and U-87 MG human glioblastoma (*1*). In order to explain these results, which seemed to contradict the findings of previous studies describing enhanced polyamine metabolism in rat and human gliomas, the authors conjectured that polyamine metabolism might vary with tumor growth fraction, and they discussed the importance of alternative pathways of putrescine metabolism (*1,4,13*) and the existence of multiple endogenous polyamine pools. In their current paper, Hiesiger et al. conclude that [^{11}C]putrescine uptake relates primarily to BBB breakdown rather than to tumor polyamine metabolism or mitotic activity and, therefore, "appears to have more limited diagnostic utility than ^{18}FDG or ^{11}CDG."

In retrospect, it is not difficult to see where things went wrong. First, the lack of a comprehensive biophysical/biochemical model for [^{11}C]putrescine uptake, based on accepted in vitro and in vivo biochemical data and taking into account BBB transport, extra- and intracellular compartmentalization and tracer metabolism to polyamines, nonpolyamine metabolites and CO_2, led to ambiguous or uninterpretable PET results. Second, the graphical evidence of irreversible tumor uptake of [^{11}C]putrescine, presented by Hiesiger et al. in their 1987 paper, was ultimately based on a *single* 50-min patient study in which, at 20 min after tracer injection, only 9% of the plasma ^{11}C radioactivity was identified by HPLC as putrescine—the remaining 91% was characterized as "[^{11}C]O_2 and nonvolatile metabolites." Third, the difficulties in interpretation occasioned by tumor heterogeneity (both histological and metabolic) and volume averaging, and the limitations of data analytic strategies relying on average regional (region of interest) or peak values were not fully appreciated (*14*). Finally, insufficient attention was paid to the mechanism of putrescine uptake, the limitations of experimental brain-tumor models, and the relative merits of other nonglucose ^{11}C and ^{18}F PET tracers employed for brain-tumor imaging (*15–17*).

In conclusion, the lessons learned from the [^{11}C]putrescine experience—the importance of tracer kinetic modeling, the need for complete radiochemical characterization of the arterial input function, and the constraints imposed by in vivo tumor biology—need not be re-learned during the evaluation of each new brain-tumor radiotracer. Claims of diagnostic and prognostic utility for novel PET tracers must be evaluated within the context of the bedside neurological examination and the results of CT/MRI scanning and standard neurodiagnostic tests. Given the biologic and metabolic diversity of human brain tumors—which extends to individual metastatic deposits—multidimensional prospective clinical trials will be required to establish meaningful estimates of in vivo sensitivity and specificity.

D. A. Rottenberg
VA Medical Center and University of Minnesota
Minneapolis, Minnesota

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Correction

In the November 1991 issue of the *Journal,* the author line for "Noninvasive Delineation of the Effects of Moderate Aging on Myocardial Perfusion", by Senneff et al (pages 2037–2042) was printed incorrectly. It should read: Martha J. Senneff, Edward M. Geltman, and Steven R. Bergmann, with the technical assistance of Judy Hartman.