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Automatic cerebrovascular segmentation methods-a review

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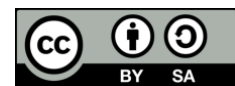
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U-Net

ABSTRACT

Cerebrovascular diseases are one of the serious causes for the increase in mortality rate in the world which affect the blood vessels and blood supply to the brain. In order, diagnose and study the abnormalities in the cerebrovascular system, accurate segmentation methods can be used. The shape, direction and distribution of blood vessels can be studied using automatic segmentation. This will help the doctors to envisage the cerebrovascular system. Due to the complex shape and topology, automatic segmentation is still a challenge to the clinicians. In this paper, some of the latest approaches used for segmentation of magnetic resonance angiography (MRA) images are explained. Some of such methods are deep convolutional neural network (CNN), 3dimensional-CNN (3D-CNN) and 3D U-Net. Finally, these methods are compared for evaluating their performance. 3D U-Net is the better performer among the described methods.

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1. INTRODUCTION

In the world, vascular diseases are one of the most common cause of death which causes stroke in about millions of people every year. Therefore, fast and accurate tools are required in order to diagnose and treat cerebrovascular diseases. MRA is the one of the common imaging techniques used to perform this function, which consists in a magnetic resonance imaging (MRI) that looks specifically the blood flow in the brain vessels when measuring. Different methods of MRA are time-of-flight (TOF), phase contrast (PC) and fresh blood imaging (FBI) and contrast-enhanced MRA [1]. TOF MRA is the most commonly used imaging modalities in non-invasive vascular research [2]. Segmentation is used to identify and separate vessels from neighborhood tissue which helps in better view and quantitative analysis. Segmentation of blood vessels done manually is having many shortcomings like it is time-consuming, prone to error. In such a situation, more accurate and faster segmentation methods are implemented. Some of the approaches used for cerebrovascular segmentation are deep CNN [3], 3D CNN, and 3D U-Net.

A CNN is a class of deep neural network [4] consisting of one or more convolutional layers, pooling layer and fully connected layer. A feature map created by the first layer i.e. convolutional layer is used to extract the features from an input image. This is possible by using a filter that scans the full image pixel wise. Pooling layer cutdown the quantity of information the first layer generated for each feature and maintains the most important information only. The output generated by the pooling layer is flattened by fully connected input layer, which converts them into a single vector that serves as an input for the next layer. After passing through the fully connected layer, the final layers use the SoftMax activation function which helps in classification. Fully connected output layer generates the final result which will determine a class for the image. The filters of different sizes are used, also known as kernels. Usually convolution layer and pool layer

are used in some combination in CNN architecture [5]. Max pooling and mean pooling are the two types of operations carried out by the pooling layer. Mean pooling or average pooling calculates the average value from the region of the feature map. Maximum Pooling also called as max pooling finds the maximum value from the region of feature map covered by filter. The error caused by the neighborhood size limitation can be reduced by mean pooling and it also retains the background information. The estimated error caused by the mean deviation can be reduced by max pooling and hence keeps more texture information.

In 3D-CNN, 3D filters can move in all the three dimensions i.e. along X, Y and Z axes. 3D CNN requires more parameters and computations compared to 2D. Improvement in computer hardware and 3D medical imaging availability gives the concept of using 3D information for segmentation. Compared to 2D and 2.5D approaches which are having one, three orthogonal views, respectively, 3 dimensional images can deliver information in any direction. For the segmentation of the brain tumor of arbitrary size, the first pure 3D models were introduced. Multiscale, dual-path 3D CNN is also used in many applications. The next pathway received the patches from a sub sampled representation of the image. More areas around the voxel can be processed by using this, which will be advantageous to the whole system [6]. For better performance, small kernel size can be preferred. A deep model is required to isolate an organ from complex images which can thereby extract highly informative features. A significant challenge for 3D models is to train such deep network.

In order to strengthen the U-Net [7] structure with richer spatial information model, 3D U-Net is developed which is a deep neural network that helps in very compact volumetric segmentation. 3D U-Net requires only some annotated 2D slices by using weighted loss function and data augmentation for training. This network takes 3D volume as input and 3D operations like convolution, pooling, and loss calculation are used to process them. For vascular boundary detection, 3D U-Net was used. One of the disadvantages of 3D U-Net is the input image size should be small because of limited memory space [8]. Therefore, the input size of region of interest (ROI) is having poor resolution. Therefore, the input image can be divided in to multiple batches to overcome this issue, which can be further used for training and testing. In this paper, these three methods are explained in detail and compared their performance with global statistical based approach (GSB) by using dice similarity coefficient (DSC) values.

