A comparison of polyacrylamide gels and radiochromic film for source measurements in intravascular brachytherapy

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Abstract. For intravascular brachytherapy with catheter-based systems, AAPM Task Group 60 has recommended measurements that should be made to characterize the sources. Beta emitters, including 90 Sr/ 90 Y are ideal for intravascular brachytherapy, but problems arise in measuring dose distributions in the high dose gradient region at short distances from the source. In this paper, measurements of radial and orthogonal dose distributions and dose profiles for a 90 Sr/ 90 Y source train using polyacrylamide gel (PAG) dosimetry and a high-field 4.7 Tesla MRI scanner are presented and compared with measurements made with two types of radiochromic film, MD-55 and HD-810. For the PAG system, the dose distributions were determined with in-plane resolutions of 0.4 mm and 0.2 mm. The measurements of absorbed dose distributions both orthogonal and parallel to the source axis show good agreement between the PAG and radiochromic film. The absolute dose at a radial distance of 2 mm in the central 32 mm of a line parallel to the axis was measured. For the PAG the measured absorbed dose was 1.25% lower, for MD-55 4% higher and for the HD-810 1.6% higher when compared with the value given by the source calibration. These results confirm that both absorbed dose and dose distributions for high gradient vascular brachytherapy sources can be measured using PAG but the disadvantages of gel manufacture and the need for access to a high resolution scanner suggests that the use of radiochromic film is the method of choice.

Recently, there has been much interest in the prevention of restenosis following angioplasty using intravascular irradiation. Different types of source are used for vascular therapy, for example ${}^{90}\text{Sr}/{}^{90}\text{Y}$ and ${}^{192}\text{Ir}$ as a chain of seeds, ${}^{90}\text{Y}$, and ${}^{32}\text{P}$ as a metallic wire and ${}^{188}\text{Re}$ as a liquid source. Fox [1] has recently given a comprehensive review of intravascular brachytherapy of coronary arteries. The American Association of Physicists in Medicine (AAPM) Task Group 60 [2] recommends that for sources used for intravascular brachytherapy the dose rate should be measured 2 mm radially distant from the centre of the source and that the dose rate should be uniform to within $\pm 10\%$ over the central two-thirds of the treated length. In addition, the relative dose should be measured from 0.5 mm to the distance where 90% of the energy from a point source has been absorbed at intervals of 0.5 mm in the plane perpendicular to the catheter axis through the centre of the source. Compliance with these recommendations requires a high-resolution dosimeter capable of making accurate measurements in regions with a high dose gradient.

Radiochromic film is one method that has been used for the dosimetry of vascular brachytherapy sources [3], but it is restricted to measurements in two dimensions, as are measurements with scintillator devices [4]. Polyacylamide gel (PAG) dosimetry has been used for measurements of several brachytherapy sources [5–10], and relies on radiation-induced cross-linking of the polymer, which alters both the optical density of the gel and the nuclear

relaxation behaviour of the gel water. Changes in optical density may be used in optical dosimetry [11, 12] but will not be discussed further in this paper. In MRI dosimetry, the changes in the nuclear transverse relaxation rate (R_2) (the inverse of the relaxation time (T_2)) with dose are exploited. Using PAG as a dosimeter has the advantages that the distributions can be measured in three dimensions, the gel is both dosimeter and phantom, and the gel is tissue equivalent [7]. To date, in-plane resolution for the dose distributions from gel dosimeters has been reported in the range from 0.1 mm to 1.5 mm for MRI [6, 7, 13–15]. In principle, the spatial resolution achievable in MRI is determined by the strength of the magnetic field gradient that is applied to achieve spatial discrimination. However, in practice, the signal-to-noise ratio (SNR) depends inversely on the third power of the spatial resolution, so that the resolution that is achievable in practice is limited by SNR, which in turn depends on the strength of the static polarising magnetic field and on the time available for scanning [13, 16]. Using a high-field MRI system, the resolution achievable may be sufficient for the needs of vascular brachytherapy dosimetry.

The purpose of this paper is to compare radiochromic film dosimetry with PAG in meeting the requirements of AAPM Task Group 60 [2].

