SPECT Evaluation of Cervical Occlusion

TO THE EDITOR: Two recent articles (*1,2*) and an editorial (*3*) on evaluating patients for permanent occlusion of the cervical internal carotid or cerebral artery with SPECT and temporary balloon occlusion are to be applauded. Both verify the work that has been done for years with stable xenon CT. Further, all the authors reference some of the previous work done with stable xenon, which is refreshing. A novice in CBF measurements would be hard pressed to learn of competing technologies (particularly stable xenon CT) from most CBF articles in the *JNM*.

I must take exception, however, to the references by all three groups which question the validity of stable xenon CT techniques based on flow activation of 30%–35% concentration of xenon as cited through Giller et al. (*4*). It is generally agreed and has been confirmed by others (*5*), that TDC-monitored flow velocity increases under the influence of xenon. Everybody associated with stable xenon and CBF agrees that xenon does significantly increase CBF, however, the results of measuring CBF with stable xenon are not significantly affected because the procedure is essentially complete before the effect takes place. Over the years, most xenon CT practitioners have reduced the total xenon breathing time to under 5 min, thus closing the barn door while the horse is still contemplating escape.

Lindstrom (*6*), also one of the Giller co-authors (*4*), did a computer simulation using a 40% flow increase and demonstrated no significant change in CBF values. That a significant flow change during the procedure produced no significant change in results is attributed to the assumption of time-invariant flows built into the Kety-Schmidt integral equation used by both the stable and radioactive xenon method.

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REPLY: The comments of Mr. Timpe regarding the validity of xenon CT in measuring cerebral blood flow (CBF) have been addressed in depth by one of my coauthors, Dr. Philip Purdy (*1*) and one of my colleagues Dr. Cole Giller (*2*). However, I will briefly summarize our reservations regarding this technique.

One of the basic tenets of CBF measurement is that the agent used to quantify CBF does not itself alter CBF, therefore the original techniques of nitrous oxide and xenon gas washout were developed. However, at the concentrations of xenon gas used in the xenon CT technique, CBF can be altered. Using transcranial Doppler measurements, Drs. Giller and Purdy (*3*) demonstrated marked alterations in measured cerebral blood velocity in normal subjects inhaling xenon gas concentrations consistent with those used in xenon CT. The troubling issue in their study was that the variability of response between subjects was high. In 15% of these subjects, velocities actually decreased rather than increased. This suggests that it is not enough to just factor in a known degree of overestimation of blood flow because the variability of the response is so great. In addition, there is little data about whether this variability might be further increased in pathologic conditions. This variability of response is also the reason why a computer simulation of cerebral blood flow using xenon CT does not adequately examine what actually happens in an in vitro model. Mr. Timpe also states that the rise in CBF seen with xenon CT occurs after inhalation of xenon is complete. Again, the Giller et al. study demonstrated that this increase occurred at variable times, sometimes as soon as 1 min (*3*).

Finally, while blood flow measured with xenon CT has been correlated with other techniques of measuring CBF such as microspheres, little work has actually demonstrated that xenon CT reliably measures CBF. At different flow rates, radioactive count rates for two techniques, e.g., microspheres and ^{133}Xe, may rise parallel to one another but produce different calculated values, especially under high flow conditions. That flow values calculated by xenon CT parallel those of the other techniques does not mean that the calculated value is the *same* as that produced by comparison with the gold standard which in this case is microsphere measurement.

Although high-resolution SPECT CBF imaging at this time is not easily quantified in terms of ml/100mg/min, we do know that the agents such as ^{99m}Tc-HMPAO discussed in our paper behave like "chemical microspheres" (*4*) in that they do not themselves affect CBF, they distribute themselves in the brain proportionally to CBF at the time of injection, and they are trapped in the brain by ligand or conformational changes. CBF imaging can be performed at a time distant to the actual balloon occlusion and the patient does not have to be transported to the nuclear medicine area with a carotid catheter in place.

I think that for the reasons stated above, if CBF imaging during trial occlusion of a carotid or intracerebral artery is desired, high-resolution SPECT imaging is more reliable, practical and more easily obtained in most institutions than CBF measured by xenon CT.

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The Scintigraphic Sign for Detection of Right-to-Left Shunts

TO THE EDITOR: In a recent paper in the *Journal*, Dogan et al. reported on lung scintigraphies in patients with right-to-left shunts (*1*). They found a new scintigraphic pattern in extrapulmonary distribution after intravenous injection of ^{99m}Tc-labeled macroaggregated albumin in 18 of 49 patients with proven cardiac right-to-left shunt, a so-called "quantum mottling" pattern, visible in kidneys and brain. Dogan et al. argued that this phenomenon is caused by too few particles, which where 50,000 to 100,000 in each patient. The size of the shunt was >10%. Dogan et al. concluded that the quantum mottling pattern allows a reliable proof of a cardiac right-to-left shunt.

