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Neuroimaging and deep learning for brain stroke detection - A review of recent advancements and future prospects

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Background and objective: In recent years, deep learning algorithms have created a massive impact on addressing research challenges in different domains. The medical field also greatly benefits from the use of improving deep learning models which save time and produce accurate results. This research aims to emphasize the impact of deep learning models in brain stroke detection and lesion segmentation. This is achieved by discussing the state of the art approaches proposed by the recent works in this field.

Methods: In this study, the advancements in stroke lesion detection and segmentation were focused. The survey analyses 113 research papers published in different academic research databases. The research articles have been filtered out based on specific criteria to obtain the most prominent insights related to stroke lesion detection and segmentation.

Results: The features of the stroke lesion vary based on the type of imaging modality. To develop an effective method for stroke lesion detection, the features need to be carefully extracted from the input images. This review takes an attempt to categorize and discuss the different deep architectures employed for stroke lesion detection and segmentation, based on the underlying imaging modality. This further assists in understanding the relevance of the two-deep neural network components in medical image analysis namely Convolutional Neural Network (CNN) and Fully Convolutional Network (FCN). It hints at other possible deep architectures that can be proposed for better results towards stroke lesion detection. Also, the emerging trends and breakthroughs in stroke detection have been detailed in this evaluation.

Conclusion: This work concludes by examining the technical and non-technical challenges faced by researchers and indicate the future implications in stroke detection. It could support the bio-medical researchers to propose better solutions for stroke lesion detection.

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1. Introduction

Stroke is one of the major reasons for adult deaths around the globe, impacting 6.2 million people every year [1]. Over the past two decades, there has been a 26 percent increase in stroke deaths, worldwide. Stroke is the second leading cause of death across the globe [2]. In turn, a great amount of research has been carried out to facilitate better and accurate stroke detection. Brain stroke occurs when the blood flow to the brain is stopped or when the brain doesn't get a sufficient amount of blood. As a result, the particular part of the brain drained of blood supply experiences a shortage of oxygen and becomes unresponsive [3]. This in turn, causes disturbances to the organs that are controlled by the affected part of the brain. The primary symptom of a stroke is partial numbness and numbness in the legs, arms and face belonging to one side of the body. Other minor symptoms are dizziness, headache, difficulty in walking and unconsciousness [4].

Depending on the obstacle in the blood supply to the brain, stroke can be classified into two types, Ischemic Stroke and Hemorrhagic stroke [5]. Ischemic stroke is caused by an obstruction in the blood vessels that carry blood to the brain. This specific type accounts for almost 87% of all stroke cases [6]. Hemorrhagic stroke is majorly caused by the breakage of weak blood vessels. Aneurysms and arteriovenous malformations are the basic types of weakened blood vessels that are responsible for Hemorrhagic stroke [7]. Another cause of Hemorrhagic stroke is high blood pressure [8].

The impact of stroke in an individual is influenced by the affected region of the brain and its severity. An extreme case could

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potentially lead to death [9]. The challenging process concerning stroke is its treatment. If the blood flow to the brain is not restored within several hours after the onset of ischemia, then the penumbral tissue will not be salvageable. The goal of stroke treatment and therapy is to save the penumbral tissue. Once the tissue is infarcted, the process is irreversible [10].

A stroke can be caused by a ruptured blood vessel or a blocked artery [11]. Images of the brain that are recorded during a scan and physical tests are utilized in diagnosing stroke among individuals. Strokes are diagnosed using advanced imaging techniques. Diagnosis is done with the help of brain imaging procedures such as Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) [12]. These imaging techniques have been proven to be essential for computing the changes in the properties of the tissues. The degree of infarction of the brain tissue is characterized by these imaging techniques. Over the past few years, various medical image investigation methodologies and statistical tools have been experimented with. The performance of these tools and methodologies in differentiating amongst the states of tissues in the brain were compared.

CT scans performed on an individual presumed to have a stroke, can be used to identify the type of stroke that they have undergone. The required information for carrying out the emergency procedures right after a stroke can be provided by CT scans [13]. CT is comparatively inexpensive and less affected by noise. CT is more accessible to patients and much faster than other imaging techniques such as MRI [14,15]. In the event of a stroke, a non-enhanced CT is the first radiological examination performed on the patient [16]. A hypodense structure in the CT images indicates the presence of an ischemic lesion [17]. However, abnormal lesions are not clearly visible in a CT. It also experiences constraints while locating minute infarcts in the cerebellum, the brain stem and the interiors of the cerebral hemispheres.

Hence, MRI is a more suitable technique for overcoming this limitation [18]. Despite the many benefits that MRI provides, MRI is expensive and accessible to only a minority of the healthcare centers. The high duration for performing an MRI scan poses serious challenges to the existing imaging techniques [19]. By using MRI instead of CT, infarcts can be detected earlier on before the appearance of symptoms.

Over the last decade, several computer-aided techniques and tools have been developed to detect abnormalities in the brain at the earliest. Specifically, Artificial Intelligence and Deep Learning are majorly used to achieve accurate and automated results for Stroke detection. These results do not play a stand-alone role in the detection process. Being a very sensitive treatment process, computer-aided techniques can be complementary to support physicians in the stroke detection process [20].

There are certain challenges involved while using computer-aided techniques to get accurate results. Firstly, high-resolution images are required. The equipment required to get these high-resolution brain images is expensive. Secondly, the diversity in brain tissues increases the difficulty in diagnosing the stroke. Another challenge is the presence of any older stroke area. This makes the distinguishing process tough between the new stroke area and the old stroke area [21]. To get an efficient and accurate computer-aided model, all these issues need to be fixed.

Through this work, we aim to achieve the following objectives

- To compare the performance of the existing deep learning techniques used for stroke lesion detection and segmentation.
- To discuss the achievements of the state-of-the-art techniques in stroke lesion detection.
- To analyze the key challenges involved in stroke lesion detection and segmentation.
- To highlight the potential research gaps and future trends related to computer-aided diagnosis of brain stroke.

2. Search strategy and organization of the review

In this study, we have referred research publication databases like Pubmed™, ScienceDirect™, IEEEXplore™, and Google Scholar™ to search the relevant publications made in the area of brain stroke detection. In addition to these sources, few significant articles were also downloaded from Springer and Wiley publications. These articles were screened in the context of deep learning methods and the search strategy process is highlighted in Fig. 1.

We applied a three level filtering process to identify the most suitable publications required to present this review. In the first degree analysis, 367 publications were filtered from a set of 620 publications based on the title and abstract. The second degree analysis filtered 196 publications from a set of 367 publications, based on the details of the datasets and methods applied. The third degree analysis employed a full length study to understand the details and implementation aspects of the deep learning method employed. Through this step, 113 publications were finally shortlisted and included in this review. To the best of our knowledge, we have considered the key contributions of all deep learning research publications reported till 2020 for stroke lesion detection and segmentation.

The search process used the keywords like ‘Ischemic stroke’, ‘Hemorrhagic stroke’, ‘Deep learning’, ‘Convolutional Neural Network’, ‘Fully Convolutional Network’, ‘Lesion segmentation’, ‘Lesion detection’, ‘Brain stroke detection’, ‘Computed Tomography’, ‘Magnetic Resonance Imaging’, ‘Perfusion Imaging’, ‘Penumbra’, ‘Core’, and ‘Computer-aided diagnostic support system’ to download the relevant publications. A period of 45 days was involved to download these publications and the inclusion/exclusion criteria to filter the final 113 publications from the list of 620 publications are highlighted in Table 1. The quality assessment form utilized to review each publication is presented in the appendix.

The year-wise distribution of the reviewed publications is presented in Fig. 2. It could be inferred that, most of the deep learning-based approaches for stroke detection were published in the last three years. To the best of our knowledge, this is the first review report consolidating the findings of different deep learning approaches for stroke lesion detection based on the input imaging modality employed.

The review is organized as follows. In Section 2, we present the details of the search strategy employed to collect and filter the research articles from different sources. Section 3 highlights the essential details behind the types of stroke and its related neuro-imaging modalities. Section 4 presents the consolidated review of different deep learning architecture employed exclusively for stroke detection, lesion segmentation and prognosis. Section 5 presents the various datasets that research works have employed in stroke detection. It also includes the future scope, research gaps, and the challenges to be addressed in stroke lesion detection and segmentation. Finally, Section 6 concludes the research work describing the significance of deep learning methods in stroke detection.

3. Neuroimaging for stroke – a walkthrough

This section presents an overview of types of stroke and its related imaging modalities employed for diagnosis and treatment.

