CenterlineNet: Automatic Coronary Artery Centerline Extraction for Computed Tomographic Angiographic Images Using Convolutional Neural Network Architectures

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***Abstract*—The prevention of cardiovascular diseases starts by a thorough examination of the coronary artery vessels for atherosclerotic plaques existence. By combining deep learning convolutional Neural Network (CNN) architectures and the biological knowledge, we introduce a novel method for the automatic extraction of coronary artery centerlines in Computed Tomography Angiography (CTA) data. The proposed method is based on a 3D convolutional neural network used as a local vessel centerline detector to extract the main and side branches of the coronary artery tree. Coupled with a pre-processing vessel enhancing step, the model takes advantage of the analytical analysis of the former as well as the feature extraction ability of the CNN. In addition, automatic aorta and heart region detections are also performed to delineate the origin and the extent of the coronary tree and phase out the false predictions. We investigate the use of Coronary Stenosis' Detection and Quantification (2012) Database to enrich the training process while ensuring the homogeneity of the scans. Our work offers a fully automatic, CNN based, pipeline for coronary artery centerline detection while circumventing the scarcity of the medical data in hand. Its validation against the ground truth annotation from the Rotterdam Coronary Artery Algorithm Evaluation Framework yields a retrieval ratio of 95% and 93%.**

1. Introduction

For the longest time, the coronary artery identification problem in computed tomography angiography images as well as other modalities has attracted researches attention due to the tediousness, time consumption and the infeasibilty of the clinical manual extraction process. The vascular structures extraction task offers numerous challenges to the research community. To start, since the CTA is a contrast enhancement protocol, the resulting data highly depends on the acquisition process (scanner type, resolution, noise, contrast intensity...) as well as the patient pathology's high variability (artery tree network, branching patterns, size and curvature of vessels). Moreover, the geometry of the latter structures can be bothered by the abnormal presence of calcification and stenoses. Finally, the dimensions of the targeted arteries are relatively small (diameter of 4 mm on average) compared to nearby anatomical structures and especially the whole CTA volume ($256 \times 256 \times 80$ mm on average).

For the last two decades, a plethora of algorithms have been dedicated to (semi-) automatically extract vascular entities centerlines in the medical imaging field [1]. The centerline is a geometrical shape that reduces the complexity of representing 3D vascular structures to a 1D curve skeleton (set of points that runs through its center). A large amount of user-interactive methods are based on a minimal cost approach that grows a vessel path from a selected point or connects user-provided start and end points by minimizing a defined cost function that runs through the center of the vessels. The variation of these approaches boils down to the different assumptions (numerical optimization schemes, cost function, termination criteria..) used to reflect the data representation. The fully automatic versions successfully replaced the user interactions by an automated selection of points however they still needed to compute hand-crafted cost function optimization. One approach was to apply tube detection filters like frangi et al [2] and sato et al. [3] which offer a geometric analysis of the structures based on the hessian matrix's eigenvalues and eigenvectors. Bauer et al. [4] and Krissian et al. [5] based their search for tubular candidates on the classical frangi filter while Yang et al. [6] twisted the step edge response of the latter en route to introducing an improved vesselness filter. Another approach is to consider the centerline extraction task as an iterative tracking process and therefore a duality of prediction and correction steps. In fact, Friman et al. [7] uses ideal tubular template matching model to conduct the prediction of a possible path continuation step with a Multiple Hypothesis Tracker leading the way. This method achieved the highest rank in the CAT08 challenge [8] even though it had resorted to a user selection points and a manual correction step in

