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Inappropriate probe positioning during radioactive iodine uptake measurements cause inaccurate 131I quantification in patients with Graves' disease

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► ***Original article***

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#J.Z., T.Z. and Y.Y. are co-first authors with equal contributions.

ABSTRACT

Background: To evaluate the effects of probe positioning on radioactive iodine uptake (RAIU) measurements and 131I quantification in Graves disease (GD) patients. ***Materials and Methods:*** We performed a cross-sectional study in GD patients between May 9 and June 27, 2013. 24 hr-RAIU was measured. Measurement A was the reference measurement and was obtained with the probe parallel to the bottom of the thyroid cartilage. Measurements B, C, D, and E were obtained by moving the probe 2.5 cm to the left, 5 cm to the left, 2.5 cm vertically upward, and 5 cm vertically upward, respectively. The ^{131}I doses were calculated. Non-reference measurements were compared with measurement A using the paired t-test or Wilcoxon signed-rank test. ***Results:*** A total of 63 GD patients (17 men, 40.3±13.6 years old) were enrolled. Among them, 57 patients had 24 hr-RAIU measurement and 37 patients chose the ^{131}I treatment. Significant changes were observed in 24 hr-RAIU and ^{131}I dose between measurement A (24 hr-RAIU 60.40±12.67% and median ^{131}I dose 8.17 mCi) and measurement E (24 hr-RAIU 48.67±11.74% and median ^{131}I dose 9.50 mCi) ($P<0.05$). In one patient, the 24 hr-RAIU was 20.3% lower in measurement E compared with that in measurement A, resulting in a 30 mCi increase in the calculated 131I dose. ***Conclusions:*** The vertically upward movement by a distance of a radius of the collimator could affect the 24 hr-RAIU measurement and thus cause inaccurate calculation of the ^{131}I dose.

INTRODUCTION

Radioactive iodine (RAI, in the form of ^{131}I) has been used to treat Graves' disease (GD) since the 1940s. Precise ^{131}I dose calculation is essential to optimize the outcome of GD treatment, reduce the incidence of iatrogenic hypothyroidism, and minimize unnecessary ^{131}I residues. In general, three different methods are used to determine the dose of 131I: frequent low-dose, fixed-dose, and calculated-dose approaches [1, 2]. The last method requires accurate thyroid weight assessments and 24-hour radioactive iodine uptake (24 hr-RAIU) tests. Therefore, measurement of the 24 hr-RAIU is vital during the treatment of GD patients. Inaccurate 24 hr-RAIU values can result in inappropriate therapeutic ^{131}I doses for GD patients [3]. However, the measurement of 24 hr-RAIU is affected by many factors, including instrument parameters, the operation process, thyroid size, standard source and background environments, iodine-containing drugs or foods, anti-thyroid drugs, and other factors. In addition, it is well known that some GD patients with severe hypermetabolic symptoms can be extremely weak and have difficulty in maintaining a position for a prolonged time period during the RAIU test. A previous study reported that the measurement of RAIU could be affected by the position of the probe on the patient's neck [4]. However, the authors in that study only investigated two inappropriate probe positions (5 cm backward and 5 cm higher). It is necessary to further investigate how much the probe position deviation in the neck could result in the inaccurate measurements during the RAIU test. Therefore, in this cross-sectional study, we examined the effects of probe position deviations in more directions (different extents of the left deviations and upward deviations) on the RAIU and the dose calculation of ^{131}I, which was never reported previously.

MATERIALS AND METHODS

Study design and participants

We performed a cross-sectional study at the Fifth Center of PLA General Hospital in Beijing, China, between May 9, and June 27, 2013. The study protocol was approved by the Institutional Ethics Committee of The Fifth Medical Center, Chinese PLA General Hospital (approval number ky-2013-2-3). All participants were informed of the study process,

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benefits, and risks and signed informed consent forms.

