AUTOMATED APPROACH FOR WHOLE BRAIN INFARCTION CORE DELINEATION

Using Non-contrast and Computed Tomography Angiography

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Abstract: This article proposes automated approach for whole brain infarction core delineation while using only non-contrast computed tomography and computed tomography angiography. The main aim is to provide additional information measuring infarction core volume while exceeding certain level is contraindication of early recanalization. Process of generation of Perfusion Blood Volume maps is described first followed by description of process of infarction core delineation. Verification of correctness is based on comparison against follow-up examinations. Discussion and future works summarizes weaknesses of the method and steps for improvement.

1 INTRODUCTION

Acute stroke is the third leading cause of death and first leading cause of disability in population over 60 years old. When we use computed tomography the best localization and stoke visualization can be reached by perfusion examination (CTP). This kind of examination has limitations depending on the device and settings restrictions. Radiation dose is another factor which must be taken into account. CTP is generally limited in width of the acquired area. Early recanalization is a treatment of choice in acute stage of ischemic stroke. This kind of treatment can be used at those patients who did not exceed certain level of infarction core. Evaluation of actual infarction core tissue volume is not possible from CTP in many cases because of limited acquired width while the volume must be summed over all the brain tissue. Our study is concerned in the detection of the necrotic tissue and computation of its volume. To cover whole area of the brain we use different examinations – computed tomography angiography (CTA) and non-contrast computed tomography (NCCT). This article deals with assumption that there exists certain level of density increase between CTA and NCCT (due to contrast material) where all voxels with lower increase are considered as the necrotic core. Study (Wintermark, 2006) present optimal level in range 2.0 ml/100g to 2.3 ml/100g using CTP method.

The method proposed here tries to find the way for fully automated detection and delineation of the infarction core. It is based on studies (Hamberg, 1996) and (Hunter, 2003). To ensure objectivity of results we compare findings with follow-up non-contrast CT examination where the final infarction core area has significant density decrease compared to the non-contrast CT acquired at the time of patient admission.

Following sections describe each step of the processing and the final section summarizes results and mentions our future plans.

2 INPUT EXAMINATIONS

Our study contained examinations of 32 patients with acute ischemia. For each patient we had 2 pairs of examinations. One pair acquired at the time of admission and the follow-up was acquired one day after. Each pair consisted of non-contrast CT examination and CT angiography.

All examinations were performed using a dual-source CT (Somatom Definition, Siemens

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Healthcare, Forchheim, Germany). First, an unenhanced brain CT using a spiral technique with the following parameters was performed in all patients: collimation 2× (32 × 0.6 mm) with simultaneous acquisition of 64 slices by means of a z-flying focal spot (double z-sampling), reconstruction slice width 6 mm without overlap, and—in addition—0.75 mm with a reconstruction increment of 0.5 mm. A medium-smooth head kernel (H25) was used for all reconstructions.

All CT angiography, ranging from the aortic arch to the vertex of the head, was performed in a dual-energy (DE) mode using 140-kV tube voltage for measurement system A and 80-kV tube voltage for measurement system B. Collimation was again 2× (32 × 0.6 mm) with simultaneous acquisition of 64 slices by means of a z-flying focal spot (double z-sampling). The examinations were performed after application of an iodine contrast medium (60 ml) of 400 mg/ml at a flow of 4 ml/s with subsequent saline flush using 50 ml of saline solution.

For each examination, we reconstructed two image data sets, one at 140 kV and one at 80 kV. A medium-smooth head kernel (H25) was used for all dual-energy reconstructions.

From all these examinations we have chosen 18 patients who had significant findings on the follow-up non contrast examination. From this group we have chosen 6 patients because of infarction core location in a white matter where the method has better results (see Discussion). Examinations of those six patients underwent following processing.

