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DETERMINING ISCHEMIC STROKE FROM CT-ANGIOGRAPHY IMAGING USING SYMMETRY-SENSITIVE CONVOLUTIONAL NETWORKS

Arko Barman[†], *Mehmet E. Inam*[‡], *Songmi Lee*[‡], *Sean Savitz*[‡§], *Sunil Sheth* [‡§] *, *Luca Giancardo*[†§] *

[†] Center for Precision Health, School of Biomedical Informatics, UT Health, Houston, TX, USA
[‡] McGovern Medical School, UT Health, Houston, TX, USA
[§] Institute for Stroke and Cerebrovascular Disease, UT Health, Houston, TX, USA

ABSTRACT

Acute Ischemic Stroke (AIS) is the second leading cause of death worldwide in 2015, and 5th in the United States. Neuroimaging is routinely used in the diagnosis and management of these patients. To create a decision support method for AIS, we propose a convolutional neural network for automated detection of ischemic stroke from CT Angiography (CTA), an imaging technique that is widely available and used routinely in stroke evaluations. The network has a novel design that makes it sensitive to changes in symmetry of vascular and brain tissue texture which allows it to detect ischemic stroke from CTA brain images. The proposed model is inspired from the paradigm of Siamese networks and applied to the two brain hemispheres in parallel. We tested the model on a clinical dataset of 217 subjects, 123 controls and 94 subjects imaged less than 24 hours after stroke onset. First, we tested the ability of the network in recognizing strokes with the original images, which contain asymmetries in both vascular structures and brain tissues. Then, we digitally removed the vasculature in order to evaluate the ability of the network to recognize strokes by analyzing brain tissue only. We achieved AUC 0.914 (CI 0.88-0.95) and AUC 0.899 (CI 0.86-0.94) on the two experiments respectively. The qualitative analysis of the network activation confirms that the model efficiently learns the vasculature and brain tissue structures in one hemisphere that does not appear in the opposite hemisphere.

Index Terms— Siamese Network, ischemic stroke, CT Angiography, brain symmetry

1. INTRODUCTION

Stroke is "the second leading cause of death and the third leading cause of disability" worldwide [1]. About 15 million people are affected by stroke worldwide every year, out of which Acute Ischemic Stroke (AIS) accounts for nearly 87% [2]. AIS alone leads to the death of nearly 3 million people annually worldwide [3]. In United states alone, every 3 minutes 45 seconds someone dies because of a stroke [2].

*Equal contribution.

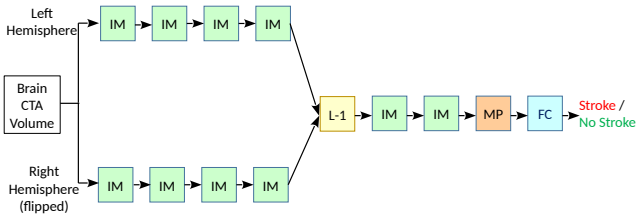
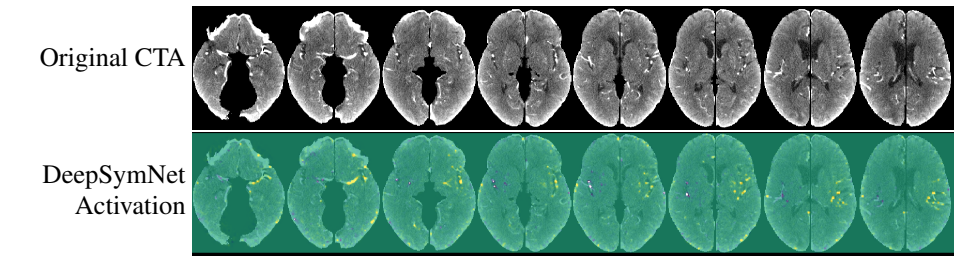


Fig. 1: Deep Symmetry-sensitive CNN (DeepSymNet). (IM = Inception Module, L-1 = Merge Layer with L-1 difference, MP = Max Pooling, FC = Fully Connected Layer)

