MULTI-RESOLUTION 3D CONVOLUTIONAL NEURAL NETWORKS FOR AUTOMATIC CORONARY CENTERLINE EXTRACTION IN CARDIAC CT ANGIOGRAPHY SCANS

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ABSTRACT

We propose a deep learning-based automatic coronary artery centerline tree tracker (AuCoTrack) extending the work of [1]. A multi-resolution 3D Convolutional Neural Network (CNN) is employed to simultaneously predict movement directions and detect bifurcations. Moreover, an automated artery endpoint detector is used to prevent premature termination of the tracking process. On Coronary Computed Tomography Angiography (CCTA or coronary CTA) scans annotated by clinical experts, an average sensitivity of 87.1% and clinically relevant overlap of 89.1% could be obtained. In addition, the MICCAI 2008 Coronary Artery Tracking Challenge (CAT08) training and test datasets were used to benchmark the algorithm and to assess its generalization capabilities. On CAT08, an average overlap of 93.6% and a clinically relevant overlap of 96.4% were achieved.

***Index Terms*—** coronary artery centerline tracking, coronary computed tomography angiography, neural networks

1. INTRODUCTION

Coronary artery disease (CAD) results in narrowing or blockage of coronary arteries due to the build-up of cholesterol and fatty deposits on the inner lining of the arterial wall. Such constrictions can result in an inadequate supply of blood to the heart muscles which can be fatal [2]. CAD is one on the leading causes of death worldwide with 9.43 million deaths reported in 2016 [3]. Coronary Angiography (CA) is an interventional procedure for CAD evaluation and treatment. The severity and anatomical extent of CAD can be assessed non-invasively by Coronary Computed Tomography Angiography (CCTA) [4]. Manual reading of volumetric CCTA images is a time-consuming task. Several advanced visualization techniques relying on coronary artery centerlines have been proven to facilitate the clinical workflow. In [5], approaches for the assisted extraction of coronary artery centerlines are categorized as: *automatic* requiring no user interaction at all [6, 7, 8], *semi-automatic* requiring one seed point per artery [9, 10, 11] or *interactive* requiring multiple user interactions per artery [1, 5, 12]. Recently, [1] proposed a CNN-based tracking scheme which iteratively predicts a movement direction and a step-size. As an interactive method, almost state-of-the-art performance could be achieved. Typically, their tracker required multiple seeds per artery in order to successfully extract the related centerline due to premature stopping. The approach did not identify and handle bifurcations. In order to render the algorithm automatic, an additional network was used for seed point extraction.

Building on [1], we propose a multi-resolution CNN-based algorithm to extract the entire coronary tree automatically without user interaction. Our approach detects bifurcation points and properly integrates them into the tracking process. In addition, the tracker is guided by another CNN in order to prevent premature termination. The algorithm does not rely on a segmentation network or any other automated method to generate multiple seed points per artery. We show that a simple automated detection of two seeds (one for each coronary tree) suffices and that the proposed method is very robust towards variations of those points. The ostium points obtained from a deformable shape model of the heart [13] are used to initialize the automatic coronary centerline extraction.

2. METHODOLOGY

Our automatic coronary artery tracker (AuCoTrack) sequentially traces the coronary artery centerline while deciding in each step forward in which direction to continue or if a new vessel branches off (direction and bifurcation classifier, DBC-Net). Simultaneously, the tracker monitors whether an endpoint of an artery is reached and the tracking should be stopped (stop classification network, STC-Net), see Figure 1. A global priority queue containing active centerline points is maintained which is initialized with points located at the left and right ostium. Two or three points are added to the queue at each step depending on the discovery of a bifurcation. We avoid double visits by only following centerline points located at a minimum distance from already found centerline points. Processing can be done in parallel and the tracker terminates once no more active centerline points are queued.

