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A Review of MRI Acute Ischemic Stroke Lesion Segmentation

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Abstract: Immediate treatment of a stroke can minimize long-term effects and even help reduce death risk. In the ischemic stroke cases, there are two zones of injury which are ischemic core and ischemic penumbra zone. The ischemic penumbra indicates the part that is located around the infarct core that is at risk of developing a brain infarction. Recently, various segmentation methods of infarct lesion from the MRI input images were developed and these methods gave a high accuracy in the extraction and detection of the infarct core. However, only some limited works have been reported to isolate the penumbra tissues and infarct core separately. The challenges exist in ischemic core identification are traditional approach prone to error, time-consuming and tedious for medical expert which could delay the treatment. In this paper, we study and analyse the segmentation algorithms for brain MRI ischemic of different categories. The focus of the review is mainly on the segmentation algorithms of infarct core with penumbra and infarct core only. We highlight the advantages and limitations alongside the discussion of the capabilities of these segmentation algorithms and its key challenges. The paper also devised a generic structure for automated stroke lesion segmentation. The performance of these algorithms was investigated by comparing different parameters of the surveyed algorithms. In addition, a new structure of the segmentation process for segmentation of penumbra is proposed by considering the challenges remains. The best accuracy for segmentation of infarct core and penumbra tissues is 82.1% whereas 99.1% for segmentation infarct core only. Meanwhile, the shortest average computational time recorded was 3.42 seconds for segmenting 10 slices of MR images. This paper presents an inclusive analysis of the discussed papers based on different categories of the segmentation algorithm. The proposed structure is important to enable a more robust and accurate assessment in clinical practice. This could be an opportunity for the medical and engineering sector to work together in designing a complete end-to-end automatic framework in detecting stroke lesion and penumbra.

Keywords: Segmentation algorithms, acute ischemic stroke lesion, brain magnetic resonance imaging, pre-processing

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1. Introduction

Stroke ranks in the top five primary reasons of death in Malaysia after heart disease, pneumonia, transport accidents, and malignant neoplasm of trachea, bronchus & lungs [1]. In Malaysia, two-thirds of the reported stroke cases were ischemic origin which gives 87% of all stroke cases [1] – [8]. A stroke normally happened as soon as the blood supply to an area of the brain is discontinued, commonly burst in a blood vessel (hemorrhagic stroke) or blocked by a clot (ischemic stroke). An ischemic stroke happens when the movement of blood to the brain is interrupted, certainly by the blockage of an artery [9]. While hemorrhagic stroke occurs when arteries inside the brain rupture or burst and cause the blood to spill into or around the healthy brain tissues. Sometimes it is also caused by uncontrolled high blood pressure and aneurysms that make blood vessels weak enough to burst [9].

With the advancement of imaging technology, neuroimaging became a standard clinical diagnosis of acute stroke and plays a crucial role in assessing patients with suspected stroke and Transient Ischemic Attack (TIA), basically done before the starting of a treatment. The primary objective of imaging of a patient with a suspected stroke is to distinguish between hemorrhage and ischemic stroke [10]. The first step in the diagnosis of acute stroke is to exclude the stroke imitators and recognition of manifestations of acute stroke [11].

The goal of this review paper is to review variously the automated and semi-automated segmentation techniques for penumbra tissues as well as stroke infarct core and the potential of multimodal Magnetic Resonance Images (MRI) for acute stroke assessment and will be explained in the next section. Moreover, the paper strives to describe a generic structure which is devised from 23 published stroke segmentation papers. The detailed of the pre-processing and segmentation techniques of the acute ischemic stroke segmentation will be explained elaborately. In addition, we will compare the performances of the stroke segmentation based on structural MR images and present the data in Table 1 which includes the evaluation of segmentation of the infarct core and penumbra tissues as well. Finally, we will critically discuss a detailed explanation of the literature and proposed a new structure of the segmentation process by considering the challenges remains for segmentation of penumbra to enable a more robust and accurate assessment in clinical practice.

