A ten-month study is presented of materials for use in heterogeneous elastography phantoms. The materials consist of gelatin with or without a suspension of microscopic safflower oil droplets. The highest volume percent of oil in the materials is 50%. Thimerosal acts as a preservative. The greater the safflower oil concentration, the lower the Young’s modulus. Elastographic data for heterogeneous phantoms, in which the only variable is safflower oil concentration, demonstrate stability of inclusion geometry and elastic strain contrast. Young’s modulus ratios (elastic contrasts) producible in a heterogeneous phantom are as high as 2.7. The phantoms are particularly useful for ultrasound elastography. They can also be employed in MR elastography, although the highest achievable ratio of longitudinal to transverse relaxation times is considerably less than is the case for soft tissues.

**KEY WORDS:** Contrast; elastography; phantoms; ultrasound.

**INTRODUCTION**

Elastography has been under development during the last decade and is recognized as having great potential as an emerging major tool for breast and prostate cancer diagnosis. It may also play an important role in other areas such as monitoring tumor ablation therapy and intravascular plaque classification. Initial clinical trials are under way and there is a great need for temporally stable heterogeneous phantoms to enable vigorous development of elastographic hardware and software.

Krouskop et al reported *in vitro* values of Young’s moduli ($E$) for normal and abnormal breast and prostate tissues using precompression and low frequency ($\leq 4$ Hz) superimposed sinusoidal loading. At 5% precompression in breast and 4% in prostate cases, $E$ ranged from $18 \pm 7$ kPa for breast fat through $241 \pm 28$ kPa for prostate cancer. (The $\pm$ values are standard deviations). $E \approx 30$ kPa for normal breast glandular and $E \approx 100$ kPa for invasive and infiltrating ductal carcinoma. Strongly nonlinear moduli were found for the latter type of cancer with $E \approx 500$ kPa at 20% precompression.

Most elastography researchers have employed phantoms composed of tissue-mimicking (TM) materials in their work. With rare exceptions, the phantoms are *ad hoc* constructions for testing ultrasound (US) or MR elastography techniques. A great many phantom versions have been investigated having different compositions and elastic contrasts. (The elastic con-
Contrast between two materials in a phantom is defined as the ratio of their Young’s moduli; if one material composed an inclusion and the other its surroundings, the elastic ratio is the Young’s modulus of the inclusion divided by that of the surroundings.) However, long-term stability of geometries (such as inclusion sizes and shapes) and of relevant physical properties in heterogeneous phantoms has not been addressed in existing literature. Heterogeneous phantoms are defined to be phantoms containing at least two volumes in direct contact but having different physical properties. If geometries and physical properties are not constant — or at least predictable over time — then important performance checks can be compromised. A review of publications involving materials and phantoms for use in elastography follows this introduction.

Even if a phantom is stable, there is another consideration that has largely been ignored in other work, viz., the degree to which US and MR properties are simulated in elastography phantoms. Because of the complexity of the physics in US and MR imaging, it is logical that the relevant US and NMR properties of the materials in a phantom should approximate those in human soft tissues of concern reasonably well, viz., propagation speed ($c$), attenuation coefficient ($\alpha$) and backscatter coefficient in US and $T_1$ and $T_2$ in MR. A simple example of the importance of mimicking physical properties involves the frequency-dependent attenuation coefficient ($\alpha$) in US. If $\alpha$ in a phantom were twice that in tissues in the frequency range involved, then at sufficient depths, the signal-to-noise would be too small for quality elastograms to be made, even if that were not the case in real tissue. Also, if the frequency dependence of attenuation is considerably different from that of tissue, elastograms might be either better or worse than those from real tissue. Thus, the more closely those properties are mimicked, the better the phantom.

One version of tissue-mimicking material that has not been investigated for use in elastography phantoms consists of oil-in-gelatin dispersions. These materials have been reported relative to use in US imaging phantoms and have been used for mimicking breast glandular tissue and fat in anthropomorphic phantoms. For fixed compositions of the gelatin matrix and of the oil droplets forming such dispersions, it is not surprising that the modulus decreases as the volume percent of oil increases.

In this paper, we describe the elastic, US and MR properties of examples of oil-in-gelatin dispersions and demonstrate that all these properties remain adequately stable in heterogeneous phantoms formed from them. Also, it has been found that the size and shape of cylindrical gelatin inclusions (0% oil) surrounded with oil-in-gelatin dispersions remained unchanged over time.

It is demonstrated in this work that heterogeneous phantoms with elastic contrasts spanning between 1/2.7 = 0.37 and at least 2.7 can be made with the oil-in-gelatin type materials. The component materials can also be made to mimic a broad range of US and MR properties. Higher elastic contrasts can be achieved by embedding sections of open-cell reticulated foam in the gelatin or oil-in-gelatin dispersion.

**LITERATURE REVIEW INVOLVING ELASTOGRAPHY PHANTOM MATERIALS**

**Reports dealing primarily with phantom materials for elastography**

Hall et al. did extensive initial work testing the elastic properties of homogeneous samples of gelatin and homogeneous samples of agar. Other than publications from the University of (1) This statement is not quite true. Insana et al. did a study regarding the effect on ultrasound echo speckle patterns with uniaxial compression of phantom materials where the scatterers in one type of material were rigid oil droplets (soft) in the other type. No study of the dependence of Young’s modulus on oil type, concentration or droplet size was reported, however.
Wisconsin Department of Medical Physics, theirs is the only relevant work found that addresses the long-term (months) stability issue of the TM materials investigated. Two types of cross-linking agents were employed in the case of the gelatin: formaldehyde and paraldehyde. Such materials have been in use in ultrasound phantoms for many years.\textsuperscript{13,14} When formaldehyde was used for cross-linking gelatin, Young’s modulus increased monotonically at room temperature for about three months; when paraldehyde was used, about two months were required. In terms of the asymptotic values of Young’s moduli, a broad range of $E$ values was found for the gelatins, including the human soft tissue range. $E$ depended on the dry weight percent of agar or gelatin and, in the case of gelatin, on the concentration of formaldehyde or paraldehyde. $E$’s for agars increased at strain values beyond 2%, whereas $E$’s for gelatins were found to be independent of strain. Strain-independent $E$’s might be desirable for heterogeneous phantoms since the elastic contrast is not a variable. Stability characteristics of contrast phantoms, containing more than one type of gelatin or agar in direct contact, were not addressed.

Erkamp et al\textsuperscript{3} investigated homogeneous gelatin and homogeneous agar and a heterogeneous phantom with a gelatin section and an agar component. They found gelatin and agar to exhibit nearly strain-independent values of $E$ for strains up to about 2%, but for strains between 2 and 7%, the modulus of the gelatin increased by about a factor of 2 – similar to the increase they found for prostate parenchyma – while the agar $E$ increased by a factor of about 6. (Krouskop et al\textsuperscript{1} found that normal fat as well as normal breast and prostate parenchyma exhibit small strain dependence of $E$ for strains less than 5% (prostate) or 10% (breast)). Thus, for strains less than 10%, agar may not be an adequate material for mimicking normal breast or prostate.

