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Coronary artery calcium score quantification using a deep-learning algorithm

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AIM: To investigate the impact of a deep-learning algorithm on the quantification of coronary artery calcium score (CACS) and the stratification of cardiac risk.

MATERIALS AND METHODS: Computed tomography data of 530 patients who underwent CACS scan were included retrospectively. The scoring (including Agatston, mass, and volume scores) was done manually. The deep-learning method was trained using data from 300 patients to calculate CACS based on the manual calculation. The automated method was validated on a set of data from 90 patients and subsequently tested on a new set of data from 140 patients against manual CACS. For the data from 140 patients that were used to analyse the accuracy of deep-learning algorithm, the total CACS obtained manually and by using the deep-learning algorithm was recorded. Agatston score categories and cardiac risk categorisation of the two methods were compared.

RESULTS: No significant differences were found between the manually derived and deep-learning Agatston, mass, and volume scores. The Agatston score categories and cardiac risk stratification displayed excellent agreement between the two methods, with kappa = 0.77 (95% confidence interval [CI]=0.73–0.81); however, a 13% reclassification rate was observed.

CONCLUSION: Deep-learning algorithm can provide reliable Agatston, mass, and volume scores and enables cardiac risk stratification.

Introduction

The presence of coronary artery calcium as assessed via computed tomography (CT) is a reliable indicator of coronary artery disease (CAD) and is commonly used as an important biomarker for predicting the risk of a serious CAD event. The characterisation of coronary artery calcification shows equivalence with the total coronary atherosclerosis load.[1] Numerous studies have established that the CT calcium score (typically Agatston) aids risk prediction[2–6]; the score is more predictive than any other single biomarker, including lipids.[7] The assessment of the coronary artery calcium score (CACS) using CT has therefore evolved to be an acceptable tool for cardiovascular risk stratification.[8,9]

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With recent innovations in the field, coronary artery calcification quantification and coronary artery imaging with the use of coronary CT angiography (CCTA) have become widely available in clinical practice for the assessment of CAD.[10,11] CT calcium score imaging is primarily used as a cardiovascular disease risk stratification tool in asymptomatic individuals; however, the disadvantage of the method as a screening test is the radiation risk associated with it.

Nowadays, CT calcium score imaging as a screening test in a priori healthy subjects has become prevalent in clinical settings. Recent guidelines and expert consensus recommend CACS scanning and measurement before CCTA.[12,13] CACS quantification still requires manual measurement, which is a time-consuming and laborious job. Besides, the value may also vary between observers with different experience. Hence, an automated assessment may be beneficial. Artificial intelligence (AI) is used increasingly in diagnostic radiology and medicine as it provides reproducible and objective diagnosis by extracting relevant features from the medical imaging data and using them in classifiers for automated detection of cardiovascular disease, thereby serving as a valuable adjunct tool in clinical practice.[14] The machine learning or deep-learning algorithm is a subset of AI that utilises algorithms to combine voluminous data comprising clinical information and coronary anatomical variables for optimal prediction of cardiac events.[15–17] Thus, it was hypothesised that a similar process using AI to quantify CACS would be suitable for learning and recalling multidimensional attributes.

Owing to the developments in imaging technologies that have enabled the capture and storage of large amounts of data, AI has attracted tremendous attention and has offered new approaches to leverage the growing volume of imaging data available for analyses. Such approaches have been successfully applied in medical imaging to improve quantification, highlight subtle findings that a physician might otherwise miss, help pathological classification, and provide recommendations for follow-up.[18]

There have been no studies to date evaluating the use of AI for the quantification of CACS from CT calcium score imaging. Thus, the present study was undertaken to investigate whether an automated CACS detector allowing quantification of CT calcium score imaging can achieve significant convenience with a comparable risk prognostication for cardiac risk stratification to manual measurement.

Materials and methods

Patients

The data pertaining to patients who underwent a dedicated electrocardiogram (ECG)-triggered calcium scan between January and April 2018 was analysed retrospectively. Patients with known CAD (prior percutaneous stent implantation or coronary artery bypass grafting) and those with implanted mechanical prosthetic valves or other cardiac devices were excluded to prevent imaging artefacts. A total of 530 patients were selected for further analysis.

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the local ethics committee. Written informed consent was obtained from all patients.

