J of Nuclear Medicine Technology, first published online December 6, 2021 as doi:10.2967/jnmt.121.262719

Thyroid Uptake Exceeding 100%: Causes and Prevention

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Running title: Thyroid uptake quality control

Key words: Thyroid uptake, Radionuclide, Quality control

Word Count: 5544

Abstract

Background: Radionuclide thyroid uptake measurements reflect the metabolic activity of the thyroid gland. Thyroid uptake is measured as a percentage of radioactivity retained by the gland at a specified time versus the activity administered to the patient; thus, uptake measurements must fall between 0 and 100%. In this study we review sources of errors that can lead to uptake >100% through a case study and describe a novel quality control (QC) indicator to improve the accuracy of uptake measurements in the clinic.

Methods: Probe efficiency is determined as the ratio between dose counts of the probe relative to the independent dose calibrator activity readings. The nominal probe efficiency value (M) was calculated as the mean of readings ($n \geq 20$) and variance was characterized using the standard-deviation (SD). Warning levels were set at $M \pm 1.96 \times SD$ and error levels were set to $M \pm 2.58 \times SD$. In subsequent routine clinical use, prior to administrating a capsule, the probe efficiency is calculated and compared with the warning and error limits. We derived M for three pairs of probe and dose-calibrator devices using several doses and measured independently by several nuclear medicine technologists.

Results: The recorded data indicated that nominal efficiency was statistically different between our old device and the one that replaced it ($p=0.01$) but coefficient-of-variation (CV% $=SD/M \times 100\%$) was not ($p=0.42$) when technologists were made aware of the expected efficiency value. Using efficiency measurements of the first 20 first patients acquired on the replacement device new QC values were derived ($M= 910$, $SD =36$). In 22 patients measured at our sister site, with the same device models but without technologists being aware of QC initiative, derived QC values were ($M =1025$, $SD =116$), demonstrating a significant difference

between nominal values of individual devices ($p<0.001$). Furthermore, variability was significantly lower ($p<0.001$) when QC was followed compared to when it was not applied. **Conclusion:** Adding the probe efficiency as a quality control indicator during thyroid uptake measurement is simple, can produce more precise clinical measurement and help mitigate operator and instrumentation errors.

Key words: Thyroid uptake, Radionuclide, Quality control

Introduction

Radionuclide thyroid uptake measurements reflect the metabolic activity as well as the iodine handling and kinetics in the thyroid tissue. It measured as the fraction of radioactivity in the neck relative to that administered to the patient with a predetermined time between measurement and administration (e.g. 24 hours). (*1*) ^{131}I- and ^{123}I-sodium iodide are commonly used as the radiopharmaceutical for thyroid uptake determination either in capsule or liquid form. Clinical applications for this procedure are to differentiate hyperthyroidism associated with thyroid dysfunction (e.g. Graves' disease or multinodular goiter) from other forms of thyrotoxicosis such as subacute thyroiditis and for calculating the activity of radioiodine (^{131}I) to be administered for treatment. (*2*) Because thyroid uptake is measured as a percentage of radioactivity retained by the gland at a specified time versus the activity administered to the patient (time = 0) uptake measurements must fall between 0 and 100%.

The basic procedure involves the following steps (as illustrated in Figure 1):

1) Measure the room background activity and administered activity using a gamma counting probe with the radio-iodine dose positioned in a dedicated neck phantom. Duplicate measurements including repositioning of the probe should be taken to avoid positioning errors; indicated by discrepant count-rates between measurements. Highly discrepant dose counts (e.g. >10%) should be investigated and addressed immediately to avoid propagation of errors.
2) Administer the entire activity to the patient in oral form.
3) At a predetermined time (e.g. 24 hours post administration at our institution) the patient returns for the uptake measurement. Measure the thyroid and patient background (thigh) counts using the same gamma counting probe. Duplicate measurements including

repositioning of the probe should be taken to avoid positioning errors; indicated by discrepant count-rates between measurements.

4) After ensuring matching repeat counts, subtracting corresponding background (BG) measurements and applying radionuclide decay correction, the ratio of net uptake count-rate to net administered count-rate is the measured thyroid uptake, as shown in the following equation in which the over-bars represent the average of multiple repeat measurements.

$$Uptake\% = 100\% \times \frac{\overline{Uptake} - Patient\ BG}{(\overline{Administrered} - Room\ BG) \times Radionuclide\ Decay} \qquad \text{Eq. 1}$$

Modern probes are equipped with software to track the measurements and perform the thyroid uptake calculation automatically.