Polyvinyl alcohol gels have also been investigated regarding their suitability for MR elastography phantoms. Chu and Rutt\textsuperscript{4} describe a rather involved cyclic freeze-thaw process for production of cross-linking and accompanying solidification. Expansion and contraction of the material occurs during the freeze-thaw process and some liquid is expelled. The authors indicate that the material does not possess long-term stability. Only homogeneous materials are reported and it is unclear whether a durable bond can be made to exist between materials of different hardness, allowing production of realistic heterogeneous phantoms.

Aqueous mixtures of agar and gelatin have been employed in phantoms for US elastography by de Korte et al.\textsuperscript{5} They produced three homogeneous samples, all containing 8% dry weight gelatin and 1%, 2% and 3% dry-weight agar. No agent was employed to cross-link the gelatin. The samples were congealed by immersing their container in ice water. The only temporal stability study was to monitor the ‘compression modulus’ for a four-hour period following congealing in ice water and raising to 20°C. The modulus increased monotonically. Other measurements were done after 6 days of aging at different temperatures between 5°C and 40°C. Since the congealing point of gelatin is about 26°C and the melting point is about 32°C, it is not surprising that the modulus at 40°C was about 5% of that at 5°C.

Reports where phantoms are ad hoc tools to demonstrate elastographic methods

A gelatin phantom with cylindrical inclusions was made with the materials described in Hall et al.\textsuperscript{2} The phantom is described briefly by Chaturvedi et al.\textsuperscript{15} One later publication by Zhu et al\textsuperscript{16} discusses use of the same data acquired for the earlier work by Chaturvedi et al.\textsuperscript{15} Varghese et al\textsuperscript{17} refer to a phantom which seems to be the same as that described in Chaturvedi et al.

Other heterogeneous gelatin phantoms with either harder inclusions or layers with different hardnesses have been reported by various investigators.\textsuperscript{10-24} Cross-linking agents were
apparently not employed. Contrast was created with different dry-weight gelatin concentrations. From our knowledge of gelatins, these phantoms were almost certainly unstable due to diffusion of liquids to equalize dry-weight gelatin concentrations.

Two reports involve heterogeneous gelatin phantoms where differences in hardness appear to have been produced through use of different concentrations of the cross-linking agent formaldehyde. Such phantoms would be unstable with time due to gradual migration of formaldehyde toward a uniform concentration.

Heterogeneous phantoms have been made from agar or agarose where the hardness differences result from differing dry-weight concentrations of agar. Agar phantoms would be suitable for mimicking tissues for both MR and US properties. However, there are various drawbacks of agar regarding its usefulness in stable heterogeneous phantoms: (1) Agar is a brittle gel; i.e., it tends to fracture with moderate strains. (2) As mentioned above, for strains greater than a few percent, agar has been found to exhibit a much more rapidly increasing Young’s modulus with strain than normal breast or prostate parenchyma; the same rapid increase would exist for the shear modulus assuming constant Poisson’s ratio. (3) When one agar section is congealed around a previously congealed section, the bond is not very strong so that for moderate strains, perhaps 5%, a break between the two sections may occur; also, this bonding weakness could mean that repeated smaller strains might result in fracture at the boundary. It should be noted that strong bonding at interfaces may not be desirable for representing some situations in the body; e.g., juxtaposed muscles can slide at their interface.

Aqueous polyacrylamide gels have been employed to test methods for assessing tissue elastic parameters. Walker et al. used separate uniform materials with different polyacrylamide concentrations; suspended Sephadex was present to provide US scatter. Parker et al. employed a phantom consisting ‘mainly’ of Zeredine, a polyacrylamide hydrogel with microscopic suspended particles to provide absorption and scattering. Spherical inclusions with stiffness seven times that of the surrounding gel were present. Taylor et al. employed a polyacrylamide prostate phantom where the ‘tumor’ was harder through increased cross-linking.

Sinkus et al. describe a breast phantom for MR elastography made from polyvinyl alcohol. The bulk of the phantom consists of a softer material surrounding a 6-mm cube of harder material. They state that polyvinyl alcohol is ‘significantly stiffer than biological tissue.’ Hardening of this material was done by the ‘freeze-thaw’ process described by Chu and Rutt.

Fowlkes et al. employed a silicone rubber phantom for MR elastography containing a cylindrical inclusion which was about 10 times the hardness of the surroundings. A sample of this material was produced in our lab for determination of ultrasound properties. The propagation speed at 22°C was found to be 1,008 m/s, precluding its use in ultrasound elastography.

A silicon-based polymer (Reston Self-Adhering Foam Pad, 3M Co., Minneapolis, MN), which was apparently not silicone rubber, was employed by Wu et al. The material seems to have been a reticulated foam permeated with an aqueous solution. If so, then the material does not constitute an incompressible constant ‘solid’ simulating tissue (i.e., when compressed uniaxially, the ultrasound scatterers that must arise at the foam surfaces will move only parallel to the compression direction, whereas in tissue, the scatterers will generally move perpendicularly to the compression direction as well as parallel to it).

‘Plastisol,’ a form of polyvinyl chloride, has been used in phantoms for MR elastography. Heterogeneous phantoms with two or three different hardness values in one phantom are described. A sample was made in our lab and with the following ultrasound properties at 22°C: Propagation speed = 1,395 m/s, and attenuation coefficient/frequency value of 1.05 dB/cm/MHz at 4.5 MHz and of 1.37 dB/cm/MHz at 8.0 MHz. Thus, the ultrasound properties make this material of doubtful value for US elastography, particularly because of
the high attenuation at the frequencies used in elastography. The propagation speed is in the range corresponding to fat rather than the mean for soft tissues.

Aqueous agar/gelatin materials have been reported as part of elastography methodology work by various investigators. Kallel et al. employed six phantoms made from aqueous gelatin/agar mixtures. In all but one phantom, the dry weight gelatin concentration was lower in the bulk of the phantom than in a cylindrical inclusion, resulting in greater stiffness in the cylinder than in the background. The five cylindrical inclusions which were stiffer than their surroundings increased in diameter by a factor of 5/3 in two weeks, and the softer cylindrical inclusion contracted as the gelatin relaxed toward a uniform dry-weight gelatin concentration. Thus, these phantoms did not possess long-term stability.

Gao et al. used agar/gelatin mixtures in a heterogeneous phantom. The gelatin concentrations were not matched in the inclusion and background; thus, the inclusion size would change due to diffusion.

