Paper

RADIOACTIVE SEED LOCALIZATION WITH ^{125}I FOR NONPALPABLE LESIONS PRIOR TO BREAST LUMPECTOMY AND/OR EXCISIONAL BIOPSY: METHODOLOGY, SAFETY, AND EXPERIENCE OF INITIAL YEAR

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Abstract—**The use of radioactive seed localization (RSL) as an alternative to wire localizations (WL) for nonpalpable breast lesions is rapidly gaining acceptance because of its advantages for both the patient and the surgical staff. This paper examines the initial experience with over 1,200 patients seen at a comprehensive cancer center. Radiation safety procedures for radiology, surgery, and pathology were implemented, and radioactive material inventory control was maintained using an intranet-based program. Surgical probes allowed for discrimination between ^{125}I seed photon energies from ^{99m}Tc administered for sentinel node testing. A total of 1,127 patients (median age of 57.2 y) underwent RSL procedures with 1,223 seeds implanted. Implanted seed depth ranged from 10.3–107.8 mm. The median length of time from RSL implant to surgical excision was 2 d. The median ^{125}I activity at time of implant was 3.1 MBq (1.9 to 4.6). The median dose rate from patients with a single seed was 9.5 μSv h^{-1} and 0.5 μSv h^{-1} at contact and 1 m, respectively. The maximum contact dose rate was 187 μSv h^{-1} from a superficially placed seed. RSL performed greater than 1 d before surgery is a viable alternative to WL, allowing flexibility in scheduling, minimizing day of surgery procedures, and improving workflow in breast imaging and surgery. RSL has been shown to be a safe and effective procedure for preoperative localization under mammographic and ultrasound guidance, which can be managed with the use of customized radiation protection controls.**

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Key words: ^{125}I; breast; diagnostic imaging; radiation protection

INTRODUCTION

Improvements in imaging techniques and increasing rates of screening mammograms have resulted in the increased detection of nonpalpable breast lesions that require localization prior to surgery to allow excision for complete histological evaluation or as part of breast-conserving therapy (Harris et al. 1981; Homer 1983; Cady et al. 1996; Montrey et al. 1996; Bartelink et al. 2001; Skinner et al. 2001; Hooley et al. 2012; Nederend et al. 2012). Breast image-guided localization is performed on nonpalpable lesions after marker clips are left in the breast following image-guided biopsy (i.e., stereotactic biopsy, ultrasound core biopsy, or MRI core biopsy) of masses or calcifications.

To date, the most common method for preoperative localization has been wire localization (WL), performed with a hooked wire (Frank et al. 1976). Because the wire is in part external, this procedure has major limitations. The wire can be inadvertently pulled, displaced, or transected before or during surgery, precluding accurate localization of the target lesion (Homer 1983; Montrey et al. 1996), or it can undergo incidental migration, kinking, or fracturing of the wire (Bronstein et al. 1988; Montrey et al. 1996). Additionally, the wire skin entry site determined by the radiologist often is not at the ideal skin incision site for the surgeon, and identifying the wire within the breast may be difficult when the incision is not at the wire entry site (Homer 1983; Davis et al. 1988; Montrey et al. 1996; Besic et al. 2002; Fleming et al. 2004). Finally, wire placement needs to be done typically on the day of surgery, linking operating room and radiology schedules (Davis et al. 1988) and increasing the chance for conflicts that result in significant delays in the operating room, and the potential for leakage of sentinel lymph node (SLN) mapping agents (e.g., blue dye and/or ^{99m}Tc colloid).

Initially, radio-guided occult lesion localization (ROLL), direct intra-tumoral injection of ^{99m}Tc-labelled colloidal serum albumin, was developed as an alternative to wire localization (Nadeem et al. 2005; Mariscal Martinez et al.

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2009). However, this technique is also subject to limitations, particularly since the injected material is not visible on radiographs, and ^{99m}Tc is the same radiotracer used for SLN mapping, potentially creating confusion, particularly with tumors in the upper outer quadrant (Nadeem et al. 2005; Mariscal Martinez et al. 2009).

Radioactive seed localization (RSL) is a recent alternative to WL using a fully implanted ^{125}I encapsulated titanium seed that is visible on both mammography and ultrasound. Given the relatively long half-life of ^{125}I (~59 d), RSL does not need to be performed on the day of surgery, and since it has a different photopeak from ^{99m}Tc, it can be performed in conjunction with SLN mapping (Gray et al. 2004) if appropriate detection probes are calibrated and used. In addition, surgical studies have suggested that RSL produces fewer positive margins and reoperation rates than WL and results in shorter operating times than WL (Gray et al. 2001; Lovrics et al. 2011a and b; McGhan et al. 2011). In addition, bracketing of lesions and post-localization mammograms are not impeded by wires.

The purpose of this study was to evaluate, from the perspective of the radiation safety specialist, the methodology, safety, and first year experience of preoperative ^{125}I RSL as an alternative to WL for lesions visible by mammographic and sonographic imaging techniques.

