

# IMAGING COLORECTAL CANCER

Colorectal cancer is the second most common cause of cancer death in the UK. However, advances being made in imaging, preoperative therapies and surgery promise to improve the outcome for patients with the disease.



**Gina Brown**

**MD MRCP FRCR**

Gina Brown is a Consultant Radiologist in the Academic Department of Diagnostic Radiology at The Royal Marsden NHS Foundation Trust.

## Introduction

In the last few years, we have successfully focused on improving the detailed information that can be obtained about colorectal tumours in order to target preoperative treatments, as well as direct surgery to improve the chances of cure. The research achievements in gastrointestinal (GI) imaging during 2006 have been accomplished through the close collaboration of the colorectal cancer network of The Royal Marsden, as well as through the multicentre MERCURY research group. The results of our studies have produced improvements in outcomes for patients with colorectal cancer both locally and nationally. In 2007, and beyond, there remain challenges in the management of colorectal cancer which include:

- Earlier diagnosis and staging of patients with suspected bowel cancer;
- Elimination of tumour at the surgical resection margins and prevention of local recurrence;
- Avoidance of unnecessary permanent colostomies and improvement of outcomes in patients with low rectal cancer;
- Improving our understanding of the biology and behaviour of tumours in order to distinguish between aggressive high-risk disease and low-risk tumours;
- Refining staging techniques to characterise and detect early spread of tumour to lymph nodes better;
- Improving surveillance of patients at high risk of recurrence.

## Earlier diagnosis and staging of patients with suspected bowel cancer

Recently, rapid developments in computed tomography (CT) scanner technology have enabled increasingly sophisticated imaging techniques. One such example is CT colonography or virtual colonoscopy which enables the internal contours of the bowel to be visualised in two or three dimensions. When the empty bowel is distended by insufflation with air or carbon dioxide, the scans can demonstrate polyps and cancers that project into the bowel. Currently studies are underway to confirm

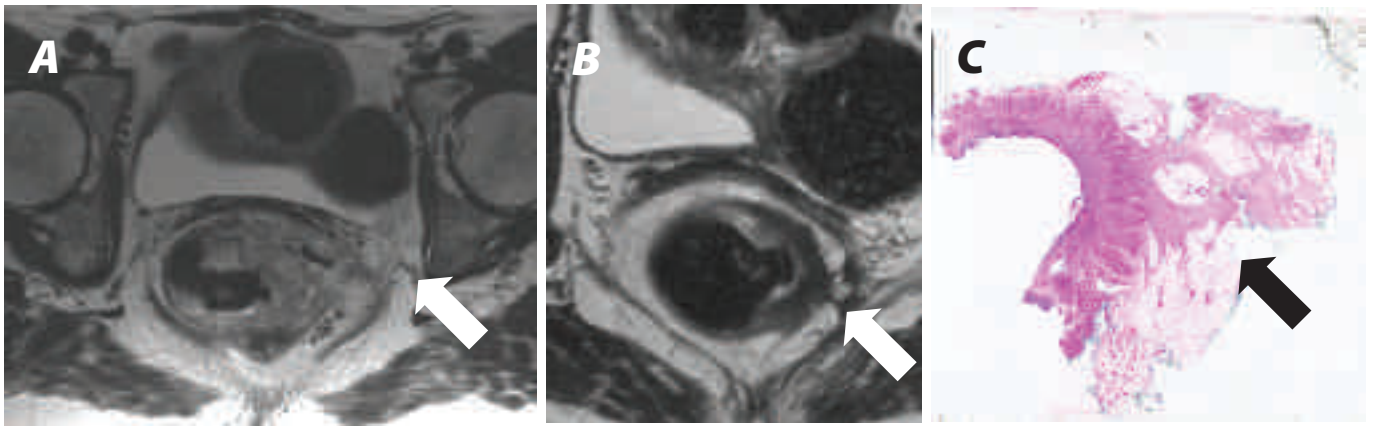


Figure 1: MRI-based stratification

Tumour identified on MRI extending to the potential margins of surgery

(A) Having identified this high-risk tumour, preoperative treatment was given in the form of chemotherapy followed by chemoradiotherapy. The tumour shrank away from the surgical margins (B) and surgery resulted in successful removal of the tumour with clear margins (C).

if virtual colonoscopy is an effective and less invasive method of diagnosing older patients with bowel cancer symptoms. The technique is also used when a conventional colonoscopy has not been successful.

### Prevention of local recurrence

Nationally, the local recurrence rate in rectal cancer is as high as 25%. This is due to instances of tumour left behind following surgery at the surgical resection margin which occurs in 15-30% of operations. Once local recurrence occurs, few patients survive. It has been our goal to use detailed preoperative imaging with multidisciplinary discussion of these findings to identify patients at risk of local recurrence before surgery and alter the preoperative therapy as well as the surgical approach to prevent positive surgical resection margins. In the last four years, we have achieved this aim with the near elimination of tumour positive surgical resection margins. This has translated into a substantial reduction in patients developing local recurrence, which in turn has resulted in improved long-term survival for our patients. Having demonstrated the success of this approach within our network, we wanted to show that this could be achieved by others.

