Journal of the Korean Physical Society, Vol. 77, No. 12, December 2020, pp. 1238∼1247

A Novel Ultrasonic Gel Phantom Dosimetry for Evaluation of the Dose Response

Neda Goharpey and Manijhe Mokhtari-Dizaji*
Department of Medical Physics, Faculty of Medical Sciences, Tarbiat Modares University, Tehran 1411713116, Iran

Mohsen Bakhshandeh
Department of Radiology Technology, Allied Medical Faculty, Shahid Beheshti University of Medical Sciences, Tehran 1971653313, Iran

(Received 1 March 2020; accepted 15 June 2020)

Ultrasonic imaging is able to detect structural changes due to chemical reactions occurring due to ionizing irradiation. The purpose of this study to create a gel phantom dosimeter (developed MAGIC gel), which has ultrasonic properties equivalent to human tissue for readout with ultrasonic imaging. The speed of sound and the attenuation coefficient were determined as a function of the absorbed dose in the range of 0–50 Gy by using this dosimeter. A gel phantom was prepared by adding MAGIC polymer gel proprietary combinations in ultrasonic soft tissue-mimicking gel. Then, the ultrasonic parameters (response) of the samples, including the propagation speed of sound (SOS) and the attenuation coefficient (BUA) were measured in the absorbed dose range of 0–50 Gy in steps 2 Gy. The dose response curve is plotted and a sigmoid function is fitted. Ultrasonic images were recorded to assess the quality of the novel gel phantom. At 24 h post-irradiation, the gel samples were imaged by using a magnetic resonance (MR) scanner. The mean values of the transverse relaxation rates (R2) were taken. The sensitivities of the speed of sound and the attenuation coefficient parameters and the R2 parameter were determined for the soft tissue-mimicking ultrasonic gel phantom. The concentrations of gel phantom, including 14% gelatin, 0.25% graphite, and 2% formaldehyde, with a maximum variation in the speed of sound (21.9 ± 2.3, 20.5 ± 2.1, and 24.3 ± 3.3 m/s) and attenuation coefficient (49.6 ± 9.1, 29.5 ± 5.5, and 47.9 ± 15.4 dB/MHz·m) were selected, respectively. The sensitivities of the speed of sound and the attenuation coefficient parameters and the R2 parameter were determined for the soft tissue-mimicking ultrasonic gel phantom as 1.01 m/s, 2.9 dB/MHz·m, and 0.48 s^{-1} per Gy and for the MAGIC-f polymer gel as 0.79 m/s, 1.9 dB/MHz·m, and 0.26 s^{-1} per Gy (R = 0.98), respectively. A significant correlation was found between the MAGIC-f polymer gel and the ultrasonic soft tissue-mimicking gel phantom with the R2 parameter (R = 0.9). Thus, the ultrasonic tissue-mimicking gel phantom can be concluded to be suitable for read-out using ultrasound waves as a free radical polymerization sensor. The cost effectiveness due to the utility of edible gelatin and the formation of breast soft tissue-mimicking ultrasonic images due to the presence of graphite scattering particles are distinctive features of the gel phantom introduced in this study.

Keywords: Gel phantom, Tissue-mimicking material, Polymerization, Dosimetry
DOI: 10.3938/jkps.77.1238

I. INTRODUCTION

Over the past two decades, interest in the advancement of three-dimension (3D) gel polymer dosimeters to evaluate and verify the distribution of absorbed doses in clinical radiotherapy treatments has been a growing. A generic gel polymer is primarily composed of water, gelatin as a main matrix, monomers such as methacrylic acid (MAG: methacrylic acid gel), and oxygen scavengers [1]. A gel polymer is basically a type of hydrogel in which monomers are dissolved, and the water content commonly is approximately 90%. Primary experimental investigations concerning whether the abundant solutions of distinct compounds in the water have demonstrated that the solute is frequently not directly affected by the irradiation, but indirectly by some entity or entities produced from water [2]. Upon radiation, the molecules of water are dissociated into multiple, extremely reactive radicals and ions by a process known as "radiolysis." The cluster size and the types of radiolysis products that are

*E-mail: mokhtarm@modares.ac.ir

generated within the first femtoseconds depend on the type of irradiation and the energies of the principal particles [3].

The products of the radiolysis of water depends on the type of irradiation and the energies of the principal particles in the radiation. The amalgamation of two radicals or disproportionation leads the polymerization. Furthermore, the transfer of radical groups to other molecules, such as gelatin biopolymers, may terminate growth of the polymer radicals [4]. The gelatin matrix affects the polymerization so that an increase in the concentration of the gelatin matrix reduces the polymerization rate by creating cross-linking between monomers and the gelatin molecules [5]. Suppose that, in methacrylic-acid-based polymer gels, the methacrylic acid polymer chains react with the gelatin biopolymer chains in a process called "graft polymerization" [3]. This presumption is based on the observed physical properties of polymer gels, such as the propagation speed of sound, Young's modulus for various doses of radiation [6], the chemical stability, and the melting temperature of the gels [2].

Several studies have investigated the radiological tissue-equivalence of gel dosimeters [3]. When applying a dosimeter over the therapeutic energy range, the most significant considerations for radiological water equivalence are the mass densities and the relative numbers of electrons. For high-energy photon radiation, most gel dosimeters can be investigated as soft-tissue equivalents [7,8]. The extent of radiation-induced polymerization in the monomers within gel dosimeters depends on the absorbed dose [2,3]. Following polymerization in polymer gels, the magnetic, optical, physical, and mechanical properties of the dosimeters undergo changes that are utilized to evaluate the 3D dose distribution. This can be done by using a number of imaging modalities, such as magnetic resonance imaging (MRI) [2], optical computed tomography (OCT) [9], X-ray CT [10,11], Fourier-transform (FT)-Raman spectroscopy [12] and ultrasonography [6].

To date, MRI has been predominantly employed to explore the changes in the features of irradiated polymer gels by using the transversal relaxation rate parameter, despite the introduction of alternative techniques to MRI [3]. Watanabe *et al.* [13] discussed 3D dose quantification techniques: MRI, OCT and X-ray computed tomography. The available ultrasound techniques were not considered in their review because of their unproven measurements. Recently, an ultrasound quantification technique has been shown to appraise properly the variations in the absorbed doses based on ultrasonic properties such as the speed of sound and the attenuation coefficient [6]. However, ultrasound technique has been demonstrated to have potential for use as a measurement tool for read-outs of polymer gels [6]; still, it is not a commonly used method. In addition to the technical limitations that may exist, one reason for this may be related to the gel's composition and some adverse intrinsic features of the ultrasound technique.

