https://www.scirp.org/journal/jbise

J. Biomedical Science and Engineering, 2020, Vol. 13, (No. 12), pp: 254-266

Investigations of CT Dose with Contrast Agent and Its Effects on the CTDI

Moshi Geso[1], Farnaz Tabatabaie[2,3], Edel Doyl[1], Salem Algithami[4]

[1]Discipline of Medical Radiations, School of Health & Biomedical Sciences, RMIT University, Bundoora Campus, Bundoora, Australia; [2]Peter MacCallum Cancer Centre, Melbourne, Australia; [3]School of Applied Sciences, RMIT University, Melbourne, Australia; [4]Department of Health Sciences, Al Dammam University, Altaif, Saudi Arabia

Correspondence to: Moshi Geso, moshi.geso@rmit.edu.au

Keywords: Computed Tomography, CTDI, Patients Data

Received: October 20, 2020 **Accepted:** December 22, 2020 **Published:** December 25, 2020

ABSTRACT

Purpose: Computed tomography is a leading imaging technique for head & neck and brain and most of these imaging protocols iodine-based contrast media are utilised. The chief aim of this research is to utilize the effects of the contrast media "CM" used in computed tomography "CT" which is used to enhance subject contrast on the delivered CT via its inclusion into the CT dose index "CTDI", and to introduce a simple method to determine this effect via the available CT numbers at the imaged targets. Method: The CT dose increase is estimated theoretically and measured experimentally and then related to the average CT number in the volume of CM uptake. A factor dependent on CM concentration and beam energy is added to the CTDI equation to represent the increased dose burden. A simple holed Perspex phantom was built to measure the variation of imaged CT number. CT Gafchromic type film was alternately imaged in a reservoir of CM and water. The relative difference in the dose burden as obtained by scanning the two films represents the dose difference and hence the CM dependent increase. Results: Measured dose effects due to the inclusion of the CM varied depending on the concentration. The increase in dose is estimated to be about 17% for 20% contrast media in the target while that for 10% by volume is around 6.6%. These are estimated from the CT numbers. Patients' data also shows influence of the CM on the CTDI values. Conclusion: The dosimetric effects of the contrast media are included into the CTDI and can be estimated by using the CT numbers obtained.

1. INTRODUCTION

Computed tomography "CT" is increasingly becoming a highly reliable imaging modality in medical imaging. Whilst computed tomography techniques had limited use during 70s and 80s, due to the in-

creased scanning speed and improved image quality, CT usage has increased dramatically since then. Today, large numbers of patients are imaged by CT techniques covering almost every part of the body. According to the ICRU, about 250 million CT scans are performed worldwide per year [1]. Even though projection imaging such as chest radiographs remains the dominant radiological imaging modality, CT is recognized as the modality that delivers the highest radiation dose to the public. As an example, according to Kalender *et al.* [2] and the German Federal Office for Radiation Protection [3] whilst only about 7% of total x-ray imaging in Germany was done by CT, 60% of the total dose to the public from all the x-ray imaging modalities was attributed to the CT scans. It is highly unlikely that Germany is unique in this regard.

Computed tomography is one of the most common imaging modalities for brain and head and neck [4]. For brain imaging CT has many advantages over other imaging modalities including the fact it is fast imaging technique, hence it less affected by patient motion, less expensive, easier to perform, provides detailed images most required in brain imaging, and can be used at no risk to the patient with implantable devices. Though CT acquired images are normally with great contrast, it is required in more than half of the cases a contrast media inclusion in the target prior imaging [4].

Whilst radiation dose delivered during CT examination is an important consideration, it is generally not measured directly but taken into account indirectly through a dose indicator. This is because the distribution of the dose delivered by CT imaging through slices is not uniform and it cannot be measured directly in the patient using known types of dosimeters. Shope *et al.* [5] introduced the definition of computed tomography dose index/indicator "CTDI" in 1981 as a parameter to indicate the level of doses delivered by CT scanners. Since then many modifications of the CTDI basic form have been introduced to accommodate new conditions and new instrumentations introduced in this field such as the pitch value which is introduced through the spiral CT techniques. The full meaning and description of this parameter "CTDI" is discussed by McCollough *et al.* [6] and also the references cited in this paper provide a comprehensive review of the changes introduced to it over the years. For example, the dose estimated over volume and the difference between the dose-levels at the centre of the slice as compared to that on the periphery are currently included as corrections. Full details of employing CTDI to estimate dose delivered by a CT scanner with all the corrections can be found in Kalender *et al.* [2]. The IAEA code of practice for dosimetry in diagnostic radiology "TRS457" recognises the concept of CTDI as defined by the IEC [7], measured using a 100 mm pencil ionization chamber. CTDI is a dose indicator and all of its modified forms such as Dose Length Product "DLP" are also dose indicators. CTDI is defined for sequential CT. For volume scanning based on the helical principle, the pitch is included and the CTDI is then termed volume CTDI, "$CTDI_{vol}$". The DLP is the product of the $CTDI_{vol}$ and the scan length and it is utilised for multislice slice and multi detector CT scanners. DLP can be converted crudely to measure the effective dose through the use of some conversion factors. Seibert *et al.* [8] recently introduced the effects of patient size on the $CTDI_{vol}$ and DLP values. Also recently a comprehensive explanation for the dose delivered by CT has been documented in an AAPM report [9]. Contrast media, such as iodine-based compounds, enhance tissue contrast due to its higher atomic number and physical density compared to the tissues. These characteristics dramatically increase the probability for the photoelectric effects & Compton interactions and this leads to enhancing the CT image contrast [10]. Though CT images show far superior details of the target compared to projection imaging *i.e.* contrast resolution is higher, in some cases still further details are required clinically; therefore, contrast media of the type traditionally used in projection imaging (iodine compound) is required and used to enhance the image details by increasing the subject contrast. The contrast media is used in CT imaging to improve the visualisation of anatomic structures (usually blood vessels or parenchymal organs) that would be indistinguishable from background tissue, in terms of their x-ray attenuating properties. A phantom based study by Jackson *et al.* [10] showed the levels of contrast enhancement by CT scan when various types of contrast media are used.

