The Status of SPECT in Tumor Diagnosis

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THE ROLE OF SPECT IN TUMOR DIAGNOSIS

Kuhl et al. introduced single photon emission computerized tomography (SPECT) in 1963 (*1*), yet it has been only during the past few years that a concentrated effort has been made to develop systems for clinical applications. Preliminary reports have been published evaluating the accuracy of SPECT in the detection of mass lesions of the brain, chest, and abdomen, using technetium-99m, iodine-123 and 131, and gallium-67 labeled compounds. The results indicate that SPECT studies have a diagnostic accuracy competitive with that of other imaging modalities. The purpose of this paper is to evaluate the current status of emission computed tomography and to suggest areas where it may be used advantageously for the examination of patients with known or suspected cancer.

For the detection of a lesion by SPECT, a target-to-nontarget (T/NT) ratio of 2 is adequate (*2*), whereas for most planar imaging a ratio of at least 5 to 6 is usually necessary. If the T/NT ratio on the planar image is increased to a level comparable to that provided by tomography, the detection of lesions by planar imaging can be markedly improved. For example, in a study of patients with cancer, background activity from the Ga-67 was reduced by using a second radionuclide (Tc-99m HEDP) and subtraction techniques (*3*). When the unprocessed Ga-67 images were compared with those obtained using the second-radionuclide subtraction method, 30% of the lesions originally interpreted as positive and 67% of those interpreted as suspicious were found to be negative after the background was diminished—twice as many true lesions were detected on the processed images as had been found on the original studies. These results demonstrated the increased accuracy of tumor detection that could be attained if the level of activity in a lesion produced a contrast satisfactory for the mode of imaging (2:1 for SPECT and 5 or 6:1 for planar). A major advantage of radionuclide tomographic imaging is the greater contrast possible without the need for more complex enhancement procedures and exposure of the patient to additional radiation. Figure 1 illustrates the difference in T/NT ratio between a planar and tomographic image of the same lesion. By film densitometry the intensity of this pulmonary lesion was three times greater on the SPECT study—the planar target-to-background ratio was 1.4:1, and tomographic 4.0:1. In a study of cerebral lesions, Jaszczak et al., reported a similar increase in contrast obtained with SPECT, a ratio 2.8 times that observed for the best planar view (*4*).

As all practitioners of nuclear medicine can attest, equivocal studies observed in planar images are a recurring, disconcerting problem. It has been our experience that tomography decreases the number of questionable interpretations. For example, Figures 2 and 3 illustrate the value of tomography for decision making, i.e., tomography increases the interpreter's level of confidence. In Fig. 2 the questionable area was delineated by tomography as an anatomical variant and in Fig. 3, as a true defect of the liver. The importance of increased certainty in diagnosis cannot be overemphasized, since the projection of confidence is readily perceived by the clinician.

In view of the results from previous Ga-67 citrate studies (*5,6*), tomographic imaging with this tracer should provide a high degree of sensitivity for the detection of tumors. In a limited comparative study using gallium-67 and both planar and tomographic imaging, Yui et al. reported the results from 23 patients—lung carcinoma (13 cases) and malignant lymphoma (10 cases) (*7*). With SPECT 91% of the lesions were detected and by conventional planar studies, 86%. In ten patients with lymphoma and five with bronchogenic

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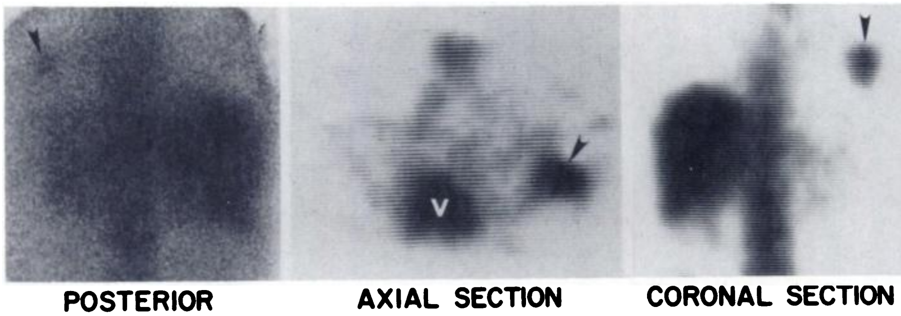

