Detecting the Early Infarct Core on Non-Contrast CT Images with a Deep Learning Residual Network

Jiawei Pan,* Guoqing Wu,† Jinhua Yu,† Daoying Geng,* Jun Zhang,* and Yuanyuan Wang,†

Purpose: To explore a new approach mainly based on deep learning residual network (ResNet) to detect infarct cores on non-contrast CT images and improve the accuracy of acute ischemic stroke diagnosis. *Methods:* We continuously enrolled magnetic resonance diffusion weighted image (MR-DWI) confirmed first-episode ischemic stroke patients (onset time: less than 9 h) as well as some normal individuals in this study. They all underwent CT plain scan and MR-DWI scan with same scanning range, layer thickness (4 mm) and interlayer spacing (4 mm) (The time interval between two examinations: less than 4 h). Setting MR-DWI as gold standard of infarct core and using deep learning ResNet combined with a maximum a posteriori probability (MAP) model and a post-processing method to detect the infarct core on non-contrast CT images. After that, we use decision curve analysis (DCA) establishing models to analyze the value of this new method in clinical practice. *Results:* 116 ischemic stroke patients and 26 normal people were enrolled. 58 patients were allocated into training dataset and 58 were divided into testing dataset along with 26 normal samples. The identification accuracy of our ResNet based approach in detecting the infarct core on non-contrast CT is 75.9%. The DCA shows that this deep learning method is capable of improving the net benefit of ischemic stroke patients. *Conclusions:* Our deep learning residual network assisted with optimization methods is able to detect early infarct core on non-contrast CT images and has the potential to help physicians improve diagnostic accuracy in acute ischemic stroke patients.

Key Words: Deep learning residual network—Infarct core—non-contrast CT—Decision curve analysis—Acute ischemic stroke

Introduction

Ischemic stroke is a high incidence disease which seriously affects the quality of human life. Identifying the location and scope of the infarct core in a short time is crucial to the treatment and prognosis of the patient.[1,2] However, currently the applying of most examination methods are limited by the patient's compliance, contraindications, or the complexity and time consuming of the examination, which is difficult to be routinely applied, especially in the emergency department. The routine head non-contrast CT (ncCT) scan is the necessary examination for each suspicious ischemic stroke patient, but its value of detecting the acute infarct core is low because of the weak contrast between the early infarct tissue and the normal brain tissue which is far beyond the differentiate limit of the naked eye.[3] Due to the rapid development of the artificial intelligence, it is now possible for us to overcome this limitation.[4,5] Machines can accurately analyze every pixel, and differences between any two pixels can be found, which is unable to be identified by human eyes. Thus, in this study, we tried to use a deep learning residual network and two optimization methods to find out the recognition information of the acute infarct core on non-contrast CT images, which has the characteristic and important diagnostic value, and hope that this new approach could assist clinical practice in the near future.

From the *Department of Radiology, Huashan Hospital, Fudan University, Shanghai, China; and †Department of Electronic Engineering, Fudan University, Shanghai, China and Key Laboratory of Medical Imaging Computing and Computer Assisted Intervention of Shanghai, China.

Received November 16, 2020; revision received March 7, 2021; accepted March 8, 2021.

Correspondence authors. E-mail: fdhszj@yeah.net.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105752

Material and methods

Material

We continuously enrolled magnetic resonance diffusion weighted image (MR-DWI) confirmed acute ischemic stroke patients and normal people in this study. They all received both ncCT and MR-DWI scans with the same scanning range, layer thickness (4 mm) and interlayer spacing (4 mm). Criteria for inclusion: (1) Age : 18−80 years old, men and women are not limited. (2) First-episode ischemic stroke. (3) Onset time: within 9 hs. (4) The time interval between MR-DWI and CT scans: within 4 h. Exclusion criteria: (1) Pregnant women. (2) Recently participated in other clinical researches. (3) People with serious internal medical diseases. The study was approved by the ethics committee. The clinical information of the training and testing dataset are summarized in Table 1.

Method

Model building

As shown in Fig. 1, the proposed infarct detection method consists of training phase and testing phase. In the training phase, we build deep learning-based classification model for acute ischemic stroke infarct core identification. Specifically, firstly, the preprocessing including the skull stripping and registration is performed on both ncCT and DWI images. Secondly, different scales of image patches including 23*23, 19*19 and 17*17 (pixel*pixel) are extracted from lesion and health regions to construct training and testing samples. Thirdly, based on above samples, a deep learning residual network (ResNet) model is established to learn differences between positive and negative samples and complete the classification. Finally, morphological operation-based maximal connected region (MCR) selection and image filling are used to optimize the infarction identification results. In the testing phase, based on the established models in training phase, the final identification result can be obtained by performing four steps, i.e. pre-processing, patch classification, maximum a posteriori probability (MAP) identification and post-processing, corresponding to the training phase on the test image.

