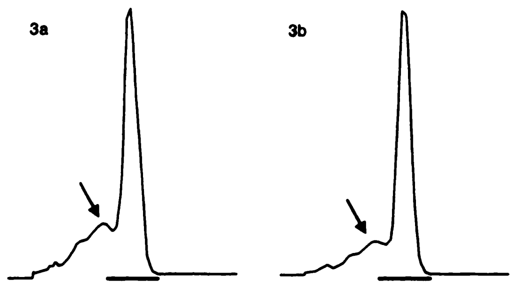

FIGURE 3
Spectrum of photon fluence, (A) 30 mm of copper (B)11 mm of copper. Bar on abscissa indicates position of 20% acceptance window. The arrows indicate the increased contribution due to scatter in (A).

In summary, the IAEA method of measuring the intrinsic count rate performance does not take into account the broad-beam conditions of the experiment. This can be easily corrected by measuring the attenuation factor of several plates rather than by measuring each plate's attenuation factor individually. The shape of the count rate curve is changed, and there is a change in the important parameter of count rate corresponding to a 20% loss.

The extra counts at low count rates are due to changes in the spectrum of the photon fluence caused by changes in the thickness of the copper. This anomaly causes slight changes in the count rate corresponding to a 20% loss. This error can be eliminated by using a decaying source to change the photon fluence; however, this procedure is time-consuming. The test recommended by NEMA and IAEA is still a useful test, as long as one is mindful of its inherent errors.

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Determination of Brain Death with Technetium-99m-HMPAO

TO THE EDITOR: Recently, Laurin et al. published their excellent results on "Cerebral Perfusion Imaging with Technetium-99m-HMPAO in Brain Death and Severe Central Nervous System Injury" (*1*). The use of ^{99m}Tc-HMPAO in the diagnosis of cerebral death has been established in our clinic for a couple of years (*2,3*) (Fig. 1). The method has shown to be useful, noninvasive, and without additional risks for the patient in comparison to other methods, especially angiography (*4*). Nevertheless, caution is requested because problems from the "instability" of lipophilic ^{99m}Tc-HMPAO may occur. Technetium-99m-HMPAO is one of the most "labile" technetium complexes used in nuclear medicine. Not only the rather fast degradation of the initial lipophilic complex to a number of hydrophilic compounds but also the extremely low content of stannous chloride (7.6 μg) may be responsible for these problems. In our opinion, this low concentration of reductant especially might have caused a number of pitfalls in ^{99m}Tc-HMPAO scintigraphy that we observed within the last three years. Figure 2 shows the scintiphoto of a ^{99m}Tc-HMPAO-study in which we used the "first eluate" of a ^{99m}Tc-generator (three patients). Obviously there is no ^{99m}Tc-HMPAO, but there is a reasonable amount of pertechnetate. This might be explained by the presence of oxidants in the generator eluate or by the addition of air-oxygen during the preparation. In a second case (eight patients), one single lot of sodium chloride used for the reconstitution of the kit has been identified to be responsible for the extremely low labeling yield.

FIGURE 1
Completely absent intracranial uptake (15 min p.i.) of the flow tracer ^{99m}Tc-HMPAO in a patient with brain death after trauma.

In regard to these observations, we recommend that in the diagnosis of cerebral death the integrity of lipophilic ^{99m}Tc-HMPAO has to be carefully examined prior to application. In our departments, we use the procedure described by the manufacturer (chromatography on ITLC-SG strips with saline and 2-butanone, respectively). The quantification can be done with a TLC-scanner, by a scintiphoto of the developed TLC-plates, or by cutting the TLC-support and counting in a well-type counter. Alternatively, a rapid HPLC-method (*5*) can be used to determine the exact labeling yield of each preparation. By using these methods, quality control of ^{99m}Tc-HMPAO can be done before injection within 10 to 15 min.

Complementary to the in-vitro quality control, we recommend an "in vivo" control by taking two additional scintiphotos. A negative scintigram of the thyroid gland will prove the

FIGURE 2
Absence of uptake in the brain (1 hr p.i.) of a patient with unknown headaches due to the low labeling yield of the flow marker ^{99m}Tc-HMPAO. Uptake in the thyroid and salivary glands indicates the presence of pertechnetate.

absence of pertechnetate in the preparation, and a scan of the lungs and the liver (10 min. p.i.) will establish the integrity of the lipophilic ^{99m}Tc-HMPAO in the administered solution.