Materials and methods

Sources

The radiation source used in this investigation was a high doserate 90 Sr/ 90 Y source train from a BetacathTM

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device (Novoste, Norcross, CA). The source consisted of a train of 16 90 Sr/ 90 Y pellets encapsulated in a strontium titanate ceramic. 90 Sr/ 90 Y is a high-energy beta emitter with maximum energy of 2.28 MeV. Each pellet had an outer diameter of 0.65 mm and a length of 2.5 mm. The sources were transported hydraulically from the source container in the BetacathTM using a catheter of 1.6 mm diameter with three lumen: one for the sources, one for the return fluid, and one for the guide wire. A syringe filled with sterile water drove the hydraulic delivery system.

Gel preparation and irradiation

The polymer gels employed in this study were prepared in a glove box using the method described by Farajollahi et al [7] with modifications to the phantom filling system developed De Deene et al [17] and Love [18]. The oxygen concentration inside the glove box was monitored, and was always less than 0.2%. As an additional precaution, the preparation was carried out in a dark room to minimize any polymerization brought about by ultraviolet light. All polymer gel preparations used gelatine of type A (acid derived), approximately 300 Bloom (Sigma Aldrich, Dorset, UK), electrophoresis-grade acrylamide monomer and N,N'-methylene-bis-acrylamide cross-linker (ICN Biomedical Ltd, Basingstoke, UK); de-ionised water was used as the solvent. Oxygen free nitrogen gas was used to remove dissolved oxygen from the de-ionised water and gel solution. Typically, the gas was bubbled through the water for a period of up to 30 min, depending on the volume of water and flow-rate of the nitrogen. It was found that the time for deoxygenation was proportional to the volume and inversely proportional to the flow-rate of the nitrogen, as would be expected. The gel was prepared in a reaction flask and transferred to different calibration tubes and phantoms inside the glove box. The composition of the polymer gel used was 5% gelatin, 3.5% acrylamide and 3.5% N.N'-methylene-bis-acrylamide by weight.

The gel samples used for calibration were irradiated in glass tubes approximately 100 mm long and 25 mm in diameter closed at one end. The phantoms used for the brachytherapy sources had either an insert of BarexTM (BP Chemicals, London, UK) with a 2 mm inner diameter and 4 mm outer diameter, or a glass insert with a 2 mm inner diameter and 3 mm outer diameter. Both types of insert were closed at one end. The dimensions of brachytherapy phantoms were 143 mm long and 28 mm outer diameter for phantom with the glass insert and 150 mm long and 25 mm outer diameter for phantom with the BarexTM insert. BarexTM has the advantage of having a relatively low density of 1.15×10^3 kg·m⁻³, with high oxygen barrier properties [19]. The insert was positioned along the central axis of the glass tube, and held in position with a rubber stopper as shown in Figure 1. This initial design of phantom was limited by the inability of the rubber stopper to keep the insert supported centrally in the glass tube and difficulties were experienced in manufacturing BarexTM inserts from sheet material. An improved design of phantom was also constructed using a glass tube with glass thickness of 0.5 mm. This tube was also closed at one end and sealed with quartz quick-fit stopper (Figure 1). Glass is more rigid with higher density $(2.33 \times 10^3 \text{ kg} \cdot \text{m}^{-3})$ and may perturb the beta radiation but gave more accurate positioning of the sources. Figure 1 also shows



Figure 1. Polyacrylamide gel (PAG) phantom with a glass (left) and a $Barex^{TM}$ (right) insert after an irradiation of 8 Gy with ${}^{90}Sr/{}^{90}Y$ sources.

the areas of radiation-induced polymerization caused by the ${}^{90}\text{Sr}/{}^{90}\text{Y}$ source train. Another phantom was made which simulated a curved coronary artery. For this phantom, a glass tube 115 mm long with 2 mm inner and 3 mm outer diameter was bent through an angle of 100° (angle of arc) and was open at both ends. The tube was then inserted into a rectangular BarexTM phantom measuring 40 mm × 40 mm × 125 mm. The rectangular phantom was then filled with gel.

