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The effect of iodine uptake on radiation dose absorbed by patient tissues in contrast enhanced CT imaging: Implications for CT dosimetry

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Abstract

Objectives To investigate the effect of iodine uptake on tissue/organ absorbed doses from CT exposure and its implications in CT dosimetry.

Methods The contrast-induced CT number increase of several radiosensitive tissues was retrospectively determined in 120 CT examinations involving both non-enhanced and contrast-enhanced CT imaging. CT images of a phantom containing aqueous solutions of varying iodine concentration were obtained. Plots of the CT number increase against iodine concentration were produced. The clinically occurring iodine tissue uptake was quantified by attributing recorded CT number increase to a certain concentration of aqueous iodine solution. Clinically occurring iodine uptake was represented in mathematical anthropomorphic phantoms. Standard 120 kV CT exposures were simulated using Monte Carlo methods and resulting organ doses were derived for non-enhanced and iodine contrast-enhanced CT imaging.

Results The mean iodine uptake range during contrast-enhanced CT imaging was found to be 0.02-0.46% w/w for the investigated tissues, while the maximum value recorded was 0.82% w/w. For the same CT exposure, iodinated tissues were found to receive higher radiation dose than non-iodinated tissues, with dose increase exceeding 100% for tissues with high iodine uptake.

Conclusions Administration of iodinated contrast medium considerably increases radiation dose to tissues from CT exposure.

Key-points

- *Radiation absorption ability of organs/tissues is considerably affected by iodine uptake*
- *Iodinated organ/tissues may absorb up to 100 % higher radiation dose*
- *Compared to non-enhanced, contrast-enhanced CT may deliver higher dose to patient tissues*
- *CT dosimetry of contrast-enhanced CT imaging should encounter tissue iodine uptake*

Keywords CT imaging · Contrast media · Iodine · Radiation dose · Radiation absorption

Abbreviations

CTDI	CT dose index
DLP	Dose length product
NECT	Non-enhanced CT
CECT	Contrast enhanced CT
PMMA	Polymethyl-methacrylate
% w/w	% weight per weight

Introduction

CT imaging increasingly dominates the cumulative dose of the population from medical exposures and CT radiation-related concerns have been recurrently subject

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of public attention [1, 2]. The ongoing debate regarding radiation dose and risk associated with CT imaging renders imperative the need for reliable tools to provide patient-specific accurate estimates of the radiation burden from CT exposures [3].

The most commonly used CT dose descriptors are the CT dose-index (CTDI) and its relatives, i.e., weighted CTDI, volume CTDI and dose-length product (DLP) while a rough estimate of effective dose is commonly derived through DLP and anatomy-specific conversion coefficients [4–6]. However, CTDI-related indices do not encounter the varying internal anatomy and tissue composition, and they fail to provide reliable individual-specific organ dose estimates, which is considered the best approach for the determination of the radiation-related risk associated with a specific CT exposure on a specific patient [7, 8]. Monte Carlo computation methods have been employed to simulate CT exposure on mathematical anthropomorphic or patient-specific phantoms [8, 9] and record the energy deposition on tissues/organs. These methods rely on the resemblance of the phantom used to the specific patient, regarding the size, tissue composition/density and internal anatomy. However, elemental composition of tissues may be altered when the patient is administered with iodine-based contrast media changing the x-ray attenuation ability of tissues. The effect of contrast media uptake on the tissue absorbed radiation dose has been adequately studied in radiotherapy yielding the conceptual basis for contrast enhanced radiotherapy [10]. The motivation of the current study originated from the limited data found in lthe iterature on the effect of contrast media administration on organ doses from CT exposures [11, 12] and the inability of available CT dosimetry tools to take into consideration contrast media administration in evaluating organ doses and effective dose.

The aims of this study were to (1) investigate the effect of iodine uptake on the dose absorbed by radiosensitive organs from CT exposure and (2) evaluate the underestimation of organ doses and effective dose from contrast enhanced CT scans if iodine uptake is not taken into account.

