Reconstruction and Analysis of Non-Contrast CT Volumes of the Brain for Stroke Detection and Localization

Karthik Desingu; **Anirudh A**
Advisor: **Prof Mirnalinee T T**

Dept. of Computer Science and Engineering
Sri Sivasubramaniya Nadar College of Engineering, Chennai, TN, India

Background

After heart disease, brain stroke is the most common reason for death around the world [19]. Due to which the majority of survivors need to live with changeless or long-term injury. Brain imaging methods like magnetic resonance imaging (MRI) and CT are quite helpful for a doctor in order to start the initial screening of the patient. There are also many imaging modalities for the analysis of brain, which may include X-ray imaging, diffuse optical imaging, magnetoencephalography, functional MRI and positron emission tomography [4, 38]. However, all these imaging techniques require high operating cost and well-trained operator, hence most of these imaging methods may not be available in all the clinics and hospitals.

Image classification is widely used in medical imaging [25]. However, for better accuracy of the classification system, results should be close to the manual diagnosis. Nowadays, deep learning has been extensively used as a classification method because it automatically calculates features within the convolutional layers of the deep system [20, 1]. The main advantage of using deep learning is that it outperforms other conventional methods for image classification [31]. Many deep learning methods have come into existence such as recurrent neural networks, long short-term memory (LSTM) [13], CNNs [23], deep belief nets (DBN) [12], etc. Among these methods, CNN has been generally utilized in computer vision and medical image processing problems like ImageNet, face recognition, house numbers digit classification, patch classification from medical images etc. Classification methods other than deep learning methods are random forest (RF), - nearest neighbors (NN), decision tree (DT), multilayer perceptron (MLP), support vector machine (SVM) and many more [34, 30, 32].

In this research, an automatic classification method has been proposed to predict the category to which brain CT scan image belongs, along with the locations of the stroke infarcts for hemorrhagic and ischemic stroke types, and normal tissue. *Hemorrhagic stroke* occurs due to fragile blood vessel which burst and drains into the neighboring brain tissues. On the other side, *ischemic stroke* occurs when blood supply in the brain stops due to the presence of blood clots. Brain hemorrhage can also occur after ischemic stroke which results in a serious complication [17]. Sample images of the two types of stroke on CT slices are depicted in Figure 1, with infarct regions demarcated in red.

Towards the diagnosis of stroke, doctors first confirm symptoms from the patient or family members. The most important thing which will help in accurate identification is the stroke history. This is usually followed by neuroimaging of the patient. The most commonly used neuroimaging method used by experts is CT scan for diagnosing brain strokes, on account of their greater affordability. The prediction of stroke from CT scan images serve as the initial step towards the proper diagnosis of a patient. These images are then sent to a cardiovascular radiologist to identify the stroke type. Thereafter, physical and manual examination of the patient is performed to determine an appropriate course of treatment. However, this manual diagnosis procedure is extremely time-consuming for the already overburdened radiologist, and is prone to human-error. Many researchers have worked in this area for providing a computer-aided diagnosis (CAD) system, in spite of the significant requirement, there is no clinically accepted CAD system for stroke [21, 24]. The system proposed by [21] was not automated and requires significant performance improvements to warrant automation. Peixoto and Filho [24] have worked on the classification of hemorrhagic and ischemic stroke CT scan images. Their method was developed for small dataset where each