Plewes et al. produced a gelatin/agar phantom in which the harder inclusion and the background had the same concentrations of gelatin. Thus, the inclusion probably would not have changed size over time. However, no monitoring of properties over any time period is reported and there apparently was no cross-linking agent present to raise the melting point significantly above room temperature.

MATERIALS AND PRODUCTION METHODS

Manufacture of the oil-in-gelatin materials is straightforward. Because the compositions are not exactly those described previously, a step-by-step procedure is given here. First, a hot gelatin solution is produced. In one realization, 154 gm of dry-weight, 200 bloom gelatin derived from calveskin (Vyse Gelatin Company, Schiller Park, Illinois, USA) is stirred into 1 liter of 18 MΩ cm deionized water at room temperature. This mixture is heated in a double boiler to about 90 °C until the mixture clarifies (becomes a solution). The resulting material is referred to as ‘molten gelatin.’

If solid particles – such as microscopic powdered nylon or glass beads – are to be added to elevate US attenuation and backscatter, these should be stirred into the hot molten gelatin at this point. Relative to MR, presence of the particles will also decrease the water concentration and, correspondingly, the 'H density. To avoid particle clumping, we mix the nylon or glass beads into a small quantity of 90 °C deionized water before adding to the molten gelatin. If cupric salt and EDTA (ethylenediaminetetraacetic acid) are to be added to reduce $T_1$, these should also be added at this point. Note that there should be at least one molecule of EDTA per Cu$^{2+}$ ion to form Cu$^{2+}$-EDTA complexes and prevent arresting of the Cu$^{2+}$ ions on the gelatin.

Next the solution is cooled to about 55 °C by immersing the lower part of the beaker containing it in cool water while stirring. Then 1 gm per liter of the fungicide thimerosal is added and stirring done until dissolving is complete. The 55 °C molten gelatin is then mixed with the amount of safflower oil (also at 55 °C) resulting in the desired percent oil in the emulsion. Note that, if the volume percent oil is greater than about 60%, the resulting cooled material will likely not possess any rigidity, the tendency being for gelatin droplets to form in the oil instead of the oil droplets in gel.

Emulsification to produce oil droplets that are sufficiently small such that separation of oil from gelatin does not occur during congealing, is accomplished by adding a surfactant and either using a variable speed blender or mixing vigorously with a spoon in a manner not allowing aeration. A commercially available surfactant is used in our lab, viz., liquid Ultra Ivory® produced by the Proctor and Gamble Company, Cincinnati, OH, USA; 15 cc of this
surfactant per liter of oil usually being sufficient. When a blender is used, a low speed is recommended, sufficiently low speed being attainable with the aid of a variable transformer. Aeration can be avoided by submerging the bowl of a spoon or similar object just below the liquid surface to prevent the formation of a whirlpool vortex. When a spoon *per se* is used for emulsifying, aeration can be avoided by using a spoon bent at right angles where the bowl meets the handle and mixing with the handle kept vertical and the submerged bowl moving in a circle around a horizontal axis. The technique is illustrated in figure 1.

After emulsifying, cool the liquid to $35\,^\circ C$ and mix in 0.7 cc of formalin solution (37.4% by weight formaldehyde) per 100 cc of gelatin. For example, if the volume percent of molten gelatin is 50%, then add 0.35 cc of formalin per 100 cc of emulsion.

Continue cooling to about $28\,^\circ C$ and pour the molten emulsion into the appropriate receptacles for congealing. The congealing temperature is about $26\,^\circ C$. If solid particles are present, and perhaps even if they are not, the molten emulsion should be sealed from the air under positive gauge pressure and rotated slowly (~ 2 rpm) about a horizontal axis for a few hours until congealing has been completed. The sealing technique has been previously described.\(^2\)

At the same time the phantom mold is filled, test samples are made from the $28\,^\circ C$ molten emulsion for measuring US, MR and elastic properties. The US test samples are 2.5 cm thick acrylic cylinders with parallel 25-mm-thick Saran Wrap\(^*\) windows. The MR test samples are 15 cm long, 5 mm diameter NMR glass tubes. (Cat. no. 512, Wilmad Glass Company, Inc., Buena, NJ, USA) The containers for forming the 2.5 cm diameter, 1 cm thick cylinders to be used in measurements of Young’s moduli are acrylic cylindrical sections with parallel Saran Wrap\(^*\) ends; the molten emulsion is introduced through a syringe barrel as in the case of the US samples. The elasticity samples are removed from their container and are stored immersed in safflower oil.

It has been observed that the elastic moduli of gelatin-type materials with formaldehyde concentration used in our materials increase monotonically for about three months following production.\(^5\) It was assumed that this slow approach to an elastic steady state related to slow completion of formaldehyde cross-linking of gelatin. To reduce the amount of time re-

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![Figure 1](image-url)  
**FIG. 1** Illustration of emulsification method using a spoon: (a) axis of rotation in the plane of the figure; (b) axis of rotation perpendicular to the figure.
quired to reach steady state, all gelled materials have been kept at an elevated temperature of about 50°C for a number of days.

**HETEROGENEOUS PHANTOMS**

One type of heterogeneous phantom made from the above materials consists a cube of background material, 9 or 10 cm on a side, with a 1 cm or 2 cm diameter cylindrical inclusion having a composition different from that of the background. An example of the geometry is shown in figure 2. Each phantom is stored in a covered flat-bottom container immersed in safflower oil. Thus, no desiccation is expected and the only rigid constraining surface is the flat bottom of the container. Because of the oil surrounding the phantom, negligible shear forces are exerted on the bottom of the phantom when it is compressed by a force on the top surface during elastographic data acquisition.

Each phantom is produced in three steps. The first step is the production of the background. The mold into which the molten background material is poured is an acrylic box open at opposite ends over which Saran Wrap® is epoxied. The barrel of a sawed-off 30 cc hypodermic syringe is also epoxied into a hole in one acrylic wall near one corner of the box. A stainless steel cylindrical rod passes through holes in opposite sides of the box. Epoxy provides a seal between the rod and the external part of the holes. Before the last Saran Wrap® layer is glued on, all surfaces to be in contact with the molten background material are coated with a thin layer of petrolatum. This layer allows removal of the stainless steel rods and then removal of the completed phantom from the mold.

After the 28°C molten background material has filled the mold and the projecting syringe barrel (through which the molten material is poured), the syringe piston is inserted in the syringe barrel and rubber bands positioned to maintain positive gauge pressure on the material as it congeals. Note that before the molten background material is poured in, acrylic constraining plates are taped over the Saran Wrap® sides to maintain flatness of those sides of the background material. After the syringe piston has been introduced, the entire apparatus is mounted on a rotator so that rotation at 2 rpm about a horizontal axis proceeds throughout the congealing period; thus, gravitational sedimentation of glass beads, etc., is avoided. Note
that the material formed after the gelatin matrix solidifies is called an oil-in-gelatin dispersion since the term emulsion refers to the suspension of droplets of one liquid in another with which the former is immiscible.