3 METHOD DESCRIPTION

3.1 Overview

We have developed prototype software processing input examinations resulting in binary volumetric maps where each voxel represents information 1=infarction core, 0=non infarction core. Whole process can be described by these parts:

- Registration
- Segmentation
- Subtraction
- Infarction core delineation

Method requires a pair of examinations - NCCT and CTA. First these examinations are registered to each other. After this step segmentation follows by removing non-brain areas and large vessels. The same way we process both examinations and afterwards we subtract non-contrast examination from angiography thus we get values of density enhancement caused by the contrast material in Hounsfield's units. Infarction core delineation follows using a threshold value. The aim of our study is to find the best threshold value which will lead to best fit with the findings of the follow-up findings. The best threshold value is found by ROC analysis described later.

3.2 Registration

Method requires a pair of examinations - NCCT and CTA. First these examinations are registered to each other. We use open source software ITK (Yoo, 2002) for registration process. First we convert all source examinations to 2 mm slice thickness to avoid memory complexity problems of using 1 mm or less of slice thickness. Reconstructions in 2 mm slice thickness are generated also by the ITK software.

We use rigid registration with Mattes Mutual Information image to image metric, multi resolution pyramidal approach and versor rigid transformation optimizer with stopping criteria of 200 iterations.
Result of the registration is angiography examination registered to non-contrast examination thus voxels of both examinations correspond to each other.

3.3 Segmentation

Segmentation step just removes “non-important” areas like skull bones, large vessels and other non-brain areas like eyes, ears, etc. from both NCCT and CTA examination. Large vessels are removed by thresholding leaving just voxels with density between 20-80 HU.

3.4 Subtraction

Simple subtraction on voxel by voxel basis does not provide satisfactory results because of high ratio of noise. Denoising pre-processing is required despite of missing information about this step in literature. Denoising process is crucial step and have high influence on detection of infarction core. We tried denoising by a method of averaging neighborhood area. The method computes average density for all voxels in a cuboid area with the voxel as the center of the area and dimensions m, n, o where m, n, o are dimensions along axes x, y and z. All voxels get new density equal to the average density of the area. Subtraction follows after the denoising process (Figure 1). It is based on voxel by voxel basis.

3.5 Infarction Core Delineation

The goal of this step is to automatically find the area corresponding to the necrotic tissue area. The procedure starts with the subtracted volume where voxels contain information about local density increase caused by the contrast material. Infarction core can be characterized by a low density increase – let's call separating threshold as τ. All values below the threshold are considered to be infarction core and all voxels above the threshold are marked as non-infarction core. Not all voxels having the value below the threshold are in fact infarction core. We may assume that infarction core is the largest continuous area formed by voxels with values below the threshold. Thus we can find all the continuous areas, measure their dimensions as a count of voxels of the group and keep just the largest group.

Nevertheless the process of finding infarction core is not that simple. Large groups of voxels below the threshold can be found also at the bottom parts of brain and head, including under-brain areas which can be present because of non-perfect brain

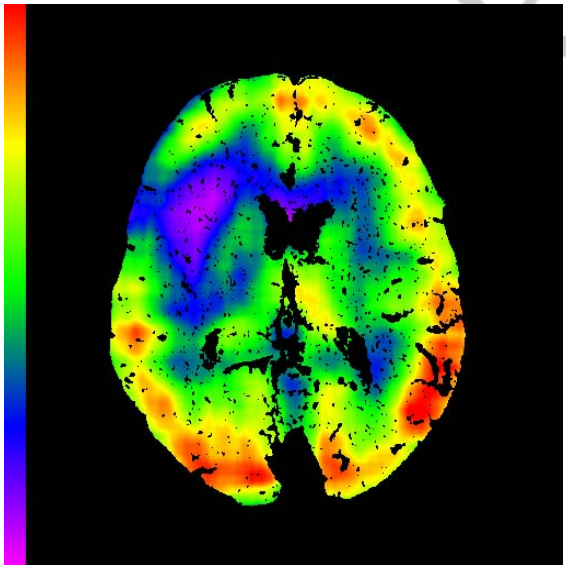

Figure 1: Subtraction on voxel by voxel basis, perfused blood volume map.

area segmentation. To get rid of these groups we calculate average density of each group and all groups having average density below -2 we remove from detection of infarction core.