3.1. Ischemic stroke

The occlusion of brain vessels inside the brain causes ischemic stroke [22,23]. This causes a reduction in the blood supply to a

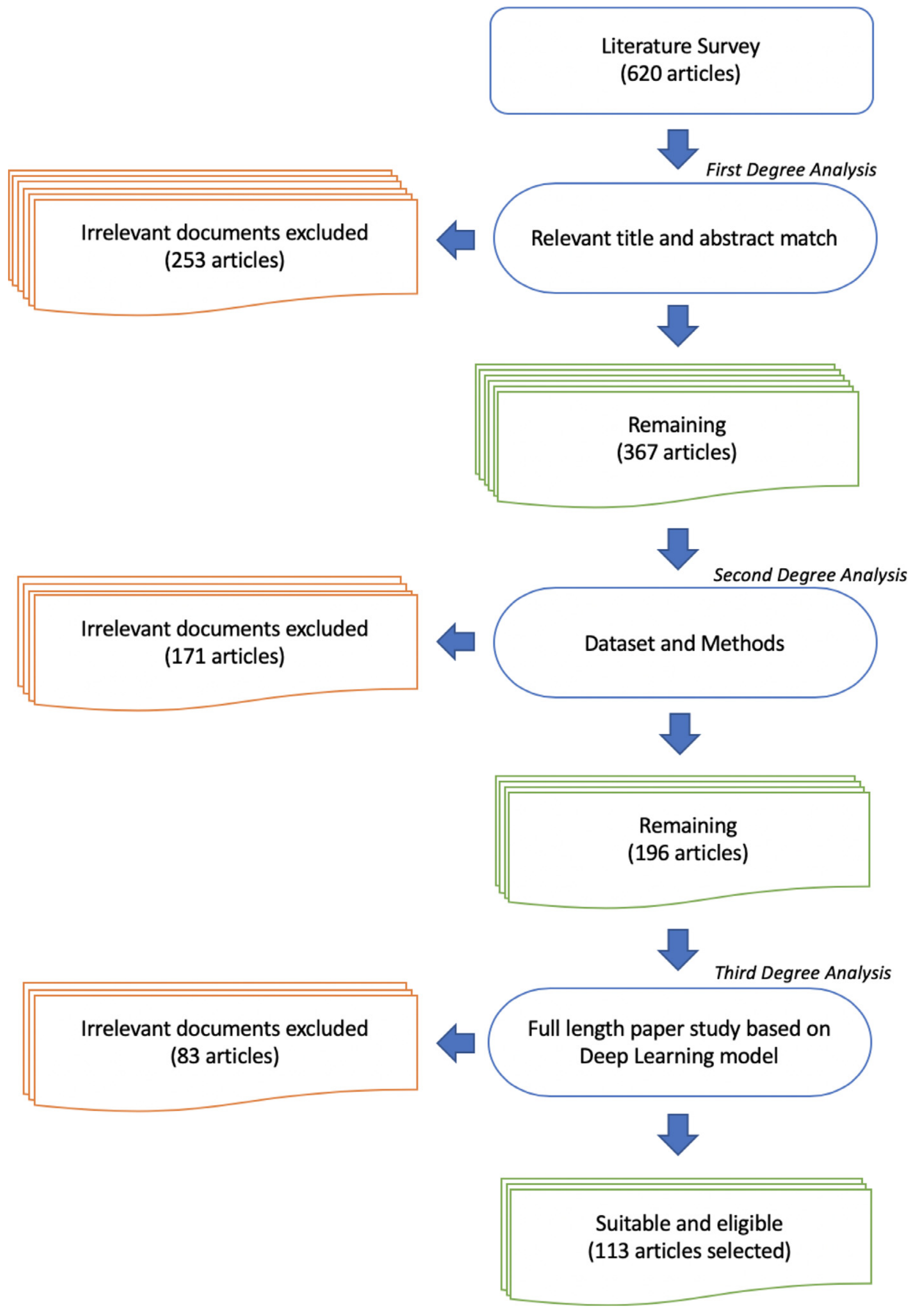
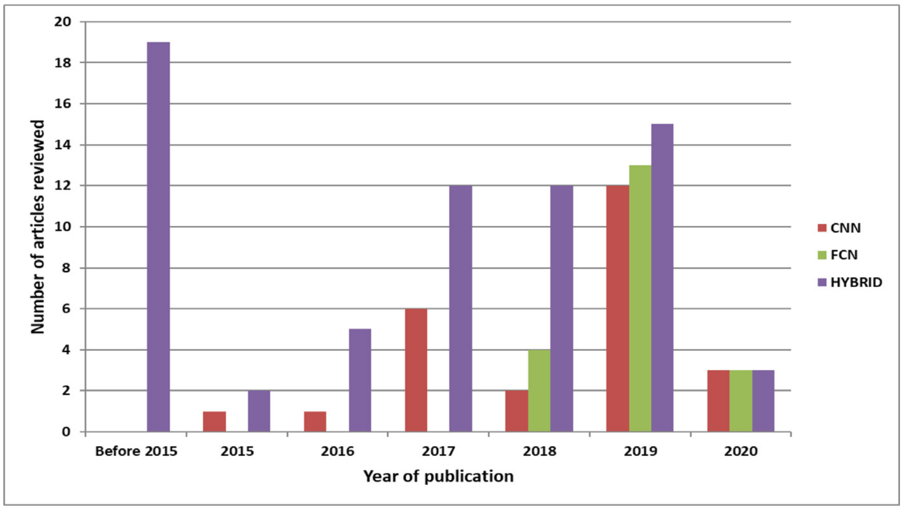


Fig. 1. Overview of the search strategy and manuscript filtering process.

Table 1
Exclusion and inclusion criteria.

Factor	Inclusion	Exclusion
Dataset and research outcome	• Studies involving ischemic and hemorrhagic stroke in humans. • Studies dealing with CT, MRI and other multimodal imaging of the lesions. • Studies using benchmark datasets for stroke lesion detection. • Studies describing the proportions of the infarct and the extent of damage. • Studies detecting the area the core and penumbra in an ischemic stroke.	• Studies involving animal data. • Studies that only considered healthy controls. • Studies involving with the treatment of the detected lesions. • Studies describing the transition of the lesion before and after the treatment. • Studies related to lesions caused by conditions other than stroke.
Study design and Methodology	• Studies that used deep learning architectures to segment and annotate the lesion regions from the image dataset. • Various studies that employed deep learning models for stroke detection.	• Statistical methods for stroke lesion detection. • The scientific working of the imaging modalities employed in the research articles. • Biochemical research studies on the properties of the lesions.



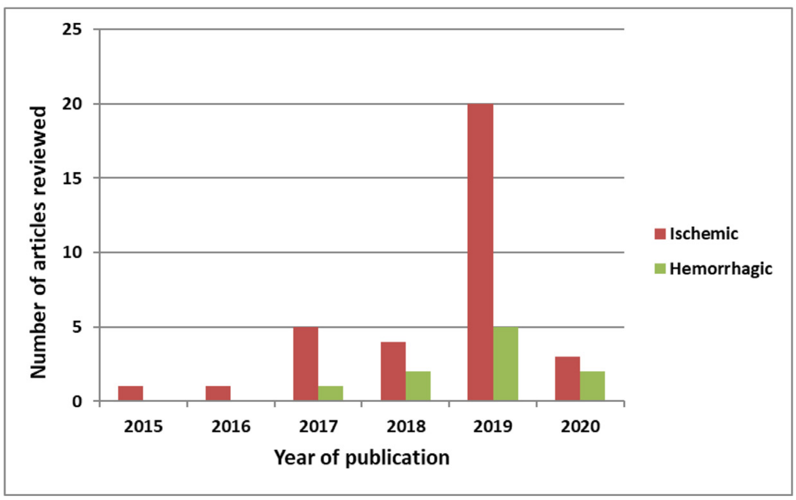


Fig. 2. (a). Year-wise distribution of the reviewed publications based on the type of deep network. (b). Year-wise distribution of the reviewed publications based on the type of stroke.

specific region of the brain. Consequently, there is a loss of oxygen and nutrients and excretes are not expelled from the brain. The regular neuronal functioning of the body ceases and ultimately leads to necrosis due to the blockage of the blood vessel [24]. Within hours, the ischemia can become permanent infarction [25]. The infarction and the changes in the brain tissue can be observed by using imaging techniques including CT and MRI [26].

After the onset of ischemia, the brain tissue gradually becomes more hypo-attenuated on the CT scan. During the first few hours after the stroke, gray matter attenuation reduces. It becomes a similar attenuation to normal white matter. However, within 24 hours, the affected brain is hypo-attenuated compared to the normal brain which is a characteristic for infarction [27,28]. Contrarily, within minutes of the onset of an ischemic stroke, MRI's diffusion-weighted imaging (DWI) can show hyper-intensity in the ischemic tissue. After a few hours, the lesion becomes hyper-intense on other T2 weighted sequences as shown in Fig. 3. This usually indicates infarction.