case had 100 images and for future work they have to test their method on large datasets. Thus, there is a need for an effective automated system for diagnosing strokes that can help physicians quickly start treatment after stroke onset. Hence, in this work, we proposed to develop a deep learning -based computation pipeline to process CT slices to detect stroke type and localize infarct location. Furthermore, we propose to reconstruct the CT slices into volumetric models while correcting errors in infarct localization, and cast the volume into a computationally pliable 3D model that can be used to draw out diagnostic measurements as well as for treatment simulations.
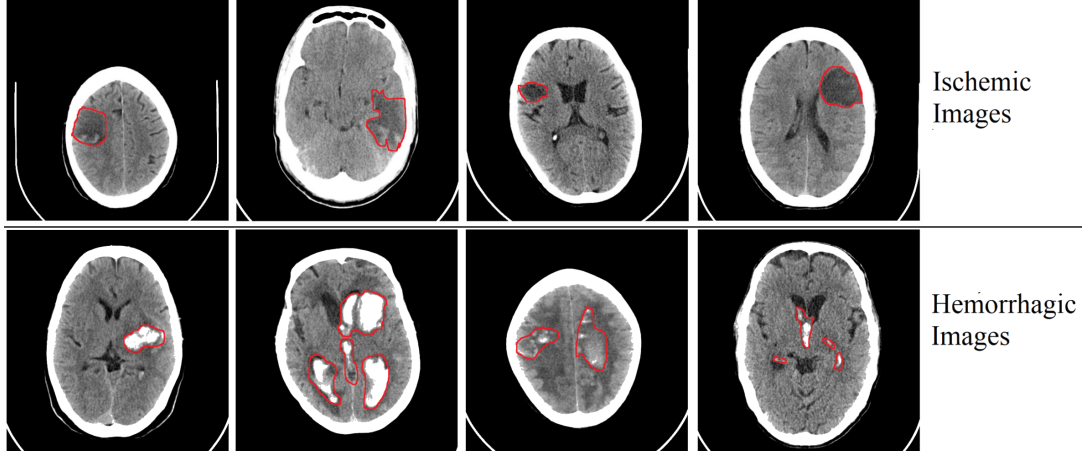

Figure 1: Samples of CT slices to depict the infarcts arising from *Ischemic* and *Hemorrhagic* strokes.

Related Work

In general, processing and analysis of medical images using computer-aided diagnosis (CAD) systems can help physicians in early identification of diseases [21, 10, 14, 36]. Herein, the proposal briefly describe some important image preprocessing and classification methods used so far in order to analyze brain strokes from medical images.

Saatman et al. [26] have discussed various classification techniques for traumatic brain injury so that proper treatment can be provided for that targeted injury. They discussed classification based on the severity of brain injury where various parameters which include Glasgow Coma Scale (GCS) have been used to identify the severity, however these procedures require many clinical trials. Other techniques which they have discussed are pathoanatomic classification, classification by physical mechanism, pathophysiology and prognostic modeling. According to them, for avoiding several clinical trails of patients new tools can be developed like dataset development, data sharing, data mining, and bioinformatics, etc. In 2008, Mozqueda et al. [33] have tested the hypothesis on clinical data of patients that acute ischemic stroke classification from CT or MR angiography images into major and minor stroke can be done by using Boston Acute Stroke Imaging Scale (BASIS) instrument. They have proved that BASIS classification instrument is better than Alberta Stroke Program Early CT Score (ASPECTS) in predicting stroke.

Chawla et al. [2] presented an automatic method for the detection and classification of an abnormality from low-contrast CT images into three categories — hemorrhage, chronic and acute infarct. Their proposed technique comprises of three steps: enhancement of the image, recognition of mid-line symmetry and classification of abnormal slices. The main limitation of their work is that they have just shown results on the dataset and have not compared their results with any of the previous state-of-the-art methods by generating their results on their dataset. The accuracy obtained by them on their dataset was also not given and have just shown precision and recall values for the experiments. Griffis et al. [9] have also worked on ischemic stroke lesions identification where they utilized the T1-weighted MRI scans and predict the stroke region using Gaussian naïve Bayes classification method. Limitations of their method was that they were unable to detect very subtle WM lesions with very small extents. Shahangian and Pourghassem [28] proposed a method to segment and classify hemorrhage, where segmentation was based on a modified version of distance regularized level set evolution (MDRLSE). Thereafter, SVM classifier