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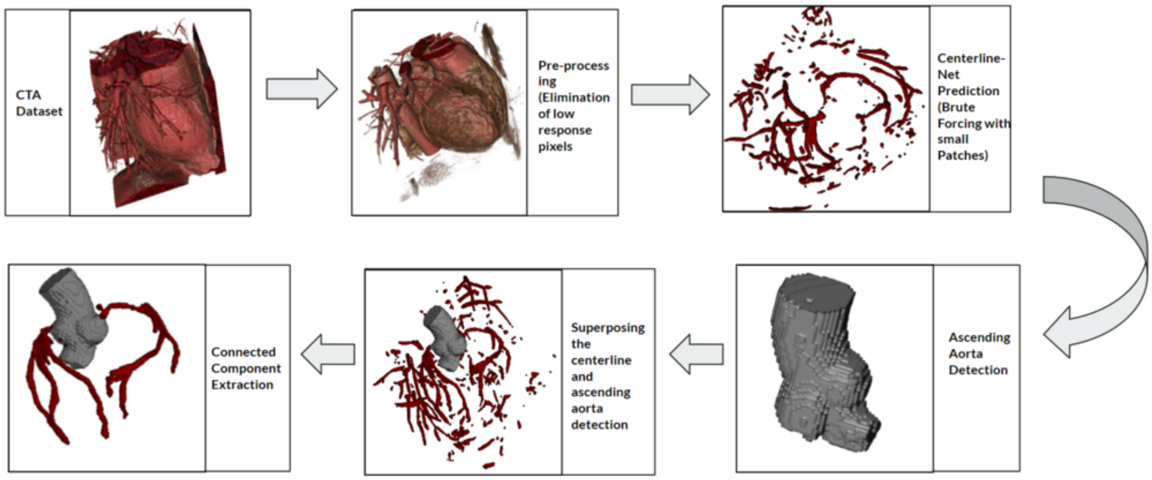

Figure 1. Centerline Extraction Pipeline

case of failure. Lesage et al. [9] in his turn, proposed a bayesian model based on particle filtering algorithm.

Regardless of the pre and post processing techniques that complement the full pipeline of these algorithms, these filters are mostly handcrafted and they require adjustments and rectification when their assumptions do not hold. So, in order to compensate for the hand-crafted feature extraction step, the researchers have turned their attention toward the deep learning approach and especially the use of convolutional neural networks for medical image analysis [10]. The latter proved to have a high understanding of the complexity of imaging tasks and a powerful capacity when it comes to learning spatial correlations and extracting features. Gulsun et al. [11] explored the use of CNN as a postprocessing technique to discriminate the true coronary arteries from the leaks. Guo et al. [12] used a CNN model to convert a segmentation map into a centerline mask and a list of endpoints as well whereas Wolternik et al. [13] put in place an iterative tracking pipeline with a similar multi-task CNN that outputs both a radius and an orientation of a candidate centerline over a set of possible directions. CNNs have been used not only for centerline extraction but also for vessel segmentation as shown in the work of Merkow et al. [14] when they enabled efficient multi-scale feature learning and voxel-wise prediction using a 3D U-net architecture for different types of vessels. Huang et al. [15] and Shen et al. [16] used similar CNN networks to predict dense segmentation probability with the former introducing an attenuation gate coupled with a level set function. In turn, Lee et al. [17] presented the idea of incorporating shape prior information (deformable tubular shape template) into an end-to-end deep learning architecture to produce a vessel segmentation of an input volume.

In this paper, we present a newly automatic method for the extraction of coronary artery centerlines. Relying on the power of the CNNs, we propose a deep learning local vessel filter that learns the shape, the distribution and the features of centerline points with no handcrafted filters nor template functions approximations. We also put in place a deep learning neural network using only 56 public patient data to train and test and thus circumventing the data scarcity challenge. Furthermore, our entire pipeline converts the local aspect of the centerlineNet to a fully detection of the main and side branches of the coronary artery. Our experiments, evaluated on the publicly available Rotterdam Coronary Artery Evaluation Framework, demonstrate that our proposed method yields a high extraction ratio without any user interaction.

