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Coronary CT Angiography (cCTA): Automated Registration of Coronary Arterial Trees from Multiple Phases

Lubomir Hadjiiski¹, Chuan Zhou, Heang-Ping Chan, Aamer Chughtai, Prachi Agarwal, Jean Kuriakose, Ella Kazerooni, Jun Wei, and Smita Patel

Department of Radiology, University of Michigan, Ann Arbor, MI 48109, USA

Abstract

Coronary computed tomography angiography (cCTA) is a commonly used imaging modality for evaluation of coronary artery disease. cCTA is generally reconstructed in multiple cardiac phases because different coronary arteries may be better visualized in some phases than in other phases due to the periodic cardiac motion. We are developing an automated registration method for coronary arterial trees from multiple-phase cCTA that has potential application in building a “best-quality” tree to facilitate image analysis and detection of stenotic plaques. Given the segmented left or right coronary arterial trees (LCA or RCA) from the multiple phases as input, the adjacent phase pairs, where displacements are relatively small, are registered by specifically designed method based on cubic B-spline with fast localized optimization (CBSO). For the phase pairs with large displacements, a global registration using affine transform with quadratic terms and nonlinear simplex optimization (AQSO) is followed by a local registration using CBSO to refine the AQSO registered volumes. 26 LCA and 26 RCA trees with 6 cCTA phases from 26 patients were used for registration evaluation. The average distances for the tree pairs between the adjacent phases with small displacements before and after CBSO registration were 0.96 ± 0.79 mm and 0.76 ± 0.61 mm, respectively, for LCA and 0.93 ± 0.97 mm and 0.64 ± 0.43 mm, respectively, for RCA. The average distance differences before and after registration were statistically significant ($p < 0.001$) for both LCA and RCA trees. The average distances for the distant phases with large displacements before registration, after AQSO registration, and finally after the CBSO registration were 2.85 ± 1.46 , 1.62 ± 0.76 , and 0.97 ± 0.43 mm, respectively, for LCA, and 4.03 ± 2.36 , 2.18 ± 1.11 , and 0.97 ± 0.44 mm, respectively, for RCA. The average distance differences between every two consecutive stages of registration were statistically significant. The corresponding phases of LCA and RCA trees were aligned to an average of less than 1 mm, providing a basis for a best-quality tree construction.

Keywords

Computer-aided diagnosis; CT angiography; registration; cubic B spline; optimization; coronary arteries; atherosclerotic plaque

¹Author to whom any correspondence should be addressed. lhadjisk@umich.edu.

1. INTRODUCTION

The accumulation of atherosclerotic plaque in coronary arteries is the main cause for myocardial infarction and death among both men and women. Recent understanding of the nature of atherosclerotic plaques indicates that myocardial infarction is often caused by soft non-calcified plaques that are lipid rich with a thin fibrous cap and therefore prone to rupture. Early detection of soft plaques and treatment may reduce the risk of myocardial infarction.

Coronary CT angiography (cCTA) scans are usually acquired with ECG-gating and reconstructed at multiple cardiac phases. The multiple phases are intended to capture each major coronary arterial segment in a stationary and good-quality state in at least one of the phases because different arterial segments may be blurred in different phases due to heart motion. However, it is time consuming for radiologists [1] or a computer-aided detection (CAD) system to search for atherosclerotic plaques in multiple-phase cCTA volumes. One potential method to increase the efficiency of radiologists or the CAD system is to automatically register the coronary arterial trees from multiple cardiac phases, select the best phase (e.g., sharpest and highest contrast filling) for each arterial segment from the multiple phases and build a best-quality composite tree for image analysis.

Extensive work related to modeling of cardiac motion can be found in the literature. Tavakoli et. al. [2] published a detailed review on the registration and segmentation techniques for various cardiac imaging modalities. Temporal registration of the cardiac images is useful for computation of the regional displacements and mechanical indices of cardiac function. In many of these studies, different registration methods were used to align the dynamic 4D (3D + time) sequence of cardiac images and to extract the non-rigid motion of anatomical objects. The majority performed registration on the entire heart region. More details about these methods were discussed in Tavakoli et. al. [2].

Baka et al [3] proposed 4D registration of the heart using statistical models and landmark points surrounding coronary arteries. These methods were utilized for the 2D+4D registration of xray coronary angiography. Metz et. al. [4] used hand segmented coronary vessels as a guide for 4D registration of the cardiac dynamic sequences.

4D registration of the segmented coronary vessels were proposed in pilot studies by Hadjiiski et. al. [5] and Habert et. al. [6]. In these studies only the segmented coronary trees were used as input to the registration algorithm and only coronary arteries were registered. The estimation of the cardiac motion based on manually or semi-automatically segmented vessels was also used for improvement of the CT reconstruction [7, 8]. Bhagalia et. al. [8] used a coronary registration algorithm (SWA) to improve the image quality of cardiac CT scans as demonstrated in an observer study using nine human cardiac CTA. Motion compensation was achieved by employing a 3D warping of a series of partial reconstructions based on the estimated motion fields. Results from the observer study showed that the SWA method successfully reduced motion artifacts in 75% of all initially nondiagnostic coronary artery segments, and in over 45% of the cases this improvement was enough to make a previously nondiagnostic vessel segment clinically diagnostic.

