Université de Poitiers
Faculté de Médecine et Pharmacie

ANNEE 2019

THESE N°

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POUR LE DIPLOME D'ETAT DE DOCTEUR EN MEDECINE

(Décret du 16 janvier 2004)

Présentée et soutenue publiquement
le 6 septembre 2019 à Poitiers
par **M. Rémy VERGNES**

Is dynamic contrast enhanced computer tomography a valuable tool to evaluate the risk of delayed cerebral ischemia in unevaluable patient hospitalized for aneurysmal sub arachnoid hemorrhage?

COMPOSITION DU JURY

Président : Monsieur le Professeur Rémy GUILLEVIN

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Année universitaire 2018 - 2019

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CONTENTS

À la médecine, si dure, si exigeante, mais si passionnante.

« Les seules causes que l'on perd sont celles qu'on abandonne. »

« Tout problème à une solution.
S'il n'y a pas de solution, c'est qu'il n'y a pas de problème. »
Jacques Rouxel

ABBREVIATIONS

A-SAH: Aneurysmal Sub Arachnoid Hemorrhage

ACA: Anterior Cerebral Artery

ACoA: Anterior Communicant Artery

AJ: Anterior Junctional

BA: Basilar Artery

CBF: Cerebral Blood Flow

CBV: Cerebral Blood Volume

CTA: Computed Tomography Angiography

DCE CT: Dynamic Contrast Enhanced Computed Tomography

DCI: Delayed Cerebral Ischemia

DSA: Digital Subtraction Angiography

FLAIR+: Positive FLAIR

FLAIR-: Negative FLAIR

IC: Internal Carotid

IPH: Intra Parenchymal Hematoma

KTRANS: Volume Transfer Coefficient

L-ACA: Left ACA

MCA: Medium Cerebral Artery

MRI: Magnetic Resonance Imaging

MTT: Mean Transit Time

NCCT: Non-Contrast CT scanner

NT-SHA: Non-Traumatic Sub Arachnoid Hemorrhage

PCA: Posterior Cerebral Artery

PCoA: Posterior Communicant Artery

PICA: Posterior Inferior Cerebellar Artery

PJ: Posterior Junctional

R-ACA: Right ACA

ROI: Region Of Interest

SA: Superficial Anterior

SP: Superficial Posterior

TCD: Trans-Cranial Doppler

TTP: Time To Peak

V-: Territories without vasospasm

V+: Territories with vasospasm

VA: Vertebral Artery

WFNS: World Federation of Neurosurgical Societies

INTRODUCTION

Non-traumatic subarachnoid hemorrhage (NT-SAH) corresponds to extravasation of blood in the subarachnoid space and represents 5% of strokes. It affects relatively young patients (average 55 years), and is associated with a poor prognosis. The incidence of NT-SAH is high with overall mortality rates of 32% to 67%. One-third of survivors remain dependent (1). The cause of SAH is a ruptured aneurysm in 85% of cases (A-SAH) (2). Despite the progress made in the management of aneurysm rupture, patients remain exposed to many complications such as hydrocephalus, convulsion, hemodynamic and respiratory failure, delayed cerebral ischemia (DCI).

Whereas most of the outlined complications can be diagnosed by hemodynamical or general parameters, delayed cerebral ischemia depiction remains challenging. Indeed, the best clinical indicator of significantly reduced brain perfusion is the presence of new neurologic deficits. However, for patients in coma or sedated after initial phase of A-SAH there are no established parameters to orientate patients management. In fact, diagnostic accuracy for DCI depiction of both trans arterial arteriography (3) and trans-cranial doppler (TCD) (4) remains low.

The need for new imaging tools has led to outline the role of perfusion CT at admission to predict DCI (5). But a recent published study illustrated that perfusion on admission was correlated with clinical scores but not with DCI development (6).
Moreover, most of the patients are transferred from other hospitals after first line treatment including resuscitation supports (5,7,8) before perfusion CT.

Some other studies suggest to perform repetitive perfusion CT acquisition assess DCI which can be both fastidious for resuscitation teams and risky for severe patients (7,9).
It is necessary to use a new imaging technic to predict DCI during patients' clinical course.

Indeed, the physiopathology of the DCI remains unclear. For some, vasospasm, defined as a diameter reduction of at least one intracranial artery, is the main cause. For others, a deregulated

cascade of crase in cerebral microvasculature would be responsible for the formation of microthrombi in the capillaries of the cerebral parenchyma leading to cerebral infarction (10).
However, one study has highlighted that the involvement of cerebral autoregulation, which initially compensates vasospasm, seems to fail at day five (11), with a wide installation window ranging from 5 to 14 days (2).
DCI seems to be multifactorial, not always related to vasospasm region of the brain, and difficult to investigate after endovascular treatment. There is a need for an evaluation of both intra vascular parameters and capillary parameters.

Dynamic contrast enhanced CT (DCE CT) is a technic allowing to study intra vascular compartment but also extra vascular compartment. Among the estimated DCE parameters, Ktrans has proven to be reliable in MRI to predict DCI (12). MRI remains challenging for patient at risk with all the resuscitation devices.

Therefore, the aim of our study is to determine whether mean global Ktrans measured by DCE CT at day 6 could predict DCI in clinically unevaluable patients with aneurysmal subarachnoid hemorrhage.
With an underlying question of should all the clinically unevaluable patient undergo DCE CT at day 6 to predict the risk of delayed cerebral ischemia?

MATERIALS AND METHODS

This retrospective study was approved by the hospital ethics committee wich did not require patients informed consent since the patient management was not modified.

Patients:

Between January 2011 and January 2017, we analyzed and collected the data of all patients hospitalized at our institution consulting for non-traumatic sub arachnoid hemorrhage.

All consecutive patient's meeting the following criteria were included:
Over 18 years old,
Ruptured intracranial aneurysm,
Hospitalization in a unit of reanimation within 24 hours,
No neurological deficit on admission,
Patient sedated or with Glasgow score < 9 before aneurism treatment,
DCE CT performed in our institution protocol between the fourth and the eight day after inclusion,
MRI performed at 3 months following.

Exclusion criteria were:
Patients with chronic vascular occlusion,
Patients with neurosurgical management,
Patients with per procedural complication during endovascular treatment such as rebleeding, insufficient coiling according to Raymond's scale or already installed vasospasm,
Patients with a DCE CT performed after treatment of DCI,
Patients with a new cerebral infarction from causes other than DCI.

Each patients file was analyzed and recorded.

Patient management was decided according to the established guidelines by a multidisciplinary team including neurosurgeons, specialist in neuro-anesthesia-resuscitation and interventional neuroradiologists (1,13–15).

