A simple, reliable and accurate approach for assessing $^{131}\text{I}$-capsule activity leading to significant reduction of radiation exposure of medical staff during radioiodine therapy

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**ABSTRACT**

**Purpose:** According to German law, the $^{131}\text{I}$-capsule activity has to be checked in the context of radioiodine therapy (RIT) immediately before application. The measurement leads to significant radiation exposure of the medical personnel, especially of their hands. We aimed to establish a method for estimating $^{131}\text{I}$-capsule activity by measuring the dose rate (DR) at contact of the delivered lead closed container carrying the $^{131}\text{I}$-capsules and to evaluate radiation exposure in comparison to conventional $^{131}\text{I}$-capsule measurement using a dose calibrator.

**Methods:** DR on the surface of the closed lead container was measured at two locations and correlated linearly with the $^{131}\text{I}$-capsule activity measured in a dose calibrator to create calibrating curves. The hand and whole body (effective) doses were determined with official dose meters during validation of our method in clinical practice.

**Results:** The determination coefficients ($R^2$) of linear calibration curves were greater than 0.9974. The total relative uncertainty for estimating $^{131}\text{I}$-capsule activity with our method was $\pm 7.5\%$ which is lower than the uncertainty of the nominal activity and quite close to the threshold limit for the maximum allowed uncertainty of $\pm 5\%$ for measuring activity in radioactive drugs. The reduction of the hand dose caused by our method was 97% compared with the conventional measurements of the $^{131}\text{I}$-capsules in a dose calibrator.

**Conclusion:** Measuring DR on the surface of the closed lead containers enables the $^{131}\text{I}$-capsule activity to be estimated simply, reliably and with sufficient accuracy leading to significant reduction of the radiation exposure for the medical staff.

**Introduction**

Radiation protection of medical personnel is of great importance. Radioiodine therapy (RIT) is a well-established, safe and effective option in the treatment of benign and malignant diseases of the thyroid gland in many countries around the world [1,2]. In Germany alone, several tens of thousands of RITs are performed every year [3]. In most cases, the radioiodine required for the therapy is administered orally as an $^{131}\text{I}$-iodide therapy capsule ($^{131}\text{I}$-capsule). According to German law the $^{131}\text{I}$-capsule have to be checked prior to RIT in order to prevent mix-ups, incorrect labelling by the supplier and application errors as an important contribution to patient safety [4]. This necessary determination of the activity level is usually performed by measuring the $^{131}\text{I}$-capsule in a dose calibrator. As $^{131}\text{I}$-iodine is a beta emitter ($E_{\text{max}} = 606$ keV; 89.3%) with an additional amount of gamma radiation ($E = 364$ keV; 81.2%) [5], the measurements can lead...
to a significant radiation exposure of the medical staff, in particular of their hands [6] - despite radiation protection measures such as usage of lead shielding, the use of lead glass for eye protection, and tweezers (distance law). Depending on the number of $^{131}$I-capsule measurements carried out and the total measured activity, this can lead to the dose limits for hands being exceeded (500 mSv/year or 150 mSv/year depending on the category of staff, A or B - based on the German Radiation protection legislation) [4,6].

There are many studies dealing with the determination of radiation exposure of nuclear medicine staff in general [7-9], or in special nuclear medical procedures such as Positron Emission Tomography/Computer Tomography (PET/CT) [10-12]. Other studies focus on the equivalent dose for the eyes [7,13-15], limbs or fingers [16-20]. Many of these studies show that the annual dose limits for the hands of 500 mSv/year can be exceeded [6,12,18,20-23]. Other studies focus primarily on the definition of general resp. specific rules for handling radioactive materials [8,9,24-28] or preventing contamination [29]. The development and implementation of new devices and methods to reduce the radiation exposure of nuclear medicine staff seems to be an important and hitherto neglected goal [30].

In a previous study we described a method of determining $^{131}$I-capsule activity by measuring the count rate on the surface of the delivery lead container in which the $^{131}$I-capsules are carried, without opening it [31]. However, the limitations of this procedure were a high inter-observer variability, as well as a large amount of time required for manual positioning.

In this work, we optimized this procedure with regard to the measurement geometry and precision, and with a view to further reducing radiation exposure of the staff. We developed a fixation device to determine $^{131}$I-capsule activity from the DR on the surface of the lead container, with the $^{131}$I-capsule remaining shielded inside. This ensures reproducibility and independence from the operator. In addition, we report on the evaluation of this new method in clinical practice, comparing the staff exposure with that measured by conventional dose calibrator measuring.

