TISSUE EQUIVALENCE STUDY AND EVALUATION OF A NORMOXIC POLYMER GEL DOSIMETER

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Abstract. We determined the mass fractions, density, attenuation coefficients, effective atomic number (Z_{eff}) and stopping power of MAGAT gel to verify its equivalence to water and tissue. We also studied the MAGAT gel response using the X-ray scanner, using a new MAGAT gel dosimeter with different concentrations of components (gelatin 8 %, methacrylic acid 6 % methacrylic acid, gelatin, tetrakis (hydroxymethyl) phosphonium chloride (THPC) 2 mM, water 86 %). We observed a small difference in the mass fraction due to the change in concentration of some main chemical compounds of MAGAT gel. The MAGAT gel has a Z_{eff} almost identical to water. The curves of mass attenuation coefficient (μ/ρ) of water and MAGAT gel as a function of energy present a relative deviation not exceeding 4 %. The relative difference between the two stopping power curves is less than 0.5 %. The response of our novel MAGAT gel to the X-ray CT scanner as a function of the dose is linear with dose sensitivity equal to 1.85±0.28 HU Gy^{-1}, while the concentrations of its components have a better tissue equivalence and a high N_{CT} dose response.

Key words: Gel polymer, MAGAT, radiobiological equivalence, X-ray scanner.

INTRODUCTION

Dosimetry techniques used in external radiotherapy, such as film, thermoluminescent detectors and ionization chambers allow the evaluation of the radiation dose in a plane or at a point. At the same time, external radiation therapy techniques have been refined to provide better irradiation conditions for tumors and have led to a better adaptation of the dose distribution to the target volume, while keeping the dose to the surrounding tissues at a relatively low level.

This development requires new dosimetry techniques to simulate the dose distribution in three dimensions. Several works have focused on the volume dosimetry systems and gel dosimetry [3].

The polymer gel is a chemical dosimeter consisting of radiation sensitive chemical compounds in an aqueous gel matrix. After irradiation, free radicals are

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Received: December 2022;
in final form March 2023.

ROMANIAN J. BIOPHYS., Vol. 32, No. 4, P. 207–218, BUCHAREST, 2022

formed in the gel, which induce polymerization. The polymerization rate is proportional to the absorbed dose [16].

Polymer formation increases the viscosity of the aqueous solution; this change in the solution can be quantified using an imaging technique. MRI is the most widely used technique in dose reading, where the spin-spin relaxation rate ($R_2 = 1/T_2$) varies as a function of absorbed dose [13].

X-ray CT scanning [10], optical computed tomography (OCT) [27] and ultrasonography [17] are alternative imaging modalities to read out of the absorbed dose.

Fricke gel and polymer gel are the two main types of dosimeter gels used in the practice. However, due to the diffusion of ferric ions Fe^{3+}, the information of dose distribution is not preserved in time [19]. Polymer gels were developed based on radical polymerization, and it is now the best technique for the experimental measurement of absorbed dose distribution in three dimensions, at the same time this dosimeter plays the role of a phantom.

In the published literature, the first gels are of the so-called anoxic type, where they are manufactured free of oxygen contamination. Oxygen acts to inhibit free radical polymerization by combining with the radiolysis product of water. The polymer gel dosimeter is composed mainly of monomer dissolved in an aqueous matrix, the addition of an antioxidant has made it possible to manufacture the polymer gel of the normoxic type in an ambient environment (in the open air). The MAGIC gel (methacrylic and ascorbic acid in gelatin initiated by copper) [6] is the first formula of the normoxic gel, using ascorbic acid that traps the dissolved oxygen. Methacrylic acid (MAA) in MAGIC gel is less toxic than acrylamide in anoxic gel.

Other normoxic gel formulations have been developed, such as the methacrylic acid, gelatin gel and ascorbic acid (MAGAS) gel [5] and the polyacrylamide, hydroquinone, gelatin gel and tetrakis (PAGAT) gel [15].

In the clinical setting, X-ray CT is the more accessible imaging modality. With radiation polymerization inducing a change in electron density, it has been shown that X-ray CT can be used as an evaluation tool for the polymer gel dosimeter. The evolution of Hounsfield Units as a function of the absorbed dose has been studied for the MAGIC [9] and MAGAT gels [22]. Because the polymer gel's sensitivity is low, an optimization study was performed on the PAGAT gel, and recommendations were made to achieve the best change in CT number with radiation dose [23].