For CT scanners equipped with current modulation, it has been shown that the indirect effect of contrast media (the tube current is increased to compensate for the attenuation of the CM, and the increased current increases the CTDI) is significant enough to change clinical practice [11]. It has also been proven, through radiobiological studies, that inclusion of the contrast media in the tissue of interest (target) di-

rectly enhances the dose locally (or radio-sensitises the cells) at the target [12-17]. Generation of copious secondary electrons, *i.e.* free radicals from the interaction of x-ray photons with the higher density and particularly higher atomic number of the iodine atoms, leads to an increase in the photoelectric effect probability of interaction and this is the main reason underlying dose enhancement. However, the direct effect of contrast media on the dose and hence on the CTDI value is currently not factored into the equation for the determination of the CTDI value. The CTDI for newer CT scanners with Tube Current Modulation is affected indirectly by an increase in tube current, and this is an active area of research [11] but currently for all CT scanners the method for calculating the CTDI does not take into account any direct change in dose due to the presence of contrast media. This research is based on the evaluation of the direct effects of the contrast media on the CT delivered doses and particularly its currently unaccounted effects on the CTDI value. The work comprises both theoretical calculations and experimental measurements. Moreover, this contrast factor for dose increase is derived in terms of the average CT number at the target. This means this contribution can easily be estimated from the known CT numbers at the target. The contribution of the contrast media to the CTDI value depends on the concentration of the media in the target and also on the kVp value. This makes it feasible to determine the levels of dose enhancement directly from the CT numbers of the imaged target.

Paul *et al.* [18] conducted a study on patients CT data to determine the effects of the contrast media on the image noise and the dose delivered. The effects on dose were inferred from the $CTDI_{vol}$ value changes between conditions of non-contrast with the existence of the contrast media to the same targets. Their results showed an increase in $CTDI_{vol}$ values between 3 to 13 per cent. A clinical study by Amaton *et al.* [19] also identified that inclusion of iodine contrast media in CT scans results in direct dose enhancement specific to various organs ranging from 20% to 70%. In addition, a recent Monte Carlo simulation based study conducted by He *et al.* [20] also demonstrated an increase in dose caused by micro-spheres containing contrast media in a modelled phantom. Whilst these studies indicate (or suggest) that contrast media does have both a direct and indirect impact on CT dose, there is a need to theoretically and experimentally examine and quantify the direct effects of contrast media on CTDI.

In particular, this paper includes theoretical and experimental dose enhancement determinations following the administration of varying concentrations of iodine-based contrast media just prior to scanning, as well as modifications in the CTDI equation. This work also relates dose enhancement of contrast media to the CT number. Hence, to estimate the contrast media effects on the CTDI it is only required to know the CT numbers at the target *i.e.* slice. The dose enhancement at these levels of low doses are calculated according to the method introduced by Corde *et al.* [12] for radiotherapy beams which agrees with the dose enhancement values obtained from the CT numbers. Moreover, in this work we also extended the notion of this simplistic method of dose enhancement estimation based on just mono-energetic beams into using spectral energy values of the x-ray photons and under more realistic conditions of low levels of contrast media concentrations (similar to those expected in humans before CT scanning). In this research the dose enhancement and its relationship to the CT numbers is derived from the first principles and related it to the measured values at certain concentrations of the contrast media.

Recently, a review article is documented on the effects of iodinated contrast media on the cells' DNA in diagnostic x-ray imaging in general [13, 14]. High dose enhancement levels are reported by these researchers in the intra and extra vascular and in the blood and in the microdosimeteric environment.

2. MATERIALS AND METHODS

2.1. Materials

The following materials and equipment were used for the determination of the effects of the contrast media on the CT numbers and those related to its effects on the dose;

- Scanner; The computed tomography scanner used in this research to investigate the contrast and dose enhancement at Alfred Hospital Victoria Australia is a 64-slice type Discovery CT590 RT, GE

Healthcare.

