Radioactive iodine (RAI) therapy with $^{131}$I is the standard of care for treatment in many patients with differentiated thyroid cancer. Because $^{131}$I is typically administered as a pill, and much of its radioactivity is excreted via the urine, there can be challenges in patients who cannot swallow pills, absorb iodine via the gastrointestinal tract, or eliminate RAI via the urine (i.e., dialysis patients and patients with renal failure). In this article, we present 3 cases in which the standard $^{131}$I treatment protocol for thyroid cancer could not be used because of these challenges, and we discuss the strategies used to overcome them. Provider collaboration and treatment customization are critical in overcoming patient-specific challenges.

**Key Words:** radioactive iodine; $^{131}$I; thyroid cancer; patient care

**CASE REPORT**

Case 1

Case 1 was a boy with a past medical history of Noonan syndrome with dysphagia diagnosed at birth. At 4 y of age, the patient came to our institution with an enlarged right thyroid lobe and was diagnosed with multiple thyroid nodules on a neck ultrasound. The ultrasound demonstrated a diffusely abnormal thyroid gland with microcalcifications, and the right and left cervical lymph nodes were abnormally enlarged with suggestive microcalcifications. These findings were highly suspected of representing thyroid malignancy, and a fine-needle aspiration of the right thyroid nodule revealed papillary thyroid cancer. The following week, CT of the neck and chest with contrast medium was performed, finding a lobulated heterogeneous mass in the right thyroid gland and multiple suggestive lymph nodes (Fig. 1). The following month, a thyroidectomy was performed with radical neck dissection to remove the suggestive nodes. A pathology report of the thyroid described a 4.2-cm primary papillary thyroid cancer with positive margins. In addition, angioinvasion and perineural invasion were present. Fourteen positive lymph nodes were identified at right neck levels II, III, IV, and VB and at left levels IIb and III. A pathologic stage classification, based on the eighth edition of the *AJCC Cancer Staging Manual* (7), was determined to be at least pT3aN1b(cMx)

Given the patient’s intermediate-risk thyroid cancer, a recommendation was made for treatment with $^{131}$I. However, this case presented challenges due to the patient’s young age and difficulty swallowing. Because of the patient’s dysphagia, it was not feasible to administer the standard $^{131}$I pill orally. A multidisciplinary joint decision was made to
proceed with liquid $^{131}$I therapy. Because the patient had extensive bilateral neck involvement on pathology, a pre-therapy scan was recommended to assess for macroscopic residual disease burden.

Since $^{131}$I is volatile, liquid administration required special preparations. Specifically, to avoid staff exposure to $^{131}$I, a pharmacist provided a 5- to 10-mL oral solution of $^{131}$I mixed with grape juice in a French square glass vial with a screw cap. The patient drank through a straw with a spinal needle that was attached to poke the Teflon (DuPont) septum within the cap. These preparations were designed to minimize evaporation of liquid $^{131}$I. An anterior and posterior whole-body scan with SPECT/CT imaging of the neck was taken 24 h after oral administration of 55.5 MBq (1.5 mCi) of Na$^{131}$I ($^{123}$I was not available as a liquid for the diagnostic scan). Focal uptake was noted in the thyroid bed region in the neck, consistent with remnant thyroid tissue. There were no visible suggestive cervical or distant foci of RAI uptake to suggest metastasis.

The following day, the patient was admitted (as per the patient’s legal guardian’s request because of situations in the home) to our hospital for high-dose RAI therapy. For the therapeutic dose of 2,775 MBq (75 mCi) of Na$^{131}$I in a liquid form, the dose was again mixed with grape juice and ingested via a method similar to that for the pretherapy scan.

The patient was discharged 2 d after being admitted and returned the following week for a posttherapy anterior and posterior whole-body scan supplemented by SPECT imaging of the neck (Fig. 2). A year after therapy, the patient returned the following week for a posttherapy anterior and posterior whole-body scan supplemented by SPECT imaging of the neck. These images are consistent with residual thyroid tissue, as focal tracer uptake was noted within thyroid resection bed. No immediate adverse events were observed.

**FIGURE 2.** Case 1 posttherapy scan. (A) Whole-body scan obtained after administration of 2,775 MBq (75 mCi) of $^{131}$I. (B) SPECT imaging of neck. These images are consistent with residual thyroid tissue, as focal tracer uptake was noted within thyroid resection bed.
Posttherapy whole-body SPECT/CT imaging of the neck the following week did not find any distant metastatic disease (Fig. 3). One year after treatment, neck ultrasound showed postsurgical findings from thyroidectomy and no new or suggestive findings. Thyroglobulin levels were 0.1 μg/L (nearly undetectable; reference range for intact thyroid, 2.8–40.9 μg/L) and thyroglobulin antibodies were 1 IU/mL (within the reference range of ≤11 IU/mL).