A broad variety of test objects and phantoms have been developed to monitor and calibrate the performance of ultrasound scanners [14]. They are called tissue-mimicking materials (TTMs) and should mimic the physical characteristics of soft tissue, such as the speed of the sound (1540 m/s), attenuation coefficient (0.3–0.7 dB/cm·MHz), and scattering coefficient [15]. TMMs are composed of different types of materials in order to prepare soft- or hard-tissue-mimicking materials. However, materials containing water, gelatin, n-propanol alcohol, formaldehydes, and scatterers, such as graphite, polysaccharide particles, and glass beads, have been commonly used. The n-propanol alcohol controls the speed of sound so that the desired speed can be achieved by varying the concentration [16]. The small-diameter particles (approximately 1 micron) change the attenuation rate and the scattering levels, and the graphite particles can act as a scattering agent similar to normal tissue [17].

The common gel polymers are water-equivalent and echo-free in terms of ultrasound, so ultrasonic systems are not able to distinguish the radiation-induced polymerization. In addition, the basic combinations and the main matrix of both polymer gels and TMMs are identical, so that the ultrasonic TMMs with the addition of proprietary combinations of the MAGIC-*f* (methacrylic and ascorbic acid in gelatin initiated by copper-formaldehyde) polymer gel, including monomers and antioxidants, have become excellent cost-effective and accessible alternatives and compete with regular dosimeters for ultrasound investigations.

In this study, a gel phantom dosimeter (developed MAGIC gel) that has ultrasonic properties equivalent to human tissue was created for readout with ultrasonic imaging. The main components of the gel phantom, including gelatin, graphite, and formaldehyde were extracted, in order to achieve the best performance of the novel gel phantom as a free radical polymerization sensor for assessments via ultrasound waves. The physical parameters responsible for the variations in the speed of sound and the attenuation coefficient in the phantom were determined as a function of absorbed doses in the range of 0–50 Gy and were found to changes in the macromolecular structure of the components of the phantom due to irradiation.

II. MATERIALS AND METHODS

Gel phantoms were fabricated based on a combination of the Mokhtari [14] and the Fernandes [17] formulations with different concentrations of the two formulations. The samples were prepared and included n-propanol alcohol (Sigma-Aldrich Co., Missouri, USA), sodium benzoate (KFDA Co., Seoul, South Korea), deionized water, gelatin, methacrylic acid (Merck Co., Darmstadt, Germany), formaldehyde (Mojallali Chemical Complexes, Tehran, Iran), ascorbic acid (Fisher Scientific Co., Acros

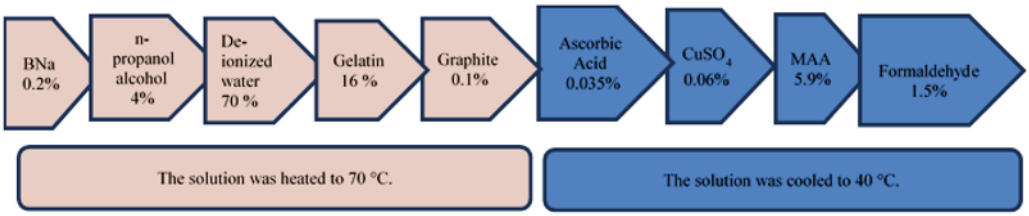

Fig. 1. The steps of preparation of the gel-phantom dosimetry.

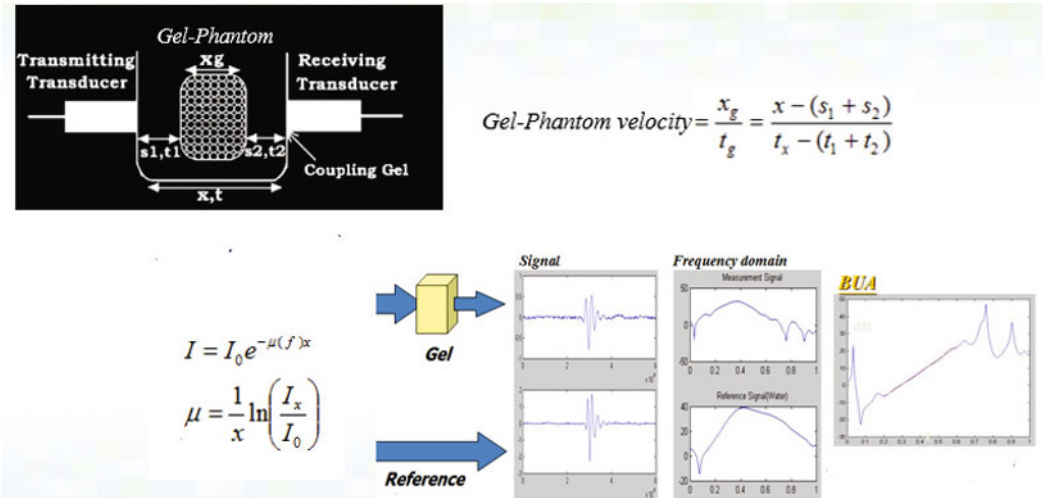

Fig. 2. Schematic of measurement of sound speed and attenuation coefficient.

Organics, USA), and copper sulfate (Merck Co., Darmstadt, Germany). The vast majority of polymer gels are made using commercial gelatin as the gelling agent, which is costly. In this study, to reduce the costs, we used flavorless edible gelatin powder [14] and added sodium benzoate to preclude bacterial contamination. The n-propanol alcohol adjusted the speed of the sound to an appropriate [15].

To prepare the gel phantom samples, after having dissolved the sodium benzoate in n-propanol alcohol by heating, we first added the deionized water and then the gelatin over a period of 120 s to the mixture, with simultaneous stirring, and heated up to 70 °C until the gelatin had entirely melted. The solution was cooled to 40 °C after having added the graphite. Next, ascorbic acid, copper sulfate, formaldehyde, and, after five min, methacrylic acid were added to the gel phantom. The obtained solution was poured into Perspex molds ($6.5 \times 3.5 \times 4.0$ cm^3) and sealed to prevent oxygen contamination. After manufacture, all samples were stored in a shaking water bath for 30 min at 10 rpm in a horizontal manner in order to make them uniform. Then, they were kept in a refrigerator for 24 h at 10 °C (Fig. 1).

