Effect of Computed Tomography Slice Thickness on Calculated Coronary Artery Calcium Score in the Assessment of Possible Radiation Induced Cardiac Toxicity

C. Alexander¹ and R. Rajapakse¹,²

¹Department of Physics & Astronomy, University of British Columbia Okanagan, Kelowna, BC, V1V 1V7, Canada
²Medical Physics, BC Cancer – Kelowna, Kelowna, BC, V1Y 5L3, Canada

E-mail: RRajapak@bccancer.bc.ca

Abstract. Studies have suggested that the occurrence of radiation induced cardiac toxicity in breast cancer patients is significantly higher in women with pre-existing cardiac risk factors. Therefore, it is important to quantify the relationship between radiation induced cardiac toxicity and a measurable level of pre-existing cardiac risk such as the patient’s coronary artery calcium Agatston score. To assess the extent of coronary artery calcium present in the walls of patients’ coronary arteries before they received treatment, Agatston scores may be calculated using thoracic CT scans acquired for external beam radiotherapy planning. However, these planning CT scans can vary in slice thickness and resolution, thus complicating the calculation of calcium scores using scans with slice thicknesses other than the 3mm routinely employed for traditional Agatston scoring. The objective of this project is to quantify the effect of varying CT scan slice thickness in the calculation of coronary artery calcium scores so that a method of standardization might be developed. This is accomplished through the design, fabrication, and scanning of an anthropomorphic phantom featuring calcium inserts of varying sizes. Analysis of how the scores change with increasing slice thickness is used to construct a simple linear scaling method of standardization which corrects for varying slice thickness and the resulting partial volume distortions. A linear scaling method was successfully validated for the calculation of coronary artery calcium Agatston scores across a range of slice thicknesses increasing from 0.625 mm to 5 mm. Scaling is applied by multiplying the score by the slice thickness and dividing by 3 mm. This method is potentially applicable in any clinical or research endeavour which calls for retroactive cardiac calcium quantification. With a simple linear scaling method, external beam radiation therapy planning CT scans with slice thicknesses ranging from 0.625 mm to 5 mm can be used to calculate coronary artery calcium Agatston scores and thereby measure a patient’s level of cardiac risk before treatment.

1. Introduction

Studies have suggested that the occurrence of radiation induced cardiac toxicity in breast cancer patients is significantly higher in women with pre-existing cardiac risk factors [1]. Therefore, it is important to quantify the relationship between radiation induced cardiac toxicity and a measurable level of pre-existing cardiac risk such as the patient’s coronary artery calcium Agatston score. To assess the extent of coronary artery calcium present in the walls of patients’ coronary arteries before
they received treatment, Agatston scores may be calculated using thoracic CT scans acquired for external beam radiotherapy planning. However, these planning CT scans can vary in slice thickness and resolution, thus complicating the calculation of calcium scores using scans with slice thicknesses other than the 3mm routinely employed for traditional Agatston scoring [2]. Among the 27361 radiotherapy planning CT scans taken at the British Columbia Cancer Agency in the past 15 years, 12% have a slice thickness of 2 mm, 4% have 2.5 mm, 12% have 3 mm, 65% have 5 mm, and 7% have 10 mm.

The objective of this project is to quantify the effect of varying CT scan slice thickness in the calculation of coronary artery calcium scores so that a method of standardization might be developed. This is accomplished through the design, fabrication, and scanning of an anthropomorphic phantom featuring calcium inserts of varying sizes. Analysis of how the scores change with increasing slice thickness is used to validate a simple linear scaling method of standardization which corrects for varying slice thickness and the resulting partial volume distortions.

2. Phantom Design

To investigate the effects of varying computed tomography slice thickness on calculated coronary artery calcium score, an anthropomorphic cardiac calcification phantom was designed and built at the British Columbia Cancer Agency Centre for the Southern Interior. The base of the phantom is composed of an acrylic material. It contains foam components acting as lungs, a rod for the spine, and ten calcium inserts.