The inclusion criteria were [5]: (1) Clinical symptoms of high metabolism and diffuse goiter on palpation and/or thyroid scan; (2) Elevated serum free triiodothyronine (>6.30 pmol/L), elevated serum free thyroxine (>22.70 pmol/L), suppressed serum thyrotropin (TSH) (<0.55 μIU/mL), and elevated TSH receptor antibody (>1.75 IU/L); (3) For two weeks prior to the test, patients agreed to stop iodine-rich foods, iodine-containing and anti-thyroid drugs. The exclusion criteria were: (1) Patients with other causes of hyperthyroidism, such as toxic multinodular goiter and single toxic adenoma; (2) Women who were pregnant or lactating; (3) Patients with a history of partial thyroidectomy; (4) Neck deformity or severe scarring and ectopic thyroid, visualized with ultrasonography.

Study procedure

Immediately before the measurement, the patient was asked to swallow water to clean the mouth and esophagus. The patient was placed in a seated position, with the neck comfortably extended. Gentle restraints were applied to immobilize the head, if necessary [6]. RAIU measurements were obtained using a thyroid probe uptake system (Beijing Hehai Hi-Tech Co., Ltd. HH6008). The scintillation probe was made of a 3.5 cm-diameter NaI crystal with a lead alloy shielding and a collimator with a 9.8 cm-diameter scan field. Before the oral administration of a capsule with 9 μCi of 131I-NaI (HTA Co., Ltd, Beijing, China), the capsule was placed in a neck phantom and was counted for 1 min at a distance of 25 cm using the thyroid probe uptake system. After the oral administration of the capsule, the counts were taken over the patient's neck and thigh for 1 min each at a distance of 25 cm, while avoiding the urinary bladder from the detector field. The background was also counted for 1 min [6]. Neck, thigh, and background counts were recorded at each counting session. Phantom counts were measured once before the oral administration of the capsule. The instrument automatically calculated the RAIU based on the measured time. During the neck counts, first, the scintillation probe was placed parallel to the bottom of the thyroid cartilage, with a distance of 25 cm from the skin according to the instruction manual (figure 1). A 1-minute measurement was obtained at the time points of 24 hr, and designated as the reference measurement (measurement A) [7]. Afterward, starting from the location for measurement A, the probe was moved left by 2.5 cm (measurement B), left by 5 cm (nearly a radius of the collimator, measurement C), vertically upward by 2.5 cm (measurement D), and vertically upward by 5 cm (nearly a radius of the collimator, measurement E). Five 24 hr-RAIUs and five calculated doses of ^{131}I were obtained for each patient using the above methods. Among the five measurements, the 24 hr-RAIU and ^{131}I dose values obtained from measurement A were considered the reference values, and other measurement data were statistically compared to them. The 24 hr-RAIU was calculated using the following equation 1:

$$\text{RAIU (\%)} = \frac{\text{Patient Neck Counts} - \text{Thigh Counts}}{\text{Phantom counts} - \text{Background Counts}} \times 100\% \text{ [6]}. \quad (1)$$

Every count was measured in triplicate consecutively under the same geometry and stable counting conditions in order to examine the reproducibility of the tests to ensure the accuracy of the results. RAIU measurement results were calculated automatically from the thyroid uptake devices when the average of these three counts were entered [8].

The dose calculation of ^{131}I was calculated using the following equation 2:

$$\text{Dose (mCi) to patient} = \frac{\text{Gland size (g)} \times \text{Dose requested (μCi/g)}}{\text{\% uptake of I at 24 hrs} \times 10} \quad (2)$$

The dose requested ranged between 75 and 200 μCi/g [9].

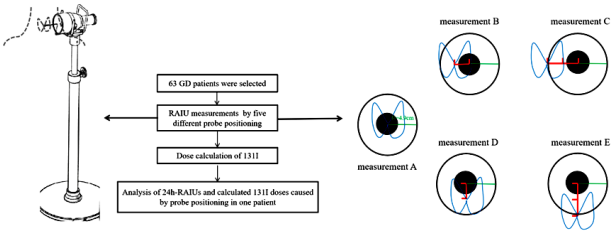


Figure 1. Study flow diagram and 24 hr-radioactive iodine uptake (RAIU) measurement. Left, the thyroid probe uptake system. The neck and thyroid gland are outlined by the dotted line. In the Middle, a schematic depicts the process flowchart of our measurements and calculations in this study. Right, the different placements of the probe. The blue butterfly refers to the shape of a thyroid gland. The black disc refers to the 3.5 cm-diameter NaI crystal. The larger circle surrounding the black disc refers to the collimator with a 9.8cm-diameter scan field. The measurement A is the reference measurement. The green straight line refers to a radius of the collimator, R=4.9 cm. The red line refers to the direction and distance of the probe movements. One red tick mark refers to the movement by 2.5 cm. Two red tick marks refer to the change in probe position by 5 cm.

