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Polymer Gel Dosimetry for Radiation Therapy

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1. Introduction

Although conventional dosimeters such as ionization chambers measure absolute dose to a high precision at single points, their finite size makes resolving areas of high dose gradient difficult. Improved spatial resolution can be achieved with thermo luminescent dosimeters (TLDs), silicon diodes and diamond detectors. Film also offers high spatial resolution in a single, two dimensional planes and provides excellent relative dose information and absolute dose measurements when appropriately calibrated. More complete three-dimensional (3D) dose measurements can be produced by positioning film in multiple planes, although accurate positioning of film in several layers can be a difficult and time-consuming process. The search for a dosimetry technique that allows full 3D imaging of a radiation dose distribution has led to the development of radiation-sensitive gels. These gels have a long history, with gels containing Folin's phenol, which change colour upon irradiation, first investigated by (Day & Stein, 1950). Later, measurements of photon and electron depth doses were made by (Andrews et al., 1957) using agar gels. Several studies subsequent to this have used Fricke solutions and gels by (Day, 1990). An alternative technique, based on radiation-induced polymerization in solutions of monomers and polymers, was studied by (Hoecker & Watkins, 1958), with dosimetry investigations carried out by (Audet & Schreiner, 1991).

The interest in the gel dosimetry technique follows on from a type of dosimetry gel proposed by (Maryanski et al., 1993). Here, acrylic molecules embedded within a gel matrix polymerize upon irradiation, with the degree of polymerization being strongly related to the absorbed dose received by the gel. The spatially localized polymerization can then be imaged by MRI or optical scanning methods. When imaged in an MRI scanner the relaxation rate of the polymerized region was reported to be linearly proportional to absorbed dose in a dose range applicable to the study of clinical radiation therapy (0-15 Gy). The first international workshop dedicated to gel dosimetry (Schreiner, 1999) took place, demonstrating the growing interest in development and application of the gel dosimetry technique. (Gore et al., 1996; Maryanski et al., 1996) demonstrated the potential of Optical CT as an alternative imaging technique to MRI for PAG-type polymer gel dosimeters. This technique was further investigated by (Oldham et al., 2001, 2003) and (Oldham & Kim,

2004). In 2000 Hilts et al demonstrated the use of x-ray CT to image PAG-type gels and subsequently used x-ray CT to investigate stereotactic dose distributions. (Mather et al., 2002b) demonstrated the use of ultrasound to image polymer gel dosimeters. (Rintoul et al., 2003) demonstrated the use of Raman imaging to evaluate an electron depth dose in an irradiated PAG dosimeter. Although polymer-type dosimeters did not have the diffusion limitations of Fricke-type gel dosimeters, there was another significant limitation to their use. Due to the nature of their free radical chemistry, polymer gel dosimeters were susceptible to atmospheric oxygen inhibiting the polymerization processes. As a result, these gel dosimeters had to be manufactured in an oxygen-free environment, for example in a glove box flushed with inert gas such nitrogen or argon (Baldock et al., 1998a; De Deene et al., 1998a). A significant development in the field of gel dosimetry was reported by (Fong et al., 2001). This development was a new type of polymer gel dosimeter, known as MAGIC, in which atmospheric oxygen was bound in a metallo-organic complex thus removing the problem of oxygen inhibition and enabling polymer gels to be manufactured on the benchtop in the laboratory. These types of polymer gel dosimeters became known as the new class of normoxic gel dosimeters. The existing PAG dosimeters subsequently became known as hypoxic or anoxic gel dosimeters. The MAGIC polymer gel formulation consisted of methacrylic acid, ascorbic acid, gelatin and copper. The principle behind removing the problem of oxygen in the MAGIC gel is in the use of ascorbic acid, commonly known as vitamin C. Ascorbic acid binds free oxygen contained within the aqueous gelatin matrix into metallo-organic complexes in a process initiated by copper sulfate (De Deene et al., 2002b). It was subsequently shown that other antioxidants could also be used in the manufacture of normoxic gels including tetrakis (hydroxymethyl) phosphonium chloride (THPC) (De Deene et al., 2002a; Baldock, 2006). Numerous authors subsequently published results of work investigating different compositions and formulations of normoxic polymer gel dosimeters which have been summarized by (Senden et al., 2006). With the introduction of normoxic gel dosimeters, MRI studies were undertaken to investigate their usefulness for IMRT (Gustavsson et al., 2003), and radionuclide therapy (Courbon et al., 2006; Gear et al., 2006; Braun et al., 2007, 2009). There have been a limited number of previous reviews on polymer gel dosimetry (McJury et al., 2000). Further additional information on gel dosimetry has been published in the proceedings of the DOSGEL conferences (DOSGEL, 1999, 2001, 2004, 2006, 2008). The fundamental science underpinning the dosimetry technique is reviewed along with the various evaluation techniques and associated issues for the purposes of clinical dosimetry applications.