The direction of movement is found by a multi-class prediction on the unit sphere whose surface is discretised into 1000 admissible directions (DBC-Net). We perform peak detection in order to find two or three likely directions depend-

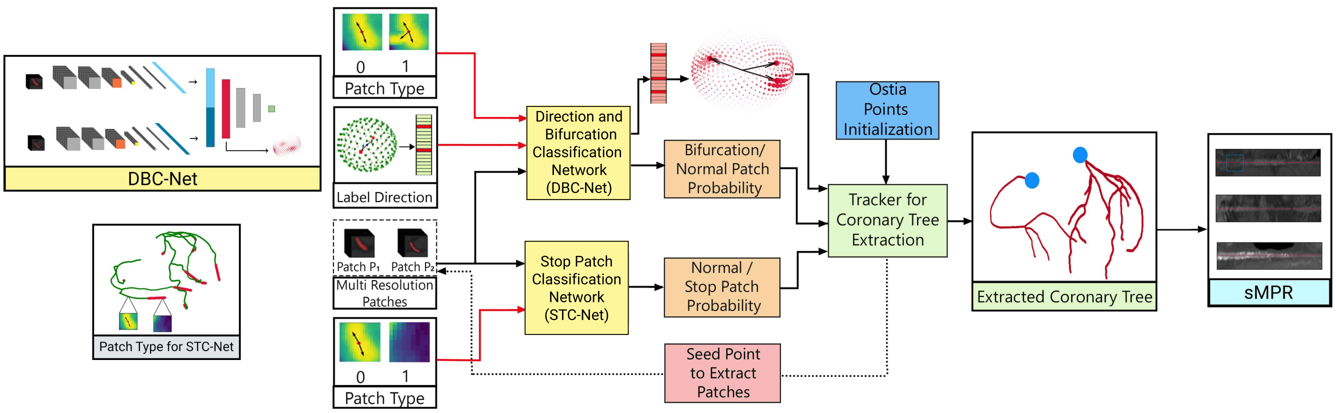

Fig. 1. Overview of the AuCoTrack pipeline. At inference time (black arrows), multiresolution image patches P_1 and P_2 are fed into the two networks (yellow boxes) which results in a predicted direction on the unit ball (red dots) and the decision whether to branch or stop (orange boxes) by the DBC-Net and the STC-Net, respectively. The stopping prediction is illustrated in the gray box on the bottom left. The main tracking loop (light green box and black dotted arrow) is initialised with the ostiae (blue dots) and results in the coronary tree (red lines). This tree can be mapped back to the underlying CCTA scan via a stretched multiplanar reformat (sMPR). The network architecture of the DBC-Net and STC-Net is essentially an encoder with parallel pathways at two different resolutions whose representations are combined (box top left). For training (red arrows), patches along with their labels (bifurcation/vessel, stop/continue, direction encoded in binary vector) are used.

ing on the prediction of a bifurcation. We employ angle constraints to concentrate on meaningful configurations i.e. we require that the (a) highest response (way back) is similar to the previous direction (angle$<60°$), (b) second response (way ahead) is different from the previous direction (angle$>110°$), and (c) third response (branching) is different from the other two (angle$>40°$). The third response is calculated only in the case DBC-Net predicts the presence of a bifurcation. A fixed step of 1 mm is taken in the predicted direction. The STC-Net casts a binary vote on whether the coronary tracking continues. Both DBC-Net and STC-Net use the same network architecture and operate locally on isotropic 3D patches P_1, P_2 of size 19^3 sampled at the two resolutions 0.5mm and 1.0mm. Each of the two network branches has 7 convolutional layers with kernels of size 3. Layers 3 and 4 use dilated convolutions with the spacing of 2 and 4 between the kernel points respectively .We use ReLu activation functions and batch normalisation. The result of the two branches is stacked and reduced to the number of direction classes to form Layer L_D. Layer L_D is then followed by two linear layers and a sigmoid activation for the patch type prediction. In case of DBC-Net, the output of layer L_D is followed by a softmax activation to get the direction response.

We train and evaluate the two networks on a set of volumetric CCTA scans where the coronary artery tree – as annotated by clinical experts – is represented by a set of centerlines and their topological connections.

