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## Effectiveness of CT Computed Tomography Perfusion in Diagnostics of Acute Ischemic Stroke

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### Background:

Stroke is the third most common death reason after the cardiovascular disorders and cancer. Cerebral ischemia is a pathology that stems from a decrease in cerebral perfusion.

Computed Tomography Perfusion (CTP) is an additional method to the conventional Computed Tomography (CT) that could be performed by using developed softwares, in a short period of time and with a low risk of complications. CTP not only allows early detection of cerebral ischemia but also gives valuable information on the ischemic penumbra which are very important in early diagnosis and treatment.

Acute Ischemic Stroke (AIS) can be cured by trombolytic treapy within 3–6 hours after symptom onset. Since rapid screening and accurate diagnosis increase the success of the treatment, the role of neuroradiology in acute ischemia diagnostics and treatment has become more important.

Our aim was to define CT skills in early diagnosis of AIS, to define its contribution to patient's diagnosis and treatment and to define its importance regarding patient's prognosis.

### Material/Methods:

We included 42 patients that presented to the emergency service and neurology outpatient clinic with the symptoms of acute cerebral incidence.

### Results:

In our study, we found that Cerebral Blood Flow (CBF) is 90.91% sensitive and 100% specific in examining ischemia.

### Conclusions:

Tissue hemodynamic data, especially sensitivity and specificity rates, which cannot be acquired by conventional CT and MRI methods, can be acquired by the CTP method.

### MeSH Keywords:

**Hypoxia-Ischemia, Brain • Multidetector Computed Tomography • Stroke**

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## Background

Acute ischemic stroke (AIS) is a common cause of mortality and morbidity all over the world. Researches show that acute ischemic stroke is on the 3<sup>rd</sup> place amongst causes of death [1]. Stroke, which is very common in the world, expands the health care costs. Considering this expansion, it is predicted that it will cost a lot by 2050. This makes acute ischemic stroke an urgent national problem [2].

While 87% of ischemias are arterial, most of the rest are hemorrhagic [3]. In recent years, it has been important for a patient to get early diagnosis and medical treatment as

it has a significant influence on patient's mortality and morbidity [3]. It is important that intravenous recombinant tissue plasminogen activator (rTPA) is introduced 3 to 4.5 hours following the ischemic stroke. It is 0–6 hours for intra-arterial treatment and 0–8 hours for mechanical treatment [3]. Advances in technology contribute to diagnostics and treatment of AIS. Methods of diagnosis and treatment of AIS, for which acute-term treatment and prophylaxis have become important because of the risk factors, are becoming widespread [4]. The fact that early imaging and accurate diagnosis increase the success in treatment has made the neuroradiologist's role in diagnostics and treatment of AIS more important [5]. For patients

who consult for AIS, computed tomography (CT) is applied to preclude bleeding, vascular incidents and tumor pathologies. Conventional CT is not only used for the preclusion of cerebral hemorrhage, but it is also a primary method for the detection of early symptoms of AIS [6]. With conventional magnetic resonance imaging (MRI) and CT scans, conducted pre and post contrast administration, irreversibly infarcted brain tissue cannot be distinguished from ischemic brain tissue (penumbra), which is under the risk of infarction [7]. Although conventional CT and MRI provide us with anatomical details, they do not give functional information on the dynamic process of ischemia and its elongation. So, perfusion imaging has become a significant method today [7]. While we can detect ischemia at an early stage with cerebral perfusion imaging, we can also obtain important details regarding the elongation and severity of ischemia of the brain tissue [6].

Our aim was to define Computed Tomography Perfusion (CTP) potential in early diagnosis of AIS, to define its contribution to patient's diagnosis and treatment and to define its importance on patient's prognosis.

## Material and Methods

Our study was conducted with a decree no. 07-2011-18 of the Medical Ethics Committee.

CTP was conducted after explaining and obtaining consent from relatives of 42 cases (**22 male and 20 female**, age range from 6 to 83 years) with no contraindications, who presented to emergency room and neurology clinic for an acute cerebral incident. First, CT was performed. In CT scans without contrast enhancement, bleeding and additional pathologies were eliminated. Early symptoms of ischemia were examined. Later on, CTP was applied to patients with no contraindications.

