The optimal time to identify residual thyroid tissue or persistent differentiated thyroid cancer on a posttreatment whole-body scan is 3 to 6 days after therapeutic radioiodine is administered

Huang BT, Huang SH, Huang YE, Wang PW. Appropriate time for post-therapeutic I-131 whole body scan. Clin Nucl Med 2009;34:339-42

SUMMARY

BACKGROUND The optimal time for performing a posttreatment whole-body scan (RxWBS) is not entirely clear. This may be the consequence of a variety of things that might alter ^{131}I uptake, such as inadequate pretherapy preparation, lack of functioning sodium–iodine symporters, poorly differentiated thyroid cancers, advanced patient age, or improper timing of the RxWBS. The aim of this study was to identify the optimal time for performing an RxWBS.

METHODS This is a retrospective study of 239 patients with differentiated thyroid cancer who were treated from January 2006 through May 2008 in the Department of Nuclear Medicine in Chang Gung Memorial Hospital, University College of Medicine in Kaohsiung, Taiwan. All patients were treated with total thyroidectomy followed by ^{131}I therapy after patients were off levothyroxine for at least 4 weeks. The patients had three sequential whole-body scans on the 3rd to 4th day, the 5th to 6th day, and the 10th to 11th day after ^{131}I was administered. Simultaneous anterior and posterior whole-body images and spot views of the abdomen and pelvis were included in some patients to more accurately localize the ^{131}I-avid tumors, which were scored by visual assessment into three grades, as follows: grade 0 = no visible uptake, grade 1 = visible uptake, and grade 2 = clearly visible uptake. Metastatic tumors and thyroid remnants were regarded as having early ^{131}I washout when uptake was no longer visible in the third RxWBS. All scans were interpreted by two experienced specialists in nuclear medicine. If the readings were conflicting, then a third reviewer evaluated the images.

RESULTS Of the 239 patients comprising the study cohort, 172 were women (72%) and 67 were men (28%), with a mean (±SD) age of 45.8±15.0 years. A total of 205 patients had

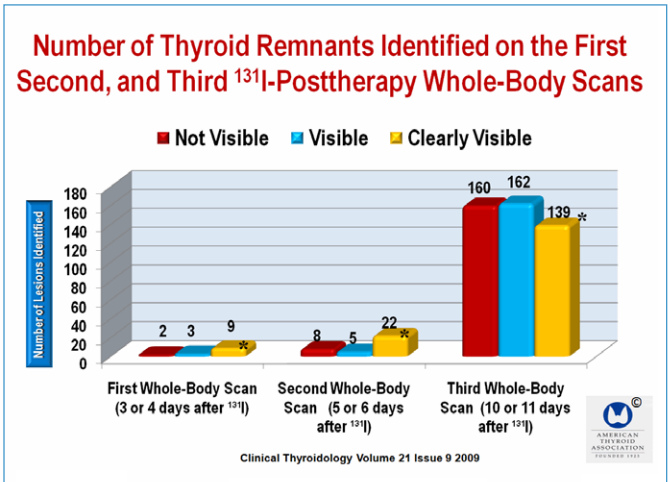

Figure 1. This figure shows a linear trend of decreasing ^{131}I uptake in sequential images of thyroid remnants. *P<0.001, comparing the first and second with the third RxWBS results. There was no statistical difference between the second and third RxWBS visualization for all of the studies, including remnant ablation and lymph-node, lung, and bone metastases. Only 9 of 170 remnants were missed on the third RxWBS (5%).