- Materials for determination of effects on CT Numbers; A purpose built simple phantom was designed to investigate the direct effect of contrast media on CT contrast enhancement and dose. The phantom was made of Perspex and cubical in shape of dimensions 3.8 cm × 3 cm × 5.9 cm. Two holes were drilled in the phantom to be filled with various concentrations of the contrast media ranging from 0% to 100%. Two identical holes were drilled in this phantom. The phantom holes' diameter and depths were 1.25 cm and 4.5 cm respectively. One of the holes was filled with water and the other one with either 10% or 20% iodine based contrast media (Omnipaque 350, GE Healthcare) as shown in **Figure 1**. This phantom was designed to be used for the investigation of the contrast media direct effect on the CT dose.
- Materials for determination of Computed Tomography Dose; Computed Tomography type Gafchromic films (XR-CT2) were placed vertically in the centre of the hole and in various concentrations of contrast media then scanned at the same conditions in computed tomography then optically scanned using Image J programme. The image regional optical density can then be related to dose via a calibration curve or used directly as relative dose since these films have a very linear dose response [21].

2.2. Methods & Analysis

2.2.1. Dose Enhancement Factor "DEF" Included in the CTDI

The dose enhancement factor "DEF", the direct effect of contrast media on the dose, will be linked to the CT number "$\mathcal{N}$" and then it will be included in the CTDI equation.

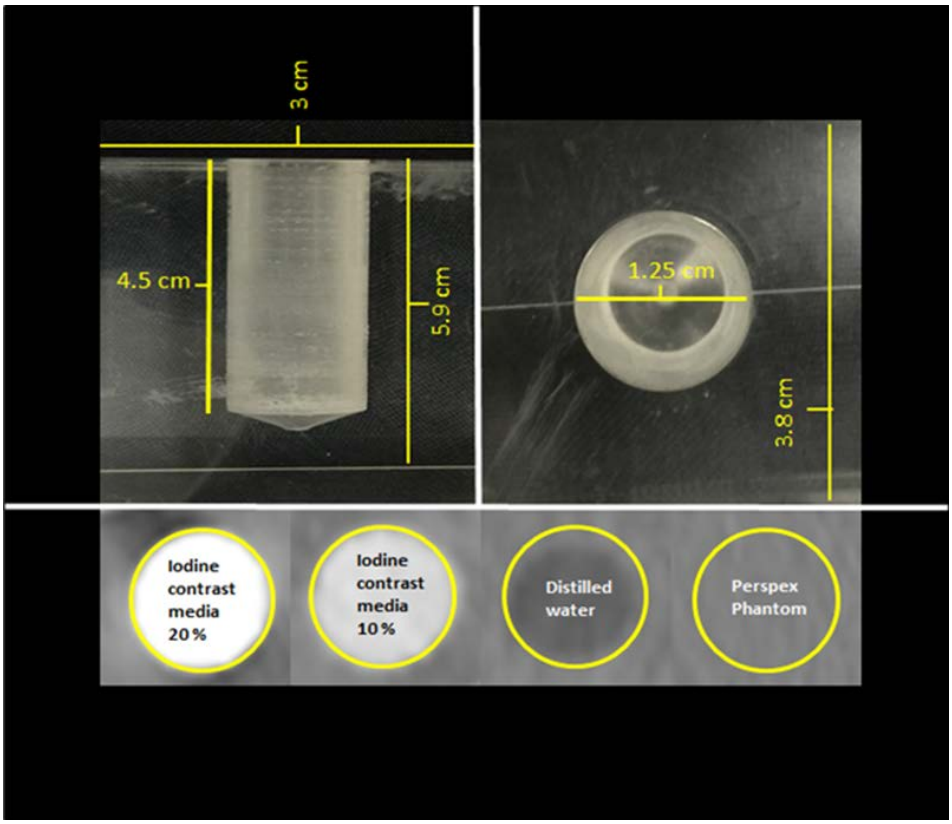

Figure 1. The area of the ten pixels values measurement from the contrast enhancement phantom at different medium; iodine contrast media 20%, iodine contrast media 10%, distilled water and Perspex phantom.

The basic formula representing the CTDI showing its value as an integral for the dose along the z direction which runs along patients' longitudinal axis and covers 7 slices on each side is displayed in Equation (1) below.

$$\mathrm{CTDI} = \frac{1}{nT}\int_{-7T}^{7T} D(z)\cdot \mathrm{d}z \tag{1}$$

where T is the slice thickness and

n is the number of slices.

