Individual Calculation of Effective Dose and Risk of Malignancy Based on Monte Carlo Simulations after Whole Body Computed Tomography

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Detailed knowledge about radiation exposure is crucial for radiology professionals. The conventional calculation of effective dose (ED) for computed tomography (CT) is based on dose length product (DLP) and population-based conversion factors (k). This is often imprecise and unable to consider individual patient characteristics. We sought to provide more precise and individual radiation exposure calculation using image based Monte Carlo simulations (MC) in a heterogeneous patient collective and to compare it to phantom based MC provided from the National Cancer Institute (NCI) as academic reference.

Dose distributions were simulated for 22 patients after whole-body CT during Positron Emission Tomography-CT. Based on MC we calculated individual Lifetime Attributable Risk (LAR) and Excess Relative Risk (ERR) of cancer mortality. EDMC was compared to ED_{DLP} and ED_{NCI}. ED_{DLP} (13.2 ± 4.5 mSv) was higher compared to ED_{nci} (9.8 ± 2.1 mSv) and EDMC (11.6 ± 1.5 mSv). Relative individual differences were up to −48% for EDMC and −44% for ED_{nci} compared to ED_{DLP}. Matching pair analysis illustrates that young age and gender are affecting LAR and ERR significantly. Because of these uncertainties in radiation dose assessment automated individual dose and risk estimation would be desirable for dose monitoring in the future.

The Euratom council directive (2013/59/Euratom) emphasizes the need for patient radiation dose monitoring in clinical routine. Computed tomography (CT) is indispensable for contemporary patient care, but many studies suggest a relation between low dose protracted radiation exposure and an increased incidence of malignancy based on the linear Non-threshold Dose-Response Model. Therefore, detailed knowledge of radiation exposure from CT examinations is crucial for radiology healthcare professionals in clinical routine to detect and address increased risks of malignancy. Widely used parameters for radiation exposure assessment like the volumetric CT dose index (CTDIvol) and the Dose Length Product (DLP) characterize scanner radiation output, but are unable to take individual patient characteristics into account. Conversion to effective dose (ED_{DLP}) is feasible using population-based conversion factors (k) that take the averaged radiosensitivity in defined anatomic regions into account. A variety of different k-factors are recommended in the literature for different volumes (e.g. head, thorax, abdomen, pelvis) and different CT-scanners. These k-factors are mostly derived from phantom models that try to represent average patient anatomy in western populations, but are unable to respect individual anatomy like missing organs due to aplasia or resection, organ hypo- or hypertrophy, skeletal deformations and metal implants. Nevertheless, these programs, like e.g. the National Cancer Institute (NCI) dosimetry system for CT, can be considered as current academic reference (ED_{NCI}). However, the routinely performed calculation of ED_{DLP} is imprecise and the degree of difference to the real ED in each individual patient is unknown. Risk estimates that...
are calculated on these imprecise data could then easily be misinterpreted. Therefore, conventionally calculated EDDLP can be used for comparison between different CT-scanners or different examination protocols, but should not be used for comparison between different patient collectives or for radiation risk estimation. Stochastic estimation of radiation exposure from CT is feasible by Monte Carlo (MC) simulations. Romanyukha et al. used computational phantoms and MC-simulations to calculate body size-specific conversion factors from regression curves. Huda et al. were able to show that this phantom based technique is also feasible to derive organ doses and to use these for cancer risk estimation. Only few studies with small numbers of mostly pediatric patients used MC simulations for individual dose and risk estimation per patient, probably due to the high computational power needed. The main drawback of MC calculations is that they are limited to the reconstructed body volume. Therefore, overexposure in z-axis and scattered radiation to the organs outside the directly exposed volume cannot be taken into account.

Detailed information about biological effects of low-level ionizing radiation is available from the National Academy of Sciences report number seven about Health Risks from Exposure to Low Levels of Ionizing Radiation (BEIR VII). The authors of BEIR VII report follow the linear Non-threshold Dose-Response Model and presume that the risk of cancer incidence and mortality due to medical examinations are mainly based on low-level ionizing radiation dose, age and gender.

The aim of this study was to provide individual calculations of ED in whole-body exposure derived from MC calculations (EDMC) and to compare them with the conventional method (ED DLP) and the academic reference (EDNCI) following an equivalence hypothesis in a heterogeneous study collective. Furthermore, cancer risk estimates that are based on EDMC should allow to evaluate the impact of patient characteristics on individual risk of malignancy. Whole body CT from combined Positron Emission Tomography (PET)-CT examinations were exclusively selected in order to minimize the indeterminate radiation dose to body parts outside the imaging volume that cannot be assessed by MC.

