Recent advances in oncological imaging

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Imaging has become increasingly important in the management of patients with cancer, reflecting a growing need to evaluate disease status not only at the time of diagnosis and staging, but also at regular intervals during treatment follow-up. Imaging is a rapidly evolving medical specialty based on technical innovations and continues to take on new roles in clinical medicine. Close co-operation between clinicians and radiologists is therefore required for optimal and appropriate use of imaging techniques. For decades, the management of cancer patients depended on the detection of disease using imaging techniques that placed a great emphasis on spatial resolution to distinguish structural (anatomical) changes within tissues or organs. More recently, highly sensitive functional imaging techniques have entered clinical practice. These image physiological/metabolic processes that often precede anatomical changes are of value for the early detection of cancer and assessing response to treatment.

In modern practice, the choice of an imaging strategy or test depends on many factors, including the:

- nature of the information being sought
- availability and accuracy of imaging techniques, and
- potential hazards to patients.

Recommendations on usage require constant reappraisal in the light of emerging evidence.

Key Points

Multislice computed tomography is the most important advance in mainstream oncological imaging

Improved contrast mechanisms in magnetic resonance imaging (MRI) provide the ability to visualise function superimposed on morphology

Advances in technology have significantly improved the diagnostic efficiency of ultrasound and reduced its operator dependent nature

Positron emission tomography using 2-{F-18} fluoro-2-deoxy-D-glucose now enables a management change in a substantial number of patients, with applications in the characterisation of indeterminate lesions, for staging and grading malignancy, monitoring response to treatment and predicting relapse following definitive treatment

Dynamic contrast-enhanced MRI is useful for detection and characterisation of lesions based on their vascular characteristics

MR spectroscopy can provide information on tumour grade and be used to monitor tumour response to therapy

Molecular imaging using tumour-specific radiolabelled agents is useful in the diagnosis and treatment of cancer

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Advances in anatomical imaging techniques

Computed tomography

Volumetric data acquisition using spiral/helical multislice technology is the latest innovation in computed tomography (CT), and has made spiral CT the preferred technique for the routine detection of pulmonary and liver lesions and for defining pancreatic and renal cancer prior to surgery. CT also makes possible more accurate radiotherapy planning. Irradiation of normal tissues can thereby be reduced to a minimum using conformal and intensity modulated radiation techniques.[1] Volumetric CT has several recognised advantages over conventional incremental CT techniques, including:

- rapid data acquisition
- improved detection and characterisation of lesions
- optimal use of contrast medium enhancement
- 3D imaging.

Rapid data acquisition. For example, the trunk can be examined in 1–2 breath-holds by multislice systems (10–20 sec), thereby minimising inconvenience to sick patients and avoiding artefacts caused by motion.

Improved detection and characterisation of lesions. Thinner axial sections improve long axis resolution, thus enabling high quality multiplanar and 3D imaging. This is being exploited to screen for lung cancer.[2] Thin axial sectioning also helps in the characterisation of lesions on the basis of their internal structure and X-ray density, particularly for liver and lung lesions.[3,4]

Optimal use of contrast medium enhancement allows internal organs to be examined at optimal levels of vascular and parenchymal organ enhancement as rapid scanning proceeds, thus improving the visualisation of a greater contrast differential between normal tissues and pathologies. In many organs such as the liver and pancreas, three main phases of enhancement can be distinguished – arterial, early parenchymal and venous – making it easier to detect primary

and secondary lesions when appropriate enhancement is undertaken. The ability to image vessels at optimal levels is now routinely used to obtain angiographic-like images and to detect pulmonary emboli in patients with parenchymal lung disease where the conventional ventilation/perfusion (V/Q) scanning method is often indeterminate.[5]