Image pre-processing

To discriminate between lesion and healthy region, DWI is needed to localize stroke on ncCT, namely image

Table 1. *The clinical information of the training and testing dataset.*

	Training dataset ($n = 58$)	Testing dataset		p (Training dataset vs Testing dataset-Patients)
		Patients ($n = 58$)	Normal people ($n = 26$)	
Age (yrs)	50 ± 11.2	52 ± 13.4	56.2 ± 10.4	0.38
Gender				
male (n)	30	25	13	0.59
female (n)	28	33	13	0.62
Onset Time (hours)	5.2 ± 2	5 ± 3	-	0.67
Main Complaint				
paralysis (n)	33	35	7	0.71
anesthesia (n)	15	12	5	0.51
aphasia (n)	12	10	2	0.64
headache (n)	12	15	10	0.51
dizzy (n)	24	20	15	0.44
Infarct Volume (ml)	16 ± 9	13 ± 8	-	0.06
Pathogenesis (TOAST classification)				
large-artery atherosclerosis	30	34	-	0.46
cardioembolism	8	6	-	0.57
small-vessel occlusion	20	17	-	0.55
stroke of other determined etiology	0	1	-	0.32
stroke of undetermined etiology	0	0	-	-
Infarct Location (anterior/posterior) (n/n)	55/3	54/4	-	0.70
Risk Factors				
hypertension (n)	12	14	7	0.73
diabetes (n)	10	10	6	1.00
coronary artery disease (n)	2	1	0	0.56
atrial fibrillation (n)	4	3	2	0.98
hemorrhagic stroke (n)	1	0	0	0.32
hypercolesterolemia (n)	7	8	1	0.78
obesity (BMI ≥ 27) (n)	2	2	0	1.00
smoking (n)	9	6	4	0.66
Baseline NIHSS Score	5.2 ± 4.4	5.3 ± 4.3	-	0.90
Thrombolysis	32	35	-	0.57

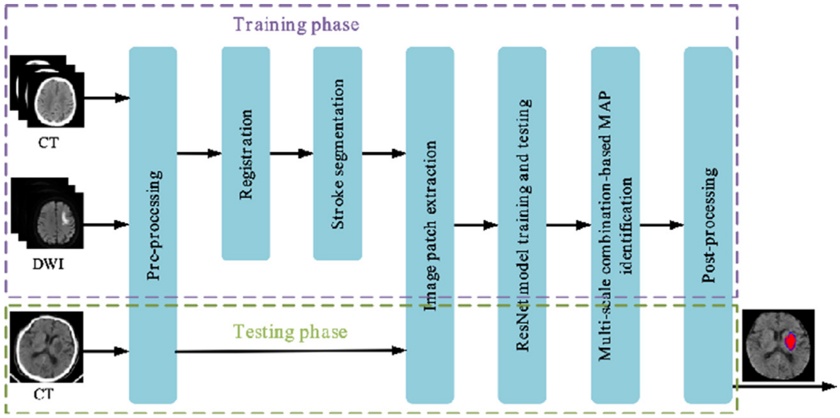

Figure 1. *The overall framework of the proposed method.*

pre-processing. Firstly, we utilized *spm12* to strip skull on both DWI and ncCT images since stroke will not happen in this area. After that, we geometrically transformed DWI to its associating ncCT template via rigid transformation including shift and rotation, followed by ellipse fitting to correct distortion. Fig. 2 shows the results of skull-stripping and registration. The first row shows the skull stripping ncCT, the skull stripping DWI and their overlapping. The second row shows registration results of the first row.

Deep learning -based image patch pair classification

The image patch pair classification consists of two steps. Firstly, we extract different scales of symmetric image patches from ncCT image. Secondly, we establish a residual network model for classifying theses image patches. Details of these steps are presented in the following two sub-sections.

▶ Image patches extraction

First we distribute the center voxels of target image patches in the ncCT image in a fixed distance. Then we locate the symmetric center voxels through the symmetry axis. Finally, we extract the symmetric image patch pair according to the symmetric center voxels. For image patch classification-based stroke identification, smaller patch contains fewer image information, which is not conducive to obtain high patch classification accuracy. While larger patch will lead to larger lesion localization error. Hence, according to,[21] we choose three patch scales, that is 23, 19, and 17, to