2. Data

This work takes advantage of two frameworks that offer not only publicly available databases but also a benchmark of the different algorithms that took part in these challenges. The first Dataset is the CAT08 dataset [8], it is part of the Rotterdam Coronary Artery Evaluation Framework. It consists of 8 patient data acquired between June 2005 and June 2006 with a 64-slice CT scanner and a dual source CT scanner(Sensation 64 and Somatom Definition, Siemens Medical Solutions, Forchheim, Germany) while the second dataset is the Stenosis and Quantification challenge [19] which offers a total of 48 patient data collected between June 2005 and June 2011 for with a dual source CT scanner (Somatom Definition, Siemens, Forchheim, Germany), a 64-slice CT scanner (Brillance 64, Philips Medical Systems) and lastly a 320-slice CT scanner (Aquilion ONE 320, Toshiba Medical Systems).

3. Methodology

The medical imaging field always presents a huge challenge when it comes to the number of datasets available for training. In fact, the small number of samples limits the ability of a neural network of catching the existing features in an image or a volume. The 3D nature of the CTA scans requires a 3D model to learn the most important correlations between the different structures of the volume. The coronary arteries are a connected vessel tree that originates from the aorta and belongs to the cardiac region. The proposed pipeline 1 translates this definition into sub-models that extracts the full coronary artery centerline tree. First, a preprocessing vessel enhancement step is used to eliminate low response pixels (see section 3.1.2), then a 3D CNN model is applied to detect the arteries in the CTA volume. As a post-processing step, the boundaries of the targeted structures are defined by extracting the aorta and heart region. Lastly, a connected component analysis retrieves the coronary tree.

3.1. CenterlineNet

3.1.1. Architecture. The culmination of this classification model is to convert a CTA patch into a probabilty value that reflects the likeliness of such volume being centered around a vessel. The full architecture of the model is shown in Fig. 2. This network is 6 layers deep and uses a convolution module highly inspired from 3D U-net module [20] which performs 3D convolutions via $3 \times 3 \times 3$ filters with stride 1. Each convolution operation is accompanied with a ReLu activation to detect the non linearities. The result is then fed to a Batch Normalization layer to adjust and scale the data to get more training speed. After that, the data enters the compression path with a Maxpooling layer that divides the resulting feature map size by 2. The data is processed

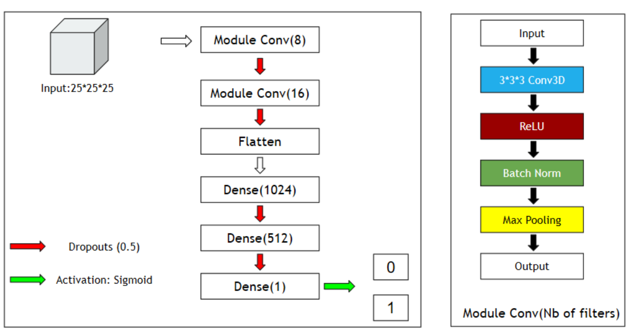

Figure 2. CenterlineNet Architecture

through the 'Module Conv' twice as the number of filters gets doubled at each stage (from 8 to 16). To minimize the phenomenon of overfitting, we add Spatial Dropout Layers with a 25% rate. After that, the output of the second layer is flattened (passed from 3 dimensions to one) then applied to three consecutive Dense layers where the last layer has a number of units equals to one (the output shape the network). In the end, the model should be able to yield the probability that an input volume contains a centered vessel using the Sigmoid activation function.

3.1.2. Data Organization. All the datasets are resampled to a voxel size of $0.8 \times 0.8 \times 0.8mm^3$ via trilinear interpolation. The Datasets's values are capped to a $[0, 700]$ range then scaled down to $[0, 1]$ range using the Min-Max normalization to eliminate the low response pixels. In fact, the hounsfield units are quantitative measurement for radiodensity and these values are significant in determining the nature of the structure in question (air $\simeq -1024$, lung $\simeq -500$, bones ≥ 700,...). With the former proposed threshold, we keep the relevant structures (soft tissues, blood, muscles,..) while eliminating those who does not constitute the vessels. In order to create a 3D vessel filter, the model is provided with different true and false vessel patches from CTA volumes. An input patch has a size of $(25 \times 25 \times 25)$ so that it can contain the largest coronary artery possible. A patch is labeled as true if it is centered on a centerline point whereas it is labeled as false if the patch does not contain a vessel or contains a vessel that is not centered as shown in Fig 3.

