Dose integration and dose rate characteristics of a NiPAM polymer gel MRI dosimeter system

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Abstract. The normoxic polymer gel dosimeter based on N-isopropyl acrylamide (NiPAM) is a promising full 3D-dosimeter with high spatial resolution and near tissue equivalency. NiPAM gel samples were irradiated to different doses using a linear accelerator. The absorbed dose was evaluated using MRI and statistical significance of the analysed data was calculated. The analysis was carried out using an in-house developed software. It was found that the gel dosimeter responded linearly to the absorbed dose. The gel exhibited a dose rate dependence, as well as a dependence on the sequential beam irradiation scheme. A higher dose rate, as well as a higher dose per sequential beam, resulted in a lower dose response.

1. Introduction
Commonly today, dosimeters used for absorbed dose distribution measurements contain diodes or ionization chambers positioned in an array [1, 2]. These dosimeters have a limitation in spatial resolution as the diodes or chambers integrates the ionization over an area or a volume and the full 3D dose is estimated from a limited number of measurement points [3, 4]. Furthermore, the diodes or chambers are placed millimeters or centimeters apart and the dose between the measurement points have to be reconstructed and calculated. This makes the uncertainties of 3D quality assurance (QA) depend on both accurate measurements and calculation algorithms provided by the vendor.

Gamma pass rate evaluation is commonly used to compare two dose distributions. The concept combines the percentage dose difference between measured and planned dose as well as the distance to agreement (DTA) [5]. However, there is research that points out that gamma pass rate for virtual 3D dosimeters that utilize arrays of detectors arranged in common 3D geometries does not capture clinically relevant dosimetric differences [6]. One suggestion is to implement dose evaluation trough dose volume histogram (DVH) analysis. This requires a true 3D dosimeter with high spatial resolution such as for example the polymer gel dosimeters.

Polymer gel dosimeters have high spatial accuracy and are near tissue-equivalent, i.e., the absorbing and scattering properties for a given radiation match those of a certain biological tissue [7, 8]. However despite the promising aspects of polymer gel dosimetry, it have yet to be a common dosimeter in clinical use [8]. There could be several reasons for this. A few of them discussed by Ibbott [8] are imaging artifacts emerging during evaluation of the gel, linear energy transfer dependence and the fact...
that there has been a limited effort to create low and high-density gels to simulate different tissues e.g. lung tissue. Another major reason to why this type of dosimeter has low acceptance in clinics could be that it is time consuming to manufacture and analyse, and, additionally, the monomer toxicity of these dosimeters makes them hazardous and inconvenient to use and manufacture [9]. As discussed by Senden [10], there are other polymer gel formulations which are less toxic. In particular N-Isopropylacrylamide (NiPAM) gel dosimeters holds great promise [10, 11].

The aim of this study was to investigate the dose response of a NiPAM gel dosimeter. The dose rate and the sequential beam irradiation dependence were investigated.

2. Materials and methods

2.1. NiPAM gel preparation

The gel was prepared by heating deionized water together with gelatin (Sigma Aldrich, U.S.A., 5% w/w) to 45°C. When the gelatin had completely dissolved, first N-isopropyl acrylamide, NiPAM, (97% Sigma Aldrich, U.S.A., 3% w/w), and then N,N'-methylene-bis-acrylamide (98% Sigma Aldrich, U.S.A., 3% w/w) was added. Subsequently, the temperature was allowed to drop to 38 °C and the antioxidant Tetrakis hydroxymethyl phosphonium chloride, THPC, (80% solution in water, Sigma Aldrich, U.S.A.) was added to a concentration of 5 mM. The gel was manufactured under normal atmospheric conditions and constantly mixed with a magnetic stirrer. The mixture was poured into glass vials equipped with plastic screw-tops and were left in dark to form a gel over night at room temperature, approximately 21°C. Under the whole process, care was taken to minimize the gels exposure to ambient light. The gel formula was inspired by Senden [10].

