Influence of gelling agents on the dosimetric performance of the Turnbull Blue gel dosimeter

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Abstract. Gelling agents such as agarose, phytagel, and several types of gelatin were used for preparation of Turnbull Blue radiochromic gel dosimeter. Their influence on gel dose response and background value was assessed. It was found that all gelatins cause significant increase of background in a short period of time after gel preparation therefore gelatin is not a suitable gelling agent for this dosimeter. Phytagel and agarose gels exhibit low and stable background and higher dose sensitivity than gelatin gels; however, the disadvantage is increased scattered light intensity in the gel in comparison to gelatin gels. A simple measurement was done demonstrating that the scattered light intensity significantly increases in phytagel and agarose gel in comparison to gelatin gels.

1. Introduction
The main advantages of radiochromic gel dosimeters in comparison to polymer gels are easy preparation procedure and the possibility to evaluate gel response using optical methods, particularly optical cone beam computed tomography (optical CBCT; [1,2]). Although new types of radiochromic gels were recently presented [3,4], the only one widely used for 2D and 3D dose distribution measurement is a Fricke-infused gel with xylenol orange Fe3+ ion indicator (the FXG dosimeter; [5]). Some researchers also use the radiochromic solid polymer dosimeter PRESAGE™ [6]. Recently, our group presented a new radiochromic gel based on radiation-induced creation of blue dye Turnbull Blue (the TBG dosimeter or the TB gel; [7]). Its main advantage - besides easy preparation - is the suppressed diffusion of dose patterns recorded in the irradiated gel. However, the gel exhibits lower dose sensitivity and higher background level in comparison to the FXG dosimeter. In this study we prepared this gel with different gelling agents in order to find a better gelling agent, resulting in higher gel sensitivity and lower background level. The final goal is a transparent solid gel with low and stable background, whose response could be easily evaluated using the optical CBCT.

2. Materials and Methods
2.1. Original gelling agents for the TBG dosimeter
The most suitable gelling agent was assumed to be gelatin because it is easy to prepare and forms a clear, colorless solid gel. However, former experiments with gelatin (gelatin form porcine skin,
type A; Sigma, G2500) revealed [8] that the TB gel with gelatin exhibits a very high background. The reason was unclear, but it was suspected it could be caused by some additives in gelatin. That is why several types of gelatin were bought to use for preparation of the TB gel.

The other already tested gelling agent was phytagel. It creates nearly as clear and colorless gel as gelatin, however it was observed that phytagel was forming lumps during addition of chemicals required for the TB gel [8].

2.2. Examined gelling agents

Eight gelling agents were chosen to study their influence on sensitivity and background level of the TBG dosimeter: gelatin from porcine skin, type A, for electrophoresis, 300 bloom (Sigma, G8150) - abbreviated as GP-1; gelatin from porcine skin, high gel strength (Fluka, 48724) - GP-2; gelatin from porcine skin (Fluka, 04055) - GP-3; gelatin from bovine skin, type B (Sigma, G9391) - GB; gelatin from cold water fish skin (Sigma, G7041) - GF; edible food gelatin (natura, Czech Republic) - GE; phytagel, plant cell culture (Sigma, P8169) - PHY; and agarose, low EEO, for routine use (Sigma, A5093) - AGA.

2.3. Gel preparation

Gel composition was as follows: 4 % w/w gelatin (or 0.25 % w/w phytagel or agarose), 1 mM potassium ferricyanide if gelatin gels or 0.5 mM if phytagel or agarose gels, 1 mM ferric chloride, and 1 mM sulphuric acid. Gelling agents were dissolved in deionized water (10 % w/w gelatin solution, 0.6 % w/w agarose or phytagel solution) placed into a water bath (60°C if gelatin, 90°C otherwise). Ferric chloride was dissolved in diluted sulphuric acid (approximately 2/5 of the total gel volume). Before gel mixing, this solution was warmed to ~35°C, while the gelling agent was cooled down to ~35°C as well. Diluted potassium ferricyanide was then added to the gelling agent, followed by ferric chloride. Well mixed gel was filled in PMMA 1.0×1.0×4.5 cm³ spectrophotometric cuvettes (1.0 cm optical path) and refrigerated.

