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Effects of iodinated contrast media on radiation therapy dosimetry for pathologies within the thorax

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Abstract The aim of this study was to establish whether the presence of iodinated contrast within the tissues of the treatment region leads to inaccurate dose representation during radiation therapy dose calculations. We reviewed the radiation therapy planning computed tomography (CT) scans for 20 previously treated lung cancer patients where both contrast and non-contrast CT scans had been performed. Planning had been carried out on the non-contrast scan. Plans were replicated to the contrast CT series and dosimetry was compared between the two plans. To account for differences in respiration and therefore lung volume between the two CT series, lung tissue was assigned a density equivalent to water. The overall data collected from this method showed that, for all chest plans examined, the presence of contrast affected the resultant dosimetry by up to ± 1.5% when compared to the identical non-contrast plan. Even when lung tissue was not assigned a density equivalent to water, the average effect of contrast was minimal, however, these results are not solely from the presence of contrast as there were additional lung volume discrepancies. In conclusion, the effect of the presence of contrast on dosimetry for lung cancer treatment is negligible.

Keywords: 3D dosimetry, heterogeneity, iodinated contrast, lung neoplasms, thorax.

Introduction

Three-dimensional radiation therapy planning systems incorporate calculation algorithms that demonstrate the effects of tissue densities on dosimetry. Anatomical structures with varying densities are represented on computed tomography (CT) scans by a two-dimensional distribution of Hounsfield units (HU). These units depend on beam attenuation properties and are defined by a relative attenuation coefficient.[1,2] Treatment planning systems convert the HUs into corresponding electron densities in order to calculate dose and therefore HU values that yield incorrect electron densities may decrease the accuracy of dose calculation, especially when applying heterogeneity correction.[1,3]

Structures with a high atomic number present within a field of view produce image artifacts that reduce image quality and create areas of misrepresented density information. These CT artifacts are unavoidable if the patient has dental fillings or metal hip prostheses and these structures are enclosed within or near the radiation treatment fields. The impact of intravenous iodinated contrast media (IVICM) should also be considered when using heterogeneity correction as these high density agents are not present in patient tissue during radiation therapy treatment. The use of IVICM during the acquisition of planning CT images is usually minimised, because it is possible that planning systems will misinterpret IVICM as high density tissue, leading to an underestimation of the actual delivered treatment dose.[4] Nonetheless, the use of IVICM with CTs for some specific tumour types is recommended to improve tumour volume definition as well as the enhancement of other regions of interest,[3] particularly for radical treatment.

Historically, intravenous (IV) contrast agents used in any medical imaging scans have been specifically developed and selected to minimise the degradation of the diagnostic quality of the image while producing minimal image artifacts.[1] The introduction of high density iodinated contrast into the blood vessels does not affect the diagnostic quality of the image by creating unwanted streaking artifacts usually caused by high density materials however, tissue densities will be misrepresented.[1] There is conflicting evidence regarding the impact of IVICM on dosimetry. Ramm *et al.*[3] (using phantoms containing materials to simulate the presence of contrast) showed that contrast agents had effects on dosimetry which were more pronounced as concentration and volume of the contrast media increased. These authors considered dose changes of 1–3% for patients displaying Hounsfield units of less than 500, in volumes of less than 5 cm to be acceptable.[3] However, Williams *et al*.,[1] also using simulation phantoms, considered that errors of 2–4% were sufficient to recommend the use of image registration. Weber *et al.*[4] studied prostate cancer patients who received bladder contrast during their planning CT scan to help localise the prostate. When comparing plans where the bladder either contained contrast or was simply assigned a mass HU of water, the median dose variation was -0.03% for the prostate volume and -1.13% for the rectum. These authors considered that the contrast mass within the treatment volume had not significantly modified the dose distribution.[4]

Currently at our centre, when the radiation oncologist (RO) requests contrast scans in order to outline the target volume, patients undergo both a non-contrast and contrast scan. After importing these CT series to our planning software (Eclipse 6.5, VARIAN®), the images are overlaid using image registration. The RO uses the contrast scans to outline the target volumes, but the

non-contrast scans are used for the final dose calculations. The aim of the present study was to determine whether the impact of IVICM during thoracic planning CT scans was sufficient to justify this duplication of scans.