CT acquisition parameters and image reconstruction

CT acquisition was performed with the aid of a 256-detector row CT (Revolution CT, GE Healthcare, Milwaukee, WI, USA). A dedicated, prospectively ECG-triggered calcium score scan at 75% (HR $<$65 beats/min) or 45% (HR $\geq$65 beats/min) of the cardiac cycle was performed with the following scan parameters: 120 kVp tube voltage, automated tube current modulation, 0.28 seconds gantry rotation time, 3mm reconstruction thickness, 250$\times$250 mm typical reconstruction field of view (FOV), depending on the patient anatomy, in a 512$\times$512 pixel image matrix.

Image analysis of CACS datasets

The extent of coronary calcification was quantified using unenhanced scans. The data were uploaded to an advanced workstation (AW4.7; GE Healthcare) for analysis. An experienced radiologist (5 years of experience in cardiac CT imaging) mapped the lesion areas at each level manually using a special customised calculation software (smart score 4.0; GE Healthcare) through which the Agatston, mass, and volume scores were obtained for each patient.

For deep-learning analysis, the datasets were divided into 300 scans for training, 90 for validation, and 140 scans as a test set, which was only used for the final evaluation. Of the coronary calcium score scans, the CT scans were first converted into three-dimensional (3D) volume data. Subsequently, all the voxel points were segmented with a radiodensity value $\geq$130 HU. Later, the connected regions in the volume were labelled as they were suspected to be the calcified regions. The suspected calcification regions were marked with different labels. These regions were then fed as input to a neural network for automated analysis. The input for the neural network was the CT calcium score imaging and the suspected calcified region. This network calculated the probability of calcium in each suspected calcified region, and its main function was to identify the coronary artery calcified regions. The neural network classified each suspected calcified area into five categories, namely non-calcium, left anterior descending calcium, left circumflex calcium, left main stem calcium, and right coronary artery calcium. This function combined the nearby voxels into local structures and summed those into overall structures. Although the algorithm did not clearly express the calcified features, it learned to recognise them by analysing the local structures. The specific neural network used in this work was the 3D-resnet architecture.[19] The calcified regions were located based on the results of the neural network classification. The number of voxels contained in the calcified region and the HU value of the corresponding voxel were estimated. The thickness and pixel spacing in

the digital imaging and communications in medicine (DICOM) meta information provided the volume of each voxel. The calcification percentage corresponding to each patient was calculated according to the integral formula. The calculation was based on the weighted density score given to the highest attenuation value (HU) multiplied by the area of the calcification speck (density factor: 1=130–199 HU; 2=200–299 HU; 3=300–399 HU; 4=400+ HU).

$$\text{Agatston score} = f \times p \times s \quad (1)$$

In equation (1), f is the density factor, p is the pixel number, and s is the area of the pixel. Similarly, the volume and mass scores were calculated by referring to the traditional coronary artery calcification scoring methods.[13]

For the 140-scan test set included in the analysis, image quality was evaluated, the total Agatston, volume, and mass scores were recorded, and the values from the different measurements were compared. The results of the Agatston score were divided into calcification and non-calcification groups to compare the detectability of the calcification between the two measurements. The Agatston score categories were 0, 1–99, 100–299, and >300, and the corresponding risk categorisations were grade 0, 1, 2, and 3, respectively.[20] Subjective image quality was evaluated by an experienced radiologist (5 years of experience in cardiac CT imaging) using a five-point Likert scale: 1 = non-diagnostic, with intense image noise and artefacts, 2 = limited diagnostic value, with image noise and artefacts, 3 = diagnostic, with moderate image quality, 4 = diagnostic, good image quality with minimal noise and artefacts, 5 = diagnostic, with excellent image quality. To estimate the radiation dose, the volumetric CT dose index (CTDI) and dose–length product (DLP) were recorded. The effective radiation dose was derived by multiplying the DLP with a standard conversion factor of 0.026 mSv/mGy·cm.[21]

Statistical analysis

SPSS software (SPSS 23.0, IBM, Chicago, IL, USA) was used for statistical analyses. Continuous variables were expressed as mean±standard deviation. Normal distribution was assessed using the Kolmogorov–Smirnov test. Categorical variables were presented as frequencies and/or percentages. The Agatston, mass, and volume scores revealed a highly skewed distribution. Therefore, the values were computed as medians and 25th and 75th percentiles. The consistency of the calcium score quantification between the two methods was evaluated by using the intragroup correlation coefficient (ICC); values >0.90, 0.75–0.90, 0.50–0.75, and <0.50 were defined as excellent, good, moderate, and poor tests, respectively. A chi-square test was used to compare the detectability of calcification between the two methods. The agreement of the Agatston score categories was compared using the kappa identity test. K values >0.75, 0.60–0.74, 0.40–0.59 and <0.40 were defined as excellent, good, moderate, and poor tests, respectively. A p-value ≤0.05 was considered statistically significant.

