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FULL PAPER

Comparison of virtual non-contrast dual-energy CT and a true non-contrast CT for contouring in radiotherapy of 3D printed lung tumour models in motion: a phantom study

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Objectives: This work aims to investigate whether virtual non-contrast (VNC) dual-energy CT (DECT) of contrasted lung tumours can be used as an alternative for true non-contrast (TNC) images in radiotherapy. Two DECT techniques and a TNC CT were compared and influences on gross tumour volume (GTV) volume and CT number from motion artefacts in three-dimensional printed lung tumour models (LTM) in a motion phantom were examined.

Methods: Two spherical LTMs (diameter 3.0 cm) with different inner shapes were created in a three-dimensional printer. The inner shapes contained water or iodine (concentration 5 mg ml⁻¹) and were scanned with a dual-source DECT (ds-DECT), single-source sequential DECT (ss-DECT) and TNC CT in a respiratory motion phantom (15 breaths/min, amplitude 1.5 cm). CT number

and volume of LTMs were measured. Therefore, two GTVs were contoured.

Results: Deviations in GTV volume (outer shape) of LTMs in motion for contrast-enhanced ss-DECT and ds-DECT VNC images compared to TNC images are not significant ($p > 0.05$). Relative GTV volume and CT number deviations (inner shapes) of LTMs in motion were $6.6 \pm 0.6\%$ and 104.4 ± 71.2 HU between ss-DECT and TNC CT and $-8.4 \pm 10.6\%$ and 25.5 ± 58.5 HU between ds-DECT and TNC, respectively.

Conclusion: ss-DECT VNC images could not sufficiently subtract iodine from water in LTMs in motion, whereas ds-DECT VNC images might be a valid alternative to a TNC CT.

Advances in knowledge: ds-DECT provides a contrasted image for contouring and a non-contrasted image for radiotherapy treatment planning for LTM in motion.

INTRODUCTION

CT has become essential for radiotherapy treatment planning (RTP). RTP benefits from new and steady developments of CT techniques. Dual-energy CT (DECT) has found its way to radiotherapy mainly for metal artefact reduction¹⁻⁴ and the reconstruction of virtual monochromatic energy (VME) images.⁵⁻⁸ DECT systems have material decomposition algorithms to reconstruct virtual non-contrast (VNC) images, which are algorithmically corrected for iodine-containing contrast agent to reflect non-iodine contrast only.^{9,10} Material decomposition relies on the use of two different energy spectra and decomposing the image into two basis materials, like in the above example: iodine and water. VNC images are not common in radiotherapy, but as Yamada et al¹¹ showed, it can improve the accuracy of dose distributions in treatment planning by

removing the iodine component from contrast-enhanced areas. Nevertheless, more complex phantom settings than in the previously mentioned study would be useful to investigate its usability in treatment planning and contouring.

Contouring in RTP relies on the right CT attenuation numbers and can be done within a contrast-enhanced CT image. As the contrast agent is eliminated from the patient's body, CT attenuation numbers will have changed until the beginning of radiotherapy treatment. However, the calculated dose distribution is still based on the contrast-enhanced tumour and organs. Treatment planning systems (TPS) have the option to define regions with corrected homogenous attenuation numbers, which is inaccurate and does not represent the real inhomogeneity of tissue.

Especially, in regions with a high accumulation of contrast region, a density correction must be considered.

Using intravenous iodinated contrast agent can be useful to estimate the grade of malignancy of solid pulmonary nodules.¹² DECT was shown to successfully add value in the evaluation of lung cancer^{13–16} and predicting lung tumour recurrence after radiotherapy.¹⁷ Generation of VME images may improve contouring of lung nodules for radiotherapy by increasing their contrast or may reduce streak or photon starvation artefacts that arise from dense accumulation of contrast agent, *e.g.* inside the subclavian vein or superior vena cava. DECT might also be an option for differentiating between lung cancer and inflammatory masses.¹⁸ Considering these potential advantages, DECT with VME and VNC reconstructions comes with additional information compared to a standard polychromatic energy spectrum of standard CT which ultimately may improve RTP for lung cancer.