The remaining part of this paper is organized is being as. In the next section, literature survey is presented. In section 3, different cerebrovascular segmentation methods are explained, in section 4, results are discussed and finally conclusion is presented in section 5.

2. RELATED WORKS

Major contributions of some of the researchers who aimed at developing a system for cerebrovascular segmentation are summarized below. Sanches *et al.* [1] proposed a cerebrovascular segmentation method using deep learning. A 3D model called uception which is inspired from U-Net architecture is discussed in this paper. When compared with the U-Net model, this 3D architecture showed better performance. In order to improve the outcome of this model, they have decided to add more details regarding the cerebrovascular anatomy in the neural network.

Hesamian *et al.* [6] summarized some of the medical image segmentation methods and their performance compared with old methods. This paper also explained some of the applications helpful in the medical industry such as training techniques used for image segmentation. Advantages and disadvantages of these techniques are also taken into consideration. The challenges faced by the deep learning networks for segmentation and its effective remedies are also explained at the end.

A fully automatic segmentation method is proposed by Gao *et al.* [9] for detection of cerebrovascular diseases. This segmentation method is very fast too. Improved curve evolution and statistical model analysis play a major role in the segmentation of 3D-cerebral vessels from MRA. Modelling of the cerebral vessels is also explained in this paper. Combination of region distribution and gradient information is used as one novel mode in curve evolution. Low contrast thin vessel boundary around brain tissue can be determined by using the edge-strength function. A fast level set method was introduced to speed up the implementation of curve evolution which helps in improving the performance of cerebrovascular segmentation.

Fatma *et al.* [10] presented a review on accurate and advanced automated methods for cerebrovascular segmentation. In this paper, old, new, automatic and semiautomatic models explained along with its advantages and disadvantages. A linear combination of discrete gaussians (LCDG) model is used for segmentation that yields the empirical marginal gray level distribution intensity in the images, while using modified expectation maximization (EM) algorithm for refinement.

A statistical method discussed by Fatma *et al.* [11] utilizes a voxel-wise classification. In order to isolate blood vessels from the background of each time of flight MRA slice, probability models of voxel intensities are determined. The marginal empirical distribution of intensity probabilities is approximated for

the purpose of classification where LCDG is employed with alternate signs. For linear combination of gaussian approximation, EM-based techniques are also utilized that helps in dealing with LCDGs.

3. RESEARCH METHOD

Cerebrovascular segmentation methods such as deep convolutional neural network (CNN), 3dimensional-CNN (3D-CNN) and 3D U-Net are used for conducting this research which are discussed in detail. These methods are compared for evaluating their performances. Dice similarity coefficient (DSC) is used for determining the segmentaion accuracy.

3.1. Convolutional neural network (CNN)

When considering time-of-flight magnetic resonance angiography (TOF MRA) images, there are chances of over-fitting in the model learning and increased processing time by the use of complex deep CNN architectures. A CNN architecture proposed by Phellan *et al.* [12] composed of two convolutional layers and fully connected layers. Figure 1 depicts the CNN architecture, where the number of filters and details of receptive field in the two convolutional layers are mentioned. There is no sub sampling in the second convolutional layer. Next layer is a rectified linear activation (ReLU) which will reduce the back propagation vanishing problem. There are two fully connected layers present in this architecture. The first fully connected layers will reduce the dimensionality from 256 to 100 neurons, and the other layer will determine the likelihood of belonging to a vessel or not [12].

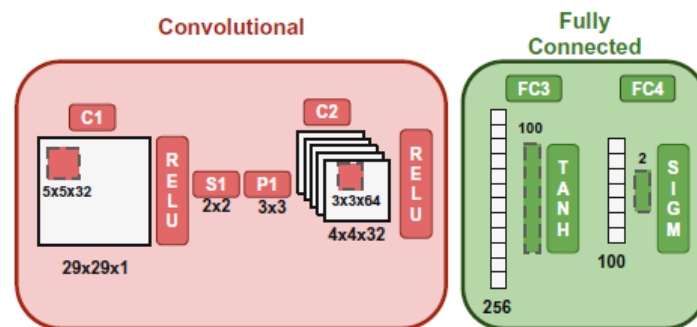


Figure 1. Network architecture [11]