**Material and methods**

**Lead containers and $^{131}$I-capsules**

The $^{131}$I-capsules and also the lead containers delivered to our hospital are manufactured by Curium, formerly Mallinckrodt London, United Kingdom. The lead containers were obtained in two different sizes (container sizes I and II). The containers are 99% lead-made and standardized with respect to their geometrical and material properties (Fig. 1, also Supplementary Material 1). The development and implementation of new devices and methods to reduce the radiation exposure of nuclear medicine staff seems to be an important and hitherto neglected goal [30].

In this work, we optimized this procedure with regard to the measurement geometry and precision, and with a view to further reducing radiation exposure of the staff. We developed a fixation device to determine $^{131}$I-capsule activity from the DR on the surface of the lead container, with the $^{131}$I-capsule remaining shielded inside. This ensures reproducibility and independence from the operator. In addition, we report on the evaluation of this new method in clinical practice, comparing the staff exposure with that measured by conventional dose calibrator measuring.

**Dose calibrator and DR measurement**

The activity of the therapy $^{131}$I-capsules was measured with an ISOMED 2010 dose calibrator (NUVIA Instruments GmbH, formerly

<table>
<thead>
<tr>
<th>Lead container</th>
<th>Thickness [mm]</th>
<th>Radioactivity range [MBq]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size I:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ø = 41 mm</td>
<td>a = 17.6 ± 0.3</td>
<td>370-1650</td>
</tr>
<tr>
<td>h = 76.9 mm</td>
<td>b = 14.6 ± 0.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>c = 19.1 ± 0.3</td>
<td></td>
</tr>
<tr>
<td>Size II:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ø = 67 mm</td>
<td>a = 26.1 ± 0.3</td>
<td>1651-7400</td>
</tr>
<tr>
<td>h = 93.1 mm</td>
<td>b = 27.6 ± 0.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>c = 26.8 ± 0.3</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1. Image of container size II and characteristics and dimensions of lead delivery containers size I and size II.
The DR on the surface of the lead container carrying the therapy \( ^{131}I \)-capsule was measured with an UMO dose rate meter (LB 123, Berthold Technologies, Bad Wildbach, Germany), assisted by steel fixation devices as can be seen in Fig. 2 and supplementary video 1. The fixation devices were developed as prototypes specifically for this purpose, in cooperation with an industrial partner specializing in radiation protection, medical and measurement engineering (Rapp-iso GmbH, Kappeln, Germany). Two fixation devices were developed to fit the different sizes of the lead containers, enabling custom-fit insertion of the protection, medical and measurement engineering (Rapp-iso GmbH, Kappeln, Germany). Two fixation devices were developed to fit the different sizes of the lead containers, enabling custom-fit insertion of the measuring device and of the respective lead container (Fig. 2). The measurement duration was selected in a way to achieve a statistical accuracy of 1% (typical measuring time < 15 s).

**Calibration**

A linear correlation between the DR measured at defined locations on the surface of the closed lead containers (\( x_i \)) and the activity of the \( ^{131}I \)-capsule measured in the dose calibrator (\( y_i \)), can be described mathematically as an equation of a straight line with the slope \( \hat{k} \) (\( \hat{k} \) being the calibration factor for estimating \( ^{131}I \)-capsule activity by measuring the DR on the surface of the lead containers):

\[
y_i = \hat{k} \cdot x_i \tag{1}
\]

As both measured values \( x_i \) und \( y_i \) are affected by measurement errors, we calculated the calibration factor \( \hat{k} \) using the compensation of a straight line for both coordinates \( X \) and \( Y \). This method, known as regular compensation or linear regression for both coordinates [32,33], ensures independence of the calibration factor regarding the units for \( X \) and \( Y \).

The calibration factors \( \hat{k} \) and the uncertainties of the calibration factors \( u(\hat{k}) \) were calculated according to equation (2) and (3) [34]:

\[
\hat{k} = \text{sign} \left[ \frac{\sum_{i=1}^{n} (x_i - \bar{x})(y_i - \bar{y})}{n \sum_{i=1}^{n} (x_i - \bar{x})^2} \right] \cdot \sqrt{\frac{\sum_{i=1}^{n} u_x^2 x_i^2 + \sum_{i=1}^{n} u_y^2 y_i^2}{\sum_{i=1}^{n} (x_i - \bar{x})^2}} \tag{2}
\]

\[
u_{\text{rel}}(\hat{k}) = \frac{\sum_{i=1}^{n} u_x^2 x_i^2 + \sum_{i=1}^{n} u_y^2 y_i^2}{\sum_{i=1}^{n} (x_i - \bar{x})^2} \tag{3}
\]

