MedAppSci
Journal of Medicine and Applied Sciences

Original Article
J Med App Sci, 2022; 1(1): 1-11

Automatic Segmentation of Cerebral Infarct Tissue by Using Computed Tomography Perfusion Maps

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Received: *23 October 2021*
Revised: *10 February2021*
Accepted: *12 March 2021*

ABSTRACT

Computed tomography (CT) perfusion maps are dependent to conditions like patient age, blood pressure, vessel structure, and parameters like arterial input choice. Thresholds for stroke infarct and penumbra are well established in literature but they may sometimes lead to misdiagnosis. The aim of the study was to develop a full automatic reliable segmentation algorithm for infarct core by making use of cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) perfusion maps. We applied the presented method first to digital phantom data. After optimization of the algorithm in phantom data, final algorithm was tried on 21 real patient data retrospectively. The results from pathology-mimicked phantom data were compared with magnetic resonance (MR) diffusion weighted images of the mimicked patient images. The results showed that infarct segmentations were consistent with real pathology information. We compared our results with the results of a commercial neuro perfusion software on identical patient group. The results showed that infarct segmentations were consistent with a priori pathology information and commercial software results with including greater true positive (TP) and less false positives (FP) rates.

Keywords: stroke, segmentation, infarct, automatic, perfusion

INTRODUCTION

Acute ischemic stroke syndrome, with a narrow time window is one of the highest mortality ranked disease in the world (1). The narrow time window after the stroke is the crucial period when all hospital-ization, diagnosis and intervention should happen (2). Within this crucial period, time is critical to save more portions of the brain. Computed tomography perfusion (CTP) is the fastest and with final ad-vancements, becoming more commonly used diagnosis method for stroke, instead of magnetic reso-nance imaging (MRI). At the final stage of the diagnosis, region of interest (ROI) analysis on CTP maps and symmetry checks are routine part of this diagnostic process. Since the developed CTP maps are highly depended on patients' condition like age, blood pressure, vessel structure, and arterial input choice of the user or the algorithm itself, the most accepted thresholds, given in literature for stroke di-agnosis, may sometimes lead to misdiagnosis (3). Blood flow in gray, white regions of the brain are dif-ferent, and selecting a global threshold for both is a problematic assumption due to brains' perfusion na-ture (4). Strokes are usually grouped in two groups: 1) Ischemic stroke or infarct (due to lack of blood supply) and 2) Hemorrhagic stroke (due to rupture of blood vessel). Among these, ischemic stroke is predomi-nant stroke type with occupying 80 percent of all strokes. Seldom, both these types may co-occur. Accu-rate early diagnosis of hyper acute ischemic stroke is crucial since the time is limited to apply thrombo-lytic therapy. Development of smart segmentation algorithms help physicians to identify patients with acute stroke. They also try to guide through suitable treatment selection.

Brain parenchyma attenuation coefficients fluctuates from patient to patient due to the differing thickness

of the cranial bones. As the cranial bone gets denser, energy of the beam lowers, and attenua-tion is increased. The variations in detector stability, x-ray source, reconstruction deficiencies and CT number calibration fluctuations add noise to final image which in some cases may mask subtle hypo dense changes in ischemic region causing hard to detect situations for physicians.

Most of the CTP algorithms of the manufacturers allow users to adjust cerebral blood flow (CBF), cerebral blood volume (CBV) and mean transit time (MTT) maps' thresholds for acute stroke diagnosis. This manual user input has many benefits however; it demands deep knowledge and experience in CTP imaging (2). Manual thresholding and segmentation are time consuming, and mostly suffers from the lack of availability, reliability and reproducibility (5). The reliance upon subjective judgments, enhances the possibility of reaching different observers to different conclusions about the presence of lesions. This may cause same observer to reach different conclusions on different occasions (6, 7). Hence, an effec-tive automatic brain lesion segmentation algorithm is beneficial and desirable for clinicians.

It has been shown that in most of the cases the size of the perfusion deficit predicted by CTP corre-lates with the prognosis of patients (8). The first worth mentioning method for detecting automatically asymmetry regions was proposed by Wintermark et al. (9, 10). Matesin et al. proposed an automatic segmentation algorithm based on seeded region growing for segmenting stroke lesions in CT scans (11). Segmentation methods in CT images based on mean and standard deviation computations were pro-posed by Usinkas et al. and Meilunas et al (12, 13). Usinkas et al. improved their method by adding pix-el intensity-based analysis like histograms and gray level co-occurrence matrices (14). In order to identi-fy acute middle cerebral artery infarcts, Maldjian et al. used an atlas as anatomical reference for register-ing target vascular region whilst in the segmentation process with a manual input demand from the user (15). A clustering algorithm based on evaluating a feature map for each pixel by using root mean square values with a square neighborhood around a pixel was proposed by Ozertem et al (16). A mismatch al-gorithm which finds mismatch between CBF, CBV and time to peak (TTP) maps were presented by Hachaj (17, 18). Chawla et al. developed an automatic histogram and wavelet-based two-level classifi-cation method to determine acute and chronic ischemic lesions (19). Segmentation methods given above determines ischemic region of the infarct without focusing on the distinction between penumbra and core. This problem was raised and challenged by Contin et al. They focused on developing a new semi-automatic method built upon the idea of computing regional mean and standard deviations, which is blended with local statistics, identify penumbra and core separately (20). They pro-posed a semi-automated method for segmenting infarct region in ischemic stroke with a different ap-proach which mean and standard deviations was chosen as a criterion to select pixels from 8-connectivity. Among all these literatures given above, only Usinkas et al emphasized the most important disadvantage in current features extraction methods. The over segmentation problem which is a common disadvantage of most proposed methods can be eliminated by using an effective feature extraction and techniques (14).

