Optimization for stability of the deformable FlexyDos3D radiation dosimeter and curing effects

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Abstract. Previous formulations of the FlexyDos3D dosimeter have shown significant changes in the dose-response over time. In this study, various formulations of the dosimeter were created and tested to see if this stability could be improved. A dosimeter that was stable over a three-day period was found. Rapid manufacture of this dosimeter for patient-specific validation of radiotherapy treatments is desirable. The use of 3D printing manufacturing techniques for thermosetting polymers require high temperatures to cure the polymer within a reasonable time. The effect of different curing temperatures and times were investigated for the FlexyDos3D radiation dosimeter for its effect on stability. No significant difference in the dose-response was found for dosimeters cured for different curing times beyond an hour. A significant dose-response offset was found between dosimeters cured at different temperatures, but the dose-response sensitivity was the same.

1. Introduction
Different 3D dosimeters currently exist, from Fricke gels, to polymer gels, and radiochromic dosimeters [1-3]. Whilst many of these dosimeters have been shown to provide accurate determination of the 3D dose-distribution within the dosimeter, the hardware requirements and difficulty to manufacture and image the dose-distribution of these dosimeters is a potential barrier to their wider implementation in clinical settings.

The FlexyDos3D dosimeter can be manufactured at standard atmospheric pressure and temperature, allowing it to be produced in any standard laboratory setting. Manufacturing the dosimeter at room temperature requires two days to cure and so is currently infeasible for rapid production. Heating the dosimeter at 65 °C has previously been shown to allow it to be cured in two hours [4]. However, these temperatures still only allow for castings of the dosimeter to be produced. Higher temperatures are required for 3D printing of the dosimeters, which would allow for complex structures to be created, such as the lungs and heart. The effect of higher temperatures on the dosimeter had not previously been tested.
Previous formulations of the FlexyDos3D dosimeter had poor stability characteristics, with the dose-response of the dosimeter changing significantly over a period of three days. In this study, the effect of different concentrations of the silicone curing agent and base mixture on the stability of the dosimeter were tested. Once a stable formulation was found, the effect of different curing temperatures and times were tested for their effects on the stability of the dosimeter.

2. Methods and materials

2.1. Dosimeter fabrication

The FlexyDos3D dosimeter consists of an optically-transparent silicone elastomer (Sylgard® 184, Merck), chloroform, and a leucodye, leucomalachite green (LMG). The silicone elastomer initially consists of a separate base and curing agent (CA), which cures when mixed together. The silicone elastomer serves as a matrix for the chloroform and LMG, and gives the dosimeter deformable properties. The chloroform aids in dissolving LMG in the elastomer and provides radiation-induced radicals that initiate the reaction with LMG. The LMG changes colour from crystal clear to green upon reaction with the initiator radicals, forming malachite green (MG). The amount of MG formed from the LMG is related to the cumulative radiation dose which causes an absorbance change that can then be read out optically.

2.2. Irradiation

In fundamental studies, samples were irradiated with UVC light. For the final dosimetry tests, samples were irradiated with high-energy X-rays on a linear accelerator (linac).

2.2.1. UVC irradiation. The dosimeter had been previously found to be sensitive to UVC light [5]. This allowed for testing of the dosimeter in the lab using a UV light source for irradiation. The cuvette samples were irradiated with a 9 W UVC germicidal lamp (TUV PL-S 9 W, Philips). The light intensity at 100 mm from the end of the lamp was measured with a UVC light reader (UVC-254, Lutron Electronic Enterprise Co., LTD) to be 5.22 W / m². From the manufacturer’s specifications, the wavelength of the UV light source was predominantly 255 nm.

The cuvettes were placed 100 mm away from the UV lamp which was suspended in a polystyrene box. The box’s internal surface was covered with aluminium foil to homogenize the UV flux. The cuvettes were enclosed on all sides but the one facing the UV lamp.

2.2.2. Linac irradiation. The cuvettes were irradiated with high-energy photon beams using a clinical Varian 21EX linac (Varian Medical Systems, Palo Alto, USA) with a beam quality of 6 MeV. All samples were irradiated together within a 10 cm × 10 cm field size at an SSD of 100 cm and were irradiated with doses varying from 0 Gy to 10 Gy in steps of 2.5 Gy and from 10 Gy to 40 Gy in steps of 5 Gy. All the cuvettes were placed in a solid water phantom with an SSD of 100 cm and the centre of the cuvettes positioned at 1.4 cm depth (Dmax).