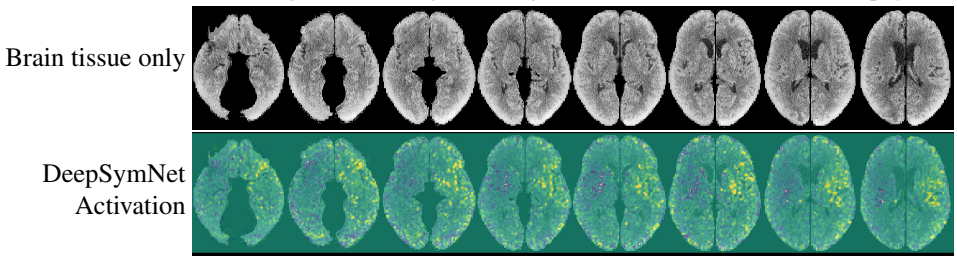
The diagnosis and management of AIS relies heavily on neuro-imaging, particularly non-contrast head CT (NCHCT) and CT angiography (CTA). These studies assist in determining whether the patient is having a stroke, whether the stroke is a severe stroke due to the occlusion of one of the major vessels of the brain, the degree of brain tissue death (i.e. infarct volume), and whether there is a significant salvageable tissue to recover. Recent studies have shown that CTA performs better than NCHCT [4] for detection of AIS and estimation of infarct volume. In this paper, we propose a novel model for the detection of AIS from CTA images that leverages the differences between the two hemispheres observed in the CTA images of stroke patients.

Related Work: Segmentation of stroke lesions from NCHCT and multispectral MRI images has been a research area in biomedical image analysis. A number of traditional machine learning algorithms [5, 6] as well as deep learning models [7, 8, 9] that segment stroke lesions in NCHCT and MRI images have been proposed in recent years. To our knowledge, models for the automated detection of AIS from CTA images have not been described in scientific literature. The only exception is a commercial package called Viz-AI (currently under development) whose underlying algorithm has not been described [10].

Our contributions: To the best of our knowledge, existing methods for detecting AIS using NCHCT and MRI need to be trained on manually segmented stroke lesions [11, 12, 13]. The need of manually segment stroke lesions for each



(a) Original CTA image of a subject with AIS and activation of DeepSymNet



(b) CTA image with brain tissue only of a subject with AIS and activation of DeepSymNet

Fig. 2: CTA images of left/right hemispheres with DeepSymNet activation. The top two rows show an example of a subject with AIS from the "Original CTA" dataset. The bottom two rows an example of a subject with AIS from the "Brain tissue only" dataset, i.e. where AIS can only be detected by the appearance of the brain tissue as vasculature has been removed. Yellow corresponds to positive network activation, purple to negative network activation. Note the high activation in the region with blood vessels in (a) and brain tissue in (b) only in one hemisphere, indicating occlusions due to AIS in the other hemisphere. The activation in (b) corresponds with the ischemic core identified by CT Perfusion (CTP) images analyzed with iSchemaView RAPID. (An interactive visualizer is available at https://lgiancauth.github.io/stroke-deepsymnet-web/)

brain volume is a significant hurdle when working with large datasets. Additionally, methods specifically trained on stroke lesions are not able to detect vasculature occlusion, which is the primary clinical sign of AIS. In this paper, we propose a Convolutional Neural Network (CNN) model that detects AIS from CTA images. The model, called Deep Symmetry-sensitive Network (DeepSymNet) (Figure 1), analyzes the symmetry information in CTA images of the brain to deduce if the patient has suffered from AIS without needing the location of the areas affected. Inspired from the observation that the two hemispheres of the brain are visibly different in CTA images both in terms of vasculature structures as well as voxel intensities in the tissue affected by the stroke, the network can robustly compare the two hemispheres both in presence and absence of blood vessels in the images to identify if a patient has suffered from AIS. We also perform a qualitative analysis of the network by visualizing the network activation for CTA images of AIS patients. The analysis confirms that the network learns to identify blood vessels and tissue structures in one hemisphere of the brain that are not present in the other hemisphere, indicating a diagnosis of AIS.

