ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 06, pp.52122-52129, June, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

ROLE OF CT PERFUSION IN ACUTE ISCHEMIC INFARCT

Dr. Rashmi Sharma, *Dr. Rajesh Sharma and Dr. Ishan Gupta

Acharya Shri Chander College of Medical Sciences, Bye Pass Road, Sidhra, Jammu, Jammu and Kashmir 180017

ARTICLE INFO

Article History:
Received 23rd March, 2017
Received in revised form
14th April, 2017
Accepted 18th May, 2017
Published online 20th June, 2017

Key words:
Ischemic infarcts,
NCCT,
CT perfusion,
Penumbra, core infarct,
Tissue at risk, hyperacute infarct.

ABSTRACT

Objective-To diagnose hyperacute(<3hrs duration of symptoms) ischemic infarct and differentiating penumbra from core infarct by using CT perfusion technique.
Material and method- The study was conducted on 40 patients of acute stroke using 128 slice MDCT scanner first NCCT were done to rule out hemmoragic infarction and other pathologies followed by 40 milliliters of a nonionic contrast agent at a rate of 4 mL/sec. 5 seconds after initiation of the injection, a cine (continuous) scan was initiated for duration of 45 seconds. CT perfusion data was analyzed at an imaging workstation *(Syngo* Acquisition workstation; Siemens healthcare Systems) equipped with commercially available software (Stroke MTT; Siemens Healthcare Systems).
Results: out of 40 patients, 8 patients presented within 3 hours of symptoms and the sensitivity of NCCT in detecting Ischemic infarct within 3 hours is 26 % whereas that of CTP was 87.4%. rCBF of tissue at risk was 0.64 ± 0.12 and that of core infarct was 0.35 ± 0.05. the rCBV of tissue at risk was 0.80 ± 0.16 and rCBV of core infarct was 0.29 ± 0.11
Conclusion:- Considering all the parameters studied, CT Perfusion was found to be more sensitive than NCCT in diagnosing acute ischemic stroke and was better in differentiating salvageable penumbra from non salvageable core infarct.

Citation: Dr. Rashmi Sharma, Dr. Rajesh Sharma and Dr. Ishan Gupta, 2017. "Role of CT perfusion in acute ischemic infarct", *International Journal of Current Research*, 9, (06), 52122-52129.

INTRODUCTION

Stroke is the rapid loss of brain function due to disturbance in the blood supply to the brain. This can be due to ischemia (lack of blood flow) caused by blockage (thrombosis, arterial embolism), or a hemorrhage (Sims *et al.,* 2012). As a result, the affected area of the brain cannot function, which might result in an inability to move one or more limbs on one side of the body, inability to understand or formulate speech, or an inability to see one side of the visual field (Donnan *et al.,* 2008). Its early diagnosis is important as its treatment is dependent on the time elapsed since ictus. Tissue at risk, or "penumbra," is defined as an area of markedly reduced perfusion with loss of function of still viable neurons (Astrup *et al.,* 1981; Donnan *et al.,* 2008). This risk increases as the time interval between the onset of symptoms and thrombolytic therapy increases. Thus, patients are more likely to have a good outcome when treated within 3hours than between 3 and 6 hours after the acute event (Wardlaw, 2001). Therefore, the primary purpose of diagnostic imaging is to ensure selection of the appropriate patients for thrombolytic therapy to reduce severe complications.

***Corresponding author:** *Dr. Rajesh Sharma*
Acharya Shri Chander College of Medical Sciences, Bye Pass Road, Sidhra, Jammu, Jammu and Kashmir 180017

For this purpose, diagnostic imaging of acute stroke should reliably help *(a)* exclude intracranial hemorrhage, *(b)* differentiate between irreversibly affected brain tissue ("dead brain") and reversibly impaired tissue ("tissue at risk"), which might benefit from early treatment.

In the assessment of acute stroke syndrome, NCCT remains the first-line imaging technique for differentiating hemorrhagic and ischemic stroke and identifying other etiologies for altered neurologic status, such as an intracranial mass (de Lucas *et al.,* 2008). Perfusion computed tomography (CT) is a relatively new technique that allows rapid qualitative and quantitative evaluation of cerebral perfusion by generating maps of cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT). It is hypothesized that tissue at risk of infarction will have decreased CBF, normal or elevated CBV secondary to activation of cerebral autoregulatory mechanisms, and elevated MTT, while infarcted tissue will have decreased CBF and CBV with elevated MTT (Wintermark *et al.,* 2001). Color-coded perfusion maps showing CBV, mean transit time (MTT), and CBF are obtained (Wintermark *et al.,* 2007; Eastwood *et al.,* 2003). Quick visual assessment of the perfusion maps is better than more accurate measurements in the emergency setting. Subsequently, we analyze the CBF and CBV maps, which are more specific for distinguishing ischemia from infarction (Schaefer *et al.,* 2006; Wintermark *et*

al., 2007). Thus with the new imaging modalities of perfusion CT stroke patients can now be evaluated more precisely and consequently treated according to their individual needs, thus avoiding the potential harm of performing thrombolysis in patients with a large amount of irreversibly damaged brain tissue or reversible cerebral ischemia, in which spontaneous reperfusion of ischemic tissue may occur (Yuh *et al.,* 2000).

MATERIALS AND METHODS

This prospective observational study (case series) was carried out in the Department of Radio-Diagnosis, Government Medical College Jammu and Superspeciality Hospital Jammu on 40 Patients presenting with acute stroke and have no hemorrhage on NCCT head. Informed and written consent was taken from the patient prior to examination.