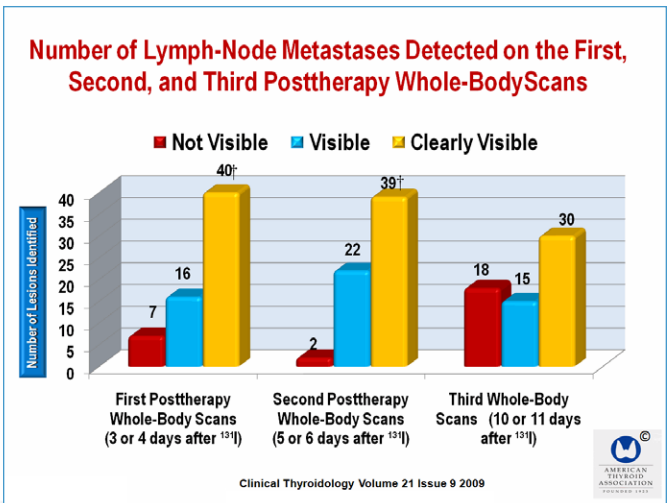

Figure 2. This figure shows the linear trend of decreasing ^{131}I uptake in sequential images of lymph-node metastases. †P<0.01, comparing the first and second with the third RxWBS.

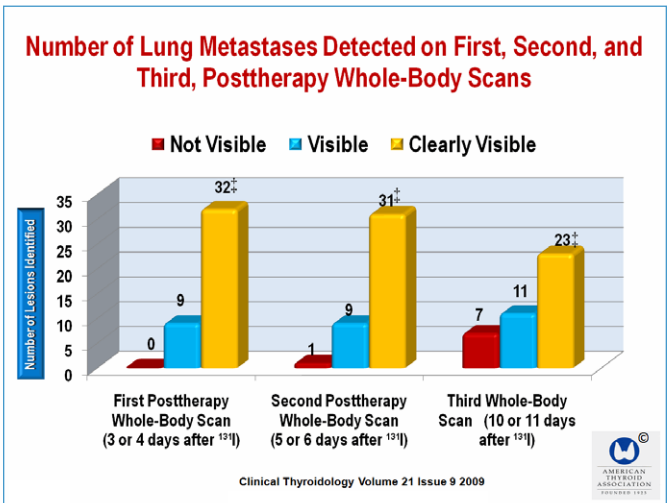

Figure 3. This figure shows the linear trend of decreasing ^{131}I uptake in sequential images of lung metastases. ‡P<0.003, comparing first and second with the third RxWBS. The third RxWBS missed 7 of 41 lung metastases (17%).

papillary thyroid (86%) cancer (PTC) and 34had follicular thyroid cancer (14%). Patients were treated with 30 to 200 mCi (1.1 to 7.4 MBq) of ^{131}I. The mean amount of ^{131}I administered was 108±32 mCi (4.0±1.2 GBq). There were a total of 295 images, 227 of which revealed uptake in the anterior neck (77%). This was interpreted as either intrathyroidal or extrathyroidal ^{131}I uptake, which was confirmed by physical examination, neck ultrasonography, and computed tomography scans. A total of 170 of the 227 images with thyroid-bed uptake (44%) were interpreted as thyroid remnants (75%), and 57 extrathyroid bed lesions were regarded as lymph-node metastasis (25%). In addition, there were metastases in the lung (n = 41), bone (n = 18), and mediastinum (n = 6). Serum thyroglobulin (Tg) levels were assessed in patients with visible RxWBS lesions, some of which were also found on fluorodeoxyglucose–positron-emission tomographic images. Here and elsewhere, percentages are rounded to an integer.

There was a difference in the early washout of ^{131}I in thyroid remnants and metastatic lesions (Figure 1). The third posttherapy RxWBS missed 18 of 63 lymph-node metastases (29%) (Figure 2); 7of 41 lung metastases (17%) (Figure 3); and 3 of 18 bone metastases (17%) (Figure 4); however, only 9 of 170 thyroid remnants were missed on the third RxWBS (5%) (Figure 5). Comparisons of the first and second scans found no statistical difference between the two scans, including observations of scans on lymph-node, lung, and bone metastases (P = 0.154, P = 0.602, and P = 0.630, respectively). However, the third scans were significantly poorer as compared with the first two, detecting significantly fewer lymph-node metastases than the first (P = 0.043) and second (P<0.001) scans. Moreover, there were no significant findings in the third scan as compared with the first two scans (Figure 5). The mean serum Tg levels were significantly different between patients with lymph-node metastases and those with lung (98.5 vs. 91.1 µg/L) or bone (98.5 vs. 4.7 µg/L) metastases. There was no correlation with serum Tg concentrations among patients with and without early ^{131}I washout.

