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Alternative Means of Estimating ^{131}I Maximum Permissible Activity to Treat Thyroid Cancer

Kenneth J. Nichols PhD,[1,2] William Robeson MA,[2] Miyuki Yoshida-Hay BS,[2]
Pat B. Zanzonico PhD,[3] Fritzgerald Leveque BS,[2] Kuldeep K. Bhargava PhD,[1,2]
Gene G. Tronco MD,[1,2] Christopher J. Palestro MD[1,2]

[1]Hofstra Northwell School of Medicine of Hofstra University, [2]Division of Nuclear Medicine and Molecular Imaging, Northwell Health, Manhasset and New Hyde Park, NY
[3]Memorial Hospital Research Laboratories, Memorial Sloan Kettering Cancer Center, New York, NY

Please address all correspondence to:
Kenneth Nichols, Ph.D.
Division of Nuclear Medicine & Molecular Imaging
Northwell Health
270-05 76th Avenue, New Hyde Park, NY 11040
Office: 718-470-7080; FAX 516-277-4923; Email: knichols@northwell.edu

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ABSTRACT

To protect bone marrow from over-irradiation, maximum permissible activity (MPA) of iodine-131 (^{131}I) to treat thyroid cancer is that which limits absorbed dose to blood (as a surrogate of marrow) to < 200 cGy. The conventional approach (Method-1) requires repeated gamma-camera whole-body measurements along with blood samples. We sought to determine whether reliable MPA values can be obtained by simplified procedures. Methods: Data acquired over multiple time points were examined retrospectively for 65 thyroid cancer patients, referred to determine ^{131}I uptake and MPA for initial treatment following thyroidectomy (N = 39), including 17 patients with compromised renal function and 22 patients with known (N=16) or suspected (N=6) metastases. Total absorbed dose to blood (D_{Total}) was the sum of mean whole-body γ ray dose component (D_γ) from un-collimated gamma-camera measurements, and dose due to β emissions (D_β) from blood samples. Method-2 estimated D_{Total} from D_β alone, Method-3 estimated D_{Total} from D_γ alone, and Method-4 estimated D_{Total} from a single 48-hour gamma-camera measurement. MPA was computed as 200 cGy/D_{Total} for each D_{Total} estimate. Results: Method-2 had strongest correlation with conventional Method-1 (r = 0.98) and values similar to Method-1 (21.0±13.7 cGy/GBq versus 21.0±14.1 cGy/GBq, p = 0.11), while Method-3 had a weaker (p = 0.001) correlation (r = 0.94), and Method-4 had weakest (p < 0.0001) correlation (r = 0.69) and lower dose (16.3±14.8 cGy/GBq, p < 0.0001). Consequently, correlation with Method-1 MPA was strongest for Method-2 MPA (r = 0.99) and weakest for Method-4 (r = 0. 75). Method-2 and Method-1 values agreed equally well regardless of whether patients had been treated with ^{131}I previously or had abnormal renal function. Conclusions: Because MPA based on blood measurements alone is comparable to MPA obtained with combined body counting and blood sampling, blood measurements alone are sufficient for determining MPA.

INTRODUCTION

Thyroid cancer is the most rapidly increasing malignancy diagnosis in the United Sates (*1,2*). The most common form of thyroid cancer is differentiated thyroid cancer, the recurrence rate of which is estimated to be 30% (*3*). Typical treatment for thyroid cancer is total thyroidectomy followed by administration of iodine-131 (^{131}I) to ablate thyroid remnants to reduce the risk of disease recurrence (*4*).

Some institutions administer empiric ^{131}I activity to all patients, but doing so delivers excessive radiation dose to some patients (*5*). The conventional approach to estimating ^{131}I maximum permissible activity (MPA) that can be administered to limit blood dose to < 200 cGy (200 rad) involves repeated gamma camera measurements and blood sampling over 5 days (*6,7*), and longer for patients with decreased renal clearance (*8*). Additional restrictions include limiting whole-body retention at 48 hours to < 4.4 GBq, and to < 3 GBq for patients with diffuse pulmonary disease (*9,10*).

The conventional approach to estimating MPA assumes total dose to blood (D_{Total}) is the sum of dose to blood from ^{131}I β emissions (D_β), measured from blood samples, and γ ray dose to blood from all other organs due to ^{131}I γ emissions (D_γ), estimated from gamma camera measurements. Some institutions find this conventional MPA approach inconvenient. Alternative techniques reduce or eliminate blood sampling altogether (*11*,*12),* estimating MPA from a single body counting radiation measurement (*13*).

Our investigation was undertaken to determine whether alternate MPA methods agree with the conventional method. Since some institutions routinely administer 7.4 GBq (200 mCi) of ^{131}I for metastatic disease (*13,14*), despite findings that 7.4 GBq ^{131}I would exceed 200 cGy of blood dose in 19% of patients (5), we also evaluated which methods indicate the need to

administer < 7.4 GBq. We also investigated effects of previous radioiodine treatment and/or abnormal renal function on different MPA methods.

