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Monoclonal Antibody Imaging of Colorectal and Ovarian Cancer

A MONOCLONAL ANTIBODY labeled with indium 111, satumomab pendetide (OncoScint CR/OV), was recently approved by the United States Food and Drug Administration and now is routinely available for the imaging of colorectal and recurrent ovarian cancers. The radiopharmaceutical is given intravenously, and imaging is done within three to five days.

OncoScint CR/OV is more sensitive than computed tomography (CT) for the detection of cancer in the pelvis (OncoScint CR/OV 74%, CT 57%), mesentery, and retroperitoneum (OncoScint CR/OV 66%, CT 34%), but less sensitive in the liver (41% versus 84%). It can detect metastatic disease in normal-sized lymph nodes and can distinguish between scar tissue and recurrent cancer. The positive predictive value of OncoScint CR/OV is 97% for colorectal cancer and 83% for recurrent ovarian cancer. Consequently, a focus of uptake usually indicates disease. The negative predictive value, however, is only 19% and 29%, respectively, so a normal scan does not rule out recurrent disease.

When used appropriately, OncoScint CR/OV can be both clinically efficacious and cost-effective. Its use can cause a false-positive elevation in carcinoembryonic antigen levels for several months, however. The $2,000 evaluation can help avoid even higher costs and influence patient management in the following four clinical settings:

- Patients with a previous history of colorectal or ovarian cancer who present with an elevated carcinoembryonic antigen or CA 125 level are at high risk for recurrent disease. In this setting CT, magnetic resonance imaging, and ultrasonography show low sensitivity and specificity. OncoScint CR/OV may identify the site of recurrence and enable earlier surgical intervention.
- Patients with "resectable" recurrence of colorectal cancer (such as a solitary liver metastasis) may be candidates for surgical resection with curative intent. If OncoScint CR/OV imaging before surgical therapy identifies unexpected nonresectable disease elsewhere, a futile operation may be avoided.
- Following resection and chemotherapy, cases of ovarian cancer are often restaged surgically because of a lack of an accurate imaging procedure for detecting residual disease. In these patients, abnormal uptake on OncoScint CR/OV imaging may make a second-look laparotomy unnecessary, or the scan can be used to direct a limited laparoscopic procedure for tissue confirmation. Because of its poor negative predictive value, however, a normal OncoScint CR/OV scan does not eliminate the need for laparotomy.
- In patients with suspected recurrence following surgical or radiation therapy for rectal cancer, CT and magnetic resonance imaging are often unable to distinguish between scar tissue and recurrent disease. OncoScint CR/OV imaging in these patients is often definitive, and the scan findings may be used to determine if palliative or possibly curative therapy is warranted.

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Regional Cerebral Blood Flow and Cocaine Abuse

COCAINE ABUSE is a major and costly problem. Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) are windows into brain function. In the past decade, they have provided information about the acute and chronic effects of cocaine abuse. An aim of diagnostic imaging is to distinguish typical changes of cocaine abuse from those of other conditions. Identifying the presence of cocaine abuse will permit appropriate treatment.

Cerebral blood flow and metabolism in patients who abuse cocaine vary with the duration of withdrawal. Within a day of their last ingestion, these patients have lower than normal flow to anterior cortical areas on PET scans using oxygen 15. After seven to ten days, blood flow to the left dorsolateral prefrontal cortex continues to be decreased in most of these patients. In contrast, global brain metabolism is above normal in these patients after a week off cocaine, with regional increases in the basal ganglia and orbitofrontal cortex. The dorsolateral prefrontal cortex directs executive brain function, whereas the orbital cortex is associated with compulsive behaviors. Both receive dopaminergic innervation from the ventral tegmental area. Longer intervals off cocaine produce minimal additional changes, with persistent cerebral blood flow decreases in the dorsolateral frontal cortex on both sides and in the right parietal cortex. In a sagittal projection, blood flow deficits produce a scalloped pattern in the frontal and parietal lobes. After as long as six months of abstinence, the metabolic and cerebral blood flow deficits failed to reduce, suggesting that cocaine-induced changes are long term and may be permanent. We have recently compared 15 nonpsychotic persons with cocaine abuse with 13 control subjects using technetium Tc 99m exametazime (hexamethyl-propyleneamine oxime). Patients were drug-free for an average of 12 days before the study. In agreement with other studies, we found that those who abuse cocaine

had below-normal cerebral blood flow in the dorsolateral prefrontal, dorsomedial, and orbitofrontal cortex.