3.2. Hemorrhagic Stroke

The rupture of the blood vessels inside the brain causes immediate destruction of the brain tissue, leading to hemorrhagic stroke [22,30]. Intracranial hemorrhage (ICH) and subarachnoid hemorrhage (SAH) are the two different types of hemorrhagic stroke. Common risk factors that are the root of hemorrhagic stroke include Hypertension (HTN), myocardial infarction (MI) and thrombolytic consumption. Within 72 hours of the onset of a hemorrhagic stroke, a hypo-dense region can be detected around lesions on CT. The lesion area becomes less intense and begins to shrink during the next 17 days. The periphery of the lesion takes an uneven profile, with a ring-like appearance, as presented in Fig. 4. MRI scans taken 12-24 hours after a hemorrhagic stroke are more sensitive than CT scans. The lesion has a hyper-intense core and is usually surrounded by hypo-intense boundaries as shown in Fig. 5. The black arrows indicate the presence of microbleeds which are reported to predict hemorrhagic stroke (Fig. 5) [31,32].

3.3. Penumbra Core Separation

Generally, interruption in blood supply to the brain causes a stroke. This leads to a drastic decline in oxygen and glucose concentration within a short period of time. This results in the leakage of ions across the membrane of neuronal cells [34]. This disrupts the tissue's ion balance causing cerebral ischemia. The territory of this ischemia consists of necrotic tissue, core, which is surrounded by a border. This border zone is called the penumbra. Penumbra tissue has a reduced blood flow as it is around the ischemic tis-

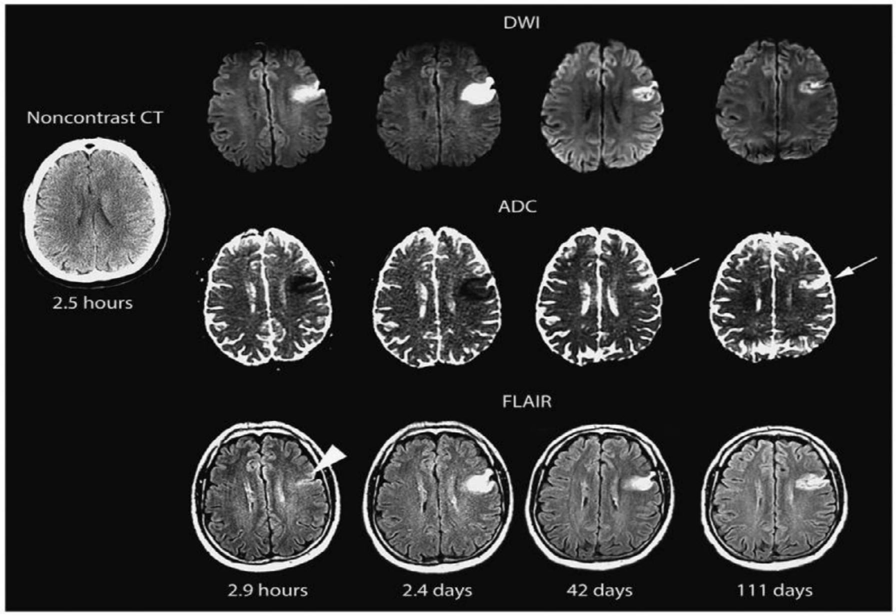


Fig. 3. Comparative visualization of ischaemia in CT and MRI modalities - (DWI – Diffusion Weighted Imaging, ADC – Apparent Diffusion Coefficient, FLAIR – Fluid Attenuated Inverse Recovery) [29].

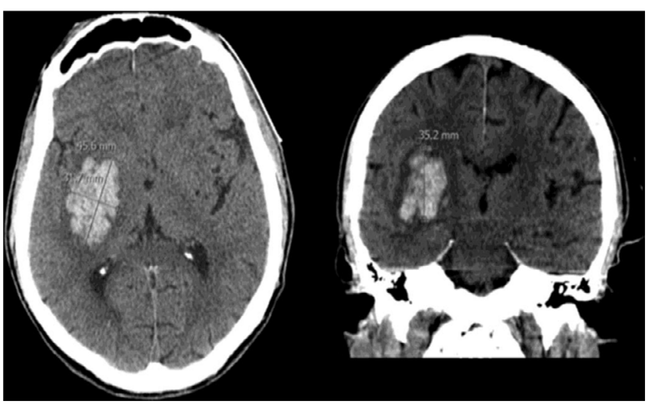


Fig. 4. Intracerebral hemorrhage evidenced in CT [33].

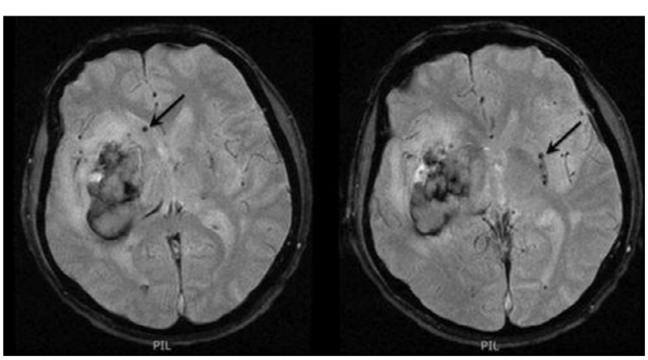


Fig. 5. Intracerebral hemorrhage evidenced by MRI [33].

sue. The blood flow to this tissue is marginally higher than the ischemic threshold [35]. When this issue is not addressed in time, the penumbra transforms itself into a core tissue. This transition process is only partially known [36–40].

Even though penumbra is an area at risk, the penumbra can be treated and cured with the help of certain suitable treatments [41,42]. But over some time, this penumbra gets converted into a core tissue, which is affected by ischemic lesions to an extent where it is irreversible [43]. Hence, it becomes very critical to diagnose the stroke at the earliest using advanced medical imaging techniques as the penumbra region is always surrounded by the core region. In this way, the penumbra and the core tissue can be differentiated. This separation is essential for adopting suitable treatments [41,44]. Fig. 6 indicates the various sections of the brain related to penumbra core separation.

4. Deep learning for stroke detection

Though Machine learning methods were successfully applied in Medical image processing for the past two decades, it suffers from few limitations. These methods relied greatly on hand crafted features designed by domain experts. As the observed data vary from patient to patient and data interpretation varies with the experience of the domain experts, it might lead to intra and interobserver error. On the other hand, deep learning in Medical imaging has made significant progress in capturing hidden representations and automatically extract features from them. Hence, it can support better data interpretation and supervision, which can assist the physicians efficiently.

As the deep network typically consists of more number of layers, the magnitude of the back propagated error derivative decreases rapidly along these layers. This causes a slight update of weights in the layers, leading to precise feature learning and classification. Hence, the trained model does not miss out on any of the significant features in the underlying data. Due to the rapid growth and development in the computational platforms like Graphics Processing Unit (GPU), processing large amount of data with deep learning is now getting simple. Hence, Deep learning stands out to be a significant learning paradigm in health care automation. This section reviews the different state of the art methods applied for stroke detection.

4.1. Ischemic lesion detection

In this section, different methods for ischemic stroke detection are reviewed and discussed based on CT and MRI modalities.

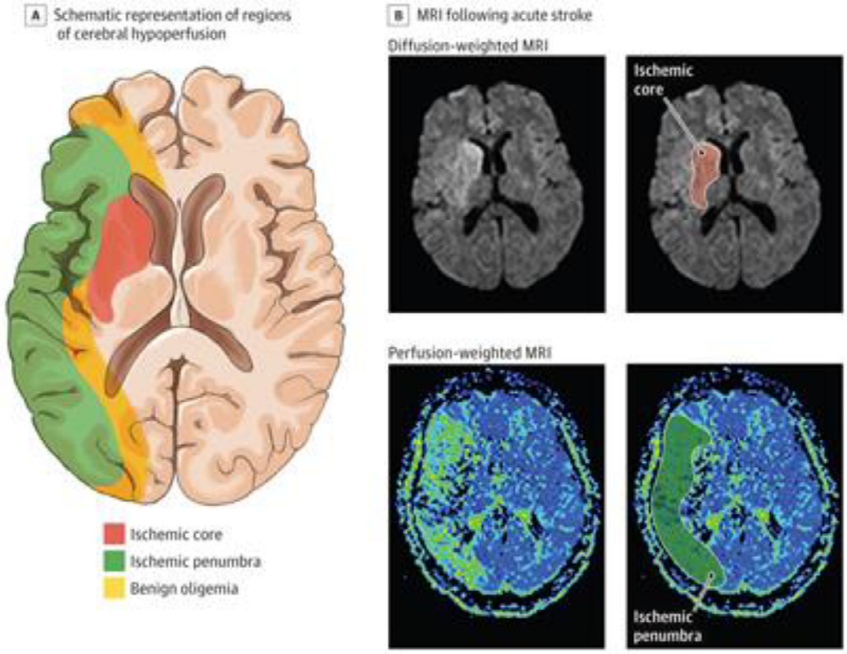


Fig. 6. Penumbra and core – a pictoric illustration [45].

