NUKLEONIKA 2012;57(4):467–472

ORIGINAL PAPER

Dose sensitivity enhancement on polymer gel with suspended gold particles

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Abstract. The presence of high Z material adjacent to soft tissue, when submitted to irradiation, enhances locally the absorbed dose in these soft tissues. Such an effect occurs due to the outscattering of photoelectrons from the high Z material. Polymer gel (PG) dosimeters were used to investigate this effect. Analytic calculations to estimate the dose enhancement were performed. Samples containing a polymer gel with 0.005 gAu/gPG and a pure polymer gel were irradiated using an X-ray beam produced by 150 kV, filtered with 4 mm Al and 5 mm Cu, which resulted in an approximately 20% greater absorbed dose in the samples with gold in comparison to those with the pure polymer gel. The analytic calculations resulted in a dose enhancement factor of approximately 30% for the gold concentration of 0.005 gAu/gPG.

Key words: polymer gel • dose enhancement • radiation therapy • X-rays

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Received: 28 November 2011
Accepted: 10 March 2012

Introduction

The challenge in radiotherapy is to deliver high doses to a tumour without exceeding the health tissue tolerance. If one could "adjust" the probability of interaction of a photon, a selective increase of the dose within the tumour would be feasible. Taking into account that the probability of a photon absorption by photoelectric effect increases drastically with atomic number of the medium, the insertion of a high Z substance into the tumour would result in an augment of the energy transmitted from the photon to the tumour, without damaging the surrounding healthy tissue [4, 5, 7, 8, 12].

This alternative could be explored by introducing contrast agents, which is a well established concept in the field of diagnostic imaging, like computed tomography (CT) and nuclear magnetic resonance (NMR). However, studies concerning the risks of the contrast agents found increased damages in tissues after diagnostic imaging procedures using them [10]. This indicates that the greater radiation damage may be associated with a higher absorption.

This effect of dose enhancement caused by the presence of high Z materials in soft tissue could be used as an application in radiation therapy. Based on this assumption, the aim of this work was to verify the dose

Table 1. Composition of the polymer gel used in this work (proposed by Berg [1])

Compound	Mass (%)
Distilled water	79.97
Gelatine (300 bloom, swine skin, Sigma-Aldrich)	13.99
Methacrylic acid 99% (Sigma-Aldrich)	5.99
Ascorbic acid (Merck)	0.035
Copper(II) sulphate pentahydrate (Merck)	0.0025

enhancement caused by adding gold microspheres (high Z) into a polymer gel (soft tissue equivalent).

Methods and materials

Polymer gel dosimetry

The polymer gel used for this work is known as MAGIC (methacrylic ascorbic in gelatine initiated by copper) [3]. Its formulation is composed of methacrylic acid, ascorbic acid, gelatine and copper sulphate. The specific composition used for this work was proposed by Berg [1], and it is presented in Table 1.

Initially, the gelatine and water are mixed in a beaker till the gelatine absorbs the whole water. Then, the mixture is placed to melt in a water bath at 55°C. When the solution is melted, the ascorbic acid and the copper sulphate are added and mixed using an electric mixer. Afterwards, the methacrylic acid is added to the solution, and mixed thoroughly. The solution stays in the water bath till it clears up and the superficial foam dissolves. The solution is finally poured into the sample flasks, and samples are left to cool and gelify.

The samples are irradiated 24 h after the production, and read 24 h after the irradiation using a NMR system (Bruker, 9.4 T). The reading sequence used is a multi-slice multi-echo (MSME) with 16 echoes, with echo times of 10, 40, ..., 320 ms and a repetition time of 2500 ms. The 16 signals obtained from the echoes are adjusted to an exponential function, which provides the transverse relaxation time (T_2) value. The inverse of T_2 ($R_2 = 1/T_2$) is called transverse relaxation rate, and is linearly related to the absorbed dose.

