Quantitative dual-energy computed tomography imaging: Evaluation of system performance regarding iodine quantification accuracy

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Aims and objectives

Computed tomography imaging is based on revealing contrast differences between materials of different composition. These contrast differences are caused by the individual physical density and absorption behavior of each specific material when it is irradiated by X-ray photons in the energy range of ~30 keV to ~140 keV. Dual-energy computed tomography (DECT) allows for the differentiation of materials based on their spectral behavior. A considerable difference in their atomic number (number of protons of the element, Z) is desirable for visual and/or quantitative identification and differentiation of different materials [1]. For iodinated contrast agents (iodine: Z=53) this difference is large in comparison with the natural occurrence of elements in the human body (i.e. hydrogen, oxygen, carbon and nitrogen (all Z<10), and even calcium with Z=20), and differentiation from body tissues is possible on the basis of the materials’ spectral behavior [2].

Attempts to visualize the distribution of iodinated contrast agent in different organs with DECT systems were already made in the 1970s [3, 4, 5]. Nowadays, DECT software packages (e.g. Syngo Via Dual Energy, Siemens Medical Solutions, Forchheim, Germany) allow for material decomposition based on two body material data points (e.g. fat and soft tissue) and the slope of the iodine enhancement vector. On the basis of this material decomposition, DECT allows for the calculation of quantitative iodine maps. These are a surrogate of tissue perfusion, i.e. the dynamic process of blood flow over time, and might thus substitute conventional perfusion imaging in the future.

For the quantitative assessment e.g. of lung perfusion, reliable visualization of contrast agent in the pulmonary capillary bed or the blood volume is crucial, as is the quantification of its concentration. Several studies have been conducted in order to measure lung perfusion by determining the iodine contrast agent content of the lungs [1, 6, 7, 8, 9, 10, 11]. As lung perfusion imaging can indicate pulmonary embolism among other lung diseases, DECT imaging might have potential for improved diagnosis [12]. Future studies will have to investigate the value of DECT perfusion in the assessment of lung diseases such as emphysema, cystic fibrosis, or interstitial lung disease.

The method of DECT perfusion imaging yielding quantitative iodine concentration maps relies on an exact and reproducible determination of CT numbers for a specific amount of iodinated contrast agent. Accuracy and stability of iodine concentration measurements should increase with a DECT system’s capability for material differentiation. The latter can be improved by enhancing the differences in spectral absorption behavior, e.g. by increasing the spectral separation between the low (80 kV_p or 100 kV_p) and high-energy (140 kV_p) X-ray tube spectra employed for DECT imaging. Dual-source DECT provides the possibility to operate two X-ray sources at different voltages and record the photons transmitted through the body under examination with two corresponding detectors [13,
Such systems offer the possibility for mechanical filtration of the 140 kV$_p$ spectrum by a tin filter, increasing the spectral separation between the low and high-energy X-ray tube spectra.

Since an exact and reproducible determination of CT numbers for a specific amount of iodinated contrast agent is an imperative for quantitative DECT imaging especially in view of DECT perfusion, the aim of this study is to objectively determine measurement variability of CT numbers of iodinated contrast agent solutions of different concentrations in dependence of the position within the acquisition field-of-view (FOV), the object attenuation, as well as the acquisition and reconstruction settings used for dual-source DECT imaging.
Methods and materials

Using a dual-source DECT system (Somatom Definition Flash, Siemens Medical Solutions, Forchheim, Germany, see Fig. 1 on page 6) CT acquisitions of 70 different well-defined iodine concentrations ranging from 0.0 - 15.0 mg/ml have been performed in order to quantitatively assess the scanner’s CT number linearity, stability, and uniformity 'free-in-air'. To this end, iodine-saline solutions were pipetted in polystyrene tubes each having a length of 10.0 cm and a diameter of 1.4 cm. For CT acquisitions, the tubes were positioned in the scanner’s isocenter (center of the scan field-of-view (s-FOV)), and their central axis was aligned with the scanners longitudinal axis (z-axis, Fig. 2 on page 6a).

