## Utility of Technetium-99m-Sestamibi to Assess Osseous Tumor Spread

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We report the staging results and the surgical outcome of a male patient with squamous-cell carcinoma in the floor of the mouth and a bone SPECT scan suggestive of local tumor infiltration of the mandible. Additional <sup>99m</sup>Tc-sestamibi SPECT imaging of the primary tumor and superimposing of both studies excluded osseous tumor spread and less extensive surgery was performed. Pathohistological examination confirmed the scintigraphic results and indicated a nonspecific periostal reaction as the cause of the positive bone scan. Nevertheless, a high-resolution camera and careful superimposition of both studies is mandatory if the differential diagnosis of an osseous tumor spread of a malignant tumor in the floor of the mouth and possibly less extensive surgery is at stake.

Key Words: squamous-cell carcinoma; technetium-99m-sestamibi; bone scintigraphy; SPECT

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Cancer of the head and neck accounts for 4%-5% percent of all cancers. The vast majority of the cancers arise from squamous epithelium. Almost 50% of the tumors occur in a horseshoe-shaped region in the floor of the mouth. Diagnosis is confirmed by fine needle biopsy, yet an exact preoperative staging is crucial for the surgical procedure. Distant metastases rarely occur without locally advanced primary disease or nodal involvement (1). Thus, bone scintigraphy is primarily applied to exclude local osseous invasion of the base of the skull, the maxilla or the mandible (2).

Scintigraphic delineation of the primary tumor has been attempted with  $^{99m}$ Tc (V)DMSA (3),  $^{67}$ Ga (4),  $^{57}$ Co-bleomycin (5) and monoclonal antibodies (6) but is not routinely applied in clinical practice. Recently,  $^{99m}$ Tc-sestamibi has been established as tumor tracer (7) and has been shown in vitro to discriminate better between normal and malignant cells than other perfusion tracers (8). Of note, this could also be shown in vivo with benign and malignant bone lesions (9). Kao et al. (10) published their initial experiences in nasopharyngeal cancer in 1993.

We report the staging results and the surgical outcome of a male patient with squamous-cell carcinoma in the floor of the mouth and a bone SPECT scan suggestive of local tumor infiltration of the mandible and who was thought to require extensive and mutilating mandibular resection.

#### CASE REPORT

The patient was admitted for bone scintigraphy after histologic confirmation of a squamous-cell carcinoma in the left anterior sublingual sulcus. Whole-body bone scintigraphy was performed 3 hr after intravenous injection of 600 MBq <sup>99m</sup>Tc-DPD (3,3-diphosphono-1,2-propane dicarboxylic acid tetrasodium salt). The left anterior part of the mandible showed increased tracer uptake, whereas no signs of distant metastases were found. Additionally, SPECT imaging of the skull was performed using a triple-head

gamma camera (LEUHR-PAR collimator;  $128 \times 128$  matrix, 3° steps; ramp filtered backprojection, three-dimensional postfiltering using a Wiener filter, reorientation in three planes; slice thickness 3.5 mm) (Fig. 1). The head was placed into a shell and taped to allow reproducible positioning. The aforementioned area of increased tracer uptake could be topographically assigned to the anterior portion of the tumor. This region showed no clinical or radiological signs of dentoalveolar pathology. Thus, bone scintigraphy suggested tumor infiltration of the mandible (Fig. 2).

Moreover, as part of an ongoing study at our institution, the patient underwent <sup>99m</sup>Tc-sestamibi (500 MBq) scintigraphy 5 min after postinjection.

Again, the study was performed using a triple-head gamma camera and identical acquisition and backprojection parameters. As the second study was performed on the same equipment, the head could be positioned identically to the bone study. The primary tumor could be clearly delineated from the physiologic uptake in the salivary glands and the mucosa but did not appear to reach the mandibular region (Fig. 3).

