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Initial Characterization of a Gel Patch Dosimeter for In Vivo Dosimetry

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Abstract

In vivo dosimetry is a greatly underutilized tool for patient safety in clinical external beam radiotherapy treatments, despite being recommended by several national and international organizations (AAPM, ICRU, IAEA, NACP). The reasons for this underutilization mostly relate to the feasibility and cost of *in vivo* dosimetry methods. Due to the increase in the number of beam angles and dose per fraction in modern treatments, there is a compelling need for a novel dosimeter that is robust and affordable while able to operate properly in these complex conditions. This work presents a gel patch dosimeter as a novel method of *in vivo* dosimetry. DEFCEL, a 6%T normoxic polyacrylamide gel, was injected into 1-cm thick acrylic molds to create 1-cm thick small cylindrical patch dosimeters. To evaluate the change in optical density due to radiation induced polymerization, dosimeters were scanned before and after irradiation using an in-house developed laser densitometer. The dose-responses of three separate batches of gel were evaluated and compared to check for linearity and repeatability. The response development time was evaluated to ensure that the patch dosimeter could be high throughput. Additionally, the potential of this system to be used as an *in vivo* dosimeter was tested with a clinically relevant end-to-end *in vivo* phantom test. All irradiations were performed with a Varian Clinac 21EX at the University of Wisconsin Medical Radiation Research Center (UWMRRC). The dose response of all three batches of gel was found to be linear within the range of 2–20 Gy. At doses below 0.5 Gy the statistical uncertainties were prohibitively large to make quantitative assessments of the results. The three batches demonstrated good repeatability in the range of 2 Gy to up to 10 Gy, with only slight variations in response at higher doses. For low doses the dosimeter fully developed within an hour while at higher doses they fully developed within four hours. During the *in vivo* phantom test the predicted patch absorbed dose was 4.23 Gy while the readout dose was evaluated to be 4.37 Gy, which corresponds to a 3.2% discrepancy. The dosimeter and densitometer pairing shows promise as an *in vivo* dosimetry system, especially for hypofractionated or MRI-guided radiotherapy treatments where higher doses are prescribed.

1. Introduction

In vivo dosimetry is an effective QA method to improve the quality and safety of radiation treatment through the direct monitoring of patient dose (Essers and Mijnheer, 1999; Leunens *et al.*, 1990; Noel *et al.*, 1995). As a result, many national and international organizations

(AAPM, ICRU, IAEA, and NACP) have recommended the use of *in vivo* dosimetry in standard clinical practice (ICRU, 1976; AAPM, 2005; NACP, 1980). Despite these recommendations, *in vivo* dosimetry has not been fully adopted by clinics due to many limitations, including cost, difficulty of use, and lack of dose sensitivity. The more popular *in vivo* dosimeters used clinically are prone to angular dependencies (AAPM, 2005) and exhibit dose supralinearity at high doses (IAEA, 2013). These issues are further exacerbated by modern increases in dose per fraction, beam angles, and the use of complex beam modulation. Due to these shortcomings, there is a need for a novel dosimeter that addresses these limitations. A potential dosimeter to address these issues is DEFGEL, a gel dosimeter that shows inherent angular independence (Gustavsson *et al.*, 2003), dose rate independence (De Deene *et al.*, 2006), near water equivalence, and is more effective at the high doses characteristic of hypofractionation (Yeo *et al.*, 2012) when compared to existing *in vivo* dosimeters. This study demonstrates a cheap, simple, and reliable method of *in vivo* dosimetry that utilizes a small, robust gel patch dosimeter paired with a high throughput laser densitometer.

2. Methods and Materials

2.1 Dosimeter Fabrication

The gel used in the patch dosimeter was DEFGEL, a type of 6% T normoxic polyacrylamide gel (Yeo *et al.*, 2012). The gel was fabricated using the method described by Yeo *et al.* The weight percentile composition of the gel was 3% acrylamide monomer, 3% N,N'-methylenebis-acrylamide (Bis) cross-linking monomer, 6% porcine skin gelatin, and 88% deionized (DI) water. In addition, 5 mM of Bis [tetrakis (hydroxymethyl-phosphonium)] sulphate, or THP, was added to act as an antioxidant and 0.01 mM Hydroquinone, or HQ, was added to inhibit polymerization due to oxygen permeation through membranes (Yeo *et al.*, 2012). The dose response mode of DEFGEL is radiation induced polymerization of the monomers, which causes the dosimeter to increase in optical density (OD) at a level proportional to the dose absorbed by gel.