After 24 hours, the gel samples were irradiated using Cobalt 60 with a field size of 30×30 cm^2) (Samples were placed at the center of radiation to deliver a uniform dose with the accuracy of ±2%) the source-to-surface distance (SSD) and the depth were 80 cm and 1.5 cm, respectively. The dose rate at a depth of 0.5 cm for the reference field was about 88 cGy per minute. For each gelatin concentration, three samples were prepared. Gel samples containing various amounts of edible gelatin were irradiated with a dose of 36 Gy and compared with non-irradiated ones. Dose calculations on the central axis of the gel phantoms at depth of 1.5 cm were performed by using the Isogray (Version 4.103.18L) treatment planning system. Masoumi *et al.* [18] suggested that the dose-response has a sensitivity to the speed of the sound and the attenuation coefficient of MAGIC-f gel at an absorbed dose of 36 Gy.

One day following irradiation, when the samples had reached thermal equilibrium at the room temperature, the gel phantoms were investigated using an ultrasonic measuring device (Version 2.01.12, Osteosys Co., Ltd., Seoul, Korea) [14,15] at a frequency of 500 kHz based on the transmission method (with resolutions of ±0.1 cm/s and ±0.1 dB/MHz for the speed of sound and the attenuation coefficient, respectively). The samples were placed in the holder of the device so that the centers of phantoms were in front of ultrasonic source and detector.

Before each read-out, the system was calibrated with a tissue-equivalent standard sample; then, the ultra-

sonic parameters (response) of the samples, including the propagation speed of sound (SOS) in m/s and the attenuation coefficient (Broadband Ultrasound Attenuation: BUA) in dB/MHz were measured in the absorbed dose range of 0–50 Gy in steps of 2 Gy (Fig. 2). The read-outs were repeated 3 times for each sample to reduce the error to below 10%. The dose-response curve was plotted, and a sigmoid function fitted with the following general formula was used to fit the experimental curve:

$$y = d + \frac{a-d}{1+(\frac{x}{c})^2}, \quad (1)$$

where a (minimum asymptote), b (steepness of the curve), c (inflection point) and d (maximum asymptote) were calculated in the calibration curve fitting by using MATLAB software.

Sigmoid functions are primarily used to fit phase-shifting phenomena, such as radiation-induced polymerization [19]. In this study, in order to have a more accurate and precise fit (fitting coefficient = 0.99), we used a 4-parameter sigmoid function [20]. The slope of the linear part of the dose-response curve from 0 to 10 Gy was assessed as the dose sensitivity ($s^{-1}\cdot Gy^{-1}$). The nonlinear response of gel samples at high doses is due to changes in the polymeric aggregates reactivity [21]. Our use of the 4-parameter sigmoid function allowed us to account for that nonlinearity. For low-dose irradiation, the dose response of gel is linearly proportional to dose and the linear slope is considered. In standard fractionation, the total prescription dose for breast cancer is 50 Gy in 25 fractions (2 Gy per fraction). Because the gel phantom mimics breast soft tissue, we investigated the dose-response of the samples until 50 Gy. In this study, B-mode two-dimensional (2D) images, with a central frequency of 10 MHz (pixel size ±0.01 mm) and a breast tissue imaging protocol to assess the quality of the novel gel phantom in terms of ultrasonic images, were recorded using an ultrasound system (Sonix TOUCH Ultrasound System, Ultrasonix Medical Co. Canada).

At 24 h post-irradiation, the gel samples (6.5 × 3.5 × 4.0 cm^3) were imaged by using a 1.5T MR scanner (Siemens Magnetom Avanto) after having achieved the thermal equilibrium. The following parameters were used: 4000 ms TR, 22 ms TE1 (16 echoes) and 3-mm slice thickness with a 350 × 350 mm^2 field of view. The mean values of the transverse relaxation rates (R2) were taken as the inverse of the transverse relaxation time (T2) average, which was determined in rectangular regions of interest located at the center of each sample.

All tests were repeated least at three times, and the resultant parameters were expressed as means standard deviations (SDs). The paired sample t-test analysis was performed to examine the differences among the samples of each group. P-values less than 0.05 were considered as significant. The dose-response curves for the parameters of speed of sound and the attenuation coefficient were achieved over the above range of radiation doses. Based on the dose-response curves, we use correlation analyses to evaluate the importance of the ultrasonic parameters on the read-out of the absorbed doses. All statistical analyses were performed using the SPSS software package (SPSS V. 16, Inc. Chicago, IL, USA).

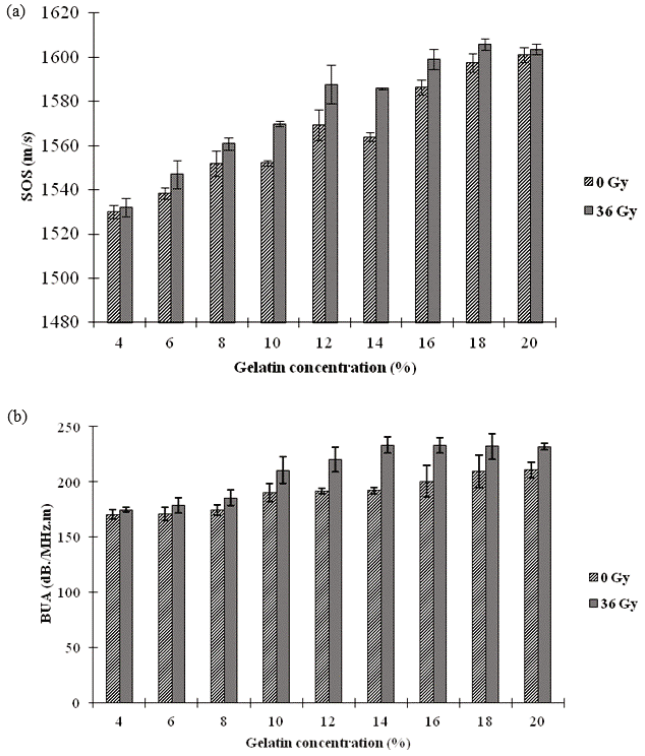

Fig. 3. The variations of a) the speed of sound (SOS) and b) attenuation coefficient (BUA) before and post-irradiation of 36 Gy containing different concentrations of flavourless edible gelatin (4–20% in 2% increments). A 14% concentration is selected as optimum.