To confirm this observation, both scintigraphic studies were superimposed to project tumor delineation on the <sup>99m</sup>Tc-sestamibi scan into the osseous structures shown by conventional bone scintigraphy. It could be clearly shown that the area with increased <sup>99m</sup>Tc-sestamibi uptake did not reach the mandible (Fig. 4). Conventional CT did not suggest osseous destruction. Technetium-99m-sestamibi scintigraphy suggested that the mandible was not infiltrated. Thus, tumor surgery was performed as en bloc resection



**FIGURE 1.** Slices of <sup>99m</sup>Tc-DPD bone scintigraphy reoriented parallel to the central portion of the mandible. Reorientation of <sup>99m</sup>Tc sestamibi scintigraphy was performed identically.

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FIGURE 2. Transaxial slices of <sup>99m</sup>Tc-DPD scintigraphy show focally increased tracer uptake in region 4/4 of the mandible. This region showed no clinical or radiological signs of dentoalveolar pathology. Other parts of the skeleton showed normal tracer distribution.

of the tumor, including the internal surface of the mandible but retaining the external surface, to spare the patient from otherwise extensive and mutilating surgery.

Histological work-up of the tissue confirmed that malignant tissue had reached the periost of the bone, which showed mild reactive changes but osseous tumor spread could be excluded.

### DISCUSSION

Bone scintigraphy is sensitive in detecting early metastases, when changes in osteoblast function precede morphologic changes (11). False-positive findings are commonly attributed to degenerative, post-traumatic or inflammatory changes. In his retrospective analysis of rib biopsies, Ikard (12) found 9 of 61 biopsies had false-positive scans. The issue of a possible tumorus invasion of the bone by an adjacent malignancy has rarely been addressed. Hudson et al. (13) found no falsepositive or false-negative scans in their study of soft-tissue sarcomas, whereas CT was false-positive in 3 of 17 patients. Our case reveals the possible hazards if a positive bone scan is incorrectly interpreted as local tumor infiltration. Bone scintigraphy is a highly sensitive image of regional bone metabolism.



FIGURE 3. Transaxial slices of <sup>99m</sup>Tc-sestamibi scintigraphy reoriented identical to the bone study show physiological tracer uptake of salivary glands and mucosal outlining of the nose and anterior part of the floor of the mouth. Faint physiological uptake can be seen in the neck muscles. The primary tumor can be delineated as asymmetrical focal uptake in the left anterior portion of the floor of the mouth clearly exceeding mucosal uptake.



FIGURE 4. Upper left image depicts <sup>99</sup>Tc-sestamibi slice showing maximal extension of the primary tumor (PT). Upper right image shows corresponding slice from <sup>99</sup>Tc-DPD bone scintigraphy, demonstrating focal uptake in the mandible (M) and normal uptake in the spine (S). The fusion image of both studies clearly proves that tumor uptake is adjacent to the mandible but does not correspond with the area of increased bone metabolism. Note physiological uptake in both parotides (PG) and right submandibular gland (SG). Left submandibular gland shows only a faint uptake.

It is by no means specific and should be interpreted cautiously in patients with malignant disease. The most probable explanation for the positive bone scan in our patient seems to be nonmalignant periostal reaction of the bone due to a subclinical inflammatory reaction at the borders of the tumor since other dentoalveolar pathologies, including mal occlusion of teeth, could be excluded. The decreased uptake in the right submandibular gland may indicate congestion due to a duct occlusion of the primary tumor. Tumor infiltration could be excluded histologically.

### CONCLUSION

In the setting of a malignant tumor adjacent to the cortical bone and a positive bone scan, the additional diagnostic utility of scintigraphic delineation of the malignancy by a second tracer has to be used. This approach seems justified even if there are no current tumor-specific tracers available for squamous-cell cancers. Given the inherent lower resolution of scintigraphic studies in comparison to radiological methods, <sup>99m</sup>Tc-sestamibi appeared to be more appropriate than other established nonspecific tumor tracers (e.g., <sup>67</sup>Ga, <sup>201</sup>Tl) due to its better imaging properties. Nevertheless, a high-resolution camera and careful superimposition of both studies is mandatory if the differential diagnosis of osseous tumor spread of a malignant tumor in the floor of the mouth, and possibly less extensive surgery, is at stake.