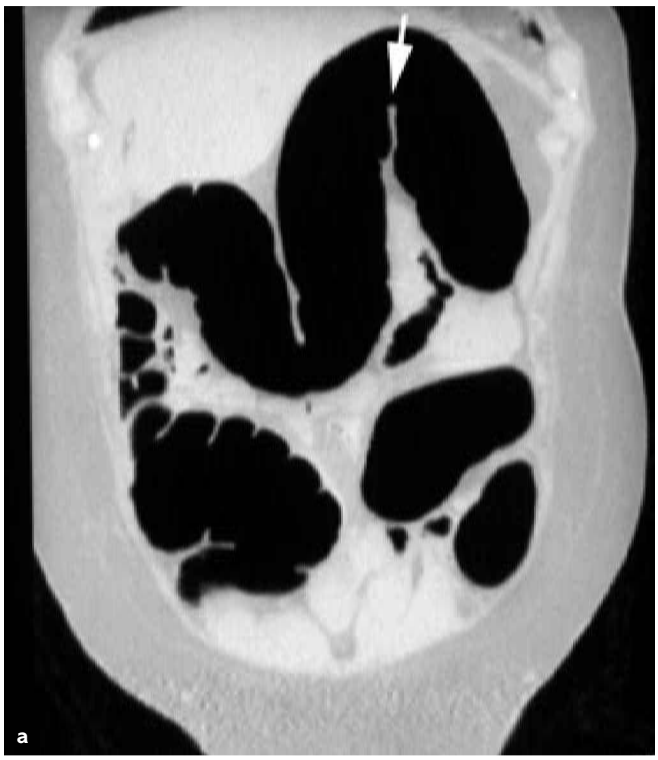
3D imaging is helpful in planning surgical and radiotherapy treatments. 'Virtual colonoscopy' is one such 3D application whereby endoscopic-like views of hollow organs are reconstructed on computers (Fig 1). This technique is being evaluated as an alternative screening tool for the colon; it may be of particular value for patients unsuitable for more invasive colonoscopy.[6]

Magnetic resonance imaging

Magnetic resonance imaging (MRI) is the test of choice for the routine staging of pelvic, brain and spinal cord malignancies[7] and for the evaluation of patients with cord compression. Advances in MR hardware and software, together with new and improved contrast agents, have resulted in greater speed of data acquisition and the ability to visualise function superimposed on anatomic images.[8] New tissue-specific contrast agents have been developed, including liver- and lymph node-specific agents:

- Following the introduction into clinical practice of *liver-specific agents* targeting Kupffer cells and hepatocytes, invasive CT arterioportogram is rarely performed for the surgical assessment of focal liver lesions.[9,10]
- *Lymph node-specific agents* using ultrasmall superparamagnetic iron oxide particles are currently under investigation and likely to enter clinical practice soon (Fig 2). These agents are taken up by macrophages within lymph nodes and can detect metastases even in normal sized lymph nodes.[11–13]

MRI assessment is also possible of functional tissue properties including perfusion, blood volume and permeability to micro- and macromolecules, and also for observing the Brownian motion of water molecules.



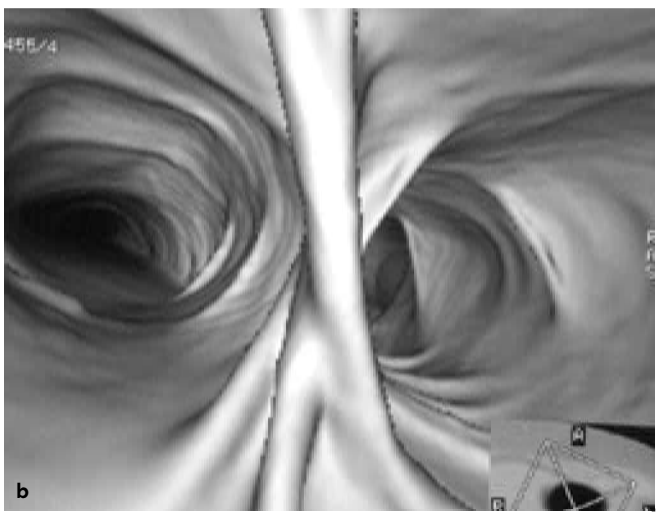


Fig 1. Virtual colonoscopy. Coronal reconstruction from a spiral computed tomography data set imaged on lung windows: **(a)** an air distended colon is visible. Arrow indicates the viewing direction of the endoscopic-like computer generated image at the splenic flexure; **(b)** the haustral folds are clearly visible.