Between 1978 and 1991 we carried out more than 500 investigations in 150 children with tetralogy of Fallot and pulmonary atresia with ventricular septal defect. We injected 2 MBq/kg body weight (minimum activity, 15 MBq) of ^{99m}Tc-labeled macroaggregated albumin intravenously in the supine position (Solco^{R} MAA, Sorin Biomedica, Italy; in more than 95%, the particle size ranged between 5–40 μm, the number of particles comes to 2,000/MBq according to the producer). If there was a perceptible extrapulmonary activity in the perfusion scintigraphies, we proceeded on the assumption that the right-to-left shunt was measurable. That was the case in 71 children. The scintigraphic right-to-left shunt varied between 7% and 63%, the average was 27.5%. A preoperative cardiac catheterization was also performed and determined a ventricular septal defect in all children. Due to the fact that the whole extrapulmonary activity was not measurable at the same time, we used the accumulation of the radioactive tracer in the kidneys as a reference to the extrapulmonary activity. Assuming that the kidneys receive about 25% of the heart-time volume, we multiplied the activity in the kidneys by a factor of 4:

$$\text{Formula 1: } \frac{\text{Activity}_{(\text{kidneys})} * 4 * 100\%}{\text{Activity}_{(\text{kidneys})} * 4 + \text{Activity}_{(\text{Lungs})}}.$$

However, we found a homogeneous pattern of activity over the kidneys and brain in all children. Depending on the size of the shunt volume, there was a corresponding strong accumulation over the kidneys and brain, which was always homogeneous. There was no evidence of a quantum mottling pattern described by Dogan et al. (*1*). Also, Gates et al. who reported on 36 children with various congenital heart defects, could not find this phenomenon in their scintigraphies (*2*). The number of particles in our study was between 30,000 and 60,000 which is comparable to Dogan et al. Thus, the small number of particles does not sufficiently explain the quantum mottling. Possibly, the activity has not been shaken up immediately before the injection causing several macroaggregates to be linked together. This might have led to a larger size of the conglomerated particles and to a decrease in the total quantity. Although in children the absolute number of particles is smaller than in adults, the specific number of particles per volume is higher. Consequently, the scintigraphy in children might be more homogeneous, on the other hand there is no significant difference in perfusion concerning the homogeneity of brain and kidneys between children and adults. Also, a smaller shunt volume is not a sufficient explanation for the quantum mottling because even in children with a small shunt (10%–20%) there was no evidence for that phenomenon. Even though Palevsky et al. mentioned quantum mottling of the brain in two adults with a right-to-left shunt, many other authors did not find this phenomenon (*3*). However, in our opinion, a quantum mottling pattern in children does not exist as illustrated in Figure 1.

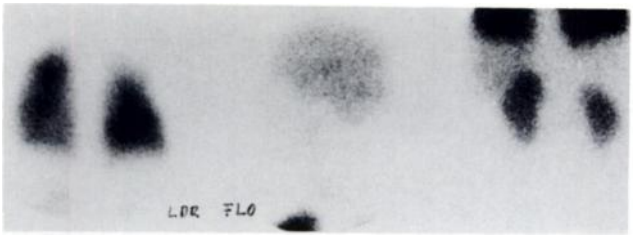

FIGURE 1. An 8-yr-old girl with a calculated right-to-left shunt of 25% shows a homogeneous distribution of activity over the brain and kidneys. Lack of activity in the thyroid demonstrates the absence of pertechnetate. For comparison of the relative distribution of radioactivity, the dorsal lung image is given. Activity used was 35 MBq with 70,000 particles.

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REPLY: We read with great interest the letter submitted to the *Journal* by Meins et al. regarding our recent article on the scintigraphic findings in patients with right-to-left shunts. We were surprised to hear that our colleagues from Hannover did not observe a quantum mottle (QM) pattern on ^{99m}Tc-MAA images obtained in patients with documented right-to-left shunts, and we were even more surprised by their suggestion that our reported finding was due to imaging artifacts or poor radiopharmaceutical preparation technique. Accepting the observations of our German colleagues, we decided to search for an explanation for the two discordant reports.

The question of imaging artifact or inappropriate radiopharmaceutical preparation was easily dismissed. In our department, all radiopharmaceutical preparations and evaluations are done under the close supervision of a board-certified radiopharmacist. Right-to-left shunt studies are done only with fresh preparations of ^{99m}Tc-MAA, and the contents of each newly prepared kit undergo meticulous quality assurance testing, including thin-layer chromatography and evaluation of particle size with a microscope and