An example of the cylindrical mold used for the dosimeter is shown in Figure 1. The outer wall of the mold is a 3 mm thick acrylic ring to ensure the dosimeter is robust enough for clinical use. The dosimeter developed for this project was approximately 45 mm in diameter and 10 mm thick, although this thickness could be decreased to 5 mm for clinical use. The gel was covered with a 15 μ m Saran™ window to ensure that it is properly sealed while allowing for some deformability and proper optical transmission. A small hole was drilled in the outer wall of dosimeter and a syringe was attached to this hole to act as a funnel during injection and allow for additional gel to be added, accounting for any contraction of the liquid during cooling. This syringe was then removed after cooling and the hole was patched with tape.

2.2 Dosimeter readout

An in-house laser densitometer was used as a readout system (Rosen *et al.*, 2015). This laser densitometer operates by scanning a tray insert along a 2D plane using a 635 nm laser paired with a photodiode. This densitometer is designed for very high precision measurements,

with a maximum spatial resolution of 25 μm , greatly decreasing dosimeter uncertainty due to readout alone. The laser densitometer measures the amount of voltage gathered by the photodiode due to optical transmission through the target.

To properly quantify the change in OD of the dosimeter due to radiation induced polymerization, referred to as the netOD, the dosimeter was scanned before and after irradiation. Each scan resulted in a 2D map related to the voltage readout of each point within the dosimeter. These voltage maps were evaluated by finding the averages and standard deviations in a small, central region of interest within the dosimeter. To calibrate the densitometer and account for any changes in the system over time, all scans were done with a set of NIST traceable OD filters in place along with an open air space, allowing for a voltage to OD calibration to be created for every scan. This is done by plotting the relationship between the absolute OD of each filter and its readout voltage, enabling a linear fit to be made of these data relating voltage to OD. After the netOD was calculated for each dosimeter, the netOD of a control dosimeter from the same batch of dosimeters was subtracted from the result to account for any polymerization induced by the background. The uncertainty of each netOD measurement was calculated through the propagation of the standard deviations of the pre-irradiation OD, post- irradiation OD, and the uncertainty of the netOD of the control (Rosen *et al.*, 2015). Each of these uncertainties arose from the propagation of the standard deviations of the voltage readouts from the densitometer and the standard deviation arising from the calibration of voltage readout to OD for the densitometer.

2.3 Irradiation Setup

To properly create dose response curves and time response curves for the patch dosimeter, a repeatable irradiation setup was used to ensure consistent irradiation conditions, shown in Figure 2. All irradiations were performed using a Varian Clinac 21EX at the UWMRRC with a 6 MV beam and 600 MU/min dose rate. The Clinac 21EX was calibrated using TG-51. Dosimeters were set up with 10 cm of Virtual Water™ (Med Cal, Inc., Verona, WI) placed directly behind the dosimeter and at a depth of 5 cm of Virtual Water™ to the front face of the dosimeter. The dosimeter was surrounded laterally with Virtual Water™ of identical thickness. The SSD of the setup was 100 cm. Dosimeter doses were calculated to the center of the dosimeters, the 5.5 cm depth, using percent dose depth curves created for the linac during commissioning. The gantry and collimator were set to 0° for all irradiations. The field size was 10 cm $\times$ 10 cm to avoid the use of scatter factors.

2.4 Dose response and repeatability

The first investigation done was to quantify the netOD as a function of dose. To evaluate this relationship, dosimeters were irradiated to a range of doses using the setup described above, ranging from 30 cGy to 2000 cGy. The dosimeters were then read out 9 days after irradiation to ensure that the dosimeters had fully developed. This procedure was repeated for three separately made batches of DEFGEL to evaluate the batch-to-batch variability.

