The Role of Biofeedback in Improving Anal Continence after Anterior Resection

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ABSTRACT

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THE ROLE OF BIOFEEDBACK IN IMPROVING ANAL CONTINENCE AFTER ANTERIOR RESECTION
By Sophie Anne Pilkington

Incorporation of routine biofeedback into the management of patients with rectal cancer who are undergoing anterior resection offers potential for improved anal continence compared with standard management. A multicentre randomised controlled trial was performed to investigate this and 121 participants undergoing major rectal resection were randomly assigned to receive biofeedback training. In the control group participants received standard management. Randomisation was stratified for preoperative radiotherapy exposure. The primary end point was Cleveland Clinic Incontinence (CCI) score at 1 year. Analysis was by intention to treat (ITT). Secondary end points were serial symptom-score, quality of life questionnaires and anorectal physiology measured during the first postoperative year.

Follow-up to one year was completed by 89 participants. A mean CCI score of 4 was recorded at 1 year in both groups. Before anterior resection, 15 (17%) participants reported severe anal incontinence. At 3 months after anterior resection, 27% of participants reported severe anal incontinence, which caused a negative impact on their quality of life. Function improved in some participants but 15% complained of severe anal incontinence at one year.

Anal continence after anterior resection is a poorly defined problem. Although no advantage was found by the addition of routine biofeedback to standard management, this study establishes a working definition for “Anterior Resection Syndrome” and evaluates methods for measuring the structural and functional abnormalities associated with it. Symptom-score and quality of life questionnaires, anorectal physiology and proctography are frequently used to evaluate pelvic floor patients but are also relevant to assess anterior resection patients.

An additional study was carried out to compare Barium (BaP) and MR proctography. BaP reproduced rectal emptying and demonstrated structural abnormalities to a greater extent than MR proctography and would be the best test for assessing structural abnormalities after anterior resection.

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Declaration of Authorship

I, **Miss Sophie Anne Pilkington**

declare that the thesis entitled

The role of biofeedback in improving anal continence after anterior resection

and the work presented in the thesis are both my own, and have been generated by me as the result of my own original research. I confirm that:

- this work was done wholly or mainly in candidature for a research degree at this University;
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- where I have consulted the published work of others, this is always clearly attributed;
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- none of this work had been published before submission

Signed:

Date:

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Abbreviations

APC	Adenomatous polyposis coli
APR	Abdominoperineal resection
ARP	Anorectal physiology
ATZ	Anal transition zone
BaP	Barium proctography
BCSP	Bowel Cancer Screening Programme
BFB	Biofeedback
CCI	Cleveland Clinic incontinence score
CRM	Circumferential resection margin
CT scan	Computerised tomography scan
DI	Diarrhoea symptoms as measured on the EORTC QLQ-C30 questionnaire
DXT	Radiotherapy
EORTC QLQ-C30 & CR29	European organisation for research and treatment of cancer quality of life questionnaire core module 30 & colorectal module 29
FA	Folinic acid
FAP	Familial adenomatous polyposis
FIQL	Fecal incontinence quality of life questionnaire
FISI	Fecal incontinence severity index
Gy	Gray
HNPCC	Hereditary non-polyposis colorectal cancer
M	Distant metastasis
MDT	Multidisciplinary meeting
MMR genes	Mismatch repair genes
MR proctography	Magnetic resonance proctography
MRI	Magnetic resonance imaging
MRP	Mean resting pressure in anal canal
MSI	Microsatellite instability
MSP	Mean squeeze pressure in anal canal
MTV	Maximum tolerated rectal volume
N	Regional lymph node metastasis
QL	Global Health Status / Quality of life as measured on the EORTC QLQ-C30 questionnaire
QOL	Quality of life
RAIR	Rectoanal inhibitory reflex

SD	Standard deviation
T	Extent of primary tumour
TME	Total mesorectal excision
TNM	Tumour, node, metastasis classification of malignant tumours

1 Introduction

1.1 Rectal Cancer

Rectal cancer (See Figure 1.1) is the fifth most common cancer in both sexes in England and Wales (Quinn, Babb, Brock, Kirby, & Jones, 2009). The five-year relative survival for adults (15-99 years) diagnosed with rectal cancer between 2001 and 2006 and followed up to 2007 was 51% for men and 55% for women (Walters et al., 2009). Rectal cancer is more frequent in men than women and the annual numbers of patients diagnosed during 2001 to 2006 were 6,340 men and 4,070 women (total: 10,410) (Walters, et al., 2009). Recent advances in surgical technique, chemotherapeutic options and radiotherapy have resulted in an improvement in survival and reduced permanent stoma rates (Kirwan, O'Riordain, & Waldron, 1989). Over the last 2 decades there has been an increase in five-year relative survival of 22% in rectal cancer (Trends in Cancer Survival in Scotland 1980-2004) (ISD National Service Scotland, 2009). It is predominantly a disease of the elderly. In 2001, the Office for National Statistics recorded that 71% of patients presenting with rectal cancer were aged 60 years or older in England and Wales and 53% were aged 70 years or older (Office for National Statistics, 2009).

Cancer of the colon is more common than rectal cancer (Figure 1.2) with 16,880 patients diagnosed annually. Colorectal cancer is the second commonest cause of death from cancer in the UK (Figure 1.3). Cancers of the colon and rectum are often considered together as colorectal cancer as they present with common symptoms either as an emergency or chronically (See Table 1.1) (M. R. Thompson et al., 2003).

Figure 1.1 Colonoscopic appearance of rectal cancer

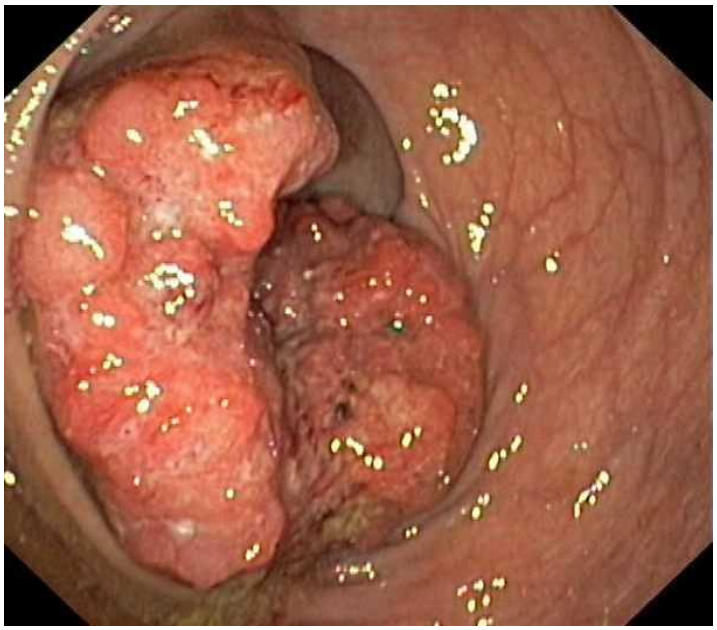


Figure 1.2 Frequency of anatomical locations of colorectal cancer (Based on data from the Royal College of Surgeons audit in Trent Region and Wales)

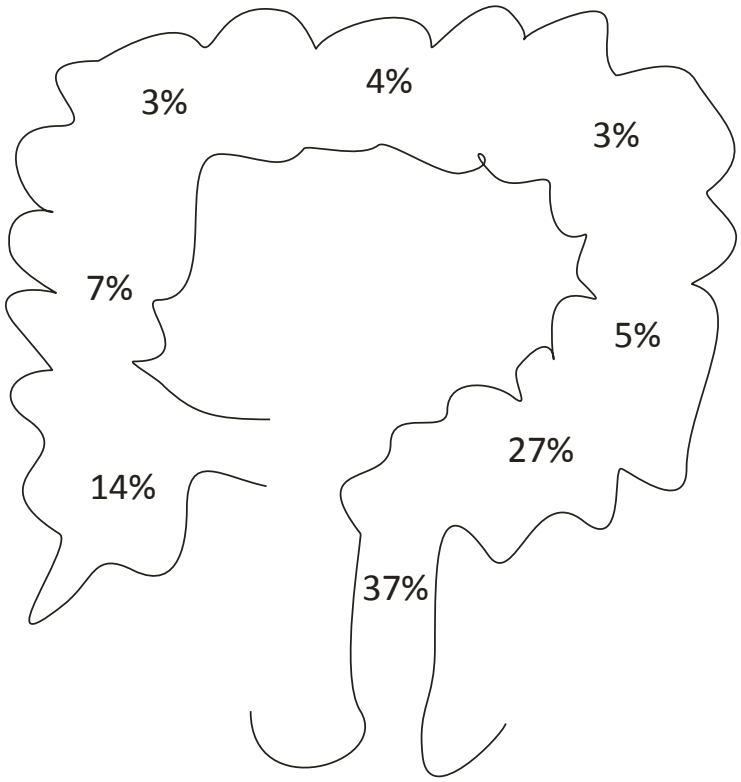


Figure 1.3 The 20 most common causes of death from cancer, UK, 2007 (Cancer Research UK, 2009)

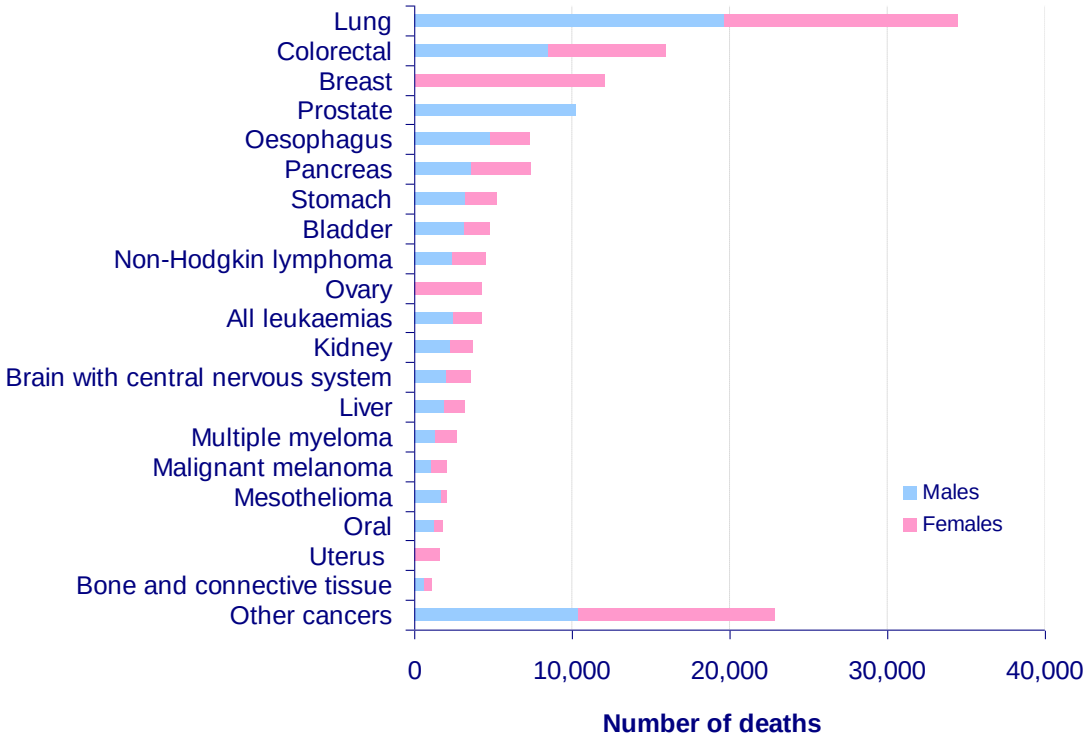


Table 1.1 UK Department of Health criteria for high and low risk of colorectal cancer

Higher risk • Rectal bleeding with a change in bowel habit to looser stools or increased frequency of defaecation persisting for 6 weeks (all ages) • Change in bowel habit as above without rectal bleeding and persisting for 6 weeks (>60 years) • Persistent rectal bleeding without anal symptoms (soreness, discomfort, itching, lumps, prolapse or pain) (>60 years) • Palpable right-sided mass (not pelvic) (all ages) • Palpable rectal mass (not pelvic) (all ages) • Unexplained iron deficiency anaemia (all ages)
Low risk ***Patients with no iron deficiency anaemia, no palpable rectal or abdominal mass and*** • Rectal bleeding with anal symptoms and no persistent change in bowel habit (all ages) • Rectal bleeding with an obvious external cause, e.g. anal fissure (all ages) • Change in bowel habit without rectal bleeding (<60 years) • Transient changes in bowel habit, particularly to harder or decreased frequency of defaecation (all ages) • Abdominal pain as a single symptom without signs and symptoms of intestinal obstruction (all ages)

Patients with higher risk symptoms should have the large bowel visualised with either colonoscopy, CT colonography (Kuwayama, Iimuro, Kitazumi, & Luk, 2002) or barium enema with sigmoidoscopy to search for suspected colorectal cancer. The gold standard for diagnosis is the presence of adenocarcinoma on histology from endoscopic biopsy. Once the diagnosis is established, preoperative imaging with a CT scan of the chest, abdomen and pelvis is used to predict staging of the cancer. In the case of rectal cancer, an MRI scan is also performed to predict involvement of the circumferential resection margin (CRM) (Brown & Daniels, 2005) and the T and N

staging of the tumour. This is important for the selection of patients for preoperative radiotherapy (Sebag-Montefiore et al., 2009). There may be a role for rectal ultrasound in selecting patients for short course radiotherapy (Garcia-Aguilar et al., 2002; Mackay, Pager, Joseph, Stewart, & Solomon, 2003; Pilkington, Winter, Harris, & Nugent, 2009).

1.2 Defining the Rectum

A precise clinical definition of the boundaries and length of the rectum is not universally recognised. This is at least in part because it is extremely difficult to measure the length of a curved distensible tube that is located deep within the bony pelvis and does not have start and end points that are easily identifiable clinically.

The sigmoid colon has a mesentery and the rectum does not. Therefore the rectosigmoid junction is located where the sigmoid mesentery ends. Anatomically this is located over the third part of the sacrum. The three taeniae coli broaden out over the sigmoid colon and then fuse together over the rectum to form a complete outer layer of longitudinal muscle with no appendices epiploicae or diverticulae. Despite its name ("rectus" comes from the Latin meaning "straight as if ruled") the rectum is curved, following the concavity of the lower sacrum, coccyx and pelvic floor (Sinnatamby, 1999). It has three lateral curves with the middle portion passing to the left. The lower part of the rectum is supported on the levator ani muscle before passing through the pelvic floor between the puborectalis sling posteriorly and the perineal body anteriorly to become the anal canal. In the upper third of the rectum, peritoneum covers the anterior and lateral surfaces. In the middle third, peritoneum covers only the anterior surface and the lower third is below the level of the peritoneal reflection. In men, the peritoneum sweeps over the upper part of the bladder to form the rectovesical pouch and in women it is reflected over the upper vagina to form the rectouterine pouch (of Douglas). The rectum is about 12cm long. When measured from the anal verge with a rigid sigmoidoscope the rectosigmoid junction is located at approximately 15cm (Lowry et al., 2001). Unfortunately the anal verge is not a fixed point and, particularly in large patients, it can be difficult to identify accurately. In addition, this measurement includes the anal canal which is of variable length. The surgeon needs to gauge whether an anastomosis can be safely performed with sphincter preservation. The height of the tumour above the uppermost part of the sphincter is critical in making this assessment. Some surgeons recommend measuring tumour height from the dentate (or pectinate) line (Phillips, 1992). The dentate line marks the embryological change from anal skin (ectoderm) to rectal mucosa (endoderm) and can be felt as a difference in "slipperiness".

The UK Coordinating Committee on Cancer Research defines a rectal cancer as a tumour within 15cm of the anal verge on rigid sigmoidoscopy (United Kingdom Coordinating Committee on Cancer Research (UKCCCR), 1989) and this definition will be used for the current research project. Additional useful clinical information about the cancer include whether the tumour is fixed or not, height of the lowermost part of the tumour and position in a coronal plane (anterior, posterior, left, right or circumferential). The height of the cancer is often summarised according to which third of the rectum it is located in (upper, mid or lower).

1.3 Genetics of Colorectal Cancer

The lifetime risk of colorectal cancer in the general UK population is about 5%. Colorectal cancer develops as the result of a complex interaction between an individual's genotype and their environment. In less than 5%, the contribution of inheritance is significant and these individuals have a high risk of developing colorectal cancer. In a further 30% genotype may influence the development of colorectal cancer but in a less predictable fashion.

It is useful to subdivide the population into three broad categories (low medium and high) according to risk of developing colorectal cancer based on their family history. See Table 1.2

Most people fall into the low-risk group. Those people in the low-risk group, who are also aged between 60 and 69 years, are increasingly being screened by the NHS Bowel Cancer Screening Programme (BCSP). The BCSP uses faecal occult blood testing to select patients for colonoscopy (Hewitson, Glasziou, Irwig, Towler, & Watson, 2007).

People in the moderate-risk group have a three to six-fold relative risk and should be offered colonoscopy at 35 to 40 years and again at 55 years (Dunlop, 2002).

Table 1.2 Classification of general population's risk for colorectal cancer

Low-risk group • No personal history of bowel cancer; no confirmed family history of bowel cancer • No first-degree relative (parent, sibling or offspring) with bowel cancer • One first degree relative with bowel cancer diagnosed at age 45 or older
Moderate-risk group • One first-degree relative with bowel cancer diagnosed before the age of 45 years (without high-risk features described below) • Two first-degree relatives with bowel cancer diagnosed at any age (without the high-risk features outlined below)
High-risk group • Member of a family with known FAP or other polyposis syndrome • Member of a family with known HNPCC • Pedigree suggestive of autosomal dominantly inherited colorectal cancer

In the high-risk group there is a 1 in 2 chance of inheriting a high risk of developing bowel cancer. These patients should be referred to a clinical genetics team. Hereditary non-polyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP) are the main conditions in the high risk group and are autosomal dominant. HNPCC is the commonest and accounts for about 2% of colorectal cancers. It is characterised by an early onset of colorectal tumours with the average of diagnosis being 45 years. Tumours tend to be in the proximal colon and are also frequently multiple, both synchronous and metachronous. Typical histological features include mucinous, poorly differentiated tumours with 'signet-ring' appearance and microsatellite instability (MSI) detected with immunohistochemistry (Frayling, 1999). In 1984, HNPCC was divided into Lynch syndrome I which includes those with colorectal cancer diagnosed at a young age and Lynch syndrome II which describes those with both colorectal and extracolonic cancers (Thorson, Knezetic, & Lynch, 1999). The frequency of developing a large bowel cancer in HNPCC is 80%. Associated cancers include gastric (15%), urothelium (5%) and in women endometrium (40%) and ovary (12%). HNPCC is due to germline mutations in mismatch repair (MMR) genes. MMR genes are responsible for repairing errors in base-pair matching during replication of DNA. They are tumour suppressor genes. Defective MMR results in multiple mutations leading to tumour formation. Genetic testing is expensive. Selection of individuals for genetic testing is based on assessment of pedigree according to the Amsterdam criteria which were proposed in 1990 and modified in 1999 (Vasen, Watson, Mecklin, & Lynch, 1999).

Although families who fulfil these criteria are very likely to have HNPCC, not all affected families will have a positive pedigree.

In HNPCC, regular colonoscopic surveillance is recommended every 2 years from the age of 25 years or 5 years younger than youngest affected relative if earlier. Alternatively prophylactic colectomy may be performed. Once a colorectal tumour has been identified, subtotal colectomy with ileorectal anastomosis or restorative proctocolectomy is recommended.

FAP is less common than HNPCC but the risk of colorectal cancer is nearly 100%. It is characterised by hundreds of adenomatous polyps in the colon and rectum. Duodenal adenomatous polyps are common and there are multiple extraintestinal manifestations including the development of desmoid tumours. The mutation responsible for FAP is in the adenomatous polyposis colic (APC) gene on chromosome 5q. The mutation varies between families but can be located in approximately 80% of affected individuals. Once the diagnosis is made, prophylactic surgery is offered before a cancer develops.

1.4 Treatment for Rectal Cancer

The aim of treatment for rectal cancer is to provide cancer cure whilst preserving quality of life and bowel, bladder and sexual function as much as possible. Therapeutic options for achieving this include surgery, radiotherapy and chemotherapy. When there is no likelihood of cure due to the extent of local disease, presence of distant metastases or patient co-morbidity, aggressive treatment with these modalities is not appropriate.

An individualised management regime for each patient with a diagnosis of rectal cancer is planned at dedicated colorectal cancer multidisciplinary team meetings (MDT). Consultants with a special interest in colorectal cancer contribute to the meeting and this includes representatives from colorectal surgery, oncology (medical and clinical), pathology and radiology. Other core members of the MDT are colorectal nurse practitioners, stoma therapists, oncology nurses, MDT co-ordinator and psychiatric support.