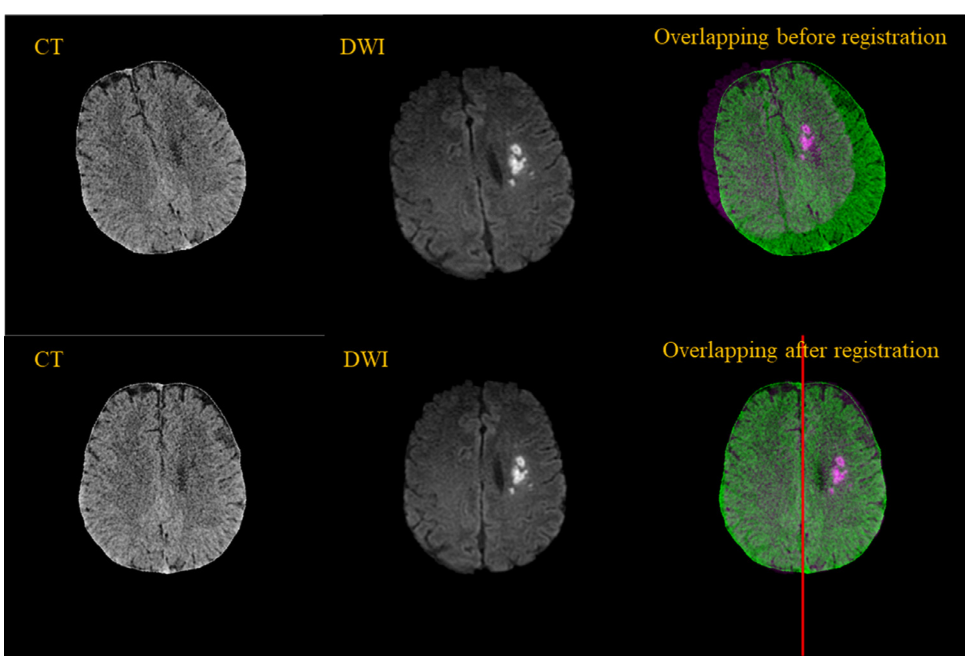

Figure 2. *The results of the image pre-process. The first row shows the skull stripping of ncCT and DWI without registration. The second row shows their registration results, respectively.*

better balance the accuracy of patch classification and lesion location. For the training dataset, we set the extracting stride of health regions to 9 pixels while lesion regions to 3 pixels to balance the number of positive and negative samples. Then we extract image patches of each patient at a patch size of 23*23, 19*19 and 17*17 (pixel*pixel), respectively. After that, we merge the extracted patches at each patch size. For the testing dataset, a similar process is performed except that the extracting strides are 3 pixels for both health and lesion regions.

▶ Residual network classification

The ResNet is a network model that not only exhibits lower training errors when the depth increases but also can easily enjoy accuracy gaining from the greatly increased depth. The concept 'shortcut connections' is used in the network. Shortcut connections means skipping one or more layers. They simply perform the identity mapping, and their outputs are added to outputs of stacked layers. By directly transferring the input information bypass to output and protecting the integrity of information, the whole network only needs to learn the difference between the input and output, which is exactly the residual to address the degradation problem by introducing a deep residual learning framework. Identity shortcut connections add neither extra parameters nor the computational complexity. Hence, in this paper, we use a ResNet with 18 layers to classify image patch pairs. Details of the network are provided in Appendix A. Three metrics, that is, the accuracy (ACC), the sensitivity (SENS) and the specificity (SPE) are calculated to assess the patch classification model.[19] The formulas of three metrics are provided in Appendix B.

Multi-scale combination-based MAP identification

Although the ResNet-based patch classification have good classification performance, there are also two shortages in the infarct region identification. On one hand, the neighborhood information between image patches that are important for stroke detection has not been used. On the other hand, it is difficult to determine the patch size in the ResNet-based patch classification. Hence, based on the ResNet-based symmetric patch classification, we built a multi-scale MAP model to integrate the patch classification results on different size and the neighborhood information between patches. For constructing the MAP model, we firstly take the sum of output results of three ResNet models as the likelihood probability. Then we define a spatial neighborhood constrain function as a prior probability. Because the neighborhood constrain function considers spatial dependencies between neighboring pixels in each scale simultaneously, multi-scale classification results can be effectively combined.

Decision Curve Analysis

Decision curve analysis (DCA) is a method introduced by Vickers and Elkin[14] in 2006 that can be used to assess benefits of a diagnostic test on patients. It is essentially a figure constructed by calculating the "net benefit (NB)—Y-axis" of one or more diagnostic tests across a range of "threshold probabilities (Pt)—X-axis". NB is the benefit gained after a patient accept one or a set of specific tests, Pt refers to the minimum probability of disease at which the diagnosis would be confirmed. The calculation formula between NB and Pt is presented in Fig. 10. The generation of DCA curve is to obtain net benefits through a series of threshold probability changes. Thus, for a particular Pt, the diagnostic method (single or combined) with the highest NB value is the best strategy. For more on the background to decision curve analysis, see.[22] DCA applies to situations where individuals have symptoms that indicate that they may be sick but have not been diagnosed, whether and what certain approaches should be used to help diagnose the disease.

By adopting the DCA in this study, we try to evaluate whether our ResNet-based method is able to help improve the benefit (offering a higher NB than currently used test methods across a range of threshold probabilities) while diagnosing stroke patients. We constructed three different combinations of test selection and used the decision curve analysis to plot and analyze the testing dataset. Diagnostic methods of the three combinations are: (1) the ResNet-based diagnostic method, (2) the traditional diagnostic method: symptoms (paralysis+anesthesia+aphasia) +CT report, and (3) combined method: the ResNet-based + the traditional.

The construction of the three combinations, the calculation of their NB at different threshold probabilities and the drawing of those curves are all realized in the R language software that contains a DCA programming package. During the process, logistic regression is used to construct models.

Results

Totally 116 acute ischemic stroke patients and 26 normal people were enrolled in this study from July 2015 to March 2018. 58 patients are allocated to the training dataset, and the rest 58 patients and 26 normal people are set to the testing dataset. There was no statistical difference in clinical data between patients in these two groups as shown in Table 1. We randomly selected 20000 samples (10000 positive and 10000 negative samples) for both the training classifier and validation. Note that, all training and validation samples are from the 58 training data. And the validation is used for the model's hyper-parametric tuning. The rest 58 patients and 26 normal people are used for testing. Table 2 shows results of different scales.