After about 24 hours the formaldehyde cross-linking will have raised the melting point of the material to above 90 °C, and the second production step is undertaken, viz., production of the inclusion. The epoxy seals around the stainless steel rod are removed and the rod is withdrawn. The hole in the gel is then quickly cleaned with a detergent solution and rinsed. Tape is applied over one opening in the acrylic wall and 28 °C molten inclusion material is poured into the remaining opening filling the hole. Since the background is at room temperature, the inclusion material congeals within minutes.

After another 24 hours, allowing adequate formaldehyde cross-linking of the inclusion material, the third step is performed which is intended to complete cross-linking so that slow increase in stiffness is avoided. The phantom and all test samples are sealed in a large plastic sack with a beaker of water and are placed in an oven at about 50 °C for either 3 or 10 days. Thus, all materials involved with a phantom are baked at the same temperature and the same length of time. (The beaker of water is added insurance that desiccation is suppressed.)

Two versions of heterogeneous phantoms are reported here. These are referred to as type A and type B. Five duplicate type A phantoms were produced at the same time. These phantoms and corresponding test samples were baked at about 50 °C for 3 days. The geometry is that shown in figure 2 where the 1 cm diameter cylindrical inclusion has its axis 2.5 cm from one surface. Powdered graphite (No. 9039, Superior Graphite Co., Chicago, IL) exists in the inclusion material to provide tissue-mimicking US attenuation, and 4 gm/liter of glass beads (type 3000E, Potters Industries Inc., Valley Forge, PA) with an approximate mean diameter of 22 mm were present throughout the phantom to provide uniform tissue-like backscatter. The bulk of the phantom, which surrounds the cylindrical inclusion, contains 32% by volume safflower oil. The emulsion also contains 4 gm/liter of type 3000E Potters glass bead scatterers. Emulsification was done with a blender set at its lowest speed (Model 688-4, Hamilton Beach Proctor-Silex, Glen Allen, VA) with speed further lowered using a variable transformer.

The other heterogeneous phantom, called type B, differs in geometry from type A in that it has a 2 cm diameter cylindrical inclusion with axis centered at a depth of 3 cm from one side. No graphite exists in the type B phantom, and the material surrounding the cylinder contains 50% safflower oil instead of 32%. Emulsification was done by the less vigorous method using a spoon as shown in figure 1; this method presumably produces a larger mean oil droplet diameter which results in a lower US attenuation coefficient slope per percent oil. Glass bead scatterers, of the same type as in the type A phantoms, are present in both background (4 g/L) and inclusion (20 g/L) of the type B phantom; the higher concentration in the inclusion provides both backscatter and significant attenuation.

After the phantom has been removed from the oven and allowed to cool to room temperature, it is removed from the mold. Both Saran Wrap® ends are cut from the box and a blade is used to cut off the congealed background material in the syringe barrel and to cut off each end of the inclusion at the inner surfaces of the acrylic walls. The cubic phantom is then dropped out of the mold through one of the square open ends. The phantom is stored submerged in safflower oil in an appropriate flat-bottomed container.

To investigate the effect of the final 50 °C baking period on Young’s moduli, six of the 1 cm-thick, 2 cm diameter samples of the plain gelatin (no oil) and six of the 50% oil-in-gelatin emulsion were produced from the same batch of molten gelatin on the same day, viz., 28 December 2001. Five samples of each type were placed in the 50 °C oven. After five days, a sample of each type was removed, after 10 days another sample of each type was removed, etc. This process resulted in baking periods of 0, 5, 10, 15, 20 and 25 days at 50 °C for each
type material. The Young’s moduli for all samples were then measured using an Instron® machine (Instron Corporation, Canton, MA).

Another type of heterogeneous phantom was made for assessing the accuracy of a NanoIndentor®, an instrument used at University of Texas-Houston for in vitro mapping of Young’s moduli of thin tissue samples. This instrument has a fixed flat stage on which the 2-4 mm thick tissue slice is placed, and a 2 mm diameter piston produces highly controlled local slight compressions with monitored positions and forces. The test phantom consisted of a 4-mm thick, 2.5 cm diameter disc of tissue-mimicking fat (50% oil) with an equilateral triangle (6 mm sides) of plain gelatin (0% oil) at its center.

MATERIAL COMPOSITIONS

Table 1 shows compositions of the variable components of all tissue-mimicking materials reported in this work as well as differences in 50° baking periods. Invariant composition values are as follows: the weight-percent concentration of gelatin in the gelatin matrix of emulsions (excluding the volumes occupied by safflower oil, glass beads and graphite powder) is 13.3%; the concentration of thimerosal in the gelatin matrix of emulsions is 1 gram per liter; the concentration of formaldehyde in the gelatin matrix of emulsions is 0.35 grams per liter; the concentration of surfactant is 15 cc per liter of safflower oil.

METHODS OF MEASUREMENT OF MATERIAL PROPERTY PARAMETERS

Prospective tissue-mimicking (TM) materials have been tested regarding Young’s modulus (E), ultrasonic propagation speed (c) and attenuation coefficients (α), and the NMR relax-
All measurements were done at room temperature of 22°C. For every version of TM material, a 2.5 cm diameter, 1 cm thick uniform cylindrical sample was produced for E measurements; each sample is bare and is stored immersed in safflower oil. Also for each version, a 7.6 cm diameter, 2.5 cm thick test cylinder with acrylic curved boundary and parallel Saran Wrap® transmission windows was made for US measurements. For NMR measurements, a 5 mm diameter NMR relaxometer tube was filled and sealed with petrolatum.

**Young’s modulus (E)**

Young’s moduli were measured quasistatically. A hydraulic servo Instron 8500 at the University of Texas-Houston Dental School is employed. Samples are compressed uniaxially with a 5 cm diameter flat compressor. When measurements are not being made, each 2.5 cm diameter, 1 cm thick cylindrical sample is stored immersed in safflower oil (to prevent desiccation) contained in a small glass bottle with Teflon® screw top.

Following is a summary of the quasi-static measurement procedure. A clean smooth 10 cm × 10 cm flat plate is placed in the Instron machine and raised until it contacts the parallel 5 cm diameter flat compressor. The compressor is connected directly to the load cell in the machine. When the load cell registers a load of 0.8 grams, the elevation of a reference point is recorded and used as the zero setting for measuring the heights of the samples. The sample is removed from the bottle; sufficient oil clings to the sample, that it is reasonable to assume that no desiccation of the sample occurs during the 5 or 10 minute period required for data acquisition. Also, the oil suppresses undesirable shear forces at the sample’s flat surfaces during measurement. The 2.5 cm diameter sample is placed on the flat plate in the Instron – centered beneath the compressor – and the system is activated to cause the sample to come into contact with the compressor; when a load of 0.8 grams is registered in the load cell, the position is recorded and used to calculate the height of the sample. The Instron is programmed to apply a load yielding 10% strain to the sample at a rate of 1% per second. After the test has been recorded in the Instron, the system is returned to zero strain position and the sample is given 3 minutes to recover. The procedure is then repeated, and if the final load is less than 1 gram different than for the first case, the test is completed and the next sample is tested. If there is a load difference of more than 1 gram, the test is repeated four times, and the data are averaged for calculating the modulus over the strain range of 0 - 10%. The gel sample is then returned to immersion in oil for storage at room temperature. Test results are stored as stress-strain curves. The slope of the stress-strain curve yields the value of E.

