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ORIGINAL ARTICLE

Determination of effective half-life of ^{131}I in patients with differentiated thyroid carcinoma: comparison of cystatin C and creatinine-based estimation of renal function

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Abstract

Purpose Renal function and effective half-life ($t_{1/2,eff}$) of I-131 have not been fully elucidated in patients undergoing radioiodine therapy (RAIT) for differentiated thyroid cancer (DTC). Aim of the present analysis was to evaluate the potential of cystatin C-based estimated glomerular filtration rate ($eGFR_{CysC}$) in comparison to conventional creatinine ($eGFR_{Crea}$) and to verify which methods to determine $t_{1/2,eff}$ are most accurate to predict $t_{1/2,eff}$.

Methods Forty-eight patients receiving whole-body I-131-scintigraphy were included. $eGFR_{CysC}$ was compared to $eGFR_{Crea}$ with regard to accuracy of $t_{1/2,eff}$ prediction. Three different methods (i.e. blood-based, gamma camera-based and probe-based) and two protocols with either three (short period,SP; up to 42 h) or four (long period,LP; up to 114 h) time points were compared using the Akaike's information criterion.

Results The $eGFR_{CysC}$ measurement is more likely than $eGFR_{Crea}$ in predicting the $t_{1/2,eff}$. High correlation coefficients were found between $t_{1/2,eff}$ assessed by gamma camera and probe measurements and blood-based determination revealed lower values. Patients with normal eGFR showed higher values of $t_{1/2,eff}$ of LP compared to SP.

Conclusions $eGFR_{CysC}$ should be included in further study protocols. As camera and probe measurements lead to almost superimposable results, one of the methods is expendable. Blood-based results of $t_{1/2,eff}$ were lower, presumably due to unspecific iodine retention, whereas the lower correlation with renal function may be caused by individual differences in intestinal iodine resorption. SP-protocols up to 42 h after I-131 administration are sufficient to determine $t_{1/2,eff}$. Further studies are necessary for specific recommendations regarding I-131 activity reduction during RAIT in patients with DTC and renal insufficiency.

Keywords Renal insufficiency · Thyroid Cancer · Radioiodine Therapy · Effective Half-life · eGFR

Introduction

Radioiodine therapy (RAIT) is a well-established method for the treatment of differentiated thyroid carcinoma (DTC). Usually, standard therapeutic activities of I-131 ranged from 1 to 11 GBq are administered without pretherapeutic dosimetry measurements [1–3]. As 90% of the I-131 is cleared through the kidneys [4], in patients with renal insufficiency, I-131 is excreted more slowly. Thus, these patients have markedly longer effective half-life times ($t_{1/2,eff}$) and hence higher radiation exposure [5]. This is particularly relevant in case of high-dose RAIT, in which the safety of blood and bone marrow represent a radiobiological limiting factor [6]. According to guidelines, the renal function, or estimated glomerular filtration rate (eGFR), must therefore be determined before any RAIT [1–3]; however, there are no specific recommendations on the percent reduction of the I-131 dose for renal patients not on dialysis.

Remarkably, systematic investigations concerning the relationship between eGFR and $t_{1/2,eff}$ after I-131 administration are rare. A retrospective study indicated that these parameters are significantly correlated and that decreasing levels of eGFR are associated with longer $t_{1/2,eff}$ [7]. All of the available literature regarding eGFR and $t_{1/2eff}$ during RAIT has focused on the creatinine-based eGFR ($eGFR_{Crea}$)

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Table 1 Overview of the study protocol

Day (d)	Timeline hour (h)	Week day	Patient status	rhTSH injection	eGFR measurement	Time point to determine $t_{1/2,eff}$
−2	−48	Mon	Out-patient	X		
−1	−24	Tue	Out-patient	X		
0	−4				X	
0	0	Wed	In-patient		Administration of 400 MBq I-131	
0	+1					X
+1	+18	Thu	In-patient			X
+2	+42	Fri	Discharge			X
+5	+114	Mon	Out-patient			X

rhTSH recombinant human thyroid stimulating factor, *eGFR* estimated glomerular filtration rate, $t_{1/2,eff}$ effective half-life

measurement. However, in the recent past, cystatin C ($eGFR_{CysC}$) has been described to be a suitable alternative, being more robust than creatinine [8, 9], as it is less dependent on variables, such as disease status, muscle mass, and nutrition [8].

Due to the lack of specific recommendations regarding activity reduction in case of RAIT, we planned to develop a mathematical model derived from prospectively acquired data. As a prerequisite, it is necessary to investigate the relationship between different eGFR measurements as well as different methods to determine $t_{1/2,eff}$.

