IS MULTIMODAL CT SUPERIOR TO MRI IN IMAGING ACUTE ISCHEMIC STROKE? NO

Lakshmi Narasimhan Ranganathan
Institute of Neurology, Chennai, India

As there is a paradigm shift from time window to issue window, MRI with its robust sequences will emerge as the winner as compared to Multimodal CT.

Restrictive time window for the thrombolytic therapy and advances in the pathophysiological insight of the ischemic process has forced penumbral rescue as the foremost goal of acute stroke therapy (1). MRI with its versatility and Multimodal CT (NECT, CT Angiography and CT Perfusion) with an apparent ease of availability are the two competing imaging modalities in acute ischemic stroke. The modality that promptly recognises, locates, estimates and delineates the ischemic zones, identifies late responders of reperfusion and is easily implementable with an acceptable side effect profile would be ideal for clinical application.

Early CT signs of ischemia lack sensitivity and are observer dependent. The ASPECT (Alberta Stroke Program Early CT) score though validated is semi quantitative and assesses only MCA territory (2) (3). Diffusion weighted imaging (DWI) identifies regions of abnormal water movement which manifests very early after onset of ischemia and this can be quantified with ADC (apparent diffusion coefficient) mapping. This sequence is acquired in less than a minute and diffusion restriction is detectable within 3 to 30 minutes of ischemic onset. DWI has revolutionised early stroke diagnosis with a sensitivity of 95% and specificity of nearly 100% within 6h of stroke onset (4). Diffusion abnormalities are transient usually lasting for one to two weeks, a feature very useful in assessing patients presenting sub acutely and those with recurrent infarct (5). DWI is helpful in predicting outcome as measured by NIHSS and Barthel index. It is also a component in prognostication of outcomes after transient ischemic attack (TIA) (6). Indisputably infarction is earlier and best identified and quantified by MRI and is also preferred to exclude other stroke mimics (7) (8) (9). MRI is equally sensitive to CT in detecting acute intracerebral haemorrhage and superior in identifying micro bleeds and chronic haemorrhage (10) (11).

In addition to DWI which is a measure of ischemic injury, perfusion imaging provides vital information about the on going ischemia. MR perfusion imaging is done by dynamic susceptibility contrast (DSC) and arterial spin labelling (ASL). Perfusion weighted imaging (PWI) is done with standard MRI and MR angiography using gadolinium contrast and can be completed within 15 min. However, PWI is semi quantitative and absolute threshold values for defining various ischemic zones are yet to be established. Perfusion imaging using continuous ASL is entirely non invasive and quantitative, but is more time consuming at present (12). Asymmetry in cerebral blood flow on CASL is found to correlate with stroke severity and outcome.

Potentially salvageable tissue at risk (penumbra) exists for as long as 48 h after onset of ischemia. Accurate identification of this tissue at risk is crucial in extending the benefit of thrombolysis beyond 3h and in selecting responders for reperfusion and neuroprotection. Although PET imaging is considered the gold standard in penumbral imaging, MRI diffusion-perfusion mismatch is evolving as a potential clinical option. Diffusion and perfusion MRI are surrogate for metabolic failure and hemodynamic compromise respectively and the mismatch between them is relevant for imaging the ischemic penumbra (13). PWI–DWI mismatch is the difference in volume of tissue between the smaller diffusion lesion and the larger perfusion lesion. A difference of at least a 20% is taken as significant and is an approximate estimate of the ischaemic penumbra (14). This mismatch is present in about 70% of the patients with anterior circulation stroke and resolved with restoration of perfusion (15) (16). If the perfusion is not restored DWI lesions expand over a period up to 24 h and this occurs almost exclusively in patients (17)presenting with a larger DWI–PWI mismatch (18). Salvage of the MRI-defined penumbra has been demonstrated and several ongoing trials are designed to demonstrate the usefulness of MRI selection of patients for late recanalization therapies (19).

