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Original Research Article

Radioactive iodine-125 seed localization as an aid in reoperative neck surgery

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ABSTRACT

Background: Scarring and disrupted tissue planes add to already-complex neck anatomy and make localization of nonpalpable pathology difficult in cervical endocrine reoperations. We describe the use of radioactive iodine-125 seed localization (RSL) in 6 patients with metastatic papillary thyroid carcinoma (PTC) and 2 with recurrent hyperparathyroidism.
Methods: Eight patients had 2-D ultrasound-guided RSL of the target lesion, 0–3 days preoperatively. Intraoperative gamma probe (Neoprobe) was used to plan incision placement and localize the implanted seed. Recorded operative variables included: number of lymph nodes (LNs) harvested, estimated blood loss (EBL), operative time, length of stay (LOS) and RSL and operative complications.
Results: All patients had successful resection of the targeted area and removal of the radioactive seed. There was no seed migration. Two complications occurred in the thyroid group.
Conclusion: Radioactive iodine 125 seeds facilitate successful localization of endocrine pathology during reoperative cervical procedures.

Background

Reoperative neck surgery and its attendant morbidity are a source of apprehension for both patients and their surgeons. With increased rates of recurrent laryngeal nerve (RLN) injury, hypoparathyroidism, missed disease, and hematoma formation,[1–5] these reservations are largely justified. However, there are ways to combine image-guided methodologies with surgery to facilitate safe and efficient removal of endocrine disease following prior neck surgery. Herein we describe the use of radioactive I-125 labeled seeds to guide and enhance surgical approaches to recurrent or persistent cervical endocrine disease.

Methods

We identified 8 patients as candidates for radioactive seed-localization of their persistent or recurrent endocrine diseases. Six patients had recurrent or persistent PTC detected on routine surveillance lymph node mapping and later confirmed with fine needle aspiration cytology. Table 1 outlines the specific operative history for each patient. Ages of these patients ranged 37–74, with a mean of 59 years. The patients in the parathyroid group were 59 and 79 years old with a mean of 69 years. One parathyroid patient had 3 prior operations and the other had 6. This latter patient presented with parathyromatosis and had underwent 2 alcohol ablations in addition to their prior operations.

Patients considered candidates for RSL were referred to radiology and had a preliminary gray-scale and color Doppler ultrasound of the neck to localize the target lesion and determine the optimal needle path. An 18-gauge needle loaded with a titanium seed labeled with 200–300 μCi of I-125 (Best Medical, Inc. Springfield, VA) was advanced under direct ultrasound observation into or directly adjacent to the target lesion. An example sonogram of pre and post seed placement is depicted in Fig. 1. Seed insertion was performed by credentialed radiologists 0–3 days prior to surgery according to institutional protocol for seed localization of other soft tissue lesions such as breast carcinomas. Intraoperative gamma probe (Neoprobe of Mammotome, Cincinnati, OH)

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Table 1
Metastatic PTC patient cohort described by prior operation(s) and RSL-aided operation.

Patient	Prior Operation(s)	Year/ Date	Number of prior OR	Location of Disease	Date	RSL-aided operation	Compartment Addressed	Complication
1	Total thyroidectomy, modified lateral neck dissection, central neck dissection	1998 2012 2013	3	Level VI	10/ 18/ 19	Redo central neck dissection	VI	Transient RLN injury
2	Total thyroidectomy	2001	1	Level VI	9/ 30/ 19	Redo central neck dissection	VI/VII	
3	Total thyroidectomy, central neck dissection + modified lateral neck dissection, redo bilateral central neck dissection	2014 2015 2017	3	Level IV	3/ 27/ 19	Modified lateral neck dissection	II-IV	
4	Total thyroidectomy, central neck dissection, lateral neck dissection	2018	1	Level II	12/ 5/18	Redo lateral neck dissection	II-III	
5	Total thyroidectomy	2016	1	Level II	12/ 12/ 18	Central neck dissection + modified lateral neck dissection	II-IV, VI	
6	Hemithyroidectomy	2019	1	Thyroid bed	1/ 24/ 20	Completion thyroidectomy + central neck dissection	IV	Transient RLN injury

guidance was used to plan incision placement and to localize the pathologic target. Reoperations in the thyroid group included: modified lateral neck dissection (1), redo lateral neck dissection (1), redo central neck dissection (2), completion thyroidectomy + central neck dissection (1), and redo central neck dissection + modified lateral neck dissection (1). Seed retrieval was confirmed with an immediate postoperative radiograph to show the seed with the specimen. After pathologic review, the seed was returned to the nuclear medicine department for disposal according to state regulations from the Illinois Emergency Agency (IEMA) on handling of radioactive medical waste. Operative variables including: number of lymph nodes (LNs) harvested, estimated blood loss (EBL), operative time and length of stay (LOS), and postoperative complications were recorded and a summary is recapitulated in Table 2.

