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● *Original Contribution*

AN IMPROVED TISSUE-MIMICKING POLYACRYLAMIDE HYDROGEL PHANTOM FOR VISUALIZING THERMAL LESIONS WITH HIGH-INTENSITY FOCUSED ULTRASOUND

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Abstract—A recipe was created to improve the tissue-mimicking (TM) bovine serum albumin (BSA) polyacrylamide hydrogel (PAG) reported in our previous study (Choi MJ, Guntur SR, Lee KI, Paeng DG, Coleman AJ. Ultrasound Med Biol 2013; 29:439–448). In that work, the concentration of acrylamide in TM BSA PAG was increased to make its attenuation coefficient the same as that of a tissue. However, this increase made the PAG stiffer and less homogeneous. In addition, the increase in acrylamide caused a significant increase in temperature over the denaturation threshold of BSA during polymerization, which required forced cooling so that the PAG did not become opaque at room temperature after polymerization. To eliminate those shortcomings, we substituted the increased acrylamide with a viscous polysaccharide liquid (corn syrup). The concentration of corn syrup was optimized to 20% (w/v, tested in the volume of 50 mL), so that the acoustic properties of the PAG would be close to those of human liver. The improved TM (iTM) BSA PAG constructed in this study had a speed of sound of 1588 ± 9 m/s, an attenuation coefficient of 0.51 ± 0.06 dB cm^{-1} at 1 MHz and a backscattering coefficient of 0.22 ± 0.09 × 10^{-3} sr^{-1} cm^{-1} MHz^{-1}. The density and acoustic impedance were 1057 kg/m^3 and 1.68 MRayl, respectively, and the non-linear parameter (*B/A*) was 5.9 ± 0.3. The thermal, optical and mechanical properties were almost the same as those of the BSA PAG (Lafon et al.2005). Experimental verification indicated that the thermal lesions visualized in the proposed iTM BSA PAG by high-intensity focused ultrasound were highly reproducible. In conclusion, iTM BSA PAG was proven to eliminate TM BSA PAG shortcomings effectively and is expected to be a promising test phantom for clinical high-intensity focused ultrasound device. (E-mail: mjchoi@jejunu.ac.kr) **© 2014 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Tissue mimicking, Phantom, Polyacrylamide hydrogel, Bovine serum albumin, High intensity focused ultrasound, Polysaccharide, Corn syrup, Visualization, Thermal lesion.**

INTRODUCTION

An optically transparent polyacrylamide hydrogel (PAG) for visualizing high-intensity focused ultrasound (HIFU)-induced thermal lesions was constructed with protein such as bovine serum albumin (BSA) or egg white as a temperature-sensitive indicator, using denaturation of protein under thermal excitation (Lafon et al. 2005; Takegami et al. 2004). However, the standard PAG proposed by Lafon et al. (2005) does not acoustically mimic biological tissues. For instance, the attenuation coefficient is much less than that of tissue, and unlike tissues, the standard PAG does not scatter ultrasound (Choi et al. 2012; Lafon et al. 2005). A tissue-mimicking (TM) BSA PAG whose acoustic properties were similar to those of human liver was reported in our previous study (Choi et al. 2013).

The thermal lesions visualized in TM BSA PAG by HIFU, however, have irregular boundaries and are often accompanied by fragments (Choi et al. 2013). Lesion formation in TM BSA PAG is less reproducible compared with that in standard BSA PAG. This is attributed to the increase in the concentration of acrylamide that affects the elastic property of TM BSA PAG. The increase in acrylamide concentration makes the PAG stiffer and less uniform after polymerization, which may result in the thermal lesions visualized in the PAG being less reproducible. In addition, the increase in acrylamide caused a significant temperature rise over the protein BSA denaturation threshold during polymerization.

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This indicated that additional cooling is required for the PAG to remain transparent at room temperature after polymerization.

The problems caused by the increase in acrylamide concentration in TM BSA PAG (Choi et al. 2013) may be solved by replacing the increased acrylamide with a viscous liquid. This approach is based on the results of our experimental observation that the PAG ultrasonic attenuation is effectively controlled using corn syrup (Donald et al. 2004), a commercial polysaccharide product that is known to enhance ultrasonic absorption and dispersion (Bamber 2004; Hawley and Dunn 1969, 1970). The increased attenuation is associated with the material relaxation process as evidenced by frequency-dependent ultrasonic losses (Edmonds et al. 1970). Unlike acrylamide, corn syrup neither causes an increase in temperature during polymerization nor changes the elastic property and uniformity of PAG after polymerization. The attenuation coefficient depends on the concentration of corn syrup, which suggests that it is a potential alternative to eliminate TM BSA PAG problems caused by the increase in acrylamide content (Choi et al. 2013).