MATERIALS AND METHODS

Patients

Data were examined retrospectively for 65 patients (age = 60±14 years; 31 females; 34 males), studied from January, 2004 through October, 2016. Thirty-nine patients were referred to determine ^{131}I uptake and MPA for initial treatment following thyroidectomy, including 17 patients with compromised renal function and 22 patients with known (N = 16) or suspected (N = 6) metastases. Two patients were studied twice, and 2 patients were studied 3 times, so that there were a total of 71 studies. Standard patient preparation procedures prior to beginning ^{131}I dosimetry consisted of counseling patients to maintain a strict low-iodine diet for 2 weeks prior to beginning the procedure and ensuring that they were either hypothyroid with thyroid-stimulating hormone levels > 0.25 μIU/mL (N = 27 studies) (*15*), or had received thyrotropin alfa 0.9 mg on 2 consecutive days before I-131 administration (N = 44 studies). Determination of whether patients had abnormal renal function (AF) was assessed by examining laboratory reports, defined as blood urea nitrogen or creatinine levels exceeding referring laboratories' internally established normal limits.

The Institutional Review Board approved this retrospective study and the requirement to obtain informed consent was waived. All data were handled in compliance with the Health Insurance Portability and Accountability Act of 1996.

Data Acquisition

Dose to blood was determined by acquiring data using conventional techniques (6,7). On the first day, 3-4 mL of blood was withdrawn prior to ^{131}I administration and counted in a well counter (Perkin Elmer 2470 gamma counter (2" crystal), Waltham, MA) for initial background activity determination. An uncollimated gamma camera detector was peaked on ^{131}I (15% energy window) and positioned at a fixed location. All subsequent camera measurements were performed on the same gamma camera with fixed camera configuration and energy settings. A ^{131}I calibration source verified consistent camera operation from one whole-body counting session to another.

One hour after ^{131}I administration, the patient began whole-body counting. Background and calibration counts were obtained at the beginning of each camera counting session, followed by anterior and posterior counts of the patient. Initial patient counts were acquired 1 hour after ^{131}I administration, measurement of which constituted 100% of counts. This process was repeated at 4, 24 and 48 hours. At 48 hours, background-corrected and decay-corrected conjugate-view counts were used to estimate the per cent retained activity. If $< 60\%$ of initial activity was retained, patients returned at 72 and 96 hours; if $\geq 60\%$ was retained, patients returned at 96 and 144 hours, but not at 72 hours. All counts were acquired for 1 minute.

Blood samples (3-4 mL) were drawn within one hour of each camera counting session. At the end of all counting sessions (i.e., 96–144 hours after capsule ingestion), 1-mL aliquots of whole blood collected throughout the week were counted in a well counter, along with a ^{131}I calibration capsule and a 1-mL water sample for background.

Data Processing

All measurements were entered into a spreadsheet (Excel, Microsoft Inc). Counts were corrected for background radiation and radioactive decay to the time of administration.

Method-1: Conventional Approach.

To accommodate multiple biologic compartments with different excretion rates (7), biologic excretion was assumed to be modeled as a series of mono-exponential functions between each pair of time points with transitory washout rate λ_i starting from time point (t_i). Cumulated activity was computed between each pair of time points as:

$$(R_\gamma(t_{i+1}) - R_\gamma(t_i))/\lambda_i \qquad \text{Equation 1}$$

for per cent retained whole-body gamma activity $R_\gamma(t_i)$. Each transitory decay constant λ_i was estimated as:

$$\ln(R_\gamma(t_i)/R_\gamma(t_{i+1}))/(t_{i+1} - t_i) \qquad \text{Equation 2}$$

We assumed there was no further biologic excretion by the last time point, t_{final}, so that terminal cumulated activity was estimated using physical radioactive decay only:

$$t_{physical} \text{ x } R_\gamma(t_{final}) / \ln (2) \qquad \text{Equation 3}$$

for ^{131}I physical half-life $t_{physical}$ = 8.03 days, and final whole body counting per cent retention $R_\gamma(t_{final})$ at the time of the final measurement. The sum of all cumulated activities yielded total cumulated activity, A_γ. Dose to blood in units of cGy/GBq of ^{131}I, due to the gamma component (*16*), was:

$$D_\gamma = 0.0141 \text{ x } A_\gamma \text{ x } G/W \qquad \text{Equation 4}$$

where G is an adjustment for body habitus (*17*), W is patient weight in Kg, and 0.0141 is the S-factor of dose to blood due to whole body ^{131}I gamma emissions (*16*).

Blood sample data were handled in a manner similar to whole-body count measurements, except for the initial time, as blood was not drawn until 4 hours after capsule ingestion. At time 0, per cent retention was estimated as:

$$100\%/(0.2 \times W) \qquad \text{Equation 5}$$

immediately following capsule ingestion, assuming patient blood volume is 20% of body weight (*16*). Blood sample well counter readings were calibrated to true activity using the ^{131}I calibration capsule to convert counts into % retained activity. Cumulated activities of blood samples for emitted betas, A_β, were computed similarly to the manner described for whole-body gamma camera counts, assuming excretion modeled as mono-exponential functions between time points. Beyond the final blood measurement the final additional number of emitted betas was estimated as:

$$t_{physical} \times R_\beta(t_{final}) / \ln(2) \qquad \text{Equation 6}$$

for final blood sample per cent retention $R_\beta(t_{final})$. Dose to blood due to the beta component, D_β, in units of cGy/GBq was:

$$D_\beta = 2.59 \times A_\beta \qquad \text{Equation 7}$$

where 2.59 is the S-factor for dose to blood caused by ^{131}I beta emissions within the blood itself (*16*). Adding the two dose estimates D_γ and D_β provided Method #1 total radiation dose to blood forming organs D_{Total} in units of cGy/GBq. Limiting the blood absorbed dose to 200 cGy yielded the MPA for Method-1:

$$MPA = 200 \text{ cGy}/D_{Total} \qquad \text{Equation 8}$$

Method-2: Blood Measurements Only.

