Rapid Washout of Technetium-99m-MIBI from a Large Parathyroid Adenoma

TO THE EDITOR: In the February 1995 issue of *JNM*, Bénard et al. (*1*) presented a case of rapid ^{99m}Tc-sestamibi washout in a large parathyroid adenoma. Their finding contrasted the good diagnostic utility of double-phase ^{99m}Tc-sestamibi scintigraphy initially described by Taillefer et al. (*2*). Histological examination of the parathyroid adenoma revealed that it was mainly composed of water-clear cells with rare dark chief cells and lacked oxyphil cells. Most parathyroid adenomas are rich in oxyphil cells that are rich in mitochondria.

The authors hypothesized that the delayed ^{99m}Tc-sestamibi washout usually observed in parathyroid adenomas is caused by tracer retention in mitochondrial-rich cells and explained the rapid washout by the lack of oxyphils. This hypothesis is based on an article written by Sandrock et al. (*3*), who showed that the detectability of abnormal parathyroid glands by ^{201}Tl/^{99m}Tc subtraction scintigraphy partially depends on the presence of mitochondria-rich oxyphil cells. Bénard et al., however, did not provide sufficient evidence on how findings from a ^{201}Tl/^{99m}Tc subtraction protocol can be implemented in ^{99m}Tc-sestamibi scintigraphy.

The pharmacological differences between ^{201}Tl and ^{99m}Tc-sestamibi are well documented. Wackers et al. (*4*) as well as others found different uptake mechanisms for ^{201}Tl and ^{99m}Tc-sestamibi, and Piwnica-Worms et al. (*5*) demonstrated the divergent kinetics of ^{201}Tl and ^{99m}Tc-sestamibi in cultured chick myocytes.

Furthermore, we challenge Bénard's hypothesis for the pathophysiological basis of dual-phase ^{99m}Tc-sestamibi scintigraphy based on our own clinical findings: We studied 37 patients with primary hyperparathyroidism who had surgery as well as pathohistological work-up and found no correlation between oxyphil cell count and the regional sensitivity of ^{99m}Tc-sestamibi scintigraphy (Spearman correlation coefficient: -0.04; $p = 0.9$). The oxyphil cell count in our population ranged between $<10\%$ and 100% (median 25%).

In conclusion, the oxyphil cell count in parathyroid adenoma does not seem to be the crucial factor for determining the sensitivity of dual-phase ^{99m}Tc-sestamibi scintigraphy in parathyroid adenomas.

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REPLY: We thank Staudenherz et al. for their interest in our report. We described an unusual presentation of a parathyroid adenoma characterized by a rapid washout of sestamibi (*1*). Our clinical observation does not stand in contrast to the good results obtained by Taillefer et al. (*2*), but reflects an atypical scintigraphic pattern. We routinely use the double-phase technique in our clinical practice with excellent results. The main point of our study is to be wary of any increased uptake close to the thyroid, even if the washout rate is not slow compared to thyroidal washout. As our article illustrates, one may not rule out a parathyroid adenoma in the face of such a scintigraphic pattern, and an iodine scintigram may be helpful in such instances.

We hypothesized that mitochondrial content influences sestamibi retention based on the observations of Chiu et al. (*3*). These authors clearly have shown that sestamibi retention is proportional to the cellular and mitochondrial transmembrane potential gradient. Subcellular fractionation has identified mitochondria as the site of sestamibi retention in the cells of many tissues (*4*). The reference to the excellent study done by Sandrock et al. (*5*) was intended to make an analogy to the effects of mitochondrial content on thallium uptake, not as proof confirming our hypothesis. It seems obvious to us that only a controlled study, not a single case report, can support or confirm our explanation for the atypical pattern observed in our patient. The lack of oxyphil cells was the only unusual finding in our case.

Staudenherz et al. cite their work in progress as evidence challenging our hypothesis. It is unfortunate that their methods and results have not yet been published. It is not clear if they also correlated the number of oxyphil cells with absolute or relative sestamibi uptake or with the washout rate from parathyroid adenomas. Without several false-negative studies, it would be difficult to correlate the number of oxyphil cells with the sensitivity of sestamibi parathyroid scintigraphy. As we explained in our previous report, adenomas may be identified despite rapid tracer release. One would need to study many adenomas presenting rapid washout to determine whether there is a true relationship to the absence of oxyphil cells or to a low mitochondria per cell ratio.

It might be better to correlate the rate of tracer washout from parathyroid adenomas with mitochondrial content of these tumors to provide better insight on the mechanisms of tumor uptake and retention. The sensitivity of sestamibi scintigraphy is probably also dependent on other factors, such as adenoma size. Because the role of mitochondrial content on the washout rate of sestamibi parathyroid adenomas remains to be clarified, we hope that the work of Staudenherz et al. will address these issues when their their findings are published.