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Technical Note: Determination of individual thyroid clearance effective half-life with a common handheld electronic dosimeter

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Abstract

Purpose: To determine the thyroid clearance effective half-life ($\mathcal{T}$) with a common handheld electronic dosimeter (ED) in patients undergoing radioiodine treatment for hyperthyroidism.

Methods: Dose rates from twelve inpatients were measured daily with an ED and with a clinical uptake counter. The ED was attached to the patient with two different setups, one using a cervical collar and another employing a neck strap. Estimation of $\mathcal{T}$ was performed by linear regression analysis of the log of both the ED and the uptake counter measurements versus time. The latter provided the reference data.

Results: Based on repeated neck strap dose rate measurements, individual $\mathcal{T}$s were determined with clinically required accuracy. The mean difference from the reference method equaled to -0.09±0.35 days.

Conclusions: Determination of individual $\mathcal{T}$ is feasible with a common handheld ED using the simple and easy to instruct neck strap measurement setup. This simple method complements stationary uptake counter measurements and thus may improve the accuracy of radioiodine treatment planning by adding an individual $\mathcal{T}$ for dose calculation..

Key words: thyroid, hyperthyroidism, radioiodine, effective half-life, electronic dosimeter

Introduction

Since its introduction more than seven decades ago, radioiodine (^{131}I) has become a standard treatment of hyperthyroidism [1]. As for all radio-therapeutic treatments, prescribed radiation doses in the thyroid gland should be planned individually to avoid overdosing and to minimize radiation burden to non-target organs [2-4]. The necessary ^{131}I activity to deposit a desired radiation dose depends amongst other factors on thyroid mass, thyroidal uptake, and uptake kinetics. A two compartment model is being used to model ^{131}I uptake kinetics [4]. However, three or more uptake measurements are suggested, namely between 4 to 6 h, 1 to 2 days and 5 to 8 days after administration of radioiodine. This practice is time consuming and often not practicable in an outpatient setting.

Given the effort and complexity of repeated uptake measurements using a calibrated stationary thyroid uptake counter on an outpatient basis, disease specific mean effective half-lives ($\mathcal{T}_{\mathrm{disease}}$) are usually employed in clinical routine instead of individually measured thyroid clearance effective half-lives ($\mathcal{T}$) [3, 5]. This semi-individual approach remains inaccurate in a substantial proportion of patients, as individual $\mathcal{T}$-values may differ considerably from $\mathcal{T}_{\mathrm{disease}}$ [6]. Therefore, an alternative to stationary thyroid uptake counter measurements is desirable to make individual $\mathcal{T}$-values available for dosimetry.

Within a quality assurance project for stationary uptake counters, a common electronic dosimeter (ED) was used for auxiliary measurements. These measurements, in a controlled setup on inpatients undergoing radioiodine treatment, allowed us to investigate the feasibility and accuracy of determining $\mathcal{T}$ by measurements with a common handheld ED.

Material and Methods

Thyroid clearance effective half-live $\mathcal{T}$ was determined in twelve patients undergoing radioiodine treatment for hyperthyroidism (Graves' disease, n=7; toxic adenoma, n=2; toxic multinodular goiter, n=3) based on measurements with a handheld ED. A dedicated thyroid uptake counter served as the reference method. The additional dose rate measurements had no influence on radioiodine therapy conduction or on the discharge of patients. All study participants provided informed consent and their data were processed anonymously.