Statistical analysis

SPSS 22.0 software (IBM, New York, USA) was used to analyze the data. The paired *t* test or the Wilcoxon signed-rank test were used to compare RAIU and ^{131}I dose values among different measurements. The difference was considered to be significant at a $P < 0.05$.

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RESULTS

Characteristics of study participants

As shown in Fig. 1, 63 GD patients (17 men, 46 women, mean age 40.3±13.6 years) were enrolled in the present study. Among 63 GD patients, 57 had the 24 hr-RAIU test and 37 chose the ^{131}I treatment.

Influence of probe position deviations on the 24 hr-RAIU results

As shown in table 1, the 24 hr-RAIU of measurement A was 60.40 ± 12.67%. The measurements B, C, and D were 60.04 ± 12.74%, 59.70 ± 12.86%, and 59.91 ± 14.30%, respectively. We also calculated the error for each patient and then calculated the average of absolute value of all the errors of 24 hr-RAIU caused by displacements. The mean of absolute values of difference of 24 hr-RAIU by measurements B, C, D and E were 3.37%, 4.89%, 7.49%, 12.87%, respectively. The 24 hr-RAIU of measurements B (t=0.63, r=0.94, P=0.53), C (t=0.91, r=0.89, P=0.37), and D (t=0.90, r=0.83, P=0.37) had no significant difference from measurement A. The 24 hr-RAIU of measurement E was 48.67 ± 11.74%, which was significantly different from the measurement A (t=12.29, r=0.81, P<0.01).

Table 1. Comparison of 24 hr- radioactive iodine uptake (RAIU) between reference measurement and non-reference measurements (paired t-test).

Measurements	Mean±SD %	Mean of absolute values of difference %	*t*	*r*	*P*
A (N=57)	60.40±12.67				
B (N=57)	60.04±12.74	3.37	0.63	0.94	0.53
C (N=57)	59.70±12.86	4.89	0.91	0.89	0.37
D (N=56)	59.91±14.30	7.49	0.90	0.83	0.37
E (N=56)	48.67±11.74	12.87	12.29	0.81	0.00*

N, number of patients. *, compared with the measurement A, P < 0.05. Measurement A was the reference value and was obtained with the probe parallel to the bottom of the thyroid cartilage. Measurements B, C, D, and E were obtained by moving the probe 2.5 cm to the left, 5 cm to the left, 2.5 cm vertically upward, and 5 cm vertically upward, respectively.

Calculated 131I doses

As shown in table 2, the ^{131}I dose calculated by measurement B (median 7.78 mCi, median difference=0.01 mCi, P=0.75), C (median 7.88 mCi, median difference=0.15 mCi, P=0.98), and D (median 8.18 mCi, median difference=0.09 mCi, P=0.34) had no significant differences compared with that calculated by the measurement A (median 8.17 mCi). The 131I dose calculated by the measurement E (median 9.50 mCi, median difference=2.23 mCi, P<0.01) was significantly higher than the ^{131}I dose calculated by the measurement A (table 2).

Since the 131I dose calculations might have a more significant deviation in a larger thyroid gland, we selected patient No. 6, who had the biggest thyroid gland, to describe the deviation of the 24 hr-RAIU and calculation of 131I dosage for the measurement E. We found that the 24 hr-RAIU values were 20.3% lower (50.3% vs. 70.5%) in the measurement E compared with the values in the reference measurement A (figure 2), resulting in nearly a 30 mCi increase (104.37 mCi vs. 74.47 mCi) in the calculated ^{131}I dose (figure 3).

Table 2. Comparison of 131I dose between reference measurement and non-reference measurements (Wilcoxon signed-rank test).