Linear regression defined empirically association between D_{β} and D_{Total} by Method #1, without reference to computed D_{γ} values. Linear regression intercept and slope predicted D_{Total} from blood measurements alone, Method-2 Dose. The MPA for Method-2 was 200 cGy/Method-2 Dose.

Method-3: Whole-Body Camera Measurements Only.

Linear regression was defined empirically as the association between D_{γ} and D_{Total} by Method-1, without reference to computed D_{β} values. Linear regression intercept and slope predicted D_{Total} based on gamma camera measurements alone, Method-3 Dose. The MPA for Method-3 was 200 cGy/Method-3 Dose.

Method-4: 48-Hour Whole-Body Camera Measurements Only.

Method-4 used whole-body gamma camera conjugate counts only for the 48-hour imaging session (*13*), from which dose to blood forming organs adjusted for patient height, weight and blood volume (BLV) was computed as

Dose/Activity (mGy/MBq) =

$$((15.12/BLV) + (0.0188/W^{2/3}) \times (-t_{48}/\ln(R_{\gamma}(t_{48})) \quad \text{Equation 9}$$

where t_{48} was the time of the single imaging session in units of hours 48 hours after ingestion of ^{131}I capsule tracer activity, and BLV(mL) (*18*) :

$$BLV(mL) = 31.9 \times H + 26.3 \times W - 2402 \text{ for males} \quad \text{Equation 10}$$

$$BLV(mL) = 56.9 \times H + 14.1 \times W - 6460 \text{ for females} \quad \text{Equation 11}$$

for height H in cm and weight W in kg. MPA for Method-4 was 200 cGy/ D_{Total} for D_{Total} by Method-4 (Equation 9).

Statistical Analysis

Analyses were performed using commercially available software ("Medcalc," Version 7.5.0.0., Medcalc Software, Inc., Mariakerke, Belgium). Values are reported as means ± one standard deviation. Continuous variables were assessed by the chi-square test to determine normality of distribution. The unpaired or paired t-test, as appropriate, compared values between groups for continuous variables that were normally distributed; otherwise, the Wilcoxon test was used. Frequencies and percentages characterized categorical variables. Chi-squared analysis of proportions compared ratios. Linear regression tested correlations between continuous variables, and Bland-Altman analysis quantified trend and bias. The kappa statistic determined strength of agreement among Methods 2-4 to identify cases for which Method-1 determined MPA < 7.4 GBq (*19*), and McNemar's test evaluated significance of differences among methods.

For all tests, probability (p) < 0.05 was defined as statistically significant.

RESULTS

D_{Total} Comparisons

D_β contributed 70±7% (47%-85%) to D_{Total}, and D_γ contributed 30±7% (15%-53%). D_{Total} correlated with D_β, with $r = 0.98$. Method-2 total dose predicted from well counter measurements alone was:

$$\text{Method-2 Dose} = -0.02 + 1.49 \times D_\beta \qquad \text{Equation 12}$$

D_{Total} correlated with D_γ, with r = 0.95. Method-3 total dose predicted from camera measurements alone was:

$$\text{Method-3 Dose} = 0.15 + 2.54 \times D_\gamma \qquad \text{Equation 13}$$

Method-1 doses were not normally distributed (35.3, $p < 0.0001$). Blood dose predicted by Method-2 was similar to Method-1 (21.0±13.7 cGy/GBq versus 21.0±14.1 cGy/GBq, p = 0.11), as was Method-3 dose (20.9±13.7 cGy/GBq, p = 0.73), but Method-4 dose was significantly lower (16.3±14.8 cGy/GBq, $p < 0.0001$). Mean % error versus Method-1 dose was 0±6%, 2±11% and -13±21% for Method-2-4, respectively. Correlation with Method-1 was significantly stronger for Method-2 than for Method-3 (r = 0.98 versus r = 0.94, p = 0.001), and Method-4 (r = 0.69, $p < 0.0001$) (Table 1). Bland-Altman limits of agreement were narrowest for Method-2 (-5.6 to +5.6 cGy/GBq), wider for Method-3 and widest for Method-4 (-26.8 to +17.5 cGy/GBq) (Figure 1).

Maximum Permissible Activity (MPA) Comparisons

Method-2 MPA was similar to Method-1 MPA (14.4±9.0 versus 14.5±9.3 GBq, p = 0.05), but MPA values were different from Method-1 estimates for both Method-3 (13.2±6.7 GBq, p = 0.01), and Method-4 (19.1±11.1 GBq, $p < 0.0001$). Mean % error versus Method-1 MPA was 0±6%, -2±11% and 13±21% for Method-2-4, respectively. Correlation with conventional Method-1 MPA was strongest for Method-2 (r = 0.99), less strong ($p < 0.0001$) for Method-3 (r = 0.95), and least strong ($p < 0.0001$) for Method-4 (r = 0.75) (Table 2). Bland-Altman analyses indicated slopes (trends) were not significant for Method-2 but were for Methods 3 and 4. Bland-Altman limits of agreement with Method-1 was smallest for Method-2 (-2.7 to +2.5 GBq), larger for Method-3 and largest for Method-4 (-9.8 to +19.0 GBq), (Figure 2).

