Is Permeability Surface Area Product of [^{18}F]Florbetaben Comparable to That of H_2O?

TO THE EDITOR: I have read with great interest the article by Fettahoglu et al. (*1*) on the comparison of early-phase amyloid PET tracer and [^{15}O]H_2O and found it to be highly captivating. The authors successfully demonstrated a linear relationship between early-phase [^{18}F]florbetaben and [^{15}O]H_2O with minimal bias.

Although numerous studies highlight the utility of early-phase amyloid PET, I was inclined to suggest the necessity for contrast correction (*2*) in early-phase images, as the first-pass extraction fraction of these tracers has not been estimated to be sufficiently high. For instance, the K_1 of [^{18}F]florbetaben was estimated to be 0.187 mL/mL/min in an Alzheimer disease patient, 0.216 mL/mL/min in a healthy control subject (*3*), and 0.226 mL/g/min in another estimation (*4*). Consequently, the first-pass extraction fraction (E) of [^{18}F]florbetaben would be approximately 0.5, considering a cerebral blood flow (F) of around 50 mL/100 g/min and $K_1 = FE$.

A low first-pass extraction fraction tracer would result in underestimation in regions with high cerebral blood flow, adhering to the Renkin–Crone equation, $E = 1-e^{-\frac{PS}{F}}$ (e is the Napier constant). The permeability surface area product (PS) of an extraction fraction of 0.5 at a cerebral blood flow of 50 mL/100 g/min is theoretically 35 mL/100 g/min. However, the data presented by Fettahoglu et al. (*1*) indicate that this underestimation was minimal, suggesting that the first-pass extraction fraction of amyloid tracers may be sufficiently high and comparable to that of H_2O. Consequently, there may be no need for contrast correction.

The perplexing dissociation between the PS value of water (more than 100 mL/100 g/min (*5*)) and the above-estimated PS value of [^{18}F]florbetaben (35 mL/100 g/min) may be attributed to various factors. First, estimating kinetic parameters using the least-square method might pose challenges. Second, there could be an overestimation of radioactivity in plasma. Third, the cerebral blood flow of the participants may be smaller than expected.

Mysteries persist in the kinetic analysis of nuclear medicine, and further investigations are essential to unravel and bridge these gaps.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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Artificial Intelligence Algorithms Are Not Clairvoyant

TO THE EDITOR: Artificial intelligence (AI) systems, and computers in general, possess several advantages over humans. They have virtually perfect recall and are not subject to fatigue, mood variations, or environmental biases such as monitor contrast or room lighting conditions. However, they are not clairvoyant. Like us, they are limited by the information provided to them.

Thus, it was with a degree of concern and trepidation that I read the review article "Artificial Intelligence for PET and SPECT Image Enhancement" highlighted in the "State of the Art" section of the January 2024 issue of *The Journal of Nuclear Medicine* (*1*). The article states that "supervised deep-learning models have shown great potential in reducing radiotracer dose and scan times without sacrificing image quality and diagnostic accuracy." However, I believe this is fundamentally impossible. If photon counts are the source of information in a PET or SPECT image, then reducing scan time (and when not above peak noise-equivalent count rate, reducing dose) necessarily means less information about the patient currently being imaged.

I believe it is imperative to keep this simple fact in mind when promoting or evaluating the capabilities of any AI technique. AI models are generally trained using data or images from a separate cohort of patients. In this way, they can add information (prior information, therefore implicitly biased information) when processing a new image set. However, this should not be interpreted as additional information about the current patient. Only additional counts, or other sources of new information about the individual patient, can do that.

If I were to look at a noisy, low-resolution PET or SPECT image, the neural network in my head could imagine (based on prior experience) what it might look like if it were less noisy or had higher resolution. But this does not mean that I am better able to see the lesions that are otherwise buried in the noise. AI techniques can also "imagine," and provide for us, images that appear enhanced in their resolution and noise levels. However, this raises the question of what image enhancement is in the context of medical imaging. Prettier images do not equate to images with higher levels of useful information. Instead, an AI-enhanced image may mislead a radiologist into thinking the image data contain more information about the patient (commensurate with the perceived noise level and resolution) than is in fact present.