Materials and methods

The effect of contrast media administration on tissue CT number

Thirty head, 30 neck, 30 thoracic and 30 abdominal consecutive multiphase patient CT examinations were retrospectively studied to evaluate the change in the CT number of radiosensitive tissues induced by contrast media administration. The study was approved by the local institutional review board. All head, neck and thoracic CT examinations included a non-enhanced (NECT) and a contrast enhanced CT (CECT) scan. Abdominal CT examinations included a NECT scan followed by CECT scans at arterial, hepatic and occasionally delayed phase. All examinations had been performed on a Siemens SOMATOM Sensation 16 CT scanner (Siemens AG, Forchheim, Germany). Following the NECT scan of the imaged body region, iodinated contrast medium (iopromide; Ultravist 300, Bayer Healthcare) containing 300 mg I/ml was administered intravenously at a dose of 1.2 ml contrast medium/kg of patient weight with maximum administered quantity of 120 ml. The CT acquisition protocols shown in Table 1 were employed. The CT numbers of healthy (1) brain parenchyma, and skull bone, (2) thyroid, parotid and submandibular salivary glands, (3) breast, heart, and muscle and (4) liver, spleen, kidneys, stomach, vertebral red bone marrow and ovaries, were recorded in both NECT and CECT image series of (1) head, (2) neck, (3) thorax and (4) abdomen, respectively. The CT numbers of the different organ tissues were determined by appropriately positioning a ROI in the healthy parenchyma of each organ avoiding vessels and delineating organ region where contrast medium was homogeneously distributed. Identical ROIs in size, shape and anatomic position were employed in non-enhanced and corresponding enhanced image series of the same patient. Contrast-induced CT number increase was thus determined for all above tissues.

The number of patient CT examinations performed with intravenous administration of iodinated contrast medium out

Table 1 Typical imaging protocols

CT examination	Boundaries of imaged tissue volume	kV	Quality reference mAs	Beam collimation (mm)	Pitch
Head	Vertex – base of skull	120	320	16x0.75	0.55
Neck	Base of skull – clavicles	120	150	16x1.5	0.75
Thorax	1st thoracic vertebrae - caudal end of diaphragm	120	100	16x1.5	1.15
Abdomen	Cephalic margin of diaphragm – iliac crest	120	160	16x1.5	0.75

of 2854 CT examinations performed in total in our institution during the period Sept 1 to Nov 30 2016 was recorded to evaluate the percentage of CT examinations that involved CECT scans.

The effect of iodine uptake on resulting CT number

Aqueous solutions of 0.0, 0.1, 0.3 and 0.5% w/w iodine concentration were prepared mixing definite volumes of deionised water and iodinated contrast medium of 300 mg I/ml (Ultravist 300). It is noted that mean iodine concentration in human tissues following contrast administration has been reported to be within that range [11]. Prepared solutions and tap water were used to fill holes of a standard polymethyl-methacrylate (PMMA) CT phantom as shown in Fig. 1. Holes were sealed to prevent liquid solution leakage. The phantom was aligned at the isocenter of the scanner and successively scanned at 80, 100, 120 and 140 kV in spiral acquisition mode on (1) a Siemens SOMATOM Sensation 16 CT scanner (Siemens AG, Forchheim, Germany) with 16x1.5 mm beam collimation to derive 3 mm thick images and (2) a General Electric Revolution GSI CT scanner (GE Healthcare, Waukesha, WI, USA) with 64 x 0.625 beam collimation to derive 3.75 mm thick images. CT image series were produced using the 'standard' and the 'lung' reconstruction filter. Circular ROIs of 8 mm in diameter were positioned in the center of the circular area corresponding to each solution, as shown in Fig. 1. The CT number of each solution was determined as the mean value of the CT numbers measured in ten consecutive images of the central area of the phantom. Plots of the CT number enhancement against iodine concentration were produced for 80, 100, 120 and 140 kV.

