Compatibility of 3D printing materials and printing techniques with PAGAT gel dosimetry

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Abstract

Polymer gel (PG) dosimetry enables three-dimensional (3D) measurement of complex dose distributions. However, PGs are strongly reactive with oxygen and other contaminations, limiting their applicability by the need to use specific container materials. We investigate different 3D printing materials and printing techniques for their compatibility with PG. Suitable 3D printing materials may provide the possibility to perform PG dosimetry in complex-shaped phantoms. 3D printed and PG-filled test vials were irradiated homogenously. The signal response was evaluated with respect to homogeneity and compared to the signal in already validated reference vials. In addition, for the printing material VeroClear™ (StrataSys, Eden Prairie, USA) different methods to remove support material, which was required during the printing process, were investigated. We found that the support material should be used only on the outer side of the container wall with no direct contact to the PG. With the VeroClear™ material a homogenous signal response was achieved with a mean deviation of $(-1.4 \pm 0.6)\%$ relative to the reference vials. In addition, the homogeneous irradiation of an irregularly-shaped gel container designed with the same printing material and technique also lead to a homogenous PG response. Furthermore, a small field irradiation of an additional test-vial showed an accurate representation of steep dose gradients with a deviation of the maximum position of $<1\text{mm}$ relative to the reference vial.

1. Introduction

In patient specific quality assurance (QA) for radiotherapy, it is of high interest to perform three-dimensional (3D) measurements of the dose distribution (Guo et al 2006, Doran 2009, Seco et al 2014, Low 2015). Besides using electronic dosimeter arrays, polymer gel (PG) dosimetry may be used to measure complex 3D dose distributions (De Deene et al 2006, Baldock et al 2010, De Deene and Vandecasteele 2013, Vandecasteele and De Deene 2013). PGs use radiation sensitive chemicals, which polymerize after irradiation as a function of absorbed radiation dose (Baldock et al 2010). This effect can be evaluated with magnetic resonance imaging (MRI) as the polymerization alters the relaxation rate $R_2$ of the transversal magnetization. PG dosimetry exhibits a high spatial resolution enabling measurements in steep dose gradients as they occur e.g. in intensity-modulated radiation therapy (IMRT) (Sandilos et al 2004, Vergote et al 2004). In addition, PG has radiation absorption properties equivalent to soft tissues (Baldock et al 2010, Schreiner 2015). However, PG handling is quite challenging as it is strongly reactive with oxygen and other contaminations (De Deene et al 2006), which limits its use in combination with common phantom materials. Yet, mostly glass and BAREX™, a thermoformable acrylonitrile-methyl acrylate copolymer with low oxygen permeability (Vergote et al 2004), are used as container materials (De Deene and Vandecasteele 2013). However, using these materials, the available container sizes and shapes are limited.

In this study, we investigate 3D printing materials and different printing techniques for their compatibility with PG. Using 3D printing would allow for designing new phantoms and to perform 3D dose measurements in...
arbitrary geometries. This may be of great advantage to test new radiotherapy treatment techniques (Schreiner 2015, Kamomae et al 2017, Oh et al 2017, Yea et al 2017).

2. Materials and methods

2.1. Polymer gel
In this study, the PAGAT-(PolyAcrylamide Gelatin gel fabricated at ATMospheric conditions) PG was used as it can be produced in-house at low costs, under atmospheric conditions and has a small dose rate dependence (De Deene et al 2006). The gel consists of a gelatin matrix (6% w/w Gelatin, 300 bloom, SIGMA Aldrich), enriched with two different monomers (2,5% w/w acrylamide and 2,5% w/w N,N'-methylene-bis-acrylamide) as active components. Due to the high reactivity of the gel with oxygen the gel was flushed with nitrogen for 5 min to reduce the amount of dissolved oxygen in the gel (De Deene et al 2002). Directly afterwards, 5 mM bis[tetrakis(hydroxymethyl)phosphonium] chloride (THPC) was added as an antioxidant to further reduce interactions with oxygen. After production, the PG was filled into small vials made of different materials (see section 2.2). Before filling, the vials were flushed with nitrogen, and were sealed with Parafilm ‘M’ Laboratory film (Bemis, Neenah, USA) afterwards to reduce the influence of penetrating oxygen. Additionally, the vials were enwrapped in aluminum foil to protect the gel from light (Koeva et al 2009), placed in a desiccator, which was flushed with nitrogen for 10 min and stored in a refrigerator at 4°C for 20 – 24 h. 4 h prior to irradiation, the vials were removed from the refrigerator to allow for adaption to room temperature.

