ischemic stroke,
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Rafał JÓŹWIAK[1], Artur PRZELASKOWSKI[1], Grzegorz OSTREK[1]

CONCEPTUAL IMPROVEMENTS IN COMPUTER-AIDED DIAGNOSIS OF ACUTE STROKE

This work presents some conceptual improvements in assistance of acute stroke diagnosis with Stroke Monitor – computer-aided diagnosis tool developed and elaborated by Telemedicine Group from Institute of Radioelectronics, Warsaw University of Technology. Based on statistical analysis of common error sources we proposed some ideas of improvement capabilities for false positive errors reduction. Simulation and experimental verification confirmed validity of further development directions.

1. INTRODUCTION

Stroke (according to WHO) is the clinical syndrome of rapid onset of focal, or sometimes global, cerebral deficit with a vascular cause, lasting more than 24 hours or leading to death. It is the first cause of disability and one of the leading causes of mortality (third major reason of death after cardiac and oncologic diseases) [2]. CT remains the method of choice for the evaluation of patients with suspected acute stroke. It provides a relatively quick way of excluding conditions that may mimic ischemic stroke and may require a different treatment approach. Early assessment of irreversible injury of brain tissues is exceedingly important because of the recent advent of thrombolytic therapy [12]. Compared to MRI, brain imaging with CT is more accessible, less expensive, quicker and more reliable, especially in severely ill patients. Although a CT image of the brain in acute stroke patients is not difficult to read, it is rather not self-evident. Reading of CT needs training and instructions, how to recognize anatomy and pathology, combined with knowledge about the physical conditions of image contrast. In the further part of this introduction we present some common difficulties concerning reading of early CT examinations and briefly introduce the conception of stroke monitor utilized as a computer-aided diagnosis tool for acute ischemic stroke diagnosis.

1.1. CT IMAGING OF ACUTE STROKE

Generally, there is need to examine a stroke patient with CT as soon as possible. A typical sign of acute infarction on CT is hypodense area within a defined arterial supply territory due to respective water content increase - increase by 1% means CT attenuation decreases by 2-3 HU (Hunsfield Unit) [11]. Early attenuation changes corresponding to irreversibly damaged brain tissue may vary within the limited range of HU scale (typically up to 10 HU) depending on cerebral infarct case, discrepant patient characteristics, non-optimum scanning and acquisition conditioning. Moreover, early indirect findings, such as obscuration of gray/white matter differentiation and effacement of sulci or “insular ribbon sign” may be additionally noticed. However, subtle visual changes are often masked due to artifacts, noise and other tissue abnormalities. In effect, during the hyperacute phase of stroke (up to 6h after symptom onset), a hypodense area as direct infarct sign is not well outlined or contrasted (with low gradient, ill defined margins) and indirect findings become imperceptible - see Fig. 1). In consequences, many infarcts do not emerge on CT even until many hours after the onset of stroke - about 50-60% of stroke cases have normal CT even before 12h after stroke onset [5]. Thus assistance of computer-aided diagnosis (CAD) support to extract subtle ischemic signs was considered [1,3].

[1] Warsaw University of Technology, Institute of Radioelectronics, Nowowiejska 15/19, Warsaw, Poland,
email: {rjozwiak, arturp, gostrek}@ire.pw.edu.pl.

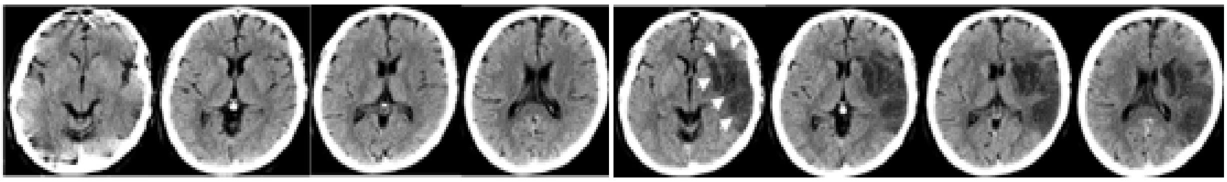

Fig. 1. CT successive scans in a patient with ischemic stroke: 11h after stroke onset, without any visible changes (1-4 from left); 4 days after the onset with clearly visible - indicated with arrows - hypodense area (5-8 from left).