Calculation of the mass energy-absorption coefficients for polymer gel and polymer gel with gold

The data base XCOM [2] provides mass energy-absorption coefficients (μ_{en}/ρ) for several materials and for pure chemical elements. The mass energy-absorption coefficients for a pure polymer gel and for a polymer gel with different gold concentrations were calculated as weighted sums over the corresponding coefficients for the elements.

The first step consisted of determining the chemical composition of the polymer gel. Excepting the gelatine, all other polymer gel constituents have a simple chemical formula. The gelatine is composed mainly of type I collagen. This collagen is composed mainly of three aminoacids: glycine, proline and hydroxyproline [6, 9]. The chemical formula of hydroxyproline was assumed as an approximation of gelatine. With these assumptions, the detailed composition of the polymer gel used in these work is presented in Tables 2 and 3.

The mass energy-absorption coefficients are available in the data base XCOM in a large range of energies; however, the values are given with very large intervals of energy. For example, between 10 and 150 keV, the data base provides only 11 values for the main elements composing the polymer gel. Therefore, these coefficients were interpolated in intervals of 1 keV, following the equation:

$$\mu_{en}/\rho = a \cdot E^b \tag{1}$$

where a and b were determined by solving the following equation system:

$$\begin{cases} (\mu_{en}/\rho)_i = a \cdot E_i^b \\ (\mu_{en}/\rho)_{i+1} = a \cdot E_{i+1}^b \end{cases} \tag{2}$$

where $(\mu_{en}/\rho)_i$ is the XCOM coefficient for the respective energy E_i.

In the case of gold, this interpolation method had to be adapted to the region of the K and L edges, due to the abrupt discontinuities when the energy of the photon reaches the binding energy of these levels.

The mass energy-absorption coefficients were interpolated for the elements: hydrogen, carbon, nitrogen,

Table 2. Detailed composition of the polymer gel with the chemical formulas of the compounds

Compound	Formula	Mass (%)
Distilled water	H_2O	79.97
Gelatine (hydroxyproline)	$C_5H_9NO_3$	13.99
Methacrylic acid 99%	$C_4H_6O_2$	5.99
Ascorbic acid	$C_6H_8O_6$	0.035
Copper(II) sulphate pentahydrate (Merck)	$CuSO_4 \cdot 5H_2O$	0.0025

Table 3. Elemental composition of the polymer gel, obtained using the program XCOM

Atomic number (Z)	Element	Mass (%)
1	H	10.33
6	C	9.72
7	N	1.48
8	O	78.35
16	S	0.0003
29	Cu	0.0006

oxygen and gold, in the range from 60 to 150 keV. The polymer gel constituents with mass percentage lower than 0.001% were neglected.

The mass energy-absorption coefficients for the polymer gel with gold were calculated as weighted sums for the following concentrations: 0.00001; 0.0001; 0.001; 0.005 and 0.01 gAu/gPG.

Calculation of the absorbed dose in short depth

Before calculating the absorbed dose, an X-ray beam was defined. The cross-section for photoelectric effect, i.e. probability of occurrence, decreases when the incident photon energy increases. However, there is a steep increase of the cross-section values for incident photon energies slightly greater than the binding energies of the atomic shell electron bounds. In order to take advantage of this steep increase in the cross-section for the photoelectric effect, ideally one could use a monoenergetic photon beam with energy slightly greater than the binding energy of the chosen shell. However, in reality, an X-ray spectrum is used. In the present work, it was wished to investigate the dose enhancement caused by those photoelectrons outscattered from the *K*-shell of the gold atom, which has a binding energy of ~81 keV. Therefore, in order to increase the probability of occurrence of the photoelectric effect, it could be possible by selecting an X-ray spectrum with a high relative intensity in the region immediately greater than ~81 keV.