However, when the contrast media is added then the whole dose will be directly enhanced due to the inclusion of the relatively high density and high atomic number of the iodine compound relative to tissue. This dose enhancement should therefore be factored into the above equation. The levels of dose enhancement have been previously determined [12] based on cell studies and termed as a dose enhancement factor $\mathrm{DEF}(c,E)$, where c stands for the concentration of the media and E the beam energy which directly depends on the applied kilovolt of the x-ray tube *i.e.* the beam energy. The DEF can be written in terms of the mass energy absorption coefficient (μ_{en}/ρ) [12] as follows;

$$\mathrm{DEF}(c,E) = \frac{\omega_I\left[\frac{\mu_{en}}{\rho}\right]_E^I + (1-\omega_I)\left[\frac{\mu_{en}}{\rho}\right]_E^{\mathrm{H_2O}}}{\left[\frac{\mu_{en}}{\rho}\right]_E^{\mathrm{H_2O}}} \tag{2}$$

ω_I represents the concentration of the iodine in the target by weight

Now including dose enhancement factor directly caused by the presence of the iodine-based contrast agent in the CTDI equation will result in;

$$\mathrm{CTDI} = \frac{\mathrm{DEF}}{nT}\int_{-7T}^{7T} D(z)\cdot \mathrm{d}z \tag{3}$$

Using the basic definition of the CT number "N" then the dose enhancing factor can be written as (**Appendix 1**);

$$\mathrm{DEF}(\omega_I, E) = \omega_I \cdot N/1000 + 1 \tag{4}$$

$$\mathrm{CTDI} = \frac{\omega_I \cdot N/1000 + 1}{nT}\int_{-T}^{T} D(z)\cdot \mathrm{d}z \tag{5}$$

Hence the CTDI becomes dependent on the concentration of the contrast media in the target and the CT number. In the case of no media in the target then ω becomes zero and the above equation reduces to the basic definition of the CTDI presented in Equation (1) above. In clinical settings the concentration of the contrast media in the target is optimised by monitoring the accumulation of the media by subsequently imaging a slice at the entrance of the blood vessels to the target. Therefore ω_i can be deduced.

2.2.2. Experimental Measurements

1) Dosimetry: Direct dose enhancement due to the inclusion of the contrast media was measured using CT type gafchromic films. The films were scanned in various media concentrations in reservoirs as depicted in **Figure 2**. The optical density at any region on the film is related to dose linearly. Therefore the measured optical density obtained from film scanning represents relative dose value within the experimental uncertainty. The gafchromic films were scanned using EPSON PERFECTION V700 PHOTO with the transmission mode and with the PTW software. The protocol followed for gafchromic film scanning can be found in the AAPM report and also some aspects of the scanning are outlined by PTW [21].

The phantoms were scanned axially (Discovery CT590 RT, GE Healthcare). The CT exposure parameters were set to 140 kV, 13 mAs and 1.25 mm slice thickness. The average value of 10 pixels in the cen-

tre of each image representing the holes is determined and used as dose indicator as depicted in Figure 2. These CT numbers are introduced into Equation (4) to determine the levels of dose enhancements.

2) Patent's data: These data are obtained using Siemens Definition Edge CT scanner [patients 1 - 8] and Siemens Perspective 128 [patients 9 - 12] for a total of 12 patients. This 3-phase Liver protocol was to scan the liver (no contrast) and the contrast media [70 ml of Ultravist 370 at 3 ml/s] was injected. A scan of the liver was obtained in the arterial phase using bolus tracking technique, followed by a scan of the abdomen and pelvis in the portal venous phase.

3. RESULTS

3.1. Theoretical Estimation of Dose Enhancement

In this section the theoretical results of the indicator for the DEF are presented using purely monoenergetic beams and at all possible concentrations of the contrast media in the target ranging from 0% to 100%. The definition of DEF in this case is simply the ratio of the mass-energy absorption coefficient difference between with the contrast to without over that of without *i.e.* just water as shown in equation 2 above. The relationship between the DEF indicator and the mono-energetic beam-energy at various concentrations of the contrast media is displayed graphically in Figure 1. Similar results are presented in reference 11. These DEF values are merely indicators and not actual DEF values for clinical circumstances for beams that are not monenergetic and contrast distributions that are not uniform. Therefore, they cannot be used to validate experimental measurements for dose enhancements caused by the inclusion of the contrast agents. However, although x-rays used in CT imaging are not monoenergetic but they have a known spectrum of energies. Such data can be used to show beam energy dependence of the DEF and also to show the direct effects of the contrast agent's concentrations on the levels of dose enhancements in general.

3.2. Empirical Dose Enhancement

The contrast enhancement, *i.e.* CT number increase due to the inclusion of the contrast media, is used to estimate the direct dose enhancement levels caused by the inclusion of the contrast media in the target. The relationship between the dose enhancement and the CT numbers is deduced as described in the methods section (Equation (4) above).