MATERIALS AND METHODS

Study Data Collection

A waiver was granted by the institutional review board (IRB) for this Health Insurance Portability and Accountability Act (HIPAA) compliant study. A retrospective review of all mammographic and/or ultrasound guided ^{125}I RSLs performed between 14 November 2011 and 14 November 2012 was conducted. One thousand two hundred twenty-three (1,223) consecutive RSLs were performed in 1,127 women prior to lumpectomy and/or excisional biopsy. Clinical and pathologic data were recorded from the electronic medical record. In addition, seed-to-target distance was measured on preoperative mammograms for a subset of the study population, and specimen radiographs were reviewed for the presence of target and seed for all cases. In 35 women, during an initial brief surgical training period, a modified Kopans wire was placed as a WL in addition to the RSL in order to ensure localization during surgery. In these cases, wire placement occurred on the day of surgery.

For this study, the following information was also collected: patient demographics (age, indications for RSL, targets, target depth, and localization method), RSL seed activity, needle size used, radiation exposure rate on contact with the skin and at 1 m, and lifecycle tracking (days from seed receipt in inventory to implant, days from implant to surgical excision).

Radioactive seeds

Sealed radioactive seeds can be used as an effective diagnostic imaging marker. Iodine-125 (^{125}I) has a long decay time, emitting low-energy photons. Disintegration of ^{125}I occurs with a half-life of 59.4 d by absorption of electrons and emission of low energy photons ranging in energy from 27.2–35.5 keV (mean energy of 27 keV). This photon energy signal differs from ^{99m}Tc (140 keV) used for concurrent sentinel node biopsy procedures, thereby enabling active discrimination during surgical excision.

The initial 76 RSL procedures were performed using a standard ^{125}I titanium seed (Standard ^{125}I Source, Best Medical International, Inc., distributed by MPM Medical, Freehold, NJ). The remaining RSLs were performed using a textured ^{125}I titanium seed (Stranded Iodine-125 Source, Best Medical International, Inc., distributed by MPM Medical, Freehold, NJ). The textured seed is coated with a bioabsorbable co-polymer made of L-lactide and polyglycolide and assists in preventing seed migration from the initial implant location. The specified seed activity was initially 4.6 MBq per seed for the first 250 procedures, but the activity was reduced to 3.7 MBq per seed for the remaining procedures consistent with the as low as reasonably achievable (ALARA) principle. The surgeons experienced no difficulty detecting and localizing the seeds with the lowered activity. All seeds came preloaded into a sterile 18-gauge needle (with a stylet fitted within the needle) ranging in needle length from 5–15 cm. The assembly includes a plastic spacer, and the tip is occluded with bone wax (Fig. 1). Prepackaged sterile seed assemblies had vendor-determined and labeled expiration dates

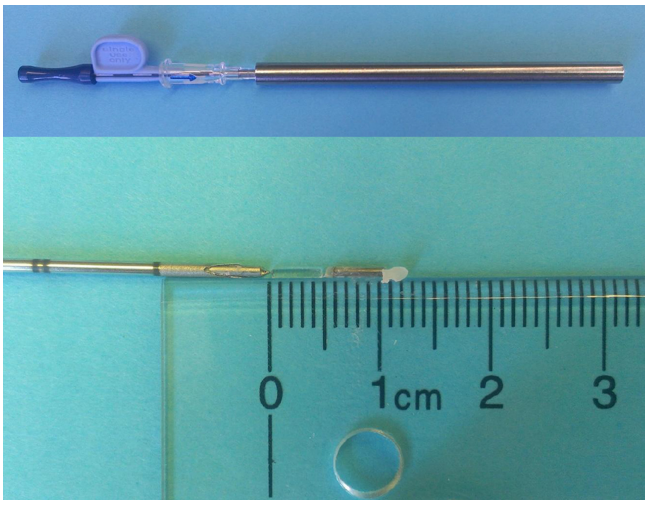

Fig. 1. RSL needle shown with stainless steel shielding in place and needle showing with bone wax, ^{125}I seed, plastic spacer, and stylet.

based on sterilization duration requirements (e.g., 2 mo). Therefore, seeds decayed over time and were maintained within the inventory. The activity in each seed was determined at the time of implant.

