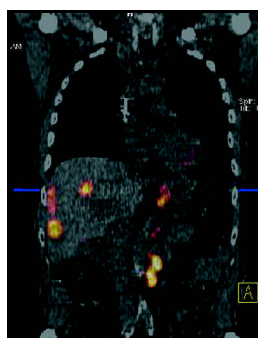


## Nuclear medicine

THROUGH IMPROVEMENTS in radiopharmaceuticals and instrumentation, nuclear medicine continues to develop and refine in-vivo approaches for diagnosis (including staging and prognosis) and treatment of disease.

**Diagnosis.** Positron-emission tomography (PET) using the glucose analogue  $^{18}\text{F}$ -fluorodeoxyglucose exploits the higher rate of glycolysis in malignant tumours relative to most normal tissues. PET is cost-effective, and is more sensitive than anatomical imaging for diagnosis, staging or restaging of patients with cancers of the lung, breast, colon, head and neck, oesophagus, lymphoma and melanoma.<sup>1</sup> Nevertheless, optimal targeting of therapy requires careful correlation of the metabolic data derived from PET with the anatomical detail provided by CT or MRI, ideally by “fusing” the datasets from these modalities. The illustration shows a “fused” PET-CT image. In Australia, the Commonwealth Government will expand its present funding of two PET facilities to six in 2002, which will improve patient access to this technology.



Myocardial perfusion imaging (MPI) using thallium-201 chloride or technetium-99m-labelled agents (sestamibi, tetrofosmin) has been validated for diagnosis of coronary artery disease (CAD) and detecting viable myocardium after myocardial infarction. More recently, its prognostic value for known or suspected CAD has been established: MPI provides incremental predictive value for overall cardiac mortality and major cardiac events over clinical evaluation, exercise testing or coronary angiography. A normal scan indicates a probability of less than 1% for death or non-fatal infarction within 12 months; this benign prognosis applies equally to patients at high risk of CAD who are to undergo non-coronary surgery. Assessment of regional and global left ventricular function is now possible, so MPI can be used to assess regional myocardial perfusion at rest and exercise, and simultaneously quantify left ventricular performance. A novel application of MPI is evaluation of patients presenting with chest pain and indeterminate ECG results. A normal MPI examination rules out myocardial infarction or significant ischaemia, and permits safe discharge of the patient for later outpatient evaluation.<sup>2</sup>

The most important prognostic indicator for breast carcinoma is axillary lymph node involvement at the time of surgery. This is conventionally ascertained by axillary clearance, which is associated with significant morbidity. Assuming that lymphatic dissemination from breast cancers is predictable, the sentinel lymph node (SLN) represents the first draining lymph node encountered by tumour cells. If the SLN can be shown to be free of metastatic disease, no further axillary exploration should be necessary. Lymphoscintigraphy following the peritumoral injection of Tc-99m-labelled microcolloid — coupled with the intraoperative use of a radiosensitive probe and (non-radioactive) isosulfan blue dye — can accurately identify the SLN in patients with apparently localised breast cancer.<sup>3</sup>

Tc-99m sestamibi imaging, particularly when coupled with high-resolution ultrasound, can accurately localise parathyroid adenomas in over 90% of patients. Confident preoperative localisation allows minimally invasive parathyroid surgery, which can be combined with the intraoperative use of a radiosensitive probe and rapid parathyroid hormone assays to shorten operating time, hospital stay, and convalescence.

**Intervention.** Several  $\beta$ -emitting radiopharmaceuticals selectively localise in skeletal metastases and reduce pain, presumably by irradiating the metastatic lesions. Strontium-89 (for metastatic prostate carcinoma) and samarium-153 lexidronam (for prostate or breast cancer) reduce pain in up to 80% of patients and have excellent safety profiles. Preliminary evidence in patients with advanced androgen-independent prostate carcinoma suggests that  $^{89}\text{Sr}$  added to doxorubicin chemotherapy improves overall survival.<sup>4</sup>

Monoclonal antibodies directed against the CD-20 antigen expressed on B lymphocytes have been conjugated with  $\beta$ -emitting radionuclides to treat non-Hodgkin's lymphoma. Two such antibodies (iodine-131-labelled tositumomab and yttrium-90-labelled ibritumomab) have entered phase III trials. In 52 patients with relapsed B-cell lymphoma treated with  $^{131}\text{I}$ -tositumomab, chemotherapy and stem-cell transplantation, progression-free survival was 68% at two years.<sup>5</sup>

Many neuroendocrine tumours express cell-surface somatostatin receptors and can be detected with  $\gamma$ -emitting somatostatin analogues. A new class of somatostatin analogues labelled with  $^{90}\text{Y}$  allows targeting of somatostatin-receptor-positive tumours with high radiation doses. In patients with refractory progressive disease, response rates of up to 80% have been reported with minimal toxicity.

As our understanding of disease increases, nuclear medicine will find new targets and roles, such as individual drug dosimetry, prediction of likely response to therapy, and early documentation of responses to therapy.

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Figure: Image courtesy of the University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.

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