**Ultrasound parameters**

The method for determining c and α is the common through-transmission, water substitution method described, e.g., in Madsen et al.44 Tone bursts are emitted by a transmitting transducer and the change in amplitude and phase of the received signal with insertion of the 22°C cylindrical sample in the 22°C distilled water path are recorded. Using the propagation speed in pure water and knowing the thickness of the sample and the phase shift allows computation of c for the sample. Knowing sample thickness, the ratio of amplitudes before and after insertion, plus corrections for transmission through the Saran Wrap®, allows computation of the attenuation coefficient. The attenuation of water is assumed negligible at diagnostic frequencies.

**NMR relaxation times, T₁ and T₂**

The methods for determining NMR relaxation times have been previously described in detail.43,45 A 40 MHz Bruker model PC140 ‘Minispec’ relaxometer was employed with T₁’s
determined with the inversion-recovery pulse sequence and $T_2$'s with the Carr-Purcell-Meiboom-Gill (CPMB) sequence. The relaxometer operates at a probe temperature of 40 °C. To obtain relaxation times at about 22 °C, the 5 mm diameter NMR tubes are kept in a 21 °C water bath and are wiped dry just before insertion into the probe; it has been verified with thermocouples that, during the data acquisition, the temperature in the sample material rises from 21 °C to about 23 °C, averaging 22 °C.

**RESULTS**

Values of physical parameters measured on homogeneous samples

In tables 2-4, elastic and ultrasonic properties are reported for seven representative gelatin and oil-in-gelatin emulsions for which the ‘baking’ time was either 3 days or 5 days. All but one of these materials exists in a heterogeneous phantom. NMR relaxation times are reported for only two of the seven types since NMR sample tubes had not been made for the other five materials.

The primary concern has been the long-term stability of the Young’s modulus. Long-term stability of ultrasonic and NMR properties have been verified previously; thus, US and NMR properties were measured only once while Young’s moduli were monitored periodically over many months. Values for US and NMR properties are shown in table 2, and for values for Young’s moduli are shown in table 3. All US and NMR measurements were made at 22 °C, and the elasticity measurements were made at ambient room temperature (about 22 °C).

Perhaps the most critical parameter regarding the stability of the heterogeneous phantoms is the elastic contrast, defined in the Introduction as the ratio of the Young’s modulus for the

<table>
<thead>
<tr>
<th>Sample identification</th>
<th>US speed (± 1 ms)</th>
<th>US attenuation coefficient (± 0.10 dB/cm) T1 (ms)</th>
<th>T2 (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.5 MHz</td>
<td>4.5 MHz</td>
<td>6.2 MHz</td>
</tr>
<tr>
<td>Plain gelatin (nanoindentor Δ inclusion)</td>
<td>1538</td>
<td>0.26 (0.10)</td>
<td>0.51 (0.11)</td>
</tr>
<tr>
<td>Tissue-mimicking fat (50% oil emulsion nanoindentor bkgd)</td>
<td>1497</td>
<td>0.99 (0.40)</td>
<td>1.71 (0.38)</td>
</tr>
<tr>
<td>Phantom A background (32% oil emulsion + beads)</td>
<td>1506</td>
<td>2.23 (0.89)</td>
<td>3.53 (0.78)</td>
</tr>
<tr>
<td>Phantom A inclusion (gelatin + graphite + beads)</td>
<td>1533</td>
<td>1.41 (0.56)</td>
<td>2.42 (0.54)</td>
</tr>
<tr>
<td>32% oil emulsion – low speed blend</td>
<td>1509</td>
<td>1.20 (0.48)</td>
<td>1.90 (0.42)</td>
</tr>
<tr>
<td>Phantom B background (50% oil emulsion + beads)</td>
<td>1496</td>
<td>0.68 (0.27)</td>
<td>1.28 (0.28)</td>
</tr>
<tr>
<td>Phantom B inclusion (beads in gelatin)</td>
<td>1536</td>
<td>0.42 (0.17)</td>
<td>0.76 (0.17)</td>
</tr>
</tbody>
</table>
Young’s moduli of materials at ambient temperature with passage of time. The final step in production of all materials was ‘baking’ at 50°C; all materials were baked for three days except for phantom B background and inclusion which were baked for five days.

### Table 3

<table>
<thead>
<tr>
<th>Sample Identity</th>
<th>8/22/01</th>
<th>9/26/01</th>
<th>12/20/01</th>
<th>1/16/02</th>
<th>2/22/02</th>
<th>3/27/02</th>
<th>4/19/02</th>
<th>5/20/02</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plain gelatin (nanoindentor inclusion)</td>
<td>28 ± 1</td>
<td>32 ± 1</td>
<td>33 ± 1</td>
<td>35 ± 1</td>
<td>31 ± 1</td>
<td>27 ± 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tissue-mimicking fat (50% oil emulsion nanoindentor bkgd)</td>
<td>16 ± 0.5</td>
<td>13 ± 0.5</td>
<td>13 ± 0.5</td>
<td>15 ± 0.5</td>
<td>14 ± 0.5</td>
<td>13 ± 0.5</td>
<td>11 ± 0.5</td>
<td></td>
</tr>
<tr>
<td>Phantom A background (32% oil emulsion + beads)</td>
<td>16, 19, 17†</td>
<td>20, 20, 23</td>
<td>(21.0 ± 1.0)</td>
<td>23, 25, 23</td>
<td>22, 25, 24</td>
<td>20, 21, 21</td>
<td>18, 19, 18</td>
<td></td>
</tr>
<tr>
<td>Phantom A inclusion (gelatin + graphite + beads)</td>
<td>29, 29, 27†</td>
<td>38, 34, 36</td>
<td>(36.0 ± 1.2)</td>
<td>41, 38, 37</td>
<td>43, 40, 40</td>
<td>39, 34, 36</td>
<td>35, 33, 31</td>
<td></td>
</tr>
<tr>
<td>Phantom B background (50% oil emulsion + beads)</td>
<td>14, 14, 14†</td>
<td>20, 17, 18</td>
<td>19, 19, 20</td>
<td>21, 20, 20</td>
<td>18, 17, 17</td>
<td>15, 16, 16</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† Three samples of this material were made for Instron measurements. Each value corresponds to a different sample.
‡ Mean and standard errors of the three values are in parenthesis.