The effect of iodine uptake on organ doses and effective dose from CT exposure

The Monte Carlo N-particle transport code (MCNP, version 4C2) was used to simulate CT exposures performed with a Siemens SOMATOM Sensation 16 CT scanner (Siemens AG, Forchheim, Germany) as previously described [13–15]. The x-ray spectra produced at 80, 100, 120 and 140 kV were obtained from Boone and Seibert [16]. Standard head and neck, thoracic and abdominal CT exposures at 120 kV, were simulated on mathematical anthropomorphic phantoms representing the average female and male adult individual. The average female was assumed to be168 cm in height and 56 kg in weight and the average male 179 cm and 73 kg, respectively. The mathematical anthropomorphic phantoms were generated using BodyBuilder software (White Rock Science, WhiteRock, NM, USA) which enables simulation of the internal human anatomy. Organs/tissues are assumed with a certain amount of mass and shape. Organ/tissue composition may be defined as either 'adult soft tissue', 'skeleton', 'lung' or 'air' with densities of 1.04, 1.4, 0.296 and 0.00102 g/ml, respectively. All soft tissue-like organs/tissues (i.e., organs categorized as 'adult soft tissue') are assumed with the same elemental composition and density. However, the BodyBuilder software allows the user to change the elemental composition of each organ separately.

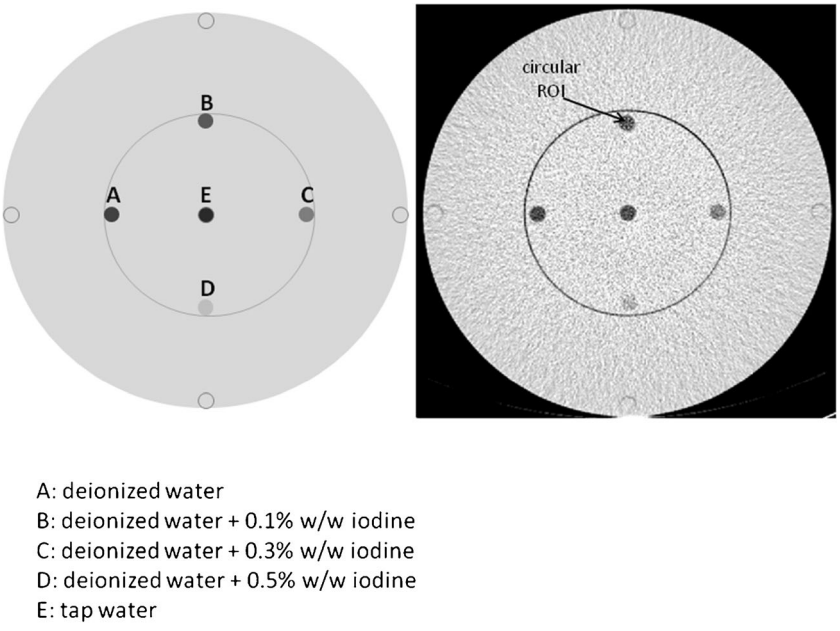

Fig. 1 CT image of the standard PMMA CT phantom containing aqueous solutions of iodine. The measuring ROI position is shown indicatively for the hole containing the 0.1% w/w aqueous iodine solution

Organ dose data were obtained for NECT and CECT imaging with identical exposure parameters. For the MC simulation of CECT imaging, the elemental composition of brain, thyroid, parotid, submandibular salivary glands, breast, muscle, heart, liver, spleen, kidneys, stomach, ovaries and red bone marrow was appropriately altered to reproduce the iodine uptake of each tissue. The iodine uptake of each tissue was determined from the recorded increase of the CT number in CECT acquisitions and the corresponding plot of the CT number enhancement against iodine concentration. The average and maximum iodine concentration were determined. The elemental composition of all other tissues was considered the same as for NECT exposure. Effective dose from NECT and CECT exposures involving identical exposure parameters was estimated according to recommendations of the International Commission of Radiological Protection [17].

