Agatston Score

calcium quantification

with arbitrary tube voltage

White paper

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Introduction

Quantification of coronary artery calcium (CAC) is an established method of stratifying risk in coronary artery disease.[3, 6] The standard quantification method, known as the Agatston Score, was developed by Arthur Agatston, Warren Janowitz, and colleagues.[1] Initially, measurements for Agatston scoring were obtained using electron-beam computed tomography (EBCT) at 130 kV. Despite the various drawbacks described in the following, the large body of available clinical data across age, gender, and race[4], and extensive clinical risk stratification studies have helped establish the Agatston Score as the primary quantification tool in clinical practice.[2, 6]

When adapting the calcium score (CaSc) acquisition protocol by changing the initial kV settings, it is essential to preserve an equivalent high level of CAC detectability, and allow comparability of the resulting Agatston Score with the original results acquired at 120 kV and 130 kV respectively. The reason for two reference voltages is mainly historical in nature, as the initial EBCT study used only 130 kV, whereas for most modern CT systems only 120 kV is available.[1, 5] This paper describes an Agatston-equivalent calcium scoring method using a dedicated reconstruction kernel (Sa36f) that allows use of all tube voltage levels offered by a given scanner model. Measurements are performed on both an anthropomorphic thorax phantom and two explanted hearts from human specimens. Furthermore, a calcium mass score conversion factor is derived that is also independent of tube voltage.

Background: Accuracy of Agatston Score

The clinical value of the Agatston Score has been demonstrated by extensive patient data initially acquired using EBCT at 130 kV. With the introduction of multidetector computed tomography (MDCT) this database was extended to include CT examinations at 120 kV. Efforts were also made to develop a consensus standard for quantification of CAC.[5] Recent studies, however, have highlighted the drawbacks of this approach. Willemink et al. investigated the inter-vendor variability of Agatston Scores obtained using state-of-the-art CT systems from the four major vendors.[8]
The resulting measurements delivered substantially different Agatston Scores among the four vendors. This variance could potentially influence the assessment of cardiovascular risk, and consequently treatment decisions.

Furthermore, the influence of chest size on Agatston Score measurements performed using fixed 120 kV acquisition protocols was evaluated in a multi-vendor phantom study.[7] An extension ring was used here to simulate differences in patient size. Results showed a systematic underestimation of Agatston Scores among vendors. This issue may be relevant to both larger patients and women with higher levels of thoracic fat and breast tissue.

Due to the quantitative nature of such risk stratification, accurate calibration is highly recommended. An established procedure for calculation of coronary calcium mass scores has been in place for several years.[5] The standardized procedure described here can easily be applied to any new scanner system or combination of tube voltage and tube filter to derive accurate conversion factors for calcium mass score calculation. Agatston scoring remains the standard method for coronary calcium quantification.

Effect on HU stability – region of interest (ROI) phantom measurements

Tube voltage is critical in Agatston scoring due to the inherent dependency between materials such as calcium and their Hounsfield units (HUs) as a function of the incident spectrum.[9, 10] In order to minimize the effect of this dependency, a new Sa36f kernel is introduced with sharpness properties equivalent to the Qr36f kernel, the standard CaSc kernel on SOMATOM® Force. A voltage-dependent lookup table based on raw data is used for image reconstruction of noncontrast CT acquisitions, producing images with Hounsfield unit (HU) values equivalent to 120 kV for bone and calcium (ART120). This enables Agatston scoring without changing the original Agatston weighting threshold, regardless of the original tube voltage chosen for image acquisition.

To illustrate the conformity between the different voltages, HU measurements were performed for the small, medium, and large phantom setup at tube voltages of 70 kV, 80 kV, 90 kV, 100 kV, 110 kV, 120 kV, 130 kV, 140 kV, 150 kV, and Sn100 kV. An anthropomorphic thorax phantom was used, combined with a calcium calibration insert consisting of nine small cylindrical calcifications of varying size and calcium hydroxyapatite (HA) density (Fig. 1). A complete, detailed description of the phantom is provided by McCollough et al.[5] All HU measurements in this section were performed on the 5 mm cylindrical calcification inserts with HA density levels of 200, 400 and 800 mg/cm³ respectively. HUs were measured by setting ROIs (3 mm diameter, blue dot) automatically centered on the respective insert. Measurements were repeated for both the Qr36f and the new Sa36f kernel. In addition, an ROI in the center of the phantom (1 cm diameter, black circle) taken from the central slice was used to measure the plastic base material of the phantom, intended to be equivalent to soft tissue. Figure 1 illustrates the reference phantom with the respective ROIs positioned for both HU measurements and the subsequent Agatston-based CaSc measurements discussed in the following chapter. All phantom images were acquired in sequential cardiac quick scan mode following the default clinical CaSc protocol of SOMATOM Force at maximum tube current so as to minimize statistical uncertainties. The effective mean water-equivalent diameter was 20 cm, 28 cm and 35 cm for the small, medium and large phantom respectively.