MPA < 7.4 Gbq

Method-1 indicated that in 22 cases (31%), MPA should be less 7.4 GBq (200 mCi), the empiric activity many institutions choose to administer (5). Using Method-1 as the reference standard, the kappa statistic indicated best agreement with Method-1 for identifying which patients should have administered activity limited < 7.4 GBq was for Method-2, and weakest agreement for Method-4 (Table 3) (*19*). Case categorization differences were not significant between Methods-1-3, but were different for Method-4 (12.1%, McNemar's p=0.02) (Table 3). Sensitivity to identify cases for which Method-1 required MPA < 7.4 GBq was higher for Method-2 (20/22 cases) than for Method-4 (10/22 cases) (91% versus 45%, p = 0.004).

Of the 2 cases missed by Method-2, MPA was estimated to be 7.7 and 10.4 GBq by Method-2 compared to 6.1 and 7.1 GBq by conventional Method-1.

Previous Treatment and Abnormal Renal Function

Of the 71 studies, 32 (45%) had previous treatment (PT+) and 39 (55%) did not (PT-), while 23 studies (32%) had abnormal renal function (AF+) and 48 (68%) did not (AF-). Method-1 D_{Total} was different among these 4 patient groups (F-ratio = 9.1, p < 0.001), as was conventional MPA (F-ratio = 15.0, p < 0.001). Patients with abnormal renal function had higher D_{Total} (30.3±10.2 versus 16.5±13.9 cGy/GBq, p = 0.0001), and lower MPA (7.4±2.5 versus 18.0±9.4 GBq, p < 0.0001) than patients with normal renal function. Patients previously treated had lower D_{Total} (16.2±12.7 versus 45.9±14.3 cGy/GBq, p = 0.01), and higher MPA (18.6±10.2 versus 11.2±6.8 GBq, p = 0.001).

For all 71 sets of measurements, D_{Total} was similar for Method-1 & Method-2 (21±14 versus 21±14 cGy/GBq, p=0.97), as was MPA (14.5±9.3 versus 14.4±9.0 GBq, p=0.38). This was the case for each patient subgroup (Tables 4, 5).

Correlation of Method-2 to Method-1 MPA was similar for PT-, PT+, AF- and AF+ subgroups (r = 0.98, 0.99, 0.99 & 0.94, respectively). Camera-only Method-3 dose estimates differed from conventional estimates for the PT+ &AF- group, and Method-3 MPA differed for both PT+ &AF- and PT- &AF+ groups, while 48-hr camera-only Method-4 dose estimates differed from conventional values for PT- &AF- and PT- &AF- groups, and Method-4 MPA differed for PT- &AF- and PT+ &AF+ groups (Table 4 and Table 5).

DISCUSSION

Our main finding was that blood sampling alone suffices to estimate ^{131}I MPA, even for patients with abnormal renal function.

The 2012 Society of Nuclear Medicine and Molecular Imaging guidelines indicates that ^{131}I activity required for thyroid remnant ablation varies with the risk of distant metastases or recurrence of disease (*14*). In many institutions a fixed empiric dose regimen is followed involving administration of 5.55-9.25 GBq (150-250 mCi) of ^{131}I, but that approach can lead to under-treating some patients while over-treating others with radiation dose > 200 cGy to blood, particularly in older patients (*20*). It is generally accepted that total dose to blood should be less than 200 cGy (*21*).

Optimizing ^{131}I activity for treatment of thyroid cancer has received considerable attention in recent years (*22*,*23*). Some investigations have reported higher success rates are obtained

with higher administered activity (2.22-3.70 GBq compared to 1.11 GBq) (2,*24*). Aggressive protocols employ repeated empiric activities of 11.1 GBq (300 mCi) at 3-month intervals (*25*). Even higher activities (38.5 GBq ^{131}I) have been used; while successfully treating thyroid cancer, these protocols sometimes necessitate hospital admission for pancytopenia (*26*). Contravening these approaches is the precaution of limiting blood dose < 200 cGy to avoid leukopenia and thrombocytopenia (6,7). So, while higher doses are recommended for patients with metastatic disease, activities usually are recommended to be below 7.4 GBq to avoid serious complications affecting bone marrow (3,*27*).

Despite being the preferred approach, conventional MPA methods are time consuming, requiring as long as 7 days for prolonged iodine retention, motivating investigations to simplify these procedures. It is not surprising that Method-2 using multiple blood samples over time agreed with the conventional method more closely than the Method-4 single 48-hour camera measurement. In contrast to blood samples that are processed on the same day under the same conditions, camera measurements performed over several days involve inherently more sources of variability, including patient positioning, and count variations due to different ^{131}I activity distributions in various organ systems over time. For Method-4 (*13*), variability is exacerbated by not knowing if a single 48-hour measurement is representative of ^{131}I excretion over time. An alternative camera-only method predicting MPA from 48-hour % retention by a non-linear bi-exponential model reported standard deviation of 14.3% (*28*), similar to the 21% standard deviation we found for Method-4, and substantially higher than the 6% standard deviation we found for Method-2. With standard error of 10%, Method-3's camera measurements at multiple time points agreed more closely with conventional techniques than Method-4's use of a single time point, comparable to an earlier camera-only method that had standard error of 11% (*12*),

but Method-3 nonetheless showed a weaker correlation than Method-2's use of blood measurements alone.

