A Novel Soft Tissue Marker for Multimodal Breast Imaging with Positive MRI Contrast

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Introduction: Radiographic tissue markers or "clips" are commonly used to mark the location of biopsies and surgeries for subsequent imaging. Most commercially-available markers were designed for visibility on x-ray mammography (MMG), and consist of a small metallic wire bent into a distinctive shape. These markers are very distinct on mammographic images, but their visibility under MRI and ultrasound (US) is suboptimal. In MRI, metallic markers are identifiable primarily by the signal void produced by local susceptibility-induced B_0 distortions. The size of these signal voids varies from ~3-18 mm, depending on the metal alloy, the MR sequence, and the orientation of the clip (*1*). In fatty and heterogeneous tissues such as the breast, these voids are not sufficiently distinct, often making it difficult to identify the clip location with confidence.

Here we present a novel tissue marker that gives a distinct, bright MRI signal using T_1 contrast (*2,3*). It can be manufactured from biocompatible materials, does not degrade over time, can be deployed with conventional interventional devices, and has x-ray and US visibility equal to or better than conventional tissue markers.

Materials and Methods: The design of the marker, shown in Fig. 1, consists of a small, solid cylinder filled with a liquid contrast agent and sealed on both ends. Several materials were evaluated for the cylinder material, including glass capillary tubes, silicone tubing, Teflon tubing, and polyethylene tubing. The liquid center is a mixture of a radio-opaque nonionic CT contrast agent (Ioversol, *Optiray 320*, Mallinckrodt) doped with small amounts of a T_1-reducing MRI contrast agent (Gd-DTPA, *Magnevist*, Berlex). After filling, cylinders were sealed either with epoxy (for the glass cylinders) or by heat-sealing the polymer tubing with a hot iron. In both the epoxy and heat-sealed systems, complete sealing was achievable with no air bubbles remaining inside the marker. A series of markers were produced with different cylinder materials and concentrations of the Gadolinium and Iodine contrast agents. Markers were embedded in a gel phantom and imaged on a 3T Siemens Trio scanner using 3D gradient echo sequences with parameters typical for dynamic contrast-enhanced breast MRI studies (TR/TE=20/5ms, flip angle 30°, resolution 0.4-2 mm). Gel phantoms were also imaged with a digital MMG system (Digital 2000 Mammo, GE) and with a US system (Philips 200) to evaluate the marker appearance in typical breast imaging modalities. Interventional deployment of the markers was then simulated by performing US-guided placement using a 10-ga introducer in a meat phantom (pork chop). After placement of the markers, the meat phantom was imaged with 3T MRI, MMG, and US.

Results: Images of the gel and meat phantoms in MRI, MMG, and US are shown in Fig 2. The top row (a-d) shows a marker made from a glass cylinder, and with a mixture of 5mM Gd-DTPA in 68% Ioversol. Under T_1-weighted gradient 3T MRI (Fig 2a), the liquid center was hyperintense and clearly distinguishable from the background signal when oriented both parallel and perpendicular to the image plane. Under MMG (Fig 2b) the liquid center was highly radio-opaque, while the glass was only slightly radio-opaque. The marker was clearly visible in both orientations. Under US the marker was highly visible when its axis was parallel to the transducer face (Fig 2c), but less visible when oriented perpendicularly (Fig 2d). The meat phantom experiments had similar findings. For this study, markers using both silicone and polyethylene materials were deployed successfully through the introducer without damage and were visible under US guidance. Figures 2e-g show several polyethylene markers under MRI (3D GRE, TR/TE = 20/4.9ms, 30° flip, resolution 0.9x0.9x2 mm), MMG, and US. In each case the marker visibility was comparable to the gel phantom results.

The gel phantom experiments were then repeated with various combinations of materials and contrast agents to optimize marker visibility. The T_1 and T_2 of the liquid contrast agent varied substantially with the concentrations of both the Gadolinium and Iodine contrast agents. A mixture of 5mM Gd-DTPA in 50% Ioversol was selected as it provided good MR contrast (T_1=95ms, T_2=30ms at 3T) and high radio-opacity. The MRI appearance of the various container materials was less variable. Polyethylene was identified as the best container material due to its high strength (and thus thin walls), good thermal workability, and potential for doping to increase radio-opacity.

