PWI/DWI Mismatch: Better Definition Required

To the Editor:

In their recent study of perfusion-weighted (PWI) and diffusion-weighted (DWI) image analysis, Coutts et al1 have demonstrated the difficulties associated with interpretation of postprocessed perfusion maps. There are, however, more fundamental problems than PWI map interpretation in identifying patients with perfusion-diffusion mismatch. The first is a lack of consensus concerning the definition of mismatch. Although a PWI abnormality that is 20% larger than the volume of the isotropic DWI lesion is often taken to represent significant mismatch, this is somewhat arbitrary.2 Furthermore, it has not been determined which PWI measure best defines the region of abnormal blood flow. Although most imaging groups have accepted that an index from the time domain is the most accurate, there is no agreement as to which is superior, ie, time to peak (TTP), Tmax (deconvolved TTP), or mean transit time (MTT) maps (Figure). In addition, the mathematical techniques used to estimate the true contrast transit times vary between groups.

To make the definition of perfusion deficits more objective, threshold techniques can be used.3 In the case of MTT maps, all voxels that represent MTT delay of less than the chosen threshold, relative to the contralateral hemisphere, are first removed. The volume of tissue with significant MTT delays can then be calculated from the sum of the remaining voxels. In the example shown, the measured volume of abnormal-appearing voxels on the original MTT map was 284 mL. Normalization of the map to the contralateral hemisphere 4 seconds resulted in the second map. The calculated volume of MTT delayed tissue on this map was 221 mL. The isotropic DWI volume at this time point was 178 mL. Thus, mismatch appeared to be present initially (48.7%), but normalization to the contralateral hemisphere resulted in a decrease in MTT delay volume and reclassification of the case as nonmismatch (19.6%). Although relatively simple tools such as this may become part of MRI workstation software in the future, some interpretation will always be required. As physicians become more experienced with these imaging tools, reliability should improve. Even in the present study, at least one of the examiners rated the example shown as 100% mismatch, indicating difficulty identifying the hyperintense signal on DWI.

As pointed out by the authors, the most important question remains unanswered. What is the true significance of the mismatch pattern? The hypothesis that PWI-DWI mismatch represents the ischemic penumbra remains unproved. In addition, the definition of the putative penumbra using MRI has been modified, with the recognition that the PWI lesion includes a region of benign oligemia and that a portion of the DWI lesion is potentially salvageable. DWI abnormalities do not always represent early tissue damage but rather bioenergetically compromised regions that may still be viable.4 Hence, patients without mismatch may also benefit from reperfusion strategies. These questions will be answered only with the completion of two investigator-driven trials, EPITHET (Echoplanar Imaging Thrombolysis Evaluation Trial) and DEFUSE (Diffusion-weighted imaging Evaluation For Understanding Stroke Evaluation). Unlike DIAS (Desmoteplase In Acute ischemic Stroke), neither of these trials selects patients on the basis of mismatch. Once we have a clear understanding of the biological significance of mismatch, the task of refining and standardizing its definition can begin.

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The perfusion-weighted image (PWI) is a mean transit time (MTT) map. The hyper-intense pixels demonstrate prolongation of MTT consistent with hypoperfusion in the right hemisphere. The diffusion-weighted image (DWI) demonstrates an area of acute bioenergetic compromise in the right hemisphere, which has a smaller volume than the abnormal MTT region (PWI-DWI mismatch). Normalization of the MTT map to the contralateral hemisphere +4 seconds results in a smaller PWI volume and mismatch is no longer present.
Response

We would like to thank Dr Butcher and colleagues for their interest in and comments on our article. We agree that there are many methods for perfusion map interpretation. They describe a method for mean transit time (MTT) analysis that attempts to reduce interpretation variability by normalizing to the contralateral hemisphere and applying a threshold of 4 seconds. Their technique of using the contralateral side to determine the normal MTT in a particular patient may help reduce interrater variability. However, selection of the contralateral region assumes that the brain is symmetrical.

It is probably premature to discuss standardization of MTT measurements and other perfusion parameters until their significance is fully understood. MTT may have fundamental limitations in that it demonstrates only the region of brain tissue that an occluded artery directly supplies, not the ability of autoregulation or collateral supply to continue to support that tissue. The use of quantified cerebral blood flow, cerebral blood volume, and MTT maps calculated using deconvolution and an arterial input function may give more accurate information about the actual perfusion of affected tissue. However, a comparison between relative measures (specifically peak height and time to peak) and quantified cerebral blood flow maps has found that the 2 methods provide comparable sensitivity and specificity for prognosis of infarct growth.1

Identification of tissue at risk in acute stroke may be improved by acquiring information from multiple MRI parameters and segmentation of gray and white matter2 to derive individual tissue thresholds. Perfusion analysis and interpretation is a rapidly evolving field that shows promise in identifying salvageable ischemic tissue and facilitating treatment decisions.

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*Stroke*. 2003;34:e215-e216; originally published online October 23, 2003;
doi: 10.1161/01.STR.0000099066.23627.24
*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/34/11/e215

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