Feasibility of polymer gel dosimetry measurements in a dynamic porcine lung phantom

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Abstract. A dynamic ex-vivo porcine lung phantom combined with polymer gel dosimetry is tested as a new tool to validate modern adaptive radiotherapy techniques (e.g. gating or tracking). The gel was inserted into the lung via a latex balloon to simulate a tumor. After irradiation, the location of the dose maximum was verified, however, the dose was higher than planned and a high background signal was seen. Potential reasons for this finding are the non-standard conditions of gel handling. These conditions were systematically studied. Besides temperature, the material of the balloon seems to be of special importance. The results identify open issues that have to be addressed in future studies.

1. Introduction

Modern adaptive radiotherapy techniques (e.g. gating or tracking) have the potential of significant normal tissue sparing [1]. This is especially relevant for lung tumors that may exhibit large displacements due to respiratory movement. Implementing these techniques for clinical applications, however, requires validation of the intended workflow that ideally includes 3D measurements of the delivered dose distribution. Although several phantom settings have been developed [2, 3], this issue is not satisfactorily solved yet as they usually do not reflect the complexity of real patient treatments and/or do not provide sufficient information on the actually delivered dose. An ideal validation phantom should provide (i) realistic motion patterns comparable to those of patients, (ii) anthropomorphic properties allowing for realistic condition for time-resolved radiological imaging, and (iii) the possibility of measuring the delivered dose distribution in 3D [4]. This study presents a new approach to meet these requirements by a combination of a dynamic porcine lung phantom with 3D polymer gel measurements.

2. Material and Methods

2.1. Dynamic lung phantom

The dynamic lung phantom consists of an artificial PMMA-thorax and contains a post-mortem explanted porcine lung [5]. Inflation of the lung is achieved by under-pressure within the thorax and a

water-filled silicon balloon simulates the diaphragm. Modulation of the water volume over time with pre-defined temporal pattern allows to ventilate the lung under conditions comparable to those in patients and to generate arbitrary breathing patterns. The phantom is MR-compatible and has been previously used to study 4D motion patterns and radiological imaging protocols of artificial tumors produced by injecting Agarose-gel [6]. Thus, the phantom meets (i) and (ii) of the above requirements.

2.2. Polymer dosimetry gel

To measure the dose distribution in the phantom, the Agarose gel has to be replaced by a polymer dosimetry gel [7], e.g. the commercially available BANG-gel (Research, Inc. Madison, USA). Polymer gels include monomers that polymerize locally depending on the absorbed radiation dose. Measuring the relaxation rate R2 of the transverse magnetization with MRI techniques, the 3D-dose distribution can be determined after establishing a linear calibration curve [7]. For MRI-evaluation, a 32-echo multi spin echo sequence [8] with an inter-echo spacing of 18.5 ms was used. Gel production and storage after production (96 h) were performed as recommended by the manufacturer. To minimize the influence of oxygen and light on the calibration samples, brown borsilicate flasks (20 ml) were used and additionally covered by aluminum foil during storage.

2.3. Insertion of the gel into the lung

There are two major challenges in using the polymer gel in our experimental setting: (i) The gel has to be inserted into the lung and protected from contact with oxygen, and (ii) due to the limited durability of the lung, the recommended time between gel injection and irradiation (96 h) and irradiation and MRI evaluation (24 h) [7] had to be reduced to 3 h and 1 h, respectively.

To protect the dosimetry gel from oxygen after injection into the lung, a latex balloon attached on top of a urinary catheter by means of two o-rings was used. Prior to inserting the lung into the thorax, the catheter was guided into the pulmonary artery and the catheter-balloon located between the o-rings was inflated to fix it. Using a syringe, 50 ml of the gel were injected into the latex-balloon. As the gel was inserted after the recommended storage period and thus had to be reheated, the calibration samples were reheated as well to assure identical temperature histories.