### Protocol

All examinations were made with a 64-row (VCT Xte Light Speed; General Electric, Milwaukee, USA) multidetector CT (MDCT).

We used section width of 5 mm, 120 kV and 160 mA on orbito-meatal plane as a conventional CT scan. CTP was detected for conventional CT and suspected areas for examination.

The CTP scan was performed by using an automatic injector, with a 5-second delay of intravenous, 300 mmol, 40 cc iodinated non-ionic contrast substance with a speed of 4 mL/sec, with 8 cm of examination area, sections of 5 mm, rotation speed of 1 sec, with 80 kV, 200 mA and with Volume Shuttle technique in 45 seconds with 276 images.

### Assesment process

For image analysis, images were sent to Advantage Windows working station. Analysis was conducted by using GE perfusion 4 software. With deconvolution method, time attenuation trajectories were made. Arterial input Regions-of-Interest (ROI) were placed automatically or to

the Middle Cerebral Artery (MCA), Anterior Cerebral Artery (ACA) and basilar arteries, (depending on our choice), and venous input ROIs were placed on the superior sagittal vein, internal cerebral vein and sigmoid sinus, depending on our choice. It was decided not to choose a morbid artery or vein.

CTP scan relies on successive images received from related tissue along the capillary bed, after the administration of a contrast agent into the vein [8].

From the dynamic images received after bolus injection of a contrast agent, an examination was made by creating mean transition time (MTT), cerebral blood volume (CBV), and cerebral blood flow (CBF) maps (Figure 1). Normal CBF value is  $85 \pm 23$  mL/100 gr/min. for cortical gray matter, 55–65 mL/100 gr/min. for white matter and 10–20 mL/100 gr/min for ischemic pneumbra [9].

In CTP, the goal is to put obtain the reduction in CBF and CBV and elongation in MTT (Figure 2).

Color maps of CBF, CBV and MTT were created by the software in less than a minute considering the given inputs.

The first analysis was made by a comparison of each hemisphere. Later, ROIs were placed on ischemic areas and on the opposite hemisphere by measuring the exact symmetry with the software to reach exact values of CBF, CBV and MTT.

While doing it, the most suitable threshold values were used, available in GE perfusion 4 software.

In the detection of penumbra and preservable tissue, "CT Perfusion with Tissue Classification" was used, which is available in GE perfusion 4 software.

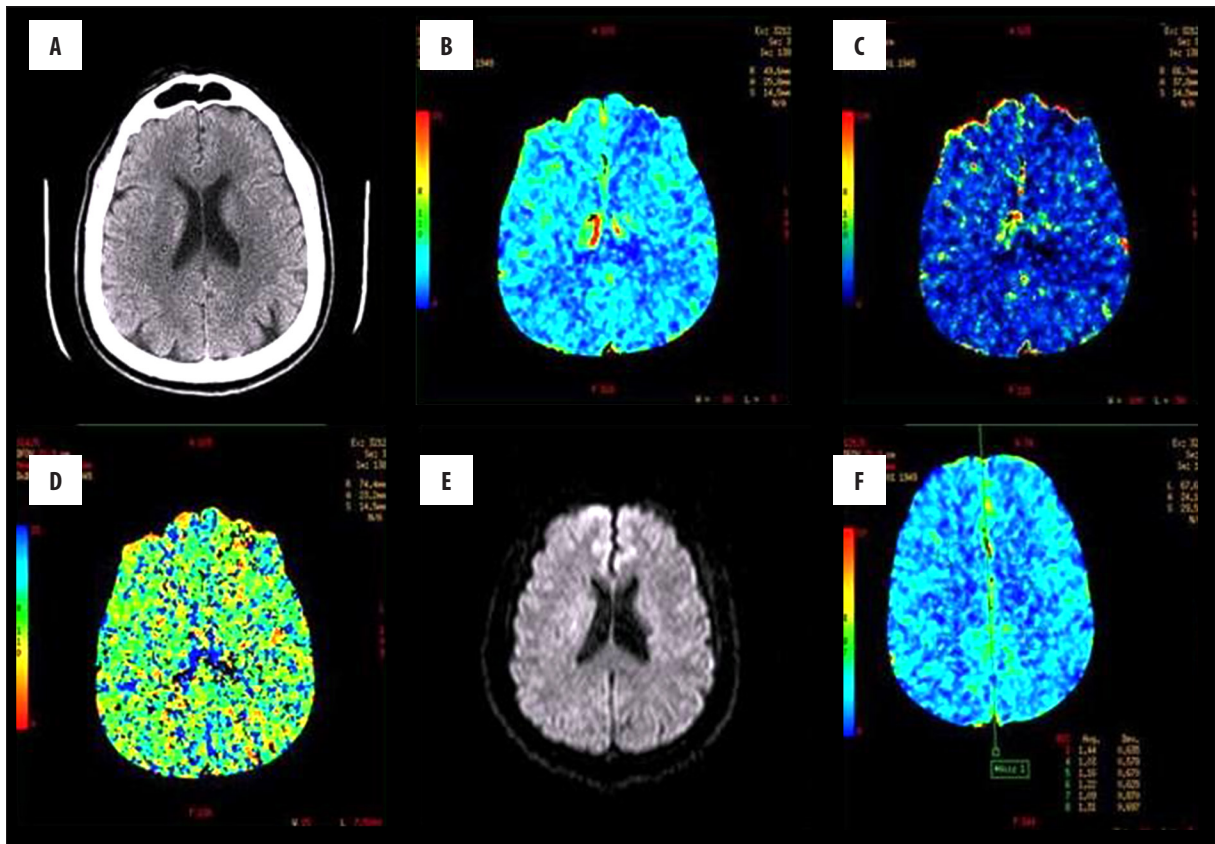
CTP findings were assessed comparatively with the diffusion MRI scans, clinical progress of the disorder and the later CT.