RSL gamma probe for surgery and pathology

Intraoperative nuclear probes have evolved into an important, well-established technology in the management of cancer (Gulec et al. 1997; Cody 2002; Mariani et al. 2008; Povoski et al. 2009; Heller and Zanzonico 2011) and have been shown to identify and localize sentinel lymph nodes expeditiously. For surgical RSL guidance and pathology explant guidance, an intraoperative gamma probe, wirelessly connected (through Bluetooth technology) with a control unit (Node Seeker 900 with Bent Tip Gamma Probe WG-140B, IntraMedical Imaging, CA) was used (Figs. 2 and 3). The system consists of a universal, computer-based control unit and a dedicated set of detector probes. The control unit was mounted to an IV pole for portability. It uses a touchscreen interface system and displays both ^{99m}Tc sentinel node and scatter corrected ^{125}I counts simultaneously on the screen. In addition, the control unit provides audio indication of the number of counts. The probe is designed with a collimated shield installed inside the probe's 12 mm tip that results in surgically useful spatial resolution (e.g., < 1–2 cm). The probe provided appropriate sensitivity for the activities used in this study. Gamma discriminator settings enabled optimization of ^{125}I versus ^{99m}Tc identification and minimization of "cross talk" between the channels. Each probe was calibrated for activity and distance-in-tissue, and the control units displayed approximate distance to the RSL seed based on entered nominal activity and seed calibration date. Assessments of system performance showed that when the probe tip was placed directly over the seed location (based on maximum displayed counts), the distance indicator was generally accurate to within

Fig. 2. RSL Probe showing wireless probe and collimated tip and probe as protected with sterile drape during surgery (Bent Tip Gamma Probe WG-140B, IntraMedical Imaging, CA).

Fig. 3. RSL monitor (Node Seeker, IntraMedical Imaging, CA).

~2 cm, adequate for determining the most direct path to the lesion, identification of the seed within the tissue, and ensuring seed removal following excision. Fresh batteries were installed in the probes each morning, and the probes were wiped with alcohol pads and placed in tied-off plastic sterile probe covers prior to each case (Fig. 2).

This center performs SLN biopsy using a dose of 18.5 MBq ^{99m}Tc injected on the day before surgery or 3.7 MBq ^{99m}Tc injected on the day of surgery (Pandit-Taskar et al. 2006). The RSL gamma probe was specifically optimized for the associated SLN biopsy agents.

RSL program licensing and prerequisites

RSL was performed at this institution under a broad scope medical radioactive material license. The sealed sources used for RSL had an active (not-withdrawn) sealed source device registry and are designated for type of use. All persons involved in handling of sealed sources under this study were trained in routine use and emergency procedures. Authorized users (AUs) were recognized as AUs in manual brachytherapy or in imaging and localization studies with work experience that included three cases of RSL, experience in performing the related radiation surveys using the appropriate instrumentation, and as approved by the institutional Committee on Radiation specific to these procedures. AUs were responsible for presenting a written directive (order) with the specified implant duration, being present during the implant, and supervising the explant (i.e., being knowledgeable and available for the procedure if requested). Persons handling seeds or who were anticipated to receive greater than 10% of the occupational dose limits were monitored in accordance with Radiation Safety procedures. Radiation safety

instrumentation was calibrated and appropriate for the types and quantities of the radioactive materials used during this study. An intranet-based RSL inventory log (i.e., database) tracked information on seed receipt, initial inventory, storage, implant, surgical excision, and pathology explant through to ultimate decay-in-storage. Institutional staff members (e.g., from radiation safety, medical physics, radiology, surgery, and pathology) were able to access and update inventory information at each interaction point of the overall RSL process.

Ordering and storage of RSL seeds

Sterile RSL seeds were ordered from a vendor licensed to distribute sealed sources for medical use with an active (not withdrawn) sealed source and device registry. Sterile seed packages were received in accordance with radioactive material receipt procedures. Information on each RSL seed was entered by radiation safety staff into the intranet-based RSL inventory log system including: nuclide, number of seeds, activity, dates of activity, seed lot number, and seed identification number. Seeds were stored in a secure location, preventing unauthorized access and removal, in a container labeled with the standard yellow and magenta trefoil and the words "Caution Radioactive Material."

Written directive (prescription) and patient consent

Based on surgical referral, the radiologist AU held patient consent discussions and obtained written consent. A specific written directive was signed by an AU prior to RSL implant. For this study, an a priori dose evaluation was performed in the event the seed was not recovered from the patient. It was estimated that the potential absorbed dose to the surrounding tissue if the seed was not removed would be approximately 70.2 cGy MBq^{-1} at 1 cm, assuming a dose rate constant of 1.01 cGy h^{-1} U^{-1} in water (Sowards and Meigooni 2002) and half-life of 59.4 d.

RSL implant by radiologist

Prior to the RSL implant, the radiologist (AU) ensured that the written directive and patient consent were in place and identified the correct implant location through mammographic or ultrasound targeting. Based on expected needle travel length, an appropriately sized preloaded needle was taken from inventory.

Needle tips were positioned within the target lesion under mammographic or sonographic guidance. RSL seeds were deployed by fully advancing the stylet fitted within the needle. If the area to be localized was very superficial, a deeper approach may be used to avoid the seed bleeding out. When any seed was placed superficially, steristrips were placed over the entry site and the patient was told to keep these in place until surgery. In some patients, two seeds were implanted in a single breast to bracket larger lesions or if there were multiple lesions. A minimum distance of 3 cm between each seed was specified for the use of more than one seed in a single breast, based on the ability of the probe to discriminate distinctly between each seed location. In some other patients, seeds were placed in both breasts.

