
AUTOMATED IDENTIFICATION OF CALCIUM IN MITRAL AND AORTIC VALVES

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Abstract

Calcification of the mitral and aortic valves is one of the main precursors to heart valve diseases. Calcified valves and coronary vessels is also an indication of risk for future cardiac events such as cardiac infarct(1)(2). During this master thesis project, a program for automatic identification and quantification of calcium in the mitral and aortic valves in CT image stacks was implemented. The program can differentiate between the aorta valve and the mitral valve and give separate scores for the valves as well as a total score which is the sum of the mitral and aorta score. The program is based on image analysis and reached a sensitivity of 100 % and a specificity of 85.4 % when the limit ≥ 100 Agatston units was used for identifying patients at risk in a comparison of 49 cases with the existing manual program syngo.via. The program can automatically go through and identify calcium in a large amount of data, and due to the high prevalence of noise it is also possible to manually go back and check and rescore images if desired.

Preface

This master thesis has been written at the department for clinical physiology at the Skåne University Hospital in Lund, to fulfill the graduation requirements of the faculty of engineering at Lund University. The automatic method that has been developed will hopefully be of use for the scientists and doctors at the department when it comes to finding out more about how common calcification of the mitral and aortic valves is.

I want to thank my supervisors Einar Heiberg, research engineer in medical image processing and Ellen Ostfeld, specialist physician Clinical Physiology Lund Cardiac MR Group for continuous feedback and sharing their expertise with me during this process.

I also want to thank the rest of the group for answering questions during the project and for sharing important and personal moments and experiences from their lives at the weekly reflection meetings, which has been very appreciated. And to my parents for unconditional love and support when it is needed the most.

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Introduction

Calcification of the mitral and aortic valves is one of the main precursors to heart valve diseases such as mitral/aortic stenosis and mitral/aortic regurgitation. Calcified valves and coronary vessels is also an indication of arteriosclerosis and risk for future cardiac events such as cardiac infarct(1) (2).

The quantification method used for calcium scoring is called Agatston Score, named after Arthur Agatston who was the first author on the first paper about Agatston's and his coauthors experience and use of the new risk score calculated from CT scans published 1990 in the Journal of the American College of Cardiology(3). In 2019, almost 30 years later, the American Heart Association (AHA) published their updated guidelines which listed coronary artery calcium (CAC) CT exams as a primary diagnostic test to better determine a patient's risk of having a coronary event(3). As a result the Agatston Score is expected to be used even more in these types of examinations(3) and it is one of the

reasons to why it is used in this project as well.

Previous studies on incidence of calcium in the mitral and aortic valves have typically come from small patient cohorts. Little is known about the prevalence of calcium in normal or cross-sectional cohorts. The access to this type of knowledge is limited by that today there are no existing software tools that can be used automatically or semi-automatically on large patient cohorts.

There are existing methods to decide how much calcium there is in the heart. These methods are based on how much x-ray radiation is attenuated in body tissues and gives the density distribution in the image. The attenuation capacity depends on what type of tissue it is and is measured in Hounsfield units, HU, (4) (5) (6).

The data used in the work leading up to this thesis originates from the Swedish CardioPulmonary bioImage Study (SCAPIS) (7).

Aims

An automatic method for quantification of mitral and aortic calcium of computed tomography, (CT), images should be implemented. The aim is that the method should be able to go through large amounts of data to be able to solve the question of what is normal or deviating amounts of calcium in the valves with good accuracy.

The resulting method should be able to quantify how much calcium, in millilitres, the relevant area of the image stack contains.

This knowledge will in the future be connected to secondary diseases and help the scientists and physicians at the department of clinical physiology to give more accurate diagnoses and prognoses to patients. It will also be of importance when deciding how this condition should be prioritised when it comes to research and economic resources.

Cardiac Anatomy

The heart is the main organ responsible for pumping out blood to the cells in our bodies and to the lungs. Figure 3.1 shows a heart with anatomy references.

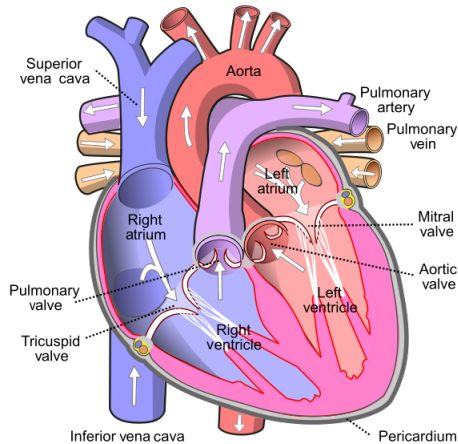


Figure 3.1: Anatomy of the heart (8)

The aortic and mitral valves together with the tricuspid valve and the pulmonary valve make up the four valves of the heart. They open and close in a certain order synchronised with the contractions of the heart and the pressure from the blood. When the blood pressure is high under a valve it causes the valve to open and the blood to flow through the valve. As the blood flows into the atrium and/or ventricle the pressure above the valve increases and the valve close.(9)

The outer shape of the valves is round and the area inside them is made up of cusps, two cusps for the mitral valve, and three cusps for the other valves. When the valves are closed the thin yet strong cusps seal tightly together to prevent blood from flowing backwards. (9)

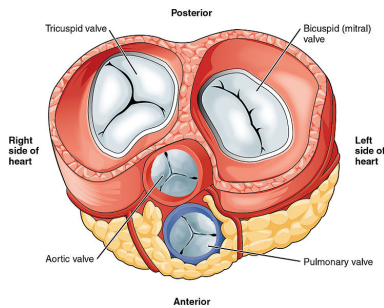


Figure 3.2: Overview of cusps in the valves of the heart, (10)

Methods

Materials

The CT image data used in the work leading up to this thesis originates from the Swedish CARDIOpulmonary bioImage Study (SCAPIS). 30 000 randomly selected men and women, 50-64 years old, participated in the study. Several different tests and examinations related to heart and lung conditions were run on each participant, including for example bloodtests, X-ray images, CT scans, MR scans and ECG. The tests were performed at six different hospitals around Sweden (Lunds universitet/Skånes universitetssjukhus, Göteborgs universitet/ Sahlgrenska Universitetssjukhuset, Linköpings universitet/Universitetssjukhuset i Linköping, Karolinska Institutet/Karolinska Universitetssjukhuset, Uppsala universitet/Akademiska sjukhuset och Umeå universitet/Norrlands universitetssjukhus) with 5000 par-

ticipants at each hospital (7). This work is based on a sample population of the Malmö- cohort of SCAPIS.

