A PATIENT-SPECIFIC CORONARY DENSITY ESTIMATE

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ABSTRACT

A reliable density estimate for the position of the coronary arteries in Computed Tomography (CT) data is beneficial for many coronary image processing applications, such as vessel tracking, lumen segmentations, and calcium scoring. This paper presents a method for obtaining an estimate of the coronary artery location in CT and CT angiography (CTA). The proposed method constructs a patient-specific coronary density estimate using CTA atlas registration. The method is evaluated by quantifying the overlap of the obtained density estimate with 24 manually annotated centrelines of the lumen. Furthermore, the method is quantitatively evaluated when applied in automatic calcium scoring of the coronary arteries, which is an important risk predictor of coronary artery disease. The obtained results were compared to manual annotations for 170 CT datasets.

Index Terms— Calcium Score, coronary arteries, CT, CTA, atlas, image registration.

1. INTRODUCTION

Cardiovascular diseases (CVD) are the number one cause of death worldwide. It is estimated that by 2030 around 23.6 million people will die from CVD[1]. Detection and quantification of atherosclerosis is essential for risk assessment of the coronary artery disease (CAD).

The imaging modalities of choice for non-invasive quantification of atherosclerosis in the coronary arteries are Computed Tomography (CT) and Computed Tomography Angiography (CTA). Obtaining a strong position estimate of the coronary arteries in CT and CTA data can be beneficial for several coronary image processing applications, such as vessel tracking, lumen segmentations, and the quantification of the amount of calcium, viz. Calcium Scoring (CS).

This paper presents a method for obtaining a density estimate for the position of the main coronary arteries, namely: right coronary artery (RCA), left anterior ascending (LAD) and left circumflex (LCX), in CT and CT angiography data. The method is quantitatively evaluated on CT images by using the density estimate for automatic calcium scoring. Studies have shown that the amount of calcified plaque is directly related to further coronary related events and are also a predictor for CAD[2, 3]. A normal scanning protocol for the assessment of atherosclerosis consist of a low resolution non contrast-enhanced native CT scan and a high resolution contrast-enhanced CTA scan. The native scan is used for calcium scoring whereas the CTA scan is used to visualize the morphology of the coronary lumen and possibly neighbouring soft plaque.

The applicability of the method in CTA is evaluated by quantifying the overlap of the obtained density estimate with 24 manually annotated lumen centrelines. The method is evaluated quantitatively by comparing the results of automatic calcium scoring to manual annotations in 170 CT datasets.

In the remainder of this paper we discuss the construction of the atlas density images and the application of these atlases for building patient-specific coronary density estimates. We conclude with the evaluation results of the proposed method on CTA and CT datasets.

2. METHOD

In an off-line stage, we build a number of CTA atlases with coronary density fields. The steps towards building these atlases, atlas selection, centreline mapping, density field generation and tuning the density fields inside the aorta, are detailed in section 2.1. The application specific details for using the application specific density estimates for calcium scoring are described in Section 2.4.

2.1. Selection of Atlases and Density Estimation

2.1.1. Atlas selection

From a training set of CTA datasets of 95 patients, a total of 10 CTA atlases were selected. We chose CTA datasets to build the atlases, because in CTA images the coronaries are clearly visible due to the presence of contrast agent. The contrast within these images gives a clear depiction of the heart chambers and the main coronary vessels. The selection criteria for the atlases were based on the quality of the images (no blurring and minimal noise), the anatomy of the heart (shape and size) and field of view (large and small). The atlas images that were selected are shown in Fig 1.

2.1.2. Centerline Mapping

Lumen centrelines in the three main coronary arteries (RCA, LAD and LCX) were manually annotated in the remaining 85 CTA datasets. Each of the three manually annotated centrelines (85) were transformed to each of the CTA atlases (10). The transformations (85x10) were obtained by non-rigid registration of the atlases to the CTA images. The 85 CTA data sets were used as fixed images and the 10 atlases as the moving images. After the registration, each of the 10 atlases had 255 centrelines (85 x 3) mapped onto them.

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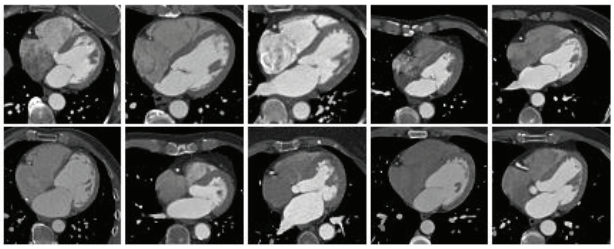

Fig. 1. Axial slices of the 10 chosen atlases. The slices were selected approximately at the centre of the heart.