The methacrylic acid, gelatin and tetrakis phosphonium chloride (MAGAT) gel [5] is composed of methacrylic acid, gelatin, tetrakis (hydroxymethyl) phosphonium chloride (THPC). THPC has a potent ability to scavenge oxygen and has good temporal stability, good spatial resolution, and excellent dose sensitivity.

The 3D dose detector must allow a quantitative measurement of the dose distribution with a good spatial resolution. In addition, it must have a response that is linear with the dose measured and must be equivalent to the modelled tissue.

The density, mass fraction, absorption and scattering of radiation within the study medium, effective atomic number, and stopping power should be the same as those of water or tissue. Radiological properties of MAGAT gel dosimeter has been investigated previously [1, 26].

The effective atomic number Z_{eff} is a physical property of multi-element materials; this parameter is used in the selection of tissue-equivalent phantom materials by comparing its value to water or tissue. The calculation of Z_{eff} for a qualitative comparison must be energy-dependent [24]. In addition, the energy and scattering angle dependencies of Z_{eff} have also been studied [14].

Many studies have already described the effect of changes in concentration of individual components on dose sensitivity and 3D distribution measurements [7, 8, 12, 18, 20]. A study of the effect of methacrylic acid concentration showed that the MAGAT gel with 6 % methacrylic acid (MAA), 8 % gelatin and 10 mM THPC had better sensitivity up to 12 Gy compared to 9 % [12]. It has been shown that the R_2 of MAGAT gel is effectively increased when the concentration of THPC is greater than 1 mM [12].

The MAGAT gel is recognized as the most common gel dosimeter with superior sensitivity and dose resolution [12, 21].

The study of the role of gelatin on radiation-induced polymerization of MAGAT gel was evaluated at a concentration of 2 mM THPC, 5 % MAA, it was found that the response of MAGAT gel to doses below 10 Gy is similar for dosimeters containing more than 8 % gelatin [21].

In contrast to previous studies (gelatin 8 %, methacrylic acid 9 %, THPC 10 mM, water 83 %) [1, 9], we used a new gel dosimeter with different concentrations of components (gelatin 8 %, methacrylic acid 6 %, THPC 2 mM, water 86 %). The aim of this study was to investigate the theoretical tissue equivalence of the MAGAT gel and to verify its response to irradiation by an external source of 6 MeV. The first manipulations consisted in preparing the MAGAT polymer gel. In order to study its sensitivity to radiation, this gel was subjected to external irradiation in order to calibrate the response. This response was investigated using an X-ray CT scanner.

MATERIALS AND METHODS

STUDY OF THE WATER EQUIVALENT

The mass fraction W_i of each element i constituting the MAGAT gel (hydrogen W_{H}, nitrogen W_N, oxygen W_O, carbon W_C, phosphorus W_P and chlorine W_{Cl}) are determined using the equation (1) below:

$$W_i = \frac{mass\ of\ the\ element\ i\ in\ the\ whole\ compound}{total\ molecular\ weight} \tag{1}$$

The density ρ of the gel MAGAT gel was determined by the equation (2):

$$\rho = \frac{m}{v} \quad (2)$$

where m is the mass, and the v is the volume of gel.

The number of electrons per gram n_e was calculated using the equation (3):

$$n_e = N_A \sum_{i=1}^{n} W_i \cdot \frac{Z_i}{A_i} \quad (3)$$

where N_A is the Avogadro number, n is the number of elements, W_i, Z_i, and A_i are the fraction, the atomic number and the atomic mass of the element i, respectively. The effective electron density, ρ_e, is as follows:

$$\rho_e = n_e\, \rho \quad (4)$$

where ρ is the density of the gel, n_e is the number of electrons per gram.

The effective atomic number Z_{eff} of the MAGAT gel was calculated using Auto-Z_{eff} software [25]. The atomic number of a gram of the gel, allows the estimation of the radiological properties and the evaluation of the equivalence in water and tissue.

The mass attenuation coefficient of photoelectric absorption, Compton scattering, pair production, and the total mass attenuation coefficient (μ/ρ) of water and MAGAT gel were calculated using the NIST XCOM database over the energy range of 0.01 to 20 MeV [11].