2. METHOD

Problem Statement: Given brain CTA volumes, $\mathcal{V}_i$, with labels, $\mathcal{C}_i \in \{0, 1\}$, $i = 1, 2, \ldots, n$, the goal is to learn a mapping $\mathcal{V}_i \mapsto \mathcal{C}_i$ that correctly classifies a brain CTA volume as having a stroke ($\mathcal{C}_i = 1$) or no stroke ($\mathcal{C}_i = 0$). We will present a brief introduction of Siamese Networks and Inception modules, which are used as building blocks to construct the proposed Deep Symmetry-Sensitive Convolutional Neural Network (DeepSymNet) that learns the mapping, $\mathcal{V}_i \mapsto \mathcal{C}_i$.

DeepSymNet learns the asymmetry between the CTA volumes of the two hemispheres of a brain in order to detect AIS. This approach is inspired from the clinical observation that, typically, in the event of an ischemic stroke, blood vessels in one hemisphere of the brain are likely to be occluded while those in the other hemisphere are less affected. Consequently, observable differences in vasculature and brain tissue structure are seen in the two hemispheres of brain from CTA images.

Inception Module: An inception module (IM) [14] is a combination of parallel convolutional layers that can be used as a building block for constructing deep neural networks, which have the ability to learn complex patterns in data. The module uses 1x1, 3x3, and 5x5 convolutions, along with max pooling, allowing the network to learn patterns at different scales from the different filter sizes used in parallel. Here, we use 3D IMs, i.e., 3D versions of the filters – convolutions with kernels of size 1x1x1, 3x3x3, and 5x5x5, and 3D max pooling since our data are 3D volumes. The relationship between the input, $\mathcal{I}_{IM}$, and output, $\mathcal{O}_{IM}$, of an IM is given by,

$$\begin{aligned}\mathcal{O}_{IM} = \{f_1^n \otimes \mathcal{I}_{IM}\} \oplus \{f_3^n \otimes (f_1^n \otimes \mathcal{I}_{IM})\} \\ \oplus \{f_5^n \otimes (f_1^n \otimes \mathcal{I}_{IM})\} \oplus \{f_1^n \otimes \mathcal{P}_3^{max}(\mathcal{I}_{IM})\}\end{aligned} \quad (1)$$

where f_k^n denotes n convolutional filters of kernel size k

Characteristic	All Subjects $n = 217$	Controls $n = 123$	Stroke Subj. $n = 94$
Sex, female (%)	106 (49%)	60 (49%)	46 (49%)
Age (year)	65 [IQR 55-75]	63 [IQR 51-72]	69 [IQR 59-79]
Race (%)			
White	74 (34%)	42 (34%)	32 (34%)
Black or African American	63 (29%)	42 (34%)	21 (22%)
Native Hawaiian or Pacific Islander	1 (0.5%)	0 (0%)	1 (1%)
Asian	1 (0.5%)	0 (0%)	1 (1%)
Other	43 (20%)	37 (30%)	6 (6%)
Unknown	35 (16%)	2 (2%)	33 (35%)

Table 1: Demographic information for the full "Original CTA" dataset. (IQR: interquartile range)

along each dimension, $\mathcal{P}_k^{max}$ denotes max pooling with kernel size k along each dimension, $\otimes$ denotes convolution, and $\oplus$ denotes concatenation of filter outputs of same dimensions.

Siamese Networks: A Siamese Network [15] is a neural network architecture that uses identical neural networks with identical weights to learn the similarities and differences between two inputs. Originally proposed for signature verification, it has been used widely for various computer vision applications [16, 17]. Although most networks employ a cost function to compare the outputs of the two identical networks for different inputs, here, we have used a significantly different approach which employs convolutional layers to learn the complex differences in structure that are embedded in the output of the identical networks learning the differences and the addition of an L-1 merge layer.

Deep Symmetry-sensitive Network (DeepSymNet): DeepSymNet is designed to take the CTA images of the two hemispheres of the brain as its inputs. We flipped the right hemispheres to facilitate the network learning process. The architecture of DeepSymNet is shown in Figure 1.