CONCLUSION The optimal time to identify residual thyroid tissue or persistent differentiated thyroid cancer metastases on DxWBS is on the 3rd to 6th day after therapeutic radioiodine has been administered.

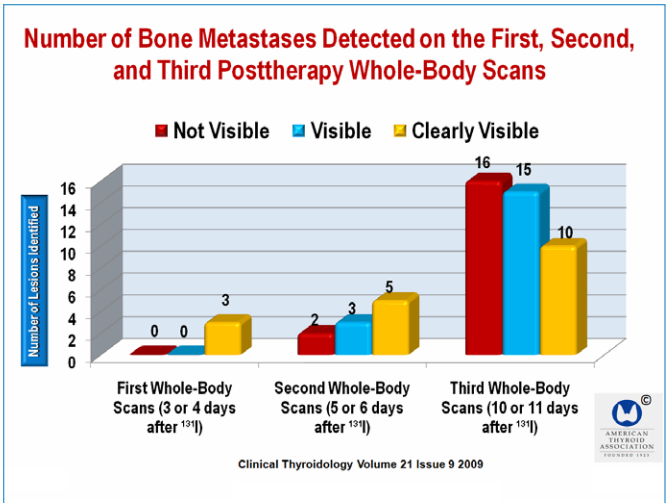

Figure 4. This figure shows the linear trend of decreasing ^{131}I uptake in sequential images of bone metastases. §P<0.0.009, comparing the first and second with the third RxWBS. The third RxWBS missed 3 of 18 bone metastases (16%).

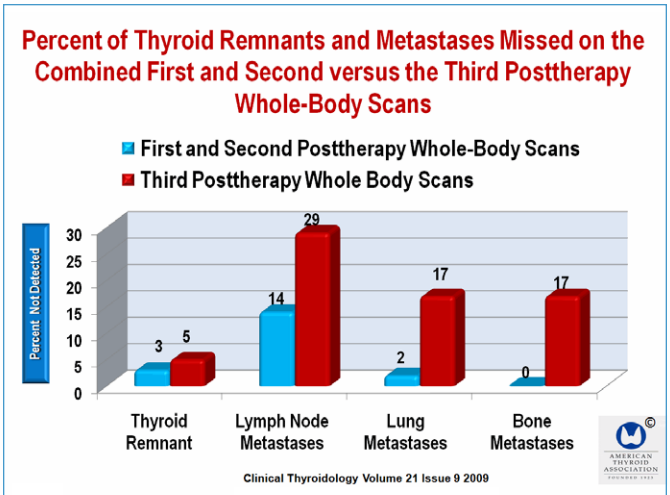

Figure 5. This figure shows the difference in the early washout of ^{131}I in thyroid remnants and metastatic lesions. The third posttherapy RxWBS missed 18 of 63 lymph-node metastases (29%), 7 of 41 lung metastases (17%), and 3 of 18 bone metastases (16%). Only 9 of 170 (5%) remnants were missed on the third RxWBS (5%).

COMMENTARY

The key question that arises after initial near-total thyroidectomy for differentiated thyroid cancer is whether or not substantial thyroid tissue—with or without lymph-node metastases—has escaped the surgeon's scalpel. Neck ultrasonography fails to immediately answer this question because of interfering postoperative cervical edema that disrupts landmarks, blocking this diagnostic path for months. Likewise, serum Tg measurements also fail to localize residual tumor.