In the current study, we focused on the development of an automated registration method for coronary arterial trees from multiple-phase cCTA. The coronary arterial trees extracted from cCTA volumes were registered up to six phases. The registration accuracy was evaluated quantitatively over the several stages of registration.

2. MATERIALS AND METHODS

An example of a 3D rendered Coronary CT angiography (cCTA) scans acquired with ECG-gating and reconstructed at 6 cardiac phases (e.g., 80%, 75%, 70%, 50%, 45%, 40%) is illustrated in Fig. 1(a). A volume of interest enclosing the heart region in the cCTA was shown for each phase.

The left coronary arterial (LCA) and right coronary arterial (RCA) trees are partially visible in the 3D volumes. In addition, some pulmonary vessels and portion of the ribs are also visible. In our registration method, we used the coronary arterial trees that have been segmented from the cCTA volume in each phase as input. The segmented coronary trees from multiple cardiac phases are then registered to a single tree in three stages. The challenge for the registration procedure is that the segmented trees may be incomplete due to factors such as image noise, motion blur or poor contrast filling. The proposed registration method is designed to handle incomplete coronary arterial trees that may have missing segments in some of the phases.

2.1 Automated coronary arterial tree segmentation

The focus of this study is on the registration of multiple-phase coronary arterial trees from cCTA. The registration algorithm uses the segmented LCA or RCA trees as input, which can be obtained from any vessel segmentation method. In this study, the LCA and RCA trees were segmented with a vessel segmentation method, referred to as the multiscale enhancement coronary artery response and dynamic balloon tracking (MSCAR-DBT) method previously developed in our laboratory [9]. MSCAR-DBT is briefly described below.

The MSCAR-DBT method includes three major steps: (1) heart region extraction, (2) vascular structure enhancement and (3) segmentation, and coronary artery tracking [9].

The heart region is extracted based on the expectation-maximization (EM) segmentation method [9], which is applied to the body region in the cCTA volume assuming there are two classes of structures in the volume: the lung region containing air as class 1 and all other structures as class 2.

The MSCAR method is designed to enhance the coronary arteries before segmentation. Initially, the VOI enclosing the heart is convolved with the partial second derivatives of 3D Gaussian functions with a range of variances (multiple scales) to cover the coronary arteries of a range of diameters. The eigenvalues of the 3D Hessian matrix are calculated at each voxel of the filtered volume at each scale. A multiscale response function [10] using the eigenvalues of the Hessian matrix was specifically designed to enhance vascular structures including bifurcations and to suppress non-vessel structures.

After vessel enhancement, a 3D dynamic balloon tracking (DBT) method is used to track the coronary arteries. The current DBT tracking algorithm starts at two manually identified seed points located at the origins of the LCA and RCA trees, respectively, to track the LCA and RCA trees. The algorithm automatically places a balloon of a diameter 1.5 times the local segmented vessel diameter at the current tracking point, searches for intersections of the local structure with the balloon surface, identifies potential branches, determines the direction of tracking and the vessel diameter at the next tracking point. The next tracking point, if found, is therefore separated from the current tracking point by a distance of 0.75 times the local vessel diameter and on the voxel closest to the calculated location. The consecutive centerline tracking points in general are separated by a distance larger than a voxel. All the possible branches are labeled and stored in a queue. The algorithm is then moved to the new tracking point. At each tracking point, a similar search process will be performed until the current vessel ends. The above procedure is repeated for each branch until the queue is empty. A continuous centerline is obtained by connecting the neighboring centerline tracking points. The collection of all connected vessel branches originated from the same seed point forms the tree and the centerlines of the vessels are given by the trajectory of the balloon.

In this study, the coronary arterial trees were enhanced with 3D Gaussian filters at four scales corresponding to vessel sizes ranging from 1 mm to 8 mm in diameter. An example of the segmented LCA and RCA coronary arterial trees in 6 phases (e.g., 80%, 75%, 70%, 50%, 45%, 40%) are shown in Fig. 1(b). Both the centerline voxels and all voxels of the segmented vessels on the coronary vessel tree constitute the input to the registration algorithm.

2.2 Automated registration of coronary arterial tree

The automated registration method for the LCA or RCA trees from multiple-phase cCTA consists of two registration modules: (1) cubic B-spline method with fast localized optimization (CBSO) for registration of the adjacent phase pairs of the tree, where displacements are relatively small, and (2) a global registration using affine transform with quadratic terms and nonlinear simplex optimization (AQSO) for the phase pairs with large displacements. The AQSO is followed by a local registration using CBSO to refine the AQSO registered volumes.

2.2.1 Cubic B-spline method with fast localized optimization (CBSO)—This registration is an iterative algorithm, in which a free-form deformation (FFD) based on CBSO is applied in each iteration to the tree being registered. The updating of the local parameters (control point positions) is guided by the minimization of a cost function. The cubic B-spline based FFD is a locally controlled transformation model and is computationally efficient even for a large number of control points [11, 12].