### Table 4

Elastic contrasts (inclusion $E$ – background $E$) for heterogeneous phantoms A and B as a function of time where $E$ = Young’s modulus as measured by Instron. Uncertainties for phantom B assume 3% uncertainty in any $E$ value except when the precision uncertainty (0.5 kPa) exceeds 3% of $E$.

<table>
<thead>
<tr>
<th>Sample Identity</th>
<th>8/22/01</th>
<th>12/20/01</th>
<th>1/16/02</th>
<th>2/22/02</th>
<th>3/27/02</th>
<th>4/19/02</th>
<th>5/20/02</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phantom A</td>
<td>1.64 ± 0.09</td>
<td>1.71 ± 0.10</td>
<td>1.63 ± 0.07</td>
<td>1.73 ± 0.08</td>
<td>1.79 ± 0.08</td>
<td>1.80 ± 0.07</td>
<td></td>
</tr>
<tr>
<td>Phantom B</td>
<td>2.70 ± 0.16</td>
<td>2.67 ± 0.14</td>
<td>2.42 ± 0.12</td>
<td>2.64 ± 0.14</td>
<td>2.80 ± 0.16</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Inclusion divided by that of the surroundings. Using the Young’s modulus values in table 3 for phantoms A and B, elastic contrast values are shown as a function of time in table 4.

Three samples of this material were made for Instron measurements; each value corresponds to a different sample. Mean and standard error of the three values are in parentheses.

Tables 5 and 6 show Young’s moduli for the six samples of plain gelatin (no oil) and six samples of 50% oil-in-gelatin emulsion with different baking times at 50°C. The purpose of the production and monitoring of these samples was to determine the effect of different baking periods on the value and temporal stability of the Young’s modulus. Table 7 is derived from tables 5 and 6 and shows the elastic contrasts for plain gelatin to 50% oil-in-gelatin as a function of number of days baked and date of measurement.

### Elastograms of the heterogeneous phantoms and values of parameters derived therefrom

In order for the materials to be useful in heterogeneous phantoms for testing elastography systems, there must be no observable long-term change in the phantoms on elastograms.
This assumes, of course, that the assessment system itself does not change significantly during the testing of the phantom. Elastograms and associated strain profiles were periodically obtained on the phantoms A and B. The strain profiles are local strains mapped along an axial or lateral line perpendicular to, and intersecting, the axis of the cylindrical inclusions.

### TABLE 5. Young’s moduli for the six plain gelatin samples with different 50°C baking periods. The samples were made on 28 December 2002.

<table>
<thead>
<tr>
<th>Number of days baked</th>
<th>1/16/02</th>
<th>1/28/02</th>
<th>2/22/02</th>
<th>3/27/02</th>
<th>4/19/02</th>
<th>5/20/02</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>104 ± 3</td>
<td>123 ± 3</td>
<td>115 ± 3</td>
<td>106 ± 3</td>
<td>107 ± 3</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>31 ± 1</td>
<td>33 ± 1</td>
<td>34 ± 1</td>
<td>31 ± 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>22 ± 0.7</td>
<td>29 ± 0.9</td>
<td>27 ± 0.8</td>
<td>27 ± 0.8</td>
<td>25 ± 0.7</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>17 ± 0.5</td>
<td>28 ± 0.8</td>
<td>24 ± 0.7</td>
<td>22 ± 0.7</td>
<td>24 ± 0.7</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>17 ± 0.5</td>
<td>17 ± 0.5</td>
<td>16 ± 0.5</td>
<td>17 ± 0.5</td>
<td>15 ± 0.5</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>22 ± 0.7</td>
<td>20 ± 0.6</td>
<td>20 ± 0.6</td>
<td>19 ± 0.6</td>
<td>17 ± 0.5</td>
<td></td>
</tr>
</tbody>
</table>

### TABLE 6. Young’s moduli for the six 50% oil-in-gelatin emulsion samples with different 50°C baking periods. The samples were made on 28 December 2002.

<table>
<thead>
<tr>
<th>Number of days baked</th>
<th>1/16/02</th>
<th>1/28/02</th>
<th>2/22/02</th>
<th>3/27/02</th>
<th>4/19/02</th>
<th>5/20/02</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>38 ± 1.1</td>
<td>43 ± 1.3</td>
<td>42 ± 1.3</td>
<td>43 ± 1.3</td>
<td>37 ± 1.1</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>13 ± 0.5</td>
<td>14 ± 0.5</td>
<td>14 ± 0.5</td>
<td>13 ± 0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>11 ± 0.5</td>
<td>13 ± 0.5</td>
<td>13 ± 0.5</td>
<td>12 ± 0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>8 ± 0.5</td>
<td>10 ± 0.5</td>
<td>12 ± 0.5</td>
<td>10 ± 0.5</td>
<td>9 ± 0.5</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>11 ± 0.5</td>
<td>11 ± 0.5</td>
<td>12 ± 0.5</td>
<td>10 ± 0.5</td>
<td>9 ± 0.5</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>11 ± 0.5</td>
<td>10 ± 0.5</td>
<td>10 ± 0.5</td>
<td>10 ± 0.5</td>
<td>8 ± 0.5</td>
<td></td>
</tr>
</tbody>
</table>

### TABLE 7. Elastic contrasts for corresponding samples in tables 5 and 6. For example, the entry for 5 days baked and measurements on both samples made on 22 February is 33/14 ± 2.4. Values for 20 and 25 days baked are not included because of the possible accidental switching of the 20 day and 25 day samples in the plain gelatin case (see end of table 5 caption).

<table>
<thead>
<tr>
<th>Number of days baked</th>
<th>1/16/02</th>
<th>1/28/02</th>
<th>2/22/02</th>
<th>3/27/02</th>
<th>4/19/02</th>
<th>5/20/02</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2.7 ± 0.1</td>
<td>2.9 ± 0.1</td>
<td>2.7 ± 0.1</td>
<td>2.5 ± 0.1</td>
<td>2.9 ± 0.1</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>2.4 ± 0.1</td>
<td>2.4 ± 0.1</td>
<td>2.4 ± 0.1</td>
<td>2.4 ± 0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>2.0 ± 0.1</td>
<td>2.2 ± 0.1</td>
<td>2.1 ± 0.1</td>
<td>2.1 ± 0.1</td>
<td>2.1 ± 0.1</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>2.1 ± 0.1</td>
<td>2.8 ± 0.2</td>
<td>2.0 ± 0.1</td>
<td>2.2 ± 0.1</td>
<td>2.7 ± 0.2</td>
<td></td>
</tr>
</tbody>
</table>
Corresponding B-mode images and elastograms of the heterogeneous phantoms were made at both the University of Texas-Houston and at the University of Wisconsin-Madison. The first of these images were made of phantom A at UT-H and are shown in figure 3. Corresponding axial strain profiles made using elastograms obtained over a 24 day period are shown in figure 4. Figures 3 and 4 indicate that the elastic strain contrast and size and shape of the cylindrical inclusion are temporally stable.