2. Principles

Polymerized gel, prepared with monomers such as Acrylamide, is widely used in biochemistry as a medium for electrophoresis for protein and nucleic acid separation (Hoecker et al., 1958; Gordon et al., 1973; Chambers et al., 1967; Alexander et al., 1954; Hsu et al., 1984). Polymer gels are typically composed of Acrylamide monomer and a cross-linking agent such as N, N'-Methylene- Bis Acrylamide (BIS). Polymerization of gels used for electrophoresis is normally initiated and controlled chemically using a free radical initiator such as ammonium/sulphate. However, polymerization can also be induced by radiation via free radical production during water radiolysis. The radiation-induced polymerization has been explained by (Charlesby, 1987). The first polymer gels designed for radiation dosimetry were made by adding the monomer Acrylamide and the cross-linking

agent BIS to a simple Agarose-based gel solution (Maryanski et al., 1993, 1994). These were given the acronym "BANANA", from Bis Acrylamide Nitrous oxide and Agarose. Greater sensitivity was later achieved with gelatin-based gel solutions, which led to the current generation of BANG (Bis Acrylamide Nitrogen and Gelatin) polymer gels (Maryanski et al., 1994). The gases nitrous oxide and nitrogen included in the acronyms are required to displace oxygen from the gel during manufacture. After irradiation, a gel will contain regions that are polymerized and cross-linked. This is the origin of the gel's spatial dose-response characteristics, as the degree of polymerization depends on the initial quantity of free radicals generated by the incident radiation and, therefore, on the absorbed dose. Within the polymerized regions, certain populations of water molecules alter their state of binding to, and exchange protons with, the polymer network. This can be investigated using nuclear magnetic resonance (NMR) relaxation time measurements. The relaxation characteristics of the trapped water protons are determined by both the polymer structure (e.g. polymer porosity, as the size of network spaces will determine the efficiency of trapping water molecules) and its concentration (which depends on the absorbed dose). The water R_2 relaxation rate (reciprocal of the transverse relaxation time T2) measured by MRI of BANG gels is linearly related to dose in the range 1-10 Gy (Maryanski et al., 1993, 1994, 1996; Back et al., 1998; Oldham et al., 1998). This range encompasses the dose used in a standard external beam radiotherapy treatment fraction (2 Gy). Previously, there are two types of BANG gel in 1996, although many variations on the basic formulation are possible. BANG-1™ and BANG-2 ™ gels are current models of BANG ™ gels. The former is made using acrylamide in powder form, while the latter replaces acrylamide with acrylic acid and NaOH to buffer the pH. Gel response is improved with acrylic acid compared to acrylamide, allowing larger relaxation-rate changes per unit dose. Acrylamide is a neurotoxin that can lead to nervous system disorders. Safe handling of acrylamide is essential and appropriate care should be taken when disposing of the gel. (McJury, 2000). BANG-3TM gels have been developed after 2000. This type of gel has strong optical and MR responses (Oldham, 2001). With the BANG-3TM gel, acrylic acid is replaced with methacrylic acid. Table 2.1 summarizes the gel types and compositions. Of the BANGTM polymer gels, BANG-3TM polymer gel reportedly has the highest MR sensitivity upon photon irradiation (Ramm, 2000).

3. Gel dosimeter manufacture

Deionized, distilled water is used, which is degassed with an inert gas such as pure N_2 to remove any dissolved oxygen. The gas is humidified to minimize water loss during the degassing process. Oxygen is a free radical scavenger that inhibits gel polymerization and must therefore be removed. To avoid exposure to oxygen during preparation, the gel is usually manufactured either in sealed reaction flasks (Oldham et al., 1998; Baldock et al., 1998; De Deene et al., 1998) or in a sealed glove box with a nitrogen environment (De Deene et al., 1998). A BANG-1 type gel is made by adding typically 5% (all percentages by weight) gelatin (type A, approx. 300 bloom) to the degassed water at room temperature (Maryanski et al., 1994; Baldock et al., 1998). This is allowed to dissolve, and is heated to approximately 50 ^{o}C to prevent gel setting. 3% Acrylamide is added to the solution, followed by 3% BIS. When the monomers have completely dissolved in the solution, the gel can be transferred to airtight containers and allowed to cool and set. Oxygen impermeable vessels, such as glass or BAREX (BP Chemicals Inc., London, UK), are usually used because plastic containers (e.g.

Perspex, polystyrene etc.) allow transfer of oxygen through the vessel wall (Maryanski et al., 1994). This may have a minimal effect on applications where the irradiated regions are distant from the container walls. It is advantageous to irradiate the gel dosimeter soon after manufacture owing to potential oxygen contamination and exposure to light. Once irradiated, the dosimeters are usually imaged, or "read", within a few days. The optimum time between irradiation and imaging is approximately 3-4 days (McJury et al., 1999).

4. Characteristics of the gel dosimeter

4.1 Light and oxygen contamination

Once the monomer and cross-linker are added to the gelatin solution, the mixture should be shielded from light as photo polymerization may begin and consequently degrade the overall sensitivity of the gel (Maryanski et al., 1993, 1994; Richmond et al., 1987).

The gel polymerization process is initiated by free radical reactions, and molecular oxygen is an efficient "scavenger" of free radicals. The effect of dissolved oxygen upon the sensitivity of Polyacrylamide gels has been reported in (Maryanski et al., 1993, 1994; Baldock et al., 1998; Richmond et al., 1987; Hepworth et al., 1999), where it was observed that even trace amounts led to a complete failure of the polymerization reaction. A typical result of oxygen contamination is shown in Figure 1.