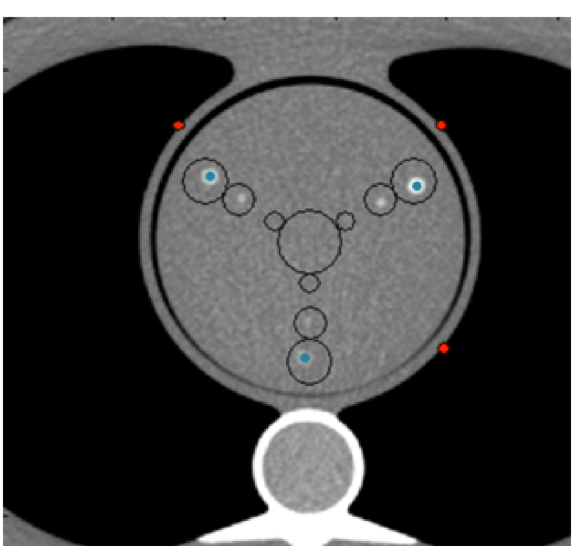
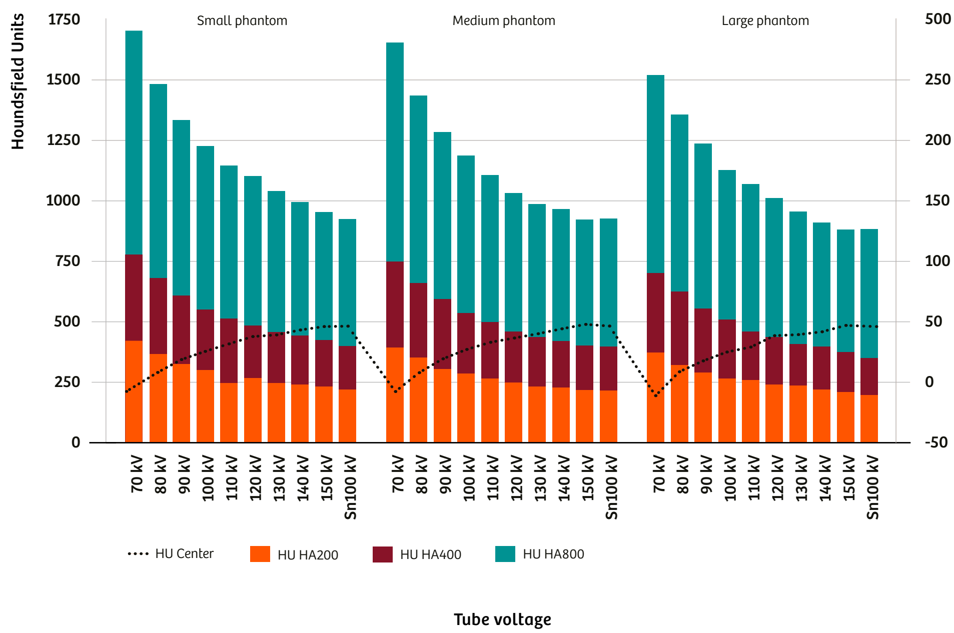


Fig. 1: A photo of the reference calcium scoring phantom used in this study with a schematic overlay showing the ROIs used for HU measurements of the large inserts (blue dots) and Agatston-based calcium scoring (black circles).
The 1-cm diameter ROI (black circle) for soft tissue equivalence measurements can be seen in the center of the phantom.