4.1.1. CT based methods

This section discusses the key strengths of various deep learning approaches applied for ischemic lesion detection using CT.

4.1.1.1. Conventional CT based methods. A conventional CT scan is obtained by an X-ray beam directed at different angles and levels of a body part. The ischemic lesion can be observed in the CT slices run over the 3D brain stack. Chin et al. used a traditional Convolution Neural Network comprising of five layers to segment ischemic lesions based on CT [46]. To improve the efficiency of the deep learning approach, Shinohara et al. came up with a Deep Convolutional Neural Network (DCNN) (Xception) model to segment ischemic lesion regions [47]. This deep network comprised of 36 layers for precise feature extraction. Lisowska et al. took a step ahead to come up with a context-based deep learning model [48]. The features in this model were self-learned in the backpropagation process. Unlike previous methods, where a general CNN was applied, this network performed better as it incorporated the context-aware features for ischemic lesion segmentation. To get more precise results, more than one convolution model was utilized. Barros et al. used three different convolution-based deep learning models depending on the properties of the lesion [49]. This network used different models for lesions with subtle, intermediate and clear hypo-dense regions. It was reported to be more consistent and effective than a single convolution model approach in successfully segmenting the lesion region from CT scan images.

4.1.1.2. Advanced CT modality based methods. Radiological Imaging technologies play a crucial role in the identification of infarcts and the diagnosis of stroke. The advanced modalities such as Computed Tomography Perfusion (CTP) and Computed Tomography Angiography (CTA) are more sensitive in detecting acute cerebral ischemia than non-contrast Computed Tomography (CT). Hence, images scanned by these techniques are widely preferred now when compared to non-contrast CT scans. These scans are used by deep learning models to detect a stroke.

Öman et al. developed a three-dimensional CNN based network by combining Cerebral hemispheric CTA images with non-contrast computed tomography (NCCT) [50]. Barman et al. proposed a Deep Symmetry-sensitive CNN (DeepSymNet) that consisted of 11 layers [51]. The network consisted of inception modules, merge-layers with L-1 difference, max-pooling layers and fully connected layers. Unlike the work of Öman et al., this research was not based on manually segmented lesions. Thereby it performed better and reported to be a fully automated method for lesion detection.

The scans produced by CTP have been used in many works for ischemic stroke detection. Lucas et al. proposed a U-Net architecture that concatenated higher-level features from different layers. This was done to exploit all the information encoded in the perfusion input [52]. A similar U-net architecture was implemented by Islam et al. as a GAN network for ischemic lesion segmentation [53]. In this model, 2 deep networks were employed namely the segmentor and the discriminator. The segmentor consisted of 23 convolutional layers and produces a segmentation label for each pixel as the output. The discriminator is an FCN with 5 convolution layers followed by leaky-ReLU and an up-sampling layer to rescale the output to the size of the input map. 2D U-nets were also utilized by Soltanpour et al. to extract information about the location of the stroke lesion from four CTP maps. The probability maps are then used to differentiate between the lesion and healthy tissue [54]. Abulnaga et al. proposed a pyramid scene parsing network (PSPNet) that when compared to U-nets and 3D V-nets performed better. The network makes use of pyramid pooling to exploit global and local contextual information [55]. Tureckova et al. utilized leaky-ReLU activation function in U-Net for ischemic lesion detection from CTP images [56].

In contrast to the architectures discussed above, Bertels et al. have employed a DeepVoxNet CNN based network and made use of Contra-Lateral Information CNN for precise segmentation of lesion core [57]. A significant improvement in performance can be seen in the GAN based work proposed by Yang et al. In this work, the segmentation network is a 3D residual U-net and the discriminator is a 7-block network containing 3 residual blocks similar to the 3D U-net. The network further enforces high-level constraints on the segmentation network to produce predictions that mimic the ground truth distribution. As opposed to the performance of other methods employed by research works, a dice coefficient of

0.87 was reported in this work [58]. The summary of the different works reviewed as part of ischemic stroke detection and segmentation are highlighted in Table 2.

4.1.2. MRI based methods

This section discusses various deep learning methods applied for ischemic lesion detection from brain MRI.

4.1.2.1. Unimodal MRI based methods. One of the most primitive modality in Magnetic Resonance Imaging is the weighted image. In T1-weighted images, the contrast between the lesion and normal tissue was better displayed than in CT images. Anatomic information from several planes can be analyzed with T1 images for diagnostic purposes [59]. Wang et al. utilized an 8 layered 3D CNN, with 6 convolutional layers and 2 fully connected layers to detect ischemia in T1 images [60].

FLAIR produces images of higher lesion clarity as compared to T1- and T2-weighted sequences. The FLAIR sequence has a high sensitivity to abnormal tissues and it suppresses the details of Cerebro Spinal Fluid [61]. Maier et al. compared various machine learning and deep learning approaches to classify FLAIR sequences for ischemic lesion detection [62]. The CNN architecture performed better than most of the machine learning classifiers like Gaussian Naive Bayes, k-Nearest-Neighbours, Generalized Linear Models, Gradient Boosting Classifier, AdaBoost, Random Decision Forests and Extra Tress Forest algorithms. The deep network employed in this work consists of 3 convolution layers with rectified linear activation (RELU) and pooling, followed by a fully connected layer. Despite the advantages of FLAIR imaging, there are a few limitations associated with this imaging technique. Subtle lesions in certain regions including the basal cisterns have been masked in FLAIR images [61].

Another significant MRI modality used in ischemic stroke diagnosis is the Diffusion-weighted imaging (DWI), where the distribution of movement of the water protons was recorded for visualizing the anatomy. Ischemic lesions can be noticed and spotted early in this modality. As water molecules relatively diffuse freely in the extracellular space than in the restrained space, DWI becomes the effective imaging method for stroke lesion region segmentation than T1 weighted and Flair imaging. Chen et al. proposed an ensemble of deep learning models to detect and segment the ischemic stroke lesion from DWI [63]. EDDnet and MUSCLEnet architectures were ensemble for precise segmentation. Joshi et al. also used the DWI images to train and test their model to detect and segment the ischemic lesion region in the brain [64]. Joshi proposed an encoder-decoder convolution neural network to serve the purpose. Zhang et al. came up with a deep learning-based approach which had three key features [65]. The first feature was to present a Detection and Segmentation Network (DSN) to handle data imbalance issues. The next feature employed a triple-branch DSN model for precise feature extraction. Finally, a Multi-Plane Fusion Network (MPFN) was employed for the segmentation process. It has been reported that this way of using 3 models to handle, detect and segment stroke lesion region in the brain from DWI gets the best results compared to the existing methods.

4.1.2.2. Multimodal MRI based methods. Multimodal MRI refers to the simultaneous production of different signals from MRI imaging techniques [66]. Ischemic lesions can be effectively detected from multimodal MRI by computer-aided techniques. The advances in CNN and FCN architectures have led to a growing trend in the field of biomedical image analytics for segmentation and detection problems. Lucas et al. used a classical shallow fully connected convolution neural network to segment ischemic lesion regions from the multimodal MRI [67]. Winzeck et al. proposed an ensemble convolution neural network to segment ischemic lesion [68]. A combination of DWI, ADC, and low b-value-weighted images from 116 subjects was used to train and test the model. Kamnitsas et al. developed an 11-layered deep pathway CNN architecture from multimodal MRI [69].

Many FCN based architectures have been utilized in stroke detection with multimodal images. A deep CNN titled Res-CNN was developed by Liu et al. to automatically segment ischemic lesions from the multimodal MRI images [70]. Zhang et al. presented a 3D FCN to exploit three-dimensional contextual information for the precise segmentation of ischemic lesion [71]. In the work presented by Karthik et al., a deep supervised FCN is used with Leaky ReLU activation for the precise reconstruction of the lesion [72]. Different hyper-parameters were analyzed in this work for the estimation of better segmentation parameters. Guerreroa et al. presented ResNet, a FCN architecture. This model comprised of two pathways namely: analysis path and synthesis path. The role of the analysis path is to learn and extract precise features for differentiating the lesion pixels from the input MRI slice. The synthesis path is used to segment the up-sample the learned features for segmentation [73]. Nielsen et al. developed a deep architecture, inspired by SegNet architecture. It combines biomarkers to predict the risk of infarct from the multimodal images [74]. Liu et al. employed a Residual-structured Fully Convolutional Network (Res-FCN) which combines DWI, Apparent Diffusion Coefficient (ADC) and T2-weighted image (T2WI) for segmentation of ischemic lesions [75].