FIG. 1. Gallium-67 citrate study was performed in patient with primary tumor of unknown origin. Posterior planar projection shows focus of radioactivity in lower aspect of left lung, about midway between vertebrae and lateral border of chest (arrow). Target-to-nontarget ratio of lesion to lung background is sufficient to suggest abnormality, however, it is marginal for unequivocal confidence. On axial and coronal tomographic sections definition of lesion is prominent and can be located precisely in periphery of left lower lobe, posteriorly (arrows). (v = vertebra)

carcinoma, Harwood et al., identified the lesions in all patients by SPECT but in only 60% of the cases by planar imaging (*8*). Yeh et al. reported that in 26 documented recurrences of Hodgkin's disease in children, 21 of those detected by tomographic Ga-67 imaging correlated with the clinical findings (*9*). In addition to an improved detection rate by SPECT, the authors observed that the more precise information obtained on tumor localization and tumor extension contributed to the overall evaluation of patient status and provided more information to the clinician. The only publication of extensive tomographic studies, an atlas (*10*), is based on the use of a linear-type instrument, and thus does not contain data on the comparison of the several imaging modalities.

Several studies recently have reported the advantages of SPECT for the detection of mass lesions in the liver. Dendy et al. (*11*) and Reid et al. (*12*) found that the sensitivity for identifying focal lesions by gamma camera tomography was approximately 92%, an 8% improvement over planar imaging. Of appreciable importance was the improvement observed in identifying true normals, which represented a true gain, since sensitivity had not been adversely affected, thus improving the diag-

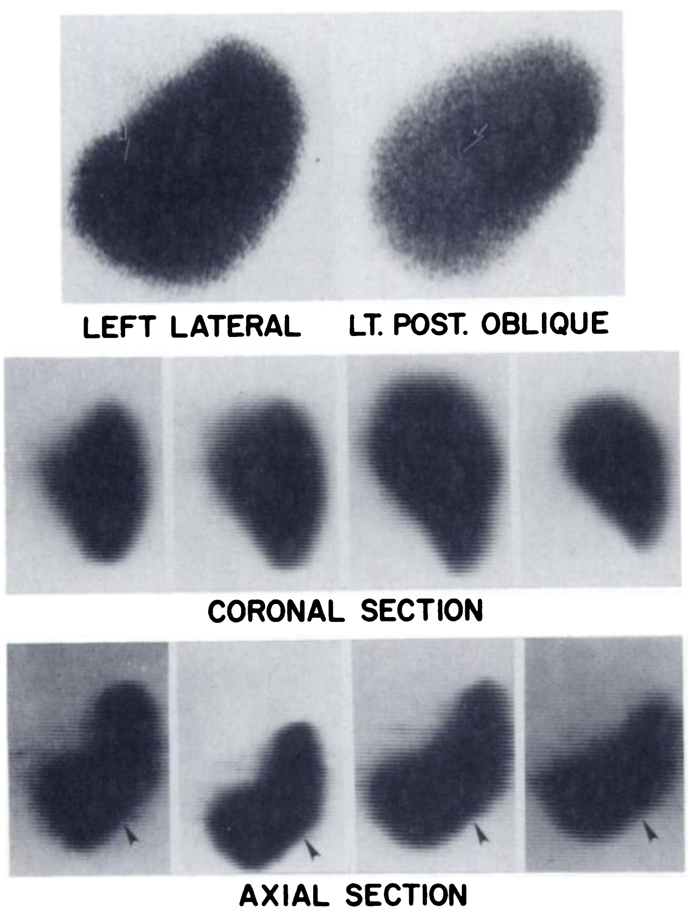

FIG. 2. Because of left hip pain Tc-99m MDP bone study was performed that demonstrated a mass lesion in left iliac bone from unknown primary. Planar images with Tc-99m sulfur colloid revealed ill-defined focus of photopenia, observed on left lateral and left posterior oblique views of spleen (arrows). Question—lesion or anatomical variant? On tomographic images mass lesions can be excluded. Axial and coronal sections demonstrate flattening of curvature in lower half of spleen (arrows) that anatomically produces central thinning overlying hilar indentation.

