Normoxic polymer gel – basic characterisation and clinical use

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1. Introduction

Polymer gel dosimeters are suitable for narrow photon beam dosimetry in radiosurgery, stereotactic radiotherapy and IMRT, where small fields and high dose gradients are frequently used and lateral electronic equilibrium often not exist. Polymer gel dosimeters show a linear dose response relationship throughout clinically used dose ranges and they are not susceptible to diffusion effects [1]. They act as absorbing medium, are integrating 3D dosimeters with variable isotropic mm spatial resolution [2,3], and can be used for absolute dose verifications [4].

However, manufacturing polymer gels is often laborious and most of the polymer gels are sensitive to any oxygen contamination which inhibits the radiation induced polymerization, because oxygen acts as a free radical scavenger. Therefore, these gels have to be manufactured, stored and used in sealed, oxygen-free containers.

The formulation for a new polymer gel, which is made under normal atmospheric conditions, has been published [5]. Because manufacturing and processing can be performed under normal atmospheric conditions, the gel is also called normoxic [6,7]. Only a few accessories for gel production are necessary, facilitating the use of this gel, which can be easily produced in a clinical environment.

The purpose of this study, which is work in progress, was to produce several gel batches with varying concentrations of their compounds, to measure dose response curves, to investigate ageing effects and to use this polymer gel in 3D absolute dose verifications in radiosurgery, IMRT and proton therapy.

2. Material and methods

Starting from Fongs formula [5], we defined our standard gel composition (water, 8 % gelatin, 18 mM hydroquinone, 9 % methacrylic acid, 2 mM ascorbic acid and 0.02 mM copper sulphate). Gel batches (1 kg each) were produced with different amounts of methacrylic acid (12, 9 and 6 %), CuSO4·5H2O (0.04, 0.02 and 0.01 mM) and hydroquinone (10, 1 and 0 mM). Gelatine and ascorbic acid concentrations have not been changed. Methacrylic acid acts as monomer, ascorbic acid together with copper sulphate builds complexes which act as oxygen scavenger [6] and hydroquinone acts as auto polymerization inhibitor. Our detailed manufacturing process is described elsewhere [8].

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The gel was filled into small glass vials, PVC and PET containers of different sizes and was kept in the dark at room temperature to solidify and was then stored in a refrigerator. The whole manufacturing procedure is very fast and simple, since no glove box or oxygen purging is necessary.

To measure dose response curves, several gel samples were irradiated with $^{60}$Co gamma rays from a Gamma Knife up to a maximum dose of 50 Gy. For analyses we used a 1.5 T MR scanner together with the head coil to measure the dose dependent spin-spin relaxation rate R2. The relaxation rate R2 varies linearly with absorbed dose and can be calculated using Hahn spin echo images with different echo times (10 and 40 ms in our case) [1]. The 3D image data sets for the different echo times were exported to an in house developed analyses software which calculates the 3D R2 distribution.

The homogeneous dose plateau region was analyzed and the dose dependent mean value and standard deviation of the measured R2-values were calculated. The geometrical image resolution chosen was 1.3 x 1.3 x 2.0 mm$^3$. In order to measure the temperature dependence of the measured R2-values a standard gel composition was scanned at temperatures between 11 and 29 °C. Also a dose response curve for the standard gel composition was measured for a maximum dose of 5 Gy in order to investigate the potential use of this gel for fractionated treatment regimes. In order to investigate ageing effects of the gel, several samples of the same batch were repeatedly scanned and their dose and time dependent R2-values were recorded. Also absolute 3D dose verifications in radiosurgery using the standard gel composition were performed. A gel container was mounted in the center of a spherical phantom and was irradiated to a maximum dose of 20 Gy using the 14 mm collimator helmet of the Gamma Knife.

The software is being currently redesigned in order to handle non-stereotactic MR images and calculated dose distributions in order to analyse 3D dose verifications in IMRT and proton therapy. Also larger gel samples (approximately 3 liters) are being produced for this purpose.

### 3. Results

![Figure 1. Relaxation rate R2 as a function of dose from 0–50 Gy for 6, 9 and 12% (by weight) methacrylic acid for the standard gel composition.](image1)

![Figure 2. Relaxation rate R2 as a function of dose from 0–50 Gy for 0.01, 0.02 and 0.04 mM copper sulphate concentration for the standard gel composition.](image2)
The dose response curves were linear up to a dose of 50 Gy (figures 1 and 2) with the slope being dependent on the chemical composition. The indicated error in R2 (range: 3 – 55 s⁻¹) increases with increasing dose to a maximum value of 5 %. The slope of the dose response curves varies between 0.79 and 0.95 (Gy.s⁻¹), the intercept between 3 and 4 s⁻¹.

Increasing the copper sulfate concentration result in decreasing slopes of the dose response curves (figure 2). The more hydroquinone (auto polymerization inhibitor) is added (0, 1 and 10 mM), the lower the slope of the dose response curves will be. The measured relaxation rate and therefore the dose to R2 relationship varies with temperature of the gel during MR imaging [9]. With decreasing gel temperature the slope of the dose response curve increases.

Figure 3 shows the linear dose response curve for the standard gel composition in the low dose region as used for fractionated treatment regimens. The maximum error in R2 was 6 %. We have also found that the R2-values decrease with increasing time after irradiation, therefore slightly decreasing the slope of the linear dose response curve and decreasing the dose resolution.

Figure 4 shows a comparison of the calculated (solid line) and measured (broken line) dose profile along the x-axis for an absolute dose distribution using the 14 mm collimator helmet of the Gamma Knife in the center of a spherical phantom (16 cm in diameter).

4. Discussion

Lowering the monomer concentration causes saturation effects to occur at rather low doses. In order to cover the dose range applied in radiosurgery we recommend 9 % by weight of methacrylic acid. Since copper sulphate acts as an oxygen scavenger, together with ascorbic acid, it has been demonstrated that an increasing concentration of copper sulfate inhibits the radiation induced polymerization [6]. To get a steep dose response curve and to scavenge dissolved oxygen within a reasonable time, a copper sulfate concentration of 0.01 mM is adequate. Increasing the hydroquinone concentration will increasingly inhibit the radiation induced polymerization. For polymer gels, the dose response is highly dependent on the gel temperature during MR scanning [9]. Therefore the read out temperature has to be known or kept constant. Also ageing effects, are demonstrated for this normoxic polymer gel. The uncertainty can be decreased by optimized MR imaging parameters such as optimized echo times. The results of first absolute dose verifications using this normoxic gel together with the
simplicity of the gel manufacturing, demonstrate the potential of this new polymer gel in small beam photon dosimetry within a clinical environment.

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