2.4. Irradiation and evaluation of gel response

Gel samples were irradiated by Co-60 photons (mean energy 1.25 MeV) to several dose values reaching up to 80 Gy. Two cuvettes per every batch were taken aside as background samples.

Evaluation of gel response was performed using an optical method. Gel samples were illuminated with red diodes light (emission maximum at the wavelength of 640 nm) and the intensity of light passed through the gel in terms of gray scale image intensity was captured by a pixelated CCD camera. Linearity of the CCD camera response and other details were described elsewhere [9]. So-called CCD absorbance is then calculated for each gel sample as ln(A/B), where A and B are median gray scale pixel values of the background cuvette and the gel sample, respectively. This quantity is linearly dependent on the gel optical density.

A calibration curve was determined between the CCD absorbance measured at the given optical conditions and spectrophotometric absorbance measured at 690 nm (maximum of Turnbull Blue absorption peak) in order to obtain and state the results in familiar quantity - the spectrophotometric absorbance. The calibration curve has the equation $A_{\text{sp}} = (0.487 \pm 0.004) \times A_{\text{CCD}}$ where $A_{\text{sp}}$ is the spectrophotometric absorbance per 1 cm optical path and $A_{\text{CCD}}$ is the CCD absorbance.

To obtain quantitative information about the intensity of scattered light in different gelling agents, dummy samples in PMMA cuvettes were prepared containing only the gelling agent in concentration used in the gel. Measurement of intensity of scattered light was inspired by [10]. Samples were inserted into a black cuvette holder, and a black color dot (4 mm diameter) glued onto a transparent plastic foil was placed just behind the sample. From the photographs, median gray scale pixel values were calculated at the central part of the dot, $I_{\text{dot}}$, and at open area, $I_0$, of the sample. Values $I_{\text{dot}}/I_0$, subtracted from that for cuvette with water, were calculated to assess the contribution of scattered light by different gelling agents to the total intensity of light passed through the gel.
3. Results and Discussion

3.1. Gelling agents

Basic dosimetric characteristics of the TB gel prepared with different gelling agents are presented in Table 1.

| Gelling agent            | Sensitivity \(^1\) (Gy\(^{-1}\)cm\(^{-1}\)) | Background level \(^2\) (cm\(^{-1}\)) | Scattered light intensity \(^3\) (%) |
|--------------------------|---------------------------------------------|---------------------------------------|-----------------------------------|
| Porcine gelatin, GP-1    | (5.5 ± 0.5) × 10\(^{-3}\) (22 h)            | 0.58 (54 h)                           | 1.6 %                            |
| Porcine gelatin, GP-2    | (5.0 ± 0.5) × 10\(^{-3}\) (22 h)            | 0.48 (54 h)                           | Not measured                      |
| Porcine gelatin, GP-3    | (4.1 ± 0.6) × 10\(^{-3}\) (2 h)             | 0.28 (8 h)                            | Not measured                      |
| Bovine gelatin, GB       | -                                           | 1.25 (54 h)                           | 5.7 %                            |
| Fish gelatin, GF         | -                                           | Did not solidify                      | Not measured                      |
| Edible gelatin, GE       | (3.6 ± 0.6) × 10\(^{-3}\) (22 h)            | 0.23 (24 h)                           | 0.8 %                            |
| Phytagel, PHY            | (7.7 ± 0.2) × 10\(^{-3}\) (22 h)            | 0.12 (66 h); 0.15 (7 days); 0.19 (18 days); 0.22 (45 days) | 3.5 %                            |
| Agarose, AGA             | (9.7 ± 0.5) × 10\(^{-4}\) (22 h)            | 0.12 (8 h); 0.14 (24 h)               | 4.3 %                            |

\(^1\) For detailed specification of gelling agents see paragraph 2.2
\(^2\) Slope of the linear part of the dose response curve at the stated time after gel irradiation (1σ confidence level)
\(^3\) Absorbance of a background sample against gelatin GP-1 at the stated time after gel preparation; stored at 5°C
\(^4\) Intensity of scattered light after 1 cm optical path in the gelling agent

A TBG dosimeter suitable for optical CBCT evaluation should fulfill three requirements: 1) it has to solidify, 2) it should be fully transparent, and 3) it has to exhibit reasonably low background at least for a sufficient period of time, enabling irradiation and evaluation of the gel.