Different DECT techniques vary in performance, especially regarding noise levels and accuracy of material decomposition, mainly because of the spectral overlap of the two used energies.¹⁹ Iodine density measurements results, however, do not seem to differ relevantly.⁶ Respiratory organ and tumour motion may lead to object blurring and change the depicted volume and attenuation numbers.^{20,21} However, tumour or organ motion was not part of previous phantom studies comparing VNC images of different DECT techniques among each other or with TNC CT. Breath-holding or 4DCT are valid techniques to image gross tumour volume (GTV) more accurately^{22–26} and to create internal target volumes (ITV) with smaller margins to the GTV for RTP compared to free breathing.²⁷ Nevertheless, these techniques are not always available. To acquire a valid breath-hold scan can be limited by patient factors, whereas for 4DCT additional technical equipment is mandatory. Multiple CT scans of unmonitored breathing can be used for these reasons to determine an ITV.

The purpose of this study is to investigate if the material decomposition algorithms of a dual-source DECT and a single-source sequential DECT device can sufficiently remove the iodine component in two differently shaped lung tumour models (LTM) in motion for the further use in RTP. As these two DECT techniques have technically different approaches to acquire VNC images, the scanner type might influence GTV contouring. A dual-source CT acquires both energies with two X-ray tubes simultaneously, whereas the approach for the single-source DECT used in this study is to acquire each energy sequentially. A comparison to a TNC CT as reference was done to reflect a standard CT in RTP without DE-capability.

METHODS AND MATERIALS

Materials

Two differently shaped lung tumour models (LTM) were created in the computer-aided design software Tinkercad (Autodesk Inc., San Francisco, CA) and made with a three-dimensional (3D) printer (German RepRap X500, German RepRap GmbH, Feldkirchen, Germany). Polylactide (PLA) was used for printing. Both LTMs are spherical and have a diameter of 3.0 cm, matching the size of self-made lung equivalent inserts of cedarwood (Figure 1). LTM-1 has a closed inner sphere with 1.5 cm in diameter, which has no structure inside (empty) due to its small size and construction restrictions of the 3D printer. The space between the inner sphere and outer shell can be filled. LTM-2 is half-empty and half-filled with a support structure needed for 3D printing (Figure 2). The inner spaces of both LTMs were either filled with demineralised water or iodinated contrast agent diluted in water (concentration 5 mg ml⁻¹; Ultravist®, Bayer Vital, Leverkusen, Germany). With two lung tumour models, CT number deviations from geometric differences were investigated.

Figure 1. Image of the opened lung insert made of cedarwood with a 3cm spherically cavity for the matching 3D printed lung tumour model. 3D, three-dimensional.

Figure 2. Implementation of the 3D printed LTM. The top images show the drafts of two different shaped LTMs and the bottom images the corresponding coronal plane in CT images. Left: LTM-1, right: LTM-2. 3D, three-dimensional; LTM, lung tumour model.

Two different DECT techniques from two vendors were used to reconstruct VNC images and to acquire a true non-contrast (TNC) CT series. For all scans, the scanning length was 14 cm, and the reconstructed slice thickness was 3.0 mm like generally used for normofractionated treatment planning.

For the DECT techniques, first, a dual-source DECT device (ds-DECT) (SOMATOM Force 2. generation, Siemens Healthineers, Forchheim, Germany) was used, which operated at 80 kV on tube A and 150 kV with tin (Sn) filtration on tube B, (table speed 12.64 cm/s, pitch 0.6, gantry rotation time of 280 ms, total collimation width 57.6 mm). $CTDI_{vol}$ was set to 7.4 mGy for a “full-dose” scan reflecting the manufacturer’s yearlong standard and to a “reduced-dose” scan with a $CTDI_{vol}$ of 3.1 mGy representing the new factory standard setting. Second, a single-source DECT device (ss-DECT) (Aquilion One Genesis, Canon Medical Systems Europe B.V., Zoetermeer, Netherlands), which operated at 80/135 kV ($CTDI_{vol}$ 12.3 mGy, gantry rotation time 500 ms, total collimation width 140.0 mm). ss-DECT uses sequential scanning, acquiring scans of the same volume with different energies consecutively. The acquisition type was a so-called “volume acquisition”, *i.e.* the whole scan volume covered 140 mm in z-axis without any table motion.