Results

Patients

Of the 140 patients, 56% were males with a mean age of 58.1±9.7 years and a mean body mass index (BMI) of 28.6±4.9 kg/m^2. The mean estimated radiation dose of the CACS acquisitions in the study population was 0.50±0.05 mSv. Other patient demographics and baseline characteristics are presented in Table 1.

Image quality

All images were scored 3 and above, indicating that the quality was diagnostic in all patients; 50 patients (36%) were scored 5, 62 (44%) were scored 4, and 28 (20%) were scored 3.

Analysis of CACS scans

Calcifications were detected in 106 patients (76%) using manual measurement and in 109 patients (78%) using deep learning. Eight patients had a score of zero with manual measurement, but displayed a positive calcium score when deep learning was used. Five patients had a score of zero when using the deep-learning algorithm but exhibited a positive calcium score with manual measurement. No statistical differences were found in detectability between the two methods (X^2=0.31, p>0.05).

No differences were discerned in the Agatston, mass, and volume scores between the two methods: ICC=0.94 (95% confidence interval [CI]=0.91–0.95), 0.93 (95% CI=0.91–0.95) and 0.92 (95% CI=0.89–0.94), respectively (Table 2). Agatston, volume, and mass scores derived from the manual and deep-learning measurements are depicted in Fig 1. The two methods agreed well with each other in terms of the Agatston score categories and risk categorisation: k = 0.77 (95% CI=0.73–0.81) (Table 3). Twenty-three patients (16%) were reclassified. Although the reclassification of most patients resulted in moving to the next risk category, one patient was reclassified from grade 0 to grade 2. Representative examples of CACS

Table 1
Patient (N=140) characteristics and procedural results.

Age (years)	58.1±9.7
Male sex n (%)	78 (56%)
Body mass index (kg/m^2)	25.4±3.2
Hypertension n (%)	77 (55%)
Dyslipidaemia n (%)	57 (41%)
Diabetes n (%)	25 (18%)
Tobacco abuse n (%)	53 (38%)
CAD family history n (%)	34 (24%)
CACS scan	
CTDI (mGy)	1.3±0.1
DLP (mGy·cm)	19.1±1.8
Effective dose (mGv)	0.5±0.05

Table 2
Calcification score values obtained by the two methods (described as medians and 25th and 75th percentiles) and the agreement between the manual and deep learning measurements.

	Agatston score	Volume score	Mass score
Manual method, median (25th, 75th)	44.1 (1.1, 227.6)	41.7 (2.7, 206.3)	8.3 (0.3, 48.6)
Deep-learning method, median (25th, 75th)	53.7 (3.8, 218.5)	51.9 (7.2, 175.8)	11 (1, 46.9)
ICC (95% CI)	0.94 (0.91–0.95)	0.93 (0.91–0.95)	0.92 (0.89–0.94)

quantification of manual and deep-learning measurements are shown in Fig 2.

Discussion

The present study investigated the feasibility of automated CACS quantification from CT calcium score imaging by using the deep-learning method. The long-term goal is to develop an automated CACS detector that can be used to provide risk markers for CAD. The present results demonstrate that the manual and automated measurements agree well for the Agatston, mass, and volume score values and risk categorisation. Thus, automated identification of CACS from CT calcium score imaging could serve as a low-cost and labour-effective strategy for the risk assessment of CAD.

The main approaches used for the quantification of the CACS were the Agatston, volume, and mass scores. The first two are the most widely used measures, especially the Agatston score; however, the volume and mass scores have shown better reproducibility.[22]

Machine-learning approaches have formed the core of many cardiovascular image acquisitions and have been used for processing several algorithms that are already in routine clinical use.[23] There are potential benefits in the algorithms designed to automate the measurements. First, automated standardised measurements permit the detection of the subtle relationship between the anatomical variance and clinical outcomes, hence helping with the analysis in case of large databases. Second, advanced measures that are expensive or time-consuming to perform can also be automated and applied to large cohorts. Third, manual measurement errors between the observers can be overcome owing to the high repeatability of machine quantification. Given the rapid evolution of machine-learning capabilities, continued advancements are being made in developing tools for optimising not only the cardiovascular imaging measurements but also the interpretation of the results from such measurements.

