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COMPUTED TOMOGRAPHY

Ischemic stroke enhancement using a variational model and the expectation maximization method

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Abstract

Objectives In order to enable less experienced physicians to reliably detect early signs of stroke, A novel approach was proposed to enhance the visual perception of ischemic stroke in non-enhanced CT.

Methods A set of 39 retrospective CT scans were used, divided into 23 cases of acute ischemic stroke and 16 normal patients. Stroke cases were obtained within 4.5 h of symptom onset and with a mean NIHSS of 12.9±7.4. After selection of adjunct slices from the CT exam, image averaging was performed to reduce the noise and redundant information. This was followed by a variational decomposition model to keep the relevant component of the image. The expectation maximization method was applied to generate enhanced images.

Results We determined a test to evaluate the performance of observers in a clinical environment with and without the aid of enhanced images. The overall sensitivity of the observer's analysis was 64.5 % and increased to 89.6 % and specificity was 83.3 % and increased to 91.7 %.

Conclusion These results show the importance of a computational tool to assist neuroradiology decisions, especially in critical situations such as the diagnosis of ischemic stroke.

Key Points

• *Diagnosing patients with stroke requires high efficiency to avoid irreversible cerebral damage.*
• *A computational algorithm was proposed to enhance the visual perception of stroke.*
• *Observers' performance was increased with the aid of enhanced images.*

Keywords Stroke · Brain · Algorithms · Tomography · Early diagnosis

Abbreviations

ASPECTS	Alberta Stroke Program Early CT Score
CPU	Central Processing Unit
CT	Computed tomography
DICOM	Digital Imaging and Communications in Medicine

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E1	Evaluation 1
E2	Evaluation 2
FN	False negative
FP	False positive
HU	Hounsfield units
MRI	Magnetic resonance image
NECT	Non-enhanced computed tomography
O1-6	Observer 1-6
TN	True Negative
TP	True Positive
VM	Variational Model

Introduction

Stroke is a cardiovascular disease that currently ranks in the fifth position among all causes of death [1]. The evaluation and initial treatment of patients with stroke symptoms require a high efficiency to avoid irreversible cerebral damage [2, 3]. Multiple medical imaging modalities appear as alternatives in the diagnosis of early signs of stroke such as magnetic resonance image (MRI) and computed tomography (CT) [4]. CT is more accessible, less expensive and faster. Non-enhanced CT (NECT) is the first radiological examination performed in emergency decisions and it is sufficient in most cases for identifying contraindications to fibrinolysis treatment [5]. The earliest signs of ischemic stroke are quite subtle on NECT. Usually, after 1–3 h of symptom onset, a slight hypodense area of infarction in either the cortices or the basal ganglia can become visible [6].

The image enhancement may aid physicians in diagnosing early signs of acute ischemic stroke. Previous studies have demonstrated approaches for enhancing ischemic stroke. Przelaskowski et al. [7] used a wavelet-based processing method for improving acute stroke detection. Chawla et al. [8] proposed an algorithm based on the contralateral symmetry to detect stroke in CT. Tang et al. [9] presented a computer-aided detection scheme for early detection of ischemic stroke using image feature characteristics.

In this paper, a novel approach to enhance the visual perception of ischemic stroke in NECT is proposed. This enhancement aims to enable less experienced viewers to reliably detect early signs of stroke. Our new contribution consists of efficiently combining different image processing techniques. Firstly, to reduce noise and redundancies, a projection of the slices likely to contain the ischemic stroke followed by a band-pass filtering is realized. Then, to enhance the contrast of the projection obtained, a variational model (VM) decomposition is used. Finally, the expectation maximization method is applied to the relevant component from VM decomposition to segment and emphasize the ischemic stroke. The performance of observers was evaluated. We compared their sensitivity and specificity performances for stroke and control cases.