One study found that 96-hour blood sampling combined with 24-hour or 48-hour sampling yielded predictions closest to conventional MPA, but still required initial camera and blood measurements (*29*). In contrast, our Method-2 uses no camera measurements. Our finding of lower MPA for patients with abnormal renal function agrees with reports of prolonged ^{131}I excretion delivering high dose in these individuals (*30*). That Method-2 agreed well with conventional values for patients with abnormal renal clearance was reassuring, as this group of patients is particularly concerning.

Limitations

Our investigation addressed the narrow question of whether conventionally estimated ^{131}I radiation dose can be predicted by blood measurements alone. Protocols have been proposed to quantify radiation dose by ^{131}I tomography (*31*), but tomography was not part of our study, and there was no other independent reference standard available for definitively identifying intrinsic radiation dose delivered to our patients. A relevant question to answer is the degree to which specific radiation doses succeed in treating thyroid cancer. Therapy success rates are reported to correlate with dose to blood rather than to administered activity (*32*), while increasing activity > 5.55 GBq did not increase blood dose (3). So, whether patients actually have different outcomes by receiving an empirical amount of activity, such as all patients receiving 7.4 GBq, as opposed to following a dosing regimen based on estimating MPA, has yet to be proven. Conducting a prospective outcomes study of that nature would be difficult, for which satisfying ethical concerns would be challenging.

CONCLUSION

Because calculated MPA based on blood measurements alone is comparable to MPA obtained with combined body counting and blood sampling, blood measurements alone are sufficient for determining MPA, even in patients with metastatic thyroid carcinoma or compromised renal function.

DISCLOSURES

No authors have any disclosures relevant to this investigation.

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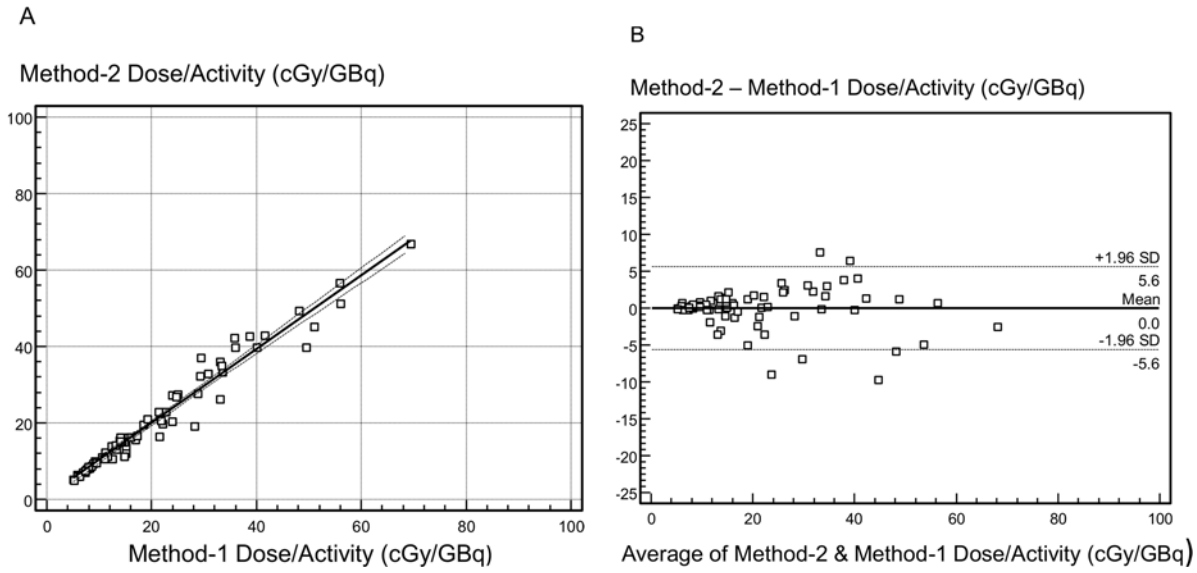

FIGURE 1. Linear regression (A) and Bland-Altman plot (B) for Method-2 versus Method-1 dose.