Cerebrovascular segmentation method is used to analyse and evaluate some TOF MRA datasets of healthy subjects. The datasets were acquired for the segmentation process. Slab boundary artefact correction was done for pre-processing and by using the N3 algorithm [13], intensity non-uniformity correction can also be done. A skull stripping algorithm [14] is also used. Based on the pre-processed TOF MRA datasets, the manual segmentation of the vessels in each dataset is done. The patches from all directions are extracted from a cubic region which is defined around all voxels inside the brain region. To calculate the vessel likelihood, each patch is fed to the CNN [15]. Then, for each orientation, three probability maps are present. Datasets consisting of TOF MRA images are randomly selected for training, the performance of the deep CNN can be evaluated. More accurate results can be obtained, if more training images are used. For each image used for testing, the training image selected will be different. Then, there is need for increasing the number of training images. In order to evaluate the performance of the cerebro vascular segmentation using CNN and ground-truth manual segmentations, dice similarity coefficient (DSC) [16] is used. DSC can be calculated as, $DSC = 2|A \cap B| / (|A| + |B|)$, where A and B defines the ground-truth and CNN segmentations, respectively.

3.2. 3D-convolutional neural network (3D-CNN)

3D-CNN architecture proposed by Kandil *et al.* [17] shown in Figure 2, consists of eight convolutional layers, two fully connected layers, and one classification layer. The eight layers are having 30, 30, 40, 40, 40, 40, 50, 50 feature maps (FMs) and the kernel size is 27. Image segments with size 25×25×25 are used as input to the network. The batch size used is 10 segments. The voxel's exact position will be lost if pooling layer is present which will inversely affect the accuracy and the strides are unary. The PReLU non-linearity is used by this 3D CNN architecture and the root mean square (RMS) Prop optimizer and Nesterov momentum with values $L1 = 10^{-6}$, $L2 = 10^{-4}$ and $m = 0.6$ are used for training. The learning rate and the

dropout are set to 10-3 and 50% rate respectively, that was used on the last hidden layers. At each optimization step for the normalization of the FM activation in all hidden layers, batch normalization technique was used. Blood flow signal strength inside the brain at a specific time varies from one area to another. In order to face this challenge, inside each compartment, blood vessels are of same features when each MRA volume is partitioned into two compartments.

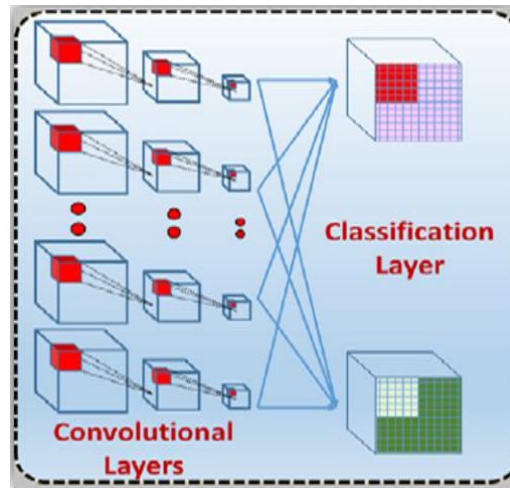


Figure 2. 3D -CNN architecture

Performance of the segmentation process can be enhanced by this. During the partitioning process, cerebral bio-marker called circle of willis (CoW) is selected. Most of the blood vessels are of different diameter size when it is existing at CoW and below it and it is having small diameter size above CoW. Based on the position of the MRA slices, whether it is above or below CoW are divided into two compartments. All the blood vessels should have same shape, appearance, and diameters of approximate sizes in each compartment; therefore, the segmentation efficiency and accuracy can be increased. A sub vascular tree is produced by the 3-D CNN manipulation during this process. The final outcome is obtained by combining two sub vascular tree [17]. 3D CNN segmentation accuracy can be tested by considering the evaluation metric DSC. In the experiment done by Kandil *et al.* [17], training set consists of 49 images and testing is done for 17 images.

3.3. 3D U-Net

Sanches [1] proposed an architecture called uception [18] which increases the network size by adding convolutional layers or by increasing their depth. Disadvantage of using 3D U-Net is that, there is a chance of overfitting when it is having a greater number of parameters. If the number of annotated images is less in biomedical datasets, this problem mainly arises. Therefore, sparsely connected architectures are preferred. In this sparsely connected architecture, the input is passed in parallel to several branches with different kernel sizes and finally concatenated in the end. In addition, this architecture with 1D convolution will dissociate the depth information in the channels and spatial information with the 3D convolutions. Moreover, processing the image in two scales is possible by using different kernel sizes. The modules which are created to be used in a 3D model are: the features map shape is retained by one model and the image size is made half with parallel strided convolutions and maxpooling operations by the other model to make contracting path [1]. In the expansive path, up-sampling was used. Uception architecture is given in Figure 3.