There are several methods developed for lesion segmentation with MRI images (21-24). Diffusion weighted imaging technique in MRI perfusion studies is a well-established and accurate method but it is not configured to provide sufficient spatial resolution in an emergency situation to establish the edges of the ischemic lesion extremely accurately, though it is sufficient to provide an initial lesion atlas that can be retained in most cases as the final size of the ischemic stroke (25). A well literature survey can be found in Rekik et al for both modalities (26). Segmenting stroke lesions by using several machine learn-ing/deep learning algorithms is gaining importance and becoming a promising field in the stroke re-search. However, there are still challenges to overcome like gathering a decent patient database and structuring proper neural networks for training the deep learning algorithms. Several recent studies can be found in Kanchana and Menaka's review article (27). One of the pioneering studies among those re-cent ones is Rubin and his colleagues work. In this work they implement a similar approach as ours and use MR images as a ground to truth to train their deep learning algorithm to segment stroke legions on CTP images (28).

The objective of this study is to improve semi-automatic diagnostic process in acute stroke CTP. We developed a fully automatic stroke segmentation algorithm building on a previous study of one of our authors, which may help radiologists and neurologists (29). The developed stroke segmentation algo-rithm does not need any threshold inputs and also needs no user input. This study aims to contribute to the stroke diagnostic process.

METHODS

A. Experimental Setup Design

It was decided that the best method to adopt for this investigation was to start developing the seg-mentation algorithm on digital brain phantoms with

well-known pathologies. Stroke diagnosed 7 pa-tients' MRI diffusion weighted imaging (DWI) images were retrieved from digital image communica-tion systems (DICOM) database. Eligibility criteria for patient images to be included in this work was to have stroke diagnosis with a defined area. The demographic structure of this patient group was homog-enous all patients were above age of 56 with no other serious health problem before stroke diagnosis. All images were anonymized. Pathologies of this patient group are given in Table 1. These 7 patients' pa-thologies were introduced to a digital perfusion phantom called strokecreator developed by Aichart et al. in MATLAB (Mathworks Inc., Natick, Massachusetts, United States) environment (7). This digital phantom allows users via a graphical user interface to mimic real patient pathologies and develops CTP maps including these pathologies (Fig. 1). We developed 7 digital CTP phantoms and maps with stroke-creator by using these real 7 patients' MRI DWI images and pathology reports. The developed stroke segmentation algorithm is tried on these CTP maps obtained from strokecreator. We compared our in-farct segmentation results with MR DWI infarct images and pathology reports.

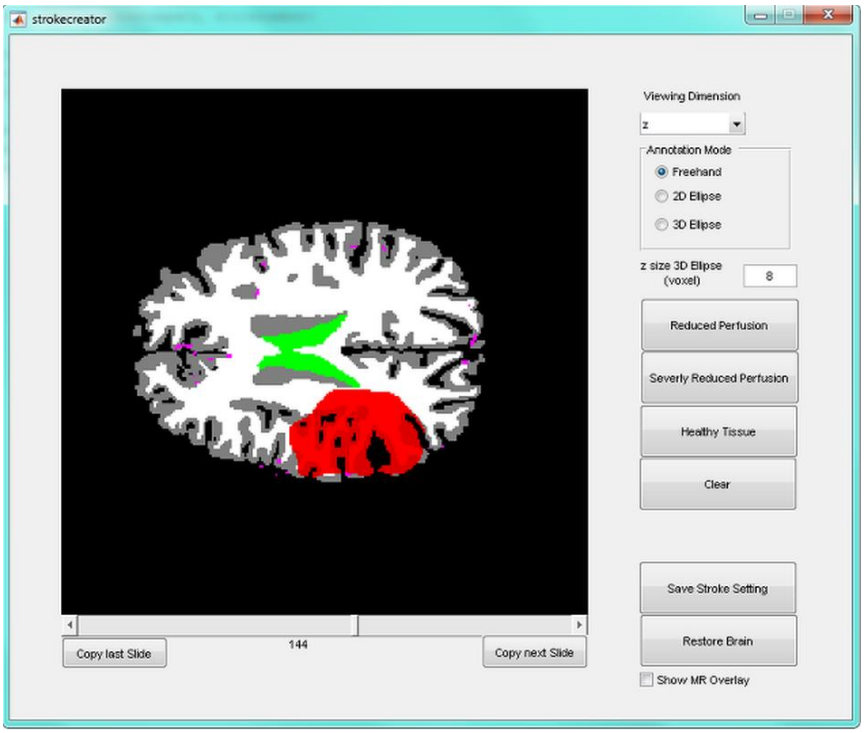

Figure 1. Stroke creator's graphical user interface. Example patient image contains infarct on left middle cerebral artery

Segmented images obtained from developed segmentation algorithm are analyzed regarding to true positive (TP), false positive (FP), true negative (TN) and false negative (FN) rates by comparing with MRI DWI pathologies. The comparison is based on their size and volumes.

Table 1. Anonymized patient group with infarct pathology

Anonymized Patient	Pathology
Patient 1	Infarct in left middle cerebral artery
Patient 2	Ischemia in middle cerebral artery
Patient 3	Infarct in right posterior cerebral artery
Patient 4	Infarct in left posterior and middle cerebral artery
Patient 5	Infarct in right posterior cerebral artery
Patient 6	Infarct in right posterior cerebral artery
Patient 7	Infarct in left posterior cerebral artery

In the second part of the study, stroke diagnosed 14 patient CTP studies are retrieved from our hospi-tals' DICOM database. This patient groups demographic structure is more heterogeneous than the MRI DWI patient group as the age range of the patients are large and some has serious health problems be-fore stroke diagnosis. In order to have a control in the patient group, a suspected but appears to be a normal (no stroke, no ischemia) case is also added to patient images. All images were anonymized. Pa-thologies of this patient group are given in Table 2. These 14 patient's CTP series are reprocessed with GE (General Electric, United States) Neuro Perfusion stroke software implemented in workstation, CTP maps are developed, and segmented with default threshold settings recommended by manufacturer. Segmentation results of GE Neuro Perfusion software

are used for cross checking with our segmenta-tion algorithm results.

