
Book Reviews

PET and SPECT in Neurology PET and SPECT in Psychiatry PET and SPECT of Neurobiological Systems

R.A.J.O. Diercks, A. Otte, E.F.J. de Vries, and A. van Waarde, eds.

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There is a series of 3 new books on PET and SPECT that is marvelous in terms of editorial coordination and comprehensiveness of content. After browsing them on and off during the last 6 mo, it took me an entire week to read all the way from the first page of *PET and SPECT in Neurology* through *PET and SPECT in Psychiatry* to the last page of *PET and SPECT of Neurobiological Systems*. Many chapters were ripe and rich in well-organized knowledge and sometimes delivered new and exciting information. I particularly enjoyed the chapters on consciousness, on anesthesia, on pharmacologic and nonpharmacologic interventions, and on the endocannabinoid system. Finding the most appealing content among the vast material in these books was like finding a needle in a haystack, but the effort was worth it.

Each of the 3 books has its own guest editor, and the difference in authors between books gives each book its own flavor. The volume on neurology was filled with details on clinical studies, some of which were repeated in separate chapters written by different authors. The authors were mainly from The Netherlands. The evidence from clinical studies in this book helps readers understand how to use PET and SPECT in clinical settings. Optimizing the clinical use of PET and SPECT is like hitting a moving target, and redundant explanations might indeed be necessary. The depth and breadth of the descriptions among chapters are relatively consistent, but certain descriptions—such as the optimal use of PET, of SPECT in epilepsy, or of acetazolamide SPECT in cerebrovascular occlusive diseases—are insufficient, and the description of the use of amyloid plaque imaging is a bit superfluous.

The volume on psychiatry is streamlined on the basis of the DSM-IV or DSM-V classification of psychopathology. Many qualified psychiatrists participated in making this book, and their description of major conditions such as depression is so full-fledged that even absolute novices—not taking care of psychiatric patients every day—can grasp the concepts. Evidence-based approaches or outcome-based concepts on the use of medical resources do not recommend the routine clinical use of PET or SPECT in psychiatric illnesses, whether for perfusion, metabolism, or neurotransmission chemistry imaging. However, the book includes an excellent, detailed literature summary that leads readers to attend to developments in that direction. This literature summary is a great introduction to the present preclinical stance of SPECT and PET in psychiatry. What is regrettable is a lack of description of the connectivity studies that recently have been developed, though many chapters include the findings of regional abnormalities even with rigorous statistical parametric mapping. Underestimation of neurodevelopmental disorders, such as attention deficit hyperkinetic disorder and disorders of the autism

spectrum, is another disappointment. They are covered only under the category of miscellaneous subjects.

The volume on neurobiological systems was written mainly by chemists, who describe the present status of progress in each field well but with varying depth and detail. The structure of the book is interesting; it was not immediately apparent to me that the topics are presented in alphabetical order by title of chapter. Discovering this fact was refreshingly entertaining after I had spent lots of time reading the details while being puzzled as to why the nicotinic system is presented after the muscarinic system or opioids after the norepinephrine system. Also amusing is the anthology of apologies at the end of this and the other books in the series. Readers will enjoy these anthologies and understand how hard it was to coordinate and organize these books. Several chapters are slightly frustrating, such as that on the nicotinic acetylcholine receptor system, which describes in too much detail the sole chemistry in chemistry fashion, and that on the *N*-methyl-D-aspartate receptor system, which unnecessarily describes the many failed attempts to develop radiochemicals for these receptors. In addition, the lack of images to complement written descriptions of representative brain-imaging radiochemicals is a limitation for readers, especially nuclear medicine physicians such as me.

In subsequent reviews, I and my colleagues will summarize and comment in more detail on each volume of this series of unprecedentedly comprehensive and charming books, revealing their uniqueness and individual merits.

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Letters to the Editor

Repeatability of Tumor SUV Quantification: The Role of Variable Blood SUV

TO THE EDITOR: The recent study by Weber et al. (1) addresses standardized uptake value (SUV) quantification repeatability in 2 multicenter trials of non-small cell lung cancer and reports repeatability coefficients of $-28\%/+39\%$ and $-35\%/+53\%$ for SUV_{peak}. No clear correlation was found between SUV test–retest variability and any of several considered parameters (body weight, age, clinical stage, blood glucose level, uptake time). We would like to draw attention to another possible explanation, namely interscan variation of the arterial blood SUV.