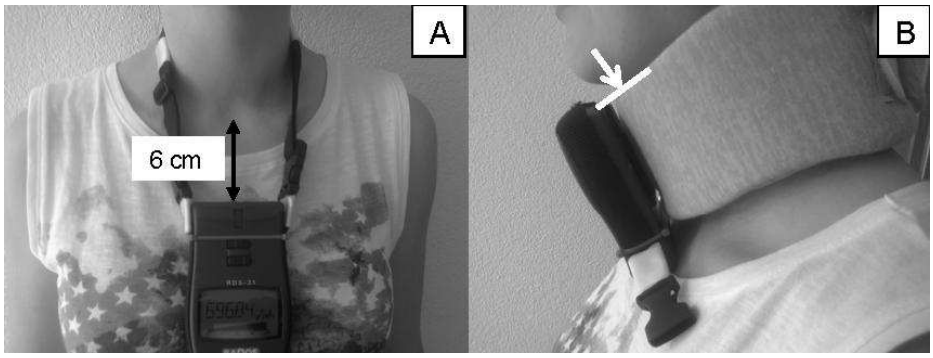
Dose rate measurements were performed with four multi-purpose survey meters (RDS-31, MIRION Technologies RADOS Oy, Finland). The technical datasheet specifies a dose rate linearity of ±15 % in the range from 0.05 μSv·h^{-1} to 0.1 Sv·h^{-1}. The dose rate linearity of all EDs was verified by comparing the measured dose rate $(\dot{D}_{\mathrm{ED}})$ of a decaying 2.1 GBq Technetium-99m (^{99m}Tc) source to its theoretical exponential decay $\dot{D}_{\mathrm{Tc-99m}}(t)$ (Equation 1). The radionuclide ^{99m}Tc was chosen for this test due to its short radioactive half-life of 6.02 h and its ubiquity.

$$\dot{D}_{\mathrm{Tc-99m}}(t) = \dot{D}_0 \cdot e^{-\lambda \cdot t} \qquad (1)$$

Here $\dot{D}_0$ equals the first measured value of $\dot{D}_{\mathrm{ED}}$, λ is the decay constant of ^{99m}Tc (0.115 h^{-1}) and *t* is decay time. For this measurement setup EDs were oriented with respect to the ^{99m}Tc-source, as the ED to the thyroid in the neck strap setup (FIG. 1A). The distance between the EDs and the ^{99m}Tc-source amounted to 8 cm and $\dot{D}_{\mathrm{ED}}$ values were stored every 5 min over the course of 5 half-lives.

Two different setups were investigated to reproducibly position the ED to the patient. In setup A (FIG. 1A), the ED was connected to a neck strap with quick release buckles and positioned 6 cm below the jugulum. All patients received an individual neck strap to ensure the same distance between ED and thyroid gland for repeated dose rate

measurements. In setup B (FIG. 1B), the ED was attached to a cervical collar with hook and loop fastener and was thereby closer to the thyroid gland. Measurements with both setups were performed twice per weekday and lasted a minimum of three



minutes each. Dose rate values were recorded automatically by the ED every 10 seconds, resulting in at least 18 recorded dose rate values per measurement. For further analysis, single dose rate values of one measurement were averaged and assigned to the time point corresponding to the center of the acquisition period. During measurements, patients were requested to cease any head and neck movements.

FIG. 1. The two setups used for dose rate measurements. Neck strap setup (A): The distance between the ED and the jugulum was about 6 cm. Cervical collar setup (B): The upper edges of the ED and the cervical collar were aligned for all patients (white arrow).

Reference measurements were performed with a dedicated thyroid uptake counter ISOMED 2162 (MED Nuklear-Medizintechnik Dresden GmbH, Germany). Whole body count rates were measured with and without shielded thyroid gland. The difference between the two measurements yielded the count rate due to the ^{131}I activity in the thyroid gland[1]. Each measurement lasted one minute and was performed twice every weekday until patient discharge.

Thyroid clearance effective half-lives derived from the thyroid uptake counter ($\mathcal{T}_{\mathrm{reference}}$), the neck strap ($\mathcal{T}_{\mathrm{strap}}$) and the cervical collar ($\mathcal{T}_{\mathrm{collar}}$) measurements were

[1] Manual Schilddrüsenprogramm Uptake 2000, Version 2.0.1.14, MED Dresden, Germany

obtained by log-linear regression analysis (SPSS Statistics Version 21.0, IBM, Armonk, NY). Only data points acquired 1.5 days after radioiodine administration were included in the analysis to ensure that measurements were performed during the clearance phase only (cf. *Supplemental Material*). The fit quality of the linear regression between averaged dose rates and uptake values versus time was measured with the coefficient of determination (R^2) [7]. Bland-Altman analysis was applied to assess differences between the three different $\mathcal{T}$s and $\mathcal{T}_{\mathrm{reference}}$.