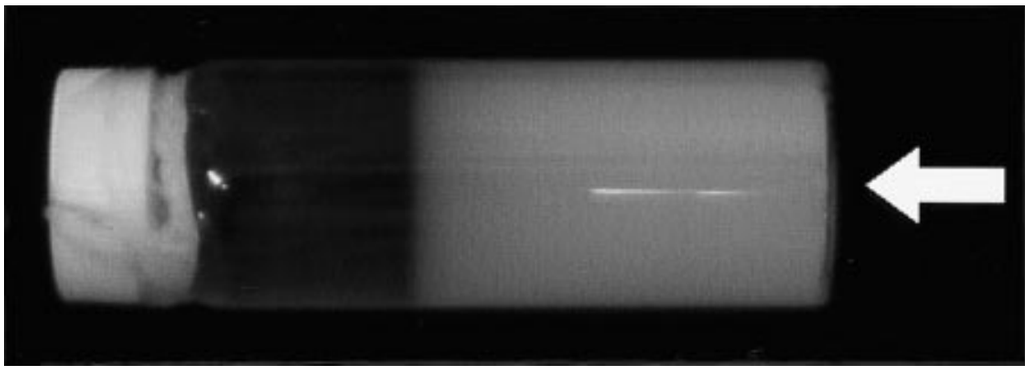

Fig. 1. 35 ml gel sample in a glass vial that has been irradiated with 6 MV photons as indicated by the arrow. Owing to oxygen diffusion through the gel, polymerization in a large component of the sample is prevented.

Here, a calibration vessel irradiated with a single 6 MV photon beam (direction indicated) had a faulty seal at the top of the flask. A strong gradient in gel polymerization is clearly seen, which renders the gel useless as a dosimeter.

4.2 Temperature

The temperature of the gel at irradiation is reported to have little effect on final R_2 measurements (Maryanski et al., 1994). However, at imaging the sensitivity of the gel increases with decreasing temperature (Maryanski et al., 1997, 1995; De Deene et al., 1998, 1999). Figure 2 shows the dose response of a BANG-1 gel imaged at a number of temperatures between 5 ^{o}C and 40 ^{o}C, as demonstrated by (Maryanski et al., 1997).

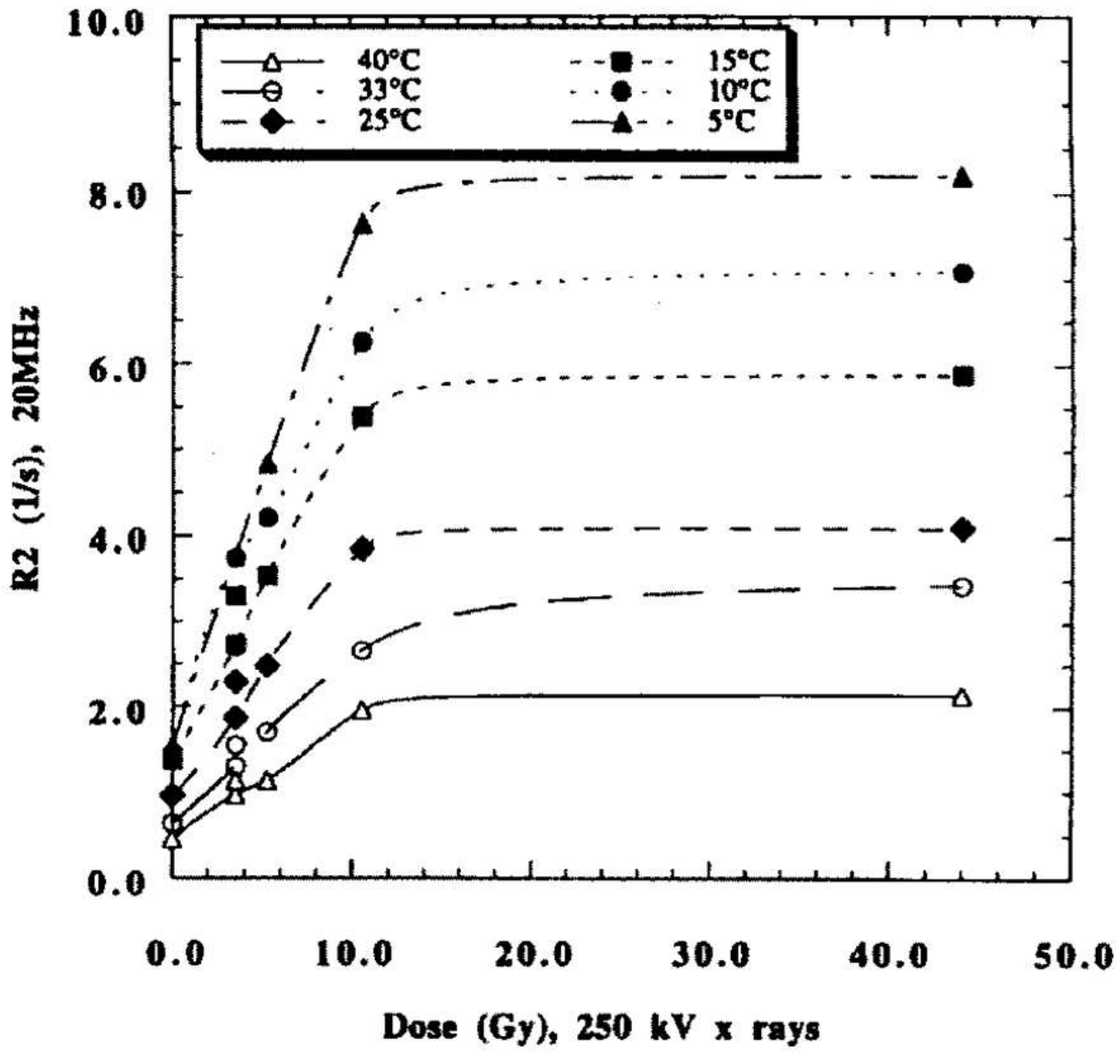

Fig. 2. The effect of temperature during imaging on the water R_2 relaxation rate dose-response curve. (Phys Med Biol 1997; 42: 303-11 [Maryanski et al., 1997])