2. MRI As a Potential Diagnostic Modality

Availability of wide options of neuroimaging technologies facilitates the assessment of lesion and brain tissue status. Neuroimaging procedures such as Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) are the top choices in imaging of acute stroke. These neuroimaging techniques offers an objective evaluation for the medical interpretations that assist in patient administration [12].

In an acute stroke assessment, the standard diagnosis of MRI sequences is DWI, PWI, T2-weighted, FLAIR and MRA [13], [14]. For the patient presenting the symptoms of acute ischemic stroke, there are two MR protocols that can be done [15]: (1) a instant stroke protocol that requires roughly 6 minutes to acquire [16] and (2) a routine stroke protocol that requires about 20-25 minutes of acquisition. The routine stroke MR imaging protocol requires an acquisition time of up to 20 minutes and another 25 minutes for the radiologist's interpretation. This time duration agrees with the FDA's recommendation of 45 minutes for a single patient which are candidates for endovascular therapy [17] – [19].

Sequence-specific MR imaging can be useful in dating ischemic stroke [20]. In a hyperacute phase of ischemic stroke (0-24 h), DWI is sensitive to detect the ischemic changes within minutes of onset and displays the high signal intensity of images [21]. The T1-weighted sequence usually displays the low signal intensity of the stroke region after 16 hours of stroke onset and isointensity during <16 hours. T2-weighted shows high signal intensity after 8 hours of stroke onset. The evolving imaging technology of MRI has been chosen as it is sensitive in classifying strokes from early hyperacute to a chronic stage. The combination of radiological images with the accurate image processing techniques gives the advantage to quantify the changes in the properties of these tissues and characterize it [22].

3. Generic Brain Ischemic Stroke Segmentation Process Flow

Recently, the advancement of neuroimaging has received attention of most scientists and engineers. With the development of user interface and software based on the image processing field, it allows the experts to ease the diagnostic and identify the abnormal parts in the human brain. There have been various methods to delineate the ischemic core from the brain image, but fewer works have been reported to segment the ischemic core and penumbra tissues simultaneously. Therefore, we propose a generic structure for a brain ischemic stroke segmentation of lesion core and penumbra tissues from MRI. This generic structure is devised from the existing segmentation works as reported in the literature. A robust segmentation system should be able to isolate the region of interest (ROI) from brain images effectively, together with the size, location, and extent of the lesion and penumbra tissues.

In this paper, several approaches were discussed for segmenting the lesion from MRI brain images. The approaches include region growing, contour-based, thresholding and even hybrid-based method. One of the challenges that was addressed was most of these methods were successfully segment the infarct core but did not focus on isolating the penumbra and infarct core separately [23] – [28]. Figure 1 illustrates generic brain image segmentation process flow. In general, raw medical images (MRI) are collected from the public database for processing. These raw images are not suitable for analysis and processing due to the presence of a various type of noise and artifact. Thus, suitable pre-processing techniques are essential to improve the quality of the image for segmentation. Raw MR images normally contain various artifacts such as brain skull, fat, and intensity inhomogeneity. MR image volumes are acquired one slice at a time thus image registration is necessary to align or register two or more images so that common and different features overlap are detected and visible for ease segmentation process [29].

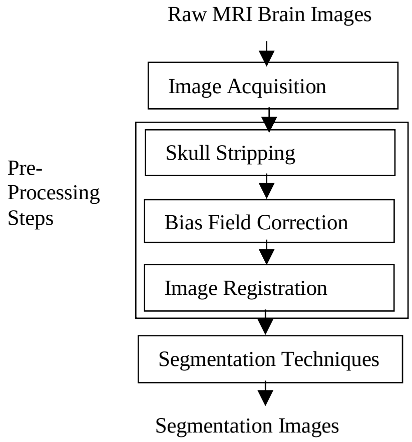

Fig. 1 - Generic Brain Images Segmentation Process Flow

4. Image Acquisition and Pre-Processing

Image acquisition is a procedure for obtaining medical images from imaging modalities. MRI modalities sequences such as DWI, PWI, T1-weighted, T2-weighted, and FLAIR have been used extensively. The magnetic field used for the sequences MRI is measured by a field strength of 1.5 T to 3.0 T. Brain MRI dataset can be obtained in public and private databases or even at medical centers.

