J of Nuclear Medicine Technology, first published online November 9, 2018 as doi:10.2967/jnmt.118.207837

Comparison of Radioiodine uptake by Gamma Camera and Thyroid uptake probe-based methodologiesand Diagnostic Radioiodine Scanin Differentiated thyroid carcinoma

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Keywords: Differentiated thyroid carcinoma;camera based neck uptake; thyroid uptake probe; Radioiodine

Abstract:

Aims and Objectives: The objective of the study was to make a quantitative comparison of 72-hrs neck uptake calculated by gamma camera–based and thyroid uptake probe–based methods after administration of low-dose (111-148 MBq) of ^{131}I capsule in thyroid carcinoma follow-up patients who have already been treated with ^{131}I.

Methods: The study group consists of 46 patients, of whom 14 were male (average 47.5 yrs) and 32 were female (average 38 yrs). All patients already had undergone thyroidectomy followed by ^{131}I treatment at least once and came to the institute after 6 months for follow-up. As per the institutional protocol the patients had their ^{131}I neck uptake and whole-body scan at 72 hours, the uptake value evaluated by both uptake probe and camera-based method using medium-energy parallel-hole collimator.

Result: Amongst a total of 46 patients, (i) neck uptake was negative in 24 patients by both probe-based (0.1% as cut-off as per institutional protocol) and camera-based methodologies and the scan, (ii) while positive in 10 patients by both the methods which was supported by scan finding.(iii) In further 10 cases thyroid uptake by probe-based uptake method showed (with 0.1% as cut-off) positive while camera-based uptake and scan finding were negative. In most of these cases scatter radiation contribution due to high non-target counts were found to be high. (iv) In two patients, thyroid uptake by probe-based method showed<0.1% where camera-based neck uptake and scan finding were positive for neck uptake. Thus, in 34 out of 46 patients (74%), both methods were found concordant, while in 12 out of 46 patients (26%), the uptakes were discordant with 0.1 % as the cut-off for probe-based uptake. Based upon the exploratory analysis of the results obtained, we propose camera-based neck uptake of 0.03% to be the cut-off for positive neck uptake. In the subgroup of patients with negative scan and systemic metastases in the vicinity of neck (n=7), an uptake cutoff of 0.1% resulted in positive results in 85.7%. All patients had true negative results with camera-based cut-off of 0.03%. Based upon the analysis of these discordant results (between probe-based uptake method and scan), we further proposethe cut-off for positivity of the ^{131}I uptake value by thyroid uptake probe-based method to be considered as 0.2% rather than 0.1% in orderto reduce false positivity with appropriate correlation with scan findings.

Conclusion:Thus, in patients of thyroid carcinoma, camera-based uptake during ^{131}I LDS canalso be reliableas conventional thyroid uptake probe-based method and can be used as a substitutein evaluating neck uptake calculation in patients with functioning metastases in the vicinity of neck or non-specific high physiological accumulation.

Introduction

The use of ^{131}I in patientsof differentiated thyroid carcinoma (DTC) is well established in both diagnostic and therapy purpose. In post-thyroidectomy patients of DTC, it is a common practice to give low diagnostic dose of ^{131}I for qualitative and quantitative evaluation residual thyroid tissue status. Although ^{123}I is a better agent for diagnostic scan, ^{131}I continues to be used in several developing nations where ^{123}I is not available(*1*).Quantitative evaluation is usually done using thyroid uptake probe while gamma camera givesqualitative imaging information. Gamma camera-based method for ^{131}I neck uptake evaluation has been reported in benign and other non-cancerous clinical conditions(*2*).Based on diagnostic scan, neck uptake value, pathology reports and disease burden,patients are planned for radioiodine ablation or therapeutic doses of ^{131}I. Following first therapy, it is customary and routine practice in our institute to call the patients for follow-up after six months. In this study we compared the % neck uptake calculated by thyroid uptake probe and gamma camera-based method in this subset of patients and compared the uptake values with scan and clinical findings.These included diagnostic radioiodine scan, serum stimulated thyroglobulin (Tg) in all cases and clinical and ultrasound finding (where appropriate).