Because thyroid uptake relies on two measurements (steps 1 and 3 above) with few redundancies, quality assurance practices are essential to have confidence in the final reading. The counting technique is an important step as the technique should include appropriate centering, distance, and positioning of the radiation counting probe, thyroid phantom, and patient. The technique should be reproducible by technologists to ensure accuracy and reproducibility, and thus all counting should be performed in duplicates. Counting time should be set to a minimum of 60 seconds to ensure adequate photon counting statistics. (*2*) Finally, prior to performing initial dose or uptake measurements, quality control (QC) must be performed on the probe, including constancy to ensure that day-to-day counting efficiency is consistent.

Case Study and Motivation

Despite these quality initiatives, errors can and do occur. When thyroid uptake values exceed 100% it is obvious that an error has occurred, but errors may not be detected if uptake values do

not significantly deviate from the expected range (by other clinical indicators). Recently, there was a patient with known hyperthyroidism referred to our clinic for thyroid uptake and scan prior to ^{131}I therapy. The thyroid uptake was measured at 139% at 24-hours (Patient 1). This event triggered an investigation by our local Quality Assurance committee, was discussed at our departmental Mortality and Morbidity rounds, and resulted in corrective actions.

Our Clinic

Our clinic consisted of two sites each performing ^{131}I uptake measurements using Captus 3000 (Capintec, NJ, United States) gamma probes that had reached the end of support by the manufacturer but were regularly maintained by our local Biomedical Engineering team. During the time in question one of the machines was deemed unserviceable (Site 1) and while a replacement was being procured all patients were referred to our other site (Site 2) with a device of the same make and model. Routine QC procedures consisted of routine maintenance and daily constancy tests according to the manufacturer and professional society guidelines.

On the day in question, three patients were referred to the clinic and all three ^{131}I capsules (370 kBq) were measured in a single session in a CRC-55t dose calibrator (Capintec, NJ, United States) and using the probe (2 duplicate measurements with room background subtraction). All three patients received their assigned capsule and returned for a 24-hour uptake measurement, consisting of duplicate thyroid measurements and duplicate thigh measurements as patient background. Results for all three patients are summarized in Table 1. The original results for patient 1 were clearly erroneous, exceeding 100% uptake, and thus investigation was started immediately by the department physician and technologists while the patient was still present. Later that day, the reporting physician also flagged the results of patient 2 and 3 to be

suspiciously high based on other clinical information. Thus we suspected a technical error and investigated the following possible sources of error (*2*):

1) Operator error at thyroid measurement: During the 24-hours visit of patient 1 uptake measured was confirmed by two independent measurements by two other technologists (3 measurements in total agreeing within 5% of each other), including repeat measurements after removal of clothing. The patient returned for repeat uptake measurements at 48-hours and 192-hours and uptake measurements were 138% and 146% respectively, indicating reproducible high-uptake and trapping of the activity (i.e. no washout).
2) Operator error at radioiodine dose measurement: The full radioiodine capsule measurement process was simulated with the technologist that had measured the three ^{131}I-capsules on the day in question. They have over 20 years experience and demonstrated proficiency in the procedure. No cognitive errors were identified. Furthermore, the count-rates for all three capsules matched, as expected as all three capsules were ordered to the same activity (~370 kBq, ~10μCi) and were from the same batch (Table 1). The three capsules were measured sequentially without repositioning the probe or phantom between capsules.
3) Background measurements: Room and patient background measurements should be performed near their corresponding administered dose and thyroid measurements respectively. Failure to do so, increases the risk of inaccurate background readings that do not reflect changes in the environment in the ensuing time. The results of our case study (Table 1 – Patient 3), revealed a previously unidentified methodological error in our clinical practice in which a single background measurement may be used for multiple

doses measured hours apart. This is unlikely to be a significant source of error in this case as the probe is housed in an area isolated from the main Nuclear Medicine department and with low patient traffic. Nevertheless, we have since revised our clinical protocol to state that all doses must be measured within 15 minutes of the corresponding background reading.

4) Instrumentation settings: The Department of Nuclear Medicine physicist was present for the 48-hour assay and verified that the system settings were consistent with the department protocol.