Two identical CNNs (with identical weights) are used for learning the low and high level volume 3D representation common to the two brain hemispheres. This CNN architecture employs 4 3D IMs one after the other. Then, instead of the commonly-used approach of directly comparing differences with a cost function (such as contrastive loss [18]), we propose a markedly different method.

We introduce a merge layer that calculates the absolute difference (L-1 difference) between the high-level convolution filter outputs common to the two hemispheres. These differences contain crucial information about the asymmetry of the two hemispheres that cannot be tackled by a simple loss function. Hence, we allow the network to learn the information in the hemisphere difference by adding two additional inception modules to the architecture. The outputs from the final inception module are then max pooled and connected to the output prediction layer through a fully connected layer. The L-1 merge layer allows the network to equally weigh stroke visual patterns generated from the left or right hemisphere, the additional inception modules to learn convolutional filters sensitive to high level differences.

In our model, 64 filters of each size have been used in all the Inception modules. The entire network uses ReLU activations, except for the prediction layer that uses sigmoid activation. Finally, the loss function used is binary cross-entropy, which is given by,

$$J(y, \hat{y}) = -\sum_i \{y_i \log \hat{y}_i + (1 - y_i) \log(1 - \hat{y}_i)\} \quad (2)$$

where y_i and $\hat{y_i}$ are the actual class and the predicted class respectively. The optimizer used for our experiments is Adam [19] with a learning rate of 1×10^{-6} for 40 epochs.

3. EXPERIMENTS & RESULTS

Subject Cohort: Experiments were conducted on a clinical dataset comprising 217 individuals, 123 controls and 94 subjects with AIS imaged with CTA scans less than 24 hours after the onset of stroke. The presence of ischemic stroke was confirmed by two experienced neuroradiologists and CT Perfusion (CTP) imaging. The distribution of ischemic core volume (ICV) was 38.3% ICV=0mL, 17% ICV=1-10mL, 20.2% ICV=11-30mL, and 24.5% ICV>30mL. Table 1 shows the demographics of the subjects. The data were collected and analyses were performed with approval from our institution IRB (HSC-MS-18-0175).

"Original CTA" dataset: The brain in each CTA volume was extracted using the FSL-based pipeline described in [20] and then linearly registered to a common MNI space. The linear transformation is computed between the CTA brain volume and the Harvard-Oxford [21] T1 atlas with 0.5mm isometric voxel size using correlation ratio as cost function, and trilinear interpolation. Using the atlas, we extracted only the two hemispheres for our experiments. Pixels were saturated to an intensity value of 100, retaining the vasculature. Finally, the volumes were rescaled to $29 \times 73 \times 20$ using bilinear interpolation. We refer to this as the "Original CTA" dataset: an example is shown in Figure 2a.

"Brain tissue only" dataset: Additionally, we also created a dataset without blood vessels by a simple "inpainting" approach. This allowed us to test the network performance when stroke can only be detected by darker textures in the brain tissue. We refer to this as the "Brain tissue only" dataset: an example is shown in Figure 2b. This dataset included only AIS subjects with infarct volume > 30 mL in order to make sure that the stroke area was visible in the CTA brain tissue information. The total Stroke/No Stroke ratio for this dataset was $24/193$. The vasculature inpainting started by selecting a vessel mask where voxel values are > 70, then voxels in the mask were replaced by the output of a large median filter on the original image. This had the effect of replacing

Brain CTA	Method	Balanced Accuracy	AUC_ROC	AUC CI (95%)	Sensitivity	Specificity
Original	Histogram	0.809	0.884	0.85 – 0.92	0.701	0.918
	DeepSymNet	0.901	0.914	0.88 – 0.95	0.859	0.943
Brain tissue only	Histogram	0.808	0.881	0.84 – 0.92	0.722	0.894
	DeepSymNet	0.979	0.899	0.86 – 0.94	1.000	0.959

Table 2: Performance comparison of histogram features with DeepSymNet using original CTA images and brain tissue only.

the vasculature with voxels values similar to the brain tissue and limiting artifacts. Finally, the volumes were rescaled to $29 \times 73 \times 20$ as before.