Thus, the goals of this study were to (1) evaluate whether $eGFR_{CysC}$ is superior to $eGFR_{Crea}$ considering correlation with $t_{1/2,eff}$ in DTC patients receiving diagnostic activities of I-131; (2) investigate the influence of different methods to determine $t_{1/2,eff}$ (i.e. blood-based, gamma camera-based and probe-based), and (3) investigate the influence of short period (SP; up to 42 h) and long period (LP; up to 114 h) protocols.

Materials and methods

Ethics

All procedures performed were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments. Informed consent was obtained from all individual participants included in the study. The study has been approved by the institutional review board (registration number: 4533-08/15).

Inclusion and exclusion criteria, measurement protocol

The target population of this prospective study consisted of patients with DTC, aged >18 years, previously subjected to thyroidectomy. The main inclusion criteria were: at least one RAIT; admission for diagnostic in-patient I-131 administration; and stimulation with recombinant human thyroid stimulating hormone (rhTSH) (Thyrogen®; Genzyme, Cambridge, MA, USA). Exclusion criteria were: large residual thyroid tissue (iodine uptake >10%); inclusion in concurrent interventional studies; insufficient thyroid hormone substitution; or after hormonal withdrawal. The planned duration per patient was 8 days (Table 1).

After blood sampling for the determination of eGFR, all patients received oral administration of 400 MBq (10.8 mCi) ± 10% I-131. Data for different methods to determine $t_{1/2,eff}$ were collected at the time points 1, 18, 42, and 114 h post administration. The $t_{1/2,eff}$ was determined using either the first three values (42 h; short period, SP) or all four values (114 h; long period, LP). The patients were instructed to void the urinary bladder before radiotracer administration, and not to urinate in the first hour between the administration and the first time point. All other measurements took place after micturition.

Laboratory tests

Serum cystatin C levels were measured by particle-enhanced turbidimetry immunoassay (Cobas Integra® 400 plus analyzer, Roche Diagnostics GmbH, Mannheim, Germany). Serum creatinine levels were assessed kinetically by means of the Jaffé reaction (Abbott, Wiesbaden, Germany). Reference ranges were 0.61–0.95 mg/l for serum cystatin C and 58–96 µmol/l (exemplary patient: female, age 59 years) for serum creatinine, respectively. The renal function based on serum creatinine ($eGFR_{Crea}$) and serum cystatin C ($eGFR_{CysC}$) was calculated using the standard formulas of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) [8, 9]. The eGFR levels were classified in 5 stages of renal function according to the KDOQI criteria [10].

Sampling for blood-based determination of $t_{1/2,eff}$

Venous blood samples (2.7 ml in EDTA K-Monovette, Sarstedt AG & Co, Nümbrecht, Germany) were divided in four samples of 0.5 ml and subjected to well-counter measurement (ISOMED 2100, MED Nuklear-Medizintechnik

Dresden, Dresden, Germany) for 1 min after assessment of the background activity. An average was calculated from the four repeats for each measurement time point.

Whole-body measurements for camera-based determination of $t_{1/2,eff}$

A dual-head gamma camera system (Symbia S, Siemens Healthcare GmbH, Erlangen, Germany) equipped with high-energy collimators and the following parameters was used: energy window width 15%; scanning speed of whole-body acquisitions 15 cm/min; acquisition matrix for whole-body scans 1024 × 256; and deactivated autocontour. The patient was in supine position with arms parallel to the body. Special attention was paid that the body was fully included in the field-of-view. The program NukDos (NukDos V 1.1, BMBF 01EZ1130) was used to define a region of interest including the whole body.

Whole-body measurements for probe-based determination of $t_{1/2,eff}$

Probe measurement (NaI scintillator, ISOMED 2101, MED Nuklear-Medizintechnik Dresden, Dresden, Germany) was performed for 1 min. The distance between patient and detector was chosen as long as possible (limited by the room's dimension), i.e. 460 cm to minimize measurement errors due to patient positioning. Nevertheless, great attention was paid to maintain an identical positioning of each patient and thus to guarantee a reproducible measurement geometry. Measurements were performed from anterior and posterior. The background count rate was subtracted from the measured values.

Calculation of $t_{1/2,eff}$

Calculations and plottings were separately performed for SP (including the first three time points up to 42 h) and LP (including all 4 time points up to 114 h) using version 3.2.3 of the statistical computing environment "R" [11]. The $t_{1/2,eff}$ was calculated using a monoexponential decay model [12, 13]. The parameters (named "Activity" in the formula below) that were used to determine $t_{1/2,eff}$ for the blood-based method, camera-based method, and probe-based method were counts/minute, total counts, and counts/minute, respectively.