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# Visualization of Myocardial Metastasis of Carcinoid Tumor by Indium-111-Pentetreotide

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We present a case of metastatic carcinoid tumor metastatic to the heart, presenting as ventricular arrhythmia and diagnosed by <sup>111</sup>Inpentetreotide scintiscan despite negative endocardial biopsy. The incidence and diagnosis of carcinoid heart disease is discussed, as well as the complementary role of high-resolution anatomical images (CT, MRI) with functional images (SPECT, PET) to determine the correct diagnosis of this rare condition.

Key Words: carcinoid tumor, indium-111-pentetreotide; heart

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Carcinoid tumor is a rare disease that originates from argentaffin cells of the gastrointestinal tract. Only 4% of these tumors lead to the carcinoid syndrome, which is characterized by flushing, telangiectasias, diarrhea, bronchoconstriction and right sided cardiac disease (1,2). Carcinoid heart disease occurs in up to 50% of the patients with carcinoid tumor, usually comprising endocardial and valvular lesions in the right heart (3,4). This is thought to be a result of excess circulating serotonin secreted by the liver metastasis. The left heart is relatively spared because serotonin is deactivated by enzymes found in the lungs (1,5,6).

In contrast, tumor metastasis to the myocardium is exceedingly rare. Less than ten cases have been reported in the past 30 yr (3,7-9).

We report here a case of malignant carcinoid tumor with metastases involving the right ventricle, presenting as ventricular arrhythmia detected during preoperative cardiac assessment.

### CASE REPORT

A 54-yr-old man was admitted initially in May 1989 for observation of abdominal trauma due to a motor vehicle accident. At that time, an abnormality of the ileo-cecal region was found on the CT scan which was considered to be most likely a hematoma secondary to trauma. However, close follow-up revealed that the mass was persistent and increasing in size; these findings were also confirmed on subsequent gastrointestinal series and barium enema. Surgical exploration was performed, revealing a large tumor in the ileo-cecal region extending inferiorly into the pelvis and superiorly to the second part of the duodenum. The omentum as well as multiple mesenteric lymph nodes were also involved. Extensive right hemicolectomy with resection of 2 feet of the terminal ileum and primary anastomosis was performed. The pathology report was consistent with carcinoid tumor of the distal ileum with metastasis extending into the omentum and involving four of six lymph nodes.

The patient was followed with yearly CT scans of the abdomen for the next 3 yr. In July 1992, abdominal CT revealed a  $2 \times 2$ -cm nodular lesion anterior to the liver suggestive of metastasis. Urinary 5-hydroxyindolacetic acid levels were also determined and showed significant elevation with abnormal results of 59.4 mg in 24 hr (normal values = 0-6 mg/24 hr). The patient also complained at that time of episodes of diarrhea together with the presence of periodic flushing of the face.

The patient underwent a second explorative laparotomy in August 1992, and the findings were consistent with extensive metastatic disease involving the small and large bowel with multiple nodules involving the entire mesentery. The patient was followed expectantly off therapy until September 1993 when he was started on 5-fluorouracil (5-FU) for impending bowel obstruction.

His disease remained stable on 5-FU until July 1994, when he presented with an episode of bowel obstruction. A palliative colonic bypass was subsequently performed.

At the time of surgery for his bowel obstruction, the patient was found to have ventricular arrhythmia. Echocardiogram revealed a large (5-cm) right ventricular mass protruding into the ventricular cavity. Mitral valve prolapse was also noted, with mild aortic insufficiency and moderate tricuspid insufficiency. Endocardial biopsy of the mass was reported as "normal heart muscle".

In September 1994, the patient was referred to the nuclear medicine department for evaluation of the extent of his disease and to determine whether or not the cardiac mass was indeed related to the carcinoid tumor.

After intravenous injection of 6 mCi<sup>111</sup>In-pentetreotide, anterior and posterior whole-body images were obtained at 4 and 24 hr. SPECT imaging of the abdomen and pelvis were also obtained at 4 hr and of the chest at 24 hr. The whole-body images showed multiple abnormal focal uptake in the abdomen, liver, mediastinum, neck, both thighs and the region of the heart just above the diaphragm (Fig. 1). Fusion of the SPECT and CT images confirmed the presence of somatostatin receptors in the right ventricular mass (Fig. 2).

Based on this information, the diagnosis of myocardial metastasis was made. In view of the strategic position of the tumor in the

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