Machine-learning based clinical plaque detection using a synthetic plaque lesion model for coronary CTA

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Summary

- Coronary CTA is an important diagnostic tool in the assessment of coronary artery disease (CAD).
- Data-driven predictive systems rely on high-quality annotated ground truth data in large abundance.
- Using a synthetic forward model we demonstrate how synthetically generated plaque lesions can help to ease the annotation burden for CTA machine learning applications.

Introduction

Coronary computed tomography angiography (**coronary CTA**) is a robust and well-established non-invasive diagnostic tool to detect and assess coronary artery disease (CAD). The accurate detection, quantification and characterization of the coronary plaque burden has become an important part of this imaging modality [1], [2].

The quality and performance of modern machine-learning-based data-driven learning approaches is often impacted by either insufficient or inconsistently-labeled training data and is further subject to additional bias from human annotators. To address these shortcomings for coronary plaque characterization, we have developed **a synthetic lesion generating framework for CTA applications**, which can produce accurate and high-quality labeled training data for data-driven learning approaches.

Our herein presented method can help to **ease the manual annotation burden**, which is often the limiting factor in data-driven learning algorithms and instead provides reliable ground truth data for modern deep learning approaches. Furthermore, this framework can easily be used to create custom tailored training data that can be used for pre- or post-training steps of already existing machine learning approaches for various CTA applications.

Figure 1 Schematic overview of the synthetic plaque lesion module integrated into a machine learning framework for coronary CTA. Starting from a clinical CCTA scan (**A**) together with a coronary artery tree segmentation (centerline and lumen segmentation) (**B**) the synthetic lesion generator can inpaint synthetic lesions in healthy coronary vessels (**C**) and therewith create high-quality annotated training data for predictive machine learning applications (**D**). The synthetic lesion generation module itself consists of three modular parts. A stochastic location generator samples lesion position and lesion length in the coronary artery tree. This step is then followed by a shape module which creates a voxelized lesion volume according to a handful of geometric parameters and a texture module which adds realistic intensity grey values to arrive at a final synthetic lesion, as exemplary shown in part (D).

Material & Methods

Clinical data base and annotation scheme

We collected and curated **92 clinical CTA** scans acquired at the Department of Diagnostic and Interventional Radiology and Nuclear Medicine, University Hospital Hamburg Eppendorf, Germany. For all of these we performed a coronary artery tree segmentation to obtain the centerline position and lumen segmentation. Within this set we identified **11 healthy patients** without any clinical findings that were used for our synthetic forward model in this work.

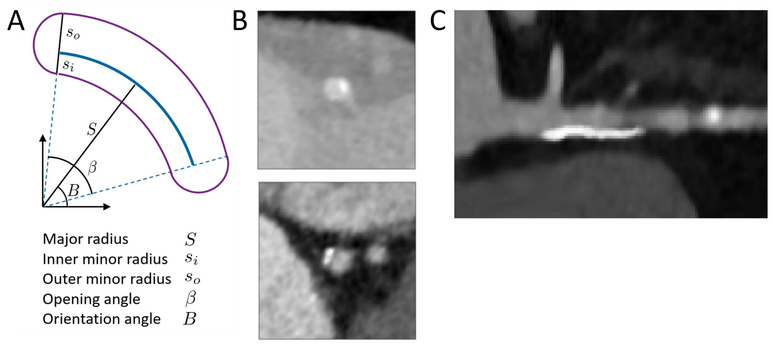

Figure 2 Synthetic plaque lesion model. **(A)** depicts the **toroidal plaque shape model** which creates the lesion shape based on the depicted geometrical shape parameters. Shown is a cross-sectional view with the center of origin in the vessel center. These five shape parameters can vary along the vessel's centerline and are sampled per inserted lesion. **(B)** shows two synthetically created lesions in cross-sectional view, while **(C)** illustrates the extent and lesion shape in a stretched MPR view.

All cases were prepared for manual annotation by a human expert reader based on a stretched multi-planar reformatted (MPR) image reconstruction based on the underlying vessel segmentation. This allows to view all vessels both in a longitudinal view and on a cross-sectional level. In this detailed annotation process we labeled various plaque types as well as other high-risk markers.

In this process labels can be created either on a per cross-section level, by annotating a certain interval in the stretched MPR view, or on a per-pixel level on a specific cross section by creating a corresponding label bitmask. For this work we focused on calcified plaque labels and pooled all labels from both label types accordingly to obtain consistent per-frame labels for calcified plaque.

Synthetic Lesion Model

The lesion model consists of a shape and a texture module (see Fig. 1 and Fig. 2 (A)) which jointly create an artificial lesion using only a few geometric parameters. Based on a coronary artery tree segmentation (centerline and lumen), the lesion shape is modulated by varying radii, angles and length parameters of a given **toroidal geometry** along the coronary's centerline (compare Fig. 2). Based on the lesion's shape, a motion vector field (MVF) is generated to capture the lesion growth process. After creating this shape and applying the growth model, a given lesion is inpainted into a given healthy vessel using a texture module. Exemplary results of this approach are depicted in Fig. 2 (B and C).