In the process of electron beam interaction with the medium, we calculated the total mass stopping power to verify the equivalence of MAGAT gel to water. We used the NIST ESTAR database over the energy range of 0.01 to 20 MeV [4].

MAGAT GEL FABRICATION

MAGAT gel was prepared using methacrylic acid (Acros Organics), gelatin 300 bloom (Sigma Aldrich), deionized water and tetrakis (hydroxymethyl) phosphonium chloride (THPC) (Sigma Aldrich) (see Table 1).

Table 1

The composition of MAGAT gel

Components	Concentration
Gelatin	8 %
Methacrylic	6 %
THPC	2 mM
Deionized water	86 %

The MAGAT gel was made under normal atmospheric conditions. The gelatin was mixed with deionized water in the beaker and stirred continuously at about 48 °C using a hot plate until the gel was completely dissolved. The solution was cooled to 40 °C, and then methacrylic acid was added and stirred continuously until the monomer is completely dissolved. Finally, the THPC is added. The gel was filled into six sample vials.

IRRADIATION

The irradiation of the vials was performed 24 hours after their fabrication, with a 6 MeV photon beam from LINAC (VARIAN) and 300 cGy/min dose rate.

Each tube was placed in the center of a water phantom under reference conditions, *i.e.*, a field of 10×10 cm and a skin source distance (SSD) = 100 cm. Two lateral and opposite photon beams (gantry at 90° and 270° angle) were used to deliver the radiation. The delivered doses were 0, 2, 4, 6 and 8 Gy for each sample tube.

DOSE READING BY X-RAY SCANNER

The response of the MAGAT polymer gel to increasing doses was studied 96 hours after irradiation on the X-ray CT scanner (General Electric, Optima 660 model, 128 slices, year of commissioning 2016). For acquisition, the gel vials were placed in a water tank, we used the following parameters: tube voltage 120 kV, tube current 180 mA, pixel size 0.45×0.45, matrix size 256×256 pixel and with 1.5 s imaging time.

The images were processed on a personal computer using the image processing toolbox in MATLAB software. The Hounsfield number (N_{CT}) was defined from a region of interest (ROI) inside the sample tube, the ROI quantifies the same number of pixels for each vial.

$$N_{CT} = \frac{\mu_{\mathrm{GEL}} - \mu_{\mathrm{H_2O}}}{\mu_{\mathrm{WATER}}}\, 1000 \tag{5}$$

where μ is the linear absorption coefficient of the gel and H_2O.

Signal-to-noise ratio (*SNR*) was calculated using the following equation [23]:

$$SNR = \frac{N_{CT}(\text{irradiated gel}) - N_{CT}(\text{un-irradiated gel})}{\sigma} \tag{6}$$

where N_{CT} is the mean value of CT number over a ROI, σ is CT number standard deviation of un-irradiated gel inside the same ROI.

RESULTS AND DISCUSSION

WATER EQUIVALENT

In order to study the equivalence to water of MAGAT gel, we calculated the mass fractions of the dosimeter elements. Table 2 allows us to compare the mass fractions of the component elements of the MAGAT gel in this study, water, the MAGAT gel presented by Venning *et al.* [26] and the MAGIC gel presented by Fong *et al.* [6].

Table 2

MAGAT gel and water mass fraction and density

Material	W_H	W_O	W_C	W_N	W_P	W_{Cl}	W_S	W_{Cu}	**ρ**
MAGAT	0.1068	0.8050	0.0741	0.0139	0.0001	0.0001	–	–	1.015
MAGAT^a [26]	0.1042	0.7928	0.0854	0.0115	0.0015	0.0017	–	–	1.032
H_2O	0.1119	0.8881	–	–	–	–	–	–	1.000
MAGIC [6]	0.1055	0.7884	0.0922	0.0139	–	–	0.0000	0.0000	1.060

Elements composing the MAGAT gel have an atomic number varying from 1 to 17, it is composed of 86 % of water, which makes the number of hydrogen atoms twice as important as the number of oxygen atoms. However, oxygen constitutes almost 80.50 % of the mass of the MAGAT gel. Hydrogen, carbon, nitrogen and (phosphorus/chlorine) represent respectively 10.68 %, 7.41 %, 1.39 % and 0.02 % of its mass.

In this study, the fraction of oxygen and hydrogen in the composition of MAGAT gel is closer to water than in MAGAT^a [26] gel and MAGIC [6] gel. We increased the water amount and decreased the methacrylic acid and THPC amount. The small difference observed in mass fraction is due to the change in concentration of some main chemical composition of MAGAT gel.