Table 2. Anonymized patient group with infarct pathology

Anonymized Patient	Pathology
Patient 1	Acute ischemia in right front parietal
Patient 2	Ischemia in left frontal temporal
Patient 3	Acute ischemia in near left frontal horn
Patient 4	Ischemia in right frontal lobe
Patient 5	Infarct in left middle cerebral artery
Patient 6	Infarct in left middle cerebral artery
Patient 7	Infarct in postcentral gyrus
Patient 8	Infarct in left middle cerebral artery
Patient 9 (the control)	Normal, no pathology
Patient 10	Infarct in left posterior cerebral artery
Patient 11	Infarct in left posterior cerebral artery
Patient 12	Infarct in right frontal lobe
Patient 13	Infarct in left posterior cerebral artery
Patient 14	Ischemia in right temporo parieto occipital

The developed and refined stroke segmentation algorithm on digital phantom data is tried on these CTP maps obtained from GE Neuro Perfusion software. By using identical patient images, we want to make sure that the dependency of the results to perfusion maps is kept at minimum. This is a commonly used methodology in CTP studies (30).

Prior to commencing the study, ethical clearance was sought from our hospitals ethical committee and since it is a retrospective study on anonymized patient images, they concluded that there is no need for an ethical approval.

Both stroke segmented images obtained from GE's software and our algorithm are compared regarding to TP, FP, TN and FN rates for all patient images. It was concluded to evaluate the results upon having TP rates equal or greater than 25% and FP rates equal or less than 75% of the whole segmented regions and none FNs as a success criterion for developed segmentation algorithm. The control patient without a stroke is used for TN evaluation.

B. Stroke Segmentation Algorithm Design

CBF, CBV, and MTT maps are the most important maps among others like TTP and permeability maps. They carry fundamental perfusion information and derived from blood flow of the brain. CBF, CBV, and MTT maps are represented in the RGB (Red-Green-Blue) color system. The RGB color sys-tem is one of the most well-known color systems and it includes three color channels, namely red, green, and blue. It combines red, green, and blue light to create the colors. Our stroke segmentation algorithm processes these 3 RGB maps along with the CT images and evaluates image features of them.

At the first step of the developed algorithm, tissue regions are segmented from CT images by remov-ing all bone structures and background objects using thresholding and morphological operators, i.e. pix-els having positive RGB channel values at the CBF maps are marked as tissue and marked regions are morphologically closed by a disk shaped structuring element (5-neighborhood). Segmented tissue re-gions are marked as input on the CT images and corresponding perfusion maps for the succeeding steps. After this, a patient movement compensation step is included in order to have a proper symmetry check in the rest of the algorithm. Patient movement compensation must be done since some patients cannot be immobilized and, in some cases,, technologist forgot to immobilize the head of the patient. It is per-formed as follows:

- First, the middle, and the last images of the CT volume are rotated -15 to 15 degrees at every 1 de-gree. Rotated images are reflected along the y-axis.

- Since reflection of an image along the symmetry axis produces nearly the same image, cross correla-tion values between CT images and reflection of rotated CT images are calculated and used as the met-ric.

- The angle Θ that maximizes total cross correlation value is determined and all CT images and perfu-sion maps are rotated Θ degrees. Similarly, the column that has the greatest cross correlation value for the angle Θ is defined as symmetry axis of brain tissue.

This approach is also done in several studies in order to establish the exact axis of symmetry by Matesin et al and Usinkas et al (11, 14). Symmetrical abnormalities are possible but the number of these kind of cases are limited (30). Usually, the symmetry axis of the brain is not always the same line that separates the hemispheres, which makes the problem complicated. The symmetry axis is selected manually in manufacturers' commercial software.

At the third step, CBF, CBV, and MTT maps are decomposed to their red, green, and blue compo-nents in case of RGB images and combined CBF maps are acquired using the formula: (1)

$$X = \frac{\sqrt{\mu B^2 - B^2}}{R + G} \quad , \quad \text{if } (\mu B^2 - B^2) > 0$$

$$X = 0 \quad , \quad \text{if } (\mu B^2 - B^2) \leq 0$$

where X, R, G, B are values of combined CBF maps, red component, green component, and blue com-ponent of the corresponding pixel respectively and **μ**B is the mean blue component value of all CBF

maps in the volume. Since a good blood flow refers to higher red and/or green component value than blue component value and higher blue component value than the mean blue component value, greater X values represent the possible infarcts' location.

In order to smooth the combined CBF maps and even not to miss a single pixel with disease information, anisotropic diffusion filtering is applied to the combined CBF maps at the fourth step. Aniso-tropic diffusion filtering is preferred for its edge and line preserving capabilities while smoothing the image. We used 5 iterations for the anisotropic diffusion algorithm by choosing kappa 30, lambda 0.25 and we applied Perona-Malik equation 2 (32). Our choice of the parameters for anisotropic diffusion was made empirically based on (33). Just after, thresholding is applied to the smoothed maps. The pixels having greater values than the mean combined CBF value of the volume are thought as a part of possible infarct and marked as 1 (foreground) and the others are marked as 0 (background). Finally, at this step, connected component labelling is applied in order to mark the possible infarct regions separately.

In most of the acute stroke cases, only one hemisphere of the brain is affected (2). This nature of the disease led physicians to make a symmetry check of suspected stroke region by manually drawing ROIs and measure blood flow, volume and transit time of the suspected region of the effected hemisphere and the opposite healthy hemisphere. With building on this behavior of the physicians, at the fifth step, our algorithm automatically makes a symmetry check of every individual stroke suspected region deter-mined from the fourth step. Similar regions from both sides are detected using measures of area, dis-tance to the symmetry axis of brain tissue, and the mean combined CBF value of the regions. Detected regions are eliminated which means that they are the healthy parts, dissimilar regions are kept and la-beled as stroke suspected regions.

At the sixth step, a modified version of fuzzy segmentation by morphological reconstruction described in (34) is applied as defined below:

- Mean red component, green component, and blue component values of the region are calculated from CBF, CBV, and MTT maps separately.