Once the diagnosis of rectal cancer is established with a biopsy showing adenocarcinoma, a search is made for metastatic disease. This includes a thorough history and physical examination as well as a CT scan of the chest, abdomen and pelvis. The extent of local disease is assessed with a pelvic MRI scan. In particular, involvement of the CRM is assessed. Where there is CRM involvement, long course

chemoradiotherapy may be offered to the patient prior to surgical resection with the aim of reducing local recurrence. If the CRM is not involved, patients either have surgery alone or if the tumour is thought to be T3 on MRI, patients may be selected for short course radiotherapy prior to resection.

Patients with a mid or upper rectal cancer who have no metastatic disease and a resectable tumour are suitable for an anterior resection, providing they do not have major co-morbidity which precludes general anaesthesia. In cancers of the lower rectum, a careful evaluation of the height of the tumour above the sphincter complex is necessary to determine whether sphincter-preservation is possible without compromising excision of the tumour. Where the anal sphincter is involved or is too close to the tumour for complete excision, an abdominoperineal resection (APR) is performed with the creation of a permanent stoma and excision of the anal canal in continuity with the rectum. Higher local recurrence rates have been found after APR (Hewitson, et al., 2007) and it is important to perform total mesorectal excision (TME) without “waisting” of the specimen.

The situation is more complicated in the presence of metastatic disease. However, where complete resection of all metastases is possible without compromising vital structures, rectal resection is still recommended. The 5-year cancer specific survival rate after liver resection for colorectal metastases is 36% (Rees, Tekkis, Welsh, O'Rourke, & John, 2008). Patients with the best prognostic indicators after hepatic surgery have a 5-year cancer specific survival of 64%.

1.4.1 Surgery

The aim of an anterior resection is to remove part or all of the rectum with its surrounding lymphovascular structures while preserving a functioning anal sphincter (Heald, Husband, & Ryall, 1982; MacFarlane, Ryall, & Heald, 1993). Intestinal continuity is maintained with anastomosis of the sigmoid colon to the remaining rectum or superior anal canal. A circular double stapling device is most commonly used to create the anastomosis and this is introduced via the anus. The development of such circular stapling devices has enabled surgeons to perform a lower pelvic anastomosis more easily and has consequently reduced the rate of permanent stomas (Kirwan, et al., 1989). Alternatively a hand-sewn anastomosis may be created. In very low anterior resections this can be performed transanally. A temporary loop ileostomy is employed in selected cases to divert the faecal stream and allow the anastomosis to heal. This is particularly important after radiotherapy and low rectal anastomosis. There is conflicting evidence to suggest that a stoma may reduce leak and re-operation rates (Tan, Tang, Shi, & Eu, 2009; Wong & Eu, 2005). The integrity of the anastomosis is

assessed after 2 months with a gastrografin enema. Providing no leak is seen, a second operation to reverse the ileostomy can be performed. Although a much smaller operation, closure of ileostomy is not trouble-free and morbidity rates of up to 23% and mortality rates of 2.5% have been reported (Gastinger et al., 2005; Machado et al., 2002; Saha et al., 2009).

The importance of performing TME, which includes removal of the entire lymphovascular package surrounding the rectum, was popularised by Professor Heald from Basingstoke in the 1980's and is now well-recognised (Heald, et al., 1982; MacFarlane, et al., 1993). A reduction in both 5-year cancer specific survival and local recurrence rates has been demonstrated after the introduction of this method (A. Martling et al., 2005; A. L. Martling et al., 2000). Sharp dissection with diathermy is used to remove the complete mesorectum under direct vision. In contrast, blunt dissection with a finger or hand passed blindly into the depths of the pelvis, results in fragmentation of the mesorectum with tissue left behind that may contain cancer.

Complications of anterior resection include general complications of major surgery such as thrombo-embolism, cardiac arrhythmias, myocardial infarction, respiratory compromise and wound problems such as infection, dehiscence, herniation and cancer implantation. More specific complications include anastomotic leakage (6%), bowel/bladder/sexual dysfunction and local cancer recurrence. The risk of death following anterior resection varies according to patient co-morbidity and anaesthetic risk, but on average the 30-day mortality rate is 2 - 3% (Branagan & Finnis, 2005).

Although intestinal continuity is preserved by an anterior resection, up to 50% of patients may experience 'anterior resection syndrome' with faecal leakage, urgency and frequency (Karanjia, Schache, & Heald, 1992). Such symptoms are distressing to the patient and adversely affect their quality of life (Mellgren et al., 1999). Changes detected with anorectal ultrasound and physiological studies of the anal sphincter before and after anterior resection have been shown to correlate with changes in anal continence reported by the patient (Farouk, Drew, Duthie, Lee, & Monson, 1996; Farouk, Duthie, Lee, & Monson, 1998; Lee & Park, 1998). Patients with pathology up to 30cm from the anal verge also undergo anterior resection and experience similar functional problems. In one small study of 39 patients undergoing stapled low anterior resection, 18% had long-term evidence of internal anal sphincter disruption and this was associated with a poorer functional outcome (Farouk, et al., 1998). Serial manometry has demonstrated a moderate reduction in maximal anal resting pressure and loss of the rectoanal inhibitory reflex. A study of 32 patients demonstrated the RAIR before surgery in 30/32 cases but in only 8/32 cases at 3 months after surgery.

There was some recovery of the reflex with 4 patients regaining RAIR. The RAIR was not essential for full continence (Lee & Park, 1998).

Health-related quality of life assesses the personal burden of illness. This is not directly related to stage of disease but by how the disease is perceived by the patient. It is important that patients assess their own quality of life rather than health-care professionals trying to guess or assume what it might be. Over the last 20 years, measurement of quality of life has gained importance, as health-care professionals have recognised the value of using treatment to improve function and how the patient feels, in addition to simply curing the underlying condition.

Faecal incontinence is one of the most debilitating complications of surgery for rectal cancer. The most commonly used endpoint of surgical treatment for rectal cancer is survival. Much emphasis is also placed on avoiding a stoma, achieving a complete surgical excision and reducing cancer recurrence rates (Scott et al., 1995). However, the functional outcome of the neorectum is also a significant factor for patients (Karanjia, et al., 1992).

1.4.2 **Radiotherapy**

Radiotherapy is useful for reducing local recurrence in an adjuvant role (short course preoperative radiotherapy with high doses usually 25Gy in five daily fractions) and for reducing tumour bulk to enable complete resection where CRM involvement is predicted (long course preoperative chemoradiotherapy with lower doses usually 45Gy over 5 weeks with fractions of 2Gy). Radiotherapy is associated with toxicity related to treatment volume, total dose, fraction size and irradiation field. Complications include altered bowel, sexual and bladder function. Surgery remains the key to cure for patients with rectal cancer but it also results in a significant insult to anorectal function. Advances in surgical technique and radiotherapy have occurred at the same time and this has obscured their relative risks and benefits.

The benefit of radiotherapy in terms of reduced local recurrence is well documented in several large trials (Colorectal Cancer Collaborative Group, 2001; Holm, Rutqvist, Johansson, & Cedermark, 1995; Kapiteijn et al., 2001; Sebag-Montefiore, et al., 2009). Preoperative function was not included in all these studies (Holm, et al., 1995; Kapiteijn, et al., 2001) and uniformity of surgery was not always rigorously demonstrated (Holm, et al., 1995). In addition, radiotherapy fields have been improved so that the anal sphincter is no longer included in the irradiation (Cedermark, Johansson, Rutqvist, & Wilking, 1995; A. Martling, Holm, Johansson, Rutqvist, & Cedermark, 2001). Despite large numbers of randomised trials (Colorectal Cancer

Collaborative Group, 2001; Peeters et al., 2005), there is still debate over the role of short course radiotherapy in rectal cancer patients who have surgery with TME dissection. The CR07 trial randomised 1350 patients to either short course preoperative radiotherapy or salvage long course postoperative radiotherapy for patients with involved resection margin. A lower local recurrence rate was demonstrated for all pathological stages in the short course group (Sebag-Montefiore, et al., 2009), but this was small for cancers with histology staging T2 or less. Although CR07 was carried out in the era of TME, there was no formal assessment of surgical technique. The excised specimens were assessed for completeness and patients who had a superior dissection (according to specimen features) and radiotherapy had a local recurrence rate of only 1% (Quirke et al., 2009). Individual surgeons often entered only a few patients into the trial and these patients may not be representative of the whole population of rectal cancer patients. The CR07 Trial did include assessment of quality of life using EORTC QLQ-CR38 instrument but completion rates were not high (Stephens et al., 2009). At baseline 87% completed the questionnaire and this fell to 61% (proportion of those alive) at one year. The assessment of overall bowel function did not differ between the two treatment arms. However the participants who received routine short course preoperative radiotherapy reported a worse score for "unintentional release of stools" at 2 years but this was not significant (p=0.12).

Many unanswered questions remain about short course radiotherapy. In particular, whether patients can be selected for short course preoperative radiotherapy with an added reduction in local recurrence which occurs in addition to TME dissection and what the cost of this is in terms of reduced anorectal function. The MERCURY study (Brown, 2006) establishes pelvic MRI as an accurate method for assessing CRM and thereby selecting patients for long course chemoradiotherapy. The group of patients who are most likely to benefit from short course radiotherapy are those with T3 disease, however MRI is not so accurate for T staging (Bolgeri et al., 2009; Branagan, Chave, Fuller, McGee, & Finnis, 2004). There may be a role for rectal ultrasound for identifying patients for short course radiotherapy (Pilkington, Winter, et al., 2009; Starck, Bohe, Fork, Lindstrom, & Sjoberg, 1995).

The long-term effect of radiotherapy on anorectal function has not been extensively studied. Surgery probably has the biggest effect on function, but there is evidence to suggest that radiotherapy has an added detrimental effect (Bordeianou et al., 2008; Jang et al., 2010; Peeters, et al., 2005; Pollack, Holm, Cedermark, Holmstrom, & Mellgren, 2006). Pollack *et al* assessed 64 patients randomised within the Stockholm Radiotherapy Trials 1 & 2 to low anterior resection only or short course preoperative radiotherapy (Pollack, et al., 2006). Mean follow-up time was 14 years (range 9 to 23).

Faecal incontinence was defined as involuntary leakage of liquid or solid faeces with a minimum frequency of “once a week or less”. This gives rather a broad definition, but no further information is provided. Irradiated patients had significantly more faecal incontinence (see Table 1.3). In this study the researcher assessing the patients was not blinded to radiotherapy treatment group and this may have introduced bias. Only 12% (64 / 528) of the original study group were included and therefore it is important to know whether anorectal function was similar in the two treatment arms before any radiotherapy was given. Unfortunately, no preoperative assessment was carried out. In addition the radiotherapy regime was changed so that the irradiated field did not include the sphincters for the Stockholm Radiotherapy Trial 2. The relative contribution of patients from the two trials is not given and again this could cause bias. Most patients in the study had an anastomosis at 10cm and did not have TME. In contrast the Dutch TME trial, had a rigorous method for ensuring good TME surgery and the anal sphincters were not irradiated in patients undergoing anterior resection (Peeters, et al., 2005). Questionnaire assessment of these patients was carried out with a median follow-up time of 5 years. Similar results to the Stockholm study were found, with increased rates of faecal incontinence in patients who had received radiotherapy (see Table 1.3) and 39% (597 / 1530) of the original study group were included. There was a surprisingly high rate of tumour margin involvement (23%) which suggests that despite attempts to standardise the TME procedure performed, a significant number of patients were undergoing suboptimal rectal dissection. There are no studies comparing anal incontinence rates in an age-matched control group without a history of pelvic disease or treatment.

Table 1.3 Functional outcome after radiotherapy

*In both studies "faecal incontinence" is defined as: involuntary leakage of liquid or solid faeces with a minimum frequency of "once a week or less"

	N	Faecal Incontinence* (radiotherapy)	Faecal incontinence* (no radiotherapy)	P
Stockholm Radiotherapy Trial (Pollack, et al., 2006) Mean follow-up = 14 years	64	57%	26%	0.01
Dutch TME Trial (Peeters, et al., 2005) Mean follow-up = 5 years	597	62%	38%	<0.001

1.4.3 Chemotherapy

Adjuvant chemotherapy is used in rectal cancer with the aim of improving the outcome of patients with lymph node involvement (stage III disease). The majority of patients will not benefit, because they will be cured by surgery alone or will ultimately develop recurrent disease despite additional treatment. Identifying those patients who will benefit is important to reduce the numbers of patients exposed to the inconvenience and toxicity of chemotherapy without any added advantage. Despite lots of research, it remains difficult to identify these patients with certainty.

In rectal cancer with lymph node involvement, chemotherapy is based on 5-fluorouracil (5-FU) and folinic acid (FA) given as a weekly bolus (Quasar Collaborative Group, 2000). Most studies have been carried out on patients with colon cancer so the relevance to patients with rectal cancer remains unknown. However the overall improvement in absolute survival is in the region of 5 to 10%. There may be increased toxicity in elderly patients and some trials have excluded these patients.

Patients with lymph node involvement typically start their chemotherapy as soon as possible after primary surgery and usually this is within 6 to 8 weeks. Those who also have a defunctioning stoma will have a delayed stoma reversal procedure to allow completion of chemotherapy.

5-FU toxicity occurs in about 10% of patients and includes diarrhoea, vomiting, nausea, fatigue, plantar-palmar erythema, epistaxis and sore eyes. Severe toxicity necessitating emergency admission to hospital occasionally causes death.

Neoadjuvant chemotherapy has already been mentioned in the section on radiotherapy. It is useful in fit patients with unresectable rectal cancer to attempt to downsize the disease before surgery and increase the chance of complete resection and sphincter-preservation. A combination of 5-FU and FA is given with a longer course of low dose radiation.

Recent advances in chemotherapeutic options for rectal cancer include the arrival of monoclonal antibodies directed at blocking tumour growth and spread. The EXPERT-C trial has recently finished recruiting patients from UK, Spain and Sweden. This randomised trial is studying oxaliplatin, capecitabine and radiation therapy to compare how well they work with and without a monoclonal antibody called cetuximab in treating patients who are undergoing surgery for high-risk rectal cancer. Eligible patients for this study have rectal cancer that is predicted to be at high risk of local recurrence according to MRI scanning. They undergo long course chemoradiotherapy with oxaliplatin and capecitabine and are randomised to receive cetuximab, prior to TME surgery. The primary outcome is pathological complete response at TME and secondary outcomes include follow up to 5 years with quality of life questionnaires and survival rates.

1.5 Anorectal function

The ability to maintain both anal continence and normal rectal evacuation depends on many inter-related factors, of which we are surprisingly unaware until something goes wrong. The resulting loss of balance between these two opposing processes causes either anal incontinence or a rectal evacuatory disorder or sometimes both. Factors responsible for this equilibrium can be divided into intestinal, pelvic and sphincteric. Structural, functional and neurological aspects of these three factors need to be considered in normal defaecation.

1.5.1 Normal anorectal function and measurement

An intact and innervated pelvic floor, rectum and anal canal are necessary for normal bowel function (see Figures 1.4 and 1.5). Stool is transferred to the rectum by high-amplitude propagated contractions. These may be stimulated by a meal or after waking from sleep. Stool delivered to the rectum can be stored until a convenient time for defaecation. Rectal capacity is determined by rectal volume, tone, compliance and

sensation. Rectal hyposensitivity and hypersensitivity have been defined as a maximum tolerated rectal volume (MTV) of greater than 400ml and less than 90ml respectively (Chan, Scott, Williams, & Lunniss, 2005). In rectal hyposensitivity the patient has little or no urge to defaecate even when the rectum is full. Conversely, patients with hypersensitivity get the urge to evacuate when there is only a small amount of stool in the rectum. The consistency and volume of stool is variable depending on diet, hydration and gastrointestinal length. The Bristol Stool Form Scale is useful for recording stool form reproducibly (Heaton, Ghosh, & Braddon, 1991; Heaton et al., 1992; O'Donnell, Virjee, & Heaton, 1990).

During defaecation, anal relaxation occurs accompanied by raised intrarectal pressure. There is relaxation of the pelvic floor especially puborectalis, to allow expulsion of rectal contents. Proctography is used clinically to assess abnormalities of rectal emptying. Changes in anorectal angle have been described in association with evacuation but the limits of normality have not been clearly defined (Shorvon, McHugh, Diamant, Somers, & Stevenson, 1989).

Sympathetic, parasympathetic and somatic nerve fibres supply the pelvic floor, rectum and anal canal and enable effective co-ordinated rectal evacuation. Sympathetic fibres are derived from the lowermost thoracic ganglion in the paravertebral sympathetic chain. They join branches from the aortic plexus to form the superior hypogastric plexus, which then divides into right and left hypogastric nerves. The hypogastric nerves unite with preganglionic parasympathetic fibres from the ventral rami of S2, S3 and S4 to form the inferior hypogastric plexus. This is located posterior to the bladder and ultimately innervates the rectum. Somatic motor innervation of the external anal sphincter and sensory input from the lower anal canal is carried via the pudendal nerve. Right and left pudendal nerve motor innervation to the external anal sphincter has an overlapping distribution. Stimulation of either nerve will cause circumferential contraction of the external anal sphincter. Distension of the rectum causes a sensation of rectal fullness which is interpreted by the individual as the need to pass stool or flatus. The anal canal is exquisitely sensitive to light touch, pain and temperature. In addition it is able to discriminate between gas, liquid and solid stool. The anal transition zone (ATZ) (Thompson-Fawcett, Warren, & Mortensen, 1998) is a highly innervated area which is thought to be crucial for assessing rectal contents. Relaxation of the internal anal sphincter allows sampling of rectal contents by the ATZ. Anal relaxation is stimulated by distension of the rectum and this reflex is called the rectoanal inhibitory reflex (RAIR). It is mediated by intrinsic nerves and is absent in Hirschsprung’s disease. In contrast when the extrinsic (sympathetic and

parasympathetic) nerves are damaged as in cauda equina lesions or after spinal cord transaction, the reflex is preserved.

Anorectal function is difficult to measure accurately, both clinically and for research purposes. There is a wide range of normality and often a poor correlation between measurements and the impact of patient symptoms on their lives. A careful, sensitive history and examination are vital to understanding the patient's symptoms. The use of validated and widely used symptom score and quality of life questionnaires is important for defining and accurately documenting the patient's symptoms. In addition to these subjective measures, objective measures such as anorectal physiology, endoanal ultrasound and proctography can be used.

One of the difficulties in trying to study anal incontinence is that there is no precise, useful definition of it. There is a plethora of studies focusing on this condition and its associated problems but the case mix tends to be heterogeneous and the assessment of incontinence haphazard without the use of validated questionnaire instruments. Anal incontinence usually refers to the uncontrolled leakage of solid, liquid or gas from the anal canal, whereas faecal incontinence refers only to the leakage of solid or liquid faecal material. Flatus incontinence can be difficult to assess but is important for many individuals. The term "anal incontinence" is misleading because it suggests that the anal canal itself is the main site for maintenance of continence. Although integrity of this structure is important for normal continence, the rectal reservoir function, stool consistency, etc. are also of importance and may be even more important than the anal canal (Chan, Lunniss, Wang, Williams, & Scott, 2005). The anal canal is the last resort for preventing or allowing the passage of intestinal contents and as such significant emphasis has been placed on assessing its structure and function. However there is an increasing awareness that this is only one component in a very complex multi-factorial process (Bharucha et al., 2005). Anal incontinence is defined by the International Continence Society as "the involuntary loss of flatus or faeces which becomes a social or hygienic problem".

