2021 43rd Annual International Conference of the
IEEE Engineering in Medicine & Biology Society (EMBC)
Oct 31 - Nov 4, 2021. Virtual Conference

Automated Cerebral Vessel Segmentation of Magnetic Resonance Imaging in Patients with Intracranial Atherosclerotic Diseases

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***Abstract*— Time-of-flight (TOF) magnetic resonance angiography is a non-invasive imaging modality for the diagnosis of intracranial atherosclerotic diseases (ICAD). Evaluation of the degree of the stenosis and status of posterior and anterior communicating arteries to supply enough blood flow to the distal arteries is very critical, which requires accurate evaluation of arteries. Recently, deep-learning methods have been firmly established as a robust tool in medical image segmentation, which has been resulted in developing multiple customized algorithms. For instance, BRAVE-NET, a context-based successor of U-Net—has shown promising results in MRA cerebrovascular segmentation. Another widely used context-based 3D CNN—DeepMedic—has been shown to outperform U-Net in cerebrovascular segmentation of 3D digital subtraction angiography. In this study, we aim to train and compare the two state-of-the-art deep-learning networks, BRAVE-NET and DeepMedic, for automated and reliable brain vessel segmentation from TOF-MRA images in ICAD patients. Using specially labeled data—labeled on TOF MRA and corrected on high-resolution black-blood MRI, of 51 patients with ICAD due to severe stenosis, we trained and tested both models. On an independent test dataset of 11 cases, DeepMedic slightly outperformed BRAVE-NET in terms of DSC (0.905±0.012 vs 0.893±0.015, p: 0.539) and 95HD (0.754±0.223 vs 1.768±0.609, p: 0.134), and significantly outperformed BRAVE-NET in terms of Recall (0.940±0.023 vs 0.855±0.030, p: 0.036). Qualitative assessment confirmed the superiority of DeepMedic in capturing the small and distal arteries. While BRAVE-NET consistently reported higher precision, DeepMedic generally overpredicted and could better visualize the smaller and distal arteries. In future studies, ensemble models that can leverage best of both should be developed and tested on larger datasets.**

***Clinical Relevance*— This study helps elevate the state-of-the-art for brain vessel segmentation from non-invasive MRA, which could accelerate the translation of vessel status-based biomarkers into the clinical setting.**

I. INTRODUCTION

Intracranial atherosclerotic disease (ICAD) is responsible for 8-10% of all strokes and is particularly prevalent in Black, Hispanic, and Asian populations.[1] Luminal imaging techniques, specifically non-invasive time-of-flight magnetic resonance angiography (TOF-MRA) is routine clinical procedure for the diagnostis and evaluation of the stenotic lesion. However, as MRA visualizes the flow within the vessels, its accuracy and reliability in the visualization of lesion might be compromised in regions with slow or turbulent flow characteristics, in particular small arteries, carotid siphon, and stenotic regions. Therefore, delineation of the lesion (lumen) and smaller vessel requires neuroradiologists to manually segment the images, which is time-consuming and introduces uncertainties and subjectivity. Therefore, tools that can automatically segment and provide accurate and reliable representation of vasculature, especially smaller arteries, can help to improve management of ICAD patients.

Efforts have been made to develop tools for cerebrovascular segmentation, but they were semi-automatic, utilizing hand-crafted features, and were insufficiently validated on independent datasets [2, 3]. More recently, with the advent of deep learning (DL) and its application to medical image segmentation, multiple DL methods have emerged [4-6]. From these DL methods, the current state-of-the-art is a 3D convolutional neural network (CNN)—BRAVE-NET [5], that mainly excelled due to the extra contextual information it provides to the CNN architecture over its predecessor—U-Net [4, 7]. DeepMedic is another context-based 3D CNN that has been used in the recent past for various medical segmentation applications ranging from brain lesion segmentation [8] to cerebrovascular segmentation of finer 3D digital subtraction angiography (DSA) [6]. Interestingly, DeepMedic has been shown to be significantly superior to U-Net for cerebrovascular segmentation from 3D DSA images [6].

To that end, we aim to do a comparative study between the two state-of-the-art context-based 3D CNNs for brain vessel segmentation from MRA. We train, and independently test the two models on a dataset of 51 retrospectively collected TOF-MRA images from patients with ICAD. Furthermore, for more accurate ground truth generation, mostly in small arteries, carotid siphon, and stenotic regions, we employ high-resolution black-blood MRI. We performed thorough qualitative and quantitative assessment to assess the performance of both the models on independent testing cohort.