was used to classify images by extracting weighted grayscale histogram features where they achieved an accuracy of 94.13%. However, the complete dataset information is not given like under what parameters images have been acquired and the details of CT scanner. The other limitation is that, the number of images which they have used for classification were also very less for 5 different categories i.e. only 627 images. The segmentation of hemorrhagic stroke from CT scan images was proposed by Gautam et al. [7] using variant of fuzzy clustering named as modified robust fuzzy c-means clustering (MRFCM) and used it with distance regularization level set evolution (DRLSE) method for the segmentation. However, their method was not able to identify very small lesions from the images. They have also proposed the method for the classification of a brain CT scan images into hemorrhagic, ischemic and normal [6]. A new feature descriptor known as the local gradient of gradient pattern (LG2P) descriptor has been proposed by them. The highest classification accuracy achieved by them on 900 image dataset is 83.11% and 86.11% using fine NN and cubic SVM. However, this accuracy is very less and for better results it must be improved. Incremental gradient descent decision boundary feature extraction method was proposed by Woo et al. [35] for the classification of UCI dataset where they have shown results on Parkinson speech, chess, molecular biology, gas sensor, and array drift datasets of UCI. Recently, some researchers have published a literature survey on feature extraction methods and they can be found in [27, 3], so readers are referred to these papers for more methods.

Subudhi et al. [30] have proposed a new method for the segmentation and classification of brain stroke from MR images where they used expectation–maximization and random forest classifier. The accuracy achieved by them was 93.4% on the dataset of 192 brain images. The limitation of this paper is that they do not have any discussion of the dataset like from where they collected it and how. Ortiz-Ramón et al. [22] also worked on MR images where they proposed a texture analysis method to identify whether the patient has a stroke or not and also identify whether that stroke is lacunar or cortical. In this paper, they have used various methods proposed by different researchers in order to carry out their work and references for them can be found in [30]. According to them the limitation of their work is inability to combine stroke and aging (old stroke lesion) datasets for the analysis of images showing recent cortical or lacunar strokes. However, image normalization techniques can solve this issue by improving the image qualities.

Apart from the conventional machine learning methods which have been used very widely for the identification of diseases from the medical images, deep learning approaches are gaining attention because of the accurate diagnosis results. In 2012, Krizhevsky et al. proposed AlexNet as the CNN architecture and won the most difficult ImageNet large-scale visual recognition challenge (ILSVRC) [15]. Thereafter, it emerged as the revolution in the field of computer vision and machine learning. AlexNet has 5 convolutional and 3 fully connected layers where 2 dropout layers have been used with 0.5 probability. The best classification prediction with it can be achieved when the softmax layer is fed with the result of the last fully connected layer. In this architecture, the input image size should be $224 \times 224 \times 3$. However, in order to improve the accuracy many researchers have tried to develop new architectures. In 2014, VGG16 has come into existence, proposed by Simonyan and Zisserman [29]. The main contribution of their network is that they have made a very deep CNN architecture for the recognition of very large image dataset by increasing the network depth to 16–19 layers with 3×3 convolution filter. VGG16 consists of five batches of 13–16 convolutional layers and 3 fully connected layers. In the first layer the number of filters starts from 64 and increases by a factor of 2 for each layer after the max-pooling till it becomes 512. The input image size for this architecture remains the same as that of AlexNet i.e $224 \times 224 \times 3$. The other CNN architecture ResNet50 proposed by He et al. [11] is a very deep residual network and it won the first place in ILSVRC 2015. It is a 50 layer architecture instead of 16–19 layers, which was trained on the 1.28 million training images. The input image size for this architecture is $224 \times 224 \times 3$. After that, many variants of CNN architectures have come into existence in order to provide better results for the diagnosis of the patients. Recently, deep learning has shown good classification accuracy on both training and testing datasets of breast cancer histopathology images [10]. The other work on the detection and classification of breast cancer makes use of four fully convolutional networks (FCN) [8]. CNN has also been used to detect colorectal cancer from the histology images [37]. Gao et al. [5] used deep CNNs to classify interstitial lung diseases (ILD) from CT images by using the entire image as a holistic input.

