosimetry allows the measurement of the energy deposited from a source of radiation to be measured in a 3 dimensional volume. This makes gel dosimetry a suitable method for measuring the dose distribution of sub-centimetre radiotherapy beams. The resolution will primarily be limited by the resolving power of the scanning technique, reducing the influence of dose averaging. The dose determination for such small fields has attracted many researchers, reflected in the recent surge of papers in the literature. Hence, this aim of the thesis is of high interest and use for radiotherapy techniques.

1.3.2. Microbeam radiotherapy dosimetry using high resistance gel dosimeters

Microbeam radiotherapy is a technique that employs the use of an extremely high dose x-ray beam very quickly (dose rate on order of 90 Gy s$^{-1}$) by very narrow planar or pencil beam geometries. These beams will be usually spaced between 100 and 200 µm apart and each will be in the range of 25 – 90 µm wide [98-103], and to generate the high dose rate, a synchrotron is usually used as the source of radiation. These microbeams strike the target (Figure 5), resulting in portions of the target where an extremely high dose is delivered, and between these regions very little dose is deposited. As previously described (section 1.3.2), this has been shown to be effective at treating tumours regions while reducing side effects.
Figure 5 Diagram of the collimation of microbeams unto a target. The highly irradiated regions are shown in black, the rest of the target receives very little radiation in comparison.

It has been shown that test animals have a much higher survival rate when very high doses of radiation are delivered via microbeam radiotherapy compared to lower doses delivered via flat broad beams [103]. As microbeam radiotherapy treatment is delivered in terms of micrometres, it is essential that the treatment be delivered very quickly, to ensure that subject motion during irradiation does not blur out the irradiated region [100].

The dosimetry of microbeam radiotherapy beams cannot be measured using typical ionisation chambers for the same reasons that very small beams cannot. The effect of dose averaging, disruption of the electronic equilibrium and perturbation of the dose disruption mean that ionisation chambers [85] are inadequate for microbeam dosimetry.

Alternatives methods to ionisation chambers are therefore required for microbeam radiotherapy dosimetry. Possibilities that have been investigated include radiochromic films [104, 105] and metal-oxide-semiconductor field effect transistors (MOSFET) [98, 106, 107]. In addition to the experimental data acquired with film and MOSFETs, Monte Carlo simulations have been performed in order to determine the dose distribution of microbeam radiotherapy [101, 102, 108-110].
In this work and for the first time, the possibility of using polymerising gels was explored as a method of dosimetry for tightly collimated microbeam radiotherapy. Typically, microbeam radiotherapy will involve very high doses, in order of hundreds of Gy), an amount well above the saturation point of a typical polymer gel dosimeter. Therefore, a new special type of gel dosimeter was developed that was capable of withstanding the very high levels of dose delivered, making measurements at these high doses possible. This was made possible by oxygen contamination within the gels, normally a hindrance in gel preparation, and using it as a method of reducing the response of the gel to ranges suitable for microbeam radiotherapy beams. In other words, a limitation/drawback of polymer gels preparation (the exclusion of oxygen to prevent inhibition of polymerisation) is turned around to be an advantage for such dosimeters to be usable at such high doses since they are made highly radiation resistive by the presence of oxygen.

Another face of this challenge is embedded in the conventional scanning procedure. The most common method of imaging used for gel dosimeters is MRI, however, MRI does not have the spatial resolution needed for measuring the dose distribution of microbeam radiation. Of the available alternatives, Raman spectroscopy holds the most promise for high resolution measurements of irradiated polymer gel. Raman spectroscopy allows for a direct determination of the polymerisation of gel [13, 14] and currently has a possible resolution of the order of 1 µm [14].

In this work, a special high resistance type of polymer gel dosimeter was developed and used to record the dose distribution of synchrotron generated x-ray microbeams. The microbeam irradiated regions were examined using Raman spectroscopy, which was able to resolve the irradiated regions. This is the first documented case where gel dosimetry has been successfully used to determine the dose distribution of microbeam irradiation. Several factors such as temperature increase during polymerisation and the consumption and movement of oxygen through the sample were found to be important factors and are addressed in this thesis in detail.
1.3.3. Development of clear-type polymer gel dosimeters

Polymer gel dosimetry holds potential to be an effective dosimeter for dose distributions of Microbeam Radiation Therapy (MRT). However, due to the light scattering effect of typical polymer gels when irradiated (which gives these gels their white colour when irradiated), Raman Spectroscopy is only able to examine the surface of a gel dosimeter, and information regarding the degree of polymerisation within the gel is difficult to obtain.

The possibility of developing a gel dosimeter that remains clear when irradiated is thus an attractive possibility. Such a gel dosimeter would still polymerise when irradiated, but would also remain clear, permitting the use of Raman spectroscopy at depths below the surface for a 3-dimensional mapping technique. Such type polymer gels were successfully developed in this work, opening a new line of application for the use of gel dosimeters.

The light-scattering of a polymerised gel is caused by the polymer structure phasing out of the solution. This is primarily due to the size and shape of the polymer chains that are formed, which is strongly dependent on the relative portions of the gel solution chemicals. Changing the formulation of the gel dosimeter (in particular, the ratio between the monomer and cross-linker) would allow polymer chains to form without having them phase out of solution, resulting in a gel that remained clear after irradiation.

In this thesis, a gel formulation was successfully developed that remained clear after polymerisation, and the process of polymerisation was verified using MRI and Raman Spectroscopy.

1.3.4. Polymer gels used to determine inhomogeneity in very small radiotherapy beams

Patient treatments for various conditions such as cerebral aneurysms warrant the use of a metallic aneurysm clip within the brain region. At a later time, these patients may require radiotherapy treatment, and the presence of a small metallic ‘surgical clip’
implant may influence the dose distribution of this treatment. In this thesis, the possibility of using gel dosimeter/phantoms to determine the effect of these metallic inhomogeneities was undertaken.

Cerebral aneurysms are balloon-like sacs formed in weakened areas of the arteries, with the potential to cause life threatening haemorrhages due to sudden rupturing, strokes, problems due to enlargement of the arteries, recurrent bleeding, hydrocephalus and vasospasm [111, 112]. An arteriovenous malformation (AVM) is a congenital disorder whereby abnormal blood vessels form a tangled web of arteries and arterialised veins. In the absence of capillaries, this creates a direct arteriovenous shunting [113]. The treatment modalities available for these conditions include microsurgery, endovascular embolisation and radiosurgery [114]. Factors that influence treatment decisions include age, neurological status, associated risk factors and angioarchitectural features of the lesion [114, 115]. Patients treated for neurological conditions such as cerebral aneurysms and AVMs sometimes have foreign objects such as aneurysm clips being inserted into their brains [111].

Historically, the first aneurysm clip (made of malleable silver) used to isolate the aneurysm from the artery was used by Walter Dandy M.D. on the 23rd March, 1937 [116]. The design of these clips was improved over time to prevent slippage. Improvements were also made in the materials used to construct the clips. By 1952, Mayfield and colleagues used clips made from stainless steel, believing that it was sufficiently malleable while maintaining adequate spring recoil [115, 117]. Since the introduction of magnetic resonance imaging (MRI) in the neurologic and neurosurgical examination of patients, magnetic compatibility of aneurysm clips has become a crucial requirement. This lead to the introduction of first titanium clips. Currently, most aneurysm clips are made of titanium [112]. These clips are much safer when conducting MRI scanning and produce smaller imaging artefacts than their steel counterparts [111, 114, 118-122].

AVMs were one of the first conditions treated by stereotactic radiosurgery (SRS) [122]. SRS has been a well-established non-invasive treatment modality alternative to surgical treatment of well-circumscribed and small intracranial lesions for over 25 years [122-131]. It offers an alternative therapeutic option to surgical extirpation for
small AVMs with excellent radio-surgical outcomes and obliteration rates. This procedure also has a relatively low risk of side effects. SRS is especially useful for patients with AVMs in deep brain locations and vital lobar areas [122].

When SRS techniques have to be performed in patients with metal implants (such as the aneurysm clip) at the treatment target, the effects of the implant are either not taken into consideration when planning for dose distribution or cannot be predicted correctly by the present treatment planning systems, such as the XKnife radiosurgery treatment or BrainLAB planning system (Radionics, Tyco Healthcare Group LP, Massachusetts). This is because the calculations are based on a homogeneous water equilibrium phantom, without taking the heterogeneity factor into consideration [111]. It is not easy to account for perturbations in dosimetry caused by small objects such as aneurysm clips.

Cheung, Yu, Chan, Ho and Yu [132] simulated the effects of various foreign metal materials such as silver, stainless steel, titanium, and platinum for Leksell Gamma Knife SRS dosimetry using the Monte Carlo technique employing Electron Gamma Shower computer code (EGS4) for calculation. Dose enhancements were observed when metal implants such as aneurysm clips and Guglielme detachable coils (GDC) were placed within the target regions. The effect was most significant for platinum objects due to its high atomic number (Z-value). A high Z-value causes a relative increase in the photoelectric effect. For metal objects with a low Z-value, dose enhancements can only be observed at the superior position of the metal–phantom interface [132].

In 2004, Cheung, Ng and Yu [133] simulated the dosimetry effects of platinum implants on SRS for 4, 6, and 10 MV (energies commonly used in SRS) using Monte Carlo calculations. Their results showed that dose enhancement is a factor of both beam size and energy whereby dose enhancement increases with increasing beam energy but decreases with increasing beam size. These investigations were based solely on simulations and were not compared against any experimental measurements yet been documented in the literature regarding the effects of metal implants such as aneurysm clips on SRS dose distribution.
The effect on SRS dosimetry of metal implants such as an aneurysm clip is of concern due to the close proximity of critical brain structures to the clip and the fact that the treatment area is small when compared to the size of the aneurysm clip (i.e. the clip size is not negligible in comparison with the field size). Therefore the clip may have a considerable effect on the dose distribution. This study is therefore aimed at investigating the effects of an aneurysm clip on the dose distribution of SRS.

In this work, a polymer gel dosimeter phantom was successfully used to simulate a patient head containing an aneurysm clip. This phantom was irradiated by an IMRT treatment plan focused on the location of the aneurysm clip. The polymerised gel dosimeter was compared against a similar control phantom that did not contain an aneurysm clip. The variation in dose distribution due to the presence of an aneurysm clip was determined, and an increase in the local dose delivered to the region around the clip in the path of the x-ray beam was found. In addition, the image artefacts caused by the metallic aneurysm clip within an MRI system were investigated.

1.3.5. Estimation of photonuclear reactions in radiotherapy beams using polymer gels

In recent years there have been several investigations aimed at measuring or estimating the contribution of photonuclear interactions (from high-energy radiation generating photonuclear activation) to the total radiation dose delivered by high energy radiotherapy beams. These investigations measured the contribution of neutron generation from high-energy electromagnetic radiations and electrons through simulations [134-137] and measurements [138-140].

High energy photon or electron beams used in radiotherapy may generate photonuclear interactions within certain targets [134, 141-143]. From these interactions, secondary radiations may also be produced, altering the dose distribution in the target.

While polymer gels are regarded as being close to energy independent [20, 72], a possible slight variation in dose response at higher energies has been reported [18,
21], with certain formulations of polymer gels showing a greater effect than others [2]. One possible reason for this is that these high energy x-ray beams have energies above the threshold for photonuclear reactions in oxygen. These photonuclear reactions generate neutrons, the dose distribution of which is not normally accounted for during treatment planning. Photonuclear reactions also produce other secondary particles such as gamma rays that can be detected to confirm the existence of the high energy photonuclear reactions.

This thesis aims to establish a method of detecting the photonuclear reactions that occur in polymer gels or other oxygen containing materials. A comparison of the gel dosimeter polymerisation at energies below and above the threshold for photonuclear interactions was made. The secondary particles from polymer gels irradiated by high energy beams were measured, confirming the presence of photonuclear reactions. The decay of these secondary particles matched the expected half-life of oxygen.

1.3.6. Extremely high dose rate radiotherapy beams examined using gel dosimetry

As described previously, gel dosimeters have been applied to very high dose rate systems such as a synchrotron. This use was extended to the possibility of using gels as a dosimeter for extremely high dose rates that are characteristic of systems such as injection type linear accelerators.

The Idaho State Induction Accelerator System (ISIS) at the Idaho Accelerator Center (Figure 6) is a special type of linear accelerator that uses a heavily charged capacitor to generate a number of electrons, which strike the tantalum target. This special type of linear accelerator can deliver an extremely high dose rate \(2 \times 10^{12} \text{ Gy s}^{-1}\) x-ray beam. This makes it difficult to determine the delivered dose with conventional techniques such as ionisation chambers, as they become saturated almost instantly.

It was hypothesised that the high resistance polymer gels developed in this work may be a suitable dosimeter for measuring the dose distribution from this special type of
accelerator. This is the first time gel dosimetry has been applied to measurements of this type of extremely high dose rate linear accelerator.

The possibility of using highly radiation-resistive polymer gels as a method of dosimetry for the ISIS linear accelerator system was investigated in this thesis. A depth dose curve using gel dosimetry was obtained and compared against radiochromic film and Monte Carlo simulations to determine the distribution of energy deposited with depth for this system. The distribution of dose measured using all the three methods were found to be similar.

![Figure 6 Idaho Accelerator Center](image)

### 1.3.7. High energy proton dosimetry using polymer gels

Proton radiotherapy techniques are increasingly becoming important [144, 145], as proton beams have several unique advantages that make them highly attractive for radiotherapy treatments. Proton beams have little dispersion, and will deposit a large amount of energy at the end of their maximum path length, a region known as the Bragg peak. Beyond the Bragg peak there is marked reduction in radiation dose. The presence of the Bragg peak can be utilised in radiotherapy, allowing a large concentration of energy to be deposited on the site of the tumour relative to the surrounding tissue.

There have been some investigations in the past to use polymer gel dosimetry as a method of dosimetry for proton beams [146, 147]. These investigations have concentrated mainly on low energy proton beams (<75 MeV). With the development
of high energy proton beams, the possibility of using polymer gels as a method of dosimetry was of interest.

In this thesis, normoxic polymer gel was transported to be irradiated at the National Cancer Center in South Korea (Figure 7) as such a beam was not available in Australia currently. These polymer gels were irradiated by a 230 MeV proton beam. A calibration curve from the irradiated gels was obtained and compared against gel irradiated in Melbourne using a 6 MV photon beam from a clinical linear accelerator. This is the first such calibration of such a high energy proton beam using polymer gels.

Figure 7 National Cancer Center of South Korea
2. BACKGROUND AND THEORY
This chapter is designed to give the reader a basic level of understanding of the physical processes by which polymer gel dosimetry works. Also covered in this section are the physics behind the operation of Magnetic Resonance Imaging and Raman Spectroscopy as methods of scanning polymer gel dosimeters. Finally, the processes by which neutrons are generated from high energy radiotherapy beams are described.

### 2.1. Irradiation and Ionisation Theory

When exposed to radiation, monomer gels will polymerise, a measurement of the incident can be obtained by measuring the degree of polymerisation. The processes that polymer gels undergo during polymerisation have been studied and reported in the literature previously [28, 56, 148, 149]. The basic process involves the irradiation of water molecules separating into free radicals (radiolysis) which then react with monomers in the gel solution to create a polymer [150]. When free radicals are present in the water, they may react with monomers and polymer dissolved in the gel. As the production of free radicals is dependent on the dose delivered to the water, the final degree of polymerisation is also radiation dose dependent.

A vinyl group is part of a molecule that has the chemical structure CH$_2$=CH$. The monomer acrylamide and the cross-linker N' N-methylene-bis-acrylamide (BIS) contain one and two vinyl groups respectively. The double bond within a vinyl group will react when exposed to a free radical or the reactive portion of a polymer chain, joining the monomer to the chain. The final chain is still able to react with further monomers in the solution (Figure 8 and equation (5)). By reacting with a crosslinker, a growing polymer chain can branch in multiple directions (equation (6)). If two reactive sites in polymer chains react with each other, they may join, terminating the growth of polymerisation at that point (equation (7)) and the polymer in total if there are no active sites anywhere within it. This includes the possibility that growing polymer chains may curl around and terminate by linking with themselves.
Acrylamide monomers will form long chains, whereas the 2 double bonds in BIS allow it to form branching chains. Chains of polymers may also wrap around and link up with the chains of parallel forming polymers or link up with themselves. The relative proportion of monomer to cross-linker thus affects how tight the polymer is. This will affect the gel dosimeter’s dose sensitivity and reaction rate [56, 151]. Other monomers and cross-linkers may be substituted for acrylamide or BIS, depending on the gel formulation.

When these gels become polymerised, they are noted for changing colour as polymer chains become too large to remain dissolved in water. This is a feature employed in optical CT measurements [7, 10, 22, 24, 25, 152]. The degree of cross-linking within the sample will influence the level of light-scattering and the polymer gel’s level of opaqueness after polymerisation. This property is important when imaging gels using optical computed tomography (CT) techniques. In this thesis modifying gels such that they remained clear when irradiated (thus possibly making three-dimensional
measurements using Raman spectroscopy possible) by altering the relative proportions of monomer and cross-linker material was investigated.

2.2. The basics of magnetic resonance imaging

2.2.1. Using MRI to image an object

Magnetic Resonance Imaging (MRI) is a technique commonly used in the measurement of gel dosimeters as well as patient analysis in general. This section describes a simplified account of how MRI scanning works.

The basis of operation is that the patient or sample is placed into a strong and nearly homogenous magnetic field ($B_0$). In the gel sample or patient, there are atoms with inherit spin (usually, as in this thesis, singular protons/hydrogen nuclei are examined, but various other atoms can also be examined).

Normally, these nuclei will be aligned at random, and there will be no net magnetisation within the sample (Figure 9(a)). The presence of the MRI scanner’s magnetic field will force all these protons to precess around the axis (labelled the z-axis, Figure 9(b)). The result is that there is a net magnetisation in the direction of the external magnetic field (z-axis, Figure 9(c)).

Figure 9 (a) a group of particles (protons) in a material. Each proton has a spin in a random direction. (b) The addition of an external magnetic field $B_0$ causes each individual spin to precess about the axis of the magnetic field. (c) Therefore, the net magnetisation of the material will be along the direction of the external magnetic field.
A second magnetic field \((B_1)\) is used to tip the nuclei’s net magnetisation (90° in this work, Figure 10). This second field is very short-lived (theoretically, it is instantaneous, but this is impossible in practice), and the nuclei now have their net magnetisation at a 90° angle to the original magnetic field.

With the net magnetisation now in the XY plane, it will undergo two processes. The first is that it will gradually return to be realigned with the main external magnetic field \((B_0)\). The rate at which this occurs is dependent on the surrounding magnetic environment and is therefore affected by the surrounding material. As a result, the rate at which the spins align back to their original position provides information on the material the nuclei is located in. This can be summarised by a single variable, the spin-lattice relaxation rate \((R_1)\), which represents the rate at which the net magnetisation returns to align with \(B_0\). The spin-lattice relaxation time \((T_1)\) is also commonly used, and is inversely related to \(R_1\) as shown in equation (8).

\[
T_1 = \frac{1}{R_1} \quad \text{(8)}
\]

While the net magnetisation is along the XY plane, it will precess about the z-axis. However, the individual spins that make up the net magnetisation will not precess at
identical rates due to the subtle differences in net magnetic field they each experience. These differences are due to the influence of the neighbouring environment. As a result, the group of spins will de-phase, that is the net magnetisation will decrease in magnitude as shown in Figure 11. The rate at which this occurs is called the spin-spin relaxation rate ($R_2$) and again the corresponding spin-spin relaxation time ($T_2$) is related by equation (9).

$$T_2 = \frac{1}{R_2} \quad (9)$$

There are two sources of net magnetisation loss that influence the value of $T_2$. The first is the variations of local magnetic field due to the influence of the nuclei’s magnetic spins upon each other ($T_2$). The second is due to the variations in magnetic field strength resulting from the impossibility of producing a perfectly homogenous magnetic field and the variation of magnetic susceptibility. The variation in magnetic susceptibility depends on the tissue type/material being examined ($T_2^+$). The total decay rate ($T_2^*$) is given by equation (10).

$$\frac{1}{T_2^*} = \frac{1}{T_2^+} + \frac{1}{T_2} \quad (10)$$
In order to extract the $T_2$ value from $T_2^*$, the initial RF pulse, and second RF pulse is applied to flip the magnetisation $180^\circ$ across the x-axis at time ($\tau/2$) as shown in Figure 12. As a result, the order of the de-phasing magnetisations are now reversed, and will re-phase at time $\tau$ as the separation between the fast and slow individual magnetisation within disappears (Figure 13). By measuring the net magnetisation at this time, a signal intensity value relating to the base $T_2$ value (dependent only on the effect of the nuclei’s magnetic spin upon each other) can be obtained.

Figure 12 After de-phasing for a time $\tau/2$, the de-phased magnetisation will be rotated $180^\circ$ about the x-axis.

Figure 13 After the 180° rotation, the net magnetisation will reach a maximum value when the entirety of the magnetisation re-aligns at time $\tau/2$ after the 180° rotation. This is equivalent to a time $\tau$ after the initial 90° rotation.
To accurately determine the value of $T_2$, many such values would need to be obtained. In this thesis, this is done with a multiple echo sequence. As noted, at time $\tau$, the loss of phase due to $T_2^+$ has been restored, and at this point the net magnetisation will begin to de-phase again. By applying another $180^\circ$ RF field at time $3\tau/2$, the net magnetisation can be unified a second time for measurement at time $2\tau$, and this can be repeated indefinitely. This is shown in Figure 14. The value of $T_2$ can thus be calculated. This sequence is called a Multiple-Spin Multiple Echo (MSME) sequence.

![Multiple Echo Train Sequence](image)

**Figure 14** A diagram of a multiple echo train sequence used in Magnetic Resonance Imaging (MRI). The $T_2$ value of a sample can be extracted at times $\tau$, $2\tau$, $3\tau$, etc. by a series of repeated $180^\circ$ RF pulses (at times $\tau/2$, $3\tau/2$, $5\tau/2$, etc.).
An alternative MRI sequence to the MSME is the Fast-Spin-Echo (FSE) sequence, also used in this thesis for 1.5 T measurements. This uses a phase shift between each read-out echo, so that each echo signal applies to a different section of the final image. By doing so, the time required to take the full image is reduced as multiple phase shifted images can be acquired using the same echo train. In this work, 8 echoes was the standard length of the echo train, thus the image acquisition time using an FSE sequence was one-eighth the time required by an equivalent sequence without phase shifts between echoes.

As previously stated, the polymerisation of a gel dosimeter like those employed in this thesis will cause a change in both $R_1$ and $R_2$ (and correspondingly, $T_1$ and $T_2$), with the change dependent on the irradiated dose. It has been reported that the magnitude of $R_2$ variation in a linear portion of polymerisation response is a magnitude greater than for the comparable $R_1$ dose response gradient [1, 3].

### 2.2.2. The resolution of MRI

Theoretically the individual nuclei within a sample can be detected using MRI, however the signal is very weak. Normally, the signal from a small volume is obtained to give information on the rate of net magnetisation signal decay. The small region is termed a voxel (in 3D) or pixel (in 2D), and one limit of their size is the hardware of the scanner. In particular, the precision and strength of the magnetic field gradient that the scanner is capable of. The stronger (steeper) the gradient of the magnetic field is, the less uncertain the localisation is, allowing the scanning of smaller pixels or voxels.

It is for this reason that in this thesis, a focus on using specialised micro-imaging systems was made. In general, clinical systems that are currently used for patient examinations have a 1.5 T strength magnetic field and are capable of a resolution in the order of half a millimetre. For polymer gels irradiated using very small fields and microbeam fields, an increased image resolution was required.
Another factor of MRI image quality is the level of noise present in the readout image. Noise generates uncertainty in the $T_2$ value measurement, leading to uncertainty in dose resolution [153]. Noise is inversely proportional to the square of the pixel size, so doubling the 2D resolution of an image will quadruple the noise. To compensate for this, the simplest way is to take and average multiple images, as the signal-to-noise ratio (SNR) is proportional to the square root of the number of averages [154]. However, this requires quadrupling the scan time to achieve the same level of noise when doubling the resolution. The SNR ratio is increased with field Strength $B_0$ [155], which is a strong incentive to use higher strength magnetic fields when imaging.

In this thesis, specialised micro-imaging systems that have inherently stronger magnetic field gradients (7 T) and are specifically designed to make high resolution images were employed in order to obtain more accurate measurements of the polymerisation of gel dosimeters, specifically in the field of examining the dose distribution of fields that had been collimated to very small field sizes ($3 \times 3$ mm$^2$ and 4 mm circular diameter field size). In addition, the uncertainty of $R_2$ measurements of polymer gel is known to decrease with an increase in the overall magnetic field of the scanner [1]. Such systems have drawbacks compared to their clinical brethren. They are more expensive and their small core size makes them quite limited in terms of the size of samples that can be scanned.

### 2.3. Raman spectroscopy

Incident photons of energy $h\nu$ on a molecule may interact with the electron cloud of the molecule’s bonds. This incident photon will excite an electron into a virtual state. Should the electron fall back to the original state, the resultant emitted photon is of the same wavelength as the incident light. This process is known as Rayleigh scattering and it is an example of elastic scattering as the scattered photon has the same energy as the incident photon. However, if excited electron doesn’t fall all the way back to the original state, but to a higher energy state between the initial and the excited state, then a photon of a longer wavelength than the incident photon will be emitted due to the difference in energy of the electron states and this is an example of Raman
scattering (specifically Stokes Raman scattering), as shown in Figure 15. If the electron falls back to a lower energy state than where it was initially excited from (possible if the electron was already excited when it interacted with the incident photon), then it will emit a photon of higher energy than the incident photon. This is known as Anti-Stokes Raman scattering. In both types of Raman Scattering, the emitted photon will have a wavelength that is different to that of the initial incident light. The difference in energy between the incident and emitted photons is equal to the differences between the energy of the excited electron’s initial and final states. This is dependent on the molecular structure that the electron is a part of. As such, different materials can be characterised by their unique Raman shifts, that is, by the quantity of various wavelengths of light that they emit when exposed to certain wavelength photons [156-158].

Figure 15 Diagram of the energy level changes due to Rayleigh scattering (left), Stokes Raman scattering (middle) and anti-Stokes Raman scattering (right). An incident photon raises the electron into a virtual energy level. If it returns to the same energy level, then it will emit a photon of the same wavelength as the incident, an example of Rayleigh scattering. If it falls to a final energy level that is different to the initial energy level, then it emits a photon with a different wavelength to the incident photon. This difference in energy will depend on the particular molecular structure of the chemical, and therefore can be used to identify it.
Raman spectroscopy uses a monochromatic laser to irradiate samples. If the light returned from the sample is of a different wavelength to the initial laser, then the difference can be used to identify the materials that make up the sample. As monomer and polymer within gels have different wavelengths of light produced by Raman scattering, this allows Raman spectroscopy to act as a direct method of determining the degree of polymerisation (and thus the incident dose) in polymer gels. By comparison, MRI relies on the degree of relaxation of water protons within the polymer network to deduce the degree of polymerisation [13].

Raman spectroscopy has a high intrinsic resolution which made it an attractive method for examining the dose distribution of microbeam irradiated gel dosimeters in this thesis. The resolution of Raman spectroscopy is dependent on the limit of diffraction of the laser at the focus point [14], and theoretically can be of the order of 1 µm. Resolution obtained by Rintoul, Lepage and Baldock [14] was of 0.5 mm. In this work, a focus of approximately 2 µm was obtained for examining microbeam irradiated gels.

The signal induced from Raman scattering is an inherently low compared to Rayleigh scattering, hence the excitation of electrons is typically done with a laser in the visible region of the spectrum. However, this can lead to the generation of a strong fluorescence signal, which masks the Raman signal [55]. The signal produced from Raman scattering is also significantly weaker than Rayleigh scattering, therefore filtering out the Rayleigh signal is important to being able to accurately measure Raman scattering.

### 2.4. Photonuclear reactions in gel

Gels are designed with the intention of mimicking tissue in relation to the spread and deposition of energy from radiation within them, and are thus made of similar materials and density. In particular, gels generally consist of approximately 90% water and so contain a significant amount of oxygen [2, 3, 159].
It is known that photoneutrons can be generated from water and other targets by high-energy photons [141, 142] if the energy of the incident photon is above a threshold level, including the higher-energy photon and electron beams used in radiotherapy. These photonuclear reactions give rise to the production of neutrons and gamma rays that alter the dose distribution within a target compared to lower energy radiations which generate only secondary electrons and photons.

When exposed to a high-energy beam containing photons with energy above 15.6 MeV, oxygen ($^{16}$O), which is present in high concentrations in water, may undergo a photonuclear reaction to form $^{15}$O along the following method as described in equation (11).

$$\frac{16}{8}O + \gamma \rightarrow \frac{15}{8}O + \frac{1}{0}n \quad (11)$$

This $^{15}$O will then decay with a half-life of 122.1 s [160], emitting a positron as shown in equation (12).

$$^{15}_0O \rightarrow \frac{15}{7}N + e^+ + \nu_e \quad (12)$$

The emitted positron will undergo matter-antimatter annihilation with an electron from the surrounding environment, producing a pair of 0.511 MeV gamma rays in opposing directions. The detection of these gamma rays is evidence that a neutron had previously been emitted and the photonuclear reaction described in equation (11) had occurred locally. Therefore, by quantifying the number of gamma’s detected, one can determine the number of neutrons that must have been produced.

As dosimetry gels are naturally sensitive to radiation, the presence of generated neutrons and photons would be expected to cause additional polymerisation. However, neutrons would deposit energy with a different dose distribution due to the neutrons different interaction cross-section compared to secondary electrons/photons produced by lower energy incident photons.
The decay of $^{15}$O (including half-life measurements) within polymer gels after irradiation from high-energy beams and thus the presence of photonuclear activation can be demonstrated using a NaI scintillation detector to detect 0.511 MeV gamma rays from positron-electron annihilation.

### 2.5. Microdosimetry concepts

Dosimetry, the measurement of dose, was developed as a macroscopic quantity for applications such as the measurement of dose to objects such as body tissue. As such, conventional dosimetry is not perfectly well defined for the dose delivered to microscopic objects such as cells. In these cases, an inherit uncertainty is introduced when applying dose to microscopic quantise and volumes [161, 162]. An important factor with such small irradiated volumes is the degree of statistical fluctuation. The associated uncertainty of the energy deposited within a volume is equal to the square root of the number of interacting particles, and within the volumes associated with microdosimetry (with very low numbers of interacting particles), the relative size of the uncertainty is thus increased [161]. Microdosimetry is essential in for dose measurements when using techniques such as microbeam radiotherapy.
3. MATERIALS, METHODS AND PROCEDURES
3.1. Gel dosimeter preparation methods

This chapter covers the overall experimental methodology of preparing and using gel dosimeters for the purpose of this thesis.

3.1.1. Polyacrylamide gel preparation background

There are various types of gel dosimeters, depending on the application intended for, and thus the formulation and preparation method will vary accordingly. However, all gel dosimeters that are based on the polymerisation of monomer as the method of measuring deposited radiation energy share similarities in the method of preparation. Various methods of polymer gel dosimeter preparation have been described in literature [3, 18, 20, 26, 31, 47-49, 63, 71, 81, 163-165].

Maryanski et al. [1] created the first case of a polymer-based gel dosimeter, although gel dosimeters that react to radiation due to other processes pre-date it [32-34, 36]. Maryanski et al. [3] created a gel dosimeter that polymerises due to radiation that was based specifically on the monomer acrylamide, and this formulation forms the basis on which the gel dosimeters of this work derive from.

Since then, there have been many attempts (as reported in the literature) that describe the preparation method for polymer gel dosimeter, as well as changes and improvements to the method as specific reasons have necessitated. Notable among these was the inclusion of an anti-oxidant to the preparation. This freed the perpetration from the necessity of being carried out in an oxygen free atmosphere. As a result, the time required to formulate a polymer gel was reduced significantly [26] and the simplicity of making gels in a clinical environment was improved [26, 63].