Matlab was used as a programming language to write plug-in functions to the software Segment developed by Medviso AB. Medviso AB is a swedish company that works in close collaboration with Lund Cardiac MR Group at Lund University and Skåne University Hospital to develop medical image analysis tools. An advantage of using segment for the project is that several anatomical reference points as well as segmentations and other image analysis tools are already available in the program.

A computer with enough memory and computing capacity for the task was provided by the cardiac MR group.

Calcium Scoring

Volume Score To calculate the volume, in mm^3 of the segmented calcium objects the following equation was used:

$$Volume = NbrOfPixels \cdot ResolutionX \cdot ResolutionY \cdot (SliceThickness + SliceGap) \quad (4.1)$$

Agatston Score The Agatston Score for one (4D) CT image stack is calculated by first creating four empty 4D-single matrices of the same size as the CT image stack, each representing one of the intervals shown in table 4.1.

Matrix	Interval	Weight
1	$130 \leq HU < 200$	1
2	$200 \leq HU < 300$	2
3	$300 \leq HU < 400$	3
4	$400 \leq HU$	4

Table 4.1: Intervals and weights used to calculate the Agatston Score

The sum of the pixels classified as calcium in each matrix, was multiplied with the weight for that specific matrix. The sum of the resulting four products is the Agatston score. (11)

Image Processing

As mentioned above a contrast image stack was used to create a mask(AM-mask) that segments out the area where the valves are located. The coordinates from the contrast image stack is then used in the non-contrast image stack to identify where to look for calcium. The non-contrast image stack consists of images that is going to be referred to as calcium images, since it is in those image calcium is going to be detected if there is any. The images in the contrast image stack is going to be referred to as contrast images.

When creating the AM-mask in the contrast image thresholding was used as a segmentation method. One of the first challenges was to find out what threshold value to use. By analysing the histogram of the intensities (in the contrast image) it was clear that what would be a good choice as a threshold value varied be-

tween different patients, since the brightness between the scans varied. Below, in Figure 4.1, an example of such a histogram is presented.

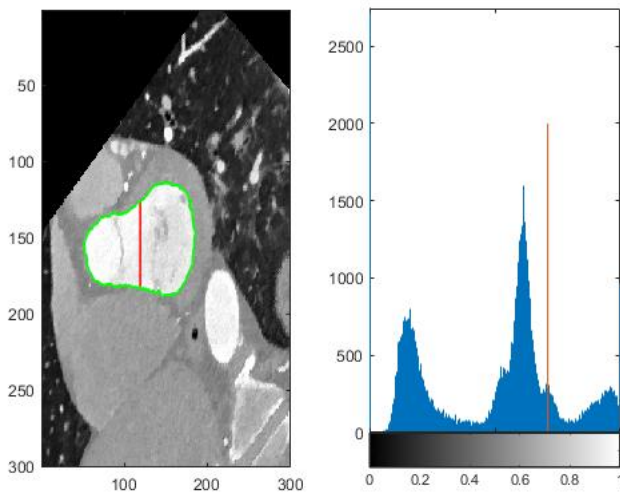


Figure 4.1

Even if the brightness of the scans varied between different patients, the general shape of the histograms was similar. After some experimenting it was clear that the threshold value should be in the right tail of the second last peak, just as the red line shows in Figure 4.1. The location of the threshold line was calculated for each image's histogram by taking the value in between the characteristic large peak (at 0.6 in Figure 4.1) and the characteristic minima (at 0.8 in Figure 4.1). The peak and the minima was found by using matlabs min and max fuctions on the relevant interval of the histogram.

When the threshold value was found it was applied to the contrast image. The left ventricle(LV) was found by using the already existing LV segmentation in the slices where it was possible, and for the other slices where there was no preexisting LV segmentation, the center coordinates from the last(most basal) slice of the preexisting LV segmentation was used as a reference point. A mean value of the 'radius' of the LV in four different directions was calculated and then a point P one mean radius to the left of the reference mean coordinates was selected. P was used to find the LV and left atrium(LA) in the following manner. Out of the large objects to the right of P (large object being the upper half, with respect to size, of all objects to

the right of P) the object with a center point closest to P was selected as the LV. In the same way, but to the left of P, the LA was selected.

Figure 4.2 shows some examples of what the AM-mask looks like. Before the AM-mask is transformed and applied to the calcium image it is dilated with square structuring element whose width is 20 pixels to ensure that no part of the valves are left out in case the segmentation is not perfect.

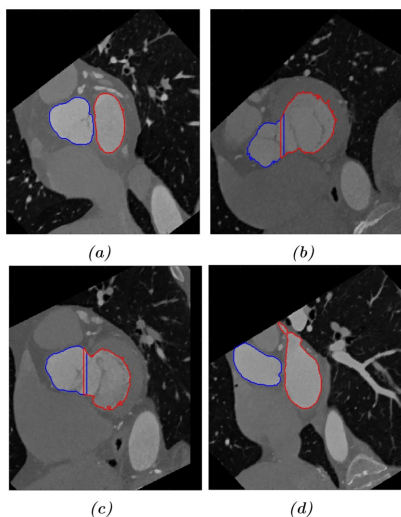


Figure 4.2: *Examples of AM segmentation masks*

It is important that the AM-mask is applied to the relevant images in the image stack, where the mitral and aortic valves are located. To find their location the pre-existing segmentation of the left ventricle was used as a reference for when to apply the AM-mask. The AM-mask was applied to 8 slices before the first slice of the pre-existing LV segmentation and to 8 slices after the first slice of the pre-existing LV segmentation, since the mitral and aortic valves was found to be located within this slice interval. When the CT image stacks are loaded into segmentct they are organised so that the first slice is closest to the base of the heart and the last slice is closest to the apex.