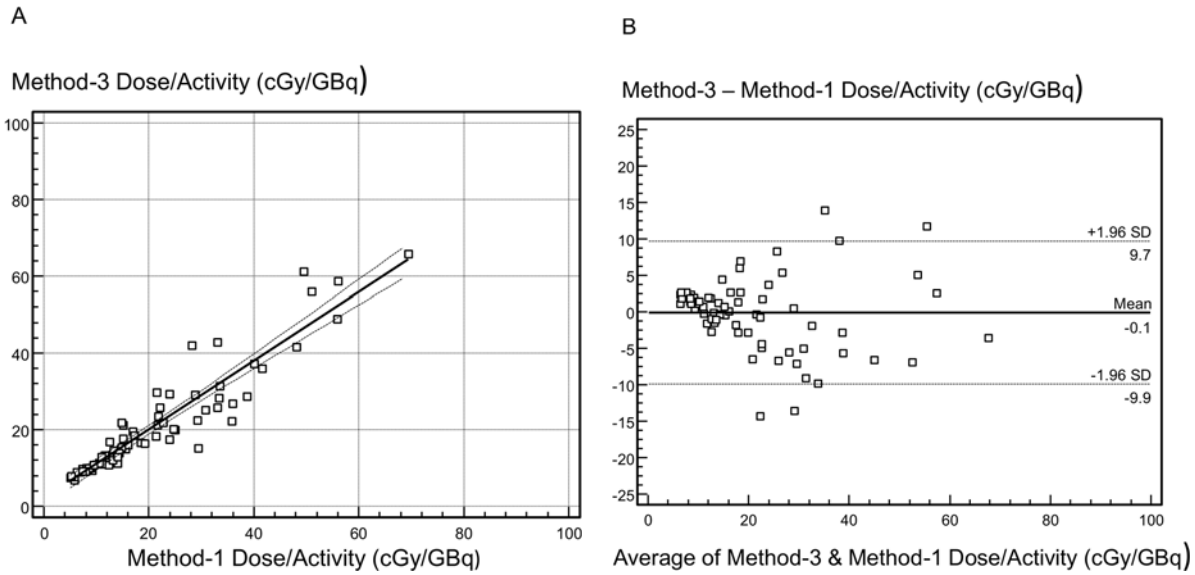

FIGURE 2. Linear regression (A) and Bland-Altman plot (B) for Method-3 versus Method-1 dose.

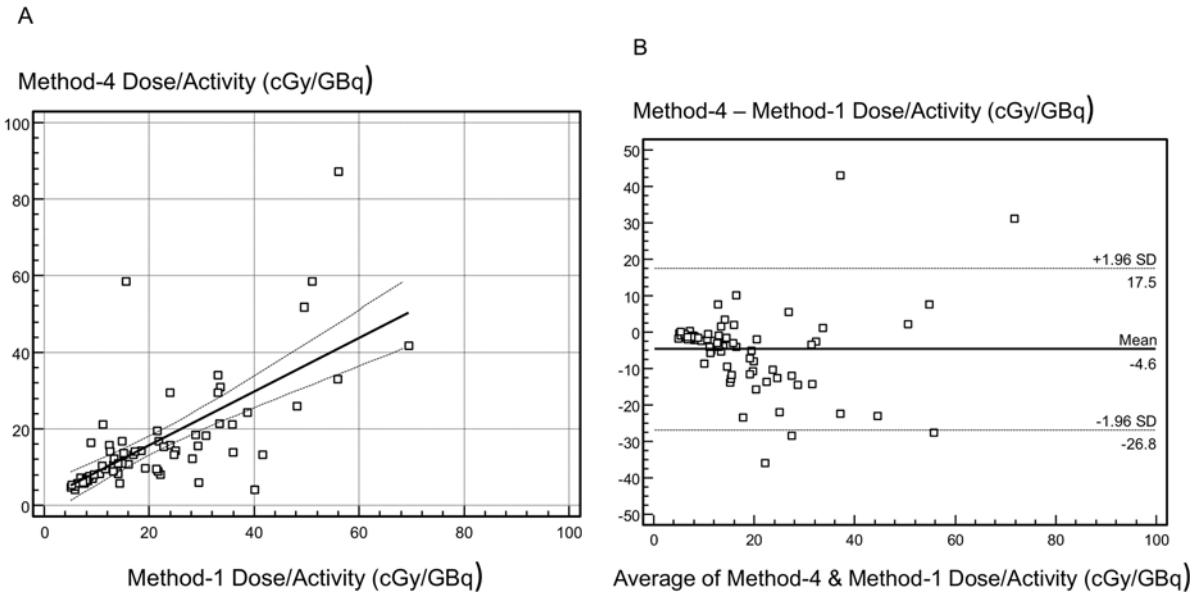

FIGURE 3. Linear regression (A) and Bland-Altman plot (B) for Method-4 versus Method-1 dose.