Calibration vials were irradiated to doses of 0 Gy, 2 Gy, 4 Gy, 6 Gy and 8 Gy using a 6 MV photon beam with a 150 mm \times 150 mm field. The response of PAG based on the formulations given by Maryanski et al [5, 6] has been reported to be independent of energy for a wide range of photon and electron beams by several authors [6–8]. More recently, some energy dependence has been reported [20] for the formulation based on acrylic acid and N,N'-methylene-bis-acrylamide [6]. This investigation related to the energy dependence of gel sensitivity, which can depend on many factors. The calibration tubes were irradiated

5 cm deep in a Perspex holder and were rotated through 180° halfway through the irradiation to give a uniform dose distribution. The phantoms were irradiated using 90 Sr/ 90 Y sources to doses of 8 Gy and 10 Gy at 2 mm radial distance from the source centre. Previous work has shown that the linearity of the gel response to absorbed dose using this formulation and method of manufacture extends to 12 Gy [7]. The absorbed doses were calculated using source calibration data traceable to NIST (USA).

MRI

High-resolution images were obtained using a 4.7 Tesla MR imaging spectrometer (Varian, Palo Alto, CA), with a corresponding proton resonance frequency of 200 MHz. A quadrature receiver coil with a 60 mm diameter was used for radiofrequency pulse transmission, and for reception of the NMR signal. The straight inserts that had contained the catheter were air filled and the curved insert was filled with water for the imaging process. Water was added to the curved insert to reduce the possibility of magnetic susceptibility artefacts that have been reported for air filled catheters [9]. The straight inserts were closed at one end and the small bore did not permit air to escape when attempts were made to fill them with water.

MRI measurements of the transverse relaxation rate (R_2) of the polyacrylamide gels took place between 20 days and 30 days after irradiation, at which time the degree of polymerization has been shown to be stable [21]. This time was longer than usually used and was governed by the availability of the spectrometer. MRI scanning was performed at room temperature using a single echo spinecho sequence, repeated with echo times (TE) of 25 ms, 150 ms and 300 ms. The repetition time (TR) was 3000 ms and the in-plane image resolution was either 0.2 mm or 0.4 mm. Slice thicknesses were 1 mm and 0.5 mm for the 0.4 mm and 0.2 mm in-plane resolutions, respectively. The k-space data matrix was 256×256 in all cases, and data were acquired at least twice and signal averaged in order to improve the SNR, and to enable phase cycling of the radiofrequency pulses, thus reducing image artefacts. Imaging times were of the order of 1 h for 0.4 mm resolution, while for 0.2 mm resolution, imaging times of 10 h were used in order to reduce the standard error in the R_2 readings to less than $\pm 3\%$.

It has been observed that change in R_2 is proportional to the radiation dose over a limited region, typically 0–12 Gy, (*e.g.* [5, 7]) and so by measuring R_2 , the absorbed dose can be estimated in this region. Neglecting any effect of diffusion through the magnetic field gradients used for imaging, in a single-echo spin-echo MRI, the signal intensity varies according to:

$$S = S_0 e^{-\mathrm{TE} \cdot R_2} \tag{1}$$

TE is the echo time, and S_0 is the signal intensity at zero echo time. R_2 was estimated on a pixel-by-pixel basis from the signal intensities of the three images at the different echo times, by non-linear regression using the Levenberg-Marquardt algorithm [22]. The relationship between R_2 and radiation dose was established by measuring the R_2 of the calibration samples, and then fitting a straight line of

the form:

$$R_2 = R_{2b} + \rho \cdot D \tag{2}$$

where R_{2b} is value of R_2 for the background (unirradiated) gel; D is the radiation dose; and ρ is the dose–response of the gel. Having established R_{2b} and ρ , subsequent estimation of R_2 as part of a dosimetric measurement allows an image of radiation dose to be computed.