To identify calcium the intensities in the calcium image is translated to Hounsfield units, HU, and then, by using a threshold value of 130 HU, the image is thresholded to get a mask for the calcified areas. In order not to risk counting noise as calcium, areas smaller than 3 mm^3 was excluded from the calcium mask.

Finally, the AM-mask was applied on the calcium mask to obtain the calcified areas within the mitral and aortic valves.

Validation

To validate the results of this project 49 images was compared to a calcium scoring made by a physician, Ellen Ostenfeld, in the clinical software syngo.via. Also, 100 preview images and resulting scores should be controlled by Ellen. The preview slices consisted of slices from the middle of the segmentation slices (every other slice was picked to cover a larger volume), they also included one of the most cranial slices of the segmentation (the first frame in the preview image) as well as one of the most caudal slices of the segmentation (the last frame in the preview image). The resulting scores were also included in the preview images. Figure 4.3 show one of the preview images.

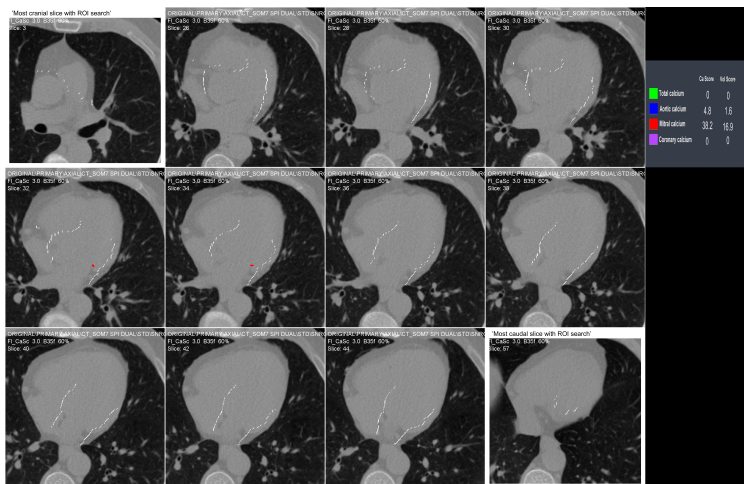


Figure 4.3: Example of a preview image

Sensitivity and specificity was used as a way to rate the performance of the final program. In an article (12) written by Shavelle DM it is suggested that an Agatston score of e.g. ≥ 150 could be used to differentiate patients of risk for aortic stenosis. This value was used as a guideline and then some error margin was added, so that ultimately a score of 100 Agatston units was used in this project to determine the true positives(TP), false positives(FP), true negatives(TN) and false negatives(FN) could be determined in order to calculate the

$$sensitivity = \frac{TP}{TP + FN} \quad (4.2)$$

and

$$specificity = \frac{TN}{TN + FP} \quad (4.3)$$

Results

Figure 5.1 shows a few examples of what the segmentation looks like in the short axis view, where it is created. As mentioned before the segmented area is then dilated with 20 pixels to be on the safe side that no part of the aortic and mitral valves are left outside the segmentation.

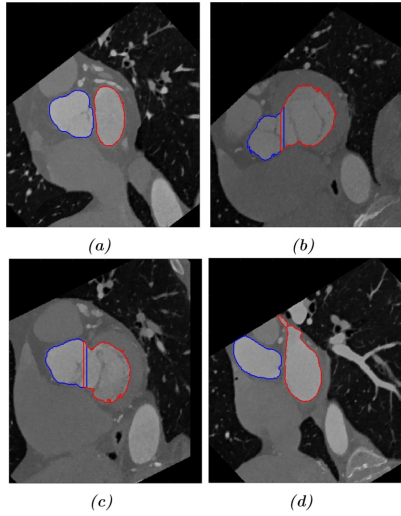


Figure 5.1: Examples of AM segmentation masks

Results from the preview images

From Table ?? , see appendix, the following main results were deduced:

1. Out of 100 preview images 33 of them had registered noise as calcium
2. All of the most cranial slices looked ok, meaning the segmentation ends outside the valve, but not too far up in the aorta.
3. All except one (99/100) of the most caudal slices looked ok, the one that did not look ok had a too large segmentation that included the vertebrae.
4. The outer segmentation was good in 86 of the postcards, not so good in 13 of the postcards(see the additional comments in the Table 4.3), and in one case it was hard to tell whether the outer segmentation was good or not.
5. 61 preview images out of 100 needed editing or at least a closer look to check up on something.
6. 2/100 had registered calcium in the coronary arteries, which is outside the valves.

7. The division between the aortic and mitral valves was good in 72 of the postcards, in 10 cases something needed to be edited and in 18 cases it was unclear whether editing was needed or not. (Meaning, there was registered calcium in the slices that was not included in the postcards).
8. None of the postcards had outer segmentations that included the liver (An earlier version of the program had failed in this way on some slices, which is the reason for this question to be included)
9. 1/199 of the preview images had missed calcium due to the aorta segmentation being too small.

Results of the developed algorithm compared to syngo.via

The results from the developed algorithm were compared to the results from syngo.via as a way to validate the developed algorithm's results. Remember the difference that the developed algorithm counts **all** objects within the segmented area that fulfills the requirements of being brighter than 130 HU and larger than 3 mm^3 (which is going to contain noise) while in syngo.via the user manually picks out the objects that should be counted, why an overestimation of calcium is expected in the developed algorithm. Results from syngo.via and results from the Ca-scoring algorithm developed in this project are presented in Table 1.