\( \hat{k} \): Slope of the regression line (calibration factor).
\( y_i \): Activity of \( ^{131}I \)-capsule measured in the dose calibrator.
\( x_i \): DR measured on the surface of the lead container.
\( \bar{x} \) and \( \bar{y} \): Mean value of \( x_i \) and \( y_i \).
\( u_{\text{rel}}(\hat{k}) \): Relative uncertainty of the calibration factor.
\( u(x_i) \): Uncertainty of \( x_i \).
\( u(y_i) \): Uncertainty of \( y_i \).

For establishing calibration curves based on a linear correlation between the activity of the \( ^{131}I \)-capsules measured in a dose calibrator (supplementary video 1) and the DR measured on the surface of the closed lead containers that carry the \( ^{131}I \)-capsules (supplementary video 2), five \( ^{131}I \)-capsules, each with a nominal activity of ca. 1.500 GBq delivered in lead containers of size I, and five \( ^{131}I \)-capsules with a nominal activity of ca. 5.500 GBq delivered in lead containers of size II, were obtained from Curium (formerly Mallinckrodt, London, United Kingdom). The DR on the surface of the consistently closed lead containers with the \( ^{131}I \)-capsules inside was measured daily within a period of 19 days, using the fixation devices and the UMO dose rate meter on the top (top measurement) and on the side (side measurement) of the lead containers. After the last DR measurement on day 19, the lead containers were opened; the activity of the \( ^{131}I \)-capsules was measured in a dose calibrator, and the exact activity for each DR measurement was

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**Fig. 2.** Top left: Fixation devices for the lead containers of both sizes (I and II), Top right: Placement of the device onto the closed lead container of size I carrying the \( ^{131}I \)-capsule, Down: Exact fitting of the dose rate meter measuring probe inside the fixation device for exact and reproducible measuring geometry, in this case on the side (side measurement) of container size I.
then inferred based on the half-life of $^{131}$I-iodine.

**Uncertainty of the $^{131}$I-capsule activity determination by our method**

In our method the $^{131}$I-capsule activity ($A$) is determined by multiplying the DR measured on the surface of the closed lead container by the calibration factor ($k$):

$$A = k \cdot DR$$

Taking into account the relative measuring uncertainty for both the calibration factor $u_{rel}(k)$ and for the DR measurement $u_{rel}(DR)$ the relative overall uncertainty for the whole procedure $u_{rel}(A)$ for the estimation of the activity of the $^{131}$I-capsule is calculated under employment of the law of error propagation by equation (6):

$$u_{rel}(A) = \sqrt{u_{rel}(k)^2 + u_{rel}(DR)^2}$$

(5)

The relative uncertainty of the calibration factor is given by equation (3). For the determination of the relative uncertainty of the DR measurement, $u_{rel}(DR)$, on the surface of the delivered closed lead containers, three uncertainties have to be considered by the law-of-error propagation (equation (6)). These are the measuring uncertainty of the dose rate meter $u_{rel}(measurement)$, the uncertainty of the lead containers $u_{rel}(lead)$, which results from the use of different lead containers during the DR measurements, and the statistical uncertainty of the count rate measured by the dose rate meter $u_{rel}(sta.)$.

$$u_{rel}(DR) = u_{rel}(measurement) + u_{rel}(lead) + u_{rel}(sta.)$$

(6)

$u_{rel}(measurement)$: Relative uncertainty of the DR measurements on the surface of the lead container.

$u_{rel}(lead)$: Relative uncertainty of the dose rate meter (estimated using a $^{137}$Cs-standard dose rate source).

$u_{rel}(sta.)$: Statistical uncertainty of count rate of the DR measurements. The measurement duration was selected in a way to achieve statistical accuracy of 1%.