Let Φ denote a $n_x \times n_y \times n_z$ mesh of control points $\varphi_{i,j,k}$ [11]. The control point $\varphi_{i,j,k}$ is placed at the ijk^{th} position of the mesh. The spacing of the mesh in the x , y , and z directions is denoted by δ_x , δ_y , and δ_z respectively. The transformation function $T(x, y, z)$ is defined in terms of control points as:

$$T(x, y, z) = \sum_{l=0}^3 \sum_{m=0}^3 \sum_{n=0}^3 B_l(u) B_m(v) B_n(w) \phi_{l+l,j+m,k+n}, \quad (1)$$

where $i = \lfloor x/\delta_x \rfloor - 1$, $j = \lfloor y/\delta_y \rfloor - 1$, $\lfloor z/\delta_z \rfloor - 1$, $u = x/\delta_x - (i + 1)$, $v = y/\delta_y - (j + 1)$, $w = z/\delta_z - (k + 1)$. B_0, B_1, B_2, B_3 are the cubic B-spline basis functions and are defined in [11]. The control points are the parameters of the transformation function and by moving the control points the VOI will be warped.

The mesh of control points for the cubic B-spline is defined within the VOI enclosing the LCA or RCA tree. The spacing of the mesh in the x , y , and z directions is 10 voxels ($\delta_x = 10$, and $\delta_z = 10$). B-splines are locally controlled. Moving the control point $\phi_{i,j,k}$ affects the transformation only in the local neighborhood of that control point.

Cost Function: For every displaced control point, $P_w(i, j, k)$, in the warped volume of interest, VOI_w , a block G with a size of $21 \times 21 \times 21$ voxels is centered at the control point. For every centerline voxel c_h within G , ($c_h \in C_G$), the shortest distance to the centerline of the reference (unwrapped) coronary tree C_U is calculated as:

$$D(c_h, C_U) = \min \{d(c_h, t) : t \in C_U\}, \quad (2)$$

where the function d is the Euclidean distance. Let $t_{h,min}$ be the corresponding voxel on C_U , at which the shortest distance $D(c_h, C_U)$ is found. The x , y , and z components of the difference in the position vectors between the points c_h and $t_{h,min}$ are calculated as follows:

$$\begin{aligned} D_x(c_h, C_U) &= t_{h,min}(x) - c_h(x) \\ D_y(c_h, C_U) &= t_{h,min}(y) - c_h(y) \\ D_z(c_h, C_U) &= t_{h,min}(z) - c_h(z) \end{aligned} \quad (3)$$

and the distance between the two points is given by:

$$D(c_h, C_U) = \sqrt{D_x(c_h, C_U)^2 + D_y(c_h, C_U)^2 + D_z(c_h, C_U)^2}$$

$D_x(c_h, C_U)$, $D_y(c_h, C_U)$, and $D_z(c_h, C_U)$ define both the distance and the 3D direction from c_h to the closest voxel $t_{h,min}$. The distance and direction of displacement $D_x(C_G, C_U)_{i,j,k}$, $D_y(C_G, C_U)_{i,j,k}$, and $D_z(C_G, C_U)_{i,j,k}$ of the control point $P_w(i, j, k)$ is estimated from $D_x(c_h, C_U)$, $D_y(c_h, C_U)$, and $D_z(c_h, C_U)$ of all the centerline voxels in the block G as follows:

The new location of the centerline voxels in the block G are obtained as:

$$\begin{aligned} \tilde{c}_h(x) &= c_h(x) + D_x(C_G, C_U)_{i,j,k} \\ \tilde{c}_h(y) &= c_h(y) + D_y(C_G, C_U)_{i,j,k} \\ \tilde{c}_h(z) &= c_h(z) + D_z(C_G, C_U)_{i,j,k} \end{aligned} \quad (4)$$

The x , y , and z components of the difference in the position vectors between the points $\tilde{c}_h$ and $t_{h,min}$ are then estimated as:

$$\begin{aligned}
D_x(\tilde{c}_h, C_U) &= t_{h,min}(x) - \tilde{c}_h(x) = t_{h,min}(x) - c_h(x) - D_x(C_G, C_U)_{i,j,k} \\
D_y(\tilde{c}_h, C_U) &= t_{h,min}(y) - \tilde{c}_h(y) = t_{h,min}(y) - c_h(y) - D_y(C_G, C_U)_{i,j,k} \\
D_z(\tilde{c}_h, C_U) &= t_{h,min}(z) - \tilde{c}_h(z) = t_{h,min}(z) - c_h(z) - D_z(C_G, C_U)_{i,j,k}
\end{aligned} \quad (5)$$