Imaging Protocol:

CT protocol

All clinically non examinable patients hospitalized for ruptured aneurysm underwent a standardized CT examination at day 6 consisting in 3 systematic series: NCCT (non-contrast CT scanner), DCE CT (Dynamic Contrast Enhanced CT scanner) and CTA (CT angiography) from the aortic arch to the vertex.

All examinations were performed on a CT scanner with DCE technology (Philips B40, Philips Medical, Eindhoven, Nederland, commissioned in 2003).

The contrast product used for the protocol was a low osmolality nonionic tri-iodinated monomer (Iomeprol 400 mg I/ml, Iomeron®400, Bracco, Milan**,** Italy).

NCCT:

NCCT was obtained from the vertex to the second cervical vertebra (C2), with the following parameters: slice thickness 3/3 mm (0.625 mm); pitch: 0.5; rotation time: 0.4 sec; 120 kV; automated mAs modulation (300 mA); reconstruction: 3/1 mm (1.5 mm).

DCE CT:

DCE CT was performed in the following way: centering was done manually by the manipulator, at the height of the central gray nuclei, avoiding to overlay the acquisition box with the surgical clip or coils, sources of radial artifacts. The box Length was 4 cm. The posterior fossa was systematically excluded from the analysis because of beam curing artifacts.

It was realized before the CTA, after injection of 40 ml of Iomeron®400 at a rate of 5 ml/sec, with a 6 seconds delay. A bolus of iso-osmolar saline solution of 50 ml was consecutively injected with a flow rate of 5 ml/sec thanks to an automatic contrast injector (Medrad®, Warrendale, USA). The following parameters were: 8 slices, thickness 5 mm; pitch: 0.5; 80 kV; automated mAs modulation (150 mA).

CTA:

CTA was obtained from the level of the left cardiac atrium to the vertex, after injection of 60 ml of the same contrast media, at a rate of 4 ml/sec, with the region of interest (ROI) in the internal carotid at C1, and an automatic departure of the acquisition at 150 Hounsfield Units. A bolus of iso-osmolar saline solution of 30 ml was consecutively with a flow rate of 4 ml/sec.
The examination was performed using the following parameters: slice thickness 0.75/0.5 mm (0.625 mm); pitch: 1; 120kV; automated mAs modulation (350 mA); reconstruction: 0.75/0.5 mm (0.67 mm).

MRI:

The control MRI was performed by an axial FLAIR sequence in 5 mm sections in 3 differents devices according to the availability: Magnetom Verio 3 Tesla, (Sequence TR: 8500 ms; TE: 103 ms) (Siemens, Erlangen, Germany); Intera 1.5 Tesla, (TR: 6000 ms; TE: 140 ms), (Philips, Eindhoven, Nederland); Optima 1.5 Tesla, (TR: 9000 ms; TE: 140 ms), (General Electric, Boston, USA).

Image analysis:

DCE CT:

Post processing was performed on a dedicated neuro imaging station Olea Sphere software, 2.2 version (Olea Medical, La Ciotat, France, 2016).
Olea Medical software deconvolution method is based on fast truncated Singular Value Decomposition (e.g. sSVD, cSVD, oSVD. Here oSVD was use).
This software especially allowed an automatical reproduction of regions of interest (ROI) and performed sampling of each territory: same area, same shape and same localization.
It allows to obtain 5 parametric maps based on the extended Toft modeling: volume transfer coefficient (Ktrans), mean transit time (MTT), time to peak (TTP), cerebral blood flow (CBF), cerebral blood volume (CBV).
Fig. 1a et 1b: *Parametric maps based on the extended Toft modeling*

The arterial input function was defined automatically from the A2, M2, M3 segments and the venous exit function from the right sinus, internal cerebral veins, cortical veins, Galen vein.

These maps were qualitatively analyzed by one general radiologist (5 years of experience) and one neuroradiologist (10 years) to assess good quality.

The quantitative analysis was standardized by the automatic placement on each of the 8 cutting levels, 7 contiguous ROI corresponding to 5 vascular territories (including white matter and gray matter) in each hemisphere: anterior cerebral, medium cerebral (superficial anterior and posterior; deep), posterior cerebral, junctional anterior and posterior.

Mean global Ktrans was calculated using average of the Ktrans of the 8 cuts for each territory and recorded as it was our main study parameter.

Fig.2: *Automatically reproduction of regions of interest (ROI, 0 to 13) in the section 1 to 4*

Fig. 3: *Automatically reproduction of regions of interest (ROI, 0 to 13) in the section 5 to 8*

The contouring of the vascular territories has been carried out in accordance with the tomodensitometric guide for the identification of the vascular territories of Damasio.

NCCT and CTA:

The NCCT and CTA treatment was performed on the Mc Kesson workstation in comparison with NCCT and CTA performed on admission and digital subtraction angiography (DSA) performed during endovascular treatment.

An angioscanographic vasospasm was evaluated on the endings of the internal carotid artery, on the segments A1 and A2 of the anterior cerebral artery, on the segments P1 and P2 of the posterior cerebral artery, on the segments M1 and M2 of the medium cerebral artery and on the basilar trunk, scored as follows: 0 = None ; 1 = <50% ; 2 = >50%.

MRI:

Delayed cerebral ischemia:

DCI was defined according to established consensus (16) :

- Cerebral infarction identified on MRI, after exclusion of procedure-related infarctions and absent in the early 24 hours imaging control.
- Clinical outcome in living patients with reference to the modified Rankin score at the 3 month control visit performed by a neurosurgeon.

Presence of FLAIR hypersignals of cortico-subcortical or lacunar areas were recorded by the radiologist and compared to the initial imaging (considered as the baseline). If FLAIR signal was positive without relevant abnormalities recorded on the base line nor procedure-related complications, FLAIR hypersignal was considered positive (FLAIR+). Topography of the FLAIR+ lesion was recorded according the DCE CT reading grid methodology by considering 8 stackable MRI sections in the 8 DCE CT sections and their 14 ROI corresponding to the 5 vascular territories described above.

Statistical Analysis

We used the non-parametric Wilcoxon-Mann-Whitney statistical test to compare mean global Ktrans of FLAIR+ and FLAIR- patients.

RESULTS

Population characteristics:

Patients characteristics are summarized in ***Table 1:*** *Population characteristics*

28 patients were enrolled retrospectively in the study. Three were excluded due to unevaluable imaging follow up.

Of the remaining 25 patients, sex ratio was 0.47 (n=17 women, 68 %; n=8 men, 32 %), aged from 30 to 77 with a median age of 54.

All included patients were hospitalized in a resuscitation unit with underlying diagnosis of A-SAH.
None of the patients were clinically evaluable, with a Glasgow Score lower than 9. The average Glasgow Score at admission was 4.2 (standard deviation was 1.65).

No patient had a history of previous neurological deficit.
DCE CT was performed on a median time of 6 days. Control imaging was performed within 2 to 4 months (average 3.1 month, standard deviation 1.76).