Ultrasound

Advances in transducer technology, digital imaging and signal processing have significantly advanced the diagnostic efficacy of ultrasound (US) in oncology and reduced its operator dependent nature. Probe miniaturisation and the use of endoluminal transducers assist in the assessment and characterisation of lesions, also enabling biopsy guidance of difficult anatomical locations (eg the pancreatic head, subcarinal space etc). Endoscopic techniques have had a significant effect on the staging accuracy of oesophageal, gastric and rectal malignancies.[14]

Non-enhanced power Doppler has a higher sensitivity for blood flow than colour Doppler, and allows real-time visualisation of blood flow within tumour masses independent of the angle

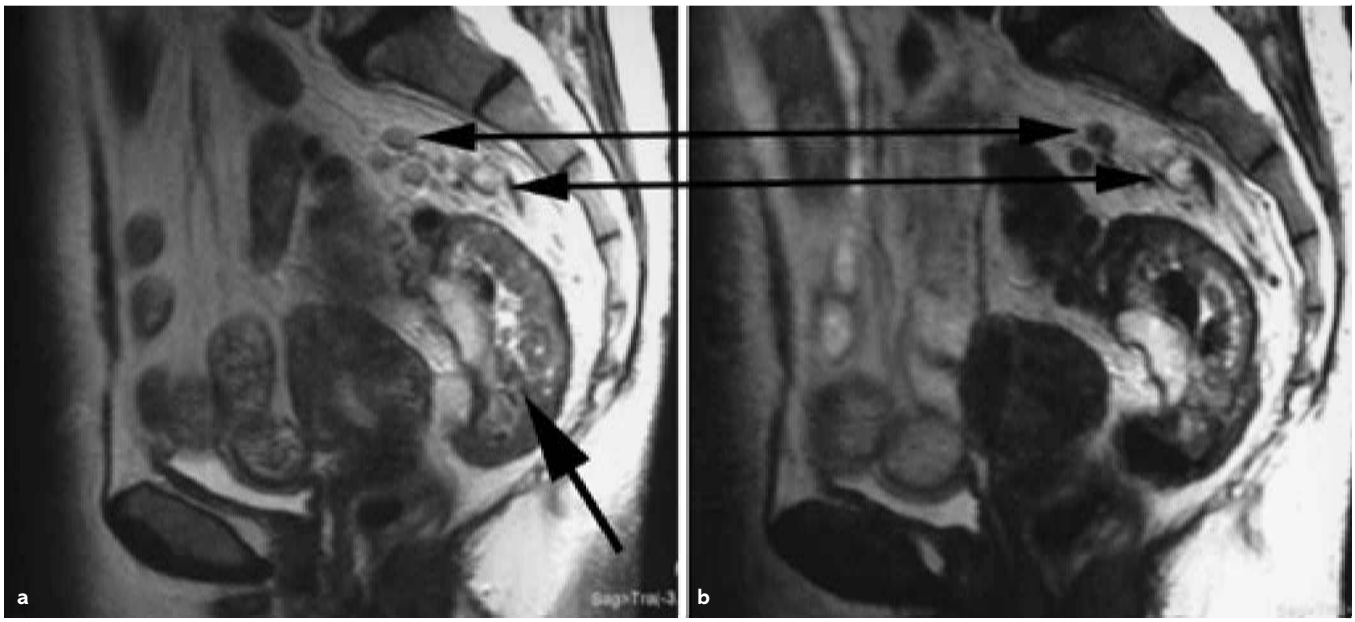


Fig 2 Magnetic resonance imaging (MRI) lymphography: (a) sagittal MRI image of the pelvis showing a large mid-rectal tumour (arrow) and enlarged presacral lymph nodes (arrows); **(b)** similar image acquired 24 hours after intravenous administration of ultrasmall superparamagnetic iron oxide particles. All but one of the lymph nodes have decreased in signal intensity (see corresponding arrows). The lymph node showing no change in signal intensity (lower arrow) was replaced by metastatic disease. All other lymph nodes were benign at pathology (reproduced courtesy of Mr S Rasheed, Northwick Park and St Mark's Hospital).