This methodology section describes new developments achieved in fabricating and using gel dosimeters during the course of this thesis, the general process for preparing various types of gel dosimeters and how these gel dosimeters were irradiated along with comparison techniques such as radiochromic film. It then describes how these
gel dosimeters were scanned by MRI, Raman spectroscopy and other techniques and how the collected data was analysed, and finally how the gel dosimeters were disposed of afterwards.

### 3.1.2. Innovative methodology aspects of this thesis

This thesis contains several aspects that are notable as being innovative in the area of polymer gel dosimetry:

- **Use of 7 T high resolution MRI and measurement of the dose distribution from small size irradiated fields**

  The use of a 7 T MRI micro-imaging scanner allowed a much higher level of resolution than previously been possible in MRI scanning using the lower magnetic field strengths and magnetic field gradients employed in literature thus far. A reduction in the pixel size down to the range of 30 µm is possible. This was applied to the measurement of dose distribution profiles in polymer gels irradiated by small field sizes, down to 3 × 3 mm size from a linear accelerator. Such field sizes are not currently used in clinical work due in part to the difficulty in obtaining an accurate measurement of the dose delivered.

- **Development of a polymer gel resistant to radiation (low sensitivity gel)**

  Polymer gels are sensitive to the level of dissolved oxygen, which inhibits the polymerisation process. By allowing a known quantity of oxygen to permeate the polymer gel, its resistance to polymerisation can be increased and can be exposed with much higher doses without saturating the level of polymerisation. Oxygen was used to this advantage during synchrotron microbeam irradiation, where a very high flux of irradiation is common.

  Highly resistant polymer gels were developed and employed for determining the dose distribution of synchrotron generated microbeam irradiation, the first time that polymer gel dosimeters have been used for such measurements.
These oxygen diffused gel dosimeters were also employed to measure the dose of a capacitor-based linear accelerator, the Idaho State Induction Accelerator System (ISIS).

- Development of a clear polymer gel
  
  Raman Spectroscopy one method by which a polymer gel can be scanned, but the colour change common in polymer gels can prevent them from being scanned below the surface. A new type of polymer gel that remains clear was developed for this.

- Measurement of the dose distribution inhomogeneity (artefact) within a stereotactic field due to the presence of an aneurysm clip
  
  An aneurysm clip is a small metal clip placed inside the brain, used to prevent blood vessels from rupturing. However, it is possible that their presence could affect future radiotherapy treatments as their presence could cause artefacts in the dose distribution. A polymer gel sample containing an aneurysm clip were irradiated with a typical stereotactic treatment plan and compared to another without to determine the extent of change in dose distribution generated by the presence of the aneurysm clip.

- Neutron activation through irradiation from high energy linear accelerator beams and detection through the induced characteristic decay sequence
  
  When irradiated by sufficiently high energy irradiation, water, polymer gel dosimeters and other materials containing oxygen should emit neutrons. Polymer gels were irradiated with 6 and 18 MV photons to determine the difference in polymerisation induced and to develop a method of quantifying the emitted neutrons.

- Proton irradiation
  
  Polymer gels were irradiated using a high energy proton beam for the first time to determine their response to such beams in comparison to photon beams.

- Gold nanoparticles as a dose enhancement medium
  
  For the first time, gold nanoparticles were added to polymer gels with the aim of demonstrating that they could be used to enhance the delivered dose.
3.1.3. General types of gel dosimeters evaluated in this thesis

Hypoxic polymer gel dosimeters (those that contain very little oxygen within) [26] were used initially in this work when a specific type of gel dosimeter was not required. These were replaced later by normoxic type polymer gel dosimeters as the standard type of polymer gel as normoxic polymer gels were found to be easier to create, more reliable and gave more consistent results.

3.1.3.1. Hypoxic gel dosimeters

It is well known that the presence of oxygen in polymer gels will hinder the polymerisation process [3, 20, 44, 47-49, 63, 70]. For hypoxic gel dosimeters, perpetration is performed inside a sealed glove box as shown in Figure 16. Oxygen is displaced from the glove box’s atmosphere and from within the solution (via bubbling) by a replacement gas that does not interfere with the polymerisation process. Initially, the nitrogen gas was used based on work present in literature [3] but in this work it was decided to use argon as the degassing agent. While both gasses are unaffected by free-radicals, argon has the benefit of being heavier than oxygen (unlike nitrogen), but is also more expensive in general. For our work, the air outlet was located at the top of the glove box, meaning that argon should be more suited to displacing oxygen than nitrogen as it would tend to settle underneath.

The amount of time spent degassing will vary depending on the size and nature of the equipment used, the volume of gel dosimeter to be prepared and the flow rate of argon into the system. In this work a time period of approximately 1.5 hours was used for degassing, and similar values between 1 and 3 hours have been reported in literature previously, depending on the setup employed [3, 47, 166].
Polymer gel dosimeters are prepared in ordinary glass beakers of size suitable to the amount of gel dosimeter solution being prepared. Because adding gelatine to the solution will cause the solution to swell the beaker should be large enough to accommodate this as well as the vortex induced by stirring. However, it should not be too wide else the solution would become too shallow for measurement devices (thermometer, oxygen reader, etc.) to be adequately placed in the solution. In these experiments the volume of the beaker was chosen to be approximately twice the volume of the final solution.

The solution is heated and stirred using a combination of magnetic stirrer and magnetic hotplate, and the temperature measured using a standard thermometer. For hypoxic polymer gels prepared in an oxygen-free atmosphere, an oxygen meter (Model OXI 330, with CellOx 325 sensor) was used to model the oxygen content of the water before the addition of the other chemicals. However, as this oxygen meter
cannot work in a solution containing monomer, it had to be removed before these chemicals where added.

The 4 main components of the polymer gel dosimeters used in this work are de-ionised water, acrylamide, N' N-methylene-bis-acrylamide and gelatine. The relative proportions of each component will vary depending on type and these along with alternative chemical components are discussed in the introduction. For the standard PAG used in this work, the relative proportions of each chemical are (percentages are relative by mass):

<table>
<thead>
<tr>
<th>name</th>
<th>formula &amp; diagram</th>
<th>standard mass %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water (18.01 g mol⁻¹)</td>
<td>H₂O</td>
<td>88%</td>
</tr>
<tr>
<td>Acrylamide (71.08 g mol⁻¹)</td>
<td>CH₂=CHCONH₂</td>
<td>3.5%</td>
</tr>
<tr>
<td>N' N-methylene-bis-acrylamide (154.17 g mol⁻¹)</td>
<td>(H₂C=CHCONH)₂CH₂</td>
<td>3.5%</td>
</tr>
<tr>
<td>Gelatine</td>
<td>(C₁₇H₃₂N₅O₆)ₓ</td>
<td>5%</td>
</tr>
</tbody>
</table>

Table 2 The basic 4 components of polymer gel used in this work. Particular polymer gels may use other or additional chemicals.

Gelatin is a protein and does not have a single molecular structure, but rather varies based on the source.

This is a similar composition as Maryanski et al. [3], but contains 0.5% more acrylamide and N' N-methylene-bis-acrylamide. This composition was chosen as it was found that improved sensitivities could be obtained, particularly if incomplete
degassing of the solution occurred. By increasing the concentration of monomers, the adverse effects of oxygen contamination could be reduced. In comparison to Maryanski’s initial formulation, this one has 1% less water to compensate for the additional monomer.

Water is the solvent in which the other chemicals are dissolved and ensures that the final solution has close to tissue-equivalent properties. Acrylamide is the basic monomer, and N’ N-methylene-bis-acrylamide (BIS) is the cross-linker. The final properties of the polymerisation (including sensitivity) will vary depending on the proportion of cross-linker to acrylamide. The gelatine serves to solidify the solution, ensuring that the polymerisation cannot move.

All the materials required to create the gel dosimeter are placed inside a custom built glove box, (Figure 16) which is then degassed for approximately 1.5 hours consuming approximately 1500 kPa of argon during that time. Using less than this amount was not found to be sufficient to degas a glove box of the size used in this work. Less time could be spent degassing by increasing flow rate, however, the glove box used in this work was not suitable for a higher flow rate.

All the materials to be used are placed into the glove box before degassing of the water and glove box atmosphere begins. After sufficient degassing has taken place, the water is heated to about 40-45 °C. This temperature is slightly less than the suggestions of some literature [3, 47], but sufficient to dissolve the chemicals in solution. The purpose of heating the solution is to ease the dissolving of the BIS, which is typically difficult to fully dissolve, but dissolves faster at higher temperatures. If the temperature is increased too far, then the sample may begin to spontaneously polymerise [47, 164].

The chemicals are dissolved into the solution one at a time. Typically, each chemical is allowed to completely dissolve before adding the next one, but this is not strictly necessary. For a typical formulation as used in this work, acrylamide will dissolve very easily, but BIS and gelatine are more difficult to dissolve into the solution. The order that the chemicals are added in is not important to the final properties of the PAG.
When the chemicals are dissolved into solution, the resultant liquid is mostly clear with a yellow tinge. It is immediately ready to pour into the separated containers that it will be irradiated in (Figure 17). For hypoxic gel dosimeters, this must also be done in the glove box until the vials are completely sealed. The choice of container and reasons for this choice are discussed in another section (3.1.5). The container should also be protected from light to prevent the possibility of photo-polymerisation [3], in this work, this was achieved by wrapping the container with aluminium foil after sealing them (Figure 18).

Figure 17 The final polymer gel solution is poured into vials before sealing them while still inside the oxygen free atmosphere of the glove box.
Figure 18 While still inside the sealed glove box, gel dosimeter containers are wrapped in aluminium foil after sealing to prevent possible photopolymerisation.

After pouring the solution into vials, the samples were typically placed in refrigeration based on the methods suggested previously in literature [3, 47] to set. The amount of time required for the polymer gel to become solid is not long (approximately 2 hours is sufficient), after which the sample considered to be ready for irradiation.

It is not strictly required to place the gel dosimeters in refrigeration, as they will set regardless assuming sufficient gelatine has been mixed into the solution. Examples include Novotný Jr., Spěváček, Dvořák, Novotný and Čechák [18] (BANG-2 type gel), who let their samples set at room temperature (protected from light) over two days. It is also possible, depending on the temperature and gel dosimeter formulation, for the polymer gel to expand when frozen, possibly breaking the container it is placed in (discovered during the course of this work). In this work, clear-type gel dosimeters were typically set at room temperature rather than in refrigeration to avoid the possibility of the gel dosimeter expanding and breaking the container.
After preparation of hypoxic gel dosimeters, it is possible that although oxygen was removed from the polymer gel solution during perpetration, it could re-enter the gel dosimeter afterwards, depending on the condition of the container it was stored in. A solution to this was the addition of a layer of castor oil as mentioned previously in literature [167]. Castor oil is added on top of the PAG solution while it is still in liquid form, and will float on top, but in this work it was not found to provide a significant aid in preventing oxygen from entering the solution. In addition, it was found that in some cases, the oil could mix later with the gelatine solution. With the introduction of normoxic gel dosimeters and the improvements in gel dosimeter storage (by sealing them in a 1 L glass flask to prevent outside oxygen from passing the plastic vial cap), the need of a castor oil barrier has disappeared.

3.1.3.2. Normoxic polymer gel dosimeters

The preparations of normoxic polymer gel dosimeters (those that are prepared in an atmosphere with a standard level of oxygen) [26] are not required to take place inside a glove box. Rather a regular fume hood will work adequately [63, 81], with a net air intake for safety reasons (to prevent acrylamide or other dangerous chemicals from drifting out to the workers).

Normoxic polymer gel dosimeters can be made in a fume cupboard, outside of a glove box, by adding an oxygen scavenger such as THPC (Tetrakis (hydroxymethyl) phosphonium chloride, formula (HOCH$_2$)$_4$PCl, Figure 19) to the solution [31, 49, 75] as used in this work. These reactants consume oxygen in the gel dosimeter solution, allowing an easier and faster creation process than using a degassing process. Our work, based on previous work reported in the literature [80] demonstrated that a 5 mmol L$^{-1}$ concentration to be adequate in removing oxygen from the final PAG solution, as overuse will not only consume the oxygen in the solution, but start to react with free-radicals produced by irradiation before the monomer can, lowering the sensitivity. The THPC or another anti-oxidant is the last addition, in order that the PAG solution may be sealed as quickly as possible from the atmosphere afterwards to
allow only the minimum amount of oxygen from entering the solution after the anti-
oxidant is included.

Although the container is sealed, it is possible that, depending on the container type, oxygen may diffuse through it. This problem was addressed by placing the vials inside another, container (a 1 L round flask) that would be degassed and sealed more thoroughly than the individual vials. This larger container does require degassing, but to a much lesser degree than the degassing required for the hypoxic polymer gel preparation method.

![Chemical structure of Tetrakis (hydroxymethyl) phosphonium chloride (THPC).](image)

Figure 19 The chemical structure of Tetrakis (hydroxymethyl) phosphonium chloride (THPC).

3.1.4. Special type polymer gel dosimeters preparation

3.1.4.1. High radiation resistance polymer gel dosimeters

For the purpose of making gel dosimeters to be irradiated by high dose and high dose rate beams emitted from a synchrotron, a new, different gel dosimeter formulation was required. A synchrotron is capable of emitting a dose-rate of several hundred Gy s\(^{-1}\) and is limited in the accuracy that low-level doses can be delivered due to the speed at which the collimation can be opened and closed. Typical polymer gel dosimeters are not capable of withstanding these high levels of dose without saturation. For typical polymer gels, the range of doses they can accept will vary depending on the composition, but will not be more than 30 Gy or so [3, 80].

The addition of an inhibitor to the gel dosimeter that will compete with the monomer reactions for the free radicals produced will slow the polymerisation process and increasing the dose to which polymer gel can be subjected without saturating polymerisation. As previously described, oxygen is an inhibitor and is present naturally, so it was chosen as the first inhibitor to be used. Aside from the lack of
degassing to remove oxygen from the PAG solution, the method of perpetration for a high-resistance polymer gel is practically identical to that of a standard hypoxic gel.

The amount of oxygen dissolved in solution is dependant on the temperature of the solution and the level of oxygen in the atmosphere. Thus by controlling the temperature of the solution when it is sealed from the atmosphere, the level of oxygen in the solution can be controlled.

The composition of chemicals in the gel dosimeter formulation was chosen to be the same as that of the hypoxic gel dosimeters that were degassed, as shown in Table 2 previously. Because the preparation doesn't require the solution to be degassed, it may be prepared in a fume cupboard instead of a sealed glove box, which eases the method procedure and reduces the time required for preparation.

3.1.4.2. Clear polymer gel dosimeters

A formulation of polymer gel designed to remain clear when irradiated was designed and created for the purpose of being examined though Raman Spectroscopy. The relative proportion of each component was altered, and some new, possibly stronger gelling agents were also experimented with.

A variety of different gel formulations was attempted to make clear polymer gels, focusing on reducing the level or cross-linking and their properties of light-scattering. Another focus was the stability of the gel dosimeters. It was found that polymer gel formulations tried were often unstable, and the monomer contained within would phase separate out of solution into visible white clumps after a period of time. Several different formulations were tried to avoid this problem. The details of these batches are recorded in the results chapter addressing them.
3.1.4.3. Application of gel dosimeters to the measurement of localised dose inhomogeneities induced by the presence of an aneurysm clip within the irradiated field

One of the applications used was to apply polymer gel dosimeters to measuring the artefacts caused by an aneurysm clip (as shown in Figure 20) during stereotactic treatment. The aneurysm clip (obtained from B/BRAUN Australia Pty. Ltd.) is made of a Ti$_6$Al$_4$V titanium alloy (6% aluminium, 4% vanadium) and has been designed in mind of reduced MRI artefacts.

![Figure 20 Yasargil standard aneurysm clip used in this study. This clip has a 7 mm straight blade and is made from an alloy of titanium.](image)

In this work, a 1 L glass round flask was used to simulate the head of a patient. These flasks had an inner diameter of 13.4 cm. Three separate flasks were prepared. Two flasks contained an aneurysm clip (one to irradiate and one to be left unirradiated) and a third (as a control comparison that was to be irradiated) did not. For the flasks that did contain an aneurysm clip, the clip was suspended inside centre of the flask by a string attached to the flask stopper until the PAG solution had solidified as shown in Figure 21. After solidifying, the flask can be orientated in any direction without the aneurysm clip moving from the centre of the flask. As both the flask and the stopper are made of glass, sealing the stopper with vacuum grease effectively prevents any additional oxygen from the outside environment from entering and contaminating the PAG solution. The round flask sample containing the aneurysm clip was then irradiated as described in the following section.
3.1.5. Gel dosimeters containers/vials

Various containers for the gel dosimeters have been considered. The choice of container is very important, as this affects the ability to create, transport, irradiate and scan the gel dosimeters. It has been noted recently that the shape of gel dosimeter phantom will affect its response to radiation [54].

The containers used must therefore satisfy various conditions, such as:

- Should not react with the polymer gel material inside – before, during or after irradiation – in any way.
- Should induce minimal artefacts when scanned. The scanning method will dictate how the gel dosimeter container will influence the results. A container such as a plastic vial will not induce great artefacts over the sample in general.
when using MRI, but will make measurement using visible Raman Spectroscopy almost impossible.

- Should be somewhat sturdy, as transport of the gel dosimeters between locations cannot be expected to be completely smooth.
- Should be easy to fill with gel dosimeter solution, and easy to clean after use to be deposed.
- Ideally, the container should be fairly inexpensive, for economical reasons, for if not that then ideally reusable.
- Should not hinder the transport of the ionising radiation into and out of the gel dosimeter. This generally implies a thin wall, but given the short nature of electron transport, what is satisfactory for photon beams may not be for electron beams. In addition, particularly thicker glass may raise concerns regarding the dose in the build-up region, particularly as this cannot be measured easily.
- Should be preventative of particles other than radiation transporting into and out of the gel dosimeter. This is particularly important regarding the prevention of oxygen from the atmosphere entering the polymer gel, and preventing monomers of the polymer gel passing out into possible contact with people.

The most common container used in this work was a Pyrex glass vial (Pyrex disposable culture tubes, Sigma Aldrich). These are 100 mm long, have an outer diameter of 13 mm and are sealed using a plastic screw cap. The glass is considered a full barrier to oxygen but the cap is not and may allow oxygen to pass through slowly.

To combat this, a layer of castor oil was considered for a time (as mentioned previously) but our results did not show any significant improvement, and in addition it complicated the gel dosimeter creation process. As a result, our attempts at using castor oil were considered non-successful.

An alternative was to use glass vials with glass vacuum sealed stoppers. These vials can be considered to be oxygen proof, but due to the nature of their design, they cannot be completely filled during the preparation process, rather a small gap of air
must be left in them. Provided that they are prepared in a glove box this problem should not be too great, but it still caused problems during this work. In general, portions of the polymer gel near the air were found to be less reactive.

A workable alternative was to use screw cap vials, and place those into a 1 L round flask that could be sealed with vacuum grease and a glass stopper. This allows the vials to be filled completely, and still keep in an atmosphere that was protected from oxygen contamination.

One disadvantage to this method is that orientation of the gel dosimeter during storage. Because the round flask is accommodating a long thin vial, it’s impossible for the vial to be standing vertical during the freezing/solidifying process. For a vial that is completely full, this is not an issue, but if a test where a glovebox air gap is left deliberately in the gel dosimeter is desired, the orientation of the vial and shape of the gel dosimeter cannot be assured when using this storage method.

Barex containers have been tested and used in limited numbers in this work. Because Barex containers are much thinner than glass, they were preferred for electron beam radiation and they are also used by several other researchers.

It has been noted in literature that the shape and volume of the vial used can have an influence on the degree of polymerisation relative to dose [54]. As a result, calibration samples should be placed into vials of the same type as being used for particular dosimetry measurement whenever possible, and this effect noted whenever the calibration samples cannot match the volume/shape of the dosimetry measurement sample.

The particular effects of glass on the final dose distribution, as calculated using Monte Carlo techniques, are assumed to be negligible compared to that of water [168].

Details on vials:

For gels scanned using MRI, the vials used were:
Main vials used for most work (13 × 100 mm) glass vial
Pyrex® disposable culture tubes, screw cap style with white markings spot
7.5 mL
CLS9944713

For polymer gels irradiated by synchrotron microbeams and scanned using Raman spectroscopy, the vials used were:
GPC vials
Kimble Glass Inc.
8 × 40 mm, 1 mL volume
Article number 608342-840
Made in USA

3.2. Irradiation methods

3.2.1. Standard gel dosimeter irradiation techniques

3.2.1.1. General setup procedure

Depending of the aspect to be examined, gel dosimeters can be irradiated through a variety of methods including radiotherapy beams from linear accelerators [3, 48, 71, 147, 169], brachytherapy seeds [170] stand alone sources [3] among others. These are usually further specialised to mimic a particular situation, such as an IMRT plan.

The method of irradiation described previously in literature is generally uniform in approach, with the gel dosimeter phantom placed inside a larger phantom to simulate the surrounding body and to provide a build-up region and scatter.

Some previous reports in the literature have described custom-shaped phantoms from materials such as Perspex [47]. In this work, irradiation of samples usually performed in a water tank (to generate scatter), and comparative ionisation diode measurements in the same. Gel dosimeters were most commonly placed at a depth of 5 cm in water, in line with standard measurement procedures at the locations where the irradiation
via linear accelerator beams took place. To support the gel dosimeter sample, either solid water or glass beakers were used to provide a medium (solid water or water respectively) to generate backscatter (Figure 22 and Figure 23). By comparison, radiochromic film measurements were made using solid water instead of water as the scattering medium.

Figure 22 Basic set up for irradiation of a gel dosimeter in a water tank. The orange material under the gel dosimeter sample is solid water to ensure backscatter is present.
Figure 23 Basic set up for irradiation of gel in a water tank. The gel dosimeter is supported by beakers so that water can surround it and provide scatter.

Irradiation was performed using a Varian 600C linac (capable of 250 MU min\(^{-1}\) at maximum) and Varian 2100C linac (capable of 400 MU min\(^{-1}\)). In order to save time, the highest dose rate available on the machine was normally used, however for PAG and MAG type gels there has been a reported effect on dose sensitivity due to dose rate [2]. In this work, unless otherwise noted all gel dosimeters from the same batch were irradiated at the same dose rate.

A comparison between gels irradiated at 0 °C and ambient room temperature performed by Maryanski et al. [3] suggested that temperature during irradiation did not affect the T\(_2\) measurement results. However, it has been suggested that the temperature polymerisation occurs at can affect the shape of the polymer formed [171, 172], which may influence the final dose distribution measurement.

In addition, the temperature of the gel dosimeter can be expected to increase during irradiation [166, 172]. This is attributed primarily to the energy released as acrylamide.
monomers release the double bonds and form polymers in an exothermic reaction [173]. This temperature increase can be fairly significant in size (>10 K) and is dependent on the ability of the surrounding medium to transport excess heat away [172]. This could cause problems by liquefying local regions of the gel, particularly if the incident dose is not homogenous, thus causing a distortion of the polymerised region.

After irradiation, the gel dosimeter samples will not fully polymerise immediately [70, 172], so a period of time for the polymerisation process to stabilise is needed before they can be scanned. The amount of time between irradiation and scanning is known to have an effect [2, 70] and it is therefore important to scan all gel samples from a batch at the same time. McJury, Oldham, Leach and Webb [70] have suggested a period of 3-4 days, after which >80% of the total polymerisation has occurred is any further polymerisation is progressing slowly in comparison to the scanning time. Some methodologies in literature have, when possible, refrigerated the samples during this time [14, 47].

It has been reported in literature the decision to expose polymer gel dosimeters to atmospheric oxygen after irradiation [70]. By doing so, further polymerisation can be prevented, although the rate of oxygen diffusion is not particularly fast and as a result, possible variances in dose may result from this [70]. However, it has been found that even samples that have been exposed to oxygen for a long time may spontaneously polymerise. However, this is considered rare, and polymer gels are in principal and general use considered to be stable.

3.2.1.2. Profile measurements for small fields

Small fields (in this work, between 18 × 18 mm² down to 3 × 3 mm²) were generated by use of the BrainLAB m3 Mini-multileaf collimator (MMLC). This collimator has leaves that are 3 mm wide at minimum, thus, this is the smallest size field they can produce in this dimension. However, due to the leaves containing tongues and grooves, the effective size of the field is less than 3 mm.
Two sets of data were employed for this work, the first set examining field sizes down to $6 \times 6$ mm$^2$ [169] and the second examined field sizes down to $3 \times 3$ mm$^2$ (to be published in Radiation Measurements). In both works, the basic method of irradiation was the same. Along with a calibration set (irradiated using a standard large field size of $98 \times 98$ mm$^2$), a series of gels were irradiated with the specified field sizes, which were then scanned with MRI to determine the profile and depth dose shape of the incoming radiation.

For each of these measurements, comparison methods were used to examine how well the results measured using gel dosimeters compared. Other methods used were radiochromic film, stereotactic diodes and micro-TLDs, which are discussed in later sections.

Polymer gel dosimeters were irradiated using a 6 MV x-ray photon beam originating from a Varian 600C linear accelerator. This linear accelerator was previously calibrated according to the IAEA TR398 protocol, with local policy implemented with a 2% action limit for recalibration, thus providing a 2% dose delivery uncertainty. Gel dosimeters were placed at a depth of 5 cm in a water tank, which is significantly farther than the $D_{\text{max}}$ value of approximately 1.5 cm. $D_{\text{max}}$ will decrease when the size of the field is reduced [174]. The change in dose with distance at 5 cm is anticipated to be relatively even compared to that at $D_{\text{max}}$, meaning that the effects of possible positioning errors are minimised [175-177]. The distance of the water surface to the target within the linear accelerator (SSD) was set to 95 cm.

Dose was delivered at a rate of 250 MU min$^{-1}$. Calibration vials were irradiated with a wide $98 \times 98$ mm$^2$ field size, under which 100 MU is calculated to be equivalent to 1 Gy. Two calibration batches were irradiated, as this data was collected in two groups.

The first batch of gel dosimeters examined field sizes of $18 \times 18$ mm$^2$ and $6 \times 6$ mm$^2$, and calibration polymer gels were made accompanying it. The second batch of polymer gels irradiated examined a 4 mm diameter circular field and a $3 \times 3$ mm$^2$. With the smaller field sizes, calibration is not easily performed as the standard method (ionisation chambers) suffers problems due to lack of electronic equilibrium and dose averaging [85, 95, 96]. The $3 \times 3$ mm$^2$ field has not been previously calibrated at the
centre in which the linear accelerator used here and thus it was impossible to determine ahead of time the calculated delivered dose. A dose of 3000 MU was delivered as it was estimated that this would deliver approximately 10 Gy to the target.

All fields except the 4 mm diameter circular field were formed by calibration using the BrainLAB m3 MMLC. The 4 mm diameter circular field was formed using a solid lead collimator. The main jaws of the linac were set to $60 \times 60$ mm$^2$ for the 4 mm diameter circular field and $10 \times 10$ cm$^2$ for the $3 \times 3$ mm$^2$ field.

The smallest leaf width available on the MMLC was 3 mm wide. This places a limit on the size of the smallest fields that can be produced, as their width must be an increment of 3 mm. There is no limit on the length dimension of the field size, as the leaves can be moved in and out to any degree. In addition, the centre of the target within the linear accelerator head is placed above the line between the two most central leaves. As a result, the smallest width field (when only one leaf is opened) cannot have the target placed above the centre of the field width; rather it must be placed along one of the edges at least. The smallest width field size that avoids this asymmetry is 6 mm. Because of this, in the case of the $3 \times 3$ mm$^2$ field, the orientation of the gel or measurement medium is particularly important. Figure 24 shows the directions of the x and y-axis, in which gel, film and diode measurements were compared.
3.2.1.3. Depth dose and scatter measurement for small fields

Depth dose measurements using gel dosimeters were made by placing them in water. Short depth dose measurements were made by measuring the dose along the vial’s diameter, and long distances by directing the dose long the vial’s length. Irradiations were made using a Varian 600C linear accelerator with a dose rate of 250 MU min$^{-1}$. The front end of the gel sample was placed 95 cm from the target inside the linear accelerator.

To determine the effect of scatter contribution to dose deposited by radiation, thin vials of normoxic polymer gel (which would not contribute much scatter themselves due to their small volume) were irradiated in air and in water. These were compared against each other, to determine the degree to which radiation scattered from the surrounding water influenced the polymerisation of the gel. For the vial surrounded by water, the top of the vial was levelled with the water surface. The vials had a flat base, an outer diameter of 8 mm and a length of 40 mm including cap. This is shown in
Figure 25. The field sizes for depth dose and scatter measurement were made for $3 \times 3 \text{ mm}^2$, and, $98 \times 98 \text{ mm}^2$ collimated fields. Depth dose measurements were made of these gels using MRI to determine the polymerisation in each gel.

![Diagram showing the comparison between irradiation scheme for vials irradiated with (left) and without (right) scattering medium (water).](image)

3.2.1.4. Clear type gel dosimeter irradiation

Clear gels preparation requires the same basic steps, but uses a different combination of chemicals to achieve a special gel that does not change colour when polymerised, instead remaining clear.

Several different variations of clear gel were developed in the course of this thesis (described individually in the relevant results section). As part of this, one change that was made was the introduction of alginate, an alternative gelling agent to gelatine. Alginate was investigated as being a possibly stronger gelling agent, allowing it to compose a lesser portion of the final gel solution compared to gelatine, hence allowing more monomer within the gel.
In samples of gel using alginate, it was combined with calcium carbonate and GDL to control the rate at which the gel solidified. The combination of chemicals listed below was found to solidify in a period of time between two hours and one day, making it suitable for the gel preparation process.

\[
\text{Alginate} = 0.02 \times \text{mass of water in gel solution}
\]

\[
\text{CaCO}_3 - \text{calcium carbonate (CaCO3) } = 20 \text{ mmol L}^{-1}
\]

\[
\text{D-\(\text{(+)-Gluconic acid}\ \delta\text{-lactone (C}_6\text{H}_{10}\text{O}_6\) (GDL) } = 20 \text{ mmol L}^{-1}
\]

![Chemical structure of GDL.](image)

### 3.2.2. Radiochromic film irradiation procedure

Radiochromic film was irradiated as a comparison to gel dosimeters, and irradiation was performed under the same conditions. In this work, Gafchromic film MD-55 (ISP Technologies Inc. Dosimetry Media, Type MD-55) was used. Film was handled using gloves to reduce the possibility of damage and contamination from affecting them, as in accordance with guidelines suggested by the AAPM [88]. Each piece of film was marked at the corners to identify the coating direction; this orientation was maintained during irradiation and film readout.

MD-55 Gafchromic film was not placed in water as gel dosimeters were, but rather between sheets of solid water which was used as the scattering medium. For calibration measurements and profile measurements of small fields, the linear accelerator beam was directed vertically downwards to the target. This setup is shown
in Figure 27. For depth dose measurements, the x-ray beam was directed horizontally to the side of the film.

Films were irradiated with small field sizes that matched those delivered to gel as a comparison, although the absolute doses at times varied because the sensitive range of radiochromic film doses not necessarily match that of gel. For depth dose measurements, the same setup was employed, but with the incident beam directed from the side. A series of films irradiated by known calibration doses using a full beam \((10 \times 10 \text{ cm}^2)\) were also irradiated to determine the response of the film.

![Figure 27 The setup of film wedged between sheets of solid water during irradiation for field profile measurements.](image)

For work related to aneurysm clip measurements, EBT type GafChromic film (International Specialty Products, Wayne, NJ) was employed. Film samples were cut into small pieces (each marked in a corner to retain orientation). Pieces of film were
irradiated for calibration and used for irradiation under the stereotactic field (section 3.2.6.2).

### 3.2.3. Ionisation diode irradiation procedure

Diode measurements were made using a Scanditronix Wellhofer SFD stereotactic diode detector. For profile measurements, the diode was placed into a water tank at 5 cm depth below the surface, and the water tank placed at 95 cm SSD. For depth dose measurements of field sizes varying between 98 × 98 mm$^2$ and 3 × 3 mm$^2$, the diode was moved between 11 cm below the water surface to 1 cm above the water surface, using a ‘stop and shoot’ method to determine the measured dose relative to a reference diode in 1 mm increments. The diode detector has an active area of 1.1 mm$^2$ and a thickness of 0.3 mm.

