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QUANTITATIVE DYNAMIC PERFUSION CT BRAIN IN PATIENTS WITH STROKE

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ABSTRACT: Limiting irreversible ischemic insult to brain parenchyma is possible with early detection using perfusion CT. Studying time to peak (TTP), cerebral blood volume (CBV) and cerebral blood flow (CBF) in patients with stroke help to identify the risk areas. **METHODS:** Of the 72 patients with stroke, 20 patients with acute symptoms of less than 4 hours were selected. Non-enhanced CT (NECT) of brain, perfusion CT in the selected area of interest and immediate contrast study for major blood vessel occlusion done. Perfusion parameters were analysed in different regions of interest and analysed for statistical significance. Follow up CT brain was done after 48 hours to assess the size of hypodensity and compared with NECT. **RESULTS:** TTP value increased in regions of hypodensity and surrounding areas. TTP, relative CBV (rCBV) and CBV ratio showed a significant statistical difference ($p<0.05$) in penumbra and infarct regions. CBV values showed a significant statistical difference ($p<0.05$) between infarct and penumbra regions of the same hemisphere. **CONCLUSION:** TTP map can be used as initial map for identifying ischemic area. rCBV and CBV ratio helps in identifying reversible ischemic area.
KEYWORDS: Perfusion imaging, Computerized Tomography, Stroke.

INTRODUCTION: Perfusion CT (PCT) of the brain is playing a vital role in acute stroke and management decisions. Functional physiological imaging helps to determine diseases before anatomical changes occur. Interpretation of varying colour pattern enables us to identify abnormal areas in perfusion CT.[1]

Due to a recent rise in the ageing population, identification of brain attack at an appropriate time reduces morbidity using early interventions. By 2030, developing nations will also count the stroke as a leading cause of death and disability.

Initially PCT was used to assess the ischaemic changes in the brain. Nowadays, it is a problem-solving tool used in complex cases requiring blood flow pattern analysis.[2] The aim of our study was to define different regions of brain parenchyma into normal, penumbra and infarct zones using intravenous contrast perfusion characteristics in patients presenting with stroke.

METHODS: Total 72 patients presenting with neurological symptoms were clinically assessed in a period of 3 months. Patients having symptoms of the stroke more than 6 hours and haemorrhagic stroke were excluded from the study. 20 patients presenting with symptoms of the stroke less than 6 hours duration included in the study.

After basic neurologic examination, stroke protocol which included plain CT brain and perfusion CT brain done. Follow up CT after 2 days taken to assess the effectiveness of therapeutic measures. The study was approved by the ethical committee of the institution. Explained consent was obtained from the patient.

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Perfusion CT was performed with iodinated intravenous contrast, repetitive sequential examination of selected brain parenchyma. Perfusion CT performed at 80/200Kv/mAs, 40s scan time, 0.6 s rotation time, and 4x5mm slice collimation, reconstruction slice thickness of 5mm and 40mL of contrast at 5mL /s.

The first pass contrast flow allows us to estimate perfusion parameters which include time to peak enhancement (TTP), cerebral blood volume (CBV) and cerebral blood flow (CBF) in abnormal areas comparing with contralateral normal brain parenchyma.

These parameters enable us to differentiate areas of penumbra and infarct zones. The area covered was 20mm thickness in 4 contiguous 5mm thick sections. The predominant area of interest was the basal ganglia, however the area of interest was selected based on hypodensity in NECT brain.

Areas having delay in peak enhancement and slightly abnormal cerebral blood volume suggested ischaemic penumbra, which is recoverable brain parenchyma.[3] Also thin slice perfusion CT help in assessing large vessel occlusion in the brain.

NECT brain was done using 120/260Kv/mAs, scan time of 7 to 8s, rotation time 0. s and 1mm slice thickness. The same protocol was used for contrast enhanced CT (CECT) brain following perfusion CT with no scan delay (Table 1).

	Characteristics	NECT/CECT	NEURO PCT
1	KV/mAs	120/260	80/200
2	Scan time	7-8 sec	40 sec
3	Rotation time	0.6 s	0.6 s
4	Slice collimation	0.6 mm	4x5 mm
5	Reconstructed Slice thickness	1 mm	5 mm
6	Contrast flow	-/contrast used for perfusion is used with out scan delay.	40 ml @ 5 ml/ sec

Table 1: Scan protocol for PCT, NECT and CECT brain.

