Evaluation of Thyroglobulin Antibody Normalization in Papillary Thyroid Cancer Patients Receiving High-Dose I-131 Therapy

Sang Hyun Hwang
Yonsei University College of Medicine

KwanHyeong Jo
Korea University College of Medicine and School of Medicine

Chun Goo Kang
Yonsei University Medical Center: Yonsei University Health System

Jiyoung Wang
Yonsei University College of Medicine

Hojin Cho
Yonsei University College of Medicine

Won Jun Kang
Yonsei University College of Medicine

Arthur Cho ( artycho@yuhs.ac )
Yonsei University Health System https://orcid.org/0000-0001-8670-2473

Research Article

Keywords: papillary thyroid carcinoma, thyroiditis, radioiodine ablation, thyroglobulin antibody

DOI: https://doi.org/10.21203/rs.3.rs-759906/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

**Purpose:** Thyroglobulin antibody (TgAb) elevation after I-131 ablation may be difficult to evaluate in cases of recurrence, especially in high-risk patients. This study aimed to evaluate factors contributing to TgAb normalization in papillary thyroid cancer patients receiving high-dose I-131 therapy.

**Methods:** From September 2009 to June 2012, 98 papillary thyroid cancer patients treated with 150 mCi radioactive iodine (RAI) were retrospectively enrolled. Early (3 day) and Delayed (7 day) post-RAI neck counts and reduction ratios were measured and correlated with clinical and pathologic findings. Patients with normal neck ultrasound and undetectable level of serum thyroglobulin (<0.1 ng/mL) and TgAb (<10 IU/mL) were defined as having successful ablation.

**Results:** Thirty-five patients (35.7%) had thyroiditis and 28 (28.6%) achieved ablation success. The thyroiditis group had lower neck counts in both Early and Delayed whole-body scans (WBS), and higher reduction rates than the thyroiditis-absent group. In the ablation success group, Early and Delayed neck counts were significantly higher and the reduction rate of RAI was lower than those in the ablation failure group (p < 0.05). In multivariable analysis, Delayed neck count was the only significant factor for predicting ablation failure (odds ratio = 54.37, 95% confidence interval = 1.33-14.32; p = 0.015).

**Conclusion:** I-131 uptake in the remnant thyroid gland and thyroiditis are factors that indicate TgAb normalization and ablation success in thyroid cancer patients receiving high-dose I-131 therapy.

Introduction

High-dose I-131 therapy (> 100 mCi) is recommended for thyroid cancer patients with late stage cancer with risk of recurrence [1], as I-131 therapy reduces recurrence rates and increases patient survival [2, 3]. An additional benefit of I-131 therapy is the ablation of the remaining thyroid gland function, which should reduce thyroglobulin (Tg) levels to undetectable levels. This increases the sensitivity of recurrence surveillance, as unablated thyroid glands have fluctuating baseline Tg levels, which may potentially delay detection of rising Tg levels. The general assumption is, and recent study results have shown, that patients treated with high-dose I-131 therapy have significantly higher thyroid remnant-ablation success rates than patients treated with low-dose I-131 therapy [4]. However, there are few studies evaluating factors for ablation failure in patients who have received high-dose I-131 therapy.

There is a high incidence for co-existing Hashimoto's thyroiditis (HT) in patients with papillary or follicular thyroid cancer [5, 6]. Although HT is considered to be a favourable prognostic factor compared to patients without HT [7], a few recent reports have shown that HT is a significant factor for remnant thyroid ablation failure [8, 9]. More importantly, evaluation of Tg levels is difficult in these HT patients as elevated thyroglobulin antibody (TgAb) levels are often detected after thyroidectomy [10]. Successful ablation in HT results in a decrease in TgAb levels; however, disappearance of TgAb levels has been shown to take years [11]. HT patients often have to undergo serial thyroid stimulating hormone (TSH), Tg, and TgAb
measurements to determine successful ablation or to evaluate recurrence due to the slower decrease in TgAb levels compared to that in patients without HT [4].