5) Instrumentation quality control: Quality control logs were reviewed for the probe indicating consistent, and in range daily QC metrics over the week preceding and succeeding the dose administration. In our clinic QC is perform according to manufacturer recommendations. (*3*) Two reference sources (^{137}Cs and ^{152}Eu) are measured daily for energy calibration and precision, linearity, and efficiency constancy. Quarterly, we also perform chi-square (χ^2) of the counting performance of the system and test the minimal detectable dose (MDA).

6) Patient contamination: At 48-hours, the physicist reviewed the emission spectrum from the thyroid assay and confirmed that the emission spectrum matched that of ^{131}I with no indication of contamination from other radioisotopes and that low counts were present in the patient background reference region (thigh). Furthermore, radioactive contamination was ruled out by our Radiation Safety physicists by biological assay of the patient and their spouse at 9 days post administration using a separate gamma counting probe. Thus, internal radioactive contamination was ruled out.

7) Correlation with prior measurement: The patient had a prior thyroid uptake measurement performed 32 months earlier, measuring at 51%.
8) Correlation with imaging: On the day of, and prior to, ^{131}I administration the patient was imaged with ^{99m}Tc-pertechnetate and a pinhole collimator. The images appeared to be visually similar between the two studies (Figure 2), however a quantitative comparison of pertechnetate uptake could not be conducted, as these images were acquired using different imaging devices (camera and collimator).

Eventually, we identified a loose contact in the cable between the probe head and data acquisition card of the device. How long this fault went unnoticed and its implications to prior measurements can only be speculated. This fault was subsequently repaired by biomedical engineering and was followed by necessary calibration and QC including Chi-square measurement.

To understand the potential implications to the three patients on the day in question we evaluated the probe efficiency as the ratio of probe counts to dose calibrator readings using equation 2 and as shown in Table 1. We compared these results to those of 14 previous patients in our clinic data (Table 2).

$$Probe\ efficiency\ \left(\frac{cps}{MBq}\right) = \frac{Probe\ net\ count{-}rate\ (cps)}{Dose\ calibrator\ activity\ (MBq)} \quad \text{Eq. 2}$$

While we could not definitively determine the reason (e.g. probe physical configuration, instrumentation failure) for the change in geometric efficiency of the probe during capsule readings on the day in question, they appeared to be off by a fixed factor. We used the ratio of efficiencies of the two cohorts to adjust the 24-hour uptake using Equation 3, which aligned with the clinical histories of all three patients.

$$Adjusted\ 24\ hour\ uptake\ (\%) = Original\ 24\ hour\ uptake\ (\%) * \frac{Current\ average\ probe\ efficiency\ (\frac{cps}{MBq})}{Previous\ average\ probe\ efficiency\ (\frac{cps}{MBq})} \quad \text{Eq. 3}$$

Nevertheless, we decided to replace this aging machine at this site (Site 2) with the same make and model as had been ordered for Site 1. Furthermore, we embarked to implement new QC practices to mitigate similar risks in the future.

Objectives

The purpose of the current study was to develop a QC method to mitigate errors when measuring radioiodine doses prior to their administration to the patient. We provide a detailed explanation of the method so that it can be applied by others. These methods include routine measurement of the probe efficiency as part of the clinical workflow and comparison to pre-derived warning levels and error levels to initiate timely action by technologists, physicists and biomedical engineering. We also explain how to derive the warning and error levels and provide a spreadsheet for data collection and calculations.

Materials and Methods

As a clinical quality assurance study, the Institutional Research Ethics Board (IRB) approved this retrospective study and the requirement to obtain informed consent was waived.

After our recent upgrade, thyroid uptake measurements were again performed at our two sites, using identical thyroid uptake systems (Captus© 4000e, Capintec, NJ, United States), using 60 seconds acquisitions with a 364 keV±10% photopeak energy window and count-rates were reported in units of counts per second (cps). To determine these devices' counting efficiencies, the activities of several ^{131}I-NaI capsules were measured in the respective site's dose calibrator. The dose calibrators (Capintec CRC-25 and Capintec CRC-55t) were previously calibrated to a reference standard. Next, the ^{131}I-NaI capsules were measured independently several times by

several technologists in duplicate and with room background count subtraction using the probes as would be performed clinically using the neck phantom holder.