Materials and Methods

Study population

Forty-six patients undergoing ^{131}I scanning between 2014 and 2015 were included in this study analysis. The study had approval by the Institutional Review Board (IRB). Fourteen were males(average 47.5 yrs) and 32 were female(average 38 yrs). As aforementioned, the patients included in this study were post-thyroidectomy DTC patients, who had undergone one ^{131}I treatment in the past and came for follow-up scan. Post thyroidectomy patients who were referred for the standard precautions for radioiodine scanning were undertaken (regarding avoidance of iodine-containing substances and thyroid medications, exclusion of pregnant or lactating female patients). All of them were post thyroidectomy patients who has undergone ^{131}I treatment and came for follow up after 6 months for check-upor for further evaluation. 111 - 148 MBq^{131}I capsuleswere orally administered and 72 hrs'

neck uptake was evaluated by both thyroid uptake probe (Nuclear Chicago) and gamma camera-based methods.

Method for Probe-Based Uptake Calculation: -

A thyroid uptake probe (Nuclear Chicago) loaded with a flat-field collimator was used to estimate the neck count.A 0.925MBq standard ^{131}I capsule was kept in the neck Lucite phantom and was counted for 100 seconds. The neck shield was added over the phantom and background measurement was undertaken. The counts were taken at 30cm from the crystalwhere the probe gives iso-response. This count was further extrapolated for the low doseradioactivityadministered to the patientafter decay correction (*3*). The patient was also positioned 30 cm from the probe, and the count was taken for 100 seconds to obtain the count used to calculate 72-hrs uptake. The neck was shieldedwith neck shield, and the count taken for 100 seconds to obtain the background count. Percentage uptake was calculated using the following formula:

$$\%Uptake = \frac{(Neckcount - PatientBackgroundcount)}{(Standardphantomcountextrapolatedforthepatientadministeredradiactivity - Phantombackgroundcount)}$$

(*2*).

Method for Camera-Based Uptake Calculation

In the same group of patients, the camera-based method was then adopted to calculate the 72-hrs neck uptake (Table 1). To obtain astandard counts, the ^{131}I capsule in the neck Lucite phantom was scanned with speed of 4cm/ min and matrix size of 1024 X 512, and the counts were calculated by drawing a region of interest (ROI) around the capsule and was then extrapolated for the patient's administered radioactivity to get net standard counts equivalent to administered large doseradioactivity. The neck scan was obtained by positioning the patient supine with neck extended. A gamma camera with a medium-energy collimator (Symbia; Siemens) was used for scanning and gamma camera-based method. The scan was acquired with scan speed 4cm/min with the energy window centered on 364 keV with 15 % window and matrix size of 1024 X 512. A ROI was then drawn on the neck to get the neck counts, and the total pixel area were noted. A background region of interest was drawn near the thyroid to obtain the average background per pixel(Figure 1). Serum Tg value was available in 39 patients to

correlate with theclinical findings.As per institutional protocol stimulated Tg value <= 5ng/ml is considered to be insignificant.

Percentageneck uptake was calculated using the following formula:

$$\%Uptake = \frac{Background\ corrected\ neck\ count}{Standard\ count} \times 100 (3)$$

Results

Thyroid uptake probe based neck uptake values were compared with gamma camera based neck uptake keeping the neck scan finding as the reference standard. As per the institutional protocol,any uptake <0.1 % by the uptake probe based method wasconsidered negative. A cut-off of 0.03% by gamma camera-basedneck uptake showed goodcorrelation with the scan findings. Serum Tg value was available in 39 patients to correlate with clinical findings. On this basis, 24 patients' neck uptakeswere negative by both uptake probe based (considering 0.1% as cut-off) and camera-based methods while 10 patients were positive by both these methods which were supported by scan finding. Thus, in 34 out of 46 patients (74%), both methods were found concordant, while in 12 out of 46 patients, the uptakes were discordant (26%). In 10 cases uptakeprobe-based uptake showed positive, while camera-based uptake and scan finding were negative (Figures 2and3). In most of these cases, scatter radiation contribution from lungs, stomach and salivary glands were found to be high. The comparison of the individual values has been tabulated in supplementary material as Table S1 and Table S2. The uptakes obtained through camera-based method and uptake probe-based methods were presented graphically in Figure 4. The Pearson correlation coefficient was measured with 0.97 between the camera-based method and uptake probe-based method findings. Both the uptakes were highly concordant. The independent performances observed through these methods were presented by mosaic plots in Figure 5. The sensitivity, specificity and agreement analysis were performed to compare the pair wise diagnostics performance between Camera based method findings, uptake probe-based method findings and scan-based findings. The cut-off value of camera-based method was selected with 0.03% arbitrarily based on observatory evidence. Similarly, two cut-off detection points

