New techniques for imaging colorectal cancer: the use of MRI, PET and radioimmunoscintigraphy for primary staging and follow-up

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Modern imaging techniques such as computed tomography (CT) and ultrasound (US) are in the majority of cases able to detect local and metastatic spread of malignancy. Increasingly, the requirement is for even more accurate pre-operative tumour staging to enable the use of new surgical techniques, neo-adjuvant therapies and, postoperatively, to enable detection of tumour recurrence on follow-up. Recent imaging research has focused on magnetic resonance imaging (MRI) for the detection of local tumour extension particularly for rectal tumours and on positron emission tomography (PET) and radioimmunoscintigraphy (RIS) for the detection of metastatic nodal and soft tissue disease. This article briefly describes these three imaging modalities and their role in primary staging, detection of hepatic metastases and local recurrence.

Imaging techniques

Positron emission tomography (PET)

PET uses unstable radionuclides such as $^{18}$F or $^{11}$C which, on decay, emit a positron. This positron then almost instantly combines, within the target tissue, with an electron to produce 2 photons which are always emitted at 180° to each other. These photons are then detected by the positron scanner and, as the photons are always emitted at 180° to each other, the exact site of their creation can be calculated. In this way, areas of tissue providing large numbers of positrons, i.e. areas of tumour, can be detected and imaged.

In practice, the most commonly used positron emitter is $^{18}$fluorine in the form of [F]-2-deoxy-D-glucose ($^{18}$FDG). All cells take up $^{18}$FDG by the same mechanism as glucose. Tumour cells have an increased expression of glucose transporters (GLUT1) and preferentially take up $^{18}$FDG compared to normal cells. Once the $^{18}$FDG is within the cell, it is phosphorylated by hexokinase to $^{18}$FDG6P which cannot cross the cell.
membrane. The normal dephosphorylation by glucose 6 phosphatase does not occur and the metabolites of $^{18}$FDG are effectively trapped within malignant cells and accumulate in sufficient quantity in comparison to normal cells to be detected by PET imaging\(^1\).

Unfortunately, $^{18}$FDG uptake is not exclusive to tumour cells. All metabolically active cells take up the tracer and it is normally seen in brain, myocardium, liver, spleen, bone marrow and kidney\(^2\). In addition to this, there is variable uptake in the lumen of the gastrointestinal tract, sites of inflammation and post-laparotomy scars\(^2\,3\).

As there can be interference in tumour uptake if blood glucose levels are high, imaging takes place with the patient fasted for at least 4 h prior to intravenous injection of $^{18}$FDG to lower both glucose and insulin levels.

Imaging takes place 45 min after intravenous injection. Images are obtained from the base of the skull to the pelvis and are displayed in the sagittal, coronal and axial planes. Areas of increased isotope activity appear as black areas on the scan in a similar way to areas of abnormality on a bone scan.

**Radioimmunoscintigraphy**

Radioimmunoscintigraphy uses monoclonal antibodies labelled with radionuclides such as $^{99m}$technetium or $^{111}$indium that produce gamma radiation detectable by a gamma camera. The antibody is targeted against antigen sites found on malignant cells, in this instance carcino-embryonic antigen (CEA). Tumour cells produce a number of distinct antigens due to alterations in cell DNA. Britton and Granowska have identified that an ideal antigen should be expressed by all malignant cells with at least 5000 epitopes per cell; it should not be expressed by normal tissue or in other diseases and should be stable\(^4\). It should also be expressed by both poorly differentiated and well-differentiated tumour. Like all ideals, this is rarely met.

Two common radiolabelled antibodies used in the assessment of patients with colorectal carcinoma are IMMU-4 and PR1A3. IMMU-4 is a monoclonal antibody that targets CEA, an onco-fetal antigen that arises from the epithelium of the digestive tract. It is found both on the cell surface membrane and in about 65% of patients within the blood stream. As such, CEA can be found in normal lymph nodes resulting in false positives in studies using anti-CEA antibody\(^5\). PR1A3 is an antibody directed against the B3 domain of CEA, which is retained by the cell membrane when CEA is shed, and is not seen in normal lymph nodes\(^6\).

