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Imaging with Pentavalent [^{99m}Tc]DMSA in Patients with Medullary Cancer of the Thyroid

TO THE EDITOR: In response to the comments of Clarke et al. (*1*) in their publication on imaging techniques in patients with medullary cancer of the thyroid (MCT), we are still having limited success with pentavalent techetium-99m (^{99m}Tc) DMSA, preparing the material as they have described. It is still our opinion that the outcome of imaging is dependent on the stage of the disease, the likelihood of a positive result being low in the early stages of the diseases (*2*).

Four patients with elevated calcitonin levels and MCT diagnosed histologically were studied recently with pentavalent [^{99m}Tc] dimercaptosuccinic acid DMSA. The results of the imaging are shown in Figure 1. Patient 1 (female, age 58 yr) had a calcitonin level of 109,000 ng/1 (normal range < 45 ng/1) at the time of radionuclide imaging. Biopsy had already confirmed the presence of MCT in the liver and ultrasound had revealed nodules in both lobes of the thyroid. As can be seen from Figure 1, there was uptake of ^{99m}Tc in both lobes of the thyroid, with that in the right lobe being much more pronounced. (There was also increased uptake of radionuclide in the liver). Patient 2 (female, age 55 yr) with a family history of multiple endocrine neoplasia, type 2a, had a calcitonin level of 3,450 ng/1 at the time of imaging. There was uptake of radionuclide in both lobes of the thyroid (Fig. 1) much more so, however, in the left lobe. No other areas of increased uptake were noted. Total thyroidectomy was later undertaken and multiple medullary carcinomas in both lobes of the thyroid were found at pathology. Patients 3 (female, age 50 yr) and 4 (female, age 25 yr) were from the same family, with a history of multiple endocrine neoplasia, type 2a. Their calcitonin levels were 494 and 2,000 ng/1, respectively, at the time of imaging. As can be seen from Figure 1, there was minimal uptake in the right lobe of the thyroid in Patient 3 but no thyroidal uptake of radionuclide in Patient 4. The distribution of radionuclide elsewhere had normal appearances. Ultrasound examination revealed thyroid nodules in both patients. Subsequent total thyroidectomy revealed MCT in the right lobe of Patient 3 and in both thyroid lobes of Patient 4.

Clarke et al. (*1*) visualized pentavalent [^{99m}Tc]DMSA uptake in all patients with proven metastatic MCT. The time from diagnosis of the disease to radionuclide imaging ranged from 2–18 yr. In our four patients with proven MCT, imaging was carried out within 2 yr of initial presentation and in only one case (Patient 1) was there proven metastatic spread of the disease. Convincing tumor uptake was observed in only two of our patients.

References

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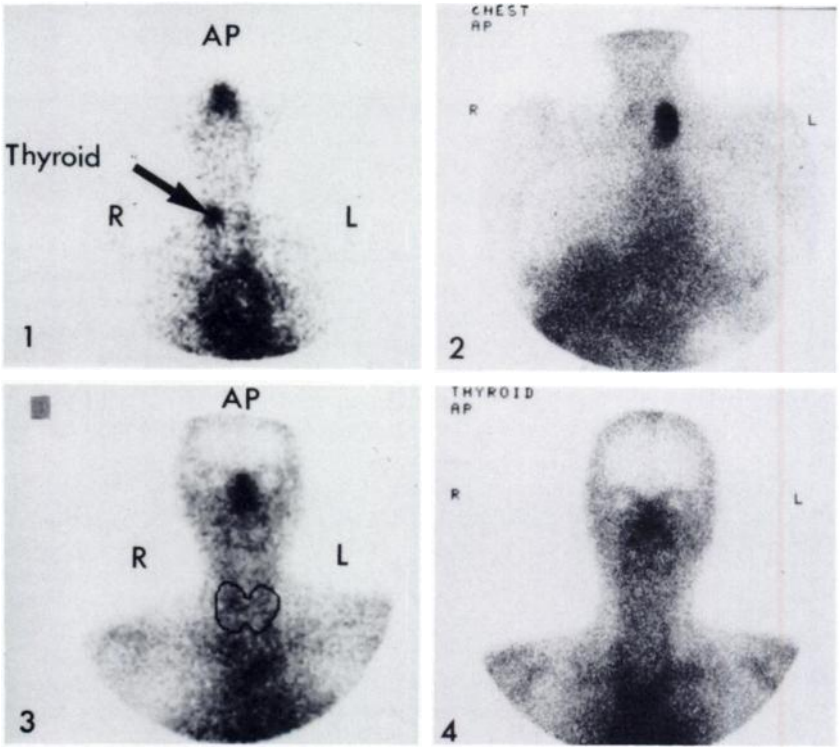