The WFNS score was 5 in 20 patients, and 4 in 5 patients.
Fischer Scale was 4 in 24 patients and one patient of the FLAIR+ group had a Fischer Scale of 3 (4%).

Descriptive analysis

Standard analysis (NCCT and CTA):

Aneurism topography:

N= 2 (8%) internal carotid (IC), N= 10 (40%) anterior communicant artery (ACoA), N= 6 (24%) middle cerebral artery (MCA), N= 0 (0%) posterior cerebral artery (PCA), N= 0 (0%) basilar artery (BA), N= 0 (0%) A2 segment of anterior cerebral artery (ACA), N= 3 (12%) V4 segment of vertebral artery (VA), N= 1 (4%) posterior inferior cerebellar artery (PICA), N= 3 (12%) posterior communicant artery (PCoA).

Aneurism treatment:

All N = 25 patients underwent radiological interventional aneurysm embolization.

Intra parenchymal hematoma:

Present in N= 10 patients; N= 2 (33%) in FLAIR+ patients and N= 8 (42%) in FLAIR-.

Vasospasms:

15 artery segments were analyzed in 25 patients.

Vasospasms was found on 52 arteries (13.9%); N = 24 arteries (26.7%) in FLAIR+ patients and N = 28 arteries (8.4%) in FLAIR- patients, distributed as follows:

Table 2: *Vasospasm repartition and severity*

Vasospasm was larger and more severe in FLAIR+ than in FLAIR-.

There was no significant difference in the topography of vasospasms.

Vasospasm treatment: ***Table 1:*** *Population characteristics*

FLAIR+

N = 2 (33%) received medical treatment.

N = 4 (67%) received interventional radiology treatment, N = 2 (50%) with angioplasty alone and N = 2 (50%) with angioplasty + chemical dilatation.

FLAIR-

N = 3 (37.5%) received medical treatment.

N = 5 (62.5%) received interventional radiology treatment, N = 5 (100%) with angioplasty alone.

Approximately two-thirds of patients in each group received interventional neuroradiology treatment.

DCE CT analysis:

112 ROI were analyzed in each patient, 2800 ROI per parameter.

Ktrans:

FLAIR+:

Mean global Ktrans (average of the Ktrans of the 8 cuts for each territory of the 14) ranged from 0.26 to 4.16 (mean: 0.87, median: 0.65, standard deviation: 0.60).

In territories with vasospasms, mean Ktrans ranged from 0.29 to 2.06 (mean: 0.98, median: 0.91, standard deviation: 0.42).

In territories without vasospasm, mean Ktrans ranged from 0.26 to 4.16 (mean: 0.78, median: 0.57, standard deviation: 0.71).

FLAIR-:

Mean global Ktrans ranged from 0.01 to 1.64 (mean: 0.52, median: 0.48, standard deviation: 0.27).

In territories with vasospasms, or with aneurysmal rupture in patients without vasospasm, mean Ktrans ranged from 0.01 to 0.95 (mean 0.48, median 0.49, standard deviation 0.20).

In territory without vasospasm and no aneurysm, mean Ktrans ranged from 0.01 to 1.64 (mean 0.54, median 0.47, standard deviation 0.29).

Others perfusion parameters

MTT:

FLAIR+:

Mean global MTT ranged from 6.11 to 9.31 (mean: 7.14, median: 7.09, standard deviation: 0.44).

In territories with vasospasms, mean MTT ranged from 6.76 to 9.31 (mean: 7.32, median: 7.18, standard deviation: 0.52).
In territories without vasospasm, mean MTT ranged from 6.11 to 7.58 (mean: 6.99, median: 6.93, standard deviation: 0.28).

FLAIR-:

Mean global MTT ranged from 1.74 to 8.68 (mean: 6.93, median: 6.95, standard deviation: 0.64).

In territories with vasospasms, or with aneurysmal rupture in patients without vasospasm, mean MTT ranged from 1.74 to 8.43 (mean: 6.78, median: 6.87, standard deviation: 0.90).
In territories without vasospasm and no aneurysm, mean MTT ranged from 5.45 to 8.68 (mean: 6.99, median: 7.01, standard deviation: 0.49).

CBV:

FLAIR+:

Mean global CBV ranged from 2.50 to 11.08 (mean: 5.97, median: 5.89, standard deviation: 1.49)

In territories with vasospasms, mean CBV ranged from 4.05 to 9.91 (mean: 6.21, median: 6.15, standard deviation: 1.21).
In territories without vasospasm, mean CBV ranged from 2.50 to 11.08 (mean: 5.77, median: 5.75, standard deviation: 1.67).

FLAIR-:

Mean global CBV ranged from 1.74 to 12.93 (mean: 5.98, median: 5.71, standard deviation: 1.70).

In territories with vasospasms, or with aneurysmal rupture in patients without vasospasm, mean CBV ranged from 1.74 to 11.08 (mean: 5.98, median: 5.89, standard deviation: 1.67).
In territories without vasospasm and no aneurysm, mean CBV ranged from 2.48 to 12.93 (mean: 5.98, median: 5.62, standard deviation: 1.72).

MRI analysis

FLAIR positive lesion:

FLAIR+ was found on N = 91 ROI (3.3% of all patients, 13.5% of ROI of FLAIR+ patients).

The FLAIR+ territories distribution is as follows: ***Fig.5 and Table 3:*** *Topography of DCI.*

Statistical analysis

Summarize statistical analysis is presented in ***Table 4:*** *Mean global values,* and ***Table 5:*** *Mean sub group values.*

Using a statistical non parametrical Mann-Whitney test, we found out a significative difference between mean global Ktrans analyzed in FLAIR+ patients and mean global Ktrans analyzed in FLAIR- patients (p=0.039).
We did not find, in this population, a significant difference between the FLAIR+ and FLAIR- patients on the MTT and CBV values, both on the global mean of all the ROI, and on the territories with vasospasm.
Subgroup analyzes in FLAIR+ patients did not provide a contributory result either.

DISCUSSION:

In this study we have shown that the measurement of mean global Ktrans on a DCE CT at day 6 can be a useful tool to diagnose clinically non evaluable patient at risk for DCI.
The other parameters were not statistically different, suggesting Ktrans is a better predictor for DCI in the conditions of our study. Moreover, mean global Ktrans calculation in the whole 8 slices explored allowed us to overcome the procedure related artifacts and sometimes complicated vasospasm depiction. Patients presenting elevated Ktrans at day 6 DCE CT should be considered at higher risk for DCI complications.

Unlike the position of the ROI on the DCE CT, the analysis of FLAIR and its superposition to the DCE CT is less standardized. Indeed, the sequences are made in 2D, with a different cut thickness and in a different orientation. Three dimensions FLAIR sequences on the 3 month control MRI could be performed and their reconstruction in the DCE CT cut axis should improve accuracy. Nevertheless, we used a reading grid to minimize the gap between DCE CT sections and MRI sections.