Therefore,

$$\begin{aligned}
D_x(\tilde{c}_h, C_U) &= D_x(c_h, C_U) - D_x(C_G, C_U)_{i,j,k} \\
D_y(\tilde{c}_h, C_U) &= D_y(c_h, C_U) - D_y(C_G, C_U)_{i,j,k} \\
D_z(\tilde{c}_h, C_U) &= D_z(c_h, C_U) - D_z(C_G, C_U)_{i,j,k}
\end{aligned} \quad (6)$$

$$D(\tilde{c}_h, C_U) = \sqrt{D_x(\tilde{c}_h, C_U)^2 + D_y(\tilde{c}_h, C_U)^2 + D_z(\tilde{c}_h, C_U)^2} \quad (7)$$

Finally, the position components, $D_x(C_G, C_U)_{i,j,k}$, $D_y(C_G, C_U)_{i,j,k}$, $D_z(C_G, C_U)_{i,j,k}$, of the control point $P_w(i, j, k)$ are obtained when the cost function, given by the average of the squared distances, is minimum:

$$ED(C_G, C_U) = \frac{1}{2} \frac{1}{N_G} \sum_{h=1}^{N_G} D^2(\tilde{c}_h, C_U), \quad (8)$$

where N_G is the number of the centerline voxels within the block G . The minimum is calculated by applying the least squares method:

$$\begin{aligned}
\frac{\partial ED(C_G, C_U)}{\partial D_x(C_G, C_U)_{i,j,k}} &= 0 \\
\frac{\partial ED(C_G, C_U)}{\partial D_y(C_G, C_U)_{i,j,k}} &= 0 \\
\frac{\partial ED(C_G, C_U)}{\partial D_z(C_G, C_U)_{i,j,k}} &= 0
\end{aligned} \quad (9)$$

As a result, the distance and the direction of the displacement of the control point $P_w(i, j, k)$ are equal to the average of the shortest distances and the directions over all the centerline voxels in the block G :

$$\begin{aligned}
D_x(C_G, C_U)_{i,j,k} &= \frac{1}{N_G} \sum_{h=1}^{N_G} D_x(c_h, C_U) \\
D_y(C_G, C_U)_{i,j,k} &= \frac{1}{N_G} \sum_{h=1}^{N_G} D_y(c_h, C_U) \\
D_z(C_G, C_U)_{i,j,k} &= \frac{1}{N_G} \sum_{h=1}^{N_G} D_z(c_h, C_U)
\end{aligned} \quad (10)$$

The average distance between the centerline C_G of the warped vessel tree within block G and the centerline C_U of the reference (unwrapped) vessel tree is calculated as:

$$D(C_G, C_U) = \frac{1}{N_G} \sum_{h=1}^{N_G} D(c_h, C_U) \quad (11)$$

Optimization: Based on the estimation in Eq. (10), the control point $P_w(i, j, k)$ is moved to the new location at the next iteration $L+1$:

$$\begin{aligned} \phi_{(x),i,j,k}(L+1) &= \phi_{(x),i,j,k}(L) - D_x(C_G, C_U)_{i,j,k} \\ \phi_{(y),i,j,k}(L+1) &= \phi_{(y),i,j,k}(L) - D_y(C_G, C_U)_{i,j,k} \\ \phi_{(z),i,j,k}(L+1) &= \phi_{(z),i,j,k}(L) - D_z(C_G, C_U)_{i,j,k} \end{aligned} \quad (12)$$

By moving the control point $P_w(i, j, k)$ as specified above, the distance $D(C_G, C_U)$ between the centerlines of the coronary vessels in G and the centerlines of the reference tree C_U is reduced. This process is repeated for all control points of the warped VOI. After all the points are moved to their new locations, the cubic B-spline is calculated based on the moved control points to obtain the new warped VOI_w.

The movement of the cubic B-spline control points is regularized. The relative displacement of the control points is limited by overlapping the blocks G positioned on the neighboring control points, reducing the occurrence of folding in the displacement field. In addition, if the average distance in Eq. (10) is larger than 30 voxels in any of the x , y or z directions the update of the control point location is not performed. This constraint is imposed during every iteration.

The average distance between the centerlines of the warped C_W vessel tree and the reference (unwrapped) C_U vessel tree is calculated based on the Euclidian distance:

$$D(C_W, C_U) = \frac{1}{N_W} \sum_{h=1}^{N_W} D(c_h, C_U), \quad (13)$$

where $c_h \in C_W$, and N_W is the number of the centerline voxels of C_W within VOI_w. $D(C_W, C_U)$ is used as a registration quality index for the CBSO registration. A smaller value of $D(C_W, C_U)$ corresponds to better quality and higher accuracy of the registration. The minimization of the local cost $ED(C_G, C_U)$ by the localized optimization reduces $D(C_G, C_U)$, which, in turn, will lead to a reduction in $D(C_W, C_U)$.

This localized optimization process is repeated for a fixed number of iterations, large enough to reach convergence. In our application, 9 iterations are used. At the end of the iterative procedure, the final registration quality index $D(C_W, C_U)$ is recorded as a measure of the accuracy of the CBSO registration.

The more complete segmented tree, i.e., the tree with a larger number of centerline voxels (larger N_w) was selected to be the reference (unwrapped) tree.