In 2006, we reported the results of the largest multicentre trial evaluating preoperative staging of rectal cancer. The data, from 428 patients enrolled over a two-year period, showed that when magnetic resonance imaging (MRI) is taught to radiologists in different centres using criteria and techniques developed by researchers at The Royal Marsden, the local spread of the tumour could be predicted very accurately as well as the likely success of the surgical resection.

■ As a result of this trial, the MRI methodology used at The Royal Marsden has been established as the standard for preoperative assessment of rectal cancer and a Department of Health-funded programme of national workshops has been set up. ■

The workshops, which are run from The Royal Marsden, are aimed at training specialist consultants in GI imaging. This approach is now available at the majority of colorectal networks and these workshops continue. The widespread adoption of high resolution MRI for staging rectal cancer has placed the UK in a unique position to lead clinical research into the important area of preoperative neoadjuvant therapy for high-risk rectal cancer. The Royal Marsden conducted the first successful clinical trial using MRI-based stratification and showed for the first time that tumour extension to the potential resection margins could be downstaged by intensive preoperative therapy (see Figure 1). This approach has been developed further with more sophisticated preoperative strategies using targeted agents and high risk patients are currently enrolled into this trial. Nationally, a similar MRI-based stratification is being used to develop a multicentre randomised preoperative therapy trial (designated ARISTOTLE).

### Distinguishing between high-risk and low-risk tumours

By careful comparison of MR images with microscopy, we have been able to learn about the behaviour of rectal tumours before surgery. This gives us the unique opportunity to undertake detailed prognostic staging

of tumours. One of the most significant findings from our recent research has been the demonstration of the impact of MRI-detected spread of tumour into veins (extramural venous invasion) and the implications for patient survival since this feature strongly predicts for the development of liver metastases. Armed with this information, we are now in a position to intensify both the treatment and follow-up of this significant prognostic group of patients.

### Improving surveillance of patients at high risk of recurrence

Colorectal cancer is unique in that good survival can be achieved following successful resection of metastatic disease. Improvements in hepatic surgery and development of a hepatic surgical unit at The Royal Marsden has revolutionised the management of our patients with colorectal cancer. Our strategies are aimed at early detection of metastatic disease and aggressive combined chemotherapeutic and surgical removal of disease (see Figure 2). We have complemented this with non-surgical approaches such as radiofrequency ablation, as well as powerful palliative chemotherapy to prolong survival in patients with irresectable liver metastatic disease. Our experience with imaging of liver disease has enabled us to demonstrate extremely high accuracy in both the early identification of liver metastases and confident characterisation of liver lesions. In a recently published study, we showed greater than 90% accuracy for detection of liver metastases using a special liver-specific contrast agent.

### Improving the management of colonic tumours

Above the rectum, imaging of the colon is much more of a challenge since the absence of the rigid bony pelvis prevents us from obtaining high resolution MR images of the colon. However, by applying our knowledge of the morphological behaviour of tumours to computed tomography (CT), we have been able to improve our staging abilities for the rest of the colon (see Figure 3).

Preoperative CT staging of non-metastatic colon cancer predicts outcome and as such has implications for clinical trials. By careful interpretation of images we have been able to show that CT can identify poor prognostic colonic tumours accurately enough for these patients to be offered novel preoperative treatment strategies. This generates an important clinical question: can the success of preoperative treatment in improving outcomes in rectal cancer be translated to the rest of the colon? The observations and validation of this improved staging method will be the subject of a forthcoming national randomised trial evaluating novel preoperative chemotherapy in CT-identified high-risk colonic tumours.

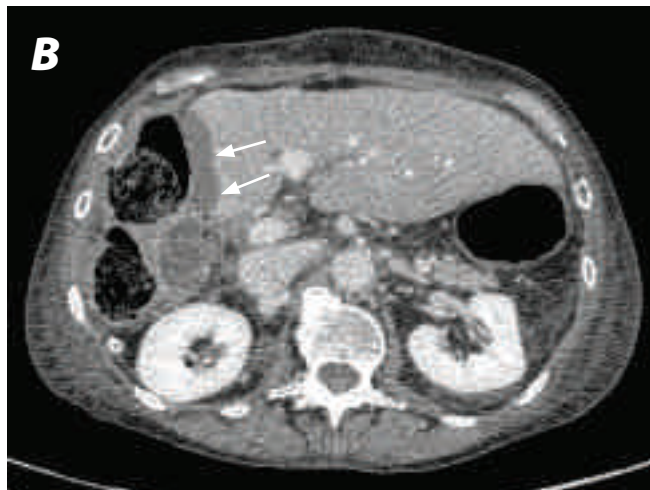
### Improving outcomes for patients with low rectal cancer

From the patient's perspective, the diagnosis of low rectal cancer, defined as tumour below the lowest 5cm of the rectum, has potentially the greatest impact on quality of life. Issues include the prospect of permanent colostomy, as well as the documented 40% risk of local recurrence. Multidisciplinary research at The Royal Marsden is focusing on these problems by:

- Improving surgery by developing new laparoscopic techniques (see article by Professors David Cunningham and Sir Ara Darzi, p.26-29);
- Conducting a clinical trial aimed at avoidance of colostomy for patients showing a complete response to preoperative chemoradiotherapy;
- Gaining a greater understanding of the role of imaging as a method of directing the surgical approach;
- Identifying patients who can safely undergo ultra low sphincter-sparing rectal cancer surgery.