Ischemic area, detected by CTP, was accepted as genuine positive if shown in the follow-up CT and difusion weighted MRI (DW-MRI). It was accepted as genuine negative if there were no findings in either examination. It was accepted as false positive if detected in CTP but not shown in the follow-up examinations. It was accepted as false negative if not shown in CTP but shown in the follow-up examinations.

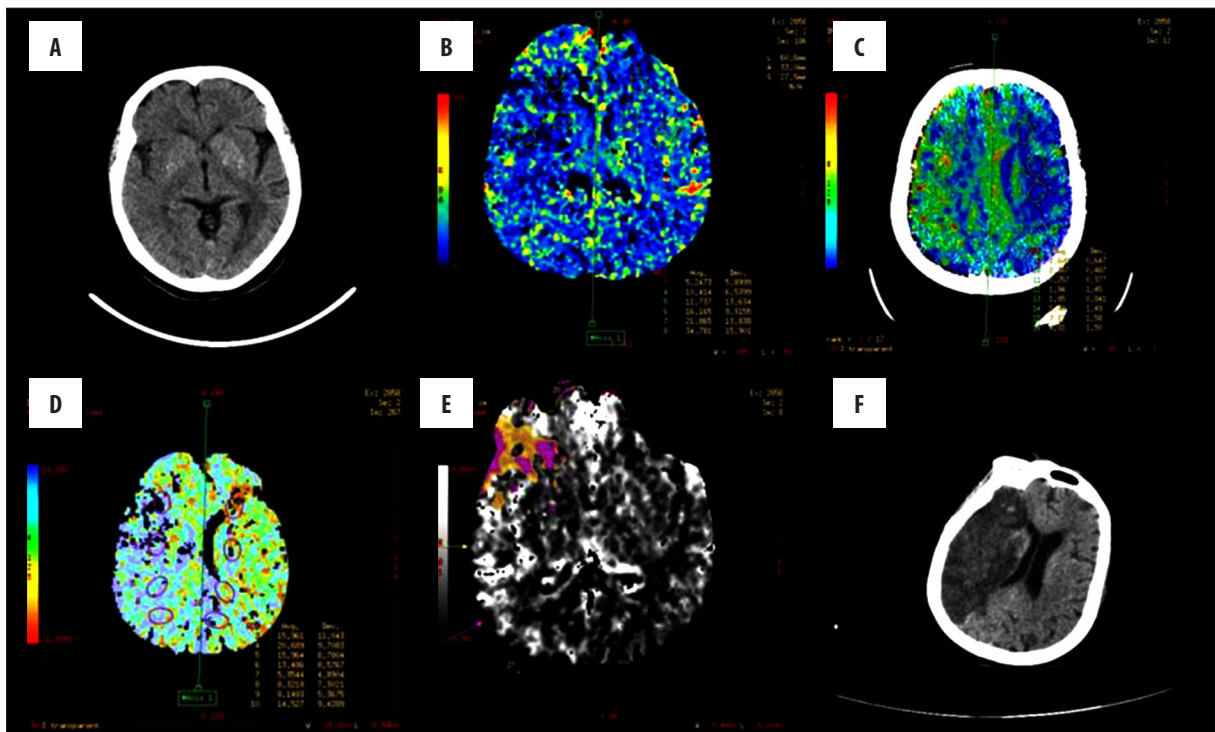
It was investigated if there was a statistical difference between specificity and sensitivity values of CBF, CBV and MTT maps and between perfusion maps and the follow-up CT.