$$\Delta_{\mathrm{strap}} = \mathcal{T}_{\mathrm{strap}} - \mathcal{T}_{\mathrm{reference}} \quad (2a)$$

$$\Delta_{\mathrm{collar}} = \mathcal{T}_{\mathrm{collar}} - \mathcal{T}_{\mathrm{reference}} \quad (2b)$$

$$\Delta_{\mathrm{disease}} = \mathcal{T}_{\mathrm{disease}} - \mathcal{T}_{\mathrm{reference}} \quad (2c)$$

Results

In FIG. 2 the percentage difference $\Delta\dot{D}/\dot{D}_{\mathrm{Tc-99m}}(t)$ between measured and theoretical dose rates is exemplarily shown for one ED

$$\Delta\dot{D} = \dot{D}_{\mathrm{ED}}(t) - \dot{D}_{\mathrm{Tc-99m}}(t) \quad (3)$$

as a function of $\dot{D}_{\mathrm{Tc-99m}}$. Percentage differences were less than 1 % for all EDs in the relevant dose rate range between 300 μSv·h^{-1} and ~4 *m*Sv·h^{-1}, demonstrating the suitability of the EDs to determine $\mathcal{T}$.

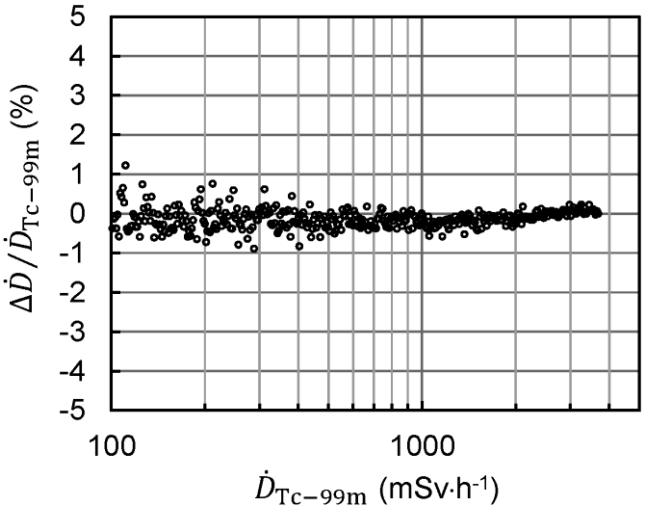


FIG. 2. Percentage difference between measured and theoretical dose rate responses of one ED in the radiation field of a decaying ^{99m}Tc source.

Dose rates measured with the neck strap and with the cervical collar setup covered a range from 350 to 1400 μSv·h^{-1} and from 700 to 4000 μSv·h^{-1}, respectively. Dose rate curves from both setups displayed similar shapes, but the cervical collar rates were positively offset from the neck strap dose rate curves (Figure 3). The average standard deviation of the single dose rate values $\dot{D}_{\mathrm{ED}}$ per measurement for all patients was 2.7 % (neck strap setup) and 3.2 % (cervical collar setup).

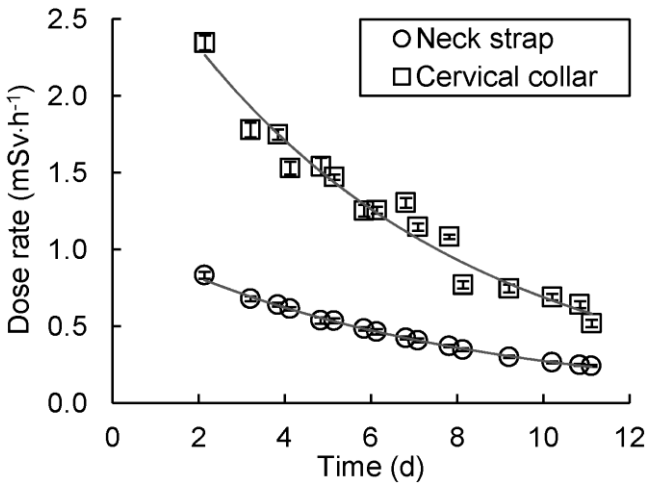


FIG. 3. Example of dose rate measurements of a single patient during hospitalization.