Meanwhile, image pre-processing is a process of improving and enhancing the quality of raw images obtained from the scanner. Pre-processing steps in segmentation techniques are crucial to eliminate the unwanted tissues and enhance the image quality by eliminating the noise and correct the intensity inhomogeneity. Some of the pre-processing operations include skull stripping, bias field correction, filtering, registration, and image intensity adjustment and enhancement.

Skull stripping is the operation to remove the skull tissues from the brain image and obtained only brain tissues only before proceeding to the segmentation. The skull stripping procedure is a significant process as the forefront to acquire better segmentation results for accurate diagnosis [30]. The related works on segmentation of acute ischemic stroke that performed skull stripping are presented in [23], [26], and [31].

Bias field signal or intensity inhomogeneity (IIH) is a smooth and low-frequency signal that degrades the quality of MR images during the imperfections of image acquisition process. This signal will distort the produced images and therefore reduces the high-frequency content of the image such as contours and edges of different intensity gradient of image pixels. As this signal is a slow variant, bias field is barely distinguishable to a human viewer and many medical image analysis approaches, such as segmentation and registration are vastly sensitive to the false dissimilarities of image intensities [32], and [33]. Thus, intensity inhomogeneity correction is needed to correct the intensities variation in producing an accurate segmentation result. The related work on segmentation of acute ischemic stroke that performed intensity inhomogeneity is presented in [34].

On the other hand, image registration of MR imaging is an approach to align two or more images from different multimodal of MRI. The ability to precisely register multimodal image is vital to distinguish the differences and identify the abnormalities displayed on the images. Image registration is an important step in which respected information delivered in more than one modality of MRI [35]. The further image registration works in acute ischemic stroke are presented in [24], [26].

5. Image Segmentation

Image segmentation is one of the significant tasks in medical image analysis and it is frequently to be the primary step in most of the clinical applications. Image segmentation is the process of dividing an image into a region with similar attributes. The attributes can either be the texture, grey level value, brightness, contrast, shape, volume, and color [36] – [39]. Various image segmentation techniques are available for medical image analysis. The type of segmentation can be clustered into four different categories: region-based, contour-based, statistical based, and hybrid methods. Thresholding technique that will be discussed later is categories into statistical based.

5.1 Thresholding

Thresholding is also known as the simplest and fastest segmentation method and founded on changes in intensity levels in an image to delineate the region of interest (ROI). The procedure primarily uses the intensity histogram and to decide the intensity values called threshold T, which divides the desired classes. Segmentation is attained by categorize all the pixels value greater than the threshold into one class and the remaining into another class. A further description about thresholding technique are available at [40] – [43].

In medical images, this method is applied to differentiate different tissue regions based on intensity values [44]. There are certain disadvantages of thresholding method. For example, the global thresholding technique of only two classes are generated and do not consider the spatial features of an image therefore it is influenced to noise and intensity inhomogeneity of MRI images [45], [46].

Karthik et al. [31] developed a technique to identify ischemic stroke region by utilizing Otsu's thresholding segmentation. This technique segments the image using a bi-modal histogram, which will differentiate the foreground and background pixels. Meanwhile, Saad et al. [47] have proposed an adaptive thresholding procedure to automatically distinguish and threshold the lesions in diffusion-weighted images of stroke. Gradient function is used to adaptively calculate the optimal thresholding values.

5.2 Region Growing

Region-based segmentation is a method that segments the image into a various ROI which comprises of clusters of pixels or voxels with comparable characteristics [48]. This approach starts with setting a "seed" point and the regions grow by adding to individual seed of those neighboring pixels that have similar characteristics to the seed (specific ranges of intensity or color) [38]. The seed point can be manually designated by a person or automatically initialized with a seed finding algorithm [48].