2.2. Irradiation, readout and data processing

All gel vials were irradiated with a 10 MV beam, placed in a water filled PVC phantom. The gel samples were irradiated approximately 24 hours after the manufacturing. To characterize the dose rate dependence of the gel, a total of 33 vials were irradiated to 11 different absorbed doses between 0.50 and 10 Gy. Three vials were irradiated to each of the predetermined doses, each with a different dose rate, 100, 300 and 600 MU/min. To characterize the sequential irradiation dependence of the NiPAM gel, a total number of 42 vials were irradiated. Doses for each beam sequence were 0.25, 0.50, 1.0, 2.0 and 4.0 Gy. During irradiation, a dose rate of 600 MU/min was used. The beam-off time between two subsequent beams was approximately 60 seconds. The gel vials were evaluated approximately 24 hours after irradiation using a 3.0T MRI scanner (Discovery 750W General Electric Medical Systems, U.S.A.). The scanning sequence used for all scans was a T2-mapping sequence, named CartiGram, supplied by GE. The gels were scanned and data from 16 echo times were acquired with an inter echo time, ΔTE, of 80 ms (80 - 1280 ms) using a repetition time of 4000 ms.

The images generated by the MRI were processed in an in-house developed software written in Matlab (Mathworks®, Massachusetts U.S.A.). To evaluate the dose rate and sequential beam irradiation dependence, the calculated R2, and the corresponding standard deviation, were plotted as a function of the absorbed dose and linear regressions were fitted to the data.

3. Results

Linear regressions for three different dose rates (100, 200 and 600 MU min⁻¹) were carried out. It was found that the dose response of the NiPAM gel was dependent on the dose rate (Figure 1). The slope of the 100 and 300 MU min⁻¹ regressions were 11.8 % and 6.5 % steeper respectively compared to the 600 MU min⁻¹ regression. All three regressions were statistically significantly different from each other (p<0.05).

The dose response of the gel dosimeter was also dependent on sequential beam irradiation (Figure 2). The response for the single, continuous beam, compared to the response for the sequential beams were all statistically significantly different from each other with the exception of the single beam versus the 4 Gy per sequence-beam.
4. Discussion

An F-test evaluation of the regressions for the dose responses with different dose rate (Figure 1) shows that there is a difference between the regressions (p<0.05), i.e. the NiPAM gel is dependent on the dose rate. This is an unwanted characteristic as it complicates or limits the area of application of the gel. This result contradicts with the result in the study by Farajollahi et al [11] but agrees with the study by Hsieh et al [12].

It was found that the dose response of the gel is dependent on sequential beam irradiation (Figure 2). Although the study by Karlsson et al [13] investigated different types of polymer gel dosimeters (nMAG and nPAG), their findings coincides with the result in this study. The rate of production of free radicals, and thereby the concentration of radicals, is directly linked to the dose rate of the beam which the gel is being irradiated with. Unlike polymer growth termination reactions, the polymer chain growth process involves one polymer radical. As a result, the rate of reactions is proportional to the concentration of polymer radicals. However, termination reactions involve two radicals, consequently the incidence of termination reactions is proportional to the square of the radical concentration which makes termination reactions the dominant reaction when high concentration of radicals are present [13]. This might serve as an explanation to why the gel demonstrates dose rate dependence where a higher dose rate gives a lower dose response and vice versa.

The sequential beam irradiation dependence of the NiPAM gel can be explained similarly; when the radiation beam is delivered in shorter bursts with no active beam in between, the radicals will approach high concentrations only for short periods and the concentration will drop in between beams. Compared to a single continuous beam, the average lifetime of the radicals generated by the sequential beam is longer, yielding more polymer formulation and increased dose response. It is likely that the sequential irradiation dependence of the gel would be different if time between the sequential beams had been altered. If the time between the sequential beams had been reduced, the sequential irradiation dependence would probably be less pronounced.

Figure 1. R2 versus absorbed dose for the dose rate dependence study of the NiPAM gel. Samples irradiated with dose rate 100, 300 and 600 MU min\(^{-1}\).
Figure 2. R2 versus absorbed dose for the sequential irradiation dependence study of the NiPAM gel. Samples were irradiated with 600 MU min\(^{-1}\).

5. Conclusion
The dosimeter was found to respond linearly to the absorbed dose within the investigated range of doses and all regressions had a R\(^2\)-value greater than 0.98. The NiPAM polymer gel dosimeter shows both a dose rate and a sequential beam dependence.

6. References
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