Materials and methods

Patients and image selection

The study was approved by the local institutional ethics committee. We collected retrospective examinations of patients. Patients were selected using the following criteria for inclusion and exclusion. Inclusion criteria: patients with confirmed acute ischemic stroke lesions who had undergone CT scan examinations within less than 4.5 h of symptom onset [10]. Exclusion criteria: patients with previous stroke lesions, intracranial malformations or haemorrhage. This study also did not consider cases of stroke with haemorrhagic transformation. Certified CT scans of stroke were checked with the clinical reports including histological, pathological and clinical results, and with the follow-up NECT examination acquired in the following days for each patient. Finally, all cases were further validated by two radiologists, and only cases approved by both of them were used. After this selection, a set of 39 CT examinations were used: 23 cases of acute ischemic stroke, and 16 normal cases used as a control group. Normal cases were obtained from the database of our institution from migraine studies in which patients did not have any anatomical or neurological alterations. CT scans were performed on multislice CT scanners. Scanner acquisition settings were: kVp = 120, automatic exposure control, exposure time = 1 s, matrix size = 512 × 512 and slice thickness = 2.5 mm. All images were stored using the DICOM format.

Methods

A computational algorithm was proposed to enhance the ischemic stroke visual perception. After selection of adjunct slices, an average image (called projection) was performed to reduce the noise and redundant information. Then, a VM decomposition was applied on the obtained projection to keep the relevant component for our analysis. Finally, the Expectation Maximization (EM) method was applied to enhance the ischemic stroke. The proposed approach steps are described in the flowchart (Fig. 1). All steps were performed using Matlab software R 2014a.

Selection of slices

The processing starts by opening one sequence of CT scan images of individual patients. The selection of slices was performed in the same region as the ASPECTS score, involving

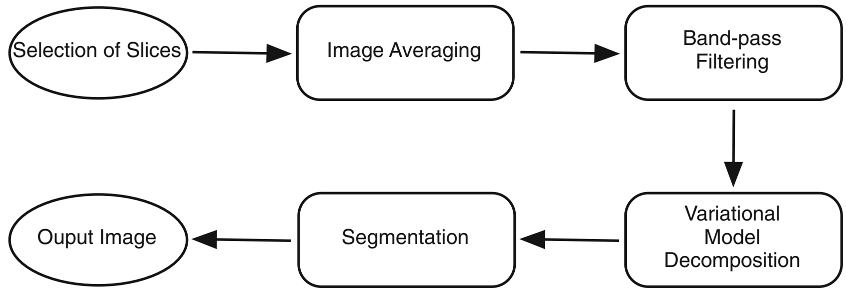


Fig. 1 Flowchart showing the main image processing steps performed

two slices, one at the level of the thalamus and basal ganglion and one adjacent to the most superior margin of the ganglionic structures, such that they were not seen [11]. These regions are most commonly affected by stroke [2]. After selecting slices, a projection is performed by summing the values of the grey levels in each slice, yielding an average image. The algorithm operates by computing an arithmetic mean of the intensity values for each pixel position in a set of captured images from subsequent slices. This approach was performed to highlight the presence of stroke and lower the image noise level. All control group images were also averaged using slices in the same region evaluated for the stroke group.

Band-pass filtering and variational model decomposition

After the projection step, a band-pass filtering was applied between 0 and 50 Hounsfield units (HU) to remove all pixels of bone tissue, background and other unwanted structures. All pixels out of this band were assigned a new value equal to zero HU. After this stage, a histogram normalization was performed by redistributing pixels intensities from [0, 50] to [0, 255] HU. The histogram normalization enabled improving the contrast between adjacent regions.

To further enhance the contrast of the projection, a Variational Model (VM) [12, 13] decomposition was applied to decompose the image into different components. The image p was modelled as the sum of three terms: $p = u + v + w$. Here, v is the smooth second order part, u is related to contours and w is linked to fine textures. Our primary interest is in the v component since it is related to contrast and brightness of the image. More details of the VM decomposition are presented in the Supplementary Material.

Segmentation

The next step concerned the image segmentation, which was applied to the v component after the VM decomposition. The Expectation Maximization (EM) method has been very popular in medical imaging and several variants of the algorithm have been proposed [14, 15]. EM is a segmentation method that assigns pixel intensities into different clusters using a probabilistic Gaussian distribution. The mixture model is composed of a sum of K Gaussian distributions, each distribution with its own parameters. The algorithm is iterative and starts from some initial estimate and then proceeds to iteratively update until convergence. Each iteration consists of an Expectation (E-step) and a Maximization (M-step) step [14]. Each pair of E and M steps are considered one iteration. This EM cycle is repeated until some preset threshold. Thus, in the final assignment each pixel of the final image will belong to only one cluster. More details on the EM method are presented in the supplementary material.