Region growing methods performed adequately when segmenting organs, such as lungs or bony structures, that have well-defined boundaries and suitable for the segmentation of volumetric images which are comprise of large connected homogeneous regions [45], [49]. Therefore, makes it effectively segment different tissue regions or lesions of a brain from MRI images. The problem existed in the region growing techniques is the sensitivity to the initialization of seed point. Hence, the outcome of the segmentation result can be entirely diverse if selected the different seed point [45]. Region growing has less noise sensitivity, but it can cause a hole in the segmented shape or could result in a disconnected area [49], [50]. These problems can be overcome by using a hemitropic region growing algorithm [51].

Aboudi et al. [52] applied both regions growing and SFCM segmentation algorithms on DWI and PWI datasets. The region growing method performs well with respect to noise. Meanwhile, a fully automated brain lesion segmentation using region growing method is proposed by Saad et al. [53] by merging the homogenous regions according to the selected criteria. The statistical features are being used as criteria such as mean, standard deviation, and entropy.

5.3 Contour-based Method

Contour-based methods normally use the edge detection techniques for segmenting images based on rapid (local) changes of intensity value [38]. While edge detection is a method based on marking of discontinuities in grey level and often these edges represent boundaries between regions [54]. Such discontinuities are noticed by by means of first and second order derivatives [38]. Contour-based methods are also known as deformable models that are substantially driven for delineating region boundaries using closed parametric curves or deform surface under the effect of two forces called internal and external [55]. The review on deformable models' approach in medical image segmentation are available in the research paper [55] – [58].

In medical image segmentation, deformable models can directly produce closed parametric curves or surfaces from images and their integration of a smoother restraint that provide robustness to noise and spurious edge [55]. In addition, this method can be employed on a continuum and accomplish sub pixels accuracy, a exceedingly necessary attribute for medical imaging applications. Furthermore, the active contour technique is more flexible and can be applied for complex segmentations [57].

Feng et al. [59] introduced a technique for segmenting acute ischemic laceration in multi modality images (DWI, T1-w, T2-w, and FLAIR) using intensity inhomogeneity correction embedded FCM and three phase level set segmentation technique with the capability of dealing with intensity inhomogeneity. Haeck et al. [60] also presented a fully automated lesion segmentation using Expectation Maximization-approach to estimate intensity models for normal and lesion tissue and signify the boundary between these regions. Meanwhile, Charoensuk et al. [61] proposed segmentation infarct areas in DW images by employing Chan-Vese active contour and localized region-based active contour algorithms. The segmented areas from this algorithm that possessed these three conditions which are intensity, connectivity and magnitude are considered as an infarct.

5.4 Hybrid Method

The main limitations of the conventional segmentation such as region growing segmentation techniques are inadequate to segment the minor lesions and have less stability [62], [63]. Thus, a normalized graph cut segmentation technique is introduced to segment the stroke affected region to overcome this limitation [62]. In a work by Khadem [64], the min-cut/max-flow algorithm of graph cut image segmentation is applied in segmenting MRI brain image. Edge and boundaries detection and histogram thresholding were applied to segment the brain images before applying the graph cut algorithm to differentiate the grey matter, white matter, and cerebrospinal fluid.

6. Discussion and Recommendations

In this review, we have carried out a complete search to classify the image processing method in segmenting the ischemic stroke lesion in human and animal data from MRI brain images. We have identified 23 papers of segmentation algorithm. 17 papers were focused on segmentation of infarct core region while 6 papers proposed on segmentation of infarct core and penumbra regions. All these papers were based on the analysis of several methods applied for segmentation of infarct core & penumbra region of the ischemic stroke disease and the performance evaluation of the reviewed techniques.

Table 1 demonstrates a comparison of the various segmentation methods of acute ischemic stroke based on structural MR imaging. For the dataset used on all these studies, all of them employed the human brain as an image source and only one study used animal brain as its image source. For the segmentation methods, we have divided the of methods implemented into five different bases which are region-based, statistical-based, data clustering, contour-based followed by the hybrid-based method. On the other hand, for the performance column, we have included result parameters such as accuracy, dice coefficient, specificity, sensitivity, computational time and other parameters from the published works.