Measurements	131I dose (mCi), median	Difference (mCi), median	*P*
A (N=37)	8.17		
B (N=37)	7.78	0.01	0.75
C (N=37)	7.88	0.15	0.98
D (N=36)	8.18	0.09	0.348
E (N=37)	9.50	2.23	0.00*

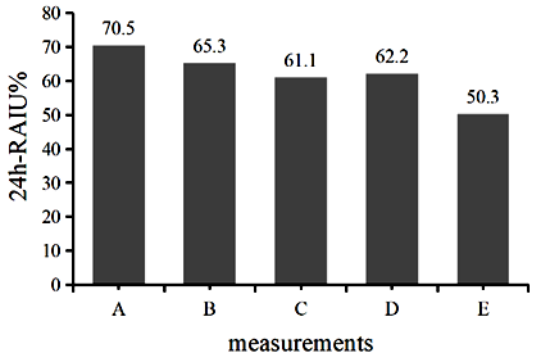


Figure 2. Deviation of 24 hr- radioactive iodine uptake (RAIU) values in five measurements for patient No. 6.

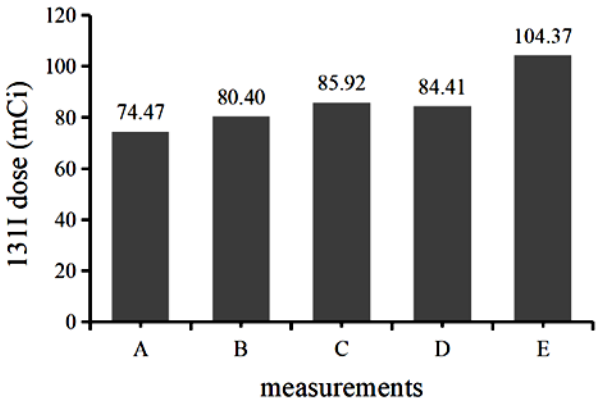


Figure 3. Deviation of calculated 131I dose in five different measurements of 24 hr- radioactive iodine uptake (RAIU) for patient No. 6.

DISCUSSION

During RAI therapy, the accurate 131I dose can improve the treatment outcomes with a low recurrence rate, reduce radiation toxicity and side effects, such as early-onset hypothyroidism (especially since most GD patients are women under the age of 40 years old), facilitate a better quality of life, and reduce environmental pollution of excessive 131I. Among the methods used to determine the 131I dose, the calculated-dose approach requires

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measuring the 24 hr-RAIU [3, 9-13]. Many factors can influence the accuracy and stability of the 24 hr-RAIU, such as various physiologic and pathologic processes, instrumental factors, measurements and operations, techniques, standard source and background measurements, iodides, foods, antithyroid drugs, iodine-containing drugs, statistical fluctuations, and other unpredictable factors. Variations in measurements and operation highlight the importance of standardized steps during the 24 hr-RAIU test and can substantially affect RAIU [3]. Especially, inappropriate probe positioning will lead to variations in RAIU, including variations in neck to detector distance and improper centering of the probe over the patient's neck [7]. Hyperthyroidism could cause increased thyroid gland function with weight loss, heat intolerance, diarrhea, fine tremor, and muscle weakness [14]. However, few studies have reported the influence of inappropriate probe positioning on the measurement of RAIU and subsequent dose calculations. This study investigated the effects of inappropriate probe positioning on the RAIU measurement and 131I dose calculation.

There are different methods to determine the ^{131}I dose. Some studies have shown that a calculated ^{131}I dose can affect the treatment of GD with a higher success rate, minimize the residue radiation dose, reduce radiation exposure to the public and family members, and is the preferred method for determining ^{131}I [2, 15-17]. Our results showed a significant difference in the 24 hr-RAIU between the measurement E (48.67 ± 11.74%) and the measurement A (60.40 ± 12.67%) with the mean of absolute values of difference 12.87%, suggesting that vertically upward movement of the probe by 5 cm (nearly a radius of the collimator, measurement E) could significantly lower the 24 hr-RAIU compared to the reference measurement A. Accordingly, the calculated dose by the measurement E (median 9.50 mCi, median difference=2.23 mCi, P<0.01) was significantly higher than the ^{131}I dose calculated by the measurement A (median 8.17 mCi).