$t_{1/2,\ eff}$ was estimated by determining the linear least-squares estimate of the decay constant λ of the function

$$\ln(\text{activity}) = -\lambda \cdot t + b$$

and calculating $t_{1/2,\ eff}$ from "λ" by

$$t_{1/2,eff} = \ln(2)/\lambda.$$

Statistical analysis

For comparison of median $eGFR_{CysC}$ versus $eGFR_{Crea}$ a paired one-sided Wilcoxon signed-rank test was used. For the evaluation which eGFR measurement is more informative with respect to $t_{1/2,eff}$ the Akaike's information criterion (AIC) was calculated for all models using the function "AIC" from the R package "stats" [14]. The relative likelihood l_i for each alternative model "i" was then calculated according to Burnham et al.[15]: where AIC_{min} is the minimal AIC of all alternative models "i" of a single model response, calculate the relative likelihood l_i for each alternative model "i" as

$$l_i = \exp((AIC_{min} - AIC_i)/2).$$

Models with a relative likelihood $l_i < 0.05$ were considered unlikely to be more informative than the most likely model.

Additionally, for the evaluation of the relationship of eGFR and $t_{1/2,eff}$ as well as for the comparison between different methods to determine $t_{1/2,eff}$ the coefficient of determination (R^2) was calculated.

RESULTS

Patients

Eighty-seven consecutive patients referred between 13-Jan-2016 and 22-Mar-2017 for diagnostic whole-body I-131 scintigraphy in the context of RAIT of a DTC were asked for participation in the study. Fifty-one patients (59%) signed an informed consent. Three patients were excluded from the present analysis due to technical problems with methods to determine $t_{1/2,eff}$ or eGFR measurements. Thus, the present analysis was based on 48 patients (Table 2).

$t_{1/2,eff}$ assessed by $eGFR_{CysC}$ and $eGFR_{Crea}$

The $eGFR_{CysC}$ values were significantly lower than $eGFR_{Crea}$ (Table 3). The correlation between both parameters was $R^2 = 0.713$ (Fig. 1). Eight patients had an $eGFR_{Crea} < 60$ ml/min per 1.73 m^2 (17%). Based on the AIC statistical analyses, $eGFR_{CysC}$ measurement is more likely in comparison to the $eGFR_{Crea}$ in predicting the $t_{1/2,eff}$ (Table 4, Fig. 2).

$t_{1/2,eff}$ measured by blood, gamma camera, and probe

The $t_{1/2,eff}$ determined by gamma camera and probe measurements showed high correlation coefficients ($R^2 = 0.992$

for SP); whereas, the comparison of both whole-body methods with blood measurements resulted in a lower correlation (Fig. 3).

$t_{1/2,eff}$ determined by SP and LP protocols

The $t_{1/2,eff}$ ranged between 5.3 and 37.3 h (Table 5). Comparisons of the $t_{1/2,eff,SP}$ vs. $t_{1/2,eff,LP}$ results showed that, for patients with renal insufficiency, there was a high agreement (Fig. 4). In contrast, for patients with normal or minimal impaired renal function the $t_{1/2,eff,LP}$ was markedly longer than the $t_{1/2,eff,SP}$.

Discussion

Studies on the relationship between renal function and $t_{1/2,eff}$ of I-131 as primary end point are scarce. Some studies have focused on the impact of rhTSH on the eGFR in DTC patients undergoing RAIT, showing that the iatrogenic hormonal withdrawal leads to a worsening of the eGFR and to a prolongation of the $t_{1/2,eff}$ [16–24]. Other studies have focused on $t_{1/2,eff}$ in RAIT for benign thyroid diseases [25]. Also, while the studies performed thus far have assessed the eGFR using the creatinine-based method [17, 21, 23], to our knowledge there are no data on the use of the cystatin C-based method.

Some of the previous studies used high (therapeutic) activities between 1 and 10 GBq [16–18, 20, 24], whereas only one study used lower (diagnostic) doses [19]. Also, the study designs largely differed, for example one long-term study assessed the whole-body activity (via probe) and the blood-based activity at 6 time points (2–168 h); whereas, the whole-body gamma camera scans were performed at 3 time points (48–168 h) [16].