Many studies are now available, which suggest automatic detection and quantification in cardiovascular imaging. A previous study by von Knebel Doeberitz *et al.* demonstrated that coronary CCTA-derived plaque markers combined with deep-machine-learning-based CT fractional flow reserve possessed incremental predictive value in identifying lesion-specific ischaemia when compared with CCTA stenosis

Table 3
Agreement between the manual and deep-learning measurements depending on the Agatston score categories.

Deep learning method	Manual method				Total
	0	1–99	100–299	>300	
0	26	5	0	0	31
1–99	7	49	3	0	59
100–299	1	2	16	2	21
>300	0	0	3	26	29
Total	34	56	22	28	140

Kappa identity test revealed excellent agreement. Kappa = 0.77 (95% CI=0.73–0.81), ($p<0.001$).

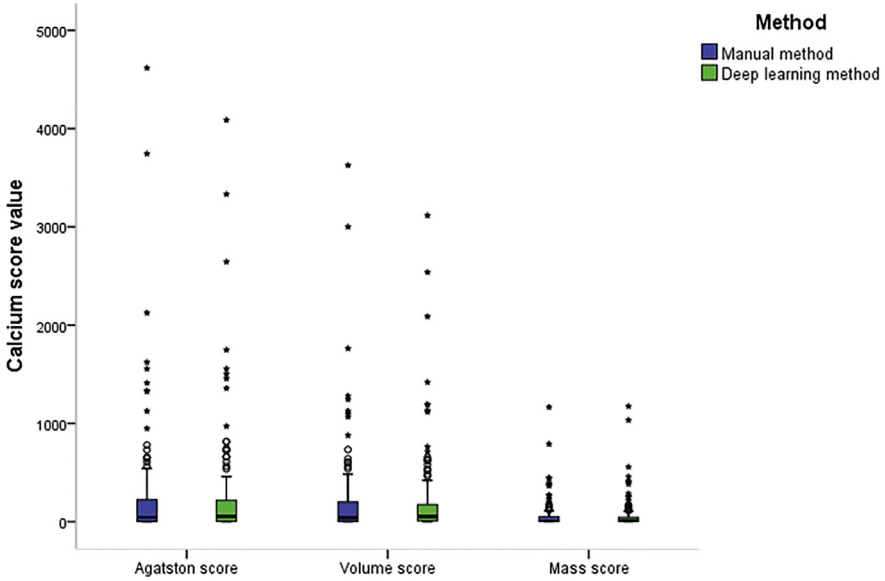

Figure 1 Box plot of Agatston, volume and mass scores derived from the manual and deep learning measurements. The overall mass score was lower than the Agatston and volume scores.