The thyroid clearance effective half-lives of $\mathcal{T}_{\mathrm{strap}}$, $\mathcal{T}_{\mathrm{collar}}$, $\mathcal{T}_{\mathrm{reference}}$ and $\mathcal{T}_{\mathrm{disease}}$ are shown in TABLE I. Considerable variations of $\mathcal{T}_{\mathrm{reference}}$ were observed for patients with Graves' disease (from 2.1 d to 7.0 d) and to a lesser extent for toxic multinodular goiter (from 5.0 d to 6.9 d) and for toxic adenoma (from 4.3 d to 5.3 d).

TABLE I. Comparison of disease specific standard effective half-lives $\mathcal{T}_{\mathbf{disease}}$ [5] and effective half-lives derived from the reference method (thyroid uptake counter) $\mathcal{T}_{\mathbf{reference}}$ and from ED dose rate measurements $\mathcal{T}_{\mathbf{strap}}$ and $\mathcal{T}_{\mathbf{collar}}$. The administered ^{131}I activity A for each patient is listed in the 2nd column.

Diagnosis	A (MBq)	$\mathcal{T}_{\mathrm{disease}}$ (d)	$\mathcal{T}_{\mathrm{reference}}$ (d)	R^2	$\mathcal{T}_{\mathrm{strap}}$ (d)	R^2	$\mathcal{T}_{\mathrm{collar}}$ (d)	R^2	Δ_{strap} (d)	Δ_{collar} (d)	$\Delta_{\mathrm{disease}}$ (d)
GD	684	5.4±1.6	7.0±0.1	1.00	7.5±0.1	1.00	6.9±0.3	0.95	0.4	-0.1	-1.6
GD	494	5.4±1.6	7.0±0.5	0.98	6.9±0.4	0.97	7.5±0.8	0.92	-0.1	0.5	-1.6
GD	451	5.4±1.6	5.7±0.8	0.93	5.4±0.3	0.97	6.4±0.4	0.96	-0.3	0.7	-0.3
GD	378	5.4±1.6	6.1±0.2	1.00	5.3±0.3	0.99	5.6±1.2	0.81	-0.7	-0.5	-0.7
GD	304	5.4±1.6	5.5±0.3	0.99	5.0±0.3	0.98	4.4±0.3	0.96	-0.6	-1.1	-0.1
GD	473	5.4±1.6	2.1±0.1	1.00	2.3±0.4	0.95	2.5±0.2	0.99	0.2	0.4	3.3
GD	271	5.4±1.6	6.8±2.0	0.92	6.7±1.5	0.91	3.5±0.8	0.91	-0.1	-3.3	-1.4
TMNG	745	6.6±1.2	5.0±0.2	0.99	5.1±0.1	1.00	4.6±0.2	0.96	0.1	-0.4	1.6
TMNG	555	6.6±1.2	6.9±0.4	0.98	6.7±0.6	0.93	6.8±0.8	0.89	-0.3	-0.1	-0.3
TMNG	763	6.6±1.2	5.5±0.1	1.00	5.6±0.1	0.99	6.2±0.2	0.99	0.1	0.8	1.1
TA	358	5.7±1.5	4.3±0.4	0.99	4.1±0.5	0.96	3.5±1.4	0.77	-0.3	-0.8	1.4
TA	533	5.7±1.5	5.3±0.2	0.99	5.6±0.2	0.99	5.9±0.3	0.95	0.3	0.6	0.4

Graves' disease (GD), toxic multinodular goiter (TMNG), toxic adenoma (TA)