The following results has been deduced from Table 1 (see appendix).

When the developed algorithm total score was ≤ 10 (23 cases), the syngo.via total score was ≤ 1 in 22 of those cases. For the one that was not ≤ 1 the developed algorithm total score was 4.6 and the syngo.via total score was 5.4.

When the developed algorithm total score was 0 (12

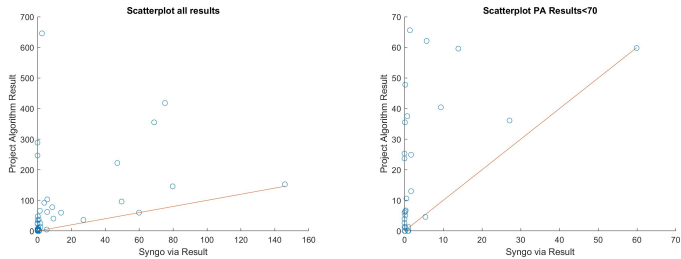
cases), the syngo.via total score was 0 in 9 of those cases. The ones that were not 0 in syngo.via were ≤ 1 .

		PA	
		-	+
Syngo via	-	41	7
	+	0	1

Figure 5.2

Figure 5.2 shows the TP, FP, TN and FN value extracted from Table 1. The resulting sensitivity becomes $\frac{1}{1+0} = 1 = 100\%$ and the resulting specificity becomes $\frac{41}{41+7} = 0.854 = 85.4\%$

In Figure 5.3a a scatter plot of the results of the 50 values from syngo.via and the developed algorithm is presented. Figure 5.3b shows the same scatterplot but with developed algorithm values larger than 100 (and their corresponding syngo.via results) omitted to get a better view of what is going on in the cluster around zero where a lot of the values are located.



(a) Scatter plot with all results from syngo.via and the developed algorithm (b) Scatter plot 5.3a with extreme values larger than 70 removed

Figure 5.3

Figure 5.4 shows a Bland-Altman plot of the 50 results from syngo.via and the developed algorithm.

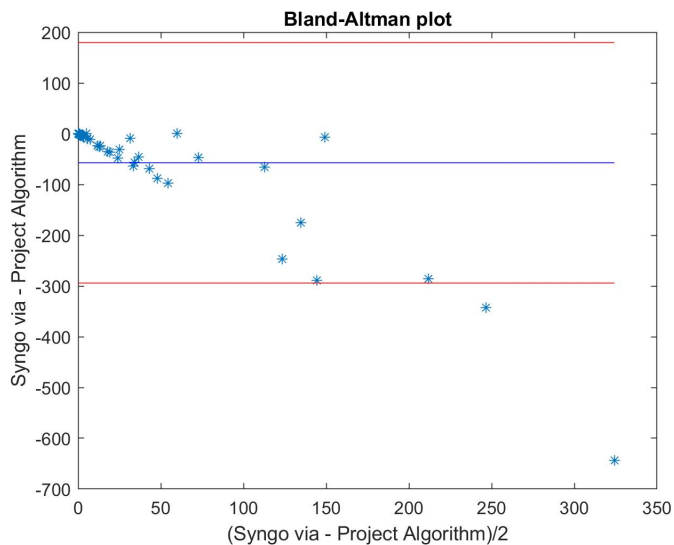


Figure 5.4: Bland-Altman plot with the results from syngo.via and the developed algorithm

Manually Corrected Algorithm

Figure 5.5 show a scatter plot similar to Figure 5.3a above, but with the manually corrected developed algorithm values on the y-axis. A manual correction of the developed algorithm was made to be able to compare with syngo.via where the calcium is manually labeled.

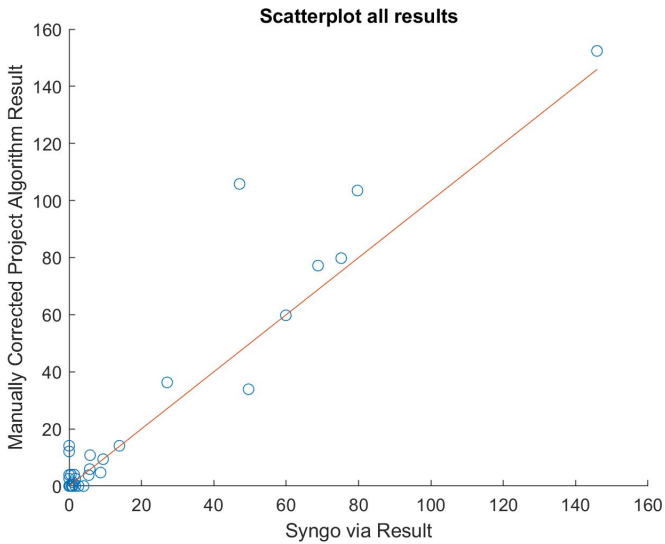


Figure 5.5

In the same way, Figure 5.4 shows a Bland-Altman plot of the 50 results from syngo.via and the manually corrected developed algorithm.