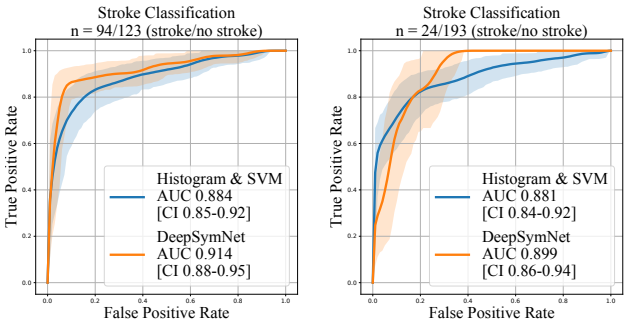
Experiment Design: In all our experiments, 4-fold cross-validation was used. The metrics used for evaluation of the models include balanced accuracy (to account for class imbalance), Area Under the ROC Curve (AUC_ROC), 95% confidence interval of AUC_ROC, sensitivity and specificity. Due to the absence of prior literature that does not require the manual segmentation of the infarct volume, we develop our own baseline approach (presented at SWITCH: Stroke Workshop on Imaging and Treatment CHallenges MICCAI workshop 2018) for performance evaluation. The performance of DeepSymNet was compared with a baseline approach of using histogram features and a SVM classifier. Histogram features were extracted using 30 bins for both the original images as well as the images with brain tissue only, and were normalized to estimate two probability density functions (PDFs). Similarly to DeepSymNet, the L1 difference between each value of the PDFs was computed and used as feature vector. A linear SVM classifier was trained to classify the CTA image volumes using these features with cross-validation.

Quantitative Analysis: In Table 2, the performance of the classification models for the two types of input brain CTA volumes are shown. Using original images for DeepSymNet achieved an AUC of 0.914 when compared with using brain tissue only, which achieves an AUC of 0.899. The balanced accuracy of prediction is 90.1% and 97.9% when using the original image and using brain tissue only respectively. The sensitivity and the specificity are better when using brain tissue only compared to using the original images. The performance of DeepSymNet is better than the baseline in terms of all observed metrics for both types of input images.

In Figure 3, ROC curves for the histogram-based method and DeepSymNet are shown for both original CTA images and brain tissue only. For original CTA volumes, the ROC curve for DeepSymNet is better than the baseline, with AUC of 0.914 (Figure 3a). For images with brain tissue only, except for the region of very low False Positive Rate (FPR), DeepSymNet has a higher True Positive Rate (TPR) compared to the histogram features (Figure 3b).

In conclusion, DeepSymNet can recognize the presence of stroke remarkably well even in the absence of vasculature information by leveraging only brain tissue information.

Qualitative Analysis: We also performed a qualitative review of the performance of DeepSymNet using ϵ-LRP [22, 23]. Network activation for an input CTA image volume with stroke using ϵ-LRP is shown in Figure 2 along with corresponding brain images. In the original images, it is interesting to note how blood vessels in one hemisphere show high activation only in places where the corresponding vessels in the other hemisphere are not visible. Similarly, in the images with brain tissue only, high activation is seen in regions of one hemisphere where the corresponding region in the other hemisphere has been affected by stroke. Moreover, the ischemic core location identified with CTP images and iSchemaView RAPID software corresponded with the negative activation shown in Figure 2b; these regions correspond with the high activation region in the opposite hemisphere where vessels and tissue information are present and visible.



(a) Original (b) Brain tissue only

Fig. 3: ROC curves (with 95% confidence intervals).

4. CONCLUSION

In this paper, we have proposed a novel model sensitive to changes in the symmetry between brain hemispheres, which enables the automated detection of AIS with CTA images. Experiments show that the model possesses the capability to learn symmetry in both vasculature and tissue structure of the brain, and can determine if these structures change or are absent in one hemisphere. The proposed Deep Symmetry-sensitive Network (DeepSymNet) achieves AUC 0.914 (CI 0.88-0.95) and AUC 0.899 (CI 0.86-0.94) for original brain CTA volumes and for images with brain tissue only respectively. In future, we will further validate the model on a larger dataset and explore the potential of DeepSymNet with other imaging modalities, diseases and test its potential to identify temporal changes for quantifying disease progression.

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