II. MATERIALS AND METHODS

A. Patient selection and Imaging

This study was approved by the institutional review board (IRB) at the University at Buffalo (Study00004370). All methods were carried out in accordance with the approved protocol and consent was waived by the IRB. We retrospectively collected MRA and black-blood MRI from 51 ICAD patients from the Dent Neurologic Institute (Amherst, NY, USA). MRI scans were acquired at the Dent Neurologic Institute (Amherst, NY, USA) on a 3T Philips Ingenia Elition

*Research supported by the Dent Family Foundation.

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X scanner. The axial MRA covered vessel from the skull base to the top of corpus callosum, reconstructed voxel size 0.6x0.7x1.1mm, scan time was 6:05 minutes. The axial VISTA sequence coverage was 8cm, with the center slice positioned over the Circle of Willis. Voxel size was 0.5x0.5x0.5mm, scan time was 8:30 minutes.

B. Ground truth generation and Pre-processing

Figure 1 demonstrates a representative case for the generation of labels from multi-model MR images as ground-truth. A radiologist (N.P) with 10 years of experience in reviewing MR neurovascular images segmented the intracranial vasculature visible in the head-and-neck MRA. Specific caution was exercised in the reconstruction of Pcom, Acom, stenotic lesion, and ICA siphon, leveraging black-blood MRI. MRI data were registered using the BRAINS registration algorithm available in the open-source software 3D Slicer (www.slicer.org). Furthermore, as a pre-processing step, to avoid inhomogeneity in the MRA dataset, we performed N4-ITK MR Bias correction on the MRA images using the open-source tool 3D Slicer.

C. Deep-Learning architectures

The architectures implemented for this study have been illustrated in detail in Fig 2. Both the CNN architectures are context-driven with dual pathways—high- and low-resolution. The detailed local appearance of vascular structures is captured in the high-resolution input whereas the higher-level features such as the connectivity of the vascular network are learned in the low-resolution pathway.

The BRAVE-NET architecture is the current state-of-the-art for TOF-MRA brain vessel segmentation, recently used by Hilbert et al. [5]. This CNN improves upon the conventional U-Net by adding contextual information around the patch to be segmented, and by borrowing the concept of 'deep-supervision' introduced to avoid the problem of exploding or vanishing gradients.

DeepMedic implemented for this study is similar to the original architecture [8]. The overall architecture contains 11 fully un-padded convolutional layers. The low- and high-resolution inputs first go through 4 independent layers each of fully connected convolutions.

D. Training scheme

All models were implemented in Python using the Keras Deep Learning library (https://github.com/fchollet/keras) with Tensorflow deep learning framework as the backend [9]. The learning rates for individual architectures were set to their prescribed values [5, 8]. The complete dataset of 51 was divided into training (n=32), validation (n=8) and testing datasets (n=11). Depending on the GPU memory footprint, each model was prescribed their respective batch sizes, BRAVE-NET: 30, and DeepMedic: 50. Similar to the original studies, training was performed in patches, with 2000 patches extracted from each image in the training/validation datasets, resulting in a total of 80,000 patches split up into training and validation cohorts in 80%:20% split. The models were trained by optimizing the loss function defined as a hybrid binary-crossentropy and Dice Similarity Coefficient (DSC) [10], optimized using the ADAM optimizer. All models were trained using the EarlyStopping criteria.

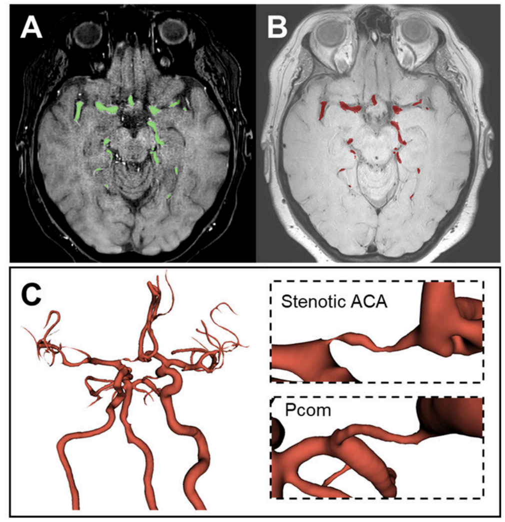

Figure 1. Ground truth label generation. From a representative case included in the training dataset, A) MRA, B) Co-registered Black Blood MRI, C) 3D Visualization of the segmented geometry, with representative zoomed stenotic ACA and healthy PCOM.