The iodine concentration capacity of patients with HT is much reduced compared to patients without thyroiditis [12]. HT has also been often reported to show positive results in perchlorate discharge tests, likely due to defective or absent thyroid peroxidase (TPO) enzymes. These findings are reflected in technetium-99m (Tc-99m) pertechnetate scintigraphy scans, where the thyroid gland is not well seen in chronic phase HT. Considering the poor iodine concentrating capacity of patients with HT, it is likely that thyroiditis will be a considerable factor in ablation failure after low-dose I-131 ablation [8, 9]. However, HT has not been cited for ablation failure in high-dose I-131 therapy. We conducted this study to evaluate the clinical usefulness of I-131 whole body scans (WBS) in patients with high-dose I-131 therapy and focused on clinicopathologic factors that correlated with I-131 washout in the thyroid, and its correlation with ablation success.

Materials And Methods

Patient selection and follow-up

The institutional review board of our university approved this retrospective study, and the requirement to obtain informed consent was waived (IRB approved no. 4-2021-0257). From September 2009 to June 2012, 245 patients were admitted to Severance Hospital for high-dose (≥150 mCi) I-131 ablation or treatment. Of those, 27 patients were excluded from this study as these patients received prior I-131 therapy, 46 patients were excluded for 200 mCi I-131 treatment for known metastasis, 29 patients were excluded due to metastatic sites found in post-RAI (radioactive iodine) WBS, and 45 patients were excluded due to loss of follow-up. Finally, a total of 98 patients were included who had no known metastasis, received initial I-131 therapy, and in whom follow-up TSH, Tg, and TgAb levels were detected for at least 2 years at approximately 6-month intervals as a routine clinical follow-up protocol. The TNM stage and serum TSH, Tg, and TgAb levels were all acquired on the ablation day, and lymphocytic thyroiditis statuses as determined by pathologic slides were recorded. Successful thyroid remnant ablation (gold standard) was defined as the absence of visualization of any structural lesions on neck ultrasound, undetectable serum Tg levels during levothyroxine administration (on-Tg) (<0.1 ng/mL), and TgAb level recordings <10 IU/mL between 6 months and 2 years after treatment.

Radioactive-iodine remnant ablation protocol

Before RAI remnant ablation therapy, all patients were instructed to discontinue levothyroxine for 5 weeks with triiodothyronine replacement for the initial 2 weeks. Patients underwent strict iodine restriction diets for two weeks before I-131 administration, which ended 3 days after RAI administration. TSH levels were confirmed to be at least 30 mU/mL before admission. All patients underwent two post-RAI WBS after hospital discharge. The first WBS was performed on the day of discharge (the third day after I-131 administration; Early scan) and on the seventh day after I-131 administration (Delayed scan).
Post-RAI whole body scan analysis

Early and Delayed post-RAI WBSs were acquired using a gamma camera equipped with a high-energy parallel hole collimator (Infinia, GE Medical Systems, Milwaukee, WI, USA). Early and Delayed scans obtained from a total of 98 enrolled patients were analysed. The count of these two scans were measured using a Xeleris workstation (GE Medical Systems) using the following method: A circular region of interest (ROI) was drawn on the neck on the Early scan to encompass the remaining thyroid, while the same size ROI was copy and pasted onto the neck of the Delayed scan. The same sized ROI was used for all patients, and the total counts in each ROI was recorded. Moreover, because whole body counts at early scans were higher compared to Delayed scans, post-RAI Early WBS scans were acquired faster than Delayed scans. To compare thyroid uptake in the Early scan compared to the Delayed scan, both Early scan speed and Delayed scan speed were factored into the analysis. This was done by first recording the scan speed on the DICOM header (Tag (0008,0008), which records scan speed as mm/sec), and then dividing neck ROI counts by scan speed for both Early and Delayed scans. Finally, Early scan counts were decay corrected to Delayed scan counts. This was done with the following formula:

\[
\text{decay corrected activity (counts) = } A_0(\text{Early scan counts})e^{-\left(\frac{0.693}{8.04}\right)\times \text{time}}
\]

where:
- \(A_0\) is the activity of the Early scan,
- \(e\) is the base of the natural logarithm,
- \(0.693\) is the natural logarithm of 2,
- \(8.04\) is the half-life of Iodine-131.

Finally, the reduction ratio was calculated with the following formula: (Delayed WBS neck count - Early WBS neck count)/Early WBS neck count * 100.

