Radiofrequency Identification Tags for Preoperative Tumor Localization: Proof of Concept

OBJECTIVE. The objective of our study was to experimentally explore the potential for tumor localization using radiofrequency identification (RFID) tags and a newly developed handheld RFID detector.

MATERIALS AND METHODS. A unique RFID detector that combines the use of multiple interchangeable detector probes with both audio and LCD display signals was invented, allowing precise localization and identification of RFID tags. Accurate localization and identification were validated using this handheld RFID detector (TagFinder) and RFID tags of 2-mm diameter and 8- or 12-mm lengths. Experiments included the following: validation in various breast phantoms; differentiation of 4- to 6-cm-diameter tissue specimens with and without tags; determination of the nearest differentiable distance between two tags; proof of visualization of tags on sonography, radiography, and MRI; and experimental localization and resection of RFID-labeled tissue specimens.

RESULTS. Both 8- and 12-mm-length RFID tags implanted ≤ 6 cm deep were accurately localized and uniquely identified. Chicken breast specimens of 4- to 6-cm diameter implanted with RFID tags were accurately differentiated from specimens without tags. Tags in proximity could be reliably differentiated and uniquely identified when placed as close as 0–2 cm apart, depending on the tags’ precise orientations. RFID tags were easily visualized with sonography, mammography, and MRI, with artifacts present only on MRI. Localization and resection of RFID tags in the labeled tissue region were successful in grocery store–bought chicken breasts.

CONCLUSION. The combination of RFID tags and a new handheld RFID detector shows promise for preoperative imaging-guided tumor localization.

Radiofrequency identification (RFID) technology shows potential for multiple medical uses, including identification of surgical sponges and monitoring of endotracheal tube position, but heretofore not for preoperative tumor localization [1, 2]. An RFID tag, about the size of a grain of rice, contains a dormant microchip that can be stimulated with radiofrequency energy, causing reemission of a radiofrequency signal used to localize and identify the unique number of the tag. RFID tags that can be implanted in humans have already been approved by the U.S. Food and Drug Administration (FDA) for purposes such as patient identification. Current preoperative imaging-guided tumor localization options for nonpalpable breast lesions include imaging-guided placement of one or more radiopaque markers and preoperative percutaneous localization with a hookwire [3–5]. Direct injection of radioactive seeds has also reportedly shown promise [6, 7]. Injection of radioactive material and intraoperative detection with a Geiger counter are also commonly used to localize sentinel lymph nodes [8].

RFID tags potentially provide radiopaque markers that can be both uniquely identified and interactively localized if used in conjunction with a handheld reader that can interactively pinpoint tags. In theory, such an RFID system could replace current metallic tumor markers, preoperative hookwire localization, and specimen radiographs and could otherwise aid surgeons and pathologists in localizing nonpalpable tumors.

Based on these theoretic advantages, a handheld RFID tag reader has been developed and tests have been performed to show the...
accuracy and feasibility of imaging-guided tumor localization using RFID technology.

Materials and Methods
RFID Technology

The RFID system consists of two components: a reader and a tag [9]. Each tag contains a microchip that stores a unique identification number and an antenna that responds to interrogation by the reader [9]. The RFID reader sends a radio-frequency signal to the tag that in turn receives, alters, and reemits the signal [9]. The reader then captures the altered signal and responds with the combination of an LCD display and audio signal. For the experiments in this study, we used cylindrical RFID tags (VeriMed, VeriChip), which were 2 mm in diameter and 8- or 12-mm long, and an RFID reader (Figs. 1A and 1B) (TagFinder, Health Beacons). The reader is powered by a standard 9-V battery; operates at 134.2 kHz; and consists of an interrogation antenna, LCD display, power on button, read button, and audio signal mechanism (Fig. 1B). The reader’s LCD screen displays a bar indicating the proximity of the reader to an RFID tag and emits an audio tone that increases in volume and pitch as the reader is moved closer to a tag. If the read button is pressed, the reader displays the unique identification of the tag being interrogated. The RFID reader has two attachable interrogation antennae—a loop probe with a detecting range of 0–6 cm and a pencil probe, intended for highly specific localization, with a shorter range of 0–3 cm (Fig. 2). The loop probe was used in the research described herein unless otherwise specified. Signal strength is strongest when the reader approaches the longitudinal ends of the tag, meaning that scanning the reader across the tag from pole to pole produces peak signals at the end points, or ends of the RFID tag, and a relatively minimal signal over the tag’s center (Fig. 3).