Materials and methods

Patient selection

All patients who underwent radiotherapy planning for lung cancer between 2003 and 2004 were considered. Eligible patients were those where both non-contrast and contrast CT chest series were requested by the radiation oncologist as part of the planning process. In the context of our quality assurance program, an opportunity to evaluate practices regarding the use of IVICM using retrospective data only, meant that with reference to the National Health and Medical Research Council's *Guidelines For Ethical Review*, such review was not warranted.[5] As part of our patient consent forms, the patient is to understand that their data may be used by the department for retrospective internal quality assurance studies. All patients selected for the project had completed their treatment courses, could not be identified from the data collected and did not have to undergo any additional studies. As this research was conducted by persons that usually have access to patient records and data, privacy and confidentiality issues were not breached.[5]

As a result of respiration and slight patient movement occurring between the two CT series, source to skin distance (SSD) variations between the non-contrast and contrast plans were detected. As SSD discrepancies influence the resulting isodose distribution, patients with SSD variations greater than 0.5 cm were excluded from the study. Phantom measurements carried out on our planning system showed that SSD variations of up to 0.5 cm yield maximum dosimetry changes of ± 0.02%. All patients had previously undergone radical radiation therapy treatment to the chest region with treatment fields encompassing the mediastinum, where large amounts of contrast agent were present within the major blood vessels. Thirty patients were excluded because of SSD discrepancies and a lack of contrast within the treatment area, leaving 20 patients who were suitable. All patients had received treatment using 6 MV photons with prescriptions ranging from 35 Gy to 60 Gy PTV doses. Field arrangements depended on individual tumour characteristics with plans featuring two to four fields (one patient: two fields, 13 patients: three fields and six patients: four fields).

Planning procedures

At the time of planning for each patient, we acquired a non-contrast image series using a GE LightSpeed diagnostic CT scanner, followed by a contrast image series in which 50 mL of saline and 50 mL of iodine contrast (Omnipaque 350®, Schering) was injected intravenously prior to performing the scan. Standard planning procedure at our clinic involves the patient breathing normally during the scans. Planning target volumes (PTV) were defined by the prescribing radiation oncologist for each patient using the non-contrast scans, while viewing the registered contrast images. The beams were designed to encompass the PTV with the prescribed dose on the non-contrast scans.

Standard comparison

The PTV and treatment fields were copied anatomically from the non-contrast scans to the contrast series. Monitor unit values were then replicated within the contrast plan. A comparison of isodose distributions of the non-contrast and contrast plans was performed and maximum point doses and reference point doses were recorded for both plans. Dose volume histograms (DVH) were used to calculate mean PTV doses. We considered the mean PTV dose to be a more reliable variable than the maximum point doses and the reference point doses, because it considers an area, not just a single point. The non-contrast dose value (in Gy) for the particular point/volume of interest was divided by the corresponding contrast dose value (in Gy). This value was then multiplied by 100 and 100 was subtracted to express the difference in dose as a percentage of the non-contrast dose ((NC/C) x 100–100). Negative values indicate that the dose of the contrast plan was less than the dose of the comparable non-contrast plan. To determine if dose variations were clinically significant, ± 2% was considered to be acceptable, with this dose uncertainty forming part of the ± 5% overall dose delivery uncertainty as described by ICRU 1976.[6]

Due to individual patient variations in contrast clearing times, as well as differences in the timing of the image capture of the contrast scans and the methods of injection (pressure injector *vs.* hand injection), the contrast CT series were carefully scrutinised for the presence of contrast within the major vessels. This was accomplished by observing whether the HU of a specific anatomical point within a major blood vessel on the contrast scan was greater than the HU of the same point on the non-contrast scan.