An illustration of the CBSO registration of the LCA and RCA trees in 6 phases is shown in Fig. 2 and Fig. 3, respectively. For the LCA tree in Fig. 2, the corresponding trees in phase

70% and 80% were registered first. The phase 75% tree was then registered to the combined tree from phases 70% and 80%. For the RCA tree, the trees in phase 45% and 50% were registered first and then the tree in phase 40% was registered to the combined tree (45%-50%). For the RCA tree in Fig. 3, the corresponding trees in adjacent phases (70%, 75%, and 80%) and (40%, 45%, and 50%) were registered, similar to the registration of LCA trees in adjacent phases shown in Fig 2.

2.2.2 Affine transform with quadratic terms and nonlinear simplex

optimization (AQSO)—An affine transform with quadratic terms and nonlinear simplex optimization (AQSO) is designed to register the trees between phases with large displacements, namely, registering the combined tree from phases 80%, 75%, and 70% to that from phases 50%, 45%, and 40% (Fig. 2 and Fig. 3).

Second order polynomial is used as a spline warping function:

$$\begin{aligned}x' &= a_9x^2 + a_8y^2 + a_7z^2 + a_6xy + a_5xz + a_4xy + a_3x + a_2y + a_1z + a_0 \\y' &= b_9x^2 + b_8y^2 + b_7z^2 + b_6xy + b_5xz + b_4xy + b_3x + b_2y + b_1z + b_0 \\z' &= c_9x^2 + c_8y^2 + c_7z^2 + c_6xy + c_5xz + c_4xy + c_3x + c_2y + c_1z + c_0,\end{aligned}\quad (14)$$

where x' , y' and z' are the coordinates of a voxel in the warped VOI_w and x , y and z are the coordinates of the corresponding voxel in the un-warped VOI . The constants a_i , b_i , c_i , $i=0, \dots, 9$ are coefficients of the polynomials, which are determined by the optimization procedure described below. The transformation is applied to every voxel in the un-warped VOI .

For every segmented voxel p_h of the warped coronary vessel tree V_w , ($p_h \in V_w$), the shortest distance to the segmented voxels of the reference (unwrapped) coronary tree V_U is calculated as:

$$D(p_h, V_U) = \min \{d(p_h, t) : t \in V_U\}, \quad (15)$$

where the function d is the Euclidean distance. The cost function for optimization is determined as a sum of the shortest distances of all segmented voxels of the warped vessel tree V_w :

$$D(V_w, V_U) = \sum_{h=1}^{N_v} D(p_h, V_U), \quad (16)$$

where N_v is the number of the voxels in the segmented coronary arterial tree within the warped VOI_w . The nonlinear simplex optimization by Nelder and Mead [13] is used to minimize the cost function $D(V_w, V_U)$ by automatically tuning the 30 coefficients of the second order polynomial. We experimentally found that convergence can be reached within 120 iterations in our application. At the end of the registration procedure, the registration quality index $D(C_w, C_U)$ from Eq. (13) is estimated for the AQSO registration. The use of $D(V_w, V_U)$ as the cost function at this AQSO step gives more weights from the thicker, clinically important portions of the vessels in the cost function, thereby registering them more closely and reliably.

Finally, CBSO is applied to the AQSO registered volumes for final refinement and the registration quality index $D(C_W, C_U)$ is estimated again at the final stage.

Both the CBSO and AQSO methods are programmed in C and are executed on a Linux DELL Precision PC with a 3GHz processor and 4GB of memory.

2.3 Data set

The registration performance was evaluated with a data set of 26 LCA and 26 RCA trees in 26 ECG-gated contrast-enhanced cCTA scans from 26 patients. The CTA scans were retrospectively collected from patient files at the University of Michigan Hospital with Institutional Review Board (IRB) approval. The cCTA scans were acquired with GE multidetector CT scanners, 100-120 kVp and 340-790 mA, reconstructed at 0.625 mm slice interval and 0.488 mm in-plane pixel size. The clinical protocol of cCTA in our department reconstructed 6 phases in a range from 40% to 87%. However, in some phases, due to substantial motion artifacts and insufficient opacification, less than 10% of the LCA (or the RCA) tree was segmented compared to the best-segmented corresponding tree in the case. Such an incompletely segmented tree was excluded from registration because the chance that they would contribute good quality arteries for building the best-quality tree was low, and the very sparse tree branches could mislead the registration. The sparsity of the LCA or the RCA tree was evaluated by automatically counting the voxels on the segmented and tracked trees, and the RCA or the LCA tree that did not pass the criterion in a given phase was excluded separately, independent of the other tree. The exclusion criterion was that the number of the voxels on the segmented and tracked tree was less than 200. After exclusion, the data set contained the following: for the segmented LCA trees, there were 16 cases with 6 phases and 10 cases with 5 phases; for the segmented RCA trees, there were 13 cases with 6 phases, 4 cases with 5 phases, 2 cases with 4 phases, 4 cases with 3 phases, and 3 cases with 2 phases. For 13 cases both the corresponding LCA and the RCA segmented trees had 6 phases. The RCA trees lost more of the individual phases because RCA trees generally have greater problem with motion blur. For 6 of the cases the RCA tree did not have distant phases.