The TNC images were acquired with a “standard” single-source CT (Canon Aquilion LB, Canon Medical Systems Europe B.V., Zoetermeer, Netherlands) as reference (tube voltage 120 kV, $CTDI_{vol}$ 4.5 mGy, table speed 6.4 cm/s, revolution time 344 ms, pitch 0.7, total collimation width 32.0 mm), which is commonly used for radiotherapy treatment planning in our department.

A respiratory motion phantom (Quasar, Modus Medical Devices, Inc., London, Ontario, CA) was used for simulating respiratory tumour motion and SPSS 26 (IBM SPSS Statistics, Armonk, NY) for statistical analysis. GTV contouring was done using the Varian Eclipse V15.5 software (Varian Medical Systems, Palo Alto, CA).

Methods

Respiratory motion was simulated with a sinusoidal waveform (amplitude 15 mm, period 4 s, motion speed 15 mm/s, 15 breaths per minute). This waveform was chosen to ensure constant motion while scanning.

Two GTV for each LTM were defined in the TPS. An outer GTV-O for the whole sphere (window level –500 HU; window width 500 HU) and an inner GTV-I (window level 40 HU; window width 400 HU) for the water or iodine filling, representing the lung tumour. Furthermore, an ITV-O and ITV-I from multiple TNC GTV-O and GTV-I in motion was created by image fusion of TNC CT scans in free breathing. GTV and ITV volumes were measured, as well as CT attenuation numbers of GTV-I, polymethylmethacrylate (PMMA) and the lung insert. The region of interest for measuring in PMMA and the lung insert was set to 10 mm in diameter in an axial plane. Scans for the contrast-enhanced LTMs were done with both DECT techniques in respiratory motion and rest.

As LTM-1 and LTM-2 have the same outer shape, absolute GTV-O volume measurements were joined for each CT technique, including water-filled and contrast-enhanced LTM. This can be done, because the GTV-O shape is encased by the surface area material. GTV-I CT numbers can only be joined for equal fillings. ITV-O and ITV-I volume deviations to TNC GTV-O and GTV-I were calculated. A two-tailed *t*-test was used to determine differences between VNC and TNC images for GTV-O volume and also for the CT number of PMMA and the lung insert. $p < 0.05$ would indicate statistical significance. GTV-I relative volume and absolute CT number differences between VNC and TNC images were calculated. Relative deviations in GTV-I volume in motion should be in the order of the deviations of GTV-I in rest ($\pm \Delta Vol_{LTM1+2}$) to be seen as comparable values between VNC and TNC images. CT number values should range between HU_{TNC} and 0 HU.

RESULTS

VNC images of LTM in motion for GTV-O volumes did not differ significantly between both DECT techniques ($p = 0.55$) as well as in comparison to TNC (ss-DECT $p = 0.09$, ds-DECT $p = 0.06$). The same goes for the lung insert CT number between both DECT techniques and TNC CT ($p > 0.05$), but significance was reached between ss-DECT and ds-DECT. PMMA measurements were affected significantly among all three CT scanners ($p < 0.05$). ITV-O volume was 60.6% larger than TNC GTV-O volume, whereas DECT GTV-O tend towards being smaller (ds-DECT $\Delta Vol_{GTV-O} = 24.6\%$, ss-DECT $\Delta Vol_{GTV-O} = 20.8\%$) (Table 1). Figure 3 shows the coronal plane of TNC and VNC images for GTV-O and ITV-O in motion.

Table 1. Volume measurements of the GTV-O, ITV-O and CT numbers of PMMA and the lung insert for all three CT scanners

Scanner	Iodine (5 mg ml ⁻¹)	GTV-O Vol. (ccm ±SD)	PMMA (Mean ± SD) HU	Lung Insert (Mean ± SD) HU
ss-DECT	Yes	16.6 ± 1.6 (n = 6)	77.7 ± 13.2 (n = 6)	-618.4 ± 17.9 (n = 6)
ds-DECT	Yes	15.8 ± 2.5 (n = 6)	156.2 ± 18.8 (n = 6)	-608.8 ± 20.2 (n = 6)
TNC CT	No	20.9 ± 7.4 (n = 11)	127.1 ± 20.9 (n = 12)	-614.2 ± 18.7 (n = 12)
TNC CT (ITV-O)	No	33.6 (n = 11)	-	-

GTV, gross tumour volume; HU, Hounsfield unit; ITV, internal target volume; PMMA, polymethylmethacrylate; SD, standard deviation; TNC, true non-contrast; ds-DECT, dual source dual-energy CT; ss-DECT, single source dual-energy CT.