2.1.3. Atlas Centerline Density Estimation

The coronary density estimate for each voxel of the atlases was determined in the following way. First for every voxel, the closest point on each of the 85 centrelines for each of the three main arteries was determined. Subsequently, Mean Shift [4] was applied to these points. The iterative Mean Shift algorithm is represented as:

$$x^{\tau+1} = \sum_{m=1}^{M} \frac{G_\sigma(|x^\tau - \mu_m|)}{\sum_{m'}^{M} G_\sigma(|x^\tau - \mu_{m'}|)} \mu_m \tag{1}$$

where μ_m represents the m^{th} data point, G_σ a Gaussian kernel with bandwidth σ and x(τ) being the mean shifted position at iteration τ. As the stopping criteria we used (x(τ+1) - x(τ)) $< \varepsilon$. Once all the points had converged to their local mode, the shifted points were clustered based on their mode. In this way, the cluster for each point and the number of clusters was determined.

Next, for each of the clusters the covariance of the points in that mode was determined, and the density at the voxel of interest was calculated by summing the contributions of each of the clusters, where each cluster is represented by a multivariate Gaussian:

$$\begin{aligned} d(x) = \frac{1}{P}\sum_{m} P_m * \frac{1}{(2\Pi)^{\frac{N}{2}} |\mathbf{\Sigma}_m|^{\frac{1}{2}}} \\ * exp(-\frac{1}{2}(x - M_m)^T \mathbf{\Sigma}_m^{-1}(x - M_m)) \end{aligned} \tag{2}$$

with $d(x)$ the density for position x, P the total number of points, P_m the number of points in the mode m, N the dimension (in our case 3), $\mathbf{\Sigma_m}$ is the covariance matrix of all points in mode m and M_m the mean of the mode.

Finally, the obtained density estimates lying within the aorta were reset to zero. The aim of this work is to obtain an automatic density estimate for the location of the arteries. However, due to anatomical variations between patients, the locations of the start of the arteries at the aorta are not always the same. Furthermore, during annotation the observers did not start the annotation exactly at the coronary's ostium. This causes some of the mapped arteries to lie partly in the aorta of the atlas, thereby causing the density estimate to give a high value within the aorta. Therefore, we included a separate automatic aorta segmentation step in our off-line calculation of the density estimates, by updating the density field such that it is zero inside the aorta. The automatic aorta segmentation is based on a multi-atlas based registration approach, which is explained in detail in recent work of Kirisli et al.[5]. The aorta is detected and segmented in all the 10 atlases and the density field is set to zero inside the segmented aorta region.

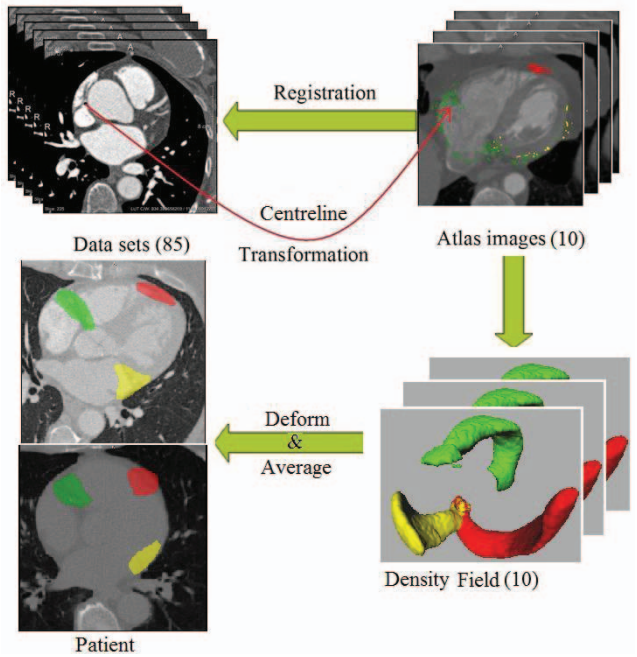

Fig. 2. Schematic representation of the method. Top left: CTA data sets with manual centreline annotation. Top right: Atlas images with mapped centrelines for all 85 datasets. Bottom right: generation of the density field. Green, red and yellow represent the RCA, LAD and RCA respectively. Bottom left: using the density estimate on a patient CTA or CT image.

2.2. Patient specific coronary artery density estimation

In order to obtain a patient specific coronary artery density estimation, the density fields obtained from the atlases are mapped onto either a CTA or CT image. This is achieved by a non-rigid registration of the atlas images to the CT/CTA images, transforming the density fields accordingly, and combining the density fields by averaging them.