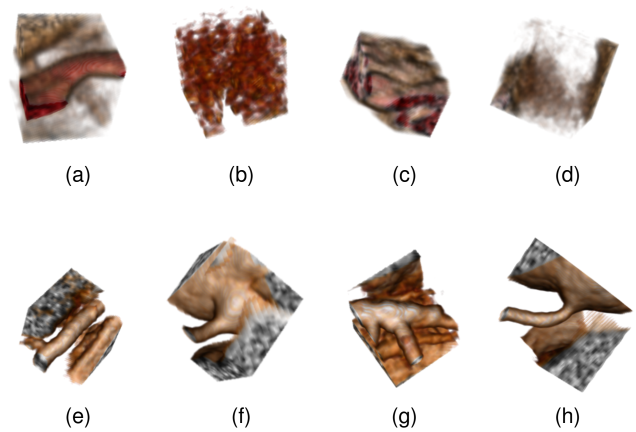

Figure 3. Example of True and False Vessels Patches: the first row displays the false vessels while the last one shows the true vessels.

To generate the training data, the actual coordinates of the centerlines provided by the Rotterdam Datasets were used. Each true vessel patch is centered on a centerline point. Let $C = (C_0, C_1, C_2) = (z_{centerline}, x_{centerline}, y_{centerline})$ be a centerline point. Let $\mathbf{d}$ be a vector that represents the size of the patch in a number of voxels.

$$\mathbf{d} = \begin{pmatrix} d_0 \\ d_1 \\ d_2 \end{pmatrix} = \begin{pmatrix} depth_{patch} \\ height_{patch} \\ width_{patch} \end{pmatrix} \tag{1}$$

Let $\mathbf{P}$ be the patch with size defined by $\mathbf{d}$ and $\boldsymbol{I}$ is the CTA volume. The i^{th} slice of the patch which corresponds to the i^{th} layer of depth is defined in the equation below as $P_d(i)$.

3.2. Aorta and Heart Region Detection

In order to delineate the origin and the extent of the coronary artery tree, an extraction of the heart region and the ascending aorta is performed. The ostium points give the start of the main coronary arteries. This biological connection allows the model to distinguish between the spurious vessels and the targeted ones. Moreover, and in the quest of eliminating the false responses, a heart region boundary is established to tune out the extra-cardiac predictions (lungs,

$$P_d(i) = \begin{pmatrix} I_{C_0-\frac{d_0}{2}+i, C_1-\frac{d_1}{2}, C_2-\frac{d_2}{2}} & \cdots & I_{C_0-\frac{d_0}{2}+i, C_1-\frac{d_1}{2}, C_2} & \cdots & I_{C_0-\frac{d_0}{2}+i, C_1-\frac{d_1}{2}, C_2+\frac{d_2}{2}} \\ \vdots & \cdots & \vdots & \ddots & \vdots \\ I_{C_0-\frac{d_0}{2}+i, C_1, C_2-\frac{d_2}{2}} & \cdots & I_{C_0-\frac{d_0}{2}+i, C_1, C_2} & \cdots & I_{C_0-\frac{d_0}{2}+i, C_1, C_2+\frac{d_2}{2}} \\ \vdots & \cdots & \vdots & \ddots & \vdots \\ I_{C_0-\frac{d_0}{2}+i, C_1+\frac{d_1}{2}, C_2-\frac{d_2}{2}} & \cdots & I_{C_0-\frac{d_0}{2}+i, C_1+\frac{d_1}{2}, C_2} & \cdots & I_{C_0-\frac{d_0}{2}+i, C_1+\frac{d_1}{2}, C_2+\frac{d_2}{2}} \end{pmatrix}$$