Many models combine multimodal data and use it as input to their network. U-nets are commonly used in many multimodal, medical image segmentation models. In the work presented by Liu, CTP and DWI data have been used in their network. The model consists of 3 components, a generator, a discriminator and a segmentor. The generator synthesizes the DWI images from the CT data. The role of the discriminator is to classify the DWI images as generated one or the true sample. The segmentation of the lesion was carried out by the segmentor. The generator and segmentor are designed based on U-Net which is an FCN. Whereas the discriminator is a 5 convolutional layered network with batch normalization, ReLU activation and an average pooling layer [76]. Dolz et al. proposed an improved U-net architecture which is inspired by the Inception architecture. They handle the various lesion sizes by extending the inception modules in the network. Two convolutional blocks having dilated convolutions of different scales are used in the inception modules [77]. Unlike the work proposed by Liu et al. [75], this work does not combine the image modalities at the input. Distinctive information is exploited by processing each modality separately which enhances the performance of this work as compared to that of Liu [76].

4.1.2.3. Advanced MR modality based methods. MR perfusion imaging is one of the advanced MRI modality which has many advantages in stroke detection. This imaging technique ensures whole-brain coverage and simpler post-processing including construction of rapid perfusion map. It can also perform diffusion imaging at the same time [78]. Hence, deep learning methods applied over these images could significantly improve the efficiency of automated computed aided assisted systems for stroke diagnosis.

Hu et al. presented a 3 dimensional residual framework called BrainSegNet, for automatic lesion segmentation from perfusion MR images [79]. Malla et al. conducted six experiments by varying different aspects of the CNN model such as the type of data and the hyperparameters. The CNN network, based on DeepMedic v0.6.1 with 8 convolutional layers performs automatic segmentation of brain lesions [80]. Ho et al. proposed a deep CNN network based on advanced MRI modality. The architecture consisted of multiple convolutional layers, fully-connected layers, pooling layers and a Softmax classifier. This model automatically learns hierarchical

Table 2
Summary of different deep learning methods employed for ischemic stroke detection.

S. No	Ref	Image modality	Datasets	Method	Loss function	No. of epochs	Optimizer	Framework/Library used	Validation system	Outcome
1	Hu et al., 2020 [79]	MR Perfusion	75	CNN	Focal loss based on Cross entropy	1500	ADAM	Pytorch	43 subjects for training and 32 subjects for tesing	Dice Coefficient: 0.30 Precision: 0.35 Recall: 0.43
2	Zhang et al., 2020 [65]	DWI	28	FCN	MSE, Cross entropy and Focal loss	Not specified	Stochastic Gradient Descent	Keras 2.0.8 and TensorFlow-1.4.1	21 subjects for training and 7 for testing	Dice Coefficient: 0.622 Sensitivity: 71.7%
3	Yu et al., 2020 [85]	PWI and DWI	182	FCN	Weighted Binary Cross-Entropy, L1 loss, Dice Loss, and Volume loss	120	ADAM	Keras 2.2.2 and TensorFlow 1.10.0	5-fold cross-validation	Dice Coefficient: 0.58
4	Barman et al., 2019 [51]	CTA	217	CNN	Cross Entropy	40	ADAM	Pytorch	4-fold cross-validation	Accuracy: 97%
5	Zhang et al., 2018 [71]	DWI	242	CNN	Dice loss	3000	Stochastic Gradient Descent	Pytorch	90 subjects for training, 62 for validation and 90 for testing	Dice Coefficient: 0.79 Precision: 92.67% F1-Score: 89.25%
6	Dolz et al., 2019 [77]	Multimodal MRI	93	FCN	Not specified	200	ADAM	Pytorch	83 subjects for training and 9 for testing	Dice Coefficient: 0.635 Modified Hausdorff distance: 18.64 mm
7	Malla et al., 2019 [80]	MR Perfusion	75	CNN	Dice	700	RmsProp with Nesterov momentum	Not Specified	5-fold cross-validation	Dice Coefficient: 0.34
8	Öman et al., 2019 [50]	CTA	60	CNN	Dice	35	RmsProp with Nesterov momentum	Theano	30 subjects for training and 30 for testing	Dice Coefficient: 0.61 Sensitivity: 0.93 Specificity: 0.82
9	Bertels et., 2019 [57]	CTP	125	CNN	Cross Entropy and Dice	4000	ADAM	Not Specified	5-fold cross-validation	Dice Coefficient: 0.45
10	Liu et al., 2019 [70]	Multimodal MRI	50	CNN	Customized loss function	70	Not Specified	Keras	25 subjects for training and 5 for testing	DC: 0.742 Hausdorff distance: 2.33 mm
11	To et al., 2019 [83]	MR Perfusion	345	FCN	L2	190	ADAM	MXNet version 1.3.1b	205 subjects for training, 64 for validation and 76 for testing	SSIM: 0.846
12	Shinohara et al., 2019 [47]	CT	18,396 samples	CNN	Not Specified	10	Stochastic Gradient Descent	Keras	Leave-one-case-out cross-validation	Accuracy: 86% Sensitivity: 82.9% Specificity: 89.7%
13	Soltanpour et al., 2019 [54]	CTP	103	FCN	SoftDice	150	ADAM	Keras	10-fold cross-validation	Dice Coefficient: 0.40
14	Abulnaga et al., 2019 [55]	CTP	103	FCN	Focal loss	200	RmsProp	Pytorch	5-fold cross-validation	Dice Coefficient: 0.44
15	Mobarakol et al., 2019 [53]	CTP	156	FCN	Adversarial loss	Not Specified	Not Specified	Not Specified	94 subjects for training and 62 for testing	Dice Coefficient: 0.39
16	Liu et al., 2019 [76]	CTP and DWI	103	FCN	Cross Entropy	700	RmsProp	Pytorch	4-fold cross-validation	Dice Coefficient: 60.65%

(*continued on next page*)

Table 2 (*continued*)

S. No	Ref	Image modality	Datasets	Method	Loss function	No. of epochs	Optimizer	Framework/Library used	Validation system	Outcome
17	Pinheiro et al., 2019 [84]	PWI and CTP	75 and 103	FCN	Dice	300	RmsProp	Pytorch	4-fold cross-validation	Dice Coefficient: 0.51
18	Yang et al., 2019 [58]	CTP	63	FCN	Adversarial loss with Cross Entropy and Dice	Applied early termination after observing 20 epochs	Not Specified	Pytorch	Training and Validation on 63 subjects	Dice Coefficient: 0.87
19	Winzeck et al., 2019 [68]	Multimodal MRI	116	CNN	Not Specified	Not Specified	Not Specified	TensorFlow	5-fold cross-validation	Dice Coefficient: 0.82
20	Barros et al., 2019 [49]	CT	1026	CNN	Not specified	Not specified	Not Specified	Not Specified	570 subjects for training and 456 for testing	Dice Coefficient: 0.57
21	Liu et al., 2019 [103]	MR Perfusion	64	FCN	Dice	60	ADAM	Not Specified	28 subjects for training and 36 for testing	Dice Coefficient: 0.57
22	Ho et al., 2019 [81]	MR Perfusion	48	CNN	Not specified	40	Gradient descent	MatLab	10-fold cross-validation	AUC: 0.871
23	Karthik et al., 2019 [72]	Multimodal MRI	28	FCN	Cross-entropy, Dice coefficient, and Tversky index	100	ADAM	Keras and TensorFlow	4-fold cross-validation	Dice Coefficient: 0.7
24	Tureckova et al., 2019 [56]	CTP	103	FCN	Not specified	300	ADAM	Keras	75 subjects for training, 19 subjects for validation and 62 for testing	Dice Coefficient: 0.37
25	Liu et al., 2018 [75]	Multimodal MRI	212	FCN	Dice	500	ADAM	Keras and TensorFlow	2-fold cross-validation	Dice Coefficient: 0.645
26	Lucas et al., 2018 [52]	CTP	75	FCN	QDice	100	ADAM	Pytorch	43 subjects for training and 32 subjects for testing	Dice Coefficient: 0.35
27	Nielsen et al., 2018 [74]	Multimodal MRI	222	FCN	Multinomial logistic loss	100	Stochastic Gradient Descent (SGD)	TensorFlow	158 subjects for training and 29 for testing	Accuracy: 85%
28	Guerreroa et al., 2018 [73]	T1 and FLAIR	250	FCN	Dice	60	RMSprop, Adam, SGD	TensorFlow	2-fold cross-validation	Dice Coefficient: 0.69
29	Chen et al., 2017 [63]	DWI	741	CNN	Cross Entropy	Not specified	SGD	Caffe	380 for training and 361 for testing	Dice Coefficient: 0.67
30	Lucas et el., 2017 [67]	Multimodal MRI	28	CNN	Cross Entropy	60	SGD	Matlab	cross-validation	Dice Coefficient: 0.39
31	Chin et al., 2017 [46]	CT	256 images	CNN	Not specified	Not specified	Gradient Descent	pyTorch	50% for training and 50% testing	Accuracy: 92.9%
32	Lisowska et al., 2017 [48]	CT	170	CNN	Hinge loss	Not specified	ADAM	Keras with Theano	71 subjects for training, 48 for validation and 51 for testing	Accuracy: 96.4%
33	Kamnitsas et al., 2017 [69]	Multimodal	64	CNN	Cross Entropy	Not specified	RmsProp with Nesterov momentum	Theano	5-fold cross-validation	Dice Coefficient: 0.66 Precision: 77% Sensitivity: 63% ASSD: 5.00 Hausdorff distance: 55.93
34	Wang et al., 2016 [60]	T1-weighted	18	CNN	Not specified	Not specified	Gradient Descent with constant momentum	Not Specified	10 for training and 8 for testing	Dice Coefficient: 0.78
35	Maier et al. 2015 [62]	FLAIR	37	CNN	Not specified	Not specified	Gradient Descent with constant momentum	Caffe	leave-one-out evaluation	Dice Coefficient: 0.67