In contrast to the above-mentioned studies, one study specifically addressed the relationship between eGFR and half-life using both therapeutic and diagnostic activities [7]. Due to the retrospective nature of this study, measurements were not performed according to a precise study protocol, therefore data were considered prone to relatively large errors. A mathematical relationship was described, but this lacked sufficient quality to allow valid conclusions for clinical applications.

The clinical significance of a nephrogenic prolongation of $t_{1/2,eff}$ (and thus of higher radiation exposure of patients

Table 2 Patient characteristics ($n = 48$)

Characteristic	Value
Age (y)	
Median (range)	62.2 (26.5-87.5)
Mean ± SD	61.2 ± 15.02
Female patients (%)	29 (60.4)
Administered I-131 activity mean ± SD	409.6 ± 18.8 MBq

Table 3 Parameters of renal function

	Serum values		eGFR	
	Serum cystatin C (mg/l)	Serum creatinine (µmol/l)	$eGFR_{Crea}$ (ml/min per 1.73 m^2)	$eGFR_{CysC}$ (ml/min per 1.73 m^2)
Median (range)	0.94 (0.63–2.55)	71.5 (55–189)	87.1 (30.3–120.6)	82.2* (19.3–125.8)
Mean ± SD	1.04 ± 0.39	79.3 ± 25.1	82.4 ± 21.2	79.1 ± 25.6

$eGFR_{Crea}$ estimated glomerular filtration rate based on creatinine, *$eGFR_{CysC}$* estimated glomerular filtration rate based on cystatin C
*$p < 0.05$ vs. $eGFR_{Crea}$

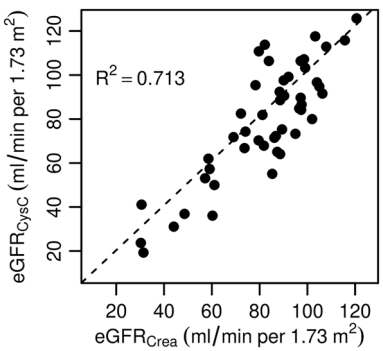

Fig. 1 Estimated glomerular filtration rate (eGFR) of creatinine ($eGFR_{Crea}$) plotted against eGFR of cystatin C ($eGFR_{CysC}$)

Table 4 Relative likelihoods of models based on different eGFR measurements

eGFR measurement	Relative likelihood of the model					
	$t_{1/2,eff}$ blood		$t_{1/2,eff}$ camera		$t_{1/2,eff}$ probe	
	SP	LP	SP	LP	SP	LP
Cystatin C	1[a]	1[a]	1[a]	1[a]	1[a]	1[a]
Creatinine	8.7E−03	1.3E−04	1.3E−04	4.8−E05	1.7E−05	1.6E−05

eGFR estimated glomerular filtration rate, *$t_{1/2,eff}$* effective half-life
[a]Most likely model