Figure 2 shows the results of these HU measurements, with the uncorrected Qr36f reconstructions (top) and the corrected Sa36f reconstructions (bottom). In the top graph, the inherent dependency between calcium and its HUs as a function of the incident spectrum is clearly apparent in the increase in calcium HU values for lower tube voltages. Conversely, the Sa36f graph below clearly shows HU stability for all insert densities regardless of the source tube voltage.



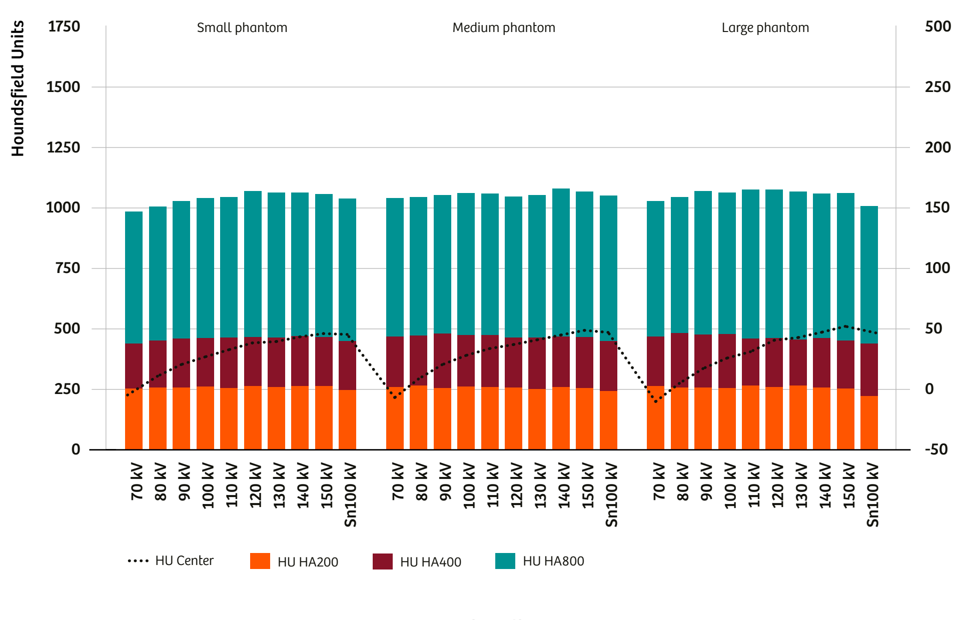


Fig. 2: HU values derived from measurements of the calcium scoring reference phantom using the uncorrected Qr36f reconstructions (top) and corrected Sa36f reconstructions (bottom). The y-axis on the left measures the HU values for the insert with different HA density values as a function of tube voltage for the different phantom sizes. The increase in the calcium HU values for lower tube voltages in the top plot is expected from the material, whereas HU stability can be appreciated in the bottom Sa36f plot. The y-axis on the right measures the HU values for the central base material ROI, shown as a dotted blue line in the plot. A relatively strong "soft tissue" dependency of the phantom's plastic base material is apparent in both plots.

In addition, both figures also show the mean HU value of the central base material ROI (dotted line) with the y-axis scale shown on the right. In both cases the base material displays a relatively strong tube voltage dependency between 70 kV and 150 kV with a delta of up to 50 HU. However, experience of clinical patient scans shows that this drop-off behavior towards lower tube voltages is not realistic for actual human soft tissue. In order to estimate the extent of this effect in cardiac tissue, two hearts explanted from human cadavers and embedded in 27 cm water cylinders were scanned using SOMATOM Force with the CaSc protocol setup described above. Manual ROI measurements were performed in multiple slices in each scan and an average HU value was extracted for each tube voltage and individual heart. Figure 3 shows the results of these measurements for each heart, clearly illustrating very little dependency between the HU value and the different tube voltages.

In light of these results, it can be concluded that a scoring method based on thresholds in HU units such as the Agatston Score should yield similar scoring results for tube voltages between 70 kV and 150 kV if the Sa36f (ART120) reconstruction method described above is applied to the data. Moreover, the intrinsic beam hardening correction properties of this method suggest that greater independence of the Agatston Score from patient diameter can be expected. This is a result of the increased Hounsfield unit stability with respect to the object size. The dependency of the score on diameter is known and reported in the literature for phantom measurements, and confirmed by patient data.[7]