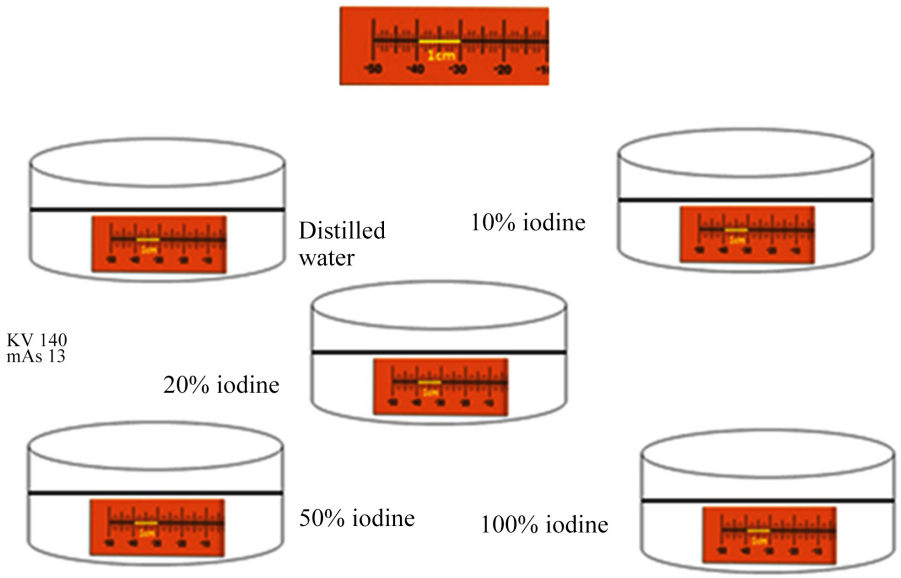

Figure 2. CT gafchromic films; top sample and the rest as immersed in the reservoirs of various concentrations of the contrast media.

The dose enhancements due to the inclusion of the contrast media (at the CT energy levels) are determined experimentally using CT type Gafchromic films. The x-ray beams used for this study are from a superficial radiotherapy machine which delivers similar beams to those generated by typical CT scanners with high enough doses to be reliably measured by the films. The reason for using similar beams from superficial radiotherapy x-ray units is to obtain adequate dose levels for the films to be able to measure doses above the threshold levels for such films. And finally, these experimental results are validated against the predictions obtained from CT number variations.

Dose enhancement was determined by measurements using CT type Gafchromic films as described in the method section and displayed in **Figure 3**. The average pixel value in the centre of the film imaged by the CT scanner at 140 kV immersed in various concentrations of contrast media are presented in **Table 1**.

The left column represents the concentration of the contrast media in the water where the film is immersed in, while the middle column represents the scanned pixels in optical density which is linearly related to dose. Dose enhancements as percentage to the optical density values of water *i.e.* zero concentration of contrast media are displayed in the third column.

The larger the measured pixel-value of the Gafchromic film the higher the x-ray absorption and also it is of higher media concentration. The difference between the average pixel values of the films immersed in reservoirs with iodine contrast media compared to those of the films in water reservoir, *i.e.* zero concentration, represents the levels of dose enhancement since the pixel value is linearly related to the dose as these films are well calibrated and show linear dose response.

Dose enhancement levels determined from the CT number variations caused by the inclusion of the contrast media using Equation (4) are displayed in **Table 2**.

Clinical Data as Example

Patient's data showing examples of the indirect effect of contrast on CTDI are listed in **Table 3**. The average values for the 12 patients are listed at the bottom of the table. Clearly, the results of both the CTDI and the DLP indicate an indirect increase by the inclusion of the contrast media. For instance, in the case of arterial liver the CTDI value increases in average by about 16%.

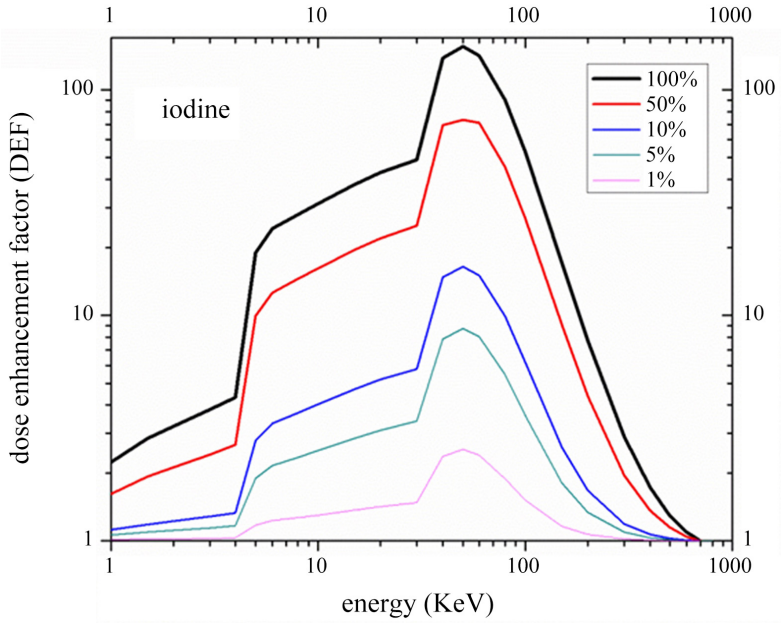

Figure 3. DEF indicators versus energy for various iodine concentrations as described in Equation (2). Calculated dose enhancement factor from mass energy absorption coefficient for different beam energies and at different concentration of iodine contrast agent in the target.