2.5 Time response

The second investigation was to evaluate how quickly the OD of the dosimeter stabilized at its full response after irradiation. Three dosimeters were irradiated to 2 Gy, 8 Gy, and 20 Gy using the setup shown in Figure 2 to evaluate the development time at a wide range of doses. Scanning of the dosimeters began within five minutes after the end of the irradiation and scan times were minimized to approximately 13 minutes to decrease time averaging.

2.6 In vivo proof-of-concept

As a proof of principle for the *in vivo* capabilities of the patch dosimeter, a 10-beam SBRT non-small cell lung cancer (NSCLC) treatment plan was made for a LUNGMAN (Kyoto Kagaku, Kyoto, Japan) phantom using Varian Eclipse™, as shown in Figure 3, and the predicted absorbed dose was compared to the readout absorbed dose of the patch. The treatment plan was made using a CT scan of the phantom with a patch placed on the lateral anterior surface of the phantom. The dose limits of the SBRT lung study RTOG 0915 (Videtic *et al.*, 2015) were followed for the skin, lung, spine, and ribs. A Virtual Water™ sphere was placed in the lung of the phantom to represent a PTV. The dose to the patch was predicted using a ROI in the central region of the patch and encompassing the entire depth of the dosimeter in the TPS. The measured dose to the patch was calculated using the raw OD readings and the associated dose response curve of the first batch of DEFGEL. The treatment plan was performed using a verified model of a Varian Clinac 21EX using 6MV photons.

3. Results

3.1 Dose response and repeatability

The dose response of the patch dosimeter is shown in Figure 4. Within the range of 2 Gy to 20 Gy the dosimeter is shown to be reliably linear and reasonably precise. The R^2 values of the linear fits of the responses for batches 1–3 were 0.994, 0.993, and 0.997, respectively. Below the range of 0.5 Gy, statistical uncertainties due to inhomogeneities in the gel make measurements not practically useful. In the range of 2 Gy to 10 Gy, the measured netOD values were reproducible batch-to-batch within the $k=2$ uncertainty of each netOD measurement ($k=1$ uncertainty of netOD within each ROI ranging from 0.0119 cm^{-1} to 0.0193 cm^{-1}), demonstrating reasonable repeatability. Specifically, at 10 Gy the repeatability of the measurements was found to be 3.8% when repeatability is defined using the method of Descamps *et al.* (Descamps *et al.*, 2008):

$$\text{Repeatability} = \frac{\sigma_{OD}}{\text{mean}_{OD}} * 100\% \quad (1)$$

3.2 Time response

The results of the time response test are shown in Figure 5. The dosimeter irradiated to 2 Gy stabilized at its full response within an hour. The dosimeters irradiated to higher doses of 8 and 20 Gy took a longer time to reach their full OD response. After approximately four hours these dosimeters consistently were within a standard deviation of each previous and

subsequent reading. Note that the time uncertainties in these measurements are due to the scan time of approximately 13 minutes, which may possibly average dosimeter response over time.

3.3. In vivo proof-of-concept

During the *in vivo* test of the dosimeter, the TPS predicted that the ROI representing the patch dosimeter would receive 4.23 ± 0.3 Gy absorbed dose. The measured dose based on OD data from the dosimeter was 4.37 ± 0.3 Gy. The measured dose was 3.2% higher than predicted, indicating good agreement between the measured patch absorbed dose and the dose predicted by the TPS.

4. Discussion

A DEFGEL patch *in vivo* dosimeter has been developed for the potential use in radiation therapy. Initial measurements revealed that the patch dosimeter was able to avoid response saturation up to 20 Gy, agreeing with the results of Yeo et al., while remaining relatively repeatable up to at least 10 Gy. It was also shown that at doses of 2 Gy the dosimeter had reached a stable OD after an hour, while at doses of 8 Gy or 20 Gy the development process takes four hours. This shows the potential for the dosimeters to be read out at the end of each day of treatments in a clinical setting. Additionally, the patch dosimeter readout doses showed promise in the *in vivo* test as a potential way to evaluate agreement between the TPS and the treatment performed. A treatment consisting of 10 beams was delivered in order to better investigate the angular sensitivity of the dosimeter. The slight disagreement between the TPS and the dosimeter is likely due to the non-uniform dose distribution created through the finite thickness of the dosimeter being integrated along during the 2D readout by the densitometer. While the addition of the bolus decreased the dose gradient within the dosimeter, it did not fully eliminate it. Fortunately, this issue could be improved by using a thinner dosimeter mold.

