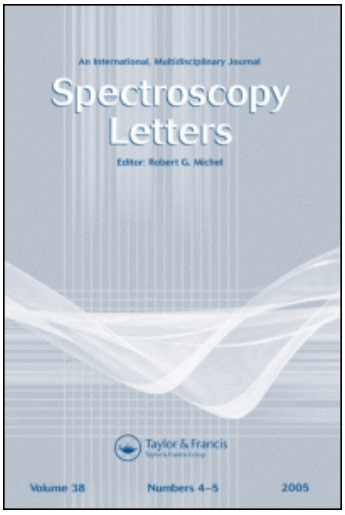

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Determination of Radiation Dose Distribution by Magnetic Resonance Imaging in the New Tissue Equivalent Gel

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DETERMINATION OF RADIATION DOSE DISTRIBUTION BY MAGNETIC RESONANCE IMAGING IN THE NEW TISSUE EQUIVALENT GEL

Keywords: MRI based dosimetry, proton relaxation, phantom

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Abstract: A new tissue-equivalent substance for the MR dosimetry has been developed. It is composed of water, bovine serum albumin, acrylamide with N,N'-methylene-bis-acrylamide, ammonium ferrous sulphate and sulphuric acid. The elemental composition, mass density, and electron density of the PIRA gel are closer to real tissue than those of dosimeter gels previously investigated. Irradiation causes the changes in the NMR properties of the gel. The dose dependence of NMR longitudinal relaxation rate, R1, is reproducible (less than 2% variation) and is linear up to about 30 Gy, with a slope of 0.023 $s^{-1}Gy^{-1}$ at 0.48 T. The gel, referred to as PIRA, can be used to obtain accurate radiation dose distribution with conventional magnetic resonance imaging devices.

INTRODUCTION

The success of radiotherapy depends on the accurate knowledge of the distributions of the radiation absorbed dose, often in respect to localization and magnitude. The irradiated regions should be well-defined to spare the surrounding healthy tissues. MRI may be convenient to determine the accurate spatial dose distributions using tissue-equivalent phantoms [1]. Usually, the phantoms for NMR - based dosimetry are made of easy to prepare aqueous gels doped with a dosimeter factor, whose NMR properties are sensitive to irradiation. A Fricke solution (a ferrous sulphate solution) is the most commonly used dosimeter. The ionizing radiation converts ferrous ions into ferric ions, the number of converted ions being proportional to the absorbed dose. The difference in the concentrations of ferric ions induces the changes of the proton relaxation times [2], and can therefore be monitored using MR imaging as first demonstrated by Gore et al in 1984 [3]. Since then, several ferrous sulphate dosimetry gels including gelatin [4], agarose [5-7], Sephadex-200 [8], Sumikagel N-100 [9] and polyacrylamide [10] were studied [11-14]. Some of them have been employed to the imaging of dose distributions in the stereotactic radiosurgery [15,16], and in brachytherapy [17-18]. Unfortunately, the Fricke gels have one serious disadvantage for the assessment of the radiation field. The post-irradiations diffusion of ferric ions leads to blur the MR image and a consequent loss of spatial resolution. Recently, Maryanski et al [19,20] have proposed an alternate type of gel, in which the radiation-induced formation of a polymer increases the water proton NMR relaxation rates in proportion to the absorbed dose. The sensitivity and stability of polymer gels are much better than of the Fricke - gels systems. In addition the polymer gels can also be used for the qualitative testing by visual inspection after the formation of cross-linked polymers in the irradiated regions of the gel, these parts becoming increasingly opalescent against a background of the clear, non-irradiated regions.

The present paper describes a new gel phantom permitting the determination of the three-dimensional radiation dose distribution - the PIRA gel (the letters stand for

Protein, IRon and Acrylamide). Our aim was to find a phantom material that can provide the similar properties to the biological tissue, for the radiation modalities being investigated. In PIRA gel, bovine serum albumin and acrylamide with N,N'-methylene-bis-acrylamide are the tissue equivalent mediums and an ammonium ferrous sulphate solution is the main dosimeter factor. The BSA and monomers of acrylamide were chosen as the basic matrix material to optimize the similarity between the gel and simulated tissue.