**Uncertainty of dose rate meter and dose calibrator**

The relative measurement uncertainty of the UMO dose rate meter, determined by means of a ring-shaped $^{137}$Cs-standard dose rate source (Berthold, Wildbad Germany; nominal dose rate $= 11.0 \pm 0.55 \mu Sv/h$). The $^{137}$Cs-standard dose rate source is shaped so that the measuring cylinder of the UMO dose rate meter fits perfectly into it. The relative measurement uncertainty of the ISOMED 2010 dose calibrator, determined by means of a $^{131}$I-standard activity source (Physikalisch-Technische Bundesanstalt, Braunschweig, Germany; nominal activity $= 100 \pm 1$ MBq). The standard sources were repeatedly measured ($n = 10$) in the corresponding device and the relative uncertainties were calculated using equation (1) according to the primary test procedure of the “German Industrial Standard” (DIN) and following the recommendations of the “Guide to the Expression of Uncertainty in Measurement” (GUM) (35,36):

$$u_{rel}(measurement) = \sqrt{\left(\frac{S_{standard}}{V_{standard}}\right)^2 + \left(\frac{S_m}{V_m}\right)^2}$$

(7)

$u_{rel}(measurement)$: Relative uncertainty of the measuring device (UMO dose rate meter or ISOMED 2010 dose calibrator).

$S_{standard}$ Standard deviation of the used standard source as stated by the manufacturer ($\pm 0.55 \mu Sv/h$ for the $^{137}$Cs-standard dose rate source and $\pm 1$ MBq for the $^{131}$I-standard activity source).

$V_{standard}$ Nominal dose rate or activity of the standard source (11.0

\[ \mu Sv/h \] for the $^{137}$Cs-standard dose rate source or $= 100$ MBq for the $^{131}$I-standard activity source.

$S_m$ Standard deviation of the measured values (activity or dose rate; $n = 10$).

$V_m$ Average of the measured values (activity or dose rate; $n = 10$).

The $^{137}$Cs-standard dose rate source (Berthold, Wildbad Germany; nominal dose rate $= 11.0 \pm 0.55 \mu Sv/h$) was also used for the daily quality control of the UMO dose rate meter. The dose rate output measured within 120 s must not deviate from the reference value by more than 5%. For Quality checks on the dose calibrator a calibrated $^{137}$Cs activity test source was used (Physikalisch-Technische Bundesanstalt, Braunschweig, Germany; nominal activity $= 7.66 \pm 1$ MBq). The activity of the $^{137}$Cs test source measured in the dose calibrator must not deviate by more than 5% from the reference value.

**Uncertainty of the lead containers**

Variation in the attenuation of radiation due to variances of the dimensions of the lead containers ($\pm 0.3$ mm) presents a further important aspect regarding measurement uncertainty.

The relative measurement uncertainty of the lead containers $u_{rel}(lead)$, which results from the use of different lead containers during the DR measurements, was estimated statistically using the primary test method (35,36). For this purpose we measured a $^{131}$I-standard activity source in five different randomly selected lead containers of each size and measurement locations and calculated $u_{rel}(lead)$ by applying equation (8):

$$u_{rel}(lead) = \sqrt{\left(\frac{S_{standard}}{V_{standard}}\right)^2 + \left(\frac{S_m}{V_m}\right)^2}$$

(8)

$u_{rel}(lead)$ Uncertainty of the measured DR on the surface of five different randomly selected lead containers containing the $^{131}$I-standard activity source.

$S_{standard}$ Standard deviation of the used $^{131}$I-standard activity source as stated by the manufacturer ($\pm 1$ MBq).

$V_{standard}$ Nominal activity of the $^{131}$I-standard activity source (100 MBq).

$S_m$ Standard deviation of the measured DR values on the surface of the containers containing the $^{131}$I-standard activity source; $n = 5$.

$V_m$ Average of the measured DR values on the surface of the containers containing the $^{131}$I-standard activity source; $n = 5$.

The statistical uncertainty $u_{rel}(sta.)$ was $\pm 1\%$ as the duration of all measurements with the dose rate meter was selected in a way to achieve statistical accuracy of $\pm 1\%$.

**Validation of the measuring technique in clinical practice**

We validated our method in practice by measuring a total of 89 $^{131}$I-capsules delivered for patient treatments, with a cumulative activity of 164.353 GBq over a period of six months. 51 of these $^{131}$I-capsules with a total activity of 52.844 GBq (0.316–1.622 GBq, average 1.036 GBq/capsule) were delivered in a lead container size I, and 38 $^{131}$I-capsules with a total activity of 111.309 GBq (1.542–6.122 GBq; average 2.929 GBq) were delivered in a lead container size II. We initially measured the DR on the surface, on the top and on the side of the closed lead container, respectively, employing the fixation device (Fig. 2). Subsequently, we opened the lead container and measured the activity of the $^{131}$I-capsule with the dose calibrator. The thus obtained measurements were correlated.