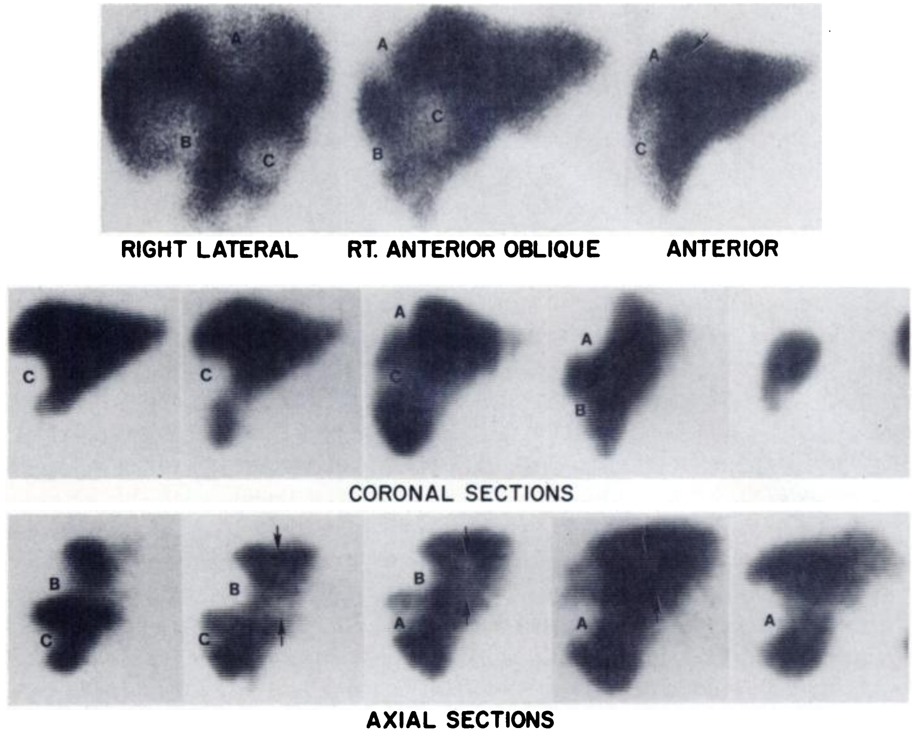

FIG. 3. Multiple mass lesions in liver are shown by Tc-99m sulfur colloid study in patient with colon carcinoma. In anterior, right lateral, and right anterior oblique projections, corresponding photopenic foci are identified with letters and same lesions are noted in tomographic views (axial and coronal). Additional defects found only by tomography are identified with arrows.

nostic accuracy. In 107 patients with proven hepatic lesions, Kahn et al. compared the results from planar scintigraphy, ECT, and transmission computer tomography (TCT), and found diagnostic agreement in 76 patients (71%) for the three modalitites (*13*). In the remaining 31 cases ECT provided the correct diagnosis in 23, false-positive diagnoses in three, a false-negative finding in one, and indeterminate results in four. The accuracy range was 78–81% for TCT and 92–96% for ECT, substantiating the advantages of SPECT.

A comparison study of metastatic disease to the liver using emission tomography demonstrated a 94% true-positive identification in 77 patients in whom masses had been detected by TCT (*14*). For lesions 2 cm or less in diameter, however, the detection rate by ECT was only 52%. In a study performed on livers that had been removed from the body (not subject to respiratory motion), Scherer et al. reported an accuracy by TCT of 90% for 2 cm lesions in the liver, decreasing to 15% for 0.5 cm lesions (*15*). The rapid exposure time of x-ray tomographic units available today virtually eliminates any motion problem, but for SPECT examinations respiratory movement remains a problem. With excursions of the diaphragm of 1.5 to 2 cm, lesions <2 cm will be difficult to define. In 72 patients with confirmed photopenic mass lesions of the liver, ECT demonstrated a sensitivity of 89%, specificity of 87%, and accuracy of 88% (*16*). The accuracy of planar imaging (2D) in this group was 79%. In 78 of the lesions that were 6 cm or smaller, the detection rate for ECT and planar imaging was: 0–2 cm,

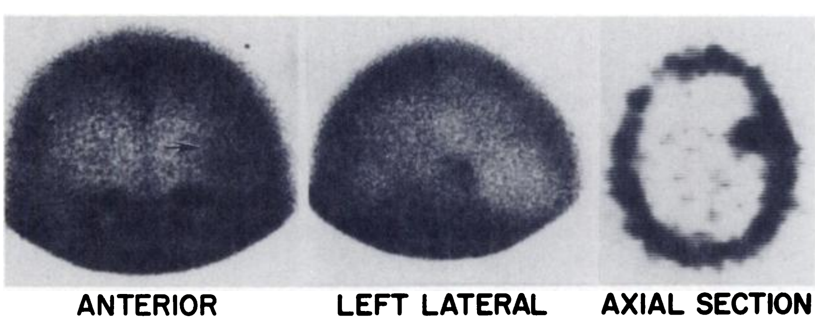

FIG. 4. Tc-99m DTPA study was obtained in patient with right-sided symptoms. Mass lesion, about 3 cm in diam, is apparent at level of left sylvian fissure (left lateral view). From anterior projection abnormal focus of radioactivity can be seen (arrow); however, edge of mass is not well defined, and relationship of mass and cortical surface is indistinct. On tomographic section lesion can be reliably located in cerebral cortex.