Case 3

Case 3 was a 59-y-old man with diabetes mellitus, hypertension, and end-stage renal disease on hemodialysis. One challenge with hemodialysis in the context of RAI treatment is ensuring radiation protection for everyone present, as there is a risk that the RAI will contaminate the dialysis machine and increase the level of occupational exposure. In addition to the contamination-control and occupational-exposure issues, there are concerns with waste-disposal, dosimetry, and patient-release issues. Finally, because the 131I is eliminated largely through the dialysate because of the negligible renal clearance, the administered dose might need to be modified from the typical protocol.

The patient was referred from outside our medical center for treatment with RAI after surgery for an 8-cm pT3aNx follicular thyroid cancer with capsular vascular invasion. The patient underwent a whole-body scan with 123I. Anterior and posterior images of the neck and entire body were taken 24 h after oral administration of 95.83 MBq (2.59 mCi) of Na123I. No distant uptake was found to suggest metastasis, and the focal uptake within the thyroid bed was consistent with residual thyroid tissue after recent thyroidectomy.

The hemodialysis requirement presented the challenge of providing radiation protection to those who would be caring for the patient during dialysis. Our workflow for managing this case is illustrated in Figure 4. Specifically, multidisciplinary meetings were held involving radiation safety, nuclear medicine, endocrinology, and nephrology personnel. The decision was made that the radiation safety team would monitor all personnel and equipment and check for contamination of the dialysis machines and ports. The training materials provided to the dialysis lab personnel are included in the supplemental materials (available at http://jnmt.snmjournals.org). Additionally, all dialysis staff received training from radiation safety personnel.

The following month, the patient received 1,102.6 MBq (29.8 mCi) of Na131I as a pill to treat his follicular thyroid cancer. After a discussion among health-care staff and consultation of the relevant literature, the dose had been lowered from an anticipated dose of 1,850 MBq (50 mCi) because of the use of dialysis, to reduce the radiation dose to the marrow secondary to the lowered clearance. The patient was admitted to our hospital at the University of California, San Francisco for this procedure.

The patient was prepared for therapy by thyroid hormone withdrawal. The outpatient dialysis record showed a normal session the day before the therapy, without any adverse events. After collaboration between the nuclear medicine team, the radiation safety team, the primary nephrologist, and the outpatient nephrologist, the patient received dialysis the day after the RAI therapy, with intermittent hemodialysis for 3.5 h planned for 3 consecutive days after RAI. The patient tolerated the intermittent hemodialysis well. The radiation safety personnel checked the dialysis machines and no contamination was detected. There were no complications or radiation risks after the careful planning.

The posttherapy 131I scan supplemented by SPECT/CT imaging of the neck found no evidence of distant metastatic disease (Fig. 5). Most recently, at 1 y 2 wk after the RAI therapy, the patient underwent anterior and posterior imaging of the neck and entire body without SPECT 24 h after oral administration of 82.88 MBq (2.24 mCi) of Na123I. No abnormal RAI uptake was observed to suggest recurrent or metastatic disease.

**FIGURE 3.** Case 2 post-RAI therapy scan with intravenous administration of 131I. (A) Whole-body scan obtained after administration of 1,850 MBq (50 mCi) of 131I. (B and C) SPECT/CT imaging of neck obtained in axial and coronal planes, respectively, showing focal tracer uptake in thyroid bed, consistent with residual thyroid tissue. No distant metastases were observed.

**FIGURE 4.** Workflow for management of patients with end-stage renal disease (ESRD) who are on dialysis and referred for RAI.

**DISCUSSION**

At present, 131I pills are the standard preparation for RAI treatment of hyperthyroidism and thyroid cancer. von Schulthess et al. concluded that...
capsular \textsuperscript{131}I is a safe formulation for treatment of thyroid disease, demonstrating that the gastric radiation dose from \textsuperscript{131}I pills was high only locally and was below the level that would cause tissue necrosis (8). However, unique patient challenges, such as dysphagia, may limit or restrict safe administration of oral \textsuperscript{131}I in pill form. The patient in case 1 was unable to take pills because of developmental anomalies and a young age and was consequently administered liquid oral \textsuperscript{131}I. No adverse events took place, and the dose was administered safely without exposing the technologist staff to radiation.