pulmonary,...). For this task, a 3 classes U-net segmentation model [21] is used and the ground truth samples are prepared by cardiologists using 3D slicer software [22] namely the segment editor module. We used a portion of 10 patients chosen randomly from the rotterdam database as our training dataset. The choice of a 2D architecture is due primarily to the scarcity of data since a slice-wise approach provides more training samples than a volume-wise 3D segmentation. The U-net model is widely used in the computer vision algorithms for its fast and precise segmentation of images. The encoding part consists of compressing the data into a small feature map code while the decoder phase elevates the feature map code to the original size of the input image. This auto-encoder architecture is finally followed by a segmentation layer that decides on the value of each pixel and classify it within one of the following classes: {0: Extra Cardiac, 1: Heart Region, 2: Ascending Aorta}. The segmentation results (Dice coefficient metric) yielded by this model are slightly over 89% (89.2%).

4. Results

We used the Rotterdam Coronary Artery Framework Stenosis and Quantification Challenge (2012) testing datasets which contains 30 patient and annotated by LKEB algorithm [6] to train our network since the manual annotation is not provided for these samples. The local nature of our model allows it to detect all the main vessels and side branches even though it was trained on a model that only detects main branches and with noisy results (not the experts annotations). The testing sensitivity on 18 patient of the training Stenosis datasets yields the results shown in table 1. On a patch-wise level, we demonstrate that our model is highly capable of identifying the manual reference points with 95.48% sensitivity largely better than LKEB prediction with 38.33% (No radius margin is considered for a prediction to be labeled as correct). Surprisingly, the CenterlineNet model reflects the manual annotated data (95.48%) more than it does to the LKEB annotated centerlines (95.18%) which validate the robustness of the feature extraction power of the CNNs.

We evaluate our approach against the CAT08 datasets. First, we noticed the model performs worse on this framework than on the Stenosis and Quantification one (88.03% against 95.48%). This decrease can be explained by the fact that both these frameworks do not have the same image quality nor the acquisition scanner protocol for the acquired data and therefore the variation between the two sets of images is considerable. To solve this issue, we provide CAT08 patches to the training data and we retrain our model using transfer-learning while validating by a leave one-out technique. Results are reported in tab.2. We observe an augmentation of 5% in sensitivity and an adaptation of the model to the new samples. Since we attempt to find all the branches of the coronary artery tree, it is not useful to report specificity because the rotterdam framework extracts only the main trunc and a random side branch. Nevertheless, the idea of having connected structures is crucial to proceed with such model. Although it is a local oriented model, the overall prediction should reflect an understanding of the data by producing an artery tree that is harmonic with its

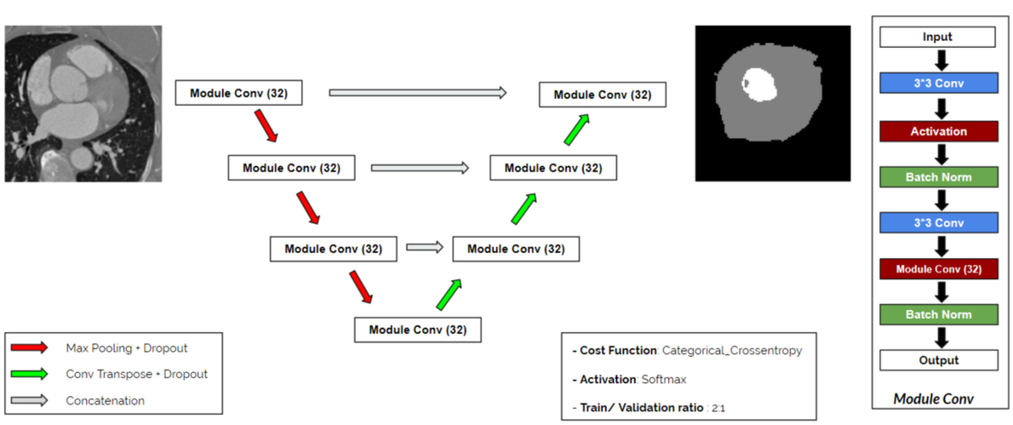

Figure 4. Aorta and Heart Region Detection

TABLE 1. EVALUATION OF CENTERLINENET PERFORMANCES ON 18 PATIENT FROM THE ROTTERDAM CORONARY ARTERY STENOSIS AND QUANTIFICATION CHALLENGE (2012) TRAINING SET [19]. THE COLUMNS CONSIDERED AS GROUND TRUTH ANNOTATION.