Monoclonal antibodies are produced by immunizing a mouse with a specific antigen. Lymphocytes from the spleen are then fused with myeloma lymphocytes to create an immortal strain. The lymphocytes
are then selected for a specific strain of antibody and cultured to yield a clone producing a single antibody. Antibodies have two heavy chains and two light chains held together by disulphide bonds into a Y-shaped configuration. The stalk of the Y is the Fc portion whilst the arms are the Fab portion. It is the tip of the Fab portion or the complementarily determinant region that reacts with the antigen.

Whole murine monoclonal antibodies can be used for imaging. This has the drawback of inducing an immune response in the recipient leading to human anti-murine antibodies (HAMA) directed against the imaging antibody. These have been found to occur in 5–40% of patients. It is debatable whether this has a significant clinical effect, but there are theoretical problems with increased serum clearance reducing the time available for the antibody to bind with the tumour and decreased sensitivity of imaging if it is used repeatedly as the monoclonal antibody is neutralised by the HAMA, and potential allergic reaction. It has been postulated that using just the Fab portion would avoid the production of HAMA as they are targeted against the Fc portion of the antibody. Indeed, Moffat found that when using IMMU-4, which contains solely the Fab portion, only 2 patients out of 240 developed HAMA. In the studies so far, HAMA have not yet been a problem, but repeated follow-up scanning has not been adequately assessed. HAMA may prove a problem if radioimmunotherapy is increasingly used.

A number of different radionuclides have been attached to monoclonal antibodies in colorectal imaging, most commonly 111indium and 99mtechnetium. 111Indium has a long half-life and requires imaging 48–72 h after injection. A further disadvantage is prominent liver and bone marrow uptake and bowel excretion, resulting in liver metastases appearing as cold spots rather than conventional hot spots. However, as urinary excretion is minimal, it has been suggested that it may be better for pelvic imaging. 99mTc has optimal energy gamma rays for gamma camera detection and a half-life which allows same-day imaging. Liver and marrow uptake is less than with 111indium but urinary excretion is greater which results in bladder accumulation, impairing imaging in the pelvis.

The patient needs to be well hydrated and, prior to imaging, the bladder is emptied. In males with benign prostatic hypertrophy, catheterisation may be necessary. Images of the pelvis, abdomen, chest and head are obtained at 2–6 h. Repeat imaging at 22 h may be necessary to see if bowel-related activity is due to bowel excretion or tumour.

**Magnetic resonance imaging**

When a hydrogen atom, which contains a single proton within its nucleus, is placed within a magnetic field, the proton will tend to align
itself in the axis of the magnetic field. If a radiofrequency wave is then applied, the atom will become excited and will need to release the excess energy to return to its original state. The time it takes to release this energy is partially dependent on the tissue character. By manipulating the timing of the radiofrequency pulse and the gradient of the magnetic field, it is possible to identify and characterise soft tissues and fluid. In addition, paramagnetic agents such as gadolinium and super-paramagnetic agents such as iron will also alter the local magnetic field within a tissue enabling these agents to be used as contrast agents.

MRI has certain advantages over CT scanning. It has superior soft tissue contrast which enables the identification of the different layers of the bowel wall as well as identification of the peritoneal reflections. In addition, multiplanar imaging is possible without the patient moving which enables the operator more accurately to define the extent of a tumour and its relation to adjacent organs. Unfortunately, despite the introduction of faster imaging sequences such as fast spin echo (FSE) and echo planar imaging, movement artefact caused by peristalsis and respiration can reduce image quality. These can be partially overcome with techniques such as respiratory gating and anti-peristaltic agents (hyoscine butylbromide). This has allowed high quality imaging of the rectum and liver, but imaging of the colon has not yet been clinically validated.