for uptake probe-based method were selected with 0.1 and 0.2 respectively based upon routine practice evidence (in supplementary material Table S3). The agreement to detect true positive and true negative between the methods were tested with kappa statistics(Table 1). The kappa values 0.69 was obtained between camera based method findings and scan based findings.Similarly, kappa value obtained between camera based and uptake probe-based finding was .52(while probe cut-off point was 0.1%) and 0.64(while probe cut-off point was 0.2%). The corresponding sensitivity and specificity values were 95%, 74.28 % (while probe cut-off was 0.1%) and 54.54%and 100% (while probe cut-off was 0.2%). Also, interestingly, in the subgroup of patients with negative scan and systemic metastases (n=7) in the vicinity of neck (supplementary material -Table S2), an uptake cutoff of 0.1% resulted in positive results in 85.7%, which would be 0% if cut-off value of 0.2% is considered. All patients had true negative results with camera-based cut-off of 0.03%.

Discussion:

Radioiodine scan with ^{131}I is well established and has been in routine use in the thyroid uptake and scan evaluation (both for malignant and benign thyroid conditions) in several countries where ^{123}I is not available. Qualitative evaluation is done by gamma camera scan while quantitative evaluation is done by using thyroid uptake probe.Since the two procedures are done separately, an alternate gamma camera-basedmethod for quantitative and qualitative evaluation in single procedure has been reported for low dose scan mainly benign thyroid disorders patients (primarily thyrotoxicosis) (*2*).In the present study, the utility of gamma camera-based neck uptake method in post thyroidectomy cases was evaluated and compared with the thyroid uptake probe-based method, which is the methodological standard for measuring thyroid uptake. Furthermore, we sought to evaluate the cases of discordance and explore the clinical correlate and advantages for either of the methodologies.

As per the institutional protocol, the neck uptake is correlated with scan findings and Tg value in all patients. Any neck uptake value of >0.1% which is considered

to be positive uptake by thyroid uptake probe-based method is re-evaluated (by doing high count scan) to confirm persistence/recurrences. It has been observed in all the population of studiesthat camera-based uptake of <.03% was found to be neck scan negative (confirmed by high count scan and serum Tgvalue in case of patients with no metastasis by scan), whose corresponding values of probe-based method were high.In the present study, camera based % neck uptake cut off of .03%was found to be a useful diagnostic parameter when compared to the thyroid uptake probe-based neck uptake cut off of >0.1 %and comparable when thyroid uptake probe cut-off was kept 0.2%especially when the patients had metastatic disease in the vicinity of the neck. In cases of camera-based uptake <0.03%, opinion of expert nuclear medicine physicians was taken, and on the basis of final scan findings and clinical evaluation, all scans were found to be negative scan(all were negative when 0.2% was considered as cut-off by probe-based method), suggestingcamera-based uptake as an alternate method over uptake probe-basedmethod (supplementary material -Table S3).

Multiple factors could contribute to the higher neck uptake value obtained by the uptake probe based method compared to the gamma camera based method, these include: (a) use of a parallel-hole vs. a flat-field collimator, (b) inclusion of non-target counts like salivary glands in the calculation by the probe method, (c) difference in thickness between the probe and camera scintillation crystals (gamma camera used by us had 5/8” crystal, while probe had 1” thick crystal). The other less probable factors could be (d) measurement during scanning vs. making a measurement at a single location and (e) the use of a medium-energy collimator for a high-energy radionuclide in the gamma camera-based method.In all cases of discordance, non-target counts were high, which contributed to the counting uncertainty in thyroid uptake probe-based method which has flat field collimator compared to gamma camera with parallel hole collimator; in the latter,the neck ROI canrestrict non-target counts to minimum.