MATERIALS AND METHODS

Preparation of the Gel Samples

The new tissue equivalent gel consists of 5% by weight bovine serum albumin (BSA) (A-7030, Sigma Chimie, St. Quentin Fallavier, France) 10%T acrylamide (A-3553, Sigma Chimie, St. Quentin Fallavier, France) with 50%C N,N'-methylene-bis-acrylamide (Bis) (A-M-7279, Sigma Chimie, St. Quentin Fallavier, France), 0.5 mM $Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$ (F-3754, Sigma Chimie, St. Quentin Fallavier, France), 100 mM H_2SO_4 (analytical grade) and high-purity water. The preparation of the gel proceeded as follows: acrylamide and N,N'-methylene-bis-acrylamide were dissolved in half the desired water volume of the gel and the colloid solution was well mixed. The solution was placed in a water bath at 80°C until it became clear. In a separate glass vessel an ammonium ferrous sulphate was dissolved in diluted sulphuric acid to make the 1/6 of the final gel volume. The final 2/6 volume of the gel was BSA solution. The BSA solution and the ammonium ferrous sulphate solution were carefully mixed. Then the acrylamide and Bis solutions were added and stirred. The gel was poured into desired containers and allowed to cool slowly at room temperature.

Irradiation of the Samples

The irradiations was completed using a γ Co-60 beam from the therapy unit ALCYON II (GE - CGR MeV, Buc, France). Two types of experiment were done.

Firstly, we quantified by NMR at 20 MHZ, the dose-response of the gels in small volumes. Secondly, we determined 3D dose distributions in the large volume phantom using MR imaging. For the dose-response experiments the gel was irradiated in test tubes embedded in a specially built polystyrene phantom. The NMR tubes containing dosimeter material were irradiated, with a large field size, at a depth of dose maximum (5 mm tissues equivalent) in a polystyrene block to provide full scatter and build-up conditions. The dose rate was about 200 cGy/min. The doses ranged from 0 to 45 Gy and were confirmed by irradiating calibrated $Li_2B_4O_7$ thermoluminescent powder under the same conditions.

For the large volume phantom studies a rectangular common plastic container (11 x 13 x 18 cm^3) filled by the gel was used. The absorbed dose at the depth p=30mm was D = 30 Gy (square field 4 x 4 cm^2, phantom top-source distance 60 cm).

Measurement of Relaxation Times

The measurements of the longitudinal proton relaxation time T1 and of the transverse relaxation time T2 were performed in a 0.48T, 20MHz for proton, spectrometer (Bruker, PC 20, Wissenburg, France). T1 was measured by inversion recovery, using eight values for the pulse delays and a three-parameter nonlinear least squares fit to the data. T2 was measured by CPMG sequence with every 8th echo sampled, using 20 or more data points so that the signal decayed by at least a factor of three. All measurements were carried out at a temperature of 21°C ±1°C. The gels were measured in the same tubes in which they were earlier irradiated. All the gel samples, between measurements, were stored in a refrigerator at 4 °C and kept away from daylight .

Magnetic Resonance Imaging

The large volume phantom was imaged in a 0.5 T MRI system (MR MAX, GE-CGR, Buc, France), using a Spin-Echo pulse sequence with a TR = 580 ms, a TE = 25 ms, a 224H x 256V image matrix, 2 Nex, and a 20 cm FOV.

RESULTS

The PIRA gel composition and concentration of the chemical compounds has been found to provide the best equivalence to the biological tissue and sensitivity for ionizing radiation. The elemental composition, specific density and electron density of the PIRA material together with those of real tissue (muscle and lung) and few dosimeter gels are summarized in Table 1. The electron density ρ_e was calculated according to

$$\rho_e = \rho N_a \Sigma W_i Z_i / A_i$$

where ρ is measured specific density, N_a is Avogadro's number, W_i is the weight fraction of the element I, Z_i and Ai are the atomic and mass numbers respectively of the element I. The chemical composition of the BSA was taken from Ref. 22.
No allowance was made for gases dissolved in the gels.

The samples (4 ml) in test tubes of outer diameter 7 mm were irradiated less than two hours after the production of the gels to reduce degradation of the gels' dosimetric properties. Directly before and after irradiation the relaxation times T1 and T2 of the gels were measured. Both T1 and T2 change with irradiation. T2 displays good sensitivity but because of better reproducibility of T1 it was chosen as irradiation indicator. Figure 1 shows the relaxation rate R1 = 1/T1, as function of the absorbed dose D. The solid line represents the fitted curve by the last square method. The relation between R1 and D is linear (R1 (s^{-1}) = 1.134 (s^{-1}) + 0.023 D ($s^{-1}Gy^{-1}$), correlation coefficient r = 0.999, a variation of less than 2% from the mean value) for a limited range of the dose (0-30 Gy).