In addition, the DCE CT was limited to the analysis of 8 sections. On the 3 month MRI, some FLAIR+ regions could not be included in the analysis because they were located outside the equivalent box on the DCE CT. A DCE CT acquisition on the entire brain would limit false negatives. The use of standard layout and size ROI has allowed reliable and repeatable analysis.

Population
We included only non-clinically evaluable patients and excluded all potential risk factors for non-related SHA ischemia to limit bias.
This serie ultimately contained only 25 patients, while 640 were initially included and analyzed (3.9%). The desire to make a retrospective analysis as reliable and reproducible as possible has forced us to lower our threshold of inclusion to the maximum.

The Glasgow score >9, the absence of DCE CT or too much delay were the three main exclusion factors. Indeed, studying DCE CT in clinically non-evaluable patients was the goal of our study. As a result, patients with a higher Glasgow score, were not included.
Patients who did not receive a DCE CT could not be included, as well as patients who had received a DCE CT too late because, in their case, the DCE CT did not change the patient management. No patient received DCE CT on admission.

Although sharpened sample, it was comparable to 640 patients and the general population, both in terms of sex ratio and average age.
Some patients had small intra-parenchymal hematomas (40%). Although patients with large hematomas and cerebral hernias have been excluded, small hematomas can be source of focal artifacts and perfusion disorders.
Coils are also a source of artifact and can alter measurements. These 2 biases are independent of the study patterns and can be partially overcomed by the use of global measurement instead of focal measurement.

Intervention
The volume transfer coefficient, Ktrans, is a combination of tissue perfusion rate and permeability surface multiplication that varies with physiological conditions and acquisition conditions. The results obtained are dependent on the acquisition mode and do not allow comparison of results from two centers using different acquisition protocols. On the other hand, their robust parameters allow efficient comparisons between voxels of the same examination or between patients if the acquisition conditions are strictly equivalent (17).
As the article by Bivard and co. shows, perfusion results are subject to great variability among various deconvolution techniques but we used same mathematical modeling for all the patients to decrease inter observer variability (18).

We did not find statistical differences in patients' parameters such as MTT or CBV nor between territories with vasospasms and territories without vasospasm. This could be related to insufficient patient recruitment. But as previously mentioned, we restricted the number to limit the non-related to SAH ischemia. Moreover, as the patients underwent resuscitation and interventional intra-arterial procedures the risk for bias increase and population became more

heterogenous. It was then challenging to include non-clinically evaluable patient, with both similar management and clinical courses.

Schema inclusion:

In line with previous studies (19), we used the FLAIR sequence on 3 month later MRI, as gold standard to judge if DCI was present or not, in accordance with the DCI definition (16). There could be some procedure related or later ischemic event but it still remains the gold standard for DCI according to its definition.

Contrary to some studies that considered DCE CT on admission, this work provided a quick answer to the question of how to guide the treatment of SAH in non-evaluable patients by performing a DCE CT at day 6.

Clinical biomarker:

By showing that DCE CT performed in the acute phase of subarachnoid hemorrhage is a good predictor of DCI, our study joins previous studies such as Nagarra's in 2016 (19), Yuxia Duan in 2017 (5) and Fragata in 2019 (20).

Nonetheless, few studies focused specifically on Ktrans as a predictor of DCI but it was on MRI (12).

To the far of our knowledge and unlike the others studies, this is the first study to provide delayed data after day 6 (8,9,21).

As already tested in one previous study, global measurement seems to be an efficient biomarker allowing to get rid of most of the artefacts (20).

Although it was not the object of our study, it also seemed that using global mean measurement instead of manually segmented values could potentially increase inter and intra observer reproducibility. It also was technically easier and decreased the rate of inconclusive reports.

Vasospasms

As shown previously and observed in this study, vasospasm is not the only cause for DCI (22,23). It is always challenging to decide whether to treat or not with interventional angioplasty the clinically unevaluable patients presenting vasospasm based only on NCCT and CTA data. Procedure related artifacts, especially coils, can hide focal vasospasms and lead to false negative.

Using a whole brain Ktrans measurement would allow us to overcome these artifacts and therefore can be seen as another tool to help in vasospasm management, including decision for interventional angioplasty.

CONCLUSION:

In the conditions of our study, measurement of mean global Ktrans on a DCE CT at day 6 can be a reliable tool to diagnose clinically non evaluable patients at risk for DCI and therefore to define appropriate management, even if they do not have vasospasm on the CTA.
We did not find any statistical link between vasospasm and DCI, suggesting that vasospasm is not the only cause of DCI in the limit of our study.
Further study, with larger amount of patients, could assess and confirm our findings.

ANNEX

	FLAIR-	FLAIR+
NUMBER OF PATIENT	19	6
SEX RATIO M/F	0.46	0.5
MEDIAN AGE	54	57
DCE CT DELAY MEDIAN (DAY)	6	6
GLASGOW SCORE AVERAGE	4.2	4
WFNS		
5	15 (79%)	5 (83%)
4	4 (21%)	1 (17%)
FISHER		
4	19 (100%)	5 (83%)
3	0 (0%)	1 (17%)
MODIFIED FISCHER		
4	13 (68%)	5 (83%)
3	2 (11%)	1 (17%)
2	4 (21%)	0 (0%)
ANEURISM SITE		
IC	2 (11%)	0 (0%)
ACoA	7 (37%)	3 (50%)
MCA	4 (21%)	2(33%)
PCA	0 (0%)	0 (0%)
BA	0 (0%)	0 (0%)
A2 ACA	0 (0%)	0 (0%)
V4 VA	3 (16%)	0 (0%)
PICA	1 (5%)	0 (0%)
PCoA	2 (10%)	1 (17%)
ANEURISM TREATMENT		
INR	19 (100%)	6 (100%)
SURGERY	0 (0%)	0 (0%)
VASOSPASM		
N	8 (42%)	6 (100%)
> 50%	5 (26%)	5 (83%)
< 50%	3 (16%)	1 (17%)
VASOSPASM TREATMENT		
MEDICAL	3 (38%)	2(33%)
ANGIOPLASTY	5 (62%)	2(33%)
CHEMICAL	0 (0%)	0 (0%)
CHEMICAL AND ANGIOPLASTY	0 (0%)	2(33%)
IPH	8 (42%)	2(33%)