Primary staging

The emphasis in primary staging of colorectal carcinoma by imaging techniques is moving slightly away from TNM categories (Table 1) towards therapy dictated by subgroups. In rectal carcinoma, prognosis is related to the depth of invasion into the mesorectal fat. At surgery, the

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**Table 1** TNM staging of colorectal cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
<td>T1</td>
<td>Tumour invades the sub mucosa</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour invades the muscularis propria</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour invades the muscularis propria and into the subserosa or into the pericolic or perirectal tissues</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour directly invades other organs or structures and/or perforates visceral peritoneum</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in 1–3 regional lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in 4 or more regional lymph nodes</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
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whole thickness of the mesorectal fat is removed and this should be curative for T1, T2 and most T3 tumours. If tumour clearance of at least 1 mm from the resection edge is obtained, it is associated with a lower rate of local recurrence and improved prognosis.

One aim of pre-operative imaging is, therefore, to determine the minimum distance from the tumour (either direct extension or nodal) to the mesorectal fascia (Fig. 1)\(^{12,13}\). In addition, the increasing use of pre-operative radiotherapy for T3 tumours requires excellent pretreatment imaging\(^{14}\). The demonstration of the relationship of low rectal tumours to the internal and external sphincter and puborectalis enables assessment of the feasibility of sphincter-preserving surgery\(^{15}\).

Some of the major limitations of radiological staging of colorectal carcinoma relate to the lack of correlation between morphological and pathological findings. For example, spiculation of the perirectal fat can reflect either early tumour infiltration (T3) or desmoplastic response to T2 disease\(^{16}\). The key to accurate staging of local invasion is identification of the five layers of the rectal wall and the mesorectal fascia as a fine low intensity line surrounding the mesorectum (Fig. 2). CT is unable to demonstrate the different layers of the colonic wall and has an accuracy of \(\sim 74-81\%\) in advanced T staging\(^{17,18}\). In addition, the poor soft tissue discrimination makes the assessment of invasion of the anal sphincters and puborectalis in low rectal carcinomas problematic.

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Fig. 1 (A) Axial and (B) coronal T2 weighted fast spin echo MRI images of a mid rectal carcinoma. Soft tissue extending from the tumour into the meso-rectal fat (arrow) suggests early T3 disease. The meso-rectal node is only 4 mm in diameter and probably reactive (short arrow).
Endorectal ultrasound has been shown to demonstrate the 5 layers of the rectal wall and is 80–90% accurate in local staging but, unfortunately, due to limited depth of penetration, is unable to detect tumour deposits in the mesorectal fascia and tends to overstage T2 tumours if there is associated desmoplastic reaction\(^\text{19}\).

Despite great initial optimism based on its superior soft tissue discrimination and multiplanar acquisitions, initial studies of pre-operative MRI staging of rectal carcinoma were disappointing. Early studies using relatively thick sections of 8 mm or greater and a body coil did not allow identification of the layers of the bowel wall nor high spatial resolution. In fact, The Radiology Diagnostic Oncology Group (RDOG) using 10 mm sections found CT to be more accurate than MRI for rectal as well as colonic staging\(^\text{17}\). Improved accuracy was achieved first by using endorectal coils, which have the advantage of demonstrating the layers of the rectal wall, but result in poor visualisation of the mesorectal fascia. This limits its use in bulky

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**Fig. 2** Axial T2 weighted fast spin echo MRI of a polyploid mid-rectal carcinoma. The normal muscularis propria causes the low signal intensity line in the rectal wall seen anteriorly and to the right (short arrow). The effacement of this low signal posteriorly indicates T2 disease. The linear extension of soft tissue (arrow) into the meso-rectal fat is difficult to interpret (tumour versus desmoplastic response). In this case, the histopathology revealed tumour extension indicating T3 disease.
tumours. The use of endorectal coils is also limited in stricturing or high rectal lesions. Despite these limitations, it has a similar sensitivity and specificity to endoluminal ultrasound.

Further advances were made using pelvic phased array coils or four element surface coils. Brown et al studied 28 patients using a surface coil; thin sections correctly assessed the T stage in all patients who went on to surgery. Another study correctly staged 67–83% of all tumours.