All the patients had undergone NCCT Head first using Siemens Somatom definition AS (Siemens Healthcare, Germany) 128 slice Multi Detector row CT Scanner. The CT images were acquired by using a 120-kV and 450-mAs technique. Images were reconstructed into a contiguous 5-mm axial dataset by using a standard algorithm. After unenhanced CT of the whole brain, four adjacent 5-mm-thick sections were selected starting at the level of the basal ganglia. At this level, all three supratentorial vascular territories were visualized. 40 milliliters of a nonionic contrast agent (370 mg of iodine per milliliter) was injected at a rate of 4 mL/sec. 5 seconds after initiation of the injection, a cine (continuous) scan was initiated with the following technique: 80 kVp, 190–200 mA, 4 × 5-mm sections, 1-second per rotation for duration of 45 seconds. CT perfusion data was analyzed at an imaging workstation *(Syngo* Acquisition workstation; Siemens healthcare Systems) equipped with commercially available software (Stroke MTT; Siemens Healthcare Systems). The software then generated color-coded CBF, CBV, and MTT maps. The final summary maps were generated by the software on free hand drawing ROIs in affected area and setting the threshold values of CBF and CBV for core infarct.

OBSERVATIONS AND RESULTS

In the present study, the age of the patients ranged from 38 years to 94 years. The maximum number of patients 12 (33.33%) was in the age group of 70-79 years and more than two third of the patients were above 65 years of age.Out of these 40 patients, 24 (55%) were female patients and 16 (45%) were male patients with a sex ratio of 1:1.5(table 1). In our study, among 40 patients, 15 patients (37.5%) presented with hemiparesis which was the most common presenting symptom followed by hemiparesis with aphasis in 20% patients. 2 patients (5%) among 40 presented with ataxia and vomiting representing posterior circulation abnormality (Table 2).

Among the 28 patients who presented within 6 hrs of symptoms, 10 (35.7%) had normal NCCT, 4 (14.2%) had well formed infarct on NCCT and rest 18 (50%) had early changes. Obscuration of lentiform nucleus was seen in 6 (21.4%) of the patient and was most common among early findings followed by dense MCA in 5(17.8%) patients(table 3).In our study, among 40 patients, 3 had normal study on CT perfusion and 4 had AMBI thus, the total no. of ROIs evaluated were 41 for penumbra and core infarcts. The sensitivity of increase in MTT was 100% in detecting hypoperfusion and was the most sensitive indicator for diagnosing infarct but cannot differentiate between penumbra and core infarct. Decrease in CBF is more sensitive than CBV in detecting hypoperfusion however decrease in CBV better depicts extent of core infarct. The sensitivity of increase in TTP is 92.68% in diagnosing hypoperfusion however there is not much difference in alteration of TTP between penumbra and core infarct (Table 4).

In our study, rCBF of tissue at risk was 0.64 $\pm$ 0.12 and that of core infarct was 0.35 ± 0.05. This shows that there is mild decrease in CBF of tissue at risk and CBF of core infarct decreases significantly. So the mean threshold value for discrimination of infarct and tissue at risk of rCBF was estimated to be 0.44.Here the rCBV of tissue at risk was 0.80 ± 0.16 and rCBV of core infarct was 0.29 ± 0.11 i.e. CBV decreased slightly in TAR whereas in core infarct is decreased significantly. The threshold absolute value for CBV to diagnose core infarct was estimated to be 1.98 ml/ 100g.In our study, there was increase in MTT in both tissue at risk and core infarct and the value of rMTT in tissue at risk was 1.69 and in core infarct it was 2.06 i.e. in core infarct MTT further increases however there is no significant difference in MTT of TAR and core infarct. The threshold value for MTT was estimated to be 147%.rTTP in TAR was 1.84 and in core infarct it was 2.39 i.e TTP is increased in both core infarct as well as TAR (Table 5).

In our study, among 40 patients, 8 patients presented within 3 hours of symptoms and out of these only 2 patients were diagnosed by NCCT. However CTP diagnosed 7 patients i.e. the sensitivity of NCCT in detecting Ischemic infarct within 3 hours is 26 % whereas that of CTP was 87.4%(table 6).In our study, among 40 patients, only 29(72.5%) patients were diagnosed by NCCT. However CTP diagnosed 37(92.5%) patients i.e. the sensitivity of NCCT in detecting Ischemic infarct is only 72.5% which can be increased to 92.5% by using CTP (Table 7).

DISCUSSION

In the past 40 years the use of medical imaging to distinguish stroke subtypes has become a mainstay at almost all medical institutions, revolutionizing acute stroke diagnosis and treatment. Currently the NCCT acquisition is the most common imaging modality used to diagnose stroke however characterization of penumbra and core infarct separately is not accurate and diagnostic sensitivity of NCCT in hyperacute stage(<3 hrs) is very low. In the present study, patients had age range between 38 years to 94 years with mean age of 69.4 ± 14.3 years and the maximum no. of patients, 12 (33.3%) were in the age group of 70-79 years. The present study also revealed that 72.5% of patients were above the age of 65 years. Out of these 40 patients 24(55%) were females and 16(45%) were male patient and we had a sex ratio of 1:1.5.Gregg. C. Fonarow *et al.* (2010) in their study found that the mean age of patients was 71.0± 14.6 years which is consistent with our finding however the maximum no. of patients in their study were seen in age group of 80-89 years which is different from our study. In their study the percentage of female patients was 52.5% and sex ratio was 1:1.2. These findings also corresponds to our study finding.In the present study, Hemiparesis was the commonest presenting feature in 15 (37.5%) patients followed by Hemiparesis with aphasia in 8 (20%) patients. Other presenting features are Altered sensorium in 5 (12.5%) patients,

Table 1: Demographic data (n=40)

AGE GROUP (IN YEARS)	TOTAL(n=40)			
	No of males(n=16)	No of Females(n=24)	Total No.(n=40)	Percentage (%)
< 50	1	3	4	10
50-59	2	3	5	12.5
60-69	4	3	7	17.5
70-79	5	7	12	33.33
80-89	3	6	9	22.5
> 90	1	2	3	7.5
Total			40	100.0