Models	*CTA Data*	*LKEB Prediction*	LKEB ∪ CTA	LKEB ∩ CTA
CenterlineNet Prediction	95.48 %	95.18%	94.83%	97.10%
LKEB Prediction	38.33 %	Nan	62.21%	Nan

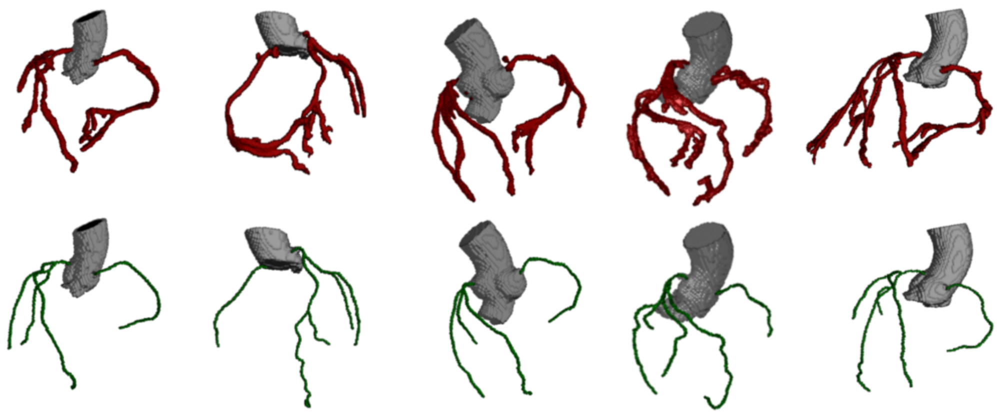

Figure 5. 3D models of the CenterlineNet predictions as well as the ground truth segmentations. The top row represents the prediction results while the bottom one displays the corresponding ground truth for the same patient and from the same view.

TABLE 2. EVALUATION OF CENTERLINENET PERFORMANCES ON 8 PATIENT FROM THE CAT08 DATASETS. WE REPORT THE RESULTS OF THE MODEL VERSION TRAINED ONLY ON THE STENOSIS DATA AND ANOTHER VERSION MIXED WITH THE CAT08 PATCHES [8]

Patient Number	**00**	**01**	**02**	**03**	**04**	**05**	**06**	**07**	**Overall**
With CAT08	85.51%	95.95%	93.23%	90.08%	98.43%	99.52%	98.21%	89.08%	93.75%
Withtout CAT08	78.44%	92.74%	88.92%	85.97%	85.99%	93.02%	95.07%	84.13%	88.03%

biological definition. Such an evaluation can only be made via visualization of the 3D predictions. So, as shown in Figure 5 the model has succeeded in reproducing the overall shape of the centerline tree.

5. Conclusion

One of the most explicit ways to tackle the centerline extraction task might be to provide a 3D neural network with the complete volume of data, but due to the scarcity of samples, the model will surely under fit and thus will poorly represent the data features. One could argue that data augmentation techniques can help solve such deficiencies but when the actual data size is relatively small then its contribution becomes minor. In this work, we have presented a novel, fully automatic method for the extraction of coronary arteries using 3D CNNs. Our approach used exclusively the publicly available Rotterdam Frameworks limited dataset to train and test. Although we used noisy predictions to train our model, it has achieved a high retrieval rate of 95.48% and 93.75% on manual annotated references for both datasets. In this work, only automatic learned features with no prior assumptions are used to navigate the pathway of the coronary tree with 3D CNNs used solely as a local centerline detector replacing the handcrafted filters and cost functions used for vesselness measurement. The full pipeline however, assures the detection of a complete connected artery tree with main and side branches originating from the aorta and limited within the heart region boundaries. Future work will incorporate a tracking method to recover the non predicted points as well as a centerline refinement technique using CMPR to tune more the center of the detected vessels.