Adjusted comparison to allow for respiration effects

We considered that differences in respiration phases and lung volume between the non-contrast and contrast series might affect overall dose distributions and possibly obscure the true impact of contrast on dosimetry. Therefore, in order to appreciate the effects of contrast on dose distributions and to overcome lung volume variation between the two CT series, all lung volume was contoured and assigned a HU value of zero (equivalent to water). Thus, with SSD differences of less than 0.5 cm deemed negligible and with all lung volume within both scans effectively removed, dosimetric inconsistencies were assumed to be generated from the presence of contrast media only.

Results

Standard comparison

The percentage variations in maximum point dose, mean PTV dose and reference point dose between non-contrast and contrast chest plans (with normal tissue heterogeneity) are shown in Table 1. In the presence of normal lung tissue heterogeneity, the average percentage difference in reference point doses was -0.8% ± 1.6 SD (range -4.9– +1.7%). The average percentage difference in maximum point dose was -0.2% ± 1.2 SD with a range of values between -2.0% and +3.9%. The reference point and maximum point dose data appear to be randomly distributed, presumably, as point doses are very dependent upon beam path length and presence of inhomogeneities such as lung. Mean PTV doses ranged from -2.3% to 0.0% with an average percentage difference of -0.8% ± 0.6 SD.

Adjusted comparison

Table 2 shows the reference point doses, maximum point doses and mean PTV doses for chest plans where lung volume was assigned a mass Hounsfield unit of zero. Reference point doses ranged from -0.9–+0.6%, maximum point doses varied from -1.5–+0.9% and mean PTV doses ranged between -0.9% and +0.7%. The average values for reference point doses, maximum point doses and mean PTV doses were -0.2% ± 0.5 SD, -0.2% ± 0.6 SD and -0.2% ± 0.5 SD respectively. Overall, the data

Table 1 Percentage variations in maximum point dose, mean PTV dose and reference point dose between non-contrat and contrast chest plans with normal tissue heterogeneity.

Pt. No.	% Diff. Max. Point dose	% Diff. Mean PTV dose	% Diff. R.P. dose
1	0.3	0.0	-0.7
2	3.9	-0.8	0.4
3	-1.5	-2.3	-1.2
4	-2.0	-1.6	1.0
5	-1.0	-0.8	-1.1
6	-1.2	-1.1	1.7
7	-0.9	-1.0	0.7
8	-1.3	-0.5	-0.7
9	0.2	-0.8	-1.7
10	1.3	-0.3	-1.4
11	-0.4	-0.6	-4.9
12	-1.0	-1.5	-3.2
13	-0.2	-0.6	-0.6
14	0.2	-0.2	1.2
15	-0.3	-0.7	-2.4
16	-0.3	-0.8	-1.1
17	0.2	0.0	-0.4
18	-0.2	-1.1	-1.1
19	-0.2	-0.2	1.2
20	-0.4	-1.3	-1.0
Mean	-0.2	-0.8	-0.8
S.D.	1.2	0.6	1.6

Negative values denoting data that are less than that of the non-contrast plan. Pt. No. = Patient Number; % Diff. = Percentage Difference; R.P. = Reference Point; S.D. = Standard Deviation

presented in Table 2 suggests that, for the majority of chest plans in our study, the presence of contrast affected the dosimetry by up to ± 1.5% when compared to identical non-contrast chest plans. Nineteen out of the 20 patients included in the study displayed dose variations within the limits of ± 1.0% with one patient (Patient 4) showing a maximum point dose greater than ± 1.0% but less than ± 2.0%.

Discussion

Few studies have examined the dosimetric effects of contrast media on radiation therapy planning and, to our knowledge, only one other patient-based project to examine this topic has been performed.[7] The anatomical region chosen for this study was the chest or mediastinum, due to the abundance of larger blood vessels in this area. Considering the high probability of the presence of contrast agent within blood vessels and surrounding tissues within the chest, we anticipated that inconsistencies between contrast and non-contrast plans would be more clearly highlighted for chest plans in comparison to other anatomical areas (such as the brain) where contrast agents do not readily concentrate within the tissues.

