

$$\begin{aligned} \text{SUV} &= C(T)/(\text{injected amount} \div \text{body mass}) \\ &= C(T)/(C_p(0)V_0), \quad \text{Eq. 2} \end{aligned}$$

where  $V_0$  is an initial distribution volume implicitly defined here.  $V_0$  would be dimensionless if the convention of using activities per unit mass for  $C$  and  $C_p$  is adopted.

To further understand FUR usage, it is helpful to have an appreciation of the relationships among FUR, SUV and Patlak parameters. Dividing Equations 1 and 2 leads to:

$$\text{FUR} = \text{SUV}k_p V_0, \quad \text{Eq. 3}$$

where  $k_p$  is an average plasma clearance rate for time  $T$ :

$$k_p = C_p(0) \left/ \int_0^T C_p(t) dt \right. \quad \text{Eq. 4}$$

If  $C_p$  were describable as  $\sum A_i \exp(-a_i t)$ , then at large  $T$  (some-what greater the smallest  $a_i^{-1}$ )  $k_p$  approaches the reciprocal of a weighted sum of the  $a_i^{-1}$ 's.

To relate FUR to Patlak analysis, one only need multiply Equation 1 by the equivalent time  $\int_0^T C_p(t) dt / C_p(T)$ . Then FUR is seen as approximately the Patlak slope—to the extent that at large  $T$  the effective distribution volume term in Patlak analysis is not important.

In summary, the FUR should be recognized as an approximation to the Patlak slope, which is an easily obtained and preferable quantifier. FUR and SUV are proportional, related by plasma clearance rate and a dimensionless initial distribution volume. These proportionality constants also provide some understandings for the unexplained scatter seen in typical (2) Patlak slope and SUV correlations in a population of varying plasma dynamics: the former not having plasma variabilities.

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**REPLY:** We entirely agree with Dr. Thie's concerns and appreciate the opportunity to further discuss this subject. In our study (1), we intended to obtain the quantitative parameter of FDG uptake in normal tissues as well as in tumors. Because the plasma clearance of FDG varies according to plasma glucose level, we introduced the concept of fractional uptake (FU) in order to normalize the variability of arterial input function. Dr. Thie indicated that FU is not a dimensionless parameter and it has dimensions of reciprocal time. He also suggested calling this parameter fractional uptake rate (FUR) and we agree with his suggestion.

$$\text{FUR} = C(T) \left/ \int_0^T C_p(t) dt \right. (1/\text{min}). \quad \text{Eq. 1}$$

In this equation,  $T$  is the middle time of the PET scan. Because static PET scan was performed from 40 to 60 min after FDG injection in our study,  $T$  was 50 min for all patients.

Dr. Thie clarified the relationships among FUR, SUV and Patlak parameters and concluded that FUR was an easily obtained and preferable quantitative parameter. FUR may not be recommended for all quantitative studies because it needs serial arterial samplings. This procedure is, however, widely performed in many quantitative studies which evaluate, for example, rate constants with compartment model analysis, cerebral metabolic rate of glucose with Phelps' method or Patlak parameters (2–4). We believe that FUR can give additional, useful information about tracer uptake in these studies.

In FDG-PET studies especially, FUR can be converted to the more physiological parameter FURglu by introduction of a lumped constant (2):

$$\begin{aligned} \text{FURglu} &= \frac{\text{plasma glucose concentration}}{\text{lumped constant}} \\ &\times \text{FUR} (\mu\text{mole}/100 \text{ g}/\text{min}). \quad \text{Eq. 2} \end{aligned}$$

FURglu does not represent glucose metabolic rate directly, but we think it is a reliable parameter of glucose uptake rate when the lumped constant is known or assumed to be a constant (5). We believe both FUR and FURglu would be simple and reliable parameters and should be estimated before calculation of more complicated parameters.

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## Early and Delayed Technetium-99m-ECD Brain SPECT in Stroke

**TO THE EDITOR:** We read with interest the article by Moretti et al. (1) dealing with the comparison of  $^{99\text{m}}\text{Tc}$ -ethylcysteinate dimer (ECD) and  $^{123}\text{I}$ -isopropylidoamphetamine (IMP) for brain SPECT imaging in subacute stroke. The study was a part of a multicenter trial on ECD. The authors compared the washout from various brain regions during early and delayed SPECT acquisition. Early acquisition was started 50–120 min and delayed acquisition 130–420 min after tracer injection, respectively. The study revealed—besides a slightly, but not significantly, higher accuracy of ECD for the detection of the infarct—a higher washout of ECD from ischemic parietal zones than from normal pari-

etal zones. The authors conclude that in spite of improved SPECT image quality, accuracy is not affected by early imaging after 1 hr.

We congratulate the authors for their excellent study. Nevertheless, we do not agree with the statement "The brain distribution of  $^{99m}\text{Tc}$ -ECD versus time in normal and ischemic tissue at the subacute phase of stroke has not yet been studied." Participating in the Phase III multicenter trial on ECD, our group performed—similarly to Moretti et al. (1)—early and delayed ECD SPECT imaging in stroke. Our data were presented in Sendai in 1993 (2). The investigation included 11 patients with subacute stroke (5–15 days), four patients in the late subacute phase (16–30 days) and two patients in the chronic phase (>30 days). We performed SPECT studies on 11 patients 60 min and 20 hr after tracer injection and observed hypoperfusion of the affected hemisphere in 16 of 17 patients on the early SPECT scan. Semiquantitative analysis of the 11 patients with early and delayed SPECT studies was performed. The ratio (infarcted to contralateral region) showed a significant ( $p < 0.01$ , paired t-statistics) decrease from the early ( $0.80 \pm 0.09$ ) to the delayed ( $0.71 \pm 0.14$ ) SPECT image. Therefore, the results of both studies (1,2) agree in demonstrating increased washout from infarcted tissue, although the time lag between early and delayed imaging was markedly different.

ECD brain uptake has been proven to be blood flow-dependent in epilepsy, dementia and cerebrovascular diseases. In contrast to other blood flow tracers such as IMP or  $^{99m}\text{Tc}$ -hexamethyl propyleneamine oxime in late posts ischemic reperfusion/luxury perfusion such as ECD shows no increased uptake, but a decreased uptake (3). In normal brain tissue, the trapping mechanism for ECD is its hydrolyzation into polar metabolites after crossing the blood-brain barrier. In stroke, particularly in the subacute phase, different binding mechanisms must be assumed, which could explain the retention differences in luxury perfusion (3) and the increased washout from infarcted brain tissue (1,2).

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**REPLY:** We were delighted to read the comments of Grünwald et al. concerning our results for comparison of early and delayed ECD and IMP brain imaging in subacute strokes (1). We agree that we forgot to quote their excellent study (2) and to discuss their results in our article. Our attention was mainly focused on comparison of ECD diagnostic accuracy with IMP within 5 hr after tracer injection. Their study, which addressed ECD with a delay in exploration (20 hr), was beyond the scope of our paper. We acknowledge that very delayed images also demonstrated significantly increased washout from infarcted tissue.

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