Localization and Depth Detection

The ability to localize and detect the depth of implanted RFID tags was tested in an opaque sonography breast phantom (Breast Ultrasound Phantom, Blue Phantom Company) with a density of 0.92 g/cm³, which is comparable to breast tissue (Fig. 4A). An insertion needle was calibrated using a millimeter-scale steel ruler. The depth of insertion was verified in a gelatin phantom control by injecting three tags at varying depths and then inserting the ruler to confirm the depths (Fig. 4B).

Three tags were then injected into the sonography phantom at depths of 1.0, 2.0, and 3.0 cm. Three independent individuals, none with prior RFID experience, blinded to the locations of the tags were given a brief tutorial about how to use the tag reader to detect the depths of the tags in the phantom. These observers’ measurements were compared with the actual insertion depths.

Differentiating Specimens With and Without Embedded RFID Tags

On three separate occasions, sets of 20 pieces of grocery store–bought raw chicken breast were cut into 4- to 6-cm-diameter specimens. These pieces were prepared slightly larger than typical lumpectomy specimens to avoid the argument that the tags could be easily identified because of the specimens’ small sizes. During trial 1, 11 of the 20 pieces were each injected with RFID tags, five tags 8 mm in length and six tags 12 mm in length. The tags were injected into the specimens so that the tags and injection tracks were not visible. The 20 chicken pieces were then placed onto five plates, four pieces per plate, with individually numbered paper labels (numbered 1–20) underneath each chicken piece. Three individuals—a board-certified anesthesiologist, a premed college student, and a high school student—were then given a short 5-minute tutorial explaining how to use the handheld RFID reader to identify tags and
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determine unique tag identification numbers. Each individual was also given a form on which to record which chicken pieces, identified by the paper labels, contained tags. To ensure accuracy, the individuals were asked to record the final four digits of the associated unique tag identification numbers. The individuals were told that no chicken piece would contain more than one tag, but they were not told how many total tags were present. They were free to pick up, turn, and otherwise maneuver the chicken pieces. Of note, the injection tracks were not visible on the chicken pieces, so tag locations could not be determined illegitimately. The individuals then separately analyzed the chicken pieces and recorded their results on the provided forms.

For trial 2, the experiment was prepared just as the experiment for trial 1 except for a few changes. The experiment for trial 2 was conducted at the University of California, Los Angeles Medical Center, with three individuals participating including a radiology resident, a radiology fellow, and a medical student. This time, 10 of the 20 raw chicken pieces were each injected with one 12-mm RFID tag. In addition, the tag injection needle was inserted into each tagless chicken piece to eliminate the chance that an injection track might provide a clue about a tag’s presence. Finally, the response forms were modified so that participants were queried whether they could determine in any way which pieces contained tags by visually inspecting the chicken pieces.

For trial 3, the experiment was prepared just as the experiment in trial 2 except the chicken pieces were not presented on plates but, instead, inside individually labeled clear plastic bags. In addition, an added functionality of the RFID reader was explained: namely, that the read button, if pressed while not actively detecting a tag, displays the most recent identification number recorded in its memory. In the event of this occurrence the letter $M$ precedes the identification number on the LCD screen, indicating that the displayed number is from memory, rather than from active detection. In trial 3, 11 individuals participated, including two radiology residents, four medical students, two radiology researchers, one engineer, and two secretaries.

Nearest Differentiable Proximity Between Tags

A grocery store–bought hotdog was used as a medium in which to determine the nearest differentiable proximity between tags (Fig. 5A). Pairs of parallel 8-mm-length RFID tags were...
inserted in a vertical orientation, perpendicular to the longitudinal axis of the hotdog, or in a horizontal orientation, parallel to the longitudinal axis of the hotdog (Fig. 5B). For each trial, tags were incrementally brought closer together, and the RFID reader was used to determine if the tags were differentiable (Figs. 5C and 5D). In the vertical orientation, distances of separation were set using an adjacent ruler. In the horizontal orientation, distances of separation were set by ruler and by slicing the hotdogs to the appropriate length and inserting the tags just into the two ends of the hotdogs.