### 3.2.4. Micro-TLD

As a comparison method to gel dosimeter measurements for small fields (4 mm diameter circular and 3 × 3 mm$^2$), micro-TLD’s were employed for profile measurements. Micro-TLDs used in this work (type Harshaw TLD-100) have dimensions 1 × 1 × 1 mm$^3$ and are made from Lithium Fluoride. The relative proportions of Li isotopes in this type are 7.5% $^6$Li and 92.5% $^7$Li [178]. For irradiation, they are placed into a groove made into solid water that has space for 7 Micro-TLDs placed into a straight line. These were placed behind the equivalent of 5 cm and above 10 cm (to provide backscatter) of solid water and then irradiated with a 3 × 3 mm$^2$ collimated x-ray beam (with the TLD’s aligned along both the x and y axis) with 600 MU (estimated dose of 2.7 ± 0.1 Gy) and a 4 mm diameter circular field with 350 MU (calculated dose of 2.05 ± .04 Gy).

Because of the expected asymmetry of the field (particularly the 3 × 3 mm$^2$ field), and small number of TLDs in comparison to the size of the fields examined, each axis was measured 3 times. Once with the centre of the beam directed at the second from the end of the 7 µ-TLD series (Figure 28), and once directed towards the middle. Together, the 3 profiles were used to establish a profile of the dose distribution.
Figure 28 Diagram of the beam placement for a $3 \times 3 \text{ mm}^2$ field in relation to the position of the micro-TLDs (looking alone z-axis). Two sets of micro-TLDs were irradiated for each field, one time aimed at the 6th micro-TLD, and one time at the 2nd. Each µ-TLD has dimensions of $1 \times 1 \times 1 \text{ mm}^3$.

After irradiation, the Micro-TLDs were read using a Harshaw TLD System 5500 Automatic TL Reader (running WinREMS software, Saint-Grobain Crystals & Detectors) in order to determine the amount of energy deposited. The micro-TLDs were then irradiated with a uniform beam from a $10 \times 10 \text{ cm}^2$ beam to determine each micro-TLD’s individual dose response, and thus determine the dose each micro-TLD had received during small field irradiation.

### 3.2.5. High dose rate and microbeam irradiation

#### 3.2.5.1. High dose irradiation by a linear accelerator

Two sets of high resistance gel dosimeters (both using the same chemical formula) were irradiated. The first set was to investigate the possibility that oxygenated polymer gels could polymerise, the second to help quantify their properties.
Both sets of gel dosimeters were irradiated by placing the samples in water at 5 cm depth and with an SSD of 95 cm. They were irradiated by a Varian 21EX using a 6 MV beam at a dose rate of 600 MU min\(^{-1}\).

The first set of gel dosimeters were irradiated in various types of glass vials to 200 and 225 Gy in increments of 50 Gy until polymerisation was observed. These were irradiated using a 10 \( \times \) 10 cm\(^2\) field from a 6 MV linear accelerator. For this irradiation, 1 Gy was equivalent to 100 MU.

For the second set of high resistance gel dosimeters, samples in standard 10 cm long glass vials were exposed to a 6 MV wide beam (15 \( \times \) 15 cm\(^2\)) beam to determine the required dose to polymerise gels that had been fully exposed to oxygen to preparation.

Doses of 0, 50, 100, 150, 175, 200, 250, 300 and 350 Gy (irradiated at 98.4 MU Gy\(^{-1}\)) were delivered to the high resistance polymer gel for form a calibration set of data. It should be noted that the expected calibration using a large field such as this is expected to differ from that of a small or microbeam field due to variations in oxygen volume and the electron scattering conditions.

### 3.2.5.2. Microbeam irradiation by a synchrotron

Microbeam irradiation is irradiation by beams which have been collimated such that at least one of their dimensions (length or width) is in the micrometre range \([99, 102, 103]\). In addition, the planned benefits of microbeam radiation come from doses which are both very high and delivered at a very high rate. Currently, these properties are achieved by use of a synchrotron to generate the beam.

Gels samples were irradiated at the SPring-8 synchrotron on the BL28B2 beamline, located in Hyogo, Japan. The incident beam has a median energy of 110 keV and is polychromatic. The collimator was made from tungsten with 25 \( \mu \)m gaps made from kapton spaced 200 \( \mu \)m apart (centre-to-centre). The microbeam array consisted of 5 beamlets, and larger arrays were made by combining multiple irradiations with movement of the gel location to simulate a greater number of beamlets. The gels were
irradiated with varying levels of dose, and the uncollimated dose rate was approximately 90 Gy s$^{-1}$. Larger gel samples were also irradiated using board beams (1 $\times$ 10 mm$^2$), and doses were delivered in 10 second increments to prevent possible damage to the collimator.

Figure 29, Figure 30 and Figure 31 show the set up of gel dosimeter irradiation. From this camera angle, the beam travels from left to right, passing through a collimator that divides the beam into a set of micro-planar beams, each 25 µm wide. The beams each have a length of 10 mm, although this can be increased up to 30 mm. The total extent of the microplanar beams is 1 mm, but by using a step-and-shoot methodology, where the sample is moved after each set of irradiation, larger regions can be irradiated using microbeams.

Figure 29 Photograph of the beam tubing emerging from the synchrotron. The beam moves from left-to-right in this photograph.
Figure 30 Photograph of the collimator grill (on the left) and the dose measurement chamber (centre) of the synchrotron beam. The gel dosimeter sample to be irradiated can be just seen on the right (see Figure 31 for clearer view of gel sample in set-up).

Figure 31 Sample of gel dosimeter (in a rectangular quartz vial) to be irradiated using a synchrotron microbeam.
In addition to the standard and oxygen-saturated samples, polymer gels that contained gold nanoparticles throughout the solution were also irradiated under the synchrotron beam.

### 3.2.5.3 Gel dosimetry measurements of the ISIS accelerator

Polymer gels of high resistance type were employed to try and quantify the Idaho State Induction Accelerator System (ISIS) as a comparison method. This linear accelerator can deliver x-rays or electrons beams in a series of pulses that deliver a large amount of dose very rapidly to a target. As such, the dosimetry of this system is not simple to quantify. Figure 32 shows the setup used in this work.

![Figure 32 The setup for gel measurements using the ISIS linear accelerator.](image)

The linac was used to expose gel dosimeters with a 3 MeV beam (x-ray and electron) with an estimated dose rate of approximately 60 Gy per 35 ns. Multiple pulses of x-rays are normally employed to increase the delivered dose. X-rays are produced by having electrons strike a Tantalum target.

### 3.2.5.4 High dose rate proton beam measurements

Normoxic polymer gel samples were irradiated from a proton beam (230 MeV) located at the National Cancer Centre in South Korea with a range of doses between 0 and 32 Gy. Irradiation set-up gave an output factor of 1.3231, or 1 Gy equal to 75.58 MU.
Polymer gels were placed inside a foam medium, surrounded by solid water (19.3 cm in front of the sample and 7 cm behind). This setup was employed to ensure the polymer gels were placed to cover the region of the spread out Bragg peak (8.7 cm width) and the adjacent drop off in dose in the region immediately afterwards. A setup of irradiation is shown in (Figure 33). Gels were placed horizontally during irradiation as shown in Figure 34.

In addition, a series of gel dosimeters from the same batch was retained in Australia and irradiated with a 6 MeV beam from a Varian 2100C located at the William Buckland Radiotherapy Centre. A $20 \times 20 \text{ cm}^2$ field size was used, with the gel dosimeters placed into water at 5 cm depth, and the SSD value of 95 cm. This data was irradiated with a set up that gave a total output factor of 1.04, or 1 Gy being equal to 95.7 MU. The dose rate was 400 MU min$^{-1}$. These gel dosimeters were irradiated to doses between 0 and 40 Gy.
Figure 33 Photograph of polymer gels within foam/solid water, to be irradiated using a 230 MeV proton therapy beam.
Figure 34 Setup of gels irradiated by proton beams at the national Cancer Centre in South Korea. The gels are placed behind 19.3 cm of solid water. A model of the dose distribution from a proton beam is shown underneath the diagram, the Bragg peak representing the region of high dose is aligned with the position of the gel dosimeters.

### 3.2.6. Application – measurement of artefacts generated by an aneurysm clip

**3.2.6.1. Gel dosimeters**

After preparation in 1 L round flasks, the gel dosimeters were to be irradiated using a Varian 2100C linac. In order to mimic a stereotactic radiosurgery treatment, each flask to be irradiated was attached to a stereotactic head ring as shown in Figure 35. This image also displays the co-ordinate system used in this work.
Figure 35 Stereotactic Radiosurgery set-up showing the flask filled with gel dosimeter representing the head for stereotactic radiosurgery, along with the co-ordinate system (note that due to the angle, the x-axis shown is negative).

Following setup, the flask was subjected to a radiosurgery treatment procedure that mimicked the treatment of a patient. A single isocentre treatment plan consisting of four noncoplanar arcs was developed using the XKnife planning system to produce a nominally spherical dose distribution centred about the aneurysm clip if present and in the equivalent region if the clip was not present. A total dose of 15 Gy (± 2 % dose uncertainty) was delivered to the isocentre by a series of 6 MV photon arcs. The beam was collimated to a circular field of 20.0 mm diameter. The exact dose delivery of the 4 arcs is listed in Table 3.
### Table 3 Beam details for SRS procedure

<table>
<thead>
<tr>
<th>Arc</th>
<th>Dose delivered</th>
<th>Gantry start angle (degrees)</th>
<th>Gantry end angle (degrees)</th>
<th>Couch angle (degrees)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.5Gy</td>
<td>30</td>
<td>330</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>2.7Gy</td>
<td>305</td>
<td>240</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>4.9Gy</td>
<td>30</td>
<td>150</td>
<td>45</td>
</tr>
<tr>
<td>4</td>
<td>4.9Gy</td>
<td>150</td>
<td>30</td>
<td>90</td>
</tr>
</tbody>
</table>

#### 3.2.6.2. Radiochromic film

When irradiating radiochromic film using a SRS field, the films were each immersed in spherical glass flasks filled with water, identical to those used in gel irradiation. Each flask contained a Perspex sheet placed centrally. Each Perspex sheet was $140 \times 20 \times 2 \text{ mm}^3$ block with a $25 \times 5 \text{ mm}^2$ rectangular hole drilled down the central axis. The central hole of one sheet was filled with the clip and the second sheet’s central hole was filled with water as a control as shown in Figure 36. Each piece of $2 \times 5 \text{ cm}^2$ film was attached on two sides of a Perspex sheet. The combined flask of films was fixed in an in-house clamp on the couch. A nominal dose of 6 Gy was delivered to the isocentre by one SRS arc. This arc began at a gantry angle of $270^\circ - 90^\circ$ with the couch at $0^\circ$. Two flasks, one with and one without the presence of a clip were irradiated under same conditions.

![Figure 36](image-url) **Figure 36** Setup of the radiochromic film irradiated to investigate artefacts induced by an aneurysm clip.


3.3. Introduction to MRI scanning

Magnetic Resonance Imaging is a popular and well-studied technique used in gel dosimetry as a method of determining the level of polymerisation [1, 46, 50, 51, 54, 179]. The polymerisation of a gel dosimeter due to energy deposited from incident radiation generates a reduction in the spin-lattice relaxation time ($T_1$) and the spin-spin relaxation time ($T_2$) [3, 47]. When measuring polymer gels, measurements of $T_2$ provide generally better images with a larger change in magnitude and higher signal-to-noise ratios (SNR) than $T_1$ measurements [3].

The value of $T_2$ is inversely proportional to dose, and the spin-spin relaxation rate ($R_2$, equal to $1/T_2$) is sometimes used instead, both give the same information. The $T_2$ and $R_2$ values of a sample in a volume can be determined by using MRI scanning and combining the echo images so produced.

While being scanned, polymer gel samples will be heated by the RF waves of the MR system [46, 180]. As the measured $T_2$ value is sensitive to temperature [46, 151, 179], a change in temperature during scanning could produce misleading results. This problem is accentuated with higher strength fields and longer scans. To counter this problem, whenever high strength fields were employed for scans that were expected to take long periods of time (> ~1 hour), the samples were temperature controlled.

3.3.1. Standard scanning (1.5 T)

In this study, a clinical Picker (now owned by Philips) “Edge Eclipse” 1.5 T MRI scanner with software T55B-1295 was used to make $T_2$ maps of gel dosimeter slices. This machine is used for patient studies and is large enough to accommodate a patient’s body.

Often, MRI machines such as the one used in this work will include a “head coil”, which is used for imaging the head specifically. The head coil provides a more even magnetic field inside it than could be achieved using the main body coil, thus generating higher quality images. The transmitter/receiver head coil was employed in
this work to image gel dosimeters as it provided higher resolution. Multiple gel dosimeters were imaged simultaneously to reduce the required scanning time. Each batch of gel dosimeters was imaged multiple times, with the positioning of individual PAG samples in the scanner altered between scans in order to detect and reduce the effect of any field inhomogeneity. An image of a set of gel dosimeters being imaged is shown in Figure 37.

![Figure 37 A photograph of a typical gel dosimeter scan using the 1.5 T MRI scanner “Edge Eclipse” made by Picker, located at the Western Private Hospital’s MIA clinic (Victoria, Australia). The gel dosimeters are placed into the head coil, and supported so that they are located within the central section of the field, increasing the field uniformity.](image)

Generally the number of gel dosimeters being imaged does not equate the full volume of the head coil and thus the gel dosimeters will need to be supported in order to place them in the middle, where the magnetic field is most homogeneous. Gel dosimeters were placed in the horizontal position when being scanned, such that the length of the vial was parallel to the z-axis of the machine. Unless otherwise specified, the vials
were placed such that the face/side closest to the incoming irradiation was placed upwards for consistency.

Due to the restrictions on possible scanning methods available on this machine, a Fast-Spin-Echo (FSE) sequence was employed. The individual parameters of TR, TE and listed separately for each scan, in the results section.

### 3.3.2. 4.7 T scanning

A 4.7 T small animal MRI scanner (Bruker) was used to perform high resolution imaging of gel dosimeters. The core size of used in this work was approximately 10 cm. An image if the scanner is shown in Figure 38. An Echo Planar Imaging Sequence (EPI) was employed for measurements using the 4.7 T scanner in order to obtain $T_2$ maps of data. The individual sequence settings are described in the respective results section. This machine was used to obtain higher resolution images than what was capable using a 1.5T MRI scanner, and was employed as part of the measurements made for photonuclear effects in polymer gel.
3.3.3. 7 T scanning

The Bruker Advance 300 MR micro-imaging system, a 7 T MRI scanner, was used in this work and is shown in Figure 39. This system differs from those used to typically study humans due to the increased magnetic field strength and decreased core size. The core space used in this work had a diameter of 1.5 cm, providing a limit on the maximum size sample that can be imaged and only allowing a single sample to be scanned at a time. Slightly smaller or larger core sizes are possible, although larger core sizes will result in a loss of some spatial resolution, and smaller cores would demand that the sample being imaged be correspondingly smaller as well. The scanner is orientated such that the z-axis is vertical, and samples of the gel dosimeters or other material are placed vertically within the machine from the bottom.
This scanner images $^1$H at 7.0 T, 300.18 MHz. Using this scanner, it became possible to scan gel dosimeters at a resolution of just under $30 \times 30 \, \mu m^2$ pixel size. As it is known that scanning temperature will influence the $T_2$ measurement [46, 151, 179], any samples that were scanned for long periods of time were maintained at $26 \pm 1 \, ^\circ C$ during scanning using a nitrogen cooling system.

The basic scanning sequence used for this work is shown in Figure 40. It is a Multiple-Spin Echo Sequence, with the number of echoes usually recorded being 128
or 256. Specific details for the scanning sequence are listed in the corresponding results section.

Figure 40 A diagram of the Multiple-Spin Multiple Echo (MSME), sequence used to scan gel dosimeter samples using the Bruker Advance 300 7 T system at high resolution (<100 µm pixel size).

### 3.4. Raman spectroscopy

In this work, Raman Spectroscopy was performed using a Reinshaw RM2000 system with a 10× lens, resulting in a focal size of approximately 2 µm. This is an upper limit to the resolution of the scan. The lens employed as a working focal distance of 8 mm, which is the maximum depth into the sample that can be examined (including the glass vial). In this work, spectra was obtained generally at the surface of the polymer gel samples, behind the <1 mm of glass.

The gel dosimeter sample inside a glass vial was fixed to a stage underneath the microscope and moved into position by visible eye. After positioning, further
movements can be made by moving the stage and this can be controlled by the associated Raman system to within 0.1 µm.

In this work, a green laser of 514 nm was used in this work to examine the spectra produced from irradiated and unirradiated polymer gel. A near-infrared laser (782 nm) was also used in a few particular samples, but in general more reliable success was achieved using the green laser. The power of the laser at the sample was measured to be between 9.5 and 13 mW. A photograph of the set-up taken during the scanning process is shown in Figure 41.

![Photograph of a gel dosimeter being examined using Raman Spectroscopy. Due to the brightness of the laser and the possibility of reflection, protective eyewear must be worn during use.](image)

Raman Spectra were obtained as point measurements, where the reflected spectra from a single point was acquired, and as linemaps in order to obtain spatial data. A linemap is a series of spectra taken at regular intervals in order to determine how the spectra changes with position (Figure 42). In this work, the ratio of the peak volume
(area under the peak) for the peaks located at 2940 cm$^{-1}$ and 3040 cm$^{-1}$ in the scanned spectra was used.

![Diagram showing the method by which a linemap is produced](image)

**Figure 42** Diagram showing the method by which a linemap is produced. In this example, the volume of a peak located between 100 and 200 cm$^{-1}$ in each spectra is used to generate the final linemap.

Spectra could be obtained over a pre-defined series of wavenumbers. The larger the extent of wavenumbers examined, the longer a scan of that region would take. Measurements of the spectra for single points were made for Raman shifts (wavenumbers) between 100 and 3200 cm$^{-1}$, while linemap measurements, while linemap spectra were made between 2758.12 and 3229.12 cm$^{-1}$. The reduced range of spectra acquired for linemaps allowed them to be performed much more quickly than the time employed for a single point spectra as a change in filter (internal to the machine) was not required mid-scan.

The same region could be examined multiple times in order to improve the signal-to-noise ratio. In this work, the time used to acquire 1 spectrum measurement made between 100 and 3200 cm$^{-1}$ was 65 seconds, whereas a single point measurement of a linemap spectra took approximately 3 seconds. In order to improve the SNR ratio
during linemap measurements, the spectra at each point was recorded 4 times and averaged to reduce noise. Prior to linemap measurements, single spectra measurements were made at each end to ensure a good signal collection.

### 3.5. Radiochromic film

#### 3.5.1. Radiochromic film scanning method

Radiochromic film was scanned using a standard transmission scanner, a method that as been reported in previous work [181]. In this thesis, the scanner used was an Epson Perfection V700 Photo scanner, set to scan via transmission mode. This scanner uses a white LED, and the image recorded is done so in TIFF format. It was been previously noted that any effect that a scanner light would have on the film should be negligible due to the short time of exposure [182]. The scanner was set-up so such that output intensity was linear with respect to transmission of light through the film. For measurements of MD-55 film used for small field measurements, the scanner was set to analyse the film at 3200 dpi, which translates to a pixel resolution of 7.94 µm, or 1 mm being 125.98 pixels.

For the images of radiochromic film, the red portion of the 3-colour scale, which is the most sensitive colour for this dose region [181], was analysed. The different colours of the RGB colour map are useful for different ranges of doses, with red being the most sensitive for low doses, and blue more suitable for high doses [183].

Scanning the same sample 5 times in a row demonstrated that there appears to be a heating effect of the scanner that affects the transmission properties of film, so this should be taken into account. This has been reported previously [183].

Scans of radiochromic film (EBT type) used for measurements of aneurysm clip artefacts small field sizes and for these measurements at a resolution of 1200 dpi, and averaged 3 times to reduce noise. Data smoothing with a linear least-squares fitting and a second-degree polynomial was performed on the profile data imaged near the aneurysm clip to remove fluctuations in the profile curve.
3.5.2. Radiochromic film analysis method

Scanned data from radiochromic films were analysed using MATLAB software. For calibration film samples, a square ROI was made in the centre of the film and the mean and standard deviation of the transmission was calculated.

For small field profile measurements, several (10) repeated line profiles were made across the irradiated region and averaged in order to improve the signal-to-noise ratio. Both the x and y-axis were analysed separately to determine if there was any variation between them, particularly for the $3 \times 3$ mm field, which was expected to show some asymmetry.

3.6. Data analysis

3.6.1. MRI analysis

An MRI scanner will initially produce data as a series of echo images of a single slice through the sample. Once obtained the MRI data will need to be analysed and combined to create a $T_2$ map from the series of echoes. This is done on a pixel-by-pixel basis, where the series of echo signal intensity value at a certain point are fitted to the equation (as mentioned previously in theory section 2.2):

$$f(t) = a \times e^{-\frac{t}{T_2}} + c$$

An example of a series of echo images is shown in Figure 43. It can be seen that over the time that the echoes were acquired, the intensity of the echo signal over the entire image decreased.
Figure 43 A series of 39 echo images from a T₂ MRI scan. Each scan is taken at a time TE after the previous.

Each point in the image needs to be fitted to determine the value of T₂ at that location. Figure 44 the shape of the decay is shown for a single pixel in the series of echo images.
Figure 44 The decay of the $T_2$ signal. Each pixel has the echo intensity measured at $t$, $2t$, $3t$, etc. In this way, the value of $T_2$ can be calculated.

Depending on the particular MRI scanner involved, this process may or may not have been automatically performed at the centre where the scan takes place (listed in Table 4).

**Table 4 List of MRI scanners used in this work**

<table>
<thead>
<tr>
<th>Scanner</th>
<th>Strength</th>
<th>Pre-fits $T_2$ image?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Picker Eclipse</td>
<td>1.5 T</td>
<td>Yes</td>
</tr>
<tr>
<td>4.7 T Bruker</td>
<td>4.7 T</td>
<td>No</td>
</tr>
<tr>
<td>7 T Bruker Advance 300 MR micro-imaging system</td>
<td>7 T</td>
<td>No</td>
</tr>
</tbody>
</table>

A series of programs written in MATLAB (The Math Works, Inc., Natick, Massachusetts, USA) code were developed in-house in order to analyse the collected MRI data.

The primary code named ‘T2Fit’ was developed to create $T_2$ maps from a series of echo images. A flowchart of the program is shown in Figure 45.
Figure 45 A flowchart of the fitting program created by Christopher Wong (the author) to produce T₂ maps.
The program requires the following input from the user each time it is run:

- The size of the image (image matrix size). The program is designed to be capable of handling images in which the x and y matrix size are not the same, but such instances are rare.
- The number of echoes per image.
- The choice of which slice to create a $T_2$ map from (if not all of them).
- The value of $TE$ (the time spacing between each echo).
- The bit size of each pixel. The program is designed to be capable of handling a variety of standard possible values (8, 16, 32 and 64-bit images), although the majority of images analysed in this work were 16-bit.
- The location of the raw data in computer memory (in terms of a filename).

From this input, the program determines the size of the data that needs to be analysed, and automatically names each slice sequentially.

The program calculates the $T_2$ map on a pixel by pixel basis using a fitting algorithm. The program will examine the data before analysing it to determine if it is a region of interest (by determining if the echo intensity at that point for the first and last slice differs by more than a pre-set value). If the point is in a region of interest, it will make a fit to determine $T_2$ at that point, but if the pixel is not in a region of interest, it will automatically skip calculating $T_2$ and assign it the value of –1. This process saves a significant amount of time, depending on how much of the image is of the gel dosimeter and how much is empty space surrounding the gel dosimeters.

It is known that eddy currents are a major source of artefacts in images. However, introducing a train of echoes that are not read, but only used for stabilising the magnetic field in the sample, is an effective method of reducing these [50].

The program records the time required to compute the $T_2$ map and automatically saves the final data. In addition to the matrixes of $a$, $T_2$ and $c$, it also saves the upper and lower limits of the fits (95% confidence level) in separate matrices.
In addition to this main code, several more basic programming codes were developed to assist in analysis of the data. These include programs to quickly determine the $T_2$ value over a region in many slices simultaneously.

### 3.6.2. Raman spectroscopy data analysis

Raman Spectroscopy of a sample will output a spectra (as example in Figure 46), where the response with varying Raman Shift or wavenumber is measured. In these spectra, peaks that can be assigned to various bonds in the sample can be assigned (for example, in Figure 46, peaks located at 2940 and 3040 cm$^{-1}$ are visible). By measuring the change in the peak volume, a measurement in the change of structure of the sample can be obtained.

![Comparison of unpolymerised and polymerised spectra](image)

Figure 46 Comparison of spectra obtained from and unirradiated and irradiated region of gel dosimeter, centred on wavenumbers around 3000 cm$^{-1}$. The two peaks in this region, located at 2940 cm$^{-1}$ and 3040 cm$^{-1}$ are used as a measure of the polymerisation of the gel.
Raman Spectra are obtained at single points of the sample. To obtain a linemap, (a measurement of the spectra of a single dimension of the sample that shows how the sample changes along a line), multiple spectra are obtained at regular intervals (as described previously). A property of each spectra (for example, in this work, the volume of the peak located at 2940 cm$^{-1}$) is then plotted against position.

Due to the large amount of data, a program was developed to read in the data, and based on user input to determine the limits, it would calculate the integrated peak volume within those limits and also the background signal. The background signal was determined by taking the signal of each end point of the Region of Interest (ROI), and multiplying the average by the linear extent of the ROI.

### 3.7. Photonuclear reactions in gel dosimeters

After a batch of gel dosimeters were prepared using a standard formulation (as described in previous sections), polymer gel samples were irradiated using 18 MV x-rays from a Varian 2100C linear accelerator. Gels were placed in a water tank (to provide scatter) centred at depth $D_{\text{max}}$. Irradiation was performed at a dose rate of 5.43 Gy min$^{-1}$ for 10 minutes.

Immediately after irradiation, the gel dosimeter was removed from the water tank and the spectrum obtained using a Rainbow I model 7010 Multichannel Analyser. This had previously been calibrated by use of a $^{137}$Cs source. The experimental set-up is shown in Figure 47. The NaI crystal scintillator as a diameter of 3.2 cm and was placed 3 cm from the vial containing the gel dosimeter. There is a short period of time (18 seconds approximately) between turning off the linac beam and starting the spectrum acquisition due to physical experimental set-up constraints. As this amount of time is not negligible in comparison the half-life of the oxygen activity, there is unfortunately some loss of signal.
The emission spectrum was measured in 30-second cycles. Each cycle was comprised of 20 seconds to record the spectrum, and 10 seconds used to save the data and prepare the multichannel analyser for the next cycle. This process was repeated 10 times, for a total acquisition time of 200 seconds over a 300 second period. This was used to determine the decay rate and allow it to be compared with that known of $^{15}\text{O}$. Because the presence of a 0.511 MeV peak is indicative of positron-electron annihilation, its presence was used as evidence of the emission of a positron by $^{15}\text{O}$ decay, thus indicating a neutron emission as well. The size of this peak was used as an indication of the number of annihilation events, and thus the number of neutrons generated within the gel from the creation of $^{15}\text{O}$ via photonuclear activations.

The spectrum was subsequently analysed using MATLAB software (The MathWorks, Inc.).
In addition, a comparison of polymer gels irradiated to the same set dose, using 6 and 18 MV x-rays and scanned using MRI, was made to determine if any difference in the degree of polymerisation could be measured. Any detected difference may indicate the effect of neutron generation in the polymerisation process.

### 3.8. Disposal of gel dosimeters

Because the chemicals used in polymer gel dosimeters (in particular, the monomer acrylamide and the cross-linker N’ N-methylene-bis-acrylamide are classified as dangerous to humans and the environment [29, 30], a safe method of disposal is required.

Polyacrylamide is not regarded as a dangerous substance, so a possible method of disposal is to complete transform the material from monomer to polymer after usage, through radiation or other methods (such as the addition of reactants or radicals). However, this method is not reliable as it is not possible to determine with certainty when all the monomer has been transformed into polymer.

Employing a third party to dispose of the chemical is the simplest method, although obviously it comes at a cost. It was decided to allow a commercial company to dispose of the PAG samples. After the usage of a polymer gel was completed, it was removed from its container by heating it through immersion in warm water. This melts the PAG inside, after which it can simply be poured out. Sections of the PAG which are polymerised do not tend to melt, and may need to be broken up through physical means (such as scrapping) in order to remove them from the container.

The containers are then cleaned and then disposed of, or ready to be used again if needed if the container is considered to be particularly expensive or unique.

### 3.9. Monte Carlo Simulations

Monte Carlo simulations refer to the use of computer software to simulate the interactions of particles, in this work the particles that make up a radiotherapy beam
originating from a linear accelerator. Each particle in generated and interacts with the geometry of the system (the linear accelerator head and the phantom). Factors such as the total energy deposited in certain regions can therefore be calculated.

In this work, Monte Carlo simulations were used to examine the amount and shape of the dose distribution from a linear accelerator for various radiotherapy beams field sizes. $18 \times 18 \, \text{mm}^2$, $6 \times 6 \, \text{mm}^2$, $4 \, \text{mm}$ circular diameter and $3 \times 3 \, \text{mm}^2$ fields were examined.

In this thesis, the Electron Gamma Shower software developed by the National Research Council of Canada (EGSnrc) was used to simulate the head of a Varian 600C linear accelerator. BEAMnrc software, an add-on to EGSnrc, was used to simulate the target phantom, either water or polymer gel. These programs were run on a Windows XP operating system, using a Pentium 2.80GHz desktop.

Polymer gel was generated using a density of 1.04 times that of water. This value was obtained from Trapp, Back, Lepage, Michael and Baldock [9], who found this to be the density of polymerised gel of the type used in the experimental part of this thesis. This value was chosen, as this value holds the greatest difference from that of water, by comparison unpolymerised water has a density of 1.02 [9], therefore any variations between water and gel should be more apparent. The atomic composition of water and gel simulated in this work was (as percentages of total mass): Hydrogen 10.7%, Carbon 4.7%, Nitrogen 1.7%, and Oxygen 82.9%.

The Monte Carlo simulation was made by first simulating the target, primary collimation, flattening filter ionisation chamber and mirror within the linear accelerator. After this, the collimating lead jaws were simulated, with their size adjusted to produce the desired field upon the target. A diagram of the combined simulated linear accelerator head and collimator jaws (across YZ-plane) are shown in Figure 48. Figure 49 shows the second set of jaws for the XZ-plane. Figure 50 shows the $4 \, \text{mm}$ circular collimator.

For the $4 \, \text{mm}$ circular diameter field, the jaws were opened to a $6 \times 6 \, \text{cm}^2$ field. Underneath those was a circular collimator made of Cerrobend (density $9.4 \, \text{g cm}^{-1}$,
elemental composition 50.0% bismuth, 26.7% lead, 13.3% tin, 10.0% cadmium, [184]) which collimated the beam to the 4 mm circular diameter field desired.

For each simulation, $4 \times 10^7$ particle histories were simulated in the phantom. The electrons striking the target had 6 MeV of energy; therefore the target emitted x-rays in a spectrum of energies and the maximum possible energy of an emitted x-ray photon being 6 MeV. Throughout the simulations, the global electron cut-off energy (the threshold energy below which electrons are not longer simulated to save computational time) was 0.7 MeV (including the electrons rest energy). The corresponding photon cut-off value was 0.01 MeV.

At a distance of 100 cm from the linear accelerator target, a phantom made of either gel or water, shaped as a block $20 \times 20 \text{ cm}^2$ wide and 15 cm thick. The simulation was designed to determine the level of dose throughout the gel or water phantom block. The resolution of the simulation was varied with position, with more resolution near the central axis of the beam (where the dose gradient would be the largest for these small beam sizes), and the z-axis resolution greatest in the first 5 cm thickness of the block. The regions and the resolution of the simulation in this block geometry is described in Table 5 (x and y-axis) and Table 6 (z-axis).