T2 weighted scans show tumour to be of higher signal than smooth muscle, but lower signal than submucosa. This enables assessment of each of the five bowel wall layers. Spread into perirectal fat is best demonstrated with T1 weighted scans.

Spiculation of the perirectal fat by both direct tumour invasion and by desmoplastic reaction may cause difficulties differentiating T2 and T3 tumours. Fortunately, as the treatment of both T2 and T3 tumours is by total mesorectal excision, the differentiation is of less importance than the ability of MRI to predict accurately clear resection margins at surgery. Patients with disease within 5 mm of the mesorectum can be identified and given pre-operative radiotherapy.

In a study with a high proportion of T1 tumours, Wallengren et al advocated the use of rectal contrast. Ferristene is a super paramagnetic contrast that reduces signal on both T1 and T2 causing a signal void in the rectal lumen. By distending the bowel wall, the authors claimed improved tumour delineation, which is further improved by intravenous gadolinium. They did, however, use relatively thick sections of 7 mm and it is unclear whether the benefits would be as great in thin section (4 mm) scanning.

Others have argued that TNM staging has little value and that the presence of invasion into puborectalis, and the internal and external sphincter is more important as it allows the surgeon to plan sphincter-preserving surgery. Using intravenous gadolinium, Urban et al had a sensitivity of 100% and specificity of 98% in assessing sphincter infiltration.

Although both PET and radioimmunoscintigraphy have been shown to detect primary colorectal tumours, their spatial resolution and lack of anatomical detail prevent accurate determination of the degree of local tumour invasion. Although they have been shown to be useful in the detection of occult synchronous tumours, their major role is in the detection of metastatic disease enabling appropriate decisions to be made on attempted curative or palliative surgery.

Lymph nodes and extra hepatic spread

The lymphatic plexus of the colon drains into lymph nodes within the superior or inferior mesenteric chain and from there to the para- and
pre-aortic nodes. The rectum drains either into the inferior mesenteric chain or via the iliac nodes into the hypogastric nodes.

CT is the main imaging method for detecting lymph node metastases. It can only assess nodes in terms of size, number and, to a lesser extent, morphology. As such, it has inherent limitations in the detection of disease in normal sized nodes. Lymph nodes are considered abnormal on CT if they are greater than 1 cm in short axis. This criterion may also lead to the misinterpretation of benign reactive enlarged lymph nodes. Zheng et al found 4 out of 14 patients had malignant involvement in lymph nodes of less than 1 cm\(^2\). Overall, CT has a reported sensitivity of 22–73\%\(^\text{18}\). Other authors suggest that smaller drainage nodes especially in clusters near the primary tumour should be considered malignant, but this reduces specificity.

**MRI**

Like CT, MRI relies principally on size to differentiate benign from malignant lymph nodes, again using a maximum short axis diameter of

![Fig. 3](A) Axial CT and (B) coronal T2 weighted fast spin echo MRI images of an upper rectal carcinoma. The relationship between the tumour (arrow) and bladder is not clear on CT. The MRI demonstrates no evidence of tumour invasion of the bladder.
Studies have looked into the use of signal intensity, shape, central necrosis and enhancement patterns with mixed results and accuracy remains low at 64%\(^24\).

Currently, the most promising avenue of research is the use of ultra-small superparamagnetic iron oxide particles. These are taken up by macrophages found in normal and inflamed lymph nodes and homogenously reduce the signal intensity on T2 weighted MRI sequences. In metastatic lymph nodes there is complete or partial replacement of the macrophages by tumour cells resulting in either no change or a heterogeneous change in signal on post-contrast scanning. It has been found to have a high sensitivity and specificity in patients with abdominal and pelvic malignancy: 47 of 49 nodes were correctly categorised as benign or malignant\(^25\).

Unfortunately, this study only included enlarged nodes and much of the difficulty in nodal staging results from tumour deposition in non-enlarged nodes. Further trials are in progress.