2.2. 3D printing material and printing techniques
To test the usability of different 3D printing materials, a first set of test vials (figure 1 (a)) was designed having a similar size and shape as BAREX™ containers (table 1). BAREX™ (VELOX GmbH, Hamburg, Germany) vials were already verified for compatibility with PAGAT dosimetry (Mann et al 2017) and therefore used as reference in this study.

2.2.1. Support material
The PolyJet/MultiJet printing technique requires the use of support material if structures with an overhanging shape shall be printed since the subsequent layer is printed while the previous layer is still liquid. After the printing is completed, this support material has to be removed. For the VeroClear™ material, different removal methods were tested: (i) purely mechanically by means of a water jet or (ii) by applying additionally a 2% sodium hydroxide (NaOH) lye for several hours to degrease the material and to remove material residues (Stratasys 2013), (iii) in addition, a printing method was tested that employs the support material on the outside rather than inside of the vials to avoid contact with the PG. In this case, the vials were printed in two separate parts, which were then glued together using the same printing material and by curing the interface of both parts with UV-light for 30 min. In case of the VisiJet M3 Crystal™ material, removal of the support material required heating to 55°C and residual support material was dissolved in a bath of sunflower oil (3DSystems Product 2012). Afterwards the vials were cleaned with a degreasing agent.
2.2.2. Irregular shapes

As the BAREX™ vials are available only in a single size and shape the purpose of this study was to find a 3D printing material compatible with PG dosimetry that allows designing gel containers in arbitrary geometries. Based on the previous investigations, the most promising technique for 3D printing and support material handling was selected to design irregularly-shaped gel containers (figure 1(b)).

2.3. Irradiation experiments

The gel-filled test vials were irradiated with a clinical 6 MV linear accelerator (Linac) (Artiste, Siemens Healthineers, Erlangen, Germany) using a dose rate of 3 Gy min⁻¹ measured under reference conditions at 5 cm depth and a source-axis-distance of 100 cm. Dose calculation was performed with the Raystation treatment planning system (RaySearch Laboratories, Stockholm, Sweden) and the dose delivery has an accuracy of about 0.5% for the setup of our experiment. For irradiation, the printed test vials were inserted into a water-filled cylinder phantom (Mann et al. 2017). The centre of the test vials was positioned to the isocentre marked by the in-room laser system (LAP GmbH Laser Applikationen, Lüneburg, Germany). After irradiation, the vials were wrapped in Aluminum foil and stored at room temperature. As a reference, all irradiations were repeated with a gel-filled BAREX™ container under identical conditions.

Two different irradiation field geometries were applied:

(a) Homogenous irradiation. Two opposing and equally-weighted beams (90° and 270°) with a field size of 10.0 × 10.0 cm² were used to prescribe a total dose of 4 Gy to the centre of the container leading to a homogeneous dose distribution over the whole volume of the BAREX™ reference vial. The homogenous irradiation was performed for all vials printed with different materials (table 1) and removal techniques of support material (section 2.2.1). The irregularly-shaped container was irradiated under identical conditions.

(b) Small-field irradiation. Based on the results in (a), the most promising printing technique and support material handling was further investigated. For this, three equally-spaced beams (0°, 120° and 240°) with a field size of 1.0 × 1.0 cm² were applied, prescribing a maximum dose of 5 Gy to the centre of the PG within the BAREX™ reference vial. The high dose gradients were located within the PG.

2.4. Evaluation

2.4.1. MR imaging

Approximately 48 h after irradiation, the gel containers were imaged on a 3T Biograph mMR (Siemens Healthineers, Erlangen, Germany). To avoid influences of temperature differences on quantitative R₂ measurements, the containers were scanned within a water-flow phantom allowing for temperature constancy within ±0.1°C (Mann et al. 2017). The phantom was placed inside a 16-channel head/neck coil and scanned using a multi spin-echo sequence with 32 equidistant echoes with echo times TE = 27.5 − 880.0 ms and an

| Material name                  | Material type         | 3D printer          | Manufacturer         | Printing technique       | Additional information                                                                 |
|-------------------------------|-----------------------|---------------------|----------------------|--------------------------|----------------------------------------------------------------------------------------|
| VeroClear™ (Stratasys 2008)   | Photopolymer          | Objet30 Pro™        | Stratasys            | Polylite                  | Printed with and without use of support material (section 2.2.1)                        |
| PLA™                          | Polycratic acid       | Ultimaker 3 Extended™ | Ultimaker            | Fused filament fabrication | —                                                                                       |
| PVB™                          | Resin based on polyvinyl butyral | Ultimaker 3 Extended™ | Ultimaker            | Fused filament fabrication | Treated with ethanol vapor for surface smoothing after printing                        |
| Clear™                        | Photopolymer          | Form 2™             | Formlabs             | Stereolithography         | —                                                                                       |
| High Temp™                    | Photopolymer          | Form 2™             | Formlabs             | Stereolithography         | —                                                                                       |
| VisiJet M3 Crystal™           | Photopolymer          | ProJet 3510 HDplus™ | 3DSystems            | MultiJet                  | Printed externally at 4D Concepts GmbH (Groß-Gerau, Germany) using support material (section 2.2.1) |