In order to also evaluate the dependence of measured CT numbers on subject absorption thickness and measurement position within the acquisition FOV (s-FOV), a second experimental setup employing a cylindrical acrylic phantom with a radius of 16.0 cm, featuring 8 bore holes of 1.4 cm diameter and fitting the polystyrene tubes of 10.0 cm length has been used. The phantom's bores are located at increasing distance from the phantom center (No. 0), the center of each bore being incremented by 2.0 cm and rotated counterclockwise by 45° with regard to its predecessor (Fig. 2 on page 6b).

One single-energy (SE) and three dual-energy (DE) protocols with different tube voltage combinations with and without tin filtration (Sn) were applied for both experimental setups (SE: 120 kVp; DE: 80/140kVp, 80/Sn140kVp, 100/Sn140kVp). The detailed acquisition parameters are listed in Table 1 on page 7. For the SE datasets and both low and high tube voltage datasets originating from the DE acquisitions two reconstruction kernels were used for image reconstruction: body soft-tissue (B30f) and body sharp (B70f). For DE blended images linearly calculated from both low- and high tube voltage datasets with a weighting factor of 0.5, a medium soft dual-energy kernel (D30f, dual-energy equivalent of the soft-tissue body kernel B30f) was applied. For the 'free-in-air' measurement a reconstruction FOV (r-FOV) of 5 x 5 cm² was chosen (Fig. 3 on page 8a). For the phantom measurement two different r-FOVs was selected in order to also allow for the assessment of a possible CT number dependence on r-FOV size: 5 x 5 cm² (Fig. 3c) and 34 x 34 cm² (Fig. 3 on page 8b). Table 2 on page 9 shows the reconstruction parameters used for both experimental setups in detail.

CT numbers in Hounsfield units [HU] were measured for all image data gained using both experimental setups with software developed in house (Fig. 4 on page 9a). It is based on "ROOT - An Object Oriented Data Analysis Framework" [15], and allows for automated region-of-interest (ROI) placement, propagation and evaluation in all image slices of a CT dataset. ROIs were manually placed at the center of the tubes imaged...
in the first and last slices of each image stack, and ROI positions were automatically interpolated for the 99 slices in between. In this manner, standardized circular ROIs with a radius of 4.5 mm were automatically evaluated for all 101 slices of each reconstructed image dataset. The amount of pixels covered by the ROI depended on the current r-FOV. The large amount of pixels inside the ROIs (app. 6700 pixels for the smaller r-FOV, Fig. 3 on page 8a and Fig. 3 on page 8c, and app. 150 pixels for the larger r-FOV, Fig. 3 on page 8b) results in a high statistic reliability and stability.

The mean and standard deviation (corresponding to image noise or measurement uncertainty, respectively) of all ROI values are the basis for the subsequent analyses and diagrams. All regressions to the measured data are done with a linear model and a chi square function.

For the phantom measurement commercially available software (LungPBV, SyngoVia, Siemens Medical Solutions, Forchheim, Germany) was used to calculate and measure the iodine concentration of the iodine-saline solutions (Fig. 4 on page 9b). ROIs were evaluated on five different images per measurement position within the phantom (Fig. 2 on page 6b), and calculated average iodine concentration was compared to the known nominal concentration in dependence on measurement position with regard to its distance from the phantom’s center, i.e. the scanner system’s isocenter.
**Fig. 1:** Dual-source, dual-energy CT system (DECT; Somatom Definition Flash, Siemens Medical Solutions, Forchheim, Germany) evaluated in this study.

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Fig. 2: a) Experimental setup of the free-in-air measurements. A polystyrene tube filled with a well-defined iodine concentration is located at the scanner’s isocenter (center of the scan field-of-view (s-FOV)), aligned with its longitudinal axis (z-axis of the scanner). The polystyrene tube has a diameter of 1.4 cm, a length of 10.0 cm, and a total capacity of 13.0 ml.

b) Image of the cylindrical acrylic phantom aligned within the scan field-of-view (s-FOV) for the phantom measurements. The phantom has an overall radius of R = 16.0 cm, featuring 8 bore holes of 1.4 cm diameter fitting tubes lengths of 10.0 cm. The bores are located at increasing distance from the phantom center (No. 0), the center of each bore being shifted by 2.0 cm and rotated counterclockwise by 45° with regard to its predecessor.