Following placement of the seed(s), a post-procedure two-view mammogram was performed to confirm the location of the seed (Fig. 4). In order to assist with seed inventory tracking and to provide readily available information to the surgeon on the day of surgery, the radiologist recorded the seed activity and reference date directly on the image. In order to assess the potential for patient release and instruction requirements (USNRC 2008), after each RSL, a handheld ion chamber (e.g., Victoreen 451P Ion Chamber Survey Meter, Fluke Biomedical, Everett, WA) was used to measure exposure rates on contact with the skin at the implant site and at 1 m from the breast.

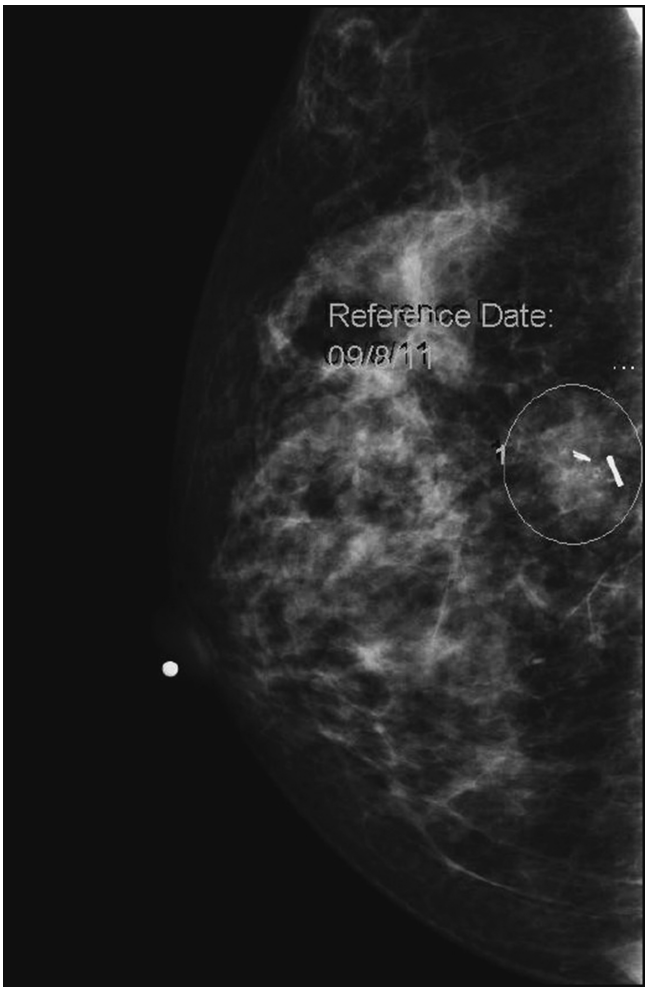

Fig. 4. Example mammogram (cranio-caudal view) following RSL.

Calibration factors for ^{125}I energies were used to convert to $\mu Sv\ h^{-1}$ rates. In addition, a radiation survey was performed to ensure that no seeds were left in the needle. The intranet-based RSL inventory log was updated to include: patient name, medical record number (MRN), date of implant, AU, nuclide, estimated activity per seed, number of seeds, seed identification number(s), on-contact survey measurement, and 1 m survey measurement.

Each patient was provided with radiation safety instructions emphasizing return for explant. The guidelines explain that the implanted seed contains a small amount of radioactive material that assists the surgeon in finding the abnormal tissue during surgery. The handout explains what can be done to minimize exposure to others. The technologist explained to the patient that it is prudent to maintain doses as low as reasonably achievable (ALARA) and that they should not hold a child to their chest for more than 30 min per day. Also the patient was told that once the seed is removed, no such precaution is necessary as there is no radiation left in the breast. The telephone number of the Radiation Safety office in the department of medical physics was provided in case the patient had any questions. If the patient was travelling, she was given a card that stated she had measurable levels of radioactivity that may be detectable. The date of the planned surgery was written on the card.

Explant by Surgeons in Operating Suite

When the patient is in the operating room, the surgeon inputs the activity and reference date for the seed into the computer, which is wirelessly connected with the probe and uses the probe to scan the breast and determine the incision site. A standard SLN biopsy was carried out (Cody 2002) using the ^{99m}Tc count window of the RSL gamma probe.

The display of the approximate distance to the seed and the audio response to count rate assisted the surgeon in placing the incision. Surgical removal of the ^{125}I seeds was performed with the guidance of the RSL gamma probe. Dissection was not performed with scissors to avoid seed transection. The specimen(s) with the seed implant(s) were removed and placed on a specimen board with a sticker noting the presence of ^{125}I isotope, the number of seeds, and a "Caution Radioactive Material" label (Fig. 5). Seed retrieval was verified by the surgeon who performed a radiation survey of the patient and specimen, verifying the presence of ^{125}I counts within the specimen and the absence of ^{125}I residual activity in the breast, as well as the presence of the seed on the specimen radiograph (Faxitron, model MX-20, Faxitron X-ray, Wheeling, IL) (Fig. 6). The surgical staff updated the intranet-based RSL inventory log with the date of the surgical removal of the seed(s). The specimen board was placed in a plastic bag and hand-delivered directly to the Pathology Department.