1.2. STROKE MONITOR

Stroke Monitor (SM) [9] is a computer tool supporting acute ischemic stroke diagnosis. Emergency noncontrast, routine CT scans are enhanced to increase visibility of hypodensity changes in hyperacute ischemic stroke cases. The processing algorithm of SM is based on multiscale image data processing, denoising, lesion pattern identification and description, and final extraction optimized by visualization procedure. Essentially the main algorithm consist of three successively performed steps:

a) image segmentation, aimed at selection of diagnostic ROIs - stroke-susceptible regions of brain tissues, containing:
   - the brain extraction (deskulling) to remove non-brain tissue (based on region growing procedure),
   - selection of the only tissue regions which are susceptible to ischemia by rejection of clear brain sulci, prior ischemic scars and other structures useless in acute stroke detection.
b) hypodensity extraction, which as an essential stage is oriented at subtle signs mining through following operations:
   - smooth complement of segmented diagnostic ROIs with mean values of neighbor areas providing the continuity of density function and absence of any lower density fields,
   - multiscale transformations and nonlinear processing according to different procedures (wavelets, curvelets and their joint combinations with adaptive modeling across scales and subbands),
   - brain tissue mapping to source CT scans space and merging with background view of the scans.
c) visualization of diagnostic image content:
   - display arrangement with contrast enhancement by adaptive histogram equalization of processed data in brain tissue area,
   - alternative and complementary view of image data processed according to four multiscale procedures.

More detail description of SM algorithm and conception is reported more exhaustively in [6-10].

Combining the effects of standard CT scans review with SM assistance may led to a better diagnosis of stroke. Stroke Monitor provide a new semantic-visualization system of empowered hypodensity symptoms, realized according to elaborated and optimized four different forms of multiscale processing, localizes suggested ischemic areas in source brain image space. Observation of suggestive ischemic density changes occurrence combined with correlation analysis of their localization related to clinical manifestation, made image content assessment and interpretation more accurate and simple. A good example of different semantic-visualization forms (semantic maps) of SM were presented in Fig. 2.

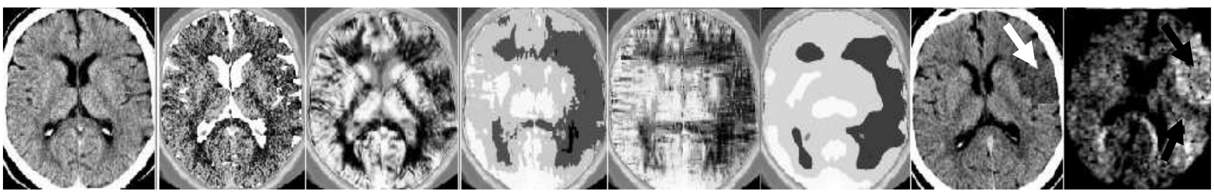

Fig. 2. The effects of SM assistance for stroke diagnosis (from left): view of CT scan, enhanced visibility of diagnostic ROI with segmented unusual areas (white), four visualization forms of SM, follow up CT and DWI with indicated visible ischemic changes.

1.3. WORKING WITH STROKE MONITOR

Aiding routine interpretation procedure with SM assumes exploiting of additional knowledge concerning localization and spacing of brain tissue hypoattenuation in susceptible to ischemia territories. This knowledge is contained in SM semantic maps where areas with diverse density, especially with density lower than normal surrounding brain tissues, are much more clearly recognizable due to improved perception of subtle tissue density distribution. Possible presence of ischemic region with local brain tissue hypoattenuation expresses itself with noticeable disorder in lower tissue density distribution symmetry. The presence and localization of the asymmetric hypodense signs should be verified related to segmentation results (to avoid diagnosis of incorrectly segmented prior ischemic scars and other structures useless for stroke diagnosis), clinical manifestation and other available domain knowledge (i.e. disease and imaging modality conditioning).

The potential gain is due to the synergistic effect obtained by combining the radiologist's competence and the computer's capability. Computer suggestions can be applied by radiologists, but they cannot replace their judgment. Thus convincing computer aid could be really useful for reliable support of the diagnosis for hyperacute cases.

As a matter of fact, SM was realized as a standalone application written in C/C++ with DICOM viewer functionality, capable to work in standard RIS/PACS environment. Image review procedure of regular CT scans is synchronized in visualization to the same number of images obtained by SM processing. These results are displayed at additional diagnostic view, independently form basic diagnostic station visualization. In spite of four complementary SM semantic maps of brain tissue hypoattenuation distribution, SM interface provides also additional visualization of segmentation results together with corresponding preview of original CT data.