Statistical Analysis

Continuous data were compared using the Mann-Whitney U test. Comparisons of categorical data were performed with the chi-square test. Correlation between post-RAI WBS neck uptake and laboratory findings were evaluated using Spearman's correlation coefficients. Univariable and multivariable logistic regression analyses were performed to evaluate the predicted ablation success. P values less than 0.05 on univariable analysis were included in the multivariable analysis. With respect to post-RAI WBS parameters, receiver-operating characteristic (ROC) curves using the Youden index were used to determine the cut-off values for predicting ablation success. All statistical analyses were conducted using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and R version 4.0.3 (http://www.R-project.org). P values less than 0.05 were considered statistically significant.

Results

Patients' characteristics

The characteristics of the enrolled 98 patients are shown in Table 1. The median patient age at the time of RAI remnant ablation was 47.5 years (range 14-79), and 68 patients (69.39%) were female. Thirty-five patients (35.7%) had lymphocytic thyroiditis on pathologic report, and 28 patients (28.6%) had ablation
success. The thyroiditis group had significantly lower serum off-Tg levels (3.1 ng/mL vs. 0.2 ng/mL) and higher TgAb levels (5.49 IU/mL vs. 29.82 IU/mL). In post-RAI WBS analysis, the thyroiditis group had lower neck counts in both Early (10,085 vs. 3,350 counts/mm/sec) and Delayed (450 vs. 95 counts/mm/sec) scans, and a higher reduction rate (-96.76% vs. -97.67%) than that of the thyroiditis absent group (Fig 1.). In addition, ablation success rates were significantly lower in the thyroiditis present group than the non-thyroiditis group (5.7% vs. 41.3%).

**Correlation between post-RAI WBS neck uptake and laboratory findings.**

There was a weak correlation between off-Tg levels acquired at the I-131 ablation and thyroid bed uptake on the Early scan (Spearman's rho = 0.542, p <0.001) and Delayed scan (r = 0.492, p <0.001). There was also a weak inverse correlation between TgAb levels acquired at I-131 ablation and thyroid bed uptake (Early: r = -0.341, p = 0.001; Delayed: r = -0.323, p = 0.001).

When patient groups were subcategorized into either a TgAb elevated group (TgAb >10.0 IU/mL) or a TgAb non-elevated group (TgAb ≤10 IU/ml), there was a slight increase in the correlation between off-Tg levels with the Early scans (Spearman's rho = 0.536, p <0.001) and those with the Delayed scans (Spearman's rho = 0.669, p <0.001). In the non-elevated TgAb group, however, there was no correlation between off-Tg levels with the Early scan thyroid bed uptake (Spearman's rho = 0.198, p = 0.221) nor with the Delayed scan thyroid bed uptake (Spearman's rho = 0.033, p = 0.841).

**Prediction of ablation success**

Patients in the ablation success group had higher counts on Early and Delayed scans compared to the ablation failure group (Table 2, Figure 2). Also, the reduction ratio tended to be higher in the ablation success group than in the failure group. Only two thyroiditis patients had ablation success (5.7%), while 26 patients out of 63 non-thyroiditis patients (41.3%) had ablation success.

ROC curve analysis was performed to evaluate the optimal cut-off values for Early neck count (6,810 counts/mm/sec), Delayed neck count (295.2 counts/mm/sec), and reduction ratio (-96.35%). Using these values, univariable logistic regression analysis showed that sex, coexisting thyroiditis, serum TgAb, Early WBS neck count, Delayed WBS neck count, and reduction ratios were significant factors (p <0.05, Table 3) for ablation success. In multivariable analyses, the Delayed WBS neck count was the only significant factor for predicting ablation failure (odds ratio = 54.37, 95% confidence interval = 1.33-14.32; p = 0.015, Table 4). The reduction rate was marginally significant (p = 0.081).

**Discussion**

This study evaluated clinical factors that contribute to ablation failure, using a relatively homogenous population of thyroid cancer patients. We selected 150 mCi treated patients as these patients underwent I-131 WBS on the same day (third and seventh days post-administration), because different days may have demonstrated different I-131 thyroid retention amounts. To our knowledge, we are the first to
correlate I-131 neck uptake with ablation success and thyroiditis pathology in the non-tumorous thyroid gland. Our findings suggest that semiquantitative analysis using I-131 WBS may provide further insight in I-131 retention patterns in remnant thyroid glands and possibly in metastatic lesions.