However, among patients who are candidates for postoperative ^{131}I therapy, the RxWBS offers an effective way to promptly identify the location and extent of residual tumor. RxWBS thus becomes the lynchpin that guides subsequent clinical maneuvers, providing major clues as to tumor location and prognosis. When posttherapy ^{131}I is not administered, or when there is little or no ^{131}I uptake on the RxWBS, the next maneuver becomes problematic on several levels. There is robust evidence that a diagnostic whole-body scan (DxWBS) using 4 or 5 mCi (148 or 185 MBq) of ^{131}I fails to identify up to 80% of the residual tumor foci (1), underscoring that RxWBS is a much more potent diagnostic test than DxWBS (1;2). A false-negative RxWBS may be the result of several problems, such as inadequate preparation for ^{131}I therapy, iodine contamination from contrast material used for computed tomography, failure to adhere to a low-iodine diet, poorly differentiated non-^{131}I-avid tumor, and in some cases—the best scenario after ^{131}I therapy—is complete excision of the thyroid and lymph-node metastases. Still, the most common problem may be appropriate timing of the

RxWBS after ^{131}I therapy. In my experience, the optimal timing of an RxWBS is one of the most frequent questions posed by clinicians. Unfortunately, until now there has been almost no detailed information to properly answer this question. However, the retrospective study by Huang et al. provides important information on the timing of RxWBS.

After studying 239 patients, Huang et al. found that the identification of thyroid remnants was influenced by timing of the RxWBS, even after treating patients with an average of approximately 108 mCi of ^{131}I. The visualization of thyroid remnants was significantly more accurate when RxWBS was performed 3 to 6 days after the administration of ^{131}I, as compared with RxWBS performed 10 to 11 days after ^{131}I therapy. Still, only 9 of 170 thyroid remnants (5%) were missed on the third RxWBS (5%). The accuracy of identifying metastases is another matter. First, there was a difference in the early washout of ^{131}I in thyroid remnants and metastatic lesions. Second, there was some difference in the type of metastasis.

The third posttherapy RxWBS performed 10 or 11 days after ^{131}I therapy missed 18 of 63 lymph-node metastases (29%), 7 of 41 lung metastases (17%), and 3 of 18 bone metastases (17%). There were no statistically significant differences between the findings in the first and second RxWBS, including scans on lymph-node, lung, and bone metastases (P = 0.154, P = 0.602, and P = 0.630, respectively). Thus, the third RxWBS performed 10 or 11 days after ^{131}I was significantly poorer as compared with the first two scans performed 3 to 6 days after ^{131}I. The Huang study thus indicates that the optimal timing for RxWBS is 3 to 6 days after ^{131}I; however, there were no data concerning day 2, and days 7 through 9 after ^{131}I.

As all of the patients in the Huang study were pretreated with thyroid hormone withdrawal (THW) before ^{131}I therapy, one might be concerned that the study findings could be different from those in patients prepared with recombinant human thyrotropin (rhTSH). In this case, intramuscular rhTSH is typically administered on days 1 and 2 (Monday and Tuesday), and ^{131}I is administered on day 3 (Wednesday), and RxWBS is performed on day 5 (Friday), which is not precisely the same timeframe used in the Huang study. The optimal timing for RxWBS might be 1 week after the administration of rhTSH (5 days after ^{131}I). However, the effective half-life of ^{131}I in follicular cells is significantly longer after rhTSH as compared with THW (3;4), which would enhance RxWBS uptake and could provide a more accurate RxWBS performed 2 days after ^{131}I (Friday). In the study by Haugen et al. (5), patients were prepared first by rhTSH and again after thyroid hormone withdrawal, and the RxWBS was obtained 48 hours after ^{131}I (i.e., on Friday) in patients pretreated with either rhTSH or THW. The RxWBS results were concordant after rhTSH and THW in 89% of the patients. Of the discordant scans, 8 (4%) had superior scans after rhTSH and 17 (8%) had superior scans after thyroid hormone withdrawal, a difference that was not statistically significant. Thus, it would seem that the Huang study could be applicable to patients pretreated with rhTSH, meaning that days 3 to 6 would be the optimal time to administer rhTSH.

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References

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