Table 2: Distribution of clinical features of patients of stroke

CLINICAL FEATURES	NO. OF PATIENTS (PERCENTAGE)
Hemiparesis	15 (37.5%)
Hemiparesis with aphasia	8 (20%)
Altered sensorium	5 (12.5%)
Hemiparesis with altered sensorium	4 (10%)
Hemiparesis with facial palsy	3 (7.5%)
Ataxia and vomiting	2 (5%)
Facial palsy	1 (2.5%)
Slurring of speech	1 (2.5%)
Generalised weakness	1 (2.5%)

Table 3: Findings on NCCT head in patients of stroke with less than 6 hours duration of symptoms

FINDING	NO. OF PATIENTS (PERCENTAGE)
Normal study	10 (35.7%)
Obscuration of lentiform nucleus	6 (21.4%)
Subtle hypodensity of parenchyma with sulcul effacement	3 (10.7%)
Loss of grey- white differentiation	2 (7.14%)
Insular ribbon sign	2 (7.14%)
Dense MCA	5 (17.8%)
Well formed infarct	4 (14.28%)

Table 4: Qualitative comparison of perfusion parameter alteration on ct perfusion in tissue at risk and non viable tissue

PARAMETER	No. of ROI (n=41)	
	TISSUE AT RISK	CORE INFARCT
Decreased CBF	40	41
Decreased CBV	29	41
Increased MTT	41	41
Increased TTP	38	41

Table 5: Quantitative comparison of perfusion parameters on ct perfusion in tissue at risk and non viable tissue

PARAMETER		CONTRALATERAL HEMISPHERE	TISSUE AT RISK	CORE INFARCT
CBF	Range	25.5 – 73.8	20.1-48.8	10.7 – 23.8
	Mean ± SD	57.8 ± 10.2	37.2 ± 7.3	16.6 ± 3.32
	Relative to contralateral hemisphere (rCBF ± SD)	1	0.64 ± 0.12	0.35 ± 0.05
CBV	Range	2.2 – 4.3	1.5 - 3.6	0.1 – 1.8
	Mean ± SD	3.4 ± 0.6	2.7± 0.57	1 ± 0.4
	Relative to contralateral hemisphere (rCBV ± SD)	1	0.80 ± 0.16	0.22 ± 0.11
MTT	Range	3.1 – 6.3	4.4 – 8.8	5.4 – 11.2
	Mean ± SD	4 ± 0.7	6.7 ± 1.4	8.2 ± 1.4
	Relative to contralateral hemisphere (rMTT ± SD)	1	1.69 ± 0.35	2.06 ± 0.35
TTP	Range	2.7 – 8.2	4.7–11.7	6.6 – 13.9
	Mean ± SD	4.39 ± 1.09	8.1 ± 1.9	10.5 ± 2.4
	Relative to contralateral hemisphere (rTTP ± SD)	1	1.84 ± 0.44	2.39 ± 0.55

Table 6: Comparison of NCCT and CTP findings in diagnosing hyperacute infarct (less than 3 hours duration) (n=8)

Diagnostic Modality	No. of Patients	
	Diagnostic	Normal
NCCT	2	6
CTP	7	1

Table 7: Comparison of NCCT and CTP findings in diagnosing acute infarct (n=40)

Diagnostic Modality	No. of Patients	
	Diagnostic	Normal
NCCT	29(72.5%)	11
CTP	37(92.5%)	3