2.4 Evaluation methods

The average distance between the centerlines of the registered trees is used as a registration quality index $D(C_W, C_U)$ as defined in Section 2.2.1, Eq. (13). In addition, a visual inspection of the registered LCA and RCA trees at the final stage of registration (AQSO method followed by the CBSO method) was performed and the misregistered vessels were counted for every tree.

3. RESULTS

The registration results are illustrated in Figs. 4 and 5. Fig. 4(a) and Fig. 4(b) show the scatter plots of the average distance $D(C_W, C_U)$ between the centerlines of the LCA and RCA trees, respectively, from different adjacent phases. $D(C_W, C_U)$ was estimated before and after CBSO registration for every registered pairs of LCA trees (Fig. 4(a)) and RCA

trees (Fig. 4(b)) in the process of registering the adjacent phase pairs in the (80%, 75%, 70%) group and (50%, 45%, 40%) group.

It can be observed that after CBSO registration $D(C_W, C_U)$ is reduced for most of the pairs. The average $D(C_W, C_U)$ over the LCA and RCA tree pairs before and after CBSO registration, corresponding to those plotted in Fig. 4(a) and Fig. 4(b), is summarized in Table 1. The average $D(C_W, C_U)$ values are smaller after the CBSO registration for both the LCA and RCA trees. The difference is statistically significant as estimated by Student's two-tailed paired t-test.

Fig. 5(a) and Fig. 5(b) present the registration results of the distant phases, where the AQSO followed by CBSO registration was applied to the combined (70%-80%-75%) tree and the combined (40%-50%-45%) tree for the LCA and the RCA trees, respectively. The average distance between the centerlines, $D(C_W, C_U)$, of the (70%-80%-75%) tree and the (40%-50%-45%) tree was estimated for the LCA and the RCA coronary trees for all of the cases. The $D(C_W, C_U)$ values were estimated before registration, after AQSO registration, and finally after the AQSO followed by CBSO registration. $D(C_W, C_U)$ was reduced after AQSO registration for both the LCA trees (Fig. 5(a)) and the RCA trees (Fig. 5(b)) for all but one of the cases. $D(C_W, C_U)$ was reduced even further after AQSO followed by CBSO registration.

The average $D(C_W, C_U)$ values at the stage of registering the distant combined trees, corresponding to those plotted in Fig. 5(a) and Fig. 5(b), are summarized in Table 2. The average $D(C_W, C_U)$ was reduced at every registration step for both the LCA and the RCA trees. The differences between the different registration steps were statistically significant ($p < 0.001$) as estimated by the Student's two-tailed paired t-test. The average $D(C_W, C_U)$ before registration was larger for the RCA trees compared to the LCA trees. After the registration using AQSO followed by CBSO, the average $D(C_W, C_U)$ values were reduced for both the LCA and RCA trees and they became comparable.

Examples of both the LCA and RCA registration are shown in Fig. 6 - Fig. 10. The number of phases available for registration after exclusion of the sparse trees was described in the caption for each tree. The different phases of the LCA and the RCA tree were registered using the CBSO method for the neighboring phases and the AQSO method followed by the CBSO method for the distant phases as shown in Fig. 2 and Fig. 3. It can be observed that reasonable registration was achieved for the variety of LCA and RCA trees.

The visual inspection revealed that, of the 46 LCA and RCA trees, 7 vessels in 7 trees were misregistered. Five of the vessels were small segments at the end of the tree pulled to the wrong vessels. The remaining two were larger vessels that were pulled to the wrong vessels.

4. DISCUSSION

The proposed registration procedure combines the localized (CBSO) and global (AQSO) registration methods in order to register efficiently and accurately the different phases of the coronary arterial tree. For the adjacent phases we proposed a fast optimization algorithm to speed up the registration based on the cubic B-spline (CBSO) method. The optimization

algorithm was able to converge for a small number of iterations. For the distant phases the global AQSO registration method used an affine transform with quadratic terms and nonlinear simplex optimization. The affine transform with quadratic terms was found to be a useful warping function for deformation of coronary trees allowing sufficient bending flexibility, but at the same time it was a sufficiently global transformation that could preserve the right spatial ordering of the objects in the volume. It also had a relatively small number of parameters to be optimized. The average distances of the adjacent LCA and RCA tree pairs before registration were comparable, revealing that the displacement due to heart motion at the adjacent phases is relative comparable for LCA and RCA in our database. However, the average distances for the distant LCA and RCA tree pairs before registration were different with the average distances of LCA substantially smaller than those of RCA. This can be explained by the physiological fact that the RCA tree undergoes substantial motion and thus larger displacements between the distant phases. However, the registration procedure was able to register both the LCA and the RCA trees to achieve similar accuracy, even in the cases when the average $D(C_W, C_U)$ before registration for the RCA trees was substantially larger than that for the LCA trees, as can be seen by comparing Fig. 5(a) and Fig. 5(b).