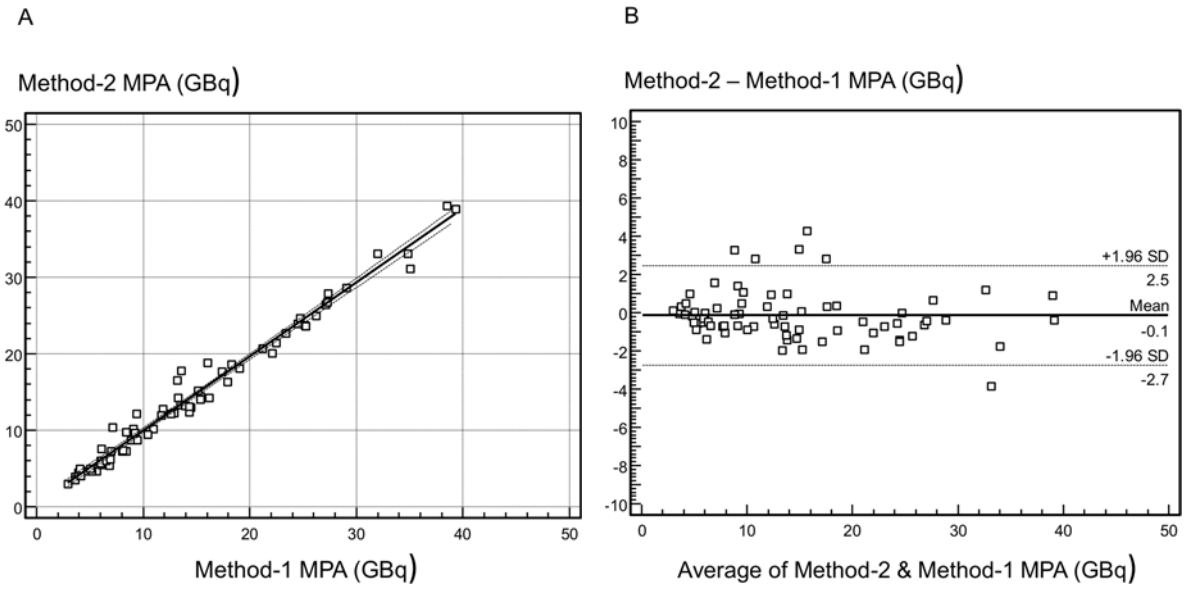

FIGURE 4. Linear regression (A) and Bland-Altman plots (B) for Method-2 maximum permissible activity (MPA) versus Method-1.

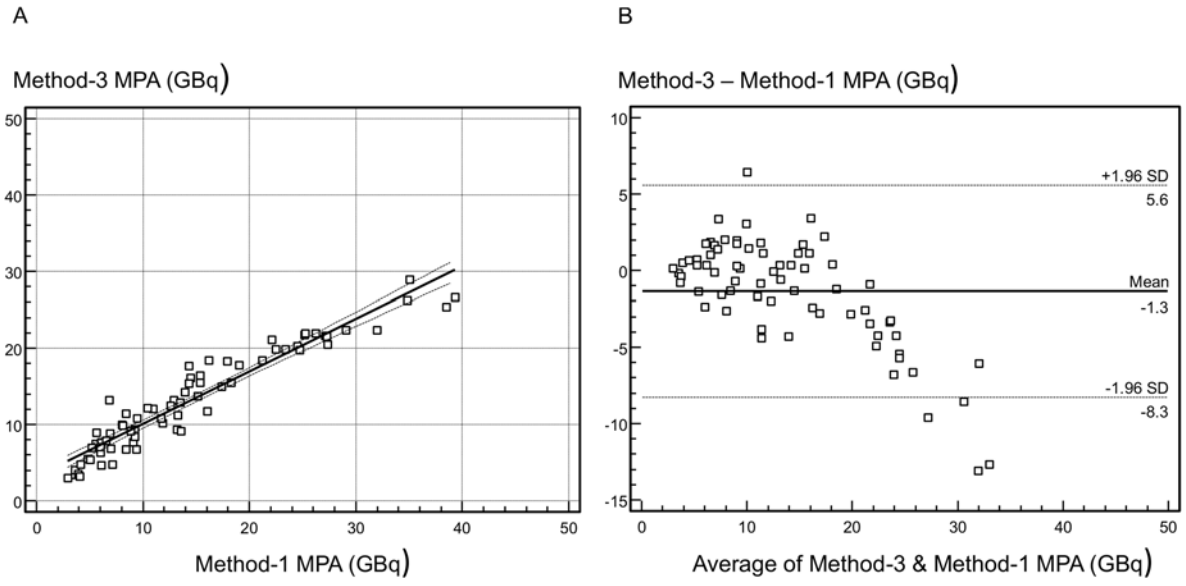

FIGURE 5. Linear regression (A) and Bland-Altman plots (B) for Method-3 MPA versus Method-1.

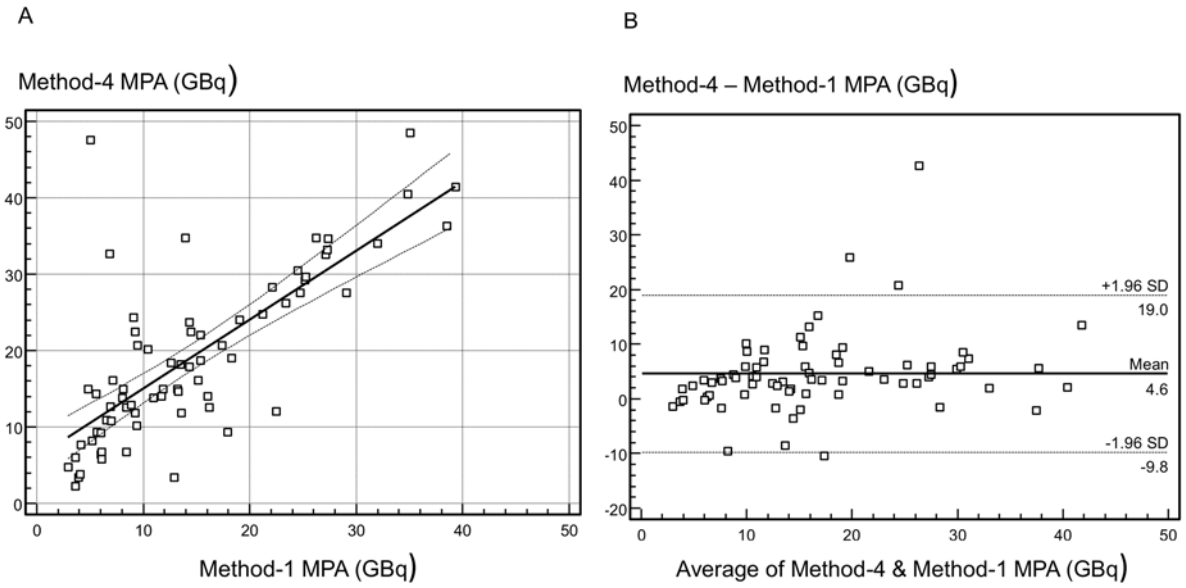

FIGURE 6. Linear regression (A) and Bland-Altman plots (B) for Method-4 MPA versus Method-1.