6.1 Comparison of acute ischemic stroke segmentation methods based on MRI

The studies that were done on acute ischemic stroke segmentation approaches based on MR imaging potentially can be a benchmark to the development of a more robust and complete stroke detection systems. The development of these algorithms could serve as a second opinion for the medical experts in decision making and improve diagnostic accuracy.

From Table 1, 12 papers from all segmentation papers discussed were using DWI as the dataset modalities, 6 papers were using MRI which include T1-weighted, T2-weighted, and FLAIR sequence whereas 5 papers were using a combination of DWI and MRI. A few of these datasets were obtained from the hospital; datasets from General Hospital of Kuala Lumpur for research conducted by [47], [65], [66]. All these datasets for segmenting core and penumbra were using DWI and PWI sequence [23] – [28]. The proposed algorithms [25], [27], [28], [53], [69], [70] listed in Table 1 have produced a segmentation outcome within the allocated time recommended by FDA's stroke protocol. The goal of producing the automated segmentation is to reduce the time taken of the radiologist's interpretation for a single patient. The shortest time of segmentation of ischemic acute stroke was recorded by Khadem [64] with the average computational time of 3.42 seconds for segmenting 10 slices of MR images followed by Ghosh et al. [69] with the computational time less than 15 seconds for one slice of MR image sequence. Meanwhile, a semi-automated method to quantify the perfusion/diffusion mismatch was proposed by Dwyer et al. [26] requires approximately 30-45 minutes of processing data and the entire process can run in a shorter duration if the processing pipeline can be run in parallel. The time taken for this method is longer than FDA's stroke protocol recommendation [17] – [19]. The interpretation of different modalities of MR imaging for a single patient is time-consuming. Thus, image fusion of different MRI modalities is necessary to reduce the time taken for assessment of a single patient which will be further discussed in this section.

From all the studies done, the highest accuracy was 99.10% achieved by [71] and [52] followed by 98.76% [62] and 98.43% [31]. The higher the sensitivity value, the higher the percentage of positives region were correctly recognized as lesion tissues. The highest sensitivity was recorded as 0.9719 [62] followed by 0.9410 [47] and 0.8935 by [64]. The specificity values indicate that the proportion of negatives region that was correctly identified by the algorithm. The highest specificity was accomplished as 0.9930 by [23] followed by 0.9828 [62] and 0.9700 by [69]. The highest accuracy reading in segmenting stroke lesion in brain MRI by the watershed algorithm is due to its effectiveness to combine elements from both discontinuity and similarity-based [70], [71]. The best sensitivity performance is by using the hybrid-based method because this method was able to analyze the figure of the inner boundary region of the small lesions [62]. The hybrid-based method is best applied to segment a hyperacute ischemic stroke. The statistical-based method gives the highest specificity value as this method is based on statistical analysis and arithmetic operation of images making the algorithm fast and computationally efficient.

Table 1 - Performance Comparison of The Acute Ischemic Stroke Segmentation Method

Overview of the segmentation methods of infarct core and penumbra. In the "Data" column, two acronyms are used: (n,h/a): n:number of patients, h:human data, a:animal data. The "A" column is automation of the system, F: Fully automatic, S: Semi-automatic. Next column is "Seg." is for segmented area either infarct core (C) and the penumbra (P). In the "Result Parameter" column, **T**: Computational Time, **DC**: Dice Coefficient, **JS**: Jaccard Score, **CR**: correlation coefficient, **FPR**: False positive rate, **FNR**: false negative rate, **TPR**: true positive rate, **NPV**: negative predictive value, **PPV**: positive predictive value, **AO**: Area Overlap, **ACC**: Accuracy, **SD**: Standard Deviation, **SI**: Similarity Index.

