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To cite this article: Caroline Boudou et al 2006 J. Phys.: Conf. Ser. 56 145

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Preliminary study of a normoxic polyacrylamide gel doped with iodine

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1. Introduction
At the medical beamline of the European Synchrotron Radiation Facility (ESRF), a new radiotherapy technique called synchrotron stereotactic radiotherapy (SSR) is under development. This 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 first placed at the centre of rotation of a tomography system. It is then irradiated continuously over 360° by a monochromatic beam, fitting the tumour dimensions. Encouraging pre-clinical results were obtained that are opening the way towards clinical trials [1, 2].

However, the particularities of SSR require the design of appropriate dose calculation tools as well as suitable experimental procedures. We thus developed a dose calculation tool (SSRdose) based on the MCNPX Monte Carlo code [3]. During a SSR treatment, it has been demonstrated that iodine should perfuse the tumour for achieving acceptable dose distributions within a human head [4]. The aim of this study was to experimentally assess the dose enhancement due to iodine. We have used a polyacrylamide gel doped with an iodinated contrast agent as a dosimeter.

A standard nPAG formulation was employed in which we added a commercial contrast agent containing iodine (named thereafter nPAGI). Our results showed (1) the conservation of a linear relationship between spin-spin relaxation rates and delivered doses (2), an increase in sensitivity (3) and no overshoot over the explored dose range.

2. Materials and Methods

2.1. Gel composition
A standard receipt of normoxic poly-acrylamide gel (nPAG) was utilized (6%T, 50%C) with 5 mMol/L of THPC as antioxidant. For 8 ml of gel, an appropriate volume of contrast agent (see table 1) was added to obtain 10 mg/ml of iodine in the final solution (after the antioxidant was added to the mother solution). Both contrast agent molecules have the same formula (C₁₇H₂₂I₃N₃O₈) but a different conformation which gives them various properties.
Figure 1. Molecular structure of the two iodinated contrast agents used in this study.

Table 1. Iodinated contrast agent volumes added to nPAG.

| contrast agent (gel denomination) | concentration of iodine in the product | Volume of contrast agent added to 8 ml of nPAG |
|----------------------------------|---------------------------------------|---------------------------------------------|
| Ioméron® (nPAGI1)               | 350 mg/ml                             | 0.229 ml                                    |
| Iopamiron® (nPAGI2)             | 200 mg/ml                             | 0.400 ml                                    |

2.2. Irradiation
Glass tubes were irradiated one day post manufacture at various doses by a monochromatic x-ray beam of 50 keV. Irradiations were carried out at the ESRF medical beamline, in tomography mode according to a procedure described elsewhere [5].

2.3. MRI readout
Tubes were imaged eight days after irradiation in a 1.5 T MRI scanner (Philips Medical Systems). Spin-spin relaxation time of proton was measured. For this feasibility study, a standard multiple spin echo sequence was used (without optimization) with following parameters: knee coil, FOV=140×140 mm² (1.094 mm resolution), slice thickness = 3 mm, echo spacing = 50 ms, first echo time = 50 ms, number of echoes= 8, repetition time= 950 ms and number of accumulations was 3.
3. Results
As displayed on figure 2, R2 values can be linearly linked to the delivered dose from 0 to 18.5 Gy (for there are only 4 points per curve fit statistics is provided, see table 2). The linearity of doped gels up to 9.4 Gy (dose delivered to water) can also be assessed (confirmed by another experiment, data not shown). The iodine compound seems to shorten the spin-spin relaxation time as revealed by the R2 values of non irradiated gels.

The dose modifications produced by the doping atom were estimated by a sensitivity enhancement ratio (SER) \[6\]. This factor, calculated from the experimental gel calibration curves, was defined as the ratio of the slope of doped versus pure nPAG gels: \[\text{SER} = \frac{\text{sens}_{\text{nPAGI}}}{\text{sens}_{\text{nPAG}}}\]. Dose enhancement due to the iodine presence was also determined by Monte Carlo calculations. The increase in sensitivity for the nPAGI1 is close to the calculated value of 2.6. The measured SER is lower for the nPAGI2, which might be due to chemical reactions.

Within the sensitivity of the imaging technique, no overshoot was observed, as shown on figure 3, where a profile across the irradiated zone at 9.4 Gy from nPAG and nPAGI1 is plotted. Another experiment confirmed this observation (data not shown).

Table 2. Parameters of linear fit for the studied gels.

|       | sensitivity (std. dev.) [s-1.Gy-1] | origin (std. dev.) [s-1] | R²   | standard deviation of the fit | p value | SER |
|-------|-----------------------------------|--------------------------|------|------------------------------|---------|-----|
| nPAG  | 0,05646 (0,0034)                  | 1,25556 (0,04053)        | 0,9964 | 0,53444                      | 0,0036  | -   |
| nPAGI1| 0,15203 (0,01849)                 | 1,43378 (0,10012)        | 0,9855 | 1,38235                      | 0,0145  | 2,7 |
| nPAGI2| 0,11469 (0,01045)                 | 1,5131 (0,04957)         | 0,9918 | 0,76074                      | 0,0082  | 2,0 |

4. Discussion
The sensitivity of iodine doped nPAG was found to be increased while preserving linearity, at least up to 9.4 Gy. The increase in sensitivity (SER) was close to the theoretical dose enhancement due to iodine, at 50 keV. This preliminary study demonstrated the interest of PAG for iodine-enhanced SSR dosimetry.
Fricke gel, that has previously been used for similar approaches, was shown to be valuable for observing the dose enhancement due to the presence of gold particles [7]. However the introduction of iodinated contrast agent in Fricke gel failed to produce any significant increase in gel sensitivity, due to gel chemical reactivity [6]. A polymer gel has also been tested to measure dose enhancement due to boron when irradiated by neutrons [8].

The possible alternative use of PAG doped with iodine is a critical issue in SSR dosimetry, before treating a patient. Further investigations regarding chemical behaviour, temporal stability and dose resolution will however be necessary for understanding the influence of the contrast agent composition on the PAG response.

5. References

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