E. Model evaluation

Qualitative comparison was performed to observe the extent of missing vessels, missing vasculature connections, and quality of segmentation of vessels for all segmentation methods, for assessing the overall segmentation quality. To assist with visualization, for each case, all predicted voxels were assigned true positive (TP), true negative (TN), false positive (FP) and false negative (FN) labels, visualized by overlaying TP, FP and FN. Furthermore, for quantitative assessment of the CNN models, dice similarity coefficient (DSC), precision, recall and 95 percentile hausdrauff distance (95HD) were computed [5].

III. Results

Quantitative results on the independent testing cohort (n=11) is reported in Table 1. Deepmedic model performed better than the current state-of-the-art MRA cerebrovascular segmentation CNN BRAVE-NET in terms of DSC (0.905±0.012 vs 0.893±0.015, p: 0.539) and 95HD (0.754±0.223 vs 1.768±0.609, p: 0.134). DeepMedic significantly outperformed the BRAVE-NET model in recall (0.940±0.023 vs 0.855±0.030, p: 0.036). Precision was higher in BRAVE-NET as compared to DeepMedic (0.884±0.028 vs 0.947±0.071, p: 0.087).

Overall quantitative comparison on the independent testing cohort showed a similar trend. Overall quantitative comparison on the independent testing cohort showed a similar trend. With significantly high recall, as expected, DeepMedic showed clear overprediction of distal vessels in the anterior and posterior circulation.

TABLE I. RESULTS ON THE INDEPENDENT TESTING COHORT (N=11)

Features	DeepMedic	BRAVE-NET	p-value
DSC (mean±SE)	**0.905±0.012**	0.893±0.015	0.539
95HD (mean±SE)	**0.754±0.223**	1.768±0.609	0.134
Precision (mean±SE)	0.884±0.028	**0.947±0.071**	0.087
Recall (mean±SE)	**0.940±0.023**	0.855±0.030	0.036*

*Indicates significant difference using the 2-sample t-test (5% significance level)