The effect is explained by the change in proton correlation times and proton exchange rates in the gel with temperature. These increase as the motions of the polymer chains become slower with decreasing temperature. The relaxation rate of gelatin increases with decreasing temperature (Vachier et al., 1996). It is therefore important that a gel is allowed to equilibrate to a uniform temperature prior to MRI and that the experimental gel and the calibration gels be at the same temperature.

4.3 Concentration of polymer and cross-linker

Both the absolute and relative weight fractions of monomer and cross-linker agents in the gel may be varied (Oldham et al., 1998; Maryanski et al., 1995, 1997; Audet et al., 1995; Baldock et al., 1996). Increasing the total monomer content of the gel, for example from 3% to 6%, increases sensitivity (Maryanski et al., 1997; Baldock et al., 1996; Farajollahi et al.,

1997) and extends the dose saturation point. The increase of dose saturation point with increasing cross-linker density can be explained by two competing mechanisms: (i) the reactivity of monomers, and (ii) the relaxation properties of the gel, which depend on polymer composition and concentration. It has been reported (Maryanski et al., 1997; Kennan et al., 1996) that as the fraction of cross-linker increases, the conversion of monomers to polymer per unit dose decreases due to the lower reactivity of the BIS cross-linker relative to Acrylamide. Therefore, the sensitivity of the gel to radiation decreases. As the cross-linker density increases, the polymerized gel becomes more rigid, with the BIS molecules cross-linking tightly with each other as well as with the residual Acrylamide.

4.4 Gel matrix

Gelatin produces clearer gels than Agarose, allowing greater visibility of the polymerized region and facilitating imaging of the gel by optical means. Other gelling agents can also be used, such as Sephadex-200 and Sumikagel N-100 (Zebrowska et al., 1995). Increasing the strength of the gelatin increases the melting point of the gel. Generally, 300-bloom gelatin is used, which has a comparatively high melting point (30-35 ^{o}C (Vachier et al., 1996)). Increasing gelatin concentration decreases R_2 and overall gel sensitivity (Maryanski et al., 1994; Audet et al., 1995), thus a gel consisting of 5% gelatin by weight is usually used.

4.5 Gel pH

For gelatin, R_2 increases with pH at all temperatures and concentrations (Vachier et al., 1996). Maryanski et al noted that a more reproducible dose-response was achieved with neutral gel pH following initial studies with acidic gels (Maryanski et al., 1993). In simple gels constructed only from solutions of Acrylamide and BIS, and polymerized by chemical means, an increase in pH (greater than pH 8) was also associated with an increase in relaxation rate (Kennan et al., 1996). This is consistent with a chemical-exchange mediated interaction between water protons and the polymer. Further work by (Gochberg et al., 1998) indicated that the dependence of relaxation rate on pH was not entirely consistent with a simple acid/base catalyzed chemical exchange.

4.6 Gel fogging

Bubbling N_2 gas through a gel during mixing can cause fogging of the gel, leading to an increased background R_2 value (Maryanski et al., 1994). This spontaneous polymerization is thought to be due to free radical impurities in some of the gel manufacturing materials (Maryanski et al., 1993; Richmond et al., 1987). It is therefore important to use high-grade chemicals when manufacturing these gels.

4.7 High dose edge effects

An increased response at the edges of irradiated regions in BANG gels has been reported (Maryanski et al., 1994). This occurs for high dose irradiations, beyond the linear region where R_2 is proportional to absorbed dose. The effect is not completely understood but is thought to be due to monomers slowly diffusing from low dose to high dose regions and interacting with long-lived macro-radicals.

4.8 Gel ageing

It is not clear whether the saturation doses employed in NMR studies lead to complete polymerization. It may take from a few hours to perhaps several weeks for the polymerization reactions to be complete after irradiation, with the reaction slowing down quasi-exponentially (McJury et al., 1999). Imaging within a few hours of irradiation, when the rate of polymerization is greatest, could lead to errors, particularly if there is a time delay between imaging a set of calibration gels and the target phantom.

4.9 Toxicity

Acrylamide is a neurotoxin. Repeated skin contact or ingestion can lead to nervous system disorders (Richmond et al., 1987; Sittig et al., 1985). Guidelines for handling Acrylamide include wearing gloves at all times and working with the powder chemicals within a fume cupboard. Care should also be taken when disposing of gels after use. Some of these concerns have been reduced by replacing Acrylamide with acrylic acid, as used in the BANG-2 gel formulation.