Our findings corroborate previous reports that HT is an important factor in low-dose I-131 ablation [8]. We have shown that thyroiditis patients have lower neck counts in Early scans, and higher reduction rates in Delayed scans, which may partially reflect the reduced iodine concentration ability of HT [12] as well as defected or absent TPO enzymes. Also, considering that the degree of reduction of I-131 marginally correlated with ablation success, our findings may suggest that delayed radioactive iodine kinetics after I-131 administration may be an important factor in ablation success. This may imply that HT patients might benefit from a longer low-iodine diet after I-131 administration, as the remnant thyroid gland might not trap I-131 efficiently, which might result in I-131 being “pushed out” after a large influx of iodine. Further studies are needed to confirm this speculation.

Our results can also explain the results of a recent meta-analysis, which showed that successful ablation is not dose dependent [13]. We have shown that there is very low uptake, and more importantly more washout, in patients with thyroiditis, which suggests that the iodine concentrating capacity of the remnant thyroid gland is more important than the administrated dose. Although complete ablation may not be critical, as HT is a favourable factor for thyroid cancer prognosis [7], persistent elevation of TgAb may result in difficulties in patient management.

The potential application of this method might be a rather simple estimate to the amount of I-131 exposure to metastatic lesions. We have only applied this study in intact, functioning thyroid glands to reduced confounding factors such as de-differentiation and lowered affinity to I-131 in metastatic lesions, as well as attenuation issues in deep tissues. However, using a similar method, Early and Delayed scan analysis using single-photon emission computed tomography/computed tomography (SPECT/CT) may help clinicians to determine the amount of I-131 retained or washed out in metastatic lesions. This may be especially useful in repeat I-131 treatments, as lesion-by-lesion analysis may be performed using SPECT/CT. All of this is highly speculative, and further studies evaluating the clinical applications of Early and Delayed WBS with SPECT/CT are needed.

This study had several limitations. First, this was a retrospective, single-centre study, with a small subset of patients in a relatively short-interval time period. Future studies in patients who did not undergo I-131 ablation should be included to determine the influence of I-131 on ablation success in thyroiditis patients. Second, we provided a rather strict definition of ablation success, as we defined undetectable TgAb levels for ablation success. This was to ensure that serum Tg levels were not influenced by serum TgAb levels and to correlate more precisely the neck counts with Tg levels. This may contribute to the lower ablation success rates compared to those in previous studies, but may more accurately evaluate TgAb level disappearance after I-131 administration. However, considering that higher I-131 uptake is seen in Early scans, we suggest that higher doses might be helpful in ablating the thyroid gland, as the higher initial amounts of I-131 in the Early scan reflect the high amount of exposure of the remnant thyroid gland.
Conclusion

I-131 uptake in the remnant thyroid gland and thyroiditis is a factor for TgAb normalization and ablation success in thyroid cancer patients receiving high-dose I-131 therapy. I-131 WBS analysis may provide information in evaluating ablation success and possibly metastasis.

Abbreviations

Tg: thyroglobulin
HT: Hashimoto’s thyroiditis
TgAb: thyroglobulin antibody
TSH: thyroid stimulating hormone
TPO: thyroid peroxidase
Tc-99m: technetium-99m
WBS: whole body scans
RAI: radioactive iodine
ROI: region of interest
ROC: receiver-operating characteristic
SPECT/CT: single-photon emission computed tomography/computed tomography

Declarations

Ethics approval and consent to participate: The protocol was reviewed and approved by the local Institutional Review Board (IRB approval no. 4-2021-0257). The institutional IRB decided to waive the informed consent of this study because it was an observational study using retrospectively collected, anonymized data. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for publication: Not applicable.

Competing interests: The authors of this work have no conflicts of interest to disclose.

Authors’ contributions: AC conceptualized the study. SHH, KJ, CGK, JW, HC, WJK, and AC collected the data. SHH, KJ, and AC performed the analysis. SHH, KJ, and AC wrote the first draft of the manuscript.
SHH and AC reviewed and edited the manuscript. All authors read and approved the final manuscript.