According to the technical requirements for the detector of probe of RAIU, the scan field diameter at the working distance was designated as 2R (with R being the radius of the collimator) where the collimator diameter of the thyroid probe uptake system we used in this study was 9.8 cm). If the point source was moved on the working distance outside the scan field and the distance from the central axis was 1.2R (nearly 6 cm in this thyroid probe uptake system), the counting rate would not be greater than 50% at the central axis. When this distance was 1.4R (nearly 7 cm in this thyroid probe uptake system), the counting rate would not be greater than 5% at the central axis [18]. However, the thyroid gland is not a point source. In fact, thyroid gland is composed of left and right lobes and isthmus looking like a butterfly. Each thyroid lobe is 2.5 to 4.0 cm long, 1.5 to 2.0 cm wide, and 1.0 to 1.5 cm thick.

Moreover, GD patients commonly have a diffused enlarged goiter. Our results suggested that, taking the base of thyroid cartilage as the center, the lateral displacement of thyroid plane in the neck and the vertical upward displacement of 2.5 cm in the vertical axis of the neck did not affect the detection of iodine uptake rate and the calculation of iodine 131 dose, but the vertical upward displacement of 5 cm (nearly a radius of a collimator) affected the accurate measurement of 24 hr-RAIU and the calculation of iodine 131 dose. The vertical upward displacement of 5 cm in the vertical axis of the neck might look unreasonable in the clinical practice. However, it emphasizes the importance of the probe positioning and its exact centering parallel to the bottom of the thyroid cartilage. For most GD patients with weight loss, heat intolerance, diarrhea, fine tremor, and muscle weakness, it is more comfortable during the RAIU examination by using a neck fixation bracket. In our study, the commercial probe with a fulcrum positioning aid did not adequately hold the neck in the vertical axis. Some other commercial probes may have no positioning aid, or have a fulcrum positioning aid but not for use during the RAIU examination. Therefore, this is an area warranting further examination.

In the present study, patient No. 6, a GD patient with a large goiter, was selected to analyze the deviation of the 24 hr-RAIU and the calculated 131I dosage with different probe positions. The weight of her thyroid was estimated to be 350 g using Single-Photon Emission Computed Tomography (SPECT) planar imaging combined with the color Doppler ultrasonography. The dose of 131I per gram was 150 μCi. The RAIU was found to be 20.3% lower (50.3% vs. 70.5%) with measurement E compared with the reference measurement A, resulting in the 131I dose exceeding the reference dose by 30 mCi (104.37 mCi vs. 74.47 mCi) that was far over the therapeutic dose. This might lead to more radiation toxicity and side effects, longer hospitalization stays and medical cost, and cause excessive radiation pollution to the environment.

In the clinic, the deviations of the probe positioning could depend on the shape and size of the thyroid gland and the neck anatomy. Our study did not explore whether retrosternal thyroid, thyroid nodule, absence of thyroid gland lobes, and ectopic thyroid tissue could affect the position of the scintillation probe. Ideally, thyroid ultrasonography, which provides information on gland morphology, especially the location, size, and sonographic features of thyroid nodules, helps adjust the probe position. In addition, the salivary glands and gastric mucosa take up a small amount of iodine. Whether they can affect the RAIU with different probe placements requires further studies.

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CONCLUSION

The vertical upward displacement of 5 cm affected the accurate measurement of 24-RAIU and the calculation of iodine 131 dose. Therefore, it is very important to fix the probe position in the vertical axis of the neck with an appropriate neck fixation bracket.

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***Conflict of Interest*:** The Authors declare that there is no conflict of interest.

***Ethical consideration*:** The study protocol was approved by the Institutional Ethics Committee of The Fifth Medical Center, Chinese PLA General Hospital (approval number ky-2013-2-3). All participants were informed of the study process, benefits, and risks and signed informed consent forms.

***Author contribution statement*:** J.Z. analyzed the data, drafted, and revised the manuscript. T.Z. analyzed the data and revised the manuscript. J.Z., T.Z., and Y.Y. are co-first authors with equal contributions. J.W. analyzed the data. X.H., Q.G. operated RAIU test. Y.F. is the corresponding author. All authors read and approved the final manuscript.

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