5. Imaging of the dosimeter

5.1 MR relaxation time imaging

MRI allows the measurement of the longitudinal and transverse relaxation rates (R_1 and R_2) of the dosimeter gels, from which dose maps can be calculated. Conventionally, the corresponding relaxation times (T_1 and T_2) are measured, from which the rates can be computed. Relaxation times are measured by applying radiofrequency (RF) pulses to excite the magnetization of the spin system, and then sampling during the return to equilibrium. The transverse relaxation time T_2 (equals to $1/R_2$) is measured by fitting data collected from at least two points on the transverse relaxation curve following excitation. Two points are the minimum needed to obtain a T_2 value, but errors will be reduced if a larger number of points on the relaxation curve are collected. Two main approaches to data collection are used, each technique having its own intrinsic advantages and disadvantages (Baustert et al., 2000). (a) Single echo or Hahn spin echo sequence method (Hahn et al., 1950). Each acquisition collects only a single echo, but can be repeated with different echo times. (b) Multiple spin echo method (Carr et al., 1956; Meiboom et al., 1958). A sequence that acquires a train of spin echoes, each corresponding to a different echo time. Concern about errors in measured R_2 values owing to imperfect refocusing with 180^o pulses, leading to standing wave effects or RF attenuation in large aqueous samples, has led to a preference for single echo sequence methods by some authors (Maryanski et al., 1994, 1996).

5.2 X-Ray CT scanning

Hilts et al showed that x-ray CT could be used to investigate changes in irradiated PAG polymer gels and demonstrated that in cases of high dose gradients this evaluation technique had potential (Hilts et., 1999, 2000). Trapp et al further evaluated the technique for investigating different compositions of PAG polymer gels (Trapp et al., 2001). It was shown that the CT-dose sensitivity increased with the concentration of co monomers used, and by varying the gelling agent from gelatin to agarose. Hill et al further investigated the change

in CT number with dose for normoxic polymer gels (Hill et al., 2003). Trapp et al showed that the observed contrast obtained in CT images of irradiated PAG gels was due to density changes in the gels (Trapp et al., 2002) and was further demonstrated for normoxic MAGIC gels by (Brindha et al., 2004). Hilts et al suggested that polymer gels for x-ray CT evaluation should have a more optimal sensitivity for an extrinsic density change and maximum polymer yield in the gel dosimeter (Hilts et al., 2004). A significant limitation of x-ray CT evaluation is the relatively small change of CT numbers or Hounsfield units in the irradiated polymer gel with absorbed dose along with image noise (Trapp et al., 2001). Hilts and Duzenli showed that the issue of image noise could potentially be tackled through image processing techniques (Hilts & Duzenli, 2004). The phantom wall material used has the potential to induce artifacts in the resulting CT image and is particularly significant for glass (Trapp et al., 2001). To overcome these artifacts, alternative plastic wall materials have been investigated (Hill et al., 2003). Audet et al undertook a clinical dosimetry study of CT gel dosimetry and showed that high dose regions produced by stereotactic irradiations could be accurately localized (Audet et al., 2002). Further clinical dosimetry studies are required to fully evaluate the potential of the x-ray CT technique. However, as a result of the easy access to x-ray CT scanners in clinical departments, CT does potentially offer a relatively simple, convenient and inexpensive method of implementing clinical polymer gel dosimetry (Hilts et al., 2004). The main advantage of this evaluation technique is that limited access to MRI facilities is not an issue or is the need to build or purchase specialized optical scanning equipment. It should be noted that where, for instance, MRI has evaluation problems such as in homogeneities or temperature dependence (De Deene et al., 2000a, 2000b; De Deene & Wagter, 2001), x-ray CT evaluation has its own limitations. However, as is the case with MRI evaluation of polymer gel dosimeters (De Deene, 2001), it has been shown that x-ray CT evaluation techniques require the CT scanner be commissioned specifically for gel dosimetry before use (Hill et al., 2005).

5.3 Ultrasound scanning

Mather et al showed that ultrasound could be used to investigate changes in irradiated PAG polymer gels (Mather et al., 2001, 2002a). In these studies, acoustic speed of propagation, attenuation and transmitted signal intensity showed a strong variation with absorbed dose indicating the potential of this technique. Comparative studies of PAG and MAGIC polymer gels indicated that differences in acoustic properties with absorbed dose were due to differences in the elastic modulus of the materials (Mather et al., 2002b). Further acoustic studies (Mather et al., 2003a) showed that the overall acoustic attenuation, dose sensitivity and dynamic range were dependant on dosimeter formulation. These studies, along with those of acoustic attenuation coefficients highlighted the complex nature of the acoustic properties of polymer gel dosimeters and indicated that further studies are required to fully understand the properties (Mather et al., 2003b). Mather and Baldock undertook a preliminary study to evaluate the potential of acoustic imaging of

irradiated PAG polymer gel dosimetry phantoms (Mather & Baldock, 2003c). An ultrasound computer tomography (UCT) system was developed and evaluated. Results from the UCT system indicated that transmission-generated images produced greater contrast than time-of-flight-generated images. However, time-of-flight-generated images produced superior

geometrical accuracy of the dose distribution than transmission-generated images. The motivation to develop UCT of polymer gels was to produce a more economically viable evaluation methodology.