Table 1. **Pixel values for CT Gafchromic film for three different concentrations.**

Mediums	Pixel values	Dose enhancement percentage from Equation (5)
distilled water	3428.1	-----
10% Iodine Contrast Media	3656.5	6.6%
20% Iodine Contrast Media	4013.6	17%
50% Iodine Contrast Media	5035.1	46.8%
100% Iodine Contrast Media	5649.9	64.8%

Table 2. **CT numbers pixel values of the phantom holes filled with two concentrations of contrast media and water.**

Medium	Pixel Value	σ Values	CNR Values
Iodine Contrast Media 20%	893.3 ± 17	17	42
Iodine Contrast Media10%	512 ± 11	11	31
Distilled Water	46.2 ± 5	5	−29
Perspex Phantom	176.6 ± 21	21	

Table 3. **Patient data from 3-phase CT scanning of the liver.**

	Weight (kg)	Height (cm)	Radius (cm)	Non Contrast		Arterial (Liver) + Contrast		Portal Venous (Abdo/Pelvis) + Contrast	
Patient				**CTDIvol**	**DLP**	**CTDIvol**	**DLP**	**CTDIvol**	**DLP**
1	75	172	12	8.21	209	8.28	167	8.12	387
2	78	180	12	6.87	167	7.16	119	7.1	307
3	92	168	13	14.29	400	14.39	403	13.08	579
4	70	176	11	6.7	147	6.74	140	7.13	319
5	64	165	11	5.55	112	6.14	151	8.18	323
6	80	165	12	15.74	398	15.87	414	15.57	739
7	102	154	15	16.89	523	16.82	522	16.79	504
8	77	165	12	6.77	140	6.8	141	8.94	383
9	89	158	13	17.54	531.01	18.08	576.73	17.01	840.95
10	60	160	11	1.15	233.9	10.4	286.57	10.73	468.99
11	110	165	15	18.31	626	18.35	797.4	18.47	1008.08
12	70	160	12	10.98	296.45	10.73	292.45	12.3	641.47
Average	82	161	12	12	422	14	488	15	740

For example, the case of non-uniform contrast distribution, reference 10 found that the presence of contrast in the ascending Aorta increased the Hounsfield number from an average of 107 to 460 at a nominal 100 kV. For instance, if we observed the same change of 353 HU at 140 kV, this gives a DEF of 6.1% for the organ, which must then be partially weighted for relative radio-sensitivity.

4. DISCUSSION

Direct dose enhancement dependence on beam energy is an important factor which has attracted the attention of many investigators in the therapy field especially those interested in heavy atom based nanoparticles [22]. The apparent disagreement between the observed therapy experimental data and theoretical predictions needs to be resolved, as all investigations showed that maximum dose enhancements occur at kV ranges of x-ray energies which include the levels of x-ray energies used in CT imaging, yet the direct effect of contrast is ignored in all diagnostic imaging dose calculations..

In this research the dose enhancement is derived from the first principles of energy deposition and then linked to the CT numbers as shown in **Appendix 2**. Moreover, Equation (5) also relates the dose enhancement to the observed CT number of the target tissue type. This means if the CT numbers for an organ with the contrast media is known it can be used to determine the levels of direct dose enhancement by the contrast agent to the organ. To proceed from the DEF to an organ to the DEF for the patient CTDI, one either has to know the weights for each organ and relative dose to each organ, or more practically in the absence of such data, to assume uniform dose to each organ.

The dose enhancement is attributed to the higher absorption rate of x-rays by iodine atoms in the contrast media leading to an increase in the generation of secondary electrons, *i.e.* free radicals including Auger electrons. More details on the principles of dose enhancement caused by iodine based contrast agents and metallic nanoparticles and gold in particular can be found in the literature [10, 22].

The direct dose enhancements caused by inclusion of set concentrations of contrast media in phantom model CT targets are displayed in **Figure 1** & **Figure 2**. For instance the dose enhancement as determined by the CT number changes due to the inclusion of the contrast media from **Table 2** at 20% concentration is about 16% as obtained using Equation (5) which relates the levels of dose enhancement to the CT number.

For standard CT clinical protocols, however, it is possible to show that the DEF for uniformly distributed contrast within the scanned volume is not more than 0.6%. The assumptions in making this estimate are crude: that the patient is a uniform cylinder, that the contrast is uniformly distributed within the irradiated volume only, that all of it is present at the time of the CT scan, but the model has the virtue of using only information generally retrospectively available for review, and the relaxation of any of these assumptions would reduce the DEF. If some of the contrast is present outside the irradiated volume, for example, the DEF will reduce. The model is so crude it should not be used to compare clinical protocols, as the model implies that reducing the scanned length increases the DEF. The only exception to this is the postulate of uniform contrast distribution. In clinical cases, contrast is not uniformly distributed; it is unevenly distributed in a way that enhances the clinical usefulness of the image. It may therefore be concentrated mainly in a relatively radiobiologically sensitive organ, and in this circumstance, it is conceivable that the presence of contrast may produce a significant DEF, as has been noted in the literature. For the case of studies with a high concentration of contrast in a radiosensitive organ, the DEF in the organ can be estimated from the CT number change due to the contrast (using the values in this work as an approximation) and the radiobiological weight factor of the organ.

In contrast, the possibility of a rescan due to a failure to inject contrast is potentially a much larger factor for individuals, but clinical cases of this are handled by legislated error reporting systems, and in studies the ethics approval often requires that studies with missed contrast are not repeated and the patient is excluded from the study.

