Current Concepts of the Ischemic Penumbra

Introduction

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The concept of the ischemic penumbra is now more than 20 years old and has become increasingly important as the potential for treating acute ischemic stroke expands. Many definitions of the ischemic penumbra have been proposed in relationship to the modalities used to derive information about the presence and evolution of this ischemic region.

Perhaps the simplest but most clinically and pharmacologically relevant definition is “ischemic tissue potentially destined for infarction but not yet irreversibly injured and the target of acute therapies.” The reliable detection of the ischemic penumbra would provide much important information for both clinicians and researchers. Imaging provides a window for the potential identification of the ischemic penumbra and much effort has been and will be expended regarding the development of reliable imaging techniques for penumbral identification. Positron emission tomography (PET) is the oldest imaging technique employed for penumbral detection in patients and is currently considered the gold standard.

PET provides spatially detailed, highly quantifiable data that is highly accurate. Unfortunately, PET availability is limited to a few centers and ease of patient access is quite limited during the acute phase of stroke, when information about the penumbra is most critical. Diffusion/perfusion magnetic resonance imaging (MRI) is increasingly available at major hospitals worldwide for the acute evaluation of stroke patients. Many groups have evaluated the utility of the diffusion/perfusion mismatch for identifying stroke patients more likely to respond to acute therapy and have shown promising results. It is, however, widely recognized that the diffusion/perfusion mismatch is at best a crude approximation of the ischemic penumbra because (1) the perfusion techniques and data evaluation are not truly quantitative and vary among centers; (2) the thresholds used for defining perfusion abnormalities have not been validated against PET thresholds; and (3) abnormal diffusion regions early after stroke onset can be reversed by timely intervention in both animals and humans.

The diffusion/perfusion concept only provides an initial attempt at using these novel MRI techniques for penumbral identification and more sophisticated data acquisition and analyses will be necessary to provide greater accuracy. Use of arterial spin-labeling perfusion and iterative, self-organizing data analysis techniques should enhance the ability of diffusion/perfusion MRI to define the ischemic penumbra more accurately. The availability of ultrafast computer tomography (CT) equipment has led to the development and increasing availability of perfusion CT. Perfusion CT can evaluate cerebral blood flow and cerebral blood volume qualitatively. Preliminary studies suggest that regions with reduced blood flow but without collapse of cerebral blood volume may represent the ischemic penumbra. Perfusion CT is currently limited by the volume of brain coverage available, the necessity to inject substantial amounts of iodinated contrast material and the lack of validated thresholds. Much additional investigative work is underway to address these concerns. The future of perfusion CT for providing at least an approximation of the ischemic penumbra is likely bright.

The ischemic penumbra session at the Princeton Conference focused primarily on several timely and important imaging aspects. Drs Warach and Kidwell presented information concerning diffusion/perfusion MRI, with Warach’s presentation providing a discussion of how tissue at risk of hemorrhage after thrombolyis can potentially be identified, and Kidwell’s presentation reviewing the current status and future direction of the diffusion/perfusion concept.

Dr Heiss presented novel and very useful information from patients who had diffusion/perfusion MRI and PET in close temporal approximation. The results suggest that abnormal diffusion MRI regions predict ultimate infarction in a fashion similar to 11C-flumazenil PET. The accuracy of perfusion MRI in comparison to PET for identifying the ischemic penumbra was more problematic. Dr Weinstein’s presentation focused on molecular aspects of the penumbra and not imaging, providing a different approach to the penumbra concept. As interest in the ischemic penumbra increases, greater efforts will continue to be expended to understand the molecular basis and how best to use imaging to identify it.

References


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