Having the largest continuous area of pixel below the threshold τ we can mark all voxels belonging to this group as those belonging to the infarction core area (Figure 2). All other voxels outside this group we can mark as non-infarction core.

3.6 Follow-up Examinations

We processed follow-up examinations in same way using only non-contrast follow-up examination (NCCT2) and non-contrast examination acquired at the time of patient admission (NCCT1). After pre-processing we made subtraction and manually we found threshold for infarction core. NCCT2 has significant density decrease in areas of real infarction core and we can mark real infarction core as shown on Figure 3. Follow-up findings were confirmed by clinician. We can use these findings for our method correctness verification and also for tuning parameters to produce best match. We found best parameters using ROC analysis separately for each patient.

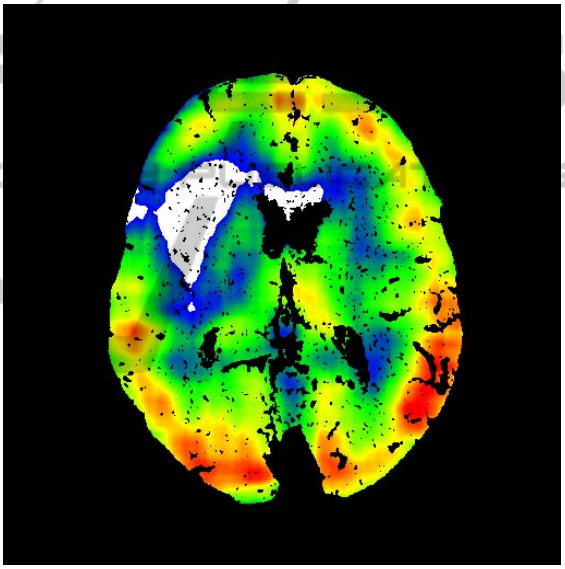

Figure 2: Method Result - Infarction Core Delineation (White Area).

4 ROC ANALYSIS

We have already described method of processing examinations and also way of preparing data for verification and tuning parameters process. We made ROC analysis for each patient separately. We set ROC analysis variables to dimensions of the considered area (for pre-processing) and threshold value for infarction core delineation. The variable for threshold value is for ROC analysis in Hounsfield units. We limited values range as follows:

- Dimensions *m*, *n*, *o* – we set *m*=*n* with range (2-8 mm) and range of *o* (2-14 mm), dimensions

are taken symmetrically, so whole considered area has size of 2**m*, 2**n*, 2**o*.

- Threshold values range from 0 to 5 HU with step 0.5 HU.

We use Matthews correlation coefficient to measure similarity between our method results and follow-up findings. ROC analysis outputs for all patients separately is summarized in Table 1.

5 ABSOLUTE VOLUME EVALUATION

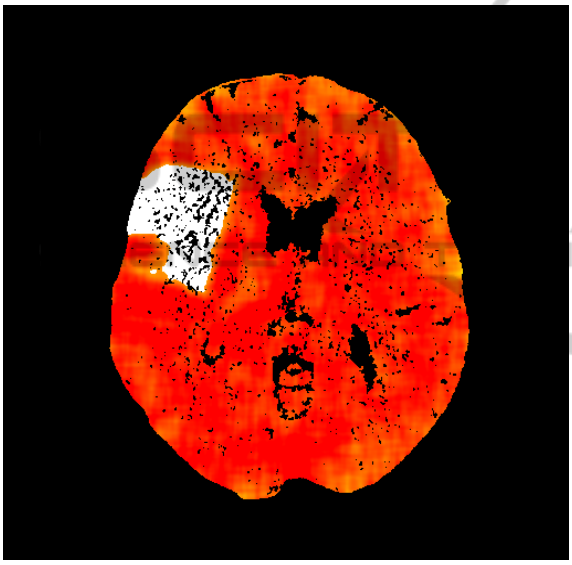

Figure 3: Follow-up examination with marked infarction core (white).