Methods

Study design. Twenty-two patients from a collective of 34 consecutive patients, with clinical indication for whole body PET-CT, were retrospectively included (Fig. 1). Inclusion criteria were the complete and artifact-free coverage of the scan volume, sufficient intra-venous contrast injection and full availability of individual patient data including age, height, weight and body mass index (BMI). Exclusion criteria were severe artifacts (n = 0) and examinations without contrast injection (n = 12). Clinical indications were infectious diseases (n = 8), bronchial carcinoma (n = 6), head and neck cancer (n = 3), cancer of unknown primary (n = 2), malignant melanoma (n = 2) and retroperitoneal fibrosis (n = 1).

Written informed consent was obtained and archived for each patient. The study was approved by the local ethics committee of the Friedrich-Alexander University Erlangen-Nuremberg and complied with the Declaration of Helsinki.

Image acquisition. All examinations were performed with continuous volume acquisition using a Siemens Biograph True Point 64 PET-CT (Siemens Healthcare GmbH, Forchheim, Germany). Indication, supervision and image analysis were performed by senior physicians with extensive experience in PET-CT (>6 years). CT was performed from head to mid-femur by a single spiral acquisition in a cranio-caudal direction using a tube voltage of 120 kV, anatomic tube current modulation with a reference tube-current time product of 170 mAs, pitch 0.8, gantry rotation time 0.5 seconds and 64 × 0.6 mm slice acquisition by 32 × 0.6 mm detector collimation and z-axis flying focal spot double sampling. Unlike in diagnostic CT, where different body parts (e.g.
head/neck and thorax/abdomen) are often examined in multiple contrast phases and different positions, PET-CT uses single spiral acquisitions with only one single bolus injection allowing for complete coverage of all body organs without overlapping of anatomic regions. Therefore, the effect of scattered radiation to all radiosensitive tissues can be taken into account by MC calculations and the effect of overranging in the beginning and end of the spiral acquisition can be neglected. All patients received body weight adapted intravenous injection of $^{18}$F-fluorodeoxyglucose (3 MBq/kg). After an average resting period of 91 ($\pm$ 25.6) minutes iodine containing contrast agent (Ultravist 370®, Bayer-Schering Healthcare, Berlin, Germany) was mechanically administered into an antebrachial cannula using a power injector (Accutron CT-D, Medtron AG, Saarbruecken, Germany), and the single spiral CT acquisition was started with a fixed delay of 70 s. The PET acquisitions were run subsequently in 7–8 steps, depending on patient length and exam volumes. For this study full field of view (500 × 500 mm) images were reconstructed using a smooth filtered back projection kernel (B31), slice thickness 5.0 mm and increment 5.0 mm. The resulting voxel size was 0.98 × 0.98 × 5.00 mm.

Conventional calculation of effective dose. Tube current time product, CTDIvol and DLP were recorded for each examination from the PET-CT scan protocol as provided by the scanner. Details about their definition and calculation are reported elsewhere in literature. The main drawback of these monitoring techniques is that they are unable to provide information about the biological impact of radiation exposure and should only be taken as an index of radiation output by the CT system for comparative purposes. The biologically relevant effective dose (ED_{DLP}) was calculated for each examination by multiplication of DLP and the region-specific conversion factor. For this study $k_{body}$ (0.015 mSv/mGy·cm) was used as recommended by the American Association of Physicists in Medicine. Dose exposition related to $^{18}$F-fluorodeoxyglucose (FDG)-PET were not considered for ED calculation.

Phantom based calculation of effective dose. Academic reference ED was calculated using a dedicated CT dosimetry software tool provided by the National Cancer Institute (NCI-CT), which combines reference phantoms provided by the International Commission on Radiological Protection (ICRP) and MC simulations of a reference CT scanner (Somatom Sensation 16, Siemens Healthcare GmbH, Forchheim, Germany). Individual examination parameters, gender, age, height and body weight were used as input for this mathematical phantom based calculation (ED_{NCI}). Dedicated descriptions about computational methods of this software are available in the literature.

Organ segmentation. All radiosensitive organs or tissues including all remainders, which are mentioned in ICRP report 103 were segmented using a dedicated software package (ITK-SNAP 1.8, Penn Image Computing and Science Laboratory, Philadelphia, USA). Semi-automatic threshold segmentation with manual corrections was used for the lungs, cortical bone, bone marrow, liver, spleen, brain, heart, muscle and skin. All other organs or tissues were segmented manually in a slice per slice fashion. Therefore, missing organs due to aplasia or resection, organ hypo- or hypertrophy, skeletal deformations and metal implants were considered. For hollow organs, only voxels contributing to the wall were considered to contain radiosensitive tissues. Segmentation of lymphatic tissues was restricted to visible lymphatic nodes (Fig. 2). All segmentations were performed by a specially trained radiologist.
Radiology resident (4 years experience) and reviewed from an experienced board-certified radiologist (9 years experience).