The contrast-enhanced GTV-I in rest and water containing GTV-I in motion had a CT number of 105.0 ± 50.4 and -30.4 ± 40.0 HU, respectively, measured within the TNC images.

GTV-I volume and CT number measurements could not be evaluated by *t*-test due to a low number of scans ($n = 4$) for each technique. Differences of ds-DECT GTV-I volume to the reference TNC measurements are comparable for LTM in rest ($\Delta\text{Vol}_{\text{LTM-1}}=0.2$ ccm, $\Delta\text{Vol}_{\text{LTM-2}}=-0.6$ ccm) and in motion ($\Delta\text{Vol}_{\text{LTM-1}}=0.1$ ccm, $\Delta\text{Vol}_{\text{LTM-2}}=-0.7$ ccm). Combining LTM-1 and LTM-2 measurements results in a relative difference in volume of $\Delta\text{Vol}_{\text{LTM1+2}}= 6.1\pm8.0\%$ in rest and $-8.4\pm10.6\%$ in motion, respectively. ss-DECT behaved similar for rest measurements ($\Delta\text{Vol}_{\text{LTM-1}}=0.3$ ccm, $\Delta\text{Vol}_{\text{LTM-2}}=-0.5$ ccm) and motion ($\Delta\text{Vol}_{\text{LTM-1}}=0.4$ ccm, $\Delta\text{Vol}_{\text{LTM-2}}=-0.4$ ccm), resulting in a combined volume difference of $\Delta\text{Vol}_{\text{LTM1+2}} = -8.3\pm4.5\%$ for LTM in rest and $6.6\pm0.6\%$ in motion (Table 2). ITV-I volumes compared to TNC GTV-O were by far the largest ($\Delta\text{Vol}_{\text{LTM1+2}} = 36.9\pm1.0\%$). A comparison between the CT techniques for GTV-I motion is illustrated in Figures 3 and 4.

Contrast-enhanced GTV-I VNC CT numbers for ds-DECT were comparable to LTMs containing water measured in the TNC images. Absolute differences were as follows: $\Delta\text{HU}_{\text{LTM1+2}} = -14.2\pm33.3$ HU for non-moving LTMs, $\Delta\text{HU}_{\text{LTM1+2}} = 25.5\pm58.5$ HU for LTMs in motion. For ss-DECT, the differences to reference are $\Delta\text{HU}_{\text{LTM1+2}} = 18.4\pm26.3$ HU for non-moving LTMs and $\Delta\text{HU}_{\text{LTM1+2}} = 104.4\pm71.2$ HU in motion. Values for each LTM separately are listed in Table 3.

The mean acquisition time for each technique was 1.02 s for ds-DECT, 2.83 s for ss-DECT and 3.14 s for TNC CT, respectively.

DISCUSSION

Although the acquisition time of ss-DECT (volume protocol) was longer than for ds-DECT (spiral protocol), there is no significant difference in GTV-O volume when in motion; actually, GTV-I volume of ds-DECT tends to differ more from the reference, which can be explained by the fact that acquisition of the TNC reference scan was performed on a rather slow 16-slice CT device with inherently longer acquisition time for the 140 mm volume. The whole

Figure 3. Coronal plane of a single scan of VNC and TNC images of LTMs in motion. The contoured lines of the outer GTV, ITV-O, inner GTV-I and ITV-I are shown (window level -500 HU; window width 500 HU). Top images show LTM-1 and bottom LTM-2. From left to right: TNC radiotherapy CT, TNC radiotherapy CT ITV,VNC dual-source DECT,VNC single-source sequential DECT. DECT, dual-energy CT; GTV, gross tumour volume; HU, Hounsfield unit; ITV, internal target volume; LTM, lung tumour model; TNC, true non-contrast; VNC, virtual non-contrast.