### Table 5 Description of the Monte Carlo simulation voxel resolution over the x and y-axis.

<table>
<thead>
<tr>
<th>x and y-axis region</th>
<th>x and y-axis resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Section 1</td>
<td>from −10 to −2 cm</td>
</tr>
<tr>
<td></td>
<td>1 cm</td>
</tr>
<tr>
<td>Section 2</td>
<td>from −2 to 2 cm</td>
</tr>
<tr>
<td></td>
<td>0.05 cm</td>
</tr>
<tr>
<td>Section 3</td>
<td>from 2 to 10 cm</td>
</tr>
<tr>
<td></td>
<td>1 cm</td>
</tr>
</tbody>
</table>

### Table 6 Description of the Monte Carlo simulation voxel resolution over the z-axis.

<table>
<thead>
<tr>
<th>z-axis region</th>
<th>z-axis resolution</th>
</tr>
</thead>
<tbody>
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<td>from 0 to 5 cm</td>
</tr>
<tr>
<td></td>
<td>0.1 cm</td>
</tr>
<tr>
<td>Section 2</td>
<td>from 5 to 15 cm</td>
</tr>
<tr>
<td></td>
<td>0.5 cm</td>
</tr>
</tbody>
</table>
Figure 48 Setup of the Monte Carlo simulation of the linac head. All units in cm. Image of the YZ-plane, \( x = 0 \). The lower collimator in the diagram is open for a 6 \( \times \) 6 mm\(^2\) field. Light blue is air, purple is tungsten, teal (target and flattening filter) is copper. Not shown due to scale are the kapton ionisation chamber and a mylar mirror, located after the flattening filter.
Figure 49 Setup of the Monte Carlo simulation of the linac head, only the jaws for the y-axis collimation are shown as the head is identical to that shown in Figure 48. All units in cm. Image of the XZ-plane, x = 0. The lower collimator in the diagram is open for a $6 \times 6$ mm$^2$ field.

Figure 50 Setup of the Monte Carlo simulation of 4 mm diameter circular collimator. All units in cm. Image of the XZ-plane, x = 0.
4. RESULTS – RADIOTHERAPY BEAMS COLLIMATED TO SUB-CENTIMETRE FIELD SIZES
Polymer gels were employed to measure the dose profiles of radiotherapy beams collimated to small field sizes, ranging from $18 \times 18 \text{ mm}^2$ down to $3 \times 3 \text{ mm}^2$. Gel dosimeters irradiated with such small fields were scanned using a high resolution 7 T micro-imaging MRI scanner, and as a comparison, radiochromic films, micro–diodes (µ-diodes) and micro-thermoluminescent diodes (µ-TLDs) were employed to determine the dose distribution within the radiotherapy beam.

4.1. Calibration curves of gel dosimeters and radiochromic film

Calibration of gel dosimeters is required to determine their response to radiation. The calibration resultant calibration curve will represent the degree of change in polymerisation against a known verified dose. This is achieved by irradiation of the gel dosimeters by a standard sized irradiation field to deliver a known dose. Ideally, this process should be repeated for each batch of gel to account for any possible inter-batch variation. The calibration curves of gel dosimeters are normally found to be close to linear in their most sensitive region, but are actually bi-exponential when evaluated over the whole dose range [164]. Gel dosimeters may still be used in dose regions that aren’t linear, with a reduced dose resolution [2].

In this thesis, each batch of gel was calibrated in this manner, an example is shown in Figure 51. Figure 51 shows the response calibration function for gel phantoms using gels irradiated with a wide field ($10 \times 10 \text{ cm}$) and full scattering conditions to 95% confidence limits with a delivered dose of 0, 1, 3, 5, 10, 15, 20 and 30 Gy. It also shows the best fit of the data points, calculated using MATLAB. The measured $R_2$ value for gels scanned with MRI can be seen to increase in a linear manner between 0 and approximately 10 Gy. At delivered doses higher than this, the rate of increase in $R_2$ is reduced, which corresponds to the decrease in available monomer to further polymerise. The most sensitive region of the calibration curve (greatest relative change in $R_2$ per delivered Gy) was found to be between 1 and 5 Gy. The $R^2$ value of the curve fit is 0.9995. Similar response and shape of the calibration curve has been previously documented by Venning, Brindha, Hill and Baldock [165], who found a
PAGAT gel with a similar chemical makeup to the one used here to be linear in its radiation dose response up to 6 Gy when scanned using a 1.5 T MRI.

Figure 51 Calibration curve for a typical gel, used to determine the dose distribution of gels exposed to x-ray beams collimated to small field sizes (4 mm circular diameter and 3 x 3 mm$^2$). The curve fit value is $R^2 = 0.9995$.

A similar process of calibration is applied to the use of radiochromic film. Figure 52 shows the calibration made for radiochromic films using 9.8 x 9.8 cm field size as with the gel dosimeter calibration. Pieces of film were irradiated at 0, 0.5 1, 2, 3, 4, 5, 8, 10, 12, 15, 18 and 20 Gy. The resultant response curve is found to be similar to that reported by Stevens et al. (1996). However, there was as expected a small deviation at very low doses [88]. The data points are fitted with a power function and the $R^2$ value of the fit is 0.9985.
Figure 52 Calibration for radiochromic films associated with film measurements of $3 \times 3$ mm$^2$ and 4 mm circular diameter field sizes. The curve fits value is $R^2 = 0.9985$.

Micro-TLD data was calibrated by exposing all micro-TLDs to a known dose (1.967 Gy) and using a large field ($10 \times 10$ cm) to determine and correct for the response of each micro-TLD individually.

4.2. Dose profile measurements of small field sizes

In this section, results relating to dose profile measurements for $18 \times 18$ mm$^2$, $6 \times 6$ mm$^2$, 4 mm circular diameter and $3 \times 3$ mm$^2$ fields using gel dosimetry and comparison techniques are described.

A high resolution MRI scanner, employing a small core and high magnetic field strength was used for this work, as it allows a more accurate measurement of the dose distribution compared to the clinically available 1.5 T MRI scanners that are more commonly used. Given the small radiotherapy beam field sizes examined in this work, the high resolution provided by these 7 T MRI scanners was valuable. However, 7 T
MRI scanners are also more expensive to use and less accessible, meaning that they could not be employed where the need for resolution was not justified.

### 4.2.1. Dose profile of an 18 × 18 mm² irradiated field

Hypoxic gel dosimeters were employed to measure the dose distribution from an 18 × 18 mm² field irradiated with a 10 Gy, 6 MV x-ray beam obtained from a linear accelerator as described in the method (section 3.2.1.2). For validation purposes, radiochromic film and μ-diodes (sections 3.2.2 and 3.2.3) were also used to measure the dose distribution from this field. These gel dosimeters were then imaged using a MRI scanning sequence in a 7 T MRI scanner as listed in Table 7 below.

<table>
<thead>
<tr>
<th>modality</th>
<th>pixel size (mm)</th>
<th>SNR</th>
<th>scanning parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 T MRI (high res)</td>
<td>0.234 × 0.234</td>
<td>35</td>
<td>MSME, 64 echoes, 4 averages, TE = 20 ms, TR = 2000 ms, read matrix = 128 × 128, FOV = 30 × 30 mm², scan time = 17m4s (alone)</td>
</tr>
<tr>
<td>radiochromic film</td>
<td>0.00794 × 0.00794</td>
<td>42</td>
<td>3200 dpi</td>
</tr>
<tr>
<td>μ-diode</td>
<td>1.1 mm² × 0.3 mm (cylinder)</td>
<td>200</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Table 7 List of MRI scanning parameters used to image a gel dosimeter irradiated with an 18 × 18 mm² field, compared to radiochromic film and μ-diode.

Figure 53 shows the beam cross-profile as measured using polymer gel dosimeters (scanned with 7 T MRI), radiochromic film and a μ-diode. As the dose profile is symmetrical for this field size, μ-diode data taken was reflected about the central point to reduce the uncertainty in the measurement. Measurements of the penumbra width and the FWHM were performed on the data and the results compiled in Table 8. Also, Monte Carlo simulations of the dose profile in water and polymer gel were made and are shown in Figure 54.
Figure 53 A comparison of the central profile across an 18 × 18 mm² wide beam with measurements made by a gel dosimeter, radiochromic film and an ionisation diode.

Figure 54 A comparison of the central profile across an 18 × 18 mm² wide beam using Monte Carlo simulations.
Table 8 Comparison of penumbra widths and FWHM data for 18 × 18 mm² cross beam profile measured using gel dosimeters, radiochromic films and µ-diodes. All units are in mm. Uncertainties are based on 1 standard deviation in the signal response to determine the maximum and minimum possible profile widths and FWHM. \( N_{\text{gel}} = 25, N_{\text{film}} = 25, N_{\mu-\text{diode}} = 40. \)

<table>
<thead>
<tr>
<th></th>
<th>gel dosimeter</th>
<th>radiochromic film</th>
<th>µ-diode</th>
<th>Monte Carlo of gel</th>
<th>Monte Carlo of water</th>
</tr>
</thead>
<tbody>
<tr>
<td>90 10%</td>
<td>3.41 ± .68</td>
<td>5.32 ± .066</td>
<td>5.99 ± .04</td>
<td>4.74 ± 1.33</td>
<td>4.99 ± .88</td>
</tr>
<tr>
<td>80 20%</td>
<td>1.98 ± .27</td>
<td>3.38 ± .36</td>
<td>3.68 ± .01</td>
<td>2.84 ± .26</td>
<td>2.75 ± .21</td>
</tr>
<tr>
<td>FWHM</td>
<td>17.92 ± .18</td>
<td>18.07 ± .33</td>
<td>17.72 ± .01</td>
<td>18.97 ± .22</td>
<td>19.01 ± .15</td>
</tr>
</tbody>
</table>

The biggest difference between the profiles Figure 53 is within the low dose regions near the edge of the penumbra, where the measured dose value for the gel dosimeter is smaller than the equivalent dose measured by radiochromic film and µ-diode. Monte Carlo profile width data falls between these values and has the largest FWHM. As desired from using gel as a phantom during dosimetry, there is no appreciable difference between Monte Carlo simulations using gel or water as the phantom. It is also observed that the diode measured penumbra data is wider at low doses than radiochromic film. Given that a µ-diode has a minimum scanning area of 1.1 mm², the effects of dose averaging from the µ-diodes coarse measurements are the most likely explanation for the diode wider penumbra observed using the µ-diode. It is demonstrated that the FWHM measurements show no significant difference between the three experimental measurement techniques.

4.2.2. **Dose profile of a 6 × 6 mm² irradiated field**

Next, a smaller radiotherapy beam field size was examined. From the same batch of hypoxic polymer gel dosimeter as used to image an 18 × 18 mm², a 6 × 6 mm² field was also irradiated and imaged using the 7 T *Bruker Advance 300 MR micro-imaging system*. The scanning parameters employed are listed in Table 9. Again, radiochromic film and µ-diode measurements were made as a comparison to gel measurements.
Table 9: List of MRI scanning parameters used to image a gel dosimeter irradiated with a 6 × 6 mm² field.

<table>
<thead>
<tr>
<th>MRI scanning parameters</th>
<th>pixel size (µm)</th>
<th>SNR</th>
<th>MRI scanning parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 T MRI (high resolution)</td>
<td>0.0508 × 0.0508</td>
<td>77</td>
<td>MSME, 128 echoes, 64 averages, TE = 7.5 ms, TR = 8000 ms, read matrix = 256 × 256, FOV = 13 × 13 mm², scan time = 36h24m32s (alone)</td>
</tr>
<tr>
<td>radiochromic film</td>
<td>0.00794 × 0.00794</td>
<td>53</td>
<td>3200 dpi</td>
</tr>
<tr>
<td>µ-diode</td>
<td>1.1 mm² × 0.3 mm (cylinder)</td>
<td>200</td>
<td>n/a</td>
</tr>
</tbody>
</table>

The gel dosimeter in this section was scanned for a very large number of averages (64) over a lengthy period of time (36.4 hours). This accounts for the low level of noise in the dose profile measurements (and thus high SNR), whereas the high resolution (pixel size 50.8 × 50.8 µm) at which it was scanned would normally mean a higher SNR. An MRI image of a R₂ map obtained from this data is shown in Figure 55. This image is a single slice through the gel 1 mm thick, and clearly shows the 6 × 6 mm² polymerised region through the gel passing from the left to the right.
Figure 55 High-resolution image of a $6 \times 6 \text{ mm}^2$ irradiated gel dosimeter obtained by a 7 T MRI scanner. The pixel size is $50.8 \times 50.8 \mu\text{m}^2$.

Figure 56 illustrates the measured cross profiles comparing gel dosimeter, radiochromic film and $\mu$-diode measurements across the centre of a $6 \times 6 \text{ mm}^2$ field. The widths of the penumbra and the FWHM for each method are listed in Table 10. Figure 57 shows the same profile simulated using Monte Carlo simulations of the linac system.
Figure 56 A comparison of the field size measurement of a $6 \times 6 \text{ mm}^2$ wide beam with measurements made by a gel dosimeter, radiochromic film and an ionisation diode.
Figure 57 A comparison of the central profile across an 18 × 18 mm$^2$ wide beam with measurements made by Monte Carlo simulations.

Table 10 Comparison of the measured penumbra size and beam width of a 6 × 6 mm$^2$ beam as calculated by gel dosimeters, radiochromic films and μ-diodes. Uncertainties are based on 1 standard deviation in the signal response to determine the maximum and minimum possible profile widths and FWHM. $N_{\text{gel}} = 25$, $N_{\text{film}} = 25$, $N_{\mu\text{-diode}} = 40$.

<table>
<thead>
<tr>
<th></th>
<th>gel dosimeter</th>
<th>radiochromic film</th>
<th>μ-diode</th>
<th>Monte Carlo in gel</th>
<th>Monte Carlo in water</th>
</tr>
</thead>
<tbody>
<tr>
<td>90 10%</td>
<td>2.44 ± .12</td>
<td>3.06 ± .21</td>
<td>3.40 ± .01</td>
<td>3.81 ± .21</td>
<td>3.85 ± .20</td>
</tr>
<tr>
<td>80 20%</td>
<td>1.67 ± .09</td>
<td>2.03 ± .13</td>
<td>2.20 ± .01</td>
<td>2.27 ± .08</td>
<td>2.23 ± .08</td>
</tr>
<tr>
<td>FWHM</td>
<td>5.66 ± .10</td>
<td>6.17 ± .13</td>
<td>6.79 ± .01</td>
<td>6.63 ± .05</td>
<td>6.64 ± .05</td>
</tr>
</tbody>
</table>

In comparison with later sets of data, here the gel dosimeter records a smaller Full Width at Half Maximum (FWHM) value than the alternatives such as radiochromic film, this point will be discussed in further detail later on (section 4.2.4.1). Monte
Carlo data displays a wider penumbra shape slightly wider compared to all methods of experimental measurement.

4.2.3. Dose profile of a 4 mm diameter circular field

A normoxic polymer gel dosimeter was irradiated by a 4 mm circular diameter collimated x-ray beam. As a comparison, radiochromic film and micro-TLDs were also irradiated with this field. The gel dosimeters were then scanned with 7 T and 1.5 T MRI with the scanning settings listed in Table 11. This table also lists the comparison resolution obtained using radiochromic films and micro-TLDs.

<table>
<thead>
<tr>
<th>Table 11 List of MRI scanning parameters used to image a gel dosimeter irradiated with a 4 mm circular diameter field.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pixel size (mm)</strong></td>
</tr>
<tr>
<td>1.5 T MRI</td>
</tr>
<tr>
<td>7 T MRI (low res)</td>
</tr>
<tr>
<td>7 T MRI (high res)</td>
</tr>
<tr>
<td>radiochromic film</td>
</tr>
<tr>
<td>μ-TLD</td>
</tr>
</tbody>
</table>

Figure 58 shows an image of a gel dosimeter sample irradiated by a beam collimated to a 4 mm diameter circular field size, imaged with a 7 T MRI scanner. Figure 59 shows an image of the gel made using a 1.5 T MRI with the polymerised region passing from top to bottom, visible as a slightly lighter colour compared to the
surrounding unpolymerised gel on the left and right portions of the image. Figure 60 shows an image of a 4 mm circular diameter field imaged using radiochromic film. Similar to the high resolution MRI scan in Figure 58, the irradiated portion on the radiochromic film can be seen clearly in the expected circular shape in the centre in both of these images.

A dose profile of the polymer gel scanned using a 7 T MRI with a pixel size of 94 µm and 186 µm, along with a comparison made using a 1.5 T MRI scan at 469 µm pixel size is shown in Figure 61. It can be seen that while scans using the higher spatial resolution 7 T MRI give a clear indication of the polymerised region’s profile, the 1.5 T is quite noisy at this level and would require a large number of repeat scans to average out the data. These profiles can be approximated to a bell-shape in which the penumbra makes up a large proportion of the field [184].

Profiles of the 4 mm circular beam using gel (of high resolution), radiochromic film and micro-TLDs are shown in Figure 62. This figure displays the cross-profiles of the gel dosimeter, radiochromic film and micro-TLD data, each of these was fitted using a double Gaussian equation in MATLAB software. Although the profile of a 4 mm circular beam can be expected to be symmetrical, a double Gaussian was employed so that the same equation could be used for examining the 3 × 3 mm² field. The cross-profile can be seen to be roughly bell-shaped in which the penumbra makes up a large proportion of the field [184] for fields of this size and less. In addition, points from the micro-TLD data and regular points from gel dosimeter and radiochromic film (at 0.44 mm intervals) are shown. Not all points from gel dosimeter or radiochromic film are shown for clarity. Table 12 shows the penumbra sizes and dose profiles FWHM for a beam collimated with 4 mm circular collimator as measured by gel dosimeters (7 T high resolution), radiochromic film and micro-TLDs.
Figure 58 $R_2 (s^{-1})$ map of a gel dosimeter irradiated with a 4 mm diameter circular beam, and imaged with a 7 T MRI scanner. The polymerised region of the gel dosimeter is clearly visible as the bright portion in the centre.
Figure 59 Image of a 4 mm circular diameter field (top to bottom) in a gel sample imaged with a clinical 1.5 T MRI system.
Figure 60 Image of radiochromic film irradiated with a 4 mm diameter circular field shown as a percentage of maximum dose. The irradiated field is clearly visible as a light portion in the centre of the image.
Figure 61 Comparison of 7 T MRI (at two different pixel resolutions) and a 1.5 T MRI scan of a 4 mm circular diameter field.
Figure 62 Comparison of the dose profiles obtained using gel dosimeters, radiochromic film and micro-TLDs for a 4 mm diameter circular field. Only points every 0.44 mm are displayed for the gel dosimeter and radiochromic film data for clarity.
Figure 63 A comparison of the central profile across a 4 mm circular diameter radiotherapy beam with measurements made by Monte Carlo simulations.

Table 12 Comparison of profile penumbra sizes for a 4 mm diameter circular beam using gel, radiochromic film, µ-TLD and Monte Carlo simulation. Uncertainties are based on 1 standard deviation in the signal response to determine the maximum and minimum possible profile widths and FWHM. $N_{\text{gel}} = 25, N_{\text{film}} = 25, N_{\mu\text{-TLD}} = 3$.

<table>
<thead>
<tr>
<th></th>
<th>gel dosimetry (7 T)</th>
<th>radiochromic film</th>
<th>µ-TLD</th>
<th>Monte Carlo with gel</th>
<th>Monte Carlo with water</th>
</tr>
</thead>
<tbody>
<tr>
<td>90 - 10%</td>
<td>1.99 ± .28</td>
<td>1.84 ± .08</td>
<td>1.89 ± 0.31</td>
<td>2.20 ± .27</td>
<td>2.27 ± .20</td>
</tr>
<tr>
<td>80 - 20%</td>
<td>1.32 ± .17</td>
<td>1.22 ± 0.05</td>
<td>1.22 ± .15</td>
<td>1.24 ± .05</td>
<td>1.25 ± .04</td>
</tr>
<tr>
<td>FWHM</td>
<td>4.40 ± .17</td>
<td>3.82 ± .05</td>
<td>3.84 ± .14</td>
<td>4.09 ± .05</td>
<td>4.10 ± .03</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.9771</td>
<td>0.9975</td>
<td>0.9555</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

The measured values of the penumbra widths for the gel dosimeter measured at high resolution are slightly larger than that measured using radiochromic film, however
this difference is not significant as they are within the level of uncertainty. For all methodologies, the measured difference between the left and right sides is very small (not significant), and the shape of both curves can be considered to be symmetrical, as expected for a circular beam. The fitted curve for micro-TLD data does show a slight asymmetry but this is not considered significant. The beam profile FWHM measured using gel dosimetry was found to be larger (4.40 mm) compared to that measured using the other dosimetric techniques (3.82 mm and 3.84 mm for film and micro-TLD), possibly due to variations in dose response accuracy.

Results obtained through Monte Carlo simulations show a profile with a shape that is similar to that obtained through the experimental methods.

4.2.4. Dose profile for a 3 × 3 mm² beam

A 3 × 3 mm² square field produced by a BrainLAB m3 MMLC attached to a Varian 600C linear accelerator was employed to irradiate polymer gel dosimeters. Measurements were taken at 5 cm depth, and compared against measurements made using radiochromic film and micro-TLDs. The MRI scanning sequence parameters (and resultant resolution) are shown in Table 13, as well as the relative noise of each method.
Table 13 List of MRI scanning parameters using to image a 3 × 3 mm² field.

<table>
<thead>
<tr>
<th></th>
<th>pixel size (mm)</th>
<th>SNR</th>
<th>scanning parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 T MRI</td>
<td>0.469 × 0.469</td>
<td>~1.4</td>
<td>8 echoes, 2 averages, TE = 12.5 ms, TR = 8000 ms, read matrix = 256 × 256, FOV = 120 × 120 cm², scan time (multiple samples imaged) = 7m28s</td>
</tr>
<tr>
<td>7 T MRI (low resolution)</td>
<td>0.234 × 0.234</td>
<td>34</td>
<td>256 echoes, 2 averages, TE = 4.015 ms, TR = 6000 ms, read matrix = 64 × 64, FOV = 15 × 15 mm², scan time = 12m48s (single sample imaged)</td>
</tr>
<tr>
<td>7 T MRI (high resolution)</td>
<td>0.059 × 0.059</td>
<td>3.7</td>
<td>256 echoes, 2 averages, TE = 5.015 ms, TR = 6000 ms, read matrix = 256 × 256, FOV = 15 × 15 mm², scan time = 51m12s (single sample imaged)</td>
</tr>
<tr>
<td>radiochromic film</td>
<td>0.00794 × 0.00794</td>
<td>85</td>
<td>3200 dpi</td>
</tr>
<tr>
<td>µ-TLD</td>
<td>1 × 1</td>
<td>35</td>
<td>NA</td>
</tr>
</tbody>
</table>

Again, the 7 T MRI is able to perform at a much higher resolution than the clinical 1.5 T system employed in this work, an important factor in imaging the dose distribution of small radiotherapy beams. This is however at the cost of much increased scanning time. These values do depend on the exact scanning sequence employed. A clinical 1.5 T scanner can easily scan multiple samples within the head coil, but the micro-imaging system is only able to scan a single sample at a time. In general, the 1.5 T system using the clinical scanning sequence has an unacceptable level of noise (the standard deviation being 70% of the T₂ change associated with a 10 Gy irradiation) when examining particularly narrow fields such as this one, as narrow radiotherapy fields mean there are a limited number of pixels that can be examined to determine the dose. While the influence of noise can be reduced when examining larger fields by averaging over an area irradiated by a homogeneous dose, or by employing a custom made sequence (in particular, a longer echo train), this could not be applied in this case, hence there is a large degree of uncertainty in the results of the 1.5 T compared
with the 7 T scan. Unlike the 1.5 T MRI scan, scans made using the 7 T MRI can
determine the dose distribution to a satisfactory degree of accuracy. As a comparison,
radiochromic films and micro-TLDs both have comparable noise levels, but
radiochromic film is a 2D technique only, and TLD only measures dose at points.
Compounded with the fact that the minimum pixel size of a micro-TLD is at least a
magnitude greater than the other techniques, this means there is a resultant loss of
resolution when using micro-TLDs.

Figure 64 and Figure 65 show the $3 \times 3 \text{ mm}^2$ field beam exposing a polymer gel
dosimeter that was scanned with 7 T MRI and radiochromic film respectively. In
Figure 64, the light central area shows the irradiated portion of the gel, and similarly
for the image of irradiated film in Figure 65. It can be seen from both these images
that the irradiated field is not square, but rectangular. This will be discussed later in
section 4.2.4.3. Figure 66 shows an image of a polymer gel sample irradiated with the
$3 \times 3 \text{ mm}^2$ beam, with the path of irradiated gel represented by a light area passing left
to right across the image. This image was scanned using a 1.5 T MRI, and as such
suffers from poorer quality compared to that of the 7 T scan at high resolution or the
radiochromic film.
Figure 64 Image of gel irradiated with a $3 \times 3$ mm$^2$ collimated beam onto gel and scanned with a 7 T MRI scanner (pixel size 234 $\times$ 234 µm$^2$). Note that $R_2$ values do not match the calibration graph due to difference in resolution at time of imaging.
Figure 65 Image of radiochromic film irradiated with a $3 \times 3 \text{ mm}^2$ collimated beam.
Figure 66 Image of a $3 \times 3 \text{ mm}^2$ field (left to right) in a gel sample imaged with a clinical 1.5 T MRI system.

4.2.4.1 Dose profiles along the x-axis

A comparison of the ability of the 7 T MRI micro-imaging system and the 1.5 T MRI scanner to measure the dose profile of a $3 \times 3 \text{ mm}^2$ field (along the x-axis) is shown in Figure 67. It is quite clear that the 7 T MRI scanner is produces a more reliable map the small beam profile with less uncertainty compared to a scan using the 1.5 T MRI scanner, given the settings shown.
Dose profiles along the x-axis of the 3 × 3 mm² field measuring gel dosimeters (scanned using the 7 T MRI scanner), radiochromic film and micro-TLDs are shown in Figure 68. The cross-profiles of the raw data from all three methods were fitted using a double Gaussian equation in MATLAB software. A double Gaussian equation was employed as the data points were approximately Gaussian in shape and there was an expected asymmetry. A single Gaussian equation would not be sufficient to reveal any asymmetry. The data points for each method are also displayed on the graph. Due to the large number of data points from radiochromic films, only points every 0.44 mm are shown for clarity. However, all data points including those not displayed were used when calculating the best fit. Measurements of the penumbra and FWHM sizes from these profiles are listed in Table 14. The fitted data shown for the gel dosimeter is from the image at 234 µm pixel resolution, which shows much less uncertainty in dose resolution than the scan at 59 µm.
Figure 69 shows a Monte Carlo simulation of the results for irradiation by an idealised $3 \times 3 \text{ mm}^2$ radiotherapy beam, using polymer gel and water as the phantom material. Due to the nature of the beam collimation, it is not expected to match the experimental data, but rather provide information about what a theoretical true $3 \times 3 \text{ mm}^2$ collimated beam profile would look like.

Figure 68 Comparison of the dose profiles obtained using gel (7 T, pixel size 234 µm), radiochromic film and micro-TLDs in the x-axis of a $3 \times 3 \text{ mm}^2$ collimated field. Only points every 0.44 mm are displayed for the radiochromic film data for clarity.
Figure 69 A comparison of the central profile across a $3 \times 3$ mm$^2$ wide beam with measurements made by Monte Carlo simulations.
Table 14 Penumbra sizes of a 3 × 3 mm² collimated field along the x-axis as measured using gel and radiochromic film. Due to the asymmetry of the irradiated beam, the negative and positive sides of the fit are listed separately. Uncertainties are based on 1 standard deviation in the signal response to determine the maximum and minimum possible profile widths and FWHM. \( N_{\text{gel}} = 25, \ N_{\text{film}} = 25, \ N_{\text{\( \mu \)-diode}} = 40. \)

<table>
<thead>
<tr>
<th></th>
<th>gel dosimetry (7 T high resolution)</th>
<th>gel dosimetry (7 T low resolution)</th>
<th>radiochromic film</th>
<th>( \mu )-TLD</th>
<th>Monte Carlo with gel</th>
<th>Monte Carlo with water</th>
</tr>
</thead>
<tbody>
<tr>
<td>90 - 10%</td>
<td>2.39 ± 0.82</td>
<td>1.94 ± 0.26</td>
<td>2.01 ± 0.15</td>
<td>2.65 ± 0.62</td>
<td>3.01 ± .14</td>
<td>2.96 ± .15</td>
</tr>
<tr>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90 - 10%</td>
<td>2.54 ± 0.74</td>
<td>2.29 ± 0.31</td>
<td>2.37 ± 0.18</td>
<td>2.43 ± 0.58</td>
<td>2.95 ± .05</td>
<td>3.03 ± .14</td>
</tr>
<tr>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80 - 20%</td>
<td>1.58 ± 0.47</td>
<td>1.28 ± 0.17</td>
<td>1.31 ± 0.11</td>
<td>1.61 ± 0.30</td>
<td>1.95 ± .04</td>
<td>1.93 ± .04</td>
</tr>
<tr>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80 - 20%</td>
<td>1.70 ± 0.49</td>
<td>1.51 ± 0.19</td>
<td>1.60 ± 0.11</td>
<td>1.55 ± 0.27</td>
<td>1.96 ± .04</td>
<td>1.94 ± .05</td>
</tr>
<tr>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FWHM (mm)</td>
<td>3.26 ± 0.33</td>
<td>3.62 ± 0.13</td>
<td>2.87 ± 0.07</td>
<td>3.08 ± 0.18</td>
<td>3.96 ± .03</td>
<td>3.98 ± .03</td>
</tr>
<tr>
<td>( R^2 ) fit value</td>
<td>0.8942</td>
<td>.9853</td>
<td>0.9997</td>
<td>0.9892</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

This data (Table 14) demonstrates that the positive side of the x-axis has a wider penumbra than the negative x-axis as measured with radiochromic film and gel dosimetry, while the micro-TLD data is more symmetrical. An explanation for the asymmetry is given below in section 4.2.4.3. Given that a double Gaussian equation was used to fit these points, and the high \( R^2 \) value for the fit (\( R^2 = 0.9997 \) for radiochromic film), it is anticipated that the asymmetry is rooted in the experimental set-up. The width of the penumbra measured using radiochromic film is narrower than that of gel dosimeters or micro-TLDs (which both are approximately equal to each other). This difference was more pronounced on the negative side of the x-axis.

The FWHM of the x-axis profile measurement obtained using radiochromic film was also narrower than that obtained using micro-TLD or gel dosimetry. In general, the
measured micro-TLD FWHM value was approximately equal to that of the field size, while gel dosimetry measured a larger FWHM. Radiochromic film suggested a FWHM that was less than the width of the collimated field (at this depth, equal to 3.15 mm).

Monte Carlo results demonstrate a wider penumbra compared to the experimental results, this is most likely due to the differences in the shape of the leaves used in the simulation. The Monte Carlo simulation is an idealised version, and therefore does not have any difference between the positive and negative sides of x-axis penumbra. The larger FWHM and penumbra can therefore be attributed to the absence of tongues from a MMLC sticking into the irradiated field.

Profile data for 3 × 3 mm² and 4 mm circular diameter fields show that in general the gel dosimeter gives the penumbra width being larger compared to techniques such as film, whereas the 18 × 18 mm² and 6 × 6 mm² show the opposite. Due to the small field sizes involved, changes in detector sensitivity when using such small field sizes may be an explanation for this.