Dynamic multi slice images were evaluated with magic view 300 software (SIEMENS, Germany). Perfusion parameters, which include TTP, CBV, CBF and CBV ratio of different regions of interest were calculated. 16areas were having hypodensity on NECT marked as Area A; 12 surrounding areas showing increased time to peak and minimal change in cerebral blood volume as Area B and 22 apparently normal TTP with the opposite hemisphere marked as C(Table 2). Corresponding perfusion parameters of all 50 areas also obtained from normal opposite hemisphere. Tabulation and appropriate statistical analysis were done.

A	Hypodensity area in plain CT
B	Normal density in NECT and increased TTP
C	Normal density in NECT and Normal TTP
A1, B1, C1	Corresponding contralateral normal regions of A, B, C regions respectively.
Table 2: Selection of regions based on NECT and TTP maps	

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RESULTS: Most of the patients presented were within 40 to 60 years of age with mean age of 52.5years. Sex ratio was 3:2.Males were outnumbering females. Pre-existing diseases like hypertension and diabetes were noted in 30 to 60% of patients.

Time to peak perfusion values of normal brain parenchyma varied from 10.05s to 12.31s with mean value of 11.3s, the B areas showed the mean value of 14.05s and area a showed 18.42s. There is statistically significant difference in time to peak value between areas marked as A (p<0.01) and B (p<0.01) on comparison with the contralateral brain parenchyma and also between A and C (p = 0.04) of same cerebral hemisphere (Fig 1).

Cerebral blood volume (Related volume ratio of blood in percentage of blood volume) of different regions ranges from 3.3 to 4.0% in normal appearing parenchyma. Mean cerebral blood volume measures 4.1% in the area marked as B and 1.6% in the area A.

There is significant statistical difference between mirror areas marked as A (p=0.02) and B (p=0.04) and also between different areas of same cerebral hemisphere marked as A & B (p=0.01) and A & C (p=0.05). Cerebral blood volume ratio of (Abnormal/normal side) different regions of diseased side showed a significant statistical difference between A & B and A & C (p<0.01) (Fig 2).

Cerebral blood flow (Cerebral blood volume/mean transit time) of normal cerebral parenchyma varied from 59 to 80mL/100mg/min. Means cerebral blood flow of areas marked as A and B measured 26.3 and 67.4mL/100mg/min respectively.

There is a significant statistical difference in cerebral blood flow of regions marked as A with contralateral normal brain parenchyma and between A & C regions of the same side (p=0.02). Cerebral blood flow ratio of different regions of abnormal hemisphere showed a significant statistical difference between A & B and A & C (p < 0.01) (Fig 3).

The hypo dense areas in plain CT showed increased time to peak, reduced cerebral blood volume and blood flow compared with adjacent areas which showed increase in time to peak value and predominantly mild increase in cerebral blood volume. There was a wide range of values of TTP, CBV and CBF parameters seen in apparently normal regions of the same hemisphere and opposite normal hemisphere. Follow up NECT after 48hrs showed no increase in size of hypodensity in all selected regions (16- Area A).

Area	TTP (sec)	CBV (% of BV)	CBF (ml/100mg/min)	CBVR	CBFR	INTERPRETATION
A	18±6	1.6 ±1.1	26±22	0.46±0.27	0.38±0.2	INFARCT
B	14±4	4.1 ±1.2	65±19	1.14±0.33	1.10±0.2	PNUMBERA
C	10-12	3.3-3.5	59-68	1.00±0.20	1.10±0.2	NORMAL

Table 3: Summery of perfusion parameters and its interpretaton

DISCUSSION: Perfusion CT is an optimal rapid decisive prerequisite for therapeutic intervention in patients with stroke. It provides a quantitative estimation of blood perfusion disturbance due to major branch vessel occlusion.[4] But it is always important to compare with apparently normal regions of the same and opposite hemispheres. There is no standardised TTP, CBV and CBF cut-off values. Baseline values are derived from the normal regions of brain parenchyma.

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The baseline values vary significantly between patients due to changes in haemodynamics of anterior and posterior circulation, due to diseases of carotid arteries and incomplete circle of Willis.

The evaluation of perfusion starts with time to peak, which is the screening map showing regions of ischaemia has increased value. The penumbra can be very well appreciated based on areas showing mild increase in cerebral blood volume, which is salvageable area by active arterial revascularisation/intervention.[5]

Planning of perfusion CT has to start when there is history of acute stroke less than 6hours. Only 27% of patients were presented with acute stroke of less than 6 hours duration, which implies the lack of understanding about the disease in public and referring physicians.

Scan duration for perfusion study varies from 40 s to 150s. longer duration is required when studying brain tumors. Scan time did not affect the CBV and CBF parameters.[6] The amount of radiation is lesser with reduced scan time, kV and coverage area. The benefit of radiation will out weight the risk.[7,8]

Publication by Lin et al, said that the perfusion CT is more valuable in patients with stroke presenting with symptoms of less than three hours duration.[9] Here, we have selected patients having symptoms of less than 6 hours, as the number of patients presenting within 4hours was very less (<10%).