**Measurement geometry**

To be able to determine the activity of the $^{131}$I-capsules by measuring the DR on the surface of the lead containers without opening them, a clearly defined and reproducible measurement geometry is
obligatory. To this aim, we developed and produced the above-mentioned fixation devices from steel with a wall thickness of 4 mm. These fixation devices are custom-made to fit the two lead container sizes (Fig. 2). The two additional cylindrical tubes of each device warrant exact positioning of dose rate meter measuring cylinder on the top and on the side of the container. The 4 mm steel wall thickness of the fixation device adds to the shielding from radiation and thus further reduces radiation exposure of the staff.

**Determination of the hand dose and the effective dose in clinical practice**

During the above-described validation procedure, we determined the hand dose (H<sub>P</sub>(0.07)) and the effective dose using thermo-luminescent ring dose meters (TLD), Type X, for beta and gamma radiation and Optically Stimulated Luminescence dose meters (OSL) obtained from Mirion Technologies Dosimetrieservice (AWST, 80,219 Munich, Germany).

The determination of the hand dose and effective dose was carried out separately for each method, i.e. for the measurements with the dose calibrator and with the dose rate meter. For this purpose, different finger ring TLD and different OSL were used for each measurement method. To minimize the risk of systematic errors and also to reduce the radiation dose per person, two different staff members were involved in the measurements.

**Results**

**Calibration**

We calculated a total of four calibration curves, as two different lead container sizes were used and each container size was measured on the side and the top of the container surface. The correlation of the DR for each container size and the respective measuring location with the corresponding activity of the [¹³¹I]-capsules resulted in a total of 19 × 5 = 95 data points each (two calibration curves per container size each with 19 × 5 data points, Fig. 3). The one standard deviation uncertainty of the calibration on the whole activity range is represented as the area between the dashed lines.

**Uncertainty of measurement**

The relative uncertainty of the measurement performed with the dose rate meter and the dose calibrator was calculated by equation (4) to be 1.5% for both devices.

Table 1 summarizes the determined calibration factors $\hat{k}$, the determination coefficients, the relative uncertainty of the DR measurement, the relative uncertainty of the calibration factor $u_{rel}(\hat{k})$ and the overall procedure uncertainty $u_{rel}(A)$ for the different sizes of the containers and the different measurement locations respectively.

Table 2 illustrates the results of the DR measurements on the surfaces of five randomly selected lead containers carrying a [¹³¹I]-standard (A = 100 MBq $u_{rel.} = \pm 1\%$) inside (columns 3–7) as well as the statistical data (columns 8–9) and the calculated $u_{rel.}(\mathrm{lead})$ for the different container sizes and measuring locations. The statistically estimated relative uncertainties for $\mu_{rel.}(\mathrm{lead})$ range between $\pm 4.2$ and $\pm 4.6\%$ (columns 10). The maximum value of $\pm 4.6\%$ was found for the side measurement on container size I which corresponds to the fact that the container dimension is the smallest for the side measurement.

**Validation of the measuring technique in clinical practice**

The method was validated in practice by measuring a total of 89 [¹³¹I]-capsules, with a cumulative activity of 164.353 GBq, which were released for patient treatment over a period of six months. Fig. 4 on the left demonstrates a linear correlation between the activities of all [¹³¹I]-capsules (measured with the dose calibrator) and the DR (measured on the surface of the lead containers of both sizes and both locations with the dose rate meter). The slope of the regression line with the value of
Table 1
Summary of calibration factors, determination coefficients and determined relative uncertainties.

<table>
<thead>
<tr>
<th>Container Size I</th>
<th>Side</th>
<th>Measurement</th>
<th>Top</th>
<th>Measurement</th>
<th>Container Size II</th>
<th>Side</th>
<th>Measurement</th>
<th>Top</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>( k )</td>
<td>0.9915</td>
<td>3.4845</td>
<td>7.9251</td>
<td>12.3581</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( R^2 )</td>
<td>0.9974</td>
<td>0.9984</td>
<td>0.9986</td>
<td>0.9992</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( u_{rel}(k) )</td>
<td>7.0%</td>
<td>7.0%</td>
<td>6.8%</td>
<td>6.8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( u_{rel}(A) )</td>
<td>7.5%</td>
<td>7.3%</td>
<td>7.3%</td>
<td>6.9%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The \([^{131}\text{I}]\)-capsule activity (A) is determined by multiplying the dose rate (DR) measured on the surface of the closed lead container by the calibration factor \( k \cdot A = k \cdot \text{DR} \).