Probe efficiencies were calculated for each probe measurement as in Equation 2. The nominal probe efficiency value (M) was calculated as the mean of all readings. Because count statistics follow a Poisson distribution and are sufficiently high (~18,000), a Gaussian distribution was assumed and therefore efficiency variance was characterized using the standard-deviation (SD) of all measurements. (*4*) Warning levels were set at M±1.96×SD and error levels were set to M±2.58×SD (see example in Table 3), corresponding to an expected false-positive rate of 5% and 1% of capsule measurements respectively. (*5*) The ratio of the standard-deviation to the mean is referred to as the coefficient of variation (CV) and we expressed is percent units. Thus, warning and error levels can be expressed as a percentage of the nominal value or in absolute units (cps/MBq).

We determined the nominal probe efficiency, warning levels and error levels for three devices: Site 1 – New Device (Site1New), Site 2 – Old Device (Site2Old) and Site 2 – New Device (Site2New). For Site1New, data was acquired from routine clinical worksheets in which no QC was performed on efficiency measurements. This served as a baseline sample of the variability of the efficiency when QC is not performed. For Site2Old technologists were explicitly instructed to perform multiple test measurements using multiple capsules on multiple days using the old probe (Captus 3000). In this case the technologists were aware of the test being performed and paid attention to expected probe count-rates. These data were used to derive a baseline measure of nominal efficiency and its variability. For Site2New, data was collected from routine clinical worksheets in which QC was performed by the technologists on the efficiency measurements

using warning and error limits derived from Site2Old (as the nominal values for these machines were similar in preliminary measurements).

In subsequent routine clinical use, prior to administrating a capsule, the probe efficiency must be calculated in the same manner as during calibration and using equation 2. The calculated efficiency is then compared with the warning and error limits corresponding to the probe and dose-calibrator used posted at the corresponding site (see example in Table 3). Directives on how to handle pass, warning and error events were also posted, and are detailed in the discussion section.

Statistical Methods

The difference between nominal values for different devices was tested for statistical significance using a Student's unpaired t-test. (*6*) Likewise, differences in CV% were evaluated using an F-Test. P=0.05 was used as a cut-off for statistical significance.

Results

Mean and CV% probe efficiencies are summarized in Table 4 for the three devices. Baseline efficiency estimates (Site2Old) consisted of 29 independent samples measured by 7 technologists, using 6 capsules on 6 separate days. The CV% was 4% resulting in warning and error levels as shown in Table 3. These exceed variability expected from count statistics alone (~0.5%). Using this baseline QC limits as estimates for the new device at the same site (Site2New), 20 routine clinical patients were worked up. The recorded data indicated that nominal efficiency was statistically different between these two devices (p=0.01) but CV% was not (p=0.42); new QC limits were derived from these data for subsequent QC in the clinic.

The 22 participants who received a thyroid uptake measurement at Site 1 (M =1025, SD =116) compared to the 20 participants at Site 2 (M= 910, SD =36) demonstrated a significant difference

between individual machines ($p<0.001$) both with regards to nominal values, further justifying that specific QC limits were required for each device. Furthermore, in the absence of QC indicators at this site variability was nearly 3-times greater (CV%=11% vs 4%).

Discussion

In this work, we set out to enhance the quality control of thyroid uptake measurements by ensuring that the measurement of the administered dose to the patient is consistent between two independent measurements: probe count-rate and dose-calibrator reported activity. We concluded that in our clinical practice 4% coefficient of variation was achievable corresponding to ~8% and ~10% warning and error limits associated with 95% and 99% confidence intervals. In other words, using these error and warning limits, we expect to experience false-warning and false-error limits one out of every 20 and out of 100 tests respectively. These would trigger further investigation which should be resolved prior to administering the dose to the patient, and therefore would lead to higher confidence in the final clinical results. It is possible that with further emphasis of QC the variability (CV%) can be further decreased, towards more precise thyroid uptake measurements.

As noted in the Case Study and Motivation section, we, as did others previously, (*2*) identified several possible sources of error in high thyroid uptake. We included this detailed description to guide readers in the event that they need to investigate a similar incident in their own clinic. Table 5 highlights a more complete list of potential sources of errors and means to mitigate their occurrence and propagation. However, for our enhanced QC we focused on the pre-administered dose measurement as it is a single point of failure that cannot be conclusively investigated after administration. Erroneous, measurements of thyroid activity, on the other hand, can be investigated within several hours, assuming they are caught early enough.