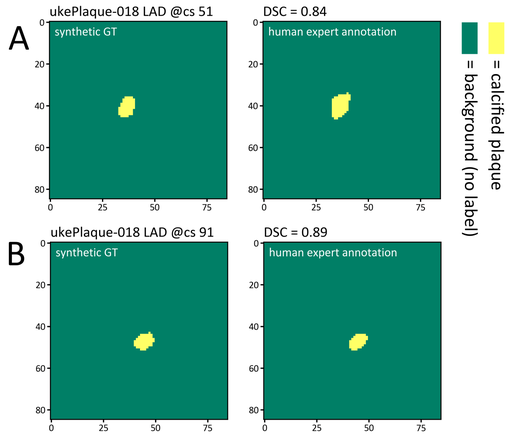

Figure 3 Comparison of automatic generated ground truth annotation and human expert labeling to verify the quality of synthetically generated lesions. **(A & B)** Two exemplary chosen cross-sectional bitmasks showing the calcified plaque lesion (yellow) as binary bitmasks for two cross sections. Shown is also the **Dice coefficient (DSC)** as an overlap measure to quantify agreement between left (automatic GT annotation) and right (human expert). **(C)** Summary statistic reporting the Dice coefficient for all N = 60 labeled cross-sectional plaque findings for a given test case, giving an average Dice coefficient of 74%.

Learning approach

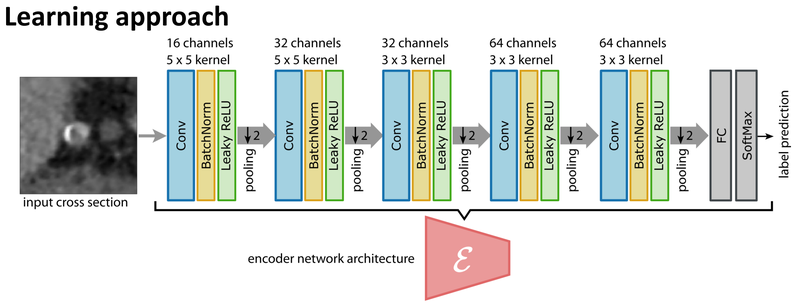

Figure 4 Encoder neural network architecture. Starting from an input cross-section at the very left, a forward pass consists of five VGG-like layers (2D convolution, batch normalization and nonlinear activation function) with a subsequent average pooling step after each layer.

In this work we use a neural **encoder architecture** (similar to Noh et al. [3]). This is a deep CNN architecture where **VGG-like neural network layers** are combined [4] (see Fig. 4). The encoder consists of five sub-blocks, each containing a convolutional layer (twice kernel size 5x5 and 3x3 in the last three blocks, all with stride 1), batch normalization [5] and leaky ReLU as activation. The single channel raw input is increased to 16 feature channels in the first sub block and then further increased to 32 and 64 as illustrated in Fig. 4. After each VGG-like sub block an average pooling operation is performed with kernel size 2x2 and stride 2. The output of the last sub block is fed into a fully connected layer (FC) followed by a softmax operation to output the class probabilities for the classification task.

In this work we looked at the **binary classification task** of predicting calcified plaque on a per-frame level and trained this encoder structure in a supervised manner. For this process we used the ADAM optimizer [6] for training and ran all models for 200 epochs using a cross-entropy loss function.

Results

- We preformed several plaque detection experiments using the described data-driven learning approach and report the classification performance by reporting normalized confusion matrices.
- A purely synthetic training, applied to synthetic test data shows on overall **classification accuracy of 93%** (see Fig.5 (A)). This demonstrates that synthetic lesions can be faithfully and self-consistently classified with high accuracy.
- **Transfer learning experiment**: Applying the same synthetically trained model to unseen clinical test data we obtain an overall **classification accuracy of 84%**. This demonstrates that synthetically generated lesions can be used to solve the much harder task of classifying real lesions. This model has not seen any real lesion during training (see Fig. 5 (B)).

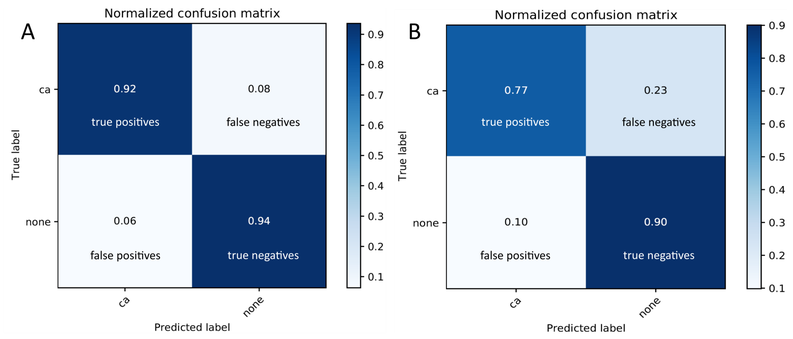

Figure 5 Normalized confusion matrices summarizing the classification performance. Rows are normalized to unity. **(A)** Results for a purely synthetic training tested on purely synthetic test data. **(B)** Results for the transfer learning experiment by applying the purely synthetically trained model on a test set with clinical plaque findings. Ca denotes the calcified plaque label in the binary classification task.