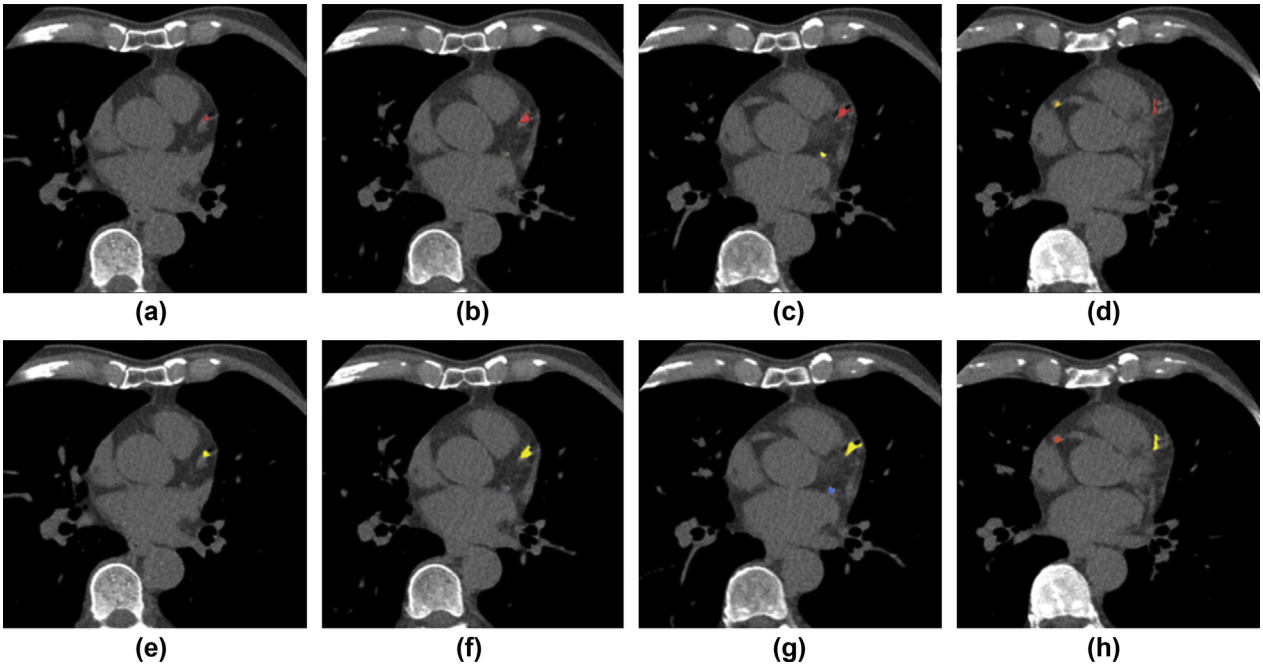

Figure 2 CACS acquisition in a 68-year-old male patient with a BMI of 21.5 kg/m^2. Transverse CT sections obtained from CT calcium score imaging. Upper row illustrates CACS quantification manually. Lower row shows CACS quantification by using the deep learning algorithm. Calcified plaques located in the coronary artery are colour-coded. Calcification in the different coronary artery branches is represented by different colours. The total Agatston scores for the manual and deep learning measurements were similar, that is 442.1 and 447.8, respectively. (The colour settings for the two methods are different.)

grading alone, thus providing an additional prognostic and predictive value in patients with CAD.[24] Lessmann *et al.* asserted that AI enabled reliable automatic cardiovascular risk assessment by detecting coronary artery, thoracic aorta, and cardiac valve calcifications in low-dose chest CT scans acquired for lung cancer screening.[25] Annika *et al.* validated that the coronary calcium score can be accurately measured using an automated standardised method on CCTA. The coronary calcium score derived from CCTA correlated extremely well with the coronary calcium score from non-contrast images obtained using commercial methods.[26] Despite these efforts, accurate and automated detection of CACS from CT calcium score imaging remains a daunting task, and the technology is far from clinical deployment. The use of unenhanced cardiac CT as a screening test is irreplaceable in clinical practice, which implies that the information of risk stratification obtained from CT calcium score imaging is of great value. The present study constitutes the first attempt to evaluate the use of AI in CACS quantification from CT calcium score imaging. Although larger-scaled studies are required to further refine the approach, the results indicate that the technique brings automated CACS quantification one step closer to clinical translation.

There are several limitations in the present study. First, the total calcium score was evaluated for every patient; however, the scores of the various coronary artery branches showed significant differences. To a large extent, this was because of the difficulty in identifying the boundaries of the branch vessels, especially when lesions continued to distribute in these arterial branches. Second, although Agatston score categories and cardiac risk stratification showed excellent agreement between the two methods, 13% reclassification was still observed. In cases with higher calcification scores from the deep-learning method than the manual method and the increment causing a reclassification of risk stratification, the increase might have stemmed from the calcification of the aortic wall and annulus as well as the adjacent high-density tissue. Third, we did not evaluate AI's ability for CACS measurement in cases where calcification of adjacent tissues exists, including annular calcification, calcification in the wall of the aorta at the root, and aortic sclerosis. In these cases, CACS quantification using the deep-learning algorithm may not be as accurate, considering it is difficult for AI to differentiate coronary artery calcification from aortic and annular calcification, even by manual method; however, through abundant data analysis and self-regulated learning of computer, the recognition of coronary artery calcification via AI can be improved step by step. This study preliminarily confirms the value of AI in measuring CACS. For some complex cases, analysis of the performance of AI in CACS quantification needs more research and good performance relies on the improvement of algorithm. Furthermore, this research was a single-centre retrospective study, which included a relatively small patient cohort, and all images were post-processed on the same workstation from one vendor using the vendor-recommended reconstruction algorithm. Variability between the calcium scores derived from different reconstruction techniques and scanner types has been documented.[27–30] Larger studies covering the impact of different scanners and reconstruction algorithms are necessary to validate the present findings.

In conclusion, this study demonstrates that the deep-learning algorithm provides reliable calcium score and risk stratification with immense convenience by automatically quantifying CACS in CT calcium score imaging. As the well-validated CACS reference values are based on the calcium score quantification in traditional ways, any measurement error will affect the clinical decisions. Therefore, caution should be exercised while using this technique in clinical practice. Quantification of CACS using AI has facilitated the potential applications, but technical refinement is still needed to define the course of the coronary artery and divide the main branches precisely.

Conflict of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: ShuKun (Beijing) Network Technology Co provided data analysis based on the deep learning algorithm.

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