Normoxic polymer gels: are they magic?

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1. Introduction

In the last few years there has been considerable interest in the use of polymer gels to measure complex dose distributions in radiotherapy. Despite considerable advantages they are still not widely used in clinical situations. This is due primarily to the difficulty in manufacture, particularly the need to exclude oxygen both from the gel and the manufacturing process, the limited number of suitable phantom materials and the need for easy access to an MRI facility.

In 2001 Fong and co-workers [1] proposed a new gel formulation, which was given the acronym MAGIC (Methacrylic and Ascorbic acid in Gelatin Initiated by Copper). In their study, they used Gelatin (300 bloom) as a gelling agent, methacrylic acid (MAA) as monomer, and HPLC grade water as solvent. Copper-sulphate (CuSO₄.5H₂O) and ascorbic acid was added to form a complex with oxygen, and to serve as a free radical source for the initiation of the polymerisation of the methacrylic acid. In addition hydroquinone was used to keep the monomer from auto-polymerisation and to absorb any free radicals introduced from the gelatin or other components. The advantages of this gel were reported to be the ease of preparation and a linear response to absorbed dose up to 30 Gy. The slope of the relaxation rate \( R_2 \) versus dose at 85 MHz was found to be 0.310, 0.567 and 0.868 s⁻¹Gy⁻¹ respectively for MAA concentrations of 3, 6, and 9. More recently further investigations have been undertaken on the stability of the MAGIC gel by De Deene et al [2]. Their results showed that the stability of the \( R_2 \) dose response is largely determined by the chemical composition of the gel dosimeters. They also showed that the compactness of the gelatin matrix has an effect on both the dose sensitivity and the \( R_2 \) value of an unirradiated gel sample and on the rate of post-irradiation polymerisation. In addition they reported that whilst the \( R_2 \)-dose sensitivity for polyacrylamide gels (PAG) increases with time (post irradiation), it decreases with time for the MAGIC gel, which indicates that the polymer structure in the normoxic gels differs from the polymer structure in the PAG gels. The radiation response for normoxic gels with different compositions gels has also been evaluated by De Deene et al [3].

The purpose of this paper is to report on an investigation of the basic properties of MAGIC gels namely: linearity of response, effects of temperature and stability.
2. Method

The “MAGIC” gel was manufactured using the formulation proposed in the literature by Fong et al [1] with no additional precautions to exclude oxygen. Type A gelatin from porcine skin approximately 300 bloom was used together with methacrylic acid, L-ascorbic acid, copper sulphate pentahydrate, hydroquinone and HPLC water. The procedures were carried out in normal atmospheric conditions. The magnetic resonance (MR) measurements were performed using a 1 T whole-body scanner using the standard quadrature knee coil for signal reception. The transverse relaxation rate $R_2$ ($1/T_2$) of the water protons was taken as a measure of radiation dose absorbed in the gel. Gel samples were placed in the MR room 24 hours prior to measurement, to obtain temperature equilibrium. Imaging was carried out 1 to 5 days after irradiation. Both spin-echo and multi spin-echo sequences were used. For the spin echo sequence, a repetition time of 3000 ms was used with echo times of 25, 50, 75, and 100 ms. For the multi spin echo sequence, an echo train length of 16 was used with an initial echo time of 22.5 ms, and fifteen 22.5 ms increments. Repetition time was 3000 ms, field of view was 300 mm with a matrix size of 192×256, slice thickness was again 3–10 mm and in-plane resolution was 1.17 mm. For generating $R_2$ images, the first two (22.5, 45 ms) and the last few echo times (due to the very low signal at the higher dose level) were discarded to minimise any image artefacts. The choice of pulse sequence was determined by irradiating 7 calibration vials filled with gel, using 6 MV x-rays to give absorbed doses of 2, 5, 10, 20, 30, 40, and 50 Gy. $R_2$ measurements were performed 56 days after irradiation using the two different pulse sequences: single echo and multi-echo sequence and the results compared.

Measurements were made of:
(1) the linearity of response;
(2) effect of MRI pulse sequence;
(3) the effect of time from manufacture to irradiation;
(4) the dependence of the dose response on time from irradiation to time of measurement;
(5) the effects of temperature on the behaviour of the gel both at the time of irradiation and at scanning;
(6) spatial stability of the polymerisation.

3. Results and discussion

The dose response was found to be linear up to 50 Gy and of the two pulse sequences used it was found that the dose sensitivity was higher for the single spin echo sequence ($0.62 \pm 0.01 \text{s}^{-1}. \text{Gy}^{-1}$) than that for the multi-echo sequence ($0.48 \pm 0.02 \text{s}^{-1}. \text{Gy}^{-1}$). No significant effect was found of time from manufacture to time of irradiation over a period 14 days and the response of the gel after irradiation was found to be relatively stable 1 day after irradiation (figure 1) which agrees with the findings of De Deene et al [2].

A linear dependence of both the slope of the gel response curve and background values on temperature at the time of measurement in the MRI scanner was found, as would be expected. In addition a dependence of the value of $R_2$ on the temperature of the gel at the time of irradiation was also found. This is shown in figure 2 for two different batches of gel with each sample irradiated to 10 Gy with 6 MV x-rays. The mean decrease in $R_2$ with increase in temperature was found to be $0.27\pm0.07 \text{s}^{-1}$ per °C.
In order to study spatial stability of the gel a rectangular glass phantom was irradiated using a single 40x40 mm photon field and the results imaged over a period of 1 month. The width of the distribution was measured using a single coronal image with the slice positioned at the centre of the irradiated area. This study was repeated three times. The results of the first study are shown in figure 3 and it was found that the measured width decreased from 40.3 ± 0.2 mm on day 1 to 34.8 ± 0.2 mm on day 56, a decrease of 14%. In the subsequent measurements the width was found to decrease by 14% over 34 days and 12% over 25 days. This behaviour indicates some long-term reorganisation of the polymer and some possible changes in water volume. In a study using x-ray CT, Trapp et al [4] have reported a density change in a PAG gel related to a volume decrease, which implies the possibility of some spatial changes within the gels. In addition, after day 1 the profiles show a “dose overshoot” at the edge of the high dose plateau. This is believed to be due to the migration of unirradiated monomers into the high dose region and subsequent reaction with long-lived radicals (5).
4. Conclusions

This work confirms that the “MAGIC” normoxic gels have many good properties and for relative measurements variations with temperature may not be of concern but that the variation in dimensions of irradiated areas with time must be investigated further if this type of gel is to used extensively in radiation dosimetry.

References

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