Binary cross entropy loss (BCE_{patch}) is used for the patch type classification and categorical cross entropy loss (CE_{dir}) is used for the direction classification. The combined loss function used to train the DBC-Net is $L = CE_{dir} + \lambda_b\, BCE_{patch}$. The weighting factor λ_b is fixed at 5. For STC-Net, we employ only binary cross entropy loss for stop patch type classification. For optimisation, we use Adam with a learning rate of 0.0001 and a mini-batch size of 64. We use several augmentation strategies during training. We use random translations (along three axes) to make the direction prediction more robust and rotational perturbations (along three axes) to introduce a certain degree of rotational invariance. The training of the DBC/STC-Nets requires carefully selected pairs of input patches and output labels in terms of binary vectors encoding the directions, stop and bifurcation indicators. The binary direction vectors are obtained by placing a sphere with radius $R = 1.5mm$ around the centerline point and a subsequent nearest neighbor matching of the vessel intersections with the sphere to the discrete sphere tessellation. The number of intersections with the sphere governs the flag in terms of bifurcation or stop patch. Care was taken to oversample the bifurcations (by a factor of 10, see Section 3). The STC-Net was trained with patches particularly selected beyond the end of the coronary artery, see Figure 1 bottom left box.

3. RESULTS

We evaluate our AuCoTrack algorithm using the evaluation metrics defined in [5]. Sensitivity was an additional metric used on the training dataset.

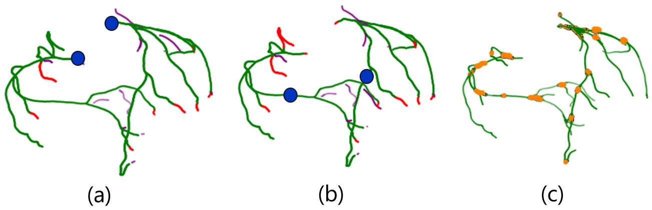

Fig. 2. Rendering of AuCoTrack result: (a) initialization at ostiae, (b) initialization approximately at center of LAD and RCA, (c) detected bifurcation overlayed on tracking result. Green = correct, blue = init points, orange = bifurcations.

3.1. Training Dataset

The training dataset consists of 43 CCTA images which were annotated by clinical experts. The number of annotated coronary arteries per CCTA scan varies from 4 to 20. The mean number of annotated coronary arteries per CCTA scan in this dataset is 9. The training dataset contains 428 annotated coronary arteries. Four-fold cross validation has been performed in-order to evaluate the proposed algorithm.

Figure 2 (a) shows that the result of the automatic coronary centerline extraction when the seed points for tracker initialization are placed at the left and right coronary ostium. Figure 2 (b) shows the result when the initialization takes place approximately at the center of LAD and RCA. The extracted coronary tree is very similar in both cases. The sensitivity obtained when the seed points are placed at the ostiae is 88.9% and it is 87.3% when the seed points are placed in the middle of LAD and RCA. This shows that the seed point can essentially be placed anywhere on the coronary tree. Figure 2 (c) shows the bifurcation detection overlaid on the tracking result. The orange marks on the coronary tree indicate that a bifurcation has been detected at that centerline point by the DBC-Net. This implies that three direction vectors will be obtained to generate the candidate points.

An ablation study was performed and revealed the optimal number of equispaced points on the direction sphere to be 1000 (using the spherical Fibonacci mapping). The number of pathways in the multi-resolution DBC-Net and STC-Net was fixed at 2 and the importance sampling parameter for the bifurcation class was found to be around 10 [14]. The patch size of 19 is selected to balance fast processing and enough field-of-view to cover average coronary artery radii. We obtained a sensitivity of $87.1\,\% \pm 3.2\,\%$, a clinically relevant overlap of $89.1\,\% \pm 2.3\,\%$ and a total overlap of $80.4\,\% \pm 2.0\,\%$. The accuracy inside was $0.34\,\mathrm{mm} \pm 0.0017\,\mathrm{mm}$ which is below the average voxel size of $0.40^2 \times 0.43\,\mathrm{mm}^3$.

3.2. CAT08 Training Dataset

The best model cross-validated on the training dataset was used to extract centerlines on the CAT08 training datasets. Table 1 shows that an average overlap (OV) of 93.4%, clinically relevant overlap (OT) of 95.9% and overlap until first error (OF) of 76.5% was obtained for these 8 CCTA scans. This is a good test of generalization as the CCTA training dataset and the CAT08 dataset used for testing are disjoint and were acquired on scanners from different vendors.