Conclusion

^{131}I iodine neck uptakecalculation with0.925MBq^{131}I administered in patients with benign thyroid disorders (thyrotoxicosis and non-thyrotoxic multinodular goiter)

have shown good correlation by these two methods [2]. It was observed that camera-based method is a good substitute for the probe-based method in this group of patients. In the present study, a different subset of patients (DTC in the follow-up),activity of 111 -148 MBq,and uptake period (72 hours) was evaluated and compared.The comparability of neck uptake value by keeping cut-off value of 0.2% by probe-based method and .03 % by camera-based method, makes the latter one as good substitute for probe-based method as in single procedure both qualitative and quantitative information are achievable.

We also propose the cut-off for 131I uptake estimated by thyroid uptake probe-based method to be considered as 0.2% on basis of comparison with camera-based method rather than 0.1% to reduce false positivity. The proposed cut-off value of 0.2% in probe method by this study was commensurate with that proposed by Bal et al in 1996 (4).

References:

1. Mettler FA, Guiberteau MJ. Emeritus Professor, Department of Radiology, University of New Mexico, Thyroid, Parathyroid, and Salivary Glands, in (Chapter 4) Essentials of Nuclear Medicine Imaging (Sixth Edition), Pg 99-131, Elsevier, 2012.

2. Menon BK, Rao RD, Abhyankar A, Rajan MG, Basu S. Comparative evaluation of 24 hour thyroid 131I uptake between γ camera-based method using medium-energy collimator and standard uptake probe-based method. J Nucl Med Technol. 2014 Sep; 42(3):194-197

3. Balon HR, Silberstein EB, Meier DA, Charkes ND, Sarkar SD, Royal HD, Donhoe KJ. Society Nuclear Medicine Procedure Guideline for Thyroid Uptake Measurement Version 3.0, approved September 5, 2006.http://snmmi.files.cms-plus.com/docs/Thyroid%20Uptake%20Measure%20v3%200.pdf. Accessed 28th April 2018.

4. Bal C, Padhy AK, Jana S, Pant GS, Basu AK, Department of Nuclear Medicine, All India Institute of Medical Sciences, New Delhi.. Prospective randomized clinical trial to evaluate the optimal dose of 131 I for remnant ablation in patients with differentiated thyroid carcinoma. Cancer. 1996 Jun 15;77(12):2574-80.

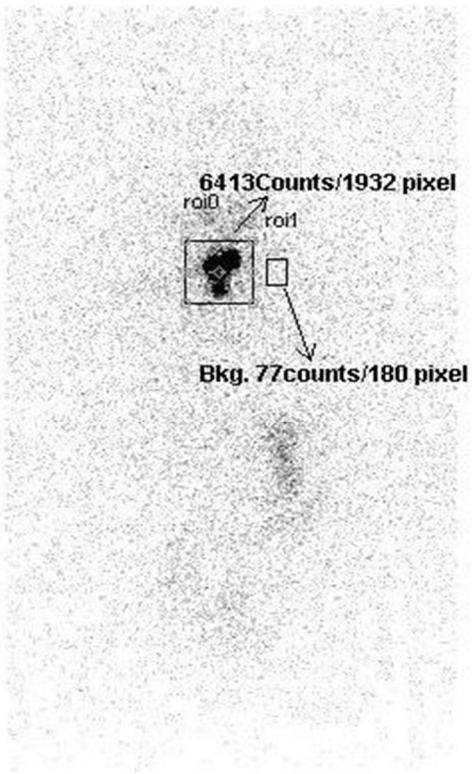

Fig 1. **Neck and background count estimation by gamma-camera based method**

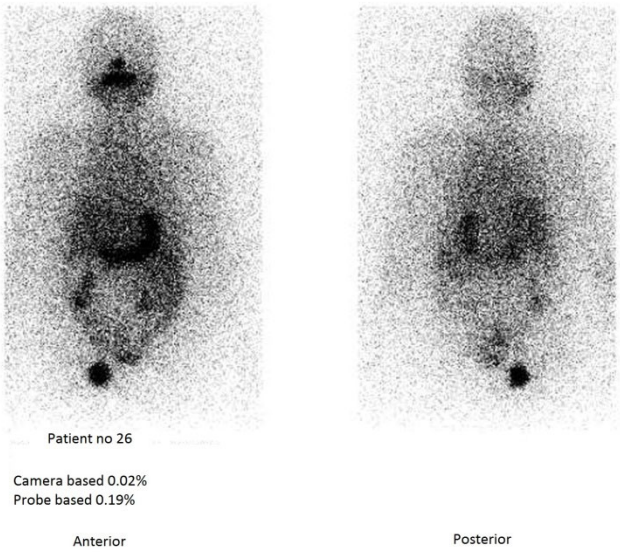

Fig 2. A 57-Year-old female patient of DTC with skeletal metastasis (following one previous therapy before) with increased stomach and salivary gland uptake.