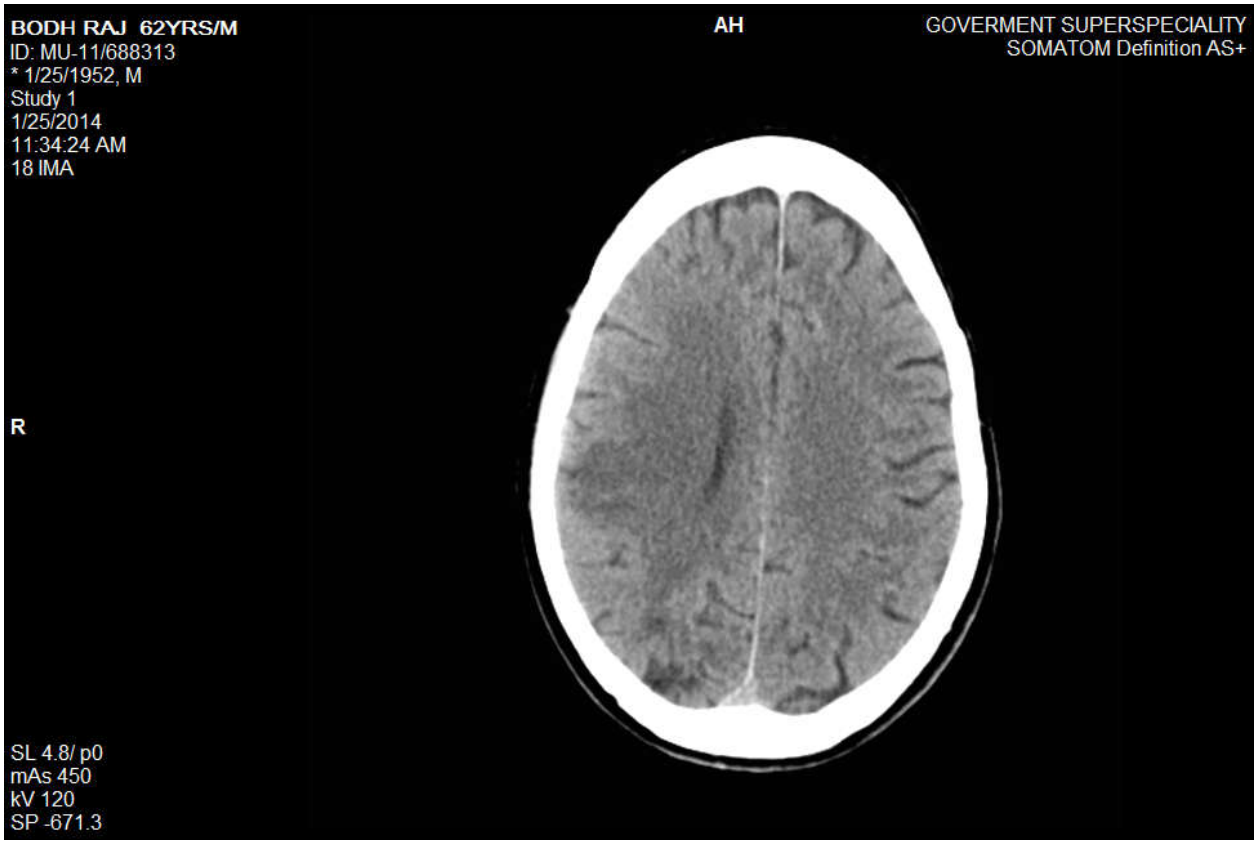

Fig 1(a) :- NCCT of 62 year old male patient presented with weakness of Left side of body of 2-3 hours duration showing subtle hypodensity in right parietal lobe.

Hemiparesis with altered sensorium in 4 (10%) patients, Hemiparesis with facial palsy in 3 (7.5%) patients, Ataxia and vomiting in 2 (5%) patients, Isolated Facial palsy in 1 (2.5%) patient, Slurring of speech in 1 (2.5%) patient and Generalized weakness in 1 (2.5%) patient.

Among 40 patients, 2 patients who had Ataxia and vomiting as presenting features were diagnosed to have posterior circulation infarction. In our study, among 28 patients, who presented within 6 hours of symptoms, early ischemic changes were seen in 14 (50%) patients with obscuration of lentiform nucleus being most common finding, seen in 6 (21.4%) patients followed by dense MCA in 5(17.8%) patients. Other early findings on NCCT were subtle hypodensity of parenchyma with sulcul effacement in 3 (10.7%) patients, loss of grey-white matter differentiation in 2 (7.14%) patients and loss of insular ribbon sign in 2 (7.14%) patients. Among 28 patients, 10 (35.7%) patient had normal NCCT and 4 (14.28%) had well formed infarcts on NCCT. Koga *et al.* (2003) and Wardlaw *et al.* (2005) in their studies found that one or more of early ischemic changes were present in 65 (62%) and 66% patients respectively with attenuation of lentiform nucleus and sulcul effacement being most common finding, seen in 43 (41%).

These finding are similar to our findings. Lin *et al*. (2009) in their study found that the sensitivity of NCCT in detecting hyperacute infarct (infarct of less than 3 hours duration) was very low and was 26.2%. Wintermark *et al.* (2005) in their study found that the sensitivity of MTT maps, TTP maps, CBF maps and CBV maps in diagnosing ischemic infarcts was 94.4%, 87.5%, 85.7% and 62.5% respectively.In our study among 40 patients, 3 had normal study on CT perfusion and 4 had AMBI thus, the total no. of ROI evaluated were 41 for penumbra and core infarcts. The sensitivity of increase in MTT was 100% in detecting hypoperfusion and was the most sensitive indicator for diagnosing infarct but cannot differentiate between penumbra and core infarct. CBF maps were 97.5% sensitive whereas, the sensitivity of CBV maps