Table 3 gives the electron density and the electron number per gram of water and MAGAT gel with 6 % of methacrylic acid. We can notice that the electron number per gram is almost similar, with a difference of 0.4 %. The electron density of MAGAT gel is lower than that of water by about 1.5 %.

Table 3

Number of electrons per gram and effective electron density

Material	n_e **10^{23} (g^{-1})**	ρ_e **10^{23} (cm^{-3})**
MAGAT	3.333	3.383
H_2O	3.348	3.343

The difference between the calculated electron density of the new MAGAT gel and the water is about 1 %. The number of electrons per gram of MAGAT gel is 0.4 % higher than that of water.

The interaction of ionizing radiation depends on the atomic number of elements and the energy of the radiation. For a multi-element medium such as water or MAGAT gel, the effective atomic number Z_{eff} is determined; it varies with the energy and indicates the electrons number of the material, which are actively involved in the photon-atom interaction.

Curves of the Z_{eff} of the MAGAT gel and water as a function of energy (Figure 1) show that the values of Z_{eff} is maximum for low energies, with the photoelectric effect being dominant in this energy range. The Z_{eff} value decreases rapidly with energy until the intermediate energy range between 0.1 and 3 MeV. In this energy range, the Compton effect is dominant and the Z_{eff} values are almost constant. From 3 MeV, where the pair production effect becomes dominant, we notice that the Z_{eff} increases and its value in this high energy range is higher than the intermediate energy range, but lower than the low energy range. The MAGAT gel has a Z_{eff} almost identical to water.

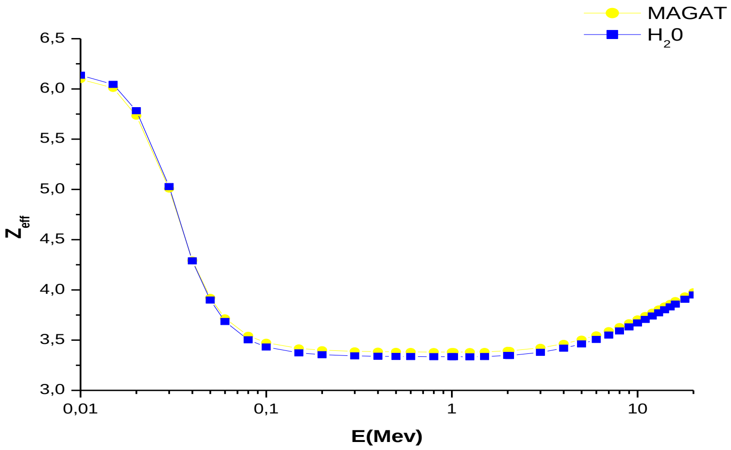

Fig. 1. Variations of the atomic number (Z_{eff}) of the new MAGAT gel and water *versus* the energy (*E*).

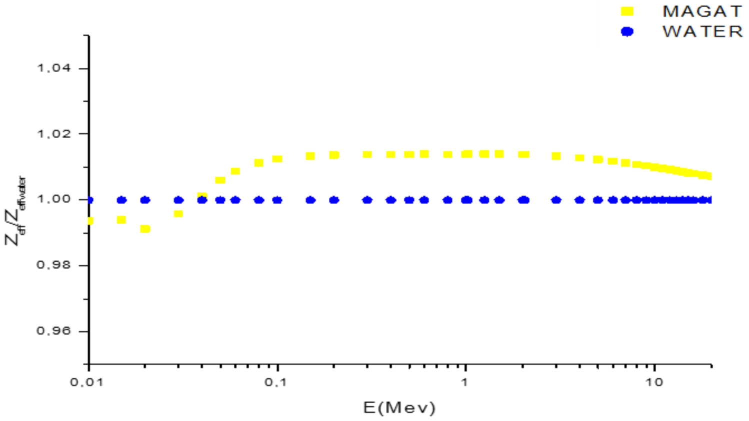

Fig. 2. The Z_{eff} values of the new MAGAT gel (2 mM THPC, 8 % gelatin, 6 % MAA) and water divided by those of water as a function of energy.