The indirect effects of contrast for CT scanners with Tube current modulation are potentially much higher, but they are adequately taken into account by the standard CTDI equation, and so they are not a

major focus in this work.

5. CONCLUSIONS

Administering contrast media to the CT patients is mainly to enhance the image contrast. However, it has been long proven experimentally that it also enhances radiation dose at the target depending on its concentration at the target. Infliction of radiation dose to patients individually and to the public in general has also been the focus of large number of investigations as documented in the literature. This research quantified this dose enhancement and introduced it into the CTDI indicator. Moreover, this work also shows a simple and direct method of estimating the dose enhancement caused by contrast media based on the CT number change due to its introduction.

The dose enhancement caused by the introduction of the contrast media into the radiation target is concentration at the target dependent. At clinically administered concentrations of contrast media, a measurable dose increase is obtained justifying its inclusion into the CTDI equation. In so doing, the level of dose enhancement inflicted by the contrast media can be estimated from the CT number change at the target in the CT slice.

However, it should be noted that inclusion of contrast in a CT scan dose equation *i.e.* the CTDI does not quantifiably increase the radiation dose burden to the patient unless there is a high concentration of the contrast aggregated in a radiosensitive organ such as breast or brain.

ACKNOWLEDGEMENTS

We thank the support of William Buckland Radiotherapy centre at Alfred Hospital in Victoria Australia for making available the radiation facilities for this work.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this paper.

REFERENCES

1. Boone, J.M., *et al.* (2012) Radiation Dose and Image-Quality Assessment in Computed Tomography. *Journal of the ICRU*, **12**, 9-149.
2. Kalender, W.A. (2011) Computed Tomography: Fundamentals, System Technology, Image Quality, Applications. John Wiley & Sons, Hoboken.
3. für Strahlenschutz, B. (2009) Jahresbericht 2008 [Annual Report 2008].
4. Mutch, C.A., Talbott, J.F. and Gean, A. (2016) Imaging Evaluation of Acute Traumatic Brain Injury. *Neurosurgery Clinics of North America*, **27**, 409-439.
5. Shope, T.B., Gagne, R.M. and Johnson, G.C. (1981) A Method for Describing the Doses Delivered by Transmission X-Ray Computed Tomography. *Medical Physics*, **8**, 488-495. https://doi.org/10.1118/1.594995
6. McCollough, C.H., *et al.* (2011) CT Dose Index and Patient Dose: They Are Not the Same Thing. *Radiology*, **259**, 311-316. https://doi.org/10.1148/radiol.11101800
7. Commission, I.E. (2002) Particular Requirements for the Safety of X-Ray Equipment for Computed Tomography: Amendment I, 2002-09. International Electrotechnical Commission, Geneva.
8. Seibert, J.A., *et al.* (2014) Dose Is Not Always What It Seems: Where Very Misleading Values Can Result from Volume CT Dose Index and Dose Length Product. *Journal of the American College of Radiology*, **11**, 233-237. https://doi.org/10.1016/j.jacr.2013.10.010
9. Dixon, R., *et al.* (2010) Comprehensive Methodology for the Evaluation of Radiation Dose in X-Ray Computed Tomography. Report of AAPM Task Group 111, 20740-3846. https://doi.org/10.37206/109

10. Jackson, P., *et al.* (2011) Evaluation of the Effects of Gold Nanoparticle Shape and Size on Contrast Enhancement in Radiological Imaging. *Australasian Physical & Engineering Sciences in Medicine*, **34**, 243-249. https://doi.org/10.1007/s13246-011-0071-7

11. Paul, J., *et al.* (2013) Effect of Contrast Material on Radiation Dose in an Adult Cardiac Dual-Energy CT Using Retrospective ECG-Gating. *Health Physics*, **105**, 156-164. https://doi.org/10.1097/HP.0b013e31828d814c

12. Corde, S., *et al.* (2004) Synchrotron Radiation-Based Experimental Determination of the Optimal Energy for Cell Radiotoxicity Enhancement Following Photoelectric Effect on Stable Iodinated Compounds. *British Journal of Cancer*, **91**, 544-551. https://doi.org/10.1038/sj.bjc.6601951

13. Harbron, R., Ainsbury, E., Bouffler, S.D., Tanner, R.J., Eakins, J.S. and Pearce, M.S. (2017) Enhanced Radiation Dose and DNA Damage Associated with Iodinated Contrast Media in Diagnostic X-Ray Imaging. *British Journal of Radiology*, **90**, Article ID: 20170028. https://doi.org/10.1259/bjr.20170028

14. Adam, J.-F., *et al.* (2005) Enhanced Delivery of Iodine for Synchrotron Stereotactic Radiotherapy by Means of Intracarotid Injection and Blood-Brain Barrier Disruption: Quantitative Iodine Biodistribution Studies and Associated Dosimetry. *International Journal of Radiation Oncology Biology Physics*, **61**, 1173-1182. https://doi.org/10.1016/j.ijrobp.2004.12.026