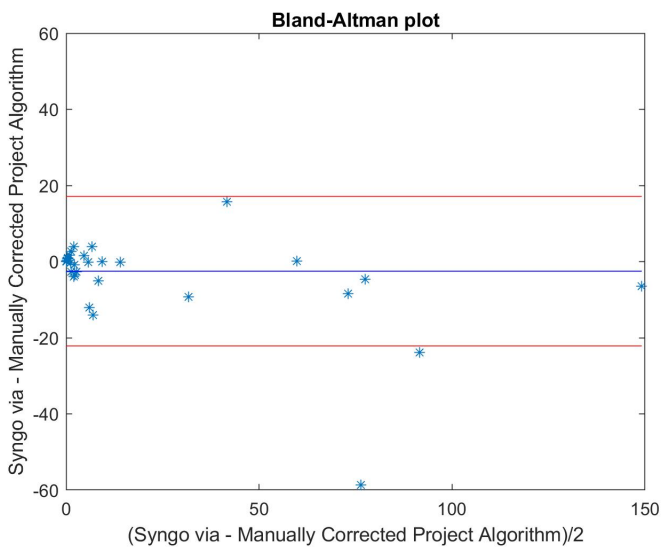


Figure 5.6: Bland-Altman plot with the results from syngo.via and the manually corrected developed algorithm

Results of the 506 files

This section describes the results from when the developed algorithm was applied on the large set of 506 image files. Out of the 506 files, the developed algorithm was not able to create a score on 226 files. This was because 199 of them did not have a calcium image, and 27 of them did not have a contrast image. For the remaining 280 files, 40 of them (i.e. 14 %) scored over 100 Agatston units.

Interface and functions

One of the requirements was for the user to be able to go in and correct the classifications in case the algorithm classified the calcium wrongly. For that purpose several different buttons and functions were implemented in the user interface of `segmentct`. Figure 5.7 shows the user interface and the buttons implemented in this project.

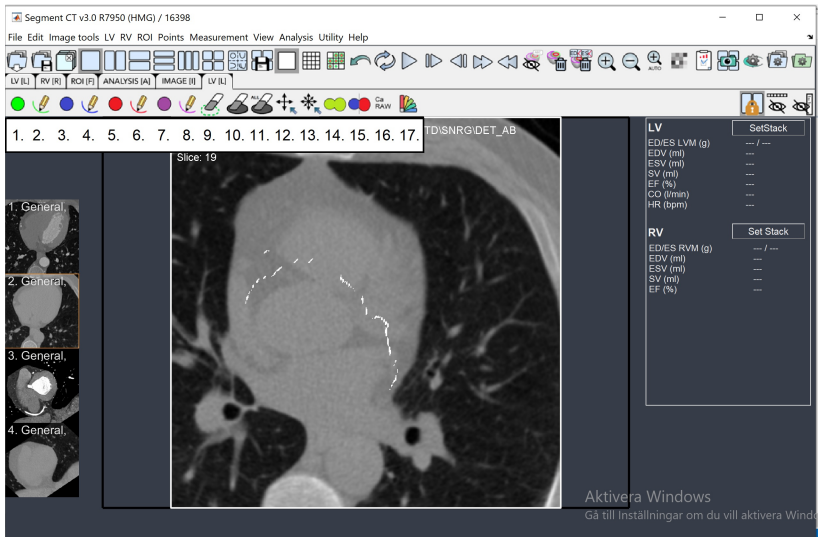


Figure 5.7

The added numbers 1-17 in Figure 5.7 are connected to the numbers in the list below which describes the functions of the different buttons above the numbers.

1. Add object(3D) to total/aortic/mitral/coronary calcium scoring
2. Add region(2D) to total/aortic/mitral/coronary calcium scoring
3. Remove region(2D) from calcium scoring
4. Remove all calcium scoring from this slice
5. Remove all calcium scoring from all slices
6. Translate Scale (These were already existing functions in Segment
7. Find calcium and show outer segmentation
8. Split outer segmentation into mitral and aortic segmentation
9. Make a 'raw' calcium scoring without aortic and mitral-segmentation
10. Show color map and calcium scores in a separate window, shown in Figure 5.8

The image shows a screenshot of a software window titled "cagu". The window contains a table with four rows and three columns. The columns are labeled "Ca Score" and "Volume Score [mm³]", with the first column listing categories. Each cell in the table contains a numerical value.

	Ca Score	Volume Score [mm ³]
Total calcium	187.1	556.9
Aortic calcium	89.4	265.8
Mitral calcium	97.7	291.1
Coronary calcium	0	0

Figure 5.8

Discussion

Summary

The results of this project shows that the developed algorithm performs quite well, but it overestimates the calcium findings due to noise and calcificated coronary arteries that got included in the mask when the mask was dilated. Therefore, the aim of being able to solve the question of what is normal or deviating amounts of calcium in the valves with good accuracy, was not fulfilled with the completely automated developed algorithm. However, a semi-automated alteration was also made (the manually corrected developed algorithm) and it can be used to fulfill that aim, if a physician takes the time to go through and correct the scorings of the developed algorithm. This is similar to the work that physicians do today in syngo.via, but, provided that we trust the low scores of the developed algorithm,

that would reduce the cases that need to be opened up for manual correction with more than 80% (83.7% in this cohort). Instead, sensitivity and specificity was calculated based on the limit value 100, classifying those with a score ≥ 100 to be at risk/need further check up. With a sensitivity at 100 % and a specificity at 85.4 % the project shows promising results, even though a larger image material should be evaluated in order for the results to be more reliable.

However, the aim of being able to quantify the calcium in mm^3 was fulfilled, for the sake of clarity only the Agatston scores are listed in the tables under Result, but the volume scores can be extracted from the method as well, see Figure 5.8. The syngo.via results were in Agatston Units, so the volume scores are not really used for anything here, why they were omitted.

In the sections below, potential sources of error, deviant results and challenges of the project are discussed more in depth, as well as what the future work relating to this project would be.

Limitations of the project

To be able to identify where in the image stack the valves are located an identical image stack, the contrast image stack, were used in which the patient was injected with contrast solution intravenously prior to the image sequence was taken. Sometimes there is a mismatch between the speed of which the heart pumps the contrast solution through the heart and the speed of which the contrast images are taken. In those cases there is a risk of getting a bad segmentation- if the segmentation is not bad enough for the method to catch that something is wrong.

The voxel size could be a possible limitation. In this project the resolution was always as good as or better than the resolution used in (11). The standard standard slice thickness is 3 mm when calculating the Agatston score. In this project, CT scans with a slice thickness ≥ 3 mm were normalised to 3 mm. The calcificated area in each slice is measured in mm^2 , so differences in x and/or y resolution will not be a problem.