The current study demonstrates that the presence of contrast within planning CT images has a negligible effect on the resultant dose distribution during radiation therapy planning. As reported, the presence of IVICM affected the dosimetry by up to ± 1.5% in the chest plans examined and when we compared non-contrast and contrast plans using Eclipse planning software, minimal variations were seen in isodose lines (data not shown). The mean values for all dose points or volumes presented in Tables 1 and 2 demonstrate that, consistently, the dose of the contrast plan is slightly less than the dose of the non-contrast plan. This data observation is consistent with radiation therapy planning principles as one would expect the dose to be less if the beams had to traverse higher density tissue. With the negligible differences in average dose values, the argument that the presence of contrast does not affect the dosimetric outcome is further substantiated.

Tissue inhomogeneity (especially lung) within treatment fields significantly modifies dosimetry.[8] Patient respiration phase dictates the amount of lung present along the beam path, introducing another variable affecting the comparison between the two sets of scans. A previous study by Henkelman and Mah [9] revealed that, during normal respiration, changes of approximately 5% were recorded in lung segment within the studied beam path length. Many other studies document variations of 1–3 cm in the placement of structures within the thorax due to respiration and cardiac motion.[10–14] We attempted to reduce this source of error by assigning all lung volume within both CT series a mass HU of zero, which is equivalent to water and essentially 'phantomised' the patient data sets.

By observing the standard deviations for each point or volume of interest in Tables 1 and 2, it can noted that the dose variation (standard deviation) between the non-contrast and contrast data is minimised in the Table 2 data where the lung heterogeneity has been removed. It is believed that the compounding effects of both the contrast and difference in the amount of lung within the beam paths caused this greater variation in the Table 1 data. Due to the removal of the lung volume variation, Table 2 data is only indicative of the effects of IVICM on the dosimetry. When comparing the standard deviation values of both Tables 1 and 2, the values in Table 1 for all dose points or volumes of interest appear to be more random. This may be due to the randomness of lung volume variation between patients and also the anatomical placement of the treatment fields. Compared to a plan encompassing a mediastinal lung volume, a beam arrangement focusing on an apical lung tumour may show less variation in lung volume between the two plans as this area does not undergo large changes in volume during respiration.[9–14] The standard deviation values described in Table 2 are all relatively similar, suggesting that differences in lung volume were impacting on the data more than the effects of IVICM. This also implies that the introduction of IVICM consistently has the same effect on dosimetry.

Because our results displayed negligible change in dose with lung inhomogeneity interfaces removed, the assumption can be made that the introduction of full heterogeneity lung correction would provide a similar outcome if lung volume and shape were identical between the two comparable CT series. In our study, lung volume was not assigned a mass HU of lung equivalent tissue (0.25 HU), in order to avoid another variable. Furthermore, identical amounts of lung volume would need to have been contoured and assigned a density of 0.25 HU, with any remaining differences filled in with tissue equivalent for both the non-contrast and contrast image sets. This difficulty in reproducing identical lung volumes between the two image studies could have been circumvented by simulating the study using a phantom. Alternatively, respiratory gating techniques could have been utilised to increase the reproducibility of the phase of respiration and thus the lung volume between the two series.

By undertaking this investigation into the effects of IVICM of dosimetry, we have, incidentally, uncovered another topic that requires further scrutiny. The variation in lung volume noted

between the two consecutive CT series (non-contrast followed by contrast) indicates that the dosimetry provided by the routine single planning CT series may not be indicative of the actual final dose delivered to the patient. The planning CT scan provides a 'snapshot' of the patient's anatomy, and with the increasing speed of CT data acquisition, organs or pathologies that may be moving up to 3 cm[10–14] in a respiratory cycle will be misrepresented due to this organ motion. This is an important issue when the ROs are determining margins for tumour volumes. If this organ/tumour motion is identified and quantified, appropriate margins may be applied to ensure during all phases of respiration, the tumour volume will be adequately covered. With respiratory gating technology increasing, further investigation into this topic is warranted.