Monte Carlo based calculation of effective dose. Extensive mathematical models in simulation techniques can be utilized to calculate dose distribution for each voxel of CT scan volumes using the attenuation values and geometry from DICOM datasets as input\textsuperscript{18,19}. All MC dose simulations were carried out using the software package ImpactMC (VAMP GmbH, Erlangen, Germany). Software details and information concerning the Monte Carlo calculation algorithms are reported elsewhere\textsuperscript{18,20}. Multiplication of the resulting relative dose values per voxel with air kerma provides the absorbed dose for each voxel. The air kerma is a scanner specific value, which describes the kinetic energy transferred in air dependent on geometry and tube settings. It can be considered as measurement of x-ray beam intensity without object, which was 18.3 mGy for this study. The averaged absorbed dose over an organ volume, defined from segmentations, provides the absorbed dose. Equivalent organ dose was calculated by multiplication with the radiation weighting factor for photons (W\textsubscript{R} = 1) and used for subsequent effective organ dose calculations (ED\textsubscript{Organ}) by multiplication with the dedicated tissue weighting factor (W\textsubscript{T}) as recommended in ICRP report 103\textsuperscript{21}. The sum of all effective organ doses provides EDMC for each individual (Fig. 3). The relative contribution of the respective EDOrgan to the EDMC was calculated following Eq. 1:

$$C\textsubscript{Organ} = \frac{ED\textsubscript{Organ}}{ED\textsubscript{MC}}$$

Individual conversion factors (k\textsubscript{MC}) were calculated using Eq. 2 to illustrate the differences compared to the conventional calculation method using DLP and k\textsubscript{body}.

$$k\textsubscript{MC} = \frac{ED\textsubscript{MC}}{DLP}$$

Radiation risk assessment. Lifetime Attributable Risk (LAR) is defined as risk of disease of an exposed cohort in comparison to a non-exposed cohort. Calculations of LAR for cancer mortality were based on report VII about Biologic Effects of Ionizing Radiation (BEIR VII). The BEIRV VII report refers to an individual radiation dose exposure of 100 mGy. Assuming a linear risk distribution between decennium age intervals LAR\textsubscript{MC} was derived from EDMC by linear interpolation between the younger (N\textsubscript{y}) and older (N\textsubscript{o}) cohort as shown in equation 3 using patient age (A\textsubscript{p}) and the age of the younger cohort (A\textsubscript{y}) as input values\textsuperscript{22}.

Equation 3: Calculation of individual LAR

$$LAR\textsubscript{MC} = \left[ N\textsubscript{y} - \left( N\textsubscript{y} - N\textsubscript{o} \right) \frac{A\textsubscript{p} - A\textsubscript{y}}{10 \text{ years}} \right] \frac{ED\textsubscript{Organ}}{100 \text{ mGy}}$$

The Excess Relative Risk (ERR\textsubscript{MC}), as a measurement of the exceeding risk of an exposed person compared to a non-exposed person, was calculated using the solid cancer mortality in the United States as baseline (female: 17500/100000; male: 22100/100000) using equation 4\textsuperscript{23}.

Equation 4: Calculation of individual ERR
Effective dose and individual radiation risk assessment. \( ED_{\text{DLP}} \) (13.2 \pm 4.52 mSv) was higher than \( ED_{\text{MC}} \) (11.6 \pm 1.47 mSv) and \( ED_{\text{NCL}} \) (9.8 \pm 2.1 mSv). Particularly high differences between \( ED_{\text{MC}} \) and \( ED_{\text{DLP}} \) were found for patients with relatively high or low radiation dose exposure. Mean difference between both methods was \(-1.7\ mSv\) (Fig. 5a). The same tendency was found for the comparison of \( ED_{\text{NCL}} \) and \( ED_{\text{DLP}} \) but with higher mean negative differences \(-3.4\ mSv\) (Fig. 5b). A comparison between the three calculation methods is illustrated as boxplot (Fig. 6). The range of radiation dose was substantially smaller in both advanced methods (\( ED_{\text{MC}} \): 5.6 mSv, \( ED_{\text{NCL}} \): 10.2 mSv) compared to the conventional technique (\( ED_{\text{DLP}} \): 19.3 mSv). Effective mAs and DLP