Table 1: *Population characteristics*

VASOSPASM SITE	FLAIR-	FLAIR+
A1 segment of left ACA	4 (14.3%)	3 (12.5%)
> 50%	3	2
< 50%	1	1
A2 segment of left ACA	2 (7.1%)	2 (8.3%)
> 50%	1	1
< 50%	1	1
A1 segment of right ACA	2 (7.1%)	3 (12.5%)
> 50%	1	2
< 50%	1	1
A2 segment of right ACA	2 (7.1%)	2 (8.3%)
> 50%	1	1
< 50%	1	1
M1 segment of left MCA	3 (10.7%)	3 (12.5%)
> 50%	3	0
< 50%	0	3
M2 segment of left MCA	1 (3.6%)	0 (0%)
> 50%	1	0
< 50%	0	0
M1 segment of right MCA	3 (10.7%)	4 (16.7%)
> 50%	2	2
< 50%	1	2
M2 segment of right MCA	3 (10.7%)	1 (4.2%)
> 50%	2	0
< 50%	1	1
P1 segment of left PCA	1 (3.6%)	0 (0%)
> 50%	1	0
< 50%	0	0
P2 segment of left PCA	0 (0%)	1 (4.2%)
> 50%	0	1
< 50%	0	0
P1 segment of right PCA	1 (3.6%)	0 (0%)
> 50%	1	0
< 50%	0	0
P2 segment of right PCA	0 (0%)	1 (4.2%)
> 50%	0	1
< 50%	0	0
Left internal carotid	4 (14.3%)	2 (8.3%)
> 50%	2	0
< 50%	2	2
Right internal carotid	2 (7.1%)	2 (8.3%)
> 50%	1	1
< 50%	1	1
Basilar artery	0 (0%)	0 (0%)
> 50%	0	0
< 50%	0	0