### Statistics

In the used IBM SPSS Statistics version 21 (IBM Corp. © Copyright IBM Corporation and other(s) 1989, 2012) software, Miller Fisher's exact test was applied. The application was made for CBF, CBV and MTT. For each, there was a statistical change to detect ischemia.  $P \leq 0.05$ .



**Figure 1.** Normal case (A) Conventional CT scan, (B–F); CBV, CBF, MTT and diffusion-weighted MRI scan and symmetrical numeric comparative CBV rates are considered as normal.



**Figure 2.** A patient who presented with loss of consciousness (A); No definite change in patient's conventional CT (B, C); On the CBF map of the same case there is a significant fall on the right MCA in comparison to its symmetry (D); Significant elongation of MTT in the right MCA (E); In the CBV map, there is a small penumbra zone in the left MCA (F); Patient's conventional CT 2 days later, distinctive hypoattenuation and minimal hemorrhage areas.

**Table 1.** The cross tabulations and Chi-Square results of the cerebral blood flow and control diffusion weighted MR images and/or CT images.**A**

Control Imaging \* CBF

Crosstab				
Count		CBF		Total
		Ischemic	Non-Ischemic	
Control imaging	Ischemia	30	3	33
	Non-ischemia	0	9	9
Total		30	12	42

**B**

Chi-square tests					
	Value	df	Asymp. sig. (2-sided)	Exact sig. (2-sided)	Exact sig. (1-sided)
Pearson Chi-square	28.636 <sup>a</sup>	1	.000		
Continuity correction <sup>b</sup>	24.355	1	.000		
Likelihood ratio	30.149	1	.000		
Fisher's exact test				.000	.000
Linear-by-linear association	27.955	1	.000		
N of valid cases	42				

<sup>a</sup> 1 cell (25.0%) with the expected count less than 5. The minimum expected count is 2.57; <sup>b</sup> computed only for a 2×2 table.

**Results**

**Forty-two cases (22 male, 20 female)**, with ages ranging from 6 to 83 years, were enrolled. Thirty-three of the 42 cases had ischemia after control CT or DW-MRI. Thirty of them were observed to have lowered CBF. However, 3 of them did not change. Those 3 were accepted as false positive genuine negative. In our study, we found out that CBF is 90.91% sensitive and 100% specific in examining ischemia (Table 1A, 1B).

In a conventional CT examination of 42 cases, examined with the prediagnosis of AIS, 20 had no distinctive change. Nine of them did not develop ischemia. Twenty-two patients (66.7%) had pre-symptoms of ischemia in the first CT with different appearances. Later, by using CBV, penumbra zones were examined. Penumbra zone in different degrees were revealed. A reduction in the number of penumbra zones was observed proportionally to the arrival hour.

**Discussion**

Early radiological symptoms of stroke, which is a clinic term, are very important for the patient to determine which treatment method he/she will benefit from. Treatment of stroke has gained on importance with the

activation of rt-PA and with the advancement of potential neuroprotective agents; and became the most important factor in the success rate of early and accurate diagnosis [10–13].

In the assessment of AIS patients, conventional CT still keeps its position despite all modern scanning techniques. CT has such advantages as easy and fast application and availability. Besides, conventional CT contributes to precluding intracranial bleeding, tumor lesions and infections. It has been reported that within the first 24 hours, CT reveals an ischemic area in 60% of cases. That is why, CT generally shows ischemia easier after its symptoms become distinctive. This restricts early treatment [14,15].