Radiochromic film dosimetry

Two types of radiochromic film were used for film dosimetry. The first type, known as HD-810 (Nuclear Associates, Hicksville, NY) consists of a single layer of radiation sensitive emulsion, approximately 7 µm thick, on a 0.22 mm polyester base. The second type of film is known as MD-55 (Nuclear Associates). This is a laminated film composed of two pieces of 0.27 mm polyester base, each with a nominal 15 µm thick coating. Recommendations on the use of radiochromic film have been given in the literature [23]. The films were read with a manual Radiochromic Densitometer (Model 37-443, Nuclear Associates) with an ultra bright LED light source with a peak wavelength of 660 nm. To improve the resolution of this device, the aperture of 2 mm was reduced to 0.3 mm by the addition of an annular insert. Initial work was carried out to investigate the energy dependence for MD-55 and HD-810 film for a range of electron energies from 1.3 MeV to 4 MeV and for 300 kV photons and 6 MV photons. A calibration curve of optical density versus absorbed dose was determined between 0 and 32 Gy for the MD-55 and between 0 and 120 Gy for the HD-810 film using 6 MV X-rays. Electrons in the range 1.3 MeV to 3.8 MeV were obtained from a Betatron (model CMB10 manufactured by the Tomsk Polytechnical University, Russia) and the 4 MeV electrons from a linear accelerator (Elekta, UK).

A solid, water equivalent phantom (WTe, St Bartholomew's Hospital, London) was designed for irradiating the film using the 90 Sr/ 90 Y source train. The rectangular phantom was constructed in two halves to form a block 38 mm × 38 mm × 50 mm with a 1.8 mm hole drilled down the central axis of the phantom into which the catheter was inserted. For each film type, two pieces of film, measuring 20 mm × 60 mm were carefully placed on either side of the central hole. The MD-55 film was nominally exposed to 20 Gy at 2 mm and the HD-810 was nominally exposed to 32 Gy at 2 mm. The AAPM recommendations for radiochromic film dosimetry were followed [23].

Results

An R_2 image in a coronal plane is shown in Figure 2 and a sagittal view is shown in Figure 3 together with an image of the curved phantom. There was no evidence of artefacts due to magnetic susceptibility variations within the phantom for either the straight insert, which could not be filled with water, or for the curved insert, which was water-filled.

A calibration curve for the PAG is shown in Figure 4; the number of calibration points was limited by the available scanner time. The parameters of the linear fit to



Signal Intensity (arbitrary units)

Figure 2. Coronal image of polyacrylamide gel (PAG) used as a vascular brachytherapy phantom and irradiated using 90 Sr/ 90 Y sources with an in-plane resolution of 0.2 mm.

the calibration data for the 4.7 T MRI scanner were $R_2=1.58+0.27D$, where D is the absorbed dose.

The measurement of the response of radiochromic MD-55 and radiochromic HD-810 film to a range of electron energies from 1.3 MeV to 4 MeV and for 300 kV photons and 6 MV photons are shown in Figure 5. The results indicate little or no dependence on energy. Calibration curves for both types for 6 MV X-rays are shown in Figure 6. For MD-55 and HD-810, the linear fit parameters were optical density=0.014+0.046D and optical density=0.029+0.009D, respectively, where *D* is the absorbed dose.

The variation in absorbed dose with distance orthogonal to the axis of the source train for both glass (0.2 mm inplane resolution) and BarexTM inserts (0.25 mm in-plane resolution) together with the results obtained using radiochromic film is shown in Figure 7. The achievable resolution was constrained by the available scan time. The data from the curved insert was found to be identical with that from the straight insert. There was no evidence



Figure 4. Calibration curve for a polyacrylamide gel measured using the 4.7 T MRI scanner. The error bars represent the standard error in the mean of several measurements made at different positions inside the calibration tubes, and the errors are a result of not only random noise but also image artefacts, the magnitude of which depended on the position of the calibration tube inside the receiver coil.

of dose overestimation in the high dose area due to monomer diffusion during irradiation [10]. The irradiation times in this experiment were quite short compared with the long iradiation times (1024 s) reported by De Deene et al [10]. Profiles parallel to the catheter axis at a radial distance of 2 mm from the source centre for PAG with a glass insert compared with measurements using radiochromic film are shown in Figure 8. In Figure 9, a measurement with 0.2 mm in-plane resolution with a glass insert is compared with measurements with both BarexTM and glass inserts with 0.4 mm in-plane resolution. A radial plot of uniformity of R_2 measured using PAG is shown in Figure 10.

The absorbed doses measured 2 mm from the centre of the source chain in the plane perpendicular to the catheter axis through the centre of the source using PAG, MD-55 and HD-810 films are given in Table 1.