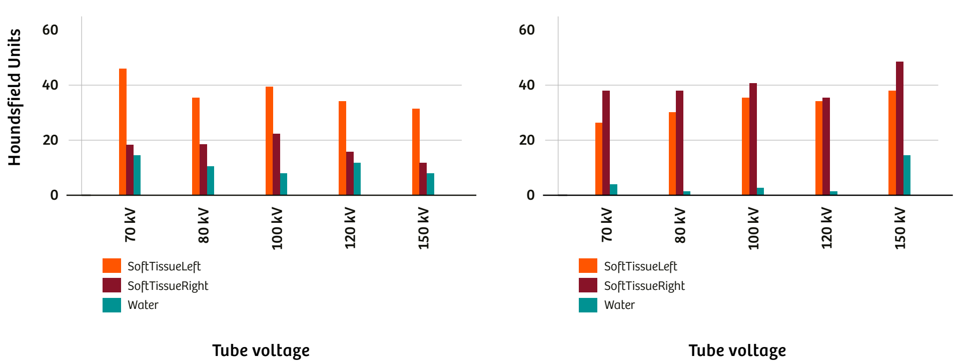


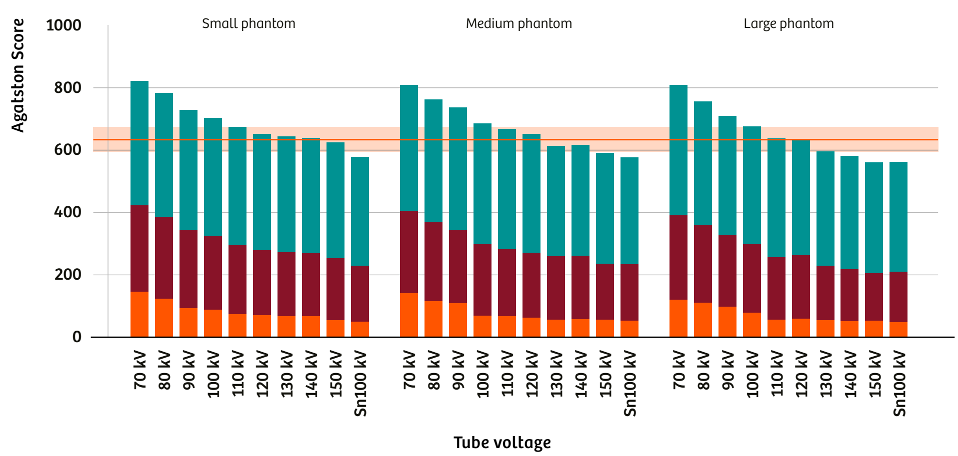
Fig. 3: HU values of the two explanted heart specimens (Heart 1 on the left, Heart 2 on the right). Only a very minor downward slope towards lower tube voltages is visible in Heart 2 and the right ventricle ROI of Heart 1. The left ventricle ROI measurement of Heart 1 exhibits a slight offset including some upslope. This effect is most likely due to the residual iodine contrast medium found in this heart specimen.

Agatston-equivalent calcium scoring using Sa36f reconstruction kernel

Anthropomorphic thorax phantom

The Agatston scoring method is based on a single 130 HU threshold for voxel count inclusion, combined with three further thresholds for lesion weighting.[1] In phantom measurements, it was possible to automatically extract and evaluate the Agatston Scores since the insert location could be predefined by setting ROIs with a radius three times larger than the size of the actual insert (Figure 1, black circles). Images were acquired as described above using the standard default CaSc protocol.

Figure 4 shows the results of the uncorrected Qr36f reconstructions (top) and corrected Sa36f reconstructions (bottom).