After each convolution layer, a ReLu activation function is applied. A sigmoid activation function was used after the last convolutional layer. Therefore, each voxel is linked to a probability which will helps to reach the probability of belonging to the vessels network during the training. Since the input is in binary segmentation, the last layer has only one channel. After each activation function, dropout was used when the regularization technique goes. The negative of the dice coefficient is used for the loss function, from (1).

$$DSC(P, T) = \frac{2 * |P \cap T|}{|P| + |T|} \quad (1)$$

Where, P is the prediction of the network and T is the ground truth. Convergence speed is high and is numerically stable as its value is between zero and one. By using the back-propagation algorithm with the Adam optimizer, the training was done. Moreover, cubic of patches of $64 \times 64 \times 64$ voxels were used to feed the data. For validation, non-superposed patches were used. In addition, more data is obtained as a result of training through patches, since data augmentation was not used; only 36 images from this dataset were disposed. A technique called snapshot ensemble [19] is used to enhance the generalization by averaging the weights of the same model at different moments of the training. During training with a cyclic learning rate schedule, these moments are chosen as the local minima of the validation loss.

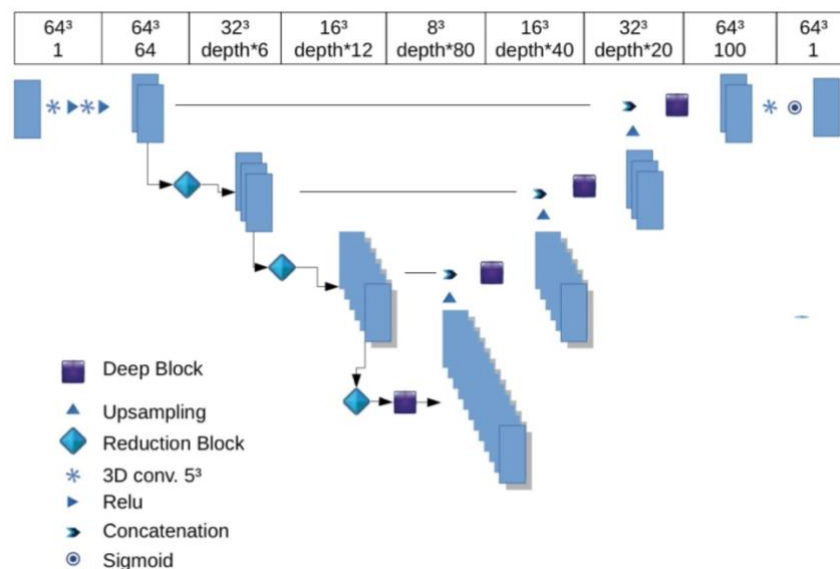


Figure 3. Uception architecture [1]

4. RESULTS AND DISCUSSION

When CNN approach [20] is used for segmentation of blood vessels in time of flight MRA images, DSC values of five datasets are averaged and obtained 0.764 ± 0.010 . From Phellan *et al.* [12] experiment, it is proved that as a greater number of images used will increase the training times and the time taking for testing are not depending on the quantity of training images and the segmentation accuracy and cannot be increased by more training images. Figure 4 shows the segmentation results using the deep CNN [21]. Figure 4(a) shows the result obtained manually and Figure 4(b) depicts the CNN approach output. For 3D-CNN [22], segmentation accuracy can be determined using a common segmentation evaluation metric called dice similarity coefficient (DSC) is used.

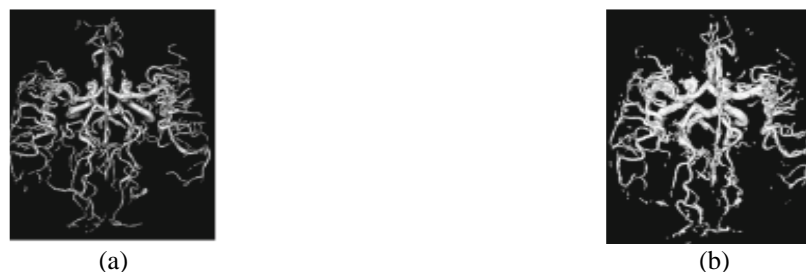


Figure 4. Segmentation results using CNN, (a) Manual and (b) Output of CNN approach

This segmentation method shows good performance in characterizing cerebral vasculature with 0.832 ± 2.30 DSC when compared with manually segmented ground truth. Each MRA volume is partitioned above CoW and below CoW to perform the segmentation [23] task locally over the entire brain. The results

of segmentation should be positive, as the other evaluation parameters of the extracted features are influenced [24]. 3D-CNN segmentation result is shown in Figure 5. Figure 5(a) shows the result obtained manually and Figure 5(b) depicts the 3D- CNN approach output.