**Acknowledgements:** This study was supported by a faculty research grant of Yonsei University College of Medicine (6-2016-0157).

**References**

1. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016;26(1):1-133.

2. Carhill AA, Litofsky DR, Ross DS, Jonklaas J, Cooper DS, Brierley JD, et al. Long-Term Outcomes Following Therapy in Differentiated Thyroid Carcinoma: NTCTCS Registry Analysis 1987-2012. J Clin Endocrinol Metab. 2015;100(9):3270-9.

3. Durante C, Haddy N, Baudin E, Leboulleux S, Hartl D, Travagl JP, et al. Long-term outcome of 444 patients with distant metastases from papillary and follicular thyroid carcinoma: benefits and limits of radioiodine therapy. J Clin Endocrinol Metab. 2006;91(8):2892-9.

4. Paris J, Mc CW, Tauxe WN, Woolner LB, Bahn RC. The effect of iodides on Hashimoto's thyroiditis. J Clin Endocrinol Metab. 1961;21:1037-43.

5. Fiore E, Rago T, Latrofa F, Provenzale MA, Piaggi P, Delitala A, et al. Hashimoto's thyroiditis is associated with papillary thyroid carcinoma: role of TSH and of treatment with L-thyroxine. Endocr Relat Cancer. 2011;18(4):429-37.

6. Paparodis R, Imam S, Todorova-Koteva K, Staii A, Jaume JC. Hashimoto's thyroiditis pathology and risk for thyroid cancer. Thyroid. 2014;24(7):1107-14.

7. Lee JH, Kim Y, Choi JW, Kim YS. The association between papillary thyroid carcinoma and histologically proven Hashimoto's thyroiditis: a meta-analysis. Eur J Endocrinol. 2013;168(3):343-9.

8. Kwon H, Choi JY, Moon JH, Park HJ, Lee WW, Lee KE. Effect of Hashimoto thyroiditis on low-dose radioactive-iodine remnant ablation. Head Neck. 2015; doi:10.1002/hed.24080.

9. Wagieh SM, El-Refaei SM, Salem SS, Al-Shiekh EA, Al-Ghamdy HA, Al-Juhani NR. Impact of histopathology of non-neoplastic thyroid tissue on ablation outcome in patients with papillary thyroid cancer. Nucl Med Commun. 2011;32(7):597-604.

10. Latrofa F, Ricci D, Montanelli L, Rocchi R, Piaggi P, Sisti E, et al. Lymphocytic thyroiditis on histology correlates with serum thyroglobulin autoantibodies in patients with papillary thyroid carcinoma: impact on detection of serum thyroglobulin. J Clin Endocrinol Metab. 2012;97(7):2380-7.

11. Spencer CA. Clinical review: Clinical utility of thyroglobulin antibody (TgAb) measurements for patients with differentiated thyroid cancers (DTC). J Clin Endocrinol Metab. 2011;96(12):3615-27.

12. Bastenie PA, Ermans A-M. Thyroiditis and thyroid function: clinical, morphological, and physiopathological studies: Elsevier; 2013.
13. James DL, Ryan É J, Davey MG, Quinn AJ, Heath DP, Garry SJ, et al. Radioiodine Remnant Ablation for Differentiated Thyroid Cancer: A Systematic Review and Meta-analysis. JAMA Otolaryngol Head Neck Surg. 2021; doi:10.1001/jamaoto.2021.0288.