These calcium inserts were created by drilling precise, cylindrical holes in the acrylic base. Five holes were arranged in a ring at the center of the phantom with respective depths of 2 mm, 3 mm, 4 mm, 5 mm, and 8 mm. The diameter of each cylinder was made equivalent to its depth. Five additional holes with equal dimensions to the first five were placed in a second ring surrounding the first to accommodate a total of ten calcium deposits. Each hole was then packed with medical grade powdered calcium microcrystalline hydroxyapatite. This particular calcium salt was used because it is known to be consistent with the inorganic composition of calcium deposits in cardiovascular tissues [3]. The sizes of these inserts were chosen to represent the range of calcification sizes typically present in coronary arteries.

3. Phantom Computed Tomography Scanning

The phantom was scanned using a GE LightSpeed 16 Slice Computed Tomography Scanner at slice thicknesses of 0.625 mm, 1.25 mm, 2.5 mm, 5 mm, and 10 mm respectively. Two independent scans were taken at each specific slice thickness for a total of 10 scans. All scans were performed on the same day.

4. Analysis

4.1. Calcium Scoring of Phantom

Preliminary analysis of these scans was done using eFilm software. The average CT number of the acrylic base of the phantom was determined to be 126 HU. This value is 84 HU above the average CT number of the cardiac tissue measured in the radiation planning scans of the patients in our cohort. Additionally, the calcium cylinders exhibited exceedingly high CT numbers, up to 983 HU. This was as expected because pure calcium microcrystalline hydroxyapatite was used. Calcium deposits formed in the body would not typically contain this high a concentration, but rather be a composite of calcific and organic material [4,5]. Because of this, they would not appear as bright on CT scans. We were unable to use a mixture with a lower calcium concentration because of issues with presence of air caused by inhomogeneous granular sizes in the respective powders. To account for both of these issues, a scaling factor was applied to the CT scans to bring all measured CT numbers down by 84 HU. This resulted in scans which could be used to reliably model the cardiac tissue and calcified lesions visible in the radiation planning scans of the patients in our cohort.
Additional considerations were made for issues caused by the presence of air along the central axial slice of the phantom. The phantom was sliced in half along the transversal plane to facilitate the insertion of the calcium cylinders and subsequently put back together with the use of tissue equivalent screws. Despite being tightly pressed back together, not all the air was removed from that central plane. This is visible in the CT scans as an overall darker image at the Z value closest to 0. To compensate for this, scaling factors were applied to the affected image to standardize the visible CT number of the acrylic background. These scaling factors must vary between scans with different slice thicknesses because the amount by which a particular image was impacted by the air slice is dependent on the depth of the whole slice in comparison to the depth of the slice of air within it.

In each of the ten scans, calcium scores were calculated for each individual cylindrical insert according to the previously described Agatston method. Areas were determined via manual contouring in the Varian Eclipse radiation therapy treatment planning software. The traditional Agatston threshold of 130 HU was used to differentiate calcific material from surrounding tissue. Additionally, consistent window and level values of 1075 and 518 respectively were utilized in the contouring of each scan. Example contours can be seen in Figure 1.

Individual cylinder scores calculated using distinct scans with equal slice thickness were averaged to provide a single score for each cylinder at each slice thickness. The average scores of inner and outer ring cylinders with equal dimensions were then averaged together, resulting in scores for each of the five calcium insert sizes at each slice thickness with as little noise as practical.

We present a standardizing scale which aims to prevent overestimation of calcium in the case of slice thicknesses smaller than 3mm and underestimation in the case of slice thicknesses larger than 3mm. This scale was applied to the averaged calcium scores extracted from the phantom scans.

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CACS_{\text{standardized}} = \frac{x \cdot CACS_x}{3}
\]

(1)

\(x\) represents the slice thickness in mm
\(CACS_{\text{standardized}}\) represents the standardized Agatston score, i.e. the total coronary artery calcium score we would expect to be calculated at a slice thickness of 3mm
\(CACS_x\) represents the total coronary artery calcium score at a slice thickness of \(x\) mm