4.2.4.2. Dose profiles along the y-axis

Similar to the analysis of the x-axis profile data above, a fit of the cross-profile along the y-axis of a beam collimated to 3 × 3 mm² using gel dosimeters, radiochromic film and micro-TLDs was made and is shown in Figure 70. This data was also fitted using a double Gaussian equation and points from all three measurement techniques at regular intervals are also displayed. The measured data relating to penumbra width and FWHM measurements of these profiles are listed in Table 15. The cross-profiles were fitted using the same double Gaussian equation as used for the 4 mm cross-profile and the x-axis of the 3 × 3 mm² cross-profile.
Figure 70 Comparison of the dose profiles obtained using gel (7 T, pixel size 234 µm), radiochromic film and micro-TLDs in the y-axis of a 3 × 3 mm² collimated field. Only points every 0.44 mm are displayed for the radiochromic film data for clarity.
Table 15 Penumbra sizes of a 3 × 3 mm² collimated field along the y-axis as measured using gel dosimeters, radiochromic film and micro-TLDs. Due to the asymmetry of the irradiated beam, the negative and positive sides of the fit are listed separately. Uncertainties are based on 1 standard deviation in the signal response to determine the maximum and minimum possible profile widths and FWHM. \( N_{gel} = 25, N_{film} = 25, N_{\mu-diode} = 40. \)

<table>
<thead>
<tr>
<th></th>
<th>gel dosimetry (7 T high resolution)</th>
<th>gel dosimetry (7 T low resolution)</th>
<th>radiochromic film</th>
<th>( \mu)-TLD</th>
<th>Monte Carlo with gel</th>
<th>Monte Carlo with water</th>
</tr>
</thead>
<tbody>
<tr>
<td>90 - 10% Negative</td>
<td>2.26 ± 0.93</td>
<td>2.45 ± 0.29</td>
<td>2.23 ± 0.16</td>
<td>2.56 ± 0.46</td>
<td>3.01 ± 0.14</td>
<td>2.96 ± 0.15</td>
</tr>
<tr>
<td>90 - 10% Positive</td>
<td>2.19 ± 0.68</td>
<td>2.93 ± 0.39</td>
<td>2.31 ± 0.16</td>
<td>2.77 ± 0.44</td>
<td>2.95 ± 0.05</td>
<td>3.03 ± 0.14</td>
</tr>
<tr>
<td>80 - 20% Negative</td>
<td>1.36 ± 0.48</td>
<td>1.69 ± 0.20</td>
<td>1.49 ± 0.10</td>
<td>1.71 ± 0.28</td>
<td>1.95 ± 0.04</td>
<td>1.93 ± 0.04</td>
</tr>
<tr>
<td>80 - 20% Positive</td>
<td>1.46 ± 0.42</td>
<td>1.96 ± 0.25</td>
<td>1.53 ± 0.11</td>
<td>1.89 ± 0.41</td>
<td>1.96 ± 0.04</td>
<td>1.94 ± 0.05</td>
</tr>
<tr>
<td>FWHM</td>
<td>3.83 ± 0.28</td>
<td>4.03 ± 0.17</td>
<td>3.78 ± 0.08</td>
<td>3.69 ± 0.22</td>
<td>3.96 ± 0.03</td>
<td>3.98 ± 0.03</td>
</tr>
<tr>
<td>Fitting R² value</td>
<td>0.8977</td>
<td>.9761</td>
<td>0.9994</td>
<td>0.9708</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

The fitted profiles display penumbras that are symmetric within the confidence limits. All three experimental methods show a similar profile shape and FWHM. The penumbra on the positive and negative sides of the centre is symmetric within the limits of uncertainty with all three experimental measurement methods. All three methods suggest similar FWHM values that are larger than the size of the collimated field, and also a larger FWHM size along the y-axis than the FWHM value determined for the x-axis direction.

The Monte Carlo data is identical to that presented for the x-axis, as the Monte Carlo simulation is of an idealised 3 × 3 mm² field does not have a noticeable difference between the x and y-axis.
4.2.4.3. Asymmetry of the x and y axis with $3 \times 3 \text{ mm}^2$ field

Overlaying the previous results of the profiles obtained for the x and y-axis, demonstrates that a noticeable difference between them can be observed, as illustrated in Figure 71, Figure 72 and as listed in Table 16.

![Comparison of X and Y-axis profile data from a $3 \times 3 \text{ mm}^2$ collimated field using gel dosimetry](image)

*Figure 71 Comparison of the central profiles along the x and y-axis of a beam collimated to $3 \times 3 \text{ mm}^2$ measured using gel dosimetry, using the profile data from Figure 68 and Figure 70.*
Figure 72 Comparison of the central profiles along the x and y-axis of a beam collimated to $3 \times 3$ mm$^2$ using radiochromic film, using the profile data from Figure 68 and Figure 70.

Table 16 Comparison of the y and y-axis of a $3 \times 3$ mm$^2$ collimated beam as measured using gel dosimetry and radiochromic film.

<table>
<thead>
<tr>
<th></th>
<th>gel</th>
<th>radiochromic film</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x-axis</td>
<td>y-axis</td>
</tr>
<tr>
<td>90 - 10% Negative</td>
<td>1.94 ± 0.26</td>
<td>2.45 ± 0.29</td>
</tr>
<tr>
<td>90 - 10% Positive</td>
<td>2.29 ± 0.31</td>
<td>2.93 ± 0.39</td>
</tr>
<tr>
<td>80 - 20% Negative</td>
<td>1.28 ± 0.17</td>
<td>1.69 ± 0.20</td>
</tr>
<tr>
<td>80 - 20% Positive</td>
<td>1.51 ± 0.19</td>
<td>1.96 ± 0.25</td>
</tr>
<tr>
<td>FWHM</td>
<td>3.62 ± 0.13</td>
<td>4.03 ± 0.17</td>
</tr>
</tbody>
</table>

There is a clear difference in the size of the profile measurements comparing the x and y-axis, when measured using gel dosimeters, radiochromic film and micro-TLDs as the dosimeter. The measurements of the profile FWHM using film show that the y-axis has a larger FWHM by 0.41 mm (11%) as measured using gel dosimetry and 0.93 mm (32%) when measured using radiochromic film. This difference can be attributed
to the differences in the penumbra widths and to the larger plateau observed on the profile of the y-axis. Differences between the radiochromic film and gel dosimeter are possibly due to dose response accuracy, noting that film generally has less uncertainty in measurement which is reflected in a higher $R^2$ fit value.

This difference between the positive and negative sides of the x-axis originates (as shown in the illustrations of the MMLC leaves) when the MMLC leaves are opened to $3 \times 3 \text{mm}^2$ (Figure 73, Figure 74 and Figure 75). As the MMLC leaves move along the y-axis, the faces of these leaves (parallel to the x-axis) are straight. As opening of a single leaf pair creates the $3 \times 3 \text{mm}^2$ field and the isocentre of radiation is aligned with the gap of the two central leaf pairs, the field cannot be symmetric about the x-axis when a single leaf is opened. Therefore, a difference between the positive and negative sides of the x-axis can be expected. In this work, the leaves were positioned such that the y-axis was similarly placed with one edge directly below the target within the linear accelerator, with a gap to generate a 3 mm wide beam.

It is known that the faces of the leaves that are parallel to the x-axis are flat, while the faces that slide along the y-axis consist of tongues and grooves to prevent leakage. Therefore, despite the leaf being 3 mm wide, the aperture of the field produced by the removal of a single leaf isn’t accurately described as being 3 mm wide. The tongues and grooves create an aperture that varies between 2 and 4 mm wide, and the net result is that the effective size of the field is smaller than the anticipated 3 mm. The x-axis profile is believed to be smaller than the y-axis for this reason. It is known from literature that the presence of the tongue and grooves on the leaves will reduce the dose penumbra [186].

Therefore, when using MMLCs to produce such small fields, these asymmetry effects are proportionally significant enough that they should also be included as part of any dosimetry measurements, as well as in the treatment planning software when such small field sizes are used.
Figure 73 Diagram of the opening of the MMLC leaves for a $3 \times 3$ mm$^2$ field size beam. The leaves move along the y-axis, and their faces are flat. In contrast the faces of the leaves adjacent to each other (represented by the striped region) have tongues and grooves, which have the effect of changing their attenuation. This diagram is not to scale.
Figure 74 Diagram demonstrating the tongues and grooves of an MMLC. The tongues and grooves run along the y-axis, resulting in the width of the x-axis to vary depending on the Z-value. This image is not to scale and is a simplified picture, the actual leaves having many more tongues and grooves.
Figure 75 Diagram showing the positions of the MMLC leaves along the x and y-axis during collimation to a $3 \times 3$ mm$^2$ field. This diagram is not to scale.

4.3. Depth dose measurements

In this work, two sets of depth dose measurements were made using gel dosimeters to measure the depth dose of a 6 MV linear accelerator beam of various small field sizes. For the first, a hypoxic polymer gel was used and the results were compared against the depth dose values measured using radiochromic film. For hypoxic gel irradiated with an $18 \times 18$ mm$^2$ and a $6 \times 6$ mm$^2$ beam, a dose of 10 Gy (at 5 cm depth) was delivered by setting 1198 and 1822 MU respectively. The second employed a normoxic polymer gel and was compared against a μ-diode, and investigated smaller field sizes than the first ($12 \times 12$ mm$^2$, $6 \times 6$ mm$^2$, 4 mm circular diameter, $3 \times 3$ mm$^2$). For gels irradiated by a $12 \times 12$ mm$^2$ field, a dose of 10 Gy required 1287 MU. The 4 mm circular diameter beam required 2250 MU for 13.16 Gy and the $3 \times 3$ mm$^2$ beam delivered 3000 MU for a calculated dose of 13.51 Gy.

Comparison of the depth dose of an $18 \times 18$ mm$^2$ field irradiated onto a polymer gel dosimeter and radiochromic film is shown in Figure 76, in this the gel data was averaged over four measurements to reduce uncertainty. A similar comparison made for the depth dose of a $6 \times 6$ mm$^2$ field irradiated onto a polymer gel dosimeter and radiochromic film is shown in Figure 77. The error bars obtained are as a standard
deviation of the signal intensity within a ROI around the point examined. This data demonstrates a clear drop in measured dose at 5 cm depth with increasing distance for both gel dosimeters and radiochromic film for a $6 \times 6 \, \text{mm}^2$ field. Results for an $18 \times 18 \, \text{mm}^2$ field also show a decrease in energy deposited with depth. This data was accepted for publication in *Applied Radiation and Isotopes* [169].

![Figure 76](image)

**Figure 76** Comparison of the depth dose of an $18 \times 18 \, \text{mm}^2$ field size beam as measured using polymer gel dosimeters and radiochromic films. The 0 mm depth is measured from 5 cm into the sample. The uncertainty displayed is 1 standard deviation ($N = 25$).
Figure 77 Comparison of the depth dose of a 6× 6 mm² field size beam as measured using polymer gel dosimeters and radiochromic films. The 0 mm depth is measured from 5 cm into the sample. The uncertainty displayed is 1 standard deviation (N = 25).
A second set of depth dose measurements was made using field sizes of $12 \times 12 \text{ mm}^2$, $6 \times 6 \text{ mm}^2$, $3 \times 3 \text{ mm}^2$ and $4 \text{ mm}$ circular diameter field sizes, collimated using the BrainLAB m3 MMLC. This was done using gels in $13 \text{ mm}$ diameter, $100 \text{ mm}$ long Pyrex glass vials, irradiated from the rounded bottom end of the vial. The end of the vial was made even with the surface of the water (as described in the method, section 3.2.1.3). The path of the irradiation was determined using MRI, and the change in normalised dose with depth was calculated and fitted in MATLAB. This is shown in Figure 78.

![Figure 78 Depth dose measurements of various field sizes measured using gel dosimeters.](image)

Because of the rounded end of the glass vial, accurate measurements of the dose near the surface are not possible (<3 mm), and the measured values are not shown nor fitted as they are subject to possible error. Fitting of gel dosimeter data was made to an equation of the form of two exponentials.

$$f(x) = a \times \exp(bx) + c \times \exp(dx)$$  \hspace{1cm} (14)
Measurements of the depth dose were made using the µ-diode as a comparison and the results are shown in Figure 79. This figure, together with Figure 78, demonstrate that along the central beam axis, the smaller the beam the more quickly, in general, the depth dose decreases compared to its maximum value. This is due to the lesser amounts of scatter available in smaller field sizes to deposit dose along the central axis. In addition, larger fields have the measured value of \( D_{\text{max}} \) at slightly greater depths as expected [174]. Because diode measurements had considerably less noise, this data is not fitted, and the raw data is shown instead. A comparison of the values of \( D_{\text{max}} \) measured for the µ-diode and gel dosimeters are listed in Table 17.

Figure 79 Depth dose measurements of various field sizes measured using a µ-diode.
Table 17 Comparison of µ-diode and gel dosimeter measurements of $D_{\text{max}}$ of various size small fields. The uncertainty is based on detector size.

<table>
<thead>
<tr>
<th></th>
<th>µ-diode $D_{\text{max}}$ (±1) mm</th>
<th>gel dosimeter $D_{\text{max}}$ (±1) mm</th>
<th>gel dosimeter fitting $R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$3 \times 3$ mm$^2$</td>
<td>9</td>
<td>10</td>
<td>0.7963</td>
</tr>
<tr>
<td>4 mm circular diameter (Ø)</td>
<td>9</td>
<td>9</td>
<td>0.7487</td>
</tr>
<tr>
<td>$6 \times 6$ mm$^2$</td>
<td>12</td>
<td>11</td>
<td>0.8214</td>
</tr>
<tr>
<td>$12 \times 12$ mm$^2$</td>
<td>13</td>
<td>11</td>
<td>0.8543</td>
</tr>
<tr>
<td>$100 \times 100$ mm$^2$</td>
<td>15</td>
<td>11</td>
<td>0.6963</td>
</tr>
</tbody>
</table>

It can be seen from these measurements that the gel dosimeter measurements of this work have a faster drop off in value compared to that of µ-diode. For both the gel dosimeter and µ-diode, the fastest drop off occurred with the 4 mm circular diameter field, although this field has a larger area than the $3 \times 3$ mm$^2$ beam ($12.6$ mm$^2$ compared to $9$ mm$^2$). The difference between the 4 mm circular diameter field and the $3 \times 3$ mm$^2$ field is not significantly large.

For a 6 MV beam, the value of $D_{\text{max}}$ for a wide beam such as $100 \times 100$ mm$^2$ is expected to be approximately 15 mm. The results obtained using µ-diode confirms this. The gel dosimeter results vary more greatly from the expected values, and are more consistent in measuring the $D_{\text{max}}$ value at approximately 11 mm. This is most likely due to the fitting algorithm. As a comparison, Sohn, Dempsey, Suh and Low [174] suggested that using radiochromic film data, a $5 \times 5$ mm$^2$ field would have a $D_{\text{max}}$ of 9.5 mm and a $10 \times 10$ mm$^2$ field a $D_{\text{max}}$ of 11 mm, which is consistent with the results obtained here.

Unfortunately, given the available MRI equipment at the time, a typical 1.5 T MRI scanner used for clinical work, there is an enhanced the uncertainty in the data compared to a 7 T MRI scanner.
4.4. Scatter measurements

Gels in small vials (4 mm long, 8 mm outer diameter) were used to attempt to measure the influence of scatter due to differences in irradiated field sizes. It would be expected that with larger field sizes, the influence of scatter would be larger compared to smaller field sizes. The $98 \times 98 \text{ mm}^2$ field was irradiated with 1000 MU (= 10Gy) and the $3 \times 3 \text{ mm}^2$ field was irradiated with 3000 MU (unknown dose, approximately 13.5 Gy based on small field measurements). After irradiation, gel dosimeters were scanned using 1.5 T MRI with standard settings (TR = 8000 ms, TE = 12.5 ms, 8 echoes, 2 averages, pixel size $0.59 \times 0.59 \text{ mm}^2$, slice thickness 2 mm).

Figure 80 shows the difference in $T_2$ measurements when comparing a $98 \times 98 \text{ mm}^2$ field size to that of a $3 \times 3 \text{ mm}^2$ field size. It is shown that there is negligible difference between the dose delivered to a gel dosimeter from a $3 \times 3 \text{ mm}^2$ beam when a scatter medium (water) was present, but a non-zero $T_2$ difference was measured near the surface for a large $98 \times 98 \text{ mm}^2$ field size beam. Thus, a wide beam of $98 \times 98 \text{ mm}^2$ shows that the presence of scatter significantly increases the measured dose in gel dosimeters near the surface. At greater depths, this difference became negligible.
It would be expected that irradiation with a wider beam would induce scatter that would deposit energy into the gel dosimeter while a smaller beam would not have this. For a thin gel dosimeter (8 mm diameter) orientated vertically, this would mean that for a $3 \times 3$ mm$^2$ beam there should be little difference in the measured $T_2$ values regardless of whether the gel dosimeter is surrounded by scatter material or not, but the larger $98 \times 98$ mm$^2$ beam would produce scatter outside the gel dosimeter that deposits energy inside and thus contributes to the polymerisation of the dosimeter. This work demonstrates the successful use of gel dosimeters to measure the influence of scatter in a radiotherapy beam, and further measurements are planned for obtaining scatter and output parameters from x-ray beams collimated to small field sizes using gel dosimeters.
5. RESULTS – MICROBEAMS AND HIGH RADIATION RESISTIVE POLYMER GELS
5.1. Introduction

In the previous chapter, polymer gels were applied to the measurement of small radiotherapy fields, down to sub-centimetre sizes (3 × 3 mm$^2$). In this section, the resolution will be further increased as polymer gels are used for the first time to examine the dose distribution in microbeam radiotherapy.

Microbeam radiotherapy (MRT) is a technique that can potentially deliver more effective therapy treatments to patients, as while healthy tissue appears highly resistance to high levels of peak dose delivered using microbeams while still being effective in treating malignant tissue. However, MRT’s nature of possessing high dose gradients means that it is difficult to accurately determine the dose distribution. Current techniques employed for dose measurement include MOSFETs [98, 106, 107] and radiochromic films [104, 105]; however, currently no method is completely satisfactory. Additionally, the predicted dose distribution of MRT has been simulated using Monte Carlo techniques [101, 102, 108-110].

The possibility of using polymer gels for microbeam radiotherapy as an alternative method of dosimetry was the motivation for this investigation. This thesis pioneered the use of gel dosimeters as a method of microbeam dosimetry, and is separated into two main sections. The first part focuses on the development of a special-type gel dosimeter capable of withstanding very high dose levels. Synchrotron radiation is characterised by very high flux levels, and is capable of saturating dosimeters very quickly. Hence, this necessitated the development of a new type of dosimeter as described in this thesis.

The second phase was to subject these gels to synchrotron microbeam radiation and then determine their dose response. While MRI is the most common technique for polymer gel examination, it was found that the limits of spatial resolution possible using MRI were insufficient for analysis of microbeam irradiated gel dosimeters. The only method known to have the required resolution was Raman spectroscopy. In this thesis, Raman spectroscopy techniques were employed and expanded upon to determine the MRT dose distributions in gel dosimeters.
5.2. Results – development and calibration of high resistance gels for microbeam radiotherapy

The first step in using polymer gel for microbeam radiotherapy was to overcome the ability of a synchrotron beam to generate very high doses and dose rates. Therefore, a new type of gel dosimeter was required for this, as the standard types of dosimeters are made for doses of approximately 10 Gy while in MRT doses in the range of 100’s of Gy are normally delivered. Here, work towards developing and characterising such a highly radiation resistive gel dosimeter is described.

Generally, the presence of oxygen is considered detrimental to polymer gels as it inhibits the polymerisation process, making the gel less sensitive to radiation [44]. In this work, the possibility of reversing this situation was tested, where the presence of oxygen in a polymer gel could be used to an advantage by including it to enhance the radiation resistance of polymer gels. Hence, it was hypothesised that making a gel deliberately diffused with oxygen would increase the dose required for polymerisation, and hence be more suitable for high dose situations.

An image of a typical batch of oxygen diffused gels is shown in Figure 81. These polymer gels were irradiated with 200 and 225 Gy, (6 MV beam from a Varian 600C linear accelerator) and demonstrate that polymerisation can occur in gels that have been prepared in an oxygen environment. In other words, the disadvantage of oxygen in polymer gels is converted into a useful benefit to measure the dose of high levels of radiation. These gels were irradiated in increments of 50 Gy, and no change in colour (which indicates response to radiation) was observed in any of the samples until 200 Gy, at which point all vials except the largest showed signs of colour change. One vial was removed and the remaining given 25 Gy, at which point the largest vial also showed colour change. At this point the irradiation was ended. It has been noted previously that the presence of oxygen in a gel delays the polymerisation process [44], so preparing a gel in a normal atmosphere should simply delay the process for a higher level of incident dose.
It was observed that the largest vial had much less polymerisation than the other three. This is believed to be due to the amount of oxygen in the vial in comparison to the amount of monomer. The largest vial is a push cap type, meaning that a significant air bubble remained in it after sealing it, in comparison to the other vials which were screw cap and therefore could be filled completely when being prepared. As a result, there was more oxygen in this sample to interact with free radicals compared to the other samples, delaying the dose level at which polymerisation occurred.

The polymerisation in the large sample can be seen to have only occurred on one side (the side closest to irradiation, left in the photograph), and is greater at the bottom of the vial, away from the air gap at the top, further suggesting that the air bubble was the source of oxygen preventing polymerisation in this sample.

Figure 81 Photograph of 4 gel vials that had been prepared in a standard atmospheric environment with oxygen, showing polymerisation after high levels of irradiation. The second vial from the left received 200 Gy, the other three vials received 225 Gy.
A figure of a typical calibration curve for such high resistance gel dosimeters irradiated by a large field (15 × 15 cm²) 6 MV beam with full scattering conditions from a clinical linear accelerator is shown in Figure 82. It can be seen that there is a level of dose for which there is no appreciable change in polymerisation, followed by a quick increase near 150-175 Gy, and final saturation at a dose near 300 Gy.

Figure 82 Calibration for high resistance gels irradiated with a wide 6 MV beam from a linac. The displayed uncertainty is 1 standard deviation (N = 33).

The shape of this calibration curve is fundamentally similar to those of normoxic polymer gels that were been designed for low dose measurements, such as that presented previously (section 4.1). The main differences being that the linear region is wider (therefore a wider range of doses are measurable) and there is a longer portion in which there is little change in T₂ before the linear region. For illustration, this comparison is simulated in Figure 83.
Figure 83 How a high resistance gel differs from a standard polymer gel in reaction to incident dose. Blue is the low dose region, which little change in polymerisation with dose. Green is the linear region, and the most sensitive portion of the curve. Red is the region where the gel is nearing the saturation dose. The most accurate measurements occur when the incident dose falls within the green region of the curve.

5.3. Microbeams

5.3.1. Microbeam irradiation

Gel samples were irradiated at the SPring-8 Synchrotron as described in section 3.2.5.2. A photograph of a sample vial irradiated by high-intensity microbeams is shown in Figure 84 and a closer view of the same sample is displayed in Figure 85 below. It can be seen that a clear polymerisation effect has occurred along the narrow paths of irradiation. These images demonstrate that it may be possible to use optical attenuation as a method of dosimetry for microbeam irradiated gel dosimeters; however, the vials used in this work are not suited to such a task as they are very narrow and the glass thus has a large amount of curvature.

In Figure 84, from left to right, the estimated dose for each set of irradiated regions is 2400, 2200, 2000, 1800 and 1600 Gy from a 150 kV synchrotron microbeam. Each
A group of irradiations was spaced 2 mm apart. As discussed later, the lower limit on dose required to make a microbeam visible is apparently dependent on the average dose per volume. By spacing the sets of microbeams closer together or farther apart, the minimum dose required to induce a visible polymerisation change will be decreased or increased respectively, a point that will be discussed in a later section in this chapter (section 5.3.3.7).

Figure 84 Photograph of a series of microbeams of differing strengths taken using an ordinary microscope. The estimated dose delivered in each group, from left to right, is 2400, 2200, 2000, 1800 and 1600 Gy. The beam grouping interspacing is 2 mm centre-to-centre.
5.3.2. Magnetic resonance imaging of microbeam irradiated gel dosimeters

While it is possible to image the polymerisation of gel dosimeters irradiated with microbeams with an MRI scanner, the resolution required for an accurate measurement is usually beyond the capabilities of the current technology available. A microbeam (as used in this work) will have an ideal width of 25 µm based on the width of the collimator slits used. To make a reasonable measurement of the dose across this microbeam irradiated field, the pixel resolution would have to be improved to at least about 5 µm in size. The best resolution that was achieved in this work, using a 7 T micro-imaging system MRI scanner, was a pixel size of 19.53 × 19.53 µm² as shown in Table 18 below.
After irradiation, these gels were scanned using two methods. The first was the aforementioned high resolution MRI techniques using 7 T MRI scanner and the second was using Raman spectroscopy more suited to the high resolution required for measuring microbeam irradiation. The MRI scan parameters used in this thesis are listed in Table 18. However, this was not expected to produce any useable result due to the minimum size of the MRI scanning resolution being approximately equal or larger than the nominal size of the beam.

Table 18 Images were scanned using a MSME sequence, TE = 10 ms, 64 echo train length and a FOV of 10 × 10 mm².

<table>
<thead>
<tr>
<th>Pixel size (µm²)</th>
<th>MRI scanning parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 86</td>
<td>78.13 × 4 averages, TR = 2000 ms, read matrix = 128 × 128, 64 echoes, FOV = 10 × 10 mm², scan time = 17m 4s</td>
</tr>
<tr>
<td>Figure 87</td>
<td>19.53 × 4 averages, TR = 5000 ms, read matrix = 512 × 512, 64 echoes, FOV = 10 × 10 mm², scan time = 2h50m40s</td>
</tr>
</tbody>
</table>

Below are images for typical gel dosimeters irradiated with microbeams and imaged at two different levels of resolutions using a 7 T MRI scanner.

The first image (Figure 86) shows a vial irradiated with two singular microbeams spaced 1 mm apart. In the final T₂ image, the two lines of polymerisation are consistently approximately 13 pixels apart, which is equal to 1.015 mm, the expected distance.
Figure 86 $T_2$ map of a $5 \times 5$ mm$^2$ portion of a $128 \times 128$ pixel 7 T MRI image. The dark wavy lines are the polymerised region, but the resolution is insufficient to determine the dose distribution.

The second image (Figure 87) shows the same image of the same gel sample as that displayed in the figure above using a $512 \times 512$ pixel resolution, which results in a pixel size of $19.53 \times 19.53 \mu$m$^2$. However, it is clear that the features representing the polymerised region are not observed in the $T_2$ map, despite this image covering the same region of the gel.
The increase in resolution is accompanied by a decrease in the SNR, to the point where the polymerised region no longer is visible. While the SNR can be increased further with longer scan times, the image in Figure 87 already had a scan time of approximately 3 hours, so further increases in scan time are not feasible for work on a regular basis. From this, it can be concluded that MRI scanning is inadequate with current techniques to determine dose distributions in gel polymerised by microbeam irradiation.

5.3.3. Raman spectroscopy

In the previous section, the limitations of MRI for use in imaging microbeam irradiated polymer gels were discussed. Hence, another technique with a much higher
resolution was required to determine the dose distribution within these gels. Raman spectroscopy, which measures the scattered light from a laser focused into the sample, was used for this purpose.

Raman spectroscopy has a much better potential intrinsic resolution (order of 1 µm) compared to MRI, hence this method was used to examine these microbeam irradiated polymer gels. The methodology is described in the previous chapters (section 3.4). Two methods of examining Raman spectra were employed for measurement of calibration data of broad beams, the first based on the peak volume ratio of two peaks of the Raman spectra, and the second used the overall total count within a pre-defined range of Raman shifts. In this work, all gel samples scanned using Raman spectroscopy were done at the gel surface, underneath the vial glass.

5.3.3.1. Scans of spectra

Scans of sample spectra are shown in Figure 88 and Figure 89. A clear variation between the spectra of an unpolymerised (control) sample and a polymerised spectra from the same gel sample can be seen. The polymerised spectra, in addition to having a different shape (consisting of different emphasised peaks) also tends to have a lower overall count number at all Raman shift values (wavenumbers), due to the polymerisation scattering light and therefore returning less light to the Raman scanning system.

Figure 89 shows a comparison of two scans (a polymerised spectra and a control one) centred around 3000 cm$^{-1}$. It can be seen that there is a large variation in the peaks of this region, specifically the peak located at approximately 2940 cm$^{-1}$, so these peaks were selected to be used in making profiles of the dose change with position.

The change of the 2940 cm$^{-1}$ peak can be attributed to the CH$_2$ anti-symmetrical stretching within polyacrylamide and gelatine [14, 57], and the variation of the peak located at 3040 cm$^{-1}$ (which varies to a lesser degree compared to the 2940 cm$^{-1}$ peak) is attributed to vinyl group in bis-acrylamide and acrylamide [14]. In this work, polymerisation was measured by the ratio of the integrated peak volume of the 2940
cm\textsuperscript{-1} peak to the 3040 cm\textsuperscript{-1} peak, as these peaks show a marked change in size with polymerisation, particularly the peak located at 2940 cm\textsuperscript{-1}.

Figure 88 Comparison of spectra from an unirradiated (top) and an irradiated (bottom) regions of a gel irradiated with microbeams.
Figure 89 Comparison of typical spectra (centred at 3000 cm$^{-1}$) taken from a polymerised and unpolymerised regions in a gel, showing the relative changes in the size of the peaks. For the purpose of this image, both spectra have the same baseline.

5.3.3.2. Calibration of high resistance gel by synchrotron generation x-rays

A calibration curve of the gel dosimeter response when irradiated with board beams (1 × 10 mm) is shown in Figure 90. It can be seen that there is a region of very low response from 0 Gy to approximately 250 Gy, followed by a large increase between 250 and 500 Gy, after which there is only a small increase in polymerisation. This shape is similar to that shown before with MRI calibration, although the range is pushed to high values, most likely due to the beam only being 1 mm wide (as opposed to covering the entire vial).
Figure 90 Calibration of high resistance gels using the gels irradiated with wide beams (1 × 10 mm) as a reference point. Peak volume ratio refers to the ratio of the selected size of the peak, in work the ratio of the number of counts in peaks 2940 cm\(^{-1}\) to the peak 3040 cm\(^{-1}\). The displayed uncertainty is 1 standard deviation (N = 3).

A validation of the above described calibration result is depicted in Figure 91. This figure shows an alternative and innovative calibration method developed in this thesis. It shows a linemap of a gel dosimeter irradiated to different levels of dose, measuring the total number of counts between a Raman shift of 2780 cm\(^{-1}\) and 2819 cm\(^{-1}\), including the background counts. This region of the spectra was chosen because it did not display any peaks and was relatively flat regardless of the degree of polymerisation in the polymer gel. It was found that a very minor drop in signal associated with the 250 Gy irradiation was detected, as well as a large signal drop associated with doses between 750 and 2750 nominal Gy. The broad beams (excluding the 250 Gy peak) have a measured FWHM of 1.11 ± 0.07 mm (1 standard deviation, N = 5). Increasing the dose further above 750 Gy causes a further decrease in total signal, but at a much lower rate than between 250 and 750 Gy, a similar result to that obtained with the first calibration method.
Figure 91 Calibration of gel irradiated with wide beams using a total count method. Regions of polymerisation show a significant drop in total counts, proportional to the dose received.

5.3.3.3. Linemaps of microbeam irradiated gels

A series of microbeams is shown in Figure 92 and Figure 93. In Figure 92, only the 3 central microbeam shave induced polymerisation, whereas in Figure 93, two sets of microbeams (a set of microbeams containing 5 beamlets spaced 200 µm apart) have been irradiated with a closer spacing, effectively a continuous group of beamlets at 200 µm intervals, and as such, there are four beamlets in each set visible. The variation in beamlet intensities is due to the diffusion of oxygen through the sample during irradiation, discussed in section 5.3.3.7.