A variety of other dosimeters have been utilized clinically for *in vivo* dosimetry. The thermoluminescent dosimeter (TLD) is often used as an *in vivo* dosimeter. The most common type of TL material used in radiation therapy is lithium fluoride doped with traces of magnesium and titanium (LiF:Mg,Ti). However, it is well known that this type of TLD exhibits supralinearity at doses above approximately 1 Gy. Other types of TL material, such as lithium fluoride doped with about 2% of phosphorous and traces of magnesium and copper (LiF:Mg,Cu,P) have shown improved linearity up to higher doses (~10 Gy) (IAEA, 2013). Another commonly used *in vivo* dosimeter is the semiconductor diode. Diodes exhibit high radiation sensitivity and offer real time readout. However, diodes exhibit strong angular dependence, particularly if the beam is incident on the detector at an angle greater than 30°. Similar angular dependencies are experienced with MOSFET dosimeters (Cygler et al., 2006). Radiochromic film is another potential *in vivo* dosimeter. Radiochromic film has only weak energy dependence and has high spatial resolution. But similar to TLD's, radiochromic film becomes less sensitive at higher doses (~7 Gy) due to the well-known lateral response artifact, which is a polarization effect during readout that is dependent on dose and distance from the center of the film (Menegotti et al., 2008; Saur and Frengen,

2008). Very recently, a new type of radiochromic film was developed to help correct for this effect (Grams *et al.*, 2015). However, film is still known to over respond when irradiated with parallel beams (Suchowerska *et al.*, 2001)

Given the linearity, potential of angular insensitivity, and energy independence (De Deene *et al.*, 2006) of this patch dosimeter, there are many opportunities for its clinical utilization as an *in vivo* dosimeter. As the use of hypofractionated treatment plans continues to increase in the clinic, this patch dosimeter can give reliable surface dose information during the many beam, high dose fractions characteristic of SBRT. Another potential treatment that the dosimeter could be utilized in is MR-guided radiotherapy. Due to the gel's inherent lack of response to MRI, it could be utilized to estimate patient entrance and exit doses. This is not the case with diode detectors, which have shown to have responses heavily dependent on magnetic field strength and orientation (Reynolds *et al.*, 2014). Additionally, its potential for angular insensitivity would allow for an accurate dose response in the presence of multiple simultaneous beams from a variety of angles. An additional useful feature is that, due to the saran windows of the dosimeter, a moderate amount of deformability allows for users to properly couple the dosimeter to the patient's skin to eliminate any air gaps.

5. Conclusion

Based on findings presented in this work, the gel patch dosimeter demonstrates great potential as *in vivo* dosimeter due to its potential to measure higher doses with minimal angular sensitivity. Furthermore, the gel should exhibit no dose rate dependence and is nearly water equivalent. The dosimeter's pairing with a laser densitometer allows for an in-house readout system that is high-throughput, cheap, and easy to use.

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Figure 1.
An example of the cylindrical dosimeter. This dosimeter is 45 mm in diameter and 10 mm thick, featuring an acrylic ring and an injection hole to be covered after injection.

(a.)

(b.)

(c.)

Figure 2. Setup used to irradiate the patch dosimeters. Each patch was surrounded entirely by Virtual Water™ as shown in (a), positioned at a depth of 5 cm under a solid slab of Virtual Water™ as shown in (b). A side view cross section schematic is shown in (c).

Figure 3.

a) A photograph of the LUNGMAN phantom treatment setup with the patch dosimeter in place on the anterior surface of the left lung and b) The isodoses colorwash overlaid on the CT scan image calculated for a 10-beam SBRT treatment plan created in Varian Eclipse™.

Figure 4.

The dose response of three separately fabricated batches of dosimeters. The R^2 values for batches 1–3 were 0.994, 0.993, and 0.997, respectively. Error bars represent an estimate of the combined $k=1$ uncertainty of each measurement.

Figure 5.

The change in dosimeter OD with respect to time since irradiation. The 2 Gy dosimeter response reached a stable OD within an hour whereas the 8 Gy and 20 Gy dosimeters reached their stable optical densities within four hours.