Table 2. Calculated differences of GTV-I, ITV-I and CT numbers between VNC and TNC images in motion or rest of LTMs

Model	Motion	ds-DECT	ss-DECT	TNC CT (ITV-I)
LTM ₁₊₂ ($\Delta\text{Mean} \pm \text{SD}$) HU	no	-14.2 ± 33.3	18.4 ± 26.3	-
	yes	25.5 ± 58.5	104.4 ± 71.2	-
LTM ₁₊₂ ($\Delta\text{Vol} \pm \text{SD}$) %	no	6.1 ± 8.0	-8.3 ± 4.5	-
	yes	-8.4 ± 10.6	6.6 ± 0.6	36.9 ± 1.0

GTV, gross tumour volume; HU, Hounsfield unit; LTM, lung tumour model; SD, standard deviation; TNC, true non-contrast; VNC, virtual-non-contrast; ds-DECT, dual source dual-energy CT; ss-DECT, single source dual-energy CT.

phantom could be scanned in one rotation with ss-DECT due to the wide-area detector of 160mm, but the high and low kV scan had to be acquired in a consecutive fashion resulting in relevant temporal inaccuracy. Larger scanning lengths than 140mm are generally needed in a real-life clinical scenario, *e. g.* for imaging of the whole lung, which may lead to even more motion artefacts and larger deviations of GTV. Hence, dual-energy with sequential scanning is considered to be prone to motion artefacts due to the temporal shift of the scans, whereas the dual-source CT simultaneously acquired dual-energy, resulting in a shorter scanning time.

The sinusoidal waveform as a breathing pattern we used in this study mimics the ideal clinical situation. Hence, four motion patterns have to be considered – LTM motion in the same direction of the CT table, where LTM and table speed are summed up; LTM motion in the counter direction of the table motion, where the speeds are subtracted; and the two turning points the maxima of the sinusoidal curve when the LTM does not move. The turning points represent deep inspiration and expiration. When the LTM and table speed are summed up, this can result in blurring or

missing reconstruction details for the LTM and therefore and in an extended GTV. Whereas the counter directions might even lead to a reduction of the volume, because of a scanning overlap of the LTM. A good way to handle irregular waveforms to mimic real patient breathing is the use of a 4DCT in radiotherapy.²¹ We did not have the option to acquire a 4D TNC CT, which is a weakness of our study, but represented a realistic clinical situation. A disadvantage of creating an ITV from image fusion of multiple CT scans in free-breathing, like we did in our study, is the incorrect representation of the CT number within the volume. GTV-O and GTV-I volumes were merged only representing the size of all GTVs. Time-resolved 4D DECT is currently not available with any commercially available DECT approach. Especially for ss-DECT, the sequential scans might be in different breathing phases, which could lead to exaggerated reconstruction artefacts.

As GTV-I volumes were small, slight variations in volume size lead to large relative deviations between VNC and TNC images, which occurred due to contouring uncertainties and image reconstruction of 3.0mm slices. Nevertheless, GTV-I mean volumes in

Figure 4. Axial plane of a single scan of VNC and TNC images of LTM in motion. The outer GTV-O and GTV-I are shown (window level 40 HU; window width 400 HU). Top images show LTM-1 and bottom LTM-2. Left: TNC radiotherapy CT, middle: VNC dual-source DECT images, right: VNC single-source sequential DECT images DECT, dual-energy CT; GTV, gross tumour volume; HU, Hounsfield unit; ITV, internal target volume; LTM, lung tumour model; TNC, true non-contrast; VNC, virtual non-contrast.

Table 3. Volume and CT number measurements of the GTV-I and ITV-I in VNC, ss-DECT and TNC CT images as reference LTM contained iodine or water and were in motion or rest

