Neuroimaging: Current Challenges, Future Trends

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According to results from the Diffusion-Weighted Imaging Evaluation for Understanding Stroke Evaluation Study 2 [DEFUSE-2; NCT01349946], Target Mismatch (TMM) patients who achieve early reperfusion have less infarct growth and more favorable clinical outcomes. Gregory W. Albers, MD, Stanford Stroke Center, Palo Alto, California, USA, presented results from the study.

The DEFUSE-EPITHET Pooled Analysis [Lansberg MG et al. *Stroke* 2011] showed that diffusion- and perfusion-weighted imaging (DWI/PWI) can identify subgroups with a differential response to reperfusion following intravenous tissue plasminogen activator (tPA) therapy. Yet, there have been controversy and contradictory data surrounding the scope and clinical relevance of DWI reversibility and uncertainty regarding the accuracy of PWI for detecting critical hypoperfusion.

The aim of the DEFUSE 2 study was to demonstrate that automated software (RAPID) can allow clinicians to prospectively identify magnetic resonance imaging (MRI) profiles that predict clinical and radiographic outcomes following endovascular reperfusion. The definitions of TMM, reperfusion (PWI criteria), reperfusion digital subtraction angiography ([DSA] criteria), and favorable clinical response are shown in Table 1.

Table 1. Definitions of TMM, Reperfusion (PWI Criteria), Reperfusion (DSA Criteria), and Favorable Clinical Response.

Variable	Criteria
TMM	PWI (Tmax >6s)/DWI≥1.8 DWI <70 ml PWI (Tmax >10s) <100 ml
Reperfusion (PWI criteria)	>50% reduction in PWI (Tmax >6s) volume at early follow-up
Reperfusion (DSA criteria)	TICI 2b or 3 at completion of procedure
Favorable Clinical Response	≥8 point improvement in NIHSS at Day 30 or NIHSS of ≤1 at Day 30

The primary imaging hypothesis was that reperfusion is associated with reduced infarct growth in TMM patients compared with patients who had other MRI profiles. The study results demonstrated that median lesion growth (5 day FLAIR volume – baseline DWI volume) was significantly less in TMM patients who reperfused (n=42) versus those who did not reperfuse (n=23). Respective rates were 39% in the former versus 412% in the latter (p<0.003). The clinical outcomes of the TMM patients were also significantly better if they experienced reperfusion. In non-TMM patients (n=19), median lesion growth was not significantly different with reperfusion than without it (56% vs 11%; p=0.5). Furthermore, the clinical outcomes of these patients were less favorable if they experienced reperfusion (OR, 0.1; 95% CI, 0.007 to 0.93).

The second imaging hypothesis focused on whether DWI lesions are reversible with endovascular therapy. Data demonstrate that DWI reversibility (volume not incorporated into coregistered 5-day FLAIR) is rare and that patients with reperfusion had slightly larger volumes of DWI reversal; median reversal volume was 2.5 cc (IQR, 0.2 to 5.0) versus 0.6 cc (IQR, 0.1 to 2.2; p=0.03).

The third imaging hypothesis was whether posttreatment PWI lesions predict the volume of infarction at Day 5. Findings indicate that among patients who did not reperfuse (n=28), 69% of PWI Tmax >6 sec voxels were incorporated into the coregistered 5-day FLAIR.

These findings indicate that baseline DWI lesions are reliably incorporated into the 5-day FLAIR lesion; ie, that "DWI reversibility" is minimal. In addition, tissue that remains hypoperfused (Tmax >6 sec) following endovascular therapy is very likely to progress to infarction.

Treatment Implications of the Malignant MRI Profile

Michael Mlynash, MD, MS, Stanford Stroke Center, Palo Alto, California, USA, discussed the endovascular treatment implications of the malignant MRI profile, which is defined as a large baseline DWI lesion and/or a large and severe baseline PWI lesion. This profile has previously been shown to predict poor outcomes following intravenous tPA therapy [Albers GW et al. *Ann Neuro* 2006] (Table 2).

