Potential Iatrogenic Alteration to ^{18}F-Fluoride Biodistribution

TO THE EDITOR: ^{18}F-fluoride PET has reemerged as a genuine clinical alternative to ^{99m}Tc-diphosphonate scintigraphy. In vivo, NaF dissociates into its salts Na^+ and F^- (fluoride). Fluoride is exchanged with OH^- (hydroxyl) ion in the hydroxyapatite matrix of the bone before migrating into the crystalline matrix (*1*). Approximately 50% of the injected dose localizes in bone, and bone retention of fluoride continues until bone remodeling (*1*). Fluoride has minimal protein binding affinity, allowing more rapid excretion of the fraction not localized in bone and favoring earlier postadministration imaging and low background activity (*1*). Elevation in plasma concentrations of unlabeled fluoride may reduce ^{18}F-fluoride uptake because of competition. In vivo competition is likely to increase the ratio of ^{18}F-fluoride excreted to ^{18}F-fluoride bound in bone, decreasing the percentage of the injected dose localizing in the bone. The effects on image quality may include a decrease in target organ count density and an increase in renal and bladder activity. The implications might be even more crucial for quantitation of fluoride bone uptake.

There are several fluoridated hydrocarbon-based general anesthetics that are metabolized to produce fluoride ion, which should be considered a potential confounder of ^{18}F-fluoride bone uptake. Of the fluoridated ethers, the most frequently used inhaled anesthetic agents in developed countries are enflurane, isoflurane, desflurane, and sevoflurane (*2*). Enflurane (Ethrane; Abbot Laboratories) has 2%−8% oxidative metabolism in the liver to produce fluoride ions to plasma levels as high as 20–40 μM (*3*). Sevoflurane (Ultane; Abbott Laboratories) has about 1%−5% liver metabolism, with one of the by-products being fluoride ions (*3,4*). Plasma fluoride concentrations in excess of 50 μM are produced; more than 50 μM is associated with renal impairment (*4*). Both enflurane and sevoflurane show serum fluoride ion levels peaking soon after completion of surgery (cessation of anesthetic delivery) (*2,3*). Nonetheless, elevated serum fluoride ion levels are high beyond 24 h. The retention of high serum levels after cessation of anesthesia is likely to represent saturation of fluoride on bone and reverse exchange from the bone surface to blood once blood concentration falls below that of bone. The implication for ^{18}F-fluoride PET is that significantly less than the usual 50% of the injected dose may localize to bone if enflurane or sevoflurane anesthesia has been used in the previous 24–36 h—perhaps longer for prolonged general anesthesia or in those with renal impairment.

Although potential competitive interaction between ^{18}F-fluoride and the by-products of inhalation anesthetics may decrease image quality, of greater importance is the potential impact of this competition on bone uptake quantitation. Further qualitative and quantitative research should be undertaken to determine the relationship and time course of interaction between fluoride ion–producing inhalation anesthetics and ^{18}F-fluoride PET image quality.

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Detection of Pulmonary Embolism: Comparison of Methods

TO THE EDITOR: We read with great interest a recent article by Gutte et al. (*1*) in which the authors compared the diagnostic accuracy of combined ventilation–perfusion (V/Q) SPECT plus low-dose CT with multidetector CT angiography. In that prospective study, a total of 81 simultaneous studies were available for analysis, with a prevalence of 38% for pulmonary embolism (PE).

Perfusion SPECT plus low-dose CT had a sensitivity of 93%, specificity of 51%, and accuracy of 68%. This low specificity is surprising and at variance with recent data using perfusion SPECT without low-dose CT, which showed high specificity and accuracy of greater than 90% (*2,3*). Moreover, the general impression is that the CT information would significantly increase the diagnostic accuracy, particularly the specificity. In this context, the authors had already showed that the specificity of V/Q SPECT was 88% and increased to 100% when low-dose CT was added. We wonder what the specificity would be had the perfusion SPECT been interpreted without the low-dose CT; could the specificity of perfusion SPECT be even less than 50%? Unfortunately, because the authors did not report on the diagnostic performance of perfusion SPECT, there was no comparison between perfusion SPECT with and without low-dose CT. It would be great if the authors could comment on the results of perfusion SPECT.

There is a growing impression that SPECT is more accurate than planar imaging in the diagnosis of PE (*2–4*). However, V/Q SPECT is underutilized because of technical issues and the high economic cost associated with the ventilation agent. Most facilities therefore will be able to perform the perfusion SPECT but not the ventilation SPECT. The perfusion SPECT can be easily performed in a single session with the planar V/Q scan and is not associated with additional radiation exposure. However, interpretation criteria for perfusion SPECT are not yet clearly defined. Gutte et al. (*1*) did mention that "PE was diagnosed if one or more mismatched perfusion defects with normal ventilation were present," but it was not clear to the readers whether only large subsegmental perfusion defects and larger defects were categorized as suggestive of PE or whether small and moderate