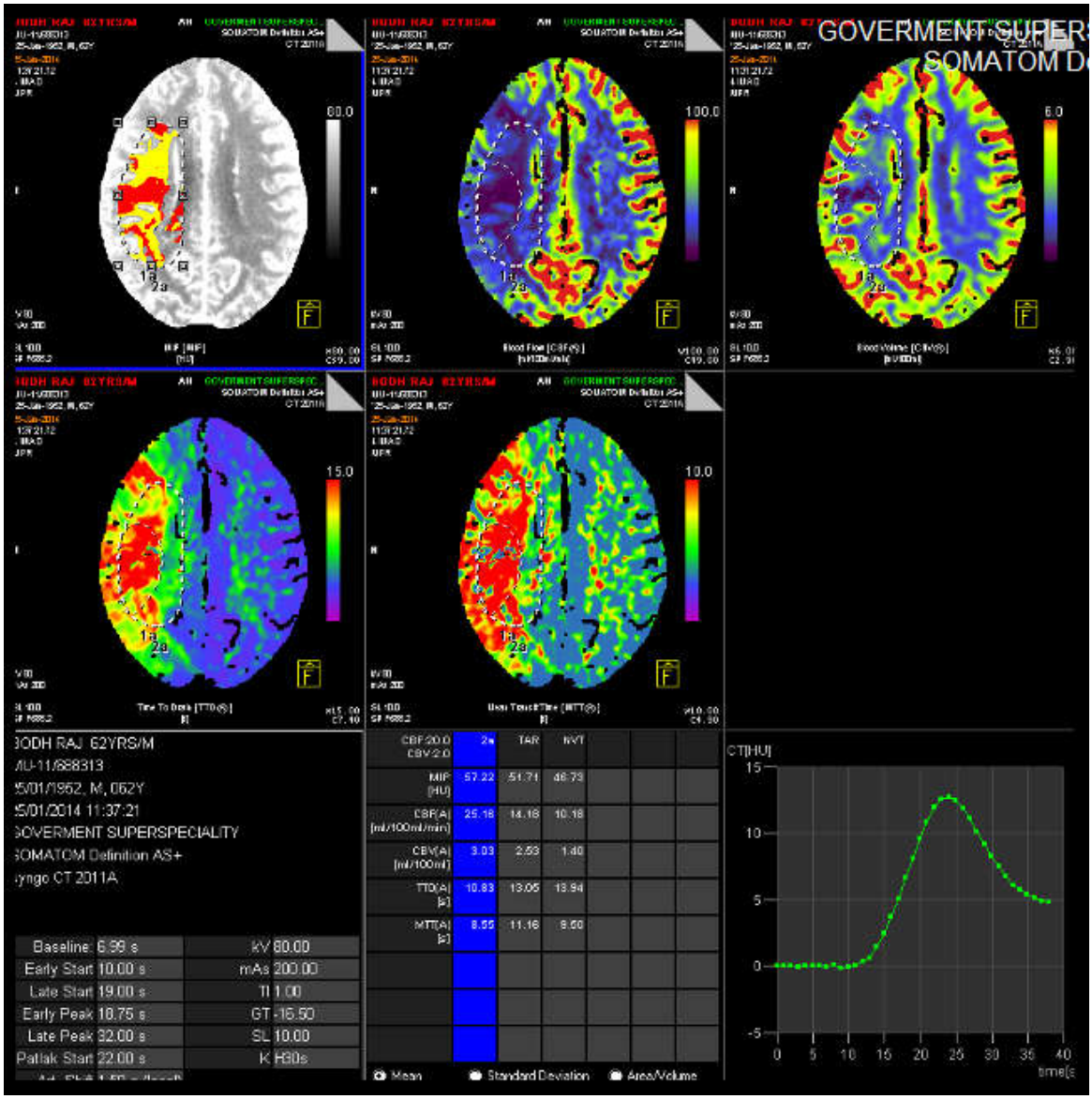

Fig 1(b):- CT Perfusion of the same patient showing Perfusion deficit on all the pefusion maps with significant amount of penumbra seen on summary map in Right MCA territory. The Perfusion parameters for tissue at risk and core infarct are shown in the table.

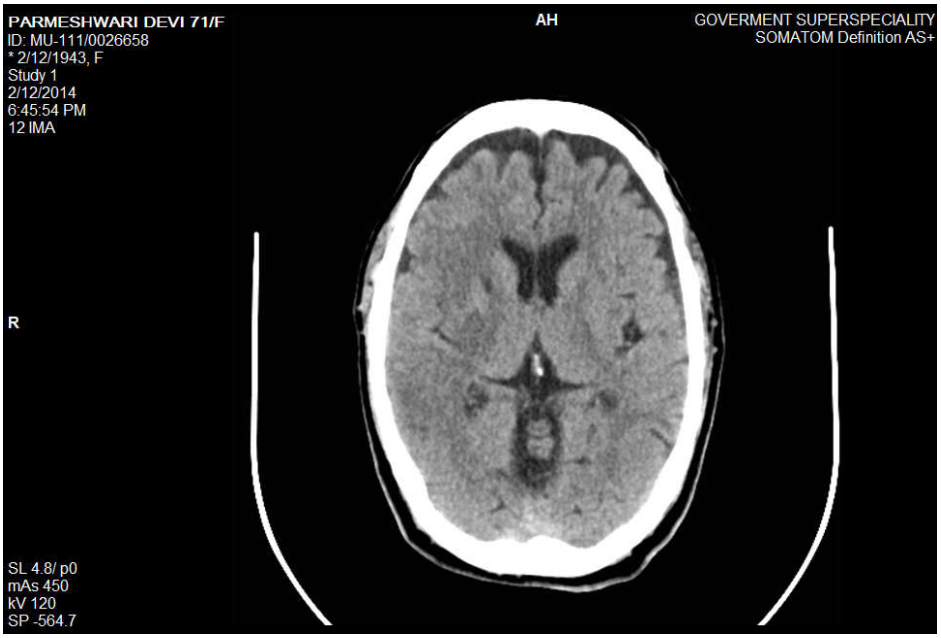

Fig 2(a) :- NCCT of 71 year old female patient presented with weakness of Left side of body and Right sided deviation of mouth of 4 hours duration showing obscuartion of right lentiform nucleus.