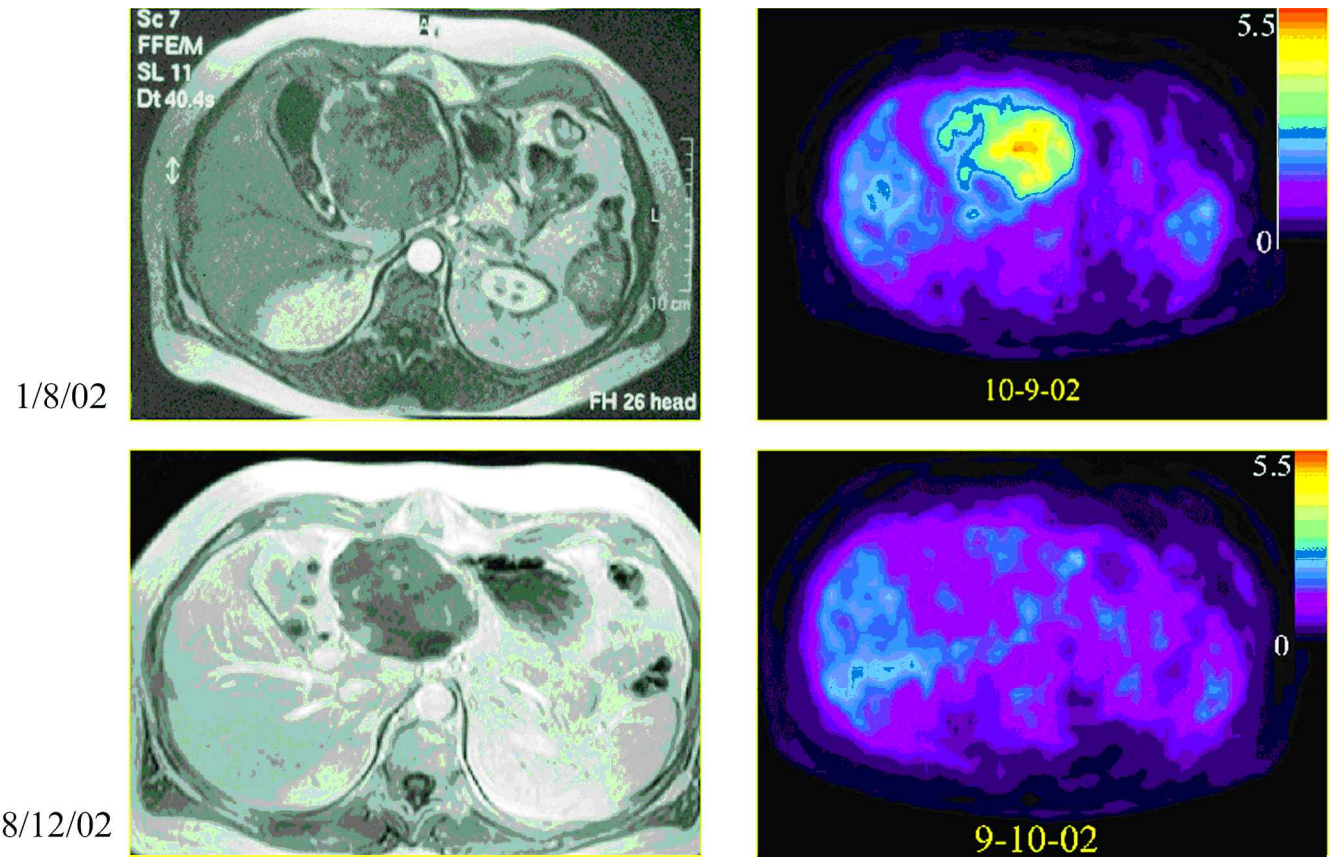


Fig 3 Positron emission tomography (PET) for monitoring Glivec tumour response: (left column) magnetic resonance images with intravenous contrast medium enhancement. A large liver mass (metastatic gastrointestinal stromal tumour) is little changed in size after nearly four months of imatinib (Glivec) treatment; **(right column)** specific uptake value (SUV) maps from 2-[F-18] fluoro-2-deoxy-D-glucose-PET scans at the same anatomic level. The tumour mass has become hypometabolic within four weeks of treatment.