The Z_{eff} values measured are approximately equal with those of water: the Z_{eff} varies by just 0.1% in the low energy range, between 1 and 1.38% in the intermediate energy range, and up to 0.7% at high energy. The curves of the ratio of Z_{eff} of MAGAT to Z_{eff} of water as a function of energy are shown in Figure 2. We compared the Zeff of the novel MAGAT gel (2 mM THPC, 8% gelatin, 6% MAA) with that of water and found that it was more like water than to another MAGAT gel (10 mM THPC, 8% gelatin, 9% MAA) [24].

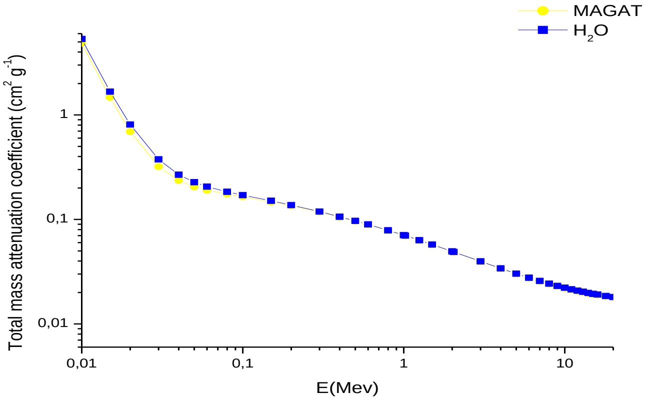

Fig. 3. Total mass attenuation coefficient of the new MAGAT gel and water.

Figure 3 shows the curves of mass attenuation coefficient (μ/ρ) of water and MAGAT gel as a function of energy. This coefficient was calculated using XCOM database [11]. The two curves have the same appearance; we note a relative deviation not exceeding 4% for low energies below 30 keV. For the rest of the energy range the difference is less than 1 %.

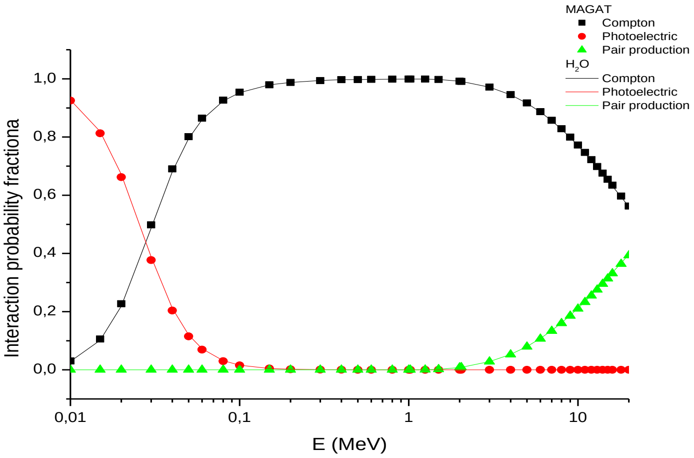

Fig. 4. Calculated interaction probability fractions of MAGAT gel and water.

Figure 4 shows the fractional interaction probability curves of the photoelectric effect, the Compton effect, and the pair creation. Water is composed of hydrogen and oxygen; the mass fraction of oxygen is dominant and has an important influence on the cross sections. In addition, oxygen has the highest mass fraction in the gel; this explains the interaction probability curves, which are almost identical with those of water.

The curves in Figure 5 show the total electron stopping power of water and MAGAT gel as a function of energy. The two curves are almost identical. The relative difference between the two stopping power curves is less than 0.5 %.

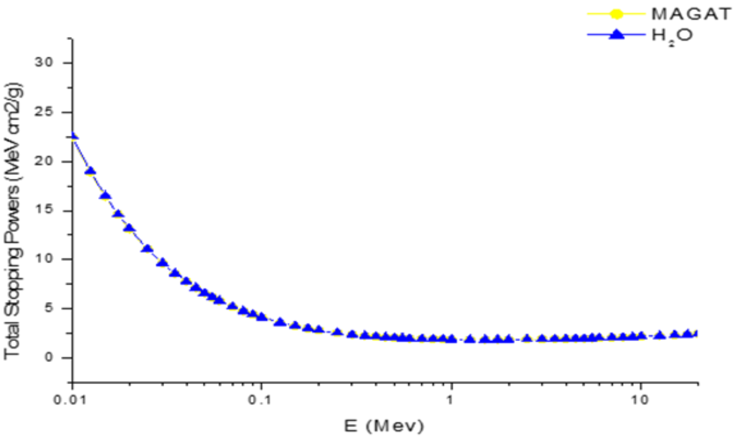

Fig. 5. Stopping power of the MAGAT gel and water.