Results

The effect of contrast media administration on tissue CT number

Out of 2854 consecutive CT examinations performed in our institution over a 3-month period, 1463 examinations (i.e., 51%) involved intravenous administration of contrast medium. The mean and maximum CT number increase following contrast medium administration recorded for the studied sample of CECT examinations are presented in Table 2. High CT number increase ($\Delta CT \geq 30$ HU) was recorded for kidneys, stomach, spleen thyroid, liver, parotid/submandibular salivary glands and heart, moderate ($30 > \Delta CT > 10$) for ovaries and red bone marrow, and minimal ($10 \geq \Delta CT$) for breast, brain parenchyma, muscle and bone. In abdominal CECT

Table 2 CT numbers* [mean (min|max)] of organs/tissues in NECT and CECT image series and CT number enhancement following contrast media administration

CT examination	Organ	CT number		
		NECT	CECT	CECT-NECT
Head	Brain	31	33	3
		(23|38)	(28|44)	(1|6)
	Skull bone	1012	1022	10
		(640|1437)	(645|1456)	(5|50)
Neck	Thyroid	80	142	63
		(28|115)	(100|220)	(20|193)
	Parotid	-6	25	30
		(-61|32)	(-31|94)	(4|63)
	Submandibular	29	76	48
	salivary gland	(-1|54)	(25|121)	(9|103)
Thorax	Breast	4	10	6
		(-34|40)	(-27|50)	(2|11)
	Muscle	44	54	10
		(16|54)	(22|73)	(3|21)
	Heart	40	87	47
		(31|49)	(63|132)	(20|90)
Abdomen**	Liver	51	103	53
		(14|65)	(51|133)	(28|79)
	Spleen	49	116	67
		(20|81)	(76|166)	(36|119)
	Kidneys	34	141	107
		(24|47)	(90-196)	(62|163)
	Stomach	33	103	70
		(14|47)	(43|176)	(13|132)
	Ovaries	42	60	17
		(28-56)	(35-74)	(9|38)
	Red bone marrow	176	194	16
		(90|247)	(100|267)	(1|40)

NECT: non-enhanced CT image series, CECT: contrast enhanced CT image series,
*rounded to the nearest whole number, **data from images obtained at hepatic phase

examinations, the highest CT number increase was observed for imaging at hepatic phase.

The effect of iodine uptake on resulting CT number

The CT numbers of non-iodinated deionised water were found to be slightly higher than tap water i.e. 2.3, 2.9, 5.4, 11.7 HU versus -7.6, 1.1, 2.1 and 5.4 HU for imaging at 80, 100, 120 and 140 kV, respectively. The CT number increase against the % w/w iodine concentration in aqueous solutions is presented in Fig. 2 for the Siemens Sensation 16 CT scanner and images produced with the standard body reconstruction filter. Linear regression equations produced for 80, 100, 120 and 140 kV are presented in Fig. 2. The use of the standard lung instead of standard body reconstruction filter was not found to affect CT numbers of iodine solutions, since corresponding CT numbers were found to differ by less than 4 HU. Regression equation coefficients obtained for the GE Revolution GSI CT scanner were found to differ by less than 6% from corresponding data obtained for Siemens Sensation 16. The CT number enhancement recorded during CECT imaging for each soft tissue-like organ/tissue (Table 2) was attributed to a certain iodine uptake via regression equations shown in Fig. 2. The regression equation corresponding to CT exposures at 120 kV was employed since all patient CT image series had been acquired at 120 kV (Table 1). Iodine w/w tissue uptake estimates, corresponding to the recorded mean and maximum CT number increase achieved by CECT imaging, are presented in Table 3 for all investigated radiosensitive organs/tissues.