However, the work on the classification and localization of origin of brain strokes from CT/MR images still requires improvements for clinical applicability. Furthermore, the presence of overlapping infarcts of the two types – ischemic and hemorrhagic – on the CT slides, as depicted in
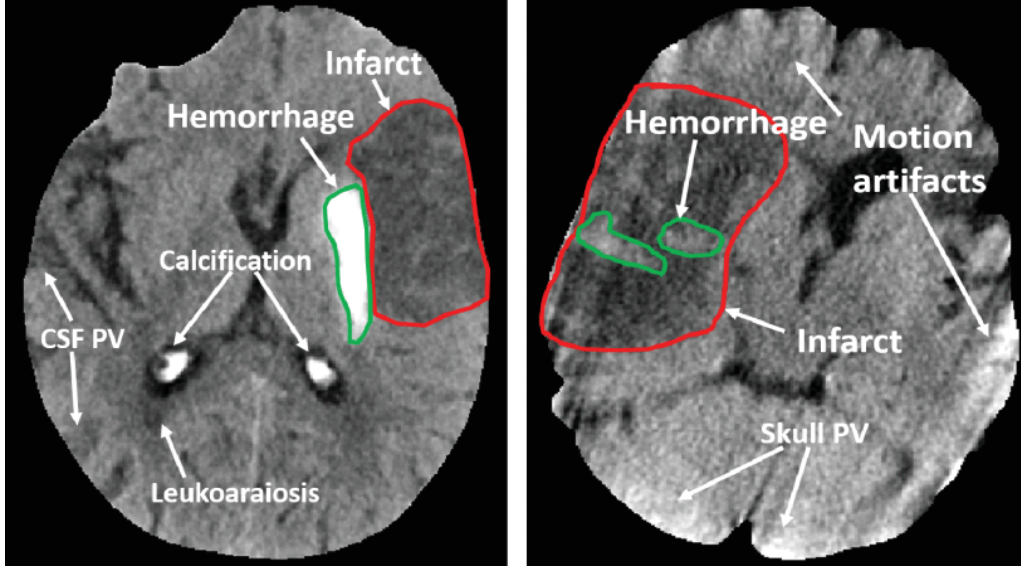
Figure 2: Samples of CT slices to depict *overlapping infarcts* – infarcts of multiple types at the same image region.

Figure 2 gives rise to a *multi-label* segmentation problem, where each image pixel may belong to more than one class. Therefore, in this research, we propose to develop a new deep learning -based processing pipeline to classify brain stroke from CT scan images, and further localize the infarct through volumetric reconstruction. Moreover, to the best of the authors' knowledge, this work is the first attempt to implement simultaneous volumetric reconstruction and correction of segmentation to improve demarcation performance and evolve a pliable computational model that can be used to infer quantitative diagnostic measures and with further extensions, for simulating surgical procedures as well.

Objectives

To this end, this research proposes to achieve the following objectives through data-driven computational modeling and analysis. The approach and methods that will be adopted in meeting these objectives is detailed in the subsequent section. An overview of this workflow is presented in Figure 3.

- To detect the presence of and differentiate between ischemic and hemorrhagic infarcts from non-contrast CT (NCCT) slices of the brain.

- To localize and segment the regions representing normal, ischemic infarcts, and hemorrhagic infarcts from the NCCT slice images.

- To reconstruct the volumetric NCCT image of the brain from the processed slices while simultaneously extrapolating and correcting infarct segmentation demarcations based on geometric constraints.

- To infer location information and other quantitative diagnostic measures from the reconstructed volumes to assess the condition such as cerebral infarct volume (CIT).