III. RESULTS

Figures 3(a) and (b) show the variations of ultrasonic parameters, the speed of sound and the attenuation coefficient, before and after irradiation at 36 Gy for different concentrations of the flavorless edible gelatin (4–20% in 2% increments). Dosimeters became milky after irradiation, which show that polymerization occurred in the samples. Manifestly, the ultrasonic parameters depend upon the gelatin's composition and the speed of sound and the attenuation coefficient increase with increasing amounts of gelatin. However, the amount of gelatin does not appear to affect the sensitivity of the dosimeters at concentrations higher than 14%, at where saturation occurs. The results of t-test statistical analyses indicate that for the speed of sound at gelatin concentrations of 10, 12, 14, 16, and 18% and for the attenuation coefficient at gelatin concentrations of 12, 14, 16, and 20%

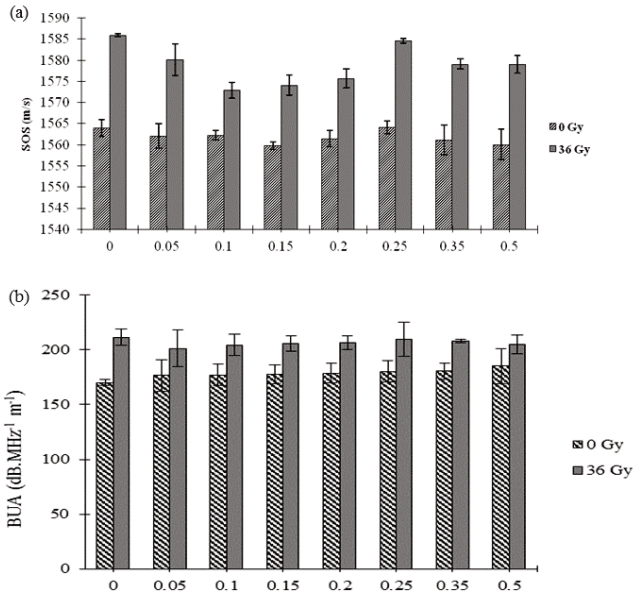

Fig. 4. Variations of (a) the speed of sound (SOS) and (b) the attenuation coefficient (BUA) before and after irradiation with 36 Gy for different concentrations of graphite powder (0.05 to 0.50%). The concentration of 0.25% is selected as optimum.

the gels fabricated with gelatin are significantly different ($p < 0.05$) before and after 36 Gy irradiation. The gel phantom containing 14% edible gelatin was chosen because its ultrasonic parameters had the greatest absolute difference before and after 36 Gy irradiation. The changes in the speed of sound and the attenuation coefficient were 21.9 ± 2.3 m/s and 49.6 ± 9.1 dB/MHz·m, respectively. Therefore, the dosimeter containing the 14% edible gelatin with maximum variations at a 36-Gy absorbed dose in the speed of sound (1.4%) and the attenuation coefficient (21.5%) was selected for further investigated.

To specify the optimized graphite concentration of the gel phantom after 36 Gy of irradiation, we prepared sets of gel phantoms containing 0.05, 0.1, 0.15, 0.2, 0.25, 0.35, and 0.5% graphite powder. The variations in the ultrasonic parameters for different concentrations of graphite 24 h after irradiation at 36 Gy at 25 °C, are shown in Fig. 4. An increase in the graphite concentration will provide images similar to breast tissue, and the amount of increase is not limited due to the transmission method used for read-out of samples. Therefore, the imaging ultrasound method was used to choose the optimal concentration of graphite in terms of imaging quality.

Figure 4 shows that the changes in the speed of sound and the attenuation coefficient before and after irradiation at 36 Gy in gel phantoms not containing the graphite powder is higher. According to the measured ultrasonic parameters, the transmission technique, and the B-mode images recorded from gels containing different concentrations of graphite samples, the ultrasonic soft tissue-mimicking phantom with a graphite concentration of 0.25% was confirmed to be the best in terms of image quality and the possibility of ultrasonic parameters being recorded using the transmission method. As Fig. 5(c) shows, the gel without graphite is echo-free. If images with ultrasonic high contrast similar to that of soft tissue are to be achieved, the ultrasound images, which are completely transparent, must be converted to soft tissue-mimicking images so that they can allow extraction of the physical parameters (Figs. 5(a) and 5(b)). The highest absolute differences in the speed of sound and the attenuation coefficient before and after irradiation at 36 Gy were 20.5 ± 2.1 m/s and 29.5 ± 5.5 dB/MHz·m, respectively. Ultrasonic images of the gel phantom containing 0.25% graphite are shown in Fig. 5.

The concentration of formaldehyde was varied from 0.5–3% in increments of 0.5%. The variations in speed of sound and the attenuation coefficient for different concentrations of formaldehyde at absorbed doses of 36 Gy are displayed in Fig. 6. The results show that with increasing formaldehyde concentration, the changes in the speed of sound and the attenuation coefficient increase after irradiation at 36 Gy. The gel phantom containing 2% formaldehyde, when compared with those containing other concentrations, has the maximum absolute differences in the speed of sound and the attenuation coefficient of samples before and after irradiation at 36 Gy, which were 24.3 ± 3.3 m/s and 47.9 ± 15.4 dB/MHz·m, respectively ($p < 0.05$).

The speeds of sound versus the absorbed dose for the ultrasonic gel phantom and the MAGIC-f polymer gel are shown in Fig. 7. The data could be fitted with a sigmoidal curve over the dose range of 0–50 Gy and with a linear curve in the range of 0–10 Gy with a correlation coefficient of 0.99. The speed of sound varied from 1540.0 to 1562.6 m/s for the ultrasonic gel phantom and from 1529.8 to 1554.3 m/s for the MAGIC-f polymer gel. The dose sensitivity (slope) in the linear region was found to be 101 ± 0.01 cm/s per Gy for the ultrasonic gel phantom and 79 ± 0.05 cm/s per Gy for the MAGIC-f gel. The variation in the coefficient was found to be less than 10% of all measurements ($p < 0.05$).