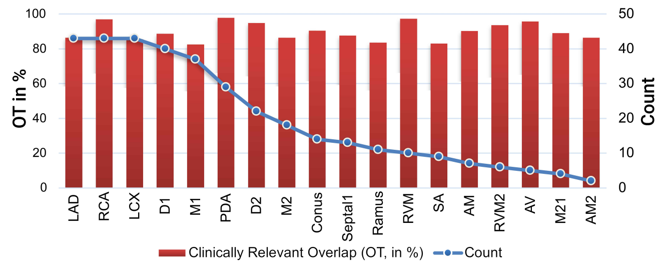

Fig. 3. Clinically relevant overlap of all the arteries present in the training dataset which occur more than 3 times evaluated using cross validation. The occurrence count of each artery is also shown in the plot.

No.	Image Quality	Calcium Score	OV	OF	OT	AI	T
0	Moderate	Moderate	94.2	77.7	95.1	0.4	55
1	Moderate	Moderate	97.3	99.4	99.6	0.32	39
2	Good	Low	98.3	99.7	100	0.31	43
3	Poor	Moderate	86.3	63.0	89.1	0.40	41
4	Moderate	Low	92.9	57.3	97.9	0.33	31
5	Poor	Moderate	97.6	77.5	99.7	0.43	33
6	Good	Low	96.7	87.2	99.6	0.30	36
7	Good	Severe	83.9	49.1	86.3	0.38	48
Avg			**93.4**	**76.5**	**95.9**	**0.36**	**41**

Table 1. Results of our method on CAT08 training set which was used as a test set. For each case, overlap (OV, in %), overlap until first error (OF, in %) and clinically relevant overlap (OT, in %), average accuracy inside (AI, in mm), time taken for coronary tree extraction (T, in s) along with subjective image quality and calcium score is shown.

3.3. CAT08 Test Dataset

We tested our algorithm on the CAT08 test set to benchmark the performance of our algorithm against methods available on the leaderboard of the CAT08 challenge. An average overlap of $93.6\,\% \pm 5.2\,\%$, clinically relevant overlap of $96.4\,\% \pm 4.1\,\%$, overlap until first error of $76.3\,\% \pm 22.7\,\%$ and accuracy inside of $0.37\,\mathrm{mm} \pm 0.05\,\mathrm{mm}$ was obtained for these 24 CCTA scans. Cases 8, 10 and 27 required one additional seed point due to failure in the detection of bifurcations for one of the vessels. There are significant motion artifacts present in case 26 which hamper the bifurcation detection. Hence, additional seed points are provided for 3 of the vessels in this CCTA image. Table 2 shows the comparison of the performance of our algorithm (AuCoTrack) with the current automatic coronary centerline extraction techniques and the state-of-the-art CNN-based technique which requires at-least one seed point per vessel for the centerline extraction. Overall,

Method	OV	OF	OT	AI	T
AuCoTrack	93.6	76.3	**96.4**	0.37	**42**
Zheng et al.	93.5	**76.5**	95.6	**0.20**	60
Kitamura et al.	90.6	70.9	92.5	0.25	160
Yang et al.	**93.7**	74.2	95.9	0.30	120
Wolterink et al. (Interactive)	93.7	81.5	97.0	0.21	10

Table 2. We compare of our AuCoTrack pipeline with the top automatic coronary artery centerline algorithms in terms of overlap (OV, in %), overlap until first error (OF, in %) and clinically relevant overlap (OT, in %), average accuracy inside (AI, in mm) and time taken (T, in s) on the CAT08 date. The interactive CNN-based tracker [1] is below the dashed line.

AuCoTrack achieves better clinically relevant overlap than other automatic methods.

4. DISCUSSION

An automatic deep learning-based coronary artery centerline tracker in CCTA images (AuCoTrack) was proposed. Our framework was evaluated on 43 training CCTA images and additional datasets available from the CAT08 challenge. On the training dataset, AuCoTrack was evaluated using four-fold cross validation. To test the generalisation of our approach, the model was applied to the CAT08 training set. For further evaluation, we trained on a combined dataset containing the 43 training CCTA scans and the 8 CCTA scans from the CAT08 training set. The resulting model was then applied to the CAT08 test set and the extracted centerlines were submitted to the CAT08 challenge evaluation framework. Our method obtained an accuracy inside of 0.37 mm, a overlap of 93.6% and a clinically relevant overlap of 96.4% on average. Moreover, an overlap rank (OR) of 9.87 was achieved outperforming the available top three automatic algorithms on the CAT08 leaderboard [6] OR=10.43, [7] OR=13.81 and [8] OR=10.55. We remark, that the state-of-the-art automatic centerline extraction algorithm by [6] requires artery segmentation masks as input for their model driven and data driven approach. Their algorithm is trained on 108 training CCTA scans. Similarly, a hybrid learning representation approach that utilizes segmentation masks proposed by [15] was trained on 100 CCTA scans.