- Distance maps are created using: (2)

$$dCBF = \sqrt{(\mu CBF_R - CBF_R)^2 + (\mu CBF_G - CBF_G)^2 + (\mu CBF_B - CBF_B)^2}$$

$$dCBV = \sqrt{(\mu CBV_R - CBV_R)^2 + (\mu CBV_G - CBV_G)^2 + (\mu CBV_B - CBV_B)^2}$$

$$dMTT = \sqrt{(\mu MTT_R - MTT_R)^2 + (\mu MTT_G - MTT_G)^2 + (\mu MTT_B - MTT_B)^2}$$

where d[MapName] represents distance maps, represents red, green, and blue com-ponents, represents mean values of red, green, and blue components of perfusion maps.

- For each of the stroke suspected regions:

i) Center point of the region is marked as the seed.

ii) A window of size 21 × 21 pixels centered at the seed is taken. Red, green, and blue components belong to those pixels from CBF, CBV, and MTT distance maps are read. The mean and the standard deviation of these values are calculated.

iii) For each of the 3 distance maps, fuzzy regions are reconstructed separately according to the fuzzy membership function, namely, not normalized Gaussian function, using the mean and the standard deviation parameters. The pixels in the window are used as seeds in this reconstruction process.

iv) Fuzzy regions are binarized using 0.5 as the threshold value.

v) Using the connected component labelling, regions those consist of foreground pixels, i.e. having values greater than 0.5are determined.

vi) Intersection of the resulting 3 fuzzy regions is accepted as final segmentation. In case of gray scale CBF, CBV, and MTT maps are used, only one component, gray component, is used in correspond-ing formulas.

The fixed threshold value and the size of the window we utilized here were determined and validated based on our experiments on the digital phantom data. At the final step of the algorithm, fuzzy recon-structed stroke labeled regions are checked and the regions those have continuity at least for 2 consecu-tive slices are accepted as final stroke regions and contoured on the CBF maps of all patients. All steps of the developed stroke segmentation algorithm are given in Fig. 2.

RESULTS

Examples from MR DWI images of the patients are given in Fig. 3. Patient 1, on the left top of Fig. 3, had a middle cerebral arterial (MCA) infarct on left hemisphere. Patient 3 had a massive infarct on pos-terior cerebral artery (PCA) on right hemisphere. Patient 6 had a relatively smaller infarct in PCA on right hemisphere. The final example, patient 7 also had a PCA infarct on right hemisphere. MR DWI images indicates pathologies well.

Stroke segmented images obtained from our segmentation algorithm are given in Fig. 4. The example patient images given in Fig. 4 are the images produced by strokecreator phantom data with mimicking the same pathology on the patients given in Fig. 3. As can be seen from Fig. 4, our stroke

segmentation algorithm segmented the infarct cores as good as MR DWI images. Boundaries of the infarct cores are sharper and well preserved in our results. At the start of the project, the main goal was to achieve correct infarct segmentation with TP rates equal and greater than 25%, FP rates equal and less than 75%, and having none FNs. These goals are achieved for this 7-patient group with 100% TP, none FPs, and none FNs. These goals are achieved for this 7-patient group without any FPs. Wintermark et al. stated that MR DWI is the gold standard for final infarct size (10). Our algorithm achieved to segment infarct cores as well as MR DWI images.

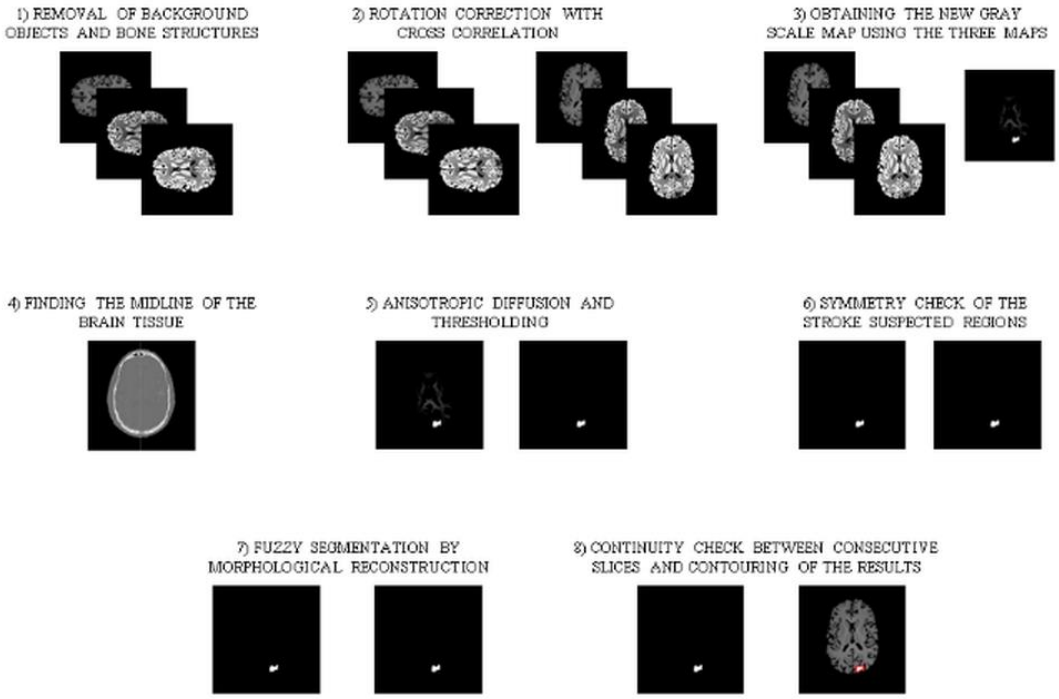

Figure 2. Stroke segmentation algorithm flow-chart, (1) result of background and bone structures removal, (2) result of patient movement compensation, (3) new grayscale map generation, (4) determination of midline (5) result of anisotropic diffusion filtering on the combined CBF map, (6) result of thresholding and symmetry check, (7) result of fuzzy segmentation by morphological reconstruction, (8) contouring of segmented infarct regions on CBF map