1.4. STROKE MONITOR EFFICIENCY

Stroke Monitor efficiency was repeatedly verified experimentally during last few years of ongoing algorithm development and optimization. The latest results were obtained on large group of 95 patients admitted to a hospital with symptoms suggesting stroke. In this group no direct hypodense signs of hyperacute ischemia were found on initial nonenhanced CT examinations of the head within first hours from stroke onset (average time between the onset of symptoms and the CT examination was 4.48 hours). Retrospective image review was performed independently at a diagnostic workstations of two radiological centers by four blinded neuroradiologists, experienced in the interpretation of stroke CT images in two configurations: without CAD and with CAD. Analysis of ROC curves indicates that SM had statistically significant, positive impact on detection of stroke for all radiologists participating experimental evaluation of diagnosis performance. Sensitivity and specificity of acute stroke detection for the readers was increased by 30% and 4%, respectively. But improved level of sensitivity was only 50% (with specificity up to 80%). More detail analysis of SM efficiency can be found in [10].

Although experimental verification of the SM confirmed its diagnostic usefulness, some algorithmic and procedural limitations still exist. Only a half of test stroke cases was detected what means still very limited diagnostic efficiency. Further optimization requires detailed analysis of common processing errors and their sources. Analysis of human and computer error causes leads to conceptual verification of assumed computer assistance procedure.

2. ANALYSIS OF STROKE MONITOR EFFICIENCY

The main goal of presented considerations was focused on identification, analysis and explanation of the nature and causes of common mistakes made by radiologists using SM. Detailed and reliable exploration of these mistakes demonstrated and expressed weak points of SM-oriented diagnostic procedure. Results of this analysis allow formulating general and particular directions for further computer-assistance concept development.

2.1. SELECTION AND ANALYSIS OF FALSE POSITIVE CASES

For that purpose of SM efficiency analysis we analyzed results of different test and verification procedures performed on dataset of about 100 cases during ongoing process of SM development and optimization. All studies were reviewed by seven radiologists with diversified experience in the interpretation of stroke CT images. Finally we selected 13 cases which turned out to be sources of false positive (FP) indications, to verify whether SM could unfavorably affect this decision.

At the beginning all selected studies and test results were reviewed and confronted in order to determine real number of all independent, different false positive indications across all cases as well as their incidence related to total number of cases and total number of FP. Finally this gave us total number of 23 standalone false positive errors indicated independently by all radiologists 29 times. Detail analysis is presented in part I of Tab. 1.

Table 1. Statistics of FP errors for selected 13 studies. Used abbreviations: case ID – case identification signature; NR_FP – number of radiologist who made FP in each case; case_FPTN – number of independent FP per each case; case_FPN – signature of independent FP in each case; NR_case_FPN – number of radiologist who made specific case_FPN in each case; case_FPN_type – common error type for specific case_FPN in each case.

part I			part II		
case ID	**NR_FP**	**case_FPTN**	**case_FPN**	**NR_case_FPN**	**case_FPN_type**
case3	1	1	FP1	1	1
case53	1	1	FP1	1	3, 4
case110	1	1	FP1	1	5
case112	2	2	FP1	1	1, 3, 4
			FP2	1	1, 2, 3
case113	2	2	FP1	1	5
			FP2	1	1,3
case114	2	2	FP1	1	1, 3, 4
			FP2	1	1, 3, 4
case120	1	1	FP1	1	5
case121	6	4	FP1	1	2, 4
			FP2	2	1,3
			FP3	1	5
			FP4	2	5
case122	1	1	FP1	1	5
case142	5	3	FP1	2	1,3
			FP2	2	3
			FP3	1	1
case147	2	2	FP1	1	3, 4
			FP2	1	1, 3
case157	4	2	FP1	3	1, 3
			FP2	1	1, 3
case164	1	1	FP1	1	1, 2, 3
TOTAL			**TOTAL**		
13	**29**	**23**		**29**	

2.2. REASONS OF COMMON ERRORS

Next all 29 FP indication were analyzed in order to establish and indicate possible sources of FP decisions. Based on that analysis we formulated 5 possible reasons of common errors made by radiologists using SM as a CAD tool. Moreover they can exists and influence the review process separately or jointly, forming complex cause and effect relationship.

2.2.1. IMPERFECT SEGMENTATION (TYPE I)

First common reason of FP indications is connected with imperfect segmentation process. Clearly noticeable low-density brain structures (e.g. sulci, prior ischemic scars, chambers, gurus) are not the subject of interest and should be omitted from processing. Unsegmented or partly-segmented compose false areas of evident hypoattenuation, which became especially clearly visible after SM processing. Example segmentation errors are presented on Fig. 3.