An analysis of the individual CAT08 cases showed that the performance is not strongly affected by the presence of coronary calcium. For example, on the CAT08 test images with low, moderate and severe calcium scores, an average overlap of 92.9%, 94.0% and 94.2% was obtained.

The number of annotated centerlines in the training dataset varied from 4 to 20. We observed a high clinically relevant overlap independent of the number of annotated arteries which demonstrates that our algorithm is capable of extracting the entire (left or right) coronary tree from a single seed. In order to address the problem of premature or late stopping, we employ a voting mechanism combining a CNN-based endpoint detection with a moving average entropy criterion.

AuCoTrack achieves a clinically relevant overlap of 96.4% on the CAT08 test set and 89.1% on the training dataset. This difference is due to the fact that the CAT08 test set contains annotations for only 4 coronaries and the training dataset contains a variable number ranging from 4 to 20.

[1] achieved near state-of-the-art performance as an interactive method for the CAT08 dataset. A main constraint of their method is that it requires one or more seed points per vessel as no functionality for detecting and handling bifurcations is available. Our method relies only on a single seed point per coronary tree and bifurcations are properly handled by the tracker. Successful vessel detection (OT $> 50\%$) was observed in 95% of the cases from the CAT08 dataset. The ostium points required for initializing AuCoTrack were automatically obtained from a deformable shape model of the heart [13]. Moreover, we observed that our algorithm is very robust towards variations of those point, see Figure 2. In [1] the tracker termination is guided by a moving average entropy criteria which fails in case of a severe stenosis. Consequently, their method may require several initialization points per vessel in order to warm-start the tracking process.

A branch-aware coronary centerline extraction approach based on Double Deep Q-Network proposed by [16] was evaluated only on the CAT08 training dataset. This method does not terminate on reaching the end of coronary artery but terminates when the tracker goes out of the CCTA scan or reaches an already visited point.

In future work, the accuracy of AuCoTrack can be further boosted by an image-based recentering step of the extracted centerline control points. Furthermore, seed points for potentially missed vessels can be obtained by a rough pre-segmentation and could be integrated into the tracking scheme by adding them directly into the priority queue. False positive detections of vessels e.g. coronary veins or thoracic arteries can be reduced by combing further anatomical prior information with the local tracker. Initialisation at intermediate landmarks different from the ostiae is feasible and can be further explored. The algorithm can be parallelized much stronger in order to decrease runtime per case or to enable intermediate assessment of a partial result. Also, multiscale processing is a possible option for future work. The tracking scheme is very generic and versatile and can potentially also be used to track other 3D tubular structures such as airways, rib centerlines and other blood vessels.

5. ACKNOWLEDGEMENTS

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6. COMPLIANCE WITH ETHICAL STANDARDS

This research was evaluated using human subject data made available in open access. Ethical approval was not required as confirmed by the license attached with the open access data.

7. REFERENCES

[1] Jelmer M. Wolterink, Robbert W. van Hamersvelt, Max A. Viergever, Tim Leiner, and Ivana Išgum, "Coronary artery centerline extraction in cardiac CT angiography using a CNN-based orientation classifier," *Medical Image Analysis*, vol. 51, pp. 46 – 60, 2019.

[2] Arup Malakar, Debashree Choudhury, Binata Halder, Prosenjit Paul, Dr Arif Uddin, and Supriyo Chakraborty, "A review on coronary artery disease, its risk factors, and therapeutics," *Journal of Cellular Physiology*, vol. 234, 02 2019.

[3] WHO, "Global health estimates 2016: Deaths by cause, age, sex, by country and by region, 2000-2016.," 2018.