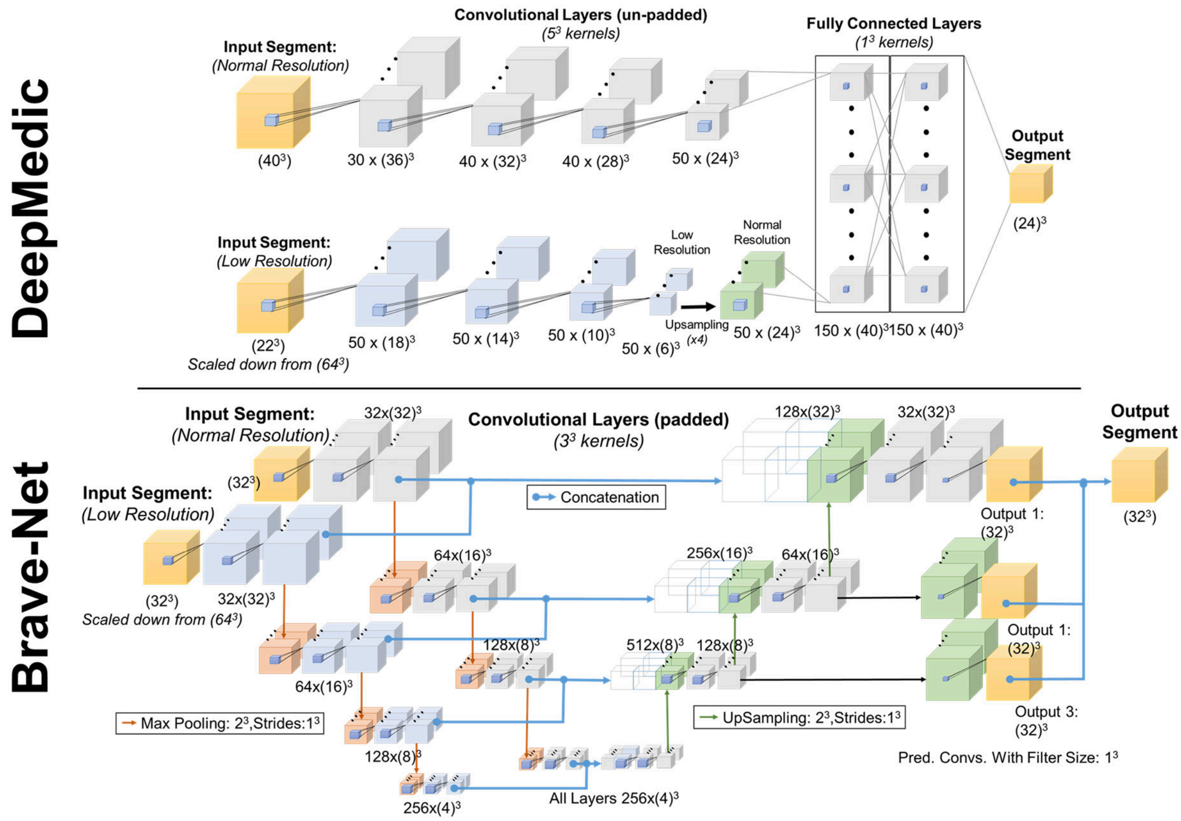

Figure 2. Context driven CNN architectures. Top-DeepMedic. Bottom-BRAVE-NET. Both networks designed to employ contextual information from the low-resolution pathway to maintain connectivity in vascular segmentation.

Qualitative comparison on 3 representative cases from the independent testing cohort is illustrated in Figure 3. Case 1 shown in Fig. 3 magnifies the overall trends observed in the testing cohort. BRAVE-NET missed the right ACOM, significant portions of left and right vertebral arteries, and smaller distal vessels, all of which was captured by the segmentation output of DeepMedic. Case 2 shows missing portions of ACOM and ACA missed by BRAVE-NET, whereas parts of both PCOMs were missed by both models.

Case 3 shown in Fig. 3 illustrates why the DeepMedic model yielded a significantly higher Recall than BRAVE-NET. In 4/11 testing cases, a considerable overprediction in terms of distal vessels from the anterior and posterior from DeepMedic. These vessels were considered non-essential/missed during the ground-truth development. This in turn led to a significantly higher recall from DeepMedic.

IV. Discussion and Conclusions

In this study, we presented a comparative analysis between the state-of-the-art for cerebrovascular segmentation of MRA images—BRAVE-NET, with DeepMedic—a 3D CNN shown to outperform U-Net for 3D DSA cerebrovascular segmentation. Our results indicate that in terms of Recall, DSC and 95HD, DeepMedic outperforms BRAVE-NET, whereas BRAVE-NET outperformed DeepMedic in terms of Precision. Further qualitative investigation showed that the reason behind such as trend was overprediction by DeepMedic, of distal vessels that were deemed non-essential/missed out during ground truth generation.

DeepMedic outperformed BRAVE-NET in terms of segmentation of smaller distal vessels, yet important for ICAD evaluation. Moreover, DeepMedic in most instances overpredicted smaller distal vessels as seen by the significantly higher Recall but a lower precision. There are two major reasons why we believe DeepMedic outperforms BRAVE-NET in small vessel segmentation. Firstly, the receptive field available for DeepMedic is larger than BRAVE-NET. DeepMedic inputs a larger high-resolution patch (40^3 vs 32^3) for a smaller output patch size (24^3 vs 32^3) compared to BRAVE-NET. Such a difference in input and output patch sizes can be explained as a pseudo-overlap in patches, allowing DeepMedic to have more context than BRAVE-NET. Secondly, DeepMedic only uses convolutions in its high-resolution pathway, whereas a BRAVE-NET uses convolution followed by max-pooling. Studies have shown previously how pooling and strided convolutions can negatively affect the contextual information, by halving the resolution after every other convolution [11]. This has also led to researches developing more innovative schemes such as dilated convolutions that systematically aggregate multi-modal contextual information without losing resolution [11].

While this study can help the current state-of-the-art to move forward, several limitations/improvements can be addressed in the future. Firstly, a larger dataset for testing the performance model is required in the future. Secondly, while BRAVE-NET is a significant step up to the conventional U-Net, next generation U-Nets designed for brain vessel segmentation such as the Iter-NET [12] should be looked into in the future. Future studies can also try to add contextual information to the Iter-NET and extend the work for segmentation of 3D cerebrovascular segmentation. Thirdly, ensemble models, shown to outperform single models [13], that leverage the best of fully convolutional model such as DeepMedic, and modern U-Net successors such as BRAVE-NET should also be developed.