The spectrum of an X-ray beam produced by a potential of 100 kV, filtered with 4 mm Al and 5 mm Cu (N-100 from ISO 4037) was calculated using the software SpekCalc [11]. The mean energy of this spectrum is ~84 keV, which is greater than the binding energy of ~81 keV. However, the air kerma rate produced by this beam is ~0.4 μGy/s (at 1 m, with a tube current of 1 mA), which would demand very long irradiation periods when performing the actual experiment. For this reason, the spectrum of an X-ray beam produced by a potential of 150 kV, filtered with 4 mm Al and 5 mm Cu (same as before) were also calculated using the software SpekCalc [11]. According to this software calculation, the mean energy of this spectrum (named 150*) is ~110 keV, the half-value layers (HVL) are 16 mm Al and 2.08 mm Cu, the air kerma rate produced by this beam is ~5 μGy/s (at 1 m, with tube current of 1 mA).

The absorbed doses at short depths were calculated for both spectra (N-100 and 150*), but only the beam 150* was experimented. The absorbed dose was calculated for a 1 mm thickness slice (Fig. 1) of a polymer gel sample 100 mm long with diameter of 12 mm, following the Eq. (3):

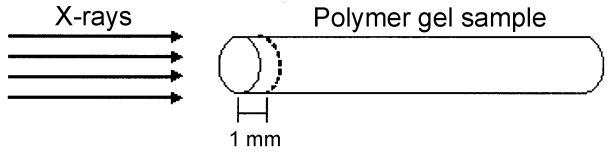

Fig. 1. Representation of the sample slice used for calculating the absorbed dose.

$$D_{\text{total}} = \sum_E D(E) = \sum_E \frac{\psi(E)\left(1 - e^{-\frac{\mu_{en}}{\rho}(E)\cdot\rho\cdot x}\right)}{\rho \cdot A \cdot x} \tag{3}$$

where $\psi(E)$ is the photon intensity with energy E (obtained with the software SpekCalc) and $\mu_{en}/\rho(E)$ is the calculated mass energy-absorption coefficient for the energy E. The sample container walls were neglected in this calculation.

The absorbed doses were calculated for the pure PG and for the polymer gel with 0.00001; 0.0001; 0.001; 0.005 and 0.01 gAu/gPG. The results of these calculations were expressed as the quotients of the doses in polymer gel with the different gold concentrations divided by the dose in the pure polymer gel. This ratio is called dose enhancement factor (DEF).

Experiment using polymer gel with suspended gold particles

One batch of polymer gel was produced following the procedure already described. Gold microspheres (with ~1 μm diameter) were added to the half of this batch in a concentration of 0.005 gAu/gPG. Forty eight samples were produced: 24 samples with a pure polymer gel and 24 samples with a polymer gel with gold.

The samples were irradiated on the next day using a Philips Industrial system with a MCN 165 X-ray tube and a tungsten anode. The X-ray 150* beam was used (produced by 150 kV, filtered with 4 mm Al and 5 mm Cu). The samples were irradiated with the nominal absorbed doses of 1, 2, 3, 5 and 6 Gy. For each absorbed dose, 4 samples with the pure polymer gel and 4 samples with the polymer gel with gold were used. As control, 8 samples were considered (4 with gold and 4 without gold).

The evaluation of the samples was performed one day after the irradiation, as already described. The R_2 values obtained for the control samples without gold ($R_2(0)$, average of 4 samples) were subtracted from the R_2 values obtained for the irradiated samples without gold. This difference ($R_2 - R_2(0)$) was related to the nominal absorbed dose. The same procedure was followed for the samples with gold microspheres.

Results and discussion

Calculation of the mass energy-absorption coefficients for polymer gel and polymer gel with gold

The mass energy-absorption coefficients obtained for hydrogen, carbon, nitrogen, oxygen and a polymer gel (as weighted sum over the corresponding coefficients for its main constituents) are presented in Fig. 2, and the coefficients for gold are presented in Fig. 3.