Cocaine abuse can lead to a paranoid psychotic state that is clinically indistinguishable from schizophrenia. Thus, persons who abuse this drug often are diagnosed with schizophrenia after several cocaine-induced episodes of psychosis. The differential diagnosis of the two conditions usually rests on the accuracy of the historical information from a psychiatric interview or on the findings of toxicologic screens of body fluids. If the patient has recurrent cocaine-associated psychotic episodes, the clinical distinction becomes even murkier. Years of cocaine abuse, unemployment, and homelessness can erode the basic personal and social capacities of a person, much like chronic schizophrenia does. Positron emission tomography or SPECT scans may help to differentiate between these two groups. Both groups show decreased flow (and metabolism) in frontal lobes and changes in caudate nuclei, but withdrawal leads to a return to normal basal ganglia metabolism in nonpsychotic persons who abuse cocaine. Both increased basal ganglia metabolism and drug abuse predict a poor response of schizophrenic symptoms to medication.

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Technetium Tc 99m Sestamibi for Parathyroid Imaging

TECHNETIUM Tc 99m sestamibi is a safe, nontoxic radiopharmaceutical that is commonly used for myocardial perfusion imaging. It was first used for parathyroid imaging in 1989. Technetium Tc 99m pertechnetate and thallous chloride Tl 201 had been used previously, but were not optimum because of the low count rate from thallium and the necessity of subtraction of the ^{201}Tl-chloride images from the ^{99m}Tc-pertechnetate images. False-negative and false-positive scans were also common. In the past few years, several groups have recommended the use of ^{99m}Tc-sestamibi as a replacement for the ^{99m}Tc-pertechnetate and ^{201}Tl-chloride combination.

The mechanism of the uptake in parathyroid adenomas and hyperplastic parathyroid glands has not been elucidated. Mechanisms may be similar to those of ^{201}Tl, namely the presence of a higher number of mitochondria in the oxyphil cells in these pathologic states than in a normal gland. Other possibilities are increased blood flow and potassium turnover.

The technique for imaging is simple and requires only the standard doses used for myocardial imaging, 10 to 30 mCi (370 to 1,110 MBq). The larger dose is preferable because it facilitates imaging in a shorter time and permits the use of single-photon emission tomography (SPECT). Imaging begins a few minutes after ^{99m}Tc-sestamibi is administered. Pinhole imaging is used in the neck because it provides greater detail. Additional imaging is done with routine techniques and includes the anterior neck area, right and left anterior oblique, and posterior views of the chest. Imaging of the neck is repeated with the pinhole technique and views of the chest and neck are obtained with a standard technique at two hours. The delayed images will often result in much better delineation of the abnormal hyperfunctioning gland(s) because the original activity in the thyroid gland will wash out with time, but the abnormal parathyroid gland retains the activity. The immediate images are useful because they define the thyroid and parathyroid gland anatomic relationship.

Experience has shown the test to have a sensitivity of 86% (31/36 patients) and a specificity of 100% (14 normal parathyroid glands). Adenomas can be found with a sensitivity of 96% (25/26). In the critical area of re-exploration for persistent or recurrent hyperparathyroidism, the technique is of particular importance because of the greater likelihood of finding the abnormal gland(s) in an ectopic location. Mediastinal parathyroid glands as small as 0.9 by 0.6 by 0.5 cm have been clearly delineated, and with SPECT, better localization has been achieved. In patients on suppressive thyroid therapy the ^{99m}Tc-sestamibi is not taken up by the thyroid, and the abnormal parathyroid gland tends to stand out. Because of the loss of the thyroid structure, localization may be more difficult. This technique has not been studied systematically to determine the usefulness of suppressive doses of thyroid. Patients with thyroid adenomas tend to have take-up of ^{99m}Tc-sestamibi on the early images, which clears on the delayed images. The presence of hypocalcemia might also increase ^{99m}Tc-sestamibi uptake.

^{99m}Tc-Sestamibi is now the agent of choice for the evaluation of patients with persistent and current hyperparathyroidism and should supplant the ^{99m}Tc-^{201}Tl technique.

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