Quantitation of Neuroreceptors: A Need to Increase Imaging Resolution?

TO THE EDITOR: van Dyck et al. (*1*) recently reported estimations of the specific-to-nondisplaceable partition coefficient V_3'' of [^{123}I]β-CIT calculated as (striatal–occipital)/occipital uptake at tracer equilibrium (18–24 hr after injection of tracer). The measurements were performed with the multislice brain dedicated GERASPECT device with a spatial resolution of 7–8 mm FWHM. The images shown, however, in their article (Figs. 1 and 5) correspond roughly to image resolution of 12–14 mm (not 7–8 mm). Imaging resolution depends on many things such as collimator used, reconstruction filtering, scatter, etc. and is not the same as the spatial FWHM resolution of the scanner. Numerical values of V_3'' are fully dependent on imaging resolution as well as on reconstruction errors of the low count density reference region (occipital) and on the regions of interest drawn. Numerical values of V_3'' from 4 to 12 are reported even in age-matched healthy control subjects. Similar numerical values of the other parameters of [^{123}I]β-CIT vary 100%–300% (*2,3*). What does this mean? The values between laboratories are not comparable.

The answer to this problem is better SPECT. With essentially all [^{123}I]β-CIT is in the striatum at 18–24 hr after injection of tracer, one might be able to increase imaging resolution by 5–6 mm. A choice of the proper reconstruction filter is important. Figure 1 shows a 2.8-mm-thick transaxial slice of a 37-yr-old healthy male imaged with the Siemens MultiSPECT 3 gamma camera with fan-beam collimators by using a Butterworth filter (order = 8) with two cutoff frequencies. The dose used was 185 MBq (5 mCi). The quality difference of these two images is impressive. In addition, the numerical value of V_3'' with the softer filter is 30% less than that of the harder one. The tracer [^{123}I]β-CIT is satisfactory and quantitation is easy, but overall results depend on the excellence of the SPECT system used. This is a sensitive and specific tracer to image patients with Parkinson's disease. It demonstrates the loss of presynaptic nerve endings in the striatum in relation to the severity of parkinsonian disability and is helpful in the early diagnosis and follow-up of Parkinson's disease. Hopefully, we will not distort its use with faulty quantitation.

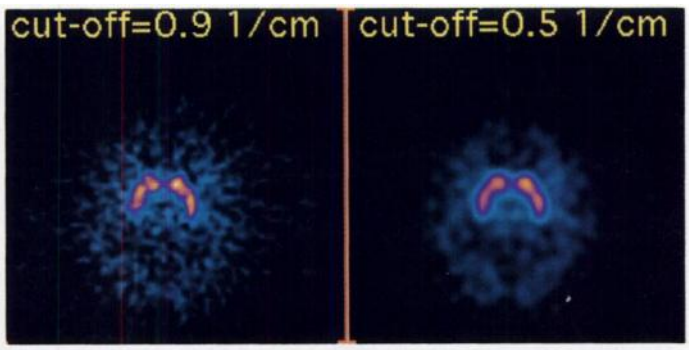

FIGURE 1. Transaxial slice of striatal [^{123}I]β-CIT uptake in a 37-yr-old healthy man using two cutoff SPECT filtering frequencies. The filter used was a Butterworth with an order of 8. There is a 30% difference in semiquantitation of (striatum-occipital)/occipital ratio between these two images.

REFERENCES

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3. Tiihonen J, Kuikka J, Bergström K, et al. Altered striatal dopamine re-uptake site densities in habitually violent and non-violent alcoholics. *Nature Medicine* 1995;1:654–657.

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REPLY: Dr. Kuikka raises timely questions for an era of increasing multicenter imaging studies (*1*). He is certainly correct that estimations of the specific-to-nondisplaceable partition coefficient V_3'' with [^{123}I]β-CIT SPECT depend on image resolution which, in turn, depends on choice of collimator, reconstruction filter, etc. He also notes that values of V_3'' and other outcome measures with [^{123}I]β-CIT vary substantially between laboratories. We should caution, however, that the studies he cites use somewhat different outcome ratios [i.e., basal ganglia/white matter (*2*) or basal ganglia/cerebellum (*3*) than that used by our group [(striatum-occipital)/occipital (*4*)]. We should further point out that, even using identical parameters, some biological variability is to be expected. Within our program, differences of twofold or greater are observed in V_3'' between healthy subjects of the same age (*4*), which are consistent with in vitro dopamine transporter binding studies (*5–7*).

To be sure, some of the variability between laboratories in outcome measures with [^{123}I]β-CIT accrues from the factors detailed by Dr. Kuikka. His example illustrates this point well: V_3'' is altered 30% by a change in Butterworth filter cutoff frequency. However, we do not believe that interlaboratory comparability will be achieved solely by increasing (or otherwise standardizing) image resolution. Enhanced resolution may come at the cost of decreased sensitivity (in the case of increased collimator resolution) or increased noise (in the case of "harder" filtering). Moreover, increased resolution alone will not address the many other issues necessary to achieve interlaboratory comparability, including camera sensitivity, attenuation and scatter corrections and regions of interest. As formal multicenter trials are organized with [^{123}I]β-CIT and other neuroligands, they will need to employ either identical imaging equipment and reconstruction algorithms or, more realistically, phantom-derived conversion factors.

We should note, finally, that the problems raised by Dr. Kuikka need not compromise the validity of results *within* a given laboratory, provided that they affect the outcome measure in a linear manner. For our studies with [^{123}I]β-CIT, we have performed phantom studies to verify linearity between known activity (across a physiologic range, including activity levels representative of the low-count occipital region) and reconstructed counts. These studies have used the same camera, collimation and filtering as utilized in our human studies. Therefore, when we report a decline in V_3'' by 51% from age 18 to 83 (*4*), we expect that this result could be reproduced by another laboratory using different imaging equipment and reconstruction algorithms.

REFERENCES

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