Figure 1.4 Coronal Section of normal anal canal anatomy (Sinnatamby, 1999)

(Reproduced with permission from Harcourt Publishers Ltd)

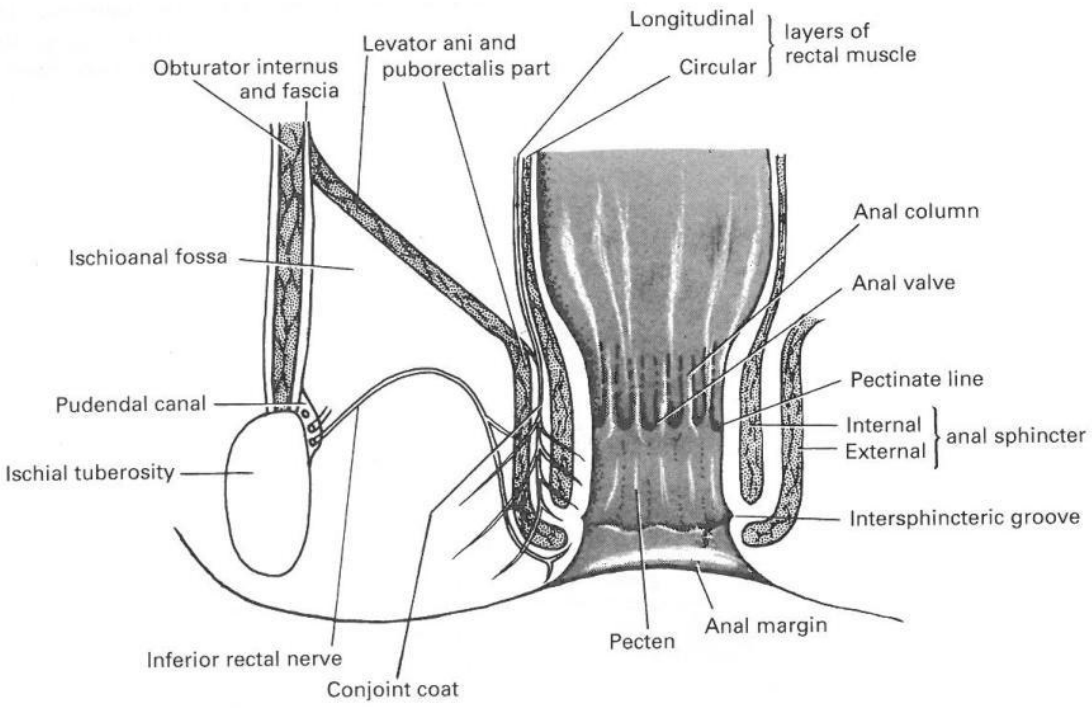
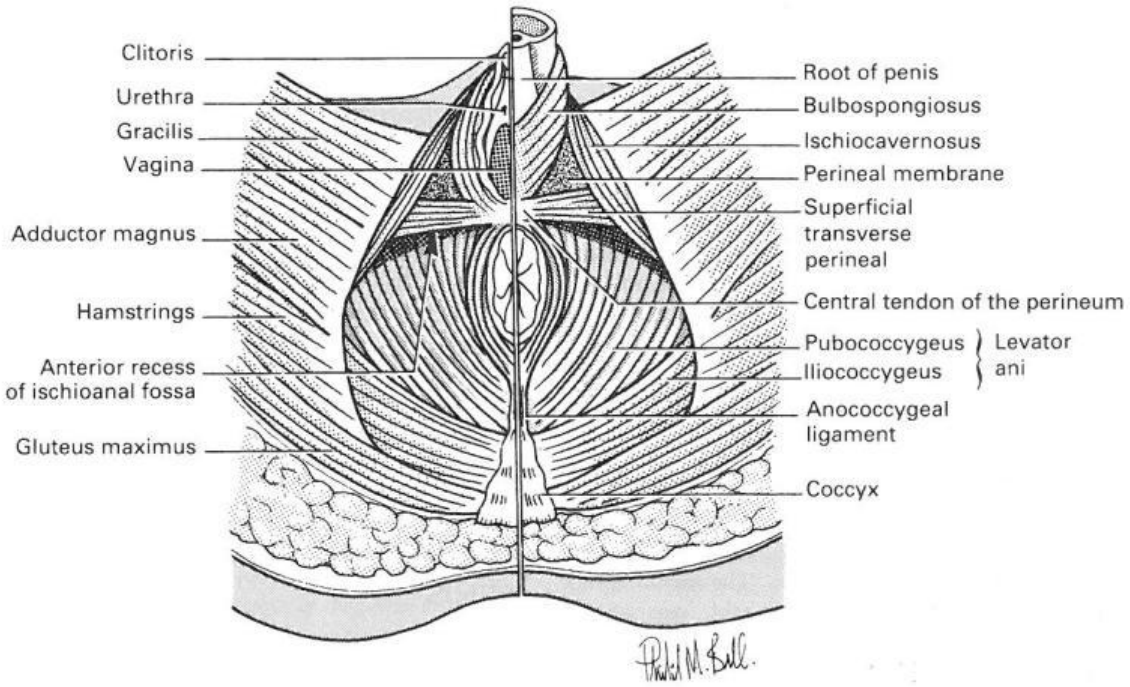


Figure 1.5 Muscles of the perineal region with female anatomy on the left and male anatomy on the right of the picture (Sinnatamby, 1999)

(Reproduced with permission from Harcourt Publishers Ltd)



1.5.2 Questionnaires

Many questionnaires have been described for assessing anorectal function. There is little uniformity in their use as each clinician or researcher tends to have their own favourites. The questionnaires can be broadly split into symptom severity indices or quality of life instruments. Frequently used symptom severity scoring systems are summarised in Table 1.5.1. Generic quality of life instruments are summarised in Table 1.5.2 and condition-specific questionnaires are summarised in Table 1.5.3.

The Cleveland Clinic incontinence score (CCI) is an anal incontinence severity score. It is easy to use and gives the patient a score of 0 to 20, where zero equates to perfect continence and twenty equates to complete anal incontinence. It was first proposed by Wexner *et a*l (Jorge & Wexner, 1993) and is widely used as a tool to measure the severity of anal incontinence (Deutekom et al., 2005; Portier, Bonhomme, Platonoff, & Lazorthes, 2005). It is already in use in the anorectal physiology laboratory in Southampton General Hospital. Rothbarth investigated the impact of CCI on patient quality of life after anterior sphincter repair (Rothbarth et al., 2001). He studied 35

patients and found that when the CCI score was between 9 and 20, there was a significant impact on quality of life. When compared with reference ranges, the quality of life scores differed significantly to those of normal individuals and equalled those of individuals confined to the home. If CCI score is 9 or greater, the individual is considered to have severe anal incontinence which is likely to significantly impact on their quality of life.

There are other formal definitions of incontinence. For example, the Rome Multinational Working Team have revised two previous definitions of functional faecal incontinence to produce the Rome III definition (Bharucha, Wald, Enck, & Rao, 2006) which is: the uncontrolled passage of faecal material recurring for >= 3 months in an individual with a developmental age of at least 4 years that is associated with:

- abnormal functioning of normally innervated and structurally intact muscles, and/or
- no or minor abnormalities of sphincter structure and/or innervations insufficient to explain faecal incontinence, and/or
- normal or disordered bowel habits (i.e., faecal retention or diarrhoea), and/or
- psychological causes

This definition is slightly broader than previous ones and does include patients with minor structural abnormalities. However Rome III still excludes patients who have an organic cause (such as diabetic neuropathy or dementia) for faecal incontinence and those who have flatus incontinence. Using the Rome definition a low prevalence rate of 6.9% (95% CI: 5.4 to 8.4) (W. G. Thompson, Irvine, Pare, Ferrazzi, & Rance, 2002) anal incontinence is found. Estimated prevalence of faecal incontinence is between 11 and 15% in other studies where sources of bias have been minimised although only one of these studies used a validated questionnaire (Johanson & Lafferty, 1996; Kalantar, Howell, & Talley, 2002; Lam, Kennedy, Chen, Lubowski, & Talley, 1999; Macmillan, Merrie, Marshall, & Parry, 2004; Marr et al., 2005). No studies have been published on the prevalence of anal incontinence as assessed with the CCI Score in a UK community-dwelling population such as the inhabitants of Southampton City.

Many quality of life questionnaires have been published, but there is little consensus about the optimal instrument to use. Generic assessment tools, such as SF-36, are often not specific enough to detect changes in quality of life in a specific patient population. Condition specific quality of life instruments such as the Faecal Incontinence Quality of Life Scale (FIQL) (Rockwood et al., 2000), EORTC QLQ-C30 and CR29 module (Aaronson et al., 1993; Whistance et al., 2009) and Manchester Health

Questionnaire (Bug, Kiff, & Hosker, 2001) are more likely to be sensitive to the effects of a given health problem, such as faecal incontinence. These examples have been validated and tested for reliability.

The European Organisation for Research and Treatment of Cancer (EORTC) was founded in 1962 with the aim of conducting, developing, coordinating and stimulating research in Europe. It is an international non-profit organisation. Through the EORTC multidisciplinary groups of clinicians and basic scientists are able to execute large, prospective, randomised, multicentre, cancer clinical trials. The EORTC created a Quality of Life Group which focuses on developing, validating and updating quality of life instruments for evaluating patients participating in cancer clinical trials. An integrated modular approach was developed with rigorous psychometric testing. The output from the Quality of Life Group includes a core questionnaire (EORTC QLQ-C30) (Aaronson, et al., 1993) and multiple supplementary questionnaires. The core questionnaire has 30-items and is designed to be cancer specific, multidimensional in structure, appropriate for self-administration and applicable across a wide range of cultural settings. It is a third generation questionnaire and is currently on its third version (Bjordal et al., 2000). The same response categories are used throughout the questionnaire except for questions 29 and 30 which assess global health status/quality of life. The responses are: “not at all”, “a little”, “quite a bit” and “very much”. The questions are either grouped together to provide multi-item scales or interpreted individually as single-item measures. The average of the items in a scale is standardised by linear transformation so that the calculated scores for each scale range from 0 to 100. A high score for a functional scale represents a high or healthy level of functioning whereas a high score for a symptom scale /single item represents a high level of symptoms or problems. There are five functional scales, three symptom scales, a global health status/QOL scale and six single items.

Supplementary questionnaire modules can be used with the core questionnaire to allow more detailed assessment and evaluation of quality of life in specific patient populations. The colorectal cancer module (QLQ-CR38) (Sprangers, te Velde, & Aaronson, 1999) has been recently updated and validated internationally (QLQ-CR29) (Whistance, et al., 2009). The new questionnaire is shortened and allows direct comparison of patients with and without stomas (Gujral et al., 2007). It consists of multi-item scales and single items which are grouped into five functional scales and eighteen symptom scales. The responses and scoring systems are the same as for the QLQ C30 questionnaire.

The relative performance of health-related QOL instruments after colorectal surgery has been compared. A study from York compared EORTC QLQ-C30 & CR38, FACT-C, SF12 and EQ5D (Wilson, Alexander, & Kind, 2006). An impressive questionnaire return rate of 95.7% was achieved to give a study group of 201. Condition-specific instruments and those in which the patient subjectively rated their overall health-related quality of life were best suited to assessing these patients. Missing data was a problem for the FACT-C summary scale which had 14 times more missing data than the EORTC QLQ global health status/QOL score.

Table 1.5.1 Subjective methods for evaluating bowel function: Symptom Severity Scores

Modality	Scoring Summary
Pescatori (Pescatori, Anastasio, Bottini, & Mentasti, 1992)	Described by Pescatori (1992), modification of Miller's score (Miller, Bartolo, Locke-Edmunds, & Mortensen, 1988) Type x frequency matrix 3 types of leakage: flatus/mucus, liquid stool and solid stool 3 frequencies: Occasional, weekly and daily Total score:
Bristol Stool Form Scale (Heaton, et al., 1991; Heaton, et al., 1992; O'Donnell, et al., 1990)	Heaton (1992) 7 stool forms described with words and pictures Valid and reproducible
Cleveland Clinic Incontinence Severity Score (CCI) (Jorge & Wexner, 1993)	Described by Wexner (1993) Type x frequency matrix 5 types: solid, liquid, gas, need to wear pad, lifestyle alteration 5 frequencies: scored 0 to 4 Frequencies: never (0), rarely (less than once a month, sometimes (monthly), often (weekly), always (daily) Total score: 0 to 20 where 0 equates to perfect anal continence and 20 is daily episodes of solid, liquid and gas incontinence requiring a pad and affecting the patients' lifestyle Widely used but not rigorously validated. Practical. Easy to use and interpret
Vaizey (Vaizey, Carapeti, Cahill, & Kamm, 1999)	Described by Vaizey (1999) Type x frequency matrix plus 3 additional items: 4 types: gas, fluid, solid, alteration in lifestyle 5 frequencies: scored 0 to 4 3 additional items:, need to wear a pad/plug, use of constipating medication, lack of ability to defer defaecation for 15mins Total score: 0 to 24(complete incontinence) Well validated but not widely used

Table 1.5.1 Subjective methods for evaluating bowel function: Symptom Severity Scores (Continued)

Modality	Scoring Summary
Fecal Incontinence Severity Index (FISI) (Rockwood, 2004)	Described by Rockwood (2004) Type x frequency matrix (see appendix)with patient and surgeon severity ratings 4 types: gas, mucus, liquid stool, solid stool 5 frequencies: scored 4 to 0 Frequencies: 1 to 3 times a month, once a week, 2 or more times a week, once a day, 2 or more times a day Total score: 0 to 61(patient ratings) or 57(surgeon ratings) Well validated but complicated to use
MSKCC (Temple et al., 2005)	Described by Temple (2005) Instrument to evaluate bowel function after sphincter-preserving surgery Frequency matrix with 18 questions 3 subscales: frequency, dietary, urgency/soilage 4 individual items Frequencies: Always, most of the time, sometimes, rarely, never Validated in anterior resection patients in America

Table 1.5.2 Subjective methods for evaluating bowel function: Generic quality of life assessment

Modality	Scoring Summary
SF-36 (Ware & Sherbourne, 1992)	36 questions 8 health domains: physical activities, role limitations due to physical health, emotional state, bodily pain, perception of general health state, vitality, social activity and mental health Well validated and very widely used
EQ-5D (Dolan, 1997; The EuroQol Group, 1990)	5 questions 5 domains: mobility, self-care, usual activities, pain/discomfort, anxiety/depression 3 severity levels: no problems, some or moderate problems, extreme problems Transform responses to 5 domains into summary utility value with range: -0.594 (worst imaginable health state) to 1 (optimal health state) Visual analogue scale: Health state today Well validated but simplistic Used for health economics

Table 1.5.3 Subjective methods for evaluating bowel function: Condition-specific quality of life assessment

Modality	Scoring Summary
EORTC QLQ-C30 (version 3) (Aaronson, et al., 1993; Bjordal, et al., 2000)	Published in 1993 and updated in 2000 Assesses quality of life of cancer patients, especially those undergoing chemotherapy trials Validated and widely used in clinical trials Core questionnaire of 30 questions • Multi-item scales and single item measures • 5 functional scales, 3 symptom scales, a global health status/QoL scale and 6 single items • Scores range from 0 to 100 after linear transformation • High score on functional scale: high/healthy level of functioning • High score on global health status/QoL: high QoL • High score on symptom scale: high level of symptoms/problems
EORTC Colorectal Cancer Module QLQ-CR29 (Whistance, et al., 2009)	Updated 2009 Supplementary questionnaire module 29 questions Accompanies core questionnaire QLQ -C30 Targeted for patients with colorectal cancer • 5 functional scales and 18 symptom scales • Same scoring process as QLQ-C30

Table 1.5.3 Subjective methods for evaluating bowel function: Condition-specific quality of life assessment (Continued)

Modality	Scoring Summary
Fecal incontinence quality of life scale (FIQL) (Rockwood, et al., 2000)	Described by Rockwood 29 items that evaluate psychometric properties of a health-related quality of life scale with issues specifically related to faecal incontinence 4 subscales: lifestyle, coping/behaviour, depression/self perception, embarrassment Validated in men and women Widely used Adopted by the American Society of Colorectal Surgeons
Functional Assessment of Cancer Therapy – Colorectal (FACT-C) (Yoo, Kim, Eremenco, & Han, 2005)	27 items from the general core questions Disease specific subscale containing 9 colorectal cancer-specific subscales Tested in cancer survivors and found to be reliable, valid and responsive
Manchester Health Questionnaire (Bug, et al., 2001)	Condition specific health-related QOL questionnaire 32 questions 8 domains: general health perceptions, incontinence impact, role limitations, physical limitations, social limitations, personal relationships, emotions, sleep/energy, severity measures Validated in women only

1.5.3 **Anorectal physiology**

Anorectal manometry, rectal distension volumes and anal mucosa sensitivity form the basis of anorectal physiology. Several different catheter systems are in use and measurements differ according to the type of catheter. Units tend to use their own reference ranges according to their equipment type and experience. Catheters are available in water-perfused or solid state forms. The whole length of the anal canal is assessed by withdrawing the catheter with either a continuous automated withdrawal device allowing vector manometry, or a hand-held system with measured withdrawal at 1cm intervals (station pull through method) (Freys et al., 1998).

Although anorectal manometry is widely used to assess anal sphincter function in pelvic floor patients, there have not been many studies on normal individuals. Normal reference ranges and reproducibility are not well established. Freys *et al* (Freys, et al., 1998) studied ten male volunteers and performed standardised anorectal physiology three times on each individual on two days separated by four weeks. They found good reproducibility in resting pressure and sphincter length but other parameters showed large inter-individual variability. No comment is made about who performed the manometry. It is important to know whether all tests were performed by the same individual and how experienced/trained that individual was. Differences in the commands used during manometry assessment and the individual technique could have a profound effect on the results. The authors suggest that the reason for the large variability was that MSP is a voluntary act and therefore dependent on participant cooperation which may be variable. Although the study group was selected for uniformity and a strictly standardised method was used, analysis demonstrated a high degree of intra individual variability leading the authors to conclude that although sphincter length and mean resting pressure were reproducible, the other parameters including MSP were not and should therefore be interpreted with caution. The study group of young men is not typical for individuals who are undergoing anorectal physiology and this may in part explain why there was a low level of reproducibility. Squeeze pressures may be too effort-dependent to be truly reliable. Anorectal physiology is most frequently tested in women with anal incontinence and who may be elderly and may also have obstetric anal sphincter injuries. A more recent study included anorectal manometry on 146 healthy individuals (72 women) with a median age of 64 years in both men and women. Although there was no gender difference in mean resting pressure of the anal canal, the maximum squeeze pressure was much lower in women (151mmHg) than in men (201mmHg), ($p=0.007$). Important age associated differences were found with both mean resting and maximum squeeze pressures decreasing with age (Gundling et al., 2010). An elegant study conducted by Williams *et al* (Williams et al., 2000) recorded anal canal pressures and 3-dimensional endoanal ultrasound on 10 male and 10 female asymptomatic subjects. No difference was found in maximal resting pressure between men and women but men had significantly higher maximal incremental squeeze pressures than women. The study also demonstrated that the maximal anal canal squeeze pressure is found where puborectalis overlaps the external anal sphincter. A study on 351 women who were evaluated for faecal incontinence found that a worse incontinence score (FISI) (Rockwood, 2004) was used) correlated with lower resting pressures (Bordeianou, et al., 2008).

1.5.4 Proctography

After anterior resection a considerable number of patients have disordered defaecation as a result of their surgery. Imaging of these patients during simulated rectal evacuation may distinguish between structural and functional causes. However, all measures whether using radiological techniques or an expulsion test, only simulate rectal evacuation. The natural process of defaecation is more complicated and involves coordination of colonic propulsion waves with abdominal and diaphragmatic effort in addition to the final event of rectal emptying. A Japanese study carried out on 62 patients who had undergone rectal resection, found that barium proctography was useful in evaluating defaecatory disorders (Morihiro, Koda, Seike, Miyauchi, & Miyazaki, 2008). They studied 62 patients who had undergone anterior resection and found that participants who were able to evacuate over 55% of the rectal contrast had a significantly lower CCI score, less soiling and less urgency.

Evacuation proctography is a clinical test for assessing the anatomical changes that occur during defaecation. For a Barium proctogram, the rectum is filled with barium paste. The vagina and small bowel are opacified with contrast medium. The patient is asked to evacuate the rectum during fluoroscopic imaging. Images are taken in the sagittal plane during rest, straining and defaecation. Until recently this was the gold standard test (Karasick, Karasick, & Karasick, 1993; Mellgren et al., 1994), but advances in Magnetic Resonance Imaging have enabled the acquisition of dynamic MR images during evacuation (Rentsch et al., 2001). Ultrasound gel is placed in the rectum and the patient is asked to evacuate during sequential MR imaging.

There is ongoing debate about which is the most appropriate test to use (Pilkington, James, Monga, Dewbury, & Nugent, 2009). Significant differences exist between these two tests:

1. Barium proctography is associated with radiation exposure to the pelvic organs. The mean effective dose equivalent has been estimated at between 3.6 and 6.5mSv, which is approximately 360 chest radiographs (Goei & Kemerink, 1990). No radiation is involved with MR proctography. Although some hospitals are using dynamic MR proctography as a substitute for barium proctography because no radiation is involved (Pilkington, James, et al., 2009), it is still not clear whether the results of these two investigations are comparable.

2. During Barium proctography the individual is seated on a radiolucent commode in a physiological position for defaecation. However, during MR

proctography the subject is supine. Studies that report poor performance of supine MR proctography when compared to barium proctography, frequently fail to include MRI scans acquired during defaecation, whereas this is always part of the barium study protocol (Bertschinger et al., 2002; Vanbeckevoort et al., 1999). When dynamic MRI scans do involve simulated defaecation, rectal intussusception can be detected (Rentsch, et al., 2001). In addition, although MRI scanning in the supine position may not simulate exactly the same mechanisms taking place in the squatting or seated position usually adopted for defaecation, it may provide useful information about the structures that will be encountered when the patient is supine on the operating table. This is likely to be particularly important when planning stapled transanal rectal resection (STARR) operations for rectal intussusception where there is a risk of forming an enterorectal fistula if the stapling device is fired through an adjacent enterocele.

