Utilization of nPAG dosimeter for synchrotron radiotherapy: first results

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1. Introduction

At the medical beamline of the European Synchrotron Radiation Facility (ESRF), the so-called synchrotron stereotactic radiotherapy (SSR) is developed to treat glioma. The technique consists in loading the tumour with elements of high atomic number (chemotherapy drug and/or dose enhancement agent) prior to an irradiation by a monochromatic low energy x-ray (up to 85 keV) beam from a synchrotron source. The tumour is placed at the center of rotation of a tomography system and is irradiated continuously over 360° with a beam restricted to the tumor dimensions. Encouraging pre-clinical results were obtained, opening the way towards clinical trials. The specificity of SSR requires new developments in dose calculation and appropriate experimental procedures. Spatially resolved dosimetry is a critical issue to the preparation of clinical trials. We developed a dose calculation tool based on the MCNPX Monte Carlo code [1]. In parallel with the development of a specific treatment planning system, we need to verify experimentally the calculated doses within anthropomorphic 3D geometries. This is only possible through gel dosimetry. We chose a standard nPAG formulation for its various advantages, recently summarized by De Deene et al [2]. The x-ray computed tomography (CT) readout of gels proposed by Hilts et al [3] is particularly interesting regarding the ESRF biomedical beamline configuration, which allows quantitative synchrotron radiation CT (SRCT) images to be obtained from monochromatic x-ray beam ranging from 30 to 85 keV [4]. All the gel dosimeters were also imaged by magnetic resonance for quantitative analysis. We present here results obtained from three experiments carried out using the same gel formulation.

2. Materials and Methods

2.1. Gel composition.

A common recipe of normoxic polyacrylamide gel (nPAG, 5%w gelatin) was utilized (6%T, 50%C) with 5 mMol/L of THPC as antioxidant. For the initial experiments (experiment n°1 and n°2) gel was poured into glass tubes. For the phantom experiment (experiment n°3), various PMMA vials and tubes were filled. During the latter experiment PMMA boxes were placed into the brain of a head phantom (tissue equivalent for x-rays from 50 keV to 25 MeV).
2.2. Irradiation.
Glass tubes and PMMA tubes were irradiated at various known doses in order to establish dose response curves with MRI and SRCT. The x-ray monochromatic beam was composed of 80 keV photons (experiments n°1 and 3) and 50 and 61 keV for experiment n°2. We performed two calibration procedures (tubes and depth dose) during the phantom experiment. Irradiations of tubes were carried out in tomography mode.

2.3. SRCT read out.
We evaluated the performance of our acquisition system by imaging some of the calibration tubes. Projections from the object were accumulated at 80 keV to optimize photon statistics for experiments n°1 and n°2 (pixel size: 350 µm; slice thickness: 1 mm) and at 49 keV with a 0.5 mm slice thickness, for experiment n°3. For image analysis, the spatial resolution was decreased to 1.05 mm (3 pixels) by linear interpolation of the data.

2.4. MRI readout.
For experiments 1 and 3, proton images were obtained with a 3 T MRI scanner (Bruker BioSpin, Germany) using a standard head coil. Glass tubes from the test experiment n°2 were imaged in a 1.5 T MRI scanner (Philips Medical Systems). In both cases multiple spin echo sequences were used with parameters reported in table 1. The R2 relaxation rate of each pixel was derived by fitting the time course of the pixel value in the consecutive raw images to a mono-exponential.

Table 1. NMR imaging parameters for the various experiments.

|                      | magnetic field [T] | FOV (resolution) [mm] | Slice thickness [mm] | TEfirst and ΔTE [ms] | NE | TR [ms] | NA | NR |
|----------------------|--------------------|-----------------------|----------------------|----------------------|----|---------|----|----|
| tubes exp. 1         | 3                  | 256*300 (1*1.172)     | 3                    | 32                   | 48 | 4500    | 1  | 1  |
| tubes exp. 2         | 1.5                | 140*140 (1.09*1.09)   | 3                    | 20                   | 8  | 5000    | 3  | 1  |
| tubes exp. 3         | 3                  | 128*192 (1*1)         | 4                    | 28                   | 56 | 4500    | 1  | 1  |
| volume exp. 3        | 3                  | 128*192*4 (1*1*2)     | 2                    | 28                   | 56 | 4500    | 1  | 1  |

3. Results
From SRCT, we obtained comparable sensitivity with previously published results for this type of nPAG gels, over a wider linearity range (table 2). No beam hardening artifacts were observed. This was expected as a monochromatic beam was used. However, the pixel to pixel calibration of the high purity germanium detector used is not perfect resulting in artifacts on the reconstructed image and consequently, loss in dose resolution.

