A MRI/US/X-Ray Compatible Breast Localization Marker: In-Vivo Histopathology

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Introduction: Pre-operative wire localization is the most common pre-operative breast procedure to guide the surgeon in tumour resection. Wire placement is usually achieved via mammographic, ultrasonographic or more recently MRI guidance. Intraoperatively, the wire location is usually detected by US; however, visibility can be suboptimal in 4-9% of surgical cases. Furthermore, a vasovagal reaction is seen in up to 20% of patients [1]. As the wire is transcutaneous, wire placement and surgery must be achieved on the same day which creates logistical challenges for the surgical and radiological departments. In our group, we have developed an interstitial marker which gives high contrast and reliable marker visualization for MRI, US and x-ray imaging. As the marker is purely interstitial, marker placement and surgery can be performed on separate days. The marker has been tested with phantoms and demonstrated excellent contrast in MRI, US and mammography [2]. In this study, we test the in-vivo contrast of the markers and explore the biocompatibility in an acute setting using a rabbit model followed by histopathology. These evaluations set the stage for future human applications of this novel marker for surgical biopsy localization.

Materials and Methods:

Marker Preparation: The marker is composed of iron containing aluminium(500 μm) and glass microspheres (400-600 μm) suspended in a gelatin matrix [2]. After dip-coated with a biocompatible Polyurethane, the size of marker is about 7.0 mm long with 2.1 mm diameter as shown in Figure 1. Sterilization for in-vivo use is achieved by x- radiation.

Figure 1: Photograph of marker

Animal Preparation: 2 New Zealand female white rabbits (3.7kg and 4.0kg) were used in this study and the thigh muscle was the site of marker insertion. The rabbits were sacrificed at 2 days and 7 days after marker placement. The animal protocol was in compliance with the Canadian Council for Animal Care Guidelines and approved by the local animal care committee of Sunnybrook and Women's College Health Science Centre.

US Experiments: Ultrasound imaging was performed with a Philips ATL HDI-5000 imaging system using a broadband linear array 5-12MHz transducer (L12-5 50mm, Philips). This was used for marker placement and determination of marker contrast throughout the study.

MRI Experiments: All MR studies were performed on 1.5 T MRI Signa, (GE Medical Systems) using a 5-inch surface coil. A 2D T1 weighted, gradient recalled sequence (SPGR, TR 18.4ms, TE 4.2ms, FA 30°, matrix 256, FOV 20cm) was used for demonstrating MRI contrast of the marker.

X-Ray Experiments: This was performed with a GE Senographe 2000D. The x-ray kilovoltage was 33kVp with a rhodium anode and filtration using a tube current of 68mA.

Histopathology Experiments: After marker removal, the dissected specimen were cut in a 20x15x5mm volume and fixed in 10% neutral buffered formalin for 2 days. After processed in paraffin blocks, sections 5um thick were cut and stained with Hematoxylin-Eosin (H&E) for histopathological analysis.

Results: In the week following localization procedures, the rabbits were scanned at three different times post-procedure intervals (1 hour, 2 days and 1 week) with MRI, US and X-Ray to monitor the contrast of marker with time. Figure 2 shows a typical marker 2 days post-procedure on MRI, US image and X-Ray image. Our objective in designing the marker for MRI is to find the optimal iron content that allows clear marker definition without excessive distortion of the MR image from the resulting B_0 inhomogeneities. This was determined to require 52μg iron which produces a clear signal void artifact of 5.15mm in diameter (figure2 (a)). The US image of marker (figure2 (b)) appears a clear hyperintense structure with acoustic shadowing. The X-Ray image of the rabbit thigh (figure 2 (c)) also clearly demonstrated the marker as a radio-opaque structure.

The H&E stained sections for the two-day and seven-day survival rabbit are shown in figure 3. Active inflammation is present two days posts insertion near the marker due to neutrophil accumulation, cell death was also found in the associated muscle fibers (figure 3 (a)). By 1 week post-procedure, neutrophils concentration was reduced and macrophages accumulation was seen. Comparing the marker position in the 7-day survival experiment, we observed evidence of modest marker migration (<5.6mm). Furthermore, no change in marker contrast was evident over the course of the experiment.

Discussion and Conclusions: In-vivo MRI/US/X-ray contrast of the marker remains stable over a 1 week post-procedure interval. Modest evidence of infection as well as macrophages accumulation was seen after 1 week. This suggests that the marker can remain interstitial for up to a one-week period. This overcomes a number of radiological and surgical scheduling challenges for the localization and surgical procedures. Modest marker migration is seen and means to minimize this effect needs further study. Additional study of the very long-term stability and biocompatibility are needed. This new marker opens new possibilities for tumour localization and surgical guidance of MRI visible tumours through intra-operative US.

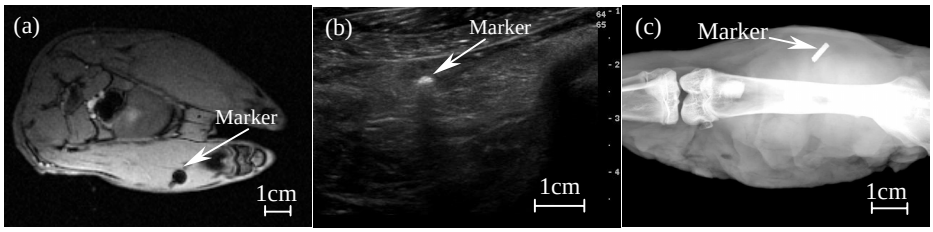

Figure 2: Axial images of marker in rabbit thigh. (a) MRI, (b) Ultrasound image, (c) X-Ray image

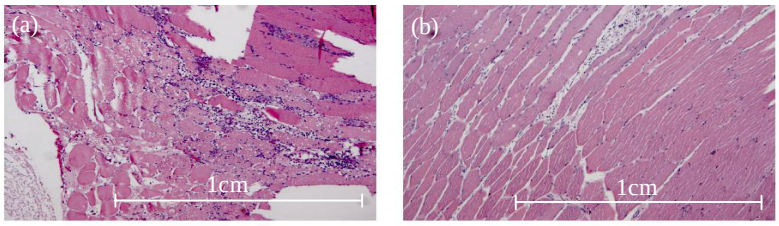

Figure 3: Histopathology at two days (a) and seven days (b) after marker injection

References:

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2. Li YM et al., ISMRM, 832, 2004.