An important finding in this work is that counting efficiencies vary between devices, even of the same make and model, and therefore nominal values and limits must be determined for each pair of devices (probe and dose calibrator) unless explicit calibration is performed. An additional key finding, is that QC of the efficiency, can reduce the variability in clinical practice as demonstrated by the CV% between Site1New and Site2New which were measured without and with QC respectively. Obvious sources of variability that should be investigated when QC fails are transcription errors, probe/phantom/source positioning, and changes in or malfunctioning of the instrumentation.

Radioactive Decay correction

Probe efficiencies were calculated using Equation 2. Note that this simple calculation ignores radioactive decay, which is acceptable if the dose calibrator and probe measurements are within 1 hour of each other and for ^{131}I which has a physical half-life of 8 days. (*7*) For shorter lived isotopes and/or delays between dose calibrator and probe measurements a decay correction may be required.

Clinical application

To apply the proposed QC in a clinical setting we propose the following instructions. Variations may be made to tailor to the clinic's specific workflow and constraints. These instructions comprise of two sequential steps; determination of QC limits and routine QC:

Determination of QC limits

For each pair of probe and dose-calibrator, nominal efficiency values and tolerances must be determined by repeat measurement of sample capsules in a manner that represents the clinical workflow. Considerations include repeat measurements by different technologists, on different days and using several doses that span the range of activities used in the clinic for the procedure.

The exact methodology will vary depending on the number of technologists operating in the clinic, but we recommend 30 independent measurements with 20 as a minimum to ensure adequate statistical power. Using the methods described in the Methods section the nominal value and tolerances can be determined and posted in the lab for routine QC. An example of this QC table can be seen in Table 3. Other, clearly marked variants including the use of color, graphics and accompanying instructions should be considered in consultation with the technologist team to ensure optimal communication of new QC practices. A sample Microsoft Excel® worksheet to derive QC limits from experimental data is provided as supplemental material.

Routine Quality Control

During clinical operations, each dose must be measured in a dose calibrator and then using the probe with the neck phantom. The ratio of probe counts to dose calibrator reading must be calculated as in equation 2 and the value compared to a table as demonstrated in Table 3. Three possible scenarios arise:

1) Quality control passes when the calculated efficiency is between the two warning levels. Proceed with the clinical procedure normally.
2) Quality control warning when the calculated efficiency is between a warning level and error level (low or high). In this case, the work should be checked and or repeated, including by an independent trained clinical staff member. If QC remains at a warning level, proceed with the clinical work if required (e.g. workflow constraints, patient has travelled from afar), but notify the physicist, quality manager, and/or biomedical engineering of the warning for further investigation. Also, notify the reporting physician.

3) Quality control error occurs when calculated efficiency exceeds either lower or upper error levels. If the source of error cannot be identified and corrected, do not proceed with administering the capsule to the patient until the physicist, quality manager, and/or biomedical engineering has been made aware of the error, has investigated the error, and has resolved the issue.

Liquid iodine

In our clinic for diagnostic procedures, we currently use radioiodine in capsule form at a single dosage. Nevertheless, the same procedure may be applied to liquid form by preparing representative samples and measuring them in both dose calibrator and using the probe. However, special accommodations may be necessary including accounting for changes in geometric efficiencies of the probe and dose calibrator depending on the container and liquid volume. (*8*)

Furthermore, one should ensure a consistent efficiency factor is achieved across the entire range of activities used (e.g. if performing uptake measurement using therapeutic doses). This requires that both systems operate in a linear range across the full range of activities, and that probe deadtimes remain below ~2%. If greater dead-time factors must be accommodated, a more complicated, activity-dependent efficiency curve may be required.

Strengths and Limitations

These additional quality practices can be implemented in a routine clinical setting with little impact on workflow. This QC provides an extra layer of assurance to boost confidence in the validity of the thyroid uptake results. However, it is important to appreciate the remaining limitation in that if the probe efficiency varies between day of capsule measurement and patient uptake (e.g. 24 hours later) erroneous thyroid uptake measurements may still result and go

undetected. Therefore, daily QC of the probe including constancy is still essential to achieving high-quality thyroid uptake measurements.

In this work, we do not report on QC outcomes in our clinic after full implementation of this QC procedure. This is due to too few data for meaningful analysis to date (n=14 at Site 1 and n=10 at Site 2) of which none have resulted in warning or error events that triggered investigations by our QC team.

