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Assessment of coronary calcification using calibrated mass score with two different multidetector computed tomography scanners in the Copenhagen General Population Study



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ABSTRACT

Objective: Population studies have shown coronary calcium score to improve risk stratification in subjects suspected for cardiovascular disease. The aim of this work was to assess the validity of multidetector computed tomography (MDCT) for measurement of calibrated mass scores (MS) in a phantom study, and to investigate inter-scanner variability for MS and Agaston score (AS) recorded in a population study on two different high-end MDCT scanners.

Materials and methods: A calcium phantom was scanned by a first (A) and second (B) generation 320-MDCT. MS was measured for each calcium deposit from repeated measurements in each scanner and compared to known physical phantom mass. Random samples of human subjects from the Copenhagen General Population Study were scanned with scanner A (N = 254) and scanner B (N = 253) where MS and AS distributions of these two groups were compared.

Results: The mean total MS of the phantom was $32.9\pm0.8\,\mathrm{mg}$ and $33.1\pm0.9\,\mathrm{mg}$ (p=0.43) assessed by scanner A and B respectively – the physical calcium mass was $34.0\,\mathrm{mg}$. Correlation between measured MS and physical calcium mass was R^2 = 0.99 in both scanners. In the population study the median total MS was $16.8\,\mathrm{mg}$ (interquartile range (IQR): 3.5-81.1) and $15.8\,\mathrm{mg}$ (IQR: 3.8-63.4) in scanner A and B (p=0.88). The corresponding median total AS were 92 (IQR: 23-471) and 89 (IQR: 40-384) (p=0.64). Conclusion: Calibrated calcium mass score may be assessed with very high accuracy in a calcium phantom by different generations of $320-\mathrm{MDCT}$ scanners. In population studies, it appears acceptable to pool calcium scores acquired on different $320-\mathrm{MDCT}$ scanners.

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1. Introduction

In current healthcare, there is an increasing demand for accurate methods to assess cardiovascular risk in asymptomatic individuals.

Abbreviations: ASA, gatston score; CT, computed tomography; CGPS, copenhagen general population study; FBP, filtered back protection; MDCT, multidetector computed tomography; MS, mass score.

A large body of evidence has demonstrated that coronary artery calcium as measured by computed tomography (CT) is a marker of cardiovascular risk [1–3]. Although substantial clinical outcome data has been accumulated using the Agatston score method (AS), this approach was not recommended in the most recent European and American guidelines on cardiovascular disease prevention [4]. It is noteworthy that most of the compiled evidence was recorded using electron beam tomography which nowadays is an obsolete technology. Nevertheless, in the guidelines it was suggested that measurement of calcium mass, might be superior to AS, and thus more clinically useful.

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As opposed to the AS method, the coronary calibrated mass score (MS) is a quantitative, measurement of the mineral weight in milligrams of the vascular calcifications [5]. MS shows higher accuracy, lower inter-observer variability as well as a lower detection threshold than AS [6–8].

Despite these advantages over AS, MS has not been widely implemented in clinical practice. This may be due to lack of reference data from large cohorts of subjects and prospective clinical follow-up using multidetector CT (MDCT). Obtaining such large data sets may require studies that use multiple inclusion sites and multiple CT scanners with different scan and reconstruction parameters. Differences in CT scanners and scanner settings have been shown to influence the measured calcium score [6–8].

There is currently no consensus on minimal technical requirements of MDCT scanners and image analysis tools acceptable for robust high accurate coronary calcium scoring in clinical practice. Methods and attempts to correct or calibrate differences between scanners have been tried, but results from large studies are not available for more modern MDCT scanners [7–12]. Technically advanced similar scanners, such as two 320-MDCT volume scanners, might provide more comparable results.

The aim of this work was to assess the accuracy of 320-MDCT for measurement of MS and AS in a phantom study, and to investigate inter-scanner differences for MS and AS recorded in a population study on these two high-end MDCT scanners.

2. Materials and methods

MS measured in a cardiac phantom with a first generation 320-MDCT (Scanner A) and a second generation 320-MDCT scanner (Scanner B) was related to physical mass of the phantom. In addition, inter-scanner differences of MS between scanner A and B were assessed. To assess clinical differences, both MS and AS were measured in two randomly selected groups of healthy subjects from the Copenhagen General Population Study (CGPS) using either scanner A or scanner B. To assess interobserver variability, all human subjects were remeasured by a single operator.