Methods and Approach

In recent years, research in deep learning has demonstrated successful application of deep learning and convolutional neural networks for image classification, including medical image analysis. In this study, we propose to develop a deep neural network -based processing pipeline for classifying different stroke patterns on NCCT images, and localizing the infarct for downstream treatment formulation.
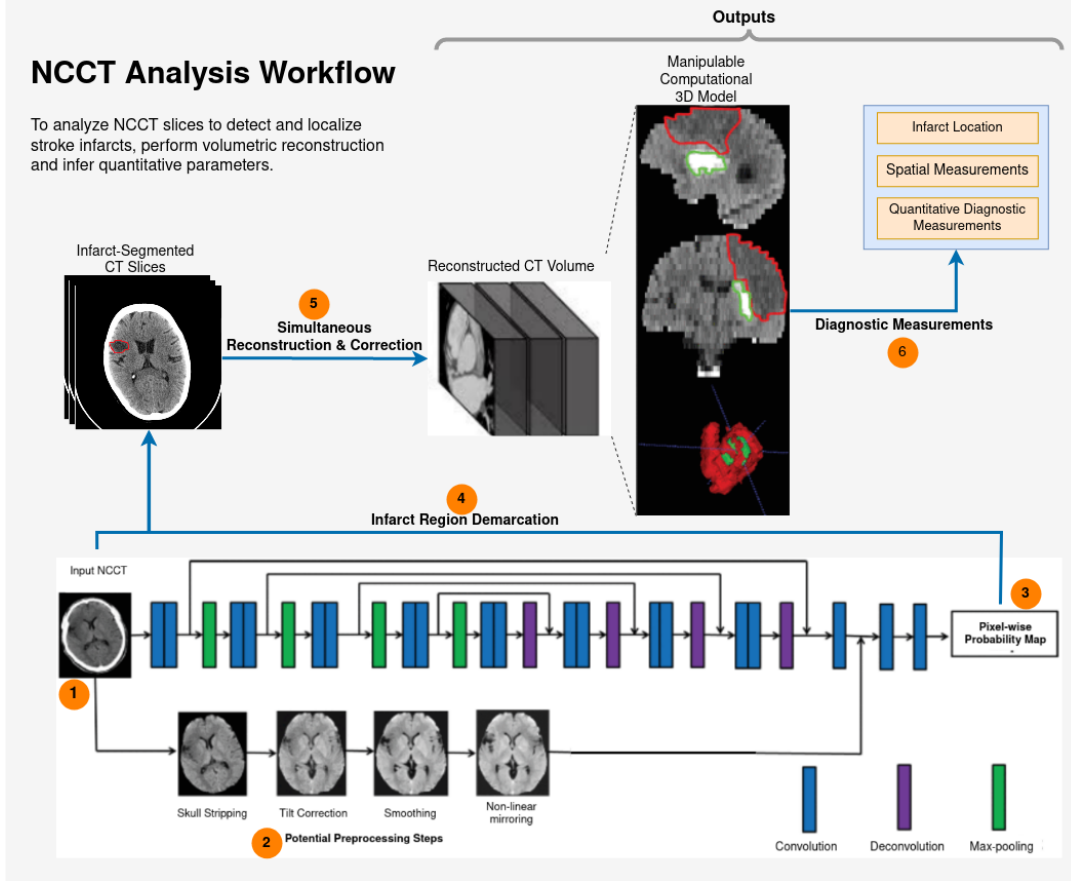
Figure 3: Overview of the NCCT analysis workflow following steps 1 through 6.

Towards this goal, we will collect NCCT imaging slides of study patients. Following this, the digital images will be randomly partitioned into two sets, one for model training and another as an independent test set for the final evaluation of the model. Care will be taken to avoid overlapping slides from a given patient across the training and test sets. Each slice will be manually assessed and its regions will be labeled as either *normal (0), ischemic infarction (1), hemorrhagic infarction (2)* by a trained cardiovascular radiologist. Thus, labeled slice image will form the input for training the deep learning -based computational pipeline. The model will be developed to take in square patches or tiles as inputs and output a prediction probability for each of the three classes: 0, 1, and 2 in a multi-label setting. Different model parameters including network weights, test for multiple network layers, learning rates, loss functions will be considered to fine-tune the model and formulate a model with optimal parameter settings. An unseen held-out subset of the slices data will be used for independently validating and evaluating performance and accuracy of the trained model. Finally, the models' ability to recognize the individual segmentation classes will be analyzed. As a final step, the processed image slides with infarct region annotations, as predicted by the developed computational model, will be used to perform volumetric reconstruction and infarct region correction. Furthermore, we will visualize the model's predictions overlaying color-coded dots on patches for which the model predicted patterns. This will aid in quickly identifying regions of the slice(s) from a given patient containing abnormal tissue.