### Results

**Demographics of the study collective.** Five out of 22 patients (23%) were female and 17 male (77%). The mean age was 57.3 \pm 14.3 years and the mean BMI was 26.0 \pm 5.9 kg/m². Three patients (13.6%) were younger than 40 years. The female patient group was younger (53.6 \pm 17.6 years) compared to the male patient group (58.4 \pm 13.6 years). Female patients had a lower mean BMI (21.2 \pm 2.5 kg/m²) compared to male patients (27.4 \pm 5.88 kg/m²). From the male subgroup 9 patients (52.9%) suffered from overweight (\( BMI > 25 \)), and three patients (17.6%) had severe overweight (\( BMI > 30 \)). One female and one male patient were considered as underweight (\( BMI < 19 \)). No overweight patient was found in the female subgroup. Detailed patient characteristics are shown in Table 1.

**Organ specific radiation dose exposure.** Mean equivalent organ dose was 13.0 \pm 3.5 mGy. Highest equivalent organ dose values were found in high attenuating structures such as the cortical bone and the thyroid gland. Lowest values were found in profound organs like the extra-thoracic (ET) respiratory region and the uterus. Many superficial organs like muscles (11.5 \pm 2.0 mGy), breast tissue (10.9 \pm 0.8 mGy) and salivary glands (14.3 \pm 2.8 mGy) also had rather low equivalent organ dose values. Despite its profound position well perfused kidneys had very high equivalent organ dose values (17.0 \pm 2.1 mGy).

Effective organ dose was mainly influenced by \( W_T \), nicely demonstrated by the thyroid gland. It has the second highest mean equivalent organ dose (21.2 \pm 5.4 mGy), but is only ranked 7th highest effective organ dose (8% of total organ dose distribution) because of the rather low \( W_T \) (0.04). In contrast, the lungs ranked only 7th in equivalent organ dose (13.4 \pm 1.9 mGy), but received highest effective organ dose levels in female and male patients (12% and 14% of the total \( ED_{\text{MC}} \)) due to high \( W_T \) (0.12). Colon, lungs and stomach contributed to more than 50% of the total \( ED_{\text{MC}} \) in male patients and to 48% in female patients (Fig. 4). Differences between \( W_T \) and the relative contribution of the effective organ dose to whole body \( ED_{\text{MC}} \) (\( C_{\text{Org}} \)) reflect the influence of individual patient characteristics on the radiation dose parameters and radiation risk estimation. Matching patient pairs, each with two comparable values and one variable parameter, were found for the parameters age, sex and BMI.

**Statistical analysis.** All statistical analyses were performed using the software package SPSS Statistics Version 21 (IBM, Somers, NY, USA). Normal distribution of the data was tested by Kolmogorov-Smirnov and Shapiro-Wilk test. Normally distributed data is presented as mean \pm standard deviation. Median and range are provided if no normal distribution was assumed. Illustration is provided as Bland-Altman plots. Spearman’s rank order test was used to test for correlations between tube current, BMI, \( EDD_{\text{LP}} \) and \( EDM_{\text{MC}} \). The significance level was defined as \( p < 0.05 \).

### Table 1. Demographic characteristics and body mass index (BMI) of the patient collective.

| BMI [kg/m²] | <20 | 20-25 | >25 | >30 | total |
|------------|-----|-------|-----|-----|------|
| Age [years] |     |       |     |     |      |
| <40        | 1♀  | 1♂    | 1♀  | 1♂  | n = 3 |
| 40-55      | 1♀  | 1♂    | 4♀  | 1♂  | n = 7 |
| 55-70      | 1♀  | 2♂    | 3♀  | 1♂  | n = 7 |
| >70        | 1♀  | 1♂    | 3♀  | 1♂  | n = 5 |
| total      | n = 2 | n = 1 | n = 5 | n = 4 | n = 22 |