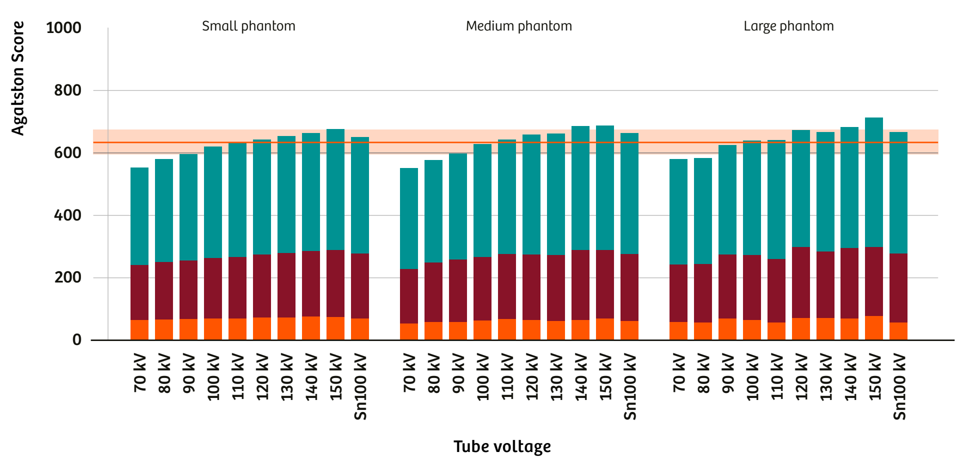
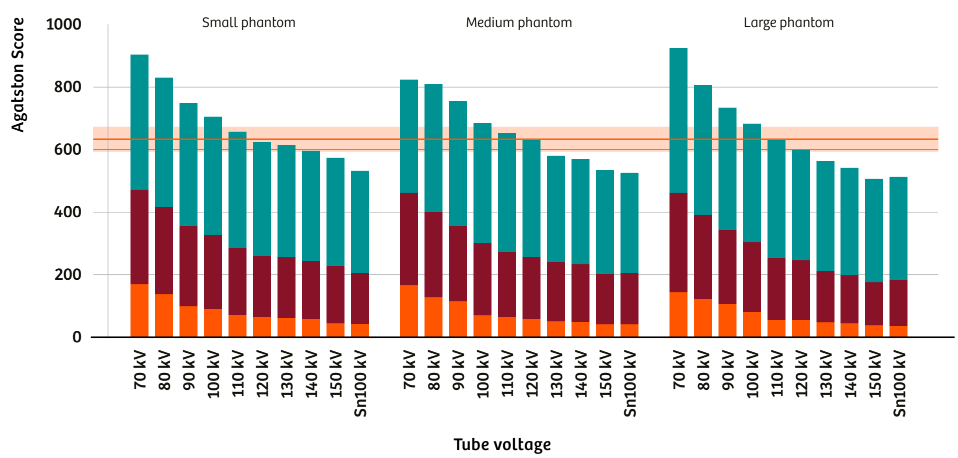


Fig. 4: Agatston Score values derived from measurements of the calcium scoring reference phantom based on the uncorrected Qr36f (top) and corrected Sa36f reconstruction (bottom) with a fixed base material threshold of 130 HU. The systematic slope of the Sa36f score caused by the strong HU dependency of the "soft tissue" base material is clearly visible. The stacked bar plots illustrate the contributions for the 200 mg/cm³ HA, 400 mg/cm³ HA, and 800 mg/cm³ HA density levels respectively (orange, berry, petrol). The red line provides a visual reference (lower: 595, upper: 672, mean: 630) based on inter-scanner variations found by McCollough et al.[5]

Although corrected, the stacked plots of the Sa36f reconstructions (Figure 4, bottom) exhibit a clearly visible systematic slope of the Agatston Score as a function of tube voltage. The primary reason for this effect is the strong spectral dependency of the base material HU values, as previously shown (Figure 2, dotted line). This behavior influences scoring due to the correlation between a fixed 130 HU threshold for pixel counting and the edge spread function of a soft reconstruction kernel. To validate this hypothesis, the scoring procedure was adjusted so that the pixel-counting threshold is expressed as a distance from the measured base material's HU value (T=Δ+HU(base)). A distance of Δ=95 HU was chosen, automatically leading to the established threshold of 130 HU for 120 kV in combination with the measured base material HU value of HU(base)=35 HU, where the variable HU(base) was adjusted for each combination of tube voltage and phantom size.

The result of the adjusted scoring procedure is depicted in Figure 5, for both the Qr36f (top) and Sa36f reconstructions (bottom). After the adjustments, the corrected Sa36f reconstructions show a constant Agatston Score within the previously defined range for the individual tube voltages and phantom sizes. The only upward fluctuation observed relates to the 70 kV measurement in the large phantom. This is most likely due to the increase in noise for this particular setting in combination with the slight noise sensitivity inherent to Agatston scoring.