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Table 1: Summary of the acquisition protocol settings used for the measurements free-in-air as well as in the phantom. For DECT acquisitions the higher-voltage tube was set to a constant tube current-time product of 50 mAs for the ‘free-in-air’ measurements, and to 150 mAs for the phantom measurements. The tube current-time product of the lower-voltage tube was automatically set to a corresponding value as defined by the manufacturer.

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<table>
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<tr>
<th>Measurement</th>
<th>Tube Voltage [kV$_p$] (Tube)</th>
<th>Eff. Tube Current-Time Product [mAs$_{eff}$/Tube]</th>
<th>Primary Collimation</th>
<th>Pitch</th>
<th>Gantry Rotation Time [s]</th>
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<tr>
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<tr>
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Fig. 3: Examples of linearly-blended (M0.5) axial DECT images acquired at tube voltage settings of 80/Sn140 kV$_p$ (tin-filtered) for an iodine concentration of 10 mg/ml reconstructed using a medium soft dual-energy kernel (D30f, dual-energy equivalent of the soft-tissue body kernel B30f). For each DECT acquisition a total of 101 axial image slices were evaluated.
a) Free-in-air measurement reconstructed with a reconstruction-FOV (r-FOV) of 5 x 5 cm$^2$. The overlain green circle represents a region-of-interest (ROI) with a radius of 4.5 mm covering over 6700 evaluable pixels.

b) Phantom measurement reconstructed with a r-FOV of 34 x 34 cm$^2$. The overlain green circles illustrate the positions of the 8 regions-of-interest (ROIs) used for analysis, each having a radius of 4.5 mm including more than 150 pixels, respectively.

c) Phantom measurement reconstructed using a r-FOV of 5 x 5 cm$^2$. The overlain green circle indicates the size and position of the analyzed region-of-interest (ROI) for bore 0 located at the CT scanner's isocenter. The analyzed ROI has a radius of 4.5 mm covering more than 6700 pixels.

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<table>
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<th>Experimental Setup</th>
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<th>Kernel</th>
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<th>Slice Thickness [mm]</th>
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<td>100/Sn140 (A/B tin-filtered)</td>
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**Table 2**: Image reconstruction parameters used. All 'single-energy' (SE) images were reconstructed with both soft-tissue (B30f) and sharp (B70f) body kernels. For the DECT acquisitions, linearly-blended (M0.5) dual-energy (DE) images were reconstructed using the dual-energy equivalent of B30f (D30f). For the phantom measurement datasets were reconstructed with two different r-FOVs.

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Fig. 4: Screenshots of the software used for image evaluation and quantitative image data analysis.

a) For every reconstructed image data set, CT numbers in Hounsfield units ([HU]) were measured on the basis of all slices in an automated fashion using custom software developed in-house.

b) Iodine concentration was measured using commercially available software (LungPBV, SyngoVia, Siemens Medical Solutions, Forchheim, Germany)

References:

a) Diagnostic and Interventional Radiology, University Hospital Heidelberg - Heidelberg/DE

b) LungPBV, SyngoVia, Siemens Medical Solutions - Forchheim/DE

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Results

The results of the CT number measurements for the 70 different iodine concentrations ‘free-in-air’ are shown in Fig. 5 on page 13. Up to iodine concentrations of 10.0 mg/ml, CT numbers increase linearly with increasing iodine concentration independent of tube voltage or reconstruction kernel. The CT numbers show a strong dependence on tube voltage, e.g. dropping to one third of their value at 80 kV compared to 140 kV (see Fig. 5 on page 13a and Fig. 5 on page 13b). The uncertainty of the nominal iodine concentration resulting from the process of pipetting the iodine-saline solutions was estimated to amount to 2.5 % of the desired nominal iodine concentration for concentrations below 2.0 mg/ml, and to 1.0 % for concentrations above 2.0 mg/ml.

Fig. 5 on page 13c shows the CT numbers for DE blended images for the three different DE acquisitions in comparison with the SE 120 kVp. The linearity of the CT numbers persists for SE images as well as for DE blended images up to iodine concentrations of 10.0 mg/ml. While sharing the same origin, CT numbers of linearly-blended (M0.5) DECT image data strongly differ for different DECT tube voltage settings and filtration. For DECT acquisitions using the tube voltage combination of 80/140 kVp without tin filtration, CT numbers of linearly-blended (M0.5) image data best match those of 'real' SE at 120 kVp.