The examples of co-registered coronary trees in Fig. 6 to Fig. 10 demonstrate the performance of the AQSO and CBSO registration procedures. The registration is not perfect. However, our ultimate goal of the registration is to automatically identify the best-quality phase of each coronary arterial segment from the multiple phases to rebuild a best-quality composite tree. The corresponding segments appear to be much closer to one another than to other arterial segments except for one of the segments on the LCA tree in Fig. 9(a).

Visual inspection also confirmed good correspondence of the registered arterial segments. Only 7 segments were misregistered. It is expected that the differences in the relative distances will allow correct identification of the corresponding arterial segments for the majority of the cases.

The registration of coronary trees in multiple phases is a difficult task due to the fact that the cardiac motion is nonlinear and different for the LCA and RCA trees. An additional challenge is that the segmentation procedure is not perfect and the segmented coronary arterial trees from the different phases are not complete in many cases. Therefore, the AQSO and CBSO registration procedures need to have a good balance between the local and global registration properties. On the one hand, because the global AQSO registration may not be able to warp enough to fit the nonlinear motion, the local CBSO registration has to complement it and refine the registration locally. On the other hand, the missing vessels and false positive vessel-like structures may cause miss-registration by the local CBSO and the global AQSO registration is crucial to make use of the other vessels to find the correct match. For a similar reason, the CBSO that we chose is not totally local. The mesh size of 10 voxels for the control points of the cubic B-spline was found to be a good compromise. Fig. 8(a) is a good example to illustrate the balance between the local and global registration of the AQSO and CBSO registration procedures. The vessel-like false positive remained a separate structure after registration and was not warped and mis-matched to the neighboring true vessels in the final co-registered LCA coronary tree.

Fig. 9(a) shows a difficult case for the registration, in which two vessel branches (indicated by the black arrow) are very close and parallel to each other. In one of the phases the upper vessel branch was missing (due to unsuccessful segmentation) and the other branch was positioned between the two branches that were segmented in the other phases. After registration, most part of the single vessel was matched to the correct branch, but was misregistered toward the end of the vessel.

Fig. 10(a) shows an example for which the registration was relatively poor. A part of the vessel (indicated by the black arrow) from the LCA tree was not pulled very close to the corresponding vessels from the other phases. This was due to the large displacement of the vessel in one of the phases. However, the rest of the LCA tree and the RCA tree were registered satisfactorily.

The average registration accuracy reported in other studies was approximately 1 mm and obtained with smaller data sets consisting of 10 cases [3], 31 vessels from 31 cases [4] and 3 cases [6]. Our method was able to achieve an average registration accuracy of 0.76 mm and 0.64 mm for the LCA and RCA trees, respectively, between the adjacent phases and 0.97 mm for both the LCA and RCA trees between the distant phases in 26 cases. Bhagalia et. al. [8] successfully reduced motion artifacts in 75% of initially nondiagnostic coronary artery segments in 9 cases; however, a direct comparison to our study is not possible because no quantitative registration accuracy was reported. From visual inspection of the registered trees, we have confirmed good correspondence of the registered arterial segments; only 7 segments were misregistered. Therefore, compared to the other studies, our method showed robust performance with slightly better accuracy on a larger data set. The result of registration will provide a basis on which a computer algorithm with proper selection criteria would be able to select the best quality segment among the corresponding segments of different phases.

A limitation of the study is still the relatively small data set. However, with 26 cases and 26 LCA and 26 RCA tree, the feasibility of our procedures for multi-phase coronary arterial tree registration is well demonstrated. To our knowledge, this is the largest data set that was used for the registration and evaluation of the coronary trees from multiple phases. We will continue to collect a larger multi-phase cCTA data set in order to further evaluate the robustness of the registration method and the subsequent applications in future studies.

5. CONCLUSION

Our study demonstrates the feasibility of using automated method for registration of coronary arterial trees from multiple cCTA phases. The registration accuracy for the LCA and RCA trees are comparable. The registration provides the basis on which we can develop methods to automatically identify the best-quality phase for each coronary arterial segment and rebuild a single best-quality composite tree for analysis of coronary arterial disease.

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Figure 1.

Coronary CT angiography (cCTA) scans acquired with ECG-gating and reconstructed at multiple cardiac phases: (a) 3D rendered cCTA volumes for 6 acquired cardiac phases (80%, 75%, 70%, 50%, 45%, 40%). Left (LCA) and right (RCA) coronary arterial tree in phase 50% are marked by white arrows. (b) Segmented LCA and RCA tree in each phase (80%, 75%, 70%, 50%, 45%, 40%) using multiscale enhancement and dynamic balloon tracking method [9].

Figure 2.

Automated registration of left coronary arterial (LCA) tree from Fig. 1 using nonlinear CBSO and AQSO methods. First, coronary trees in phases 70% and 80% were registered (70%-80%), then the coronary tree in phase 75% was registered to (70%-80%) to obtain the (70%-80%-75%) tree using the CBSO method. Similarly coronary trees in phases 45% and 50% were registered (45%-50%), then the coronary tree in phase 40% was registered to (45%-50%) to obtain a registered coronary tree (45%-50%-40%), again using the CBSO method. Finally the (45%-50%-40%) tree was registered to the (70%-80%-75%) tree by using the AQSO method followed by the CBSO method. For all images in Figs. 2 and 3 the reference (unwrapped) coronary tree is presented in red, the warped coronary tree in white, and the overlap between the trees in green.