The coefficients of determination R^2 were greater than or equal to 0.92 for $\mathcal{T}_{\mathrm{reference}}$, 0.91 for $\mathcal{T}_{\mathrm{strap}}$ and 0.77 for $\mathcal{T}_{\mathrm{collar}}$. The best estimate of $\mathcal{T}_{\mathrm{reference}}$ was provided by $\mathcal{T}_{\mathrm{strap}}$. The difference Δ_{strap} was smaller than Δ_{collar} in 9 out of 12 patients and smaller than or equal to $\Delta_{\mathrm{disease}}$ in 11 out of 12 patients. A Bland-Altman plot of $\mathcal{T}_{\mathrm{strap}}$ versus $\mathcal{T}_{\mathrm{reference}}$ placed all data points within the 95% confidence interval (FIG. 4). Mean difference and mean absolute deviation of Δ_{strap} were -0.09±0.35 d and 0.29±0.20 d, respectively.

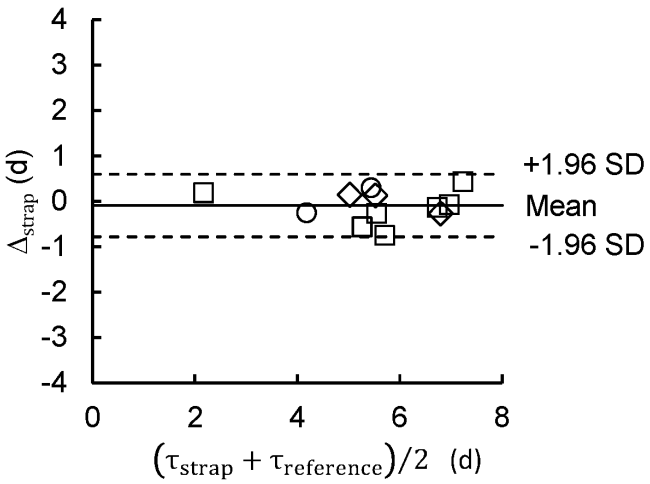


FIG. 4. Bland-Altman plot of $\boldsymbol{\mathcal{T}}_{\mathbf{strap}}$ versus $\boldsymbol{\mathcal{T}}_{\mathbf{reference}}$ Data labeled according to the underlying thyroid disease (GD (□), TA (○) and TMNG (◇)).

In FIG. 5 the Bland-Altman plot $\mathcal{T}_{\mathrm{collar}}$ versus $\mathcal{T}_{\mathrm{reference}}$. for the cervical collar setup is shown. For this setup mean difference and mean absolute deviation of Δ_{collar} yielded -0.27±1.13 d and 0.77±0.84 d, respectively.

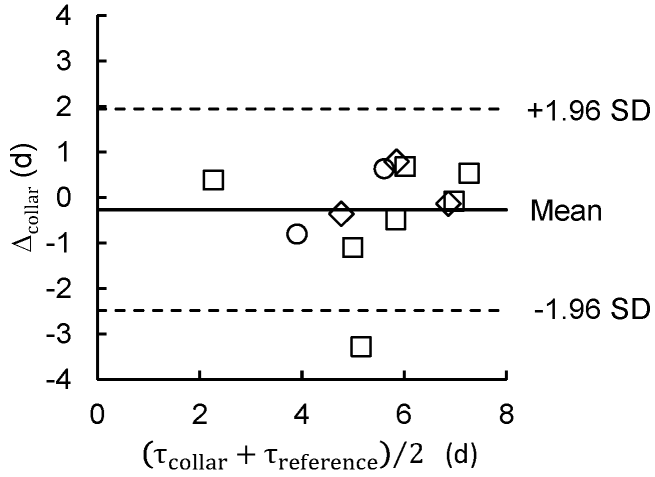


FIG. 5. Bland-Altman plot of $\mathcal{T}_{\mathbf{collar}}$ versus $\mathcal{T}_{\mathbf{reference}}$. Data labeled according to the underlying thyroid disease (GD (□), TA (○) and TMNG (◇)).