The effect of iodine uptake on organ doses and effective dose from CT exposure

Mean and maximum percentage increase of absorbed dose and effective dose from CECT exposure over the corresponding values from NECT exposure are presented in Table 4 for head and neck, thoracic and abdominal CT examinations performed at 120 kV. The maximum contrast induced organ dose increase was found to be 100% for thyroid, 74% for kidney, 64% for stomach, 51% for spleen, 51% for salivary glands, 37% for heart, 29% for liver, 24% for red bone marrow, 23% for ovaries, 12% for muscle, 6% for breast and 5% for brain. The sex-averaged mean contrast induced increase in the resulting effective dose from CECT exposure of head and neck, thorax and abdomen was found to be 23%, 9% and 13%, respectively.

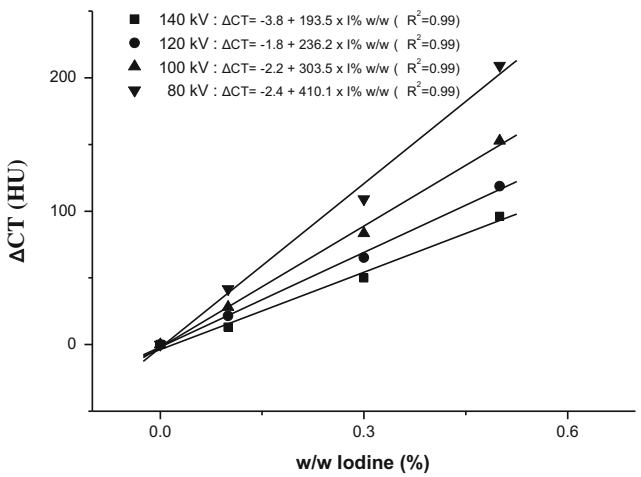

Fig. 2 CT number increase of aqueous solutions against iodine w/w concentration

Table 3 Estimated iodine concentration corresponding to recorded tissue CT number increase in contrast enhanced CT imaging

	Iodine concentration w/w (%)	
	mean	max
Brain	0.02	0.03
Thyroid	0.26	0.82
Parotid	0.14	0.27
Submandibular salivary gland	0.21	0.44
Breast	0.03	0.05
Muscle	0.05	0.10
Heart	0.21	0.39
Liver	0.23*	0.34*
Spleen	0.29*	0.51*
Kidneys	0.46*	0.70*
Stomach	0.31*	0.57*
Ovaries	0.08*	0.17*
Red bone marrow	0.08*	0.18*

*values corresponding to CECT imaging at hepatic phase

Discussion

Despite the recent advances in CT technology and the concomitant upgrade of CT image quality, many CT examinations involve contrast-enhanced image acquisitions [18]. In our institution, more than half of CT examinations performed were recorded to involve CECT imaging following intravenous administration of contrast medium. Considered the most sophisticated approach for reliable estimation of patient organ doses and effective dose from CT exposures, MC-based CT dosimetry software tools employing either mathematical anthropomorphic phantoms or patient-specific voxelised phantoms rely on the assumption that all soft tissue-like tissues such as brain, salivary glands, thyroid, breast, stomach, liver, spleen, kidney, liver, ovaries, red bone marrow, muscle, etc., are assumed to have the same elemental composition. Given the notable similarity of all those tissues to water and consequently between each other, this approach may yield reliable organ dose estimates for NECT exposures. The question is how

Table 4 Increase (%) of organ dose and effective dose in CECT exposures with respect to NECT exposures for female and male patients