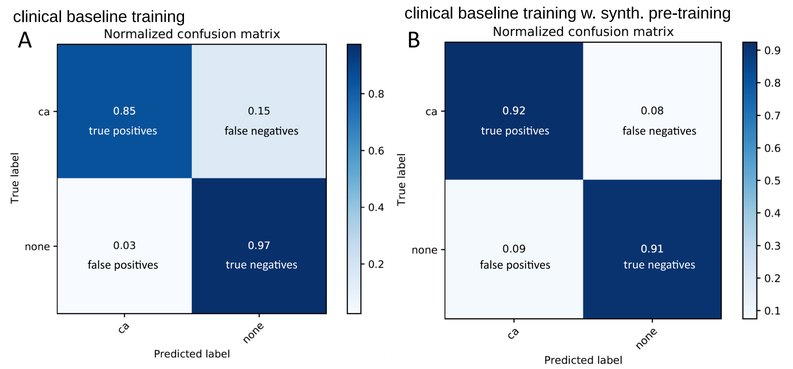

Figure 6 Normalized confusion matrices similar to Fig. 5. **(A)** Results for a purely clinical baseline training without any synthetic lesions. **(B)** Results for the same setup as in (A) but this time using a pre-trained model that was trained on purely synthetic lesions.

- Using a synthetically trained plaque detector model as a **pre-training** for a fully clinical training we can **improve the baseline classification accuracy** (Fig. 6 (A)) from 91% to 92% (Fig. 6 (B)) with a much higher true positive count (increase to 92% from a baseline value from 85%).

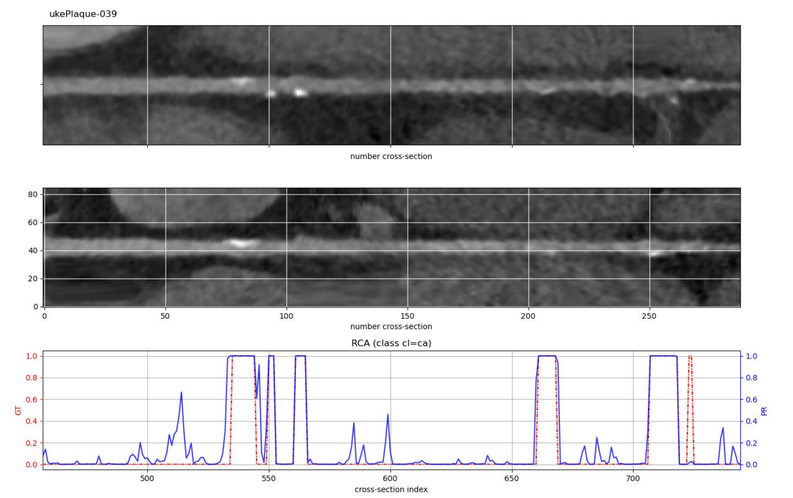

Figure 7 Predicted class probabilities as a function of the cross-sectional position along the RCA vessel of a clinical test case. This shows sample predictions from the clinical training with synthetic pre-training (compare Fig. 6 (B)). Here, the red-dashed lines indicate the ground truth annotation and the blue curves show the network prediction for the calcified plaque detection as probability values.

Conclusions

- The proposed synthetic lesion framework can create exhaustively annotated high-quality ground truth data for coronary CTA.
- We demonstrated the application and advantages of using such a synthetic forward model by performing various plaque detection experiments using a machine learning framework.
- The fast algorithmic nature of this forward model and its customization possibilities to site-specific requirements render this a valuable tool for data-driven predictive system for coronary CTA.

References

(1) Maurovich-Horvat P, Ferencik M, Voros S, Merkely B, Hoffmann U. *Comprehensive plaque assessment by coronary CT angiography.* Nat Rev Cardiol. 2014;11(7):390-402. doi:10.1038/nrcardio.2014.60

(2) Kolossváry M, Szilveszter B, Merkely B, Maurovich-Horvat P. *Plaque imaging with CT - a comprehensive review on coronary CT angiography based risk assessment.* Cardiovasc Diagn Ther 2017;7(5):489-506. doi: 10.21037/cdt.2016.11.06

(3) Noh, H., Hong, S., Han, B, *Learning Deconvolution Network for Semantic Segmentation*, Proceedings of the 2015 IEEE International Conference on Computer Vision (ICCV), IEEE Computer Society, 1520-1528, (2015)

(4) Simonyan, K. and Zisserman, A., *Very Deep Convolutional Networks for Large-Scale Image Recognition*, in [3rd International Conference on Learning Representations, ICLR 2015, Conference Track Proceedings], (2015)

(5) Ioffe, S., Szegedy, C., *Batch normalization: Accelerating deep network training by reducing internal covariate shift*, arXiv preprint arXiv:1502.03167, 2015

(6) Kingma, D. P. and Ba, J., *Adam: A method for stochastic optimization*, in [3rd International Conference on Learning Representations, ICLR 2015, Conference Track Proceedings], (2015).

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