Table 1. Applied 3D printing materials and printing techniques.
Echospacing of 27.5 ms. The signal-to-noise ratio (SNR) was optimized to $\text{SNR} \approx 290$ ($\text{SNR} = \frac{R_2}{\sigma}$ with mean $R_2$ value $\overline{R_2}$ in an exemplary region of interest within the BAREX™ reference and the corresponding standard deviation $\sigma$). The scans were performed with a resolution of $1.0 \times 1.0 \times 1.0$ mm$^3$, bandwidth of $\text{BW} = 130$ Hz/pixel and a repetition time $\text{TR} > 4000$ ms to exclude influences of $T_1$-relaxation. For comparison of the different MR images, an additional high-resolution ($0.5 \times 0.5 \times 0.5$ mm$^3$) 3D-image of the gel containers was acquired, which was used for registration purposes. For this, a standard true fast imaging sequence with steady state precession (TrueFISP) (Scheffler and Hennig 2003, Chavhan et al 2008) as implemented by the MRI vendor was applied with the following imaging parameters: $\text{TR} = 5.43$ ms, $\text{TE} = 2.72$ ms, number of averages = 2, and a flip angle of $30^\circ$.

Figure 2. Relative transversal $R_2$ profiles for the homogenous irradiation of the different gel vials and printing techniques (table 1). The VeroClear™ vial (a) was printed in two separate parts and glued together afterwards without using support material on the inner side of the vial. 100% refers to the average $R_2$-signal in the BAREX™ vial.

Figure 3. Relative transversal profiles for the homogenous irradiation of the VeroClear™ material when using different techniques for the support material. The support material was removed (a) mechanically using a water jet, (b) by applying additionally NaOH, (c) by using the support material only on the outer side of the vial. 100% refers to the average $R_2$-signal in the BAREX™ vial.
2.4.2. Post processing

The MR data was processed on a personal computer using an in-house developed Matlab (The Mathworks Inc., Natick, USA)-based PG evaluation tool (Mann et al 2017) to calculate the spin–spin relaxation rate \( R_2 = 1/T_2 \). To compare the \( R_2 \)-profile between the different materials, MR images were co-registered by means of a point-based 3rd order B-Spline interpolation algorithm using three uniquely defined points as indicated by external markers (Beekly Medical, Bristol, USA). This was done with the image processing platform MITK (Nolden et al 2013).

3. Results

3.1. Homogenous irradiation

3.1.1. Printing material

The relative \( R_2 \)-profiles of the homogenous irradiation are displayed for the tested materials using a representative transversal slice (figure 2). The VeroClear material showed a homogenous profile with a mean deviation of \((-1.2 \pm 0.4)\%\) relative to the BAREX™ reference material (\( n = 279 \) voxel). The whole evaluated volume (15 slices) within the PG revealed a mean deviation of \((-1.4 \pm 0.6)\%\) (\( n = 4072 \) voxel). The maximum difference between voxels in the two vials was < 3%. In contrast, the signal for PLA™, PVB™ and VisiJet™ decreased in the regions close to the walls of the vial (figures 2(b), (c) and (f)). In the vials printed with the stereolithographic technique (Clear™ & High Temp™, figures 2(d) and (e)), perforations of the container wall were found in the vial during the filling with PG (see discussion).

3.1.2. Support material

Based on the promising results in section 3.1.1, VeroClear™ was evaluated in more detail. Figure 3 shows a comparison of the transversal profiles for the homogeneously irradiated VeroClear™ material when using different techniques for the removal of the support material. Only the gluing technique without the use of support material on the inner side of the vial showed a good agreement with the BAREX™ reference material, while the other techniques exhibit a lower signal, which decreased further towards the wall of the vials. Based on these results, the VeroClear™ material without the use of support material on the inner side of the vials was investigated in further experiments.