The interspacing between peaks in these figures matches the expected value of 200 µm. The measured FWHM of these peaks was 35 ± 2 µm. This is approximately 10 µm larger than the nominal width of the beam. The variation could be due to polymerisation diffusion with time, the possibility of penumbra from beam divergence and the presence of secondary electrons from the collimator [105].
Figure 92 Profile of a set of five microbeams. Only the three central microbeams have induced polymerisation.
5.3.3.4. Peak-to-valley signal and dose ratios

The Peak-to-Valley Signal Ratio (PVSР) is a representation of the Raman signal (in this case, the peak volume ratio) based on the data before application with the calibration data. The series of microbeams shown in Figure 93, demonstrates that the valley signal to be 3% of the maximum peak signal (the valley being directly adjacent to the peak in question). This translates to a PVSR of approximately 33, however, it needs to be accounted for the fact that not all peaks are of equal intensity. As this is a factor of the uneven consumption of oxygen (section 5.3.3.7) in the sample, this factor needs to be accounted for.

A Peak-to-Valley Dose Ratio (PVDR) is similar, but more useful concept, as it is the comparison of the direct amount of energy between absorbed by the peak compared to the valley regions. It’s obtained converting the raw data used for the PVSR in conjunction with the calibration data. In this work, the calibration curve obtained
previously Figure 90 was used for conversion of the PVSR to the PVDR. It was found that the PVDR was approximately 28.

It is known that a measured PVDR value for a series of microbeams will depend on several factors. Aside from the beamlet thickness and interspacing, these factors include the choice of beamlet and valley to measure [185], and the PVDR will also vary depending on the array size (both the beam height and the number of beamlets in the array [187, 188]). The beam energy [187, 188] and depth within the sample at which the measurement is made are also important as the PVDR will typically decrease the further into the sample a measurement is made [185-189]. These are all factors that must be taken into account when comparing the measured PVDR. One example is the work by Crosbie et al. [105], which used the same setup for the irradiation as used in this work, and found the PVDR measured with film to be 65 at the surface of the phantom.

It is important to recognise that the dose delivered is designed for macroscopic purposes [162], and therefore the application of dose to micro-sized regions introduces uncertainties.

One possible solution would be to use two separate batches of gel for irradiation, one designed as a high resistance gel, and the other a more typical normoxic type gel that would have a sensitive range between 0 and 15 Gy. This second gel could be used for valley measurements while the high resistance gel is used for the peak measurements. The use of two separate gels does introduce another source of possible uncertainty, and this work is beyond the scope of the thesis due to the limited time available at the synchrotron facilities.

One of the limitations in obtaining a full microdose calibration curve that was not anticipated initially was that at high doses some of the gels melted due to the high temperature due to the large amount of heat generated by polymerisation reactions in the gel. Recently, a new formulation of gel was developed that raises gel’s melting point, possibly allowing polymer gels to be used in these high dose rate experiments. This topic is covered in the next section.
5.3.3.5. Temperature induced effects on microbeam irradiated polymer gel

It was observed in a few instances that the polymerised regions within the gel dosimeter had temporarily melted and resolidified as demonstrated in Figure 94 and Figure 95.

The process of polymerisation (the conversion of monomer to polymer) for an acrylamide based gel is known to be exothermic. The conversion of acrylamide and N’N-methylene-bis-acrylamide (BIS) into polymer chains releases energy stored in the double bonds of these molecules, equivalent to 81.5 kJ mol$^{-1}$ of available double bonds [172, 173, 190]. This energy is transformed into heat.

An approximate estimation of the amount of heat generated in a typical polymer gel used in this thesis can be made based on the known chemical composition of the gel. The acrylamide-based gel used in this work consists of 3.5 % acrylamide (71.08 g mol$^{-1}$) and 3.5 % BIS (154.17 g mol$^{-1}$) by weight. As acrylamide has a single instance of a double bond and BIS has two, it can be inferred that approximately $9.46 \times 10^{-4}$ mol of monomer double bonds are present in a gram of gel dosimeter material prior to irradiation. The procedure for the calculation is shown in equation (15) below is derived from the work published by Salomons, Park, McAuley and Schreiner [172].

$$
\Delta N_{max} = \frac{0.035g}{71.08g \cdot mol^{-1}} + \frac{2 \times 0.035g}{154.17g \cdot mol^{-1}}
$$

Assuming full polymerisation due to irradiation, which may be possible in a short space of time due to the synchrotron’s very high flux rate, the polymerisation process will release approximately 77 J g$^{-1}$ of gel material. If a region of microbeams is irradiated, it may increase the temperature markedly compared to the surrounding regions, by the order of 15 K. It has been previously shown that the polymerisation of an acrylamide-based gel will result in a significant increase in the local temperature [172].
So far the estimation of heat due to polymerisation is discussed and found to be significant. However the heat generated from the irradiation itself is very small compared to that generated by polymerisation. For instance the heating of the gel dosimeter due to incident radiation with a 3000 Gy entrance beam would only release about 3 J g\(^{-1}\) of energy relative to the 77 J g\(^{-1}\) due to polymerisation, assuming a 100% conversion of that energy to heat. Or, while the process of polymerisation will produce approximately 15 K of heat in a gram of gel material, the incident radiation would raise the temperature of the gel by less than 1 K.

As microbeam radiotherapy only irradiates thin slices of the gel dosimeter, some regions will become much warmer than others. As a result, there may be localised regions sustaining large amounts of heat, causing them to melt and creating convection inside the gel sample. This may explain the wavelike patterns that form in some gels such as those shown in Figure 94 and Figure 95.

Figure 94 Image of gel irradiated by microbeams. Near the top of the photograph, the waves in polymerisation due to the melting and resolidifying of the gel are visible.
Figure 95 Photograph of a vial of gel dosimeter irradiated by synchrotron beams 1 mm wide and 6 mm long. The curve in the gel can be attributed to the gel melting during the polymerisation process and re-solidifying afterwards.

Fernandes, Pastorello, de Araujo and Baffa [191] demonstrated that the addition of formaldehyde could increase the melting point of a type of polymerising gels called MAGIC gels (first produced by Fong, Keil, Does and Gore [26]). It is possible that a similar approach for PAG formulations may also increase its melting point and reduce the possible effects of the polymerisation induced temperature increase. This could be expanded into a separate project.

5.3.3.6. Raman spectroscopy measurement of dose at depth

The ability to measure the dose at depth within a polymer gel using Raman Spectroscopy is limited due to the inherent light scattering properties of polymerised gel. As a result, there is a marked drop in the signal that can be collected at depths below the surface. It can be seen in Figure 96 that the Raman signal collected from a laser focused at depth (focused at 1.5 mm below the glass) in a gel sample is greatly reduced in comparison to that collected at the surface. In addition, the beam also
appears to be wider, meaning there has been a loss of resolution, with the FWHM of the microbeam increasing from $30 \pm 2$ to $69 \pm 5 \mu m$ in this instance (uncertainty based on 1 standard deviation in signal response to determine the maximum and minimum possible FWHM, $N = 10$). Hence, depth dose with high resolution is currently a challenging task using this kind of Raman spectroscopy. A possible solution to this is discussed in a later chapter (section 7.2).

Figure 96 A comparison showing the microbeam peak from a high resistance gel measured at the surface (+) and measured at a depth of 1.5 mm below the glass vial surface (×).

5.3.3.7. Effects of oxygen contamination

It is well known that oxygen competes with acrylamide monomers for the free radicals produced through irradiation of the sample [3, 44]. Oxygen inhibits the polymerisation within these PAG dosimeters by consuming these free radicals that would have otherwise polymerised the monomer. This means a larger density of free radicals is required to compensate for those lost to oxygen interactions.
Throughout these experiments, microbeams were always irradiated in groups of 5, and the distance between these groups varying between samples. However, 5 microbeams were not always realised in the final gel polymerisation. For instance, Figure 92 demonstrates only the 3 central microbeams, while Figure 93 demonstrates groups of 4, even thought the gel received less irradiation overall.

The availability of oxygen explains this limitation in gel reaction to microbeam irradiated dose. That is, microbeam irradiation not only consumes oxygen within the irradiated volume, but also from the surrounding regions as oxygen can move through the gel dosimeter. During a single set of five microbeams irradiation, the central beamlet is exposed to less oxygen than those on the outside, which have a larger source of oxygen to the sides that they must consume before any polymerisation takes place as illustrated in Figure 97.

![Diagram](image)

**Figure 97** Diagram demonstrating the presence in a gel irradiated by a series of microbeams. Each microbeam consumes oxygen, those in the centre have less oxygen to consume, and therefore have a larger degree of polymerisation than microbeams on the outside.

Table 19 shows the ratio of microbeam intensity between the three central beams that were visible in gels where the microbeam sets were placed 5 mm apart for 2500 and 3000 Gy. It suggests that the two outer peaks have similar intensity compared to each other and that the central peak also has a reasonably constant intensity relative to the other two peaks despite an absolute difference owing to the difference in incident radiation. This is indicates that until the majority of oxygen in the sample is consumed, only a small amount of polymerisation will take place, even when using
this high intensity beam. As a result, the relative uncertainties of dose measurements in this region will be greater. This is in line with Hepworth, Leach and Doran [44], regarding the inhibition of oxygen contaminated polymer gels at relatively low intensity irradiations. One aspect of future planned work is to further characterise the motion of oxygen in these types of gel.

Table 19 The relative sizes of the outer peaks relative to the centre and to each other for a gel irradiated with microbeams of nominal dose 3000 Gy and 2500 Gy, with spacing between the beam sets 5 mm. Uncertainties listed are 2× the square root of the number of counts in the spectra data.

<table>
<thead>
<tr>
<th>dose (Gy)</th>
<th>Left peak to adjacent Centre peak Ratio</th>
<th>Right peak to adjacent Centre peak Ratio</th>
<th>Left peak to Right peak Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>3000</td>
<td>0.804 ± 0.011</td>
<td>0.823 ± 0.011</td>
<td>0.976 ± 0.016</td>
</tr>
<tr>
<td>2500</td>
<td>0.899 ± 0.012</td>
<td>0.893 ± 0.013</td>
<td>1.007 ± 0.009</td>
</tr>
</tbody>
</table>

5.4. Conclusion

Microbeam radiation therapy (MRT) is a technique with great potential to treat damaged tissue with reductions in side effects to nearby healthy tissue, but currently has several difficulties in terms of obtaining an accurate assessment of the dose distribution. In this work, a reduced the reaction rate of polymer gel by allowing the diffusion of oxygen throughout the sample was successfully achieved, and polymerisation was successfully generated along the paths of synchrotron induced microbeam radiation. High resolution MRI scanning using a 7 T system was shown to be inadequate, usable only down to approximately 20 µm and with too large an amount of noise at that level. As an alternative, the dose distribution of these microbeams could be measured successfully using Raman spectroscopy. In particular, profiles of the level of polymerisation as it varies with position accurate to 2 µm have been obtained.

The Peak-to-Valley Signal Ratio for a series of beams spaced 200 µm apart (irradiated with an entrance dose of 1400 Gy) was observed to be 33 when comparing the maximum peak with the maximum adjacent valley. This translated to a PVDR of 28
after calibration. While it is beyond the scope of this thesis due to the limited time available on the synchrotron, a possible solution to reduce the uncertainty in this measurement may be to use a normal resistance gel to measure the valley dose while using a high resistance gel to measure the peak dose.

Several aspects of these special high resistance gels warrant further investigation. The distribution and consumption of oxygen during irradiation was found to be an important factor in determining the final level of polymerisation. As oxygen can travel through the sample during the irradiation, the proportion of oxygen consumed at one location can impact the availability of oxygen and the degree of polymerisation at other locations. Therefore, the dimensions and interspacing of the microbeam radiations are important factors alongside the delivered dose in determining the final degree of polymerisation.

It was observed that they polymerisation induced is fast enough that the heat generated locally (from the exothermic polymerisation process) was sufficient to temporarily melt the gel dosimeter. In future work, this possibility needs to be accounted for when performing irradiations using high flux rate sources such as the synchrotron to prevent the loss of positional information.

The colour change of typical polymer gels is a difficulty for Raman spectroscopy, as the scattering of light greatly reduces and smears the dose distribution obtained. In this work, a new special-type clear gel (section 7.2) was developed as a solution towards solving this problem.

While it can be said that gel dosimeters are capable of imaging synchrotron microbeam irradiation, there is room for further work in developing the gel dosimeter’s chemical formulation as well as the best method of irradiation and imaging techniques, and future work in this field is proposed.
6. SMALL FIELD INHOMOGENEITY DOSIMETRY USING PAG (EFFECTS OF AN ANEURYSM CLIP ON DOSE DISTRIBUTION)
6.1. Introduction

The application of PAG for the dose determination in small fields may be altered by small metallic objects. The results of investigations into an example of such an inhomogeneity using polymer gels are presented in this section.

The use of aneurysm clips to treat patients with various neurological conditions such as arteriovenous malformations (AVMs) has lead to the possibility of having to give radiotherapy treatment to patients that contain metallic implants that could possibly affect the dose distribution. This study aimed to investigate the possible effects on the dose distribution by using an aneurysm clip placed into a 1 L round flask of polymer gel (to simulate a patient’s head) and then irradiated with a stereotactic treatment plan (as described in the method section).

It was determined that the addition of the aneurysm clip to the gel phantom resulted in an increase to the dose distribution of approximately 20% in the region immediately in front of the aneurysm clip. A drop in the delivered dose was also observed in regions of the gel located behind the aneurysm clip. The presence of the aneurysm clip was determined to induce nearby artefacts in MRI scanned images. These results were found to be in agreement with those reported [132, 133] as measured using Monte Carlo simulations and radiochromic film techniques.

6.2. Results

6.2.1. Gel results

Figure 98 shows a photograph of the 1 L round flask phantom containing the aneurysm clip after irradiation by 15 Gy of 6 MV radiation using the stereotactic arcs listed in the methodology section. The irradiated portion can clearly be seen in the centre of the flask.
After a period of 24 hours to allow for polymerisation, the polymer gel phantoms were examined using a 1.5 T MRI scanner. A Fast Spin Echo (FSE) sequence was used for $R_2$ measurements of the gel phantoms. The parameters used were: $TR = 4$ s, $TE = 12.5$ ms for 8 Echoes. The FOV = 25 cm in a $256 \times 256$ matrix, which results in a pixel size of $0.977 \times 0.977$ mm. Five slices, each 4 mm thick, were obtained at 4 mm intervals throughout the region of interest for the 3 flasks of gel dosimeter. One flask containing an aneurysm clip that had undergone irradiation, a second without an aneurysm clip with the same radiation treatment and a third containing an aneurysm clip, but without any radiation to act as a control comparison to determine the aneurysm clip’s possible imaging artefacts. The flasks were imaged in the Picker Eclipse 1.5 T MRI scanner head coil with the neck placed outwards horizontally (the same orientation as a patient’s neck).

Image analysis and a pixel-by-pixel subtraction between images of irradiated and non-irradiated gel phantoms were then carried out on slices containing the clip using MATLAB software. This minimises (but cannot be assumed to completely remove) the effects of image artefacts caused by the aneurysm clip due to magnetic susceptibility differences of the aneurysm clip compared to the surrounding gel material. The resultant image was then used to compare with the control images of the flask irradiated without the presence of an aneurysm clip.
A typical slice through the gel dosimeter flask that was irradiated, but did not contain an aneurysm clip, is shown in Figure 99. This image clearly displays the polymerised region of the gel dosimeter as a yellow region in the centre of the phantom. This region was anticipated to have a fairly uniform $R_2$ value, and this was confirmed by $R_2$ profile taken across the central region of the stereotactic field as shown in Figure 100. This validates the stereotactic plan to provide a uniform dose distribution across the central 2 cm diameter field.

Figure 99 Image of a slice through the gel dosimeter without the clip exposed to a stereotactic dose of 15 Gy. The yellow coloured area represents the central part of the irradiated area formed by the intersection of the arc shaped beams.

Figure 100 Dose profile across the stereotactic field in the gel dosimeter without the clip.
The introduction of a metallic clip, (such as the aneurysm clip) was expected to act as an inhomogeneity that could influence the final dose distribution due to the differences in the atomic number and the physical and free electron densities of the clip material (titanium) compared to the surrounding tissue-equivalent gel dosimeter [132, 133]. The dosimetric effects of titanium were not documented experimentally before this work. Figure 101 illustrates the effects on the dose distribution due to the presence of a titanium aneurysm clip within the irradiated field. Specifically, Figure 101(a) shows the MRI imaging artefact due to the presence of the aneurysm clip in an otherwise unirradiated gel dosimeter. Figure 101(b) is an image of a gel dosimeter containing an aneurysm clip after irradiation by the stereotactic treatment plan, and shows the polymerised region as a light blue area surrounding the aneurysm clip. Figure 101(c) shows a comparison phantom that underwent the same treatment plan of 15 Gy, but did not contain an aneurysm clip. Aside from the artefact induced from the aneurysm clip itself, there is a clear difference in the polymerisation of the central region in a comparison of images (b) and (c).
Figure 101 (a) An MRI image of a gel phantom containing the aneurysm clip before irradiation. (b) The same phantom of part a, now irradiated according to a stereotactic plan to 15 Gy of 6 MV x-ray beam. (c) Same gel phantom as a & b but without the clip and irradiated with the same beam and the same amount of radiation dose as that in part b.
A comparison of the dose profiles through the central irradiated region of the gel dosimeter, one containing the aneurysm clip and the other an irradiated control without the aneurysm clip, are shown in Figure 102 (y = 0, z = +2 mm from surface of clip).

From Figure 102 it is clear that the dose in the irradiated field has been enhanced by the presence of the aneurysm clip, which agrees with the predictions of Monte Carlo simulations [132, 133]. The dose enhancement to the gel phantom in front of the aneurysm clip (as shown in Figure 102) is 20 ± 3 % (uncertainty is 1 standard deviation, based on variation in MRI signal response, N = 25), excluding the MR signal from the aneurysm clip itself. The observed dose enhancement inside and outside the central field can be primarily attributed to increased scatter radiation from the aneurysm clip. Clinically, such an increase in dose within the target volume is potentially useful while that outside the target volume is possibly hazardous to healthy tissue. If the aneurysm clip is located at the edge of the irradiated region, a similar amount of dose enhancement can be anticipated outside the target region, resulting in a dose increase to healthy tissue. The uncertainty associated with this measurement is approximately what would be expected for MRI measurements of the gel dosimeter type [192]. It should be noted that towards the centre of the irradiated field, the possibility of susceptibility artefacts may influence the measured reading further. As all phantoms were made from the same batch of gel dosimeter solution, variations in response between samples to radiation is expected to be negligible.
Figure 102 Dose profiles of two slices sampled at the same depth in the gel dosimeters exposed to the same dose. The red dotted line shows the profile whereby an attempt has been made to subtract the effects of the clip artefacts on the profile, such that only the effects caused by the change in dose distribution remains (profile along x, y = 0, z = +2 mm from surface of clip).

It is anticipated that the beam will be somewhat attenuated in the regions of gel that lie behind the aneurysm clip relative to the direction the beam originates from. Hence some dose reduction behind the beam should be observed. Figure 103 shows approximately a 6 ± 2 % reduction (1 standard deviation in signal response, N = 25) in the dose immediately behind the clip (y = 0, z = −2 mm compared to back surface of clip) due to the aneurysm’s clip greater attenuation of radiation due to its higher density.
Figure 103 Dose reduction due to beam attenuation through the clip (profile along x, y = 0, z = −2 mm from back surface of clip region).

6.3. Radiochromic film measurements

Corresponding to the gel measurements previously, the dose profiles with and without the clip obtained from scanning the EBT films and converting their optical density readings into dose using the calibration data are displayed in Figure 104. A data smoothing with linear least squares fitting and a second-degree polynomial was performed to remove the fluctuations of the profile curves. It can be seen that a 6 ± 2 % (1 standard deviation in film signal response, 3 repeats of the film image, using the central 500 × 900 pixels) dose enhancement occurs due to the clip’s existence in the beam is observed. An attenuation of the beam by the clip is displayed on the other side of the profile as was observed in the dose distribution in the gels. This can be attributed to the influence of the clip, which is anticipated to attenuate x-rays more than the surrounding tissue due to its high density. Such attenuation of the beam by the clip is indicated in Figure 105 below. The uncertainty associated with film
measurement can be attributed to possible errors in calibration, non-uniform thickness of the film and reading uncertainties of the densitometer [193].

Figure 104 Measured dose before the clip using radiochromic film. This image was made with the film 2 mm from the clip, under the same conditions as used to generate Figure 102.
6.4. Discussions

Differences between polymer gel and radiochromic film measurements can most likely be attributed to differences in the set-up due to the nature of the mediums. Radiochromic film, being a 2-dimensional film, cannot completely surround an aneurysm clip as polymer gels can, leaving a small air gap nearby. The 0.1 mm protective layer of EBT film may also render the film as less sensitive to radiation, but is unlikely to make a significant difference in comparison to gel dosimeters. Additionally an air gap between the clip and the radiochromic film, due to the nature of the set-up, may also contribute to this difference compared to the gel dosimeter.

Another factor that could generate differences in measurements between the gel dosimeter and radiochromic film is the potential for magnetic susceptibility artefacts in MRI images. The magnetic susceptibility of water and tissue is approximately $-9.05 \times 10^{-6}$ [194], while the titanium alloy the aneurysm clip is composed of has a
magnetic susceptibility of $14.6 \times 10^{-6}$ [115]. Schenck [194] also describes titanium as a material that borders the line between those that produce noticeable but non-significant image distortion and those that result in obvious artefacts in images that are still useful in various applications. While titanium alloy aneurysm clips are designed to be compatible with MRI scanning, the differences in magnetic susceptibility between the aneurysm clip and the tissue-equivalent gel are expected to cause artefacts in MRI. Examples such as Figure 102 demonstrate that such visible artefacts are present in the final MRI scan. Therefore, care needs to be taken when determining the degree of enhancement at locations very near the titanium clip.

The measured dose enhancement here is approximately within the level of those predicted by Monte Carlo simulations for other higher atomic number and density materials (approximately 10% are very close distances to the clip) [132, 133]. However, these Monte Carlo predictions are at closer distances to the clip and employ a monoenergetic gamma beam of somewhat different energy to this study’s use of a clinical 6 MV x-ray beam.

From these studies, it is postulated that the enhancement is due to the photoelectric effect and the differences between the results presented here and those obtained using Monte Carlo [132] are possibly due to the higher proportion of lower energy x-rays in this work originating from the spectrum of initial beam energies.

Recently, many works have been published about the effects of various metallic materials (such as gold, dental materials and titanium mesh) inserted into tissue during radiotherapy treatments, and the dose effects determined using radiographic films and ionisation chambers [195-198]. All of the measurements employ large field sizes and involve relatively large inhomogeneities. The dosimetric effects of such inhomogeneities range between a few percent up to approximately 25%.

6.5. Conclusions

The dosimetric effects of an aneurysm clip on the dose distribution of a small field stereotactic radiosurgery treatment were determined by using applied gel dosimetry.
An increase in the recorded dose of approximately 20% at a distance of a few millimetres from the aneurysm clip was found. Measurements using radiochromic film demonstrate a similar increase, although smaller in magnitude (6 ± 2 %). The differences can be attributed to the geometry of the imaging, as gel dosimeters allow measurements closer to the aneurysm clip inhomogeneity than film. These results confirm the findings of dose enhancement seen in Monte Carlo simulations for other types of metallic clips, although the magnitude of the effect seen was less in these measurements. In addition, these results showed beam attenuation inside the field in regions of the gel phantom past the aneurysm clip, which was not indicated by Monte Carlo study. Further studies in the research would be to include the effects of aneurysm and other metallic clips into the dose distribution and treatment planning algorithms.
7. INNOVATIVE SPECIAL AND
MISCELLANEOUS APPLICATIONS OF
GEL FORMULATIONS
This chapter investigates the application of polymer gel dosimeters in some special areas of radiotherapy such as the determination of the level of photonuclear interaction contribution into the doses delivered in radiotherapy when high energy x-rays or electron beams are used. In this chapter innovative types of gel formulations are tested, in particular those that lead into formation of types of polymer gels that do not change colour when irradiated (clear gels). Extremely high dose rate beams are also determined using special type polymer gels, and the sensitivity of polymer gels to a high energy proton beam was investigated for the first time.

7.1. Photonuclear reactions in gel

The details of photonuclear reactions are described previously in section 2.4. When high energy (>15.6 MV x-rays or equivalent electron) beams are used to irradiate polymer gels it is expected that some photonuclear reactions in the polymer gels will occur, particularly within the oxygen in water molecules. This will result in emission of a positron followed by 0.511 MeV gamma rays as described in section 2.4. Therefore detection of these gammas from an irradiated polymer gels with the beams is a reliable confirmation of the generation of neutrons in the interaction process.

7.1.1. Results

A typical gamma ray energy spectrum obtained from an activated PAG sample as recorded by a NaI scintillator with a Multichannel Analyser (MCA) (previously calibrated using a $^{137}\text{Cs}$ source) is shown in Figure 106. A peak corresponding to the detection of a 0.511 MeV photon is displayed and this is clearly indicative of $^{15}\text{O}$ decay that was certainly the result of a photonuclear interaction within $^{16}\text{O}$, as described in section 2.4. The larger peaks at lower energies could be attributed to the activations in other atoms in the gel, the system noise and background plus the Compton edge of the 0.511 MeV peak.
Figure 106 Energy spectrum recorded from a polymer gel sample after irradiation by use of a scintillator and MCA. A peak corresponding to the emission of 0.511 MeV photons is clearly visible. This spectrum has had environmental background counts removed.

Figure 107 demonstrates that the size of the peak in the spectrum that is attributed to the 0.511 MeV photons emitted from the gel sample varies with time. The detection of a peak at 0.511 MeV is highly indicative of an electron-positron annihilation event. It can be seen that it decays in an exponential manner as would be expected for a material decaying according to a half-life. The measured half-life of the decay is 126.6 ± 5.1 s (fitted using MATLAB Trust-Region fitting algorithm to 95% confidence limits), which encompasses the known half-life for $^{15}$O of 122.1 s. The primary source of 0.511 MeV gamma rays is therefore attributed to the decay of $^{15}$O, and as such, an equivalent number of neutrons were produced in creating this $^{15}$O as required by the decay scheme listed previously (section 2.4).
Figure 107 The decay of number of counts within peak located at 0.511 MeV with time. The half-life measured is 126.6 ± 5.1 s.

In addition, two gel samples were irradiated to the same dose (10 Gy), with two different energy x-rays; one with beam energy below the threshold for photonuclear activation of oxygen (6 MV) and the other above the threshold value (18 MV). These gels were scanned with MRI (4.7 T Bruker animal scanner), using the parameters shown in Table 20. The recorded spin-spin relaxation time ($T_2$) values from these measurements are presented in Table 21. The measured $T_2$ value for an 18 MV beam is found to be slightly lower (representing a higher deposited dose), but not significantly so.
Table 20 Scanning parameters for gel samples irradiated by 10 Gy by a 6 and 18 MV radiotherapy beam. SNR refers to the standard deviation relative to the $T_2$ variation induced by a 10 Gy dose.

<table>
<thead>
<tr>
<th>4.7 T</th>
<th>pixel size (mm)</th>
<th>SNR</th>
<th>MRI scanning parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.391 × 0.391</td>
<td>10.</td>
<td>MSME, 40 echoes, 1 average, TE = 30 ms, TR = 11185 ms, read matrix = 128 × 128, FOV = 50 × 50 mm², slice thickness = 1 mm, scan time = 23m 15s</td>
<td></td>
</tr>
</tbody>
</table>

Table 21 Measured $T_2$ values for a gel irradiated at 10 Gy with a 6 and 18 MV beam. Uncertainty is 1 standard deviation (N=121).

<table>
<thead>
<tr>
<th>10 Gy at 6 MV</th>
<th>10 Gy at 18 MV</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_2$ (ms)</td>
<td></td>
</tr>
<tr>
<td>225. ± 11.</td>
<td>212. ± 7.</td>
</tr>
</tbody>
</table>

7.1.2. Discussion

This experiment was designed to detect evidence of photonuclear reactions in polymer gels. Experiments were made using 6 and 18 MV x-ray beams to irradiate the same batch of polymer gel. Any variation in the dose measured in polymer gel quantitatively is a measure of the secondary neutron contribution since 6 MV beams are below the threshold for generation of neutrons while 18 MV is anticipated to generate photonuclear reactions.

The detection of a 0.511 MeV peak (Figure 106) in the emission spectra of a gel irradiated by an 18 MV x-ray beam is indicative of electron-positron annihilation taking place. Due to the series of decays needed to produce the positron, it can be deduced that neutrons must also have been emitted. Figure 107 demonstrates an activity decay that matches the decay rate of $^{15}$O and therefore is correctly attributed to the neutrons generated by the photonuclear reactions occurring in oxygen. These emitted photoneutrons can be expected to cause further polymerisation of the gel but with a different energy deposition pattern compared to the secondary electrons and...
photons produced in lower energy interactions and may influence the dose distribution and degree of energy deposited.

PAGs are known to be energy independent at energies below the threshold for photonuclear reactions, but there are some indications that at higher energies (in the region that photonuclear interactions become present) that some variation in the degree of polymerisation occurs at higher energy levels, although not beyond the limits of experimental uncertainty [2, 20]. A similar result was found in this work, and this is consistent with the idea that photonuclear reactions involving oxygen within the gel are taking place and could be included into dose determination if high accuracy is required.

The amount of neutrons produced from this reaction is not negligible, though it is not expected to be large in comparison to the other elements of the interaction. Estimates from literature vary, but are of the order of 0.2% [199]. It should also be noted that photonuclear reactions may occur in a variety of materials, not only in the gel dosimeter but in the surrounding environment (such as collimators, flattening filters, etc.), which may also contribute to variations in the energy deposited within the gel [200].

This method of detecting neutrons may also be employed as a quality assurance test of a linear accelerator’s beam quality. Having a known pre-set high-energy beam irradiate a known gel dosimeter sample and recording the resulting gamma energy spectrum would allow any changes in the spectrum recorded at later times to be possibly used as an indication that the quality of the beam has changed, therefore indicating that the equipment needs maintenance.

### 7.1.3. Conclusions to photonuclear reactions in gels

In the recent years there has been an increasing interest in investigation of neutrons generated by the high-energy x-ray radiotherapy beams [136, 138-140, 201-203]. However, most of the work in the literature is focused on simulation-based investigations.
This work demonstrates a simple and reliable method for measuring the amount of neutron activation in a sample of gel, and hence is a good estimate of the photonuclear induced dose in a patient as gel is tissue equivalent. The presence of 0.511 MeV gamma rays emitted from polymer gels after irradiation by high-energy (>15.6 MeV) beams and the series of interactions needed to produce these gamma rays leads to the conclusion that neutrons were also being emitted within the gel (specifically from the decaying oxygen atoms) during the irradiation via photonuclear interactions. It should be possible to extend this method to detect photonuclear interactions to other types of samples. This measurement can possibly be improved in future work by reducing the uncertainty in the measurement through extended (and hence more accurate) MRI scan times.

In addition to obtaining a greater understanding of the dose distribution of high energy beams and the polymerisation of gels by radiotherapy beams of various energies, it is possible that the neutrons generated via photonuclear reactions from high energy photons or electrons could be used as a method of radiotherapy beam quality assurance. A change in the high-energy beam spectra from a known standard test target would change the proportional amount of positron-electron annihilations and the detected 0.511 MeV gamma spectra (i.e. the 0.511 MeV peak could be used as a measure of the beam quality).

### 7.2. Clear polymer gel development

Polymer gels are usually designed to undergo a colour change from clear to milky white as they polymerise (for instance, by radiation). This colour change is a basic sign of polymerisation, and can be used in methods such as optical tomography to measure the radiation dose delivered to the gel. The colour change is due to the scattering of light, mostly induced by the cross-linking.

It was proposed that decreasing the amount of cross-linking chemical within a gel chemical solution when polymerised would reduce the light scattering effects of the
polymer chains. Hence, a new type of polymer gel that remains clear despite a measurable polymerising effect could be developed.

A gel dosimeter that remains clear during polymerisation would have useful applications in dose measurement, in particular it would enhance the Raman Spectroscopy measurements efficiency, potentially allowing measurements to be made below the surface. In this work, it has previously been demonstrated (section 5.3.3.6) that at depths below the surface of a polymerising gel, the measurement using Raman spectroscopy of the dose distribution is compromised due to the presence of light scattering from polymerised regions. This lead to investigations into the development of a formulation of a polymer gel that would remain clear when irradiated, and finally resulted in a successful formulation of gel that detectably polymerised without colour change. The chemical formulations and stabilities of these various gel dosimeters leading up to and including the final clear gel formulation are described in the following sections.