Though dynamic CT Perfusion can quantitatively assess CBF, CBV and MTT it has limited coverage of 2cm (16MDCT scanner) to 4cm (64 MDCT scanners) thickness of brain tissue. The posterior fossa of brain could not be assessed accurately due to beaming artefact. It is two dimensional, requires complex postprocessing and enhanced multidetector CT capabilities are not as widely available as conventional CT. Another serious drawback of CT Perfusion is lack of direct visualisation of injured tissue as compared to MRI (20).

MRA is done with TOF using internal contrast. It is around 90% sensitive and specific compared to DSA, which is comparable with CTA.
A complete multimodal CT protocol for stroke delivers a larger mean effective dose of radiation of 16.4 mSv (21). Though short-term effects of radiation from acute stroke imaging are rare, long term outcome is unknown. Based on the National Council on Radiation Protection and Measurements the estimated risk of a fatal cancer is 5% per sievert. This would result in a fatal cancer in approximately one in 1,200 patients for a mean dose of 16.4 mSv. Inadvertent radiation overdose during CT perfusion has been reported and following this the FDA has published a list of recommendations for undertaking CT perfusion scans (22).
Overall incidence of contrast induced nephropathy (CIN) after CT Angiography in acute stroke patients with normal renal function is around 2-3% (23). Incidence of CIN would be more if CT perfusion is also done. Recommended preventive steps for CIN is not feasible as stroke imaging is very time sensitive (24). Whereas, incidence of nephrogenic systemic fibrosis following gadolinium contrast is low and occurs predominantly in patients with renal dysfunction (25).
Duration for stroke CT protocol is between 10 and 20 minutes (mean 13 minutes) and for MRI it is between 16 and 32 minutes (mean 23 minutes) (26). Newer ultrafast MRI imaging protocols using a sensitivity encoding (SENSE) technique are being evaluated which could assess parenchymal ischemia and vascular compromise within 3 min, an essential option for handling restless and uncooperative patients (27).
Though conventional CT scanners are widely available, the enhanced Multidetector CT scanner's availability is as limited as MR scanners.
Though Multimodal CT appears to be a cost effective over short term, additional data are needed before long term cost effectiveness is ascertained (28).
MR Imaging in acute ischemic stroke has evolved from parenchymal imaging to penumbral imaging and now to a more holistic and therapeutically relevant physiological imaging (Fig-1).
MRI is an ideal one stop solution for structural, vascular and physiological imaging in acute stroke except in less than 10% of patients who have safety issues with MRI.
As there is a paradigm shift from time window to tissue window, MRI with its robust sequences will emerge as the winner as compared to Multimodal CT.
Summary of role of MRI and Multimodal CT in acute stroke is given in table-1.