STUDY OF THE GEL RESPONSE BY X-RAY TOMOGRAPHY

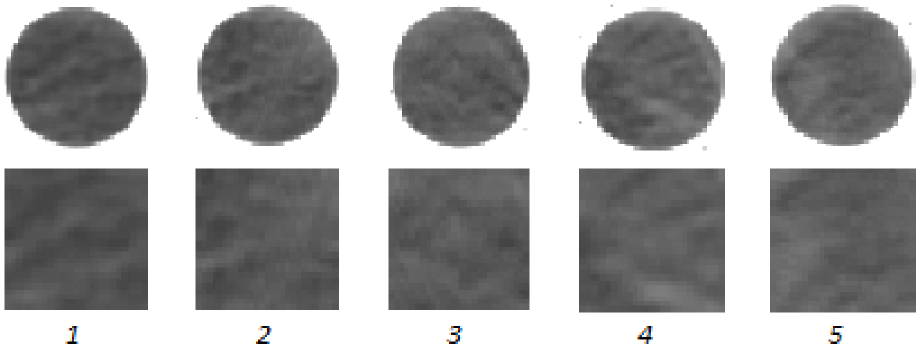

Fig. 6. The X-ray CT image of the new MAGAT gel dosimeter irradiated at 0, 2, 4, 6 and 8 Gy.

Figure 6 shows our measured X-ray CT images of the novel MAGAT gel. The response of the MAGAT gel to the X-ray scanner as a relation to dose is shown to be linear with a correlation coefficient $R = 0.97$. Figure 7 shows that the N_{CT} increases as the dose increases from 0 to 8 Gy. The *SNR* analysis of the images showed a variation of value between 41 and 43, which represents a good quality image. The dose sensitivity of the MAGAT dosimeter is found to be equal to 1.85±0.28 HU Gy^{-1}. The dose sensitivity of the number of our CT scans was 1 HU Gy^{-1} more than that in the previous study by Aljamal *et al.* [2]. These variations can be explained by the difference in time between the irradiation of the gel and the CT imaging and the differences in impurity of the main materials used in the preparation of the MAGAT gel. These results show that the MAGAT gel is suitable for use as a dosimeter for external irradiation.

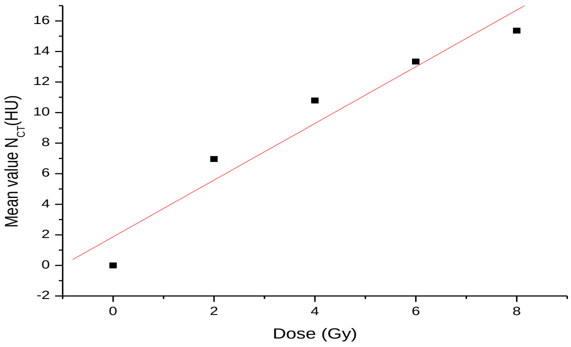

Fig. 7. MAGAT ΔN_{CT} (D) gel response.

CONCLUSION

We studied the radiological properties of a new MAGAT gel in order to determine its equivalence to water and tissue, knowing that water is considered as tissue equivalent in the clinical environment.

The new MAGAT gel dosimeter has a better tissue equivalence than others. Radiological properties such as the mass fraction of the elements composing the gel, the density, the cross section, the effective atomic number, and the stopping power show that the difference does not exceed 1 %, except in the photon energy range between 10 and 60 keV, where the total attenuation coefficient differs by 4 %. However, a slight difference of 1.38 % in Z_{eff} is observed in the intermediate energy range.

The new MAGAT gel prepared at a concentration of 6 % of methacrylic acid is a stable material with easy preparation under normal atmospheric conditions. This type of gel makes it possible to reproduce three-dimensional shapes and to model the different organs and biological tissues.

We proved that the novel MAGAT gel dosimeter is sensitive to ionizing radiation, its rate of polymerization grows with the absorbed dose, and its X-ray scanner reading is linear. The new MAGAT is tissue equivalent and it has a linear response, which allows us to conclude that it provides a valuable tool for the validation of the distribution of complex doses in radiotherapy.

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