Observers' evaluation

A test was established to evaluate the performance of observers based on a scoring system used by Tang et al. [9]. Four resident radiologists from the first (Observer 1 – O1 and Observer 2 – O2), second (Observer 3 – O3) and third (Observer 4 – O4) years of residence and two experienced radiologists (Observer 5 – O5 and Observer 6 – O6) with 10 and 20 years of experience in radiology, worked as observers. All radiologists were from Botucatu Medical School Hospital, Brazil. They had no previous knowledge regarding the history of the patients. First, the set of original images was analysed in a random order combining stroke and control cases. Observers were allowed to adjust contrast, brightness and magnification of images according to their own experience. Each observer was required to give a score relating to the presence of acute stroke (definitely absent: 1, absent: 2, uncertain: 3, present: 4 and definitely present: 5). Then, as a second step, the observers evaluated the enhanced images that were created from our proposed approach. The change of the score in diagnosis was tracked after the observation of enhanced images. Improvement changes were considered when the observer changed his evaluation to the correct score. These analyses permitted testing the confidence of the diagnosis both before and after the image enhancement.

We also measured both sensitivity and specificity of the performance of the observers before and after the enhanced images. The formula for both quantitative measures is given in Eqs. 1 and 2. The scores 1, 2 and 3 were considered as negative evaluations and the scores 4 and 5 were considered as positive.

$$\text{Sensitivity} = \frac{TP}{(TP+FN)} \quad (1)$$

$$\text{Specificity} = \frac{(TN)}{(TN+FP)} \quad (2)$$

where TP are true positives, TN are true negatives, FP are false positives and FN are false negatives.

We tracked the difference scores that resulted from the analysis of both original and enhanced images. For the difference scores, one can consider a positive score when the observer changes his previous score from any given value to a higher one. For example, the original score was 3 and the observer changed after analysing the enhanced image to a score of 4, which means that the stroke can now be visualized. Additionally, negative scores represent false-negative cases.

Results

In this study the mean age of patients was 68.45 ± 9.56 years for stroke and 65.12 ± 9.22 for control. No significant difference was found between the stroke patients and controls for age (*p*-value = 0.1735) using Student's t-test. Stroke patients had a mean NIHSS of 13±7 and mean ASPECTS of 7±2. The complete results of NIHSS and ASPECTS are presented in the Electronic Supplementary Material. All sequence of images analysed passed through the image processing steps described in the flowchart in Fig. 1. Figure 2 A-E illustrates the ischemic density changes in adjunct CT slices of the same patient. Figure 2 F presents the resulting image after computing the projection using slices A–E.

Our approach provided enhanced images that helped physicians to achieve a more reliable diagnosis of ischemic stroke in CT examinations. Representative examples of those enhanced images from different patients are presented in Fig. 3. On the top, corresponding to letters A, B, C and D, are presented the images resulting from the image averaging step of three different patients with stroke and one control case (Fig. 3 D). In the second row, corresponding to letters E, F, G and H, are presented the enhanced images according to our proposed approach accounting the band-pass filtering, followed by the VM decomposition and the EM segmentation method.

The overall sensitivity of the observer's analysis was 64.5 % and changed to 89.6 % after the evaluation of the enhanced images. The overall specificity was 83.3 % and increased to 91.7 %. The sensitivity and specificity obtained for each observer both before and after evaluating the enhanced images are summarized in Table 1. We also compared the difference scores for all observers analysing the original images and then the enhanced images for stroke cases. In this manner, one could see each case in which enhanced images provided a more reliable diagnosis. For a better visualization of scores, the observers O1, O2 and O3 were joined in the graph of Fig. 4 and observers O4, O5, and O6 in the graph of Fig. 5.

The improvement of sensitivity was more remarkable for the three least experienced physicians. This great improvement was also shown in the difference score graphs. The maximum difference score was 2 (Fig. 4 and Fig. 5), since the maximum changes occurred when observers first assigned the score 3 and then changed to score 5 after analysing the enhanced images. For those cases, enhanced images provided greater reliability in the diagnosis of ischemic stroke.

Discussion

In this paper, we proposed an approach to enhance the visual perception of ischemic stroke to be used in clinical routine as a support to the diagnosis of this disease. One limitation of our approach is that it is not entirely automatic, since it depends on the physician selection of the slices before the application of the algorithm. Two experienced radiologists selected all ground through stroke cases with the support of the follow-up CT in the same patient to confirm the occurrence of stroke. The image averaging technique was used to reduce noise and improve the perception of stroke while using subsequent slices with slightly different anatomical structures (Fig. 2). This was considered an acceptable tradeoff by the physician's analysis. The VM decomposition helped to enhance the contrast and the brightness of the images.