At our institution thyroid uptake is typically measured at 24 hours following oral administration of an ^{131}I capsule. Ideally, the thyroid uptake should be measured at multiple time points to accurately characterize the biological process, including identification of patients with rapid turnover time with higher uptake at 4 or 6 hours. These additional timepoint data may also benefit QC and investigation of anomalous measurements.

Likewise, ^{99m}Tc-pertechnetate count-rate measurements from the imaging studies may have aided investigation in the case-study, but quantitative comparison was hampered by the use of different devices between time points. Use of standardized imaging equipment and protocols within the clinic is therefor, advised whenever possible.

Conclusion

Thyroid uptake measurements can be prone to operator and instrumentation errors that cannot be detected without quality control. The ratio between dose counts of the probe relative to independent dose calibrator activity readings is a simple quality control indicator that can be readily applied in a clinic to reduce such errors.

Disclosures

Ran Klein receives revenue shares from the sale of Rubidium generators from Jubilant-DraxImage and from the sales of myocardial flow quantification software from Invia Medical Solutions. None of the authors have conflicts of interest to disclose related to this work.

Acknowledgements

The authors are thankful for the support of The Ottawa Hospital, Department of Medicine staff for their collaboration in investigating this case and their ongoing support to improve quality in our department.

Key Points

Question: Can a thyroid probe efficiency test serve as a quality control measure towards accurate thyroid uptake measurements?

Pertinent Findings: Prior to administering the radioiodine dose to a patient, the dose can be used to test the thyroid probe count-rate reading against the dose-calibrator reported activity to identify errors exceeding approximately 10%.
Many other potential sources of error are listed to facilitate investigation of anomalous thyroid uptake measurements.

Implications for Patient Care: This quality assurance measure can be easily implemented into a nuclear medicine clinic to improve quality and confidence in thyroid uptake measurements.

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Tables

Table 1. Workup of thyroid uptake using ^{131}I capsules for three patients described in the Case Report section. The original 24-hour thyroid uptake results are shown along with their corresponding adjusted values after compensating for deviations in probe efficiencies from previous patients (Table 2).

Patient	Dose calibrator		Probe							24-hour uptake	
	Activity (MBq)	Time	Count 1 (cps)	Count 2 (cps)	Room Background counts (cps)	Net capsule counts (cps)	Time	Room Background time	Probe efficiency (cps/MBq)	Original (%)	Adjusted (%)
1	0.420	9:16	213	210	1	211	8:26	8:23	501	139.6%	71%
2	0.435	10:35	214	216	1	214	8:29	8:23	490	34.8%	18%
3	0.388	9:08	208	206	1	206	13:24	8:23	534	47.0%	24%

Table 2. ^{131}I capsule activity, probe net capsule count, probe efficiency results at the clinic for previous patients.

Patient	Dose calibrator		Probe						
	Activity (MBq)	Time	Count 1 (cps)	Count 2 (cps)	Room Background counts (cps)	Net capsule counts (cps)	Time	Room Background time	Probe efficiency (cps/MBq)
4	0.370	9:22	474	477	1	475	11:33	11:16	1287
5	0.383	10:35	466	464	1	464	13:26	11:16	1217
6	0.310	10:45	294	294	3	291	10:43	10:16	939
7	0.290	8:42	286	281	3	281	8:39	8:06	967
8	0.350	9:20	353	349	1	350	15:20	15:18	1009
9	0.420	13:44	410	408	3	406	10:51	10:16	962
10	0.390	9:40	389	389	4	385	9:31	8:18	987
11	0.410	9:00	362	366	4	360	8:57	8:18	878
12	0.305	10:53	265	269	4	263	10:30	10:24	862
13	0.292	10:10	280	280	3	277	10:07	9:56	949
14	0.302	9:11	271	272	4	268	9:15	8:50	886
15	0.350	11:30	346	346	3	343	10:55	10:52	979
16	0.389	10:30	402	406	3	401	10:05	9:41	1030
17	0.360	9:02	355	348	3	349	8:59	8:35	968

Table 3. Example quality control limits for probe efficiency with three levels: pass, warning, and error. (for baseline QC - Site2Old device)

Quality control limits - Probe efficiency (cps/MBq)			
Status	Lower limit	Upper limit	±% range
Pass	808	955	8%
Warning	784-807	956-978	11%
Error	<783	>979	-

Table 4. Comparison of probe efficiencies and their variability for the three devices (and practices)

Device	n	Nominal efficiency (cps/MBq)	Measured CV%	Comment
Site2Old	29	881	4%	QC limits derived with explicit test misstatements that served as QC estimates for Site2New.
Site2New	20	910*	4%	From clinical data using QC estimate from Site2Old as a guideline.
Site1New	22	1025*	11%*	From clinical data without using any efficiency QC.