Discussion

The thyroid clearance effective half-life $\mathcal{T}_{\mathrm{strap}}$ determined with the neck strap setup agreed well with $\mathcal{T}_{\mathrm{reference}}$ from the reference method as verified by the small mean difference and standard deviation (SD) of -0.09±0.35 d. The mean difference and SD between the cervical collar setup $\mathcal{T}_{\mathrm{collar}}$ and $\mathcal{T}_{\mathrm{reference}}$ were larger and equaled -0.27±1.13 d. One reason for the larger SD is the outlier at Δ_{collar}=-3.3 d in FIG. 5. Assuming this data point was a still unclear measurement error, recalculating the mean difference yields 0.00±0.65 d. Even after exclusion of the outlier from the cervical collar setup data set, the neck strap setup remains superior due to its smaller SD. Another possible reason for the higher variance of the cervical collar setup is given by its proximal location to the thyroid. Here, steeper dose gradients will amplify positioning errors. This explanation is as well supported by the larger variation of R^2 values (TABLE I) encountered with the cervical collar setup. In contrast, the neck strap setup provided better reproducibility of the ED position with respect to the thyroid gland, and thus yielded better estimates of $\mathcal{T}$. It also appeared simpler and easier to

instruct compared to the cervical collar setup. Our data demonstrate the feasibility and accuracy of dose rate measurements using a neck strap setup to determine individual thyroid clearance effective half-lives in a therapeutic setting.

One limitation of the proposed method is that ED measurements are suited for effective half-life determination only. This restriction is caused by non-thyroid uptake contributions to the dose rate measurements. Only at times past the uptake maximum the ratio between the contribution of thyroid and non-thyroid uptake to the dose rate measurements approximates a steady state and allows for determination of the effective half-life by an ED. In addition, at the clearance phase the non-thyroid uptake is small compared to the uptake in the thyroid gland.

Absolute measurements, such as those of radioiodine uptake, still need to be obtained with calibrated thyroid uptake counters. Therefore, ED measurements can only supplement thyroid dosimetry, and necessitate at least one single stationary uptake measurement. Moreover, reproducibility of ED positioning on the patient may not be as precise as with dedicated thyroid uptake counters, and thus a higher number of dose rate measurements has to compensate for this higher uncertainty.

Given the high variability of individual and disease specific $\mathcal{T}$-values reported in the literature and also determined in our small patient sample, the use of standard effective half-lives $\mathcal{T}_{\mathrm{disease}}$ bear the risk of over- or under-treatment in a substantial portion of patients. While underdosing may not affect the clinical outcome, overdosing unnecessarily increases the radiation burden on healthy tissue [3, 6]. Accordingly, the Euratom Council directive states that individual dosimetry is strongly recommended in treatment planning in any radiation therapy [8]. In this context, neck strap setup ED measurements appear to be a promising method to determine individual patient $\mathcal{T}$ not only in the therapeutic, but also in the pre-therapeutic setting. The use of an individual $\mathcal{T}$ for radioiodine dose calculation, determined by portable radiation detector

measurements in an outpatient setting, could complement already common individual determinations of target thyroid tissue mass and uptake counter measurements in a simple and cost-effective way. In patients with hyperthyroidism, the availability of individual $\mathcal{T}$ to replace disease specific average half-lives would allow for an individually more accurate pre-therapeutic ^{131}I dosimetry, and reduces the risk of either under- or over-dosing.

Conclusion

In patients undergoing radioiodine treatment for hyperthyroidism, $\mathcal{T}$ could be determined with the clinically required accuracy from measurements with a common handheld ED. Of the two tested setups, the neck strap setup better fulfilled the requirement of reproducible ED positioning. The prospect of individual $\mathcal{T}$ determination based on outpatient measurements holds the potential for a simple and cost-efficient optimization of pre-therapeutic dosimetry in radioiodine treatment.

Acknowledgments

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Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the principles of the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Competing interests

None declared

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