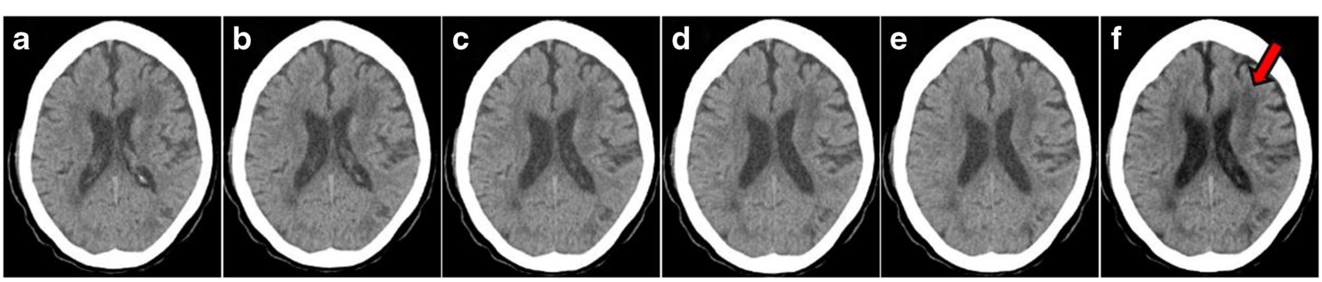


Fig. 2 (**A-E**) Adjunct slices sequence with the presence of the subtle density changes in the same patient. **F** is the result of the projection involving slices **A, B, C, D** and **E**. Stroke is present in the left frontal lobe of the brain, as indicated by the red arrow

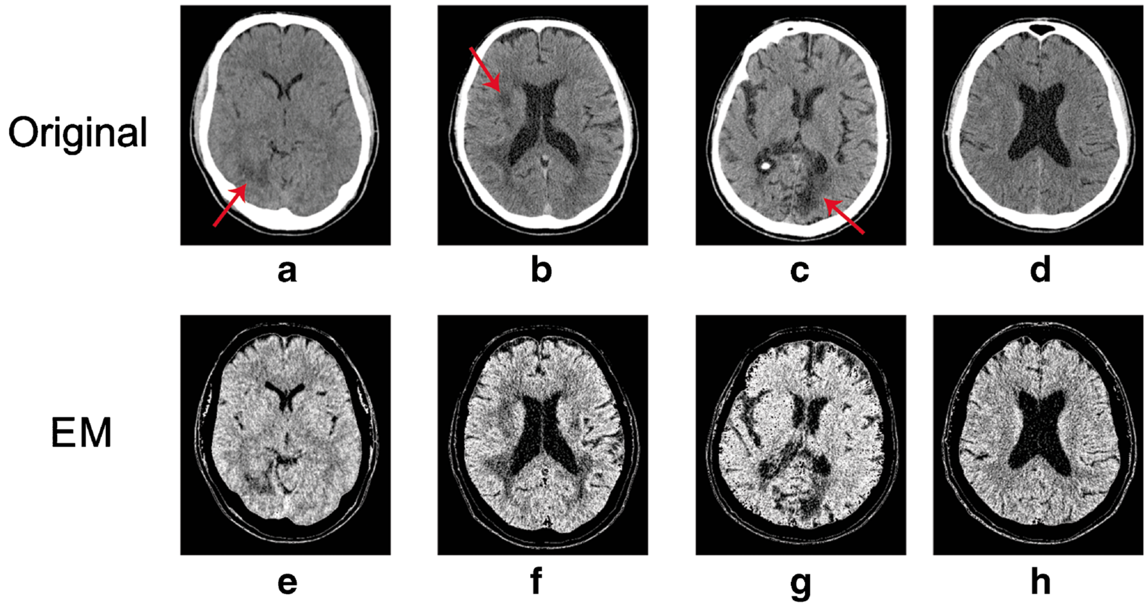


Fig. 3 Average images for three different patients with strokes (**A, B, C**) and one control (**D**). Enhanced images are shown in second row with the Expectation Maximization (EM) approach (**E, F, G, H**).