Table 2. Optimal Definitions for Predicting Poor Outcomes Following Reperfusion.

	mRS 5-6 DWI >55 mL and/or PWI Tmax>10s>95mL	mRS 3-6 DWI >45 mL and/or PWI Tmax>10s>80mL
Sensitivity	0.27	0.35
Specificity	0.91	0.92
PPV	0.50	0.86
NPV	0.78	0.50

PPV=positive predictive value; NPV=negative predictive value; mRS=modified Rankin Scale; DWI=diffusion weighted imaging; PWI=perfusion weighted imaging.

According to Dr. Mlynash, patients who meet these criteria are likely to have unfavorable outcomes and infarct growth despite endovascular reperfusion. Mlynash et al. [*Stroke* 2011] found that among patients with a malignant profile who achieved reperfusion following intravenous tPA (n=9), 89% had a Rankin score of 5 to 6 at 90 days versus 39% of patients without reperfusion (n=18; p=0.02). The respective figures for parenchymal hemorrhage were 67% and 11% (p<0.01).

The aims of the DEFUSE-2 malignant profile substudy were to investigate whether those who have the malignant profile are more likely to suffer severe disability, parenchymal hemorrhage, infarct growth, or death following endovascular reperfusion and to clarify the optimal definition of the profile in endovascular patients. Clinical response was assessed at 30 and 90 days.

Study results show that 0% of malignant profile patients who achieved reperfusion (n=8) had a Rankin score of 0 to 2 at 30 days versus 48% of non-malignant profile patients who reperfused (n=50; p=0.02). The Rankin 5-6 outcomes were 50% in the malignant profile patients versus 22% in the non-malignant group (p=0.19). The respective figures for parenchymal hematoma (PH)1 or PH2 hemorrhages were 63% versus 20% (p=0.02). Those for median (IQR) infarct growth were 136 mL (92 to 209; n=8) versus 31 mL (5 to 67; n=45; p<0.001).

Optimal definitions for predicting poor outcomes following reperfusion are approximately 50 mL for DWI and/or 90 mL for Tmax>10. According to Dr. Mlynash, automated imaging software can prospectively and rapidly identify these patients, improving the efficacy and safety of reperfusion therapies.

Whole-Brain Perfusion CT Imaging – A New Method for Mapping Cerebral Vascular Territories

Collateral blood supply is believed to be a key determinant of tissue survival in acute stroke. It sustains the penumbra before recanalization and offsets infarct growth [Bang OY et al. *Stroke* 2011]; yet, its characterization remains elusive. Soren Christensen, PhD, Aarhus University Hospital, Aarhus, Denmark, discussed computed tomography perfusion-based (CTP) Vascular Territory Maps.

The hypothesis was that such maps would display redistribution of flow territories that were concordant with CT angiography (CTA). The research entailed a quantitative comparison of territory maps with the CTA-determined site of occlusion.

Subjects were 19 acute stroke patients who were imaged <6 hours from symptom onset. Data were acquired on a Toshiba Aquilon One 320 slice system using standard perfusion protocol. Regions of interest (ROI) were placed in the middle cerebral artery, posterior cerebral artery, and anterior cerebral artery. An algorithm tracked the inflow patterns from the ROIs, and the territories were then labeled with colors.

Fourteen images were interpretable; 5 were excluded due to head motion and/or poor signal enhancement during the bolus passage. The CTA findings included 2 M1 and 1 internal carotid artery occlusion. In the affected hemisphere, the vascular territory of the occluded vessel was either diminished or absent, with the tissue supplied instead by adjacent territories. In 2 of 14 cases, the estimated collateral territory appeared inconsistent with physiological expectations.

According to Dr. Christensen, the initial results are promising. Vascular territory imaging using CTP data would open a window on the importance of the extent and origin of collateral blood supply in acute stroke by quantifying it with a technique that is complementary to standard perfusion and requires no additional hardware or higher radiation doses.