Studies	Data	Modalities	Basic method principle	A	Seg.	Result Parameter
[69]	(2, h) (4, a)	T2-w MRI for Animal, DWI for Human patients	Symmetry-Integrated Region Growing (SIRG), Hierarchical Region Splitting (HRS), Modified Watershed Segmentation (MWS)	**F**	C	**TPR**: SIRG = 0.8800, HRS = 0.8800, MWS = 0.7000. **TNR**: SIRG = 0.9700, HRS = 0.9500, MWS = 0.9700. **SI** : SIRG = 1.34, HRS = 1.31, MWS = 0.98. **T** : SIRG & MWS = <5 minutes, HRS = 15 seconds
[53]	(23, h)	DWI	Splitting and Merging for region detection	**F**	C	**ACC =** 70.89 %, **TPR** = 0.7855, **TNR** = 0.9234, **FPR** = 0.0766, **FNR** = 0.2145
[72]	(28, h)	T1-w, T2-w, DWI and FLAIR	Histogram-based thresholding and random forest	**F**	C	**DC =** 0.67**, RECALL =** 0.71
[23]	(10, h)	DWI, PWI	Hierarchical Region Splitting (HRS)	**F**	C P	**ACC**= 82.10 %, **TPR** = 0.788, **TNR** = 0.993.
[31]	(45, h)	T2-weighted	Otsu's thresholding segmentation	**F**	C	**ACC** = 98.43%.
[47]	(75, h)	DWI	Adaptive Thresholding	**F**	C	**TPR** = 0.9410, **TNR** = 0.8580, **FPR** = 0.1420, **FNR** = 0.0590, **JS** = 0.799.
[65]	(19, h)	DWI	Thresholding with Gamma-law transformation and contrast stretching	**F**	C	**TPR** = 0.8200, **TNR** = 0.8600, **FPR** = 0.1400, **FNR** = 0.1800, **AO** = 0.6800.
[24]	(14, h)	DWI, PWI	Generalized Linear Model Algorithms (GLM) and Thresholding	**F**	C P	GLM: **TPR** = 0.6600, **TNR** = 0.8400. Thresholding: **TPR** = 0.6600, **TNR** = 0.8300.
[73]	(10, h)	DWI	Gaussian Mixture Model (GMM) and Binary Morphological post-processing	**F**	C	**DC** = 0.85 ± 0.08, **JS** = 0.76 ± 0.07, **CR** = 0.86 ± 0.08.
[34]	(13, h)	T1-W, T1-G, T2-W, FLAIR	Gaussian Mixture Model (GMM) and Expectation-Maximization (EM)	**F**	C	**DC** = 0.51.
[25]	(30, h)	T1c, T2, DWI, PWI	Modified Random Forest algorithm	**F**	C P	**DC** = 0.82, **SD** = 0.08, **T** = 6 minutes.
[26]	(5, h)	T2, FLAIR, DWI, PWI	Hidden Markov Random Fields	**S**	C P	**T** = 30-45 mins to produce output. **Mean absolute error** = 34.2%.
[27]	(11, h)	DWI, PWI	Thresholding and Morphological Filtering	**S**	C P	**T** = <15 mins per patient data set.
[52]	(5, h)	DWI, PWI	Spatial FCM (SFCM) Clustering Algorithm and Region Growing	**F**	C	**SFCM: ACC** = 99.10%**, R.G: ACC =** 71.30%. **T** = 5 s
[66]	(50, h)	DWI	Fuzzy C-Means Clustering Segmentation	**F**	C	**DC** = 0.84, **JS** = 0.7, **FPR** = 0.049, **FNR** = 0.205. **Acute stroke: ACC** = 90%, **TPR** = 0.8438. **Chronic Stroke: ACC** = 75%, **TPR** = 0.8333.
[71]	(45, h)	MRI	Watershed Segmentation	**F**	C	**ACC** = 99.10 %.
[70]	(142, h)	DWI	Watershed Segmentation	**F**	C	**Random Forest (RF): ACC** = 96.00 %, **T** = 0.06s. **Multi layer Perceptron (MLP): ACC** = 85.00 %, **T** = 0.84s.
[59]	(58, h), (56, h)	MRI	Embedded FCM and Three Phase Level Set Method	**F**	C	**DC:** (Training Data Set), SPES = 0.82 ± 0.05, SISS = 0.63 ± 0.28. (Test Data Set), SPES = 0.76 ±0.09, SISS = 0.55 ± 0.30.
[60]	(58, h), (56, h)	MRI	Expectation Maximization (EM) and Level-set approach	**F**	C	**DC:** (Training Data Set), SPES = 0.78 ± 0.08, SISS = 0.53 ± 0.26. (Test Data Set), SPES = 0.67 ±0.24, SISS = 0.37 ± 0.33.
[28]	(10, h)	T1-w, T2-w, DWI, DSC PWI	Prediction using energy minimization function	**F**	C P	**T** = <1 minute. **DC :** Infarct = 0.13 ± 0.19, Penumbra = 0.61 ± 0.22.
[61]	(6, h)	DWI	Adopted Active Contour algorithms, global active Contour (Chan Vese), and localized region-based active contour	**F**	C	**TPR**= 0.8548 ± 0.0384, **PPV** = 0.8787 ± 0.0860, **DC** = 0.8511 ± 0.0475.
[62]	(45, h)	DWI, PWI, T2-w, FLAIR	Normalized Graph Cut	**F**	C	**TPR** = 0.9719, **TNR** = 0.9828, **PPV** = 0.9673, **NPV** = 0.9528, **ACC** = 98.76 %.
[64]	(10, h)	T1-w	Min-cut/max-flow	**F**	C	**T** = 3.42 s, **TPR =** 0.8935**, FPR =** 0.0331, **TNR =** 0.9401**, FNR =** 0.0307.