PCT has good sensitivity, specificity and negative predictive value in patients with stroke so excluding ischemic disease of the brain. The cerebral blood volume and flow ratio measurements are better parameters to analyse, as they are reproducible especially in MCA territory.[10]

MRI diffusion helps in defining acute infarct areas, especially smaller lacunar infarcts. Areas having increase in TTP in PCT can be regarded as ischemic. The mismatch between MR diffusion and increased TTP map is the area of risk.[11]

Recent advancements of whole brain perfusion will make management of acute stroke more interesting.[12,13] but limited due to availablility. Even though the identification of whole infarct core is much better with the whole brain perfusion.[14-17] Localising signs of hyperacute infarct or normal NECT brain with significant localising clinical history helps in defining of the area of coverage.

So rapid focussed evaluation of suspected ischemia is possible.[18] Considering the radiation dose to the whole brain, percentage of difference in volume of the infarct core between limited PCT and whole brain PCT(~10%), can be taken as negligible.[14,19]

CONCLUSION: PCT is a better non-invasive modality for diagnosis of infarct, penumbra and normal brain regions based on quantitative perfusion parameters especially rCBV, CBV ratio and CBF ratio.
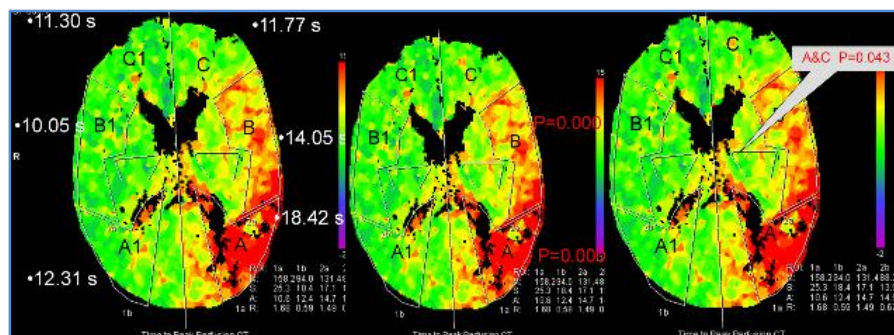

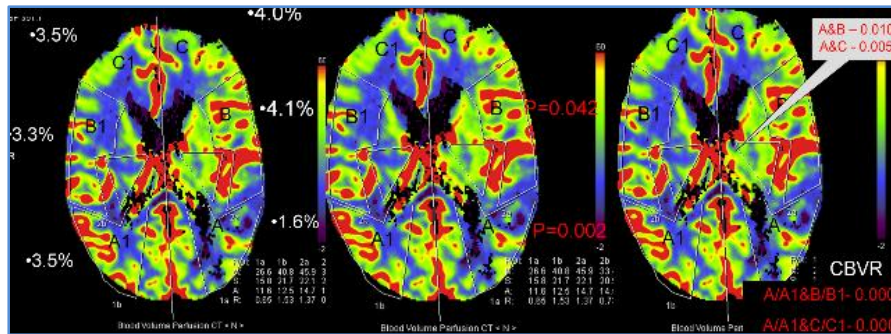*Fig. 1: TTP Map Representing Different Regions of Ischemia and Their Statistical Significance*

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Fig. 2: CBV and CBV Ratio in Different Regions of
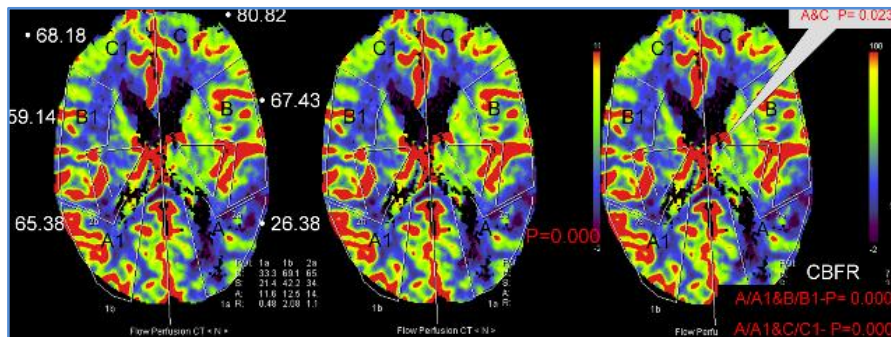*Ischemia and Their Statistical Significance*

Fig. 3: CBF and CBF Ratio in Different Regions of
Ischemia and Their Statistical Significance

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