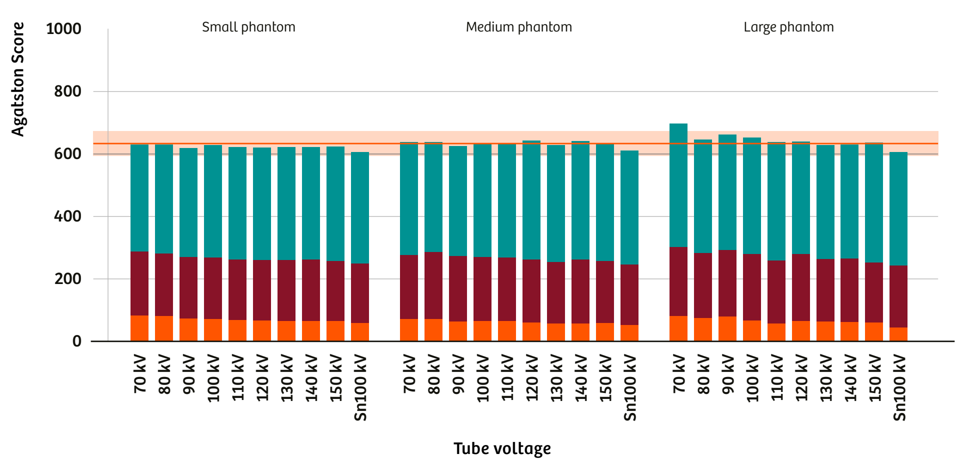


Fig. 5: Agatston Score values derived from measurements of the calcium scoring reference phantom based on the uncorrected Qr36f (top) and corrected Sa36f reconstruction (bottom) with a variable base material threshold of T = HU(base) + 95 HU expressed as a distance from the measured base "soft tissue" material in the phantom. For 120 kV this approach yields the same established 130 HU threshold. The stacked bar plots illustrate the contributions for the 200 mg/cm³ HA, 400 mg/cm³ HA, and 800 mg/cm³ HA density levels respectively (orange, berry, petrol). The bottom plot demonstrates the tube voltage independence of the Agatston Score of the Sa36f (ART120) reconstruction after taking into account the spectral shortcomings of the base material.

In addition, a calcium mass conversion factor can be derived to enable calculation of a calcium mass score in most calcium scoring applications. The calcium mass score was originally introduced to eliminate tube voltage dependency from the scoring by introducing a calibration step. This step correlates the HU values measured to the actual mass density of calcium. To support the score, a typically tube voltage-dependent conversion factor is provided as a DICOM entry with each reconstruction. In the case of a corrected Sa36f reconstruction, only a single average value of c=0.81 is derived from the measured HU values of the phantom and the nominal HA density value of the respective insert (Figure 6).

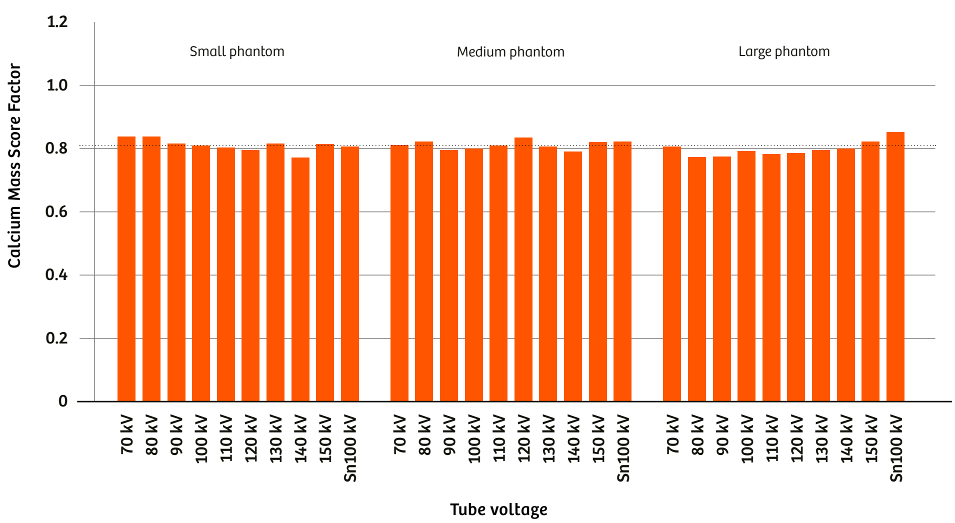


Fig. 6: Calcium mass score conversion factor derived from the measured HU values of the individual inserts for the corrected Sa36f reconstruction.