2.4. Feasibility test with the lung phantom

As a first feasibility test of the intended experimental setting, the complete chain of insertion of the gel-tumor into the lung, irradiation and dosimetric evaluation was performed. Calibration samples were taken from the same batch and were irradiated in a water phantom under reference conditions with doses between 0 and 7 Gy correcting for the influence of the flask wall. In the treatment planning system (*VIRTUOS*) a small target volume (≈15 ml) within the measurement volume was defined and a 5-field treatment plan with a maximum target dose of 6 Gy was generated and subsequently irradiated using 6 MV beam (*Artiste*, Siemens). Due to the durability of the lung, MRI evaluation of the gel was performed 1 h after irradiation of the phantom and in a liquid-filled holding device for the calibration samples, respectively. The entire experiment was performed under static conditions.

2.5. Systematic investigation of gel response

As the feasibility test revealed several problems which are most likely related to the non-standard conditions of the gel handling, the gel response were systematically studied under these conditions.

2.5.2 Temperature effect

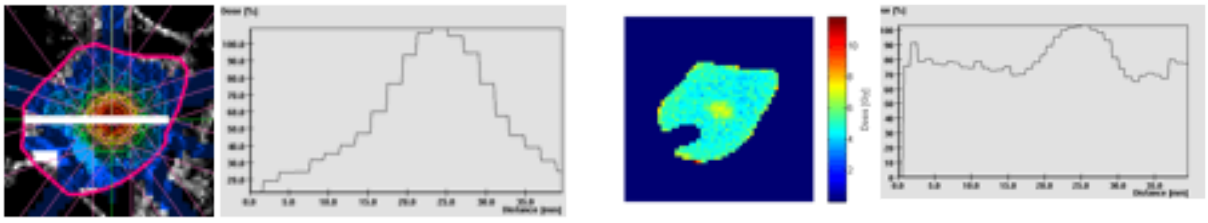
As temperature is a critical factor [8], the cooling behavior of our gel was measured placing the fiber of an MR-compatible optical thermometer (Fotemp Polytec 4.16) within the balloon. In addition, the response of unirradiated gel samples (latex balloon, 20ml flasks) was analyzed regarding its dependence on temperature during MRI evaluation. For this, the samples were measured 0, 43, 53, 66 and 104 minutes at room temperature (21°C) after removing it from storage at 12°C.

2.5.2 Oxygen permeability of the balloon
As continued oxygen contact may change the gel response to irradiation [8], the permeability of the latex balloon for oxygen was investigated. Four balloons and a set of calibration samples were filled with gel and stored light-shielded for either 3 or 24 hours at room temperature. For each storage time, one balloon was irradiated homogeneously with 4 Gy while the other remained unirradiated. During MRI measurement all samples were placed in a thermobox to assure constancy of temperature.

2.5.3 Water permeability of the balloon
As the influence of penetrating water may impact the dose response, it was investigated, if the thin-walled latex balloon is permeable for water in an aqueous environment. Two gel-filled balloons and a set of calibration samples were stored in water for 24 hours. One of the balloons was subsequently irradiated with 4 Gy. For constancy of temperature, all samples were placed inside a water filled thermobox 3 hours prior to the MRI measurement taking place 92 hours after irradiation.

3. Results

3.1 Lung experiment
Figure 1 shows the result of the lung experiment. Although the position of the dose maximum could be verified with the gel, there were two unexpected findings: (i) the maximum dose was measured to be 7.3 rather than the planned 6 Gy, and (ii) there is a significant background level of about 4.2 Gy. As these problems are likely to be related to the non-standard conditions of the gel handling potentially disturbing factors were further analyzed.



(a) (b) (c) (d)

Figure 1. CT-based dose-distribution (a) and normalized dose profile (b) along the white line. (c) and (d) show the respective results of the gel measurement.

3.2 Temperature effect
After reheating to 55°C, the gel cooled down and reached thermal equilibrium after 3h. Analyzing the temperature dependence of the MRI-signal over the first 104 min, an increase in T_2-values of 50% for the glass flasks and 33% for the balloon was found.