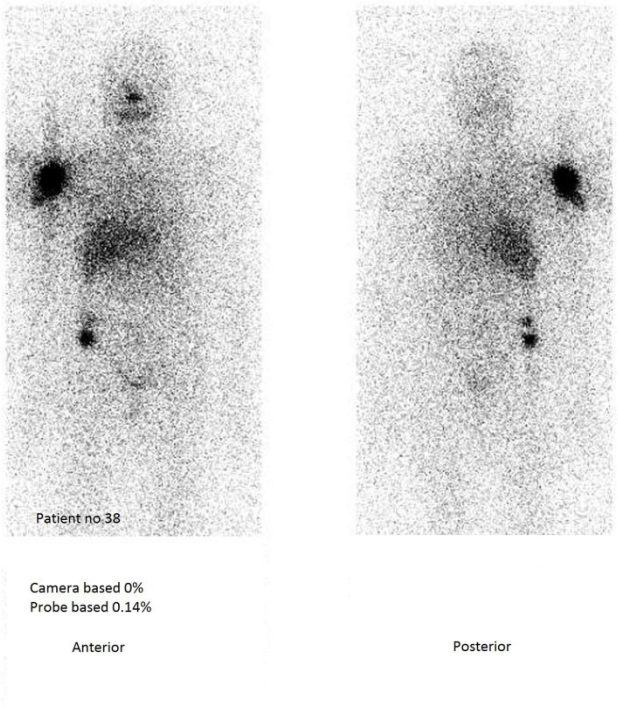

Fig 3. A 67-year-old female DTC patient with shoulder metastasis. Neck uptake by thyroid probe was positive, while scan finding and camera-based uptake were negative.

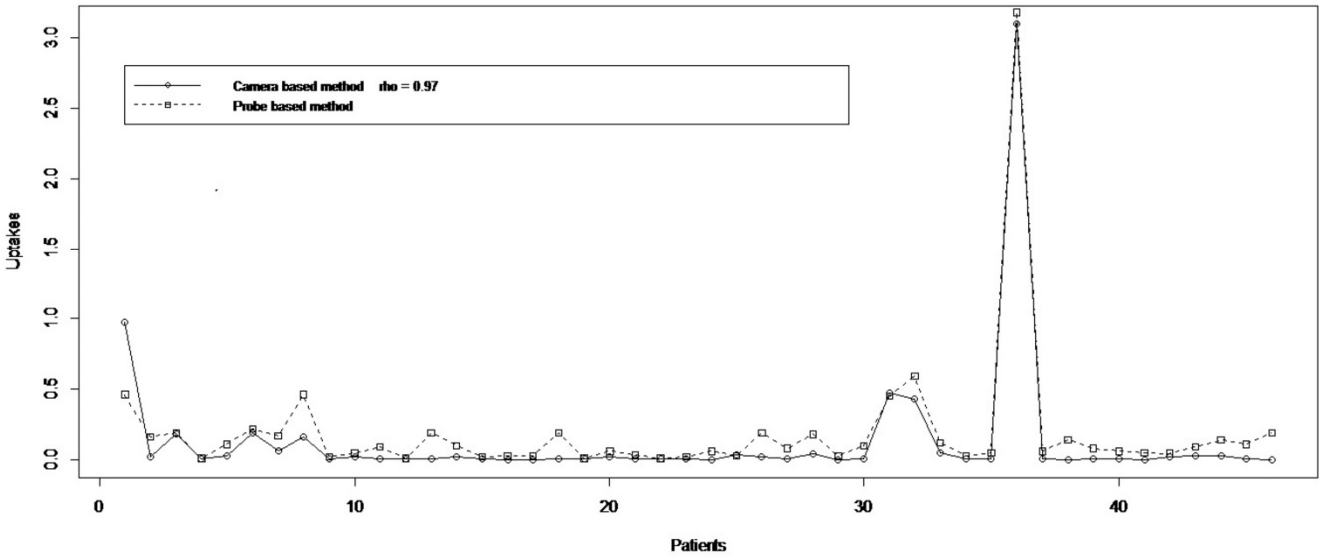

Fig 4. Measurements obtained through Camera based and uptake probe-based methods are highly concordant with Pearson Correlation coefficient 0.97.