imaging features from only the source pre-treatment perfusion images. [81].

Recently, FCNs have been implemented advanced MRI modalities for precise segmentation of the lesion regions in the brain. These advanced MRI modalities help the FCN to learn more precise features to differentiate the lesion and the normal brain tissues. Liu et al. proposed a DCNN to detect and classify lesion regions [82]. This work used dense blocks for feature extraction. To et al. proposed a three-dimensional Deep Regression Neural Network (3D-DRNN) to effectively segment the lesion regions in the brain [83]. 3D-DRNN used an encoder-decoder framework for semantic segmentation. The encoder is employed for high dimensional feature representation and the decoder reconstructs the output from the encoder to match it with the ground truth for validation. Pinheiro et al. compared the two state-of-the-art models for stroke lesion segmentation, V-Net and U-Net [84]. Pinheiro et al. worked with different configurations of pixel interpolations, depth variations, etc. in both models. According to this work, deeper U-Net was reported as the best model for stroke lesion segmentation in the brain images obtained from advanced MRI. Yu et al. proposed an attention-gained U-Net instead of a conventional FCN to classify lesion regions in the brain [85]. This research claimed that the model achieved significant results from base imaging without reperfusion information. This was proposed as the state-of-the-art model for lesion segmentation in the brain images. The summary of the different works reviewed as part of hemorrhagic stroke detection and segmentation are highlighted in Table 3.

From Table 2, it could be inferred that deep learning models using CNN and FCN were quite effective in classifying and localizing the ischemic lesion from brain images. These methods were evaluated with different evaluation metrics like Dice co-efficient, Hausdorff distance, ASSD, Accuracy, Precision, Sensitivity, SSIM, etc. Most of the deep architectures for ischemic lesion segmentation have applied a single point loss function at the very end of the network. This makes it difficult for the inner layers to tune its parameters for the global loss. Hence the initial layers of the network fail to effectively capture the global perspective when it comes to single point losses. Apart from loss function, other hyper-parameters required for training the model need to be initialized properly for optimal convergence.

4.2. Hemorrhagic stroke detection

Hemorrhagic stroke is a particular type of stroke which contributes to 15% of the entire stroke population in the world [86]. Several CNN and FCN models have been proposed in recent times to identify and segment the hemorrhagic lesion region in the brain from CT images. Islam et al. presented a deep learning method to detect and classify brain hemorrhages [87]. Islam integrated a CNN to automate the segmentation process. Several features were concatenated from different layers by sampling pixels. Another CNN based hemorrhagic stroke detection approach was proposed by Barros et al. [88]. In contrast to the above two works, Patel et al. proposed a three-dimensional convolution neural network to detect and segment stroke lesion regions in the brain [89]. Patel reported that 3D-CNN performed better than traditional CNN in identifying the hemorrhagic region in the brain from CT images.

Arbabshirani et al. proposed a deep CNN to spot hemorrhagic lesion regions from CT images [90]. It included FCNs for segmenting stroke lesions regions in the brain. Majumdar et al. came up with a 9-block convolution network for the segmentation process [91]. Each block was reported to have several convolution layers of size 3×3 followed by a Re-LU activation function. Cho et al. used a hybrid cascaded deep model for hemorrhagic lesion detection [92]. Two deep networks were involved out of which one of them was a CNN and the other one was an FCN. Phong et al. compared

Table 3
Summary of different deep learning methods employed for hemorrhagic stroke detection.

S. No	Ref	Datasets	Method	Loss function	No. of epochs	Optimizer	Framework/ Library used	Validation system	Outcome
1	Islam et al., 2019 [87]	89	CNN	Dice	40	SGD	Caffe	5-fold cross-validation	Dice Coefficient: 0.876
2	Patel et al., 2019 [89]	75	CNN and FCN	Categorical Cross Entropy	Not Specified	SGD	Theano and Lasagne	Radboudumc dataset: Total: 51 patients Training and Validation: 21 Testing: 25 Patch dataset: Training: 40 Validation: 10 Test: 50	Dice Coefficient: 0.91
3	Cho et al., 2019 [92]	135974 images	CNN and FCN	Not Specified	50	ADAM	Caffe	5-fold cross-validation	Accuracy: 98.28% Dice Coefficient: 0.84
4	Patel et al., 2019 [94]	1940	CNN and RNN	Binary Cross Entropy	Not Specified	ADAM	Keras with Theano	Training and Validation: 1554 Testing: 386	Accuracy: 87% AUC: 0.96
5	Kuo et al., 2019 [95]	4,396 head CT scans	FCN	Cross Entropy	30	SGD	PyTorch	4-fold cross-validation	AUC: 0.991
6	Arbabshirani et al., 2018 [90]	46,583 head CT scans	CNN	Not Specified	Not Specified	SGD	Caffe	Training: 75% Cross validation: 5% Testing: 20%	Accuracy: 84%
7	Majumdar et al., 2018 [91]	134	CNN	Not Specified	Not Specified	Not Specified	Not Specified	Training: 60, Validation: 5, and Test: 69 cases	Sensitivity: 81% Specificity: 98%
8	Phong et al., 2017 [93]	100	CNN	Cross Entropy	4000	SGD	TensorFlow	Training: 80% Testing: 20%	Accuracy: 99.7%
9	Barros et al., 2020 [88]	302	CNN	Not Specified	Not Specified	Not Specified	Not Specified	Training: 268 Validation: 34	Dice Coefficient: 0.63

three well defined different deep learning architectures to find the best among them for hemorrhagic stroke detection [93]. LeNet, GoogLeNet and Inception- ResNet architectures were used to detect and spot the lesion region in the brain. It was concluded that LeNet based network yielded optimum results for hemorrhagic lesion detection. Patel et al. came up with an innovative method to combine the CNN and Recurrent Neural Network (RNN) as a bidirectional long short-term memory (LSTM) model for hemorrhagic lesion segmentation [94]. Slice level sequential information was used for classification by the LSTM model. Kuo et al. trained a patch-based FCN model [95]. Patch-based FCN does not only depend on the hyperdensity relative to brain features, but also the subtlest features.

Most of these methods utilized pre-trained architectures for classification. These pre-trained architectures were trained with millions of color images derived from different category of real world objects. When the knowledge is transferred from these architectures to handle medical imaging classification, the performance of these methods might be limited. Hence, these networks need to be re-trained from the scratch with a wide range of Stroke datasets to effectively detect and delineate the hemorrhagic lesion from brain images.

4.3. Hybrid methods for stroke detection

Certain hybrid deep learning networks have been employed to classify both ischemic and hemorrhagic stroke from unimodal and multimodal images. In the work presented by Pereira et al., they have made use of three different types of CT images for each brain lesion case. A CNN optimized by Particle Swarm Optimization (PSO) selects the best hyper-parameters that achieve the lowest value of loss function [96]. Another method based on CT images was presented by Marbun et al. for the detection of ischemic and hemorrhagic stroke [97]. Carlos et al. presented an exhaustive study with different deep architectures like InceptionV3, MobileNet and VGG16 and well-defined machine learning approaches like Random Forests, SVM, etc. [98]. The MobileNet architecture with a Bayesian classifier performed best and achieved an accuracy of 91.57%. The research work carried out by Xuea et al. used multimodal MRI images for the detection of ischemic and hemorrhagic stroke. A modified U-network was extended as a multi-modal, multi-path network. This architecture had a 3D convolutional kernel for post-processing. The images from the various sources were combined to take advantage of a larger dataset [99].