Acute ischemic zones can be detected and localized better with conventional MRI in comparison to CT. As much as 80% of acute infarcts can be seen in standard spin-echo MR images received in the first 24 hours [15]. However, there may be difficulty in distinguishing between acute and chronic lesions. Moreover, it may be insufficient in distinguishing infarct zones and penumbra. Also, MRI is not that available, takes too much time and it is easily affected by movement. Diffusion-weighted MRI is a radiological scanning method which can reveal acute cerebral ischemia at an earlier stage. DW-MRI shows cerebral infarct minutes after it has started and it has a significant role in

the diagnostic assessment of stroke patients. However, in this method, infarct zone and penumbra cannot be distinguished clearly either [16–20].

In the assesment of AIS, such methods as Single-Photon Emission Computerized Tomography (SPECT) and Positron Emission Tomography (PET) show local blood flow and metabolism changes with high sensitivity and specificity. However, these changes are not thought to reflect the neuronal damage. In addition, these methods have low accessibility [21,22].

With all these methods being used, CTP, a dynamic CT method because of its limitations, is more accessible, gives results in minutes and is used routinely to monitor the dynamic process of ischemia and penumbra zone. Specificity and sensitivity of CTP are very high in ischemia [23].

CBF maps have shown that there is a good correlation between SPECT images and follow-up CT and MRI findings ( $r=0.81$ ) [24]. In a study of 12 patients, conducted by using a multidetector CT scanner, CBF maps were acquired by choosing a single-section plane and they showed that those maps gave accurate results in comparison to Stable Xenon CT. In that study, there was no statistical difference between CTP and Xenon CT CBF rates for those 12 patients [25].

In the diagnosis of CTP MCA occlusions, it was put forward that Digital Subtraction Angiography (DSA), which is the first-line option in monitoring insufficient perfusion and collateral nutrition, is beneficial [26].

In a study of 22 patients, conducted using a single-section plane, CTP was applied within the first 6 hours after the emergence of symptoms. Later, it was compared to the follow-up CT. The result showed a correlation between perfusion maps and follow-up CT findings [27].

In our study, specificity and sensitivity of CBF maps were 100% and 90.91%, respectively. It revealed that CTP has an acceptable role in early diagnosis of ischemia, detecting ischemic zones and calculating CBF maps.

We found 90.91% sensitivity and 100% specificity in 30 out of 42 patients, all of whom were subjected to CTP. In the follow-up CT and/or DW-MRI, the ischemia zones seen in CTP all developed infarct.

In the previous studies, as the perfusion CT scan was based on single-section plane assessment, areas outside the section could not be examined. With new-technology multidetector CT, cerebral perfusion examination (4, 8 and 12 cm) can be conducted in a shorter time. Also, the sensitivity rate increases with high accuracy.

With the available software, we distinguished the ischemic core and penumbra in areas with perfusion abnormality.

As we cannot distinguish the penumbra zone in a conventional CT and diffusion-weighted MRI, we saw that core and penumbra cannot be distinguished in the ischemia zone in comparison to CTP.

Within the light of these findings, when false negative results outside the perfusion CT section plane are precluded, sensitivity and specificity of CTP increases. As this ratio is close to the one in similar studies in the literature, we need studies with larger patient groups, for more accurate statistical data.

In the diagnostics of AIS, such modern monitoring methods as DW-MRI, perfusion MRI, SPECT and PET are used with high sensitivity and specificity rates. However, the fact that these methods are not as popular as CT, that they are much more expensive and that they are very sensitive to patient's movements (for DW-MRI and perfusion MRI) makes them disadvantageous.

As the majority of the patients with AIS pre-diagnosis are assessed with CT as the first-line method, we conducted dynamic CTP after about 3–5 minutes of intracranial hemorrhage and lesion ecartation in cases who presented to the emergency room with a prediagnosis of AIS.

## Conclusions

As a result, tissue hemodynamic data, especially sensitivity and specificity rates, which cannot be acquired by conventional CT and MRI methods, can be acquired by the CTP method. With the widespread use of MDCT which permits to acquire simultaneous images from more than one section plane and with more advanced softwares, we believe that dynamic CTP scan will obtain a more significant role in the early diagnosis and treatment of AIS.

## Statement

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