FIGURE 1
Radionuclide images in four patients with proven MCT, taken 2 hr after the administration of 200 MBq pentavalent [^{99m}Tc]DMSA. In these cases where thyroidal uptake was observed, 300 mg sodium perchlorate were given intravenously at the end of the study to check that uptake of the radionuclide was not due to the presence of free pertechnetate.

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REPLY: We appreciate the opportunity to reply to the letter of Hilditch, Murray, McLellan et al. in which they report continuing limited success with [^{99m} Tc](V)DMSA for imaging patients with medullary carcinoma of the thyroid (MCT).

We would disagree somewhat with the authors' interpretation of their own data, as three of four patients reported demonstrate uptake of [^{99m} Tc](V)DMSA, namely Patients 1, 2, and 3. Uptake in Patient 3 is much less than seen in Patients 1 and 2 but the authors do not comment on the volume of tumor resected from this patient. We would agree that Patient 4 gave a false-negative result.

In our article (*1*) we, in fact, report uptake in seven out of eight patients imaged and not all patients as Hilditch et al. suggest. We would entirely support the statement that "the outcome of imaging is dependent on the state of disease" as microscopic foci of tumor would be unlikely to take up enough tracer to be successfully imaged. However, our experience now indicates that positive results can be obtained in patients with small volumed disease, although more false negatives are obtained in this subgroup.

In light of our further experience with [^{99m} Tc](V)DMSA we continue to believe that this agent can play a significant role in the management of patients with MCT, particularly in patients with local recurrence when successful repeat surgery can significantly prolong the disease free interval.

References

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Reproducibility of Hepatic Perfusion Index

TO THE EDITOR: We have read with interest the article by O'Connor et al. (*1*) on dynamic hepatic scintigraphy. We take issue with the comment "Parker et al. administered a 25 mCi bolus of ^{99m}Tc but failed to obtain good reproducibility in a study of eight patients" on the following grounds.

1. The author's name is Parkin.
2. We used sulfur colloid labeled with technetium.
3. We administered 3 mCi per patient not 25 mCi.
4. We carried out repeat studies on 12 not eight normal subjects and found a mean difference between paired observations of 17%.
5. On reanalyzing the data from 20 studies drawn at random using a second observer we found the degree of correlation between the two results was 0.94 and in no case was the change sufficient to alter the diagnostic result.

In retrospect we should, perhaps, have included some patients with abnormal Hepatic Perfusion Index in the group who had repeat scans but this, we feel sure, would have further improved the reproducibility since the major source of error is the poor statistics in the arterial component of the liver time activity curve. In patients with hepatic metastases, the statistics of the arterial phase are improved.

References

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REPLY: We thank Parkin and Robinson for their comments and would like to apologize for the typographical error in the spelling of Parkin and for incorrectly stating the administered dose used in their study (*1*). However, these facts do not change the substance of our statement that their study failed to show good reproducibility.

Parkin et al. stated that reanalysis of 20 studies showed little interobserver variation. Although it is not stated in their study, the upper limit of normal for the hepatic perfusion index (HPI) would appear to be 0.4. A cursory glance at their data shows that at least one subject had a change from 0.45 to 0.27 on reanalysis. Furthermore, in the normal subjects who underwent repeat studies, several subjects showed a large difference in the HPI which was sufficient to alter the diagnostic result from normal to positive or borderline positive. Their value of 17% for the root mean square difference between paired observations should be compared with a value of 4.4% obtained with Method 3 in our study (*2*). We would also refer readers to the detailed analysis of the method of Parkin et al. published by Tindale and Barber (*3*). They found that the HPI was dependent, among other things, on the extent of bolus smearing and the level of tracer extraction and concluded that this technique should be used with caution when interpreting abnormal values.

Despite this poor reproducibility of the slope based methods, Parkin and his co-workers (*1,4*) have clearly demonstrated that measurement of the relative contribution of hepatic artery to total hepatic blood flow may be a valuable technique in the detection of liver metastases.