The attenuation coefficient (BUA) parameter is indicated in Fig. 8 for both the ultrasonic gel phantom and the MAGIC-f dosimeter. The results show that the dose sensitivities in the linear region (0–10 Gy) were 2.9 ± 0.1 dB/MHz·m per Gy for the ultrasonic gel phantom and 1.9 ± 0.2 dB/MHz·m per Gy for the MAGIC-f gel. The variations in the attenuation coefficient were 127.8 to 201.9 dB/MHz·m for the ultrasonic gel phantom and 154.2 to 205.1 dB/MHz·m over the dose range of 0–50 Gy for the MAGIC-f polymer gel.

The R2 dose-response curves over the dose range of 0–50 Gy and the linear response of R2 in the range of 0–10 Gy for the ultrasonic gel phantom and the MAGIC-f polymer gel are shown in Fig. 9. The R2 parameter changes were from 7.1 to 21.2 s^{-1} for the ultrasonic gel

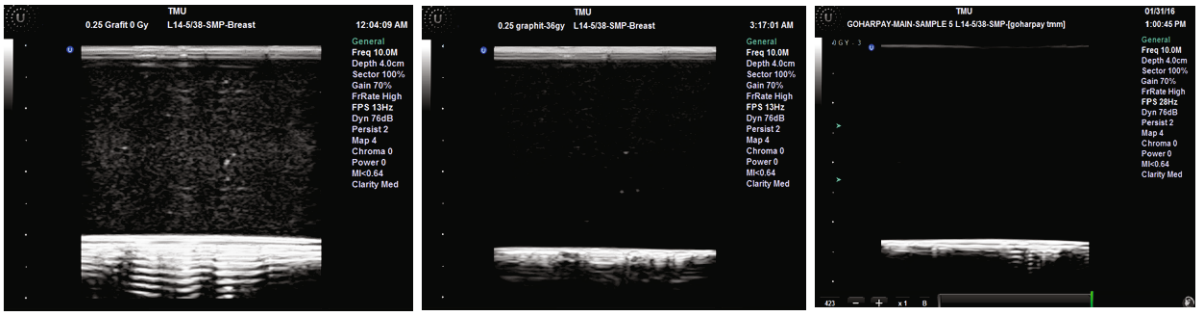

Fig. 5. B-mode images of a gel phantom containing 0.25% graphite (a) before and (b) after irradiation with 36 Gy. (c) Ultrasonic image of the gel-phantom without graphite. (The images were taken in the Ultrasound Laboratory of Tarbiat Modares University.)

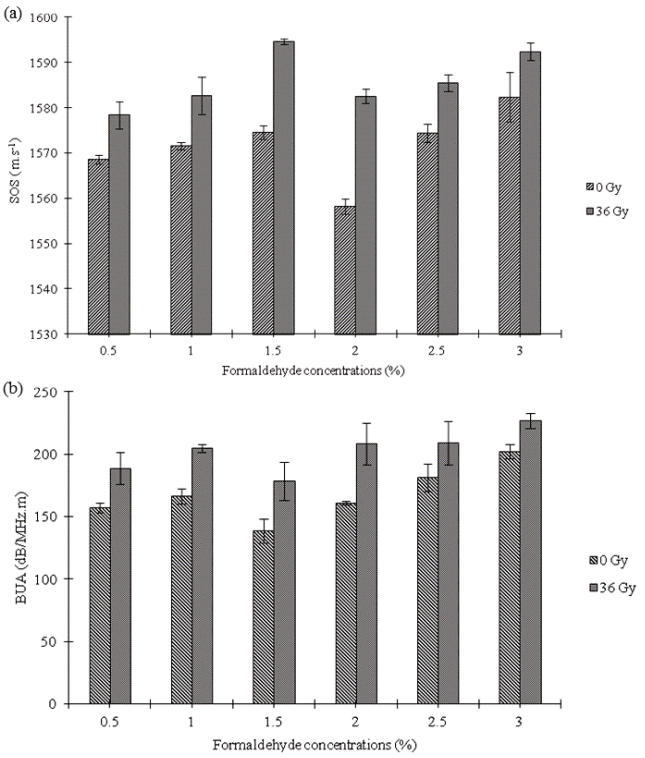

Fig. 6. Variations of (a) the speed of sound (SOS) and (b) the attenuation coefficient (BUA) before and after irradiation with 36 Gy for different concentrations of formaldehyde (0.5 to 3.0%). The concentration of 2% is selected as optimal.

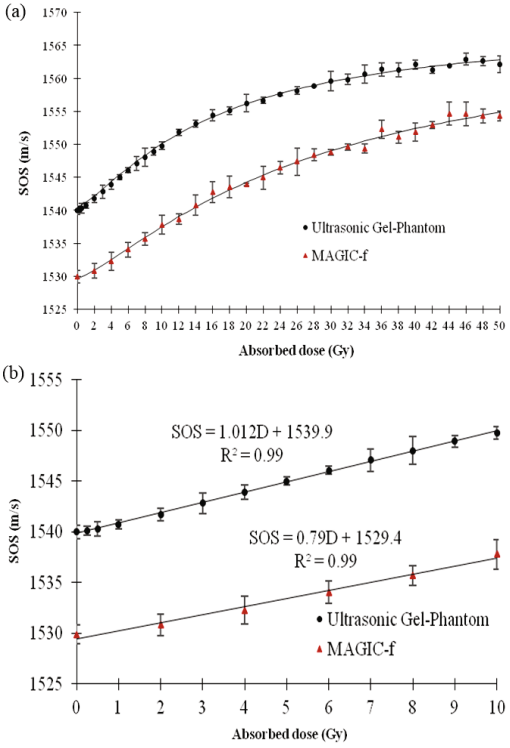

Fig. 7. Speed of sound versus the absorbed dose for the ultrasonic gel phantom and the MAGIC-f polymer gel fitted with (a) a sigmoidal curve over the dose range of 0–50 Gy and (b) a linear curve in the range of 0–10 Gy with a correlation coefficient of 0.99.

phantom and 1.8 to 9.1 s^{-1} for the MAGIC-f gel. The dose sensitivities obtained were 0.48 ± 0.01 s^{-1} per Gy for the ultrasonic gel phantom and 0.26 ± 0.01 s^{-1} per Gy for the MAGIC-f gel in the linear region. The results obtained from the ultrasonic parameters and the R2 dose-response curves are summarized in Table 1. In Table 1, the 4-parametric sigmoidal function values obtained from MATLAB are shown for the ultrasonic gel phantom and the MAGIC-f gel polymer.

