Blood-Brain Barrier Permeability in Patients with Systemic Lupus Erythematosus

We read with much interest the article by Chi et al¹ in the March 2019 issue of the *American Journal of Neuroradiology*, “Alterations in Blood-Brain Barrier Permeability in Patients with Systemic Lupus Erythematosus.”

Reportedly, dynamic contrast-enhanced (DCE) imaging supports the hypothesis that patients with systemic lupus erythematosus have increased blood-brain barrier (BBB) permeability, specifically in the hippocampus, compared with other brain regions.¹ However, some technical issues in the current study may limit its conclusions.

First, the authors stated that the pharmacokinetic 2-compartment exchange model used to calculate BBB leakage was the Tofts extended permeability model, but they provided only 2 derived parameters: the transfer constant (K^{trans}) and the extravascular extracellular volume fraction (V_e), despite the fact that the Tofts extended model is supposed to provide the blood volume fraction (V_b) in addition. V_b corresponds to the volume of vessels per volume of tissue (in milliliters/100 mL of tissue or in percentages). Thus, it is likely that the model used was a Tofts-Kety model or the Tofts and Kermode model using the Olea Sphere software (Olea Medical, La Ciotat, France), which provides only V_e and K^{trans} .^{2,3} The more complex extended Tofts model was developed to overcome some important limitations of the Tofts-Kety model, which imperfectly models DCE data and loses a significant amount of information and might not be suitable to detect subtle changes, as is the case with BBB leakage.

Second, the K^{trans} parameter is a combination of tissue blood flow (F_t), corresponding to the blood flow entering and exiting a volume of tissue, and of permeability surface-area product (PS), corresponding to the flow of molecules through the capillary membranes per volume of tissue, in varying proportions. Therefore, the K^{trans} method of calculation includes both perfusion- and permeability-related phenomena, leading to a possible misinterpretation of the parameters, even when accurately fitting the data. As a result, its use should be avoided when exploring permeability. Using a more complex and robust pharmacokinetic model like the 2CX, which provides 4 distinct parameters, including 2

perfusion-related parameters (F_t and V_b) and 2 permeability-related parameters (PS and V_e), would be more suitable.^{3,4}

Third, the authors did not provide the exact duration of their DCE sequence, though this should have been a critical part of their method. Indeed, the leakage process occurs late after contrast injection, and pharmacokinetic models calculate permeability-derived parameters on the basis of a long acquisition time. A minimal duration of 10 minutes for DCE acquisitions is therefore recommended to provide accurate data, especially when observing subtle changes, as is the case in BBB leakage.³

In conclusion, one should remain cautious when interpreting these results, especially given the very low number of patients. Using a more complex and robust model such as the 2CX, as well as optimized DCE acquisitions, might substantially improve detection and understanding of BBB leakage in patients with systemic lupus erythematosus.

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