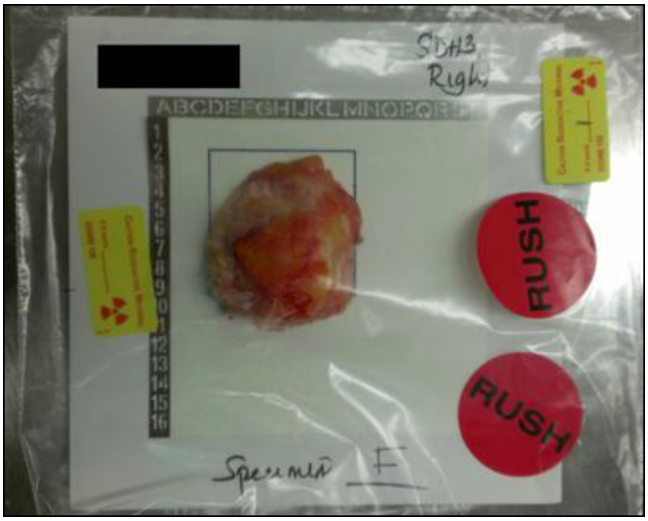

Fig. 5. Labeled specimen packaged for transport to pathology service.

Specimen handling in pathology

Upon arrival of the labeled specimen containing the RSL seed(s), pathology staff processed the accession as a rush and carried it immediately to the pathologist's assistant, who documented the receipt of the radioactive specimen in the intranet-based RSL inventory log. Prior to sectioning, a trained pathologist's assistant used a RSL gamma probe to identify the location of the seed(s) within

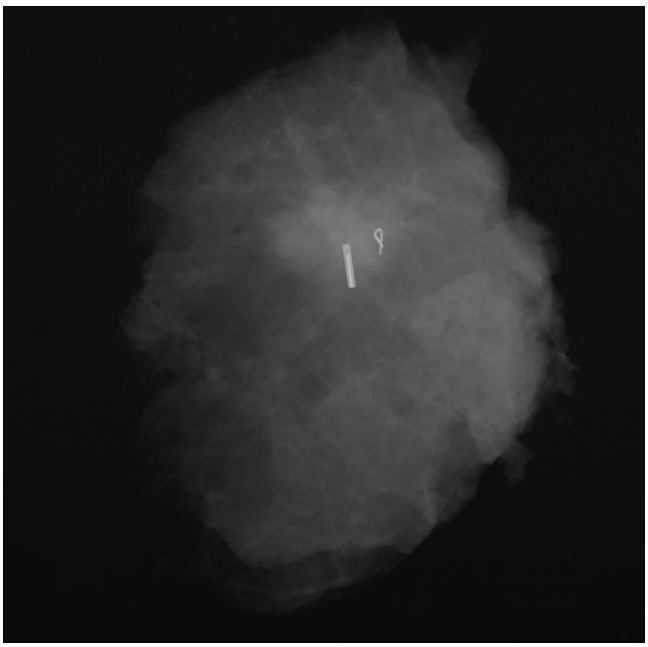

Fig. 6. Specimen radiograph confirming seed in removed tissue.

the specimen, removed them with non-puncturing long handled tools such as forceps, placed individual explanted seeds in small specimen bags labeled with the patient's name, and placed these bags in a lead shielded storage container. Placement of the explanted seeds into the waste collection container was documented in the intranet-based RSL inventory log. A final radiation survey of the remaining specimen material was performed using the RSL gamma probe to verify the absence of any remaining implants. This important step was emphasized during training of the pathology staff to preclude the possibility of cutting of the seeds during microtome sectioning of specimens (Classic et al. 2009).

Decay-in-storage

Radiation safety staff monitored the intranet-based RSL inventory log on a daily basis. Each week, a staff member retrieved the collected seeds from the lead waste storage container in pathology and delivered them to a controlled location. Disposition of each individual seed was updated in the log. After a minimum of 10 half-lives for decay, the spent seeds will be surveyed with an appropriate radiation detection instrument (e.g., calibrated GM probe and meter) on its most sensitive setting. When seeds are verified as indistinguishable from background radiation levels, the package radioactive markings will be defaced and the material placed in non-radioactive medical waste.