A measurement of the 3D absorbed dose distributions was made with the large volume phantom (about 2500 ml). Figure 2a shows the MR image of the square field irradiated phantom. A 5 mm slice, parallel to the irradiated surface was acquired at a depth of 30 mm from the outer surfaces of the top of container. The postirradiation MR image density profile taken in the plane perpendicular to the beam central axis for PIRA gel is shown in Figure 2b. Figure 2c shows the isodoses calculated for water phantom with the treatment planning program TARGET II (GE - CGR, Buc, France)

TABLE 1

Elemental Composition of Muscle, Lung and Few Selected Dosimeter Phantoms (percentage by mass).

	H	C	N	O	Na	S	Cl	Fe	others	density g/cm^3	electron density 10^{23}/cm^3
Muscle[22]	10.20	14.30	3.40	71.00	0.10	0.30	0.10	-	0.60	1.05	3.48
Lung[22]	10.30	10.50	3.10	74.90	0.20	0.30	0.30	-	0.40	1.05	3.48
Water	11.111	-	-	88.889	-	-	-	-	-	1.00	3.35
SDA[13]	11.049	0.691	0.0014	88.029	-	0.227	-	0.0027	-	1.005	3.36
Gelatin[13]	10.763	1.959	0.665	85.757	0.0021	0.847	0.0033	0.0026	-	1.005	3.35
BANANA*	10.710	4.720	1.516	83.091	-	-	-	-	-	?	?
BANG+	9.889	6.315	1.935	88.436	-	-	-	-	-	?	?
PIRA	10.461	6.877	2.373	79.892	-	0.394	-	0.0029	-	1.03	3.42

* based on the gel used by Maryanski et al [20]

+ based on the gel used by Maryanski et al [21]

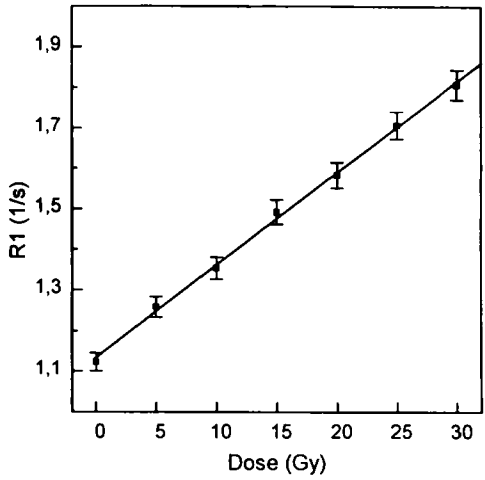

FIG 1. Dose response R1 curve for PIRA gel obtained at 20 MHz. 2% error bars are shown.

assuming irradiation conditions identical to those employed during the experiment. This image was obtained within one hour of irradiation.

DISCUSSION AND CONCLUSIONS

Several phantom substances used in NMR - based radiation dosimetry have been proposed in the past but the gel described is the first to include a bovine serum albumin, the smallest and most abundant of the plasma proteins. The presence of the protein molecules in the gel systems provides a more accurate representation of the properties of the tissue. Comparison of the data in Table 1 indicates that the elemental composition, mass density, and electron density of the PIRA gel are closer to real tissue than the gels previously investigated [11,13].

The above - mentioned parameters are very important in the dosimetric studies of the substitute materials [13]. The phantoms in which these criteria are satisfied will demonstrate radiation transport characteristics, for any type of radiation and energy,

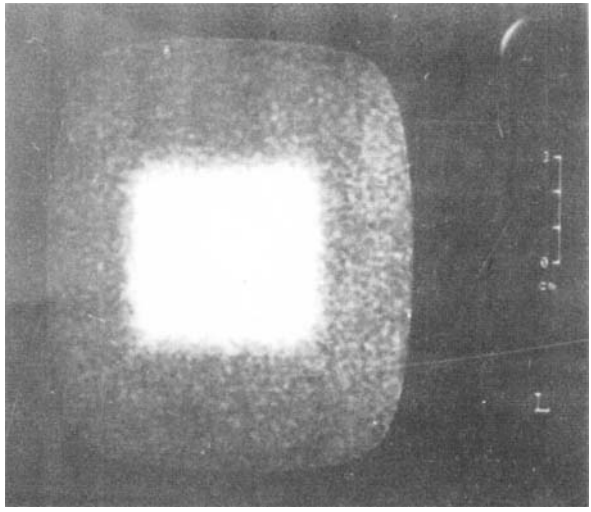

FIG 2a. Transversal MR image (SE, TR = 580 ms, TE = 25 ms) of the PIRA large volume phantom irradiated with D = 30 Gy at the depth p = 30 mm, field 4 x 4 cm^2, SSD = 60 cm.

