Ultrasound in Med. & Biol., Vol. 32, No. 2, pp. 261–270, 2006

0301-5629/06/$–see front matter

ELSEVIER

doi:10.1016/j.ultrasmedbio.2005.10.009

● *Original Contribution*

STABILITY OF HETEROGENEOUS ELASTOGRAPHY PHANTOMS MADE FROM OIL DISPERSIONS IN AQUEOUS GELS

ERNEST L. MADSEN, MARITZA A. HOBSON, HAIRONG SHI, TOMY VARGHESE, and GARY R. FRANK

Department of Medical Physics, University of Wisconsin, Madison, WI, USA

(*Received* 13 *June* 2005, *revised* 10 *October* 2005, *in final form* 18 *October* 2005)

Abstract—A set of five tissue-mimicking phantoms with cylindrical inclusions were produced for assessing long-term stability of geometry and elastic properties and assessing accuracy of determination of elastic properties. The base aqueous materials were either gelatin or a mixture of agar and gelatin. Stiffness was controlled by selection of the volume percent consisting of microscopic safflower oil droplets. Cylinder diameters remained unchanged within 1% or 2% over many months. Strain ratios from elastograms of the phantoms were stable over many months, implying that elastic contrasts were also stable. Test samples, called production samples, for measurement of Young's moduli were made at the time of manufacture of each phantom and were stored separately from one another. Each production sample was homogeneous and consisted of either inclusion material or background material. For all five phantoms, it was found that the elastic contrast computed using Young's modulus values determined using the production samples accurately represented the true elastic contrasts in the corresponding phantom. This finding was established by the fact that the (true) elastic contrasts determined using samples excised from the phantoms themselves agreed with the elastic contrasts obtained using the homogeneous production samples. (E-mail: elmadsen@wisc.edu)

Key Words: **Elastography, Elasticity, Phantom, Stability, Oil, Dispersion, Gelatin, Agar.**

INTRODUCTION

Use of oil-in-gelatin dispersions to make heterogeneous phantoms for use in elastography has been previously reported. (Madsen et al. 2003) In that work, two different 9 cm × 9 cm × 9 cm phantoms with 1-cm diameter cylindrical inclusions were used to assess temporal stability of geometry (cylinder diameter) and accuracy of elastic contrast determination. Temporal stability of geometry was verified by comparison of strain profiles made over an 8-week period. Samples for measurement of the quasistatic Young's moduli were made for the inclusion and background materials at the time of production of each phantom; such samples are referred to in the current report as production samples. Evidence was given that the elastic contrast (Young's modulus of the inclusion material ÷ Young's modulus of the background), computed using Young's moduli determined using the production samples, correctly specified the elastic contrast for the phantoms, themselves. This evidence involved comparing the strain ratios determined from elastograms of the phantoms with elastic strain ratios predicted by the model of Kallel et al. (2001), using the elastic contrast corresponding to the production samples. The two strain ratios agreed well for both phantoms, implying that the elastic contrasts obtained using the production samples equaled those inside the corresponding phantoms.

In the present study, more direct methods were used for assessing temporal stability of geometry and elastic contrast[1] and for assessing the reliability of the assumption that elastic contrast for a heterogeneous phantom is correctly given by that computed from Young's moduli of samples of inclusion and background materials made at the time of production of the phantom. The methods include manufacture of cubic heterogeneous phantoms with cylindrical inclusions along with production sam-

Address correspondence to: Dr. Ernest L. Madsen, Department of Medical Physics, 1300 University Avenue, Room 1530, University of Wisconsin, Madison, WI 53706 USA. E-mail: elmadsen@wisc.edu

[1] Elastic contrast is defined as the ratio of the storage modulus of the material composing an inclusion to the storage modulus of the background material surrounding the inclusion. The storage modulus is the real part of the complex Young's modulus.

ples for measurement of Young's moduli. Cylinder diameters were monitored periodically using an ultrasound (US) scanner and, 7 weeks or more after production of a phantom, it was sliced perpendicularly to the cylindrical inclusions into 1-cm and 2-cm slabs allowing samples of those thicknesses to be excised for determination of Young's moduli. Young's moduli for the excised samples and for the production samples were then compared. Before excising the samples, however, cylinder diameters were accurately measured directly on the slabs with a machinist's calipers.