of insonation or direction of blood flow. This improvement in sensitivity helps to detect neovascularisation of lesions and thus allows differentiation of malignant and benign lesions. Recently developed ultrasonographic microbubble contrast agents[15] have further improved the sensitivity of US by enhancing the signal strength from within small vessels. The roles of US contrast media are currently being evaluated for assessing focal liver lesions, non-palpable breast masses and prostate cancer.

Advances in functional imaging techniques

Positron emission tomography

Positron emission tomography (PET) enables the representation in image form of metabolic activity of underlying tissue processes such as glucose, oxygen and amino acid metabolism. Parameters that can be assessed by PET may allow new clinical perspectives in the diagnosis and management of cancer as well as improving the understanding of tumour physiology and biochemistry.

PET differs from conventional nuclear medicine techniques in that, in contrast to a radiation photon, positrons are released from nuclides attached to clinically relevant pharmaceuticals. These positrons are rapidly annihilated in soft tissues by electrons to release 511 MeV radiations identified by a ring of coincident detectors. The most commonly used radiopharmaceutical is 2-[F–18] fluoro-2-deoxy-D-glucose (FDG), a glycolytic pathway tracer with a wide range of clinical applications in oncology, especially for melanoma, lymphoma, colon, lung and breast tumours. FDG-PET is useful in the characterisation of indeterminate lesions seen on conventional imaging, staging and grading malignancy,[16] monitoring response to treatment (Fig 3) and predicting relapse following initiation of therapy.[17]

Recent advances in PET hardware include the simultaneous acquisition of CT and PET using combination scanners, allowing better and uninterrupted colocalisation and image registration. Research applications of PET include:[18]

- evaluation of drug pharmacokinetics
- determining the effect of treatment on tumour proliferation
- physiology, and
- biochemistry.