5. Results

The scans with the smallest slice thickness, 0.625 mm, represent the most detailed information because they are subject to less partial volume effects caused by averaging over the entire depth of the slice. The larger the slice thickness, the more the calcium scores are affected by the location of the scan origin. With a large slice thickness, offsetting the location of the scan origin by some distance in the direction orthogonal to the image plane can cause significant variance in the calcium score. If the
offset is a multiple of the slice thickness, the score remains constant because the slices have lined up and the locations of the image slice boundaries have not moved. Smaller slice thicknesses produce more slice boundaries to line up with and therefore mitigate the offset dependent score variance. Therefore, these scans yield the most accurate estimations of the extent of calcification and most meaningful CAC scores. With this in mind, the averaged and standardized CAC scores of each cylindrical insert size calculated at each slice thickness were compared to those calculated at 0.625 mm. This allowed for an evaluation of the CAC score precision at varying slice thicknesses. Figure 2 displays the CAC score deviations relative to the scores calculated at 0.625 mm plotted against the slice thickness. The expected loss of precision with increasing slice thickness is clearly apparent in the data. However the scores calculated with thicknesses up to 5 mm are all still within 50% of the most accurate estimates. This is a reasonable range in the context of the large bin sizes used in assigning levels of cardiac risk from CAC scores shown in equation [4]. Therefore, scans with slice thicknesses in this range may be deemed relevant in coronary calcium scoring.

Figure 2. CAC score deviations relative to the scores calculated at 0.625 mm plotted against the slice thickness.

At slice thicknesses as large as 10 mm not only precision is lost, but also accuracy, as systematic errors due to partial volume effects consistently underestimate the amount of calcium present. Because of this, scores calculated from scans with slice thicknesses of 10 mm or more do not provide reliable estimates of cardiac calcification.

Averaged CAC scores calculated with slice thicknesses within the established range of reasonable precision and accuracy, below and including 5 mm, can be seen in Figure 3. The graph also displays the cardiac risk category ranges.
Figure 3. Averaged CAC scores of specific cylinders plotted against slice thickness with standard deviations and cardiac risk category ranges.

After standardization, almost all scores fell within consistent risk brackets, as can be seen in Figure 4.

Figure 4. Averaged standardized CAC scores of specific cylinders plotted against slice thickness with standard deviations and cardiac risk category ranges.

The standardized CAC scores remained reasonably constant over this range of thicknesses. No overall trend of scores increasing or decreasing with larger scan slice thickness was found. Hence the plaque burden was neither overestimated nor underestimated.
6. Discussion
The objective of this project was to establish and verify a method of calculating and standardizing coronary artery calcium scores from CT scans which corrects for various slice thicknesses. This was done by designing, building, scanning, scoring, and standardizing an anthropomorphic cardiac calcium phantom. We found that CT scans taken with slice thicknesses of up to 5 mm are may be used to calculate coronary artery calcium scores comparable to those calculated using the traditional method involving 3 mm slices, but slice thickness much larger than this are prevented from yielding meaningful scores by increasingly dominant partial volume effects. Because of this, we are unable to extract reasonable calcium score estimates for the 7% of the patients in our cohort who had scans taken with slice thicknesses of 10 mm. After the standardizing scale presented in equation [5] was applied, CAC scores calculated from scans with slice thicknesses of 5 mm or less were reasonably constant. Their variations due to noise and partial volume effects did not exceed 50% of the most accurate scores. Because of this, they yielded consistent risk level categorizations.

No overall trend of scores increasing or decreasing with larger scan slice thickness was found. This differs from the results of Muhlenbruch et al, who found higher scores for 1 mm slices and lower scores for 3 mm slices [6]. This is because, in their phantom study, a threshold of 350 HU was used rather than the traditional 130 HU. They made this adjustment because they were using an entirely automated calcium scoring program which contoured every voxel with a CT above the threshold. In the 1 mm slices, this highlighted random noise pixels, causing them to change the threshold to 350 HU in an effort to automate the exclusion of these voxels. However, this higher threshold not only excluded noise, but also small calcifications averaged out by partial volume effects in larger slices. This is why they found lower CAC scores with larger slice thicknesses [6]. We do not encounter the same issue because we manually contoured all calcifications, allowing us to maintain the traditional threshold of 130 HU and therefore not overlook small calcifications that would otherwise be obscured by partial volume effects.

In summary, our results support the utility of CAC scores calculated from CT scans with slice thicknesses up to 5 mm. Using the presented method of standardization, scores calculated with slice thicknesses within this range are a reliable indicator of cardiac risk level. This provides a validated process for the evaluation of coronary artery calcium scores across different slice thicknesses.

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