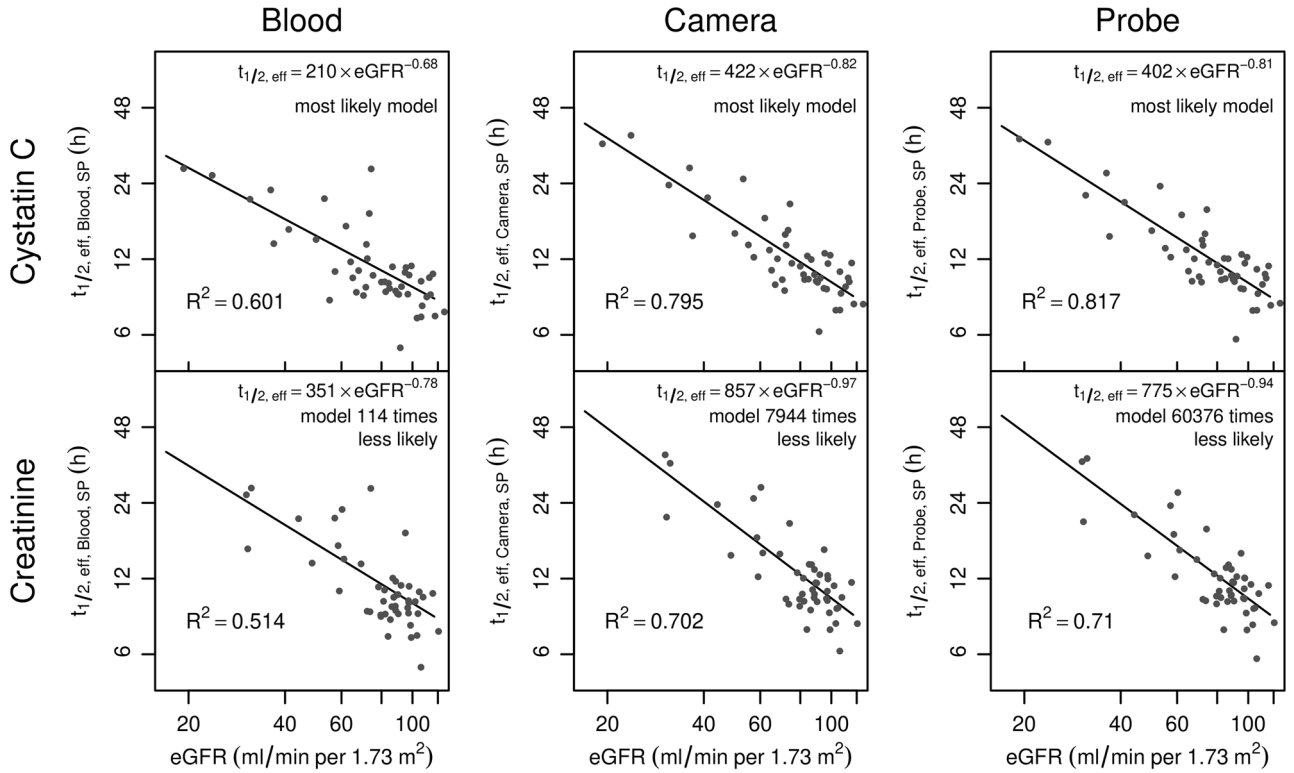

Fig. 2 Estimated $t_{1/2,eff,SP}$ plotted against estimated glomerular filtration rate (eGFR). GFR were estimated based on the concentrations of cystatin C (top row) or creatinine (bottom row). $t_{1/2,eff,SP}$ were estimated based on the three different methods: blood samples (first column), gamma camera scans (second column), and probe measurements (third column). The plotted lines show power functions fitted to the data. The resulting models are reported in the top right corner of each subplot. Models were compared column-wise using the Akaike's information criterion (AIC); the corresponding relative likelihood is reported in the top right corner of each plot. Models based on $eGFR_{CysC}$ are most likely. The coefficient of determination (R^2) of each model is also displayed

with renal insufficiency) is very high in patients receiving high-dose RAIT. However, in the present study, only patients scheduled for diagnostic whole-body I-131 scintigraphy receiving ~400 MBq were included due to three specific reasons: First, it has been shown that biokinetics of diagnostic and therapeutic activities are comparable [26]. Second, measurement errors due to dead-time effects are avoided [16]; and third, diagnostic whole-body I-131 scintigraphy is performed more frequently than high-dose RAIT, therefore shortening study recruitment time.

$eGFR_{CysC}$ and $eGFR_{Crea}$

Our results show significant lower values for $eGFR_{CysC}$ compared to $eGFR_{Crea}$ and a moderate correlation of both parameters (Fig. 1, Table 3). This is in line with previously published data [27, 28]. Intraindividual comparison of both parameters frequently leads to diverging results, either with higher $eGFR_{CysC}$ values or lower $eGFR_{CysC}$ values compared to the clinical standard $eGFR_{Crea}$. In general, slightly lower $eGFR_{CysC}$ values are most common. This is presumably attributable to patient-related factors, such as disease status, muscle mass, and nutrition as it is known that the standard method for the assessment of renal function using creatinine depends on these variables [8]. $eGFR_{CysC}$ is rapidly growing in importance in nephrology, particularly as confirmatory test after an initial serum creatinine test and is considered less dependent on these variables [9]. However, the $eGFR_{CysC}$ measurement is more expensive than determination of $eGFR_{Crea}$ (fivefold in our clinic) and may also depend on factors, such as diabetes, high body-mass-index, and inflammation [29].

The relationship between eGFR and $t_{1/,2eff}$ shows that the $eGFR_{CysC}$ measurement is more likely than $eGFR_{Crea}$ in predicting the $t_{1/2,eff}$ (Table 4). All three substances (creatinine, cystatin C, and iodine) are filtrated by the renal glomeruli [30–32]. The renal secretion process is not described for cystatin C and iodine, whereas it is known that 15% of the creatinine undergoes tubular secretion [33, 34]. The resorption process is very different, with 99% resorption for cystatin C, 75% for iodine, and nearly none for creatinine [30, 31, 35]. Apparently, the excretion process of cystatin C is more similar to iodine than creatinine. Therefore, we conclude that future study protocols focusing on relationship between renal function and iodine excretion should additionally include $eGFR_{CysC}$ measurement, but in order to