The composition of the aqueous gel components of each phantom was the same throughout that phantom; this gel component was either gelatin-based or agar-plus-gelatin-based. The agar-plus-gelatin type phantom contained Cu^{2+}-ethylenediaminetetraacetic acid (EDTA) to lower the magnetic resonance imaging (MRI) longitudinal relaxation time (T_1) to tissue-like values and NaCl to produce realistic coil loading (Rice et al. 1998). Three of the gelatin-based phantoms contained propylene glycol to raise the US propagation speed to tissue-like values. Also, some materials contained a small concentration of microscopic glass beads to provide adequate backscatter for US elastography systems.[2]

MATERIALS AND PRODUCTION METHODS

The materials composing the inclusions and background in each phantom were oil-in-gel dispersions, where the (aqueous) gel was either gelatin or a mixture of agar and gelatin. The method of production of the oil-in-gelatin dispersions has been described in detail previously. (Madsen et al. 2003) When the aqueous gel suspending the dispersion of microscopic oil droplets was an agar + gelatin mixture, the same basic procedure was used to produce the oil-in-agar/gelatin dispersions as in the case of the oil-in-gelatin dispersions.

However, because the detailed procedure for producing the oil-in-agar + gelatin dispersions has not yet been reported, an example is given here, where the method for producing about 1200 mL of the background material corresponding to phantom B is described. First, make an aqueous gelatin solution by mixing together 307 mL of distilled water (at room temperature) with 54 g of (dry) 200 bloom gelatin derived from calfskin. (Vyse Gelatin Co., Schiller Park, IL, USA) After covering the beaker with a thin plastic membrane, such as Saran Wrap®, heat the mixture in a double boiler to about 90 °C until the mixture becomes optically transparent. The hot clarified mixture is referred to as "molten gelatin." At the same time that the molten gelatin is being made and, in the same manner, prepare a quantity of molten agar starting with a mixture of 533 mL of distilled water at room temperature and 10.9 g of dry agar (Fisher Scientific, Pittsburgh, PA, USA). Mix together 307 mL of the molten gelatin at 90 °C and 480 mL of the molten agar, also at 90 °C. After raising the beads to 50 °C in an oven, add 4.8 g of 48 to 53 micrometer diameter E-type glass beads (Potters Industries, Parsippany, NJ, USA) to the hot mixture of molten gelatin and molten agar. Add 2.73 g of EDTA tetrasodium salt hydrate (catalog no. E26290, Aldrich Chemical Co., Inc., Milwaukee, WI, USA), 0.93 g $CuCl_2$-$2H_2O$, 6.4 g NaCl and 12 g of liquid Germall-plus® (Sutton Laboratories, Inc., Chatham, NJ, USA). Next, combine, in a 1.5-L beaker, 600 mL of the above mixture at 50 °C with 600 mL of safflower oil (Hollywood brand, The Hain Celestial Group, Inc., Melville, NY, USA), also at 50 °C. Using a stainless-steel tablespoon bent at a right angle where the spoon bowl and handle meet, stir the mixture, keeping the bowl well below the surface and stirring with a motion about a horizontal axis to minimize introduction of air bubbles. This procedure should produce oil droplets of 1-mm diameter or less. Add 12 mL of surfactant (liquid Ultra Ivory®, Proctor and Gamble, Cincinnati, OH, USA) and continue the vigorous stirring for 1 or 2 min, producing an off-white emulsion. Cool to 40 °C by partially immersing the beaker in cold tap water while stirring continuously. Add 3.2 g of formalin and cool to about 35 °C, stirring well to assure uniformity of all components. (Note that formalin is 37% formaldehyde.) Pour the emulsion into one or more molds and seal under positive gauge pressure. To avoid possible gravitational sedimentation during congealing, attach the mold and contents to an apparatus that rotates about a horizontal axis at a constant rate of about 2 rpm for a sufficient time that congealing and cross-linking of gelatin molecules by the formaldehyde has occurred (24 h is sufficient).

At the time of manufacture of each component material in the phantoms (inclusion or background), test samples, called production samples, were made for measurement of Young's moduli. These test samples were 2.6 cm in diameter, 1.0- or 2.0-cm thick discs. Except for phantoms C and D, samples for determination of US and nuclear magnetic resonance (NMR) properties were also made. For ultrasonic measurements, 2.5-cm thick, 7.6-cm diameter samples were enclosed in a cylindrical container with 6-mm thick acrylic walls and 25-μm thick Saran Wrap® (polyvinylidene chloride, Dow Chemical Co., Midland, MI, USA) covering the parallel faces. For NMR relaxation time measurement, a 5-mm diameter glass NMR tube (catalog no. 512, Wilmad LabGlass, Buena, NJ, USA) was filled to within 5 mm of the top and was then sealed from air with petrolatum.

[2] Compression refers to the percent decrease in thickness of the sample (*e.g.*, a 5% compression of a sample having an uncompressed thickness of 2.00 cm would result in a thickness of 1.90 cm).