Results

All patients had successful resection of the targeted lesion/area and removal of the radioactive seed. There was no seed migration. For the thyroid cohort, operations yielded lymph nodes positive for metastatic PTC in all but one patient. In this exception, fibromuscular tissue was invaded by PTC, but no nodal tissue was present. Parathyroid tissue was pathologically-confirmed for the two patients belonging to that cohort. All patients had correction of their hypercalcemia to within the range of normal. Length-of-stay averaged one day and most patients were able to discharge home the same day or postoperative day 1. Two complications occurred in the thyroid group which, specifically, were 2 transient RLN injuries. One of the RLN patients was required to stay until postoperative day 4 for concerns of aspiration risk related to laryngeal dysfunction. These complications are shown with the operation performed and the respective prior operative history in Table 1. Laryngoscopy was not performed for either of the RLN palsies in our cohort, but each patient had regained their baseline voice by 3 months after their operation. Operative characteristics are shown in Table 2.

Discussion

Radioactive seed localization (RSL) has established applications in other surgical procedures including resection of breast cancer, lung cancer, and sarcoma.[6,7] Applying the same principles used in these procedures, we have demonstrated usefulness of RSL in both reoperative thyroid and parathyroid surgery. Experience with RSL in endocrine operations has been limited and our series represents one of the largest. As can be seen in Table 2, these procedures are feasible with operative times that are to be expected in complex reoperations. We believe that this technology has shortened operative times, but the small case numbers and operation heterogeneity preclude a direct analysis at this point in our experience. Several reasons for this belief include: 1) it assists with incision planning, 2) it obviates the need for obtaining frozen section with immediate confirmation of the target lesion and 3)it helps focus the dissection around intricate anatomy.

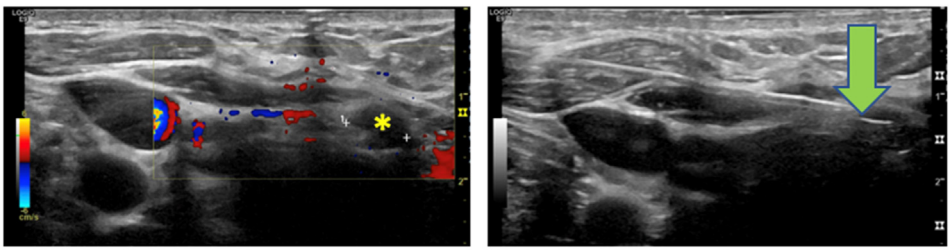

Fig. 1. Pre and post seed placement ultrasound images. The yellow asterisk denotes the lesion of interest. The green arrow shows the placement of the seed (transversely-oriented hyperlucency) within the target lymph node. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 2
Operative variables collected for both metastatic PTC and recurrent hyperparathyroidism cohorts. Mean values are followed by the range of values observed.

Metastatic Papillary Thyroid Carcinoma			Recurrent Hyperparathyroidism		
	Mean Value	Range		Mean Value	Range
Operative Time (min)	140	106–190	**Operative Time (min)**	125	70–177
EBL (mL)	66	5–200	**EBL (mL)**	10	–
LOS (days)	1.0	0.1–4	**LOS (days)**	1	–
LNs harvested	8.2	1–27			
Positive LNs	1.5	0-4[b]			
Incision length (cm)	6.2	4–9	**Incision length (cm)**	4.5	4–5
Complications[a]			**Complications**		
RLN palsy	2		RLN palsy	0	
Hematoma	0		Hematoma	0	

[a] None of the complications occurred as part of the RSL placement procedure.
[b] One patient, excluded from analysis, had target lesion removed but proved to be fibromuscular tissue invaded by PTC without any microscopic evidence of nodal tissue.