Figure 5. Segmentation results using 3D-CNN, (a) Ground truth, (b) output of 3D-CNN approach

By using 3D U-Net [25] approach, DSC obtained when compared with the ground truth is 0.671 ± 0.01 . Figure 6 shows the segmentation results of 3D U-Net when compared with its ground-truth. Figure 6(a) shows the result obtained manually and Figure 6(b) depicts the 3D U-Net approach output.

Finally, these methods are compared with the global statistical-based approach (GSB) proposed by El-Baz *et al.* [26] and the DSC value obtained in this method is 0.801 ± 2.7 . Figure 7 shows the segmentation result using GSB. Figure 7(a) shows the result obtained manually and Figure 7(b) depicts the GSB approach output.



Figure 6. Segmentation results using 3D U-Net, (a) Ground truth and (b) output of uception approach



Figure 7. Segmentation results using GSB, (a) Ground truth and (b) output of GSB approach

Comparing the DCS values, we are able to find that the performance of 3D U-Net is higher compared to other methods. 3D U-Net shows less similarity with the manual method which proves it as a better method. The DSC values obtained for the three segmentation methods when comparing with the ground truth are shown in Table 1.

Table 1. DSC values based on the type of segmentation used

Types of segmentation	DSC value
CNN	0.764 ± 0.01
3D-CNN	0.832 ± 2.30
3D U-Net	0.671 ± 0.01
GSB	0.801 ± 2.7

5. CONCLUSION

Nowadays, cerebrovascular diseases are becoming one of the major causes for increasing the death rate of the world population. Diagnosis and testing of such diseases are still a challenge for healthcare providers. Therefore, segmentation of the cerebrovascular structure is a very important step for the diagnoses process. Computer-aided diagnosis (CAD) system is used by the clinicians in the prediction process. In this paper, some of such automatic segmentation methods like CNN, 3D-CNN and 3D U-Net are explained and compared their performance. In this paper, some of such automatic segmentation methods like CNN, 3D-CNN and 3D U-Net are explained and compared their performance. In the CNN approach, only a smaller number of segmented ground truth images are needed to obtain good results which makes this application easier in many places such as in research or clinical field. 3D CNN is very helpful in the segmentation of small as well as complex blood vessel. For either healthy or unhealthy vessels, this method is applicable. But, CNN shows better performance than 3D-CNN. 3D U-Net architecture is proposed as a result of the inspiration from the inception architecture. When compared with the original U-Net, this model showed better performance. Loss function needs to be selected with much care; therefore, the total number of voxels in the data is not considered by the dice coefficient. By comparing the three segmentation methods, 3D U-Net showed the better performance.

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Fatma Taher is an associate professor and assistant dean for research and outreach in the College of Technological Innovation at Zayed University, Dubai, UAE. Her research interests are in the areas of signal and image processing, pattern recognition, deep learning, Machine learning, artificial intelligence, medical image analysis, especially in detecting of the cancerous cells, kidney transplant and autism. In addition to that, watermarking, remote sensing and satellite images researches. Dr. Fatma Taher has published more than 70 papers in international Journals and conferences. She served as a member of the steering, organizing and technical program committees of many international conferences, and has served on many editorial and reviewing boards of international journals and conferences. Dr. Fatma is the chair of IEEE UAE section and the chair of the Education Committee in British Society in UAE. Dr. Fatma has received many distinguished awards such as: Best paper award of the first prize in the PhD Forum of the 20th IEEE International Conference on Electronics, Circuits, and Systems (ICECS), PhD Forum, Dec. 8-11, 2013. And recently, she was awarded the UAE Pioneers award as the first UAE to create a computer aided diagnosis system for early lung cancer detection based on the sputum color image analysis, awarded by H.H Sheik Mohammed Bin Rashed Al Maktoum, 15th Nov. 2015. In addition to that she was awarded an innovation award at the 2016 Emirati Women Awards by H. H. Sheik Ahmed Bin Saeed Al-Maktoum. Chairman of Civil Aviation Authority, and Loreal-UNESCO For Women in Science Middle East Fellowship 2017.



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