In a previous publication (2), we demonstrated a distinctly improved linear correlation between tumor-to-blood SUV ratio (SUR) and K_m , the metabolic rate of ^{18}F -FDG, in comparison to SUV versus K_m correlation. In a later publication (3), we provided strong evidence that SUR possesses a distinctly improved prognostic value in comparison to SUV.

Our results, together with other data (4,5), support the notion that SUV normalization (either to body weight or lean body mass) does not reduce interscan blood SUV variability below 20%–30% (single SD). This implies an equally large test–retest variability of SUV parameters (SUV_{peak} , SUV_{mean} , SUV_{max}) since tracer uptake is proportional to the scaling of the arterial input function. This variability can be eliminated by replacing SUV by SUR, that is, by normalizing tumor SUV to arterial blood SUV.

Weber et al. (1) did not detect a notable influence of uptake time differences on the SUV variability coefficients although irreversible binding of ^{18}F -FDG will cause continuously increasing SUVs over time in the presence of nonnegligible residual blood SUVs. We have quantitatively investigated this effect and were able to demonstrate that a variation in uptake time from T_0 to T might be corrected approximately (6) according to $\text{SUV}_0/\text{SUV}_T \approx (T_0/T)^{1-b}$, where $b \approx 0.31$ is determined by the given (essentially invariant) shape of the arterial input function. Since Table 1 of the present paper yields some 15%–20% (SD) uptake time variability for the respective scan groups in both trials, one arrives at roughly 12% SUV variability (SD). Together with a conservative low estimate of 22% for the variability of tracer supply (blood SUV), one then can estimate by gaussian error propagation that both (uncorrelated) effects lead to a cumulative variability of about $\Delta\text{SUV}/\text{SUV} \approx \sqrt{(22^2 + 12^2)} \approx 25\%$. Since the uptake time variability is moderate in the investigation of Weber et al., the predicted tumor SUV variability is thus mostly due to interscan blood SUV variation, which might explain that the uptake time effect alone does not clearly manifest itself in the investigation of Weber et al.

Overall, comparing the 25% estimate given above with the actual SUV variability reported by Weber et al., we conjecture that a large part of the observed variability might be a consequence of blood SUV variability (plus an additional component due to uptake time variability). On top of this approximately 25% effect, other factors are operational such as imperfect scanner calibration and inaccuracies of body weight and dose information (all of which should also be accounted for when moving from SUV to SUR since they cancel out from the ratio computation).

If our conjecture is correct, one would expect that the test–retest stability of tracer uptake quantification would be distinctly improved if instead of SUV the SUR corrected for uptake time were used. SUR (which equals the left-hand side of the Patlak equation) can be shown to have a better linear correlation to K_m than SUV theoretically as well as experimentally (2), which has rather obvious consequences for the prognostic value of both quantities (3). We would therefore find it highly desirable to test the hypothesis of superior performance of SUR in the valuable data of Weber et al. This could be done retrospectively by performing an image-based determination of the blood SUV in a suitable 3-dimensional region of interest placed in the aorta.

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REPLY: My coauthors and I thank Drs. van den Hoff and Hofheinz for their comment. Our paper (1) focused on commonly used parameters for quantifying tumor ^{18}F -FDG uptake (SUV_{peak} and SUV_{max}). However, we fully agree that there are several other potential ways to normalize tumor ^{18}F -FDG uptake. Normalizing tumor SUV by arterial blood SUV is supported by tracer kinetic analysis as described by Drs. van den Hoff and Hofheinz in their letter and their previous publications. One caveat, however, is that defining a second region of interest to measure the blood activity concentration introduces an additional source of variability. Also, tumor-to-blood ratios will be more dependent than tumor SUVs on the time after injection, because the activity concentration in the blood steadily decreases with time whereas that in the tumor typically increases.

Therefore, it needs to be determined whether the repeatability of tumor-to-blood ratios is better than the repeatability of SUVs. The image data of our trial are stored at the American College of Radiology Imaging Network, and data access can be requested to evaluate the repeatability of other quantitative parameters of tumor glucose metabolism. We encourage Drs. van den Hoff and Hofheinz to apply their interesting approach to our data and compare the repeatability of SUVs and tumor-to-blood ratios.

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