\[ ERRL_{MC} = \frac{LAR_{MC}}{LAR_{baseline}} \]
linearly increased with higher BMI in Spearman's rank order test ($r_s = 0.961$ and $0.949$). This effect should be mainly due to the anatomy-based tube current modulation algorithm. Therefore, also BMI and ED$_{DLP}$ had a high correlation coefficient ($r_s = 0.949$). The correlation between ED$_{MC}$ and BMI ($r_s = 0.644$) was less and differences between ED$_{DLP}$ and the advanced techniques was especially high in over- and underweight patients. For example, the highest ED$_{DLP}$ of 26.3 mSv was found in a 77-year-old man suffering from adiposity grade 3 (BMI 40.0 kg/m$^2$) while ED$_{NCI}$ (17.3 mSv) and ED$_{MC}$ (13.9 mSv) were substantially lower (34% and 47% less). Lowest ED$_{DLP}$ of 7.0 mSv was calculated for a 30-year-old underweight man (BMI 16.8 kg/m$^2$), which was close to ED$_{NCI}$ (7.1 mSv), but substantially lower than ED$_{MC}$ (8.5 mSv, 21% higher). Consequently, the individually calculated conversion factors ($k_{MC}$) have a range from 53% to 140% when referred to $k_{Body}$ from literature. The mean $k_{MC}$ ($0.014 \pm 0.004$ mSv/mGy cm) approximately reflects the established value ($0.015$ mSv/mGy cm), which therefore seems to be suitable for regular weight patients. However, only one fourth of the patients in this study ($n = 6, 27.2\%$) had less than 10% difference between $k_{MC}$ ($0.0135–0.0165$ mSv/mGy cm) and $k_{Body}$ (mean BMI $22.95 \pm 1.58$, range 20.7–25.0 kg/m$^2$).

The values of LAR were especially high in young female patients. The highest value (60/100,000) was calculated for a 30-year-old, normal weight woman (BMI 21.6 kg/m$^2$). In contrast, low LAR values were calculated for older, predominantly male patients. The lowest value (23/100,000) was found for a 76-year-old, overweight man (BMI 29.8 kg/m$^2$). Extent of EDMC, EDDLP and LAR often differed considerably when compared between young and old or underweight and obese patients, while the interaction between these individual parameters was rather difficult to predict. Detailed results of radiation dose and risk calculations are provided in Table 3.

**Pairwise patient comparison.** Two male patients with matching constitution (BMI 24 vs. 23 kg/m$^2$) but different age (36 versus 67 years) had comparable DLP (783 vs. 724 mGy · cm, $-7.5\%$), ED$_{DLP}$ (11.8 vs. 10.9 mSv, $-7.5\%$), ED$_{NCI}$ (9.4 vs. 9.0 mSv, $-4.3\%$) and ED$_{MC}$ (10.9 vs 10.0 mSv, $-8.4\%$). Nevertheless, calculations for LAR of cancer mortality (41.3 vs. 27.1/100,000; $-34.4\%$) and ERR (0.19 vs. 0.12%, $-36.8\%$) differed considerably.
### Table 2. Illustration of equivalent organ dose, tissue weighting factors ($w_T$), effective organ dose ($ED_{ORGAN}$), the relative contribution of $ED_{ORGAN}$ to whole-body effective dose ($C_{ORGAN}$) and estimation of organ-specific Lifetime Attributable Risk (LAR) of cancer mortality based on Monte Carlo simulations and report VII about Biologic Effects of Ionizing Radiation (BEIR VII).