Figure 3.

Automated registration of right coronary arterial (RCA) tree from Fig. 1 using nonlinear CBSO and AQSO methods. First, coronary trees in phases 70% and 80% were registered (70%-80%), then the coronary tree in phase 75% was registered to (70%-80%) to obtain the (70%-80%-75%) tree using the CBSO method. Similarly, coronary trees in phases 40% and 50% were registered (40%-50%), then the coronary tree in phase 45% was registered to (40%-50%) to obtain a registered coronary tree (40%-50%-45%), again using the CBSO method. Finally, the (40%-50%-45%) tree was registered to the (70%-80%-75%) tree by using the AQSO method followed by the CBSO method.

(a)

(b)

Figure 4.

The average distance between the centerlines of LCA trees (a), and RCA trees (b) from different neighboring phases. The average centerline distances were estimated before and after CBSO registration for every available LCA tree pair (a) and RCA tree pair (b) obtained from the neighboring phases in the (80%, 75%, 70%) group and the (50%, 45%, 40%) group.

Figure 5.

The average distance between the centerlines of the (a): (70%-80%- 75%) LCA tree and the (40%-50%-45%) LCA tree, and (b): (70%-80%-75%) RCA tree and the (40%-50%-45%) RCA tree. The average centerline distances were estimated before registration, after AQSO registration, and finally after the AQSO followed by CBSO registration. For better visualization, the cases are sorted by the magnitude of the average distances before registration.

Figure 6.

Automated registration of coronary tree phases by using CBSO and AQSO: (a) LCA tree: 5 phases (40%, 45%, 70%, 75%, 80%); (b) RCA tree: 5 phases (40%, 45%, 70%, 75%, 80%). For all images in Figs. 6 to 10 the reference (unwrapped) coronary tree is presented in red, the warped coronary tree in black, and the overlap between the trees in green if the centerline distance $D(c_h, C_U)$ is $0mm < D(c_h, C_U) < 1mm$, in blue if $1mm < D(c_h, C_U) < 2mm$, and the vessels are kept in red or black if $D(c_h, C_U) > 2mm$. Some of the thin vessels appear discontinuous due to imperfection of the 3D rendering.

Figure 7. Automated registration of coronary tree phases by using CBSO and AQSO: (a) LCA tree: 6 phases (40%, 45%, 50%, 70%, 75%, 80%); (b) RCA tree: 6 phases (40%, 45%, 50%, 70%, 75%, 80%).

Figure 8.

Automated registration of coronary tree phases by using CBSO and AQSO: (a) LCA tree: 6 phases (40%, 45%, 50%, 70%, 75%, 80%); (b) RCA tree: 6 phases (40%, 45%, 50%, 70%, 75%, 80%). The black horizontal non-registered vessel like structure in (a) (indicated by black arrow) is a false positive vessel.

(a)

(b)

Figure 9.

Automated registration of coronary tree phases by using CBSO and AQSO: (a) LCA tree: 6 phases (40%, 45%, 50%, 70%, 75%, 80%); (b) RCA tree: 4 phases (50%, 70%, 75%, 80%). A difficult case in which a vessel was close to other two vessels on the LCA tree (a) as indicated by black arrow.

(a)

(b)

Figure 10.

Automated registration of coronary tree phases by using CBSO and AQSO: (a) LCA tree: 6 phases (40%, 45%, 50%, 70%, 75%, 80%); (b) RCA tree: 6 phases (40%, 45%, 50%, 70%, 75%, 80%). The vessel marked by the black arrow was not correctly registered.

Table 1

The average distances between pairs of closest points along the centerlines of the registered vessels over all 26 cases for adjacent phases for both the LCA and RCA registrations. The average distances were estimated before and after the CBSO registration at the stage of registering adjacent tree pairs. The p-values were estimated by Student's two-tailed paired t-test.

	LCA tree	RCA tree
	Average Distances (mm)	Average Distances (mm)
Before registration	0.96 ± 0.79	0.93 ± 0.97
After CBSO registration	0.76 ± 0.61	0.64 ± 0.43
P-value	<0.001	<0.001

Table 2

The average distances between pairs of closest points along the centerlines of the registered vessels over all 26 cases for registration of both the LCA trees and RCA trees. The average distances were estimated at the stage of registering the (70%-80%-75%) tree and the (40%-50%-45%) tree. All differences between the average distances are statistically significant ($p < 0.001$) for LCA and RCA, respectively. The p-values were estimated by Student's two-tailed paired t-test.

	LCA tree	RCA tree
	Average Distances (mm)	Average Distances (mm)
Before registration	2.85 ± 1.46	4.03 ± 2.36
After AQSO registration	1.62 ± 0.76	2.18 ± 1.11
After AQSO + CBSO registration	0.97 ± 0.43	0.97 ± 0.44