\( k \): Calibration factor. \( k = \frac{\text{MBq}}{\mu\text{Sv} \cdot \text{h}} \)

\( R^2 \): coefficient of determination.

\( u_{\text{rel.}(\text{lead})} \): Maximum relative uncertainty for the lead containers \( (=\pm 4.63\% \) estimated using a \([^{131}\text{I}]\)-standard).

\( u_{\text{rel.}(\text{DR})} \): \( (= \sqrt{u_{\text{rel.}(\text{measurement})}^2 + u_{\text{rel.}(\text{lead})}^2} \) \) relative uncertainty of the DR measurements on the surface of the lead container.

\( u_{\text{rel.}(\text{measurement})} \): Relative uncertainty of the used dose rate meter \( (=\pm 1.5\% \) estimated using a calibrated \([^{137}\text{Cs}]\)-standard dose rate source).

\( u_{\text{rel.}(k)} \): \( = \frac{\sqrt{\sum x_i^2 - 2 \cdot \hat{k} \sum y_i^2} + \sum x_i^2} {2 \cdot n \cdot r^2} \) relative uncertainty of the calibration factor.

\( u_{\text{rel.}(A)} \): \( = \sqrt{u_{\text{rel.}(k)}^2 + u_{\text{rel.}(\text{DR})}^2} \) uncertainty of the activity estimation with our method.

\( Y_1 \): activity of the \([^{131}\text{I}]\)-capsule measured in the dose calibrator.

\( X_i \): DR measured on the surface of the closed lead container that carries the \([^{131}\text{I}]\)-capsule.

\( 0.9991 \) and the determination factor \( R^2 = 0.9971 \) revealed very high correlation of both measurement methods.

Fig. 4 on the right represents the Bland-Altman-Analysis for the \([^{131}\text{I}]\)-capsule activity determination using both methods. The Bland-Altman-Analysis shows that the percentage differences of the measured activities with the two measurement methods lie in a 95% confidence interval between \( \pm 1.96 \times \text{SD} \) \( (\pm 6.5\%) \). The mean of the errors (red line in Fig. 4 right) is \( +0.02\% \) indicating no relevant systematic error.

Difference between nominal activity by the supplier and measured activity

Fig. 5 shows on the left a linear correlation between \([^{131}\text{I}]\)-capsule activity measured in the dose calibrator and the nominal activity stated by the supplier. The slope of the regression line with the value of \( 0.9963 \) and the determination factor \( R^2 = 0.9995 \) revealed high correlation. Fig. 5 on the right represents a Bland-Altman-Analysis for the \([^{131}\text{I}]\)-capsule activity measured in the dose calibrator and the nominal activity. The differences between the nominal \([^{131}\text{I}]\)-capsule activity and the activity measured in the dose calibrator at the reference time range between \(-8.0\% \) and \(+8.2\% \) for \([^{131}\text{I}]\)-capsule activities ranging between \( 1651 \) and \( 7400 \text{ MBq} \) and \(-12.9\% \) and \(+12.3\% \) for \([^{131}\text{I}]\)-capsule activities ranging between \( 370 \) and \( 1650 \text{ MBq} \). The most percentage differences lie in a 95% confidence interval between \(-6.5\% \) and \(+8.2\% \) \( (\pm 1.96 \times \text{SD}) \). The mean of the differences (red line in Fig. 5 right) shows a shift of \( +0.8\% \) indicating a little systematic error.

Discussion

Linear calibration

The attenuation of the gamma radiation depends on the absorption coefficient of the shielding material and the gamma radiation energy. With the same nuclide and shielding material, the attenuation of the radiation depends exclusively on the dimensions of the shielding material. Since the nuclide is \([^{131}\text{I}]\)-Iodine and the shielding material is lead in our case, with standardized composition and dimensions and a low dimension tolerance of \( \pm 0.3 \text{ mm} \), the measured DR at defined locations directly on the surface of the shielding (lead container) should only depend on the activity of the \([^{131}\text{I}]\)-capsule inside the container. Because of the identical geometry of the measurements, this also applies to the accompanying "bremsstrahlung" resulting from the beta radiation of the \([^{131}\text{I}]\)-Iodine. The beta radiation itself is completely absorbed by the shielding.

Having ensured the exact measurement geometry by means of the fixation device, the overall attenuation coefficient of the measuring system should be consistent; thus we assumed that there is a linear correlation between the activity of the \([^{131}\text{I}]\)-capsule and the measuring signal of dose rate meter. Such assumption was verified by the excellent correlation obtained in the calibration phase (Fig. 3).

