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Relative Recirculation: What Does It Mean?

No longer simply a research tool, dynamic contrast-enhanced MR imaging has become a clinically useful tool in brain imaging. T2 or T2* changes during the bolus passage of a paramagnetic contrast agent through the cerebrovascular system are converted to concentration values, and indicator dilution theory is applied to calculate a number of hemodynamic variables. Since Rosen et al first reported dynamic contrast-enhanced MR imaging of the human brain in 1990 (1), tremendous progress has been made in the use of the technique for noninvasive assessment of cerebral vascular physiologic behavior. Cerebral blood volume (CBV) measurements indicate the vascularity of lesions and can be used to identify and characterize brain tumors. Tumor capillary blood volumes measured by dynamic contrast-enhanced MR imaging have been shown to correlate with and predict glioma grade and hence provide insight into tumor malignancy and potential for recurrence. CBV measurements also may provide information on tumor angiogenesis that could be critical in detecting early tumor recurrence, developing novel antiangiogenic chemotherapeutic agents, and monitoring treatment response. Cerebral blood flow (CBF) measurements complement MR diffusion measurements in assessment of stroke by revealing the volume of tissue at risk, the so-called ischemic penumbra.

Dynamic contrast-enhanced MR imaging represents an important transition in radiology from a purely anatomy-based discipline to one in which physiologic patterns and tissue microstructure also can be investigated. Like diffusion and functional MR imaging, dynamic contrast-enhanced MR imaging provides quantitative maps that complement the purely anatomic information available from conventional MR imaging. Dynamic contrast-enhanced MR imaging–derived hemodynamic maps offer a new dimension to imaging in which both anatomic structures and cerebral microcirculation can be depicted with superior spatial resolution. In vivo measurements of regional hemodynamics offer tremendous research and clinical opportunities. It is important to remember, however, that the underlying theories of tracer kinetics are based on a complex set of assumptions that may or may not prove valid in a heterogeneous biological system such as the brain.

In this issue of the *AJNR*, Jackson et al (page 7) introduce another variable, relative recirculation (rR), derived from dynamic contrast-enhanced MR imaging that may reflect the degree of vascular tortuosity and disturbances in blood flow within brain tumors. The authors believe that rR represents "inadequate and deranged blood flow" and is independent and distinct from CBV. They found that the skewness of rR correlated with glioma grade and concluded that rR may be a surrogate marker for angiogenesis. This mathematically technical work represents an important field of research that may have a tremendous impact on how brain tumors are monitored clinically and how therapeutic efficacy is measured.

Traditionally, tumor size and enhancement margins, measured from static anatomic images, have been used to assess therapeutic response. This approach has been problematic, because contrast enhancement is nonspecific, and it is difficult to differentiate active tumor and therapy-related necrosis. There is therefore an acute need for objective variables that can be used to assess tumor response accurately so that toxic and ineffective therapies can be discarded and alternative, potentially active therapies can be initiated.

Jackson et al have found an interesting empiric correlation between rR skewness and tumor grade. Unlike CBV and CBF measurements, however, the biological meaning of rR is unknown. Is it related to contrast agent leakage due to blood-brain–barrier disruption, disturbance in flow dynamics due to tortuous vasculature, or both? Interpretation is further complicated, because it is the skewness of rR, rather than rR itself, that correlates with tumor grade. Without knowing what rR is measuring, it is difficult to regard it as a reliable arbiter of successful therapy. Their hypothesis that "abnormalities in contrast recirculation provide independent information" from CBV measurements also must be treated as provisional.

Like other dynamic contrast-enhanced MR imaging variables, rR measurements raise the question of how the technique should be used in the everyday practice of neuroradiology. The postprocessing methods are computer-intensive, and the variables are not obtained directly from MR systems but from off-line workstations with sophisticated computer algorithms. For this and other similar methods to have a clinical impact, we need some means of standardization so that comparisons can be made among different institutions performing dynamic contrast-enhanced MR imaging as part of routine brain tumor imaging. Also, the variables measured should be referable to image maps that reveal the distribution of values; after all, MR imaging is, and always will be, an image-based technique.