Discussion: The bright appearance of the marker's liquid center under MRI will allow the marker to be unambiguously identified under normal T_1-weighted MRI scans. Since it does not depend on B_0 distortion to produce contrast, this marker is more compatible with other MR techniques such as spectroscopy and is less sensitive to different field strengths. The use of a liquid mixture of contrast materials allows fine adjustment of the contrast for specific applications or to balance the magnetic susceptibility of the container material. If the contrast agents were to leak out it would reduce the bright MRI effect, making the marker difficult to see on MRI but still comparable to conventional markers on MMG and US. Leakage would not be a safety problem since these agents are regularly injected intravenously in large quantities.

The bright MRI contrast is improved with increased liquid volume, higher resolution imaging, and close matching of magnetic susceptibility between the liquid center, container, and surrounding tissue. The x-ray contrast comes from the radio-opacity of the iodine contrast agent and, to a lesser extent, the radio-opacity of the container material. The US contrast is produced by reflection of sound waves off the tissue-container and container-liquid interfaces, and can be increased by scoring or otherwise roughing the container surface. Future development of this device includes additional optimization of materials and manufacturing methods, and *in vivo* studies for measuring visibility, biocompatibility, and migration.

References: 1) S Meisamy et al., ISMRM 2004; 2) US Patent Pending, Application #11/281,801; 3) P Bolan et al, RSNA 2005

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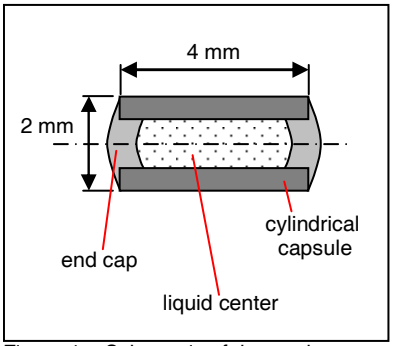

Figure 1 – Schematic of the marker design.

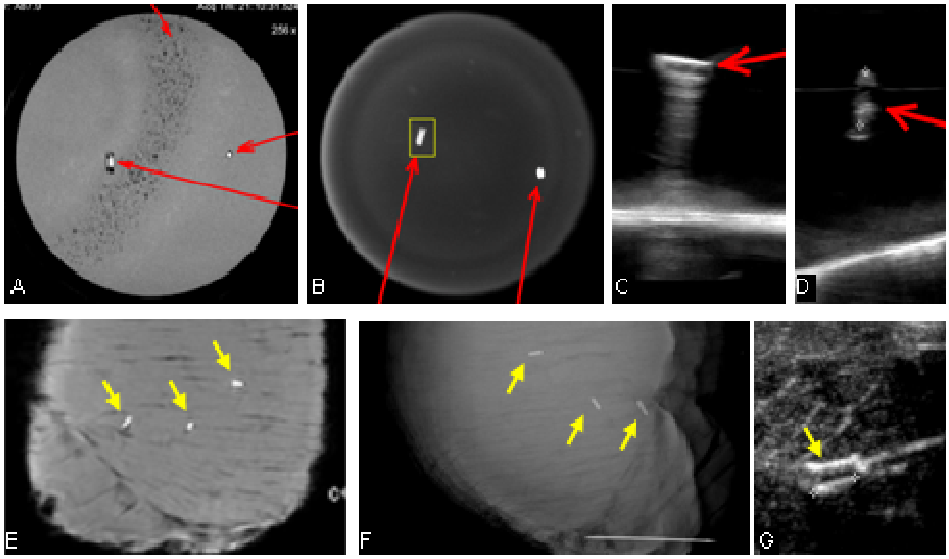

Figure 2 – In vitro imaging of the marker. Top row shows a glass marker in gel phantom in **a)** 3T T_1w-GRE MRI, **b)** MMG, and US in the **c)** parallel and **d)** perpendicular orientations. Bottom row shows a polyethylene marker in a pork phantom under **e)** 3T T_1w-GRE MRI, **f)** MMG, and **g)** US.