The read button on the TagFinder was used to ensure differentiation between two tags by confirming each tag’s unique identification number. In the vertical orientation, two signal maxima occurred, one over each tag. In the horizontal orientation, four signal maxima occurred, one over each of the four tag poles. The read button was used while the reader passed over the farthest-apart maxima. To the question of differentiability, three different responses were possible: yes, with difficulty, or no. Yes indicated that the tags were differentiable; no, that they were not; and with difficulty, that the tags were differentiable after two or three repeated attempts.

A second nonblinded trial was conducted using a detector equipped with the pencil probe designed with a narrower range of 3 cm, but with more precise localizing capability (Fig. 6).

**Visualization of Tags on Sonography, Mammography, and MRI**

Radiography of a silicone breast phantom with an embedded tag was performed using a commercial full-field digital mammography unit (Selenia, Hologic). A tag embedded in a sonography phantom was imaged as it was introduced using a 12-gauge needle and again after introduction. Tags embedded and placed on an MRI phantom were imaged on a 1.5-T commercial MR system using a variety of gradient-echo and spin-echo pulse sequences that mirror techniques typically used in clinical breast MRI, including gradient-echo (TR/TE, 5.0/1.9; flip angle, 12°) and fast spin-echo (6,050/121; flip angle, 18°) techniques.

**Localization and Resection in Specimens**

An RFID tag was implanted into a grocery store–bought, 5-cm-thick, boneless, skinless chicken breast fillet. Two physicians, on separate occasions, were provided with the RFID reader and some basic surgical tools including a scalpel, a scissor, and a forceps. One of the physicians was an American Board of Radiology-certified radiologist and MQSA-certified mammographer with more than 20 years of experience; the other was a breast surgeon (Fellow of the American College of Surgeons) with more than 30 years of clinical experience. During the experiment, a physician was asked to use the reader to localize the tag and then to use the surgical tools to resect...
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**TABLE 1: Radiofrequency Identification (RFID) Tag Localization and Depth Detection in a Sonography Phantom**

<table>
<thead>
<tr>
<th>Depth of Tag (cm)</th>
<th>Depth of Tag (cm) Measured Using RFID Reader</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Observer 1</td>
</tr>
<tr>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>2.0</td>
<td>1.8</td>
</tr>
<tr>
<td>3.0</td>
<td>3.0</td>
</tr>
</tbody>
</table>

The independent observers successfully used the RFID reader to localize and detect the depth of the tags implanted in a sonography breast phantom (Table 1). One observer slightly underestimated the depth of one of the tags, but the remaining results were accurate and precise.

**Results**

**Localization and Depth Detection**

The independent observers successfully used the RFID reader to localize and detect the depth of the tags implanted in a sonography breast phantom (Table 1). One observer slightly underestimated the depth of one of the tags, but the remaining results were accurate and precise.

**Differentiating Specimens With and Without Embedded RFID Tags**

In trial 1, the three individuals were able to successfully identify which chicken pieces contained RFID tags and the associated unique identification numbers with only a single error of omission. One of the individuals (the high school student) overlooked one of the tags. All chicken pieces containing 12-mm RFID tags were identified successfully.

In trial 2, none of the individuals was able to identify chicken pieces containing tags by visual inspection. In the combined results, the combined results, twice a tag-containing specimen was missed, and once a specimen not containing a tag was identified as containing a tag (57 of 60 correct identifications).

In trial 3, none of the individuals was able to identify chicken pieces containing tags by visual inspection. Of the 11 individuals, nine returned perfect response forms, correctly finding and identifying each tag and specimen. For the two individuals with incorrect responses, one missed two tags and the other correctly identified a tag in a specimen but listed the tag number incorrectly (217 of 220 correct identifications).

**Nearest Differentiable Proximity Between Tags**

Using the loop detector, tags in the vertical orientation could be differentiated consistently for distances of separation of 2.5 cm or greater and after repeated attempts for distances of 1.0 cm or greater. Tags in the horizontal orientation could be differentiated consistently for distances of separation of 1.5 cm or greater and after repeated attempts for distances of 0.5 cm or greater (Table 2).