Table 2: *Vasospasm repartition and severity*

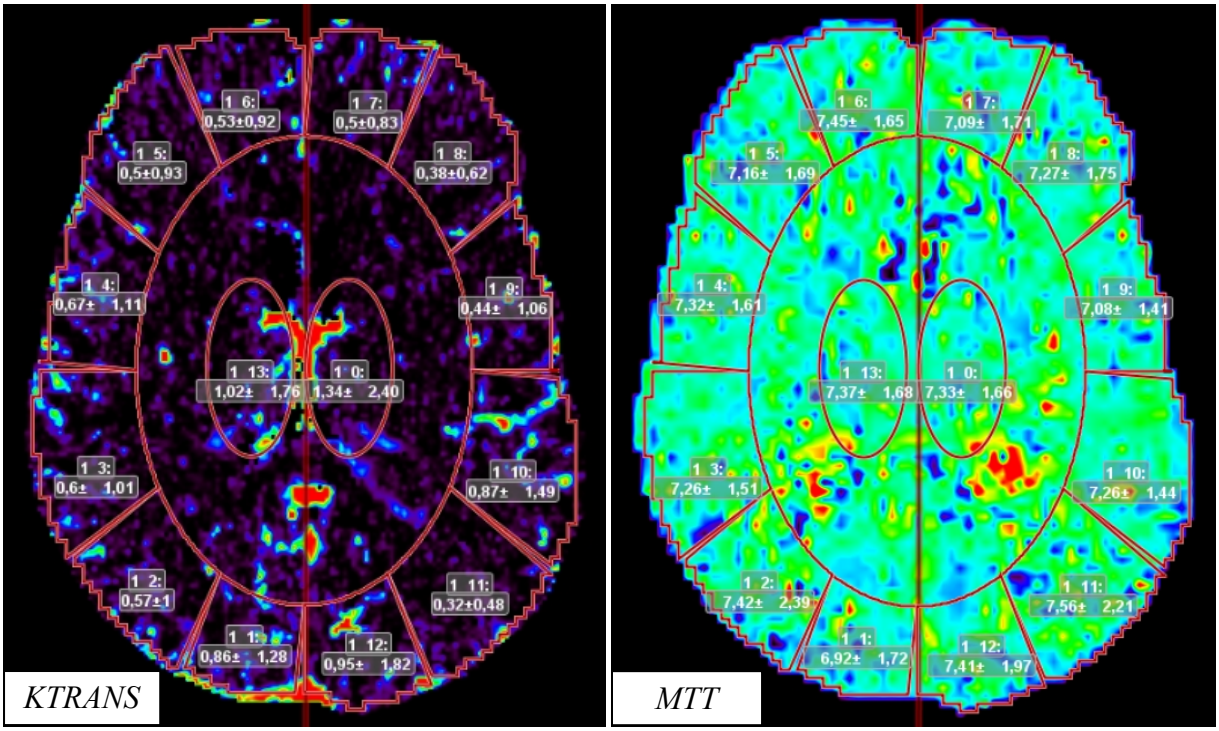

Figure 1a: *Parametric maps based on the extended Toft modeling*

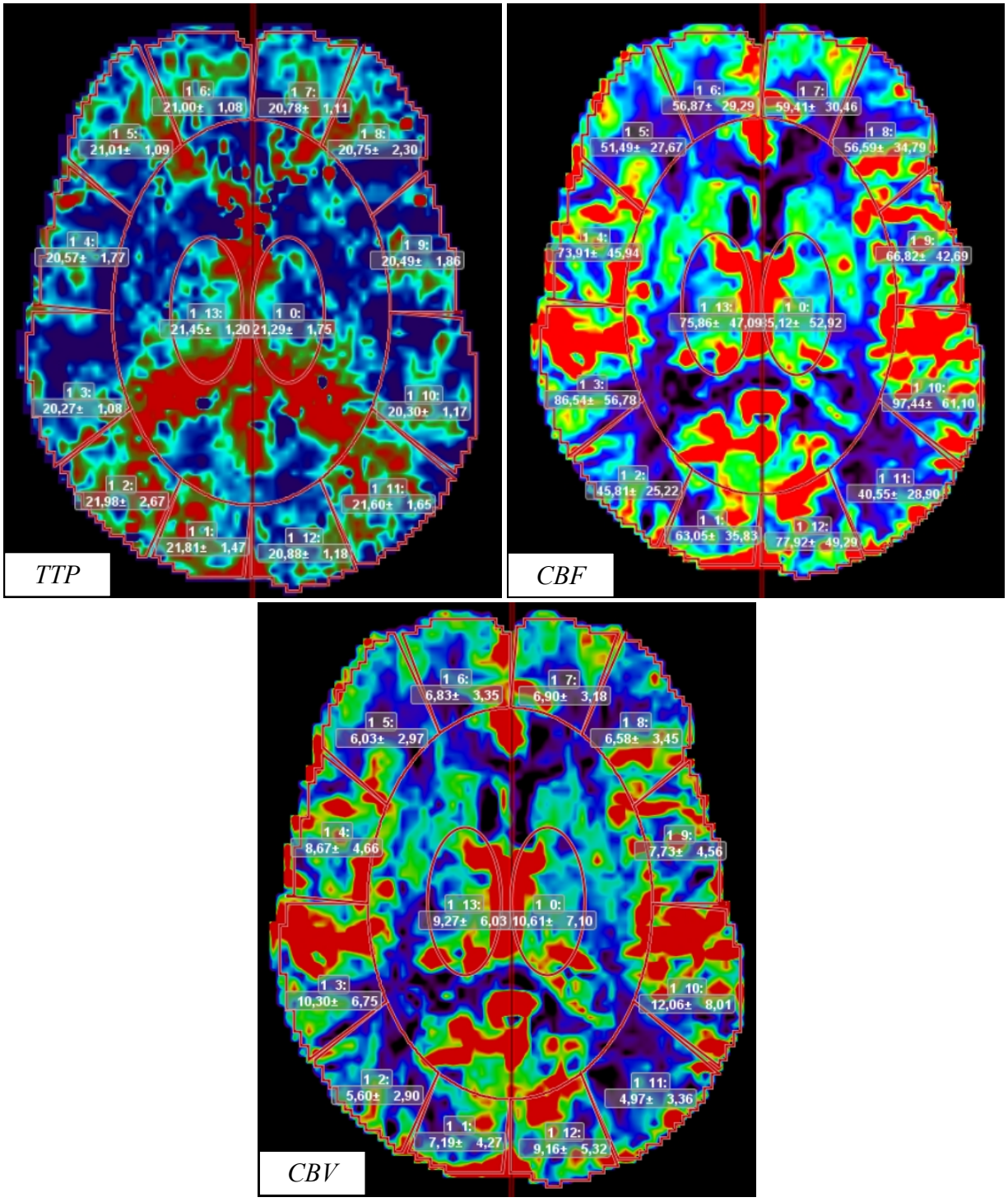

***Figure 1b**: Parametric maps based on the extended Toft modeling*

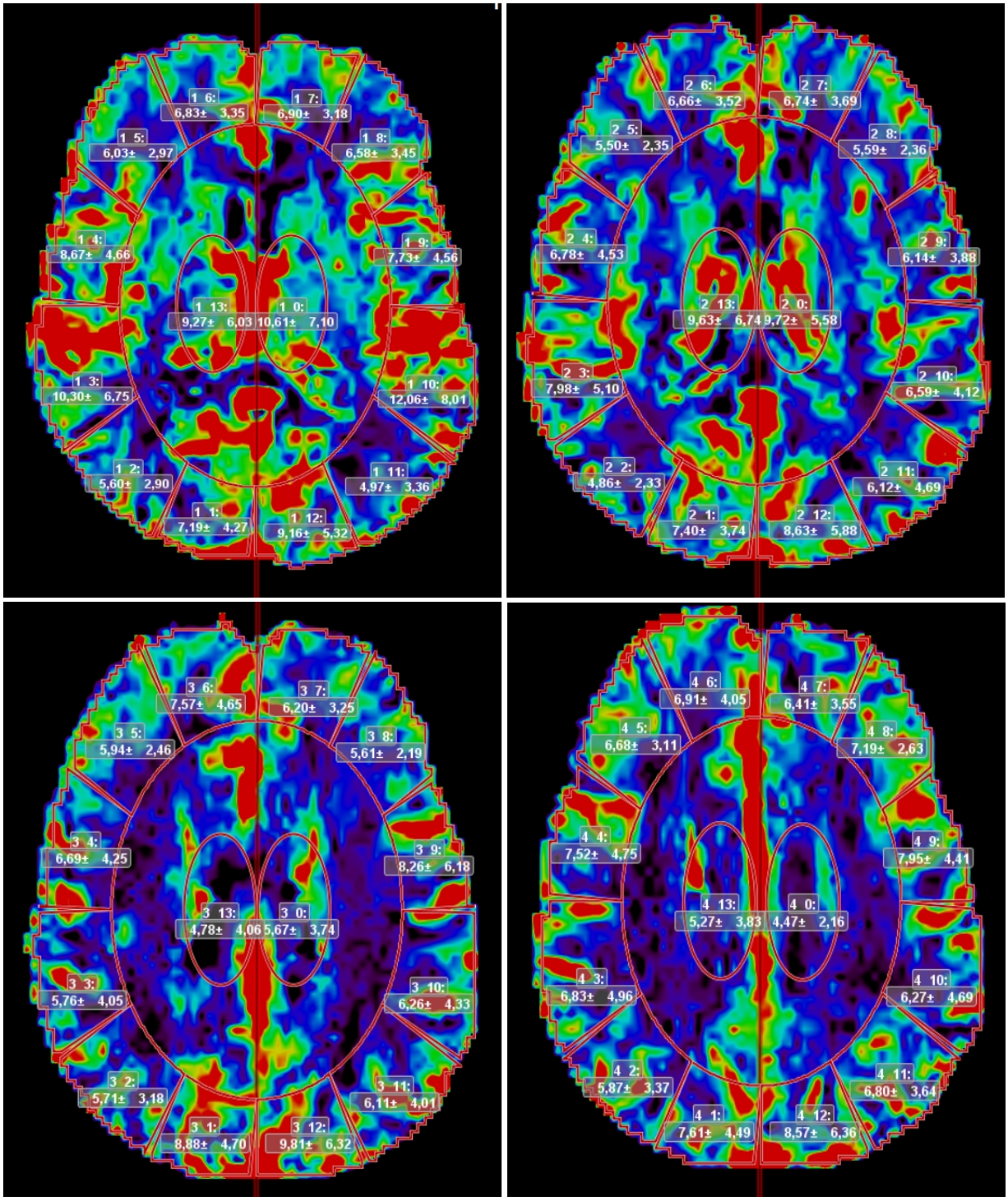

Figure 2: *Automatically reproduction of regions of interest (ROI 0 to 13) in the section 1 to 4*

