

Cerebral Blood Flow-to-Blood Volume Imaging by SPECT

TO THE EDITOR: In a recent article, Knapp et al. (1) described a method to determine the regional cerebral flow-to-volume ratio by single photon emission computed tomography (SPECT). They used iodine-123 (^{123}I) iodoamphetamine (IMP) to assess flow and technetium-99 ($^{99\text{m}}\text{Tc}$) pertechnetate-labeled red blood cells to image volume. This approach is based on the work of Gibbs et al. (2) with $^{15}\text{O}_2$ and positron imaging who found this ratio indicative for the cerebral vascular reserve in patients with cerebrovascular disease (CVD). The results of Knapp et al. are indeed promising despite the fact that Powers et al. (3) demonstrated the variability of this ratio in patients with CVD.

There are, however, some disadvantages in using IMP. Our group has demonstrated (4) that regional brain uptake of IMP still increases from 20–40 min after injection. Employing the same SPECT machine as Knapp et al. (double head ROTA gamma camera) we performed [^{123}I]IMP-SPECT at three different periods of time after injection (13–27 min, 33–47 min, 5.5 hr) and measured the regional IMP density. Figure 1 illustrates the increasing uptake, even in defect areas (difference to contralateral ROI: <10% = normal, 10–20%, 20% = defects). This “filling in” during the later period (30 min–4 hr) has been confirmed by Creutzig et al. (5). In addition, a comparison with results of xenon-133 DSPECT revealed that IMP in CVD represents rCBF only during the first 30 min after injection (4). Therefore, employment of a rCBF marker with stable distribution, like hexamethylpropyleneamineox-

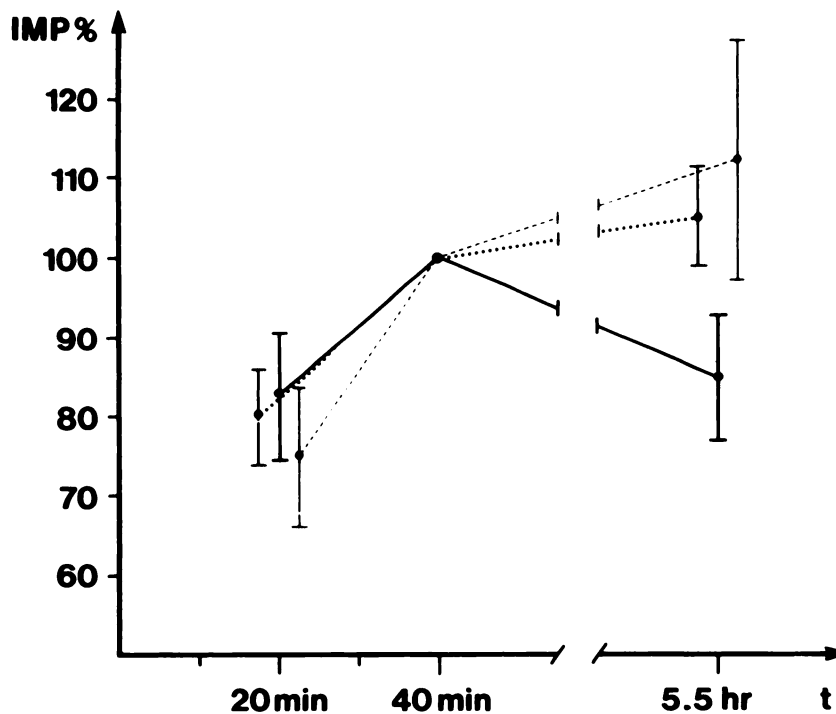
ime (HM-PAO), may be preferable for this approach. Besides the sophisticated corrections which have to be done using ^{123}I in combination with $^{99\text{m}}\text{Tc}$, one problem has not been mentioned in the paper; that is, the blurred border between the high blood volume of the skull and the low blood volume of the cerebral periphery. Thus, by the resolution of SPECT machines and by reconstruction filters employed, we face the inherent problem of unspecificity of flow-to-volume ratios in the outer hemispherical periphery. To overcome this drawback, attenuation and/or Compton correction should be employed.

In our current approach with SPECT, we are using 500 MBq $^{99\text{m}}\text{Tc}$ -labeled red blood cells and 500 MBq [$^{99\text{m}}\text{Tc}$]HM-PAO in one session to obtain volume or volume + flow data in two consecutive 360° rotations. The subtraction of volume from the flow + volume data is simple and is done for each single projection (6°) before reconstruction of the flow slices. We feel that flow-to-volume obtained with this technique could become useful also in diseases other than CVD. Within this scope, epilepsy might be of interest since HM-PAO-SPECT has already yielded helpful results in preliminary studies (6).