Human heart specimens

To compensate for the shortcomings of Agatston scoring in the reference phantom described in the previous chapter, a decision was made to further validate the method in a realistic tissue environment. Given the need for repeated acquisition at different tube voltages, a test involving patients was considered unethical. Accordingly, two explanted human hearts were scanned using SOMATOM Force in collaboration with University Hospital Wuerzburg, Germany. All measurements reported in this section are based on a CARE Dose4D™ and CARE kV dose modulation approach using the attenuation information derived from the topogram of the measurement setup. This approach mimics clinical practice, where the applied dose is also dependent on the size of the patient to be imaged. The initial quality reference value used for 120 kV was set to 80 q.ref.mAs/rot, corresponding to the established clinical default value for SOMATOM Force. The values for all other tube voltages were derived semi-automatically using CARE kV based on exactly the same reference starting point, a target material contrast setting of "bone/calcium" and manual setting of the target voltage. The system automatically adjusts the tube current based on the changed tube voltage in combination with the user-defined material contrast target setting. This makes it possible to potentially save dose due to the contrast increase if scanning is performed at lower kV settings compared to the reference point.

The results of the measurements were reconstructed using Qr36f (uncorrected) and Sa36f (corrected) with the standard 3 mm slice thickness and 1.5 mm increment. Manual Agatston scoring was performed with a commercially available standard software package (*syngo*.via VB20) on three selected groups of calcifications by an experienced professional. These three groups were assigned the labels RCA, LCA and CX in the software. They were not limited to calcifications of the vessels, but also included calcifications of the aortic valve and aorta. This results in relatively high total score values, but prevents the evaluation from being dominated by the statistical uncertainties of small calcifications. Example image snapshots of the manual scoring procedure are shown side by side in Figure 7 (Heart 1, top; Heart 2, bottom).

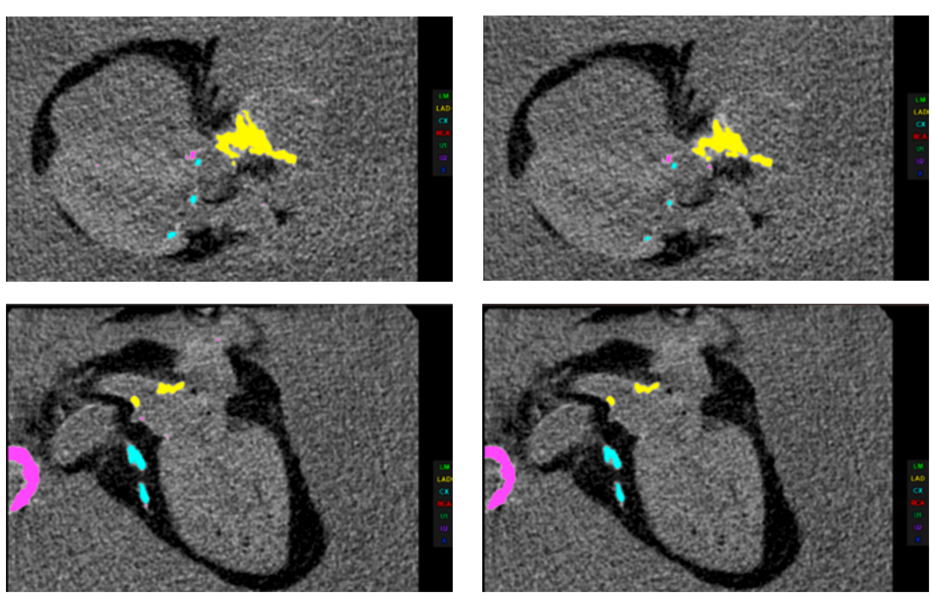


Fig. 7: Example image snapshots from the calcium scoring application (*syngo*.via VB20) of two explanted human cadaver hearts (Heart 1, top; Heart 2, bottom) at 70 kV using the uncorrected Qr36f reconstruction (left column) and the corrected Sa36f reconstruction (right column).