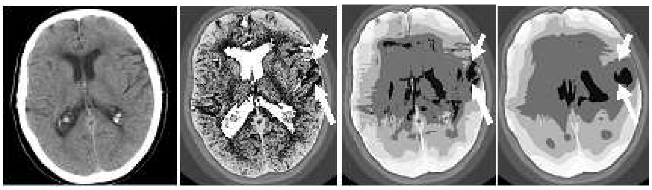

Fig. 3. Example of imperfect segmentation influence on SM indications. From left: original image, segmentation results, two forms of SM visualization. White arrows indicate unsegmented insular ribbon and corresponding false indications.

2.2.2. BRAIN STRUCTURE ASYMMETRY (TYPE II)

Norman human brain is nearly symmetrical. Presence of stroke (ischemic region) disturb brain tissue density locally (produce a hypoattenuation area). This local disorder in normal tissue density symmetry (normal brain symmetry) is extracted and enhanced by SM processing algorithm. Specific form of SM visualization project this information into four simplified forms of tissue density semantic maps, which much more clearly represent tissue density distribution. Unfortunately many times non-optimum scanning and acquisition conditions (e.g. patient asymmetry) result in brain structures asymmetry in successive frames. SM is very sensitive for an form of asymmetry. Even such a technical imperfection, which lead to natural form of tissue density asymmetry, can be captured, enhanced and thus sometimes easily misinterpret. Suggestive examples are presented on Fig. 4.

2.2.3. LACK OF SLICE-TO-SLICE CORRELATION (TYPE III)

Generally Stroke Monitor processing algorithm work independently frame by frame across whole CT volume. Standard interpretation process also assume successive frames analysis. Even though stroke area most often covers considerable part of brain. It is well-founded to assume that hypodensity changes should be visible consequently on few following slices. Moreover these changes should be correlated according to their size and localization. Review procedure should thus always take into account slice-to-slice correlation of local ischemic findings. Singular, uncorrelated changes on SM visualization maps should be considered as not much reliable and sometimes casual. Examples are presented on Fig. 5.

2.2.4. ARTIFACTS AND DIFFICULT LOCALIZATIONS (TYPE IV)

Sometimes non-optimum scanning and acquisition conditions (e.g. patients movement) result in characteristic and unpleasant artifacts like bone and movement artifacts. These artifacts are often localized and present in relatively small and diagnostically difficult cerebellum region. As a result common false indication can be observed (see Fig. 6).

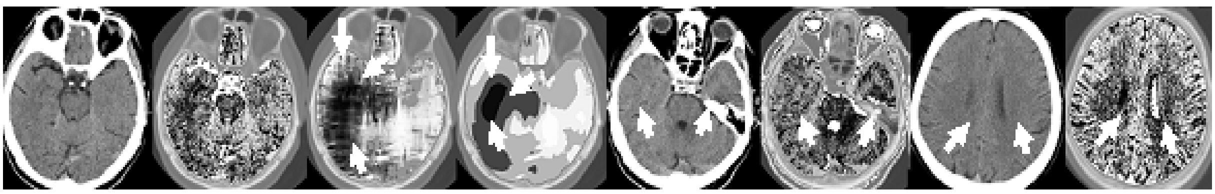

Fig. 4. Example of false indication (see white arrows on image 3 and 4) due to brain structure asymmetry. This asymmetry is much more clearly seen on other slices (white arrows indicate evident brain structures asymmetry on images 5-8). From left we can see original image, segmentation results, two forms of Stroke Monitor visualization maps, two other slices and their segmentation results.

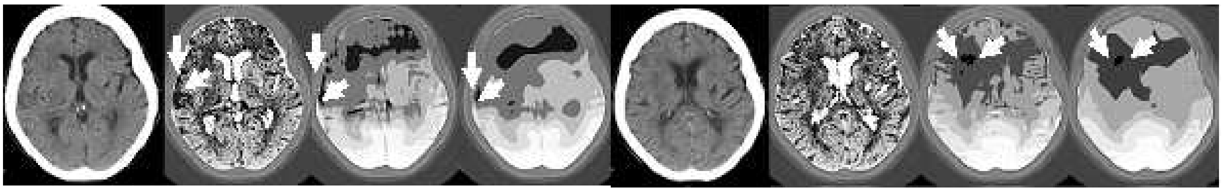

Fig. 5. Examples of unreliable indications due to lack of slice-to-slice correlation. From left we can se original image, segmentation results and two forms of SM visualization maps. White arrows indicate two independent false positive indications (made separately by two radiologist) on adjacent slices. We can see that this indications are standalone and do not correlate with each other. It is worth to notice that first false positive indication is also a result of imperfect segmentation (see white arrows on segmentation result image).