The development of open configuration MRI scanners has allowed MRI scanning to be carried out with the patient in an upright position during defaecation (Mortele & Fairhurst, 2007). A suspension of gadolinium is placed in the rectum and T-1 weighted images are taken during defaecation. One study has compared these two MRI techniques using patients who presented with stress urinary incontinence and/or symptoms of pelvic prolapse (Bertschinger, et al., 2002). Although they report that all rectal intussusception was missed on supine MRI, only 3 patients in the study group of 38 patients had rectal intussusception and there was no information as to whether these patients were symptomatic or not. In addition, although MRI during straining was carried out in the closed coil scanner, images were not acquired during defaecation due to restrictions imposed by the institution guidelines.

3. The Barium paste is thicker than the ultrasound gel used during MR proctography and this may affect the ease of evacuation.

There is considerable variation in the appearances on proctography in “normal” subjects. Trying to define the boundaries of “normal” appearances is difficult and symptoms often do not correlate closely with proctogram findings. In 1989, Shorvon *et al* (Shorvon, et al., 1989) studied 47 healthy student volunteers who denied faecal incontinence or difficulty with defaecation and had no history of anorectal surgery. There were 23 women in the study and they were all nulliparous. In this asymptomatic group of men and women, Shorvon found a wide range in values for anorectal angle as

well as a high frequency of structural abnormalities such as rectal intussusception. In most studies participants are recruited from pelvic floor patients undergoing proctography as part of their routine investigation and therefore they are likely to have symptoms.

For the purposes of quantitative research it is possible to measure the change in position of the pelvic organs during defaecation with respect to their neighbouring bony and soft tissue structures even though the normal ranges for these values are not known and are not likely to be useful clinically. The pubococcygeal line (PCL) connects the inferior aspect of the symphysis pubis with the last coccygeal joint (Mortele & Fairhurst, 2007) and is an important landmark for assessing pelvic floor movement. At rest in a normal patient the base of the bladder, the upper third of the vagina and the peritoneal cavity (including small bowel and sigmoid colon) are usually situated superior to the PCL (Healy et al., 1997). The anorectal junction (ARJ) is the point at which a line along the posterior border of the rectum transects a line along the central axis of the anal canal. This point is usually situated within 3cm of the PCL and perineal descent can be measured by movement of the ARJ with reference to the PCL.

Several methods for measuring rectoceles on imaging have been described. A reference line may be drawn along the anterior wall of the anal canal and extended (Healy, et al., 1997), or the maximum distension of the rectocele beyond the predicted margin of the anterior rectal wall is measured (Mellgren et al., 1995; Mellgren, et al., 1994). Mellgren *et al* classified rectocele size into three groups according to the maximum distension. In addition to grading the size of the rectocele, the presence of post-defaecatory trapping can be demonstrated. Invagination of the rectal wall, known as rectal intussusception, frequently co-exists with a rectocele. Rectal intussusception may be anterior, posterior or circumferential. The intussusception may be contained within the rectal ampulla or it may extend into the anal canal or beyond, where it is known as a rectal prolapse. The Oxford Radiological Grading of Rectal Intussusception is a useful and reproducible system for describing rectal intussusception (Collinson, Cunningham, D'Costa, & Lindsey, 2009) (Table 1.5.4).

It is important to remember that during proctography the process of defaecation is merely simulated and may not be a true reflection of what happens to the patient in the privacy of their bathroom seated on their own toilet. Patient embarrassment may inhibit what is normally a very private process and the findings on proctography must be interpreted with caution.

Table 1.5.4 Oxford rectal intussusception grading

Grade of intussusception	Radiological characteristics of intussusceptum
I (high rectal)	Descends no lower than proximal limit of the rectocele
II (low rectal)	Descends into the level of the rectocele, but not onto sphincter/anal canal
III (high anal)	Descends onto sphincter/anal canal
IV (low anal)	Descends into sphincter/anal canal
V (overt rectal prolapse)	Protrudes from anus

1.5.5 Anorectal function after anterior resection

Altered bowel function, faecal leakage and incomplete evacuation are recognised problems after anterior resection and cause a major problem for many survivors of rectal cancer. Rectal cancer is a common disease in the UK and recent advances have led to improved overall survival, making the functional outcome even more important for patients.

Poor functional results have been reported in 50 to 60% of patients undergoing resectional surgery (Emmertsen & Laurberg, 2008). The main focus of rectal cancer research has been directed at improving survival, reducing local recurrence rates (Sebag-Montefiore, et al., 2009) and maximising sphincter preserving surgery (Marr, et al., 2005; Morris et al., 2008). However the functional result following anterior resection can have a significant impact on the patients' physical, mental and social capabilities in both the short and long-term. Identifying patients at high risk of a poor functional outcome would allow appropriate preoperative counselling and early management.

The term "anterior resection syndrome" (Karanjia, et al., 1992) has been used to describe patients who experience persistent problems with anal incontinence, urgency and frequency of defaecation (fragmented defaecation) after anterior resection. The aetiology of these symptoms is not clear but is likely to be multifactorial. Causes may include height and configuration of the rectal anastomosis, post surgical scarring, reduced rectal capacity and compliance, denervation, altered stool consistency and in some cases anal sphincter disruption.

Health-related quality of life after anterior resection is not routinely measured despite recent advances in treatment and quality of life assessment. Reasons for this may include the confusing number of QOL assessment instruments available and difficulties with interpreting the data collected by these tools. Wilson *et al* carried out health-related QOL assessment at 6 weeks after surgery in the follow up of 201 consecutive patients after potentially curative surgery for colorectal cancer (Wilson, et al., 2006). Poorer health-related QOL was associated with the presence of a stoma and symptoms of constipation and diarrhoea. Younger participants (<65 years old) were also found to have a poorer health-related QOL. It is important to detect poor health-related quality of life after anterior resection so that the contributing factors can be recognised and appropriate treatment initiated.

A study from Stockholm assessed anal manometry using vector volumes in 71 patients who had been randomised to receive a low anterior resection with either a colonic J-

pouch anastomosis or a side to end anastomosis. They found that postoperative anal sphincter pressure volumes were halved after anterior resection compared with the preoperative values (Machado, Nygren, Goldman, & Ljungqvist, 2005). This did not recover during 2 years follow up and was not related to anastomotic configuration.

Functional impairment and recovery after anterior resection has been assessed with serial anorectal physiology to try to identify contributing factors. A Korean study evaluated 32 patients with preoperative and 1, 3, 6 and 12month postoperative anorectal physiology (Lee & Park, 1998). Mean resting pressure and rectal capacity were reduced. Residual rectal length after surgery was calculated by subtracting the length of the high-pressure zone measured on manometry at 3 months, from the height of the anastomosis measured with rigid sigmoidoscopy. Stool frequency, urgency and incontinence score were worse if the residual rectum length was less than 4cm.

Although proctography is widely used in pelvic floor patients to assess structure and function (Savoye-Collet, Koning, & Dacher, 2008), it has not been used extensively after anterior resection. There is some evidence to suggest that it is useful in this context (Morihiro, et al., 2008).

Large prospective studies that combine serial evaluation of condition-specific symptom severity and health-related quality of life questionnaires with anorectal manometry, ultrasound and proctography before and after anterior resection are lacking from the published literature but would be important for defining “anterior resection syndrome” so that it can be targeted for appropriate management.

1.6 Biofeedback: The evidence

Historically biofeedback was born from psychological learning theories such as "operant conditioning" or "task reinforcement" in the 1950's and 60's. Initially this behavioural approach was applied to all areas of medicine but cardiovascular medicine and subsequently gastroenterology received most attention. Despite research efforts, no evidence was found to substantiate this approach in most aspects of medicine. Over the last 30 years, a behavioural approach has been found to be useful in disorders of defaecation (Enck, van der Voort, & Klosterhalfen, 2009).

Biofeedback refers to the process of amplifying a bodily function so that the individual is more aware and consequently may be able to improve function with training (Enck, et al., 2009). Biofeedback is a specific form of behavioural modification and is thought to involve cortical reconditioning. In the treatment of faecal incontinence, manometry or electromyographic (EMG) recording from the anal canal is used to provide a visual display of anal sphincter muscle activity. With the help of a specialist nurse, the individual is able to recognise from the visual display when they are achieving an adequate anal squeeze. Most biofeedback programmes include a series of exercises similar to pelvic floor exercises to improve muscle strength and co-ordination (Norton & Chelvanayagam, 2001). Many similar biofeedback techniques are in use but there is little uniformity between treatment centres. The method in use at Southampton General Hospital involves 30-minute sessions. During the biofeedback sessions the patient is advised about methods of efficient defaecation. A visual display based on anal pressures is used to give feedback to the patient as they attempt to squeeze the anal sphincter. Using this to demonstrate when the patient is achieving an adequate squeeze pressure, the patient is taught a series of exercises to practise to improve sphincter function.

In addition to the specific techniques taught in the biofeedback sessions, the nurse-patient relationship is also thought to be beneficial. Faecal incontinence is an embarrassing condition which is often difficult to verbalise (if you don't ask, they won't tell) (Whitehead, 2005; Whitehead et al., 2009). Providing the patient with a forum for discussing this problem may be therapeutic in itself and the importance of such "non-specific factors" in psychotherapy treatments is well recognised (Chelvanayagam & Stern, 2007; Koch, Selim, & Kralik, 2002). Individuals with faecal incontinence often feel alone, stigmatised and hopeless about any improvement in their condition. Providing them with the vocabulary to explain and explore what they are experiencing within a safe and confidential environment is beneficial. Trying to determine how much the effect of biofeedback is due to the physical side of the treatment and how much is

due to the nurse-patient relationship is difficult to unravel. Indeed attempts to separate these two components are artificial as they are interdependent upon each other. A recent study by Norton *et al* (Norton, Chelvanayagam, Wilson-Barnett, Redfern, & Kamm, 2003), attempted to evaluate the isolated roles of advice, advice and verbal instructions, hospital based biofeedback and both hospital and home based biofeedback. Although over 50% of patients reported clinical improvement, there was no difference between the four groups. In this particular study no benefit was seen with biofeedback. However this study was carried out by nurses who run the biofeedback service. It is not possible to predict whether the same improvement could be achieved in a unit that does not provide biofeedback.

Telephone follow-up after initial sessions with biofeedback have been demonstrated to be effective instead of repeated face-to-face sessions (Byrne et al., 2005). Compliance with BFB programmes is one of the main determinants of outcome and patients who are most likely to complete biofeedback are usually more severely affected, female and older than those who discontinue treatment (Byrne, Solomon, Young, Rex, & Merlino, 2007). Other factors indicative of likely success are a high level of motivation, intact cognition and absence of depression.

Biofeedback has been shown to be beneficial in the treatment of faecal incontinence with an overall efficacy of up to 80% (Norton & Kamm, 1999). However, there is a lack of high quality randomised controlled trials that address the role of biofeedback in treating faecal incontinence (Norton, Hosker, & Brazzelli, 2000). Studies that have been carried out use a wide variety of outcome measures making direct comparisons difficult. There are few long term follow-up studies and a wide variety of different methods, equipment and training programmes are in use.

The routine use of biofeedback to prevent faecal incontinence after surgery for rectal cancer has not been studied in detail. Only one study has looked at the role of biofeedback in patients who are symptomatic after rectal surgery with excessive stool frequency or incontinence following anterior resection or total colectomy (Ho, Chiang, Tan, & Low, 1996). The number of patients in this study was small but biofeedback was found to be safe and effective. Ten out of 13 patients treated had at least 90% reduction in their incontinence episodes.

Poor bowel function after anterior resection is thought to relate to many factors including reduced reservoir capacity of the rectum because the proximal colon is anastomosed to the rectal stump. Poor rectal compliance results in less efficient storage of stools. Loss of colonic length may cause reduced fluid absorption capacity

so that the stools are looser. These factors would make anal continence more difficult to maintain. In addition there may be loss of rectal sensation and poor coordination with the anal sphincter. There is some evidence to suggest that the stapling process injures the anal sphincter in some cases (Farouk, et al., 1998). The surgery itself may distort the supporting structures of the anal canal and reduce innervation. Biofeedback may improve the functional outcome after anterior resection by improving anal sphincter coordination, rectal and anal canal sensation, strengthening the muscles of the pelvic floor and anal sphincter and improving rectal capacity. The mechanism by which biofeedback works, is not well described. Previous studies have not found a correlation between incontinence symptoms and anorectal physiology measurements done before and after biofeedback (Loening, 1990).

Despite the lack of high quality randomised trials (Pares, Norton, & Chelvanayagam, 2008), biofeedback programs have emerged as a popular and successful treatment for faecal incontinence with reported success rates of between 50 and 92% (Norton, et al., 2003; Solomon, Pager, Rex, Roberts, & Manning, 2003) and a clinical improvement lasting at least 2 years. The method is safe, painless, well tolerated and does not preclude further treatment if it is unsuccessful. It is a promising technique for avoiding the debilitating complication of anterior resection syndrome.

2 Hypotheses

- Rectal function and quality of life are not affected by anterior resection
- Routine biofeedback training started before surgery does not improve anal continence after anterior resection
- MR proctography is no better than Barium proctography for assessing pelvic floor problems

3 Aims

- To determine anal continence before anterior resection
- To assess anal continence after anterior resection
- To determine whether biofeedback improves outcome after anterior resection
- Define anterior resection syndrome
- Determine predictive factors for poor outcome after anterior resection
- Validate methods for assessing functional outcome: Barium proctography versus dynamic MR proctography

The overall aim of this thesis is to assess the impact of major rectal resection on rectal function and quality of life and to determine whether routine biofeedback improves the outcome of surgery.

4 Methods

4.1 Randomised controlled trial of biofeedback for anal incontinence after anterior resection

4.1.1 Trial Design

This is a single blind prospective randomised controlled trial to assess the role of biofeedback in improving anal continence after anterior resection. Participants were randomised to either no biofeedback (control group) or biofeedback (BFB group) in a ratio of 1:1. Randomisation was stratified for exposure to radiotherapy. See Appendix VII for Protocol.

This study was reviewed by the Southampton and South West Hampshire Ethics Committee. No objections were raised on ethical grounds. All participants gave informed written consent. Detailed information about the trial was given in both written and oral form. See Appendix I for patient information sheet. Ethical approval was granted to recruit participants from Southampton General Hospital, Royal Hampshire County Hospital and Salisbury District Hospital.

Initial recruitment was from Southampton General Hospital. Recruitment was extended from 12 to 21 months to allow for adequate accrual. Potential participants at Salisbury District Hospital were not willing to travel to Southampton General Hospital for the research tests and recruitment from this site was abandoned after inviting 12 eligible patients who all declined. Patients at Winchester Hospital were more willing to travel the shorter distance to Southampton and 3 were successfully recruited. Patients who lived on Jersey but were having their surgery in Southampton were also invited to participate and 11 accepted.

All adverse events that occurred during the investigation (i.e. after the participant had given informed consent) were documented in the Case Report Form. Postoperative complications such as chest infection, wound infection, cardiorespiratory problems, thromboembolism and anastomotic leak resulting in further surgery or death were recorded in the case report form. SUHT Research related SAE/SUSAR initial reporting form was completed for all deaths and for adverse events. The researcher made an assessment of severity and causality. The participants were encouraged to phone directly the principal investigator (SP) or their GP if they experienced a problem.
The participant could choose to withdraw from the study at any time and for any reason. Completion of the study was at one-year post surgery. A participant lost to follow up was defined as a participant who was recruited to the study but did not turn up for follow-up visits. They were sent a letter with another appointment and were

contacted by telephone to ascertain the reason for their non-attendance (e.g. patient withdrawal of consent).

4.1.2 Participants

Patients undergoing anterior resection for pathology within 30cm of the anal verge who fulfilled the inclusion and exclusion criteria shown in Table 4.1.1 were eligible for recruitment to this study.

Table 4.1.1 Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
Booked for anterior resection for pathology within 30cm of the anal verge	Patients considered by their surgeon as being unlikely to comply with the protocol
Aged 18 years or older	Mentally incompetent
Patient knows diagnosis and treatment plan	Pregnant and nursing mothers
Written informed consent	

Southampton General Hospital provides services for the 1.3 million people living in Southampton and South Hampshire. All patients with colorectal cancer in the Southampton and South Hampshire region are discussed at the weekly Southampton MDT meeting. Patients with potentially curable disease are offered a combination of surgery, chemotherapy and/or radiotherapy. In general the policy in Southampton is to give preoperative short course radiotherapy for rectal cancers and preoperative long course chemoradiotherapy for rectal cancers where the CRM is threatened or breached. Radiotherapy is thought to be detrimental to bowel function and therefore randomisation was stratified for preoperative radiotherapy exposure. Potential research participants were identified at the MDT meeting by the researcher (SP). They were approached by the colorectal nurse specialists who offered them a verbal explanation of the project and a standard Participant Information Sheet (See Appendix I). Patients were given at least 2 days to decide whether they were willing to participate. Participants were recruited to the study and asked to sign a consent form to document fully informed consent. A similar process took place in Winchester although it was not possible for the researcher (SP) to attend all the MDT meetings so the colorectal nurse specialists were responsible for identifying potential participants. A letter was sent to the patient's GP to inform the GP about the recruitment of the patient to the trial (See Appendix III). A full register of patients screened and recruited to the study was kept.

Data collection took place in the Pelvic Floor Unit at Southampton General Hospital. Postal questionnaires were sent out to the participants at 6 and 9 months for completion at home.

4.1.3 Intervention

The Pelvic Floor Unit in Southampton offers biofeedback training to patients with pelvic floor disorders including anal incontinence and rectal evacuatory disorders. The sessions are carried out by a specifically trained GI motility nurse specialist (SG).

Participants who were randomised to the BFB group were given their first BFB training session preoperatively. Each session lasted 10 to 30 minutes and took place immediately after baseline data collection. The second session was 3 months after restoration of intestinal continuity (either after closure of defunctioning ileostomy or after anterior resection if no stoma was used). Subsequent sessions were carried out by telephone.

During the biofeedback sessions, advice was given about methods of efficient defaecation including positioning on the toilet. Participants were taught a series of exercises to practise to improve sphincter function based on the exercises devised by Christine Norton(Norton et al., 2001). The nurse specialist (SG) used an anorectal probe with visual feedback display to demonstrate to the participant when they were achieving an adequate squeeze pressure. The participant was encouraged to repeat the exercises 5 times each day. The exercises began before surgery and participants with a stoma were advised to continue with the exercises while defunctioned.

The control group had minimal contact with the BFB nurse. After collecting the baseline data the researcher left the room so as to remain blind to the treatment allocation. The nurse then opened the envelope to determine which arm of the trial the participant was entering. If the participant was in the control group (no biofeedback) they were free to leave and were given no additional information.

4.1.4 Outcomes

No changes were made to the trial outcomes after the trial commenced. The primary outcome was final CCI reported at 1 year. Table 4.1.2 shows the timetable for data collection.

Table 4.1.2 Timetable of outcome measures

	Baseline	3 months	6 months	9 months	12 months
Questionnaires	✓	✓	✓	✓	✓
Anorectal Physiology	✓	✓			✓

Secondary outcome measures included changes over the first postoperative year in CCI, EORTC QLQ-C30 & CR29, FIQL, MSKCC and anorectal physiology.

Questionnaires

Four questionnaires were administered for self-completion (See Appendix V & VI).

- Cleveland Clinic Incontinence Score (Jorge & Wexner, 1993)
- European Organization for research and treatment of cancer and the new colorectal cancer module (EORTC QLQ-C30 and CR29) (Miller, et al., 1988; Whistance, et al., 2009)
- Fecal incontinence quality of life questionnaire (Rockwood, et al., 2000)
- Memorial Sloan Kettering Bowel Function Instrument (Temple, et al., 2005)

Severe faecal incontinence was defined as CCI of 9 or greater because previous studies have demonstrated that at this level quality of life is reduced (Rothbarth, et al., 2001). Participants who failed to return their questionnaire within 1 month were contacted by telephone and invited to go through the questionnaire. A small group of participants requested telephone follow-up instead of postal questionnaires.

Anorectal physiology

A standard technique was used for all patients. Baseline anorectal physiology was performed by the author (SP) in all except 5 cases, which were performed by the GI motility nurse specialist (SG). The author was trained by SG prior to starting participant recruitment to ensure that a standard, reproducible method was used. A stationary pull through technique with a 4-channel Medtronic catheter was used to measure resting and squeeze pressures within the anal canal at 1cm intervals from 6cm to 1cm above the anal verge. Recordings at each station from 6 to 1cm were an average of the pressure recorded by the four channels in the catheter tip. The manometer was calibrated before each patient. A computerised system (Polygam Lower GI, Synectics Medical, Stockholm, Sweden) was used for data acquisition.

The rectoanal inhibitory reflex was assessed using rapid inflation of 50ml of air into the balloon. No relaxation response after 3 attempts was recorded as an absent reflex. Maximal tolerable rectal volume was assessed by inflating a rectal balloon on the Medtronic catheter with water at body temperature. The patient was asked to report "first sensation", "first urge" and maximum rectal volume when they felt they could hold on no longer. A balloon expulsion test was carried out with 50ml of water at body temperature. The patient was asked to bear down and try to push out the balloon. Anal canal pressures were measured to evaluate paradoxical contraction or relaxation of the internal anal sphincter as evidenced by a fall in resting pressure.

