

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 Although the radiosynthetic method (2) used by these authors has been superseded by more regioselective synthesis (3,4), we found their studies on the stability of 6-FD to be very useful to the routine production of this radiotracer.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- $[\beta$ -3,4-dimethoxy-6-mercuric-trifluoroacetyl-phenyl]alaninate (obtained from BIS Chem. Inc., Quebec, Canada) and ^{18}F -acetylhyperfluorite 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 0.02M 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 0.02M NaOAc pH 3.5 + 0.15% Na_2EDTA) into four sterile and capped vials. Two vials were neutralized to pH 7 using 1M 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.