Restrictions added during the project are for instance the threshold value used for making the segmentation, and different specifications in the code of how to pick

out the right object after thresholding.

Potential Errors of the developed algorithm

Potential errors are discussed below:

- One of the challenges during this project has been to locate the mitral and aortic valves in the image stack, ie which slices to look at. As described above solution used in this project is to look at ± 8 slices (i.e 2.4 cm) from the first slice in the LV segmentation which me and my supervisors thought should cover all cases. But also locating the valves within each slice, making a good automated segmentation, has been a challenge in some cases. Even though the interval of ± 8 slices used in the project should cover all potential variations anatomy wise there is still a risk that it doesn't get all the valve slices if, for example, there is someone with a very big heart.

-When it comes to the threshold value for the segmentation a quite thorough solution was implemented where the histogram of the image was analysed. The threshold value was chosen as the the value in between the characteristic large peak (at 0.6 in Figure 4.1) and the characteristic minima (at 0.8 in Figure 4.1). One could

discuss whether the optimal value is really in the middle of those characteristic maxima/minima or if it is for example at $2/3$. There could be that the optimal value changes throughout the image stack, which would then affect the segmentation for some of the slices. However the segmented area is then dilated quite much to be on the safe side that the whole area of interest is inside the final segmentation. So the effect of not hitting the optimal value exactly should be small compared to how much the area is later dilated.

Transferring segmentation from short axis image to transversal image

The pixel size also matters when it comes to moving between different image stacks. The segmentation of the mitral and aortic valves is made from a short axis stack that is resampled from the original DICOM file which is a transversal stack. In the early stages of developing the method the intent was to be able to apply the method (AM segmentation and calcium scoring) on both image stacks. However, the calcium score didn't end up to the same value in the two stacks. After extensive debugging the problem seems to be outside my method, most likely when the transversal stack is

resampled into a short axis stack. In Figure 6.1 an attempt to visualise the problem has been made. The black boxes represent voxels in the transversal plane. They are square in the xy-plane but have a large slice thickness. The ratio between the x/y values and the slice thickness is about 5. (The figure is not made to scale but is just trying to show the principle)

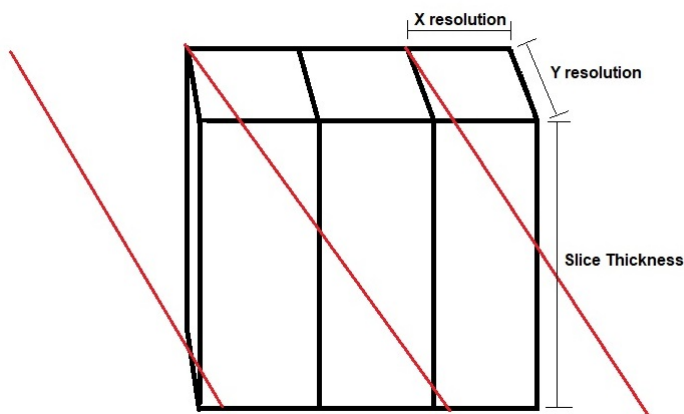


Figure 6.1: Schematic figure of the resampling process

The red lines represent the new image view plane, ie how the short axis image voxels should be represented. The voxels in the images are highly an-isotropic ($x \cdot$

x · 3 mm) and the new voxel orientation means that it cuts through several voxels in the transversal plane. Hence the value of the new voxel is some sort of mean value of the transversal voxels it cuts through and this is most likely the cause of the error I got.

While debugging the masks were of course also checked. The difference between the image stacks were a few hundred pixels which is about 1 % of the total mask volume, which is acceptable. (Remember that the masks are also dilated so the risk of not getting the whole valves is minimal) However, when it comes to the calcium findings the volumes are so small that a hundred voxels are a much larger percentage of the volume and therefore becomes a problem. The conclusion from this is that it works to create the mask on the contrasted short axis stack and apply it on the transversal stack (and on the short axis stack as well), but, it does not work to detect calcium in the short axis stack- only in the transversal stack which is the original DICOM file.

Analysing Table 1

In the paragraph below follows some discussion of deviant results in Table 1.

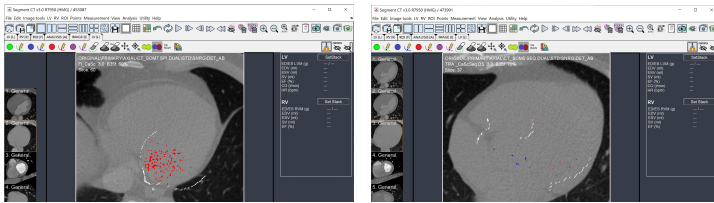
Another result in Table 1 that stands out is file 483946. The reason why it has such a high score in the developed algorithm is that there is a lot of noise and there is calcium included in the segmentation that is outside the valves, for example there is calcium in the aorta.

For file 443312 the result in Table 1 says that the developed algorithm has overestimated the amount of calcium in the valves. When opening up the file in segmentct it's clear that calcium outside the valves has been registered mitral calcium (in the coronary arteries). The preview image for this file did not show the slices where this could be seen why the result for this file in Table 4.3 looks very good.

For file 487044 the result in Table 1 says that the developed algorithm has overestimated the amount of calcium in the valves. When opening up the file in segmentct it's clear that calcium outside the valves has been registered, both mitral and aortic calcium in the coronary arteries. The preview image for this file also

showed calcium in the coronary arteries but no noise, as can be seen in Table 4.3.

The two files 473991 and 453087 also over classifies. Both of them has a lot of calcium, which is shown in Figure 6.2



(a) file 453087

(b) file 473991

Figure 6.2

Analysing Table 2

When it comes to the method of creating preview images to be able to go through the results fast there was both pros and cons of this method. The pros were that a lot of measurable data was collected in a relatively short amount of time once the scoring was done. The cons was that since the preview images consisted of quite few slices, a lot of information was left out. This

is also reflected in the additional comments in Table 2 where many of the comments are about not being able to tell if the segmentation is correct or not.