* indicates $p<0.05$ in comparison to Site2Old

Table 5. Potential sources of error leading to erroneous thyroid uptake measurements

Source		Means to mitigation error
Operator	Probe misalignment during: dose assay	Review efficiency against dose calibrator activity measurement; Review count-rate against typical values for similar dose
	room background assay	Use phantom and probe ruler, reproducing positioning for dose assay; Ensure low count-rate consistent with background radiation
	uptake assay	Palpate for thyroid location; Use probe ruler, repositioning between duplicate measure to verify consistency; Cross-validate with other time-points; Cross-validate with imaging
	patient background assay	Use probe ruler; Ensure low count-rate; Investigate high count-rates including patient/clothing contamination
	Wrong uptake time	Preschedule visits according to protocol; Automated time logging by probe software; Record all steps in clinical worksheet/software
	Wrong dose administered	Label doses with patient identifiers; Verify matching patient using multiple identifiers; View energy spectrum to confirm correct isotope
	Wrong patient	Confirm multiple patient identifiers against software recorded entry and/or clinical worksheet; Use electronic patient worklist
Instrumentation	System malfunction	Ensure appropriate quality control using quality management system; Clearly label and communicate system serviceable status
	Clock error	Configure time server synchronization
	Acquisition settings	Use predefined acquisition protocols; Password protect software administrator settings including protocol settings
Patient	Motion	Monitor patient during acquisition; Repeat acquisition if patient has moved
	Incomplete ingestion/vomiting	Monitoring patient at dose administration; Debrief patient prior to uptake acquisition
	Missed appointment(s)	Time stamps all patient encounters and counting of administered dose; Consider delaying/repeating procedure due to erroneous uptake time
	Internal/external contamination	Inspect energy spectrum for signs of other isotopes; Review patient history for exposure to radionuclides (previous medical procedures and occupational or environmental exposures); Apply energy windowing
	Changes in patient health	Implement intake questionnaire; Review adherence to preparation instructions; Correlate with other medical data (*1*)
	Diet	Follow societal guidelines for patient preparation including abstinence from high-iodine containing foods. (e.g. kelp) (*1*)
	Medication	Follow guidelines for patient preparation including extensive list of medications and iodinated contrast agents that interfere with thyroid uptake (*1*); Review patient list of medications and medical history
Environmental	Background radioactivity	Remove potential sources of radiation including from neighbouring rooms. (e.g. patients, x-ray equipment); Use radioiodine appropriate energy window; Ensure that background measurements are near in time to assay, and QC for low background count-rates