Table 2. *The results of three scales.*

	DSC	ACC	SENS	SPE
23*23	0.81	89.71%	88.17%	91.25%
19*19	0.77	87.46%	85.17%	89.75%
17*17	0.76	86.79%	85.91%	87.67%

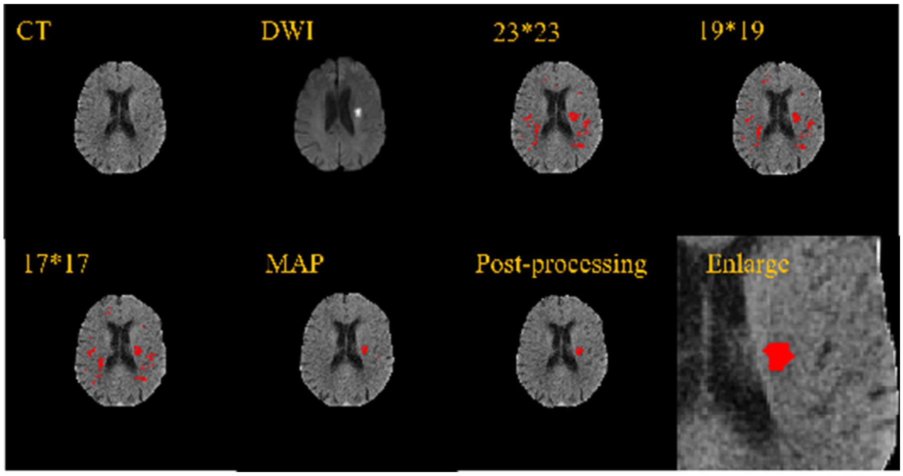

Figure 3. *The identification result for one subject. The red areas on 3rd to 5th sub-figures are detection results of three patch sizes. The 6th and 7th sub-figures shows the results after MAP and post-processing. The last sub-figure enlarges the final identification result, which is small but almost the same as ground truth on DWI.*

Fig. 3 and Fig. 4 illustrate detection results of two subjects. From top to bottom and left to right, eight sub-figures are the original ncCT image, DWI image, patch classification results on size of 23*23, 19*19 and 17*17, identification results of the MAP model, post-processing results and the enlarged identification region, respectively.

As shown in Fig. 5, according to the output of the softmax layer in the ResNet, we give the probability of the detected infarct area . In this way, doctors can set different thresholds of the probability to identify the stroke region adaptively.

Once the detected infarct cores are obtained, we use the Dice similarity coefficient (DSC) to evaluate detection results.[6] The DSC can measure the coincidence degree and the area difference of two regions. By comparing a large number of results, two radiologists agree that DSC of 0.6 is an appropriate value to determine whether the infarction area is identified or not. Finally, 44 subjects are correctly identified from the 58 subjects in the whole testing dataset, achieving an identification accuracy of 75.9%, furthermore, our method shows stable detection rate in different subgroups: anterior circulation vs posterior circulation (Table 3) and onset time more or less than 4.5 h (Table 4), which indicates its potential widespread application value in clinical practice. Fig. 6 shows the comparison between the identification results and the ground truth. Most strokes with a volume greater than 10 ml have been correctly detected (26/29), and these detected volume is close to the ground truth. The Spearman correlation coefficients for the lesion volumes by the proposed method and DWI lesion volumes is 0.5.

The decision curve analysis (DCA) is shown in Fig. 7, which is consisted of five curves. These five curves represent the net benefit rate of five different factors; when all subjects have no ischemic infarction, the benefit is 0 (represented by None, horizontal line); when all subjects are ischemic infarction, the benefit is represented by line All.

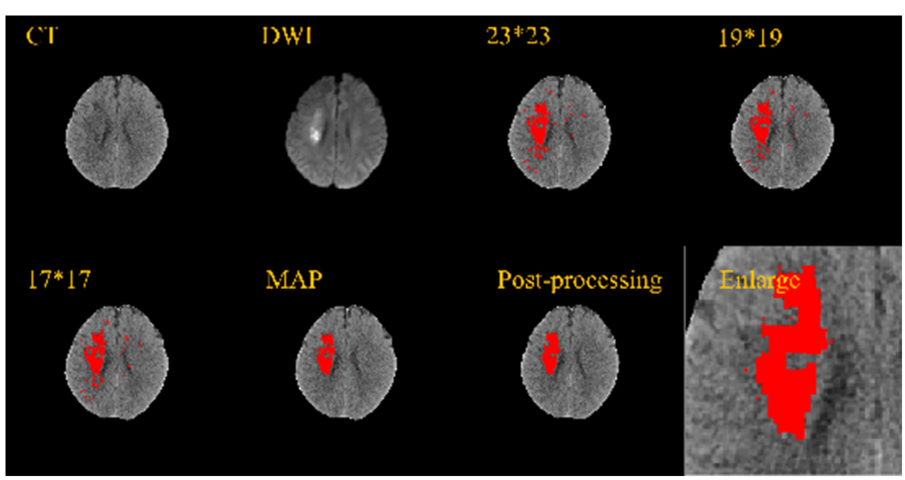

Figure 4. *The identification result for another subject. The red areas on 3rd to 5th sub-figures are detection results of three patch sizes. The 6th and 7th sub-figures shows the results after MAP and post-processing. The last sub-figure enlarges the final identification result, which almost overlaps the ground truth on DWI.*