The mass energy-absorption coefficients obtained for the polymer gel were compared with the coefficients for the ICRP soft tissue (also obtained by interpolating the XCOM data), and are presented in Fig. 4. The mass energy-absorption coefficients for polymer gel showed a maximum variation of 6% for low energies

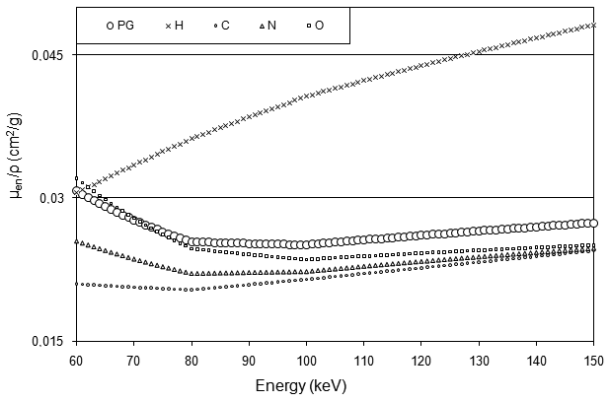

Fig. 2. Mass energy-absorption coefficients in relation to incident photon energy for hydrogen, carbon, nitrogen, oxygen and polymer gel.

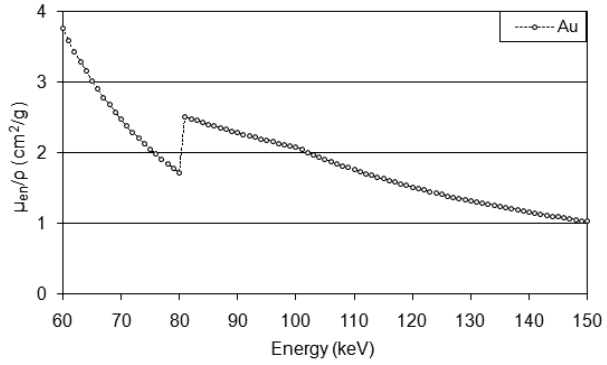

Fig. 3. Mass energy-absorption coefficients in relation to incident photon energy for gold.

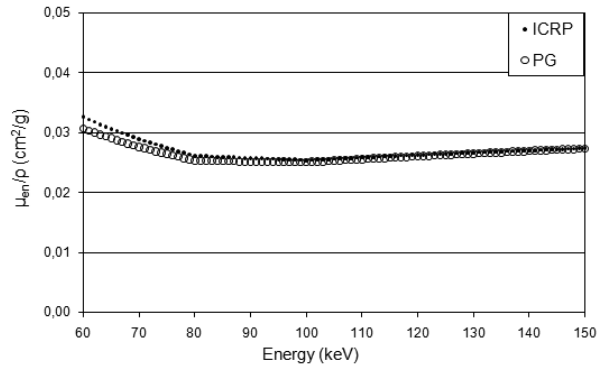

Fig. 4. Mass energy-absorption coefficients in relation to incident photon energy for polymer gel and ICRP soft tissue.

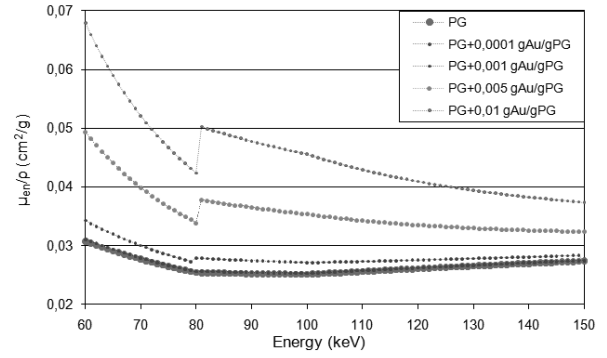

Fig. 5. Mass energy-absorption coefficients in relation to incident photon energy for polymer gel with different gold concentrations.

in relation to those coefficients for the ICRP soft tissue, confirming, therefore, the soft tissue equivalence of the polymer gel.