As shown in Fig. 3 and Table 1, the linear regressions for the correlation of the measured activity \( Y_i \) and DR \( X_i \) at all measurement locations

Table 2
Results of the measured DR on the surfaces of five different lead containers carrying the \([^{131}\text{I}]\)-standard inside, statistical data and the calculated \( u_{rel}(\text{lead}) \) using the primary test method by equation (8) [35,36].

<table>
<thead>
<tr>
<th>Container</th>
<th>Measuring location</th>
<th>DR measured on the surface of five different randomly selected lead containers carrying a ([^{131}\text{I}])-standard activity source</th>
<th>( V_a ) (Mean)</th>
<th>( S_a ) (SD)</th>
<th>( u_{rel}(\text{lead}) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>size I</td>
<td>side</td>
<td>[( \mu\text{Sv} \cdot \text{h} )]</td>
<td>107.0</td>
<td>104.0</td>
<td>104.0</td>
</tr>
<tr>
<td>size II</td>
<td>top</td>
<td>27.0</td>
<td>28.3</td>
<td>26.2</td>
<td>29.4</td>
</tr>
<tr>
<td>size II</td>
<td>side</td>
<td>12.7</td>
<td>12.4</td>
<td>12.8</td>
<td>11.7</td>
</tr>
<tr>
<td>size I</td>
<td>top</td>
<td>8.6</td>
<td>8.20</td>
<td>7.80</td>
<td>8.10</td>
</tr>
</tbody>
</table>

\( u_{rel}(\text{lead}) \): Uncertainty of the measured DR on the surface of five different randomly selected lead containers containing the \([^{131}\text{I}]\)-standard activity source.

\( S_{\text{random}} \): Standard deviation of the used \([^{131}\text{I}]\)-standard activity source as stated by the manufacturer \( (\pm 1 \text{ MBq}) \).

\( V_{\text{random}} \): Nominal activity of the \([^{131}\text{I}]\)-standard activity source \( (100 \text{ MBq}) \).

\( S_{\text{a}} \): Standard deviation of the measured DR values on the surface of the containers containing the \([^{131}\text{I}]\)-standard activity source \( (n = 5) \).

\( V_{\text{a}} \): Average of the measured DR values on the surface of the containers containing the \([^{131}\text{I}]\)-standard activity source \( (n = 5) \).

\( u^* \): calculated maximum relative uncertainty for \( u_{rel}(\text{lead}) \).
and both container sizes result in four straight lines with determination coefficients $R^2$ between 0.9974 and 0.9992. The correlation observed for the calibration of the size II container ($R^2 = 0.9986$ - side measurement and $R^2 = 0.9992$ - top measurement) is a little higher than that for the size I container ($R^2 = 0.9974$ - side measurement and $R^2 = 0.9984$ - top measurement). This is due to the fact that the container dimension of size II is larger than of size I (Fig. 1). Therefore, the effect of the lead dimension tolerance of $\pm 0.3$ mm is higher in container size I than in size II. Consequently, the uncertainty of the measurements is greater for small containers. The same applies to the relative uncertainty of the entire measuring process for estimating the activity by means of the DR measurement on the surface of the containers (Table 1).

As shown in Table 1, the overall uncertainty of our method $u_{rel,\text{in}}(A)$ range from 6.9% to 7.5%. The lowest value was found for the top measurement on the surface of container size II and the highest value was found for the side measurement on the surface of container size I. Based on the determined relative uncertainties for the side and top measurement positions (Table 1), the top measurement positions with the smaller relative uncertainties of 7.3% and 6.9% are preferred compared to the side measurement positions that shows higher relative uncertainties (7.5% and 7.3%).
The uncertainty values for the activity estimation with our method are thus for all containers and measuring locations quite close to the threshold of ± 5% (maximum allowed uncertainty in radioactive drugs according to the European pharmaceutical regulations) [37,38].

**Difference between nominal activity and measured activity**

The Bland-Altman analysis for the $^{131}$I-capsule activity measured in the dose calibrator and the nominal activity (Fig. 5 right side) demonstrates that most of the percentage differences between nominal and measured activity are within the 95% confidence interval between −6.5% and 8.2% but some differences are clearly outside of the 95% confidence interval with values up to 12.9%. On the other hand, the 95% confidence interval for the nominal activity exhibits a shift of + 0.8% indicating that the nominal activity tends to be + 0.8% higher than the measured activity. The data indicates that the nominal activity cannot therefore be considered perfectly accurate.