**TABLE 2: Distances Between Radiofrequency Identification (RFID) Tags At Which RFID Reader Can Differentiate Tags from One Another**

<table>
<thead>
<tr>
<th>Distance Between Tags (cm)</th>
<th>Can the Two Tags Be Differentiated from One Another?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vertical Orientation</td>
</tr>
<tr>
<td>8.0</td>
<td>Yes</td>
</tr>
<tr>
<td>7.0</td>
<td>Yes</td>
</tr>
<tr>
<td>6.0</td>
<td>Yes</td>
</tr>
<tr>
<td>5.0</td>
<td>Yes</td>
</tr>
<tr>
<td>4.0</td>
<td>Yes</td>
</tr>
<tr>
<td>3.5</td>
<td>Yes</td>
</tr>
<tr>
<td>3.0</td>
<td>Yes</td>
</tr>
<tr>
<td>2.5</td>
<td>Yes, with difficulty</td>
</tr>
<tr>
<td>2.0</td>
<td>Yes, with difficulty</td>
</tr>
<tr>
<td>1.5</td>
<td>Yes, with difficulty</td>
</tr>
<tr>
<td>1.0</td>
<td>Yes, with difficulty</td>
</tr>
<tr>
<td>0.5</td>
<td>Yes, with difficulty</td>
</tr>
</tbody>
</table>

*With difficulty is defined as differentiation of tags requiring either two or three attempts.*

Using the pencil probe, when two adjacent 8- or 12-mm tags were placed in continuity with each other end-to-end, the separate serial numbers were not recognizable when scanning neighboring ends of the tags. However, even with the tags touching end-to-end, separate serial numbers could be read with the pencil probe directed over the nonopposing ends of each tag (Fig. 6B). When neighboring tags were placed in parallel, the pencil probe enabled individual identification of tags separated by greater than 0.5 cm (Fig. 6A).

**Visualization of Tags on Sonography, Radiography, Mammography, and MRI**

The RFID tags were found to be easily identified on mammography and sonography. On MRI, artifacts were greatest on gradient-echo images, as large as 3.2 cm in diameter for the 12-mm RFID tag and 2.6 cm for the 8-mm RFID tag (Fig. 7).

**Localization and Resection in Specimens**

Each of two physicians successfully localized the RFID tag using the reader and resected the tag and surrounding tissue, removing an approximately 3-cm-diameter collection of tissue, from a grocery store-bought chicken breast. After resection, the physicians confirmed with the reader that the tag was in the resected mass and no longer present in the chicken breast.

**Discussion**

RFID tags combined with a newly developed handheld reader show tremendous promise for imaging-guided preoperative and intraoperative tumor localization. Both 8- and 12-mm RFID tags can be easily introduced using a 12-gauge coaxial needle system, previously well established for use in humans and animals [10]. The newly invented RFID reader enabled accurate localization, unique identification, and even differentiation of neighboring tags in multiple tests with various phantoms and chicken breasts. Highly accurate results were obtained when individuals were asked to distinguish specimens containing RFID tags from specimens not containing tags, even though the users had no prior experience with the RFID reader and underwent only brief training.

A major theoretic advantage of using RFID technology is the potential benefit of identification of the tag in a surgical specimen. The current standard for breast tumor resection requires obtaining a specimen radiograph while the patient remains in the operating room. However, the new RFID system is capable of greatly improving identification of the original tag present in the specimen.
room, lengthening operating room time. If the specimen is found to be inadequate, with current methods it may be difficult to determine how to proceed further. With the RFID system, the surgeon could theoretically interactively use the reader to find any tags remaining in the patient. Furthermore, the need for a specimen radiograph could potentially be eliminated in some cases, particularly if RFID tags are used to bracket the margins of a lesion. When human research proceeds, if tags are placed days or weeks before surgery, we may find that it is useful to obtain an immediate preoperative mammogram or sonogram to confirm that the tags have not migrated. Although we may find that specimen radiographs are still essential in cases with microcalcifications, in other cases, such as lesions only visible on sonography, properly placed tags may lend more assurance than a specimen radiograph with regard to adequate lesion resection.

Although specimens can be marked with surgical sutures and other markers, specimen orientation can be problematic today. In theory, using RFID technology, multiple tags could be placed, each with a unique identification number, bracketing the margins of a targeted lesion, which might aid in specimen orientation. Our preliminary findings suggest that multiple tags can be placed closer than would likely ever be clinically required and still can be easily identified and differentiated.

Another potential advantage of RFID technology is the use by pathologists who may sometimes struggle to locate a tissue marker in an excised surgical specimen. The ability to interactively localize the marker in an excised specimen can potentially facilitate pathologic inspection of the excised tissue. Therefore, RFID technology presents several theoretic advantages over currently widely used metallic tissue markers.