For an automated segmentation algorithm, 21 papers employed automatic segmentation while 2 papers employed semi-automated segmentation algorithm. Among all the 21 papers on automatic segmentation, only 4 papers addressed the limitation of segmentation of the penumbra tissues and the infarct core automatically in a distinctive way. The highest accuracy recorded for segmenting the infarct core and penumbra tissues that were recorded are 82.1% [23] by employing automated Hierarchical Region Splitting method. The drawback of current segmentation techniques is not only the segmentation algorithm of whole lesion structure but also the lack of focus on isolating the penumbral tissues from infarct core [22]. A supervised method proposed by James et al. [27] was compared against manually traced lesion by a neuroradiologist showed that the proposed method is consistent with the gold standard. In another published study, McKinley et al. [25] proposed a fully automatic technique for segmenting ischemic penumbra by applying Modified Random Forest algorithm. The algorithm was tested on SPES dataset and achieved an average Dice Coefficient (DC) of 0.82 in 6 minutes. Bauer et al. [28] employed energy minimization function approach to segment infarct core and penumbra in stroke patients and have produced dice coefficient of penumbra by 0.61. Wu et al. [24] developed a thresholding and generalized linear model (GLM) algorithm to predict tissue outcome of infarct core and penumbra tissues combining DWI and PWI datasets. The performance of two algorithms were compared and GLM algorithm showed higher specificity value.

6.2 Pre-Processing Approach

From Table 1, it is shown that conventional MRI combined with DWI and PWI has preferred imaging modalities in segmentation of infarct core and penumbra tissues. For image pre-processing, it shows that most of the existed work applied skull stripping, bias field correction, image normalization or image enhancement prior to the segmentation process to achieve acceptable accuracy. Our search for the existing published work for the segmentation of the acute ischemic stroke lesion have discovered several developed methods that applied pre-processing steps prior to segmentation [23], [24], [26], [31], [33]. Future acute ischemic stroke segmentation should aim to include a complete pre-processing pipeline to achieve higher accuracy of segmentation because each pre-processing step contributes to the success of segmentation of the region of interest.