One patient out of 20 (Patient 4 in Tables 1 and 2) showed a maximum point dose greater than ± 1.0% but less than ± 2.0%. This patient's scan revealed the presence of an abnormal amount of contrast within the left brachiocephalic vein, where pathological obstruction of this vessel caused pooling of contrast media. This mass of contrast enhanced tissue was situated within the fields encompassing the PTV and contained HU values ranging from 300–400 in a volume of 4 cm (wide) x 1 cm (high) x 3 cm (long). Nonetheless, even in the presence of this high contrast mass, the mean PTV and reference point doses for this patient showed a dose variation of less than ± 1.0%. The maximum point dose was reduced by approximately 1.5% in the contrast plan due to the high-density contrast acting as shielding. Data from the patient in our study where there was left brachiocephalic vein obstruction indicated that larger, concentrated volumes of contrast media could influence the resultant dose distribution by more than ± 1.0%. While our results are comparable with those of Ramm *et al*.[3] they are not entirely comparable with those of Weber *et al*.,[4] where no evidence was found to suggest that the presence of larger, concentrated volumes of contrast adversely affected dosimetry.[4] As a consequence of this uncertainty, we recommend that patients whose thoracic neoplasms concentrate abnormal amounts of IVICM by disrupting the usual flow of blood through the vessels, should undergo both a non-contrast and contrast scan. In these specific, rare cases, radiation therapy planning should be carried out on the non-contrast scan in order to obtain true dose representation.

In areas such as the thorax where there is an abundance of large blood vessels, the probability of the presence of contrast within the treatment volume will be at a maximum. In comparison, for other anatomical areas (such as the brain) where blood vessels are small, the probability of the presence of contrast within the treatment volume would also be small. Because the results from our study showed minimal dose variation between the non-contrast and contrast plans in the thoracic region, we suggest it may be plausible to apply this methodology to other anatomical regions without any major discrepancies. Further investigation is indicated to determine the distribution of IVICM throughout other anatomical sites and tissues to validate the results we obtained using chest and mediastinum CT data sets. Care should be taken, however, when applying this methodology to treatment fields encompassing contrast-enhanced bladder or kidneys. Because these organs readily accumulate large amounts of contrast media, it may be prudent in all cases to outline these structures and assign a 'normal' HU value, in order to obtain the most accurate dosimetry. Additional examination is needed to determine the maximum size, volume and density of contrast enhanced areas before significant changes in dosimetry can be observed.

Table 2 Percentage variations in a maximum point dose and reference point dose, mean PTV and reference point dose between non-contrast and contrast chest plans with the lung volume assigned a mass Hounsfield unit of zero.

Pt. No.	% Diff. Max. point dose	% Diff. Mean PTV dose	% Diff. R.P. dose
1	0.0	-0.6	-0.2
2	0.0	-0.6	0.2
3	-0.4	-0.8	-0.6
4	-1.5	-0.9	-0.5
5	-0.5	-0.3	0.0
6	-0.7	0.0	-0.2
7	-1.0	-0.8	-0.8
8	-0.7	0.0	-0.2
9	-0.4	-0.2	-0.8
10	0.8	0.0	0.6
11	0.4	0.7	0.5
12	0.2	-0.5	-0.9
13	-0.4	-0.6	-0.4
14	-0.6	-0.4	-0.9
15	-0.7	0.4	0.0
16	0.9	0.6	0.6
17	-0.2	0.0	-0.6
18	-0.4	-0.9	-0.7
19	0.7	0.5	0.5
20	-0.3	-0.4	-0.5
Mean	-0.2	-0.2	-0.2
S.D.	0.6	0.5	0.5

Negative values denoting data that are less than that of the non-contrast plan. Pt. No. = Patient Number; % Diff. = Percentage Difference; R.P. = Reference Point; S.D. = Standard Deviation

In conclusion, our results have shown that the presence of IVICM within a thoracic planning CT series has a negligible effect on dosimetry for radiation therapy planning. Exceptions to this would include patients with concentrated contrast media in obstructed vessels, causing a pooling effect. In these cases, either the contrast enhanced areas should be contoured and assigned a 'normal' Hounsfield unit or, both non-contrast and contrast CT scans should be acquired and registered with planning occurring on the non-contrast images. In all other cases, we will perform planning of lung cancer patients with a single set of contrast-enhanced CT scans.

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