One of the results from Table 2 two preview images had registered calcium in the coronary arteries. The coronary arteries are located very close to the valves in the image, so it is not surprising that they ended up inside the segmented area when the AM-segmentation was dilated.

One of the preview images (filename 516749) had missed calcium in the valves. When investigating the reason behind this result afterwards it was found that a couple of slices of the aorta segmentation were deleted since the segmentation was too big. The lines in the code that made this was originally written to prevent the program from counting slices where too much of the aorta had been included in the segmentation (since that was supposed to imply that the slice was not including the valve).

Challenges in manual classification based on preview images

Several files that had additional comments in Table 2 were opened up afterwards to take a closer look on the segmentation to be able to tell if something went wrong or if it was just the preview image that did not provide enough information. In most cases the segmentation had done what it was supposed to do (except the case with the catch statement mentioned above) in the short axis view. So what is the cause of the additional comments then? One reason to why it is hard to tell sometimes if the segmentation is good or not is that the outer segmentation is discontinuous in the transversal view. It is continuous in the short axis view where it is created, but when it is resampled to the transversal view it becomes discontinuous. It makes it harder to tell what is inside the segmentation and not. In some(few) cases the segmentation looks like it is shifted a little bit to the right for example. But when looking at the segmentation in the shortaxis view it looks good. In those cases the most likely explanation is that the patient moved between the scan with contrast solution and the calcium scan.

Analysing plots

The resulting scatterplots in Figure 5.3 implies the same thing as the Total Difference column in Table 1, and that is that the developed algorithm overestimates the presence of calcium. In Figure 5.3 this is the case since more or less all dots are above the red reference line $y=x$.

From Figure 5.4 a conclusion can be made that in general the developed algorithm is more accurate the smaller the resulting calcium score. Figure 5.4 also confirms that the developed algorithm overestimates, since all values are negative. `syngo.via` vs manually corrected developed algorithm In figure 5.5 more of the low values in `syngo.via` are low in the manually corrected developed algorithm as well. Which implies noise and/or registrations outside the valves was reduced. Most of the values are close to the reference line $x=y$, but there are about 5 cases that were not very close to the reference line, that is, cases where the manually corrected developed algorithm did not correlate with the `syngo.via` result. This could most likely be explained by me not being a physician, I find it hard to tell when the valves actually begin and end, especially

in the transversal view plane. In noisy images it is also very hard to distinguish noise from small calcium findings, so that might also be a reason. But over all the results from the manually corrected developed algorithm looks better than the developed algorithm without manual interference.

When it comes to the Bland-Altman plot with manually corrected developed algorithm values, Figure 5.6, it is clear that the mean value is closer to zero, which is good, and the standard deviations is about 1/10 of what it was in Figure 5.4 where there was no manual interference, which is also a very good improvement.

Conclusion

The developed algorithm, which is based on image analysis, works for identifying and quantifying calcium in the mitral and aortic valves. It is more reliable for low scores, since noise is included in the segmentation, in contrast to manual methods where only the calcium findings are counted. Despite that, the fully automated developed algorithm ended up with a sensitivity of 100 % and a specificity of 85.4 %.

The developed algorithm can be used to sort out files that need to be controlled manually. When a limit score of 100 Agatston units was used the number of files that required manual control decreased with about 80-85 % in this cohort.

Future Work

To improve this method and being able to use this in reality, more extensive testing of the method would be needed. The preview images did not provide as precise information as intended, so perhaps all of those files would need to be opened manually to be able to really tell if the segmentation for the files was successful or not. It would also be desirable with a continuous edge in the transversal view, so some future work with the visual presentation would also be needed.

Also, the manual correction in this project was made by me, an engineering student, and the scoring in syngo.via was made by Ellen Ostenfeld who is a physician. So having a physician do the manual corrections for the developed algorithm results and then compare if the difference between the programs is in parity with the difference between different users is an important step

in the future work of this method.

The idea of using machine learning(ML) to train the method at making a good segmentation and telling what is noise and what is not, is very tempting. There is also quite likely that a ML algorithm would learn to recognise the expected shape of the valves and the location of the coronary arteries, leading to less wrong registrations inside the segmentation. However, that would require a large material of manually segmented cases to train on, which was not available for this project.