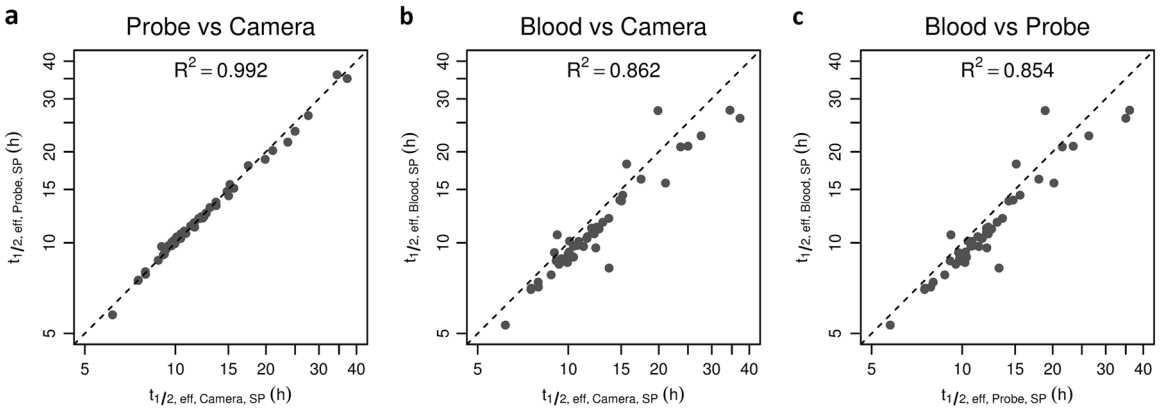

Fig. 3 $t_{1/2,eff,SP}$ were estimated based on the three different methods: blood samples, gamma camera scans, and probe measurements. Plots show pairwise correlation between the three setups **a**–**c**. The blood-based setup yielded systematically lower estimates, while the other two methods were nearly superimposed (leftmost panel). Coefficient of determination (R^2) is also displayed

Table 5 $t_{1/2,eff}$ (h) of the three methods to determine $t_{1/2,eff}$

		SP	LP
Blood	Median (range)	10.1 (5.3–27.5)	12.2 (6.7–33.3)
	Mean ± SD	11.9 ± 5.4	13.8 ± 5.1
Gamma camera	Median (range)	11.4 (6.2–37.3)	13.8 (10.7–35.2)
	Mean ± SD	13.4 ± 6.6	15.5 ± 5.4
Probe	Median (range)	11.3 (5.8–36.1)	14.0 (10.2–35.4)
	Mean ± SD	13.2 ± 6.3	15.6 ± 5.2

SP short period protocol, *LP* long period protocol

maintain comparability with previous studies and worldwide clinical standards $eGFR_{Crea}$ measurement should be retained.

Other methods are available to determine renal function; however, they were not considered in this study: Inulin- and 51Cr-EDTA-clearance are assumed to be more precise to measure GFR, but are very elaborate and poorly available in some regions. In the current analysis, previously used equations for estimating creatinine-based GFR as MDRD-(Modification of Diet in Renal Disease) [36] and Cockcroft-Gault [37] produced similar results (mean 84.3 ± 22.4 ml/min/1.73 m^2; median 85.1; range 32.5–127.1 and mean 99.0 ± 34.1 ml/min/1.73 m^2; median 96.9; range 36.6–169.3, respectively). However, statistic evaluation showed significantly lower AIC-values (data not shown), which indirectly confirms the superiority of the CKD-EPI equation. Therefore, eGFR based on CKD-EPI equations was chosen for further analysis for its reliability and as it has served as clinical standard worldwide for many years.

$t_{1/2,eff}$ measured by blood, gamma camera and probe

The highest R^2 was found for $t_{1/2,eff}$ assessed by probe measurements, albeit the R^2 for gamma camera measurements was only slightly inferior. The results of both whole-body measurements, therefore, proved almost superimposable, in agreement with a retrospective study, including 14 patients with DTC [38]. Based on these considerations two different scenarios for whole-body assessment of $t_{1/2,eff}$ are suitable. First, measurement only by gamma camera via multiple sets of images, which is elaborate but could be preferred if lesion based internal dosimetry is planned. Second, assessment of $t_{1/2,eff}$ by the exclusive use of gamma probe measurements might be more practical. Considering a clinical approach at least one camera scan is mandatory due to its clinical relevance for imaging and in compliance with the current guidelines of diagnostic and post-therapeutic imaging [1–3]. Blood-based determination of $t_{1/2,eff}$ revealed lower values than both whole-body measurements, as also shown in other studies [16, 19]. A likely explanation is the retention of iodine in extra-thyroidal iodine-avid tissues, e.g., gastric wall, salivary glands, nasal mucosa, intestine, and urinary tract [39, 40]. In our study, blood-based assessed $t_{1/2,eff}$ showed a lower correlation with eGFR compared to both other methods. This may be due to individual differences in the resorption of radioiodine from the bowel after oral administration. Especially early blood measurements 1 h p.a. may have influenced the assessment of $t_{1/2,eff}$. In contrast, whole-body measurements include the entire activity including intestinal activity.

