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# Advances in Stroke : Imaging

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# Advances in Stroke
## Imaging

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Over the past 2 years, there have been substantial advances in many areas of stroke imaging; in this review, due to space limitations, we highlight major themes with a focus on acute stroke as well as vessel imaging. We recognize that there has been a much larger body of important work including imaging in animal models, stroke recovery, and cognitive impairment that we anticipate is covered in other sections.

In acute ischemic stroke, there continues to be steady progress toward identifying the best imaging profiles that can be used to select patients for therapies and/or predict outcomes. Several studies have continued to highlight the need for greater consistency and standardized approaches in identifying perfusion thresholds for tissue viability with both CT and MRI.[1,2] Real-time analyses for postprocessing of multimodal imaging data show promise and feasibility,[3] but also potential pitfalls, including overestimation of perfusion deficits.[4]

Secondary analyses from the Echoplanar Imaging Thrombolytic Evaluation Trial (EPITHET) and Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) studies have underscored the importance of absolute volumes of baseline perfusion and diffusion deficits (as opposed to the mismatch profile) in predicting outcome and response to therapy.[5] The optimal definition of the malignant profile (time to maximum >8-second volume >85–100 mL)[6] has also been further refined. The EPITHET investigators reported the importance of coregistration in determining mismatch, which led to a positive trial result.[7] In the CT realm, regional specific thresholds for tissue viability have been identified and will likely be important in refining future predictive models.[8] There continues to be strong interest in randomized controlled trials using imaging selection for late recanalization therapies. One nonrandomized, retrospective analysis of imaging-based selection for endovascular therapy beyond 8 hours demonstrated feasibility.[9]

Positron emission tomography continues to serve as the gold standard for determining tissue viability thresholds in acute stroke and positron emission tomography has become the method of choice in animal studies with the advance of microtechniques.[10] Arterial spin labeling perfusion MRI systematically overestimated cerebral blood flow relative to $H_2{}^{15}O$[11] and T2*-weighted MRI was not sensitive to high oxygen extraction fraction, the marker of critical ischemia.[12] For the detection of the perfusion-weighted imaging–diffusion-weighted imaging mismatch as a surrogate of the penumbra, a reliable definition of a critical flow threshold is necessary. In comparative studies of perfusion-weighted imaging and $H_2{}^{15}O$-positron emission tomography, time to maximum of 5.5 seconds, cerebral blood flow of 21.7 mL/100 g/min, and time to peak of 4.2 seconds correlated best to the penumbra threshold of 20 mL/100 g/min from positron emission tomography,[13] values similar to those from another validation study (mean transit time delay 4 seconds, absolute mean transit time 8 seconds, mean transit time ratio 200%).[14] The high interindividual variability of perfusion-weighted imaging parameters can be improved by scaling to the mean from the contralateral hemisphere[15] and by careful placement of the area for recording the arterial input function.[16]

Imaging of the peripheral benzodiazepine receptor, now referred to as the translocator protein 18 kDa, has attracted much attention in recent years because it detects activated microglia, the most important cellular component of poststroke neuroinflammation.[17] The expression of translocator protein 18 kDa has been observed both in the infarct core and the peri-infarct tissue where it might be an indicator for progressive secondary damage. Similar patterns of microglial activation in poststroke patients were observed by 11C-vinpocetine.[18] Microglial activation remote from the infarct is also seen along fiber tracts or in relay nuclei, which might indicate changes secondary to Wallerian degeneration.[19] Differential temporal dynamics of local and remote activated microglia might indicate differences in neuroprotective or regenerative activity.[20] Together with diffusion tensor imaging, microglial activation is a measure of pyramidal tract damage, which is highly correlated with residual motor function in acute and chronic stages after stroke.[21]

There have also been further advances in identifying imaging markers and profiles predicting hemorrhagic transformation after recanalization therapies. Regional low cerebral blood volume may be a better predictor of hemorrhagic transformation than absolute diffusion-weighted imaging or

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thresholded apparent diffusion coefficient volumes.[22] Blood–brain barrier permeability analyses also continue to show promise in predicting hemorrhagic transformation.[23] An additional study of note suggests that evidence of recent, silent ischemia on acute MRI is frequent and does not increase the risk of symptomatic hemorrhage with intravenous thrombolysis.[24]

A growing number of studies have demonstrated the added use of imaging, particularly diffusion-weighted imaging, in prognostic scores (eg, ABCD2/3) for transient ischemic attack outcome.[25] Further studies have continued to demonstrate the importance of collaterals not only in acute stroke,[26] but also in determining stroke risk in patients with intracranial atherosclerosis.[27]

In the past 2 years, advanced imaging of intracerebral hemorrhage has led to several important new insights. MRI studies including diffusion-weighted imaging sequences have demonstrated that ischemic infarcts remote from the primary hematoma are common in intracerebral hemorrhage and may be associated with acute blood pressure-lowering and poor outcome.[28] Further data have emerged on the prevalence, risk factors for, and clinical significance of microbleeds, including their association with increased risk of future stroke and cognitive decline.[29–33]

Noteworthy advances continue in vessel imaging. Both ultrasound techniques[34,35] and high-resolution MRI can identify high-risk plaques.[36] A new technique of "vessel size imaging" has the potential to demonstrate pathological changes in the microvasculature during ischemia.[37] Inflammation in atherosclerotic plaques can be identified by both [18F]-2-fluoro-2-deoxy-d-glucose positron emission tomography and MRI techniques.[38] [18F]-2-Fluoro-2-deoxy-d-glucose selectively detects inflammatory portions of arteriosclerotic plaques, which is an indicator of macrophage load, inflammatory activity, and collagenolytic plaque destabilization[39] as the source of microemboli and vessel wall inflammation as the cause of spontaneous cervical artery dissection.[40] Intraplaque inflammation can also be imaged with 11C-PK11195, which can distinguish between recently symptomatic and asymptomatic plaques.[41] Importantly, vessel imaging studies are now being used to monitor response to secondary prevention therapies.[42]

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## Disclosures

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