Figure 2: (A) Patient with colorectal cancer who has developed a liver metastasis (double arrow). Such patients can often be treated radically and in this patient, chemotherapy was administered to reduce the size of the metastasis and to eliminate the risk of smaller micrometastases. The patient then underwent a right hemi-hepatectomy and follow up at two years shows no evidence of any further metastatic disease (B).



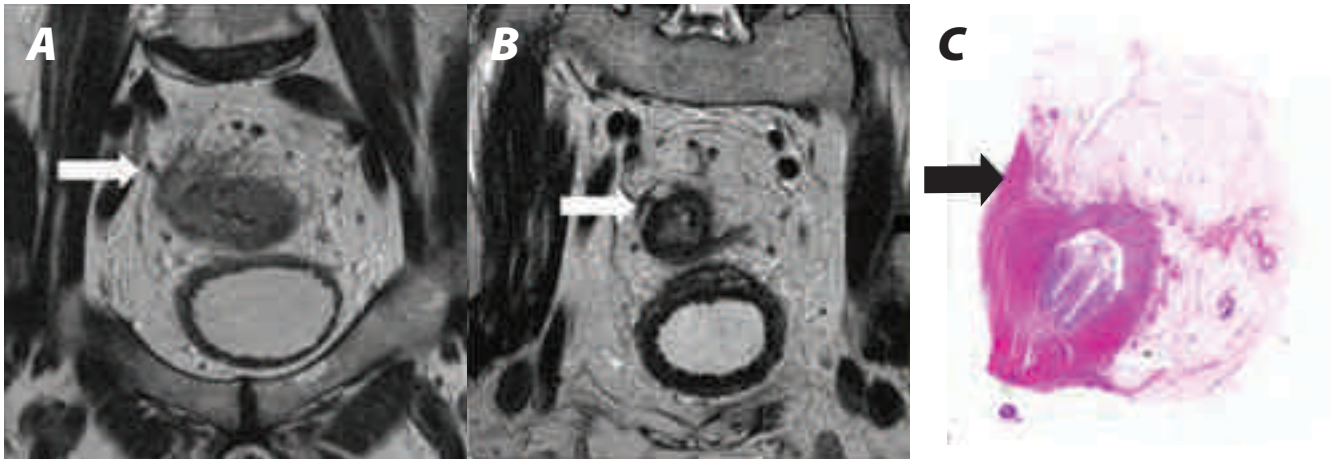


Figure 3: Staging colonic tumours

(A) Patient with a tumour in the sigmoid colon which extended to the potential surgical resection margin. Preoperative chemoradiotherapy was given to enable the tumour to shrink away from the resection margins (B). The surgical specimen shows no tumour at the resection margins (C). This example illustrates that non-rectal tumours can be treated in a similar aggressive fashion.

We have shown that using our new staging system we can identify, with certainty, those patients at risk of getting a positive margin. As such, we can recommend appropriate patients to receive more intensive preoperative therapy as well as a more radical operation (see Figure 4). This will be the subject of a national trial being launched in 2007 aimed at eliminating the unacceptably high risks of local recurrence and reducing permanent colostomy formation.

### Detection of tumour spread to lymph nodes

Rectal cancer is common and nodal disease is an independent adverse prognostic factor for patient survival. Accurate demonstration of the presence and location of nodal disease preoperatively may influence management strategies. The detailed internal architecture of lymph nodes can be visualised using our MRI techniques and we have shown this to be much more accurate than simply measuring lymph nodes. In recent years, several advances in imaging have become available and may improve nodal assessment; examples include the development of lymph node-specific contrast agents

and the availability of higher magnetic field strength MRI systems. The distinction between a benign and malignant node relies on the identification and separation of tumour cells within the lymph node from normal lymphatic tissue. For this reason, lymph node-specific contrast agents have been developed and Dr Mu Koh (Cancer Research UK Clinical Magnetic Resonance Research Group at The Institute) and Dr Aslam Sohaib (Department of Diagnostic Radiology at The Royal Marsden) have been leading the investigation of this agent. Our early results are promising and we have been able to develop criteria that distinguish between malignant and benign nodes by the pattern of nodal enhancement. The forthcoming installation of a new 3T MRI system is an exciting development for imaging research at The Royal Marsden and The Institute, and we hope to improve our staging abilities with this new innovation.

Figure 4: Illustration of the challenge faced by surgeons when operating on low rectal cancers. Only a very small amount of tissue around the rectum is removed during conventional surgery. In this case, a clear resection margin was achieved, but if MRI had identified tumour beyond the red line then this would have resulted in an incomplete resection (A). More radical surgery is being developed (B) which enables a much more generous amount of tissue removal reducing the risk of incomplete resections.