ECT-18%, 2D-0%; 2-4 cm, ECT-71%, 2D-49%; 4-6 cm, ECT-100%, 2D-98%. The authors were able to define photopenic masses of one cm by ECT in phantom studies performed without simulated respiratory motion. With respiratory gating this level of detection could be accomplished, since lesions as small as 1.6 cm had been demonstrated in their patient studies.

In defining tumors of the brain, primary or secondary, several publications have reported that SPECT has greater sensitivity than the planar studies. In a prospective study of 50 patients with confirmed tumors, Carril et al., found a true-positive rate of 88% with ECT, about 10% greater than that obtained in the same patients with planar imaging (*17*). In 29 studies Dendy et al. found an improvement of 7% in detecting lesions with radionuclide tomography (*18*). Furthermore, they observed that tomography displayed the information in a format more useful to the clinician (Fig. 4). SPECT has also shown a competitive accuracy with TCT. Ell et al., reported on 82 patients with proven malignant lesions of the brain, and the results by ECT and TCT were in agreement in 74, in three the lesion was detected by ECT only, and in five by TCT only (*19*). The authors observed that the depth relationship available with ECT was of particular advantage in differentiating neoplastic deposits in the brain from those in the skull and in locating lesions precisely in the cerebellopontine angle, posterior fossa, and base of the brain. In a similar study Oyamada et al., reported that ECT detected 12 lesions and TCT 13 in 14 patients with proven primary or metastatic cancer to the brain or skull (*20*).

A rapidly developing area of nuclear medicine is radioimmunodetection, the in vivo detection of cancer with radiolabeled antibodies-to-tumor antigens (*21*). Because the target-to-nontarget ratio of radioactivity averages only 2.5, the definition of tumor masses is suboptimal without data manipulation. In a comparison of planar and tomographic radioantibody studies, only nine of 21 tumor sites were observed on planar views, whereas 16 of 17 sites were seen by ECT (*22*). Of greater importance, however, was the improvement in the detection of tumors with volumes less than 50 cm^3 (5 cm diam)—only one of nine tumors of this volume size were detected by routine imaging, whereas eight of eight were revealed by tomography.

What factors should be considered when selecting a diagnostic imaging procedure for tumor detection? Aside from the availability of a particular examination, the reasons governing the choice of a specific diagnostic method should be based on: (a) the need for anatomic, physiologic, metabolic, or immunologic information; and (b) consideration of the cost/benefit ratio. Although tracer materials are used in most diagnostic imaging techniques, the variety of tracers available for nuclear medicine procedures far exceeds that available for other types of imaging examinations. Since many of the tracers used in nuclear medicine are uniquely designed to reflect various pathways, these types of procedures need to be expanded in the context of tomography. In view of the changing socioeconomic milieu of medicine today, if the diagnostic information required is merely a "yes or no" answer (e.g., are metastases present or absent?), then the question of cost/benefit becomes pertinent. Radionuclide procedures are generally less expensive than other types of imaging.

What will or should be the role of SPECT in the detection of tumors? The answer to this question will depend on the user and the manufacturer. Unfortunately, from the clinical standpoint, there are relatively few comparison studies of emission computer tomography. In addition it is necessary to develop new approaches to the application of emission tomography, such as volume quantification of lesions and use of imaging to determine the results of therapy in cancer. At this stage in the development of emission tomography precise attention to the procedural parameters by the user is mandatory, and, as emphasized by Keyes, the full potential of SPECT will be realized only if the manufacturers produce quality systems and develop sophisticated software (*23*). Because of a number of factors including the problem of attenuation correction and a high noise level with inadequate spatial resolution as noted by King et al., the image quality of SPECT has not been optimal (*24*). These authors demonstrate that significant improvements in image quality can be obtained with the appropriate software.

Single photon emission computerized tomography not only improves the sensitivity and specificity of radionuclide studies, but also, and of equal importance, it shows the relationship of lesions to other structures, defines the size and configuration of lesions, measures various functional processes, and provides an index of therapy. In the studies that have been published on tumor detection, it appears that single photon emission computerized tomography can provide diagnostic information essentially equal to that of other diagnostic modalities. The data now available are not yet sufficient, however, to demonstrate convincingly the accuracy of emission tomography, particularly to the clinician who is directly responsible for patient care. It is imperative that this potentially valuable modality be advanced to assume its role in the diagnostic process. In this era of fixed payments, selection of the examination that offers a definitive answer at the least cost is the most desirable course. SPECT can provide the diagnostic information needed in many types of diseases, has a high safety factor, and it is more than competitive cost-wise with other types of imaging procedures.

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