| Organs                  | Equivalent organ dose (mGy·cm$^2$) | $w_T$ | Effective organ dose (female) [mSv] | Effective organ dose (male) [mSv] | $C_{ORGAN}$ (female) | $C_{ORGAN}$ (male) | LAR of cancer mortality [n/100000] |
|-------------------------|-------------------------------------|-------|-----------------------------------|----------------------------------|---------------------|-----------------|----------------------------------|
| Red bone marrow         | 12.3 ± 2.3                          | 0.12  | 1.94 ± 0.24                      | 1.47 ± 0.28                     | 0.125               | 0.126           | 4.69 ± 1.88                     |
| Colon                   | 11.2 ± 2.8                          | 0.12  | 1.28 ± 0.08                      | 1.36 ± 0.38                     | 0.108               | 0.116           | 4.69 ± 1.88                     |
| Lung                    | 13.4 ± 1.9                          | 0.12  | 1.48 ± 0.15                      | 1.64 ± 0.38                     | 0.125               | 0.14            | 13.25 ± 4.24                   |
| Stomach                 | 12.2 ± 1.5                          | 0.12  | 1.39 ± 0.06                      | 1.48 ± 0.23                     | 0.117               | 0.127           | 1.43 ± 0.47                     |
| Breast                  | 10.9 ± 0.8                          | 0.12  | 1.30 ± 0.09                      | 0.11                            |                    | 2.46 ± 1.62      |
| Gonads                  | 14.6 ± 4.1                          | 0.08  | 0.74 ± 0.07                      | 1.29 ± 0.26                     | 0.063               | 0.111           | 1.94 ± 0.84                     |
| Bladder                 | 11.7 ± 2.0                          | 0.04  | 0.40 ± 0.05                      | 0.49 ± 0.06                     | 0.034               | 0.042           | 1.88 ± 0.47                     |
| Liver                   | 12.0 ± 1.2                          | 0.04  | 0.46 ± 0.04                      | 0.49 ± 0.08                     | 0.039               | 0.042           | 1.22 ± 0.41                     |
| Esophagus               | 11.1 ± 1.4                          | 0.04  | 0.42 ± 0.05                      | 0.45 ± 0.01                     | 0.035               | 0.039           |                                |
| Thyroid gland           | 21.2 ± 3.2                          | 0.04  | 0.90 ± 0.04                      | 0.83 ± 0.05                     | 0.076               | 0.071           |                                |
| Skin                    | 11.0 ± 2.1                          | 0.01  | 0.09 ± 0.00                      | 0.11 ± 0.03                     | 0.08                | 0.01            |                                |
| Bone surface            | 26.6 ± 4.7                          | 0.01  | 0.24 ± 0.01                      | 0.27 ± 0.03                     | 0.02                | 0.023           |                                |
| Salivary glands          | 14.3 ± 2.8                          | 0.01  | 0.12 ± 0.01                      | 0.15 ± 0.03                     | 0.01                | 0.013           |                                |
| Brain                   | 12.7 ± 3.3                          | 0.01  | 0.10 ± 0.00                      | 0.14 ± 0.03                     | 0.08                | 0.012           |                                |
| Spleen                  | 12.4 ± 1.7                          | 0.0092| 0.11 ± 0.01                      | 0.12 ± 0.02                     | 0.009               | 0.01            |                                |
| Kidney                  | 17.0 ± 2.1                          | 0.0092| 0.16 ± 0.01                      | 0.15 ± 0.02                     | 0.014               | 0.013           |                                |
| Heart                   | 12.5 ± 1.5                          | 0.0092| 0.12 ± 0.01                      | 0.12 ± 0.01                     | 0.01                | 0.01            |                                |
| Pancreas                | 11.7 ± 1.2                          | 0.0092| 0.11 ± 0.01                      | 0.11 ± 0.01                     | 0.009               | 0.009           |                                |
| Oral mucosa             | 13.5 ± 3.1                          | 0.0092| 0.12 ± 0.01                      | 0.13 ± 0.03                     | 0.009               | 0.011           |                                |
| Lymph nodes             | 12.6 ± 2.2                          | 0.0092| 0.12 ± 0.02                      | 0.12 ± 0.02                     | 0.009               | 0.01            |                                |
| Muscle                  | 11.5 ± 1.9                          | 0.0092| 0.11 ± 0.01                      | 0.11 ± 0.02                     | 0.008               | 0.009           |                                |
| Small intestine         | 13.2 ± 1.9                          | 0.0092| 0.12 ± 0.00                      | 0.13 ± 0.02                     | 0.009               | 0.011           |                                |
| Gall bladder            | 11.6 ± 1.3                          | 0.0092| 0.11 ± 0.01                      | 0.11 ± 0.01                     | 0.008               | 0.009           |                                |
| Adrenal gland           | 10.2 ± 1.3                          | 0.0092| 0.09 ± 0.01                      | 0.10 ± 0.01                     | 0.008               | 0.008           |                                |
| Prostate                | 11.4 ± 3.2                          | 0.0092| 0.10 ± 0.03                      | 0.10 ± 0.03                     | 0.008               | 0.008           | 0.74 ± 0.25                     |
| Uterus                  | 9.9 ± 1.1                           | 0.0092| 0.09 ± 0.01                      | 0.09 ± 0.01                     | 0.008               | 0.008           | 0.28 ± 0.09                     |
| Extrathoracic respiratory (ET) region | 8.7 ± 7.1 | 0.0092| 0.08 ± 0.06                      | 0.07 ± 0.07                     | 0.009               | 0.006           |                                |

Young age seems to be the decisive factor among all the considered factors, accounting for about 50% higher risk estimates (Fig. 7a).

Two male patients with matching age (76 and 77 years) but different BMI (29.7 vs. 40.0 kg/m²; +34.7%) were exposed to considerably different DLP (998 vs. 1751 mGy·cm, +75.4%) based on anatomic tube current modulation. Therefore, $ED_{DLP}$ calculations provided very high values for the obese patient (15.0 vs. 26.3 mSv; +75.5%). Dose differences calculated with $ED_{NCGI}$ (10.5 vs. 17.3 mSv; +64.5%) were also considerably high, while $ED_{MC}$ values were nearly comparable (11.9 vs. 13.8 mSv; +15.9%). Differences in $LAR_{MC}$ (22.8 vs. 25.1/100.000; +9.6%) and ERR (0.10 vs 0.11%; +10.0%) were even less (Fig. 7b). BMI seems to have only a minor influence on effective dose and risk estimation, while conventional methods would have resulted in an overestimation of almost 100%.