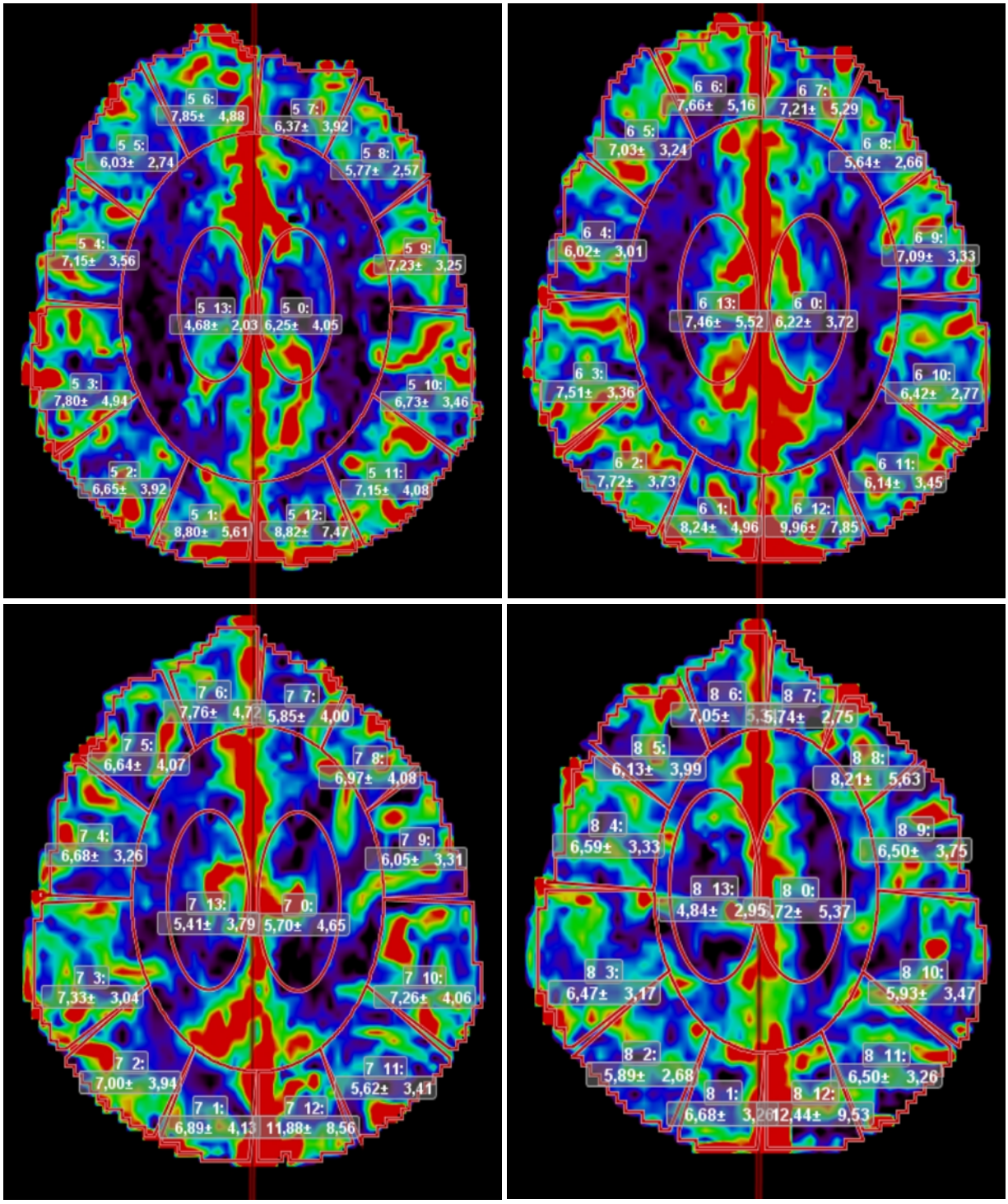

Figure 3: *Automatically reproduction of regions of interest (ROI 0 to 13) in the section 5 to 8*

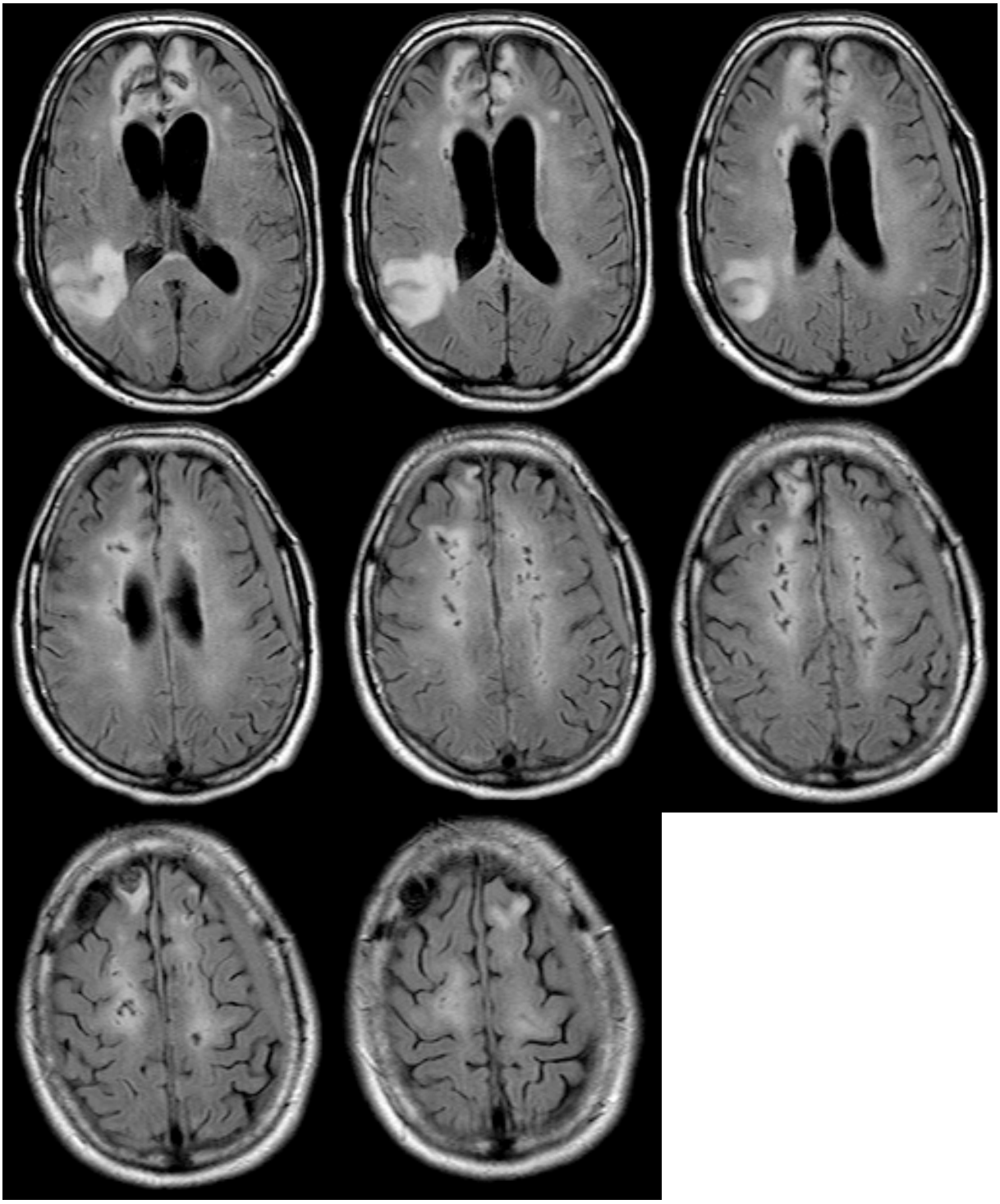

Figure 4: *Example of 8 stackable MRI sections in the 8 DCE-CT sections in a FLAIR+ patient*