Similar data on phantom A were obtained during a later period at UW-Madison. Figure 5 shows 3 sets of B-mode images and elastograms obtained 4, 5 and 6 months after production of phantoms A. Lateral and axial elastic strain profiles, derived from the three elastograms are shown at the bottom of the figure. The data again give strong evidence of long-term stability of strain contrast and long-term stability of size and shape of the cylindrical inclusion.

Figure 6 shows images and strain profiles for phantom B. On the upper left is an elastogram and on the upper right is a T₂-weighted MR image. Both images were made about one month after production of the phantom. Recall that the diameter of the cylindrical inclusion in phantom B is 2 cm.

Elastic strain contrasts were derived from elastograms using the method followed by Kallel et al. Then the contrast transfer efficiency relation in Kallel et al. can be employed to estimate elastic contrasts from experimental elastic strain contrasts (Table 8). The three steps for computing the elastic strain contrasts from elastograms are as follows.

1. Mean elastic strains in four 7mm x 7mm square areas of the background material were averaged to yield the background strain, S_b. To avoid the 'cross' strain enhancement in the
elastograms of cylinders, the four square areas were positioned about 2 cm away from the inclusion at map positions NW, NE, SE and SW where north (N) is defined to be upward. The brighter strain enhancement ‘cross’ arms extend N, E, W and S from the inclusion.

(2) The mean strain, $S_r$, over a 7 mm x 7 mm square area centered in the inclusion was computed.

**TABLE 8.** Experimentally-determined strain contrasts, (true) elastic contrasts (Instron), and strain contrasts computed from elastic contrasts for phantoms A and B. The uncertainties are propagated assuming a 3% uncertainty for all Instron-measured $E$ values.

<table>
<thead>
<tr>
<th></th>
<th>Phantom A</th>
<th>Phantom B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elastic strain contrast from elastograms and date</td>
<td>1.35 (7/18/01) †</td>
<td>1.65 (1/4/02)</td>
</tr>
<tr>
<td></td>
<td>1.30 (9/16/01)</td>
<td>1.57 (1/15/02)</td>
</tr>
<tr>
<td></td>
<td>1.30 (1/15/02)</td>
<td></td>
</tr>
<tr>
<td>True elastic contrast (Instron)</td>
<td>1.7±0.1</td>
<td>2.7±0.1</td>
</tr>
<tr>
<td>Elastic strain contrast computed from the true elastic contrast ‡</td>
<td>1.4±0.1</td>
<td>1.7±0.1</td>
</tr>
</tbody>
</table>

† Elastogram and strain contrast by F. Kallel at UT-Houston
‡ Kallel et al

**FIG. 4** Axial strain profiles for phantom A through the axis of the cylindrical derived from elastograms. Involved elastograms were made on the dates indicated in the key for each profile. Over the monitored period of 24 days, little change in profiles occurred.
FIG. 5 US images (top) and elastograms (bottom) over 2 months of phantom A. Lateral (a) and axial (b) strain profiles from elastograms where 16 Nov = solid, 15 Dec = dashed, 15 Jan = dotted; vert axes = strain and horizontal axes in cm.
(3) The elastic strain contrast, \( C_s \), is then defined to be \( C_s \equiv S_b/S_c \).
Elastic strain contrasts for phantoms A and B, with dates of acquisition of elastograms involved, are shown in the first row of table 8. In the second row are shown the elastic contrasts (inclusion Young’s modulus ÷ background Young’s modulus) as determined on homogeneous samples via Instron, and in the third row are shown elastic strain contrasts computed from elastic contrasts using the Contrast Transfer Efficiency (CTE) method described in Kallel et al. These values of elastic strain constant are 1.40 for phantom A and 1.91 for phantom B, using the elastograms made on 15 January 2002.

DISCUSSION

US and MR properties at room temperature (22 °C)

It is apparent from the US and MR properties of the seven types of materials reported in table 2 that there was generally no attempt by us to produce materials with US and/or MR

(2) Note that some researchers in elastography consider an alternative definition of elastic strain contrast, where the background strain \( S_b \) is taken to be the local mean strain in the strain enhancement “cross” which results in the largest absolute value for \( S_b/S_c \).

These values of elastic strain constant are 1.40 for phantom A and 1.91 for phantom B, using the elastograms made on 15 January 2002.
properties that closely mimic those of soft tissues. Regarding US, however, we required that propagation speeds and attenuation coefficient slopes be lower than those in soft tissues to be mimicked since it is rather easy to increase values of these properties independently; e.g., propagation speed can be elevated through addition of a salt, such as NaCl, and attenuation slope can be increased by adding a finely-powdered solid such as graphite. Also, such additives should have little effect on elastic properties; e.g., compare \( E \) values for the plain gelatin (no graphite) in the first row of table 3 with those for the gelatin + graphite + glass beads in the fourth row of table 3.

Thus, the propagation speeds in the background materials for phantoms A and B (rows 3 and 6 in table 2) could have been elevated by 40 m/s. Corresponding elevations of speed in the inclusions (rows 4 and 7) would be unavoidable because of the direct contact between the background and inclusion materials; however, since the propagation speed in a tumor typically exceeds that in the surrounding normal tissue, the result would be reasonable in the phantoms.

The background material in phantom B mimics human liver, breast glandular parenchyma or muscle reasonably well in terms of \( T_1 \). The \( T_1 \) value of 562 ms at 22 \( ^\circ \) C is in the range of the value of 561 ms for human liver at 40 \( ^\circ \) C and a frequency of 40 MHz obtained by Grodd and Schmitt.\(^{47}\) Note that the value obtained by Grodd and Schmitt was actually 397 ± 1 ms at 20 MHz; assuming a \( T_1 \) frequency dependence of (frequency)\(^{-1/2}\), 397 ms converts to 561 ms at 40 MHz. At 37 \( ^\circ \) C and 50 MHz, Koenig and Brown\(^{49}\) found a \( T_1 \) value of 305 ms for human breast glandular parenchyma; the 562 ms value for the background in phantom A seems to be a reasonable approximation. For human muscle at 37 \( ^\circ \) C and 43.5 MHz, Borghi et al\(^{50}\) found a \( T_1 \) range of 650 to 800 ms. The 562 ms value for the background of phantom B is just below this range.