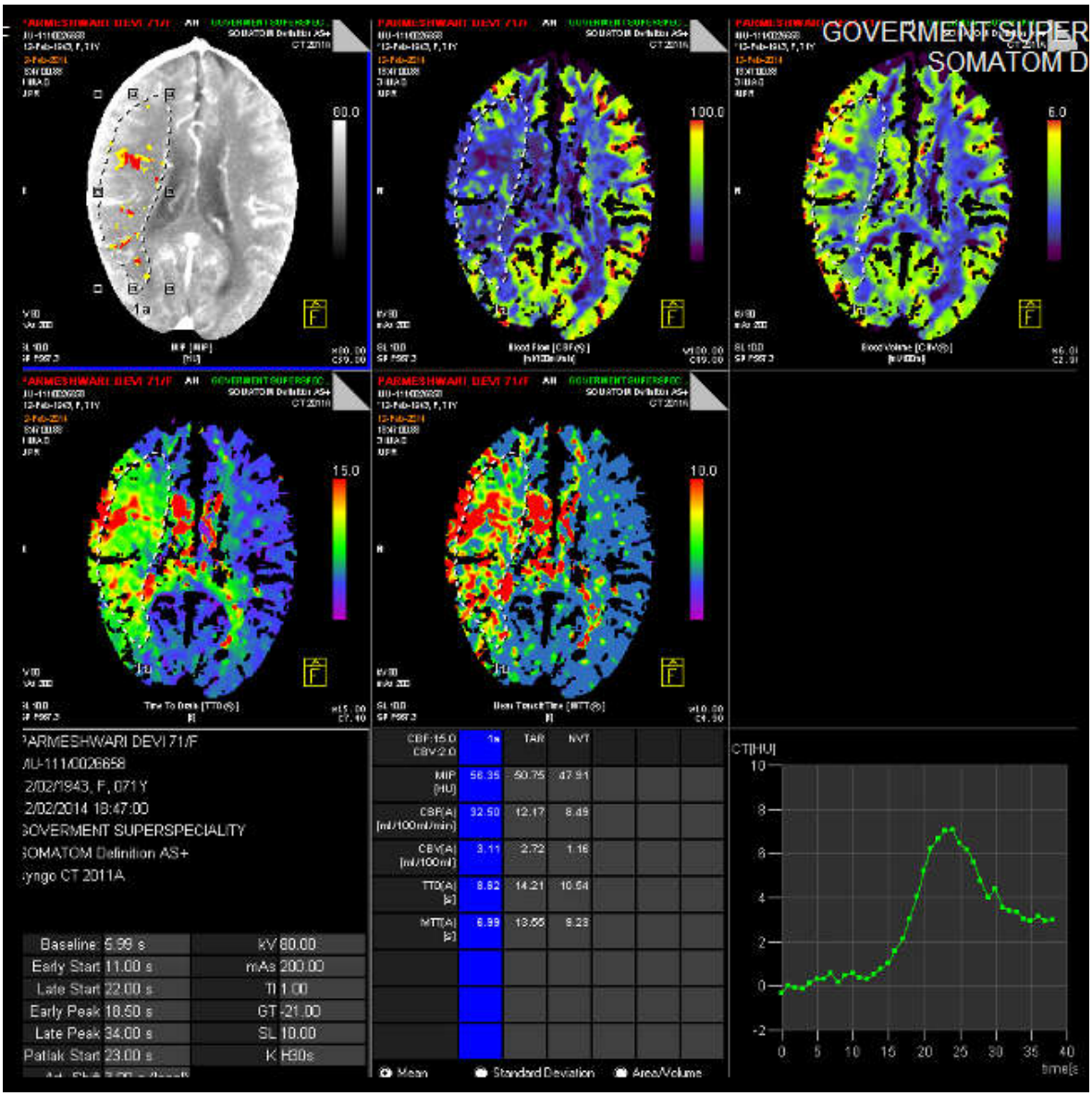

Fig 2(b):- CT Perfusion of the same patient showing Perfusion deficit on all the pefusion maps with significant amount of penumbra seen on summary map in Right MCA territory. The Perfusion parameters for tissue at risk and core infarct are shown in the table.

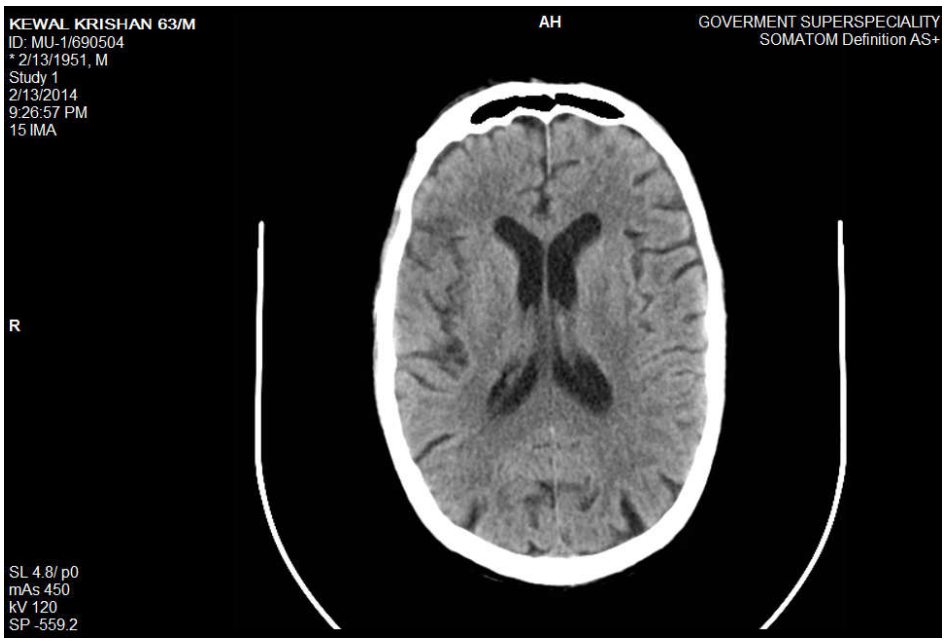

Fig 6(a):- NCCT of a 63 year old male patient presented with weakness of Left side of body with Aphasia of 5 hours of duration showing subtle hypodensity in right fronto parietal region and normal left cerebral hemisphere.