Another potential future application is the use of RFID technology to replace preoperative hookwire localization. In current common practice, hookwire localization procedures must be scheduled in a mammography, MRI, or sonography suite immediately preceding surgery, which can be logistically difficult, and subject the patient to the cost and discomfort of an additional procedure even though a metallic marker may have been previously placed. Today, after the hookwire localization, the surgeon is left with little time to communicate with the radiologist and analyze the images obtained after hookwire placement. With RFID, markers could be placed days or weeks before surgery, providing the surgeon ample time to review imaging studies obtained after RFID marker placement, to understand the identification and location of each RFID marker, to empirically confirm that the markers can be detected from the skin’s surface, and to consult as needed with the radiologist.

The percutaneous approach for safely placing a hookwire may differ from the optimal cosmetic or surgical approach for resecting a lesion. In theory, the RFID system could be used as an alternative to preoperative hookwire localization, allowing placement at a more convenient time and enabling the surgical approach to more easily differ from the percutaneous imaging-guided placement approach. Finally, although hookwires today are not typically used to mark tumor margins, multiple RFID tags could theoretically be used to bracket the margins of a lesion.

With regard to the reader, the development of a combined auditory cue and LCD display to indicate the proximity to a tag enhanced the user’s subjective ability to localize the tag. Because of the geometry of a tag’s generated field, the signal is greatest as one approaches the distal ends of a tag rather than the center of a tag. This understanding is essential for the user and can even be beneficial. The reader itself is small and is light enough to be used easily in an operating room or pathology laboratory environment. Furthermore, it can be easily contained in one of many sterile sleeves, such as those used to drape ultrasound probes. Because the reader emits an RF signal, use of the RFID reader adjacent to cardiac pacemakers introduces theoretic risks that have not been evaluated. Of note, the reader is slightly responsive to metallic objects, but it was developed in such a way to minimize this interaction. Furthermore, the ability of the reader to display the tag’s unique identification number eliminates false-positives because extraneous metal objects do not generate any identification number.

One disadvantage of RFID technology is the surrounding artifact on MRI. For now, this limitation may prevent routine placement of an RFID tag at the time of biopsy until a diagnosis is established and one determines whether preoperative MRI is required. However, if the size of the artifact can be reduced with further development of the technology, the presence of a low-signal artifact on MRI may actually prove to be advantageous in visualizing the RFID tags. Furthermore, preoperative staging MRI is most useful in detecting additional lesions and in sizing large lesions, so if one can achieve an artifact of less than 1 or 2 cm, this artifact may not practically detract from the information provided by MRI.

Tag migration after insertion is another potential problem. Tags with antimigration sleeves exist already. Today’s non–RFID tissue markers can also potentially migrate, but studies show that they seldom do [11].

With regard to safety in humans, the FDA has already cleared RFID tags for long-term implantation in humans, although not specifically for the use described herein. Currently, the RFID system is approved by the FDA as “a device intended to enable access to secure patient identification and corresponding health information” [10]. As described further, the “system may include a passive implanted transponder, inserter, and scanner” [10]. Although we are unaware of any specific evaluation of the long-term effects of RFID implantation in the human breast, we have no reason to believe that implantation in the breast would be any less safe than in any other human tissues or less safe than implantation of non–RFID metallic markers. A human implantable RFID tag vendor (VeriChip) reports safety and compatibility of RFID tags in an MRI environment [12]. In addition, a well-respected MRI safety organization reports that “patients with the VeriChip Microtransponder may safely undergo MRI diagnostics, in up to 7-Tesla cylindric systems” based on the manufacturer’s representation [12]. Finally, the results of our independent tests performed by Shellock R & D Services, which are beyond the scope of this article, showed no significant heating (< 0.6°C) in a 3-T MRI environment.

On the basis of these encouraging results, further study in humans seems warranted first to establish the safety and efficacy of the RFID system as a replacement for embedded metallic tissue markers and thereafter to determine whether this technology can be used to replace preoperative hookwire localization.

References
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**FOR YOUR INFORMATION**

Mark your calendar for the following ARRS annual meetings:

- April 26–May 1, 2009—John B. Hynes Veterans Memorial Convention Center, Boston, MA
- May 2–7, 2010—Grand Hyatt San Diego, San Diego, CA
- May 1–6, 2011—Hyatt Regency Chicago, Chicago, IL
- April 29–May 4, 2012—Vancouver Convention Center, Vancouver, BC, Canada