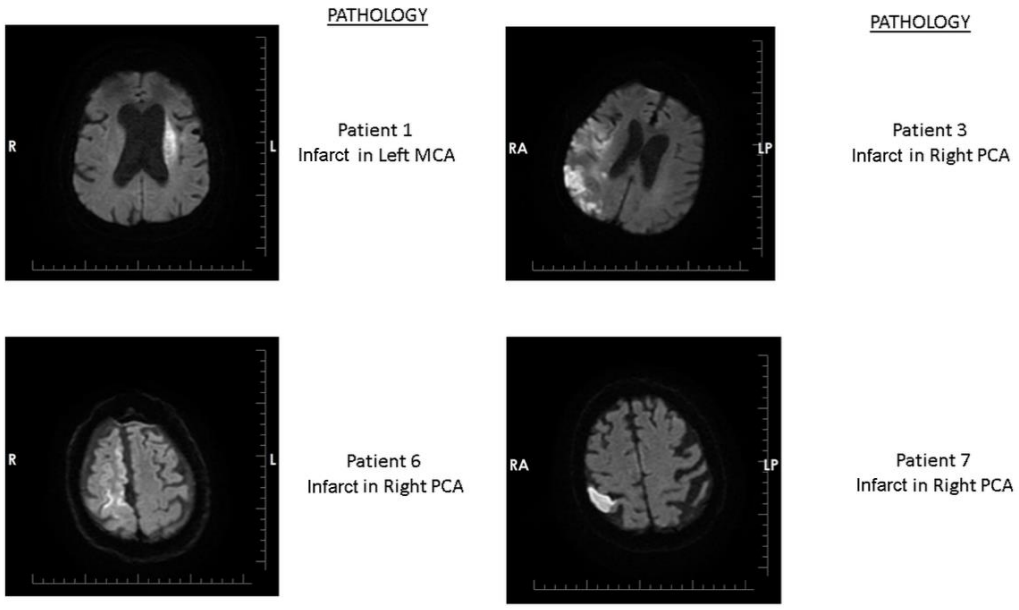

Figure 3. Examples of stroke indications in MR DWI images of the patients

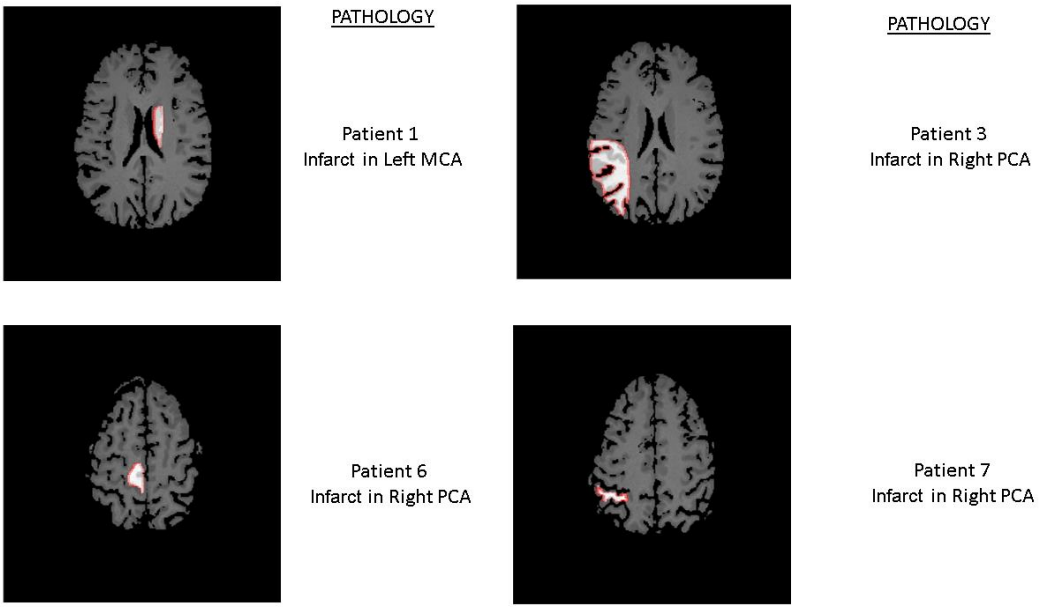

Figure 4. Stroke segmented images obtained developed stroke segmentation algorithm

Examples from the resultant stroke segmented images obtained from GE Neuro Perfusion software are given in Figure 5. Patient 5, on the left top of Fig. 5, had a middle cerebral arterial (MCA) infarct on left hemisphere. It appears that, GE's software segmented the infarct region well but with many FPs on the right hemisphere. Patient 13 had a massive infarct on PCA on left hemisphere and the segmented region is well super imposed with the pre-known pathology but like in Patient 5 image, it includes many FPs at all over the brain labeled in blue. Patient 9, who was the control patient without a pathology. As can be seen from Fig. 5, GE's software also labeled some regions, which are FPs in the PCA region. The final example, patient 11 had a PCA infarct which is well segmented, but the image also includes a lot of FPs labeled as red and blue. GE Neuro software uses red labels for infarct and blue for penumbra regions. These results are produced with recommended thresholds for both infarct and penumbra by GE's soft-ware and it suffers from FPs. In diagnostic process, in order to have accurate diagnosis, using these im-ages will force radiologists or neurologists to make symmetry ROI measurement checks. In some pe-numbra dominant cases they might need an MRI scan to support their diagnosis.