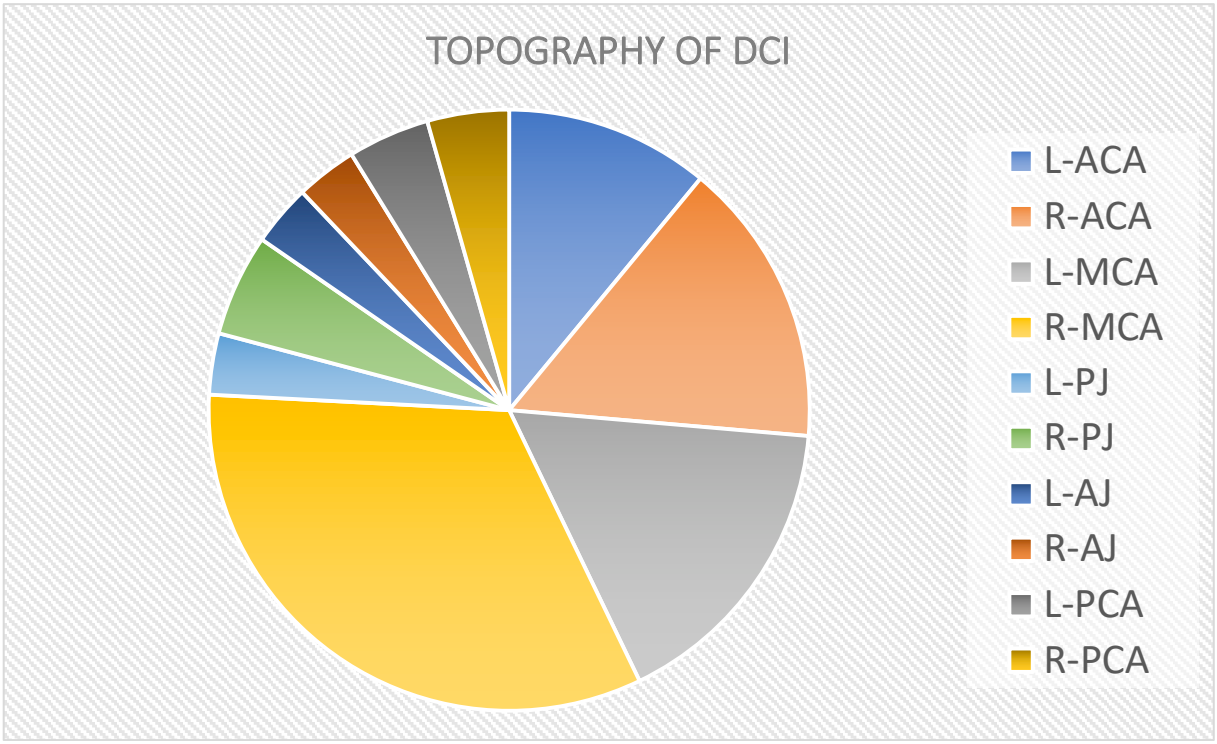

Fig.5: *Topography of DCI*

TOPOGRAPHY OF DCI	N
L-ACA	10
R-ACA	14
L-MCA	15
SA	*1*
SP	*5*
D	*9*
R-MCA	30
SA	*6*
SP	*11*
D	*13*
L-PJ	3
R-PJ	5
L-AJ	3
R-AJ	3
L-PCA	4
R-PCA	4
TOTAL	91

Table 3: *Topography of DCI*

	FLAIR -	FLAIR +	p-value
Ktrans	0,52	0,87	0.0039
MTT	6,93	7,14	NS
CBV	5,98	5,97	NS

Table 4: *Mean global values*

	FLAIR -	FLAIR +
Ktrans V+	0,48	0,98
Ktrans V-	0,54	0,78
p-value	NS	NS
MMT V+	6,78	7,32
MMT V-	6,99	6,99
p-value	NS	NS
CBV V+	5,98	6,21
CBV V-	5,98	5,77
p-value	NS	NS

Table 5: *Mean sub group values*

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ABSTRACT

INTRODUCTION

Non-traumatic subarachnoid hemorrhage represents 5% of strokes. For patients in coma or sedated after initial phase of aneurysmal subarachnoid hemorrhage (A-SAH) there are no established parameters to orientate patient management.

The aim of our study is to determine whether mean global Ktrans measured by dynamic contrast enhanced CT at day 6 could predict delayed cerebral ischemia (DCI) in clinically unevaluable patient with A-SAH.

MATERIALS AND METHODS

Between January 2011 and January 2017, all patients hospitalized at our institution consulting for non-traumatic subarachnoid hemorrhage were analyzed.

Inclusion criteria were: >18 yo, A-SAH, hospitalization in a unit of reanimation within 24 hours, no neurological deficit on admission, Glasgow score <9, DCECT performed in our institution protocol between the 4th and the 8th day after inclusion, MRI performed at 3 months following.

All patients had systematically: non-contrast CT scanner, DCECT and CT angiography.

5 parametric maps have been obtained: volume transfer coefficient (Ktrans), mean transit time, time to peak, cerebral blood flow, cerebral blood volume.

The quantitative analysis was standardized by the automatic placement of 112 ROI.

DCI was defined by a new cerebral infarction identified on MRI at 3 months on FLAIR sequence (FLAIR+ patient).

Primary endpoint: is there a link between alteration of Ktrans and occurrence of DCI?

RESULTS

25 patients have been included, 19 on FLAIR- group, 6 on FLAIR+ group.

Using a statistical non parametrical Mann-Whitney test, we found out a significative difference between mean global Ktrans analyzed in FLAIR+ patients and mean global Ktrans analyzed in FLAIR- patients ($p=0.039$).

We did not find in this population a significant difference between the FLAIR+ and FLAIR- patients on the MTT and CBV values, both on the global mean of all the ROI, and on the territories with vasospasm.
Subgroup analyzes in FLAIR+ patients did not provide a contributory result either.

CONCLUSION

Mean global Ktrans measurement on a single DCE CT at day 6 of A-SAH in unevaluable patients predicts the occurrence of DCI and could influence the management of patients at risk.

KEYWORDS

Subarachnoid hemorrhage - Delayed cerebral ischemia - Dynamic contrast enhanced CT - Ktrans - Clinically unevaluable patient - MRI - CT angiography

SERMENT

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En présence des Maîtres de cette école, de mes chers condisciples et devant l'effigie d'Hippocrate, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la médecine. Je donnerai mes soins gratuits à l'indigent et n'exigerai jamais un salaire au-dessus de mon travail. Admis dans l'intérieur des maisons mes yeux ne verront pas ce qui s'y passe ; ma langue taira les secrets qui me seront confiés, et mon état ne servira pas à corrompre les mœurs ni à favoriser le crime. Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses !
Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque !

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ABSTRACT

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