[4] Dan Paech and Adèle Weston, "A systematic review of the clinical effectiveness of 64-slice or higher computed tomography angiography as an alternative to invasive coronary angiography in the investigation of suspected coronary artery disease," *BMC Cardiovascular Disorders*, vol. 11, pp. 32, 06 2011.

[5] Michiel Schaap, Coert Metz, Theo Walsum, Alina van der Giessen, Annick Weustink, Nico Mollet, Christian Bauer, Hrvoje Bogunović, Carlos Castro, Xiang Deng, Engin Dikici, Thomas O'Donnell, Michel Frenay, Ola Friman, Marcela Hernandez Hoyos, Pieter Kitslaar, Karl Krissian, Caroline Kühnel, Miguel Luengo-Oroz, and W.J. Niessen, "Standardized evaluation methodology and reference database for evaluating coronary artery centerline extraction algorithms," *Medical Image Analysis*, vol. 13, pp. 701–14, 07 2009.

[6] Yefeng Zheng, Huseyin Tek, and Gareth Funka-Lea, "Robust and accurate coronary artery centerline extraction in CTA by combining model-driven and data-driven approaches," *International Conference on Medical Image Computing and Computer-Assisted Intervention*, vol. 16, pp. 74–81, 09 2013.

[7] Yoshiro Kitamura, Yuanzhong Li, and Wataru Ito, "Automatic coronary extraction by supervised detection and shape matching," *Proceedings - International Symposium on Biomedical Imaging*, pp. 234–237, 05 2012.

[8] Guanyu Yang, Pieter Kitslaar, Michel Frenay, Alexander Broersen, Mark Boogers, Jeroen Bax, Johan Reiber, and Jouke Dijkstra, "Automatic centerline extraction of coronary arteries in coronary computed tomographic angiography," *The International Journal of Cardiovascular Imaging*, vol. 28, pp. 921–33, 06 2011.

[9] Karl Krissian, Hrvoje Bogunović, Jose Pozo, Maria-Cruz Villa-Uriol, and Alejandro Frangi, "Minimally interactive knowledge-based coronary tracking in CTA using a minimal cost path," *The Insight Journal*, 01 2008.

[10] Suheyla Cetin Karayumak, Ali Demir, Anthony Yezzi, Muzaffer Degertekin, and Gozde Unal, "Vessel tractography using an intensity based tensor model with branch detection," *IEEE Transactions on Medical Imaging*, vol. 32, 11 2012.

[11] Suheyla Cetin Karayumak and Gozde Unal, "A higher-order tensor vessel tractography for segmentation of vascular structures," *IEEE Transactions on Medical Imaging*, vol. 34, 04 2015.

[12] Ola Friman, Caroline Kuehnel, and Heinz-Otto Peitgen, "Coronary centerline extraction using multiple hypothesis tracking and minimal paths," *International Conference on Medical Image Computing and Computer-Assisted Intervention*, 08 2008.

[13] Olivier Ecabert, Jochen Peters, Hauke Schramm, Cristian Lorenz, Jens Berg, Matthew Walker, Mani Vembar, Mark Olszewski, Krishna Subramanyan, Guy Lavi, and Jürgen Weese, "Automatic model-based segmentation of the heart in CT images," *IEEE Transactions on Medical Imaging*, vol. 27, pp. 1189–201, 10 2008.

[14] Zohaib Salahuddin, Matthias Lenga, and Hannes Nickisch, "Multi-resolution 3d convolutional neural networks for automatic coronary centerline extraction in cardiac CT angiography scans," *arXiv preprint arXiv:2010.00925*, 2020.

[15] Jiafa He, Chengwei Pan, Can Yang, Ming Zhang, Yang Wang, Xiaowei Zhou, and Yizhou Yu, "Learning hybrid representations for automatic 3d vessel centerline extraction," in *Medical Image Computing and Computer Assisted Intervention*. 2020, pp. 24–34, Springer International Publishing.

[16] Yuyang Zhang, Gongning Luo, Wei Wang, and Kuanquan Wang, "Branch-aware double DQN for centerline extraction in coronary CT angiography," *International Conference on Medical Image Computing and Computer-Assisted Intervention*, pp. 35–44, 2020.