Influence of preparation and calibration method of PAGAT dosimeter on TSE MR readout results

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Abstract. In this study PAGAT dosimeter evaluation by TSE sequence was tested. PAGAT dosimeter preparation procedure was modified to increase the dosimeter sensitivity. Because THPC reacts with gelatin, adding THPC to monomer solution prior to dissolved gelatine helps exploit THPC as an antioxidant. Turbo spin echo sequence enables to evaluate gel dosimeter with 3D equidistant resolution in a reasonable scanning time. Glass walls of the phantom cause problems both by computing inaccuracies and MR imaging artefacts. The inner dosimeter volume is not affected by these inaccuracies and should be used for radiotherapy plan verification.

1. Introduction
Polyacrylamide gel [1] containing tetrakis (hydroxymethyl) phosphonium chloride as an antioxidant [2, 3] is widely used but still should be more studied [4]. We show that only chemicals order modification can increase the dosimeter sensitivity that was evaluated by turbo spin echo magnetic resonance measurement.

2. Materials and methods

2.1. Gel preparation
A bulk of 3000 ml of PAGAT gel was prepared using 5% gelatin (from porcine skin, Type A, Sigma-Aldrich, USA), 3% (w/w) acrylamide (AA) (electrophoresis grade, >99%, Sigma-Aldrich, India), 3% (w/w) N,N'-methylenebisacrylamide (BIS) (4K ultrapure, AppliChem, Darmstadt, Germany), and 4.5 mM tetrakis (hydroxymethyl) phosphonium chloride (THPC) (80% solution in water, Sigma-Aldrich, Switzerland).

To prepare PAGAT dosimeter [5], distilled water was heated to 47°C using water bath with temperature control. Two separated Erlenmeyer flasks were used: 150 g gelatin was allowed to dissolve in 1500 ml and 45 g BIS in 1000 ml of hot distilled water. When gelatin completely dissolved, 45 g BIS was added, and after BIS dissolving 90 g AA and appropriate amount of water was added as well. When all components completely dissolved, the temperature was lowered to 37°C and both solutions were bubbled with nitrogen gas for about 10 min. Subsequently, during rapid stirring of the BIS solution 2.5 ml 80% aqueous solution of THPC was injected, the solution was
transfused into the first flask and bubbled again with nitrogen gas for about 20 min. Four purpose-
made glass flasks (700 ml, 9.5 cm in diameter and 9.5 cm the cylinder part long) were filled with the
gel in a nitrogen environment to avoid oxygen contamination and placed in a refrigerator (8°C) to
solidify over the night. Whole gel dosimeters preparation took about 5 h.

2.2. Irradiation

Gel dosimeters were irradiated 2 days after preparation. Before irradiation, gels were allowed to
equilibrate to a room temperature. Each glass flask was placed in a purpose-built holder and irradiated
by a Varian linac with a Millenium 120 MLC in The London Clinic, United Kingdom.

A highly complex VMAT H&N plan with spine sparing was used. Although not applied clinically,
the dose was delivered in a gated mode with approx. 50% duty cycle. 6 MV photon beam was used
and the dose was proportionally adapted to dynamic dose range of the gel. One flask was irradiated by
four 2x2 cm fields and appropriate depth dose curves were used for gel dosimeter calibration. For
comparison purposes, EBT2 Gafchromic films (ISP, Wayne, NJ, USA) were irradiated by identical
calibration fields. The films were held vertically inside the water filled flask by a narrow slit in the
rubber cap.

2.3. Magnetic resonance imaging

MR readout was performed on a 1.5 T whole body scanner Magnetom Avanto (Siemens, Germany) in
the Institute for Clinical and Experimental Medicine, Prague, Czech Republic. Each glass flask was
placed in a purpose-built holder and scanned using a head coil. 3D Turbo-Spin-Echo (TSE) sequence
with TR = 4000 ms, TF = 90, 1 acquisition and effective echo times TE = 31, 102, 204, 307, 409, 511,
613, 707 was used. Field of view was 150x192 mm and the whole flask was scanned with voxel size
(1x1x1)mm within 1.5 h (11 min per echo).