Emergency procedures

In the existing regulatory environment, positive control of radioactive material is critical (Rao et al. 2010); therefore, particular attention was paid to ensure seed inventory throughout the seed lifecycle. In the case of a loss of seed, immediate contact with radiation safety was to be initiated, and all personnel were kept in the area. Radiation safety would scan all personnel with the appropriate radiation detection instrumentation [i.e., thin windowed Geiger Mueller (GM) or low energy gamma (LEG NaI) scintillation probe] and scan the facility/room. Located seeds were to be handled with forceps and placed into the decay-in-storage inventory. If a patient failed to return for surgery, surgery staff would attempt to contact the patient to determine the reasons. Any loss requiring follow up would be documented in the patient medical record, including an absorbed dose estimate. Breached or leaking seeds were not expected using typical surgical procedures (Classic et al. 2009); however, in the rare event of unexpected seed leakage, Radiation Safety would be contacted to conduct a radioactive contamination assessment. If leakage were confirmed, all contaminated materials would be handled as radioactive waste. Thyroid bioassays would be performed as necessary.

RESULTS

Patients

A total of 1,127 patients underwent RSL procedures with a total of 1,223 seeds implanted. Patients ranged in age from 26.7 to 92.3 y (median 57.2, mean 57.9, s.d. 11.8). Table 1 shows the number of RSL procedures for each indication, the target, and imaging guidance used. Just over half (51%) of the procedures were for invasive carcinoma, with 19% for ductal carcinoma in situ. Most of the targets were clip/biopsy sites (82%), performed under mammographic guidance (93%). Table 2 shows the number of patients and implants according to the number of seeds used. Most of the implants were single seeds into one breast (85%).

RSL placement, activity, and radiation dose rates

A 5-cm-length needle was used most often for seed placement (46%). Other length needles, such as 7 cm (38%), 10 cm (15%), or 15 cm (1%), were used less often. When considering all RSL cases, the implanted seed depth ranged from 10–108 mm (median 38, mean 42, s.d. 19) from needle entry point to target by mammography guidance view used for placement. The numbers of days from RSL implant to surgical excision ranged from 0 to 47 d (median 2, mean 3, s.d. 3).

The ^{125}I activity at time of implant ranged from 1.9 to 4.6 MBq (median 3.1, mean 3.0, s.d. 0.6). Table 3 summarizes contact and 1 m dose rates according to the number of seeds used. The maximum contact dose rate was 187 μSv h^{-1} from a superficially placed seed. The median dose rate for single seeds was 9.5 μSv h^{-1} and

Table 1. RSL procedures by indication, target, and guidance method.

Category	Number
Total RSL implant procedures	1,223
Indication:	
Invasive carcinoma	624
Ductal carcinoma in situ	228
Multiple indications	75
Atypia	50
Atypical ductal hyperplasia	46
Excisional biopsies of suspicious imaging findings	45
Papillary carcinoma	42
Lobular carcinoma in situ	32
Atypical lobular hyperplasia	30
High risk lesions	21
Intraductal papilloma	15
Radial scar	8
Adenocarcinoma	4
Phyllodes tumor	3
Target:	
Clip/Biopsy sites	997
Masses/Focal asymmetries	117
Calcifications	75
Other	34
Guidance:	
Mammographic	1,143
Ultrasound	80

Table 2. Number of patients and RSL implants according to the number of seeds used.

# Seeds	Description	# Patients	# Implants
1	Single breast	1,037	1,037
2	Single breast, two seeds in breast	55	110
2	Bilateral breasts, one seed each breast	30	60
3	Bilateral breasts, two seeds in one breast, one in other	4	12
4	Bilateral breasts, two seeds each breast	1	4
Totals		1,127	1,223

0.5 μSv h^{-1} for contact and 1 m distances, respectively. Dose rates were higher for multiple seed cases, with the median for four seeds (two in each breast) as 23.1 μSv h^{-1} and 1.2 μSv h^{-1}, at contact and 1 m distance, respectively. As expected, personal monitoring results for the extremity for radiologists, mammography technologists, and pathology were all reported as "M" (minimal, <30 mrem per month) and were less than 1% of the annual extremity limit (50,000 mrem).

In most cases, the seeds were removed within 2 or 3 d of implant. In a few cases, the timeframe was longer. For example, in one case the patient was not cleared for surgery due to medical complications (and was rescheduled within the month). In another case, the patient canceled her surgery because of health issues (and rescheduled about 7 wk later). In two patients, an individual seed was not retrieved. In one case, the patient chose not to return for surgery. In the other, the surgeon made the decision to leave the seed in place for surgical safety reasons. Each of these cases was discussed by the institutional Quality Assurance Committees and assessed for medical event reportability in accordance with the institutional broad scope human use license.

In a separate instance, an implanted seed was "dropped" in pathology during explant from the specimen but was subsequently located (in the pathology staff person's shoe) during immediate response survey. It was determined that there was minimal dose to the extremity skin of the pathologist's assistant.

Patient flow in the operating room

This study found significant benefits with RSL for patient flow and efficiency in the operating room. The length of time from when the patient arrives for preoperative setup to when she is in the operating room was significantly reduced from a median of 243 min (s.d. 78) when wire localization was used to a median of 103 min (s.d. 72) when RSL was used. In addition, patients did not have to arrive earlier on the day of surgery to have a wire localization performed.