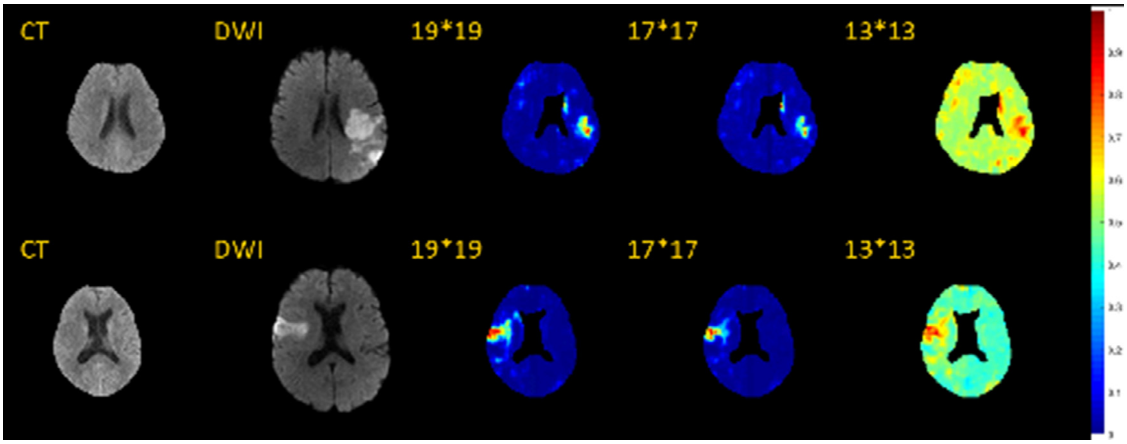

Figure 5. *The probability of infarct areas for two subjects of three patch sizes. The redder the area is, the more likely it is to be a stroke lesion.*

Table 3. *The detection rate of 58 patients in the testing dataset according to the location*

Location	Detected	Undetected	Detection Rate	*p* value
Anterior Circulation	39	15	72.22%	0.646
Posterior Circulation	3	1	75.00%	

Table 4. *The detection rate of 58 patients in the testing dataset according to the onset time (4.5 hours).*

Onset Time	Detected	Undetected	Detection Rate	*p* value
Less than 4.5 h	20	5	80.00%	0.522
More than 4.5 h	24	9	72.73%	

These two lines represent two extreme situations to define the threshold probability of the model and the range of net benefits. The red line represents our new method VS infarction, the green line represents the traditional diagnostic method VS infarction, and the blue line is the combination of these two.

Discussion

The non-contrast head CT scan has advantages of rapidity, safety, and convenience, and it has long been widely used as a routine emergency radiological examination.[7] However, the weak contrast between the infarct tissue and the normal brain tissue in the early stage and naked eye's low ability in detecting subtle differences limit the diagnostic value of ncCT in acute ischemic stroke patients. With the help of the AI, we can overcome this defect. It can not only recognize the image data available for the naked eye (form, quantity, distribution, size, intensity of grayness, etc.), but also analyze image features invisible to the naked eye, such as texture, intensity gradient and skewness.[8] The deep learning residual network is a convolutional neural network structure model proposed by He Kaiming in 2015. This method ranks first in the ImageNet Large Scale Visual Recognition Competition (ILSVRC) 2015 with 152-tier network model, which is far ahead of the second place in five data sets, including the image classification, recognition, location, detection and segmentation. The main advantage of the ResNet is that it can use a deeper network to solve the problem that the training error increases with the increase of network layers.[9]

Unlike previous studies reported on the stroke detection that have some weaknesses, including: 1) MR-DWI images were not always used as an independent gold standard. 2) Wide ranges of the onset time. 3) The long time interval between ncCT and MR scans. 4) Different scanning ranges, layer thickness and interlayer spacing, which lead to the poor lesion registration on the ncCT from the MR-DWI. 5) The number of subjects in many studies was small.[10–13] We not only used the MR-DWI as the gold standard of the infarct core, but also set two scans with the same scanning range, layer thickness (4 mm) and interlayer spacing (4 mm) to ensure that the location and scale of the infarct core on the ncCT image are consistent with that of the MR-DWI. At the same time, since the infarct core will change its range as the time goes by, we controlled every patient's two scanning interval time within 4 h. Those quality control methods can guarantee that the location and scope of the infarct core on ncCT images are real and reliable and so as the results that are carried out by those images processed with the ResNet.

From results of Fig. 3 and Fig. 4, we can see that all three patch-based classification models identify most regions of the lesion while over-identify some false positive regions. This is because the three models separately