**Tables**

**Table 1. Patient demographics**

| Characteristics                       | All patients | Thyroiditis absent | Thyroiditis present | P value* |
|---------------------------------------|--------------|--------------------|---------------------|----------|
| Number of patients                    | 98           | 63                 | 35                  |          |
| Age                                   | 47.5 (14~79) | 48 (15~79)         | 42 (14~72)          | 0.217    |
| Male:Female                           | 30:68        | 29:34              | 1:34                | <0.001   |
| Pathologic TNM stage:                 |              |                    |                     |          |
| Primary tumour size                   | 1.2 (0.1~5.0)| 1.3 (0.1~5.0)      | 1.1 (0.1~4.5)       | 0.570    |
| T3N0-1a:T1a-3bN1b                     | 13:85        | 9:54               | 4:31                | 0.689    |
| Assay at ablation:                   |              |                    |                     |          |
| TSH (mIU/mL)                          | 81.3 (22.2~247.1)| 81.3 (22.2~150.5)| 81.3 (22.2~247.1)  | 0.237    |
| Tg (ng/mL)                            | 1.4 (0.1~93.4)| 3.1 (0.1~60.8)     | 0.2 (0.1~93.4)      | <0.001   |
| TgAb (IU/mL)                          | 11.21 (5.49~2,001)| 5.49 (5.49~93.7)| 29.82 (5.49~2,001) | <0.001   |
| I-131 WBS analysis                    |              |                    |                     |          |
| Early WBS neck count†                 | 6,765 (261~94,375)| 10,085 (682~94,375)| 3,350 (261~12,439) | <0.001   |
| Delayed WBS neck count†               | 239 (6~7,124)| 450 (7~7,124)      | 95 (6~454)          | <0.001   |
| Reduction ratio (%)                   | -97.06       | -96.76             | -97.67              | 0.027    |
|                                       | (-99.21~-71.92)| (-98.97~-71.92)| (-99.21~-87.86)    |          |
| Months between surgery and ablation   | 3.74 (1.8~10.82)| 3.64 (1.8~10.82)| 3.87 (2.52~9.18)  | 0.226    |
| Ablation failure ≤ 2yrs (success:failure)| 28:70        | 26:37              | 2:33                | <0.001   |

Continuous values are presented as median (range).
*chi-squared for bivariate values, Mann-Whitney U test for continuous values.

†Scan speed adjusted neck count = neck counts/scan speed (mm/sec)

TSH, thyroglobulin stimulating hormone; Tg, thyroglobulin; TgAb, thyroglobulin antibody; WBS, whole body scan.

**Table 2.** Clinical and I-131 WBS characteristics in predicting ablation success

|                          | Ablation success (n=28) | Ablation failure (n=70) | P value |
|--------------------------|-------------------------|-------------------------|---------|
| Age                      | 46 (18-70)              | 47.5 (14-79)            | 0.878   |
| Sex                      |                         |                         | 0.008   |
| Male:Female              | 14:14                   | 16:54                   |         |
| Pathology:               |                         |                         |         |
| Primary tumour size (cm) | 1.35 (0.3-5.0)          | 1.2 (0.1-4.5)           | 0.486   |
| T3N0-1a:T1a-3bN1b        | 5:23                    | 8:62                    | 0.397   |
| Thyroiditis absent : present | 26 : 2                | 37 : 33                 | <0.001  |
| Assay at ablation:       |                         |                         |         |
| TSH (mIU/mL)             | 81.3 (45.8-117.9)       | 81.3 (22.2-247.1)       | 0.188   |
| Tg (ng/mL)               | 1.5 (0.1-17.7)          | 1.3 (0.1-93.4)          | 0.868   |
| TgAb (IU/mL)             | 5.49 (5.49-29.82)       | 15.085 (5.49-2001)      | 0.004   |
| I-131 WBS analysis       |                         |                         |         |
| Early WBS neck count†    | 9,953 (682-31,247)      | 5,361(261-94,375)       | 0.012   |
| Delayed WBS neck count†  | 502 (9-5,953)           | 179 (6-7,124)           | 0.001   |
| Reduction ratio (%)      | -96.22 (-98.62- -71.92) | -97.17 (-99.21- -84.09) | 0.055   |
| Months between surgery and ablation | 3.8 (1.8-10.8) | 3.8 (1.8-9.2) | 0.643   |

Continuous values are presented as median (range).

†Scan speed adjusted neck count = neck counts/scan speed (mm/sec)
TSH, thyroglobulin stimulating hormone; Tg, thyroglobulin; TgAb, thyroglobulin antibody; WBS, whole body scan.