2.1. Phantom study

For the phantom measurements, a cardiac phantom was used (D100, QRM, Forchheim, Germany), which contained 100 small calcium deposits varying in size and density (0.33–3.44 mg) as described previously [13]. The calcium deposits were divided over 4 planes and in addition the phantom contained a 5th plane to calibrate a CT scanner for MS. The cardiac phantom was embedded in an anthropomorphic thorax phantom (QRM, Forchheim, Germany).

2.2. Population study

For the measurements in humans, a random sample of healthy subjects was selected from the ongoing CGPS[14] and evenly distributed between scanner A and B. The CGPS is a large ongoing Danish cross-sectional population study in which data of relevance to a wide range of health-related conditions are registered [15]. Inclusion criterion for CT scan was >40 years of age. The Danish National Committee on Biomedical Research Ethics approved the research protocol (H-KF-01-144/01) and all participants gave informed written consent.

A cardio selective beta-blocker (Metoprolol 25–150 mg) was administered orally approximately 1 h before scanning in subjects with a heart rate above 60 bpm and nitroglycerine was given sublingually 2 min before each scan.

2.3. MDCT image acquisition

For image acquisition we used a first generation 320-MDCT (Toshiba Aquilion ONE, Japan – Scanner A) and a second generation 320-MDCT scanner (Toshiba Aquilion ONE ViSION Edition, Japan -Scanner B). Gantry rotation time in scanner A was 350 ms and in scanner was 275 ms. Scanner B had a 40% increase in light output and a 28% decrease in electronic noise compared with the detectors of scanner A. Scan parameters were the same for both scanners: sequential acquisition mode and collimation 320×0.5 mm. The phantom was scanned at 120 kVp, 200 mAs and 0.5 mm slice thickness on both scanners with 19 repeat scans on scanner A and 12 repeat scans on scanner B. For human subjects, tube voltage was 120 kVp and current was depending on participant's body mass index. All scans included a phantom calibration pad (INTableTM Calibration Phantom, Image Analysis, KY, USA) in the scan field for calibrated MS. Two image reconstructions were performed for each scan; one 3.0/3.0 mm slice thickness/increment reconstruction for assessment of AS and one 0.5/0.5 mm reconstruction for assessment of MS, following a patient protocol with kernel FC12 and filtered back protection (FBP) as previously described [8].

2.4. MDCT image analysis

For both phantom study and population study, calibrated MS measurement was performed with N-VivoTM (Image Analysis, KY, USA) and AS measurement was performed with Vitrea 6.3 (Vital Images Inc, MN, USA), both commercially available software, on external dedicated workstations. The scoring threshold for AS was adjusted based upon the scanning parameters as described previously [13]. For assessment of AS in healthy subjects a standardized procedure with clear-cut definitions of the delineation of the coronary arteries was used to lower variability in image analysis [16]. MS was assessed as previously described. [17] Demarcation points were set between left coronary cusp and left main coronary artery to distinguish between them.

The calcium scores from the phantom study were used to compare the performance of the MDCT scanners. For each scanner, the mean value of total MS from assessments of the phantom scans were compared to the physical mass. The distribution of total MS and AS is presented in the population study.

2.5. Statistics

We used SAS version 9.4 (SAS Institute, Cary, NC, USA) in all statistical analyses. For continuous variables, mean value and standard deviation were calculated in the phantom study and median value and interquartile range (IQR) were calculated in the population study; differences were assessed as difference between means with an unpaired t-test. T-test for difference between mean calcium scores was performed after logarithmic transformation. For categorical variables, amount and percentage were calculated; differences were assessed with a chi-square test. Correlation between physical mass and calibrated MS was assessed by Pearson's R^2 and correlation plot. A p-value < 0.05 was considered statistically significant. Interobserver variability was assessed with Bland-Altman's method for assessment of agreement.

3. Results

3.1. Phantom study

MS pr. calcium deposit was closely correlated with physical calcium mass in the phantom, R^2 = 0.99 for both scanners (Fig. 1). The mean total MS was 32.9 ± 0.8 mg and 33.1 ± 0.9 mg (p = 0.43) assessed by scanner A and B averaged over all scans. The physical

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