4.4. Deep learning for penumbra core separation

Penumbra is the damaged tissue around the irreversibly injured ischemic core of the brain. Faster separation of the penumbra and the core helps to salvage the damaged penumbra as early as possible. However, in the majority of the cases, the penumbra is left untreated in patients due to various constraints [100]. Hence, it is important to detect the penumbra and core infarction region. Clèrigues et al. used CT images for detecting the infarct core using a 2D patch-based deep learning model [101]. Robben et al. also employed a deep learning architecture to predict core and penumbra regions of the brain from acute CTP scans. Each input is operated with convolutions and up-sampled. The outputs of these pathways are then concatenated and fed into a common pathway that gives the voxel-wise prediction [102].

Liu et al. proposed a Multi-Kernel Deep Convolutional Neural Network (MK-DCNN) model that is based on the U-net architecture [103]. Multi- Sequence Network (MSNet) architecture was presented by Gupta et al. for the identification and segmentation of core and penumbra [104]. The work presented by Sathish et al. makes use of adversarial trained CNNs for semantic segmentation.

Table 4
Summary of different deep learning methods employed for penumbra core segmentation.

S. No	Ref	Image Modality	Datasets	Method	Loss function	No. Of epochs	Optimizer	Framework/ Library used	Validation system	Outcome
1	Clèrigues et al., 2019 [101]	CTP	156	FCN	Sum of Generalized Dice Loss (GDL) and Cross Entropy	30	Adadelta	Torch	5-fold cross validation: Training: 75 Validation: 19 Testing: 62	Dice Coefficient: 0.49
2	Robben et al., 2020 [102]	CTP	188	FCN	Weighted Cross Entropy	Not Specified	SGD with Nesterov momentum	Keras	5-fold cross validation	Dice Coefficient: 0.48 AUC: 0.54
3	Liu et al., 2019 [103]	MR Perfusion	50	FCN	Dice	60	ADAM	Not Specified	28 subjects for training and 36 for testing	Dice Coefficient: 0.57
4	Gupta et al., 2019 [104]	Multimodal MRI	50	FCN	Binary Cross Entropy	31	Adam	Keras	Training: 80% Testing: 20%	Dice Coefficient: For Penumbra: 0.82 For Core 0.73
5	Sathish et al., 2019 [105]	Multimodal MRI	50	CNN	Binary Cross Entropy	200	Adam	Not Specified	3-fold cross-validation Each fold, Training: 20 subjects Validation: 5 subjects Testing: 5 subjects	Dice Coefficient: For Penumbra: 0.69 For Core 0.68

The model makes use of unlabelled MRI data which is used by the discriminators to employ a relativistic visual Turing test. Here, the discriminator learns to identify the ground truth (GT) annotation for penumbra and core from the segmented map by minimizing the binary cross-entropy loss. The parameters are optimized so that the penumbra and the core can be visualized in finer detail. This method performed better than the MRI scan based methods proposed by Pereira et al., Liu et al. and Gupta et al. for penumbra and core lesion detection. It reported a dice score of 0.82 for lesion detection in the penumbra region and 0.73 for the core region. [105]. The summary of the different works reviewed as part of penumbra and core segmentation are highlighted in Table 4.

The application of deep learning methods to analyse penumbral and infarct tissues is in the early stage. A lot of analysis is further required to extensively evaluate these models and incorporate suitable architectural enhancements to study the characteristics of these brain tissues. Most of the existing deep architectures utilize single scale features for segmentation. If features are extracted in multiple scales, it can support effective feature learning. This can enhance the prediction process robust and ensures that any gain from additional context manifests decisively towards the outcome.

4.5. Deep learning methods for stroke prognosis

The prognosis of brain stroke depends on various factors like severity of the stroke, the age of the patient, the location of the infarct and other clinical findings related to the stroke. However, accurate prediction of the stroke patient's condition is necessary to comprehend the course of the disease and to assess the level of improvement. This will aid the doctors and physicians to provide better treatment and adopt appropriate patient management techniques. The use of deep learning models in the prognosis of stroke can greatly benefit the current approach to stroke treatment. Yu et al. presented a U-net architecture that aimed at predicting the final shape of the lesion [85]. Another extension of U-net architecture was proposed by Lucas et al where a 3D U-net with a Convolutional auto-encoder was used. The Convolutional auto-encoder learns core and penumbra shapes in the training phase and passes this information as input to the U-net. This network forecasted the form of the final lesion from core and penumbra segmentations [106]. Feng et al. mentioned how predicting stroke prognosis can be done by deep learning models using radiographical images as input. [107]. Cheon et al. presented a DNN model that used Principal Component Analysis (PCA) to extract relevant features to predict stroke prognosis. This technique completely discarded the need for manual segmentation of features [108]. In the work proposed by Hilbert et al. the requirement of having to manually annotate the data was removed as they utilized a Residual Neural Network (ResNet) and adapted it with Structured Receptive Field Neural Networks (RFNN) [109]. However, these models do not perform as efficient as CNN architectures on small sample sizes. Choi et al. presented a shallow CNN network combined with a logistic regression model to perform prognosis of stroke [110]. It was found that deep CNN models were better at retaining spatial information and performed with more accurate results. Nielsen et al. proposed a deep CNN architecture based on SegNet and measured the predictive performance of the network. This architecture performed best at stroke prognosis with an Area Under the Curve (AUC) of 0.88±0.12 [74].

5. Discussion

A comprehensive study has been carried out in this work by examining various deep learning approaches applied to different imaging modalities. To the best of our knowledge, this is the first report, presenting the modality-wise deep learning approaches employed exclusively for stroke lesion detection.

5.1. Dataset description

In this section, the description of different datasets used in the aforementioned research papers has been briefly presented. Most of the researches reported above has worked with limited datasets acquired from restricted clinical sources/hospitals. Few researches have utilized the benchmark datasets. The details of the benchmark datasets employed for stroke detection are presented in Table 5.

5.2. Evaluation metrics for lesion segmentation

There are different evaluation metrics used to measure the performance of the deep learning algorithms implemented for the segmentation process. The most widely metrics include Dice Coefficient (DC), Average Symmetric Surface Distance (ASSD), Hausdorff Distance (HD), and Intersection over Union (IoU).

5.2.1. Dice Coefficient (DC)

The overlapping volume between two segmentations is measured using DSC. DSC is sensitive to the lesion size [62]. The relation for DC is presented in Eq. (1).

$$DSC = \frac{2|A \cap B|}{|A| + |B|} \tag{1}$$

where,

A' and 'B' denote the voxel sets for segmentation and ground truth respectively.

5.2.2. Average Symmetric Surface Distance (ASSD)

The ASSD determines the average deviation among the volumes surface points averaged over both directions. Let 'A' and 'B' denotes the two sets of surface points. The relation for ASSD is presented in Eq. (2).

$$ASSD\ (A_S,\ B_S) = \frac{ASD(A_S,\ B_S) +\ ASD(B_S,\ A_S)}{2} \tag{2}$$

where,

$$ASD\ (A_S,\ B_S) = \frac{\sum_{a\in A_S} min_{b\in B_S}\ d(a,b)}{|A_S|}$$

A_S and B_S denote the voxels of segmentation and ground truth respectively.

$d(.)$ denote the Euclidean distance

5.2.3. Hausdorff Distance (HD)

The HD metric yields the maximum distance between two volumes of surface points and hence indicates the outliers obtained as part of segmentation. The relation for HD is presented in Eq. (3).

$$HD\ (A_S,\ B_S) = \max \left\{max\ _{a\in A_S}\ min_{b\in B_S}\ \mathrm{d}(\mathrm{a,b}),\ max\ _{b\in B_S}\ min_{a\in A_S}\ d(b,a)\right\} \tag{3}$$

where,

$d(.)$ denote the Euclidean distance

5.2.4. Intersection over Union (IoU)

IOU or Jaccard Index is determined as the area of overlap between the segmented(predicted) region and the actual ground truth, divided by the area of union between the predicted region and ground truth. The relation for IOU is presented in Eq. (4).

$$\mathrm{IoU} = \frac{\mathrm{A \cap B}}{\mathrm{A \cup B}} \tag{4}$$

where,

'A' and 'B' denote the voxel sets for segmentation and ground truth respectively.

Table 5
List of benchmarked databases for brain stroke detection and segmentation.