References

[1] David Lesage and Elsa D. Angelini and Isabelle Bloch and Gareth Funka-Lea: A review of 3D vessel lumen segmentation techniques: Models, features and extraction schemes. Medical Image Analysis **13**(5), 819 - 845 (2009).

[2] Frangi, Alejandro F. and Niessen, Wiro J. and Vincken, Koen L. and Viergever, Max A.: Multiscale vessel enhancement filtering. Medical Image Computing and Computer-Assisted Intervention — MICCAI, Springer Berlin Heidelberg(1998).

[3] Sato, Y, Nakajima, S, Shiraga, N, Atsumi, H, Yoshida, S, Koller, T, Koller, T, Kikinis, R: Three-dimensional multi-scale line filter for segmentation and visualization of curvilinear structures in medical images. Medical image analysis, 143-68 (1998)

[4] C. Bauer and H. Bischof: Edge Based Tube Detection for Coronary Artery Centerline Extraction. Midas Journal (2008) http://hdl.handle.net/10380/1403

[5] K. Krissian and H. Bogunovic and J. Pozo and M. Villa-Uriol and A. Frangi.: Minimally Interactive Knowledge-based Coronary Tracking in CTA using a Minimal Cost Path. Midas Journal (2008), http://hdl.handle.net/10380/1435.

[6] Guanyu Yang, Pieter Kitslaar, Michel Frenay, Alexander Broersen, Mark J. Boogers, Jeroen J. Bax, Johan H. C. Reiber, Jouke Dijkstra: Automatic centerline extraction of coronary arteries in coronary computed tomographic angiography. Cardiovasc Imaging, 28:921–933 (2012)

[7] Friman, Ola and Hindennach, Milo and Kühnel, Caroline and Peitgen, Heinz-Otto: Multiple hypothesis template tracking of small 3D vessel structures. Medical image analysis, 160—171 (2010)

[8] Schaap M, Metz CT, van Walsum T, van der Giessen AG, Weustink AC, Mollet NR, Bauer C, Bogunović H, Castro C, Deng X, Dikici E, O'Donnell T, Frenay M, Friman O, Hernández Hoyos M, Kitslaar PH, Krissian K, Kühnel C, Luengo-Oroz MA, Orkisz M, Smedby O, Styner M, Szymczak A, Tek H, Wang C, Warfield SK, Zambal S, Zhang Y, Krestin GP, Niessen WJ. Standardized evaluation methodology and reference database for evaluating coronary artery centerline extraction algorithms. Medical Image Analysis (2009) 701-14.

[9] David Lesage, Elsa D.Angelini, Gareth Funka-Lea, Isabelle Bloch : Adaptive particle filtering for coronary artery segmentation from 3D CT angiograms. Computer Vision and Image Understanding, 151 (2016) 29–46

[10] Alexander Khvostikov and Karim Aderghal and Jenny BenoisPineau and Andrey S. Krylov and Gwenaelle Catheline : 3D CNN-based classification using sMRI and MD-DTI images for Alzheimer disease studies, (2018), http://arxiv.org/abs/1801.05968

[11] Gülsün, Mehmet A. and Funka-Lea, Gareth and Sharma, Puneet and Rapaka, Saikiran and Rapaka, Saikiran : Coronary Centerline Extraction via Optimal Flow Paths and CNN Path Pruning. Medical Image Computing and Computer-Assisted Intervention - MICCAI 2016, Springer International Publishing, (2016) 317–325.