15. Cho, S.H. (2005) Estimation of Tumour Dose Enhancement Due to Gold Nanoparticles during Typical Radiation Treatments: A Preliminary Monte Carlo Study. *Physics in Medicine and Biology*, **50**, N163. https://doi.org/10.1088/0031-9155/50/15/N01

16. Mesa, A., *et al.* (1999) Dose Distributions Using Kilovoltage X-Rays and Dose Enhancement from Iodine Contrast Agents. *Physics in Medicine and Biology*, **44**, 1955. https://doi.org/10.1088/0031-9155/44/8/308

17. Callisen, H.H., Norman, A. and Adams, F.H. (1979) Absorbed Dose in the Presence of Contrast Agents during Pediatric Cardiac Catheterization. *Medical Physics*, **6**, 504-509. https://doi.org/10.1118/1.594613

18. Paul, J., *et al.* (2011) Effect of Contrast Material on Image Noise and Radiation Dose in Adult Chest Computed Tomography Using Automatic Exposure Control: A Comparative Study between 16-, 64- and 128-Slice CT. *European Journal of Radiology*, **79**, e128-e132. https://doi.org/10.1016/j.ejrad.2011.05.012

19. Amato, E., *et al.* (2013) Can Contrast Media Increase Organ Doses in CT Examinations? A Clinical Study. *American Journal of Roentgenology*, **200**, 1288-1293. https://doi.org/10.2214/AJR.12.8958

20. He, W., *et al.* (2014) Does Administering Iodine in Radiological Procedures Increase Patient Doses? *Medical Physics*, **41**, Article ID: 113901. https://doi.org/10.1118/1.4898594

21. Niroomand-Rad, A., *et al.* (1998) Radiochromic Film Dosimetry: Recommendations of AAPM Radiation Therapy Committee Task Group 55. *Medical Physics*, **25**, 2093-2115. https://doi.org/10.1118/1.598407

22. Rahman, W.N., *et al.* (2011) Influence of Gold Nanoparticles on Radiation Dose Enhancement and Cellular Migration in Microbeam-Irradiated Cells. *BioNanoScience*, **1**, 4-13. https://doi.org/10.1007/s12668-011-0001-x

APPENDIX

The basic definition of the dose enhancement factor "DEF" as a function of concentration "c" and energy "E" is as follows

$$\mathrm{DEF}(c,E)=\frac{c_I\left[\frac{\mu_{en}}{\rho}\right]_E^I+(1-c_I)\left[\frac{\mu_{en}}{\rho}\right]_E^{H_2O}}{\left[\frac{\mu_{en}}{\rho}\right]_E^{H_2O}}$$

Here ω represents the concentration of the solvent [in this case Iodine CM] and

μ_{en}/ρ is the mass-energy absorption coefficient

However, $[\mu_{en}/\rho]$ is mass-energy absorption coefficient which is related to the linear attenuation coefficient in the following way {The Physics of Radiation Therapy Chapter 3 section 5-4B by Faiz M. Khan 5th edition 2015}

$$\mu_{en}=\mu_{tr}(1-g)$$

where μ_{tr} is the transfer energy factor and it is directly related to the linear attenuation coefficient μ as follows;

$$\mu_{tr}=\left(\bar{E}_{tr}/h\nu\right)\cdot\mu$$

where E_{tr} represents average energy transfer

Therefore

$$\mu_{en}=\left(\bar{E}_{tr}/h\nu\right)\cdot\mu(1-g)$$

Assumptions:

- Since transfer energy "E_{tr}" will be almost the same for both cases of tissue equivalent material with and without the iodine contrast agent.
- The "g" factor representing the energy generated inside the target and deposited outside which is not balanced by the electron equilibrium and assuming that the g factor is also the same in both cases. Moreover, radiative loss factor is negligible in case of the beam qualities typically used in CT.
- Also, the density "ρ" is considered to be un-effected by the inclusion of small amount of iodinated compound. Otherwise the final relationship will still be the same however with another factor related to this difference. The CTDI factor is a dose indicator based on many assumptions and approximations which justifies neglecting this difference. Therefore

$$\mu_{en}=Y\cdot\mu$$

where $Y=\left(\bar{E}_{tr}/h\nu\right)\cdot(1-g)$

Inserting the above relationship in the DEF equation will be;

$$\mathrm{DEF}(c,E)=\frac{\omega_I\cdot Y\cdot\mu_I+(1-\omega_I)Y\cdot\mu_\omega}{Y\cdot\mu_\omega}$$

This can be re-written as;

$$\mathrm{DEF}(c,E)=\frac{\omega_I\cdot\mu_I+(1-\omega_I)\cdot\mu_\omega}{\mu_\omega}$$

and can further re-written as;

$$\mathrm{DEF}(c,E)=\frac{\omega(\mu_I-\mu_w)}{\mu_w}+1$$

But the fraction in the above equation is nothing but CT#/1000
Call CT# = N
Hence

$$\mathrm{DEF}(c,E) \approx \omega_I \cdot N/1000 + 1$$

In case of no added contrast media the CT number should be that of the target. For instance if we deal with water then CT # *i.e.* $N = 0$ and there will be no dose enhancements and its value will become one.