To convert threshold values (relative density increase in Hounsfiled's units) to absolute numbers in mL/100g (column PBV in Table 1) we use equations from (Hamberg, 1996). First we compute correction factor CF using Equation 1.

$$CF = \frac{1 - Hct_{WB}}{1 - 0.85 * Hct_{WB}} \quad (1)$$

Hct_{WB} means large-vessel hematocrit. We use value 0.4 which comes as average value (for man and woman). Next value which we must find is ΔHU_{Blood} which means an average density increase in large vessels. We need to find this value in an automatic way. First we find all brain tissue voxels with densities in range from 40 HU to 50 HU in NCCT1. For all these voxels we find corresponding voxels in angiography examinations, but only those having increases more than 300 HU aiming to select only increases of the large vessels. Finally we take median from all these increases and we call it as ΔHU_{Blood}. Having ΔHU_{Blood} value, we can use Equation 2:

$$CBV = \frac{\Delta HU}{\Delta HU_{Blood}} * CF * \frac{100}{1.05} \quad (2)$$

where ΔHU is density increase in any place of the map as described in the part of our method description. Constant 1.05 is density of brain tissue in g/100ml (Sabatini, 1991). If we put ΔHU value of the threshold we get absolute threshold value in mL/100g.

Table 1: ROC Analysis Results, m, o,= dimensions of area used for denoising, τ = infarction core threshold, PBV = threshold τ in absolute values, Matthews = correlation coefficient.

Patient	m [mm]	o [mm]	τ [HU]	PBV [mL/100g]	Mat-thews
1	8	8	4,5	1,15	0,48
2	5	8	5	1,64	0,42
3	5	11	2	0,5	0,37
4	4	8	4,5	1,17	0,28
5	3	8	4,5	1,4	0,23
6	2	14	3,5	1,17	0,16

6 RESULTS

We processed examinations of 6 patients resulting in volumetric maps with additional information which voxels correspond to infarction core and which not. We made an ROC analysis for each patient separately to find the best tuning of parameters and thus getting the best match against follow-up infarction core findings. The best match is supposed to reflect high ratio of similarity expressed by Matthew's coefficient.

We had group of 32 patient where only 16 of them had significant finding on follow-up examinations. From these 16 patients our method correctly determined infarction core only at 6 patients with precision from 16% to 48%.

Results are not yet sufficient enough for method to be used in clinical practice. But the method seems like a good starting point for automated infarction core delineation.

7 DISCUSSION

Although results are not sufficient there are many new ideas which can lead to provide better results in future. The main point is that the method provide satisfactory results in the white brain matter. White matter can be generally characterized by a lower density increase due to injected contrast material than in gray matter. White matter ischemic areas have even lower increase and such areas is easier to find by thresholding with threshold below the normal increase for the white matter.

Ischemia in the grey matter is another point. Ischemic area are optically well visible on our pefusion maps but automatic process of infarction core delineation fails to mark them. The reason is that there is significant density decrease in cortical gray matter areas compared to non-ischemic cortical gray matter areas but the decrease is not enough to fall down below normal values for the white matter. Thus making threshold value higher above the normal white matter increase leads to marking larger area containg also normal (non ischemic) areas of the white matter.

Having threshold values lower then normal density increase of white matter leads to selection of smaller infarction core areas than on the follow-up findings. That is why Matthew's coefficient gives the highest values at relatively low level and ROC analysis does not find better combination of parameters to produce better match.

8 FUTURE WORK

We believe that we can improve our results by introduction of symmetry as mentioned in (Hunter, 2003). Symmetry information can lead to detect ischemic areas also in cortical gray matter despite of any threshold used by current method. The technique of symmetry can provide information like local density decrease compared to the other side. We may put this decrease some kind of weight and use it as another criterion available when deciding whether the voxel belongs to the infarction core.

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