Data Collection. To develop and evaluate our computational model for detecting distinctive infarct patterns in CTs, we will acquire volumetric NCCT slices in a digital image format, typically DICOM or NIfTI. Following this, the images will be randomly partitioned into two sets: (a) one for *model building* – i.e., training and validation (about three-fourths of the dataset), and (b) for *model evaluation* (about one-fourth of the dataset).

Slice-level Annotation to Establish Ground Truth. All NCCT slice images will be manually labeled by one or more medical experts. Each image corresponding to the model building dataset will be annotated with scan regions as as either one of the two patterns or normal/non-applicable. These are: *normal (0), ischemic infarction (1), hemorrhagic infarction (2)*. Ideally, we

would resort to multiple independent annotation results by the experts and correct for inter-rater biases to ensure high quality of the ground truth. For the purpose of annotations, a granulated user-friendly tool will be provided to the medical expert(s) to perform manual annotation at the super-pixel image region level, with the ability to select large regions of the image at a time and label them. This will save time and effort on their part. In addition, case-specific comments will be collected for downstream evaluation and analysis of the developed processing framework. The test set will be used, once the model development is complete, to evaluate its performance and compare it against that of expert annotators.

Data Pre-processing The input data in the form of CT slices will be processed by a computation processing pipeline that comprise deep learning network to analyze images and draw inferences. Initially, basic pre-processing methods to ensure consistency of image quality and exposure statistics across the dataset will adopted, and further pre-processing workflows may be integrated at a later stage during model building by empirically determining the specific image artifacts to be managed and the method required to do so. Some of the basic methods include: automatic resizing of training images to contain a fixed dimension of pixels; apply color jittering on the brightness, contrast, saturation, and hue of each image to neutralize the differences across the dataset; and augmentation of image data to randomly flip and rotate them along the horizontal and vertical axes to obtain variability in the training data, and to ensure robust model development, among others. Some more potential pre-processing methods that may be employed, should the need arise, are depicted in Figure 4.
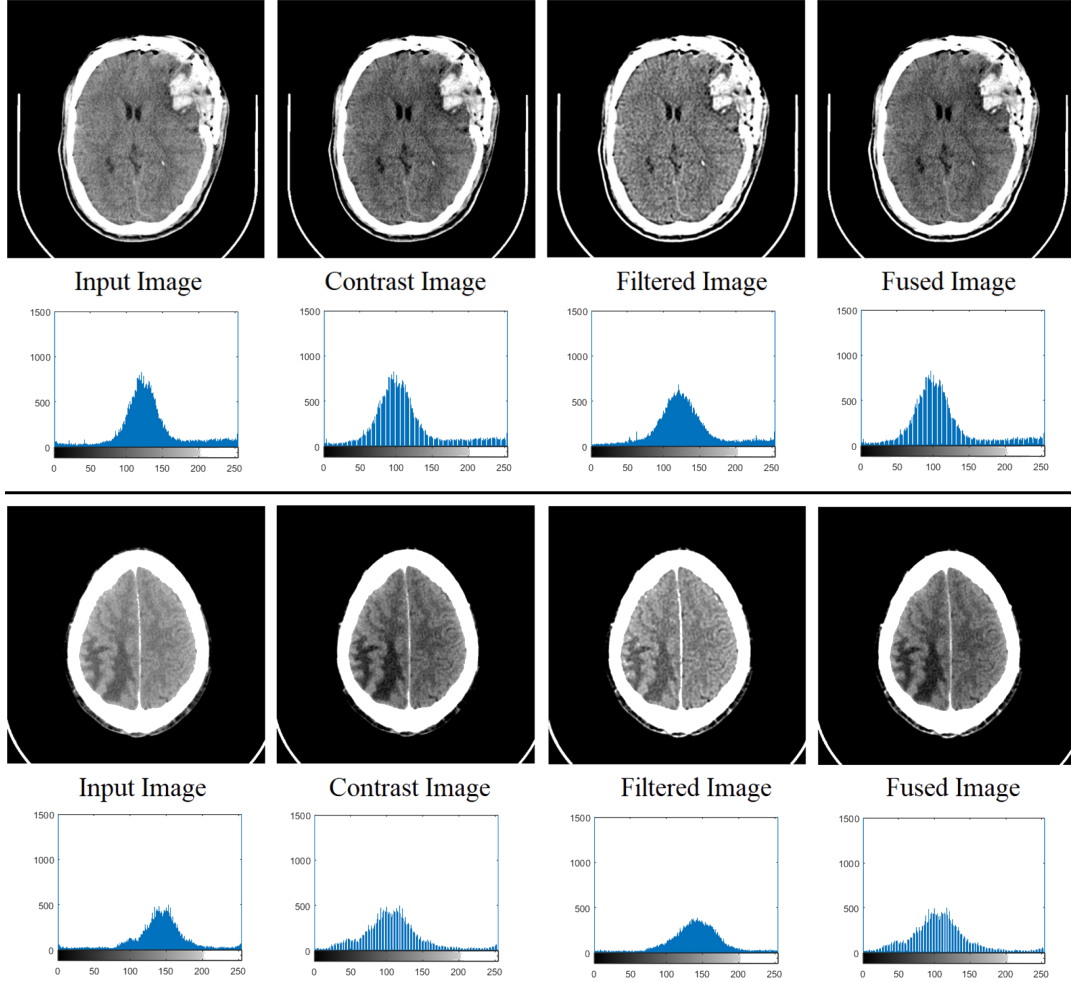