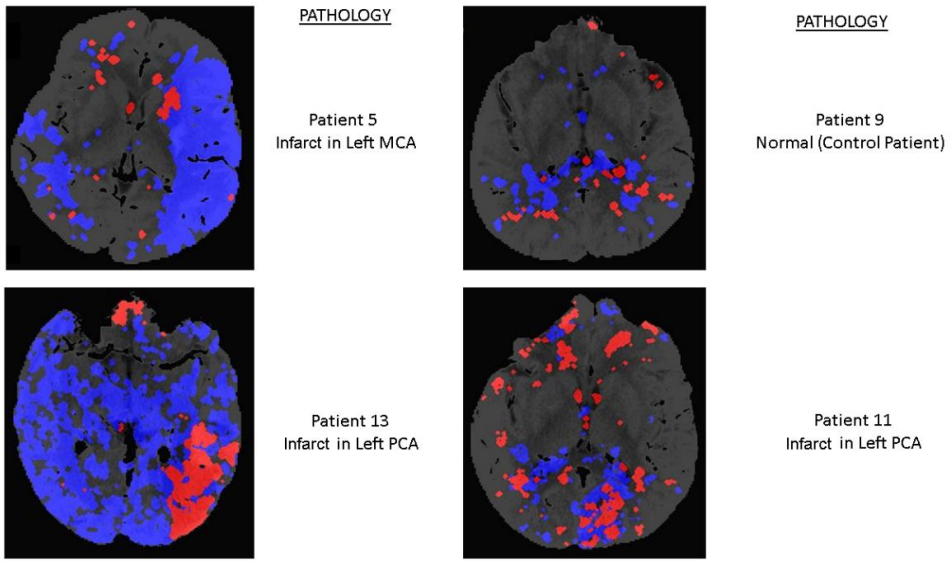

Figure 5. Stroke segmented images obtained from GE software

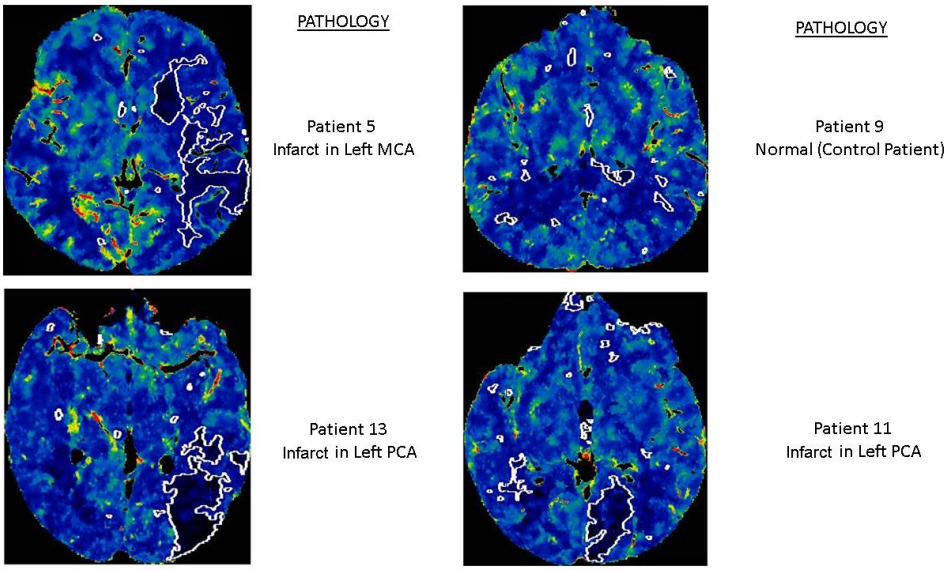

Figure 6. Stroke segmented images obtained developed stroke segmentation algorithm

Stroke segmented images obtained from our segmentation algorithm are given in Fig. 6. The example patient images given in Fig. 5 are the same patients given in Fig. 6. As can be seen from Fig. 6, our stroke segmentation algorithm segmented the infarct cores as good as GE Neuro Perfusion software with much less FPs. Our algorithm suffers from FPs like GE's software but with lower percentages per image. Hachaj et al. developed a neural network based automated algorithm which also produces FPs at a rate of 27% (17). In such kind of algorithms FPs are inevitable, and the goal is to lower the FP rate. In our results, boundaries of the infarct cores are sharper and well preserved. Patient 9, the control patients' image includes less FPs then GE Neuro software result. At the start of the study, the main goal was to achieve correct infarct segmentation with TP rates equal and greater than 25%, FP rates equal and less than 75%, and having none FNs. These goals are achieved for this 7-patient group with 100% TP, none FPs, and none FNs. These goals are achieved for this 14-patient group. Optimization of the algorithm is still an ongoing study.

In order to assess our results while comparing with the GE's commercial software, we counted all pix-els that are segmented as TP and FP by both algorithms and compared segmented volume, TP and FP rates. Result are given in Table 3.

DISCUSSION

Segmentation of acute ischemic stroke is a difficult task since perfusion maps are dependent to variety of parameters mentioned above. The semi-automatic segmentation algorithms as GE Neuro Perfusion suffers from manual threshold inputs and may sometimes enhance the workload of physicians during the diagnostic process. In stroke cases, where time is critical to save portions of the brain, it is not desired to lose time with ROI analyses and time-consuming MRI examinations.

In order to improve semi-automatic diagnostic process in acute stroke CTP, we proposed and imple-mented a fully automatic stroke segmentation algorithm. We assessed the results of the proposed algo-rithm and the results of GE Neuro Perfusion software on the same dataset.

One of the most interesting finding was that GE Neuro Perfusion software results show greater FP rates than our proposed algorithms results almost in all patients. Likewise, it also shows less TP rates when compared to our algorithms TP rates. As can be seen in Table 3, while GE Neuro Perfusion soft-ware has 13.44% TP and 86.56% FP, our proposed algorithms have 42.54% TP and 57.46% FP rates on the average. Segmented volumes differ for each algorithm since GE Neuro Perfusion software is a semi-automated software and demands user input for CBF, CBV and MTT threshold values. As mentioned earlier, these thresholds were chosen as GE's recommendations, which are coherent with the broad thresholds given in the literature (8-10). Since our proposed algorithm does not require any user input resultant segmented volumes differs from each other. For this reason, comparing TP and FP rates rather than segmented volumes makes sense when it comes to compare very different segmentation algorithms, which are aiming the same function: segmenting infarcted regions in the brain. Author believe this is one the strongest aspect of proposed algorithms and results are complying with this belief. Segmented vol-umes are given for just to give the readers an idea about both algorithms segmentation results.