5.4 Optical scanning

As the gel polymerizes it becomes opaque. It is therefore possible to use optical scanning to generate two-dimensional dose distributions. A prototype optical tomography system has been designed previously for reading the optical density of irradiated BANG gels (Gore et al., 1996). The technique depends on light scattering from the polymer micro particles within an irradiated gel. A detailed study of light attenuation within a BANG-1 gel (Maryanski et al., 1996) indicated that light was not absorbed by the polymer particles, only scattered. Light attenuation can therefore be related to polymer density and, consequently, to absorbed dose. Using a gel sample irradiated with a series of uniform dose regions the attenuation coefficient for 500 nm wavelengths light increased by approximately 0.7 mm^{-1} when the dose increased from 0 to 5 Gy. The attenuation was directly related to absorbed dose over the range 0-10 Gy. The shape of the dose-response curve was also found to depend upon the fraction of the cross linking monomer in the initial mixture and on the wavelength of light used. The main conclusion of the preliminary optical scanning studies was that the technique could replace, or at least complement, the NMR imaging method of dose measurement.

5.5 Calibration of the dosimeter

The accuracy and sensitivity of an individual gel batch is dependent upon the exact conditions of manufacture and the purity of chemicals used. It is therefore recommended that each gel batch is calibrated separately at the time of use (Baldock et al., 1998). Several different methods of dosimeter calibration have been reported. In all cases, a quantity of the gel batch to be used experimentally is transferred to a calibration phantom (or phantoms) and irradiated with a range of known doses. MRI of the calibration phantom produces a T_2 relaxation map and a plot of known dose against relaxation rate R_2 ($1/T_2$). This can then be used to calibrate the rest of the experimental data (Maryanski et al., 1994). The quality of a calibration method may be judged by the errors in fitting the calibration data and, to a lesser extent, on the quantity of gel needed for calibration. There are three main calibration methods reported in the literature.

5.5.1 Multibeam method

A large (approx. 1-1.5 litres) flask filled with gel is irradiated with several small beams (either using stereotactic cones or small square fields) to a number of doses over the sensitivity range of the gel. Figure 3a shows the T_2 map of a calibration phantom using the "Multibeam" method.

The phantom had a diameter of 20 cm and a thickness of 6 cm, and was filled with 1.5 litres of BANG-1 gel. It was irradiated with six 2x2 cm^2 fields to doses of 2, 4, 6, 8, 9 and 10 Gy (Oldham et al., 1998). The resulting calibration plot is shown in Figure 3b, with errors on the slope and intercept of 1.5% and 5.0%, respectively.

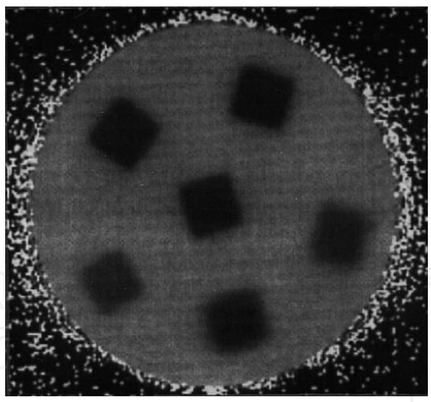

Fig. 3(a). T_2 image through a calibration gel using the "Multibeam" method. The gel sample received 2 x 2 cm^2 irradiations of 2, 4, 6, 8, 9 and 10 Gy. (Phys Med Biol 1998; 43:1113-2 [Oldham et al., 1998]).

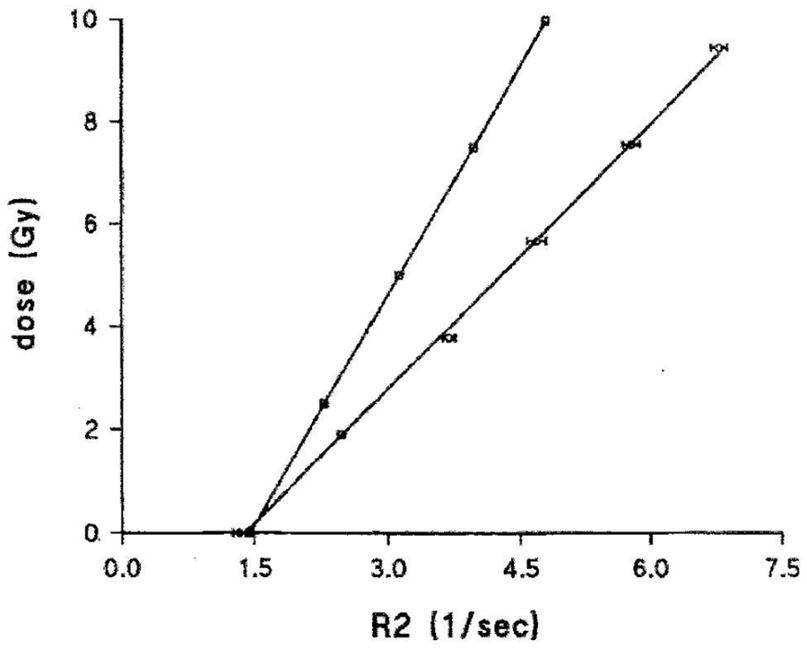

Fig. 3(b). Calibration plot of water relaxation rate R_2 against dose obtained using the "Multibeam" method for gel with a 3% N, N'-methylene-bis-acrylamide (BIS) and Acrylamide formulation and a gel with 6% BIS and Acrylamide. The plot demonstrates the enhanced sensitivity obtained when using higher concentrations of monomers. (Phys Med Biol 1998; 43: 1113-2 [Oldham et al., 1998]).