A major challenging factor in the use of these clear-type gels is their stability as the following results indicate. The method of making a polymer gel clear (by decreasing the cross-linking fraction) has had the noted effect of rendering the final gel material unstable in many cases. By unstable, it is meant that a polymer gel experienced irregular phase separation, where one or more white beads of polyacrylamide would form out of the surrounding clear gel solution. Thus, this work was directed towards finding a formulation of gel that remained stable for a period of time that could be considered sufficient for a clinical environment (which is where the use of polymer gels aims to be eventually employed).

7.2.1.1. Chemicals for the preparation of clear gels

The creation of a gel that polymerises but remains clear requires investigation into a new formulation of gel. This requires a modification to the previous methodology presented for standard polymer gels to overcome instability that causes them to spontaneously phase separate. This instability has been noted by Jirasek, Duzenli, Audet and Eldridge [55] who found that that reducing the degree of cross-linker in
certain types of gel may make them unstable in some cases. To solve this problem, in this work, a variety of different gel formulations were made to develop a type of gel that not only remained clear, but was stable enough to last sufficient time that it could be used in a clinical setting.

Samples of clear gel were scanned using Raman spectroscopy and MRI. These gels were examined using Raman spectroscopy (as described in the methodology section 3.4) in the same manner as the examination of microbeam irradiated gel polymer gels. A Renishaw RM2000 (Renishaw plc, Wotton-under-Edge, Gloucestershire, UK) system was employed to examine these samples, using a 782 nm (infrared) laser with approximately 3 mW power at the gel sample and a 10× objective lens. Examinations of both the clear regions and the suspected solid polyacrylamide were made.

### 7.2.2. Results

Throughout this section, various properties of the clear-type gels (such as the viscosity, the colour change and the degree of polymer bead formation) are rated using a scale between 0 and 5, as described in Table 22. These values are measured using subjective means, and are not absolute values. This method of description is used to provide insight as to how each gel formulation performs in comparison to its peers in regard to achieving a clear-type gel that is stable and remains clear when irradiated.

| Table 22 List of scales used in this chapter to describe clear-type gel formulations and their stability with time. |
|---|---|
| Viscosity | 0 (free flowing) – 5 (completely solid) |
| Colour change | 0 (completely clear) – 5 (heavy opaque white) |
| Phase separation beads | 0 (none) – 5 (many and/or large numbers of beads) |

In the following sections, various clear-type gel formulations are proposed and described, and their suitability as a clear gel is investigated and reported. These are described in the order in which they were developed.
7.2.2.1. Hypoxic alginate based gel

Described in Table 23 is the list of clear gel formulations that were developed without the use of any gelling agent, and those using alginate as a gelling agent. The method of gel preparation was the standard one, and after preparation, all gel samples were observed to be clear. These gel phantoms were irradiated at 1.5 cm depth in water using a Varian 600C, 6 MV beam at 100 cm SSD. The irradiated field size was $20 \times 40$ cm, resulting in 96.625 MU per Gy, which was delivered at 400 MU min$^{-1}$.

Table 23 also lists the properties of the gel 6 days after irradiation. The most obvious result from this experiment is the formation of polyacrylamide beads within the solution. These tend to only occur at the middle range of doses, whereas very high or very low doses do not exhibit this feature. Proposed reasons for this are discussed later. The fact that such visible phase separation occurred demonstrates that this particular gel solution is unsuitable as a dosimeter, being unable to retain a measure of localised dose. This result occurred to both batches of gel, with and without the addition of a gelling agent. In addition, the gel formulation without gelling agent became solid with irradiation, as expected, a result that has been reported previously in literature [204].
Table 23 List of gel formulations and dose schemes for hypoxic alginate based gels and properties after irradiation for various given doses.

<table>
<thead>
<tr>
<th>gel formula</th>
<th>dose (Gy)</th>
<th>notes: after irradiation (6 days later)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water 85%, Aa 14.25%, BIS 0.75%</td>
<td>0</td>
<td>Clear, liquid</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Clear, liquid</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>Various phase separations throughout the gel sample</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>Phase separation through the sample, fewer, but larger beads than in sample C (10 Gy)</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>Clear, solid</td>
</tr>
<tr>
<td>Water 83.5%, Aa 14.0%, BIS 0.74%, Alginate 1.7%, CaCO₃ 20 mmol L⁻¹, GDL 20mmol L⁻¹</td>
<td>0</td>
<td>Clear, solid</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Solid, faint even phase separation.</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>Solid, 2.5 cm of phase separation near bottom of sample vial</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>Solid, Phase separation throughout.</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>Solid, phase separation throughout as a few large beads</td>
</tr>
</tbody>
</table>

7.2.2.2. Normoxic gel stability study

Another two gel formulations were developed without using any sort of gelling agent. However, these gel dosimeter formulations (Table 24) have the anti-oxidant THPC added to the gel solution unlike those described in Table 23 which were degassed to remove oxygen, resulting in a reduced production time and simplified method (as previously discussed in the method section). As with the previously described gel solutions without any gelling agent, it was intended that these polymer gels would remain liquid until after irradiation.

However, a formulation of gel solution in which THPC was added at a concentration of 10 mmol L⁻¹ was observed to solidify almost immediately, and was unsuitable for use as it could not be separated and poured into individual vials. The gel solution
containing only 2.5 mmol L\(^{-1}\) showed no such solidification. It is unknown whether the solution of polymer gel containing 10 mmol L\(^{-1}\) of THPC polymerised immediately or became solid for other reasons. As such, only the 2.5 mmol L\(^{-1}\) THPC concentration solution could be irradiated and examined. These gels were irradiated by a Varian 600C to the doses listed in the table using a 6 MV beam at a dose rate of 400 MU min\(^{-1}\) and a 16 × 32 cm field size. They were placed into a water tank at a depth of 5 cm below the surface and 90 cm SSD.

Table 24 Series of clear-type gel formulations, the irradiated delivered dose and the degree of visible phase separation after irradiation.

<table>
<thead>
<tr>
<th>gel formula</th>
<th>irradiated dose (Gy)</th>
<th>notes, degree of phase separation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water 85%, Aa 14.25%, BIS 0.75%, THPC 10 mmol L(^{-1})</td>
<td>NA</td>
<td>Solidified during preparation process, unsuitable for use</td>
</tr>
<tr>
<td>Water 85%, Aa 14.25%, BIS 0.75%, THPC 2.5 mmol L(^{-1})</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>2.5</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>7.5</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>60</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>80</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

Notably, these clear-type gel samples demonstrated a tendency to phase separate as did other samples, but unlike other examined samples, there was no distinct correlation between the delivered dose and the extent of phase separation observed. It was noted that the unirradiated control samples did experience phase separation. While there was a tendency for the clear-type gel samples of this batch to not form phase separation beads at high levels of irradiation, at low doses the formation of these phase separations beads was seemingly random. As such, this formulation of gel
is not suitable as a dosimeter, as it demonstrates a lack of reliability. The gels in this section were scanned using Raman spectroscopy as reported in section 7.2.2.5 to determine if any polymerisation change could be detected.

7.2.2.3. THPC variation in a normoxic clear gel

A series of normoxic polymer gels were developed and irradiated to determine how they would react under irradiation and if it would stay clear, free of phase separation beads. It was previously observed that gel samples that contained 15 T, 5 C and 5% gelatine suffered phase separation at certain concentrations of anti-oxidant (THPC at 5 or 7 mmol L$^{-1}$), while at other concentrations, the formation of beads before irradiation was minimal, but when irradiated the gels did change colour.

Based on this, possible reasons for the colour change are:
1. Adding 5% gelatine means there is no longer enough water to fully dissolve the polymer chains any more.
2. The gelatine prevents the polymer from dissolving properly, and reducing the level of gelatine should reduce this effect.

A list of gel formulations, the dose delivered, the appearance/viscosity of the gel before irradiation and the appearance of the gel after irradiation are shown in Table 25. The only variation in the gel formula between various batches was the level of anti-oxidant (THPC) used. For the base chemicals, the amounts used were: de-ionised Water 85 % (% by weight), acrylamide 10.69 %, N’ N-methylene-bis-acrylamide (BIS) 0.5692 % and Gelatine 3.75 %. That is the values of total monomer were 11.25 % and the cross-linker was 5 % of the total monomer.

After preparation, the vials were placed into a 1 L round flask degassed with argon. In addition, 2 vials in each batch were not stored this way, but rather stored outside the flask with only the glass vial and plastic cap to protect it from the atmospheric oxygen contamination. The purpose of this was to determine the magnitude of effect that this storage method would have on the degree of polymerisation. These samples were
allowed to set overnight at room temperature, on the basis that a previous similar gel formula had frozen and shattered the glass vial it was in when placed in refrigeration.

These gel phantoms were irradiated at 5.5 cm depth in water using a Varian 2100C linear accelerator, with the water surface placed at 90 cm SSD. The irradiated field size was 16 × 32 cm, resulting in 1 Gy being equivalent to 91.7 MU, which was delivered at a dose rate of 400 MU min\(^{-1}\).
Before irradiation the clear-type gels were, in general, not solid except for the solution containing 5 mmol L\(^{-1}\) THPC which was close to, but not quite, solid. It also exhibited a significant level of phase separation. The aqueous nature of the unpolymerised clear-type gels demonstrates that the gelling agent was not strong.
enough in this case. Gels can be solidified via irradiation, however this defeats the purpose of using gels as a three-dimensional dosimeter. As the only formulations of clear-type gels that remained solid were those that exhibited phase separation, a link between these phenomena can be suggested, however more research would be needed to further investigate this point. When made using 5 mmol L\(^{-1}\) of THPC, 15 T, 5 C clear-type gels show significantly more phase separation before irradiation, forming many white beads. This feature was absent from other formulations of gels with different concentrations of THPC. The reason for this is unknown; however such a formulation of clear gel is unsuitable for use. It was observed that most vials did undergo colour change in proportion to the incident radiation. As such, these gel formulations are not suitable as a clear-type gel.

7.2.2.4. Study of total monomer concentration in clear gel

Three types of clear gels were developed in this series of tests. In this set of 3 clear-type gels, the level of total monomer was varied between 5 and 11% of the total mass, while the amount of cross-linker (BIS) relative to monomer (acrylamide) was kept constant at 5% (a 19:1 ratio). The level of gelatine in each solution was kept at 5% of the total solution mass (based on the previous gel solutions, which did not solidify using 3.75% gelatine, greater amounts of gelatine were employed in this instance). The mass of water was adjusted in each case to match the quantity of total monomer. The amount of THPC was also kept constant at 9 mmol L\(^{-1}\). Data relevant to this is listed in Table 26. This proportion of THPC was chosen on the basis of previous results (Table 25), in which gel solutions containing 9 mmol L\(^{-1}\) of THPC showed less phase separation than other values. It was found that while all of the prepared gels were clear or almost clear before irradiation, the degree of viscosity varied slightly, but was generally consistent within a batch of gel. After irradiation to doses between 0 and 40 Gy, all gels were observed to be completely solid and in general only underwent very slight colour change. This data is listed in Table 27. It was noted that the formulation of polymer gel using 11 T of THPC showed some signs of early phase separation, before irradiation.
These gel phantoms were irradiated at 5.5 cm depth in water using a Varian 2100C with 90 cm SSD. The irradiated field size was 16 × 32 cm, resulting in 91.7 MU per Gy, which was delivered at 400 MU min⁻¹.

Table 26 Gel solution chemical formulations for gel dosimeters of varying total monomer concentration. All values (except THPC) are percentages of total mass.

<table>
<thead>
<tr>
<th>total monomer concentration (%)</th>
<th>water (%)</th>
<th>acrylamide (%)</th>
<th>BIS (%)</th>
<th>gelatine (%)</th>
<th>THPC (mmol L⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>90</td>
<td>4.75</td>
<td>0.25</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>7</td>
<td>88</td>
<td>6.65</td>
<td>0.35</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>11</td>
<td>84</td>
<td>10.45</td>
<td>0.55</td>
<td>5</td>
<td>9</td>
</tr>
</tbody>
</table>
Table 27 Series of clear-type gels (varying total monomer concentration) and their properties before and immediately after irradiation. All solutions contain 5% gelatine by weight, the cross-linker makes up 5% of the total monomer and each contains 9 mmol L\(^{-1}\) of THPC.

<table>
<thead>
<tr>
<th>total monomer concentration (%)</th>
<th>irradiated dose (Gy)</th>
<th>phase separation (beads) before irradiation</th>
<th>viscosity before irradiation</th>
<th>colour after irradiation</th>
<th>viscosity after irradiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>0</td>
<td>4</td>
<td>&lt;1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>0</td>
<td>4</td>
<td>&lt;1</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0</td>
<td>3</td>
<td>&lt;1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>0</td>
<td>3</td>
<td>&lt;1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>0</td>
<td>3</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>&lt;1</td>
<td>2</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>&lt;1</td>
<td>2</td>
<td>&lt;1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>&lt;1</td>
<td>2</td>
<td>&lt;1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>&lt;1</td>
<td>2</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>&lt;1</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

These gels were examined 3 and 11 days after irradiation to inspect for visual changes, which are listed in Table 28 and Table 29 respectively. It was found that phase separation occurred, causing beads of white material to form inside the gel of various sizes, although in this case, it took some time for the beads to form rather than forming instantaneously as with previous gel formulations (section 7.2.2.3).
Table 28 Series of clear-type gels (varying total monomer concentration) and their properties 3 days after irradiation.

<table>
<thead>
<tr>
<th>total monomer concentration (%)</th>
<th>irradiated dose (Gy)</th>
<th>colour</th>
<th>viscosity</th>
<th>estimated number and size of phase separation beads</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>&lt;1</td>
<td>5</td>
<td>1 × 1 mm</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0</td>
<td>5</td>
<td>2 × 5 mm</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>0</td>
<td>5</td>
<td>1 × 3 mm</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>&lt;1</td>
<td>5</td>
<td>none</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>&lt;1</td>
<td>5</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>&lt;1</td>
<td>5</td>
<td>1 × 3 mm</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>&lt;1</td>
<td>5</td>
<td>1 × 2 mm</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>1</td>
<td>5</td>
<td>none</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>2 × 1 mm</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>&lt;1</td>
<td>5</td>
<td>1 × 10 mm</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>&lt;1</td>
<td>5</td>
<td>1 × 12 mm</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>1</td>
<td>5</td>
<td>2 × 10 mm</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>2</td>
<td>5</td>
<td>1 × 1 mm</td>
</tr>
</tbody>
</table>
Table 29 Polymer gel of varying monomer concentration, listing the properties of the gel 11 days after irradiation. Bead size refers to the estimated diameter of a spherical object. At this time, the gels samples were scanned with 1.5 T MRI.

<table>
<thead>
<tr>
<th>total monomer concentration (%)</th>
<th>irradiated dose (Gy)</th>
<th>colour</th>
<th>viscosity</th>
<th>estimated number and size (diameter) of phase separation beads</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>2 × 4 mm</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>&lt;1</td>
<td>5</td>
<td>2 × 7 mm</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0</td>
<td>5</td>
<td>3 × 10 mm</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>0</td>
<td>5</td>
<td>1 × 10 mm</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>&lt;1</td>
<td>5</td>
<td>none</td>
</tr>
<tr>
<td>7</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>&lt;1</td>
<td>5</td>
<td>8 × 5 mm</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>&lt;1</td>
<td>5</td>
<td>5 × 4 mm</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>&lt;1</td>
<td>5</td>
<td>8 × 4 mm</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>1</td>
<td>5</td>
<td>none</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>1 × 4 mm</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>&lt;1</td>
<td>5</td>
<td>1 × 12 mm</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>&lt;1</td>
<td>5</td>
<td>2 × 12 mm</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>1</td>
<td>5</td>
<td>2 × 12 mm</td>
</tr>
<tr>
<td></td>
<td>40</td>
<td>2</td>
<td>5</td>
<td>2 × 6 mm</td>
</tr>
</tbody>
</table>

It can be seen in Figure 108 that an MRI scan of clear gel across a phase-separated bead shows the bead clearly in the $T_2$ map. Figure 109 shows the variation of the average $T_2$ of the formulation of clear gel measured against the delivered dose, only in clear regions away from any polyacrylamide beads that may have formed. It is observed that in general, there is an expected decrease in the $T_2$ value, and that this decrease saturates at approximately 20 Gy (10 Gy for the 5T gel formulation). This decrease is considered significant based on a t-test to 95% certainty. This is consistent with the drop in $T_2$ measurements in standard acrylamide-based polymer gels. This is a similar value to the saturation dose for the 6T & 50C polymer gels made from acrylamide and BIS.
Gels containing 5 T of monomer showed little variation in measured $T_2$ value, because there was insufficient monomer. Any polymer chains that did form could not significantly alter the movement of water particles in the gel dosimeter, which is the primary method of altering the $T_2$ value. Whereas higher concentrations of total initial monomer would lead to a greater number of polymer chains which would restrict the motion of water particles in the gel to a greater degree, leading to a greater difference in the unirradiated and fully polymerised $T_2$ values.

Figure 108 MRI $T_2$ map of two clear-type gels with examples of phase separation. The light blue regions are locations within the gel where visible phase separation has occurred.
A noted artefact during the preparation and use of these gel formulations was the development of phase separation in the gel after irradiation, the estimated total phase separation of these gel phantoms in a 9 mL volume vial is shown in Figure 110. A similar outcome has been noted for other formulations of gel previously by Jirasek et al. [55]. In general, these phase separations were smallest for gels that had been irradiated with very low (<5 Gy) or very high doses (>40 Gy), while gels that had received middle levels of dose (e.g. 10-20 Gy) suffered the largest phase separations (collaborating the results obtained by Jirasek et al. [55]). Jirasek et al. confirms that for their polymer gels containing low BIS concentrations, the white beads that they observed are tight polyacrylamide chains, although they did not offer any suggested reason why they should not be observed at low or high doses. Furthermore, it may be that gel samples which are exposed to oxygen but do not have any counteracting anti-oxidant are immune to this effect, as no phase separation has ever been observed in gels that were made containing atmospheric levels of oxygen.
Figure 110 The estimated phase separation in clear gel formulation (of various T values, 5% C) 11 days after irradiation at various doses. The uncertainty is the square root of the estimated size. It is demonstrated that there is little phase separation at no dose or at very high doses, but intermediate doses (5 – 20 Gy) show a significant level of phase separation for concentrations of total monomer between 5 and 11%.

It can also be seen that there is no discernable correlation between the degree of phase separation and the recorded T$_2$ value (note: T$_2$ values were only obtained for the clear regions, and not within the phase separated particles, which have dramatically lower T$_2$ values compared to their surroundings) as shown in Figure 111.
Figure 111 The measured T$_2$ value of clear-type polymer gel related to the estimated volume of phase separation at time of scanning, comparing clear-type gels of various total monomer concentration. There is no apparent relationship between these factors. The displayed uncertainty is 1 standard deviation (N = 50).

This apparent discrepancy whereby very low or very high doses remain clear while middle ranges of doses cause beads of phase separation may possibly be explained by the numbers of free radicals produced. In very low dose situations, few free radicals exist, and not much polymerisation takes place, hence the gel phantom remains clear. In a high dose situation, a great number of free radicals are produced, and the monomers interact quickly where they are. As a result, it also remains clear. But in a mid-level dose situation, with an intermediate number of free radicals, some locations within the gel become sites where the free radicals interact with the monomer, giving rise to chains where other monomers (which have not reacted themselves due to the lack of free radicals for all monomer molecules) migrate to these sites. They clump together into large molecules that fall out of solution. Thus it is possible that intermediate levels of dose to the clear-type gel dosimeters will generate beads of phase separated monomer/polymer chains. The development of these white beads of
phase separation is the major obstacle of a workable clear gel that is stable over a long (>1 week) period of time.

### 7.2.2.5 Raman spectroscopy analysis of clear-type gels

The differences in polymerisation between a sample irradiated to a low level dose and a high level dose are displayed in Figure 112. The low dose irradiated gel sample (green) displays narrow and tall peaks, whereas a sample irradiated to a very high level of dose (red, 120 Gy, well beyond the expected saturation level) displays broader and more subdued peaks. In addition, several of the peaks of the high dose rate sample have split into multiple peaks, such as the acrylamide peak located at 1439 cm\(^{-1}\) splitting into 1456 cm\(^{-1}\) and 1431 cm\(^{-1}\). In addition, the blue line in Figure 112 represents a Raman spectra measured from a region of the white phase separation bead within the gel sample. The locations of the peaks for these 3 spectra are listed in Table 30.

![Figure 112 Comparison of 3 spectra obtained from a batch of clear-type gel, examining the difference between a low irradiated gel sample, a high dose sample and a region of a sample that has experienced phase separation.](image)
Table 30 Raman spectra peak locations for 3 clear-type gels irradiated to a low dose, a high dose and the spectra of a bead within a gel sample, as shown in Figure 112. Values are listed in cm$^{-1}$.

<table>
<thead>
<tr>
<th>low dose (green)</th>
<th>high dose (red)</th>
<th>solid bead (blue)</th>
<th>chemical assignment</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1654</td>
<td>1657</td>
<td>BIS</td>
<td>[14, 205]</td>
<td></td>
</tr>
<tr>
<td>1668</td>
<td></td>
<td>Aa</td>
<td>[14, 205]</td>
<td></td>
</tr>
<tr>
<td>1634</td>
<td></td>
<td>Aa</td>
<td>[14, 205]</td>
<td></td>
</tr>
<tr>
<td>1598</td>
<td>1620</td>
<td>1615</td>
<td>Aa, polyacrylamide</td>
<td>[14, 205]</td>
</tr>
<tr>
<td>1439</td>
<td>1456</td>
<td>1459</td>
<td>Aa, polyacrylamide</td>
<td>[14, 205]</td>
</tr>
<tr>
<td>1439</td>
<td>1431</td>
<td>1431</td>
<td>Aa, polyacrylamide</td>
<td>[14, 205]</td>
</tr>
<tr>
<td>1332</td>
<td></td>
<td></td>
<td>polyacrylamide</td>
<td>[205]</td>
</tr>
<tr>
<td>1287</td>
<td></td>
<td></td>
<td>Aa, polyacrylamide</td>
<td>[14, 205]</td>
</tr>
<tr>
<td>1200</td>
<td>1200</td>
<td></td>
<td>polyacrylamide</td>
<td>[205]</td>
</tr>
<tr>
<td>1123</td>
<td></td>
<td></td>
<td>Aa</td>
<td>[14, 205]</td>
</tr>
<tr>
<td>1109</td>
<td>1111</td>
<td></td>
<td>BIS, polyacrylamide</td>
<td>[14, 205]</td>
</tr>
<tr>
<td>1055</td>
<td></td>
<td></td>
<td>Aa</td>
<td>[14, 205]</td>
</tr>
<tr>
<td>973</td>
<td></td>
<td></td>
<td>Aa</td>
<td>[205]</td>
</tr>
<tr>
<td>837</td>
<td>843</td>
<td>837</td>
<td>Aa, polyacrylamide</td>
<td>[14, 205]</td>
</tr>
<tr>
<td>783</td>
<td></td>
<td></td>
<td>unknown</td>
<td></td>
</tr>
<tr>
<td>625</td>
<td>634</td>
<td>642</td>
<td>Aa, polyacrylamide</td>
<td>[205]</td>
</tr>
<tr>
<td>481</td>
<td>487</td>
<td></td>
<td>polyacrylamide</td>
<td>[205]</td>
</tr>
<tr>
<td>495</td>
<td></td>
<td></td>
<td>acrylamide</td>
<td>[205]</td>
</tr>
<tr>
<td>306</td>
<td>306</td>
<td></td>
<td>acrylamide</td>
<td>[205]</td>
</tr>
</tbody>
</table>

It should be noted that the gel compositions for this gel differ from others presented in works such as Rintoul et al. [14], so the final polyacrylamide gel will have longer chains and less cross-linking on average. This would affect the distribution of peaks comparatively.

It is observed that the region of solid white bead (phase separation) has a much higher background Raman signal compared to the clear region samples, but in general the
locations and integrated sizes of the peaks match approximately that found for the high irradiated dose (and thus polymerised) sample. Thus, it can be concluded that the white phase separated regions are primarily polyacrylamide as opposed to the base monomers, a finding supported by Jirasek et al. [55]).

Raman spectroscopy of these special clear-type gels demonstrates that while they exhibit no visible colour change, a measurable polymerisation does occur.

### 7.2.3. Conclusions

Gel formulations based on acrylamide can be made clear by reduction of the cross-linking fraction. However, such gels as described here are also unstable, possibly owing to the greatly increased monomer in proportion to solvent, compared to regular polymer gels which have been demonstrated to be stable over long periods of time.

A type of polymer gel that remains clear when irradiated has been developed, and the polymerisation of these gels confirmed using MRI and Raman spectroscopy. These gels may be of use in situations such as the synchrotron irradiated beam, where the high resolution of Raman spectroscopy is required, but the light scattering of a normal gel prevents measurements below the surface. However it is still relatively unstable compared to a standard acrylamide based polymer gel, and has an approximate timeframe of 1 week in which it is useable before significant phase separation into white beads occurs. Further work is required, particularly to examine and improve the stability of the final product.

### 7.3. Extremely high dose rate dosimetry with PAG

Injection-styled linear accelerators are capable of delivering x-rays at extremely high doses and dose rates ($2 \times 10^{12}$ Gy s$^{-1}$, compared to 90 Gy s$^{-1}$ from the synchrotron beam used in this thesis for microbeam measurements) as mentioned previously (section 1.3.6), making it a challenging task to measure the dose distribution delivered by such beams. These results describe the use of PAG dosimeters specifically designed to measure such high dose rate beams.
7.3.1. Results

High resistance gel dosimeter (containing oxygen diffused throughout the sample, as described in section 3.1.4.1) was irradiated by the ISIS system located in Idaho, USA, at the Idaho Accelerator Center (IAC). The gel dosimeter was irradiated by 3 MV x-rays as described in the method section (section 3.2.5.3).

After irradiation, gel dosimeters were transported back to Australia and scanned using the 1.5 T Picker Eclipse MRI scanner with the sequence parameters listed in Table 31. The $T_2$ images obtained for the gel dosimeter irradiated by 800 Gy of x-rays by the ISIS accelerator are shown by slice (from within the sample to the surface) in Figure 113. This image shows a series of $T_2$ maps from a typical gel irradiated by the ISIS system, each image represents a 2 mm thick slice of the gel, with the last image (bottom right) being the surface facing the beam.

<table>
<thead>
<tr>
<th>pixel size (µm)</th>
<th>SNR</th>
<th>MRI scanning parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>469 × 469</td>
<td>~7.5</td>
<td>8 echoes, 2 averages, TE = 12.5 ms, TR = 5279 ms, read matrix 256 × 256, FOV 12 × 12 cm$^2$, scan time (multiple samples imaged) = 4m 55s</td>
</tr>
</tbody>
</table>

Table 31 MRI sequence parameters for imaging gel irradiated by the ISIS system. The SNR value is based on the maximum variation in $T_2$ observed.
Figure 113 Axial images showing the variation of a typical gel dosimeter $T_2$ map with slice, each slice corresponding to a 2 mm thickness component of the depth dose. The rightmost image is nearest to the surface.

A normalised depth dose comparison of the gel dosimeter, compared against similar depth doses simulated by Monte Carlo simulations and measurements using radiochromic films are shown in Figure 114. Note that the Monte Carlo simulation and the radiochromic film measurements were performed based on the ISIS data, and were not acquired as part of this work.

A general agreement between the three techniques is shown in Figure 114, as all show a similar increase and drop in the normalised response with depth, and for all three methods the increase and drop occur over the same length distance. $D_{\text{max}}$ determined using gel dosimetry was found to be $3 \pm 1$ mm (uncertainty originates from MRI slice thickness), not significantly different equivalent (based on the possible overlap) to the value calculated by Monte Carlo simulations, $1.9 \pm 0.3$ mm. Radiochromic film has a slightly lower value for $D_{\text{max}}$, $1.3 \pm 0.3$, which is just barely within possible agreement with Monte Carlo simulations (if the true value of $D_{\text{max}}$ was located at 1.6 mm depth), but the calculated $D_{\text{max}}$ value using film does not overlap the range suggested by gel dosimetry. The shape of the depth dose curve obtained using all three methods are similar to each other.
Possible reasons for the variation in $D_{\text{max}}$ values when comparing gel dosimeters with alternative methods include the averaging out of the maximum dose. Due to the MRI scanning set-up, MRI slices were acquired at 2 mm intervals, the resolution of the step size in this work. It is possible that the maximum value (at 2 mm depth) is thus lower than the measured value. Another factor is the glass vial the gel is contained in will attenuate and harden the beam, increasing the value of $D_{\text{max}}$. These would result in the depth dose appearing to decrease slower than in reality. Monte Carlo simulations and radiochromic film measurements were made at higher resolutions, and therefore any averaging effects they may suffer would be reduced in comparison to those of gel dosimetry.

Another possible reason for the variation in $D_{\text{max}}$ is the 2 mm slice thickness for gel dosimetry images, due to the MRI sequence parameters. In this case, gel dosimetry has a greater degree of uncertainty compared to the alternative methods. This could be remedied in future work by the use of more customised sequence parameters or by more specialised MRI scanners such as the 7 T scanner used in this thesis for small field analysis.

In most clinical linear accelerators, a flattening filter is used to more evenly distribute the x-ray field, and also to remove lower energy x-rays from the beam [206, 207]. In this work, no flattening filter exists, meaning that the beam would not be as hard as a typical clinical x-ray beam. Therefore the value of $D_{\text{max}}$ for this beam will be lower compared to the same energy beam from a clinical accelerator.
A general agreement between gel dosimeters and comparison methods of dosimetry for the depth dose of the ISIS accelerator was found. This work demonstrates as a first test for the use of gel dosimeters in the dosimetry of extremely high dose and extremely high dose rates from the unique injection style accelerators. Future work in this area still needs to be performed to determine which types of gels are most suitable and how they compare with other dosimetry methods.

7.4. High-energy proton dosimetry using polymer gel

Proton radiotherapy is rapidly increasing in importance and may soon become one of the major methods of radiotherapy treatments as stated previously in section 1.3.7. A preliminary investigation into dose measurements using gel dosimetry was made in South Korea in this work, with the normoxic gel dosimeters placed behind scattering
material such that they were within the Bragg peak of the dose distribution (as described in the method, section 3.2.5.4). The response of gel dosimeter samples irradiated by high energy (230 MeV) proton beams was compared against a calibration made using 6 MV x-rays.

7.4.1. Results

A normoxic gel dosimeter was irradiated by 230 MeV protons at the National Cancer Centre in South Korea at various doses in the Bragg peak ranging between 15 to 32 Gy. Another set of gels made from the same batch was irradiated to within the same range of doses by a 6 MV x-rays from a Varian 600C linear accelerator in Melbourne, Australia. This was done to compare relative changes in polymerisation caused by photons and protons in the gels.

Calibration of the gel dosimeters was performed by comparing the measured $T_2$ value of the gel (measured using a 1.5 T MRI scanner, the parameters are listed in Table 32) against the delivered dose. The results are shown in Figure 115. A linear fit over the data points for photon and proton data was made. The equations are shown in (16) and (17). The displayed uncertainties are calculated from the maximum variation in the linear fit gradient from the calculated uncertainties in the individual points (which are 1 standard deviation). It can be seen that over the region where the calibration graphs share data points, both photon and proton data were shown to vary in $T_2$ values at approximately the same rate.

Table 32 MRI sequence parameters for imaging gel irradiated by 230 MeV protons and 6 MV photons. The SNR value is based on the maximum variation in $T_2$ observed. SNR is calculated based on the signal due to a dose of 10 Gy.