Minimal in-hospital observation of patients is required with an average length-of-stay at less than 24 h. This represents substantial progress from the first radio-guided operations performed in the early 2000s. These early protocols employed large doses of I-131 for tumor localization and required hospital stays of 7 days due to the high levels of radioactivity.[8] Patients were pre-admitted for administration of the radioactive iodine, and after several days of allowing the isotope to decay, they were taken to the operating room. Whole body scans were performed pre- and postoperatively to determine the success of the surgery at removing the I-131-localized tumor deposits. An additional advantage of RSL over these first applications of radio-guided surgery, is that RSL is not limited to only radiosensitive tumors that concentrate I-131.

Our average LN harvest of 8.2 LNs underscores that although the technique is used for berry picking concerning lesions, it achieves an adequate pathologic yield for oncologic/diagnostic purposes. Again, we did not compare our reoperative cohort against a control as the variability in operations limited meaningful comparisons, but other groups such as Cambil et al. do report in their recent experience of using RSL for thyroid metastases that they were able to achieve a reduction in their operative times.[2]

Two recurrent laryngeal nerve (RLN) palsies were noted in our thyroid cohort. Higher risks for procedure-related complications in reoperative surgery are broadly reported.[3,4] For example, Hardman et al. reported a 2.2-fold increase in RLN palsy and a 2.5-fold increase in postoperative hematoma with reoperative thyroid surgery.[5] This increased risk for complications is counterbalanced by the excellent and enduring treatment responses most patients can expect from reoperative surgery for persistent PTC. In their 13-year follow-up of reoperated thyroid cancer patients with persistent or recurrent disease, Onuma et al. showed an additional 30–40% of patients have all physical and biochemical evidence of their disease eliminated for the duration of their follow-up period.[9]

RSL for parathyroid localization during minimally-invasive parathyroidectomy was previously described by Danschutter et al.[10] While they showed that this methodology was feasible, they ultimately concluded: “we believe that this technique should be reserved for difficult cases.” This was largely because they noted hematomas around their seed markers in 40% of the patients. No seed placement-related complications were experienced in the present series. However, reoperative surgery qualifies as a “difficult case” and, it would seem that the increased operative risks, outlined above, help offset potential risks during seed placement.

Reoperative parathyroidectomy, like reoperative thyroid surgery, is challenged by lower cure rates, increasing the importance of preoperative localization; an absolute requirement for RSL. Patel et al. propose that preoperative localization is optimal for reoperative parathyroid surgery when there is concordance between 2 or more localizing modalities.[4] This concordance is key, because prior surgical intervention decreases the sensitivity of the two most commonly used imaging modalities-ultrasound and sestamibi scanning. Other methods such as 4DCT, SPECT-CT, or IR-performed venous sampling for parathyroid hormone levels can further improve this sensitivity.[3] FNA of a suspicious lesion for parathyroid hormone assay is a single test that can confirm the presence of an abnormal parathyroid gland by finding a high level of PTH within them before proceeding to the OR.

One of the advantages of the current RSL technique is that seed placement and operative intervention can be uncoupled.[1] It is not necessary to coordinate radiologic and operative schedules as must occur with intraoperative sestamibi scanning or wire-localization. Most authors suggest a 4-day period between seed placement and the patient’s operation. Times of longer than 1 week with the seed implanted raises concerns for prolonged radioactivity exposure for the patient and loss of radioactivity prior to surgery. This is largely based on a recommendation from the United States Nuclear Regulatory Commission on the use of ‘Low dose I-125 seeds for the Localization of Non-Palpable Lesions’, where it states “RSL can be performed up to 5 days before surgery”.[11] However, the radioactivity exposure to both the patient and the operating team has been shown to be minimal with these I-125 seeds.[1,2,6] With a half-life of 90 days, the latter concern is not substantiated by the physical decay of the isotope. Due to extenuating circumstances, one of our patients who had seed placement required rescheduling of their operation later than this 4-day threshold. At day 7, the seed was easily located with the Neoprobe.

Limitations of RSL reoperative endocrine surgery include the occasional technical inability to insert the seed within a target lesion and need to settle for placing it adjacent to an area of interest. Seed placement in close proximity to the target still allows for detection of the area of interest and a compartment-based dissection. Intraoperatively, surgeons are limited to dissection without suction to avoid unwittingly removing the seed from the operative field before identification of the target area. Since this technique utilizes radioactive material, this approach is limited to only those centers with a radiation safety program already in place.

Conclusion

The use of radioactive iodine 125 seed localization facilitates safe and efficient localization of endocrine pathology within reoperative surgical fields. From planning incisions to confirming pathology retrieval, it is an asset in these difficult cases. No seed placement complications were noted and operative complications were consistent with reported rates for reoperative surgery.

Declaration of competing interest

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