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Technical note

Phantom study quantifying the depth performance of a handheld magnetometer for sentinel lymph node biopsy

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ABSTRACT

Purpose: The use of a magnetic nanoparticle tracer and handheld magnetometer for sentinel lymph node biopsy (SLNB) was recently introduced to overcome drawbacks associated with the use of radioisotope tracers. Unlike the gamma probe, the used magnetometers are not only sensitive to the tracer, but also the diamagnetic human body. This potentially limits the performance of the magnetometer when used clinically.

Methods: A phantom, mimicking the magnetic and mechanical properties of the human axilla, was constructed. The depth performance of two current generation magnetometers was evaluated in this phantom. LN-phantoms with tracer uptake ranging from 5 to 500 μg iron were placed at clinically relevant depths of 2.5, 4 and 5.5 cm. Distance-response curves were obtained to quantify the depth performance of the probes.

Results: The depth performance of both probes was limited. In the absence of diamagnetic material and forces on the probe (ideal conditions) a LN-phantom with high uptake (500 μg iron) could first be detected at 3.75 cm distance. In the phantom, only superficially placed LNs (2.5 cm) with high uptake (500 μg iron) could be detected from the surface. The penetration depth was insufficient to detect LNs with lower uptake, or which were located deeper.

Conclusion: The detection distance of the current generation magnetometers is limited, and does not meet the demands formulated by the European Association for Nuclear Medicine for successful transcutaneous SLN localization. Future clinical trials should evaluate whether the limited depth sensitivity is of influence to the clinical outcome of the SLNB procedure.

1. Introduction

Sentinel lymph node biopsy (SLNB) is the standard of care for staging the axilla of early-stage breast cancer patients. It achieves equal overall and disease free survival compared to axillary lymph node dissection, while it reduces morbidity [1–3]. The current standard for SLNB is the combined technique, which uses a radioisotope tracer (^{99m}Tc-nanocolloid) and blue dye. Both tracers are injected interstitially in the breast, and subsequently distributed to the sentinel lymph nodes (SLNs). In the operating theatre, the surgeon detects the tracers within the SLNs using a gamma probe and/or visually by blue colorization of the node(s) [4]. First, the SLNs are transcutaneously localized with the gamma probe to determine the optimal incision site. Post incision, the SLNs are identified and removed. The combined technique performs very well with an identification rate of 96% and a false-negative rate of approximately 5–10% [5].

This is explained by multiple factors; the high sensitivity of the probe to low amounts of tracer, penetration depth of several centimeters, and specificity to the tracer. Despite these advantages, the use of radioactivity is also associated with drawbacks. Firstly, the handling and disposal of radioactive material is subject to stringent regulations. Secondly, the 6 h half-life of the ^{99m}Tc tracer complicates theatre scheduling. Finally, the radiotracer is only produced in a limited number of reactors, hampering availability of the procedure worldwide. These drawbacks have stimulated the search for alternative radioisotope-free techniques for SLNB [6]. The use of a magnetic nanoparticle tracer and handheld magnetometer is one of these alternative techniques. The magnetic tracer consists of superparamagnetic iron oxide (SPIO) nanoparticles, which have a long shelve life. The use is not restricted by radiation

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related regulations, and therefore overcomes the drawbacks associated with the use of radioisotopes.

The use of a magnetic tracer and handheld magnetometer for SLNB was recently evaluated in several clinical trials [7–10]. The used magnetometer (SentiMAG®, Endomag Ltd., UK) is a magnetic susceptometer, meaning that the device is not only sensitive to the magnetic tracer, but to all magnetic materials present near the probe; e.g. human tissue. The magnetic tracer produces a positive signal in vicinity of the probe whilst the diamagnetic tissue produces a negative signal. The resulting displayed signal is the sum of both the positive and negative components. Therefore the positive signal from the tracer can be 'obscured' by the negative signal from the tissue, potentially resulting in failed sentinel lymph node detection. Since the response of this magnetometer is highly distance dependent, this poses a fundamental limitation for the detection of deeply located sentinel nodes with low tracer uptake [11].

To compensate for the undesired diamagnetic signal, the probe is balanced on the skin, away from the injection site. The measured negative signal from the tissue in this position is added to the displayed signal for compensation. However, during SLN localization the probe is not used in a static position. By pressing the probe against the skin or placing it in the incision the amount and geometry of the tissue in vicinity of the probe changes, and therefore the magnetic tissue contribution is not constant during the SLNB procedure. This can result in a false positive signal when no tracer is present, or obscure the signal when tracer is present.

The goal of this study is to quantify this balancing effect, and to evaluate whether it limits axillary sentinel lymph node detection. We developed a phantom with magnetic and mechanical properties similar to human tissue, in which lymph node phantoms filled with magnetic tracer can be placed at clinically relevant depths. The performance of the magnetometer was evaluated with different quantities of magnetic tracer placed at different depths in this phantom.