<table>
<thead>
<tr>
<th>MRI scanning parameters</th>
<th>SNR</th>
<th>pixel size (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 T MRI FSE sequence, 8 echoes, 2 averages, TE = 12.5 ms, TR = 6630 ms, read matrix 256 × 256, FOV 15 × 15 cm², scan time (multiple samples imaged) = 6m 31s</td>
<td>~10</td>
<td>586 × 586</td>
</tr>
</tbody>
</table>
Figure 115 Comparison of the change in $T_2$ with dose for photon and proton irradiated normoxic gel. Uncertainties shown are 1 standard deviation (N = 100).

<table>
<thead>
<tr>
<th></th>
<th>$T_2$ (ms)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Photons</td>
<td>$2.14 \pm 0.35 \text{ ms Gy}^{-1}$</td>
<td>(16)</td>
</tr>
<tr>
<td>Protons</td>
<td>$2.12 \pm 0.38 \text{ ms Gy}^{-1}$</td>
<td>(17)</td>
</tr>
</tbody>
</table>

The difference in absolute value can be explained by the difference in time between each set (photon and proton) difference. It has been previously reported [70] that the polymerisation of a sample will increase with time (and hence the measured $T_2$ value will decrease correspondingly).

The dose distribution with depth from these proton irradiated gels should be consistent with that of a Bragg peak as the gel dosimeter is located within the peak region. That is the maximum dose should be followed by a rapid decline in dose deposited with distance to a negligible amount. Figure 116 displays an example of a gel dosimeter irradiated by protons of 230 MeV (32 Gy maximum dose) with a smoothing spline fit applied ($R^2 = 0.99$), and shows the relative maximum dose as the
Bragg peak. Past the Bragg peak, the dose is seen to fall to a non-measurable level within 1.3 cm (based on the width of the 80 – 20\% slope). As a comparison, an ionisation chamber measurement was also made, the differences between the gel and ionisation chamber measurement are possibly due to a reduction in gel sensitivity that is known to occur in polymer gels when irradiated by particles high linear energy transfer (LET) properties. Previous studies [146, 147, 208] have demonstrated that a polymerising gel will have a decrease in sensitivity when exposed to high LET particles such as protons relative to particles such as clinical energy electrons or photons. As well, the end of the spread-out Bragg peak will have a lower radiation sensitivity compared to the middle, as demonstrated in Figure 116.

Figure 116 Depth dose of a gel irradiated by 230 MeV protons, demonstrating the Bragg peak. The gel was placed behind 19.3 cm of scattering material (solid water) to ensure that the Bragg peak was located within the gel.

7.4.2. Conclusion

A comparison of normoxic gel dosimeters irradiated using proton and photon beams determined that the relative change in $T_2$ value per Gy in the range of 15-30 Gy was
approximately equal, but varied in absolute value. This variation is likely due to the
difference in time between irradiation and scanning, unavoidable due to the transit of
gel dosimeter samples between South Korea and Australia. This work represents the
first high energy proton dosimetry using polymer gels, previous attempts at proton
dosimetry having focused on low energy (<75 MeV) beams.
8. CONCLUSION

The use of smaller and more tightly collimated fields that deliver higher therapeutic doses to target regions and lesser doses to surrounding healthy tissues is an important development in future radiotherapy. Gel dosimetry has many advantages that make it highly desirable as a dosimeter. This thesis has examined several new and innovative aspects of gel dosimetry, particularly for small and micro-sized radiotherapy fields, as well as other new uses such as special gels for high dose rate applications.

• Gel dosimeters were prepared and tested for determining dose profiles of small radiotherapy fields, with these measurements compared against other established techniques such as radiochromic films, stereotactic diodes and micro-thermoluminescent diodes. A range of field sizes down to $3 \times 3 \text{ mm}^2$ were examined. In general, gel still matched well with these other techniques, and can be used as a reliable dosimeter for radiotherapy beam measurements. In addition, depth dose of such small fields have also been made using polymer gels and validated against other dosimetry techniques, and measurements of the scatter from a wide beam compared to a narrow $3 \times 3 \text{ mm}^2$ one were made.

• These gel dosimeters were scanned to high spatial resolution with a specialised 7 T MRI scanner, but it was found that doing so to the highest resolutions resulted in a loss of SNR, and in addition required a long scanning time, more than what would be considered practical currently. Scans using more standard clinical 1.5 T MRI scanners with reasonable scanning times did not have a SNR high enough for clear images of these small field sizes. Further developments in MRI technology will alleviate these problems.

• The use of a $3 \times 3 \text{ mm}^2$ field in particular was notable due to the asymmetry inherit in the beam, which was detected through gel dosimeters, radiochromic films and micro-thermoluminescent diodes. This factor is dependent on the type of MMLC used to generate the beam, and if $3 \times 3 \text{ mm}^2$ radiotherapy
beams are to be used clinically in the future this asymmetry will need to be accounted for.

• High resistance gel dosimeters that are capable of withstanding high dose levels (hundreds of Gy) that have been diffused with oxygen have been developed and demonstrated. These were applied to the use of microbeam radiotherapy, with microbeams spaced 200 µm apart successfully generating polymerised regions within the gel.

• It was also shown that the irradiation by a series of microbeams onto this gel can generate a polymerisation that may be determined through the use of a high resolution scanning method such as Raman spectroscopy. Raman spectroscopy was successfully applied to gel dosimeters to measure the degree of polymerisation in synchrotron generated microbeam irradiated gel dosimeters.

• Through the use of an aneurysm clip, the effects of a small metallic inhomogeneity on the dose distribution of radiation have been demonstrated. The use of polymer gel as both a phantom and dosimeter has allowed for measurement of the increase in delivered dose near the aneurysm clip. This information would be useful in treatment planning as the presence of a metallic implant near regions of tissue to be irradiated can be taken into consideration during treatment planning. This would results in more accurate treatment of the patient.

• It has been demonstrated that high energy x-ray photons will undergo photonuclear reactions with oxygen as expected, and that can be detected through the emission of 0.511 MeV gamma rays that are a by-product of the reaction. The decay of gamma emission matches the known half-life of activated oxygen, supporting this conclusion. Measurements made to determine the degree of change in polymerisation between a 6 and 18 MV x-ray beam did not detect a significant effect beyond the level of uncertainty of the degree of polymerisation. Differences in the polymerisation between low
and high energy x-rays (of the same dose) in gel are known to be minimal. Improvements to scanning techniques or different types of gel that have greater differences in their response to low and high energy x-rays may possibly clear this matter up in future work, and therefore tell us more accurately how the presence of neutrons alters the final dose in high energy x-ray beams.

- It was found that by altering the gel formulation to include a much higher proportion of monomer relative to the cross-linker, that a gel that remains clear when polymerised could be obtained. It was demonstrated that these clear gel formulations displayed a measurable variation in their structure with dose, as measured by both MRI and Raman spectroscopy.

- Extremely high dose rate linear accelerators such as the injection style ISIS accelerator present a difficult problem in terms of accurate dosimetry measurements. In this work, special-type high resistance gel dosimeters were applied for the first time to generate a depth dose curve of a 3 MV x-ray beam generated by such a linear accelerator. This was compared against and found similar to measurements with film and predictions made by Monte Carlo simulations.

- Polymer gels were successfully used in a preliminary investigation for measuring the dose distribution from a high energy (230 MeV) proton beam, and the gel sensitivity was found to be consistent within uncertainties to the comparable gel sensitivity to a 6 MV x-rays from a clinical linear accelerator.

Gel dosimetry is an area of study in which there are still many challenging and interesting aspects to be explored. The focus of future radiotherapy techniques on precision and reduction of dose to healthy tissues means that a dosimeter that can be used as both a phantom and three-dimensional dosimeter such as gel will become increasingly valuable. Microbeam dosimetry, with its promise to deliver very high doses to tumours with minimal side effects to the patient is another area of radiotherapy where gel dosimetry has a role as a valuable tool in dose determination.
Future plans for research include further enhancement of the techniques of gel dosimetry measurements. These include studies into gels irradiated by microbeam radiotherapy, with more research into oxygen diffusion and heat generation in gel irradiated by very high dose rate beams. Another area of future research is improvement of the special-type clear gels, increasing the length of time that they remain stable, thereby making them more user friendly and less subject to uncertainties. Another future area of research is the use of special types of gel that contain dose enhancement agent or contrast agents dissolved in them, such as nanoparticles, to determine the effect that they have on the deposited dose.

Gel dosimetry has also shown itself useful in practical applications such as inhomogeneity and extremely high dose rate measurements. As such, research into gel dosimetry and its applications for these radiotherapy techniques will continue for the foreseeable future.
APPENDIX – SOFTWARE CODE

Analysis of data in this thesis was performed using custom made software, programmed in MATLAB code. All programs listed here were developed by the author of this thesis.

MRI image data

MRI data was analysed using MATLAB software. In general, data acquired from the high resolution 7 T MRI scanner was in the format of individual echoes that required merging into a single T2 map, whereas the clinical 1.5 T MRI scanner images did not need this, as this was taken care of the 1.5 T scanner’s own software. Several programs were developed by the author in particular for processing and analysing MRI data. They are listed here:

T2FIT

This program was developed to calculate the T2 value of a sample at every point. It is described in more detail in the method chapter.

```matlab
% T2Fit
% Script to calculate the T2 values of a series of images from a file.

% STEP 1: SETTING THE PARAMETERS OF THE DATA

% These set up the size of the image along the x and y axes.
xsize = input('number of pixels along x axis of image = ');
ysize = input('number of pixels along y axis of image = ');
```
% Self-explanatory.
necho = input('number of echoes per slice = ');

% Self-explanatory. The program will probably still work fine if a number less than the actual number is entered, only calculating images for the first nslices of data.
nslice = input('number of slices in data = ');

% ROISlice = Region of Interest Slice Ask which slice the program should fit for
ROISlice = input('which slice no. do you want to fit (0 = all) = ');
if ROISlice > nslice
    error('slice selected does not exist');
end

% the total number of images in the data.
nimage = necho * nslice;

% TE is the echo time (time between echoes in MEI sequence).
te = input('enter TE (in ms) = ');

% Function to determine if 8, 16, 32 or 64-bit info and adjust for it
bitsize = input('size of data (8, 16, 32 or 64-bit) = ');
if bitsize ~= 8
    if bitsize ~= 16
        if bitsize ~= 32
            if bitsize ~= 64
                % Further handling for 64-bit information
            else
                % Default handling for 32-bit information
            end
        end
    end
end

error('selected bitsize not allowed, ending program');
  end
end
end
end

bitsize = int2str(bitsize);

pathdir = input('the path directory F:\Gel Data\Analyze Data\?? = ');

% STEP 2: Loading the data

% FID = FileIdentifier (number)
FID = fopen(['F:\Gel Data\Analyze Data\\',pathdir, '\\',... pathdir, '\.img']);

TimeBegin = clock

% ImData = Image data. The data is unit 16 in the raw form, and is
% organised into a 2D matrix with each image lined adjacent to the next.
ImData = fread(FID,[xsize,ysize * nimage],['uint',bitsize]);

% ImDataMax = the largest value in ImData. If needed, this value could be
% used to restore ImData to its original form.
ImDataMax = max(max(ImData));

% This normalises the data to the range 1-64, useful for the 'image'
% command.
ImData = ImData ./ ImDataMax .* 64;

% This will re-arrange the 2D ImData matrix into a new 3D matrix, where
% each plane is one image of a slice at a certain echo time, arrange so
% that slice 1, echoes 1->end, then slice 2, echoes 1->end, etc.
% Will work up to 999 images.
for counter = 1:nimage
    if counter >= 100 % adjust number of zeros in filename as needed
        z = '';
    elseif counter >= 10
        z = '0';
    else
        z = '00';
    end % end of 'if counter >= 100'

    % use flipud because the data is upside down, this will match the
    % co-ordinates in the correct direction, however, the image will
    % now is viewed upside-down and needs the 'axis xy' command to be
    % viewed upways again.
    GelImage.(['Echo',z,int2str(counter)]) =
        flipud(shiftdim(ImData(...
            1:xsize,((counter - 1) * ysize + 1):((counter * ysize))),(1));
end % 'for counter = 1:nimage' loop

% clear z and counter to make things cleaner.
clear z;
clear counter;
clear ImData;

% STEP 3: ORGANISING THE DATA

% Here, we want to change the one big 3D array into many smaller 3D arrays, such that each 3D array contains all the echoes of only 1 slice. If there is only 1 slice to begin with, we can skip this step.

%some problems may occur if EchoData is not cleared before starting
clear EchoData;

if nslice == 1 %skips step if only one slice
    for echono = 1:necho

        if echono >= 100 % adjust number of zeros in % name of GelImage
            zimage = '';
        elseif echono >= 10
            zimage = '0';
        else
            zimage = '00';
        end %'if imageno >= 100

        EchoData.GelSlice001(:,:,echono) = ...
        GelImage.(['Echo',zimage,int2str(echono)]);
    end
else % continues step if more than one slice
    for imageno = 1:nimage
sliceno = floor(imageno ./ necho) + 1;
echono = rem(imageno, necho);
if echono == 0
    sliceno = sliceno - 1;
    echono = necho;
end % echono == 0

if sliceno >= 100 % adjust number
    zslice = '';
elseif sliceno >= 10
    zslice = '0';
else
    zslice = '00';
end % 'if sliceno >= 100

if echono >= 100 % adjust number
    zecho = '';
elseif echono >= 10
    zecho = '0';
else
    zecho = '00';
end % 'if echono >= 100

if imageno >= 100 % adjust number
    GelImage as needed
    % name of
else
    GelImage as needed
    % name of
end
zimage = '';
elseif imageno >= 10
    zimage = '0';
else
    zimage = '00';
end % 'if imageno >= 100

EchoData.(['GelSlice',zslice,int2str(sliceno)])(:,:,echono) = ...
    GelImage.(['Echo',zimage,int2str(imageno)]);
end % 'for imageno = 1:nimage'

clear imageno;
%clear echono;
clear sliceno;
clear zecho;
clear zimage;
clear zslice;
clear GelImage;

end % nslice = 1

% STEP 4: CREATE THE TIME MATRIX

t = zeros([1,necho]);

for n = 1:(necho)
    t(n) = te .* n;
end

clear n;
clear n1;
clear n2;

% STEP 5: REMOVING THE FIRST DATA POINT

% Note: The first Data point is removed because the echo
signal it comes
% from is inaccurate, due to interference of T1 effects
(Spin-lattice)

% fix t to remove first element
t(1) = [];

% fix EchoData to remove first echo of each slice

for sliceno = 1:nslice

    if sliceno >= 100
        % adjust number of
        % name of EchoData as
        % needed
        zslice = '';
    elseif sliceno >= 10
        zslice = '0';
    else
        zslice = '00';
    end % 'if sliceno >= 100

    EchoData.([GelSlice',zslice,int2str(sliceno)])(:,:,1) = [];
end % sliceno = 1:nslice

% STEP 6: MAKING THE FIT
% The following was produced by automatically generated code of the
% curve-fitting algorithm.
fo_ = fitoptions('method','NonlinearLeastSquares','Lower',[-Inf 0 -Inf ]);%
% start point for variables a, b and c
st_ = [40 0.002 0 ];
set(fo_,'Startpoint',st_);
ft_ = fittype('a*exp(-b*x)+c',... %
    'dependent',{'y'},'independent',{'x'},...
    'coefficients',{'a', 'b', 'c'});

% this if statement is so that the following for loop will always use the
% number 1 for whatever slice was chosen, unless all slices were chosen.
if ROISlice ~= 0
    nsliceused = 1;
else
    nsliceused = nslice;
end % ROISlice ~= 0

for sliceno = 1:nsliceused
    % start for loops to fit each point in the data

    if sliceno >= 100
        % adjust number of zeros in % name of EchoData as needed
        zslice = ''; %
    elseif sliceno >= 10
        zslice = '0';
    else
        zslice = '00';
    end

end

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end % 'if sliceno >= 100

for xcount = 1:xsize
    for ycount = 1:ysize
        % need to test to see if point is of interest
        and should be
        % calculated
        if (EchoData.(['GelSlice',zslicexint2str(sliceno)])(ycount,xcount,1) -
            EchoData.(['GelSlice',zslicexint2str(sliceno)])(ycount,xcount,end) > 10)

            if sliceno >= 100 % adjust number of
                % name of EchoData as
                % needed
                zslicex'';
                elseif sliceno >= 10
                    zslicex'0';
                else
                    zslicex'00';
                end % 'if sliceno >= 100

                cf_ =
                fit(t(:,squeeze(EchoData.(['GelSlice',zslicexint2str(sliceno)])(ycount,xcount,:)),ft_,fo_);

                % stores limits of 95% confidence
                Lim95 = confint(cf_);

                A(ycount,xcount,sliceno) = cf_.a;
T2(ycount,xcount,sliceno) = 1 ./ cf_.b;
c(ycount,xcount,sliceno) = cf_.c;

ALim95High(ycount,xcount,sliceno) = Lim95(2,1);
% Lim95 matrix address reversed for T2Lim due to division
T2Lim95High(ycount,xcount,sliceno) = 1 ./ Lim95(1,2);
cLim95High(ycount,xcount,sliceno) = Lim95(2,3);

ALim95Low(ycount,xcount,sliceno) = Lim95(1,1);
T2Lim95Low(ycount,xcount,sliceno) = 1 ./ Lim95(2,2);
cLim95Low(ycount,xcount,sliceno) = Lim95(1,3);

else
% default values for non-interest areas
A(ycount,xcount,sliceno) = 1;
T2(ycount,xcount,sliceno) = -1;
c(ycount,xcount,sliceno) = 0;

ALim95High(ycount,xcount,sliceno) = 1;
T2Lim95High(ycount,xcount,sliceno) = -1;
cLim95High(ycount,xcount,sliceno) = 0;

ALim95Low(ycount,xcount,sliceno) = 1;
T2Lim95Low(ycount,xcount,sliceno) = -1;
cLim95Low(ycount,xcount,sliceno) = 0;
end % if
(EchoData.(['GelSlice',zslice,int2str(sliceno)]))...
    % (ycount,xcount,1) -
EchoData.(['GelSlice',zslice,...
    % int2str(sliceno)])(ycount,xcount,end) > 10)

    end % ycount = 1:ysize
end % xcount = 1:xsize

end % sliceno = 1:nslice

clear nsliceused;
clear Lim95;
clear cf_;
clear st_;%clear EchoData;

% STEP 7: SAVING THE DATA TO AN EXTERNAL FILE

% A
FID_.A = fopen(['G:\MATLAB files\',pathdir,'A.dat'],'a+');
fwrite((FID_.A),A,'double');
fclose(FID_.A);

FID_.AHIGH = fopen(['G:\MATLAB files\',pathdir,'AHIGH.dat'],'a+');
fwrite((FID_.AHIGH),ALim95High,'double');
fclose(FID_.AHIGH);

FID_.ALow = fopen(['G:\MATLAB files\',pathdir,'ALow.dat'],'a+');
fwrite((FID_.ALow),ALim95Low,'double');
fclose(FID_.ALow);

% T2
FID_.T2 = fopen(['G:\MATLAB files\',pathdir,'T2.dat'],'a+');
fwrite((FID_.T2),T2,'double');
fclose(FID_.T2);

FID_.T2High = fopen(['G:\MATLAB files\',pathdir,'T2High.dat'],'a+');
fwrite((FID_.T2High),T2Lim95High,'double');
fclose(FID_.T2High);

FID_.T2Low = fopen(['G:\MATLAB files\',pathdir,'T2Low.dat'],'a+');
fwrite((FID_.T2Low),T2Lim95Low,'double');
fclose(FID_.T2Low);

% c
FID_.c = fopen(['G:\MATLAB files\',pathdir,'c.dat'],'a+');
fwrite((FID_.c),c,'double');
fclose(FID_.c);

FID_.cHigh = fopen(['G:\MATLAB files\',pathdir,'cHigh.dat'],'a+');
fwrite((FID_.cHigh),cLim95High,'double');
fclose(FID_.cHigh);

FID_.cLow = fopen(['G:\MATLAB files\',pathdir,'cLow.dat'],'a+');
fwrite((FID_.cLow),cLim95Low,'double');
fclose(FID_.cLow);
% STEP 8: CLEANING UP

clear xcount;
clear ycount;

TimeEnd = clock

MRIview and variants

This series of programs was designed to convert data acquired from the 1.5 T Pecker Eclipse into a useable form. They transform the raw data by removing the header and placing it into a matrix.

Two programs are listed here. MRIview is simply a program to simply the importing of data to MATLAB. The second program, MultiMRIview enables this to be performed on multiple files at once, counting along filenames in a hexadecimal counting system (base-16), it works as a function that calls MRIview multiple times.

MRIview

% MRIview
% % This program reads in the raw data of 1.5 T scans

ImageNo = input('Input the first image number (3 digits, hex, string) = ');

FID = fopen(['F:\Gel Data\1.5 T dbase 2007-10-04\files\image-00000', ImageNo]);
Im.(['Im', ImageNo]) = fread(FID, 'uint16');
Im.(['Im', ImageNo])(1:104) = [];
Im.(['Im', ImageNo]) = reshape(Im.(['Im', ImageNo]), 256, 256);
Im.(['Im', ImageNo]) = Im.(['Im', ImageNo])';
fclose(FID);

clear FID;

### MultiMRIview

% MultiMRIview

%Does many MRIview processes at once

StartName = 'DEB';
EndName = 'E0D';

ImageNo = StartName;

NoSlice = 35;

while isequal(ImageNo,EndName) == 0
    MRIview2

    NoSlice = NoSlice + 1; % Increment number of slices counter.
    ImageNo = dec2hex(hex2dec(ImageNo) + 1); %move name to next image
end

MRIview2

### EasyMean and variants

This series of programs was designed to quickly analyse MRI data from the 1.5 T Picker eclipse. Data from this machine is already fitted to give the $T_2$ value at each point, however, to quickly analyse the data from several slices, this program will
calculate the mean T2 from a specified location in each image, along with the associated standard deviation.

The region of interest is inputted by the user, and the size of the ROI determined by the value ‘SRad’, which the user can control. It is up to the user to ensure that this value is of adequate size. A larger size will possibly exceed the boundaries of the gel material (thus giving incorrect values), and is effectively a drop in resolution, but also overcomes local noise and generally leads to a smaller standard deviation.

Because the image data is obtained with the image plane perpendicular to the axis of the gel vial in the majority of cases, the position of the centre of the vial should remain constant with each slice. However, this is not always the case due to incorrect positioning during imaging. The program EasyMeanMulti is designed to calculate the mean and standard deviation for multiple slices, and will automatically determine the centre of the region of interest for each slice given the relevant ROI points for the first and last slice. It counts filenames in hexadecimal.

_EasyMean_

```matlab
SRad = 2; % thus 2 + 2 + centre (1) is 5 sized square
XCentre = input('centre of X =');
YCentre = input('centre of Y =');

imagemame = T2;

meanans = mean(reshape(imagename((YCentre-SRad):(YCentre+SRad),
                               (XCentre-SRad):(XCentre+SRad)),(SRad*2+1)^2,1))
stdans = std(reshape(imagename((YCentre-SRad):(YCentre+SRad),
                              (XCentre-SRad):(XCentre+SRad)),(SRad*2+1)^2,1))
SNR = meanans / stdans;
```
clear imagename;

*EasyMeanMulti*

% EasyMeanMulti
% Same idea as EasyMean, but does a lot of slices at once, given only
% the start and end points coordinates (it deduces the rest)

clear meanans;
clear stdans;

SRad = 2; % This value determines the size of the area examined.
          % This is equal to 2xSRad + 1, in both directions (X and Y)

XStart = 92; % The centre of X in the first slice.
YStart = 150; % The centre of Y in the first slice.
XEnd = 87; % The centre of X in the last slice.
YEnd = 145; % The centre of Y in the last slice.
NoSlice = 23; % The number of slices to be examined.
FirstSlice = 'D79'; % The first slice in the data. This must be a hex
                     % string, 3 digits.

XDiff = XEnd - XStart;
YDiff = YEnd - YStart;

% First, we need to have a method of moving the XStart to XEnd locations
% as we move along the slices. We know the vials are straight, so this
% should be constant. Same goes for YStart to YEnd.

ImName = FirstSlice; %hex is always string.

for counter = 1:NoSlice;

    % XUse is the value of X used in each calculation
    XUse = round(XStart + round(XDiff .* (counter - 1) ./
    (NoSlice - 1)));

    % repeat for YUse
    YUse = round(YStart + round(YDiff .* (counter - 1) ./
    (NoSlice - 1)));

    meanans(counter) = mean(reshape(Im.(['Im',ImName]))...
    ((YUse-SRad):(YUse+SRad),... 
    (XUse-SRad):(XUse+SRad)),(SRad*2+1)^2,1));

    stdans(counter) = std(reshape(Im.(['Im',ImName]))...
    ((YUse-SRad):(YUse+SRad),... 
    (XUse-SRad):(XUse+SRad)),(SRad*2+1)^2,1));

    SNR(counter) = meanans / stdans;

    ImName = dec2hex(hex2dec(ImName) + 1); %move name to
    next image
end

%clear XDiff
%clear XEnd
%clear XStart
%clear XUse
%clear YDiff
Raman Spectroscopy

Raman spectroscopy data was analysed using MATLAB software. The raw data was a text file that listed the Raman shift and the intensity measured at that point. The location (in terms of an X and Y coordinate) was also listed in the case of linemap data.

PeakCalc

This program was designed to quickly calculate the peak volume of a selected peak from a Raman spectrum. It is also capable of calculating the background volume, although ultimately these values were not employed in this work.

PeakCalc determines the location of a peak based on user input in defining the endpoints, the space in the data is called the region of interest. In addition to calculating the volume of the selected region of interest, the program calculates the volume of the background, which is determined as the size of the peak capped at the average height of the region of interest end points. In cases where the user has poorly defined the edge of the peak, the calculated background volume is likely to be a poor estimation of its true value.

Before data can be analysed, it must be imported into MATLAB, this can be done using MATLAB’s own import data function.

As input, PeakCalc requires the end points of the peak, entered as the index values from the raw data. In the code shown below, the index values of 172 and 231 are used as an example, as the 172\text{nd} and 231\text{st} listed values in the raw data correspond to a
peak located between 3016 and 3064 cm\(^{-1}\) for data relating to Raman spectroscopy measurements collected during this thesis.

```matlab
%PeakCalc
TempSpectra = input('Spectra name = ');
LowIndex = 172; %input('Low Index = ');
HighIndex = 231; %input('High Index = ');
%Centre = inout('PeakCentre = ');

TempSpectra(HighIndex,2);
TempSpectra(LowIndex,2);

% Peak + Background
TotalPeak = sum(TempSpectra(LowIndex:HighIndex,2));

% Background
Background = (HighIndex - LowIndex) .* (TempSpectra(HighIndex,2) ... + TempSpectra(LowIndex,2)) ./ 2;

% Peak - Background
PeakOnly = TotalPeak - Background;

ans = [TempSpectra(HighIndex,2), TempSpectra(LowIndex,2), TotalPeak, Background]
```

**RamanSort**

RamanSort is a program that calculates the volume of a preselected region of interest (defined by the user’s input) in the same was as PeakCalc. It is also capable of calculating the background volume for the same ratio. RamanSort is a more advanced
program than PeakCalc, as it is able to calculate the volume of the region of interest for linemap data (data consisting of multiple spectra measured at differently locations within a gel sample)

RamanSort requires the variable name the data is stored under and the end points of the region of interest. As RamanSort is more advanced than PeakCalc, it is able to calculate the relevant index values when given input in the form of the Raman Shift values (in units of cm\(^{-1}\)), thus making RamanSort more user friendly compared to its predecessor PeakCalc.

It outputs a list of the peak volume for the region of interest for each spectra in the input data, along with a similar list for the background values.

```matlab
% RamanSort

% TempArray = Linemap5;
TempArray = input('Linemap name = ');

% Find #Steps, and # of different cm-1 values
BinSwitch = 0; % (Binary Switch, 0 = off, 1 = on)
Counter = 1;

while (BinSwitch == 0)
    if (TempArray(Counter,3) > TempArray(Counter+1,3))
        Counter = Counter + 1;
    else
        NoCM = Counter; % NoCM is the number of points in the spectra
        BinSwitch = 1;
    end
end

clear BinSwitch;
```
clear Counter;

% NoCM = 3113;
NoStep = size(TempArray,1) ./ NoCM;

% Create a re-organised matrix so that each spectra can be identified
% more easily.

k = 0;
for i = 1:NoStep

    for j = 1:NoCM
        Tem(j,i) = TempArray(k+j,4);
    end
    k = k + j;
end

clear k;

% Find the LowLimit and HighLimit

% The values for LowLimit and HighLimit need to be calculated by inputting
% wavenumbers as limits, else it gets to unwieldy.

LowWave = input('Low Wavenumber (units cm\(^{-1}\)) = ');
HighWave = input('High Wavenumber (units cm\(^{-1}\)) = ');
CentreWave = input('Centre of peak? = ');
% Start the search at the first index, and go until the list surpasses % the value.
HighLimit = 1;
LowLimit = 1;
CentreLimit = 1;

while (TempArray(LowLimit, 3) > HighWave)
    LowLimit = LowLimit + 1;
end

LowLimit = LowLimit - 1; % Because otherwise it's not inclusive.

% LowLimit doesn't need to go back to be inclusive.
while (TempArray(HighLimit, 3) > LowWave)
    HighLimit = HighLimit + 1;
end

% Find the centre of the peak as based on input for now...
while (TempArray(CentreLimit, 3) > CentreWave)
    CentreLimit = CentreLimit + 1;
end

for StepCounter = 1:NoStep
    TotalPeak(StepCounter) = 0;
    for Counter = LowLimit:HighLimit
        TotalPeak(StepCounter) = TotalPeak(StepCounter) + TempArray(Counter + ((StepCounter - 1) * NoCM), 4);
    end
end
end

LowLimit2 = LowLimit;
HighLimit2 = HighLimit;
BaseArray = TempArray;

for Counter = 1:NoStep
    Y1 = TempArray(LowLimit2,4);
    Y2 = TempArray(HighLimit2,4);
    Ystep = (Y2 - Y1) / (HighLimit - LowLimit);
    j = 1;

    for i = LowLimit2:HighLimit2
        BaseArray(i,4) = BaseArray(LowLimit2,4) + j * Ystep;
        j = j + 1;
    end

    LowLimit2 = LowLimit2 + NoCM;
    HighLimit2 = HighLimit2 + NoCM;
end

clear j;
% clear Ystep;

% Area under BackGround of peak
LowLimit2 = LowLimit;
HighLimit2 = HighLimit;
CentreLimit2 = CentreLimit;

% In case BackGround already exists and is a larger matrix than what
% the new one will be.
clear BackGround;

for Counter = 1:NoStep

    PeakBG = 0;

    for i = LowLimit2:HighLimit2
        PeakBG = PeakBG + BaseArray(i,4);
    end
    BackGround(Counter) = PeakBG;
    LowLimit2 = LowLimit2 + NoCM;
    HighLimit2 = HighLimit2 + NoCM;
end

clear PeakBG;

% Area under peak
LowLimit2 = LowLimit;
HighLimit2 = HighLimit;

% In case PeakHeight already exists and is larger than what the new one % will be.
clear PeakHeight;

for Counter = 1:NoStep

    Peak = 0;

    for i = LowLimit2:HighLimit2
        Peak = Peak + TempArray(i,4);
    end
    PeakHeight(Counter) = Peak;
LowLimit2 = LowLimit2 + NoCM;
HighLimit2 = HighLimit2 + NoCM;

end

clear i;
clear Peak;
clear LowLimit2;
clear HighLimit2;
clear Counter;

APPENDIX – PUBLISHED PAPERS

The author has contributed to the following publications during this time:

**Journal articles**


W. N. Rahman, M. Geso, N. Bishara, T. Ackerly, C. He, P. A. Jackson, C. J. Wong, and R. Davidson, “Enhancement of radiation effects by gold nanoparticles for superficial radiotherapy,” *Accepted for publication in Nanomedicine: Nanotechnology, Biology, and Medicine*

**Oral presentations**


**Poster presentation**

REFERENCES


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