Figure 10 shows the correlation between the speed of sound and the attenuation coefficient with R2 for both the ultrasonic gel phantom and the MAGIC-f polymer gel. The correlation coefficient over the dose range of 0–50 Gy was determined to be 0.99 in the gel phantom and 0.98 in the MAGIC-f polymer ($p < 0.05$). The slopes of the diagram were 0.53 for the gel phantom and 0.36 for the polymer gel. The results show a significant correlation between the speed of sound and the attenuation coefficient extracted from ultrasound measurements with the spin-spin relaxation rates (R2) obtained from MRI

Table 1. Sigmoidal function parameters and linear regression function of the dose-response and the linear regression functions: the speed of sound, the attenuation coefficient and R2 for the ultrasonic gel phantom and the MAGIC-f polymer gel over the range from 0 to 50 Gy (linear region of 0–10 Gy).

		Index	SOS (m/s)	BUA (dB/MHz·m)	R2 (s^{-1})
Ultrasonic gel- phantom	Sigmoidal function	a	1540	126.9	7.2
		b	1.3	1.3	1.5
		c	16.2	20.4	21.8
		d	1568	212.5	25.8
	Fitting coefficient		0.99	0.99	0.99
	Linear regression function		SOS = 1.0 × D + 1539.9	BUA = 2.9 × D + 126.4	R2 = 0.5 × D + 6.9
	Sensitivity (Gy^{-1})		1.0 ± 0.01	2.9 ± 0. 1	0.5 ± 0.008
	p-value		<0.05	<0.05	<0.05
MAGIC-f polymer gel	Sigmoidal function	a	1530	155	1.8
		b	1.3	2.3	1.1
		c	28.4	28.8	26.9
		d	1567	243.5	12.6
	Fitting coefficient		0.99	0.98	0.99
	Linear regression function		SOS = 0.8 × D + 1529.4	BUA = 1.9 × D + 154.3	R2 = 0.3 × D + 1.9
	Sensitivity (Gy^{-1})		0.8 ± 0.1	1.9 ± 0.2	0.3 ± 0.0
	p-value		<0.05	<0.05	<0.05

for the ultrasonic gel phantom and the MAGIC-f polymer gel. The slope of the linear regression function for the ultrasonic gel phantom was greater than that of the MAGIC-f polymer gel, where indicates a higher radio sensitivity for the ultrasonic gel phantoms.

IV. DISCUSSION

In this study, the gelatin, graphite, and formaldehyde concentrations of an ultrasonic gel phantom were varied, and the appropriate concentration of formaldehyde for 14% gelatin and 0.25% graphite with the best ultrasonic response to 36 Gy absorbed doses was selected. Subsequently, the dose-response curves of the gel phantom containing selective and specific compositions of the MAGIC-f polymer gel (methacrylic acid as monomer and ascorbic acid as antioxidant) were investigated. The changes in the speed of sound, the attenuation coefficient, and R2 due to variations in the chemical structure of the gel phantom post-irradiation were measured as functions of absorbed doses over the range of 0–50 Gy in increments of 2 Gy.

The extent of the free radicals released through water radiolysis within the gel was proportional to the dose delivered to the gel dosimeter. Consequently, the resultant quantity of the formed polymer was also proportional to the absorbed dose until an upper limit had been reached, after which the consumption of monomers led to saturation, so the value of polymerization plateaus after the optimal range was exceeded [4]. In 2002, Mather *et al.* [6] demonstrated that ultrasonography had the potential to detect and evaluate these chemical variations in polymer gel dosimeters.

Gelatin is a network of biopolymer chains composed of collagen connections (with an approximate length of 280 nm) and a combination of three polypeptide chains [21]. This structure helps to form a helix structure, which is called "gelation." Polymerization of methacrylic acid occurs through the interaction between the monomer and the gelatin in a particular locality of the gelatin (along the main chain or side chains) or cross-links in it [2].

For the investigated gel phantom, which contained various concentrations of edible gelatin (4–20%), an increase in the amount of gelatin led to an increase in the ultrasonic dose-response of the speed of sound and the attenuation coefficient. A 14% concentration was selected as the optimum amount of gelatin because higher concentrations appeared not to affect the dose-response having reached saturation. This result indicated that using gelatin at concentrations above a value had a slight impact on the consumption of monomers [5]. The results of this study are consistent with the findings of other researchers and show that higher amounts of gelatin can improve the response of radiosensitive gels to radiation. The concentrations used in this study (4% to 20%) were different from those used other studies (4% to 11.5% [22] and 0% to 12%), [1] which could be due to the replacement of the commercial gelatin with an edible one.

In this study, the effects of the presence and an increase in the amount of graphite used as a scattering

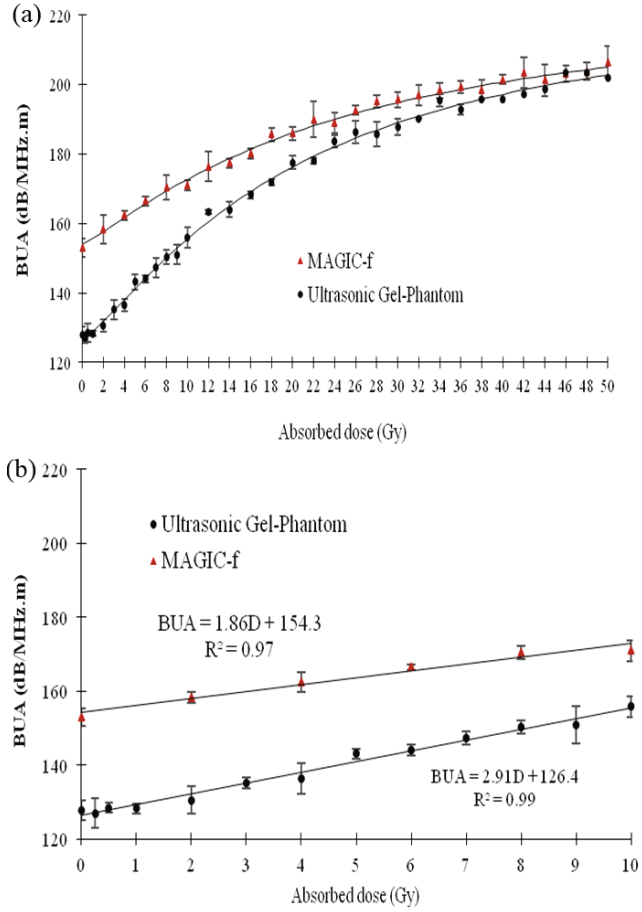

Fig. 8. Attenuation coefficient (BUA) parameter versus the absorbed dose for the ultrasonic gel phantom and the MAGIC-f polymer gel fitted with (a) a sigmoidal curve over the dose range of 0–50 Gy and (b) a linear curve in the range of 0–10 Gy with a correlation coefficient of 0.97.