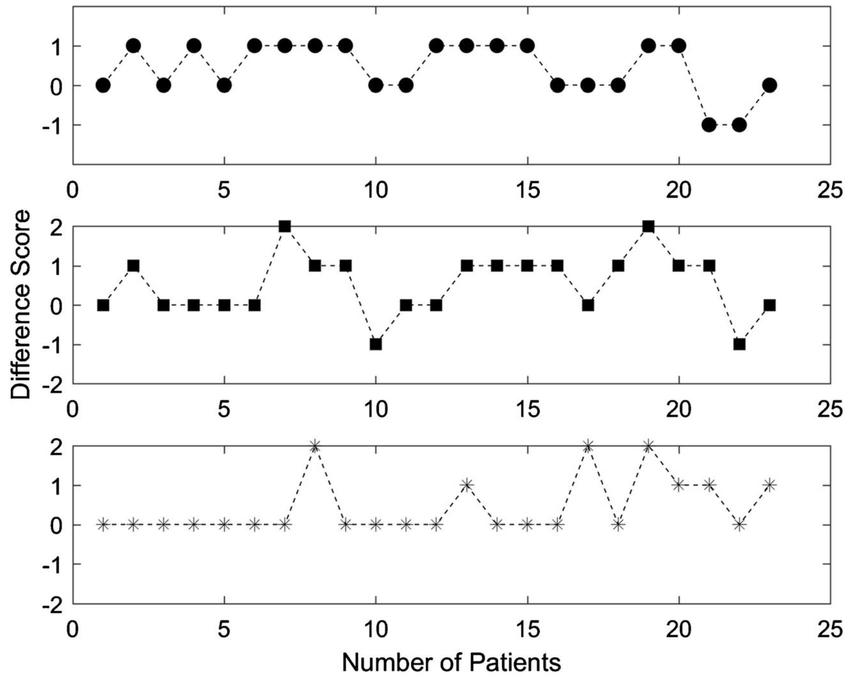
The purpose of the EM segmentation was to enhance the visual perception of ischemic stroke. A key aspect for the EM approach is to choose the number of clusters for segmentation. Our target was to achieve a number that would both benefit the visual enhancement and have no additional cost in computational time. This is an important issue since the main goal is to apply this algorithm to a medical diagnosis workstation. The best achieved results were found for six clusters. The average elapsed time for each patient analysis is 141.6 ± 1.5 s. Our experiments were performed on machines running Intel® processors with 2.4 GHz CPU frequency and having 32 GB of memory.

Regarding previous studies, Przelaskowski et al. [7] proposed a method to enhance the subtle signs of ischemic stroke in NECT. They analysed a small cohort of 11 CT examinations and improved the sensitivity of two observers from 12.5 % to 56.3 %. Tang et al. [9] proposed a method with a Circular Adaptive Region of Interest to analyse stroke in NECT scans. With a cohort of 40 examinations, they showed a significant improvement in sensitivity and specificity for three observers. They also demonstrated a great correlation between the experience of physicians and its performance. Our results corroborate that the ability of observers to detect early signs of ischemic stroke highly depend on their experience. With the aid of the enhanced images, inexperienced physicians achieved the ability to diagnose stroke, very close to the average or even higher when compared to other published papers. Patel et al. [17] found 31 % sensitivity for these early infarct signs, while von Kummer et al. [18] found that this rate increases to 82 % 6 h after symptoms onset. In general, the observers' ability to detect stroke in NECT without enhancement is less than 67 % in cases imaged within 3 h [19]. Our results indicate an initial sensitivity of 63.9 % with an improvement to 78.9 %.

Table 1 Observers' sensitivity and specificity before (evaluation 1– E1) and after (evaluation 2 – E2) of the enhanced images. Confidence intervals (CIs) for sensitivity and specificity are calculated with the Wilson score method [16]