The linearity of the CT numbers is neither influenced by subject absorption thickness nor measurement position within the s-FOV, which is verified by the phantom measurement. However, additional absorption leads to a decrease in CT numbers of up to 20 % for 80 kVp and <10 % for Sn140 kVp (Fig. 6 on page 13). The relative difference decreases with the tube voltage.

The size of the r-FOV does not influence the CT numbers of the phantom measurement (Fig. 7 on page 14). CT numbers of both sizes of the r-FOV are comparable within measurement accuracy for low iodine concentration and low tube voltage (Fig. 7 on page 14a) as well as for high iodine concentrations and high tube voltage (Fig. 7 on page 14b).

A linear regression of measured CT numbers by the distance from the isocenter (Fig. 8 on page 15) yields a flat slope for all iodine concentrations. The slopes of each linear regression can be found in Table 3 on page 16. For most combinations of iodine concentration, acquisition and reconstruction settings tabulated slopes are compatible with 0 within measurement accuracy, indicating independence of CT numbers from measurement position within the s-FOV. Only for 80 kVp and/or iodine concentrations...
larger than 5.0 mg/ml CT numbers decrease in isocenter vicinity, and the slope of the linear regression is notably higher than 0 (cf. red highlighting in Table 3 on page 16).

The absolute iodine concentration is distinctly overestimated for the 80/140 kVp DECT acquisition mode without tin filtration independent of the iodine concentration. Additionally, the overestimation increases with increasing measurement distance from the isocenter (Fig. 9 on page 16a). The ratio between measured and nominal iodine concentration is close to 1 for the DECT acquisition modes with tin filtration for iodine concentrations above 1.0 mg/ml and independent of the distance from the isocenter (Fig. 9 on page 16b and Fig. 9 on page 16c). However, for reliable quantification accuracy with a relative measurement error below 20 % the iodine concentration should be higher than 5.0 mg/ml.
Fig. 5: CT numbers in dependence of iodine concentration measured ‘free-in-air’ for three different reconstruction kernels: a) body soft-tissue (B30f), b) body sharp (B70f), and c) dual-energy equivalent of B30f (D30f). Linear regression over all concentrations measured at each tube voltage setting illustrates linear dependence independent of tube voltage. CT numbers show a strong dependence on tube voltage, e.g. dropping to one third of their value at 80 kVp for Sn140 kVp with tin filtration, and a slighter dependence on reconstruction kernel. While sharing the same origin, CT numbers of linearly-blended (M0.5) DECT image data strongly differ for different DECT tube voltage settings and filtration. For DECT acquisitions using the tube voltage combination of 80/140 kVp without tin filtration, CT numbers of linearly-blended (M0.5) image data best match those of 'real" SE at 120 kVp.
Fig. 6: CT numbers measured 'free-in-air' and in the phantom for increasing iodine concentration. Due to the increased overall absorption introduced by the phantom causing X-ray beam hardening the CT numbers drop considerably in comparison to acquisitions performed 'free-in-air'. This does not affect CT number linearity, and can be observed independent of tube voltage.

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Fig. 7: CT numbers measured at increasing distance from the phantom center applying two reconstruction field-of-views (r-FOV) of different size (34 × 34 cm² or 5 × 5 cm²):

a) Measurement for an iodine concentration of 0.1 mg/ml and 140 kVₚ tube voltage.
b) Measurement for an iodine concentration of 15.0 mg/ml and 140 kVₚ tube voltage.

Independent on iodine concentration and tube voltage, r-FOV size does not have an influence on measured CT numbers.