Discussion

The measurements of absorbed dose orthogonal to the source axis (Figure 7) show good agreement between the



Figure 3. Sagittal images of polyacrylamide gel used as a vascular brachytherapy phantom and irradiated using 90 Sr/ 90 Y sources. (a) Straight insert with 0.2 mm in-plane resolution; (b) curved insert with 0.4 mm in-plane resolution.



Figure 5. Calibration curves for radiochromic film irradiated with a range of energies and sources.



Figure 6. Calibration curves for radiochromic MD-55 film and radiochromic HD-810 film irradiated using 6 MV X-ray. Error bars are too small to be shown on this figure.



Figure 7. Relative absorbed dose measured orthogonally to the centre of the source train using polyacrylamide gel (PAG) and radiochromic film. Results are normalized to 2 mm from the centre of the source train. The error bars for the gel data were omitted for the sake of clarity. Errors for the PAG data were estimated to be $\pm 5.6\%$ (1 standard deviation) based on the variation in dose in the low dose region.



Figure 8. A comparison of profiles measured using polyacrylamide gel and radiochromic film parallel to the catheter axis at a radial distance of 2 mm from the source centre.



Figure 9. Measured profiles using polyacrylamide gel (PAG) and imaged with in-plane resolutions of 0.4 mm compared with PAG with a glass insert imaged with 0.2 mm in-plane resolution.



Figure 10. Radial plot of R_2 measured at 2 mm radial distance from the source centre at 15° intervals.

 Table 1. Comparison of absorbed doses measured at 2 mm

 from the source centre

Dosimeter type	Given dose (Gy)	Measured dose (Gy)
PAG gel Radiochromic MD-55 Radiochromic HD-810	8.0 ± 0.4 20.0 ± 0.6 32.2 ± 0.9	$7.9 \pm 0.4 \\ 20.8 \pm 0.9 \\ 32.7 \pm 1.7$

PAG, polyacrylamide gel.

PAG and MD-55 radiochromic film. The HD-810 gives some slightly higher measured absorbed doses. The thin glass-walled insert does not appear to make a significant difference compared with the tissue equivalent BarexTM insert. Normalized dose versus radial distance from the source centre at three different positions (left, middle and right) of the curve phantom were also compared with the depth dose curve of the cardiovascular glass phantom; no significant differences were observed except the fall off in dose at the end of the middle position.

For the profiles parallel to the source axis there is good agreement between the PAG with a glass insert (in-plane resolution 0.4 mm) and the two measurements with radiochromic film (Figure 8) with the exception of the fall off in dose at the end of the train. Similar distributions were measured with the BarexTM insert. The profiles measured with the highest resolution (0.2 mm) with a glass insert (Figure 9) show much more variation in the profile than the other measurements, with the exception of the measurements with the BarexTM insert (Figure 9). Undulations were also observed for all profiles, for which there are several possible explanations. First is that the outer diameter of the source train was 0.64 mm while the inner diameter of the catheter was 0.81 mm, so it could be that the sources were slightly displaced from the catheter axis with different source positions for each irradiation. Second, it is possible that the catheter was bent inside the phantom; however special care was taken to keep the catheter straight, at least in the vicinity of the sources. Finally, there might have been variations in source position giving rise to small gaps between one seed and the next. The radial plot of R_2 values (Figure 10)

shows the angular variation to be within $\pm 5\%$ of the mean value. It was not possible to measure this distribution using radiochromic film and the current setup.

The ability of PAG gels to measure absolute doses accurately has been the cause of much debate, and large differences have been recorded [7, 24, 25]. It is possible that the difference in size between the main phantom and calibration tubes is a contributory factor. Farajollahi and Bonnett [26] reported that the slope of the gel dose response had been measured as $0.24 \pm 0.01 \text{ s}^{-1} \text{ Gy}^{-1}$ for small calibration vials, and $0.33 \pm 0.003 \text{ s}^{-1} \text{ Gy}^{-1}$ for a large phantom. Another possible contributory factor is the temperature difference between the phantoms and calibration vials at the time of scanning, since R_2 is strongly dependent on the temperature. McJury et al [9] commented on this effect in the context of heating inside the radiofrequency coil. In addition, variations in the manufacturing process [27] or the thermal history of the samples [28] may cause differences between calibration samples and phantoms. In this present set of experiments, calibration vials and phantoms had almost identical dimensions, so temperature and size difference should not have affected the results to any significant degree.