Fig.1 : Evolution of MRI imaging in stroke

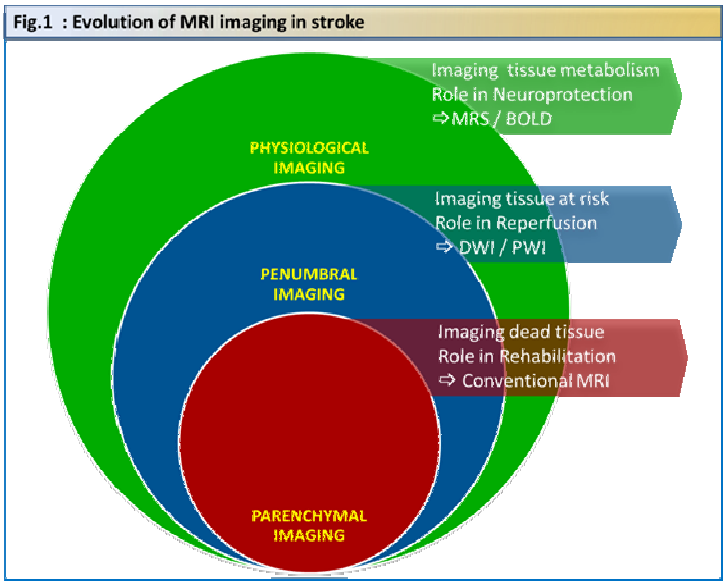

Table-1: Comparison between MRI & Multimodal CT (Role in Acute Stroke Imaging)				
		MRI	**MULTIMODAL CT**	**COMMENTS**
DIAGNOSIS	**ISCHEMIC STROKE**	DWI (Sensitivity - 95% Specificity - 100%)	NECT (Sensitivity:40-70%)	DWI Superior
	ICH	GRE -Equally sensitive in Acute Superior in Chronic & Microbleed	NECT is Standard	MRI &CT comparable MRI Superior in Chronic
PATHOPHYSIOLOGICAL ASSESSMENT **(Role in Reperfusion & Neuroprotection)**	**Hemodynamic Profile** **"Penumbra"**	DWI-PWI Mismatch CASL	CTP	CTP – Limited coverage Risk of Contrast & Radiation Poor sensitivity in posterior fossa MRI - CASL is Non Invasive
	Metabolic Profile -OER / CMRO2	MRS Perfusion with OER,CMRO2 / T2*	Not Possible	Potential Future Role for MRI
VASCULAR IMAGING		MRA	CTA	MRA as Good as CTA MRA – No Contrast

Bibliography

1. *Tissue plasminogen activator for acute ischemic stroke. .* Group., The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study. s.l. : N Engl J Med, 1995, Vol. 333. 1581-7.
2. *Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score.* Barber PA, Demchuk AM, Zhang J, et al. s.l. : Lancet , 2000., Vol. 355. 1670-4.
3. *Use of the Alberta Stroke Program Early CT Score (ASPECTS) for assessing CT scans in patients with acute stroke.* Pexman JH, Barber PA, Hill MD, et al. s.l. : AJNR Am JNeuroradiol , 2001, Vol. 22. 1534-42.
4. *Acute human stroke studied by whole brain echo planar diffusion-weighted magnetic resonance imaging.* Warach S, Gaa J, Siewert B, et al. s.l. : Ann Neurol, 1995., Vol. 37. 231.
5. *Diffusion-weighted MRI in 300 patients presenting late with subacute transient ischemic attack or minor stroke. .* Schulz UG, Briley D, Meagher T, et al. s.l. : Stroke , 2004, Vol. 35. 2459.
6. *Addition of brain and carotid imaging to the ABCD(2) score to identify patients at early risk of stroke after transient ischaemic attack: a multicentre observational study.* Merwick A, Albers GW, Amarenco P, Arsava EM, Ay H, Calvet D, et al. s.l. : Lancet Neurol, 2010, Vol. 9. 1060 – 1069.
7. *CT and diffusion-weighted MR imaging in randomized order: diffusion-weighted imaging results in higher accuracy and lower interrater variability in the diagnosis of hyperacute ischemic stroke.* Fiebach JB, Schellinger PD, Jansen O, et al. s.l. : Stroke , 2002, Vol. 33. 2206.
8. *Magnetic resonance imaging versus computed tomography for detection of acute vascular lesions in patients presenting with stroke symptoms. .* Brazzelli M, Sandercock PA, Chappell FM, et al. s.l. : Cochrane Database Syst Rev , 2009. CD007424.
9. *Evidence-based guideline: The role of diffusion and perfusion MRI for the diagnosis of acute ischemic stroke: report of the Therapeutics and Technology Assessment Subcommittee of the*