Figures

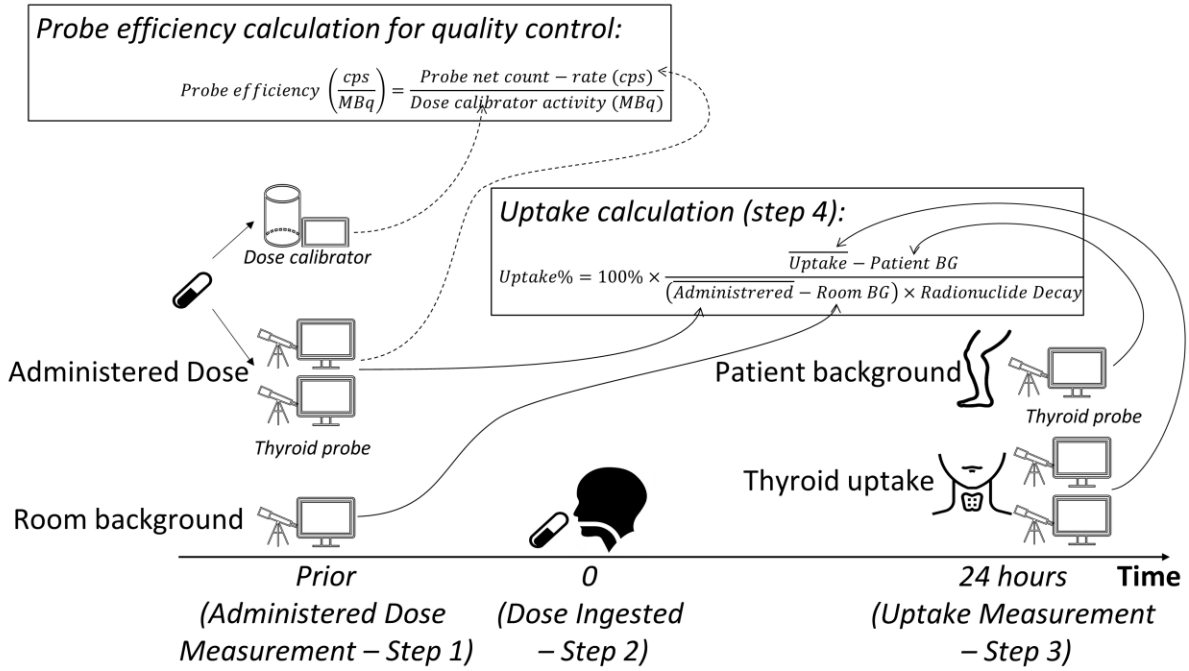

Figure 1 – Thyroid uptake workflow diagram. At time 0, the patient ingests a dose of radioiodine that was previously (prior) measured using a thyroid probe. At 24 hours (post-ingestion) the patient returns to the department for thyroid uptake measurement using the same thyroid probe. Room and patient background measurements are performed with the probe at time of dose and thyroid uptake measurements respectively for background subtraction prior to calculating the uptake ratio as a percentage. An optional measurement of the administered dose with a dose calibrator can be used to calculate the probe efficiency to be used for quality control.

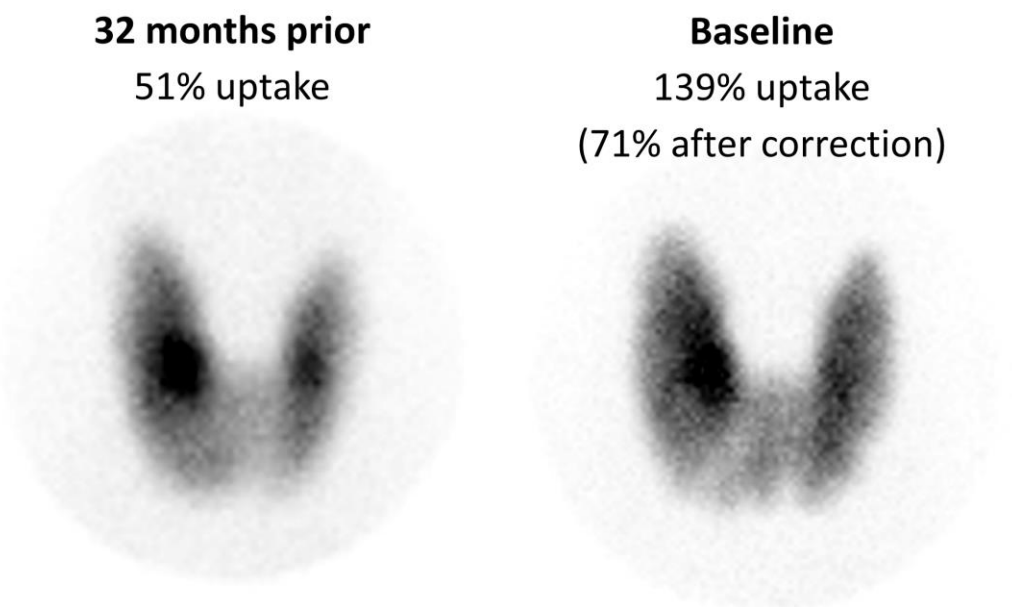

Figure 2 – Patient 1 ^{99m}Tc-pertechnetate uptake images at time of investigation (Baseline) and 32 months prior. Image intensities were manually normalized to have similar contrast. Biodistribution is similar, contradicting large thyroid uptake change between time points.

Supplementary Material

We provide a template Excel® spreadsheet (Probe Efficiency Calculator.xlsx) to laboratories that wish to implement thyroid probe efficiency quality control. The spreadsheet uses repeat measurements by laboratory technologists to determine the nominal efficiency in the laboratory, its variance and confidence intervals for quality control. Four levels of quality control are determined: low error, low warning, high warning, and high error. See the discussion section for usage instructions.

Graphical Abstract