**Table 3. Univariable analysis in predicting ablation failure**

| Variable                        | Univariable analysis |   |   |
|---------------------------------|----------------------|---|---|
|                                 | OR                   | 95% CI     | P value |
| Age                             | 1.00                 | 0.98-1.04  | 0.781   |
| Sex (vs. male)                  | 3.38                 | 1.34-8.53  | 0.010   |
| Thyroiditis present (vs. absent)| 11.60                | 2.55-52.64 | 0.001   |
| **Assay at ablation:**          |                      |             |         |
| Tg (vs. <10 ng/mL)              | 1.64                 | 0.49-5.45  | 0.422   |
| TgAb (vs. <25 IU/mL)            | 8.16                 | 1.79-37.20 | 0.007   |
| **I-131 WBS analysis:**         |                      |             |         |
| Early WBS neck count† (vs. >6,810) | 4.78               | 1.79-12.75 | 0.002   |
| Delayed WBS neck count† (vs. >295.2) | 7.50            | 2.76-20.39 | <0.001  |
| Reduction ratio (vs. >-96.35) (%)| 2.56                 | 1.04-6.26  | 0.040   |
| Months between surgery and ablation | 0.94             | 0.70-1.25  | 0.655   |

†Scan speed adjusted neck count = neck counts/scan speed (mm/sec)

OR, Odds Ratio; CI, confidence interval; Tg, thyroglobulin; TgAb, thyroglobulin antibody; WBS, whole body scan.

**Table 4. Multivariable analyses in predicting ablation failure**
| Variable | Multivariable analyses |
|----------|------------------------|
|          | Model                  | Model | Model |
|          | with Early WBS neck    | with Delayed WBS neck | with reduction ratio |
|          | count                  | count | ratio  |
|          | OR    | 95% CI | P value | OR    | 95% CI | P value | OR    | 95% CI | P value |
| Sex (vs. male) | 1.40 | 0.50-3.94 | 0.529 | 0.98 | 0.32-3.03 | 0.968 | 1.31 | 0.46-3.76 | 0.610 |
| Thyroiditis present (vs. absent) | 4.31 | 0.74-25.08 | 0.104 | 3.04 | 0.49-18.97 | 0.233 | 5.04 | 0.91-27.86 | 0.064 |
| Assay at ablation: | | | | | | | | | |
| TgAb (vs. <25 IU/mL) | 2.72 | 0.49-15.13 | 0.254 | 3.38 | 0.57-20.12 | 0.181 | 3.87 | 0.68-22.20 | 0.129 |
| I-131 WBS analysis | | | | | | | | | |
| Early WBS neck count† (vs. >6,810) | 2.10 | 0.69-6.40 | 0.193 | | | | | |
| Delayed WBS neck count† (vs. >295.2) | 4.37 | | | | | | | | 0.015 |
| Reduction ratio (vs. >-96.35) (%) | | | | | | | | | 2.48 | 0.89-6.87 | 0.081 |

†Scan speed adjusted neck count = neck counts/scan speed (mm/sec)

OR, Odds Ratio; CI, confidence interval; TgAb, thyroglobulin antibody; WBS; whole body scan.

Figures
Figure 1

Early and Delayed whole body scan neck counts in patient with and without thyroiditis (a). Lower I-131 uptake in thyroiditis patients compared to non-thyroiditis patients in both Early and (b) Delayed scans.
Figure 2

Representative cases thyroid remnant retention in I-131 whole body scan (WBS) and spot views in patients with and without thyroiditis. All spot views were acquired until 300,000 counts were detected. (a-b) A 61-y-o man with papillary thyroid carcinoma had bilateral total thyroidectomy with central compartment neck dissection and right modified radical neck dissection. This patient had no evidence of thyroiditis. Early WBS (a) neck count was 11,766 and Delayed WBS (b) neck count was 1,063. Reduction ratio was -90.96%. After radioactive iodine (RAI) ablation, serum Tg and TgAb level were <0.1 ng/mL and <10 IU/mL. (c-d) A 27-y-old woman with papillary thyroid carcinoma had a bilateral total thyroidectomy with central compartment neck dissection and left modified radical neck dissection. This patient had pathologic proven thyroiditis. The Early WBS (c) neck count was 2,151 (counts/mm/sec) and the Delayed WBS (d) neck count was 17 (counts/mm/sec). The reduction ratio was -99.2%. After RAI ablation, follow-up serum Tg and TgAb level were 0.4 ng/mL and 80.7 IU/mL. Notice the low I-131 uptake in the whole body compared non-thyroiditis patients.