Figure 4: Potential pre-processing methods to apply on the NCCT slices before passing them to the neural network and computational analysis pipeline to correct artifacts.

Detection and Segmentation Model Building. Before training the classification and segmentation models, 90% of the model building data will be randomly selected for training and 10% for internal validation. The models will be implemented using the deep learning library Torch

available for Python. Torch is a high-level neural networks API, capable of running on top of various backend architectures. The models will be trained under a supervised setting, with NCCT slices fed as input, and outputs corrected against their corresponding expert-annotated and inter-rater corrected NCCT slices. Different tests will be conducted to optimize for the number of epochs, initial learning rates as well as the optimal depth of the neural network and other functionally configurable portions of the computational pipeline. The output of the models will be configured to output probability vectors p per stroke type, normalized to 1. Finally, the learning curves (accuracy vs. no. of iterations) for both training and testing will be plotted to determine if there is a generalization of the deep learning network model(s) to the unseen validation/test data i.e., no over-fitting has occurred.

Visualization of Predicted Patterns on the TAB sections. The processed and region-predicted NCCT slices will be visualized by overlaying color-coded dots on patches for which our model predicted a stroke infarct pattern, or each type of the stroke. This visualization will allow us to the decisions generated by the model and further aid to gain insights into the model's classification method.

Volumetric Reconstruction and Correction. With the infarct segmentation workflows in place, the subsequent steps involve reconstructing the volumetric CT of the patient's brain with annotated infarct regions, labeled by type – ischemic and hemorrhagic.This process will involve stacking the processed NCCT slides whilst simultaneously correcting the neighbors for potential errors in region segmentation. These corrections will be automated based on geometric, spatial, and shape-based constraints of adjacent slides such as contour evolution methods [16], depicted in Figure 5. The correction strategy will not only improve the overall localization accuracy of the ischemic strokes facilitating subsequent use of the reconstructed volume, but will save compute time due to simultaneous reconstruction and correction and improve model inference through a more interpretable basis for reconstruction. Ultimately, this step yields an annotated volumetric model of the brain region that is pliable for exploratory analysis on a computer.
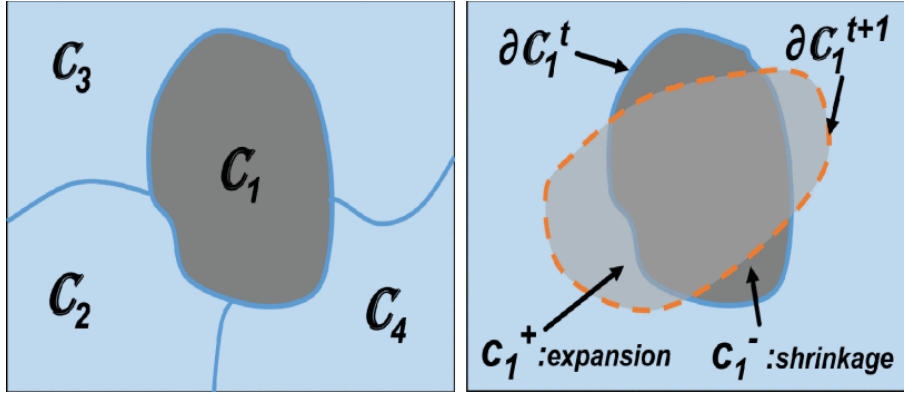

Figure 5: An abstract depiction of the *contour evolution* method, as an example of the correction methods that can be applied during volumetric reconstruction.