From MRI measurements we obtained slightly lower sensitivities to that reported in literature [2] and a wide acceptable range of linearity (1 to 23 Gy). Assuming that the photon energy dependence of the dose response is small, no significant differences in sensitivity or in the R20 values were found whatever the magnetic field. However, according to experiment n°3 the oxygen concentration seems to affect these values. Indeed, a decrease in R2 values is expected with increasing oxygen content [7].

The minimal detectable dose MDD (defined in [5]) achieved in the last experiment is 0.4 Gy for a measurement volume of 48 mm³. The boxes used for the phantom irradiation and the long box used for depth dose measurements have the same characteristics (same material and walls thickness). The gel chemistry is supposed to be similar within all these samples, so we chose this calibration method.
Table 2. Fitting parameters of x-ray CT analysis.

| Date          | Vial Type | Exp n° | Photon Energy | Sensitivity [H.Gy⁻¹] | Dose Range Explored [Gy] | Dose Range of Linear Fit [Gy] | MDD (95%) [Gy] |
|---------------|-----------|--------|---------------|-----------------------|--------------------------|------------------------------|----------------|
| tubes exp. 1  | 80 keV    |        | 0.3331        | (0.0126)              | 0-50                     | 0-26                         | 27.5           |
| tubes exp. 3  | 49 keV    |        | 0.3098        | (0.0070)              | 0-26.6                   | 0-26.6                      | 5.7            |
| Brindha 2004  | 135 KVp   |        | 0.31 (0.03)   |                       | 0-40                     | 0-15                         | -              |

Figure 1. Superimposed dose maps (MC calculation: surfaces and MRI: lines) for a dose to the centre of 10 Gy (values are in Gy).

Table 3. Fitting parameters of NMR analysis for various experiments.

| Vial Type (Photon Energy) (MRI Magnetic Field) | Sensitivity [s⁻¹.Gy⁻¹] | R2₀ [s⁻¹] | Dose Range Explored [Gy] | Dose Range of Linear Fit [Gy] | MDD (95%) [Gy] |
|-----------------------------------------------|-------------------------|-----------|--------------------------|------------------------------|----------------|
| Glass tubes (80 keV) (3T) exp. 1              | 6.955E⁻² (0.386E⁻²)     | 1.144 (0.020) | 0-10                     | 0-10                         | 0.98           |
| Glass tubes (50 keV) (1.5T) exp. 2            | 5.646E⁻² (0.340E⁻²)     | 1.256 (0.040) | 0-18.6                   | 0-18.6                       | 4              |
| Glass tubes (61 keV) (1.5T) exp. 2            | 6.001E⁻² (0.266E⁻²)     | 1.196 (0.022) | 0-18.4                   | 0-18.4                       | 4              |
| PMMA tubes (80 keV) (3T) exp. 3               | 6.208E⁻² (0.069E⁻²)     | 1.134 (0.005) | 0-26.6                   | 0-16                         | 0.3            |
| PMMA box (80 keV) (3T) exp. 3                 | 7.328 E⁻² (0.049E⁻²)    | 1.264 (0.004) | 0-15                     | 0-15                         | 0.4            |

On figure 1, high dose gradients around the target are well conserved, whereas some discrepancies are observed at lower dose, below 2.5 Gy. As the mismatch is close to the walls, oxygen or impurities contamination might have inhibited polymerization. It is noticeable that the dose maps agree well in
term of absolute dose. Furthermore, no overshoot was observed neither by MRI nor SRCT. Additional 3D results will be presented during the communication.

4. Conclusion
Experimental dosimetry with nPAG gel and MRI read out applied to SSR irradiation configuration seems promising in terms of spatial resolution and absolute dosimetry. The technique we used is however perfectible and the inhibition of polymerization observed close to the walls requires investigation. From an experimental point of view, SRCT measurement is convenient for our application since the gel dosimeter can be read with the same set up as the irradiation system and the domain of linearity is particularly wide.

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