Previous studies concerning \textsuperscript{131}I therapy describe administration difficulties and alternative treatment protocols similar to those discussed here (Table 1). Aside from difficulty swallowing pills, Aamri et al. reported pill-related issues such as a patient-caused radiation hazard, pill adherence to the container, and technologist mishandling of the substance (9). Halpern et al. suggested that formation of iodine–gelatin complexes in the gastrointestinal tract may reduce thyroidal uptake of capsular \textsuperscript{131}I relative to the liquid form (10). One proposed solution involved endoscopically depositing the solid \textsuperscript{131}I pill into the stomach—effectively minimizing risk of spillage, exposure, and incorrect administration (11). However, endoscopy is invasive and carries risks for the patient.

Rini et al. commented on the greater-than-intended irradiative impact of encapsulated \textsuperscript{131}I—particularly when used as a diagnostic tracer—compared with liquid-form \textsuperscript{131}I (12). Using a pill-form \textsuperscript{131}I tracer, this group observed a mean diagnostic \textsuperscript{131}I uptake 14\% lower than the corresponding therapeutic \textsuperscript{131}I uptake (44\% vs. 58\%), reflecting the higher uptake for a pill that delivers a therapeutic dose than for a pill that delivers a diagnostic dose. They concluded that in hyperthyroid patients treated with liquid \textsuperscript{131}I, compared with encapsulated \textsuperscript{131}I, uptake of diagnostic doses of liquid \textsuperscript{131}I better predicts uptake of therapeutic doses of liquid \textsuperscript{131}I (12). It is therefore recommended that health teams familiarize themselves with administrative techniques and safety for liquid and intravenous \textsuperscript{131}I. Although administration of \textsuperscript{131}I in pill form is the first option, it is important to remember that liquid administration remains a safe and effective alternative, provided appropriate radiation safety precautions are followed (3,13).

Unlike case 1, the patient in case 2 did not have dysphagia and could swallow but had significant gastrointestinal dysmotility, which often manifested as episodes of pseudo-obstruction with gastroparesis. Therefore, the patient was largely dependent on total parental nutrition, and oral or gastrostomy tube treatment was precluded. The decision to use intravenous treatment was made after months of ongoing discussion. The advantages of intravenous treatment relative to oral \textsuperscript{131}I therapy include enhanced diagnostic accuracy, rapidity, and the ability to treat patients with impaired gastrointestinal absorption (14). The risks include the liquid iodine’s volatility, which makes it more dangerous to handle and increases the risk of major spills and exposure of technologists to radiation. Meticulous care was undertaken, and no spills or other adverse event took place.

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<td>Rini et al. (12)</td>
<td>Capsular \textsuperscript{131}I tracers exposed patients to higher-than-intended amounts of radiation, compared with liquid \textsuperscript{131}I tracers</td>
<td>Not applicable</td>
<td>Inclusion criterion: Graves disease; radiation uptake compared</td>
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<td>Al Aamri et al. (9)</td>
<td>Several capsule-related mishaps were cited (i.e., acrylic-glass tube adherence, swallowing difficulty, radiation exposure)</td>
<td>Pill dysphagia</td>
<td>Radioactive mishandling and misuse described</td>
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<td>Honour et al. (15)</td>
<td>Case series of 144 RAI patients documented minimal fluid intake for speedy recovery</td>
<td>Not applicable</td>
<td>High-dose solid \textsuperscript{131}I therapy</td>
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<td>Shields and Johnson (17)</td>
<td>Novel presentation was made of capsular \textsuperscript{131}I administration via endoscopic stomach implantation</td>
<td>Successful pill dysphagia workaround</td>
<td>Endoscopy required; capsule \textsuperscript{131}I administered</td>
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**TABLE 1**

Other Studies on Liquid \textsuperscript{131}I Administration
Patients are more prone to experience nausea as the $^{131}$I dose increases (15,16). Additionally, patients with gastrointestinal reflux disease, gastroparesis, gastric outlet obstruction, and other similar conditions are at increased risk of vomiting (16). Overall, case 2 demonstrated that intravenous administration of $^{131}$I is a safe and effective alternative when there is great difficulty with oral administration and gastrointestinal absorption is anticipated.