In conclusion, we should continue to develop and validate new MR methods of measuring physiologic variables that can provide insight into understanding the pathophysiology of brain tumors. As the authors point out, the clinical role, if any, of the rR measurements is as yet unproven. Ahead lie the far more difficult tasks of correlating dynamic contrast-enhanced MR imaging–derived variables with histopathologic findings, standardizing imaging acquisi-

tion and data processing among different institutions, validating the robustness and accuracy of the variables in everyday clinical practice, and, ultimately, improving the lives of patients with brain tumors.

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References

1. Rosen BR, Belliveau JW, Vevea JM, Brady TJ. **Perfusion imaging with NMR contrast agents.** *Magn Reson Med* 1990;14:249–265

Watching the Brain Work: Looking at the Network Connections

A cursory glance at the article *High-Resolution Line Scan Diffusion Tensor Imaging of White Matter Fiber Tract Anatomy* by Mamata and colleagues (page 67) may initially appear to the reader as a primarily technical investigation extolling the virtues of yet another MR technique tailored for academic rather than clinical applications. The greater importance of this investigation, however, is evident regarding the potential scope of new anatomic information disclosed by the recent efforts with this technique. In vivo depiction of the underlying neuronal infrastructure of the brain not only promotes greater understanding of the complexity of everyday motor and sensory processes and the ways that disease can affect these functions; it also will allow us to begin to visualize the underpinnings of more profound neurologic phenomena such as consciousness, attention, and awareness. Therefore, the importance of these network connections is not a trivial issue, and this brief but broad editorial introduction will try to provide a perspective for the information generated by Mamata et al as well as others who have already and will continue to publish on this topic.

In today's clinical practice, most routine MR imaging (including functional MR imaging) used to determine the functional implications of cerebral lesions largely relies on an analysis of the relationships and functional imaging correlates to deep and superficial gray matter structures. This is an understandable natural consequence of readily identifiable gray matter landmarks such as sulcal and gyral anatomy as well as many well-defined deep gray matter margins. In addition, the discrete motor and sensory functions associated with the gray matter anatomy are assessable to clinical observation when mapping or in the presence of disease-related injury. The underlying white matter tracts, on the other hand, are more opaque to routine imaging and clinical evaluation owing to less visible margins and more complex functional associations.

It is also easy to oversimplify brain activity by only considering structures that encode sensory information and command movements because of the misperception of white matter fibers as mere conduits for the appropriate gray matter centers involved in sensory and motor function. This absurd scheme can reduce most brain functions to one large reflex arc. Motor and sensory regions, however, account for only a fraction (approximately 20%) of the cerebral cortex. Most of the brain consists of the so-called association cortices that enable diverse functions collectively referred to as "cognition." Some of these functions include awareness of physical and social circumstances (consciousness), the ability to have thoughts and emotions, sexual attraction, expressions of these thoughts with language, emotional memory, etc. It can be argued that cognitive abilities represent the most complex, important, and intriguing cerebral functions. In other words, these are the very psychological and neurologic processes that help to define our selves and our lives.

A closer look at association white matter tracts illuminates the complexity of the neuronal network and readily dispels the notion of a simple one-to-one connection from one cortical neuron to another. The signals these fibers project to other association cortices via the thalamus have already been processed in the primary motor and sensory areas and are fed back to the association regions for further processing. The information, therefore, is a relay from other cortical areas rather than of primary motor or peripheral sensory signals. This type of corticocortical connection explains the observed enrichment or multiplication of input fibers from other cortical areas to any one particular association area. The functional implications for this increasingly complex network foster the speculation about subcortical processing of complex behavior. For example, the association fibers that project to and from the inferior temporal lobe are more closely scrutinized in patients with agnosias such as prosopagnosia (inability to identify familiar individuals by their facial features). The structure of the connecting fibers may be a key component to understanding this type of neurologic dysfunction. Attention disorders may also require evaluation of the white matter fibers projecting to the parietal cortex in addition to the surface structures. Parietal cortex dysfunction may, in fact, reflect disorganization of the underlying association fibers.

Most of the evidence that supports our anatomic understanding of these white matter tracts is derived from anatomic tracing studies in nonhuman primates supplemented by limited pathway tracings done in postmortem human brain tissue. The inferred functional association of this information then depends on critical correlation with clinical observations of patients with cortical lesions. The ability to demonstrate these tracts in vivo, therefore, represents a huge advantage in direct observation and may even generate