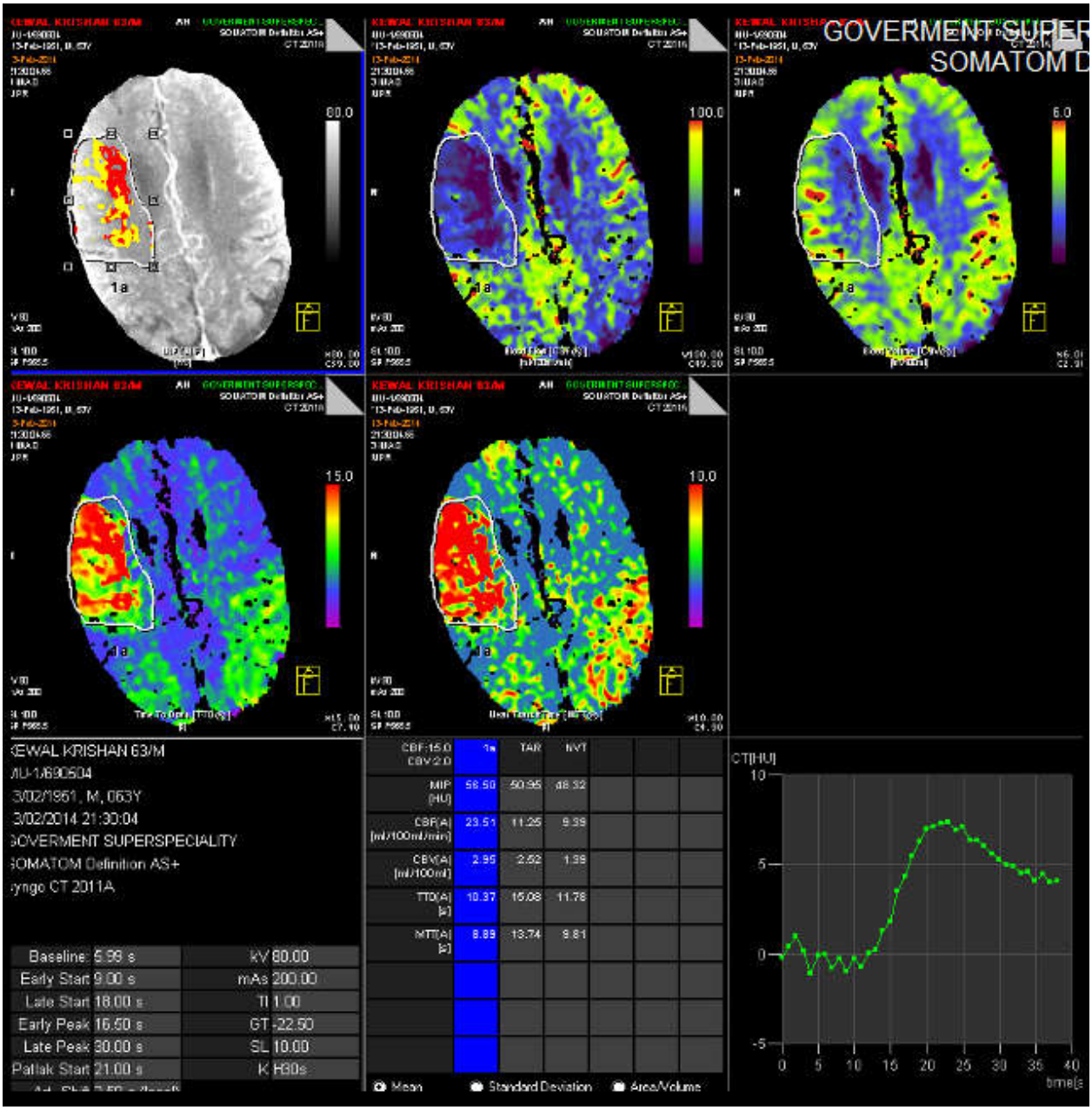

Fig 6(b):- CT Perfusion of same patient showing multiple areas of Perfusion abnormality involving both the hemispheres. The Perfusion deficit is more in Right fronto parietal region and the various perfusion parameters of this area are shown in the table.

was only 70.7%. The sensitivity of increase in TTP was 92.68% in diagnosing hypoperfusion however there is not much difference in alteration of TTP between penumbra and core infarct.

Thus our study showed good correlation with the studies mentioned above. In our study, the mean value of CBF in penumbra i.e. tissue at risk was 37.2 ± 7.3 ml/100gm/min (mean± SD) and in core infarct it was 16.6± 3.32 ml/100gm/min whereas, the mean CBF value of normal contralateral hemisphere was 57.8± 10.2 ml/100gm/min. these values showed that the CBF is reduced to approximately 60% of normal in penumbra and to less than 35% of normal in core infarct.In our study , the mean value of CBV in penumbra i.e. tissue at risk was 2.7± 0.57 ml/100gm (mean± SD) and in core infarct it was 1.0± 0.4 ml/100gm/min whereas, the mean CBV value of normal contralateral hemisphere was 3.4±0.6 ml/100gm/min. These values showed that the CBV was only mildly reduced in penumbra however there was significant decrease in CBV of core infarct as compared to normal contralateral hemisphere. The threshold absolute value for CBV to diagnose core infarct was estimated to be 1.98 ml/ 100g.In our study, there was increase in MTT in both tissue at risk and core infarct and the value of rMTT in tissue at risk was 1.69±0.35 and in core infarct it was 2.06±0.35 i.e. in core infarct MTT further increases however there was no significant difference in MTT of TAR and core infarct. The threshold value for MTT to diagnose hypoperfusion was estimated to be 147%. rTTP in TAR was 1.84±0.44 and in core infarct it was 2.39±0.55 i.e. TTP is increased in both core infarct as well as TAR however there is no significant difference in the two regions. Wintermark *et al.* (2006) in their study found that the mismatch between the absolute CBV, with a threshold at 2.0 ml/100 g, and the relative MTT, with a threshold at 145%, was the most accurate parameter for delineation of the tissue at risk of infarction. These threshold values are consistent with estimated values in our study. Abels *et al.* (2010) measured perfusion parameters quantitatively and found that absolute

values of CBF and CBV in tissue at risk were 29±6.6 ml/100gm/min and 2.9± 0.6 ml/100gm respectively, and in core infarct they were 12±4.2 ml/100gm/min and 1.1±0.44 ml/100gm respectively, when calculated using deconvolution analysis method. These findings are similar to the findings we obtained using same method of analysis. P W Schaefer et al (2006) in their study found that Mean CBF ratios for core infarct, penumbra and oligemic tissue were 0.19 ± 0.06, 0.34 ± 0.06, and 0.46 ± 0.09,respectively (all $P < .001$). Mean CBV ratios for regions were similarly distinct (all $P < .05$). All regions with CBF ratio <0.32, CBV ratio <0.68, CBF <12.7 mL/100 g/min, or CBV <2.2 mL /100 g were infracted and no region with CBF ratio >0.44 was infracted.