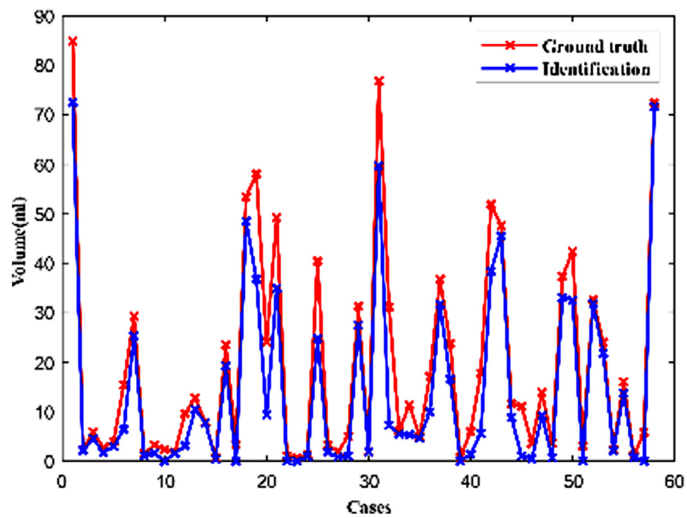

Figure 6. *Comparison between the identification results and the ground truth.*

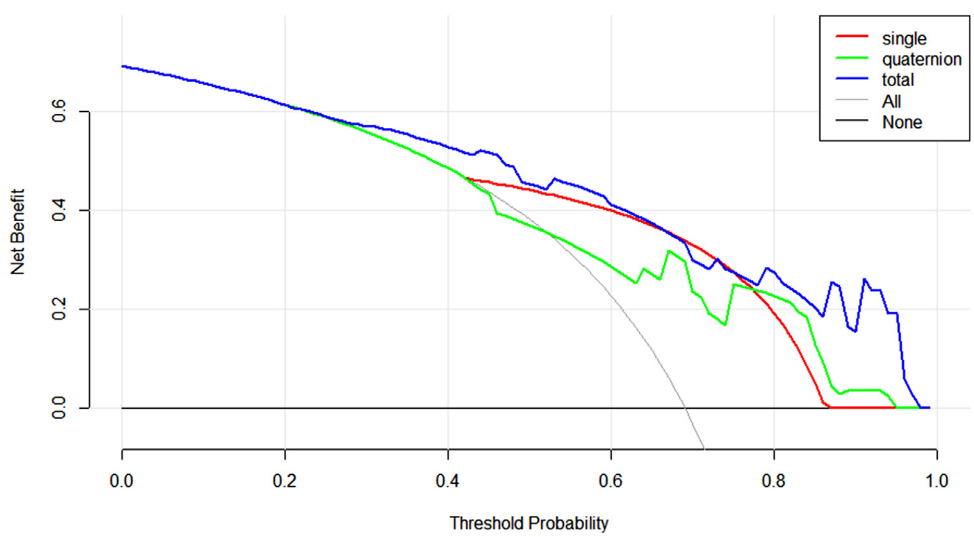

Figure 7. *The decision curve analysis of different models VS infarction. The curve None with zero benefit indicates that none of subjects has ischemic infarction while the curve All is the opposite extreme case. The red and green curves correspond to the proposed method and the traditional diagnostic method, respectively, and the blue one is the combination of these two.*

classify each image patch without considering the relevant information among the patches. The MAP identification model using the statistical estimation method is able to modify detected results by integrating the multiscale classification results and the relevant information among the patches. By performing post-processing to remove most wrongly identified isolated points, the final detected infarct region which is highly consistent with the real infarct core on the DWI image can be gained, as most isolated points that are wrongly identified have been removed. Unlike Fig. 3 and 4, which directly show the detected infarct area on the ncCT image, Fig. 5 shows the probability of stroke in different areas, the redder place indicates the greater probability of infarction, while the bluer place indicates the less probability of infarction. These displays may help doctors combine the probability with other clinical information and their experience to make clinical decisions.

The reasons for false positive results include two aspects:First, stroke identification, the number of negative samples is much larger than that of positive samples, which increases the possibility of false positive from the experimental data. Second, In terms of model, because the patch classification-based detection model is adopted in our method, and the information contained in each image block is limited, the accuracy of the classification model is limited, and some misjudged samples will appear.

The decision analysis curve was first introduced by Andrew J. Vickersand and Elena B. Elkin and published in Medical Decision Making 2006.[14] The most appropriate scenario of the DCA is whether and what screening methods should be used to diagnose diseases when symptoms

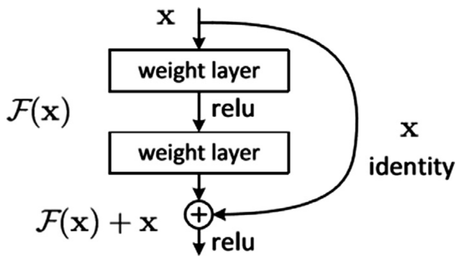

Figure 8. *The ResNet: a building block.*

indicate the possible illness but are not confirmed.[15] From Fig. 7, we can see that the line total which combines traditional and new methods shows a relatively high and stable net benefit rate. Except in the range of 0.70−0.75, which is slightly lower than that using the new method alone, the total model has the highest net benefit rate under other threshold probabilities, so it can be considered that the prediction value of the total model is highest, which means physicians are able to increase the diagnostic accuracy of ischemic patients with the help of our new method. Provided that this new method was applied in practical use, there is no need to carry out additional examinations for patients, but only combining our new non-contrast head CT images detecting method with traditional diagnostic methods of ischemic stroke, can simply and effectively improve the net benefit rate of patients and save their time of receiving treatment afterwards.