The study described here proposes a new recipe for an optically transparent improved TM (iTM) BSA PAG that acoustically and elastically mimics biological scattering tissues. In addition, the iTM BSA PAG eliminates the shortcomings of TM BSA PAG that are caused by the increase in acrylamide concentration for increasing ultrasonic absorption (Choi et al. 2013). The proposed recipe substitutes a viscous polysaccharide liquid (corn syrup) for acrylamide. The acoustical, elastic, optical and thermal properties of iTM BSA PAG were tested, and HIFU lesions visualized in iTM BSA PAG were compared with those in standard BSA PAG and TM BSA PAG. Note that the lengthy acronyms of the three PAGs—BSA PAG, TM BSA PAG and iTM BSA PAG—are hereafter referred to as PAG 1, PAG 2 and PAG 3, respectively.

MATERIALS AND METHODS

Preparation of PAG

The recipe for PAG 2 of Choi et al. (2013) was modified to construct PAG 3 by substituting corn syrup for acrylamide. The corn syrup concentration (20% w/v) was empirically determined so that the speed of sound in tissues and the attenuation coefficient of PAG 3 were close to those of human liver. The addition of corn syrup increases the attenuation coefficient, speed of sound and *B*/*A* of PAG 3, but decreases the Young's modulus. The influence of corn syrup concentration on the acoustical property of the PAG was experimentally tested to determine the appropriate concentration for PAG 3 (details are provided in the Discussion). Water was reduced by the same amount of the newly added corn syrup. Glass beads (0.002% w/v) were added so that PAG 3 could scatter ultrasound. The components and proportions of the modified recipe of 50 mL of PAG 3 are listed in Table 1.

PAG 3 was prepared by first dissolving 20% (w/v) corn syrup (Chungjungwon, Daesang Corporation, Dongdaemun-Gu, Seoul, Republic of Korea) and 7% (w/v) BSA (A7906, Sigma Chemicals, St Louis, MO, USA) in 25 mL of distilled, de-ionized and degassed water. The corn syrup solution is an equilibrium mixture of 100% corn starch and about 55% maltose which has a high viscosity of 1.4 Pa·s and a pH value of 4.5–6.5. Corn syrup is readily available from many manufacturers or suppliers throughout the world, for example, Karo corn syrup (ACH Food, Albany, NY, USA), and Golden Barrel corn syrup (Good Food, Horseshoe pike, PA, USA). The mixture was gently stirred until BSA and the corn syrup were completely dissolved in water. Gases are likely reintroduced into the solution and rapid mixing results in

Table 1. Comparison of composition of 50-mL volume of the proposed PAG 3 with those of PAG 1 (Lafon et al. 2005) and PAG 2 (Choi et al. 2013)*

	PAG 1		PAG 2		PAG 3	
Components	Quantity (mL)	Proportion (%, w/v)	Quantity (mL, g)	Proportion (%, w/v)	Quantity (mL, g)	Proportion (%, w/v)
Distilled water	35.8	71.6	29.64	59.28	27.5	55.0
Bovine serum albumin	3.5 g	7 w/v	3.5 g	7.0 w/v	3.5 g	7.0 w/v
Polysaccharide (corn syrup)	—	—	—	—	10 g	20.0 w/v
1 M TRIS buffer (pH 8)	5.0	10.0	5.0	10.0	5.0	10.0
Acrylamide:bis monomer	8.75	17.5	15	30.0	8.75	17.5
Glass beads (40–80 μm)	–	–	0.1×10^{-2} g	0.2×10^{-2} w/v	0.1×10^{-2} g	0.2×10^{-2} w/v
Ammonium persulfate solution	0.42	0.84	0.42	0.84	0.25	0.5
TEMED	0.025	0.05	0.025	0.05	0.10	0.2

PAG = polyacrylamide gel; TEMED = *N*, *N*, *N*′, *N*′−tetramethylethylenediamine; TRIS = trizma hydrochloride.

* Quantities are in units of milliliters unless otherwise specified, and proportions are in units of % unless specified. Polysaccharide is a highly viscous liquid; hence, its volume could not be accurately measured using a micropipet. Bovine serum albumin is supplied in the solid state.