S. No	Source	Modality	Description	No. of datasets	Link
1.	ISLES 2015 – SISS [111]	FLAIR, T2w TSE,T1w TFE/TSE, DWI	Sub-acute ischemic stroke lesion segmentation	Training: 28 Testing: 36	http://www.isles-challenge.org/ISLES2015/
2.	ISLES 2015 – SPES	T1c, T2, DWI, CBF, CBV, TTP, Tmax	Acute stroke outcome/penumbra estimation	Training: 30 Testing: 20	http://www.isles-challenge.org/ISLES2015/
3.	ISLES 2016	ADC, MTT, Tmax, TTP, rBV, rBF	Lesion outcome and clinical outcome prediction	Training: 35 Testing: 40	http://www.isles-challenge.org/ISLES2016/
4.	ISLES 2017	DWI, ADC, CBV, CBF, MTT, TTP, TMAX	Prediction of lesion outcome	Training: 43 Testing: 32	http://www.isles-challenge.org/ISLES2017/
5.	ISLES 2018	DWI, CBF, MTT, CBV, TMAX, CTP	Segmentation of acute stroke lesions	Training: 63 Testing: 40	http://www.isles-challenge.org/
6.	ATLAS - Anatomical Tracings of Lesions After Stroke [112]	T1-weighed MRI	Segmentation of stroke lesions	Total: 304	http://fcon_1000.projects.nitrc.org/indi/retro/atlas.html

5.3. Challenges and future trends

There are many challenges involved in stroke lesion imaging and analysis. A few of these challenges have been discussed in this section.

5.3.1. Availability of benchmark datasets

There is a lack of publically available datasets for stroke lesion analysis and only a very few among these datasets are labeled. Most of the researches reviewed in this study employ less than 100 datasets. Also, the annotation of the data is another major challenge in stroke lesion detection. This is an expensive and tedious process, as it requires support from trained radiologists. Another major issue in stroke lesion segmentation is the class imbalance problem. This imbalance occurs both in voxel level and slice level i.e. the ratio of lesion pixels to non-lesion pixels is evenly distributed to train the deep learning model. The data is usually skewed towards the normal and non-stroke related images. Though few works employ GAN based models to augment the data for handling the class imbalance problem, it can be addressed by extending these datasets by collecting and organizing samples from multi-center clinical sources.

5.3.2. Implementation aspects of deep learning models

Due to the limited availability of datasets, few approaches apply a transfer learning approach to train the model. Though the results are promising, the underlying architecture is developed for handling real-time generic color images. Hence, there arises a strong need to train the deep learning model from scratch to exclusively handle medical imaging data. Also, the selection of proper hyper-parameters plays a vital role in getting good accuracy of the trained network.

Overfitting is another major effect of training the deep learning model with minimum datasets. Though few works apply data augmentation and create new samples, the discriminative power of the trained network can be further improved by applying patch-based training extracted from multiple views. The training period of the deep learning models is another parameter to be properly examined. The performance of the trained network needs to be analyzed after each epoch to avoid overfitting. This can be addressed by employing measures like batch normalization of input data, early stopping, etc.

5.3.3. Computed aided systems for assessing the prognosis of stroke

Though several deep learning-based CAD systems have been developed to diagnose stroke, only a few researches have been reported to assess the prognosis. Hence, the strength of deep learning models has to be exploited further to develop solutions, which will help the physicians to assess the level of improvement in the treatment procedures. Deep reinforcement learning-based methods can be explored to develop CAD systems for predicting the level of improvement in the treatment process.

5.3.4. Future trends

Despite all the advancements made in deep learning for stroke diagnosis, there exists a great demand for research work to be carried out in the areas of intraoperative management and the effect of anticoagulation. All these procedures were carried out as restricted clinical trials. Hence, deep learning models can greatly support these problems to gain significant insights. The data used in stroke detection is usually insufficient for training on deep learning models. Hence, synthetic data generation using Generative Adversarial Network's (GANs) have been employed to overcome this challenge. These GANs are reported to generate CT images from MRI images [113]. Hence, this supports multimodal analysis of the data without going for different physical data acquisition procedures. It also minimizes the effect of ionizing radiation and contrast agents, as data can be simulated from another modality.

Many deep learning approaches were reported for detection, classification and segmentation of ischemic and hemorrhagic stroke. But there exists a vital need to develop deep regression algorithms in the assessment of the modified Ranking Scale (mRS) for stroke. This will help the physicians to decide appropriate treatment procedures based on the severity of the patients.

5.4. Limitations of this Study

The following are some of the limitations of this study.

1 This review considered only manuscripts published in English. The research works presented in other languages were not included.
2 Many research databases were explored in a systematic method to find the research manuscripts that were reviewed here. The keywords used in the searching process were limited to a certain set of words. Hence, it may have neglected a few other relevant works that dealt with stroke detection based on deep learning approaches.
3 This study targets to provide an overall survey on the various imaging, processing, and analysis advancements in stroke lesion detection and characterization. Therefore, the transformation of the lesion before and after treatment is not given much significance in this review.

6. Conclusion

Deep learning models can never replace doctors and radiological experts. But it can make a huge impact on the automation process in image processing and analysis. Computer-aided techniques for analysis of medical images have grown significantly in recent times, contributing to medical research and clinical applications. Recent progress in deep learning has shown continuous optimization in the segmentation process of stroke lesion regions from the brain. This research aimed to observe the improvements and the growth of deep learning architectures in the detection and segmentation of stroke lesions over the past few years. Despite these advancements, there are still some limitations and thus scope for more improvements as well. This pattern of gradual enhancements in stroke lesion region segmentation can potentially become a scientific revolution, if the medical doctors and radiological experts also play a part in the conception and building of the framework for deep learning models.

Though Deep learning has yielded significant results in the medical domain, there exist remarkable research prospects in exploiting the above-discussed methods and deep architectures to solve complex image segmentation problems. Currently, the segmentation algorithms based on deep learning are limited by factors like overfitting due to data insufficiency, training time and resources, etc. If efficient methods are devised to overcome these limitations, deep learning can definitely create several breakthroughs in the field of biomedical image processing.

Declaration of Competing Interest

None.

Appendix-evaluation form for review

First level Questionnaire for Initial Screening

S. No	Question	Yes	No	Other (NR/CD)
1.	√ *Is this publication an original research paper that proposes a new deep learning method for stroke detection/segmentation?*			
2.	Are the objectives of this research clear and specific? √ Is the work completely focuses on the deep learning approach for stroke lesion detection/segmentation? √ Is there valid motivation for this research to be carried out? √ Is the methodology reported in this research is clearly discussed and explained? √ Are the observations made in this research show significant meaning and clarity? √ Are the numerical results presented in this research precise and clear?			

If the answer for question no: 2 is ‘no’, do not proceed to the further assessment

Second level scrutiny: Detailed Questionnaire for filtering based on datasets and methods

S. No	Question	Yes	No	Other (NR/CD)
1.	Research Methodology √ *Is there a clear ‘Related Works/Literature Survey’ section which clearly justifies the reason for adopting the proposed method?* √ *Are the modules clear and precisely defined?*			
2.	Dataset acquisition √ *Does the research present the details of the source from where the datasets were obtained/downloaded?* √ *Are the subjects considered are from a distinct population?* √ *Is the sample size clearly mentioned for this research?* √ *Are the details of the validation system presented clearly ?*			
3.	Development and performance analysis √ *Are the details of the deep learning methodology explained clearly with all preliminaries/fundamentals?* √ *Whether the specifications required to implement the deep learning method are clearly presented?* √ *Is the proposed deep learning method compared against the state of the art methods reported in their literature?* √ *Is the validation metrics applied for performance comparison in line with the problem definition?*			
4.	Key findings: √ *Do the researchers give enough justification for the claims against the problem statement?* √ *Are the limitations and constraints of this research clearly presented?* √ *Does this paper have a measurable conclusion?*			

Third level scrutiny: Detailed Questionnaire for deep learning methods based on architecture, design elements and validation

S. No	Question	Yes	No	Other (NR/CD)
1.	Type of Deep architecture involved √ *Is the proposed method involves CNN ?* √ *Is the proposed method involves FCN ?* √ *Is the proposed method involves a hybrid deep architecture ?*			
2.	Architectural Parameters and Design elements √ *Is the proposed method clearly present an layer wise architectural diagram ?* √ *Is the proposed method clearly list out the details of activation function applied on each convolutional/deconvolutional layer ?* √ *Is the proposed method clearly list out the details of filter dimensions ?*			
3.	Training and Validation √ *Is the proposed method clearly list out the batch size and the details of the implementation platform ?* √ *Is the proposed method clearly list out the hyper parameter details like?* ➢ *Learning rate* ➢ *No. of epochs trained* ➢ *Type of regularization function* ➢ *Type of optimization function* √ *Is the proposed method clearly list out the details of loss function applied for validation ?* √ *Is the proposed method clearly list out the performance metrics of the validated results ?*			

(NR: Not Reported and CD: Cannot Determine)

Final Decision: ☐ Accept ☐ Reject ☐ Seek Further details

Comments:

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