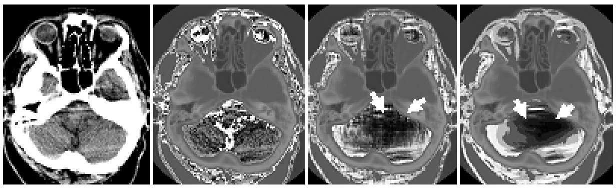

Fig. 6. Example of false positive indication (white arrows) as a result of strong artifacts covering diagnostically difficult cerebellum region. From left: original image, segmentation, two forms of SM visualization.

2.2.5. UNFORCED AND UNEXPLAINED ERRORS (TYPE V)

The last group of typical errors reasons concern unforced and unexplained errors. Sometimes false positive indications occur as a result of radiologist confidence to their own knowledge and experience. Their conviction of possible stroke indication is probably based on some early indirect findings. These suspicions are not confirmed be SM so we classify this errors as unforced. From the other hand we can also find cases where SM gives quite clear indication of possible ischemia in region where in fact detail review procedure reveal some subtle obscuration of brain tissue. Although SM suggestion seems to be reliable it won’t find any confirmation in follow-up study. Examples are presented on Fig. 7.

2.3. COMMON ERROR STATISTICS

Based on presented above common error source categorization we classified all 29 FP indications. Each of them was labeled with the most appropriate error source types. Detail common error sources statistic is presented in second part of Tab. 1.

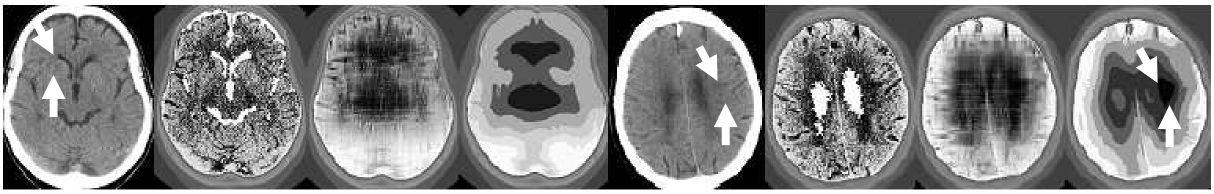

Fig. 7. First example shows false positive indication (see white arrows on original image) based probably on radiologist knowledge and analysis of indirect stroke findings. From left: original image, segmentation results, two forms of Stroke monitor visualization. False indication is not confirmed by SM. Second example shows FP confirmed by SM indication (see white arrows). Although this indication corresponds to subtle obscuration of brain tissue visible on original image (indicated by white arrows) it has no confirmation in follow-up study.

The most common reason (14 times) is type III related to lack of slice-to-slice correlation. Similarly frequent (11 times) is type I connected with imperfect segmentation. Moreover this two error reasons occur also most often together (10 times) – this is typical and common situation where imperfect segmentation on single slice effects with lack of slice-to-slice correlation in SM indications. Other FP reasons occur less frequent – type II (asymmetry) 3 times and type IV (artifacts) 6 times. Type III and type IV occurs jointly 5 times. Six FP were classified as type V (unforced and unexplained).

3. STROKE MONITOR ROADMAP

3.1. IMPROVED SEGMENTATION

Presented statistical results reveals weakness of segmentation algorithm used in SM. If segmentation results were better analyzed and correlated with SM indications, much more false indications would be avoided. The simplest way to reduce FP is than to pay much more attention to segmentation results images presented simultaneously in SM interface during standard review procedure. Nevertheless it seems obvious that segmentation algorithm should be also improved for better automatic operation. The relevance of segmentation improvement was confirmed in experiment where for all 11 segmentation specific FP (type I) we individually adapted segmentation algorithm parameters. This way 8 FP indications were efficiently reduced (see examples on Fig. 8). Although there is still problem with automation and repeatability of such an adaptation procedure this development direction seems to be well-founded.