3.1.3. Irregular shape

The homogeneous irradiation of an irregularly-shaped container printed with the VeroClear™ material revealed a homogenous signal response and showed a similar profile as the BAREX™ reference vial (figure 4), whereas the absolute signal was about 3% smaller in the 3D printed container compared to the reference (see discussion).

3.2. Small-field irradiation

Figure 5 shows the transversal and sagittal profiles of the small-field irradiation for the BAREX™ and VeroClear™ material without the use of support material on the inner side of the vial. The profiles are well comparable and the maximum position shows only minor deviations of < 1 mm.
4. Discussion

In this work, it has been shown that the VeroClear™ material in combination with the Objet30 Pro 3D printer (StrataSys) can be used to produce containers, which are compatible with the PAGAT polymer gel. With this material, a homogenous irradiation lead to a uniform signal response with only small deviations (< 3%, figure 2(a)) relative to the BAREX™ reference vials. All other tested materials showed a signal decrease in the vicinity of the container wall and can therefore considered as incompatible with the use of PG. This ‘wall-effect’ may be explained by an oxygen-permeability of the materials, which leads to a partial inactivation of the PG. In case of the stereolithographic printing technique (Clear™ & High Temp™) tiny holes with a diameter of approx. 1 mm were found in the material. These holes may origin from the mechanical removal of support struts required for the printing process.

Using the VeroClear™ material allows printing of arbitrary gel containers. However, this was only possible, if no support material was used on the inner side of the container wall during the printing process as direct contact of the support material with the gel lead to a change of the signal response (figure 3). Most likely, this change is a result of chemical reaction of the PG with either residual support material or with remaining contaminations of the NaOH lye used for the removal of the support material (Baldock et al 2010).

For containers with varying cross section it is necessary to use support material and for PG container production this is still possible as long as the support material is used only on the outer side of the gel containers. This, however, requires printing of the containers in two separate parts, which have to be glued together afterwards (see section 2.2.1). The gluing uses the same printing material and after curing the interface by UV-light, a highly homogenous signal response similar to that of the BAREX™ reference vial was obtained (figure 3). The advantage of 3D printing is the generation of arbitrarily-shaped gel containers as demonstrated by the irregular container (figure 1(b)), for which a homogeneous irradiation still leads to a homogeneous signal response (figure 4).

Compared to the BAREX™ reference vial, the homogenous irradiations of the regularly-shaped test vials revealed a mean signal difference of (−1.4 ± 0.6)% (figures 2(a) and 3(c)). In the irregularly-shaped container a slightly larger difference of 3% was found (figure 4). This larger deviation may result from differences in the volume and shape of the containers, leading to a different temperature equalization and as a consequence to a difference in the chemical polymerization rate (Sedaghat et al 2009). Especially, the temperature during and after irradiation may influence the polymerization rate (De Deene and Vandecasteele 2013). Depending on the gel container size, a small temperature difference may equalize differently leading to a small offset in the gel response. However, for relative dosimetry performed in this work, an offset in $R_2$ is of not critical.

In addition, using the VeroClear™ test vials, steep gradients could be measured with high accuracy (figure 5) and the position of the maximum signal agreed well with that in the BAREX™ reference vial with deviations of < 1 mm.

Having identified a combination of a 3D printing technique and a printing material, which is compatible with PG, it is now feasible to design almost arbitrarily-shaped gel containers. This is a very important feature to perform 3D dose verification in various geometric or anthropomorphic phantoms. These phantoms can be used for QA measurements and end-to-end tests, especially when new treatment techniques are introduced. One important example is MR-guided radiotherapy (MRgRT) (Lagendijk et al 2008, Fallone et al 2009), where it is intended to adapt the treatment plan at each fraction to compensate for changes of the patient anatomy. Validating the adapted treatment plan with PG dosimetry in a clinically relevant setting could be an important application of the proposed method.
5. Conclusion

In this study, the compatibility of 3D printing materials and printing techniques with PAGAT gel dosimetry was investigated. The VeroClear™ material has been identified as a suitable material, when the support material is used only on the outer side of the container during the printing process. For this, the container has to be printed in two parts and glued together afterwards. Relative PG measurements in homogeneous irradiation fields revealed an agreement of the gel response of < 3% when compared to measurements in the BAREX™ reference container, if similarly shaped test vials are used. Using this method, also steep dose gradients can be measured accurately.

Acknowledgments

This project has received funding from the EMPIR programme co-financed by the Participating States and from the European Union’s Horizon 2020 research and innovation programme. Additionally, we would like to thank Professor Dr K Kopka for providing the lab space for the production of the polymer gel.

Conflict of Interest

One of the authors, Dr Mann is shareholder of the company HQ-Imaging.

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