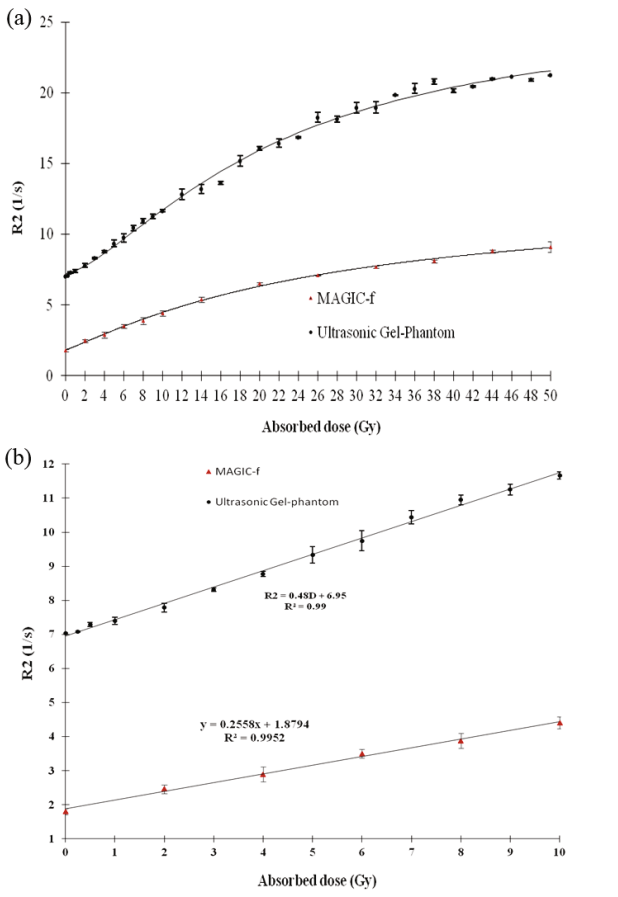

Fig. 9. R2 versus the absorbed dose for the ultrasonic gel phantom and the MAGIC-f polymer gel fitted with (a) a sigmoidal curve over the dose range of 0–50 Gy and (b) a linear curve in the range of 0–10 Gy with a correlation coefficient of 0.97.

agent on the dose-response of the soft tissue-mimicking gel phantom were investigated. Note that the scatterers were the main factors of the ultrasonic gel phantom used to create tissue equivalent images. The acquired results show that the 0.25% concentration was the optimal for achieving the maximum ultrasonic properties through transmission measurements. The increase in the graphite concentration improved the quality of the breast tissue equivalent images. However, due to the use of the transmission read-out method, the amount of graphite that could be used was limited. For concentrations greater than 0.35%, saturation occurred, resulting in variations in the percentages of the ultrasonic parameters, rather than the achievement of an optimal concentration, lessening the post-irradiation difference at 36 Gy; however, the B-mode imaging method presented no such problem. With the addition of graphite, the ultrasonic parameters' dose-responses lessened, but an acceptable trend was still seen. The graphite concentration determined the attenuation coefficient and generated ultrasonic scattering in the sample [14].

Formaldehyde was used to increase the melting point of the ultrasonic tissue-mimicking gel. Formaldehyde increased cross-linking and led to an increase in the melting point. A number of researchers have applied this idea to increase the melting temperature of the MAGIC-f gel dosimeter [21]. In this study, 2% formaldehyde, in comparison with other concentrations, resulted in the greatest physical parameters' dose-response. With that considerations, in this study, for the gel phantom containing 14% edible gelatin and 0.25% graphite, the 2% formaldehyde concentration led to a stiff of the gel structure despite its high melting point. However, the 2% formaldehyde composition, in addition to improving the ultrasonic dose-response and thermal stability, made the gel phantom a very good soft tissue equivalent in terms of quality and flexibility.

We should note that formaldehyde increases the gel's melting point by increasing the cross-linking reactions in gelatin molecules [17]. On the other hand, based on our

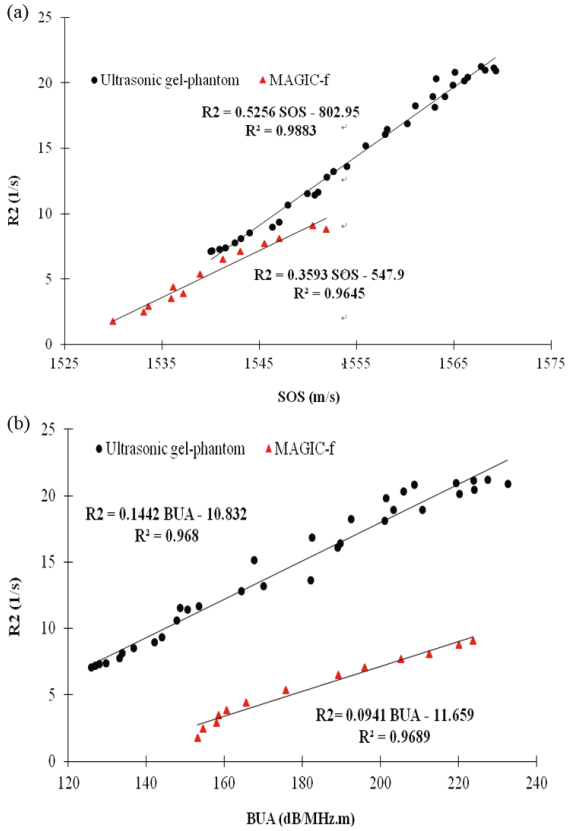

Fig. 10. Correlation of (a) the speed of sound and (b) the attenuation coefficient with R2 for both the ultrasonic gel phantom and the MAGIC-f polymer gel in the range of 0–50 Gy.

knowledge, no study of the interactions between graphite and gelatin and the graphite particles dispersed in the gel phantom have been published. Thus, we actually find the optimum concentration of formaldehyde for the mixture of 14% gelatin plus 0.25% graphite.