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Fig. 8: CT numbers measured at increasing isocenter distance for tube voltages of a) 80 kVₚ and b) Sn140 kVₚ (tin-filtered) for different iodine concentrations. Ideally, for any chosen iodine concentration CT numbers should be constant independent of isocenter distance. However, at 80 kVₚ beam-hardening lowers CT numbers in isocenter vicinity, whereas otherwise CT-number dependence on iodine concentration and measurement location within the s-FOV is only very slight. Note the different y-axis scaling in a) and b). A selection of corresponding slope values are listed in Tab. 3.
Table 3: Slopes determined by linear regression over the CT numbers measured at increasing distance from the isocenter in the phantom (8 measurement positions) for selected combinations of iodine concentration and tube voltage (cf. measurement data plotted in Fig. 8). For most combinations of iodine concentration, acquisition and reconstruction settings tabulated slopes are compatible with 0 within measurement uncertainty, indicating independence of CT numbers from measurement position within the scan field-of-view (s-FOV). Only at low tube voltage (80 kV$_p$) and/or for high iodine concentrations CT numbers are affected. In these cases, beam-hardening lowers the CT numbers in isocenter vicinity (marked in red).

**Fig. 9:** Ratio of measured to nominal iodine concentration determined for increasing distance from the isocenter for three different linearly-blended dual-energy image datasets: a) 80/140 kV$_p$, b) 80/Sn140 kV$_p$ (tin-filtered), and c) 100/Sn140 kV$_p$ (tin-filtered). Ideally, this ratio should be equal to one independent on measurement position (isocenter distance) and DECT acquisition mode (tube voltage/filtration). However, on average nominal iodine concentration is overestimated independent on DECT acquisition mode.
Quantification accuracy is best for tin-filtered DECT acquisitions with relative errors below 20% (>1.0 mg/ml), and accuracy increases with increasing iodine concentration.

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Conclusion

The goal of this study was the objective assessment of quantitative iodine concentration measurement accuracy and reliability achievable with DECT. To this end, CT number measurements over a range of 0.0 - 15.0 mg/ml of iodine concentration have been quantitatively assessed for different combinations of acquisition and reconstruction settings in dependence of the position within the acquisition field-of-view (FOV) and of object attenuation using a state-of-the-art dual-source DECT system.

The 'free-in-air' measurements show distinct linearity, stability, and uniformity of quantitative CT number measurements for both SE and DECT. The strong dependence on the tube voltage is associated with the probability of a photon being absorbed by material. The lower the energy of the X-ray photons is, the higher their absorption probability. For low tube voltages a higher amount of low-energetic photons are present in the spectrum. The CT number mirrors the attenuation of the photons traversing through the gantry of the CT. A higher CT number is associated with a higher attenuation at this location.

For iodine concentrations higher than 10.0 mg/ml a systematic underestimation of the CT numbers leads to notable deviations from the regression line. This effect decreases with increasing tube voltage: With Sn140 kV_p measured data above 10.0 mg/ml agrees well with the linear regression estimation.

As shown in Fig. 5c, the CT numbers obtained from three different DE blended image datasets have the same intercept, whereas the intercept of SE 120 kV_p data is notably different. This should be due to a different calibration of reconstruction kernels. Although the D30f kernel technically is the dual-energy equivalent of the B30f kernel, two different calibration schemes seem to cause this disparity. The slopes of the linear regressions of SE 120 kV_p and DE 80/Sn140 kV_p are compatible, such that the CT numbers of SE 120 kV_p data and DE 80/140 kV_p data only differ slightly, cf. Fig. 5 on page 20c.

The phantom measurement illustrates the effect of the presence of further absorption material and different measurement positions within the s-FOV. The additional absorption does not affect the linearity of the CT numbers but their absolute values. Low-energetic photons have a higher probability of being stopped by the phantom material and hence not reaching the detector of the CT scanner. Effectively, the photon spectrum becomes 'harder' and CT numbers are lower compared to the 'free-in-air' measurements (beam-hardening effect [16]).
effect is stronger for low tube voltages because of their relatively larger amount of low-energetic photons within the X-ray spectrum.

Different sizes of the r-FOV affect the amount of pixels inside the evaluated ROIs. The fact that the uncertainties of the CT numbers in Fig. 7 on page 20a and Fig. 7 on page 20b are of the same magnitude indicates a statistically stable evaluation method. The total of 150,000 evaluated pixels from measurements in the large r-FOV already cover all statistical outliers.