Two patients with matching age (56 and 54 years) and BMI (21.5 vs 21.0 kg/m²) but different sex had similar DLP (634 vs. 630 mGy·cm; +0.63%). ED was the same using the conventional method in both patients ($ED_{DLP} = 9.5$ mSv) and almost the same with the NCI method ($ED_{NCGI} = 8.9$ mSv; −3.3%). $ED_{MC}$ calculation was slightly higher for the female patient (12.3 vs. 10.3 mSv; +19.4%), but LAR (53.1 vs. 35.4/100000; +50.2%) and ERR (0.3% vs. 0.16%; +87.5%) were substantially higher. Sex seems to have a dominant impact on the risk estimation. Moreover, the unfavorable combination of age and sex leads to the highest values in the entire study collective, despite average ED values (Fig. 7c).

**Discussion**

Individual radiation dose assessment and risk calculation is feasible by image based Monte Carlo simulations and organ segmentations in an adult clinical routine collective that underwent full body exposure in a single spiral acquisition. This is in good agreement with the findings of Li et al. and Tian et al. who evaluated comparable techniques for radiation dose estimation in small pediatric collectives ($n=2$ and $n=4$)\cite{16,24}. A comparable approach for cancer risk estimation in adults based on anthropomorphic phantoms was described by Huda et al.\cite{11}. In contrast to these prior studies, we provide a combination of individual radiation dose analysis, voxel-based organ...
Figure 5. (a) Bland-Altman plot for the difference between conventional effective dose calculation (ED_{DLP}) and calculation based on Monte Carlo simulations (ED_{MC}): The difference between both methods increases with high and low values of mean ED. This implicates that in high and low mean ED the conventional ED_{DLP} over- and underestimates radiation dose exposure compared to ED_{MC}. (b) Bland-Altman plot for the difference between ED_{DLP} and calculation by the National Cancer Institute dosimetry system for CT (ED_{NCI}): The difference between both methods increases especially with high values of mean ED. This suggests that in high mean ED the conventional ED_{DLP} overestimates radiation dose exposure compared to ED_{NCI} (red triangles indicate female patients).

Figure 6. Comparison of effective dose for ED_{DLP}, ED_{NCI} and ED_{MC} illustrated as boxplot.

segmentation and cancer risk estimation in direct comparison to such phantom based estimation and the DLP method. The need for such an advanced dose monitoring method, due to several uncertainties with the conventional techniques, has been raised elsewhere in literature\textsuperscript{20,25}.

In our study high equivalent organ doses were strongly related to radiodensity (e.g. bone surface and high contrast medium uptake in the kidneys, the thyroid gland and the extra-thoracic respiratory region), which seems to
Table 3. Individual patient and radiation exposure characteristics with illustration of dose length product (DLP), volume computed tomography dose index (CTDvolel), effective mAs (eff. mAs), effective dose based on conventional calculation method (ED_{DLP}), Monte Carlo simulations (ED_{MC}), and the dosimetry system for CT provided by the National Cancer Institute (ED_{NCI}). ED_{NCI}/ED_{DLP} and ED_{MC}/ED_{DLP} deviations, conversion factors (k_{MC}), Lifetime Attributable Risk (LAR_{MC}) and Excess Relative Risk (ERR_{MC}) are individually calculated.

[Table 3 content]

be a much stronger predictor for equivalent organ dose than anatomical organ position. This is in good agreement with the contrast media related increase of DNA double-strand break foci after radiation exposure reported in a prior study for CT. W_T is the strongest predictor of effective organ dose. For example, the thyroid gland and the kidneys have the second and third highest equivalent organ dose (21.2 ± 3.2 mSv and 17.0 ± 2.1 mSv). However, due to low tissue weighting factors (W_T = 0.04 and 0.0092) effective organ dose of the thyroid gland and the kidneys were only sixth and twelfth highest.