The correct diagnosis of cerebral death will be much safer using these quality control procedures, especially with regard to the fast and easy handling of the methods mentioned above.

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REPLY: We agree that radiopharmaceutical quality assurance is especially important in the case of ^{99m}Tc-HMPAO because of its short half-life. This quality assurance takes the form of both chromatography and assessment of the in-vivo distribution. With such a short-lived radiopharmaceutical, the chromatographic assessment may, in our view, be properly performed after the fact analogous to common practice with short-lived positron pharmaceuticals. The cases presented by Brandau et al. demonstrate the importance of attention to the extra-cranial biodistribution and we thank them for pointing that out.

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Synthesis of ^{18}F-6-FD

TO THE EDITOR: In a recent report in *The Journal of Nuclear Medicine*, Chen et al. (*1*) reported a "Quality Control Procedure for 6-[^{18}F]-fluoro-L-DOPA (6-FD)." Although the radiosynthetic method (*2*) used by these authors has been superseded by more regioselective synthesis (*3,4*), we found their studies on the stability of 6-FD to be very useful to the routine production of this radiotracer.

We synthesize ^{18}F-6-FD in our institution using L-ethyl-N-trifluoroacetyl-[β-3,4-dimethoxy-6-mercuric-trifluoroacetyl-phenyl)]alaninate (obtained from BIS Chem. Inc., Quebec, Canada) and ^{18}F-acetylhypofluorite produced from ^{18}F-F_2 made from proton reaction on ^{18}O-O_2 (*5*). Purification of the ^{18}F-6-FD product essentially followed the method by Adam and Jivan (*4*) except the semi-prep HPLC mobile phase we used was 0.02*M* NaOAc pH 3.5. As Chen et al. (*1*) and others have observed, we found that shortly after neutralization to pH 6-7, the HPLC purified ^{18}F-6-FD solution turned brownish in color which further darkened with time. In light of the finding by Chen et al. (*1*) that the addition of 0.15% Na_2EDTA prevented or at least significantly slowed decomposition of ^{18}F-6-FD, we included 0.15% Na_2EDTA to the HPLC mobile phase used without affecting the separation of ^{18}F-6-FD. However, even with this added EDTA, slight darkening of the solution containing the ^{18}F-6-FD HPLC peak was observed within an hour after neutralization even though the solution was kept in ice and in the dark as recommended by Chen et al. (*1*).

Due to the known instability of L-DOPA at pH 7 and above (*6*), we suspected pH to be a most critical factor in the decomposition of ^{18}F-6-FD. To test this hypothesis, we divided a dose of ^{18}F-6-FD (8 mCi, 500 mCi/mmol, 10 ml 0.02*M* NaOAc pH 3.5 + 0.15% Na_2EDTA) into four sterile and capped vials. Two vials were neutralized to pH 7 using 1*M* NaOH while the other two were kept at pH 3.5. One pH 7 sample and one pH 3.5 sample were bubbled with He gas while another pH 3.5 sample was bubbled with O_2 gas. These vials were kept overnight in ice and in a dark room. As seen in the photograph (Fig. 1), low pH is indeed critical to the stability of ^{18}F-6-FD while the effect of oxygen is more pronounced at neutral pH. HPLC analysis using three detectors, UV = 254nm, electrochemical = +0.9V, and a pair of coincidence detectors, showed unchanged ^{18}F-6-FD in both pH 3.5 samples. On the other hand, more complicated chromatograms were seen in the UV and radioactivity tracings for both pH 7 samples. No electrochemical trace was seen in the pH 7 sample under ambient air while a late eluting peak was seen for the pH 7 sample under He. Further studies to identify the products are under way to elucidate the mechanism of

FIGURE 1
Effect of pH and oxygen on the stability of ^{18}F-6-FD. 6-FD samples from left to right are: (1) pH 7 under ambient air; (2) pH 7 under helium gas; (3) pH 3.5 under helium gas; and (4) pH 3.5 under oxygen gas. Note that samples (3) and (4) are clear, sample (2) is slightly colored, while sample (1) is dark.