Anorectal sensitivity was measured using an Anuform electrical stimulation probe. Three assessments were made at 3 different levels (1, 2 and 3cm from the anal verge). The patient was asked to report a change in sensation as the current was increased from 0 to a maximum of 25mA. The test was complete when the patient reported a change in sensation and the current at that level was recorded.

4.1.5 Sample size calculation

Using a standard deviation (Portier, et al., 2005) of 10, an analysable sample size of 45 patients in each arm could detect a 30% (Solomon, et al., 2003) difference in Cleveland Clinic incontinence scores. In a recent study of 239 patients treated with biofeedback for faecal incontinence, 11% failed to start treatment and a further 6% failed to complete treatment (Norton & Kamm, 1999). Assuming that a similar dropout rate of about 20% is encountered, 110 patients would need to be recruited to ensure that a final sample size of 45 per treatment arm was achieved.

Recruitment began on 27 November 2006. Trial progress was reviewed at 18 months (25 June 2008). Analysis of the first 10 patients completing follow-up suggested that if

45 similar patients in each arm completed, with a common standard deviation of 4 and 80% power, then a difference of 2.4 in CCI score could be detected.

The dropout rate at 18 months was approximately 30%. The sample size was therefore increased to 120 to account for the higher dropout rate. With a dropout rate of 30%, this would give an analysable sample of 84. Assuming a common SD of 5 and 80% power, difference of 3 could be detected. This would be clinically significant.

4.1.6 Randomisation

In this multicentre randomised controlled trial, 121 participants undergoing anterior resection for colorectal cancer were randomly assigned to control or BFB groups. Randomisation was stratified for radiotherapy treatment. The decision to give radiotherapy or not was made at the MDT meeting. Only preoperative radiotherapy was used but both short course radiotherapy and long course chemoradiotherapy were included.

The method used to generate the random allocation sequence was computer-generated permuted blocks. The random allocation sequence was concealed in sequentially numbered sealed envelopes. The envelope was not opened until after the baseline data had been collected.

The random allocation sequence was generated by the trial statistician (Scott Harris) who also performed the allocation concealment in envelopes. The researcher (SP) enrolled participants and carried out the data collection. Participants were assigned to control or biofeedback groups by the GI motility nurse specialist (SG) who also performed the intervention.

4.1.7 Blinding

The researcher (SP) assessed the outcome measures and was blinded to the assignment of intervention. After assessment of baseline outcomes, the researcher left the Pelvic Floor Unit and the GI motility nurse (SG) opened the envelope to assign the intervention. When the participant was seen in the Pelvic Floor Unit at 3 months, the outcome measures were assessed by the researcher first. After this the researcher left the Pelvic Floor Unit and the participant saw the GI motility nurse for BFB intervention. Participants in the control group left after the researcher but did not have any discussion with the GI motility nurse.

4.1.8 Statistical methods

The primary outcome measure is sphincter function as measured by the Cleveland Clinic incontinence score at one year compared to baseline function. The one-year Cleveland Clinic incontinence score was examined in a linear regression model adjusted for the baseline level. A comparison of treatment groups was conducted with its 95% confidence intervals. This primary comparison was conducted on an intention to treat (ITT) basis. The secondary analyses were carried out using similar regression models. The percentages of severe incontinence before and after surgery were compared using McNemar's test. Paired samples T-test and Wilcoxon signed ranks test was used to compare parametric and non-parametric data respectively.

Advice was sought from Dr Steven George (Epidemiologist) and Mr Scott Harris (Medical Statistician) regarding statistical analysis.

4.1.9 Finance

This project was funded by a

- BUPA Research Fellow Grant
- Joint Dunhill Medical Trust and Royal College of Surgeons Research into Aging Grant

Participants were given a free car-parking ticket to attend the Pelvic Floor Unit for assessment. Participants from Jersey were given £100 as a contribution towards their travel expenses for each additional trip for research assessment.

4.2 Barium proctography versus dynamic magnetic resonance proctography

4.2.1 Study design

This cohort study compared BaP and MR proctography on 42 consecutive consenting patients (See Appendix XIII for protocol). The proctograms were reported by two consultant radiologists (DT and CT) who specialise in pelvic floor disorders. At the time of reporting, the radiologist was blinded to the results of the other investigation.

It was not anticipated that additional conditions such as cancer would be found during magnetic resonance imaging because volumetric data through the pelvis was not collected. Instead just one slice in a dynamic sequence was performed.

Data handling and record keeping

Source data will be stored in the radiology departments at Poole and Dorchester Hospitals for 5 years. The Data Protection Act 1998 was adhered to. A screening and recruitment log was maintained.

4.2.2 Participants

All patients in the study group had been referred for BaP as part of their NHS management. Patients who fulfilled the inclusion/exclusion criteria (see Table 4.2.1) were invited to take part in the research and offered an additional appointment at Dorchester Hospital for MR proctography. Participants were also asked to complete a questionnaire (Table 4.2.2).

These patients had been seen at the colorectal or gynaecology clinics at Poole or Dorchester Hospitals as part of the pelvic floor service. This was an appropriate group of patients to study because they had been referred for proctography already as part of their NHS management.

The patient invitation letter and information sheet were posted to the patient so that it was received a minimum of 2 days before the proctogram. At the appointment in the radiology department in Poole Hospital, the study was explained to the potential participant by a senior radiographer (Jane Brenner) and consultant radiologist (Dr Tarver). Every participant signed a consent form (see appendix IX) to document informed consent. An appointment for an MR proctogram was arranged at Dorchester Hospital for participants.

Participants who did not attend the MR proctogram after informed consent were contacted by telephone to determine whether they had withdrawn from the study or not. One further appointment for an MR proctogram in Dorchester was arranged if the patient had not withdrawn consent.

Table 4.2.1 Inclusion and Exclusion Criteria

Inclusion criteria	Referred for proctography as part of routine NHS management
	Patient gives informed consent
	Patient is aged greater than 18 years old
Exclusion criteria	Patient incompetent to give informed consent
	Claustrophobia or unable to tolerate MRI
	Contraindications to MRI such as pacemaker, high BMI
	Patient unable to lie flat

Table 4.2.2 Participant questionnaire

Q1	Do you feel that you opened you bowels as usual during the test today? YES / NO
Q2	Would you have this test repeated if it was necessary for your treatment? YES / NO
Q3	Which test did you prefer and why?

4.2.3 Outcomes

The primary objective was to demonstrate whether BaP or MR proctography would be best for investigating rectal function after anterior resection. The presence of measureable differences between pelvic floor structures visualised on BaP and MR proctography was assessed. The length of rectocele demonstrated on erect BaP and supine MR proctography was compared.

The secondary objectives were:

- A comparison of proctogram measurements including anorectal descent and change in anorectal angle

- Comparison of presence of complete rectal emptying, anismus, mucosal prolapse, rectal intussusception, uterovaginal prolapse, cystocele, enterocele, rectocele and rectocele emptying between the two proctograms
- Determine tolerability and patient preference for the two procedures
- Determine whether differences between the two investigations have any clinical significance

4.2.4 **Proctography techniques**

During BaP, the rectum was filled with contrast (Barium paste) and the vagina and small bowel were opacified with contrast medium. The participant was seated on a radiolucent commode behind a screen. Fluoroscopic images were taken in the sagittal plane during rest, contraction and rectal evacuation. The commode is fixed to the floor and the fluoroscopic equipment is centred on the commode at a standard distance from the commode for all imaging to ensure reproducibility of radiological magnification. A correction factor of 0.7 is used in the radiology department at Poole based on measurements taken with a radio-opaque ruler placed on the commode.

The technique for MR proctography was similar to BaP in that the participant had contrast (ultrasound gel) placed in the rectum. However no contrast was placed in the vagina or small bowel. The MRI scanner had a 1Tesla magnet (Phillips Intera). The participant was positioned supine during scanning with a support for the feet so that the knees and hips were flexed. The MR sequence was recorded over a 40-second time period while the participant attempted rectal evacuation whilst lying in the scanning machine. Twenty T2-weighted single midsagittal sections each 5mm thick were taken at 2-second intervals to build-up a dynamic sequence as the participant was bearing down and evacuating the rectum.

A standardised case report form was used to collect data from the proctograms (See appendix XI). A record was made of the presence or absence of rectocele, complete rectocele emptying, rectal intussusception, complete rectal emptying, anismus, mucosal prolapse, enterocele, uterovaginal prolapse, cystocele. Rectal intussusception was classified according to the Oxford Radiological Grading of Rectal Intussusception (Collinson, et al., 2009) as summarised in Table 1.5.4. Rectocele size was measured as the maximum length from an extended anterior wall of the anal canal. To provide an estimation of pelvic floor descent, the distance (ARJ) from the anorectal junction to the pubococcygeal line was measured during rest, squeeze and evacuation. The anorectal angle (ARA) was measured at the intersection between a line along the posterior wall of the rectum and a line along the central axis of the anal canal. All length measurements on BaP were multiplied by a correction factor of 0.7 to allow for radiographic

magnification. Intra-observer variability and inter-observer variability in rectocele length measurement was assessed by comparing repeated measurements on the last 20 proctograms.

4.2.5 Sample size

This was an exploratory study and there was inadequate previous data to base a sample size calculation on. An analysable sample of 60 patients was proposed based on feasibility in the given time frame of one year. Assuming a dropout rate after recruitment of 20% we planned to recruit 75 patients. Between 16/07/2006 and 17/07/2007 a total of 115 barium proctograms were carried out in Poole Hospital. So if the recruitment rate was 70%, we expected to recruit the proposed sample size of 75 patients in 11-12 months.

With a sample size of 60 and standard 80% power, allowing for a maximum difference in rectocele size of 0.5 cm, we could pick up a standard deviation of 1.5, at most. This is a clinically relevant difference to detect.

4.2.6 Statistical analysis

All participants who attended both proctograms were included in the analysis. Cohen's Kappa was used to assess agreement between BaP and MR proctography. A paired T-test was used to look at difference with a 95% confidence interval and 0.5cm equivalence. Bland and Altman plots were used to assess agreement between the measurements made on BaP and MR proctography.

4.2.7 Research Governance, Monitoring and Ethics & R&D approval

The study was conducted in compliance with the Research Governance Framework for Health and Social Care and Good Clinical Practice (GCP). A favourable ethical opinion was given for this study by the Dorset Research Ethics Committee meeting on 20th December 2007 and a subsequent amendment to the study was also approved on 10th April 2008.

Dorset REC number: 07/H0201/154

4.2.8 Finance

A Research Bursary was awarded by the Bowel Disease Research Foundation to support the running costs of this project.

Patients were reimbursed with £12 as a contribution towards their travel expenses. Free car-parking at Dorchester Hospital was provided for the additional proctogram.

5 Study Results and Discussion

5.1 Rectal function and quality of life before anterior resection

A persistent change in bowel habit to looser stools or increased frequency of defaecation are recognised symptoms associated with an increased risk of colorectal cancer in patients older than 60 years (UK Department of Health Criteria: Table 1.1). This chapter explores why some patients may complain of anal incontinence as a manifestation of their change in bowel habit.

Results

Study procedures were carried out as described in Section 4.1. Data on 121 consecutive consenting participants undergoing anterior resection for pathology within 30cm of the anal verge were collected as part of a randomised trial. One participant withdrew from the study shortly after randomisation and therefore is not included. Data on 120 participants is investigated. A summary of the raw data is given in Appendix XIV.

5.1.1 Anal incontinence and Quality of Life before Surgery

Figure 5.1.01 shows the CCI score in a group of 120 patients awaiting anterior resection for suspected cancer. Fifty-four (45%) reported perfect anal continence (CCI = 0) and 22 (18%) had severe anal incontinence as recorded by a CCI score of 9 or greater (Rothbarth, et al., 2001).

Tables 5.1.01 and 5.1.02 show the EORTC Quality of Life Questionnaire (QLQ)-C30 and CR29 results for constructed scales. The Global health status, all 5 functional scales and 5 of the 9 symptom scales/items are of most relevance to this study and have been included. The EORTC has published QLQ-C30 reference data from 1773 colorectal cancer patients (EORTC Quality of Life Group, 2010) and this is also shown in Table 5.1.01 for comparison. The reference data is from patients with all stages of colorectal cancer and 29% had stage I to IV, 37% had recurrent disease and 34% had an unknown stage of disease.

The EORTC Colorectal Cancer Module QLQ-CR29 consists of 5 functional scales and 18 symptom scales. Four of the functional scales and 13 of the symptom scales are most relevant to this project and have been included in the analysis. High scores on the functional scales of QLQ-C30 and CR29 represent a high/healthy level of functioning. A high score on global health status also means a high quality of life. However a high score in the symptom scale indicates a high level of symptoms or problems.

Figure 5.1.01 Bar chart showing anal incontinence before anterior resection measured with CCI

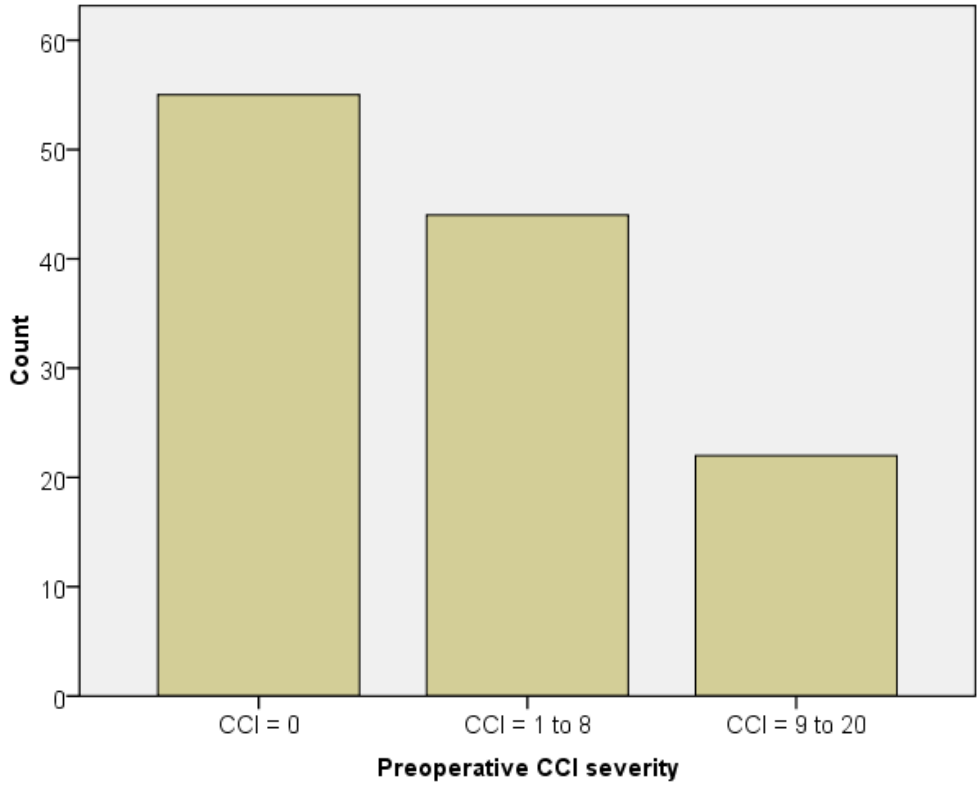


Table 5.1.01 QLQ-C30 constructed scale results from this study (preoperative data) and EORTC reference data from colorectal cancer patients (all stages) (2010) (in italics)

		Preoperative data		*EORTC Reference data*	
Constructed scales	**Abbreviation**	**Mean**	**SD**	***Mean***	***SD***
Global health status /QoL	QL	73.4	20.3	*60.7*	*23.4*
Physical functioning	PF	88.5	14.5	*79.2*	*21.1*
Role functioning	RF	82.4	28.5	*70.4*	*32.8*
Emotional functioning	EF	79.1	19.7	*68.9*	*24.5*
Cognitive functioning	CF	84.9	20.6	*85.2*	*20.4*
Social functioning	SF	86.6	21.2	*76.0*	*28.6*
Fatigue	FA	23.3	22.6	*34.7*	*28.4*
Nausea and vomiting	NV	3.6	9.9	*7.3*	*17.2*
Pain	PA	16.4	24.5	*24.0*	*29.6*
Constipation	CO	16.7	26.6	*15.8*	*27.9*
Diarrhoea	DI	20.8	28.0	*16.6*	*27.6*

Table 5.1.02 QLQ-CR29 constructed scale results from this study (preoperative data)

	Mean	Std. Deviation	N
body image	88.3	19.6	118
anxiety	61.7	27.2	120
sexual function men	31.9	30.7	68
sexual function women	13.9	20.4	48
urinary frequency	35.0	23.8	120
stool frequency	25.4	23.1	119
urinary incontinence	8.9	18.7	120
dysuria	1.1	6.0	119
abdominal pain	16.7	25.2	120
buttock pain	13.1	23.0	120
bloated feeling	24.7	31.6	120
flatulence	27.5	27.3	119
faecal incontinence	12.2	21.1	120
sore skin	13.3	21.8	120
embarrassed by bowel movement	16.7	27.5	118
impotence	38.5	39.3	52
dyspareunia	3.9	13.6	34

Table 5.1.03 shows the single item results for QLQ-C30 global health scale. Preoperative data from this study and the EORTC reference data from colorectal cancer patients (all stages) (EORTC Quality of Life Group, 2010) are shown.

Table 5.1.03 Frequency table (%) showing participant response to QLQ-C30 single items from this study (preoperative data) and EORTC reference data (EORTC Quality of Life Group, 2010) (in italics)

Response to single items	1 (very poor)	2	3	4	5	6	7 (excellent)	TOTAL (n)
Q29 overall health (preop)	0	4	5	13	23	34	20	**100% (120)**
Q29 overall health (EORTC)	*3*	*4*	*12*	*26*	*27*	*18*	*10*	***100% (1735)***
Q30 overall quality (preop)	0	2	5	14	26	31	22	**100% (120)**
Q30 overall quality of life (EORTC)	*4*	*5*	*12*	*23*	*26*	*20*	*11*	***100% (1733)***

Using an independent samples T-test to compare mean Global Health/Quality of Life (QL) status, participants with severe anal incontinence had a worse QL status with a mean difference of -10.6 (95% CI: -19.9 to -1.2) compared to those with a CCI of less than 9 (P=0.027) (see Table 5.1.04).

Table 5.1.04 EORTC Quality of life (QL) in participants with severe anal incontinence compared with perfect or moderate incontinence (CCI < 9)

	N	Mean global health status (QL)	SD
Severe anal incontinence	22	64.8	19.1
CCI < 9	98	75.3	20.2

Simple linear regression indicated that baseline CCI was a predictor of QL (b=-0.789, p=0.034, 95%CI -1.410 to -0.057). Using multiple linear regression to control for tumour height, cancer diagnosis and female gender there was a significant relationship between baseline CCI and QL as shown in Table 5.1.05.

Table 5.1.05 Multiple linear regression for preoperative Quality of life (QL) adjusting for preoperative CCI score, tumour height, cancer diagnosis and female gender

		95% Confidence Interval		
	B	Lower limit	Upper limit	p
Preoperative CCI	-0.880	-1.609	-0.152	0.018
Tumour height	-0.266	-0.828	0.296	0.350
Cancer diagnosis	-5.894	-16.98	5.195	0.295
Female gender	-2.815	-10.71	5.081	0.482

Tables 5.1.06 and 5.1.07 show the mean and standard deviation for relevant scales from QLQ C-30 and CR29 when the group is split for severe anal incontinence (CCI >= 9). The QLQ-C30 questionnaire recorded diarrhoea (DI) as a symptom in 52 participants (43%). Participants with no severe incontinence (CCI less than 9), reported significantly less diarrhoea symptoms (mean difference 13.4, p= 0.041, 95% CI: 0.53 to 26.4) than those with CCI of 9 or greater. Tables 5.1.06 and 5.1.07 also summarise the results from independent T-test comparison of means when divided into groups depending on severity of anal incontinence. The Mean CCI of participants with no

severe incontinence is subtracted from mean CCI of participants with severe incontinence to give the mean difference. The following functional and symptom scales have been omitted as the mean differences were not significant: emotional and cognitive functioning, nausea/vomiting, pain, constipation, body image, anxiety, sexual function in men and women, urinary frequency, dysuria, abdominal pain, bloated feeling, impotence and dyspareunia.