Scanner	LTM model	iodine (5 mg ml ⁻¹)	Motion	GTV-I Vol. (ccm ±SD)	GTV-I (Mean ± SD) HU
ss-DECT	LTM-1	Yes	No	8.2	20.8 ± 23.1
			Yes	7.1 ± 0.9	61.9 ± 60.3
	LTM-2	Yes	No	4.4	15.9 ± 29.5
			Yes	4.1 ± 0.0	62.3 ± 54.4
	LTM ₁₊₂	Yes	No	-	18.4 ± 26.3
			Yes	-	62.1 ± 57.6
ds-DECT	LTM-1	Yes	No	8.2	-12.4 ± 34.8
			Yes	6.9 ± 1.1	-7.7 ± 42.7
	LTM-2	Yes	No	3.4	-16.0 ± 31.9
			Yes	3.1 ± 0.3	-26.6 ± 35.7
	LTM ₁₊₂	Yes	No	-	-14.2 ± 33.3
			Yes	-	-17.1 ± 40.7
TNC CT	LTM-1	No	No	7.9	3.0 ± 26.0
			Yes	6.7 ± 2.8	-22.0 ± 40.4
		Yes	No	7.8	122.8 ± 38.7
	LTM-1 ITV-I	No	Yes	15.8	-
	LTM-2	No	No	3.9	-13.0 ± 33.4
			Yes	3.8 ± 1.5	-57.5 ± 41.6
		Yes	No	4.2	87.2 ± 62.1
	LTM-2 ITV-I	No	Yes	9.1	-
	LTM ₁₊₂	No	No	-	-5.0 ± 29.7
			Yes	-	-30.4 ± 40.0

GTV, gross tumour volume; HU, Hounsfield unit; LTM, lung tumour model; SD, standard deviation; TNC, true non-contrast; VNC, virtual-non-contrast; ds-DECT, dual source dual-energy CT; ss-DECT, single source dual-energy CT. LTM contained iodine or water and were in motion or rest.

motion were smaller than in rest for all scanners (Table 3), which is related to blurring artefacts caused by motion.²¹ ITV volumes were the largest, indicating a margin concept for DECT and TNC CT GTVsin treatment planning is needed.²⁸ CT numbers for ss-DECT VNC images were far above TNC values (HU_{LTM1+2} = 62.1±57.6 HU), also seen visually in Figure 4. An explanation could be that the temporal and for this reason, locally displacement of both energy scans leads to an insufficient material decomposition of iodine and water. Anyhow, volume measurements of GTV-I in motion deviated in ss-DECT and ds-DECT in the order of GTV-I in rest, though only GTV-I CT numbers from ds-DECT were comparable to TNC. Material decomposition in ds-DECT is, in this case, superior to ss-DECT, because of simultaneous acquisition of both energies.

The different shapes of LTM-1 and LTM-2 seem not to influence the mean CT number of the contrast-enhanced GTV-I in VNC images when measured as a volume. Measurements of CT number in VNC images of PMMA and the lung insert showed that there is a significant difference between both DECT techniques, which is

in correlation with other studies revealing variations among dual-energy systems.^{6,8,29}

GTV-I and GTV-O volume measurements relayed on a small number of scans ($n = 4$ to 6) for both DECT techniques. If the available number of scans had been higher than in this evaluation, the deviations between the DECT techniques and the TNC CT would probably have been more robust. Still, the question remains open if, e. g. 120 keV monoenergetic DECT images are suitable for contouring and vice versa VNC images for dose calculations for these LTMs. This situation has to be investigated in further studies.

The calculation and comparison of the contrast to noise ratio was not part of this study. For this purpose, equal CTDI_{vol} values for each scanner had to be chosen. The influences of different CTDI_{vol} are for the measurement of CT number and GTV volume in this case negligible.³⁰ For the further use of VNC DECT images in RTP, a calibration of the CT number to electron density is necessary. Commonly, the conversion relationship can be obtained from electron density phantoms.³¹ Other methods specifically using VNC

image are the single linear relationship conversion method^{32,33} or a stoichiometric calibration approach.^{34,35}

CONCLUSION

GTV-O and GTV-I volumes of moving and non-moving LTMs contoured in ss-DECT and ds-DECT VNC images are comparable to TNC CT images. Exact GTV definition is a requirement for the further definition of a planning target volume.

Only for ds-DECT VNC imaging, it was obtained that GTV-I CT number measurements for both moving LTMs are comparable to TNC images. For non-moving LTMs, material decomposition algorithms of both DECT techniques were sufficient, subtracting iodine from water comparable to TNC images.

In the future, detailed radiation treatment planning within VNC images of tumours in motion and dose evaluation is needed to see the potential clinical use of DECT.

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