As expected for a well-calibrated modern CT scanner, the CT number distribution over the distance from the isocenter is flat (Table 3 on page 21 and Fig. 8 on page 21). Over a range of 32 cm in diameter the CT numbers determined for the iodine-saline solutions are reliable for all tube voltages above 100 kV_p. For 80 kV_p and/or for high iodine concentrations the beam-hardening effect lowers the CT numbers in the isocenter vicinity and leads to a notable slope of the linear regression (cf. red highlighting in Table 3 on page 21). For higher iodine concentrations the additional amount of dense material affects the photon absorption and hardens the photon spectrum. The resulting CT numbers decrease, and the material seems to be less dense than expected.

The quantification of iodine concentrations with a commercially available software tool (LungPBV, SyngoVia, Siemens Medical Solutions, Forchheim, Germany) is reliable for iodine concentrations above 1.0 mg/ml and tin-filtered DE acquisitions. The relative uncertainties in order of 20 % of the measured data result from the small measurement statistics due to limiting the evaluation to only five ROIs.

In summary, this study shows that CT numbers quantitatively measured using dual-source DECT neither depend on s-FOV position nor on r-FOV size. Despite their almost perfect linear dependence on iodine concentration, their absolute values nonetheless strongly vary with acquisition (e.g. tube voltage and total subject absorption) and reconstruction (kernel) parameters. For fixed acquisition and reconstruction parameters, however, quantitative CT numbers as well iodine concentrations can be reliably determined within the subject under examination, thus allowing stable and reproducible calculation of quantitative DECT iodine maps. This result is essential for all quantitative DECT procedures, especially those focusing on quantitative iodine imaging, e.g. lung perfusion measurements.
Fig. 5: CT numbers in dependence of iodine concentration measured ‘free-in-air’ for three different reconstruction kernels: a) body soft-tissue (B30f), b) body sharp (B70f), and c) dual-energy equivalent of B30f (D30f). Linear regression over all concentrations measured at each tube voltage setting illustrates linear dependence independent of tube voltage. CT numbers show a strong dependence on tube voltage, e.g. dropping to one third of their value at 80 kVp for Sn140 kVp with tin filtration, and a slighter dependence on reconstruction kernel. While sharing the same origin, CT numbers of linearly-blended (M0.5) DECT image data strongly differ for different DECT tube voltage settings and filtration. For DECT acquisitions using the tube voltage combination of 80/140 kVp without tin filtration, CT numbers of linearly-blended (M0.5) image data best match those of ‘real” SE at 120 kVp.

Fig. 7: CT numbers measured at increasing distance from the phantom center applying two reconstruction field-of-views (r-FOV) of different size (34 × 34 cm² or 5 × 5 cm²): a) Measurement for an iodine concentration of 0.1 mg/ml and 140 kVp tube voltage. b) Measurement for an iodine concentration of 15.0 mg/ml and 140 kVp tube voltage.
Independent on iodine concentration and tube voltage, r-FOV size does not have an influence on measured CT numbers.

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<table>
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<tr>
<th>Tube Voltage [kV&lt;sub&gt;p&lt;/sub&gt;]</th>
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<td>80</td>
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<tr>
<td>Sn140 (tin-filtered)</td>
<td>0.75 ± 0.43</td>
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Table 3: Slopes determined by linear regression over the CT numbers measured at increasing distance from the isocenter in the phantom (8 measurement positions) for selected combinations of iodine concentration and tube voltage (cf. measurement data plotted in Fig. 8). For most combinations of iodine concentration, acquisition and reconstruction settings tabulated slopes are compatible with 0 within measurement uncertainty, indicating independence of CT numbers from measurement position within the scan field-of-view (s-FOV). Only at low tube voltage (80 kV<sub>p</sub>) and/or for high iodine concentrations CT numbers are affected. In these cases, beam-hardening lowers the CT numbers in isocenter vicinity (marked in red).

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Fig. 8: CT numbers measured at increasing isocenter distance for tube voltages of a) 80 kV<sub>p</sub> and b) Sn140 kV<sub>p</sub> (tin-filtered) for different iodine concentrations. Ideally, for any
chosen iodine concentration CT numbers should be constant independent of isocenter distance. However, at 80 kV\textsubscript{p} beam-hardening lowers CT numbers in isocenter vicinity, whereas otherwise CT-number dependence on iodine concentration and measurement location within the s-FOV is only very slight. Note the different y-axis scaling in a) and b). A selection of corresponding slope values are listed in Tab. 3.

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