Alternatively, a "spoke" irradiation can be carried out where a phantom is irradiated with an odd number of coplanar, circular beams, arranged equidistantly around the midline and converging on a centrally located target point (Maryanski et al., 1996). The dose is calibrated at a depth d_{max} for each beam. The main disadvantages of this technique are that a considerable amount of gel must be used and only a small number of data points are obtained for a calibration plot.

5.5.2 Multi flask method

Here, a number of small flasks are filled with gel and each flask is irradiated to a known dose with a parallel-opposed dual beam arrangement to produce a uniform dose distribution throughout the entire gel sample (Back et al., 1996; Baldock et al., 1998; Ibbott et al., 1997). Depending on the number of gel samples used, similar errors in a calibration fit may be found as with the Multibeam method, but less gel will be required. A potential drawback to this calibration technique is the risks of inter flask variability. Care must also be taken to ensure full backscatter conditions are met so that the gels receive a uniform irradiation dose, i.e. flasks should be thin walled, be completely filled with gel leaving no air cavities and be surrounded by a tissue/water equivalent phantom that is thick enough to ensure charged particle equilibrium.

5.5.3 Depth-dose method

A long test tube of gel is positioned vertically in a water tank and irradiated from the closed end with a single radiation beam. This results in the gel recording a characteristic R_2 "depth-dose" distribution. These data may be plotted against a known depth-dose distribution for the beam size and energy, or against ion chamber measurements in an identical geometry. To adequately cover the dose range 0-10 Gy, a number of short test tubes of gel irradiated to different doses should be used in preference to a single, long test tube owing to the potential limitations of RF coil homogeneity. At each depth, several adjacent points may be averaged together to increase the signal-to-noise ratio.

Two 80 ml flasks irradiated to 8.5 Gy and 5 Gy were used in this example. The gel shows good sensitivity and linearity up to 7 Gy. Errors on the slope and intercept are 0.4% and 0.6%, respectively. Overlaid onto this figure are data points obtained using the "multi flask" method with gel from the same batch. The five points correspond to flasks irradiated with 10x10 cm^2 fields to doses of 2, 4, 6, 8 and 10 Gy. Errors on the slope and intercept for the five-point fit are 2.5% and 3.7%, respectively. Other calibration methods have also been reported. Rather than generating a T_2 map of the calibration phantom, two T_2 weighted images with widely differing echo times may be used to generate a look-up table of transverse relaxation rates for known absorbed doses (Maryanski et al., 1994; Ibbott et al., 1997).

6. Applications of gel dosimetry

Polyacrylamide gel dosimetry has been used to verify a number of increasingly complex treatment techniques using a variety of radiation modalities. Attention was first focused on validating the response of the gels to simple radiation fields to assess their response characteristics (Maryanski et al., 1993, 1994, 1996; De Deene et al., 1998). Following this, more complex treatment deliveries have been investigated, exploring more thoroughly the versatility of the 3D imaging sequences.

6.1 Brachytherapy

Clinical brachytherapy systems are capable of delivering very high doses with high dose gradients. It is important therefore to be able to verify accurately the doses calculated by brachytherapy treatment planning. Conventional dosimetry has limited resolution and may give rise to large errors through the use of TLDs or mini ionization chambers that measure

the dose only at a single point. BANG gel dosimetry has been used to investigate the dosimetry of clinical ^{192}Ir (Maryanski et al., 1996; McJury et al., 1999) and ^{137}Cs (Maryanski et al., 1994; Audet et al., 1996) sources with considerable success. Good spatial and dosimetric agreement with treatment planning calculations has been demonstrated. Figure 4 illustrates a T_2 weighted image obtained using a clinical ^{192}Ir high dose rate source irradiating a spherical phantom filled with BANG-1 gel (McJury et al., 1999).

The catheter was positioned within the phantom so that the iridium source would irradiate from a single point at the centre of the phantom. The source was positioned using remote after loading equipment and the absolute dose was found to be within 7% of that at the dose prescription point. Dose maps have also been derived from gels exposed to multiple positions of a ^{192}Ir source (Maryanski et al., 1996). To resolve sharp dose gradients in close proximity to a brachytherapy source, high field strength (5 T+), and small bore MR scanners can be used (Hasson et al., 1998). With such equipment, resolution down to 0.1 mm x 0.1 mm x 0.1 mm is achievable.

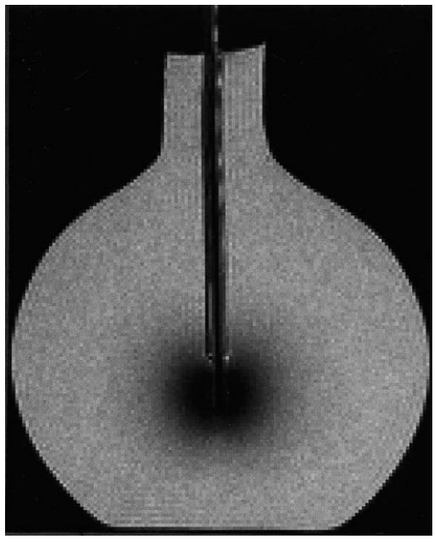

Fig. 4. T_2 weighted image of a brachytherapy phantom. Signal loss close to the source indicates a high degree of polymerization of the gel. (Phys Med Biol 1999; 44: 2431-44 [McJury et al., 1999])

6.2 Conformal and intensity modulated radiotherapy

Advances in conformal and intensity modulated radiotherapy techniques allow highly complex field shapes with high dose gradients to be planned and delivered. The capacity for imaging dose distributions fully in three dimensions is graphically illustrated by the photograph of a gel phantom in Figure 5.