The results obtained for the gel phantom indicated that the ultrasound parameters in the linear region increased and then reached saturation with increasing absorbed dose from 0 to 10 Gy. The nonlinear response to high doses is conventional for polymer gels and occurs due to changes in the polymeric mass reaction. When the gel absorbs a high dose, polymers or polymer radical are generated in high concentrations and reduce polymerization diffusion. That is why a high concentration of polymeric masses diminishes the polymerization diffusion rate through the reaction site, thus, hindering the penetration of available monomers. However, this is not a limitation for gel dosimetry, so the calibration curve can be assessed by fitting the appropriate curve at lower and higher doses [22]. The dependency of the speed of sound on the absorbed dose for the gel phantom was compatible with that of Mather *et al.*'s study [6] of the MAGIC-f gel polymer. In the present study, the highest sensitivity of the speed of sound obtained over the dose range of 0–10 Gy was 101 ± 0.10 cm/s per Gy, which demonstrated greater variations than Mather *et al.*'s study (17.8 ± 0.6 cm/s·Gy). The sensitivity of the attenuation coefficient was 2.9 ± 0.1 dB/MHz per Gy, which is less than that of the Mather *et al.*'s study (4.7 ± 0.3 dB/MHz·Gy), but is more sensitive than that of Khoei *et al.*'s study (1.4 ± 0.08 dB/MHz·Gy) [23]. This may be because of the differences in the frequency of the measurement device used in this study (0.5 MHz versus 4 MHz). According to Fig. 6, the slope had a slight increase in sensitivity. The proposed gel phantom was not supposed to replace the MAGIC-f gel in this study, meaning this gel was not introduced as an alternative to the MAGIC-f gel. Our goal is the increased efficiency of gel dosimeters based on read-outs using ultrasonic imaging. Because the MAGIC-f gel is not tissue equivalent in terms of ultrasound images (it is water equivalent), by changing the concentration of gelatin and formaldehyde and by adding graphite as a dispersion, we were able to define this gel as tissue equivalent in terms of acoustics.

Polymer gel dosimeters are hydrogels containing abundant (90%) water, and the speed of sound through them is due to a combination of compressibility and mass density. The speeds of sound in water, fat, muscle, soft issue, and bone are 1480, 1459, 1580, 1540, and 4080 m/s, respectively [14]. The soft tissues and muscles speeds within in the range of 0–50 Gy vary (1540 to 1562.6 m/s). According to the results obtained from the dose-response curve, the sensitivities of the ultrasonic soft tissue-mimicking gel phantom to the speed of sound, attenuation coefficient, and R2 parameter were 27.85%, 52.63%, and 84.61%, respectively, greater than those of the MAGIC-f gel.

V. CONCLUSION

By adding a monomer and an antioxidant to the TMM and evaluating the effects of diverse concentrations, we fabricated a novel gel phantom with the highest compatibility to ultrasonic soft tissue. This study indicated that flavorless edible gelatin is a suitable substitute for commercial gelatins and that a ultrasonic soft tissue-mimicking gel can be introduced as a novel gel phantom in ionizing radiation dosimetry using ultrasound parameter read-outs based on the absorbed dose. Ultrasonography is able to detect the chemical changes upon radiation. The manifest features of this gel phantom are its cost effectiveness due to the use of an edible gelatin and its ability to form US images of breast tissue equivalence due to the scattering by graphite particles.

ACKNOWLEDGMENTS

This study was approved by Faculty of Medical Sciences, Tarbiat Modares University.

REFERENCES

[1] S. Hayashi *et al.*, Radiat. Phys. Chem. **79**, 803 (2010).
[2] Y. De Deene, J. Phys. Conf. Ser. **3**, 34 (2004).
[3] C. Baldock, J. Phys. Conf. Ser. **777**, 12 (2017).
[4] Sh. Smith *et al.*, Med. Phys. **42**, 6798 (2015).
[5] M. Lepage *et al.*, Med. Biol. **46**, 2827 (2001).
[6] M. L. Mather *et al.*, Phys. Med. Biol. **47**, 4397 (2002).
[7] A. J. Venning, K. N. Nitschke, P. J. Keall and C. Baldock, Med. Phys. **32**, 1047 (2005).
[8] S. Brown *et al.*, Appl. Radiat. Isot. **66**, 1970 (2008).
[9] M. Oldham and L. Kim, Med. Phys. **31**, 1093 (2004).
[10] M. Hilts, C. Audet and C. Duzneli, Phys. Med. Biol. **45**, 2559 (2000).
[11] J. V. Trapp, S. A. Back and M. Lapage, Phys. Med. Biol. **46**, 2939 (2001).
[12] L. Rintoul, M. Lepage and C. Baldock, Appl. Spectrosc. **57**, 51 (2003).
[13] Y. Watanabe, L. Warmington and N. Gopishankar, World J. Radiol. **9**, 112 (2017).
[14] M. Mokhtari-Dizaji, Ultrasound Med. Biol. **27**, 1713 (2001).
[15] E. L. Madsen, G. R. Frank and F. Dong, Ultrasound Med. Biol. **24**, 535 (1998).
[16] M. O. Culjat, D. Goldenberg, P. Tewari and R. S. Singha, Ultrasound Med. Biol. **36**, 861 (2010).
[17] J. P. Fernandes, B. F. Pastorello, D. B. Araujo and O. Baffa, Phys. Med. Biol. **53**, N53 (2008).
[18] H. Masoumi, M. Mokhtari-Dizaji, A. Arbabi and M. Bakhshandeh, Dose-Response **14**, 1 (2016).
[19] M. V. Papoutsaki *et al.*, Phys. Med. **2**, 1 (2013).
[20] J. W. A. Findlay and R. F. Dillard, AAPS J. **9**, 260 (2017).
[21] J. F. Pavoni and O. Baffa, Radiat. Meas. **47**, 1074 (2012).
[22] J. J. Luci, H. M .Whitney and J. C. Gore, Phys. Med. Biol. **52**, N241 (2007).
[23] S. Khoei, J. V. Trapp and C. M. Langton, J. Phys. Conf. Ser. **59**, 444 (2014).