Organ	Head and neck CT				Thoracic CT				Abdomen CT			
	CECTmean-NECT		CECTmax-NECT		CECTmean-NECT		CECTmax-NECT		CECTmean-NECT		CECTmax-NECT	
	f	m	f	m	f	m	f	m	f	m	f	m
Brain	2	3	4	4	2	4	3	4	1	2	1	5
Salivary glands	21	22	43	43	20	26	41	48	21	27	40	51
Thyroid	33	31	98	96	30	36	92	97	30	19	100	78
Breast	4	–	6	–	4	–	6	–	1	–	2	–
Muscle	6	6	11	12	6	6	11	12	5	6	10	11
Heart	19	17	33	33	22	21	37	35	16	12	28	29
Stomach	38	29	63	60	32	32	58	55	36	36	64	63
Liver	20	17	27	25	20	19	26	25	21	20	29	28
Spleen	33	31	49	48	31	30	51	49	32	30	51	49
Kidneys	45	43	62	59	46	46	64	64	52	50	74	72
Ovaries	10	–	19	–	11	–	26	–	11	–	22	–
Red bone marrow	9	9	22	20	10	11	20	18	10	12	21	24
Effective dose	22	23	64	66	7	10	15	20	12	13	23	23

reliable are the organ dose estimates from CECT exposures, if the contrast-induced change in elemental composition of tissues is not taken into account.

The clinically occurring iodine uptake in several radiosensitive tissues was evaluated by attributing the recorded CT number increase to a certain w/w concentration of iodine aqueous solutions. The mean iodine uptake range was found to be 0.02-0.46% w/w for the investigated tissues, while the maximum observed iodine uptake was recorded for thyroid as 0.82% w/w. The estimated iodine concentration of contrast enhanced tissues occurring in CECT imaging was reproduced in mathematical anthropomorphic phantoms representing the average adult female and male individual. Our results revealed that organ doses from CECT exposures determined using modern CT dosimetry tools that do not account for the iodine uptake may suffer underestimation errors up to 100% for the clinically occurring levels of iodine uptake due to contrast medium administration. As the underestimation of absorbed dose was found to increase with iodine uptake, high underestimation may occur for tissues with high iodine uptake at the time of acquisition such as thyroid, kidney, stomach, spleen, salivary glands and liver, while the underestimation for tissues with low uptake such as muscle, breast and brain was estimated to be minor. Evidently the absorbed dose to any radiosensitive organ/tissue from a multiphase CT examination including one or more CECT acquisitions should not be derived by multiplying the number of phases to the organ dose from the NECT exposure, even if NECT and CECT exposures have been performed with identical exposure settings/geometry. Apparently, if automatic current modulation is employed, the tube current may be changed between NECT and CECT exposure, and this change should be also taken into account. Current findings render the consideration of the change in elemental composition of tissues, induced by contrast medium administration, imperative for accurate CT dosimetry. Regression equations presented in Fig. 2 are consistent with previously reported data [18] and allow the determination of iodine w/w concentration of each primarily exposed radiosensitive tissue given the CT number enhancement between NECT and CECT imaging, which may be easily determined.

It is remarkable that tissue uptake of iodinated contrast medium resulting in a w/w iodine concentration of as low as 0.3% may considerably alter the x-ray absorption efficiency of that tissue resulting in an increase of absorbed dose by about 30%. Absorbed dose D depends on material density ρ, i.e., $D \propto \rho$ and effective atomic number Z, i.e., $D \propto Z^3$ [19]. Iodine concentration of 0.3% in an adult male human liver, reported to have a mass of 1561 g [20], is achieved by accumulation of only 4.7 g of iodine. Apparently, the considerable increase in the absorption efficiency of iodinated tissue may not be attributed to the increase of density. In addition, the relative increase of effective Z for soft tissue when iodine concentration increased to 0.3% w/w, was estimated with AutoZeff software [21] as 10% for a 120 kV CT beam. Consequently, the dose absorbed by the 0.3% w/w iodinated tissue is expected to be $1.1^3 = 1.33$ higher or equivalently 33% higher than non-iodinated tissue. Evidently, the relative increase in dose of iodinated tissues may be attributed to the increase of effective atomic number induced by iodine uptake.