**Radioimmunosintigraphy (RIS)**

Extrahepatic metastases appear as areas of increased uptake within the abdomen which cannot be explained by normal distribution of the radioisotope. RIS has been reported to detect strands of tumour within the peritoneum as well as within lymph nodes. Unfortunately, radionuclide imaging suffers from poor spatial resolution, with a minimum spatial resolution of approximately 4 mm. Moffatt et al reported an accuracy below 1 cm of only 60% and other studies confirm that accuracy is increased above 2 cm\(^9,26\). Despite these limitations, RIS has been reported to detect accurately tumour deposits in lymph nodes less than 1 cm in size\(^8,27\).

**PET**

There have been only a few studies assessing PET scanning in patients with primary colorectal carcinoma. PET, as with radioimmunosintigraphy, suffers from poor spatial resolution and may fail to demonstrate nodal disease adjacent to the primary tumour\(^22\). In studies containing patients with both primary and recurrent tumours, PET has been shown to be superior to CT in detecting metastatic disease with a sensitivity of greater than 85% and specificity of greater than 65%\(^22,28–30\).

Unfortunately, as with mucinous malignancy elsewhere in the body, PET has been shown to have reduced sensitivity in patients with colorectal mucinous adenocarcinoma\(^29\). There have also been a number
of other false negative studies. PET may fail to demonstrate pseudomyxoma peritonei and necrotic mesenteric metastases\textsuperscript{28,30}.

Peritoneal and mesenteric deposits can be difficult to identify on CT but may be identified on PET\textsuperscript{29} although small volume deposits of less than 1 cm may still missed\textsuperscript{30}. As PET enables whole body scanning, it may identify unsuspected pulmonary metastases\textsuperscript{31,32}.

**Hepatic metastases**

Up to 40\% of patients with colorectal cancer will develop liver metastases. Ultrasound is currently the commonest choice of imaging, but is operator dependent and may be unreliable at detecting hepatic lesions under 1 cm in size. CT is more sensitive, particularly for small lesions, but still only has a sensitivity of 70–85\%. This can be improved by using CT arterial portography (81–93\%) or multislice, contrast-enhanced CT\textsuperscript{33,34}. One of the major issues in hepatic imaging is that as sensitivity increases with improvements in imaging techniques, more benign lesions indistinguishable from liver metastases due to their small size (1 cm) are detected. In one study of patients with known colorectal carcinoma, only 14\% of small hepatic lesions were eventually found to be metastases\textsuperscript{35}.

**MRI**

Colorectal hepatic metastases most commonly appear as lesions that are moderately hyper-intense on T2 weighted images and hypo-intense on T1 weighted images (Fig. 4). If there is diagnostic doubt, a number of features can be used to help differentiate suspected liver metastases from simple cysts or hepatic haemangiomas. Simple cysts and hepatic haemangiomas return a higher signal on T2 weighted sequences than metastases. T2 weighted sequences tend to show metastases as having an ill-defined margin with slightly heterogeneous signal, or, occasionally, a ring of surrounding high signal, or halo due to central necrosis or biliary or vascular obstruction. In addition, they may also appear as target lesions with central high signal and adjacent low signal corresponding to compressed hepatic parenchyma\textsuperscript{36}.

Gadolinium-based intravenous contrast agents can improve the sensitivity of MRI in detecting metastases.

Most metastases are hypovascular and receive their blood supply from the hepatic artery in contrast to normal liver parenchyma which receives 60–70\% of its blood supply from the portal vein. During dynamically enhanced scanning, metastases may be of increased signal during the
Fig. 4 (A) Coronal T1 and (B) axial T1 weighted MRI images of the liver in a patient under consideration for hepatic metastectomy demonstrating typical hypo-intense hepatic metastasis (arrow). (C) Axial T2 weighted images in the same patient, the metastasis has a high signal centre (arrow) with an ill-defined margin (thin arrow) which is unusual in a benign lesion.
arterial phase, and decreased signal in the portal phase. There may also be peripheral washout, whereby the periphery of the metastasis is of lower signal than the centre and adjacent liver. On delayed scanning, metastases may have increased signal.

