Imaging is still playing a major role in acute stroke management, stroke recovery, and stroke prevention. Each of these areas continued to see marked activity in the imaging field over the past year; this review will focus just on the first of these because of space constraints. With the need of more effective therapies for acute ischemic stroke, the search for a clinically applicable and reliable method to detect functionally impaired but still viable and potentially salvageable tissue—aka the penumbra—continues. Positron emission tomography using $^{15}$O-tracers still represents the best available method for the identification of brain regions with reduced cerebral metabolic rate of oxygen use (CMRO$_2$) that are thought to distinguish them from the ischemic core where oxygen extraction and use is greatly diminished. The mismatch between perfusion-weighted and diffusion-weighted imaging (PW–DWI) signals provides an estimate of the extent of the penumbra, but as shown in a comparative study, the volume of mismatch often is not in agreement with the volume of increased oxygen extraction fraction. This resulting overestimation of the volume of the penumbra, as identified by PET, is partly due to reversibility of diffusion-weighted changes but more importantly to inaccuracies in the assessment of perfusion values. In order to overcome controversies on the best approach to quantify the penumbra by MR methods, a roadmap has been proposed which seeks to standardize perfusion and penumbral imaging techniques, to validate the accuracy and clinical use of imaging markers of the ischemic penumbra, to validate the imaging biomarkers relevant to clinical outcomes, and to create a central repository to achieve these goals.

Several recent studies underline the need of such efforts: whereas the DEFUSE study demonstrated that early reperfusion was associated with a favorable response in patients with a perfusion/diffusion mismatch, EPITHET (the placebo-controlled trial of alteplase beyond 3 hours) did not meet its primary end point; whereas it showed that alteplase was significantly associated with reperfusion in mismatch patients, there was not a statistically significant association with attenuation of infarct growth in patients who had mismatch. The penumbra selection phase II DIAS II and DEDAS trials were also negative and could not support the hypothesis that selection of patients with mismatch improves outcome of reperfusion therapy. As a consequence from these and other published results, Kane et al doubt that the presence or absence of mismatch affects prognosis—a conclusion supported by the occurrence of infarct growth even in the absence of mismatch—and postulate larger studies applying more rigid definitions. Several studies applied refined concepts of mismatch to the previously presented data sets of DEFUSE$^9,10$ and EPITHET, but the results of these subanalyses in even smaller cohorts are not considered convincing by many with regard to diagnostic accuracy in patients with acute stroke. Despite these controversies PW-DWI remains of great clinical value for selecting patients which might benefit from thrombolysis after 3 hours or with tandem occlusion of the internal cerebral and the middle cerebral arteries and for estimating the risk of symptomatic intracerebral hemorrhage in potential candidates for thrombolysis.$^{14,15}$ This upcoming year most likely will see continued efforts to identify how imaging can best select patients for late thrombolysis.

The inaccuracy in defining the penumbra with PW/DWI mismatch is thought to be mainly related to perfusion-weighted data acquisition which is a complex process, and the parameters used to define perfusion lesions are variable and somewhat arbitrary. As a consequence, perfusion lesion size differs markedly depending on the parameter calculated. In 2 studies various PW parameters were compared to quantitative H$_2$O PET studies. In 5 stroke patients, relative distribution images were remarkably similar between perfusion MR and PET, but perfusion MR overestimated absolute cerebral blood flow and underestimated mean transit time. The calculation of cerebral blood flow by bolus tracking on MRI proposed by Oestergaard was reliable in identifying a threshold of 20 mL/100 g per minute set by PET in 24 stroke patients and despite a considerable variance could serve in clinical studies.

The alternative method for assessing the presence of salvageable time-at-risk is CT/CT perfusion which is often used in clinical practice because of its cost-effectiveness and availability and the advantage of combined CT angiography. With regard to identification of infarct size/ischemic core and low perfused tissue at risk, in certain patient populations (such as those with hemispheric symptoms and large ischemic lesions) the results are comparable to PW-DWI.$^{20–24}$ CT angiography source imaging might be of help in predicting outcome in posterior circulation stroke,$^{25}$ and angiographic collateral flow and volume of critically perfused tissue might provide complementary information guiding treatment decisions.$^{26}$ However, larger controlled studies proving the validity of CT/PCT/CT angiography in selecting patients for therapeutic interventions are still lacking.
A novel approach for identification of ischemic tissue uses differences in tissue oxygen extraction: in an innovative application of analyzing T2* signal intensity, Santosh et al used the diamagnetic and paramagnetic effects of high flow oxygen induced on oxygenation status (oxy-hemoglobin versus deoxyhemoglobin) and T2* signal intensity to identify ischemic core and penumbra. This study used arterial spin-labeling to define the perfusion abnormality in one single slice and, therefore, this method requires confirmation with whole brain imaging in a larger sample. Another CMRO2 imaging method could use the change on MRI of 17O-labeled metabolic water produced by oxygen metabolism in the brain mitochondria during a short (2 to 3 minutes) inhalation of 17O2 containing oxygen gas. Changes in CMRO2 can be detected by 17O magnetic resonance spectroscopy mapping or by imaging the conversion of inhaled 17O into H217O, which perturbs the proton signal thus resulting in a negative contrast on T2-MRI. However, these methods require further validation such as in comparative PET studies.

Disclosures

None.

References


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