TABLE 1. Linear regression and Bland-Altman comparisons versus conventional Method-1 of alternative methods to compute total blood dose.

	Blood only Method-2	Camera only Method-3	48-hr camera only Method-4
Regression r	0.98, p <0.0001	0.94,* p<0.0001	0.69,* p<0.0001
Regression intercept	0.7±0.6 cGy/GBq, p=0.22	2.1±1.0 cGy/GBq,* p=0.05	1.6±2.2 cGy/GBq, p=0.49
Regression slope	0.97±0.02, p<0.0001	0.90±0.04,* p<0.0001	0.70±0.09,* p<0.0001
Bland-Altman r	-0.07, p=0.54	-0.12, p=0.31	0.02, p=0.84
Bland-Altman intercept	0.3±0.6 cGy/GBq, p=0.59	0.8±1.1 cGy/GBq,* p=0.44	-5. 0±2.3 cGy/GBq,* p=0.04
Bland-Altman slope	-0.01±0.02, p=0.54	-0.04±0.04,* p=0.31	0.02±0.10,* p=0.84

* $p < 0.05$ versus Method-2

TABLE 2. Linear regression and Bland-Altman comparisons among methods of maximum permissible dose, MPA.

	Blood only Method-2	Camera only Method-3	48-hr camera only Method-4
Regression r	0.99, p<0.0001	0.95,* p<0.0001	0.75,* p<0.0001
Regression intercept	0.4±0.3 GBq, p=0.20	3.2±0.5 GBq,* p<0.0001	6.1±1.6 GBq,* p=0.0001
Regression slope	0.96±0.02, p<0.0001	0.69±0.03,* p<0.0001	0.86±0.09, p<0.0001
Bland-Altman r	-0.18, p=0.14	-0.74,* p<0.0001	0.26,* p=0.03
Bland-Altman intercept	0.2±0.3 GBq, p=0.43	3.3±0.6 GBq,* p<0.0001	1.2±1.7 GBq,* p=0.48
Bland-Altman slope	-0.03±0.02, p=0.14	-0.33±0.04,* p<0.0001	0.20±0.09,* p=0.03

* $p < 0.05$ versus Method-2

TABLE 3. Comparison of Methods 2-4 against cases for which MPA < 7.4 GBq by conventional Method-1.

	Blood only Method-2	Camera only Method-3	48-hr camera only Method-4
κ (agreement)	0.86 ("very good")	0.70* ("good")	0.43* ("moderate")
McNemar Δ	0.0%, p = 0.62	5.6%, p = 0.29	14.1%,* p=0.02
sensitivity	90%	70%	40%*
specificity	96%	96%	96%
accuracy	94%	89%	80%*
PPV	90%	88%	80%
NPV	96%	89%	80%*

* $p < 0.05$ versus Method-2

TABLE 4. Comparison of dose estimates of Methods 2-4 against conventional Method-1 dose estimates for patients grouped by prior treatments and abnormal renal function.

	Conventional Method-1	Blood only Method-2	Camera only Method-3	48-hr camera only Method-4
PT+ & AF- (N=26)	12±9 cG/GBq	12±9 cG/GBq, p = 0.63	13±8 cG/GBq,* p = 0.03	13±11 cG/GBq, p = 0.76
PT- & AF- (N=22)	22±17 cG/GBq	21±16 cG/GBq, p=0.22	23±17 cG/GBq, p=0.25	14±12 cG/GBq,* p=0.002
PT- & AF+ (N=17)	29±9 cG/GBq	30±10 cG/GBq, p=0.54	27±11 cG/GBq, p=0.17	20±13 cG/GBq,* p=0.0008
PT+ & AF+ (N=6)	34±13 cG/GBq	35±11 cG/GBq, p=0.51	30±14 cG/GBq, p=0.11	29±29 cG/GBq, p=0.52

* $p < 0.05$ versus Method-1

PT+, patients who had prior ^{131}I treatment; PT-, patient who did not have prior ^{131}I treatment; AF+, patients with abnormal renal function; AF-, patients with normal renal function

TABLE 5. Comparison of MPA of Methods 2-4 against conventional Method-1 MPA for patients grouped by prior treatments and abnormal renal function.

	Conventional Method-1	Blood only Method-2	Camera only Method-3	48-hr camera only Method-4
PT+ & AF- (N=26)	21.4±9.3 GBq	20.9±9.0 GBq, p=0.14	18.0±6.1 GBq,* p=0.0003	23.4±11.9 GBq, p=0.08
PT- & AF- (N=22)	13.9±7.8 GBq	14.1±7.7 GBq, p=0.61	12.6±6.2 GBq,* p=0.03	21.0±10.8 GBq, p=0.002
PT- & AF+ (N=17)	7.6±2.4 GBq	7.6±2.7 GBq, p=0.92	8.5±2.9 GBq, p=0.09	13.3±7.4 GBq,* p=0.003
PT+ & AF+ (N=6)	6.7±2.7 GBq	6.5±2.8 GBq, p=0.29	7.6±2.5 GBq, p=0.12	10.6±4.5 GBq,* p=0.04

* $p < 0.05$ versus Method-1

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