2. Materials and methods

The performance of the magnetometer used in the previous clinical trials in breast cancer patients and the currently sold version were evaluated in this study. The SentiMAG® system consist of a handheld probe (previously used version with a diameter of 24 mm; Probe 1) (currently sold version with a diameter of 18 mm; Probe 2) (Fig. 1a), and a base unit which displays the measured signal.

2.1. Phantom

To evaluate the performance of the magnetometers a phantom resembling the magnetic and mechanical properties of the human axilla was constructed. A Perspex container (0.25 × 0.25 × 0.25 m) was filled with a 0.9% saline solution. The susceptibility of water (-9.05×10^{-6}) matches the magnetic susceptibility of tissue (-11×10^{-6} to -7×10^{-6}) [12], therefore saline was used as diamagnetic medium. To simulate mechanical tissue properties, a double layer of thin latex sheet (0.38 mm) was spanned across a Perspex cover with a circular aperture (diameter 60 mm) in the center. When the probe is pressed in the phantom, forces are exerted on the probe as during clinical transcutaneous hotspot detection. Furthermore, the sheet deforms in a similar geometry as tissue, mimicking the tissue deformation during an SLNB procedure. A scale bar on the side of the container was used to determine the depth of the probe in the phantom. Five height adjustable nylon wires were used to place a lymph node phantom at the desired depth. The phantom with a lymph node, and the probe pressed in the phantom is displayed in Fig. 1b.

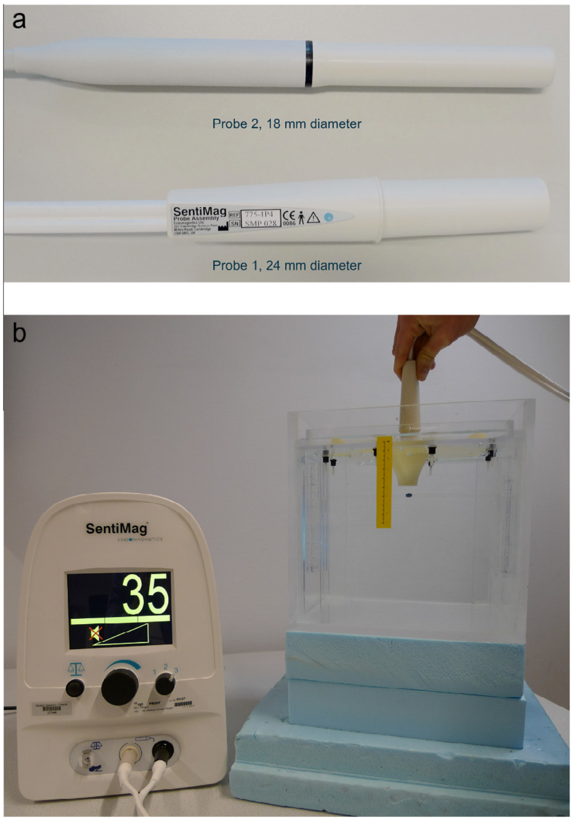

Figure 1. (a) A picture of both magnetometer probes used in this study. Probe 1 (Bottom) with a diameter of 24 mm was used in the reported clinical trials [7–10], Probe 2 (Top) with a 18 mm diameter is the currently sold version. (b) The phantom filled with saline, in which a lymph node phantom is placed. The probe is pressed through the circular aperture, covered by latex sheets. The deformation around the probe, mimicking tissue deformation, is visible. The yellow scale bar is used to measure the depth of the probe in the phantom. The magnetometer base unit (left) displays a positive signal due to presence of magnetic tracer. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Hollow PVC beads with an internal volume of 35 μL (Pharmabotics Ltd., UK) developed for use in a training simulator for SLNB with radioisotopes were used as lymph node phantoms [13]. Lymph node phantoms containing different amounts of iron were made by filling the beads with a dilution of magnetic tracer (Sienna+®, Endomag Ltd., UK, 27.9 mg iron/mL) and demineralised water.

2.2. Lymph node phantoms iron content and depth-placement

Before each measurement, a lymph node phantom was placed at a clinically relevant depth, determined based on the study of Mathelin et al. [14]. In their study, a ruler was used during surgery to measure the depth of all SLNs before excision in 11 breast cancer patients. The reported depth of the SLNs ranged from 1.5 to 8.5 cm. When only the depth of the most superficial SLN per patient is analysed, this results in a mean depth of 4.0 cm (SD 1.8, range 1.5–7.5 cm). In our study the LN phantoms were therefore placed at a depth of 2.5 cm (superficial SLNs), 4.0 cm (intermediate SLNs) or 5.5 cm (deep-seated SLNs) to evaluate the performance of the magnetometer in different clinical scenarios.

Besides the depth, the iron content of the LN phantoms was also varied to simulate SLNs with low, intermediate or high tracer uptake. Currently, there is no quantitative data available on the uptake of magnetic tracer by SLNs in humans. Waddington et al.