The mass energy-absorption coefficients for polymer gel with different gold concentrations are presented in Fig. 5. For the polymer gel with gold concentration of 0.005 gAu/gPG, it was possible to observe an increase of 50% in the coefficient at ~81 keV in relation to the coefficient for pure polymer gel. This result is due to the increase in the photoelectric absorption caused by the gold atoms.

Calculation of the absorbed dose in short depth

The spectra of the X-ray beams N-100 and 150*, used to calculate the absorbed dose, were obtained using the software SpekCalc [11], and are presented in Fig. 6.

The ratios between the absorbed doses for the polymer gel with gold and the absorbed dose for the pure polymer gel, i.e. dose enhancement factor, for the concentrations: 0.00001; 0.0001; 0.001; 0.005 and 0.01 gAu/gPG and for the spectra of the beams: N-100 and 150* are presented in Fig. 7.

The dose enhancement factors obtained show that the absorbed dose for the polymer gel with 0.005 gAu/gPG is by 43% greater than the absorbed doses for the pure polymer gel, when irradiated with the beam N-100, and 32% greater, when irradiated with the beam 150*.

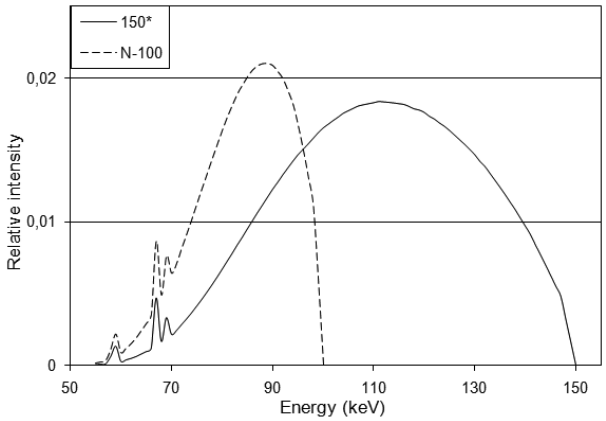

Fig. 6. Spectra of the X-ray beams N-100 and 150*.

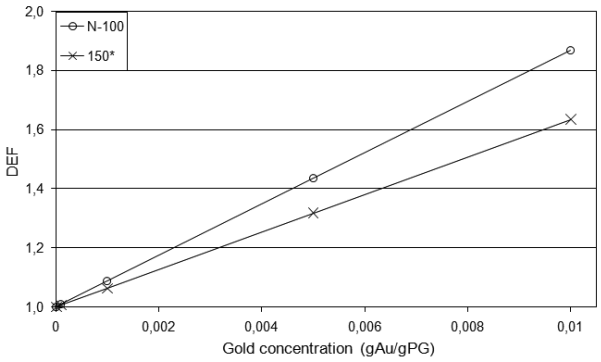

Fig. 7. Dose enhancement factor (DEF) in relation to the gold concentration in the polymer gel for the beams N-100 and 150*.

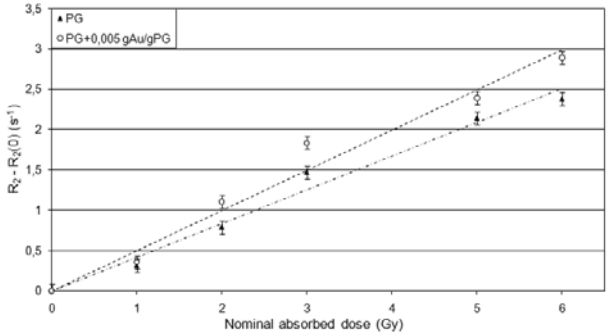

Fig. 8. Relaxation rates ($R_2 - R_2(0)$) in relation to the nominal absorbed dose for pure PG and for PG with 0.005 gAu/gPG irradiated with the beam 150*.