Table 3. Segmentation results for both algorithms

Patient No	Segmented Volume									
	The Commercial Software (GE)					The Proposed Algorithm				
	Total (mm^3)	TP (mm^3)	FP (mm^3)	TP (%)	FP (%)	Total (mm^3)	TP (mm^3)	FP (mm^3)	TP (%)	FP (%)
Patient 1	352032.9	22759.9	329273.0	6.47	93.53	8074.6	1064.6	7010.0	13.18	86.82
Patient 2	346669.3	2818.3	343851.0	0.81	99.19	2203.1	56.0	2147.1	2.54	97.46
Patient 3	258567.2	55373.2	203194	21.41	78.58	5587.9	1679.4	3908.5	30.05	69.95
Patient 4	225382.4	22396.3	202986.1	9.94	90.06	40863.3	12365.3	28498.0	30.26	69.74
Patient 5	387071.2	265411.2	121660.0	68.57	31.43	121445.4	114585.6	6859.8	94.35	5.65
Patient 6	554481.4	103737.9	450743.5	18.71	81.29	118082.2	55105.1	62977.1	46.67	53.33
Patient 7	285355.3	1542.6	283812.7	0.54	99.46	34966.7	10736.8	24229.9	30.71	69.29
Patient 8	341700.3	30458.3	311242.4	8.94	91.06	39144.1	7699.1	31445.0	19.67	80.33
Patient 9	186042.7	0.0	186042.7	0.00	100.00	34680.6	0.0	34680.6	0.00	100.00
Patient 10	55275.6	730.8	54544.8	1.32	98.68	478.0	54.8	423.2	11.46	88.54
Patient 11	171792.5	7265.1	164527.4	4.23	95.77	57178.3	13502.6	43675.7	23.61	76.39
Patient 12	201686.6	5692.6	195994.0	2.82	97.18	29193.0	2515.5	26677.5	8.62	91.38
Patient 13	676568.2	22593.0	653975.2	3.34	96.66	115186.4	21417.5	93768.9	18.59	81.41
Patient 14	152450.5	22961.4	129489.1	15.06	84.94	50512.8	38982.0	11530.8	77.17	22.83
SUM	4195076.1	563740.6	3631335.9	13.44	86.56	657596.4	279764.3	377832.1	42.54	57.46
MEAN	299648.3	40267.2	259381.1	13.44	86.56	46971.2	19983.2	26988.0	42.54	57.46

In this study, we developed a novel algorithm for fully automated segmentation of stroke lesions from brain CT images and have shown its effectiveness for both simulated and real stroke lesions. The main methodology in these kinds of studies is to develop the algorithm on digital phantoms first and then verify the results with real patient data. Results are compared with MRI DWI images and patholo-gy reports of the patients. Preliminary results on this 7 patient group show that the proposed method segment accurate infarct regions with none FPs and FNs. In order to verify and test the developed fully automatic stroke segmentation algorithm, real patient data with known pathologies were also used at the second stage of the study. Results are compared with a commercially available segmentation algorithm, GE Neuro Soft. Preliminary results on this 14-patient group show that the proposed method has good performance with segmenting accurate infarct regions and having less FPs than a commercially available software. The present results are significant in at least major two respects.

This study has some limitations. First limitation can be regarded as the low number of patient data that is available during the study. It is difficult to gather this kind of a niche data since CT perfusion is not widely used in our country. We have ongoing negotiations with some institutions to gather more pa-tient data. The final limitation is the pathologies of the patient group. Some pathologies are well suited with the goals of the study, but some are not like patient 6 and 7. More refined and suitable patient data will be added to patient group while gathering new patient data. A user-friendly graphical user interface is being developed for the algorithm in order physicians to interact with the developed segmentation algorithm. One of the major pitfalls of the presented algorithm is its incapability of detecting hardly vis-ible lesions.

CONCLUSIONS

Authors proposed a novel algorithm for fully automated segmentation of stroke lesions from brain CT images to improve the current semi-automatic diagnostic process. They believe that standard segmenta-tion algorithm alone is not a challenge, the challenge lies behind producing an automated, reproducible and clinically accepted method which uses strict, true segmentation at the starting phase. A method which will work in case of abnormalities and which can be used for further processing like computing volume, growth prediction and treatment. All discussion reveal that ischemic stroke lesions are complex structures, including large variations, and which has a relative unpredictable nature in their spa-tial/temporal evaluations.

In future work, authors will focus on delineation of penumbra and infarct core with building upon this method since, to date; only a single study has addressed the problem in a given CT volume (20).

Conflict of Interest Disclosure

The authors declare no conflicts of interest.