References

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FIGURE 1
Regional kinetics of [^{123}I]iodoamphetamine in hemispherical periphery over time after injection in patients with unilateral CDV. IMP data represent relative uptake (\pm s.d.) in selected ROI (n = 116) versus count-rate densities measured 33–47 min after injection (~40 min = 100%). All data are half-life corrected. Difference-to-contralateral uptake <10%: normal; 10–20% or >20%: defects. (—) Normal (n = 32); (.....) Defect <20% (n = 8); (---) Defect >20% (n = 18)



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REPLY: Buell et al. encourage the use of one of the technetium-99m-(^{99m}Tc) labeled cyclic amines now becoming available for estimations of regional cerebral blood flow (CBF) distribution. This label is much more convenient to use and less costly than iodine-123. Thus, [^{99m}Tc]HM-PAO could represent a major advance towards routine single photon emission computed tomography imaging in cerebral diseases.

It appears that [^{99m}Tc]HM-PAO exhibits—when the most recent compound (d,l isomer) is used—a higher stability of its initial brain distribution. However, this isomer which is favorable with respect to constant uptake gives rise to a relatively high intravascular activity. The blood contains a considerable amount of the injected material, exceeding 10% as late as 2 hr p.i. (1). Besides, radiochemical impurities up to 15-20% (2,3) must be faced. They consist of free pertechnetate or secondary complex (2), both of which do not cross the blood-brain barrier. Therefore they can interfere with the lipophilic complex in case of cerebral lesions.

As to CBF/CBV imaging, it must be taken into account that the increased negative contrast obtained by this method in diseased areas, as compared with CBF images alone, is purchased by potentiation of noise. This is caused by the pixel-for-pixel division of two separately acquired images and reduces the detectability of details, whatever method is used. However, the side-to-side differences are so dramatic in instances of CVD that the display of relatively rough anatomical structures does not compromise the efficacy of the method. The premise is that the CBF-related image does not overestimate flow in areas with increased blood volume or with tissue damage. The relatively high intravascular activity continuing after [^{99m}Tc]HM-PAO (d,l isomer) injection and the above-mentioned radiochemical impurities must be considered as a potential source of degradation of the CBF/CBV image contrast.

In conclusion, our concept of CBF/CBV imaging with SPECT may profit from new radiopharmaceuticals like [^{99m}Tc]HM-PAO. Using this compound, careful studies will be needed to analyze and solve the problems of potential artifacts by intravascular activity and radiochemical impurities in diseased foci.

References

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Perfusion Patterns in Dementia

TO THE EDITOR: We were interested in Dr. Holman's George Taplin Memorial Lecture (1) and would like to amplify and qualify some of the comments he makes.

We would not claim that our results (2), or those reported in Cohen's paper (3), showed "distinctive perfusion patterns in MID in most patients." As our experience in imaging such patients has increased (4) we have found that the MID perfusion pattern can vary from gross focal defects to completely normal. In our reported series the normal pattern was found in a patient with grade 3 cognitive impairment and a Hachinski score of 9. As this patient has definite cognitive impairment related to the presence of infarcts we must conclude that, at least in this case, they are too small to be visualized by our technique. As a corollary to this we must also question whether the infarcts visualized in the other patients with MID in our study are involved in the dementia per se or are simply the result of this group of patients being predisposed to infarcts.

We are also puzzled by Dr. Holman's comment on the uptake pattern in Korsakoff's psychosis. We can find no mention of it in Dr. Cohen's paper to which he refers; our experience is that the pattern is normal.

As was suggested in our paper, it may be necessary to reconsider some of the negative findings in the light of improvements in the technique. We recently reported that the d,l isomer of hexamethylpropyleneaminooxime labeled with technetium-99m (5) is a potential rCBF agent with excellent imaging characteristics. We can confirm, as Dr. Holman suggests, that this radiopharmaceutical is indeed suitable for investigating dementia (6). Using this agent with a high resolution tomographic imager (7), we have observed changes in uptake in the head of the caudate nucleus in patients with Huntington's Chorea which support the findings made with PET imaging (8). Incidentally, we must apologize for giving an incorrect reference to this in our paper.

Finally, although SDAT is characterized by bilateral reduction in uptake in the temporo-parieto-occipital regions, contrary to Dr. Cohen's hypothesis these changes are not necessarily symmetrical.

It is interesting to see that adequate imaging can be performed with a rotating slant hole collimator but we would strongly urge centers interested in this work to utilize rotating