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Appendix A

Filename	syngo.via			Developed algorithm			Total Difference
	Aorta	Mitral	Total	Mitral	Aorta	Total	
345575	0	0	0	0	0	0	0
349484	0.7	0.3	1	0	0	0	-1
350433	0.1	0.1	0.2	0	0	0	-0.2
353614	35	24.9	59.9	35.8	24	59.8	-0.1
257421	0	0	0	0	0	0	0
361473	1.4	67.4	68.8	43.2	311.8	355	286.2
362470	0	0	0	0	0	0	0
363502	8.5	0.2	8.7	72.9	4.7	77.6	68.9
378834	0.1	0	0.1	23.2	12.3	35.5	35.4
387549	0	0	0	3.2	2.8	6	6
388489	0	0.2	0.2	1.2	0	1.2	1
395729	0.6	0.3	0.9	0	0	0	-0.9
398270	0	0	0	13.2	12.1	25.3	25.3
403037	9.4	0	9.4	8.3	32.1	40.4	31
407463	5.4	0	5.4	1	3.6	4.6	-1.1
410191	0.3	0	0.3	6.7	0	6.7	6.3
415515	2.7	3	5.7	58.3	3.8	62.1	61.8
427891	79.4	0.3	79.7	0	145.7	145.7	66
430199	93.2	52.7	145.9	90.1	62.3	152.4	6.5
430771	0.8	0.9	1.7	23.9	1	24.9	23.2
433132	0	0	0	0	0	0	0
434185	0	0	0	0	0	0	0
437092	4	0	4	92.1	0	92.1	88.1
440968	25.6	1.5	27.1	0	36.3	36.1	9
443312	47.1	0	47.1	96.8	125.2	222	174.9
452468	1.4	0	1.4	34.2	31.4	65.6	64.2
453087	0.3	2.3	2.6	645.8	0	645.8	643.2
454545	0.1	0.9	1	0.7	0.6	1.3	0.3
458540	0.1	0.1	0.2	47.8	0	47.8	47.6
459351	0	0	0	2.6	0	2.6	2.6
461886	0	0	0	0	2.6	2.6	2.6
462135	0	0.2	0.2	2.3	2.8	5.1	4.9
473991	0	0	0	180.7	65.9	246.6	246.6
481128	1.7	0	1.7	9.3	3.7	13	11.3
482101	0	0	0	0	0	0	0
482366	75.2	0	75.2	323.7	94.4	418.1	342.9
482844	0	0	0	0	0	0	0
483611	13.9	0	13.9	40.8	18.8	59.6	45.7
483946	0	0	0	167.2	121.4	288.6	288.6
487044	4.9	0.9	5.8	32.2	70.9	103.1	97.3
487839	0	0.7	0.7	0	37.5	37.5	36.8
493404	0	0	0	0	0	0	0
494448	0	0	0	0	3.9	3.9	3.9
498249	0	0	0	0	1.3	1.3	1.3
498543	0	0.2	0.2	6.4	0	6.4	6.2
509693	0	0	0	12.1	11.6	23.7	23.7
516215	0	0	0	0	0	0	0
516749	2.2	47.4	49.6	92.7	3.5	96.2	46.6
525285	0.5	0	0.5	10.6	0	10.6	10.1

Table 1

693594	1	1	x	1	x	1	1	0	0	0	0	1	0	
459351	0	1	x	1	x	1	0	0	0	0	0	0	0	
733984	0	1	x	1	x	1	0	0	0	0	0	0	0	
349484	0	1	x	1	x	1	0	0	0	0	0	0	0	
793469	1	1	x	1	x	1	1	0	0	0	0	1	0	
697200	0	1	x	1	x	1	0	0	0	0	0	0	0	
805355	0	1	x	1	x	0	1	0	3	0	0	0	0	missing piece of aorta
360329	0	1	x	1	x	1	0	0	0	0	0	0	0	
378834	0	1	x	1	x	1	0	0	3	0	0	0	0	
357421	0	1	x	1	x	1	0	0	0	0	0	0	0	
454545	0	1	x	1	x	1	0	0	0	0	0	0	0	
363502	1	1	x	1	x	1	1	0	0	0	0	1	0	
438185	0	1	x	1	x	1	0	0	0	0	0	0	0	
482101	0	1	x	1	x	1	0	0	0	0	0	0	0	
704108	1	1	x	1	x	1	1	0	0	0	0	1	0	
410191	1	1	x	1	x	1	1	0	0	0	0	1	0	
494448	0	1	x	1	x	1	1	0	0	1	0	0	0	
826147	0	1	x	1	x	1	0	0	0	0	0	0	0	
498543	0	1	x	1	x	1	1	0	0	0	0	0	0	
462135	0	1	x	1	x	3	1	0	3	0	0	0	0	can not tell if the aorta seg is correct
766661	1	1	x	1	x	1	1	0	0	1	0	1	0	
398270	0	1	x	1	x	1	1	0	0	3	0	0	0	can not tell if the aorta seg is correct
345575	0	1	x	1	x	1	0	0	0	0	0	0	0	
458540	3	1	x	1	x	1	1	0	3	0	0	3	0	
361473	0	1	x	1	x	1	1	0	0	3	0	0	0	
387549	0	1	x	1	x	1	1	0	3	3	0	0	0	can not tell if the aorta seg is correct
388489	0	1	x	1	x	1	0	0	0	0	0	0	0	
427891	0	1	x	1	x	1	0	0	0	0	0	0	0	
430771	1	1	x	1	x	1	1	0	0	3	0	1	0	can not tell if the aorta seg is correct
433032	0	1	x	1	x	1	0	0	0	0	0	0	0	
437092	1	1	x	1	x	1	1	0	0	0	0	1	0	
440968	0	1	x	1	x	1	1	0	1	1	0	0	0	can not tell if the aorta seg is correct
453087	1	1	x	1	x	1	1	0	0	0	0	1	0	
461886	0	1	x	1	s	1	1	0	0	3	0	0	0	can not tell if the aorta seg is correct
482366	0	1	x	0	k	0	1	0	3	3	0	1	0	missing piece of aorta, vertebra partly included in seg
487044	0	1	x	1	x	0	1	1	3	3	0	0	0	coronary arteries included in seg

493404	0	1	x	1	x	1	0	0	0	0	0	0	0	0	
642134	0	1	x	1	x	0	1	0	3	0	0	0	0	0	need more slices of the aorta in the preview image
658039	0	1	x	1	x	1	0	0	0	0	0	0	0	0	
663364	0	1	x	1	x	1	1	0	1	0	0	0	0	0	missing aorta?
698527	1	1	x	1	x	1	1	0	0	0	0	0	1	0	
701697	1	1	x	1	x	1	1	0	0	0	0	0	1	0	
761757	0	1	x	1	x	1	0	0	0	0	0	0	0	0	
809367	0	1	x	1	x	1	0	0	0	0	0	0	0	0	
821524	1	1	x	1	x	1	1	0	0	3	0	0	1	0	
821915	0	1	x	1	x	1	1	0	0	1	0	0	0	0	can not tell if the aorta seg is correct
83348	0	1	x	1	x	1	0	0	0	0	0	0	0	0	

Table 2: Results from the 100 preview images. 1=yes, (0,x)-no, 3-can't tell from the image, *(not the valve)