Compared with some existed stroke identification methods, the proposed method has the following contributions and novelties. Firstly, our stroke identification method is based on ncCT image while most existed methods are based on enhancement CT or MRI.[16−18] For example, a "fuzzy c means" classification method was proposed to detect the stroke on the contrast enhancement CT image.[18] P. Sivakumar et al.[16] segmented ischemic stroke on MRI images. Mirajkar et al.[17] proposed to use the fusion of CT and MRI images to detect stroke. Because the ncCT images are easier available within the limited diagnosis and treatment time, using the ncCT image to early identify the stroke is of great practical value in clinical. Secondly, we use the deep learning-based patch classification method to detect the stroke, which can well balance the classification accuracy and location accuracy. In,[19] Tyan et al. used voxel intensity-based threshold comparison to detect the stroke. Although this method has the potential to accurately locate stroke edge. Voxel intensity-based classification is difficult to achieve high accuracy classification. In contrast, Takahashi et al. proposed to divide the brain into 10 regions in advance, then used their extracted features to determine whether they contain the stroke or not.[20] Compared with the voxel wise-based method, the region classification-based method may utilize sufficient image features to achieve high classification accuracy, but it is difficult to determine the final specific location of stroke. In our method, we first train the ResNet model to identify each image patch extracted from CT images, then take the identification result as the label of the central pixel. This patch classification-based method can not only obtain the high identification accuracy, but also accurately determine the location of the stroke. Thirdly, although Wu et al. proposed an image patch classification based stroke detection on ncCT images,[21] the process of the patch classification is complex because it includes the feature extraction, feature selection and classification. In particular, the extraction of 513 high-throughput features for each patch greatly increases the detection time. However, for the ResNet based patch classification model in this method, the feature extraction and

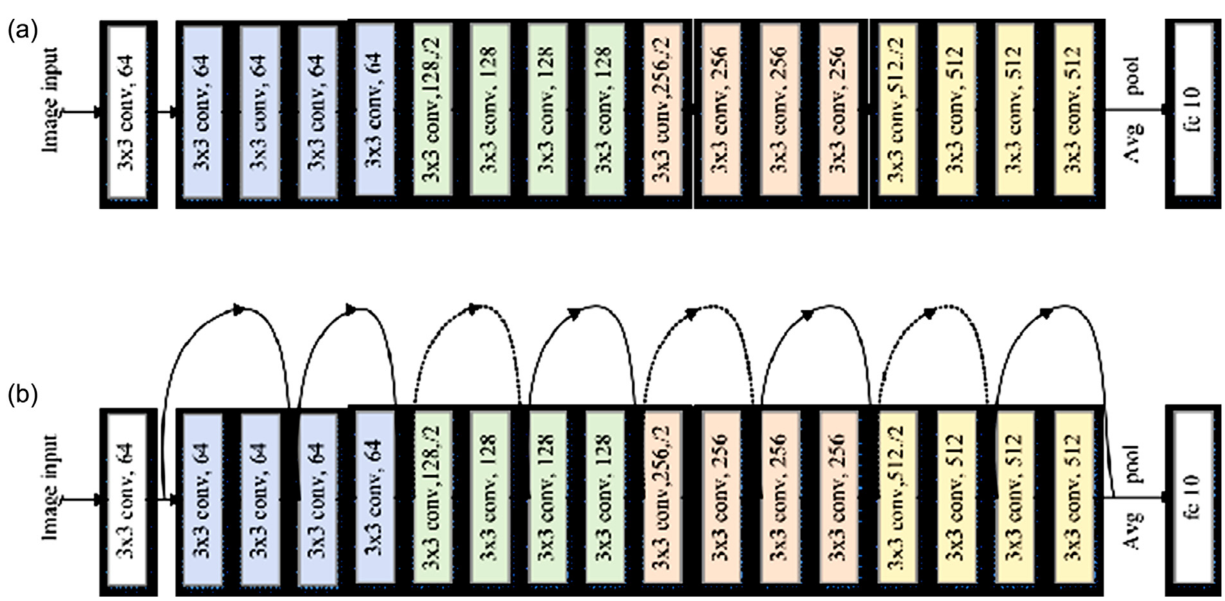

Figure 9. *(a) The plain Net with the 18-layer plain and (b) the ResNet with the 18-layer residual.*

$$\text{Net Benefit}=\frac{TruePositiveCount}{n}-\frac{FalsePositiveCount}{n}\left(\frac{p_t}{1-p_t}\right)$$

Figure 10. *The calculation formula between Net Benefit and Threshold Probability.*

feature selection is eliminated in the training process, and image patches are directly fed into the network for the classification in the testing process. The proposed method is efficient. It takes about 10 s to detect a case, including 5 s for image block extraction, 3 s for image block classification and 2 s for post-processing. As a result, the whole detection method is simplified and the universal applicability of the method is improved.

Conclusion

A deep learning residual network has the ability to detect early ischemic infarct core which is difficult to be recognized by human eyes in most cases. We hope this new approach for identifying the infarct core in ncCT images will play an important role in the diagnosis of acute ischemic stroke in clinical practice.

Declaration of Competing Interest

The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Sources of Funding: This work was supported by the grants from Science and Technology Commission of Shanghai Municipality)19411951200(

Appendix

A ResNet

Fig. 9 is the general structure of the plain network and residual network with 18 layers. The ResNet has some extra shortcuts, as shown in Fig. 8, compared to the plain one and the dashed means the mismatch in the dimension.

