Selected Controversies of Radioiodine Imaging and Therapy in Differentiated Thyroid Cancer

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KEYWORDS

• Thyroid cancer • Radioiodine scanning • I-131 • Remnant ablation
• I-131 adjuvant treatment • Radioiodine refractory disease

KEY POINTS

- Radioiodine isotopes of iodine-123 and iodine-131 (I-131) remain valuable diagnostic staging tools, and I-131 remains a valuable therapy for differentiated thyroid cancer.
- Properly performed radioiodine scans are valuable diagnostic staging tools.
- Before patients are considered radioiodine refractory, which thereby eliminates an I-131 treatment that may be potentially beneficial to patients, the physician must confirm patients are truly radioiodine refractory; the classification of radioiodine refractory is rapidly changing with new research developments.
- The classification of differentiated thyroid cancer as radioiodine refractory warrants reassessment and reclassification.

INTRODUCTION

Radioiodine is important in the diagnostic and therapeutic armamentarium of differentiated thyroid cancer (DTC); however, many controversies persist. This article addresses some of these controversies, namely, the utility of pretherapy staging radioiodine scans; the prescribed activity for iodine-131 (I-131) remnant ablation, adjuvant treatment, and distant metastases; preparation with thyroid hormone withdrawal (THW) versus recombinant human thyroid-stimulating hormone (rhTSH); and the classification of radioiodine refractory DTC. Discussion of these controversies requires definitions of selected terms in the first section.

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TERMINOLOGY

Remnant ablation is the use of I-131 to destroy normal thyroid tissue with the objective of improving serum thyroglobulin (Tg) levels to be a better tumor marker. Additional secondary objectives of *remnant ablation* are potentially to improve the quality of future radioiodine imaging studies and/or therapies. As defined by the American Thyroid Association's (ATA) guidelines from 2009 and 2015, remnant ablation does not have any objectives to reduce recurrences or to increase survival or progression-free survival.[1,2] *Adjuvant treatment* is the use of I-131 to treat suspected but unproven residual DTC with the objective of reducing recurrence, increasing survival, or increasing progression-free survival. *Treatment* is the use of I-131 to treat known residual locoregional disease and/or distant metastases having goals such as progression-free survival, overall survival, or even cure. *Therapy* is the generic use of I-131 for remnant ablation, adjuvant treatment, or treatment of known locoregional or distant metastases. These definitions are different from the 2015 guidelines from the ATA in the use of the words *treatment* and *therapy*,[1,2] but this author submits that the usage of these terms herein is more consistent with the usage of the terms in oncology of *chemotherapy* and *chemo treatment* and the terms in radiation therapy for *radiation therapy* and *radiation treatment*.

Two additional terms, *dose* and *dosage*, require distinction and definition herein. The term *dose* is frequently used with competing and, therefore, confusing definitions. In the specialty of nuclear medicine and radiation therapy, *dose* refers to absorbed dose of radiation to an organ or tumor. This value is measured in *radiation absorbed dose* (rad) or gray. Unfortunately, some individuals use the term *dose* to mean the amount of prescribed activity of I-131 administered to a patient. We measure such amounts in millicuries or megabecquerels (MBq). Millicurie and becquerel are not interchangeable with rad or gray, respectively. Although the amount of millicuries or becquerels administered will be a factor that affects how many rad or grays are delivered to normal tissue or a tumor, there are many other factors that affect the absorbed dose, such as I-131 uptake, dose rate, and residence time. As alternatives to using the same word to mean to 2 different measurements, the term *dosage* is frequently used to indicate prescribed activity administered. An additional alternative is using the term *prescribed activity* itself.

UTILITY OF RADIOIODINE SCANS

The utility of radioiodine scans remains one of the more frequently debated controversies. However, in order to better understand the arguments for and against radioiodine scanning, radioiodine scanning must be subdivided; this author proposes the following subdivisions (1) pre–I-131 therapy staging scans performed after patients' first surgery, (2) post-therapy scans performed 3 to 10 days after an I-131 therapy, (3) follow-up surveillance/baseline scans performed 6 to 18 months after the initial I-131 therapy, and (4) restaging scans performed when recurrence and/or progression of DTC is suspected.

Postoperative Pretherapy (Iodine-131) Staging Scans

In regard to postoperative pretherapy (I-131) staging scans, **Table 1** (column 1) lists many of the arguments presented against performing these scans, with the counter arguments in **Table 1** (column 2). However, with the development of single-photon emission computed tomography (SPECT) imaging, the literature overwhelmingly supports the utility of such scans (**Table 2**).[3–17] **Table 3** shows the ATA's 2015 guidelines. This author thinks that one of the reasons that there is such widespread difference of