Figure 8 shows the result plots illustrating the Agatston Score for Heart 1 using the uncorrected Qr36f (left) and corrected Sa36f reconstructions (right). Figure 9 provides the same plots for Heart 2. As shown by the uncorrected distribution, the score behaves as expected with a strong increase towards low voltages below 120 kV, while decreasing sharply at Sn150 kV. Here, the combination of high tube voltage and additional tin filtration yields a very hard spectrum. By contrast, the plots of the corrected Sa36f reconstructions clearly show that a kV-independent Agatston Score is achieved across the entire tube voltage spectrum, ranging from 70 kV to Sn150 kV, with approximately 10% relative uncertainty. This is well within the current precision limits achieved in Agatston Score-based calcium scoring for different scanner systems. It should also be noted that this uncertainty level is derived from a limited dataset from two heart specimens involving a manual scoring step. Accordingly, a higher degree of precision may be possible with this method. However, demonstrating it would require a much larger dataset.

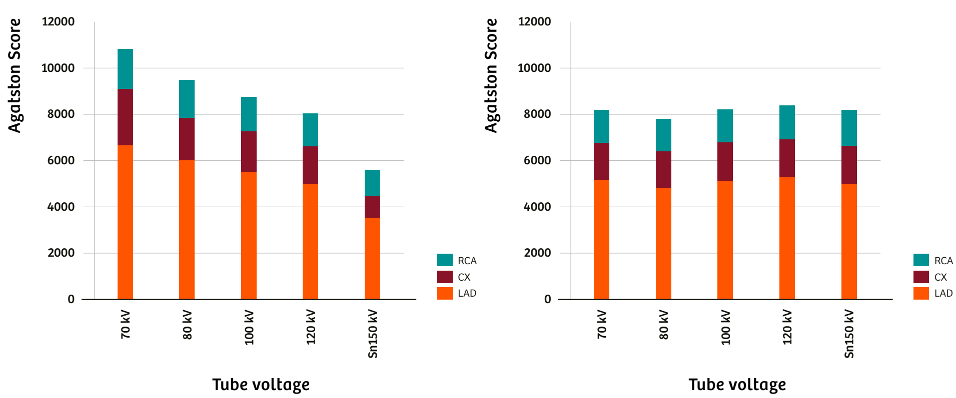


Fig. 8: Agatston scoring results as a function of tube voltage, derived from measurements performed in an explanted human cadaver heart (Heart 1) used to validate the method (Qr36f, left; Sa36f, right).

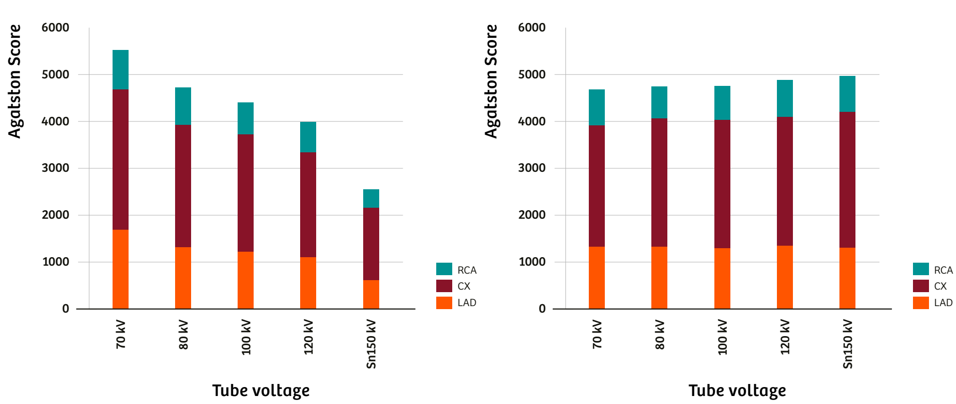


Fig. 9: Agatston scoring results as a function of tube voltage derived from measurements performed in an explanted human cadaver heart (Heart 2) used to validate the method (Qr36f, left; Sa36f, right).

Conclusion

The findings show that applying the dedicated Sa36f reconstruction method to non-contrast CT data enables generation of artificial 120 kV equivalent CT images suitable for Agatston-equivalent calcium scoring based on the established fixed set of scoring thresholds, regardless of the tube voltage of the original CT acquisition. Moreover, a calcium mass score conversion factor of c=0.81 can be derived based on phantom HU measurements regardless of the tube voltage for the dedicated Sa36f reconstruction.

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