2.3. Dosimeter stability study

Table 1 provides an overview of the composition of the different samples that were used in the stability study. Equal concentrations of chloroform and LMG were used for all samples whilst the curing agent of the Sylgard® 184 was varied from 1 % to 15 % [w/w] of the overall mass of the mixture. The amount of Sylgard base was adjusted so that the total amount of elastomer was kept the same at 97 % [w/w].

The mixtures were thoroughly stirred before being poured into PMMA cuvettes. The cuvette samples were then placed in a vacuum desiccator and a cycle of vacuum pumping and releasing to atmospheric pressure was used until all visible air bubbles were removed from the samples. The cuvette samples were cured at 60 °C for 1 hour and then allowed to cool at room temperature for an hour.

The cuvettes were exposed to UV light for different exposure times ranging from 0 s to 160 s. Spectroscopic measurements were taken after each UV exposure and then every 24 hours for the next
three days. The samples were kept in the dark and at room temperature when not being irradiated or measured.

Table 1. Concentrations of Sylgard base and curing agent for the stability study. The optimal composition of FlexyDos3D dosimeter is indicated in bold font and is used in the following experiments.

| Sample Name | Sylgard Curing Agent [% w/w] | Sylgard Base [% w/w] | CHCl3 [% w/w] | LMG [% w/w] |
|-------------|------------------------------|---------------------|--------------|------------|
| FlexyDos3D 1 % CA | 1 | 96 | 3 | 0.03 |
| FlexyDos3D 2 % CA | 2 | 95 | 3 | 0.03 |
| FlexyDos3D 3 % CA | 3 | 94 | 3 | 0.03 |
| **FlexyDos3D 4 % CA** | **4** | **93** | 3 | **0.03** |
| FlexyDos3D 4.5 % CA | 4.5 | 92.5 | 3 | 0.03 |
| FlexyDos3D 5 % CA | 5 | 92 | 3 | 0.03 |
| FlexyDos3D 7.5 % CA | 7.5 | 89.5 | 3 | 0.03 |
| FlexyDos3D 10 % CA | 10 | 87 | 3 | 0.03 |
| FlexyDos3D 12.5 % CA | 12.5 | 84.5 | 3 | 0.03 |
| FlexyDos3D 15 % CA | 15 | 82 | 3 | 0.03 |

2.4. Dosimeter curing temperature and time dependence study

Two samples of the stable composition dosimeter were fabricated and poured into quartz cuvettes, with one sample cured for 60 minutes at 120 °C and the other for 60 minutes at 60 °C. Quartz cuvettes were used as quartz glass has a low absorbance of UV light, allowing UV light to penetrate the cuvette and irradiate the dosimeter, and quartz can withstand higher temperatures than PMMA. After cooling for an hour, the cuvettes were exposed to the UVC light for increasing exposure times and absorbance spectra were acquired with the spectrophotometer (Ocean Optics, USB4000).

A broader range of curing times was investigated on 8 glass cuvette samples that were filled with the optimal composition of FlexyDos3D 4 % CA and that were irradiated with high-energy X-rays on a linac. The samples were all cured at different temperatures and times: two curing temperatures of 60 °C and 120 °C were used, and curing times of 30 minutes, 60 minutes, 120 minutes, and 180 minutes were used for each temperature.

All cuvettes were cooled for 2 hours before irradiation using the linac and spectral scans were performed between each irradiation.

2.5. Optical spectroscopy and absorbance measurements

LMG is transparent but when irradiated it converts to MG which shows an increase in absorbance at red wavelengths of light. The wavelengths measured for absorbance were 630 nm and 480 nm, with 630 nm undergoing a maximal change in absorbance when LMG is converted to MG, whilst at 480 nm the absorbance is the same for both LMG and MG. The total dose delivered to the dosimeter could then be calibrated against the difference in these two wavelengths:

$$\Delta OD = OD_{630nm} - OD_{480nm}$$

Optical spectra were acquired with a high-resolution spectrophotometer (USB4000, Ocean Optics) equipped with a cuvette holder. All optical absorbance measurements were calibrated against a cuvette filled with de-ionised water.

3. Results

3.1. Dosimeter stability

The dose response of 10 % and 4 % curing agent FlexyDos3D samples are shown in figure 1a and 1b, respectively. From figure 1a, the dose sensitivity decreases significantly after the initial irradiation of the dosimeter. However, figure 1b shows negligible change in the sensitivity of the dose response to
radiation. Only a small offset in the absorbance between the first measurement and the measurements on the following days can be seen in figure 1b which may be attributed to an incomplete curing of the sample as from day 1 onward no further measurable change is observed. Another sample with the same 4% curing agent composition was made and was cured for 2 hours at 60 °C and is shown in figure 1c. It is shown that the offset has significantly decreased, likely the result of further curing within the sample.