2.3. Implementation

All image registrations were performed using Elastix, a publicly available medical image registration software package[6].We used a multi-stage registration approach. Initially a multi-resolution coarse-to-fine affine registration was performed in three steps. For each resolution level we applied 256 iterations of a stochastic gradient descent optimizer[7]. As cost function, the Mean Square Difference (MSD) was calculated using 1028 image samples randomly chosen in each iteration. The results of the affine registrations were used to initialize a B-spline registration. A four step coarse-to-fine strategy was used, with 1024 iterations of a stochastic gradient descent optimizer in each step. A B-spline grid was defined by control points with 20mm separation. The Mutual Information (MI) cost function was calculated using 2048 randomly chosen image samples in each iteration.

For the centreline density estimation, the Approximate Nearest Neighbour[8] was used to determine the closest point on each centreline. To speed up the processing, voxels for which all centrelines further away than 10 mm received a density value of zero. In the Mean Shift clustering ε was set to 0.01 and the bandwidth

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for the Gaussian kernel G_σ was set to 1mm. A small offset of 0.6 mm was added to the diagonal elements of the covariance matrix to guarantee invertability of this matrix. For the calcium score calculation, to avoid noise being detected as a false calcification, the connected components having a volume of less than 0.02 ml were removed.

2.4. Calcium Scoring

The coronary artery density estimate can be used for fully automate calcium scoring. In conventional calcium scoring, first candidate calcifications are selected by thresholding (130 HU) followed by manual removal of false positives.

For our fully automated implementation of the automatic calcium scoring, first a pre-processing step was performed on the CT images. Dense bony structures (ribs, sternum and vertebra) were identified as objects having an intensity above 130 HU and a volume exceeding 1 ml, the intensity of these objects were set to zero. This step was performed to make the method more robust. The density field failed (for one patient) to spatially differentiate the ribs lying very close to the coronaries (especially LAD), thus intersecting the density field. The pre-processing step helped in removing the rib being detected as coronary calcification.

Subsequently, a ROI was obtained for the vessels by averaging the density fields from the 10 atlases, a threshold value of 0.01 was used. This threshold value was empirically found by visual inspection on a separate set of CT datasets. Subsequently, the CT image was thresholded at 130 HU to obtain all the calcifications. Calcium scoring can be performed with several different methods. To evaluate the automatic calcium scoring method on the CT dataset we use the most widely used method, the Agatston score[9]. It is calculated as:

$$AS = \sum_{i=1}^{n} A_i * w_i \tag{3}$$

where i is object's index, A_i is the area of the lesion on the respective slice and w_i the weighting factor of the lesion. The value of w_i is defined by:

$$w = \begin{cases} 1 & 130HU \leq I_i < 200HU \\ 2 & 200HU \leq I_i < 300HU \\ 3 & 300HU \leq I_i < 400HU \\ 4 & 400HU \leq I_i \end{cases}$$

where Ii is the maximum intensity value of the calcification.

The Agatston scores of all the calcifications are summed to obtain the final Agatston score. In the standardized Agatston score, CT images are resampled in the z-direction to produce a slice thickness of 3mm.

3. EXPERIMENTS

3.1. Data acquisition and manual annotations

All datasets used in this study were acquired at the Erasmus MC, Rotterdam, The Netherlands. The scans were acquired on two different CT scanners (Somatom Definition and Somatom Sensation, Siemens Medical Solutions, Forchheim, Germany). A tube voltage of 120 kV was used for both scanners. The CTA images were acquired with ECG dose pulsing[10] and reconstructed with B30f (medium to smooth) or B46f (sharp) convolution kernels. The CTA datasets have an image dimension of approximately 512 x 512 x 350 voxels and a voxel size of approximately 0.35 x 0.35 x 0.4 mm^3. A total of 95 CTA images (10 atlas images and 85 centreline images) and 24 additional CTA images were used for the quantitative evaluation of our method. The manual annotation in the 85 CTA images for the density atlases and 24 CTA images for the quantitative evaluation was performed by trained observers. Details about the manual annotation can be found in[11].

A total of 170 CT datasets were used for the evaluation on CT data. The datasets have an image dimension of approximately 512 x 512 x 87 voxels and a voxel size of approximately 0.35 x 0.35 x 1.5 mm^3. The kernel used for constructing the CT images was B35f (medium smooth).