$t_{1/2,eff}$ determined by SP and LP protocols

The initial rationale to include late measurement points was that patients with renal insufficiency still have a relatively high residual activity in the body after 114 h (which corresponds approximately to tenfold the $t_{1/2,eff}$ in patients without impaired renal function) (Fig. 5) [12]. The present data demonstrate that patients with renal insufficiency (and hence longer $t_{1/2,eff}$) had comparable results for SP and LP

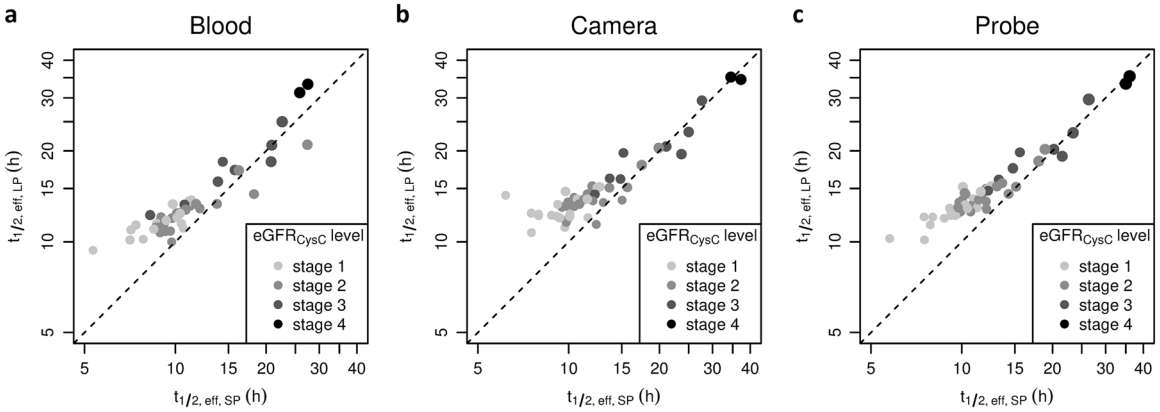

Fig. 4 $t_{1/2,eff}$ were estimated by fitting exponential curves to activity data. Plots show comparison of estimates based on a short period (SP; three time points, up to 42 h p.a.; *x*-axis) versus a long period (LP; four time points, up to 114 h p.a.; *y*-axis) protocol. Correlations between the two estimates depended on the $eGFR_{CysC}$, which is displayed with a gray scale gradation based on the KDOQI criteria (stage 1: eGFR ≥ 90 ml/min/1.73 m^2; stage 2: eGFR 60–89 ml/min/1.73 m^2; stage 3: eGFR 30–59 ml/min/1.73 m^2; stage 4: eGFR 15–29 ml/min/1.73 m^2; stage 5: eGFR < 15 ml/min/1.73 m^2). Estimates based on the LP seemed to be over-estimated in patients with short $t_{1/2,eff}$. The comparison is shown for the three different methods to determine $t_{1/2,eff}$: activity measured from blood samples **a**, whole-body scan by camera **b**, whole-body measurements by probe **c**

(Fig. 4). In contrast, patients with normal eGFR (and hence short $t_{1/2,eff}$) showed higher values of $t_{1/2,eff}$ of LP compared to SP. This overestimation is conceivably due to a minimal residual body activity (limit-of-sensitivity) in 114-h scans in patients with normal renal function. Additionally, a biphasic clearance of iodine, resulting from some retention of I-131 in iodine-avid tissues may have contributed to the phenomenon [39]. Thus, based on these considerations, it was concluded that the last measurement point at 114 h was not suitable for the assessment of $t_{1/2eff}$ in a population including all stages of renal function.

