Correlation of Apparent Diffusion Coefficient and Computed Tomography Density in Acute Ischemic Stroke

To the Editor:

We read with interest the recent article by Kucinski et al.1 The authors observed a decrease in the apparent diffusion coefficient (ADC) in diffusion-weighted MR imaging and a corresponding decrease in CT density in patients suffering from acute ischemic stroke of the anterior cerebral circulation. CT measurements showed a continuous linear decrease of 0.4 Hounsfield U/h, whereas the decrease in ADC was almost complete after 1.5 hours. Thus, a different time course was found between the 2 phenomena. A correlation between the decrease in ADC and that of CT density was found. They concluded that the severity of diffusion restriction correlated with net water uptake in acute ischemic stroke.

However, as the authors stated, the underlying pathophysiology and different time courses indicated a common reason rather than a direct causality for both phenomena. The underlying pathophysiology was explained as follows: Changes in CT density are known to correlate linearly with the specific gravity of the nervous tissue, i.e., with net water changes in ischemic brain tissue, thus describing the course of water uptake after ischemia. The decrease in ADC in acute ischemia correlates with the reduction in extracellular space caused by a shift of extracellular water into intracellular compartments with consecutive restriction of molecular water diffusion. This water shift results from ion pump failure caused by a severe decrease in oxygen and glucose supply.

The different time courses of ADC and CT values do not support a direct causality between diffusion restriction (brought about by intracellular volume expansion and extracellular volume restriction) and water uptake. This is consistent with previous results showing sudden ADC drop within minutes after induction of ischemia.

The authors propose a common underlying reason for both phenomena: the severity of regional cerebral blood flow reduction. The water increase is suggested to be a consequence of an evolving osmotic gradient between the intravascular and extracellular compartment evoked by the water shift into the intracellular space. Thus, the early ischemic edema is suggested to be a passive “net water uptake” delayed to the steep, initially occurring decrease in ADC. It occurs before the blood-brain barrier breaks down (vasogenic edema).

Although it is generally believed that the ADC changes measured by diffusion-weighted MRI (DWI) in brain pathologies are related to the alterations of the water compartments, the authors should also consider that despite the widespread use of the DWI, the underlying mechanisms that cause the ADC changes are still unclear. Theories independent of water shift from the extracellular space to the more viscous intracellular space were also published such as (1) loss of cytoplasmic streaming and/or the increased intracellular viscosity result in the ADC drop; (2) extracellular space becomes more tortuous during the aforementioned water shift; and (3) the transition of water from sol to gel state.

Although van Zijl et al.10 provided evidence that complete separation of the intracellular and extracellular space was feasible also by diffusion weighted spectroscopy in cell culture, the work of Niendorf et al carried out on rat brain outlines that, in vivo, the correspondence between the water populations determined by localized diffusion weighted spectroscopy and extra-, intracellular compartments is not straightforward.10 In recent years it became apparent that a sufficiently high b value water signal decay in neuronal and other tissues is not mono-exponential. The understanding of the diffusion properties of the water molecules in the nervous tissue becomes even more demanding by the extension of the b value range over 10 000 mm$^2$/s, where more than 2 exponentially decaying components can be determined.11 The fast and the slow apparent diffusing components can be assigned to free and bound water rather than to the extra- and intracellular compartments, respectively, as suggested in some previous studies.2–4

On the basis of these data, the observation of Kucinski et al that a difference exists in time courses of ADC and CT values may also be interpreted as a finding that supports the notion that the drop in the ADC values in the acute phase of cerebral ischemia is not caused by intracellular volume expansion and extracellular volume restriction but rather by the changes of the physical character of water.
diffusion component to signal intensity at low b values; however, the nature of the fast and slow components awaits further investigation.

ADC decrease due to association of water protons to macromolecules is unlikely, since the net water uptake results in an increase of free water. This can be shown by an increase in the spin-spin relaxation time T2 which correlates linearly with the ADC decrease (unpublished results). In case of macromolecular binding, T2 should decrease. For the patient shown in our article, mean T2 increased from 99±8 ms (control region) to 105±7 ms (Figure).

Even such basic phenomena like spin-spin relaxation are confounded by net water increase, diffusion restriction and T2* effects form deoxyhemoglobin. The term “apparent” diffusion coefficient, originally introduced for physical reasons, reminds us that there are a lot of uncertainties concerning the nature of the ADC decrease in acute stroke. Despite this, diffusion-weighted imaging is not a tool of uncertain value.

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