Furthermore, the comparison of the Bland-Altman analyses illustrated in Figs. 4 and 5 shows that the 95% confidence interval for the percentage differences for our measuring method which ranges between −6.5% and + 6.5% (13%) is smaller than the one for the nominal activity ranging between −6.5% and 8.2% (14.7%). This means that our activity measurement method is slightly more precise and more accurate than the nominal activity. Above all, our method fulfills the law request of individual activity measurement, while the simple consideration of the nominal activity would not.

In addition, there is still a very small but not ruled out possibility of incorrect labelling of the activity by the supplier. On the other hand, the difference between the nominal $^{131}$I-capsule activity declared by the manufacturer and the actual activity is particularly important for internal dosimetry after administration of radiopharmaceuticals. Since the difference can be up to 12.9%, this source of error must therefore be taken into account when calculating the internal dose in addition to the other sources of error, such as fit uncertainty, imaging uncertainty, S values uncertainties etc. Each capsule activity should therefore be measured, optimizing the procedure to reduce operators’ hand exposure (ALARA principle).

**Validation of the measuring method in clinical practice**

We have validated the calibration results for our method in clinical practice with additional 89 $^{131}$I-capsule measurements with both our method and the conventional method using a dose calibrator. Fig. 4 on the left shows the correlation between the $^{131}$I-capsule activity measurements with the dose calibrator versus the activity estimated with our method measuring the DR measured on the surface (side and top measurements) of the closed lead containers (size I and II). The slope of the correlation is 0.999 which presents a very high correlation with a high determination coefficient $R^2 = 0.9971$.

**Dose reduction**

The person that measures the activity of the $^{131}$I-capsule by means of the standard procedure (dose calibrator measurement) requires an equal amount of time for transporting the $^{131}$I-capsule from and back to the place where it is stored to the measuring station as the person that determines $^{131}$I-capsule activity with our method. Transporting the $^{131}$I-capsule back and forth from the storing place to the measuring station requires the same amount of time with the two measuring methods. Consequently, the employee would be exposed to the same radiation dose to the hands and to the body with both methods so far. However, the radiation exposure during the following measuring time is different for the two methods. Since the measurement with dose calibrator of the $^{131}$I-capsule is usually carried out in a well-shielded workplace, mainly hands are exposed after opening and removing the $^{131}$I-capsule from the lead container (supplementary video 1). Radiation exposure for the rest of the body remains minor and negligible thanks to the well-shielded workplace setup. Our measuring method does not require to open the lead containers, strongly reducing the radiation exposure to the hands and body results from residual radiation coming out of the closed lead container.

The determination of the dose in practice in our study using official dose meters for the hands and body showed a reduction for the hand dose of 97% in favour of our method, independent from the size of the container and the measuring location compared to the measurement method with the dose calibrator (Table 2). Furthermore, it can be assumed that the value for the hand dose for the proposed method can be assumed half of what we measured is lower in reality, as in our study the measurements of the DR were carried out at two locations (top and side), on the surface of the containers. While in practice DR measurements of the DR would only take place at one location.

The determined whole body effective doses were under the detection limits detection of the dose meters for both methods.

To ensure the consistency of our measuring method in clinical routine, regular cross-calibration should be performed in analogy to the calibration of exposure measuring devices once per year. In cases of extreme discrepancies between the measured activity using our method and the activity declared by the capsule supplier, these need to be resolved by additional measurements of the unshielded $^{131}$I-capsule in the dose calibrator. By observing these rules any unforeseen changes to the specifications of the lead containers can be detected promptly and safely. Due to its advantages of significant dose reduction for the employees’ hands and its high reliability and ease of use, we have established the described measuring method as a routine standard for measuring $^{131}$I-capsule activity at our institution. Everyday clinical routine has confirmed the high reliability and usability of this procedure.

**Conclusion**

In Germany, the activity of the $^{131}$I capsules has to be checked by law before the RT. Application of our measuring method leads to substantial reduction of radiation exposure of the medical staff and in particular their hands. It enables simple, accurate and precise determination of $^{131}$I-capsule activity irrespective of the person measuring it. Moreover, the manufacturer’s activity specifications regarding the delivered capsule activity are entirely fulfilled, while making an important contribution to radiation safety. The time required for measuring is comparable to that of the conventional dose calibrator measuring method. However, it must be ensured that only standardized lead containers with consistent material properties and dimensions are used. The method presented here contributes as a simple and practical approach to a significant reduction of the radiation burden for medical personnel in nuclear medicine.

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**Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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References