The absorbed dose along the source axis at 2 mm distance from the source centre was measured (Table 1). Uncertainty in the given dose was 1.6% (0.13 Gy for 8 Gy) according to the source calibration data. In addition, since we used a manual transportation system, there are also potential timing errors. Estimated timing errors are of the order of 2 s, giving a further error in dose of ± 0.24 Gy at 2 mm radial distance. Thus, the total uncertainty for the errors summed in quadrature for a dose of 8 Gy was ± 0.3 Gy (4%), and the measured dose is not significantly different from the given dose (1.25%). Both phantoms and calibration vials were measured on the same day. Additional measurements indicated that if all measurements were not carried out at the same time then the difference between the given and measured absorbed doses could be of the order of 7%. Within a region 36.4 mm along the source axis, the maximum dose recorded was 8.5 Gy, which is 6.8% higher than mean dose and the minimum dose recorded was 7.3 Gy, 7.5% lower than the mean. One possible cause of the difference between the maximum and minimum doses was the bending of the catheter within the tube, since the inner diameter of the phantom tube was approximately 2 mm, while the outer diameter of the catheter is around 1.6 mm. Some of the sources may also have been slightly displaced from the catheter axis.

In both experiments the measured absorbed dose was slightly lower than the given dose, which could be because of extra absorption by the glass insert, which is denser than tissue. The BarexTM tube was neither uniformly circular, nor perfectly straight, so it was difficult to measure absolute dose accurately and this was not attempted.

For the MD-55 film, the dose was measured along a line parallel to the catheter axis, 33 mm in length, at a radial distance of 2 mm from the axis. In this experiment the measured dose was only 4% higher than that prescribed. Along the treated length the highest recorded value was 22.5 Gy, which is 8.2% higher than the mean value, and the lowest value was 18.8 Gy, 9.6% lower than the mean. The standard deviation was $\pm 4.2\%$ for the dose measured along the central 33 mm, 2 mm from the catheter axis. For HD-810, similar results were obtained. The mean measured dose was 1.6% higher than that prescribed. Along the treated length, the differences between the highest and lowest values and the mean value were 9.9% and 7.6%, respectively. The standard deviation was $\pm 5.2\%$ for the dose measured 2 mm from the catheter axis. It should be noted that in these experiments the source train met all the AAPM Task Group 60 acceptance criteria.

With the relatively high field strength used in our study, we were able to achieve in-plane resolution of down to 0.2 mm, with slice thicknesses of 0.5 mm. However, this required long scan times in order to achieve good SNR. The strength of the relationship between resolution and scan time shows, however, that with only slightly poorer resolution, more acceptable scan times of around 1 h would give adequate resolution for scanning intravascular brachytherapy dosimeters.

Conclusion

These results indicate that PAG dosimeters can be used to measure the dose distributions specified by the AAPM [2] for vascular brachytherapy sources with high resolution MRI, and that more complex geometries can be investigated in future. If a higher resolution of 0.2 mm is used, then the results show more variation in the absorbed dose profiles and this requires further investigation. This technique is, however, restricted to centres with access to high resolution MRI, which is an obvious disadvantage. A further disadvantage is that stringent procedures must be followed to exclude oxygen during the gel manufacturing process, although this can now be avoided since commercially-prepared gels are now available for pur-chase, *e.g.* BANGTM gels, MGS Inc., USA. Alternatively, it may be possible to use new types of gel that are currently under investigation, and which are claimed to be less affected by dissolved oxygen (the so-called "MAGIC" gels [29]). On the other hand, radiochromic film is readily available and only requires the use of a relatively inexpensive densitometer. These investigations indicate that, whilst it would be difficult to measure radial distributions, the use of radiochromic film would be the method of choice for the measurements of absorbed dose distributions parallel and orthogonal to a source train used for intravascular brachytherapy.

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