Figure 1d shows that the change in sensitivities of the dosimeter do not change significantly after three days for curing agent concentrations less than 4.5%. Greater changes in sensitivity are seen with increasing curing agent concentrations.

![Figure 1](image)

**Figure 1.** Stability of the dose response for (a) FlexyDos3D 10% mixture and (b) FlexyDos3D 4% mixture cured for 1 hour at 60 °C, and (c) FlexyDos3D 4% mixture cured for 2 hours at 60 °C. Note that (c) was investigated for a longer exposure time and with more sample points. (d) Sensitivity of dosimeters with different curing agent concentrations after 3 days relative to the first measurement.

### 3.2. Curing temperature dependence for dose-response

The effect of curing temperatures and curing times upon the FlexyDos3D dose-response is shown in figure 2a and 2b and for UV exposure and high energy X-ray radiation, respectively. A linear dose-response is observed for the X-ray radiation, whilst a non-linear response is observed in the UV irradiated samples. This is attributed to a greater attenuation of the UV light in the dosimeter as compared to the X-rays and a likely saturation of the LMG reactions in the layers closest to the UV source.
Figure 2. Optical density difference between 630 nm and 480 nm versus UV exposure time for two FlexyDos3D 4% C samples cured at different temperatures for 60 minutes (a). Optical density difference between 630 nm and 480 nm versus radiation dose for different curing temperatures and times (b). The use of the difference in optical densities at the two wavelengths can compensate for some of the artefacts in the cuvettes caused by the contraction of the dosimeter after cooling.

The difference in the unirradiated absorbance is significant between the 120 °C and 60 °C cases. However, the curing time appears to have little effect on the dose-response of the 120 °C samples. In figure 2b, all the 120 °C samples have a similar dose-response. For the 60 °C samples, the dose-response does show a decrease in sensitivity with increasing curing times. The sensitivity of the 60 °C samples approach the same rate of change in absorbance as the 120 °C samples as the curing time is increased whilst still maintaining a large optical density offset.

These results demonstrate that incomplete curing of the dosimeters during irradiation is likely the cause of some dose-response effects and that the curing temperature does affect the initial absorbance of the dosimeter. However, the dose-response is unaffected by curing times once the dosimeter has cured for a sufficiently long time, which is more than 30 minutes at 120 °C. The incomplete curing effects have also been shown in [4] for 65 °C temperatures with curing times between 30 minutes and 5 hours, agreeing with our results.

4. Discussion
The FlexyDos3D dosimeter displayed a stable dose-response for compositions with curing agent concentrations between 3 % and 4.5 % over a period of 3 days after manufacture. Curing agent concentrations at 1 % and 2 % resulted in silicone matrices that were not fully cured which would be unsuitable as a solid 3D dosimeter. For concentrations above 4.5 % the dosimeter became unstable with increasing instability for increasing concentrations of the curing agent. Previously it was suggested that the elastic modulus of the dosimeter would be able to be tuned to the organ of interest, by varying the ratio of the curing agent and base concentrations of the silicone mixture to simulate different tissues within the body. It was believed that this would have a negligible effect upon the dosimetric properties [4, 6]. However, the current results show that silicone matrix concentrations affect the stability of the dosimeter and so tuning of the elastic properties of the dosimeter may be restricted to the range in which the dosimeter displays a stable response.

Building upon the results of [4], further investigation of the curing temperature found that higher temperatures had a significant effect on the zero-dose absorbance of the dosimeter but the dose sensitivity was found to be independent of curing temperature. It was found that the curing time had no
effect on the dose-response for dosimeters for curing times larger than an hour at 120 °C. This demonstrates that additive manufacturing techniques, such as 3D printing, could be potentially used to manufacture FlexyDos3D dosimeters. The current study was targeted towards the effect of possible heterogeneities in temperature history during 3D printing which could lead to inconsistencies in the dose response. Our studies have shown that these factors are not significant for the curing times and temperatures investigated.

5. Conclusion
A stable composition of a deformable 3D dosimeter, FlexyDos3D, was found that consisted of 0.03 % LMG, 3 % chloroform, and Sylgard® 184 with 4 % curing agent and 93 % base. Investigations into the effect of higher curing temperatures upon the dosimetric properties of this stable dosimeter composition revealed that by increasing the curing temperature, the curing time could be significantly reduced without significantly distorting the dose-response sensitivity.

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7. References
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