Table 5.1.06 EORTC QLQ-C30 mean function scores in participants with severe anal incontinence compared with no severe anal incontinence (CCI<9)

		n	Mean	Std Deviation	Mean difference	95% CI Lower	95% CI Upper	p
Global health status/qol	**Severe**	22	64.8	19.1	-10.6	-19.9	-1.2	0.027
	Not severe	98	75.3	20.2				
Physical functioning	**Severe**	22	80.6	17.7	-9.7	-16.3	-3.1	0.004
	Not severe	98	90.3	13.2				
Role functioning	**Severe**	22	70.5	34.1	-14.6	-27.7	-1.5	0.029
	Not severe	97	85.1	26.5				
Social functioning	**Severe**	22	76.5	23.4	-12.3	-22.0	-2.6	0.013
	Not severe	97	88.9	20.1				

Table 5.1.07 EORTC QLQ-C30 and CR29 mean symptom scores in participants with severe anal incontinence compared with no severe anal incontinence (CCI<9)

Mean difference = mean severe incontinence – mean CCI < 9

		n	Mean	Std Deviation	Mean Difference	95% CI Lower	95% CI Upper	p
Fatigue	**Severe**	22	32.3	25.4	11.0	0.6	21.4	0.039
	Not severe	97	21.3	21.6				
DI	**Severe**	22	31.8	34.9	13.5	0.5	26.4	0.041
	Not severe	98	18.4	25.8				
Urinary incontinence	**Severe**	22	21.2	30.1	15.1	6.8	23.4	0.000
	Not severe	98	6.1	13.8				
Buttock pain	**Severe**	22	33.3	30.9	24.8	15.0	34.5	0.000
	Not severe	98	8.5	18.1				
Flatulence	**Severe**	22	45.5	26.3	22.1	9.9	34.3	0.000
	Not severe	97	23.4	26.0				
Faecal incontinence	**Severe**	22	36.4	28.9	29.6	21.2	37.9	0.000
	Not severe	98	6.8	14.3				
Sore skin	**Severe**	22	27.3	33.5	17.1	7.3	26.8	0.001
	Not severe	98	10.2	16.9				
Stool frequency	**Severe**	22	39.4	26.0	17.2	6.9	27.6	0.001
	Not severe	98	21.9	21.2				
Embarrassed by bowel movement	**Severe**	22	37.9	40.2	26.1	14.1	38.1	0.000
	Not severe	96	11.8	21.1				

Table 5.1.8 compares the frequency of faecal incontinence measured on the CR-29 questionnaire with the CCI severity groupings. There are some interesting differences with 4 patients in the severe incontinence group who report no faecal incontinence on the CR-29 questionnaire. The CR-29 questionnaire only detected 7 patients with faecal incontinence symptom scores of “quite a bit” or “very much”.

Table 5.1.08 Comparing Preoperative CCI severity with single items of Faecal Incontinence symptom scale(CR-29)

		CCI severity			
		CCI = 0	CCI = 1 to 8	CCI = 9 to 20	Total
Faecal Incontinence (CR-29)	Not at all	50	29	4	83
	A little	3	15	12	30
	Quite a bit	1	0	3	4
	Very much	0	0	3	3
	Total	54	44	22	120

5.1.2 **Anorectal manometry before surgery**

Tables 5.1.09 and 5.1.10 display the preoperative anorectal manometry results. All participants contributed to the results (n = 120)

Table 5.1.9 Preoperative Mean Resting Pressure

Height above anal verge (cm)	Mean (mmHg)	Standard Deviation
4	33	22
3	46	23
2	49	22
1	38	23

Table 5.1.10 Preoperative Mean Squeeze Pressure

Height above anal verge (cm)	Mean (mmHg)	Standard Deviation
4	67	48
3	85	58
2	91	62
1	91	58

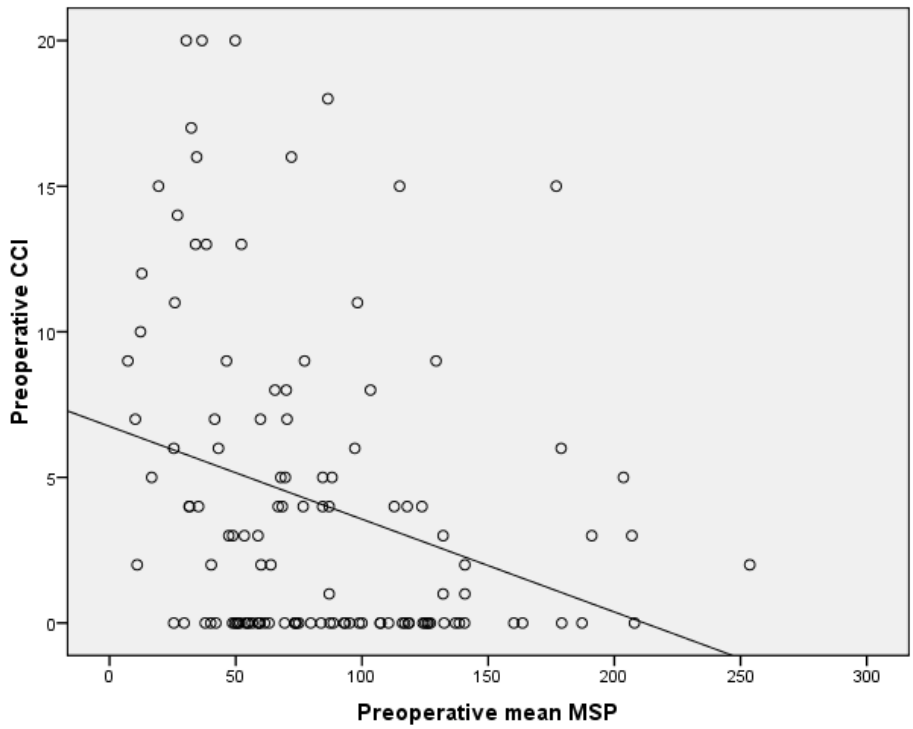
Table 5.1.11 shows the preoperative mean and maximal values for MRP and MSP, comparing participants with CCI less than 9 with participants with severe anal incontinence. Participants with severe anal incontinence had significantly lower squeeze pressures (mean difference in max MSP = 40mmHg, p = 0.002; 95%CI: 14.6 to 65.8) but there was no difference in resting pressures.

Table 5.1.11 Preoperative anorectal physiology for participants with CCI < 9 (n = 98) and severe anal incontinence (n = 22)

		Mean (mmHg)	SD
Mean MRP	**CCI < 9**	41.5	15.6
	Severe incontinence	41.8	12.7
Max MRP	**CCI < 9**	59.7	21.5
	Severe incontinence	62.4	18.3
Mean MSP	**CCI < 9**	89.85	48.6
	Severe incontinence	55.2	43.2
Max MSP	**CCI < 9**	119.3	56.2
	Severe incontinence	79.1	47.2

Using linear regression, there was a significant negative relationship between CCI and MSP before surgery as shown in Figure 5.1.02 (B = -0.032, p = 0.001, 95%CI: -0.051 to -0.013). There was no correlation between mean MRP and CCI.

Figure 5.1.02 Scatter graph showing the relationship between Mean MSP and CCI



There were significant differences in MSP between men (n = 71) women (n = 49) over the first 4cm from the anal verge (mean difference = -58mmHg, $p < 0.001$; 95%CI: -73 to -43) as shown in Table 5.1.12. There were no clinically relevant and significant differences in MRP between men and women.

Table 5.1.12 Preoperative gender differences in mean squeeze pressure
(Women - Men)

Height (cm)	Mean difference in MSP (mmHg)	95% Confidence interval		P value
		Lower	Upper	
4	-59	-73	-45	<0.001
3	-73	-90	-57	<0.001
2	-60	-80	-40	<0.001
1	-38	-58	-17	<0.001
Average over anal canal	-58	-73	-43	<0.001
Maximal	-61	-80	-42	<0.001

Before surgery, proportionally more women than men had severe anal incontinence (Chi-squared test: p = 0.003) (see Table 5.1.13).

Table 5.1.13 Frequency table of anal incontinence severity in men and women

	CCI = 0 to 8	**CCI = 9 to 20**	**TOTAL**
Men	65 (92%)	6 (8%)	71 (100%)
Women	33 (67%)	16 (33%)	49 (100%)
TOTAL	98	22	120

A highly significant relationship was found between preoperative CCI and mean MSP (B = 6.752, p = 0.001, 95%CI: -0.051 to -0.013). However when a general linear model was used to adjust for female gender, Global Health Status, diarrhoea symptom and stool frequency symptom this relationship was no longer significant (Table 5.1.14).

Table 5.1.14 Preoperative CCI adjusted for female gender, global health status, diarrhoea symptom and stool frequency symptom

Parameter	B	95% Confidence Interval		p
		Lower	Upper	
Mean MSP	-0.017	-0.039	0.004	0.115
Female gender	-2.688	-4.809	-0.567	0.013
Global health	-0.021	-0.066	0.024	0.362
Diarrhoea	-0.025	-0.010	0.060	0.167
Stool frequency	0.063	0.022	0.105	0.003

Discussion

The preoperative EORTC QLQ-C30 data from this study is similar to published EORTC reference data, suggesting that quality of life in the study group is likely to be typical and representative for colorectal cancer patients. In general the study group tended to score more highly in the Global health status and function scales, and had less severe scores on the symptom scales than the reference group. There are some important differences between the two groups which may account for this. Most of the patients in the reference group were post-operative whereas the study data in this chapter is from preoperative patients. The reference group included metastatic or recurrent cancer in 37% and these patients are likely to have a worse score. In addition the reference data is taken from patients with cancers distributed throughout the colon and rectum whereas the present study is limited to left sided cancers. The reference data includes patients with stomas and some of these were permanent stomas after APR. In the preoperative group there were no participants with permanent stomas, although 4 participants did go on to have APR. The CR-29 module reported high symptoms scores in urinary frequency, flatulence and stool frequency.

Rothbarth *et al* (Rothbarth, et al., 2001) investigated patients with varying degrees of incontinence as measured by CCI and demonstrated that patients with a CCI of 9 or greater, had a significantly lower quality of life which was comparable to house-bound individuals. Using this information, the research participants were grouped into a severe group which included all participants with a CCI of 9 or greater and a non-severe group (CCI < 9). There were 22 (18%) participants in the severe incontinence group. The non-severe group had 54 participants with perfect anal continence (CCI = 0) and 44 participants with mild to moderate incontinence (CCI between 1 and 8). Severe anal incontinence was associated with a significantly lower mean EORTC global health status (GL) of 65 compared to 75 (maximum score equating to excellent GL is 100). Although the mean difference was 10, the 95% confidence interval was between 20 and -1. Although there was a significant difference between GL in those with severe incontinence and those with no severe incontinence, the clinical relevance of this difference cannot be determined by the present study. From the 95% confidence intervals, we can estimate that the magnitude of the difference in GL is between 20 and -1. A difference of 10 or above would be clinically relevant but if it is smaller than this it would not be clinically relevant (Osoba, Rodrigues, Myles, Zee, & Pater, 1998). A larger sample size is needed to demonstrate more precisely what the difference in the groups is likely to be.

Using “severe incontinence” as defined by CCI of 9 or greater, the prevalence of anal incontinence in this study before surgery was 18%. This is a fairly high level of

incontinence and has not been extensively investigated with prospective studies. In a group of patients with colorectal cancer a higher level of incontinence than in the general community might be expected because these patients often have a change in bowel habit to looser stool. This symptom can present with faecal incontinence as the patient's continence mechanisms have more difficulty controlling the looser stool and are therefore more likely to leak.

Attempts to quantify the community prevalence of faecal incontinence have been limited by poor response rates and inappropriate data-collection methods. Faecal incontinence is an embarrassing condition and there is no universally accepted definition. A systematic literature review to estimate the prevalence of faecal incontinence was carried out by Macmillan *et al* (Macmillan, et al., 2004) and 16 studies were identified. However, only 3 of these adequately attempted to reduce sources of bias. These population studies (Johanson & Lafferty, 1996; Kalantar, et al., 2002; Lam, et al., 1999) reported a faecal incontinence prevalence in the general community of 11-15%. Different definitions of anal incontinence were used including:

1. Any involuntary leakage of stool or soiling of undergarments
2. Unwanted release of liquid or solid faeces at an inappropriate time or place
3. At least two of: stool leakage, pad for faecal soiling, incontinence of flatus > 25% of the time.

Although these definitions would include participants in the severe incontinence group, they would also include some participants in the non-severe group. If the definitions were applied to the present study, the estimation of faecal incontinence would be even higher.

A study from Korea (Jang, et al., 2010) has analysed preoperative anorectal manometry data on 80 patients with rectal cancer and reported anal incontinence in only 4/80 patients (5%). This was a retrospective study and therefore may have missed some cases of incontinence. Faecal incontinence was defined as daily leakage of gas or loose stool. These symptoms alone would give a minimum CCI score of 4. Anal incontinence is difficult to measure accurately in a retrospective study because patients often do not report this embarrassing symptom. Usually it is necessary to carefully ask about the symptom of anal incontinence and the use of a scoring system such as CCI is essential for maximising the uniformity of the data collected.

The CR-29 module uses a single question to assess faecal incontinence: "Have you had leakage of stools from your back passage?" Like most symptoms, anal incontinence

has many facets to it and the exact wording of the question will have slightly different meanings to different people. In addition, “a little” faecal leakage will have a different impact on different people. Some people may be able to ignore it altogether so that it has no effect on their quality of life or daily activities and other people may need to wear a pad in case of leakage and may feel very anxious about trying to continue with their daily activities with the risk of an embarrassing episode. The CCI scoring system tries to assess anal incontinence in more depth than a single question and may unmask the extent of anal incontinence more accurately.

A low anal squeeze pressure is often associated with anal incontinence. Consistent with this, was the finding that participants with severe anal incontinence had a significantly lower squeeze pressure than those with no severe incontinence (CCI < 9). The squeeze pressure is thought to reflect activity of the external anal sphincter primarily whereas resting pressure is thought to be more dependent on internal anal sphincter activity. No difference was found in resting pressures between continent and incontinent participants prior to surgery.

In clinical practice pelvic floor exercises and anal sphincter exercises are often recommended for patients with faecal incontinence. The aim of this treatment is to improve sphincter strength, endurance and speed of response. Biofeedback can be used to facilitate this process and monitor progress. A programme of exercises is started often in combination with other treatments such as diet, evacuation training and drugs that alter stool consistency. The evidence for exercise programmes is not strong, but recent NICE guidelines recommend their use in patients with faecal incontinence (NICE Clinical Guideline, 2007). In theory, the exercises would enable the patient to avoid faecal leakage by improved external anal sphincter and pelvic floor muscle function. Resting pressure might also be improved due to increased muscle tone, although the internal anal sphincter is thought to be primarily responsible for resting pressure. This is a smooth muscle and therefore not influenced by voluntary muscle exercises. Again, in theory, patients with low squeeze pressures may be most likely to benefit from biofeedback exercises. A significant improvement in squeeze pressures with exercises has not been demonstrated in previous research (Ho, et al., 1996; Loening, 1990).

Before surgery, women were 4 times more likely than men to have severe anal incontinence. Women are known to have lower squeeze pressures than men and in this study there was a significant mean difference of 58mmHg. Although simple linear regression confirmed a highly significant relationship between preoperative CCI and mean squeeze pressure, after adjustment for female gender, this relationship was no

longer significant. It is possible that with a larger sample size a significant relationship would be demonstrated as the 95% confidence intervals were close to zero after adjustment. On the basis of the current results we can conclude that female gender alone was the most important factor in the relationship with preoperative CCI.

In this study 18% of participants reported severe anal incontinence before surgery. The symptom of diarrhoea was reported in 43% of participants and 71% reported frequent bowel movements. Patients with a low squeeze pressure will be less able to control their diarrhoea and frequent bowel movement and may present with faecal incontinence as their primary symptom rather than a change in bowel habit. This is likely to be particularly true in women who have a lower MSP than men. It is important to exclude a diagnosis of colorectal cancer in patients who present with faecal incontinence.

To investigate whether patients with colorectal cancer do have a higher level of incontinence than non-cancer patients, it would be interesting to record the CCI for all patients presenting to the colorectal clinics with suspected cancer (two-week wait patients). It would then be possible to compare the CCI results for patients who had been diagnosed with cancer and those who were not.

5.2 Loss of anal continence at 3 months after anterior resection

The functional outcome following anterior resection is often overlooked as the main focus is usually cancer cure. However loss of anal continence has a profound effect on the patient's quality of life. Identifying patients at high risk for anal incontinence would allow appropriate counselling and may influence treatment options.

Results

Study procedures were followed as described in Chapter 4.1.

5.2.1 Anal incontinence at 3 months after surgery

Preoperatively 49% (40/81) of patients had perfect anal continence (CCI=0), 42% (34/81) of patients had mild incontinence and 9% (7/81) of patients had severe incontinence (Table 5.2.01).

After surgery 22% (18/81) of patients maintained their preoperative level of continence. Anal continence improved in 27% (22/81) with a range in CCI of 1 to 16 and a median 4, but deteriorated in 51% (41/81) patients (range 1 to 16 and a median of 5.5).

Seventeen percent (14/81) of patients with no preoperative severe incontinence (CCI <=9) reported postoperative incontinence (CCI>9), compared with 2.5% (2/81) of those who had preoperative incontinence and no incontinence postoperatively (See Table 5.2.02). This difference in proportions was significant (difference=15%, 95% CI: 5% to 25%, McNemar: P=0.004). In those patients who developed severe anal incontinence, quality of life (FIQL: Fecal Incontinence Quality of Life questionnaire) decreased in all domains postoperatively although this did not reach significance (Table 5.2.03: test statistic Wilcoxon Signed Ranks Test).

Patients who had severe anal incontinence at baseline, were 10.7 times more likely to still have severe anal incontinence at 3 months follow-up than those who did not have severe incontinence preoperatively (95% CI: 1.88 to 61.0, p = 0.008).

Table 5.2.01 Count of patients with perfect, mild and severe anal incontinence before and 3 months after anterior resection

	Perfect anal continence CCI=0	Mild to moderate anal incontinence CCI>0 and CCI<=9	Severe anal incontinence CCI>9	TOTAL
Preoperative	40 (49%)	34 (42%)	7 (9%)	**81 (100%)**
Postoperative 3 months	22 (27%)	40 (49%)	19 (24%)	**81 (100%)**

Table 5.2.02 Frequency table of change in clinical status from preoperative incontinence to postoperative incontinence at 3 months after surgery

Figures are number (total percentage)

	Preoperative incontinence	Preoperative no incontinence	TOTAL
Incontinence at 3 months	5 (6%)	14 (17%)	19
No incontinence at 3 months	2 (3%)	60 (74%)	62
TOTAL	7	74	**81(100%)**

Table 5.2.03 Test statistic (Wilcoxon Signed Ranks Test) comparing preoperative and 3 months postoperative FIQL domains

	Change in lifestyle domain	Change in coping / behaviour domain	Change in depression self perception domain	Change in embarrassment domain
Z	-1.66	-1.64	-0.98	-1.50
Significance (2-tailed)	0.10	0.10	0.33	0.13

Preoperative and postoperative EORTC quality of life domains were assessed for equality using a 2 sided Wilcoxon signed ranks test. A significant result was found for deterioration in emotional functioning (P=0.043), social functioning (P=0.043), constipation (P<0.01) and defaecatory problems (P<0.01) hence significant evidence against preoperative and 3 month EORTC QoL domains being equal

5.2.2 Predicting severe anal incontinence at 3 months

A Pearson Chi-squared test was used to investigate the strength of relationships between postoperative anal incontinence (CCI score greater than 9) at 3 months and the following variables: gender, age, height of pathology, anastomotic height, presence of rectal anastomosis, length resected and exposure to preoperative radiotherapy.

Gender

After anterior resection, 31% (11/35) of women reported incontinence (CCI>9), compared with 17% (8/46) of men (Table 5.2.04). This difference was not significant (difference=14%, 95% CI: -5% to 33%, P=0.14).

Table 5.2.04 Frequency table of clinical status by gender
Figures are number (percentage)

	Women	**Men**	TOTAL
Incontinence	11 (31%)	8 (17%)	19
No incontinence	24 (69%)	38 (83%)	62
TOTAL	**35 (100%)**	**46 (100%)**	**81**

Using logistic regression to adjust for preoperative severe anal incontinence, women were 1.7 times more likely to have severe anal incontinence postoperatively than men, however this was not statistically significant (95% CI: 0.581 to 5.35, p = 0.317).