The \( T_1 \) value for the inclusion in phantom B is 1,610 ms. Typically, the \( T_1 \) value for a human tumor \textit{in vivo} is higher than that of the surrounding normal tissue; thus, the higher \( T_1 \) value here is consistent. For human breast carcinoma, \( T_1 \) ranges from 550 to 980 ms. For hepatomas, \( T_1 \) ranges from 784-1,080 ms, and for muscle carcinomas, \( T_1 \) ranges from 762-1,052 ms.\(^{5}\)

The \( T_2 \) value of 230 ms for the background material in phantom B is 4 or 5 times the value for most normal human soft tissues, excluding brain. For example, Nyman et al\(^{52}\) found a value of 51 ± 6 ms for human liver \textit{in vivo} at 15 MHz. (Note that \( T_2 \)'s have little frequency dependence.\(^{48}\)) Ehman et al\(^{53}\) found a \( T_2 \) value of 32 ms for human muscle \textit{in vivo} at 15 MHz.

The \( T_2 \) value of 416 ms for the inclusion in phantom B is about 4 or 5 times higher than is generally the case in tumors. For liver hepatomas \( T_2 = 84 \pm 26 \) ms, and for breast carcinomas \( T_2 = 94 \pm 48 \) ms.\(^{51}\)

### Elastic properties

The study reported in tables 5 and 6 was done to determine whether baking the samples at 50 \( ^\circ \) C enhanced stability of Young’s moduli and, if so, what is an optimal number of baking days. The results indicate that the only significant effect of the baking is to lower the \( E \) value which, after returning to room temperature, remains relatively constant, even when the number of baking days is zero. Thus, the baking can be used to adjust \( E \) rather than to contribute to long term stability of \( E \). The range of \( E \)’s available for the plain gelatin (0\% oil) formulation is then about 15 kPa through 107 kPa and from 10 kPa through 37 kPa for the 50\% oil emulsion.

There is not a great deal of information on elastic properties of soft tissues in the literature. Krouskop et al\(^{1} \) reported \textit{in vitro} values for normal and abnormal breast and prostate tissues. For quasistatic conditions, normal prostate was found to have a Young’s modulus of 60 kPa, BPH (benign prostate hyperplasia) a value of about 38 kPa, and cancer about 100 kPa. Thus,
the elastic contrast for prostate cancer in normal tissue is about 1.7, which is the elastic contrast measured via Instron® by Krouskop for the components of phantom A. The actual values of $E$ in phantom A (Table 3, rows 3 and 4) are about 1/3 of those for the tissues, but that is not very important because elastic contrast is the most important parameter. Also, referring to tables 5 and 6, eliminating the 3-day 50°C baking period to which phantom A had been subjected, the $E$ values of the tissue-mimicking materials should actually closely approximate the tissue values. (Note that table 6 involves a 50% oil emulsion whereas the background of phantom A is 32% oil, so $E$ should be higher in the latter than in the 50% oil case.) Thus, mimicking $E$ values and elastic contrast for normal prostate and prostate cancer appears to be easily achievable.

The materials described in connection with tables 5, 6 and 7 are good candidates for use in heterogeneous phantoms to represent breast cancer in normal glandular tissue. For breast glandular tissue, Krouskop et al found normal human glandular to have Young’s moduli (and standard deviations) of 28 ± 14 kPa at 5% compression and invasive infiltrating ductal carcinoma to have values of 106 ± 32 kPa. These values translate to an elastic contrast of 3.8 ± 2.2. Referring to the 0 baking days rows in tables 5, 6 and 7 and taking the plain gelatin as tissue-mimicking cancer and 50% oil-in-gelatin as tissue-mimicking normal breast glandular tissue, the mean value of $E$ for the tissue-mimicking cancer is 111 kPa and that for the TM glandular is 41 kPa; these values are well within the ranges of the corresponding tissues. Also, the phantom elastic contrast of 111kPa/41kPa = 2.7 is well within the range of elastic contrasts for breast cancer in normal glandular tissue.

**Long term stability**

In table 2, values of Young’s moduli typically show an increase followed by a decrease over the periods of time monitored. For example, the mean value for the background material for phantom A increased from 28.3±0.7 kPa in August 2001 to 41.0±1.0 kPa in February 2002 followed by a decrease to 33.0±1.2 kPa in May 2002. The higher values occurred in the winter and lower in the summer.

Whether there is such a temperature effect on $E$ values or not, it is significant that the Instron®-determined elastic contrasts for phantoms A and B in table 4 are nearly invariant; i.e., long-term stability of elastic contrasts exists.

Evidence for long-term geometric stability of the inclusions in the two heterogeneous phantoms is given in elastograms and elastic strain profiles derived from them. Three lateral strain profiles made over a 24-day period using phantom A are shown in figure 4. The profiles are nearly indistinguishable when noise is accounted for. All three profiles were made within one month after completion of production of the phantom.

Similar evidence for geometric stability of phantom A is given in figure 5 where both lateral and axial elastic strain profiles are shown overlapping over a period from four to six months following production of the phantom.

Excellent long-term stability of elastic strain contrast, computed from elastograms, is shown in row 1 of table 8. phantom A was monitored over a 6-month period with no significant change in elastic strain contrast. Elastic strain contrast for phantom B was monitored only over a 10-day period, but again there was negligible change.

In the second row in table 8 are shown the mean elastic contrasts for phantoms A and B computed from values in table 4. Elastic contrasts (ratios of Young’s moduli) computed from these mean elastic strain contrasts using the Contrast Transfer Efficiency method of Kallel et al agree rather well with the Instron®-measured elastic contrasts (row 1) for both phantoms A and B.
SUMMARY

Materials have been developed that can be used for mimicking soft tissues, including fat, nonfat and cancer, in terms of elastic, US and MR properties. A broad range of Young’s moduli is attainable from about 10 kPa to about 110 kPa. The materials can be produced in stable configurations in heterogeneous phantoms for use in quality control and performance testing of US and MR elastography systems. A range of elastic contrasts as high as 2.7 can be included in these phantoms where materials with different compositions can be in direct contact without change in elastic contrast or geometry over many months and perhaps years. Anthropomorphic phantoms representing, e.g., breast or the prostate region, could be produced and used to test elastography systems in a way more closely related to actual patient conditions than are available through simpler performance phantom geometries. Different safflower oil concentrations in the oil-in-gelatin emulsions used allow some control over the elastic contrast, but additional control may be afforded by variations in baking the materials at 50 °C. An elastic contrast as high as 100 kPa/12 kPa might be attainable in a heterogeneous phantom by baking a background 50% oil-in-gelatin emulsion at 50 °C for 10 days and then, after cooling to room temperature, introducing a plain gelatin (0% oil) inclusion no subsequent baking. Thus, the range of elastic contrasts from 1 through about 8 may be achievable with the oil-in-gelatin emulsions. Long-term stability regarding heterogeneous phantoms in which different components experience different baking times needs to be investigated.

ACKNOWLEDGEMENTS

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REFERENCES


