Study of marker component for low susceptibility tri-modalities breast tumor localization

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Introduction:

Wire localization is the traditional preoperative procedure for surgical demarcation of breast lesions and is usually guided by X-ray or ultrasound (US) and more recently MRI. However, the wire visibility is suboptimal in 4-9% of surgical cases and generates vasovagal reactions in up to 20% of patients [1]. We have developed and reported an MRI, US and X-ray visible marker as an alternative to wire localization. Contrast was achieved on the basis of the susceptibility, echogenecity and atomic number of the marker components. Ultrasound and X-ray contrast was achieved by the use of small glass microspheres to control echogenicity and atomic number. While MRI contrast was achieved by modulating marker susceptibility with the glass microspheres and the addition of small amounts of iron in aluminum microspheres. In-vitro and in-vivo experiments have demonstrated that the marker is appropriate for localizing breast tumors [2,3]. While currently useful, a more ideal construct would demonstrate positive contrast in standard T1 weighted breast MRI [4] so as not to be confused with other mechanisms for signal loss. By eliminating susceptibility altering components would allow for quantitative measurements in breast MRI such as Gd-DTPA contrast uptake or proton spectroscopy. For this purpose, we replaced the glass microspheres with copper which more closely matches the susceptibility of tissue. We then added Gd-DTPA to the gel to shorten its T1. This study details the optimization of the marker components and early studies in in-vitro leading toward in-vivo application for imaging guided breast surgery.

Materials and Methods:

Materials: The marker is composed of biocompatible copper microspheres (Salem Specialty Co.,USA, diameter 0.4mm) suspended in a Gd-DTPA gelatin solution. The magnetic susceptibility of copper (9.06×10^{-6}) is similar to that of water (9.63×10^{-6}) and does not create induce sizeable signal void [5] in T1 weighted images. In order to control the T1 and T2 of the marker, varying concentrations of Gd-DTPA were added, and the optimal Gd-DTPA was determined to provide maximum contrast. As the copper microspheres have a substantially higher acoustic impedance difference from tissue [6], the US contrast of the marker was modulated by adjusting the number of copper microspheres included in the marker. Similarly, the copper exhibit 46 fold increase in X-ray absorption coefficient compared to water at energy of 20KeV [7], thus ensuring good X-ray contrast. To optimize marker composition, gel solutions with different components were cast into glass tubes with 0.6cm diameter for MRI contrast study. After determined the optimal marker mixtures, a final marker (Fig.1) made of 61 copper microspheres (5% copper volume to total volume) with a cylindrical structure 7mm long with 2.05mm diameter using the fabrication methods outlined in [2]. The final marker was placed in a chicken breast for comparative study by MRI, X-ray and Ultrasound imaging as described in [2].

MRI Experiments: All MR studies were performed on 1.5 T MRI system, Signa, GE Medical System using a 3-inch surface coil. A 2D GRE (TR 18.4ms, TE 4.2ms, FA 30°, and matrix 256) was used for demonstrating the contrast of marker in T1 weighted MRI. This pulse sequence is typical for our breast MRI work [4].

US Experiments: US images were acquired with a Philips ATL HDI-5000 imaging system using a Broadband linear array 5-12MHz transducer (L12-5 50mm, Philips).

X-Ray Experiments: This was performed with a GE Senographe 2000D was used for X-Ray imaging using a tube voltage of KVP 25 and tube current of 87mA.

Fig.1: Photograph of a final marker

Results:

A series of in-vitro experiments were used to determine the optimum marker composition. Our objective is to find the optimum Gd-DTPA content to provide biggest MRI signal in T1 weighted MRI. We have found this condition was met with Gd-DTPA concentration of 10mmol/l. This is shown in Fig.2 where we show a coronal MRI of gel solutions with different Gd-DTPA concentrations and demonstrated that beyond 10mmol/l T2 shortening starts to reduce signal contrast for our choice of pulse sequence parameters.

To evaluate the effect of copper on MRI contrast, we compared the MR images of four kinds of marker components: gel, gel added 10mmol/l Gd-DTPA, gel added 5% copper volume to total volume, gel added 10mmol/l Gd-DTPA and 5% copper volume, the T1 weighted MR image is shown in Fig.3 and demonstrated that a variation in the marker MRI visibility mostly results from the Gd-DTPA concentration instead of the copper and the small variations in susceptibility does not substantially influence image contrast.

To evaluate the marker visibility with three imaging modalities, we placed the final marker in a chicken breast for comparative imaging, the marker appears as a clear hyperintense structure in MRI (Fig.4 (a)), US (Fig.4 (b)) and X-ray images (Fig.4 (c)) without any degradation in the quality of the images.

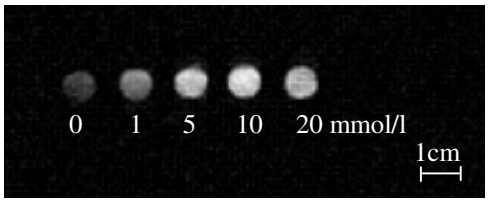

Fig.2: T1 weighted MR image of five marker components with different Gd-DTPA concentration

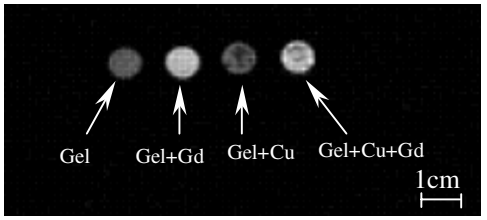

Fig.3: T1 weighted MR image of four different marker components

Discussion and Conclusions:

A low susceptibility marker has been designed which can provide positive contrast in T1 weighted MRI, US and X-ray imaging. The optimal Gd-DTPA concentration is 10mmol/l for the MRI contrast, the ratio of copper volume to the total marker volume of 5% allows the high US contrast of the marker [2] while provide no MRI distortion. Although designed for breast applications, the same marker construct could be used for other applications such as liver and kidney interventions. In future studies, we will coat the marker with a biocompatible membrane for in-vivo animal evaluation.

References:

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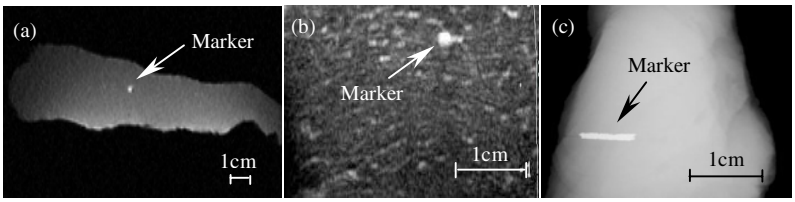

Fig.4: MRI (a), US (b) and X-ray image (c) of the final marker in a chicken breast