Experiment using polymer gel with suspended gold particles

The relations between $R_2 - R_2(0)$ and the nominal absorbed dose for the samples with pure polymer gels and for the samples with polymer gel with gold microspheres (0.005 gAu/gPG) are presented in Fig. 8. Each data group (pure PG and PG with gold) was adjusted to linear regressions. The slope from the linear regression of the measurements of the samples with polymer gel with gold (0.49) is 19.5% greater than the slope obtained from the measurements of the samples with pure polymer gel (0.41). This result means that there was an enhancement of 19.5% of the absorbed dose for the polymer gel with 0.005 gAu/gPG in relation to the absorbed dose for the pure polymer gel.

The dose enhancement predicted by the calculations was 32%. This difference may be due to the fact that the calculations assumed that the gold atoms were homogeneously mixed within the other elements that compose the polymer gel, whereas the actual experiment consisted of gold microspheres with a 1 μm diameter suspended in the polymer gel. The size of the gold microspheres has the same order of magnitude of the range of low energetic photoelectrons. Thereby it is believed that low energetic photoelectrons have been re-absorbed by the gold particles themselves, preventing them from ionizing the polymer gel.

Besides these results, an absolute increase in the sensitivity for measuring R_2 of the polymer gel with gold in relation to the pure polymer gel was observed. The absolute R_2 measured values are presented in Fig. 9.

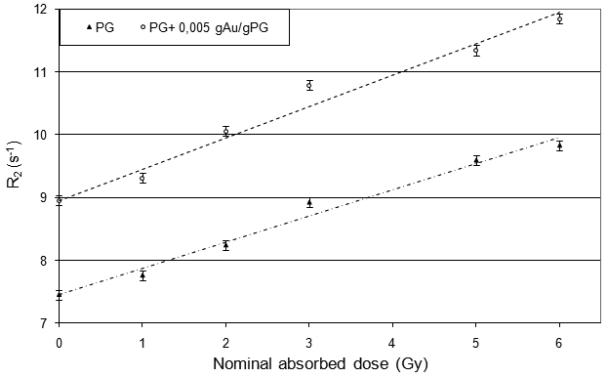

Fig. 9. Absolute relaxation rates (R_2) in relation to the nominal absorbed dose for pure PG and for PG with 0.005 gAu/gPG irradiated in the beam 150*.

Conclusions

The mass energy-absorption coefficients for polymer gel samples and for polymer gel samples with different gold concentrations were calculated. The mass energy-absorption coefficients obtained for the polymer gel were compared to the coefficients for ICRP soft tissue, and they also confirmed the polymer gel soft tissue equivalence in the considered range of energies.

Two spectra were calculated using the software SpekCalc, N-100 and 150*, to be used in the absorbed dose calculations. The considered spectra present a high relative intensity of photons at energies immediately greater than the binding energy of the *K*-shell of the gold atom.

Using the calculated mass energy-absorption coefficients and the spectra of the beams N-100 and 150*, the absorbed doses in a 1 mm slice of the samples adjacent to the X-rays entrance were calculated. The dose enhancement factors were obtained from the ratio between the absorbed dose in the polymer gel with gold and the absorbed dose in the pure polymer gel, resulting in the enhancements of 32% for the beam 150* and 43% for the beam N-100, caused by the concentration of 0.005 gAu/gPG.

The experiment using polymer gel with suspended gold microspheres (with concentration of 0.005 gAu/gPG) irradiated with the beam 150* presented a higher sensitivity to R_2 measurements using the nuclear magnetic resonance technique. The absorbed dose of the samples containing gold was 19.5% greater than the absorbed dose of the pure polymer gel. Although the calculations predicted a dose enhancement of 32%, the experimental result is positive, because the size of the gold microspheres has the same order of magnitude of the range of low energetic photoelectrons. Therefore, it is believed that low energetic photoelectrons have been re-absorbed by the gold particles, preventing them from ionizing the polymer gel.

Acknowledgment. The authors would like to thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for the partial financial support.

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