The first requirement was not met by the gel made of gelatin from cold water fish skin. Gels with 4 % and even 30 % of this gelatin did not solidify in a refrigerator. Porcine skin gelatin should be represented by at least 3.5 % of gel weight to sufficiently solidify.

Gel transparency is indicated in the last column of Table 1. Scattered light causes fogging of the gel and adds inaccuracy to the optical CBCT evaluation. Mild fog was observed for agarose and bovine skin gelatin gels, milder for phytagel dosimeter. Bovine skin gelatin exhibited very high background as well, therefore it was not studied further. On the other hand agarose gel possessed very low background, which was stable during a long period of time if stored in a refrigerator. That is why this gelling agent could be recommended preferably for non-optical CBCT evaluation methods. It was found out that, besides the gelling agent itself, the gel fogging is generally caused when potassium ferricyanide is present in an insufficiently acidic gel. The fogging was sometimes also observed in gelatin gels with high potassium ferricyanide and gelatin concentration. Lowering the concentration of potassium ferricyanide from the initial 1.5 mM [7] up to 0.5 mM or adding more sulphuric acid decreases fogging of the phytagel dosimeter and gelatin gels become transparent.

The third requirement of "reasonably low background" was not met for all gelatin gels. Generally, all gels prepared with gelatin exhibit significant increase of background and over 1.5 × lower dose sensitivity than phytagel dosimeter. However, gelatin gels are colored yellow just after mixing, indicating that no reduced Fe\(^{2+}\), which would create Turnbull Blue, is present at that time in the gel. After preparation, the gel darkens slowly and continuously (gel changes color from yellow to green). The reason of this effect is unknown but it is assumed that some reducing radicals or impurities are present in gelatin. To suppress them, one batch of gel made with gelatin GP-3 was prepared with 0.15 % w/w of hydrogen peroxide added into the diluting gelatin. However, the background value of this gel was even higher than without the additive.
3.2. TBG dosimeter with phytagel gelling agent

Gel with phytagel gelling agent proved to be the most perspective variant of the TBG dosimeter, therefore this gel will be used for next studies. In addition to the already published characteristics [7], Figure 1 shows the dose dependence of the phytagel TB gel presented in this paper. The dose response is linear from 0 Gy up to 90 Gy with the sensitivity of \((7.7 \pm 0.3) \text{ Gy}^{-1} \text{cm}^{-1}\) (measured 22 h after irradiation). Post-irradiation behavior is pictured in Figure 2. A gel sample was irradiated to 7.5 Gy in 4.5 min and immediately photographed in 5 s intervals. It can be seen that the stable response is reached approximately 40 min after irradiation.

![Figure 1: Dose response of the TB gel with phytagel gelling agent. Green dots show values beyond the gel linear response.](image1)

![Figure 2: Post-irradiation behavior of the TB gel with phytagel gelling agent.](image2)

4. Conclusions

Presented paper describes dosimetric performance of the Turnbull Blue radiochromic gel dosimeter prepared with different gelling agents. It was found out that every type of gelatin tested causes continuous increase of gel background values of optical density, making the evaluation of 3D dose distributions recorded in gelatin gels of large dimensions very difficult. Agarose gel possesses low background, however it is not fully transparent because it scatters light, which also limits the use of optical cone beam CT for gel response evaluation. The best performance is exhibited by a gel with phytagel gelling agent, although the concentrations of chemicals can only vary by a narrow margin, otherwise phytagel forms lumps. Until the cause of spontaneous reduction of \(\text{Fe}^{3+}\) in gelatin is found and eliminated, phytagel remains the most suitable gelling agent for Turnbull Blue dosimeter.

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