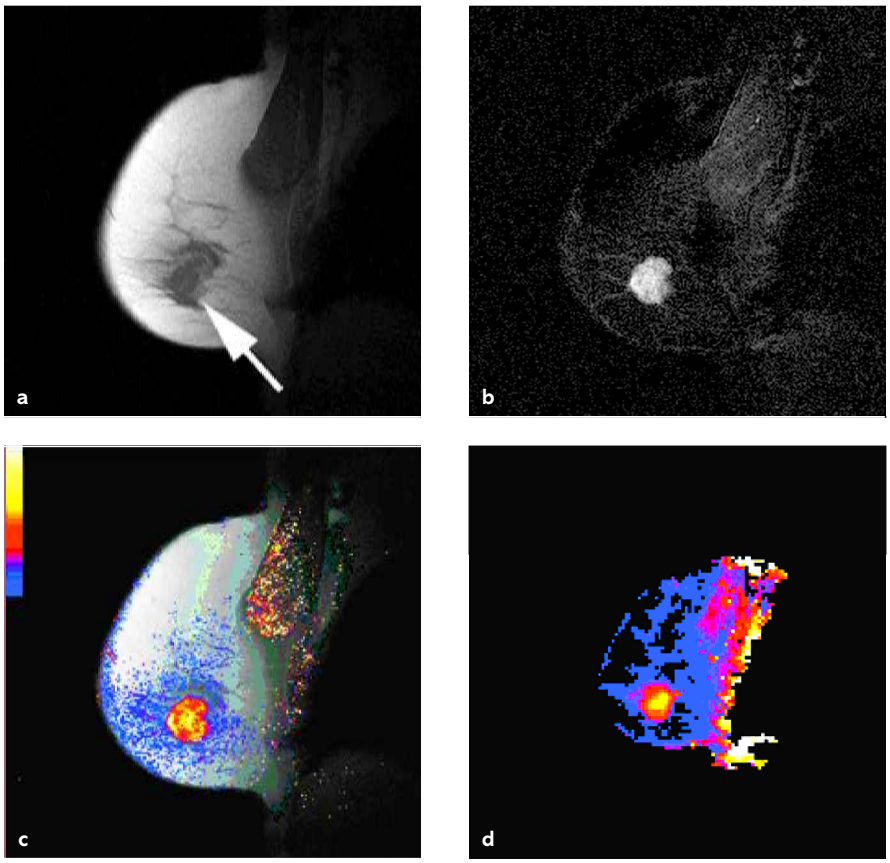


Fig 4 Dynamic contrast-enhanced magnetic resonance imaging of invasive ductal breast cancer: (a) sagittal anatomical image of the breast shows a mass in the lower part of the breast (arrow); **(b)** subtraction image after administration of contrast medium shows an enhancing mass. No other enhancement is visible; **(c)** and **(d)** corresponding images mapping permeability surface area product and relative blood volume at the same anatomic position within the mass, fat and muscles. The blood volume image is at lesser resolution.

Other nuclear medicine advances

A number of other advances in nuclear medicine have had a profound effect on the management of cancer patients. For example, the identification of 'sentinel' nodes (ie lymph nodes draining the site of a cancer) using radiolabelled colloid, particularly in breast cancer and melanoma. Identification of draining lymph nodes enables them to be selectively sampled.[19] This technique may potentially minimise the extent of nodal resection for these malignancies, reducing coincident treatment-related morbidity including lymphoedema.

Tumour-specific imaging techniques using radiolabelled compounds such as Sestamibi (^{99m}Tc MIBI) are useful in patients with questionable or indeterminate mammograms, avoiding unnecessary biopsies. Somatostatin analogues (octreotide, lanreotide etc) and meta-iodobenzyl guanidine (^{123}MIBG) are employed for imaging and treatment (using ^{131}I) of neuroendocrine tumours. Antigenic markers in the form of radiolabelled monoclonal antibodies are another type of tissue-specific agent targeting antigens expressed (or overexpressed) by tumours. Carcinoembryonic antigen and prostate specific membrane antigen for the diagnosis of

colorectal and prostate cancer are good examples of this type of application.

Dynamic contrast-enhanced magnetic resonance imaging

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI), performed after the administration of intravenous contrast medium, non-invasively accesses tumour vascular characteristics.[20] DCE-MRI techniques utilising low-molecular weight contrast media have successfully transferred from methodological development to pre-clinical and clinical validation and are now rapidly becoming mainstream clinical tools. Vascular characteristics that can be evaluated include:

- tissue blood volume and flow
- microvessel permeability, and
- lesion extravascular-extracellular space (Fig 4).

DCE-MRI using macromolecular contrast medium (MMCM) can also assay microvascular characteristics of human tumour xenografts. MMCM approval for human use will be granted soon. The success of both techniques (DCE-MRI and DCE-MRI using MMCM) depends on their ability to demonstrate quantitative differences of contrast medium behaviour in a variety of tissues.

Evidence is mounting that kinetic parameters correlate with immunohistochemical surrogates of tumour angiogenesis, including microvessel density, and with pathologic tumour grade. DCE-MRI is being applied to monitor the clinical effectiveness of a variety of treatments, including antiangiogenic drugs. Kinetic parameter changes following treatment correlate with histopathological outcome and patient survival.

Magnetic resonance spectroscopy

A powerful non-invasive tool to study tumour biochemistry and physiology is magnetic resonance spectroscopy (MRS). Most clinical MRS studies in cancer are concerned with signals from ^{31}P or ^{1}H atoms in endogenous metabolites or ^{19}F signals from anticancer drugs. ^{31}P MRS provides information on tissue 'energetics' (^{31}P in phosphorus-containing compounds, eg adenosine triphosphate) and pH. ^{1}H MRS conveys information about cell membrane synthesis and degradation, reflecting cellular proliferation and necrosis.[21] MRS resonance can provide diagnostic information on tumour grade and is used to monitor tumour response to therapy.[22] It has the potential to trace the pharmacokinetics of certain agents used in chemotherapy.[23] MRS has yet to become a mainstream clinical tool.

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