6.3 Challenges Remain for Segmentation of Infarct Core and Penumbra Tissues

Medical image fusion has been used to acquire important information from modality medical image data. The benefit of image fusion is to reduce the time to diagnose multiple image modalities. Computational time is critical for decision making because “time is brain” [28]. The primary objective of image fusion is to merge all important visual information from multiple input images into a single new image contains a more accurate information without introducing any artifacts [74]. One advantage of fusion of two or more images of the same scene and modality which with blurred and noise can lead to a de-blurred and de-noised image. Existing works on image fusion related to lesion has been done by [23], [75], [76]. Related work in image fusion done by Vupputuri et al. [23] implemented an image fusion technique from various derived MRI volume (DWI and PWI) to estimate core and penumbra region. To detect ischemic injuries efficiently, different modality of MRI is needed to separate ischemic core and penumbra. Hernandez et al. [76] combined two MR sequences (T2*W and FLAIR) that produced different intensity range in the tissues to segment White matter lesion (WML). This combination has proven to differentiate WML and CSF in a brain image.

Meanwhile, a semi-automatic detection system which can identify stroke lesion was proposed by Mirajkar et al. [75] from image fusion of non-contrast CT and MRI. The fusion methodology of segmenting stroke region in two different multimodal images has proven to diagnose the anomalies in a short time and can possess a great potential in the future in developing a fully automated stroke detection in brain images. Image fusion techniques can be proposed to improve the segmentation algorithm as seen in a study done by Kabir et al. [77] for multimodal sequence data (T2-w, FLAIR, and DWI) which compared the segmentation performance obtained by single sequences with multiple sequences. Although most of the published works reported potential impacts on the success of the isolation of infarct core and penumbra tissues from the MRI, it still does not make the best use of all modalities of MRI and only applied one or two types of MR imaging. Thus, future works should attempt to integrate all the modalities of MRI to achieve more robust and accurate assessment in segmentation of infarct core and penumbra tissues for the clinical application.

All the discussed existing segmentation methods only segment MR brain images in a grayscale image which is also known as a monochromatic image. The grayscale image is comprised of many shades of gray, varying from black to white. The difficulty existed in the segmentation of brain lesion in the monochromatic image is that the lesions often belong to the similar intensities with the normal brain tissues. To overcome this problem, the color image segmentation was proposed as it produced more advantages and can deliver more details than monochromatic images. Nowadays, the applications of color images in computers are increasing rapidly. The color-converted and clustering segmentation algorithm is showing promising results for MRI applications in segmenting tumor in brain images [78] – [80] compared to the conventional image segmentation methods. The segmentation of brain tumor images in color-converted gives a result of 100% accuracy [78], and 95.10% recall [80]. The encouraging results in color-converted and data clustering segmentation could contribute in segmentation of acute ischemic stroke lesion.

6.4 Future Direction of Segmentation of Ischemic Core and Penumbra Tissues

The early promising results on the segmentation techniques of ischemic stroke and penumbra tissues could be valuable as providing second opinion in treatment choices for acute ischemic stroke. The limitation that currently exists in the development of robust algorithm is the availability of structural MRI dataset for acute ischemic stroke. Most of the published works employed private dataset which are difficult to obtain. Thus, the obstacles of data sharing can be resolved if the dataset providers can consider creating a repository that are accessible across the globe.

7. Conclusions

A different segmentation algorithm emphasis on the detection infarct core and the penumbra tissue of ischemic stroke were presented in this review. The presented algorithms were able to detect the presence of stroke lesion from a medical image. The computational time for processing and accuracy of the algorithm remains a challenge for researchers to develop a more robust algorithm. The best accuracy thus far is 82.1% for segmentation of infarct core and penumbra while 99.1% for segmenting infarct core only whereas the shortest average computational time recorded was 3.42 seconds for segmenting 10 slices of MR images. This paper presents an inclusive analysis of the discussed papers based on different categories of the segmentation algorithm. Moreover, the gap arises when all the state-of-the-art methodologies inadequately implemented in clinical practices. This could be an opportunity for the medical and engineering sector to work together in designing a complete end-to-end automatic framework in detecting stroke lesion and penumbra.

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