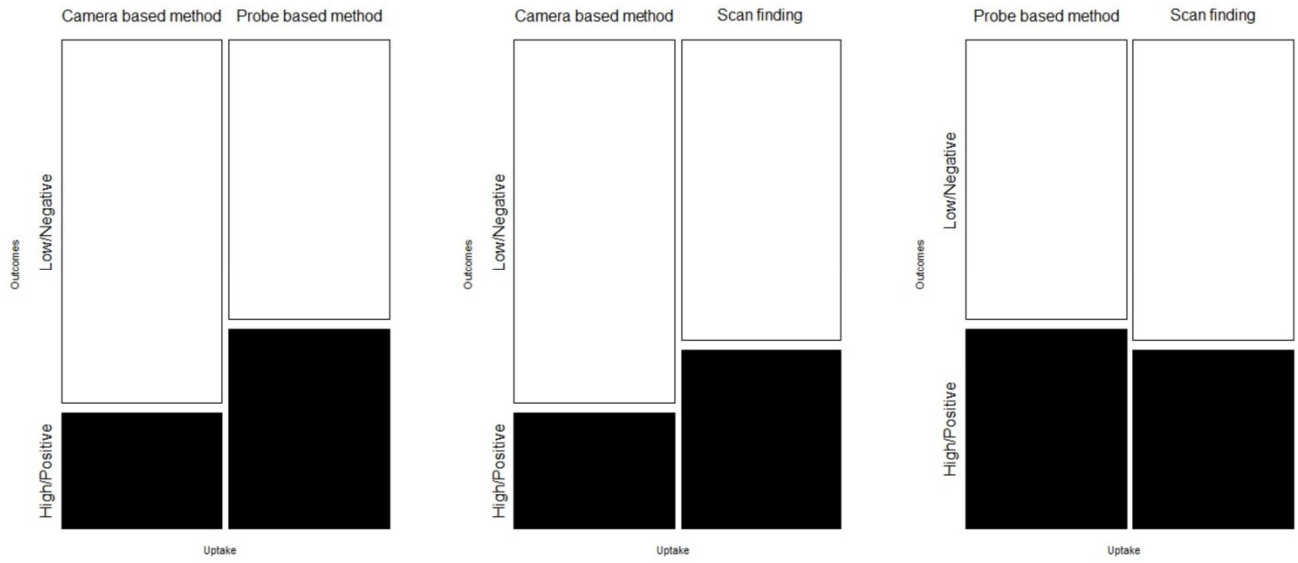

Fig 5.The pairwise comparison between Camera based, Uptake probe based and Scan findings to detect the positive and negative cases.

Table 1. Kappa test statistics obtained between performance of Camera Based Method, Probe Based Method and Scan finding in patients with thyroid carcinoma

Camera Based Method					Scan Finding is reference	
	Outcome	High/Positive n(%)	Low/Negative n(%)	Kappa Value	Sensitivity	Specificity
Scan Finding	High/Positive n(%)	11(23.91)	6(13.04%)	0.69	64.70%	82.85%
	Low/Negative n(%)	0(0.00%)	29 (63.04%)			
Scan Finding					Scan Finding is reference	
		High/Positive n(%)	Low/Negative n(%)		Sensitivity	Specificity
Probe Based Method (at cut off point 0.1)	High/Positive n(%)	12(26.08%)	5(10.86%)	0.45	79.16%	75.86%
	Low/Negative n(%)	7(15.21%)	22(47.82%)			
Scan Finding					Scan Finding is reference	
		High/Positive n(%)	Low/Negative n(%)		Sensitivity	Specificity
Probe Based Method(at cut off point 0.2)	High/Positive n(%)	6(13.04%)	0(0.00%)	0.40	100%	72.5%
	Low/Negative n(%)	11(23.91%)	29(63.04%)			