In our study, the values of rCBF in tissue at risk and core infarct were 0.64±0.12 and 0.35±0.05 respectively. Thus the threshold value of rCBF estimated to differentiate between penumbra and core infarct was 0.44. The values of rCBV were 0.80± 0.16 and 0.22±0.11 in tissue at risk and core infarct respectively. This data showed that the difference in values of rCBV in tissue at risk and core infarct was more significant than difference in values of rCBF thus, in our study rCBV was superior in discriminating between tissue at risk and core infarct. All these findings are similar to the findings of above mentioned studies. In our study, among 40 patients, 8 presented within 3 hrs of symptoms and only 2 were diagnosed on NCCT (sensitivity of NCCT was 26%) however CT Perfusion diagnosed 7 patients accurately thus the sensitivity of CTP in diagnosing hyperacute ischemia was 87.4% in our study, significantly more than NCCT. Lin *et al.* (2009) in a comparative study of NCCT and CTP in patients of hyperacute ischemia (< 3 hours duration) fount that NCCT revealed only 17 (26.2%) acute infarcts without false positives however, CTP revealed 42 (64.6%) acute infarcts with one false positive. Thus our study showed good correlation with the study mentioned above.

Conclusion

Considering all the parameters studied, CT Perfusion was found to be more sensitive than NCCT in diagnosing acute ischemic stroke and was better in differentiating salvageable penumbra from non salvageable core infarct.

REFERENCES

Astrup J, Siesjo BK, Symon L. 1981. Thresholds in cerebral ischemia: the ischemic penumbra. Stroke, 12:723–725.

Wardlaw, AU., JM, Mielke O *et al.* 2005. Early signs of brain infarction at CT: observer reliability and outcome after thrombolytic treatment--systematic review. Radiology. 235(2):444.

Abels, B., E. Klotz, B.F.Tomandl , S.P. Kloska, M.M. Lell. 2010. Perfusion CT in Acute Ischemic Stroke: A Qualitative and Quantitative Comparison of Deconvolution and Maximum Slope Approach. *Am J Neuroradiol.,* 31:1690 –98.

de Lucas EM, Sanchez E, Gutierrez A, et al. 2008. CT protocol for acute stroke: tips and tricks for general radiologists. *Radiographics*, 28*:* 1673–87.

Donnan GA, Fisher M, Macleod M, Davis SM. "Stroke". Lancet 2008; 371 (9624): 1612–23

Eastwood JD, Lev MH, Wintermark M, *et al*. 2003. Correlation of early dynamic CT perfusion imaging with whole-brain MR diffusion and perfusion imaging in acute hemispheric stroke. AJNR 2003; 24*:* 1869– 75.

Gregg C. Fonarow, Mathew J. Reeves, Xin Zhao, DaiWai M. Olson, Eric E. Smith, Jeffrey L. Saver and Lee H. Schwamm. 2010. Age-Related Differences in Characteristics, Performance Measures, Treatment Trends and Outcomes in Patients with Ischemic Stroke. Circulation. 121:879-891.

Hakim AM. 1998. Ischemic penumbra: the therapeutic window. *Neurology*, 51:S44–S46.

Lin K, DoKG, Ong P, *et al.* 2009. Perfusion CT improves diagnostic accuracy for hyperacute ischemic stroke in the 3- hour window: study of 100 patients with diffusion MRI confirmation. *Cerebrovasc Dis.* 28(1):72-79.

M Koga, Y Saku, K Toyoda, H Takaba, S Ibayashi, M Lida. 2003. Reappraisal of early CT signs to predict the arterial occlusion site in acute embolic stroke. *J Neurol Neurosurg Psychiatry,* 74:649-653.

Schaefer PW, Roccatagliata L, Ledezma C, Hoh B, Schwamm LH, Koroshetz W, *et al.* 2006. First-pass quantitative CT perfusion identifies thresholds for salvageable penumbra in acute stroke patients treated with intra-arterial therapy. *Am J Neuroradiol.,* Jan; 27(1):20-5.

Sims NR, Muyderman H. 2009. "Mitochondria, oxidative metabolism and cell death in stroke". *Biochimica et Biophysica Acta, 1802* (1): 80–91.

Wardlaw JM. 2001. Overview of Cochrane thrombolysis meta-analysis. *Neurology,* 57:S69–S76.

Wintermark M, Flanders AE, Velthuis B, Meuli R, van Leeuwen M, Goldsher D, *et al.* 2006. Perfusion-CT assessment of infarct core and penumbra: receiver operating characteristic curve analysis in 130 patients suspected of acute hemispheric stroke. *Stroke*; 37:979-85.

WintermarkM, Fischbein NJ, Smith WS, et al. 2005. Accuracy of dynamic perfusion CT with deconvolution in detecting acute hemispheric stroke. *AJNR*, 26: 104–112.

WintermarkM, Maeder P, Thiran JP, Schnyder P, Meuli R. 2001. Quantitative assessment of regional cerebral blood flow by perfusion CT studies at low injection rates: a critical review of the underlying theoretical models. *Eur Radiol.,* 11: 1220–1230.

WintermarkM, Reichhart M, Michel P, Bogousslavsky J. 2007. CT perfusion imaging. In: Miles KA, ed. Multidetector computed tomography in cerebrovascular disease. Abingdon, England: *Informa Healthcare,* 2007; pp 83–97.

Yuh WT, Maeda M, Wang AM, *et al.* 1995. Fibrinolytic treatment of acute stroke: are we treating reversible cerebral ischemia? AJNR, 16:1994–2000.

****