Our results confirm that individual patient characteristics have a considerable impact on radiation dose calculation, which is underrepresented by the conventional method. The calculated error in our adult collective (−48 to 39%) is comparable to the previously published study results for children (−63 to 28%)19. Individually calculated k_{MC} from our study reveals that the routinely used k_{MC} from literature can be applied to larger clinical collectives, but are limited in their value for individual risk assessment9. The DLP-method slightly overestimates the effective dose in general, but it seems to be appropriate in regular weight male patients. However, especially in female and underweight patients, underestimation of the effective dose may be critical for risk perception in the clinical setting. Moreover, its overestimation in obese patients may lead to restrained use of high exposure parameters, and then to poor or insufficient image quality. Individual anatomic characteristics (e.g. missing organs due to aplasia or resection, organ hypo- or hypertrophy, skeletal deformations, metal implants) may lead to considerable changes of radiation dose distribution and consequently of individual risk. Even phantom based estimation methods, like ED_{NCI} in this study, are unable to take these individual properties into account7. Bland-Altman analysis demonstrated that these phantom based estimates have the tendency to underestimate the effective dose in general, while the effect of only moderate increase of ED in obese patients despite the very high energy exposure is confirmed.

The influence of personal risk profiles on cancer risk estimates are not yet represented in standard radiation dose reporting systems. It can further increase the error of perceived and true risk of radiation dose from CT examinations. The combination of individual dose distributions and risk assessment has been presented for a few other examinations in literature, such as absorptiometry and spine radiographs, but not for spiral CT examinations27.
Pairwise patient comparisons provide a comprehensive overview of the extent of error with regard to age, BMI and sex. Especially younger patients are prone to higher LAR and ERR since more active cell division and longer life expectancy after radiation exposure is presumed. In our example the ERR of a patient in his mid-thirties was 1.6-fold the ERR of a patient in his mid-sixties and the ERR for a female patient in her mid-fifties was almost doubled compared to a matching male patient. The increasing tube current by anatomy-based modulation in obese patients seems to be of less importance to the patients’ cancer risk. CTDI and EDDLP were 1.8-fold higher for a high-grade obese patient compared to an overweight patient with matching age and sex, while the ERR was only 10% higher. Therefore, future dose assessment strategies should not only focus on absolute dose values. Furthermore, reporting LAR or ERR seems to be much more appropriate in clinical routine and a more comprehensible value for the patient-physician interaction.

Some limitations have to be considered while interpreting this study. First, the study population consisted of a heterogeneous, small and retrospectively selected patient collective with an imbalanced ratio of female to male patients. The small number of patients is mainly due to the high computing power required for MC calculations and the work intense manual organ segmentation that we used for this study. We estimate that the increasing computing power and automated organ segmentations by the application of artificial intelligence could overcome this limitation in the near future. Second, only full body dose exposure is reported in this study. This avoids indeterminate scattered radiation to radiosensitive structures and over-ranging effects, but limits the findings to this clinically rather rare indication. Further evaluations for limited examination volumes could become feasible with retrospective simulations from these data in larger collectives by future studies. Third, all examinations were conducted on the same scanner. The findings of this study can therefore not automatically be transferred to other CT systems. Forth, all tissue weighting factors that are provided in literature so far are averaged for sex and age, which may probably limit their applicability for patient specific risk estimation. Fifth, the linear Non-threshold Dose-Response Model itself is discussed controversially among experts for diagnostic dose levels. Sixth, LAR and ERR calculations in this study are only related to low dose radiation exposure. They illustrate the individual radiation dose related risk to develop cancer. Obviously, the overall individual cancer risk for a primary or even a secondary cancer and also the life expectancy is potentially much more influenced by age, genetic make-up, efficiency of DNA damage repair, therapy-related adverse effects and many other influencing factors.

**Figure 7.** Pairwise comparison of dose length product (DLP), effective dose (ED), Lifetime Attributable Risk (LAR) and Excess Relative Risk (ERR) in dependence of age (a), Body Mass Index (b) and sex (c).
The importance of patient specific dose surveillance is illustrated by this study. ED_{CLP} can be used for radiation dose assessments in larger collectives, but individual considerations require advanced techniques like ED_{MC}. Conventional methods tend to underestimate radiation dose in underweight and female patients. Therefore, these patients have to be evaluated with special care. The influence of young patient age and female gender on cancer risk estimates is very high. Thus, radiation dose assessment should not only provide whole body or organ dose measurements but also individual risk calculations, which could be included in future surveillance programs.

Data availability

The datasets generated during and analyzed during this study are available from the corresponding author on reasonable request.

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Contributed to the writing of the manuscript: M.K., M.M., T.L. and W.W. Study design, measurements and statistical analysis: M.K., M.M., W.W., M.Br., M.W., T.L., W.N., B.S., D.S., M.Be. and M.U. All authors reviewed the manuscript.

Competing interests
M.K., M.M., W.W. and M.U. are members of the Siemens Speaker’s Bureau. B.S. is an employee of Siemens Healthineers GmbH. M.W., T.L., M.Br., W.N., D.S. and M.Be. declare no competing financial interests. All authors declare no competing non-financial interests.

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