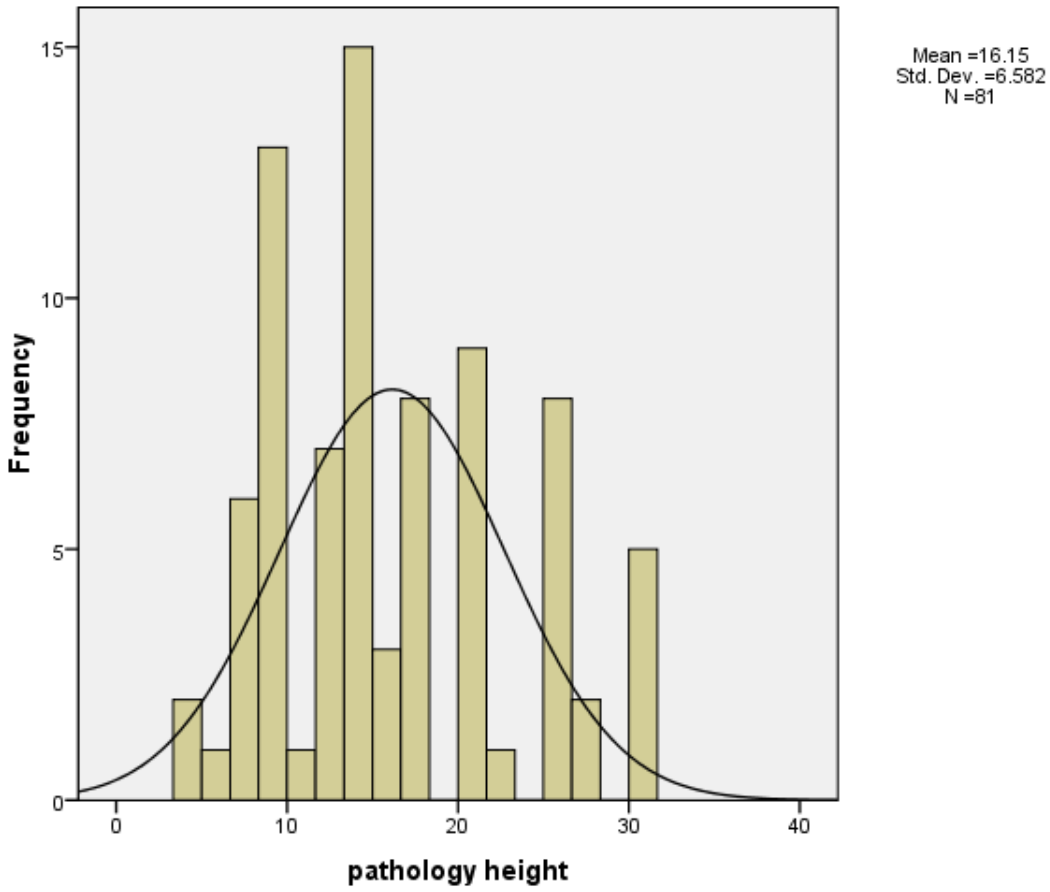
Age

There was no difference in continence levels between patients younger than 70 years and those 70 years and older. There was no linear relationship between postoperative anal continence and age (b = 0.060, 95% CI: -0,057 to 0.177, p = 0.309), even when the baseline preoperative CCI was taken into account.

Pathology height

One of the inclusion criteria for participants was that their pathology must be within 30cm of the anal verge. The mean height was 16cm (SD 6.6cm) from the anal verge(Figure 5.2.01).

Figure 5.2.01 Bar chart showing distribution of height of pathology (cm)



After anterior resection, 15% (9/59) of patients who had pathology at greater than 10 cm from the anal verge (upper third of rectum) reported incontinence (CCI>9), compared with 55% (12/22) of patients who had pathology at or below 10cm (Table 5.2.05). This difference was significant (difference=40%, 95% CI: 16.4% to 59.1%, P=0.004).

Table 5.2.05 Frequency table of clinical status by tumour height
(low: 10cm or less from anal verge; high: greater than 10cm)
Figures are number (percentage)

	Low pathology	High pathology	TOTAL
Incontinence	10 (45%)	9 (15%)	**19**
No incontinence	12 (55%)	50 (85%)	**62**
TOTAL	**22 (100%)**	**59 (100%)**	**81**

Controlling for baseline CCI, there was a significant linear relationship between anal continence at 3 months (CCI) and height of pathology (p = 0.001, 95% CI: -0.437 to -0.114), which can be described by the following equation (Table 5.2.06):

Postoperative (3 months) CCI = 9 - 0.3 (pathology height) + 0.2 (preoperative CCI)

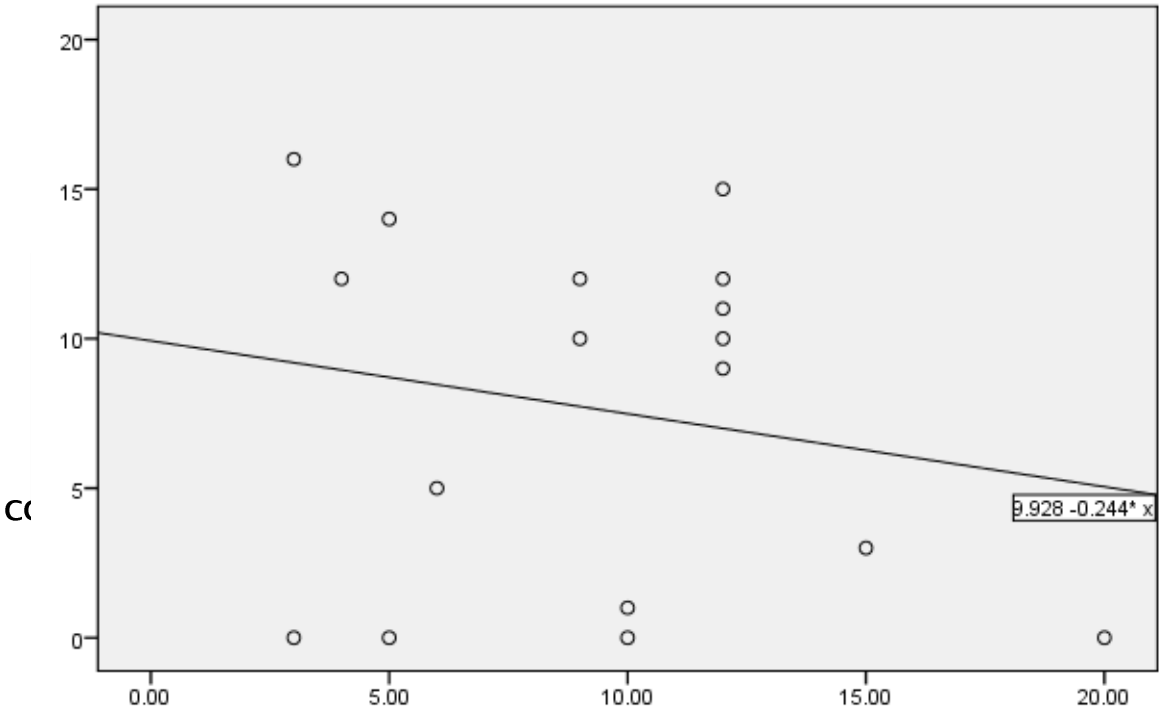
Table 5.2.06 showing 95% CI and significance of linear relationship between preoperative and postoperative (3 months) anal continence

	Constant	95% Confidence Interval Lower	Upper	P
Constant	9	6.3	12.2	< 0.01
Pathology height	-0.3	-0.4	-0.1	0.001
Preoperative CCI	0.2	-0.08	0.4	0.17

Anastomotic height

Anastomotic height is thought to be a determinant of functional outcome. In this study anastomotic height and 3 month outcome data was available in only 17 cases. Simple linear regression showed a negative linear relationship between anastomotic height and CCI at 3 months (Figure 5.2.02) but this was not statistically significant (b=9.928, P=0.462, 95% CI: -0.932 to 0.444).

Figure 5.2.02 Measured anastomotic height and CCI at 3 months



Presence of rectal anastomosis

In this study patients who had pathology within 30cm of the anal verge were included in an attempt to capture all patients who would have a rectal anastomosis. Pathology reporting recorded the presence or absence of the peritoneal reflection. Where the peritoneal reflection was included in the specimen, it was assumed that the patient had had a rectal anastomosis. The functional result between patients with a rectal anastomosis (n = 62) and no rectal anastomosis (n = 19) was compared.

Using an independent samples t-test to compare means of these two groups, there was no difference in means preoperatively (difference 0.02, P = 0.5) but postoperatively there was a difference of 4.4 (95% CI 2.6 to 6.2; P < 0.01). At 3 months follow-up, patients who had undergone rectal anastomosis had a significantly worse CCI with a mean difference in CCI of 4 (Table 5.2.07). This is shown in the Box and Whisker Plots shown in Figure 5.2.03 and 5.2.04.

Table 5.2.07 Comparing mean CCI preoperatively and at 3 months postoperatively between patients with and without a rectal anastomosis

	Rectal anastomosis	Higher anastomosis
Preop CCI (mean)	3.1	3.1
3 month CCI (mean)	6.4	2.0

Figure 5.2.03 Preoperative anal incontinence scores and in groups who underwent rectal anastomosis or no rectal anastomosis (higher anastomosis)

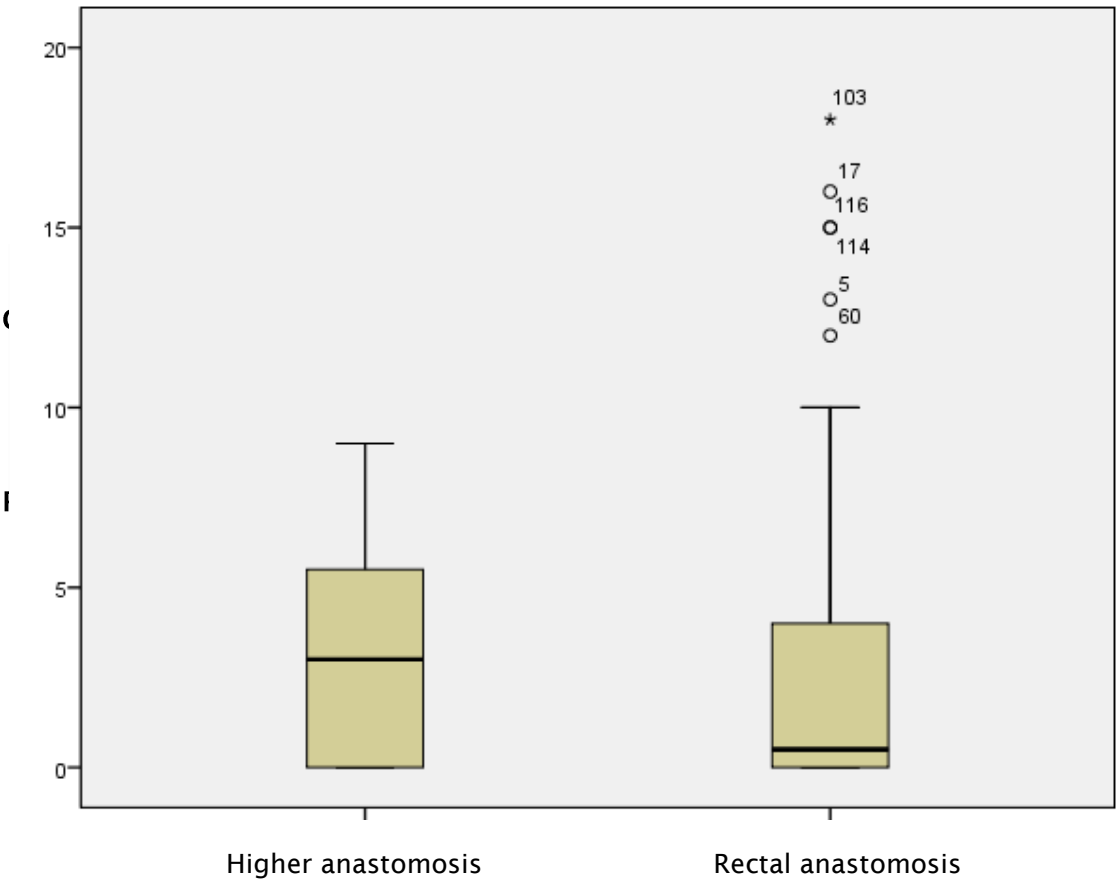
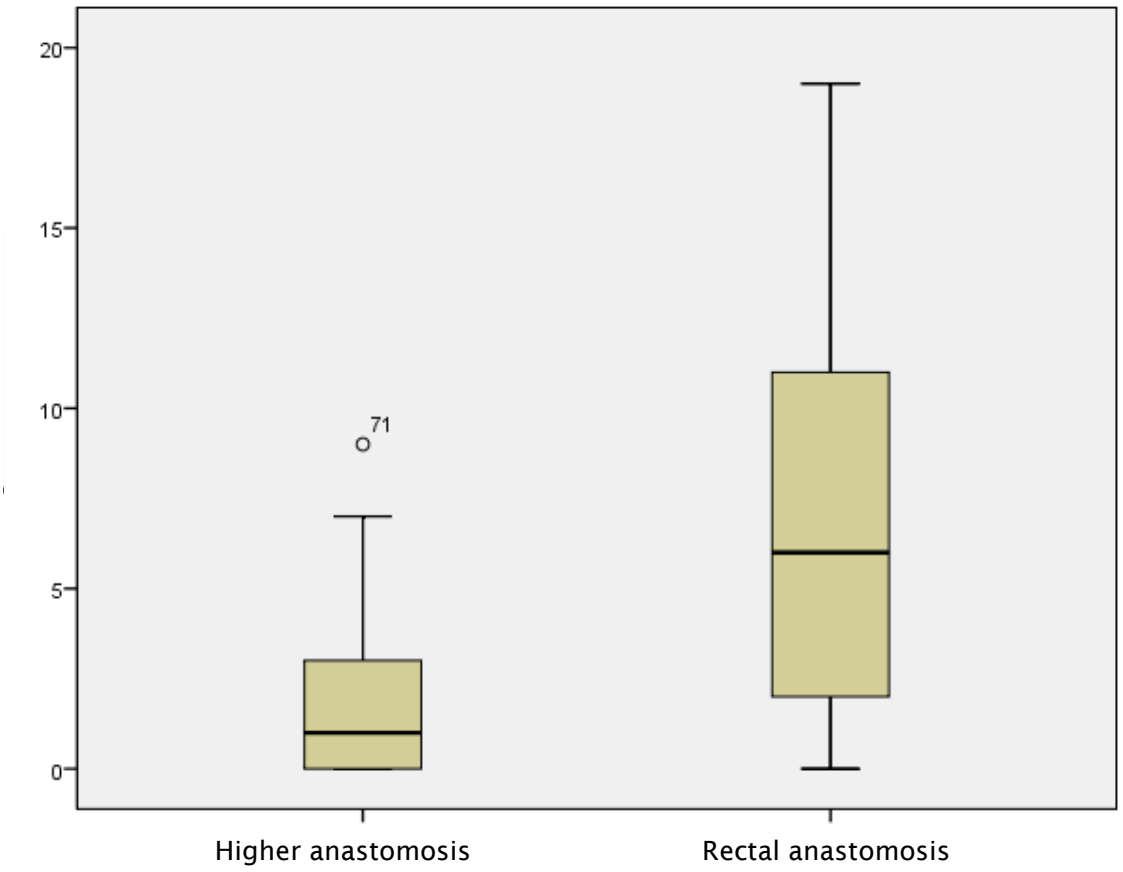


Figure 5.2.04 Postoperative (3 months) anal incontinence scores and in groups who underwent rectal anastomosis or no rectal anastomosis (higher anastomosis



After anterior resection, 31% (19/62) of patients with a rectal anastomosis complained of severe incontinence compared to none of those with a higher anastomosis. This difference was significant (difference=31%, 95% CI: 11% to 43%, P=0.006) (Table 5.2.08).

Table 5.2.08 Comparing proportions of patients with severe incontinence or no severe incontinence split for presence of a rectal anastomosis

	Rectal anastomosis	Higher anastomosis	TOTAL
Incontinence	19 (31%)	0 (0%)	**19**
No incontinence	43 (69%)	19 (100%)	**62**
TOTAL	**62 (100%)**	**19 (100%)**	**81**

After adjusting for preoperative anal incontinence, the presence of a rectal anastomosis increases the postoperative CCI by a constant of 4.4 (95% CI 1.9 to 6.9, P = 0.001) using multiple linear regression.

Length resected

The length of bowel resected may affect continence after anterior resection. In this study, patients with severe incontinence at 3 months had slightly longer lengths of bowel removed (mean 20.4cm) when compared to those with mild or no incontinence (mean 17.3cm) (Figure 5.2.05). This mean difference of 3.1cm was significant (95% CI: 0.3 to 5.9; P=0.03). There was no relationship between length of bowel resected and height of anastomosis (Figure 5.2.06)

Figure 5.2.05 Box and whisker Plot showing mean length of bowel resected for patients grouped according to presence or absence of severe anal incontinence after surgery (3 months)

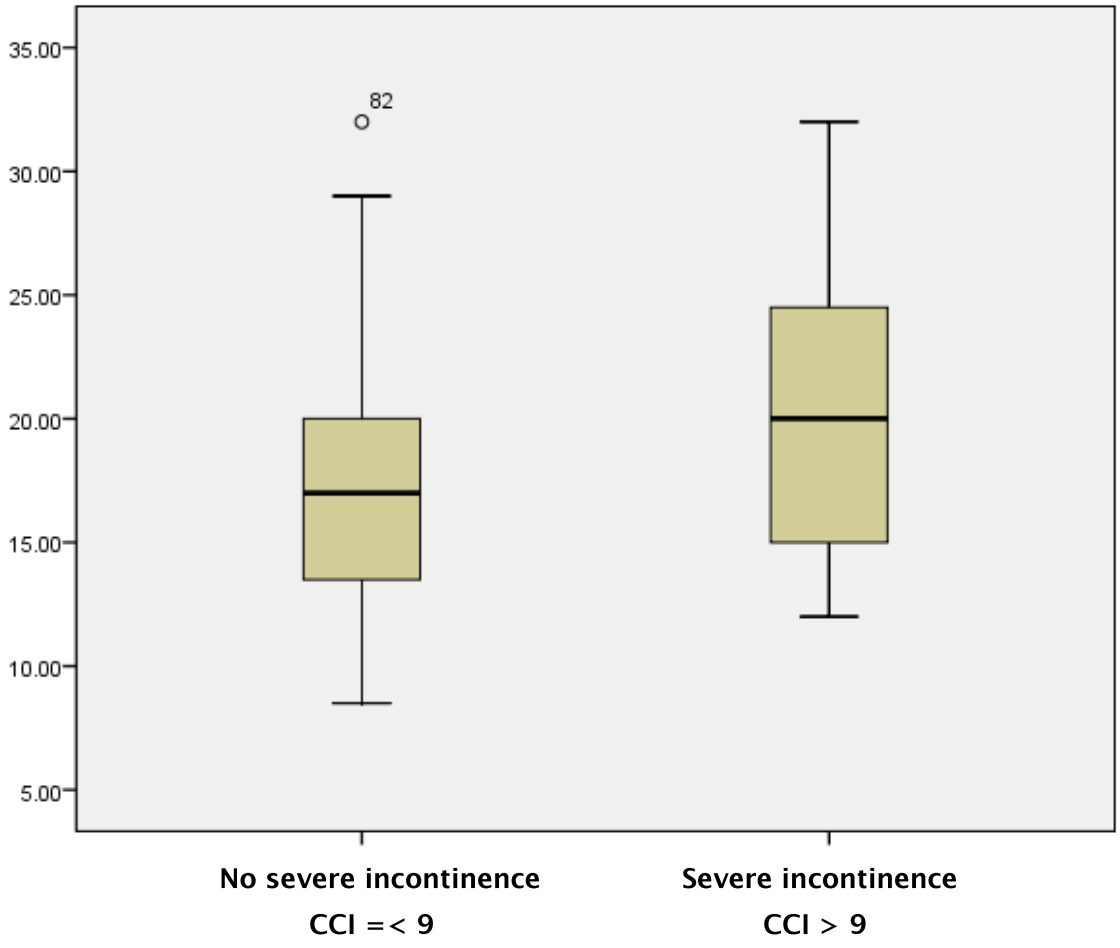
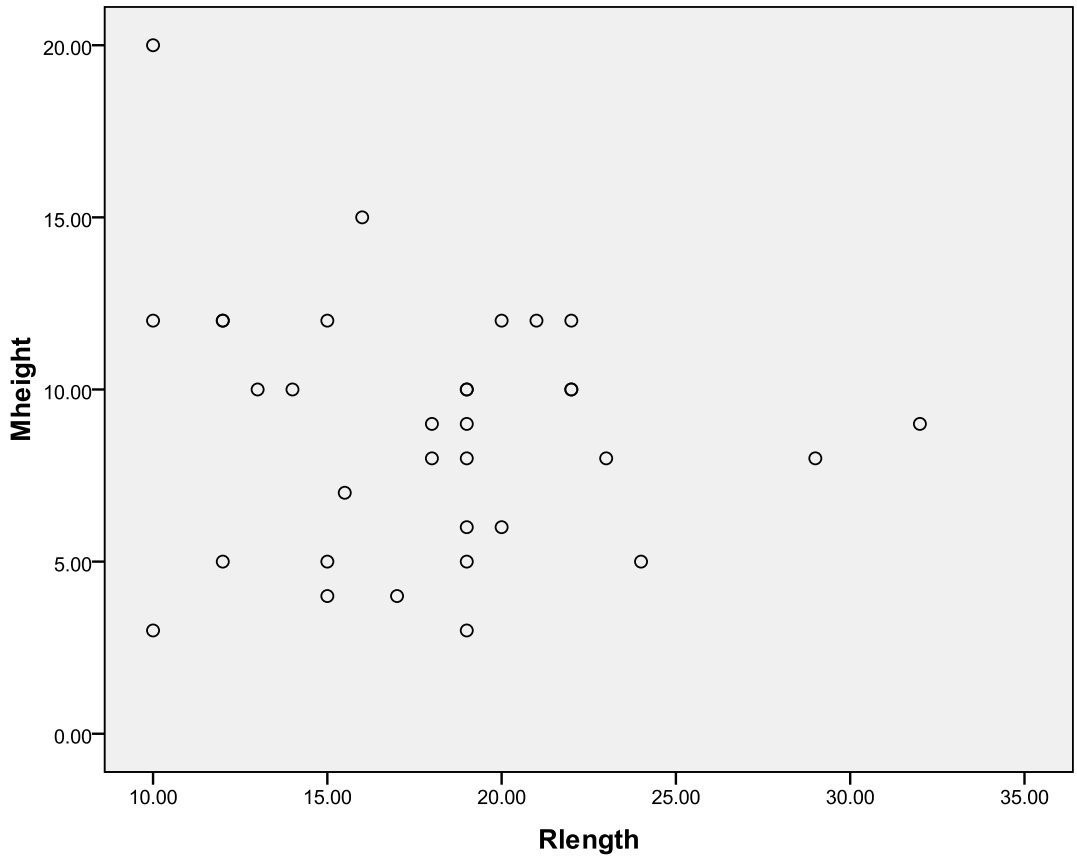


Figure 5.2.06 Scatter plot showing length of bowel resected (Rlength) against measured height of anastomosis (Mheight) (n=29)



Radiotherapy

An independent samples T-Test was used to compare the mean CCI at baseline and 3 months, with exposure to radiotherapy (Table 5.2.09).