In conclusion, this preliminary works shows DeepMedic to be a viable option to the current state-of-the-art for brain vessel segmentation from TOF-MRA images, due to its various advantages over BRAVE-NET. The study demonstrates how DeepMedic excels in prediction of smaller intracranial vessels as well as more distal smaller vessels compared to BRAVE-NET on a smaller dataset. Future studies on larger datasets are required to further the state-of-the-art and bring it closer to clinical translation.

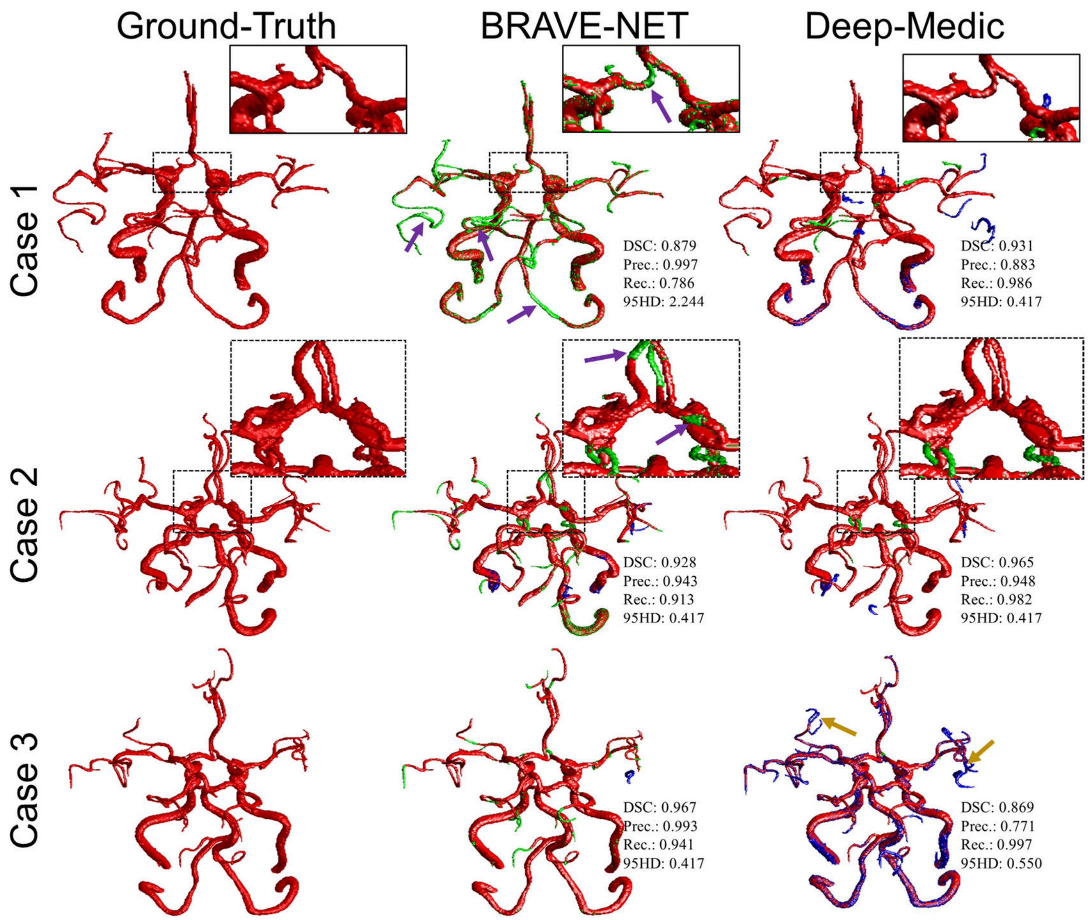

Figure 3. Three representative cases from the independent testing cohort predicted by BRAVE-NET and DeepMedic compared against the ground truth. In the predictions Red indicated true positives, Green indicated false positives and Blue indicates false negatives. Case 1: small yet important artery ACA, and other more distal vessels indicated by purple arrows missed by BRAVE-NET. Case 2: part of ACA and ACom, indicated by purple arrows missed by BRAVE-NET whereas PComs missed by both networks. Case 3: DSC indicates a better performance of the BRAVE-NET compared to DeepMedic against the ground-truth, but qualitative comparison shows overpredictions of distal vessels indicated by golden arrows.

ACKNOWLEDGMENT

The authors would like to acknowledge Ciprian N. Ionita and Sandeep Ganji for the constructive discussions.

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