DISCUSSION

Radiology aspects

These results suggest that RSL can be performed a day or more prior to surgery, with very low incidence of adverse events. The RSL methodology can be used to localize successfully any mammographic or sonographically visible targets. In this study, indications and imaging targets for RSL included the full range of instances in which preoperative WL might be used. For lesions within the breast, ability to localize and remove the seed and target successfully was not limited by preoperative lesion characteristics, type of imaging target, mode of localization, seed type, target location, depth, or breast density, consistent with evidence that suggests RSL is an effective localization procedure (Hughes et al. 2008; Jakub et al. 2010; van Riet et al. 2010; Alderliesten et al. 2011).

Surgical aspects

The intraoperative RSL gamma probe was able to identify ^{125}I seeds and assist in determining the optimal surgical pathway, as well as distinguish ^{125}I seeds from ^{99m}Tc SLN mapping agents in all surgical procedures. All nonpalpable targets were retrieved with concordant final histopathology. A single seed placed sonographically within the axilla was not retrieved at initial surgery. A comparison of the initial 431 single seed localization procedures performed during the first 6 mo using this technique to the 256 single wire localizations performed in the preceding 6 mo demonstrated that the positive margin rate for the seed group was 7.7% compared to 5.5% in the wire localization group ($p = 0.38$), and the median excision volumes did not differ. Operating times, including axillary surgery, were a median of 50 and 45 min, respectively (Murphy et al. 2013). These findings indicate that the technique is easily acquired by surgeons experienced in WL excisions and results in equivalent patient outcomes.

Table 3. Dose rates (μSv h^{-1}) from patients following RSL implants according to the number of seeds used.

		Contact with entry point			1 m		
# Seeds	Description	Min–max	Median	Mean (s.d.)	Min-max	Median	Mean (s.d.)
1	Single breast	0.2–187	9.5	11.3 (9.5)	0.2–28	0.5	0.6 (1.2)
2	Single breast, two seeds in breast	5–35	16.5	16.7 (8.0)	0.3–4.0	0.9	1.0 (0.8)
2	Bilateral breasts, one seed each breast	0.3–36	8.9	11.3 (9.2)	0.1–1.7	0.5	0.6 (0.4)
3	Bilateral breasts, two in one in other breast	7–31	18.0	19.0 (8.8)	0.6–11	1.2	2.7 (3.9)
4	Bilateral breasts, two seeds each breast	17–30	23.1	23.3 (6.9)	1.0–1.3	1.2	1.1 (0.1)

A separate study of a subset of 356 RSLs from this patient population found that the mean seed-to-target distance was 1 mm (range 0–20 mm); however, the seed and target were retrieved successfully even in cases where there was a distance of as much as 20 mm, consistent with WL (Frank et al. 1976).

In a separate study of another subset of this patient population during a brief surgical training period (King et al. 2012; Sung et al. 2013), 35 women who underwent RSL also subsequently had a WL on the day of surgery for the same lesion. In 31 of these women, the same lesion was localized under mammographic guidance using both RSL and WL (Fig. 7). The median procedure time for RSL was 9.0 min (range 4–14 min), and the median procedure time for WL was 7.0 min (range 4–26 min) (p = 0.91). Among those 31 women who underwent mammographically guided RSL and subsequent WL, the distance between the target and the seed was compared on both craniocaudal and lateral views on the day of seed placement versus the day of surgery. Twenty-eight of those 31 localizations were performed with the standard seed, and three were performed with the textured seed. The median distance of migration between RSL and day of surgery was <1mm (range 0–15 mm) over a median duration of 2 d (range 0–13 d). Two standard seeds migrated more than 1 cm: one migrated 11 mm over 4 d in a fatty breast, and the other migrated 15 mm over 1 d in a breast with scattered fibroglandular tissue. The latter case was associated with a 12 mm hematoma (from prior percutaneous biopsy) at the site of localization. These results suggest that seed migration is not generally significant enough to result in non-retrieval of the target.