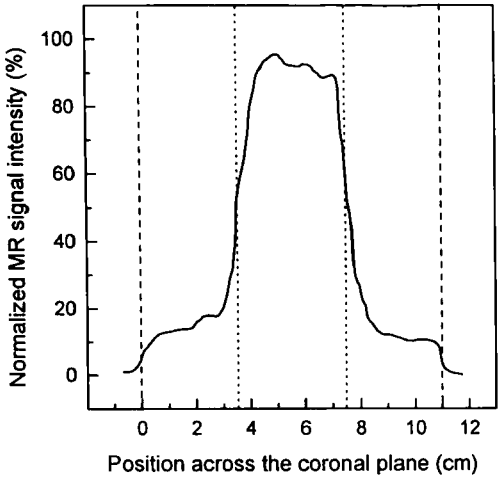

FIG 2b. The postirradiation MR image density profile taken in the plane perpendicular to the beam central axis for the PIRA large volume phantom.

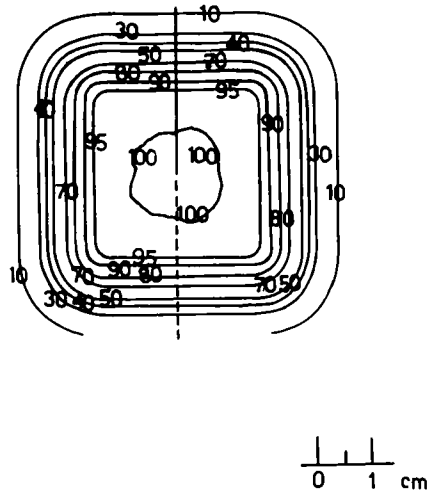

FIG 2c. The calculated isodose curves for the water phantom irradiated with D=30Gy at the depth p = 30 mm, field 4 x 4 cm^2, SSD = 60 cm.

TABLE 2

Slopes of Dose-Response R1 Curves for Different Gels.

Gel Type	Dosimeter Factor	Sensitivity (s^{-1} Gy^{-1})
SDA	Fe 2+	0,084±7%⁺
Gelatin Gel	Fe 2+	0,042±5%⁺
BANANA	cross-linked acrylamide	0,024±10%*
PIRA	Fe 2+	0,023±2%*

⁺ obtained at 64MHz
*obtained at 20 MHZ

similar to that of biological tissue. Chan et al [23] verified the radiation properties of different types of FeMRI gels using Monte Carlo simulations. They compared the calculated energy depositions ratios in the gels with the values obtained for water and bone. They concluded that standard dosimetry agarose (SDA) and gelatin gels are suitable substitutes for water in the therapy range of electron and photon energies. The PIRA could simulated real soft tissue. The basic composition of the gel which was presented can be modified by variations of the concentration of bovine serum albumin and acrylamide monomers without dramatically changing the radiation properties of the gel.

The PIRA gel is sensitive to ionizing radiation. The relaxation time T1 is changed according to the absorbed dose. The observed dose-response R1 is linear for a dose range of 0-30 Gy and reproducible (see Fig. 1). The slope of a dose - response curve is of the same order as value given by Maryanski for BANANA gel at the same NMR frequency [19], but lower then those obtained for standard FeMRI gels, shown in Table 2.

The mechanism inducing R1 changes in the irradiated PIRA gel is not already determined. However, the most important role in the increase R1 for the described gel plays the well - established effect of the oxidation of ferrous to ferric ions upon irradiation in the presence of organic substances and oxygen [12]. The spontaneous oxidation causes a subsequent increase in relaxation rates over several days following irradiation. The other processes, which could increase the proton relaxation rates, is the radiation-induced polymerization of the acrylamide monomers. The role of this proses is less significant because of the inhibiting action of oxygen and the presence of sulphuric acid [19]. However, the mechanism of the polymerization of acrylamide and the possible changes of BSA in examined gel require further investigation, as well their influence on changes in the relaxation times.

The irradiation effects in the PIRA gel can be imaged with a clinical magnetic resonance imaging devices (Fig. 2a). The shapes of calculated isodoses (Fig. 2c) fit with MR image for the same setup used in the experiment with the large volume phantom. The relationship between absorbed dose and MR image of the PIRA gel can

be determined using the technique developed by Evans and Schreiner [18]. They suggested that the MR signal intensity can be related directly to the absorbed dose by an M&D calibration curve, analogically to the film dosimetry. Figure 2b shows that the MR signal intensity of nonirradiated and irradiated regions of PIRA gel phantom can be distinguished. The maximum of the MR signal intensity corresponds to the region of a maximum absorbed dose.

The PIRA gel may be useful for 3D radiation treatment planning of soft tissues, as it offers: i) a higher similarity to soft biological tissue than the previously described phantom gels, ii) a high radio sensitivity easily detectable by MRI.

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