3.2. SOFTENING ASYMMETRY INFLUENCE

Reliable assessment and arrangement of any form of brain structure asymmetry index is quite problematic. Nevertheless rational usage of such an index can provide additional form of information augmented standard review procedure during working with SM, capable of avoiding errors in especially asymmetry cases. In Fig. 9. we present an idea of exploiting segmentation result as form of asymmetry measure. Two consecutive slice show false SM indications evolved as a result of brain structures asymmetry. If we compare asymmetry of segmentation results according to simulated brain symmetry line (white lines on segmentation result images) with asymmetry of SM indications we can easily noticed existing correlation.

High sensitivity level for brain structures asymmetry can by also soften by exploiting advantages of three dimensional multiscale processing. An attempt to use higher dimensional form of multiscale transformation (e.g. 3D wavelets, 3D curvelets) connected with volumetric nonlinear modeling of coefficients space seems quite promising.

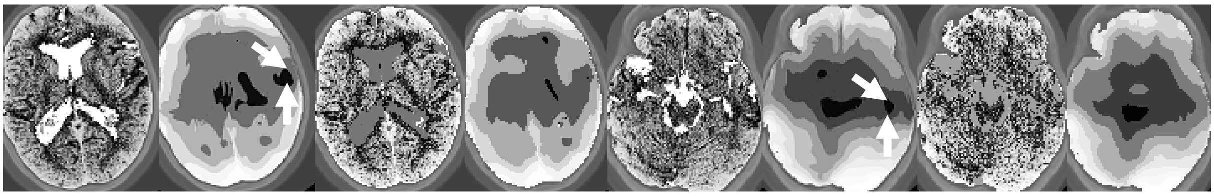

Fig. 8. Two examples of segmentation improvement. From left: original segmentation, FP indication (white arrows) on SM visualization, improved segmentation and SM visualization – false indications are efficiently reduced.

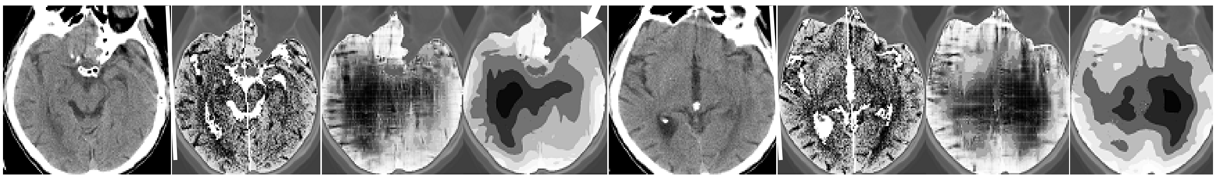

Fig. 9. Illustration of asymmetry measure based on segmentation result related to brain symmetry line. From left: original image, segmentation results with simulated brain symmetry line (white line), two forms of SM visualization. Existing correlation between segmentation asymmetry and SM indications asymmetry is obvious.

3.3. EXPLOITING SLICE-TO-SLICE CORRELATION

As it was mentioned above it is very important to exploit slice-to-slice correlation between Stroke Monitor indications. This can be done in form of standard 2D review analysis where we can observe adjacent slices related to suspicious SM indication. If any correlation related to localization and size of indications can be found we can assume higher reliability of such an indication. Additional possibility simplifying slice-to-slice correlation analysis lie in 3D visualization of relevant semantic information. Introduction of additional 3D visualization forms of SM semantic maps, localized in standard SM review interface would probably essentially facilitate analysis of volumetric, slice-to-slice correlations. Suggestive example of such a 3D visualization (prepared in MeVisLab environment [4]), which confront spatially correlated TP stroke indications with uncorrelated FP, is presented in Fig. 10.

4. CONCLUSIONS

Combining the effects of standard CT scans review with SM assistance used as a CAD tool provided a better diagnosis of acute ischemic stroke. According to all verification procedures and opinions, SM semantic visualization improved the diagnosis of early ischemic changes because of increased visibility and clarity of hypodense signs. Reliable display of hypodense signs can considerably accelerate the diagnosis of hyperacute ischemic stroke because of increased sensitivity. However some FP indication were also noticed during verification tests. FP have to be avoided since treating ineligible patients with intravenous thrombolysis is associated with an unacceptable risk of hemorrhage and death. Presented statistical analysis of common error sources allowed to formulate some ideas for further improvements, which can lead to limitation of FP indications. Proposed SM improvements ideas and their simulation and experimental verification confirm validity of further SM development direction.

Fig. 10. Example 3D visualization of SM semantic map. On the left side example successive slices of TP indication. High slice-to-slice correlation between regions with asymmetrically lower tissue density is clearly visible. On the right side example successive slices of FP indication. Lack of correlation between suspicious ischemic regions is evident.

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