For comparison purposes, a few slices were also measured with multiple spin-echo (CPMG)
sequence with following parameters: TR = 4000 ms, 32 equidistant echos with TE = 30, 60, 90, ...
960, 1 acquisition, pixel size 1x1 mm, slice thickness 3 mm, FOV = (156x256)mm, 12 min per slice.

2.4. Data processing

The R2 relaxation rate of each pixel was derived by fitting the time course of the pixel value in the
consecutive buse images to a mono-exponential decay using a linear fit of log values. For data
processing Matlab (The MathWorks, Inc., USA) and Microsoft Office Excel (Microsoft Corporation,
USA) were used.

Films were digitized 3 times with an EPSON Perfection V700 Photo scanner (Seiko Epson
Corporation, Japan) in the transmission mode. Results were averaged and the calibration curve was
derived from max values of each film compared with Eclipse AAA plan data.

3. Results and discussion

3.1. PAGAT preparation

We modified preparation method of PAGAT dosimeter. Our experiments showed that over 95%
THPC added in dosimeter was exhausted due to its reaction with gelatin. Therefore, a system of
separated reservoirs and THPC adding first in solely monomer solution prior to dissolved gelatin was
used. Moreover, to reduce oxygen contamination of dosimeter we bubbled both solutions with
nitrogen gas prior and after THPC adding and final glass flasks filling was performed in nitrogen
environment as well.

Dose response study of PAGAT dosimeter prepared in an anoxic environment made by Sedaghat et
al. [4] showed decreasing sensitivity of the gel dosimeter with increasing THPC concentration. We
point out to the fact that only chemicals order modification increases the dosimeter sensitivity again.
For 4.5 mM THPC concentration the slope change was more than 30%. Our preparation method is
only partially anoxic, so THPC acts as the rest of dissolved oxygen cleaning agent. It is presumable
that lower THPC concentration would be sufficient to scavenge all dissolved oxygen in this case. On the other hand, an excess of THPC reduce the post-irradiation polymerization, which leads to flatter profiles next to edges [6] and which is proposed to stabilize crosslink density of the polymer [7].

3.2. TSE vs CPMG sequence
Turbo spin echo sequence as the fast imaging protocol was proposed to offer great promise in polymer gel dosimetry [8], but is still rarely used [9, 10]. We test this protocol because of the time effectiveness as well as the 3D approach. A sample slice of the glass flask scanned in air acquired by CPMG and TSE sequence is shown in Figure 1. Although the TSE data near the glass interface are affected by ring artifact, the middle part response is stable and comparable to the CPMG data.

![Figure 1](image1.png)

**Figure 1**: Comparison of the same slice of the PAGAT gel acquired by CPMG and TSE sequence.

![Figure 2](image2.png)

**Figure 2**: Depth dose curves in glass flask calculated by Eclipse AAA (—) and measured by EBT2 Gafchromic film (---) and PAGAT gel dosimeter (…..)

![Figure 3](image3.png)

**Figure 3**: Isodose comparison of VMAT H&N plan, Eclipse AAA (---) and PAGAT gel dosimeter measured by TSE sequence (—)
3.3. Gel calibration and plan verification
To eliminate volume effects, PAGAT gel dosimeter calibration was performed by depth dose curve measurement of four fields irradiated in one flask. Although it is not recommended [7], the use of maximum dose data for calibration was more accurate comparing film measurements (Figure 2) than calibration curve created by plan and gel data from the depth behind maximum [8]. In our case, the area before dose maximum does not correspond with planned data. It is probably due to incorrect interpretation of the glass walls by the planning system.

The same glass flask with PAGAT gel dosimeter was irradiated by complex VMAT H&N plan with spine sparing. Resulting comparison of one slice is depicted in Figure 3.

4. Conclusion
Regarding PAGAT dosimeter properties we would like to point out to possible preparation procedure modification which slightly increases the dosimeter sensitivity. Because THPC reacts with gelatine, adding THPC to monomer solution prior to dissolved gelatin helps exploit THPC as an antioxidant.

Turbo spin echo sequence enables to evaluate gel dosimeter with 3D equidistant resolution in a reasonable scanning time. Using glass flask for TSE gel measurements does not allow to compare data near the glass walls with plan because of: 1) wrong plan computing next to the glass wall and 2) the TSE ring artefact. The inner dosimeter volume is not affected by these inaccuracies and should be used for radiotherapy plan verification.

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