3.3 Oxygen permeability of the balloon
Figure 2 shows the dose maps determined with the calibration curve. For all measurements, the dose decreases towards the centre. Comparing the irradiated (figure 2c, d) with unirradiated balloons (figure 2a, b), an increased dose was found in the center, however, this hotspot occurred only after 3h (figure 2d). Doses after 3 and 24h differed by up to 1.7 Gy in corresponding regions. For irradiated calibration vessels (e.g. at 2 Gy, figure 2e and 3c) a homogeneous dose distribution is visible.

3.4 Water permeability of the balloon
Figure 3 shows the influence of the aqueous environment of the balloon on the dose response of the gel. Although homogeneously irradiated, the irradiated balloon shows a hot-spot of 4.4 Gy in the centre (figure 3a). The unirradiated balloon shows doses between 2.2 and 3.8 Gy. Excluding the hot spot, a similar dose distribution with an average dose of 3.2 Gy and 3.4 Gy is visible, respectively.

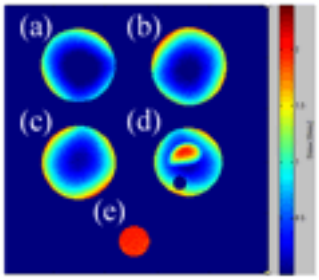


Figure. 2. Dose distribution measured in the gel-filled balloon stored in air for 24 h (a, c) and 3 h (b, d) prior to irradiation with 4 Gy (c, d) and no irradiation (a, b). The calibration sample (e) was irradiated with 2 Gy.

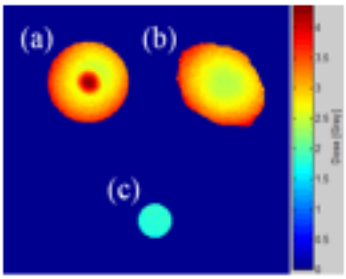


Figure 3. Dose distribution measured in the gel-filled balloon: (a) irradiated with 4 Gy (b) unirradiated. Prior to irradiation, the samples were stored in water for 24 h. The calibration sample (c) was irradiated with 2 Gy.

4. Discussion

The lung phantom was demonstrated to be a versatile tool for 4D-imaging studies [6]. Combining the phantom with polymer-based dosimetry-gel would allow to measure delivered dose distributions in radiotherapy and thus to validate complex treatment techniques like gating or tracking.

In the initial test of the gel in the lung phantom, the location of the dose maximum could be successfully verified, however, the measured maximum dose was markedly higher than planned, and there was a significant background signal. These results indicate the existence of additional uncontrolled factors that influence the gel response. Since the lung explant was stored in a freezer prior to preparation, temperature differences between the gel in the lung phantom and in the calibration flasks may occur. Thus, it is important to standardize the experimental procedures such that both pass the same temperature history. Other reasons may be related to deviations from the manufacturer's recommendations concerning the gel handling, which was necessary due to our experimental setting. With this respect, three aspects are important: (i) reheating of the gel prior to injecting it into the lung, (ii) reduced time between gel injection and irradiation as well as between irradiation and evaluation, and (iii) the use of balloons instead of glass to protect the gel from the environment.

While it can be expected that (i) and (ii) could be solved by carrying along calibration samples under the same conditions, it appears that oxygen and water may penetrate the latex-material. While the first might inhibit polymerization and thus reduce dose, the latter seems to increase the measured dose.

5. Conclusion

The combination of the dynamic anthropomorphic lung phantom with 3D gel dosimetry is a new promising approach to validate complex treatment techniques like gating or tracking geometrically as well as dosimetrically. As a first application of the phantom, the location of the dose maximum of a treatment plan could be verified. Regarding dosimetric measurements, the behavior of the gel under non-standard conditions is highly complex and although some influence factors have been identified in this study, further work is necessary to optimize protocols for use in the lung phantom.

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