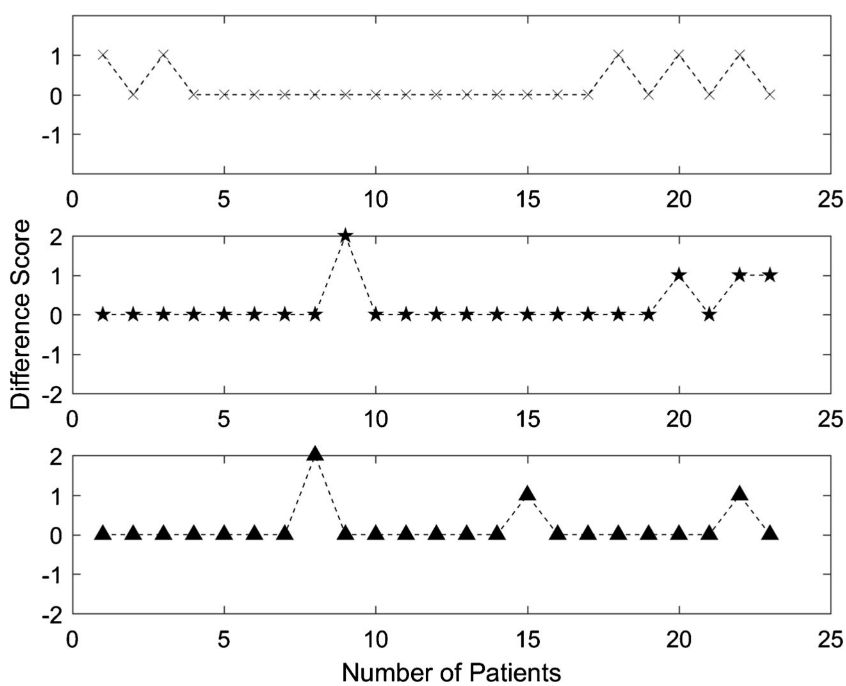
Observers	Sensitivity				Specificity			
	E1		E2		E1		E2	
	Mean	CI	Mean	CI	Mean	CI	Mean	CI
O1	26.1	(12.5–46.7)	60.9	(40.8–77.8)	81.3	(57.0–93.4)	87.5	(63.9–96.5)
O2	52.2	(32.9–70.7)	78.3	(58.1–90.4)	93.7	(71.7–98.9)	93.7	(71.7–98.9)
O3	65.2	(44.9–81.2)	82.6	(62.9–93.0)	93.7	(71.7–98.9)	93.7	(71.7–98.9)
O4	78.3	(58.1–90.4)	87.0	(67.9–95.5)	100	(80.7–100)	100	(80.7–100)
O5	73.9	(53.3–87.5)	91.3	(73.2–97.6)	75.0	(50.5–89.8)	75.0	(50.5–89.8)
O6	91.3	(73.2–97.6)	100	(85.7–100)	93.7	(71.7–98.9)	100	(80.7–100)
Overall	64.5	(56.2–72.0)	89.6	(81.8–94.2)	83.3	(76.3–88.7)	91.7	(84.4–95.7)

Fig. 4 Difference scores for the observers O1 (circle), O2 (square) and O3 (asterisk). The difference was obtained when the scores given for the enhanced images are compared to the scores given for the original images. Positive values indicate an enhancement in diagnosis. Negative changes indicate false-negative cases



Chawla et al.'s [8] method used the dissimilarity between the left and right hemispheres of the brain, which was used it to classify different types of stroke. According to the authors, this approach fails when the same type of stroke occurs symmetrically in both hemispheres. The same applies for Tang et al. [9], whose proposed scheme is not applicable when the brain is asymmetrical. Our proposed approach does not rely on brain symmetry. Most patients with stroke symptoms are agitated and there is a high risk that their heads were tilted during image acquisition, which compromises hemisphere comparison. According to the opinion of the observers who participated in this study, the enhanced images were particularly useful when displayed together with the original images. We strongly suggest that the enhanced images be displayed in association with the original images instead of standalone.

Fig. 5 Difference scores for the observers O4 (cross), O5 (star) and O6 (triangle). The difference was obtained when the scores given for the enhanced images are compared to the scores given for the original images. Positive values indicate an enhancement in diagnosis. Resident 4 results were included in this analysis since they were more similar to the experienced radiologists



A novel approach based on a VM and EM method was used to enhance the ischemic stroke perception in non-enhanced CT examinations. We demonstrated that enhanced images improved physicians' performance to diagnose early signs of acute ischemic stroke. These results show the importance of a computational tool to assist neuroradiology decisions, especially in critical situations such as institutions that do not have stroke specialists. Enhanced images may largely increase the potential candidates for thrombolysis treatment.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is José Ricardo de Arruda Miranda from São Paulo State University, Brazil.

Conflict of 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.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was not required for this study because all CT scans used were retrospective and no confidential patient information was used throughout this study.

Ethical approval Institutional Review Board approval was obtained.

Methodology
• retrospective
• diagnostic or prognostic study
• performed at one institution

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