3.2. CTA evaluation - Centerline detection

The averaged density fields were used on a set of 24 CTA images with manually annotated centrelines to estimate the accuracy of the manual centrelines lying within the obtained field. Statistical analysis was performed on these data sets to determine whether centrelines lie in the field, by using a mask (by thresholding the density field) for the ROI and determine the percentage of centreline in the ROI. The results are shown in Table 1.

3.3. CT evaluation - Calcium scoring

The automatically obtained Agatston scores for the 170 CT datasets were compared to the manually obtained Agatston scores. The scores were found to be linearly related with a Pearson regression coefficient R^2 of 0.88. A scatter plot of the manual versus the automatic scores is shown in Fig 3.

4. DISCUSSION AND CONCLUSION

A method for automatically obtaining patient-specific coronary artery estimates in CTA and CT has been proposed. The results show that the density estimates provide a reasonable estimate for the locations of the main arteries in both CTA and CT images. These estimates can be used for various cardiac image processing applications e.g. fully automated calcium scoring as presented in this paper.

The calcium scoring results are currently still different from the manual quantification, but we believe the method can easily be made more accurate by incorporating a classification technique which could differentiate between a calcium spot and noise by using a appearance feature as presented in[12]. The elegance of the method used for calcium scoring is that it is possible to derive calcium scores per vessel. Reporting the three calcium scores separately is expected to give better insights about the calcified plaque. Other methods that could be used to increase the accuracy of the calcium scoring method would be to use a wider set of atlases, covering more anatomical variations. The density fields can be improved by increasing the number of centrelines being mapped onto the atlases. The application to CTA showed a good overlap of the density estimates with manual annotations.

When inspecting the cases where the automated approach was not very accurate, often the registration of some of the atlases to the patient data had failed. We intend to address this issue by a further tuning of the registration, and by incorporating additional atlases and possibly an atlas selection scheme. We conclude that we presented a method that allows construction of a patient-specific coronary vessel estimate, and showed the application of this estimate in calcium scoring.

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	RCA	LAD	LCX
Min	0.567	0.749	0.327
Max	1.000	1.000	0.949
Avg	0.816	0.914	0.577
SD	0.305	0.177	0.439

Table 1. Percentage of the manually annotated centreline lying within the ROI of the 24 CTA data.

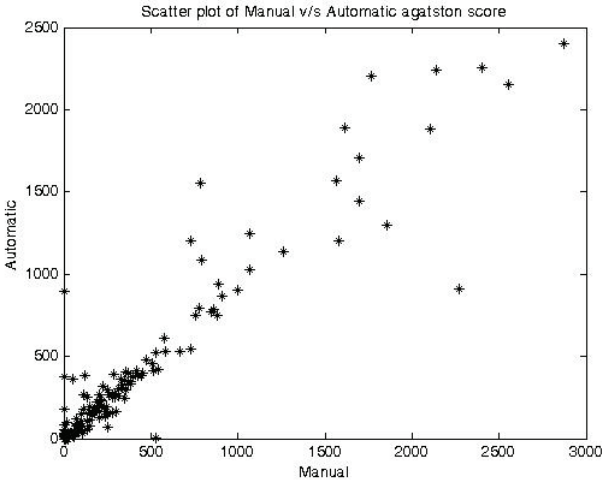

Fig. 3. Scatter plot of the Manual versus the Automatic Agatston scores.

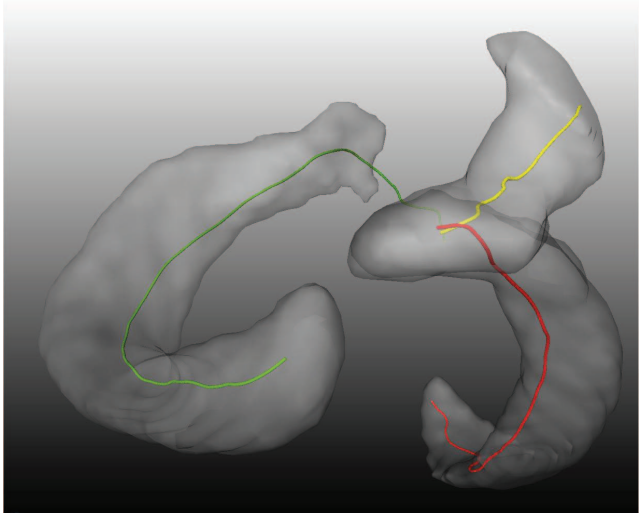

Fig. 4. 3D image of the density fields with the manual centerline passing through it. Green: RCA, Red : LAD, Yellow: LCX

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