There are three steps in general for the classification. In the first step, we divide above processed training samples into the training set and testing set and make sure that the ratio of positive to negative samples equals one. Then, we exploit a deep learning residual network model to train the datasets. In the second step, we use whole training samples to train the classification model and randomly extract small number of samples from the testing dataset to test the model's performance. Through adjusting parameters of the network, we can select some models that behave well. At last, whole testing samples are used to test chosen models and select three classification models presenting the best performance of different scales respectively.

B Three metrics

Assuming that image patches in lesion regions and normal regions are positive and negative samples, respectively. The ACC, SENS and SPE of classification results can be formulated as follow[21]:

$$\mathrm{ACC}=\frac{\mathrm{TP}+\mathrm{TN}}{\mathrm{TP}+\mathrm{TN}+\mathrm{FP}+\mathrm{FN}} \tag{1}$$

$$SENS=\frac{TP}{TP+FN} \tag{2}$$

$$SPE=\frac{TN}{TN+FP} \tag{3}$$

where the TP, TN, FP and FN denote the true positive, true negative, false positive and false negative, respectively.

References

1. Zoppo GJD, Saver JL, Jauch EC. Expansion of the time window for treatment of acute ischemic stroke with intravenous tissue plasminogen activator, a science advisory from the American heart association/American stroke association. Stroke 2009;40:2945-2948.
2. Hacke W, Kaste M, Bluhmki E. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. New Engl J Med 2008;359:1317-1329.
3. Nowinski WL, Gupta V, Qian G. Automatic detection, localization, and volume estimation of ischemic infarcts in noncontrast computed tomographic scans: method and preliminary results. Investig Radiol 2013;48:661-670.
4. Qiu W, Kuang H, Teleg ESA. Machine learning for detecting early infarction in acute stroke on non-contrast-enhanced CT. Radiology 2020;294:638-644.
5. Srivatsan A, Christensen S, Lansberg MG. A relative noncontrast ct map to detect early ischemic changes in acute stroke. Neuroimaging 2019;29:182-186.
6. Li Z, Wang Y, Yu J. Low grade glioma segmentation based on CNN with fully connected CRF. J. Healthc. Eng 2020. [Online]. Available: https://www.hindawi.com/journals/jhe/aip/9283480/.
7. Furie KL, Jayaraman MV. 2018 guidelines for the early management of patient with ischemic stroke. Stroke 2018;49(3):509-510.
8. Lee JG, Jun S, Cho YW. Deep learning in medical imaging: general overview. Korean J Ra-diol 2017;18:570-584.
9. He K, Zhang X, Ren SQ. Deep residual learning for image recognition. In: IEEE Conference on Computer Vision and Pattern Recognition, 1; 2016. p. 770-778.
10. Takahashi N, Tsai DY, Lee Y. Z-score mapping method for extracting hypoattenuation areas of hyperacute stroke in unenhanced CT. Acad Radiol 2010;17:84-92.
11. Gillebert CR, Humphreys GW, Mantini D. Automated delineation of stroke lesions using brain CT images. NeuroImage: Clinical 2014;4:540-548.
12. Takahashi N, Tsai DY, Lee Y. Usefulness of z-score mapping for quantification of extent of hypoattenuation regions of hyperacute stroke in unenhanced computed tomography: analysis of radiologists' performance. J Comput Assist Tomogr 2010;34:751-756.
13. Tang FH, Ng DKS, Chow DHK. An image feature approach for computer-aided detection of ischemic stroke. Comput Biol Med 2011;41:529-536.

14. Vickers AJ, Elkin EB. Decision curve analysis: a novel method for evaluating prediction models. Med Decis Making 2006;26:565-574.
15. Vickers AJ, Cronin AM, Elkin EB. Extensions to decision curve analysis, a novel method for evaluating diagnostic tests, prediction models and molecular markers. BMC Med Inform Decis Mak 2008;8:53-69.
16. Sivakumar P, Ganeshkumar P. An efficient automated methodology for detecting and segmenting the ischemic stroke in brain MRI images. Int J Imag Syst Tech 2017;27(3):256-272.
17. Mirajkar P, Bhagwat KA, Singh A. Acute ischemic stroke detection using wavelet-based fusion of CT and MRI images. IEEE Confer. ICAC. 2015:1123-1130.
18. Yahiaoui AFZ, Bessaid A. Segmentation of ischemic stroke area from CT brain images. IEEE Confer. ISIVC. 2016:13-17.
19. Tyan YS, Wu MC, Chin CL. Ischemic stroke detection system with a computer-aided diagnostic ability using an unsupervised feature perception enhancement method. Int J Biomed Imaging 2014;1:1-12.
20. Takahashi N, Tsai DY, Lee Y. Usefulness of z-score mapping for quantification of extent of hypoattenuation regions of hyperacute stroke in unenhanced computed tomography: analysis of radiologists' performance. J Comput Assist Tomogr 2010;34(5):751-756.
21. Wu GQ, Lin JX, Chen X. Early identification of ischemic stroke in noncontrast computed tomography. Biomed Sig Process Control 2019;52:41-52.
22. Andrew JV, Angel MC, Elena BE. Extensions to decision curve analysis, a novel method for evaluating diagnostic tests, prediction models and molecular markers. BMC Medical Inform Decis Making 2008;8:53.