To our knowledge, the first and only, attempt to quantify the effect of iodine uptake level to the absorbed dose from CT exposure was done by Amato et al. [11, 12]. The authors

developed a theoretical model to relate the CT number enhancement to the expected relative dose increase and a simplistic mathematical phantom of the neck and the abdomen to quantify the relative dose increase for different iodine tissue uptake values [11]. The authors used this approach to estimate relative dose increase in iodinated thyroid, liver, spleen [11] pancreas and kidney tissues [12]. They reported mean relative dose increase of 41%, 19%, 33%, and 71% for thyroid, liver, spleen and kidneys, respectively, for a patient series subjected to thoracoabdominal CT. The corresponding values derived in the present study with different methodology were 32%, 21%, 50%, and 51%, respectively. The moderate differences may be attributed to the use of a more realistic anthropomorphic phantom in the present study and the differences in the recorded tissue enhancement values determined from different samples of contrast enhanced patient CT examinations. In the present study, relative dose increase was additionally provided for brain, parotid, salivary glands, breast, heart, muscle, stomach, red bone marrow and female gonad tissues. Moreover, the effect of contrast induced increase of organ doses on the estimated effective dose was investigated. The relative increase in the estimated effective dose was found up to 66%, 20% and 23% for head and neck, thoracic and abdominal CECT imaging.

The main limitation of the current study originates from the inability to estimate iodine uptake in CECT studies for some radiosensitive tissues involved in the estimation of effective dose. Contrast induced enhancement measurement was not feasible for lung, oesophagus, colon, bladder, male gonads and skin, which are tissues with specific weighting factors in the effective dose formula. Lung CT number depends strongly on the respiratory phase at the time of CT exposure, and it is not possible to warrant the same lung ventilation at the time of NECT and CECT image acquisitions. Oesophagus, colon, bladder and skin are very thin tissues rendering measurement of CT number vulnerable to high inaccuracies. Contrast induced enhancement measurement was not feasible for male gonads because male gonads are typically excluded from the image volume of multiphase abdominal CT examinations. In addition, contrast-induced enhancement for bone tissue, despite minimal, could not be translated to iodine uptake since data shown in Fig. 2 refer to soft tissue-like tissues only. Since estimation of the contrast induced relative increase in dose was not possible for these organs, no uptake was considered for these organs, and; therefore, the relative increase of effective dose from CECT exposures reported here has been underestimated. Also, the minimum, mean and maximum CT number enhancement values reported here for several radiosensitive tissues, refer to the specific patient examination series studied. Data from a much larger patient cohort subjected to CECT examinations is apparently needed to determine more accurately the range of CT number enhancement values that may occur in clinical practice. Another source of inaccuracy regarding the presented estimates of contrast-induced increase of organ doses originates from the method employed here to determine iodine uptake value for each tissue. The CT number enhancement of each tissue corresponded to a specific w/w iodine concentration of aqueous iodine solution. Namely, all iodinated soft tissue-like organs/tissues were assumed as aqueous solutions of iodine. Given, however, the close resemblance of soft tissues to water, the corresponding introduced uncertainty is expected to be minor.

In conclusion, iodine uptake of tissues induced by intravenous contrast medium administration for contrast enhanced CT imaging may considerably affect radiation dose absorbed by these tissues. Consequently, the use of modern CT dosimetry tools to determine patient dose from CT exposures performed following contrast medium administration may involve considerable underestimation errors if iodine uptake to radiosensitive tissues is not encountered. Therefore, Monte Carlo-based CT dosimetry tools should incorporate the change in elemental composition of tissues induced by iodinated contrast medium uptake to provide reliable organ dose data for contrast enhanced CT exposures.

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Kostas Perisinakis.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

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Statistics and biometry One of the authors has significant statistical expertise.

No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was not required for this study because it was a retrospective study.

Ethical approval Institutional Review Board approval was obtained.

Methodology

- retrospective
- observational
- performed at one institution

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