[12] Guo, Zhihui and Bai, Junjie and and Lu, Yi and Wang, Xin and Cao, Kunlin and Song, Qi and Sonka, Milan and Yin, Youbing" : DeepCenterline: A Multi-task Fully Convolutional Network for Centerline Extraction. Information Processing in Medical Imaging, Springer International Publishing, (2019) 441–453.

[13] Jelmer M. Wolterink and Robbert W. van Hamersvelt and Max A. Viergever and Tim Leiner and Ivana Isgum : Coronary Artery Centerline Extraction in Cardiac CT Angiography Using a CNN-Based Orientation Classifier (2018). {http://arxiv.org/abs/1810.03143}.

[14] Jameson Merkow and David J. Kriegman and Alison Marsden and Zhuowen Tu : Dense Volume-to-Volume Vascular Boundary Detection (2016). {http://arxiv.org/abs/1605.08401}.

[15] Weimin Huang and Lu Huang and Zhiping Lin and Su Huang and Yanling Chi and Jiayin Zhou and Junmei Zhang and Ru San Tan and Liang Zhong : Coronary Artery Segmentation by Deep Learning Neural Networks on Computed Tomographic Coronary Angiographic Images.40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBC 2018, Honolulu, HI, USA, July 18-21, 2018 (608–611) {https://doi.org/10.1109/EMBC.2018.8512328}.

[16] Ye Shen and Zhijun Fang and Yongbin Gao and Naixue Xiong and Cengsi Zhong and Xianhua Tang : Coronary Arteries Segmentation Based on 3D FCN With Attention Gate and Level Set Function. IEEE Access 42826–42835 (2019) {http://arxiv.org/abs/1704.03379}.

[17] Matthew C. H. Lee and Kersten Petersen and Nick Pawlowski and Ben Glocker and Michiel Schaap : TeTrIS: Template Transformer Networks for Image Segmentation With Shape Priors. IEEE Trans. Med. Imaging 2596–2606 (2019)

[18] Pim Moeskops and Jelmer M. Wolterink and Bas H. M. van der Velden and Kenneth G. A. Gilhuijs and Tim Leiner and Max A. Viergever and Ivana Isgum : Deep Learning for Multi-Task Medical Image Segmentation in Multiple Modalities (2017).

[19] H.A. Kirişli and M. Schaap and C.T. Metz and A.S. Dharampal and W.B. Meijboom and S.L. Papadopoulou and A. Dedic and K. Nieman and M.A. de Graaf and M.F.L. Meijs and M.J. Cramer and A. Broersen and S. Cetin and A. Eslami and L. Flórez-Valencia and K.L. Lor and B. Matuszewski and I. Melki and B. Mohr and I. Öksüz and R. Shahzad and C. Wang and P.H. Kitslaar and G. Unal and A. Katouzian and M. Orkisz and C.M. Chen and F. Precioso and L. Najman and S. Masood and D. Ünay and L. van Vliet and R. Moreno and R. Goldenberg and E. Vuçini and G.P. Krestin and W.J. Niessen and T. van Walsum: Standardized evaluation framework for evaluating coronary artery stenosis detection, stenosis quantification and lumen segmentation algorithms in computed tomography angiography. vol. 17, pp. 859 - 876. Medical Image Analysis (2013).

[20] Özgün Çiçek and Ahmed Abdulkadir and Soeren S. Lienkamp and Thomas Brox and Olaf Ronneberger : 3D U-Net: Learning Dense Volumetric Segmentation from Sparse Annotation (2016) http://arxiv.org/abs/1606.06650.

[21] Olaf Ronneberger and Philipp Fischer and Thomas Brox : U-Net: Convolutional Networks for Biomedical Image Segmentation (2015). http://arxiv.org/abs/1505.04597.

[22] Kikinis, Ron., Pieper, Steve D., Vosburgh, Kirby G.: 3D Slicer: A Platform for Subject-Specific Image Analysis, Visualization, and Clinical Support. Intraoperative Imaging and Image-Guided Therapy (277–289). Springer New York (2014)