Diagnostic Inference from Volumes. The ultimate goal is to localize infarct types and locations in the spatial context. In addition, we also propose to estimate quantitative diagnostic measures. The annotated volume of the patient's brain can be easily exploited to draw out any form of geometric, spatial, or structural measurements, and even a combination thereof. Furthermore, the presence of each type of infarct can be individually quantified to present summary inferences of the patient diagnosis to help clinicians devise an ideal treatment strategy.

Validation from Radiologists. At the completion of the complete processing pipeline, two sets of validations will be performed to ensure correctness of the overall computational pipeline – *(1) the volume-level annotations* will be validated by radiologists, and *(2) the slice-level annotations* of the held-out test-set will be compared to the model predictions. *Evaluation 1* will be qualitative in nature, owing to the tediousness of manually annotating volumetric regions. However, this evaluation will be supported by *evaluation 2*. In conjunction, the two sets of validations will provide sufficient evidence to verify the complete proposed computational pipeline. To evaluate the slide-level performance, the model's labels will be compared against those of the radiologists' by calculating an inter-rater reliability metric called Cohen's kappa score [18], as it has been adapted

as a standard metric when it comes to annotation of medical images. Thus, between every two sets of annotations from radiologists and/or the computational pipeline, both $_{pd}$ scores and kappa score per class will be computed. K_{pd} refers to the percentage of NCCT slices in which two annotators agreed on the same annotation. Kappa scores per infarct class, on the other hand, estimates the detection of a given infarct pattern or type between two sets of annotations. The annotations will be quantified using a suitable metric as deemed suitable during discussions with the experts.

Anticipated Results, Potential Pitfalls, and Alternatives. We anticipate that the predictive model developed as part of this study will be able to accurately predict all stroke infarct features associated with patterns specific and non-specific to ischemic and hemorrhagic strokes. If this is not the case and/or model tends to accurately predict only the class labels having majority instances/samples, the authors will generate image slices with different overlapping areas for each class to accommodate for a *uniform distribution* through augmentation techniques across all classes (0-2) defined in this study. Further, we envision that there will be a good agreement i.e., 75% or higher, between the internal radiologist and the deep learning pipeline annotations. If it is less than what is expected, randomly selected image tiles annotated by the annotators will be cross-compared for their mutual agreement. This will allow us to reflect on whether the developed predictive models are capable of learning from a given training dataset provided by a single study radiologist. If the models perform worse in agreement compared to the two human experts themselves, then the models will be re-trained using the curated inputs from different radiologists on the whole training dataset. It is very important to provide high quality gold standard data set for training a deep learning network.

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