This specially designed phantom was used to verify a stereotactically guided conformal treatment plan of a small brain lesion. The measurement is useful quantitatively for visualizing the irradiation geometry, while NMR scans of the phantom will provide dose maps to compare with the treatment plan. BANG-1 gels were used to verify the planning and delivery of intensity modulated radiotherapy using the NOMOS MIMiC tomotherapy system (NOMOS Corp., Sewickley, PA, USA) (Oldham et al., 1998). The MIMiC is a multiple

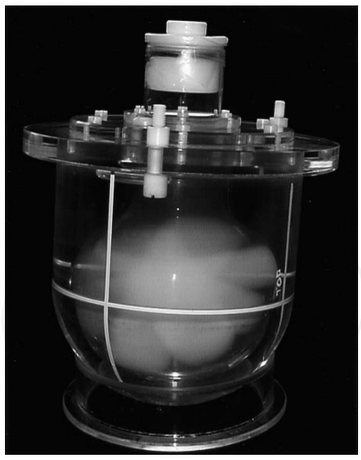

Fig. 5. Phantom used to verify a stereotactically guided conformal treatment plan. The phantom consists of an inner glass bulb containing the Acrylamide gel, which is surrounded by water in a Perspex container.)

vane, slit shaped collimator with two banks of 20 moveable leaves along the slit (Carol et al., 1992). As the MIMiC is rotated around a target, the leaves are programmed to open and close, generating intensity-modulated beam. Dose distributions measured using the BANG-1 gel was compared with those produced by the Peacock planning system and by an in-house optimized version of the planning system.

6.3 Stereotactic radiosurgery

Stereotactic radiosurgery dosimetry must be performed with high spatial resolution as the irradiated target volumes are both small and contain regions of steep dose gradient. Ibbott and co-workers have performed a series of experiments, from the placement of simple, single target points (Maryanski et al., 1996; Ibbott et al., 1996) to complicated dose distributions planned with multiple target points using a Gamma knife system (Ibbott et al., 1997). In the single target experiments there was good agreement with the calculated dose in the isocentric region, with differences increasing to 10% at the 20-30% isodose level. Although the measured isodose distribution agreed well with planning data (within 2-3 mm), doses measured by the gel were consistently lower than those predicted by the Gamma knife planning system.

7. Conclusion

Polymer gel dosimetry offers a method of acquiring 3D maps of complex radiotherapy dose distributions with a spatial resolution of the order of 1 mm, depending upon the scanning and imaging specifications. If care is taken during manufacture, particularly ensuring that there is no oxygen contamination, gels with good reproducibility can be obtained. As an alternative, it is possible to purchase ready-made gels (MGS, Guildford, New Haven, CT, USA). However, continued care is required between gel storage, irradiation and imaging to prevent any alteration or degradation of response. The dosimetry technique has been applied to a number of different radiation modalities and applications where measurements with conventional dosimeters are either difficult or of limited scope. One particular

advantage of the gel is that it can be used in phantoms of any shape so that realistic irradiation geometry can be reproduced (De Deene et al., 1998). Polymer gels are still in a period of rapid development. There are many choices for each component of the gel, such as solvent, gelling agent, monomer and cross-linker. More sensitive, accurate and easier to manufacture polymer gel formulation is expected. The requirement for MRI makes the use of the gels prohibitively expensive for many radiotherapy departments. The possibility of using optical techniques to measure polymer density distributions could extend the use of gel dosimeters beyond research groups with easy access to MRI scanners. Further research has to be undergone to characterize the optical properties of the polymer gels and to produce a precise and effective optical scanner.

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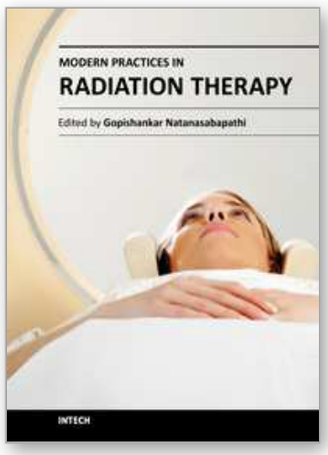

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Cancer is the leading cause of death in economically developed countries and the second leading cause of death in developing countries. It is an enormous global health encumbrance, growing at an alarming pace. Global statistics show that in 2030 alone, about 21.4 million new cancer cases and 13.2 million cancer deaths are expected to occur, simply due to the growth, aging of the population, adoption of new lifestyles and behaviors. Amongst the several modes of treatment for cancer available, Radiation treatment has a major impact due to technological advancement in recent times. This book discusses the pros and cons of this treatment modality. This book "Modern Practices in Radiation Therapy" has collaged topics contributed by top notch professionals and researchers all around the world.

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