Tumour also differs from normal liver as it lacks Kupffer cells. This is exploited by MRI using ferumoxides. This super-paramagnetic agent is taken up in Kupffer cells resulting in lower signal in normal liver but no change in the signal of the metastasis, thereby increasing its conspicuity. MRI performed post-ferumoxide has been found to have a similar sensitivity to CT arterioportography (CTAP) or contrast enhanced multislice CT. In addition, MRI post-feruxomides appears more specific than CTAP. Other new agents taken up only by hepatocytes such as Mangafodipir Trisodium or gadobenate dimeglumine also increase sensitivity above unenhanced MRI.

Radioimmunoscintigraphy

Dependent on the radionuclide used, hepatic metastases may appear as areas of increased isotope activity or photopaenic areas. There is considerable hepatic uptake of 111indium-labelled antibodies and consequently hepatic metastases appear as photopaenic areas against a background of moderate uptake. CT is more accurate in the detection of hepatic metastases than 111indium-labelled antibodies.

Scans using technetium-labelled antibodies against CEA-derived antigens show hepatic metastases as either areas of increased isotope activity or photopaenic areas with a high uptake rim presumably due to central necrosis. Sensitivities of 70–75% and specificities of greater than 90% have been reported. As yet, no study has compared RIS with optimal CT or MRI scanning.

PET

As previously discussed, most studies of PET in colorectal cancer contain patients with both primary and recurrent disease. In one study of primary staging alone, liver metastases were present in 8 patients and PET correctly identified 7, missing just 1; only 3 of these were seen on CT. However, only 1 patient with a liver metastasis identified on PET also had histological confirmation. There were no false positives. Vitola et al reported that, in patients with suspected liver recurrence, PET had a sensitivity of 90% with an accuracy of 93% and, although CTAP was more sensitive, a large number of false positives made it less accurate (76%). Other studies have found similarly high sensitivity.
and specificity. Only one study has so far found PET to be of limited sensitivity in detecting hepatic metastases. In a study by Lai et al in patients with hepatic metastatic disease under consideration for hepatic metastectomy, 32% of patients had previously unsuspected extrahepatic disease, half of which were within coeliac lymph nodes. As such, PET has an important role in demonstrating extrahepatic metastasis especially in patients with recurrent disease. This is of particular importance if curative surgery for recurrent disease, such as hepatic metastectomy, is being considered (Fig. 5).

Fig. 5  (A) Coronal PET scan in a patient under consideration for hepatic metastectomy demonstrating two liver metastasis (arrow), only one had been seen on a CT scan. (B) Sagittal PET scan in the same patient demonstrating local pelvic recurrence (short arrow).
Locally recurrent tumour

Unfortunately, up to 30% of patients develop local recurrence. Routine surveillance with CT is currently the mainstay of monitoring colorectal carcinoma post-surgery. Differentiation between local recurrence and postsurgical and radiotherapy change within the pelvis can be extremely difficult.

Post-surgical change can appear on CT as increased soft tissue with streaking of the adjacent fat. This soft tissue will frequently regress in size in the majority of patients. Currently, the CT criteria for detecting local recurrence rely on morphological changes such as the presence of a globular mass as opposed to streaking of the fat, and increase in size of the mass on follow-up scans or a change in shape\textsuperscript{18}.

CT has been shown to have a specificity and a sensitivity of 65–70%. If there is diagnostic doubt, CT-guided biopsy (Fig. 6) or second-look surgery can be performed. Second-look surgery provides a diagnosis in 90% of patients, but is associated with a significant morbidity and only a small proportion of recurrences can be resected.