References

1. Carandang R, Seshadri S, Beiser A, et al. Trends in incidence, lifetime risk, severity, and 30-day mortality of stroke over the past 50 years. JAMA 2006; 27:2936-2946.
2. Lee TY, Murphy B, Chen X, Miles KA. Image Processing. In: Miles KA, Eastwood JD, König M, ed. Multi detector computed tomography in cerebrovascular disease. 1st ed. London, 2007; 57-69.
3. Dani AK, Thomas RGR, Chappel FM, et al. Computed tomography and magnetic resonance perfu-sion imaging in ischemic stroke: definitions and thresholds. Arch Neurol 2011; 70:384-401.
4. Wintermark M, Flanders AE, Velthius B, et al. Perfusion –CT assessment of infarct core and penumbra receiver operating characteristics curve analysis in 130 patients suspected of acute hemispheric stroke. Stroke 2006; 37:979-985.
5. Shen S, Sandham W,Granat M, Sterr A. MRI fuzzy segmentation of brain tissue using neighborhood attraction with neural network optimization. IEEE Trans Inf Technol Biomed 2005; 9(3):459-467.
6. Kabir Y, Dojat M, Scherrer B, Forbes F, Garbay C. Multimodal MRI segmentation of ischemic stroke lesions. In: Proceedings of the 29th Annual International Conferenceof the IEEE Engineering in Medicine and Biology Society; 2007 Aug 22-26; Lyon France. IEEE Press;2007 p.1595-1598.
7. Fiez JA, Damasio H, Grabowski TJ. Lesion segmentation and manual warping to a reference brain: intra-and interobserver reliability. Hum Brain Mapp 2000; 9(4):192-211.
8. Alves JS, Carneiro A, Xavier J. Reliability of CT perfusion in the evaluation of the ischaemic penumbra. Neuroradiol J 2014; 27:91-95.
9. Wintermark M, Reichart M, Thiran JP, et al. Prognostic accuracy of cerebral blood flow measure-ment by perfusion computed tomography, at the time of emergency room admission, in acute stroke patients. Ann Neurol 2002; 51:417-432.
10. Wintermark M, Reichart M, Cuisenarie O, et al. Comparison of admission perfusion computed tomography and qualitative diffusion and perfusion weighted magnetic resonance imaging in acute stroke patients. Stroke 2002; 33:2025-2031.
11. Matesin M, Loncaric S, Petravic D. A rule based approach to stroke lesion analysis from CT brain images. In: Proceedings of the 2nd International Symposium on Image and Signal Processingng and Analysis; 2001 Jun 19-21; Pula Crotia. IEEE Press;2002 p.219-223.
12. Usinskas A., Pranckeviciene E., Wittenberg T., Hastreiter P., Tomandl B.F. Automatic Ischemic Stroke Segmentation Using Various Techniques. In: Rutkowski L., Kacprzyk J. (eds) Neural Networks and Soft Computing. Advances in Soft Computing 2003; vol 19. Physica, Heidelberg.
13. Meilunas M, Usinkas A, Kirvaitis R, Dobrovolskis R. Automatic contouring of segmented human brain ischemic stroke region on CT images. Mathematical Modelling and Analysis 2003; 8:43-50.
14. Usinkas A, Dobrovolskis R, Tomandl B. Ischemic stroke segmentation on ct images using joint features. Informatica 2004; 15:283-290.
15. Maldjian JA, Chalela J, Kasner SE, Liebeskind D, Detre JA. Automated CT segmentation and analysis for acute middle cerebral artery stroke. Am J Neuroradiol 2001; 22:1050-1055.
16. Ozertem U, Gruber A, Erdogmus D. Automatic brain image segmentation for evaluation of experimental ischemic stroke using gradient vector flow and kernel annealing. In: Proceedings of the IEEE International Joint Conference of on Neural Networks; 2007 Aug 12-17; Orlando, FL, USA. IEEE Press; 2007.
17. Hachaj T. An algorithm for detecting lesions in CBF And CBV perfusion maps. Bio-Algorithms and Med Systems 2008; 7:35-41.
18. Hachaj T. The unified algorithm for detection of potential lesions in dynamic perfusion maps cerebral blood flow, cerebral blood volume and time to peak. Journal of Medical Informatics & Technologies 2008; 12:117-122.
19. Chawla M, Sharma S, Sivaswamy J, Kishore L. A method for automatic detection and classification of stroke from brain CT images. In: Proceedings of IEEE Annual International Conference of the IEEE Engineering in Medicine and Biology Society; 2009 Sept 3-6; Minneapolis, MN, USA. IEEE Press;2009 p.3581-3584.
20. Contin L, Beer C, Bynevelt M, Wittsack H, Garrido G. Semi-automatic segmentation of core and penumbra regions in acute ischemic stroke: preliminary results. In: Proceedings of IWSSIP Inter-national Conference on Systems, Signals and Image Processing; 2010 Jun 17-19; Rio de Janerio, Brasil.p.178-181.
21. Stamatakis EA, Tyler LK. Identifying lesions on structural brain images validation of the method

and application to neuropsychological patients. Brain Lang 2005; 94:167-177.

22. Seghier ML, Ramlackhansingh A, Crinion J, Leff AP, Price CJ. Lesion identification using unified segmentation-normalisation models and fuzzy clustering. Neuroimage 2008; 41:1253-1266.

23. Li M, He H, Zheng Z, et al. Segmentation of infarct in acute ischemic stroke from MR apparent dif-fusion coefficient and traced-weighted images. In: Proceedings of 6th International Symposium on Multispectral Image Processing and Pattern Recognition; 2009 Oct 30; Yichang, China. SPIE Press.p.74971U:1-7.

24. Wilke M, de Haan B, Juenger H, Karnath HO. Manual, semi automated and automated delineation of chronic brain lesions: a comparison of methods. Neuroimage 2011; 56:2038-2046.

25. Wardlaw JM, Farral AJ, Perry D, et al. Factors influencing the detection of early signs of cerebral ischemia: an internet-based, international multiobserver study. Stroke 2007; 38:1250-1256.

26. Rekik I, Allassonniere S, Carpenter TK, Wardlaw JM. Medical image analysis methods in MR/CT-imaged acute-subacute ischemic stroke lesion: segmentation, prediction and insights into dyna-mic evolution simulation models. A critical appraisal. NeuroImage Clin 2012; 1:164-178.

27. Kanchana R, Menaka R. Computer reinforced analysis for ischemic stroke recognition: a review. Indian Journal of Science and Technology 2015; 8(35):1-9.

28. Rubin J., Abulnaga SM. CT-to-MR conditional generative adversarial networks for ischemic stroke lesion segmentation. Proceedings on IEEE Conference on Healthcare Informatics 2019.

29. Ozsavas EE, Telatar Z, Dirican B, Sager O, Beyzadeoglu M. Automatic segmentation of anatomical structures from CT scans of thorax for RTP. Comput Math Methods Med 2014; 1-14.

30. Ganesan V, Ng V, Chong WK, Kirkham FJ, Connelly A. Lesion volume, lesion location and outco-me after middle cerebral artery territory stroke. Archieves of Disease in Childhood 1999; 81:295-300.

31. Aichert A, Manhart MT, Navalpakkam BK, et al. A Realistic Digital Phantom for Perfusion C-arm CT Based on MRI Data. In: Proceedings of IEEE Nuclear Science Symposium and Medical Im-aging Conference; 2013, Oct 27-Nov 2; Seoul, South Korea. IEEE Press.

32. Perona P, Malik J. Scale-space and edge detection using anisotropic diffusion. IEEE Trans Pattern Anal Mach Intell 1990; 12:629-639.

33. Tsiotsios C, Petrou M. On the choice of the parameters for anisotropic diffusion in image processing. Pattern Recog 2013; 46:1369-1381.

34. Banik S, Rangayyan RM, Boag GS. Automatic segmentation of the ribs, the vertebral column, and the spinal canal in pediatric computed tomographic images. J Digit Imaging 2010; 23:301–322.