American Academy of Neurology. Schellinger PD, Bryan RN, Caplan LR, et al. s.l. : Neurology , 2010, Vol. 75. 177.
10. *Comparison of MRI and CT for detection of acute intracerebral hemorrhage.* Kidwell CS, Chalela JA, Saver JL, et al. s.l. : JAMA, 2004, Vol. 292. 1823–30.
11. *Stroke magnetic resonance imaging is accurate in hyperacute intracerebral hemorrhage: a multicenter study on the validity of stroke imaging.* Fiebach JB, Schellinger PD, Gass A, et al. s.l. : Stroke, 2004, Vol. 35. 502–06.
12. *Magnetic resonance perfusion imaging in acute ischemic stroke using continuous arterial spin labeling. .* Chalela JA, Alsop DC, Gonzalez-Atavales JB, et al. s.l. : Stroke, 2000, Vol. 31. 680.
13. *Imaging the ischaemic penumbra.* Joseph V. Guadagnoa, Geoffrey A. Donnanc, Romesh Markusc, Jonathan H. Gillardb. s.l. : Current Opinion in Neurology, 2004, Vol. 17. 61–67.
14. *The ischemic penumbra: operationally defined by diffusion and perfusion MRI.* Schlaug G, Benfield A, Baird AE, et al. s.l. : Neurology , 1999, Vol. 53. 1528–1537.
15. *Absent middle cerebral artery flow predicts the presence and evolution of the ischemic penumbra. .* Barber PA, Davis SM, Darby DG, et al. s.l. : Neurology , 1999, Vol. 52. 1125–32.
16. *Relationship between magnetic resonance arterial patency and perfusion-diff usion mismatch in acute ischemic stroke and its potential clinical use.* Staroselskaya IA, Chaves C, Silver B, et al. s.l. : Arch Neurol , 2001, Vol. 58. 1069–74.
17. *Imaging of acute stroke.* Keith W Muir, Alastair Buchan, Rudiger von Kummer, Joachim Rother, Jean-Claude Baron. s.l. : Lancet Neurol , 2006, Vol. 5. 755–68.
18. *Prediction of stroke outcome with echoplanar perfusion- and diff usion-weighted MRI.* Barber PA, Darby DG, Desmond PM, et al. s.l. : Neurology , 1998, Vol. 51. 418–26.
19. *Evolving Paradigms in Neuroimaging of the Ischemic Penumbra.* Chelsea S. Kidwell, MD, Jeffry R. Alger, PhD and Jeffrey L. Saver, MD. s.l. : Stroke, 2004, Vol. 35. 2662-2665.
20. *Imaging of acute stroke.* Keith W Muir, Alastair Buchan, Rudiger von Kummer, Joachim Rother, Jean-Claude Baron. s.l. : Lancet Neurol, 2006, Vol. 5. 755–68.
21. *Radiation dose from multidetector row CT imaging for acute stroke.* Symons, Anisa Mnyusiwalla & Richard I. Aviv & Sean P. s.l. : Neuroradiology, 2009, Vol. 51. 635–640.
22. *FDA Investigates the Safety of Brain perfusion CT.* Wintermark, M. s.l. : AJNR, 2010, Vol. 31.
23. *Incidence of radiocontrast nephropathy in patients undergoing acute stroke computed tomography angiography. .* Krol AL, Dzialowski I, Roy J, et al. s.l. : Stroke, 2007, Vol. 38. 2364–66.
24. *Renal safety of CT angiography and perfusion imaging in the emergency evaluation of acute stroke. .* Hopyan JJ, Gladstone DJ, Mallia G, Schiff J, Fox a J, Symons SP, et al. s.l. : AJNR. American journal of neuroradiology , 2008, Vol. 29(10). 1826–30.
25. *Enhanced Computed Tomography or Magnetic Resonance Imaging: A Choice between Contrast Medium-Induced Nephropathy and Nephrogenic Systemic Fibrosis?* Thomsen, H. S., Marckmann, P. and Logager, V. B. 6, s.l. : Acta Radiologica, Vol. 48. 593 - 596.
26. *Comparison of Perfusion Computed Tomography and Computed Tomography Angiography Source Images With Perfusion-Weighted Imaging and Diffusion-Weighted Imaging in Patients With Acute Stroke of Less Than 6 Hours' Duration.* Peter Schramm, MD and Peter D. Schellinger, MD. s.l. : Stroke. , 2004, Vol. 35. 1652-1658.
27. *Utility of an ultrafast magnetic resonance imaging protocol in recent and semi-recent strokes.* U-King-Im JM, Trivedi RA, Graves MJ, et al. s.l. : J Neurol Neurosurg Psychiatry , 2005, Vol. 76. 1002–1005.
28. *Cost effctiveness of Multimodal CT for evaluating acute stroke.* Kate C. Young, PhD, Curtis G. Benesch, MD, Babak S. Jahromi, MD. s.l. : Neurology, 2010, Vol. 75. 1678–1685.