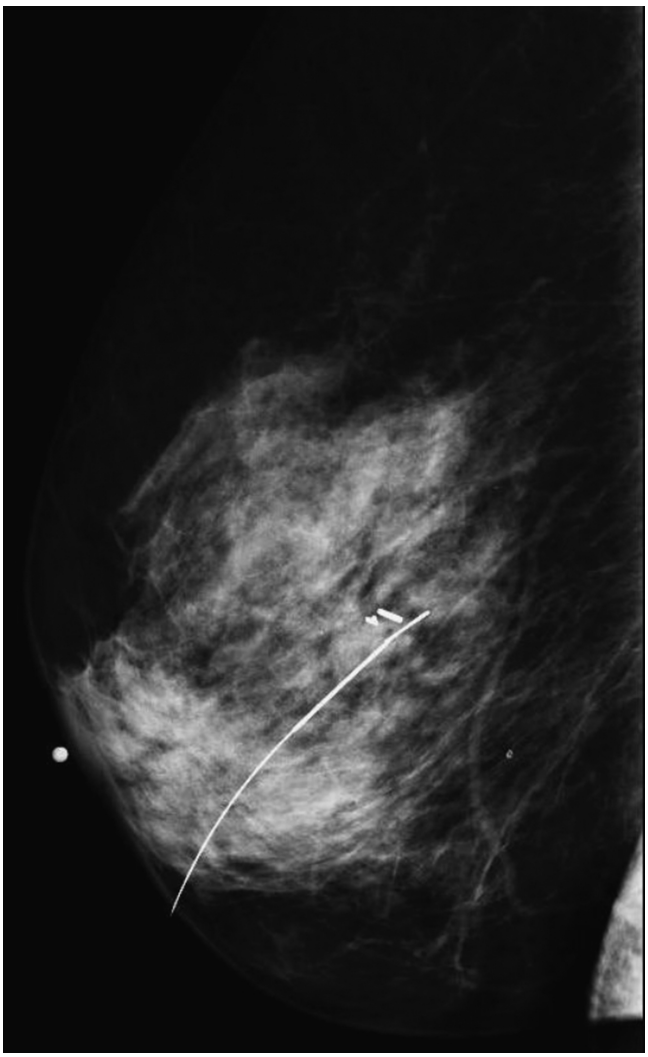

Fig. 7. Example mammogram for case where WL and RSL were performed together.

No significant difference was seen in positive or close margin rates in women who received the WL versus those who underwent RSL alone (King et al. 2012; Sung et al. 2013), suggesting that surgical outcomes are comparable between the two procedures, consistent with the literature (Hughes et al. 2008; Rao et al. 2010; van Riet et al. 2010; Dua et al. 2011; Lovrics et al. 2011a and b; McGhan et al. 2011). Surgical literature has also found that RSL is an easier technique for surgeons and has been rated more convenient by both patients and surgeon (Hughes et al. 2008; Lovrics et al. 2011a and b).

Radiation safety aspects

The United States Nuclear Regulatory Commission (NRC) has provided guidance on RSL for localization of nonpalpable lesions (USNRC 2012). They note that RSL uses radioactive seeds approved previously for the treatment of cancerous tissues and that the use of such seeds for RSL procedures is regulated under Title 10 of the Code of Federal Regulations Part 35.1000, "Other medical uses" and equivalent Agreement State regulations. NRC provides guidance on AU qualifications and training, written directives, safety precautions and instructions, survey instrumentation, and emergency response equipment. This guidance and any equivalent Agreement State regulations and guidance should be consulted prior to initiating any RSL program license amendments.

These results demonstrate that typical dose rates from patients following single RSL ^{125}I seed implants were about 10 μSv h^{-1} on contact and 0.5 μSv h^{-1} at 1 m. These dose rates are about three times lower than those measured following ^{125}I prostate seed implant procedures (Dauer et al. 2010). As in prostate seed implant procedures, patients provided RSL seeds for localization of nonpalpable lesions in the breast do not represent a radiation risk to members of the public (including children and pregnant women) when required radiation safety instructions are observed.

Although radiation exposure due to seed placement is low, the goal is to keep exposure ALARA. For a specimen with a mean diameter of 4 cm, the radiation dose to residual breast tissue for RSL has been shown to be similar to that of a two-view mammogram, approximately 2 cGy (Pavlicek et al. 2006). To minimize patient exposure, this study indicates that the activity of the seed can be minimized consistent with the ability of the intraoperative RSL gamma probe to locate the ^{125}I seed adequately and to distinguish it from ^{99m}Tc used for SLN mapping. In addition, the intent following seed placement is to remove all seeds at surgery. Since the seed is intended for removal, it is also important that a seed not be placed until all preoperative testing has been completed and a definitive plan for surgical excision exists so that cancellation of surgery is unlikely.

CONCLUSION

These results suggest that RSL is a safe and effective procedure for preoperative localization of nonpalpable lesions within the breast under mammography and ultrasound guidance, not limited by indication for localization, target type, breast density, or localization. For breast lesions, RSL performed more than 1 d before surgery is a viable alternative to wire localization (WL), allowing flexibility in scheduling, minimizing day of surgery procedures, and improving workflow in breast imaging and surgery. RSL procedure time and margin status after surgery is comparable to that of WL with very few adverse events. Special consideration should be given to localizing structures outside of the breast, such as in the axilla.

RSL can be performed according to pre-planned methodology and procedures within the current radiation safety regulatory guidance. The use of an intranet-based RSL inventory log that followed the ^{125}I RSL seeds from receipt, initial inventory, storage, implant, surgical excision, pathology explant, through to ultimate decay-in-storage is an effective tool in ensuring immediate seed status and regulatory compliance at any given time.

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