MRI

MRI suffers from similar limitations to CT, relying on morphological changes. It was initially hoped that increased signal on T2 weighted

Fig. 6 CT-guided biopsy of a pre-sacral soft tissue mass in a patient who had an anterior resection for rectal carcinoma. The convex margins of the mass had suggested recurrence but the biopsy revealed only scar tissue.
scans may help differentiate fibrosis from tumour, but this appearance may persist for at least 2 years after surgery in some patients. In addition, both benign scar and malignant recurrence can enhance on delayed scanning post-intravenous gadolinium41.

There is increasing interest in the use of dynamic enhancement, performed by obtaining pre-contrast T1 and T2 images and then imaging during intravenous gadolinium injection and for up to 10 min afterwards. Different authors have used different post-processing techniques to determine whether tumour recurrence is present. Muller-Schimpfle et al used pharmacomapping which has the disadvantage of being slow, Kinkel et al used subtraction techniques and Dicle et al a time-intensity curve to calculate the rate of lesion enhancement41–43. All have found that recurrence shows early enhancement allowing differentiation from scar tissue. Dicle et al concluded that a quantitative assessment of total enhancement was unhelpful, but tumour enhanced earlier than benign disease41. Muller-Schimpfle et al reported that recurrence had an earlier and higher degree of enhancement43. It is not clear yet whether dynamic enhancement is more accurate than PET or RIS in the detection of recurrence.

Radioimmunoscintigraphy

Numerous studies have reported on the usefulness in RIS in identifying pelvic recurrence. Stomper et al studied 61 patients of whom 29 had recurrence and found that IMMU-4 was accurate in 82%, identical to CT. In their series, all 17 pelvic recurrences were correctly identified. They showed that if there was suspicion of recurrence on CT and uptake on RIS, all patients had recurrence and suggested that in these cases biopsy might not be necessary. The most common false negatives were due to anastomotic recurrence or peritoneal disease measuring under 1 cm in size. They also found that the common false positives due to faecal material and bladder activity could be avoided by correlating the RIS study with CT26. Other studies have shown [111In]-santumomab and [99mTc]-anti-CEA scanning to be more sensitive than CT in detecting local disease and in detecting distant metastases (Fig. 7)8,9.

A common problem on follow-up of patients post-surgery is a rising blood CEA with no source of recurrence demonstrated on conventional imaging. Moffat et al reported that, in 88 patients with suspicion of occult disease identified by either a rising CEA, abnormal liver enzymes or clinical suspicion, 36 recurrences were identified on CEA scanning alone. There were 11 false positives (3 of these were later identified to be true positive by longer clinical follow-up than the study protocol allowed). As in their earlier study in patients with known disease the best results were by using RIS and CT combined9.
There have been a number of studies confirming that PET is accurate in detecting pelvic recurrence. In a study by Ito et al, PET correctly identified all 11 pelvic recurrences. No other studies have found PET to be as accurate, but Johnson et al reported that, in their series of 41 patients all of whom had surgical confirmation, PET had a sensitivity of 84% and specificity of 94%. Whiteford found PET was more sensitive than CT and colonoscopy (92% versus 71%) and as specific, and also reported that PET was superior to CT in identifying extrahepatic and hepatic metastases. As PET may demonstrate uptake in inflammation as well as tumour, false positives may occur due to recent surgery and
radiotherapy. It is, therefore, recommended that PET should be performed at least 4 months after surgery.

In 22 patients with abnormal CEA levels but normal conventional imaging, PET identified 17 with increased uptake of \textsuperscript{18}FDG. There were 2 false positives, one of which represented a bladder diverticulum and the other normal liver. However, the positive predictive value was 89\% and the specificity 100\%, confirming other smaller study results that PET is useful in the investigation of an occult CEA rise\textsuperscript{46}.

**Conclusions**

There is no doubt that these three techniques will have an increasing role to play in the management of colorectal cancer. There is increasing use of MRI in the staging of rectal tumours and detection of liver metastases. Both PET and RIS have been found to be useful in detecting occult disease and local tumour recurrences; they offer an extremely important adjuvant to conventional imaging particularly if major surgery such as hepatic resection or pelvic penetration for recurrence is being considered. Both PET and RIS should be combined with cross sectional imaging for optimal results.

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