Case 3 evidenced an instance of end-stage renal disease complicating RAI treatment for follicular thyroid cancer. In patients with normal renal function, the $^{131}$I would be excreted through the urinary system; thus, impaired renal function complicates iodine clearance and theoretically potentiates blood radioactivity risks. Although the dialysis machine would likely compensate to some extent for this decreased clearance, hemodialysis patients are still impacted by decreased clearance of $^{131}$I (17). In addition, there is a risk that the dialysis staff and machinery will become contaminated (17). In fact, the main challenge with case 3 was in dealing with the radioactive dialysate waste, managing staff exposure, and training the staff. Contingency plans are necessary for addressing fluid spills during dialysis (18). Murcutt et al. supplied an illustrated schematic and protocol for safe hemodialysis of patients in need of ablative $^{131}$I RAI therapy, much of which mirrors the methods described here (19). Additionally, under dosimetry guidance, high-dose intravenous treatment of differentiated thyroid cancer patients is safe and may also reduce the radiation dose (20). To limit risks of bone marrow toxicity and further renal insult, therapy doses should not exceed the prescribed amount in any patient, including those patients on dialysis, as Magné et al. have recommended (21). Table 2 describes other instances of successful oral $^{131}$I administration in patients with end-stage renal disease on hemodialysis.

Prior studies have suggested that dialysis patients have increased systemic retention of $^{131}$I, and reductions in the administered $^{131}$I dose have therefore been suggested, although no uniform consensus exists. Citing rapid iodine clearance, Morrish et al. concluded that dialysis reduces the effective radiation dose and necessitates larger $^{131}$I treatment doses to achieve outcomes equivalent to those in patients with normal renal function (22). Jiménez et al. administered to hemodialysis patients the same $^{131}$I doses as are received by patients with normal renal function. In their small cohort ($n = 3$), this protocol avoided overexposure of patients to radiation (23). Alevizaki et al. used a 40%–50% activity reduction of $^{131}$I and found that none of their patients experienced short-term side effects or had detectable thyroglobulin levels on their first posttherapy evaluation ($n = 5$; the inclusion criterion was end-stage renal disease) (24). Vermandel et al. concluded that an approximately 30% reduction from the nominal $^{131}$I dose struck the best balance between hematologic toxicity and treatment efficacy ($n = 6$; the inclusion criterion was end-stage renal disease undergoing hemodialysis) (25). Following their lead, we chose to reduce the dose despite the fact that some of the literature recommended no change in, or even increased, doses; our case involved a 40% reduction from our typical 1,850 MBq (50 mCi) to 1,110 MBq (30 mCi) to minimize radiation exposure of marrow secondary to reduced clearance of $^{131}$I.

**CONCLUSION**

$^{131}$I is a common treatment for hyperthyroidism and thyroid cancer, and most patients may be treated using standardized protocols as defined by the Society of Nuclear Medicine and Molecular Imaging (13). We have presented 3 cases that created technical difficulties for nuclear medicine and radiation safety staff, who had to come up with alternative protocols to meet each specific challenge. Knowledge of these alternatives should be of particular

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<td>Vermandel et al. (25)</td>
<td>Six ESRD patients were administered reduced RAI formulas to treat thyroid cancer; bone marrow toxicity was analyzed to define optimal dosimetry</td>
<td>ESRD; successful removal of $^{131}$I remnants</td>
<td>Dosimetry used to minimize toxicity</td>
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<td>Magné et al. (21)</td>
<td>Hemodialysis was safe and effective during oral $^{131}$I RAI treatment of differentiated thyroid carcinoma</td>
<td>ESRD; metastases; successful excretion</td>
<td>Papillary thyroid carcinoma; metastases in 9 of 16 cervical nodes</td>
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<td>Shields et al. (11)</td>
<td>Safe hemodialysis techniques and protocol were shared for minimizing radiation risks and maintaining RAI treatment</td>
<td>ESRD; successful excretion; patient interaction minimized</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Bhat et al. (17)</td>
<td>Radioactive ablation in ESRD patient after complete thyroidectomy remained successful 4 y later</td>
<td>ESRD; history of hypertension, diagnostic prescan with $^{123}$I</td>
<td>Goiter; presented with shortness of breath after left thyroidectomy</td>
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ESRD = end-stage renal disease.
value to nuclear medicine technologists and physicians who encounter similar cases. The cases we have described highlight the importance of provider collaboration and treatment customization to overcome patient-specific challenges.

**DISCLOSURE**

No potential conflict of interest relevant to this article was reported.

**REFERENCES**