Limitations

As known also from other studies, the proportion of DTC patients with an eGFR < 60 ml/min per 1.73 m^2 is rather limited [7]. The current analysis included 48 patients with DTC (only 8 of whom had an $eGFR_{Crea}$ < 60 ml/min per 1.73 m^2). The prevalence of renal insufficiency (16.7%) is comparable to the retrospectively gained data of Vogel et al. (11.5%) [7]. In general, the prevalence of renal insufficiency stages 3–5 in the European population aged 30–79 years is 11.9%, which is also only slightly lower than in our study population [41]. Inclusion of more patients with impaired renal function should be pursued when developing a mathematical model to reduce the administered activity in RAIT and further studies focusing on renal insufficiency only are needed.

Aiming at the introduction of eGFR in pretherapeutic dosimetry, the goal of the current analysis was to assess whether eGFR alone is appropriate for the prediction of $t_{1/2,eff}$ and which method of GFR estimation should be chosen for that purpose. Therefore, this study does not allow for conclusions on how GFR estimates exactly contribute to pretherapeutic dosimetry before RAIT. Up to date, in patients with DTC, most RAIT are performed without pretherapeutic dosimetry and standard activities are administered. GFR estimates could be considered when choosing standard activities; however, there is no formula available by how much the activity should be reduced. This will be the goal of future studies.

Conclusions

$eGFR_{CysC}$ is more likely in predicting $t_{1/2,eff}$ than $eGFR_{Crea}$ and should therefore be included in further study protocols aiming at the analysis of the relationship between renal function and $t_{1/2,eff}$. As whole-body camera and whole-body probe methods produce superimposable results, the camera approach should be preferred to determine $t_{1/2,eff}$ because it is part of clinical routine for imaging purposes in any case, thus no additional examination needs to be performed. Blood-based results of $t_{1/2,eff}$ were lower, presumably due to unspecific iodine retention. SP protocols including three time points up to 42 h after I-131 administration are sufficient to determine $t_{1/2,eff.}$ In contrast, LP protocols up to 114 h produce erroneous results in patients with regular renal function.

Further studies, including higher patient numbers and particularly more individuals with impaired renal function are necessary for the development of a mathematical model for specific recommendations regarding I-131 activity reduction during RAIT in patients with DTC.

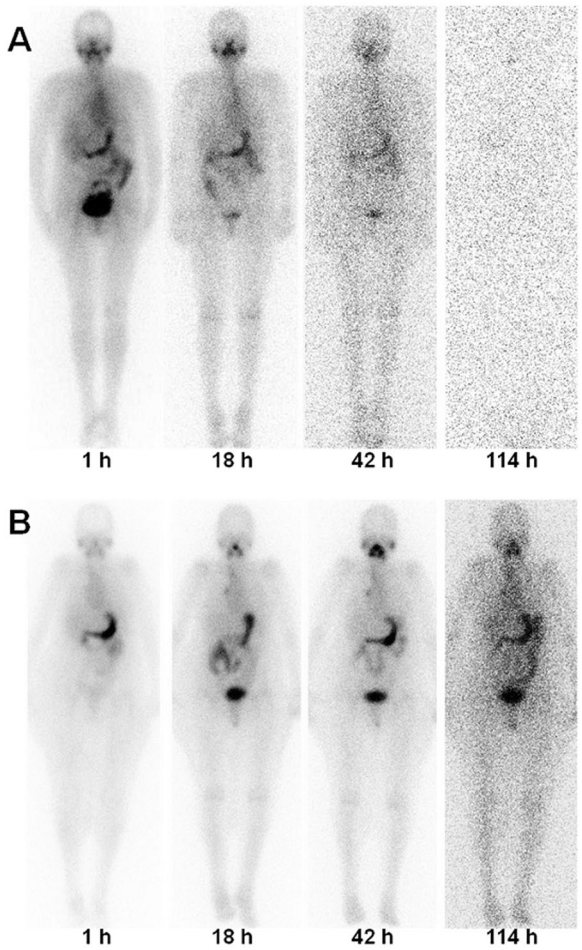

Fig. 5 Diagnostic whole-body scintigraphy at 1, 18, 42, and 114 h after administration of 400 MBq I-131, ventral view. **a** Patient with mildly decreased eGFR and rapid iodine clearance ($eGFR_{CysC}$ 106.4 ml/min per 1.73 m^2; $eGFR_{Crea}$ 83.9 ml/min per 1.73 m^2; $t_{1/2,eff,SP}$ 7.8 h). **b** Patient with severely decreased eGFR and prolonged iodine excretion ($eGFR_{CysC}$ 19.3 ml/min per 1.73 m^2; $eGFR_{Crea}$ 31.4 ml/min per 1.73 m^2; $t_{1/2,eff,SP}$ 32.4 h)

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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