Table 5.2.09 Mean CCI at baseline (preoperative) and 3 months postoperatively, split for exposure to radiotherapy

	N	Mean CCI	Standard deviation
CCI preop (radiotherapy exposure)	16	4.3	6.4
CCI preop (no radiotherapy exposure)	65	2.8	3.7
CCI postop (radiotherapy exposure)	16	8.2	6.4
CCI postop (no radiotherapy exposure)	65	4.7	4.5

When comparing radiotherapy (n = 16) versus no radiotherapy (n = 65), there was no mean difference in these two groups before surgery and exposure to radiotherapy (difference = 1.48, p = 0.225) (Figure 5.2.07). However there was a significant mean difference of 3.5 in CCI at 3 months after surgery (p = 0.013, 95%CI: 0.780 to 6.272) (Figure 5.2.08).

Figure 5.2.07 Preoperative CCI Scores in patients with no radiotherapy exposure and those with radiotherapy exposure

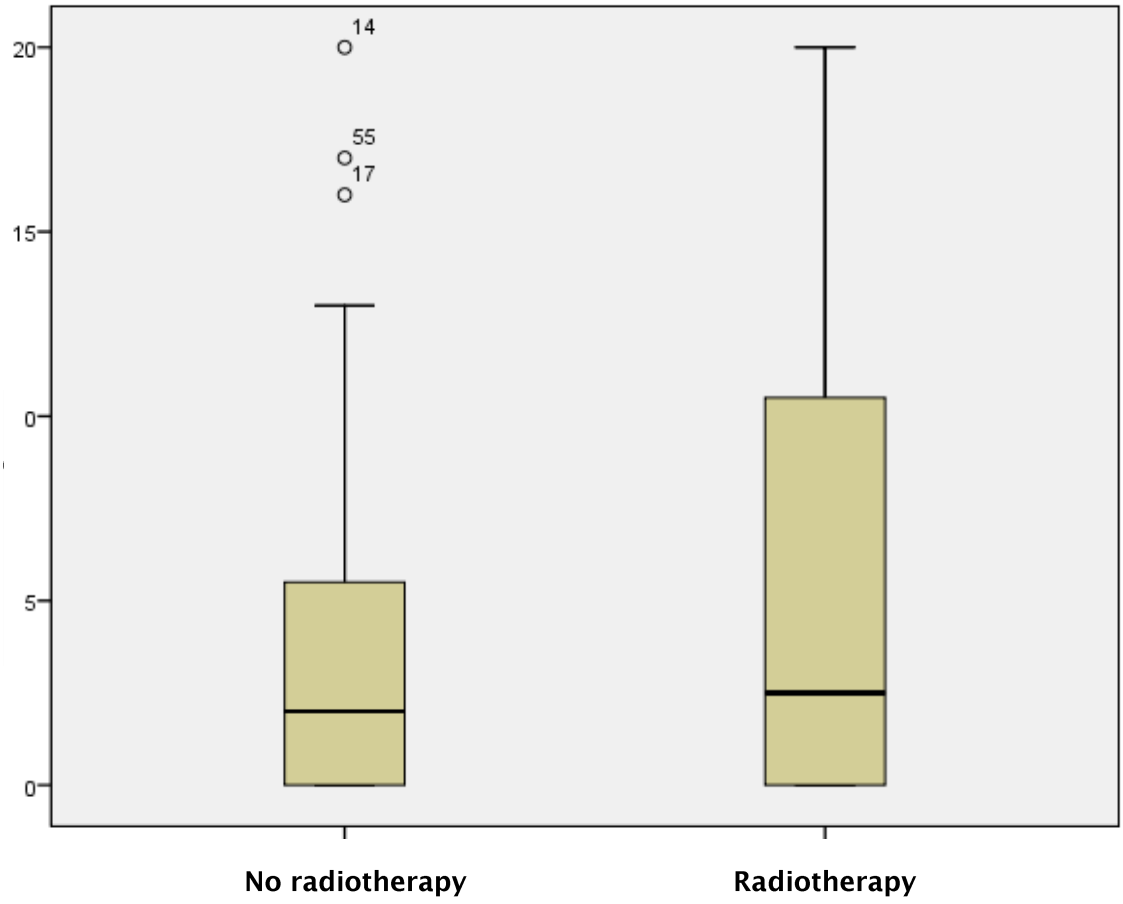
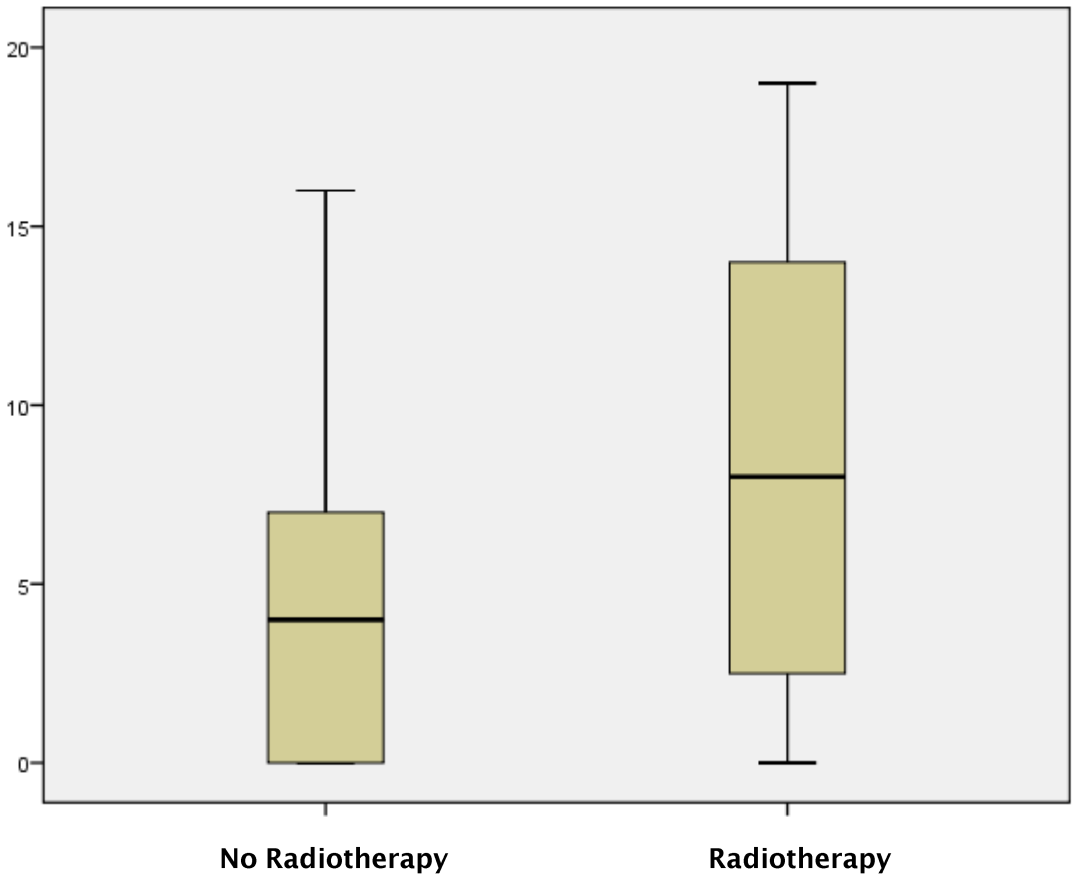


Figure 5.2.08 Postoperative CCI Scores in patients with no radiotherapy exposure and those with radiotherapy exposure



Using paired samples t-test to compare means of CCI baseline and 3 months split for radiotherapy exposure, the mean difference in CCI between 3 months and baseline was 1.8 (worsening of CCI) (P = 0.014, 95%CI: 0.38 to 3.29) in the no radiotherapy group. In the radiotherapy group, the mean difference in CCI between 3 months and baseline was 3.9 (worsening of CCI) (P = 0.044, 95%CI: 0.11 to 7.64)

After anterior resection, 17% (11/65) of patients who did not have radiotherapy reported incontinence (CCI>9), compared with 50% (8/16) who did have preoperative radiotherapy (Table 5.2.10). This difference was significant (difference=33%, 95% CI: 9% to 56%, P=0.007).

Table 5.2.10: Frequency table of clinical status by exposure to radiotherapy
Figures are number (percentage)

	Radiotherapy	No radiotherapy	TOTAL
Incontinence	8 (50%)	11 (17%)	**19**
No incontinence	8 (50%)	54 (83%)	**62**
TOTAL	**16 (100%)**	**65 (100%)**	**81**

5.2.3 Assessing for independent factors that predict poor anal continence

Logistic regression indicates that height of pathology (2.8x) (OR=0.22, 95% CI: 0.07 to 0.65, p=0.006) and exposure to radiotherapy (2.5x) (OR=0.20, 95% CI: 0.06 to 0.66, p=0.008) are significant predictors of incontinence at 3 months. However when the combined effect on postoperative incontinence was assessed, neither term was significant (pathology height p=0.14, radiotherapy exposure p=0.21). This result probably indicates that height of pathology and exposure to radiotherapy are not independent factors. Alternatively the sample size may be too small.

There is a significant linear relationship between postoperative CCI (CCI2) and exposure to radiotherapy (p = 0.013) which is described by the following equation:

CCI2 = 4.662 + 3.526 (radiotherapyYN)
95% CI 0.780 to 6.272

However when the combined effect of rectal anastomosis, radiotherapy exposure and preoperative anal continence (CCI1) were assessed with multiple linear regression, the only independent predictor of CCI2 was rectal anastomosis (b = 3.827, 95% CI: 1.276 to 6.378, p = 0.004) (Table 5.2.11). Patients with a rectal anastomosis had an increase in CCI of 3.8.

Table 5.2.11 Predicting CCI after anterior resection using multiple linear regression

Model	B	95% CI lower bound	95% CI upper bound	Significance
(Constant)	1.468	-0.805	3.741	0.202
CCI1	0.171	-0.071	0.414	0.163
Radiotherapy	2.153	-0.122	4.894	0.122
Rectal anastomosis	3.827	1.276	6.378	0.004

Discussion

Anorectal function is difficult to assess and quantify. It is important to measure the effect of anterior resection on anorectal function and to try to predict which patients will be at risk of a poorer outcome. A robust measuring stick is needed in the form of a validated symptom questionnaire with ranges for the general population.

Prospective studies assessing outcome after anterior resection often do not include preoperative quality of life and symptom assessment (Karanjia, et al., 1992). Interpretation of postoperative continence and quality of life therefore is more difficult because there is nothing to compare the postoperative scores with. In addition, normal ranges according to age for the Cleveland Clinic Incontinence Score are not available.

This study shows that before anterior resection anorectal function is compromised with 42% of patients reporting mild incontinence (CCI 1 to 9) and 9% of patients reporting severe incontinence (CCI>9). It is important to take this into account when interpreting postoperative anal continence. “Normal” anorectal function in a group of patients with rectal cancer is difficult to define as many of them will have altered bowel function due to their pathology. Using preoperative values as the baseline is likely to be better than asking the patient to retrospectively recall what their normal bowel function was but is certainly not ideal. This group of patients is likely to have worse baseline bowel function than an age-matched group who do not have bowel pathology.

Although anal incontinence improved in 27% of patients after surgery, it worsened in 51% by an average CCI score of 5.5 and 17% of patients developed new severe faecal incontinence when assessed 3 months after anterior resection. In those patients who developed severe anal incontinence after surgery, quality of life decreased in all domains although this did not reach significance.

Patients who had severe anal incontinence at baseline were almost 11 times more likely to still have severe anal incontinence after surgery than those who did not have severe incontinence preoperatively.

Women are at higher risk of anal incontinence than men due to injuries to the anal sphincter and pelvic floor during childbirth (Dudding, Vaizey, & Kamm, 2008). In this study 17% of men and 31% of women reported anal incontinence. Although a difference of 14% was observed between men and women, it was not significant. A larger study would be needed to confirm or refute this finding.

Age was not associated with anal incontinence, although population studies have shown that anal incontinence is commoner in elderly people (Perry et al., 2002). Preoperatively 40 patients had perfect anal continence (CCI=0), 34 patients had mild incontinence and 7 patients had severe incontinence. After surgery 18 (22%) patients maintained their preoperative level of continence. Anal continence improved in 22 (27%) with a range in CCI of 1 to 16 and a median 4, but deteriorated in 41(51%) patients (range 1 to 16 and a median of 5.5). There were 14 (17%) patients who developed severe incontinence postoperatively ($p<0.01$). In these patients quality of life (FIQL: Fecal Incontinence Quality of Life questionnaire) decreased in all domains postoperatively.

EORTC quality of life assessment demonstrated a deterioration in emotional functioning postoperatively ($p<0.05$) and a higher level of defaecatory problems ($p<0.01$).

Anorectal physiology showed a decrease in maximal rectal volume from 139ml (SD 59) to 106ml (SD 55) at 3 months postoperatively ($p<0.01$).

The functional outcome following anterior resection may be overlooked, as the main aim of surgery is usually cancer cure. Loss of anal continence has a negative effect on the patient's quality of life. Although the present study does include this information, the stress of imminent major surgery may depress preoperative scores and make interpretation of postoperative changes from baseline difficult to interpret. In this study, participants were assessed three months after anterior resection and 17% had developed a new symptom of severe anal incontinence which caused a negative impact on their quality of life. Participants who were exposed to radiotherapy had a 3-fold increased risk of severe anal incontinence, although it was not possible to determine whether this variable was independent of height of pathology.

5.3 Severity of anal incontinence during first year

In this section, trends in the first postoperative year are assessed for the participants who completed one year of follow-up. Table 5.5.4 summarises the baseline characteristics of these patients (n = 89). Participants with a poor functional outcome at one year were defined as those participants with severe anal incontinence (CCI 9 or greater) at one year. A good functional outcome was defined as CCI < 9 at one year. These two outcome groups were investigated for predictive factors.

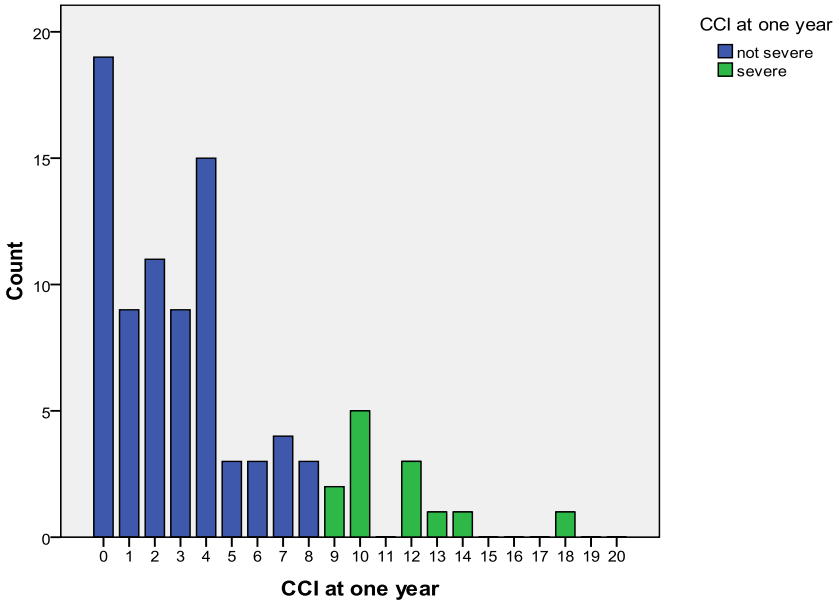
Results

Study procedures were carried out as described in Section 4.1.

5.3.1 Trends in severe anal incontinence

Figure 5.3.01 shows the count of CCI scores at one year in the analysed participants. Graphs showing individual trends in CCI at 3 monthly time intervals over the first year are included in Appendix XVa and b.

Figure 5.3.01 Summary showing count of CCI scores at one year after anterior resection (n = 89)



Although all of the 89 participants contribute to the preoperative and one year data, there is some loss of data at the 3, 6 and 9 month data collection times as shown in Table 5.3.01. Over the first postoperative year mean CCI rose to just over 5 and then returned to preoperative levels by one year. Before surgery 17% had severe anal incontinence. At 3 months 27% had severe anal incontinence and this fell to 15% at 12 months.

Table 5.3.01 Anal incontinence (CCI) over the first postoperative year (n = 89)
*Percentages given are "valid" percentages and therefore do not include missing data

	Preoperative	3 months	6 months	9 months	12 months
Mean CCI	3.9	5.3	4.7	4.9	4.0
SD	5.2	4.9	4.2	3.8	3.9
CCI severe	15 (17%*)	22 (27%)	16 (22%)	12 (17%)	13 (15%)
CCI not severe	74 (83%)	60 (73%)	57 (78%)	59 (83%)	76 (85%)
Missing data (count)	0	7	16	18	0

Table 5.3.02 shows the mean CCI scores over the first year for participants with a poor functional outcome at one year (n = 13). Table 5.3.03 shows the mean CCI score over the first year for participants who had a good functional outcome at 12 months.

Table 5.3.02 Mean CCI over the first year in participants who had a poor functional outcome at 12 months (n = 13)

	Mean	SD	Missing data (count)
CCI preoperative	4.8	6.6	0
CCI 3 months	11.0	5.2	1
CCI 6 months	9.9	3.6	5
CCI 9 months	11.1	3.2	3
CCI 12 months	11.5	2.5	0

Table 5.3.03 Mean CCI over the first year in participants who had a good functional outcome at 12 months (n = 76)

	Mean	SD	Missing data (count)
CCI preoperative	3.8	4.9	0
CCI 3 months	4.2	4.2	6
CCI 6 months	4.0	3.9	11
CCI 9 months	3.9	2.8	15
CCI 12 months	2.7	2.3	0

There was no significant or clinically relevant difference between preoperative CCI in participants who had severe incontinence at one year and those who didn't. However, after surgery there was a sustained and significant mean difference between these two groups which increased over the first year as shown in Table 5.3.04. Although participants in the good functional outcome group showed a small improvement in postoperative CCI, in the poor functional outcome group there was no improvement.

Table 5.3.04 Mean difference in CCI when comparing functional outcome at 12 months

Mean difference = (Good functional outcome group) – (Poor functional outcome group)

		95% Confidence Interval		
	Mean difference	Lower	Upper	P
CCI preoperative	-1.2	-5.3	2.9	0.543
CCI 3 months	-6.7	-10.1	-3.3	0.001
CCI 6 months	-5.8	-8.9	-2.8	0.002
CCI 9 months	-7.2	-9.6	-4.8	<0.001
CCI 12 months	-8.8	-10.3	-7.2	<0.01

The CCI score is comprised of 5 domains each of which is scored from 0 to 4 to give a final score with a maximum value of 20. Figure 5.3.02 shows the contribution of the five components of CCI to the final score. None of the participants had leakage of solid stool on a daily basis and some of the participants with severe incontinence did not have any incontinence to solid stool. The relative numbers of participants in the severe anal incontinence group can be seen to increase in all of the CCI domains as the scores worsen. Gas incontinence was fairly common even in participants without severe anal incontinence.

Figure 5.03.03 shows the components of CCI in the participants with severe anal incontinence. They all had some leakage of liquid stool. One participant did not wear pads at all and three participants did not think that their bowel symptoms affected their quality of life.

Figure 5.03.02 Components of CCI at one year

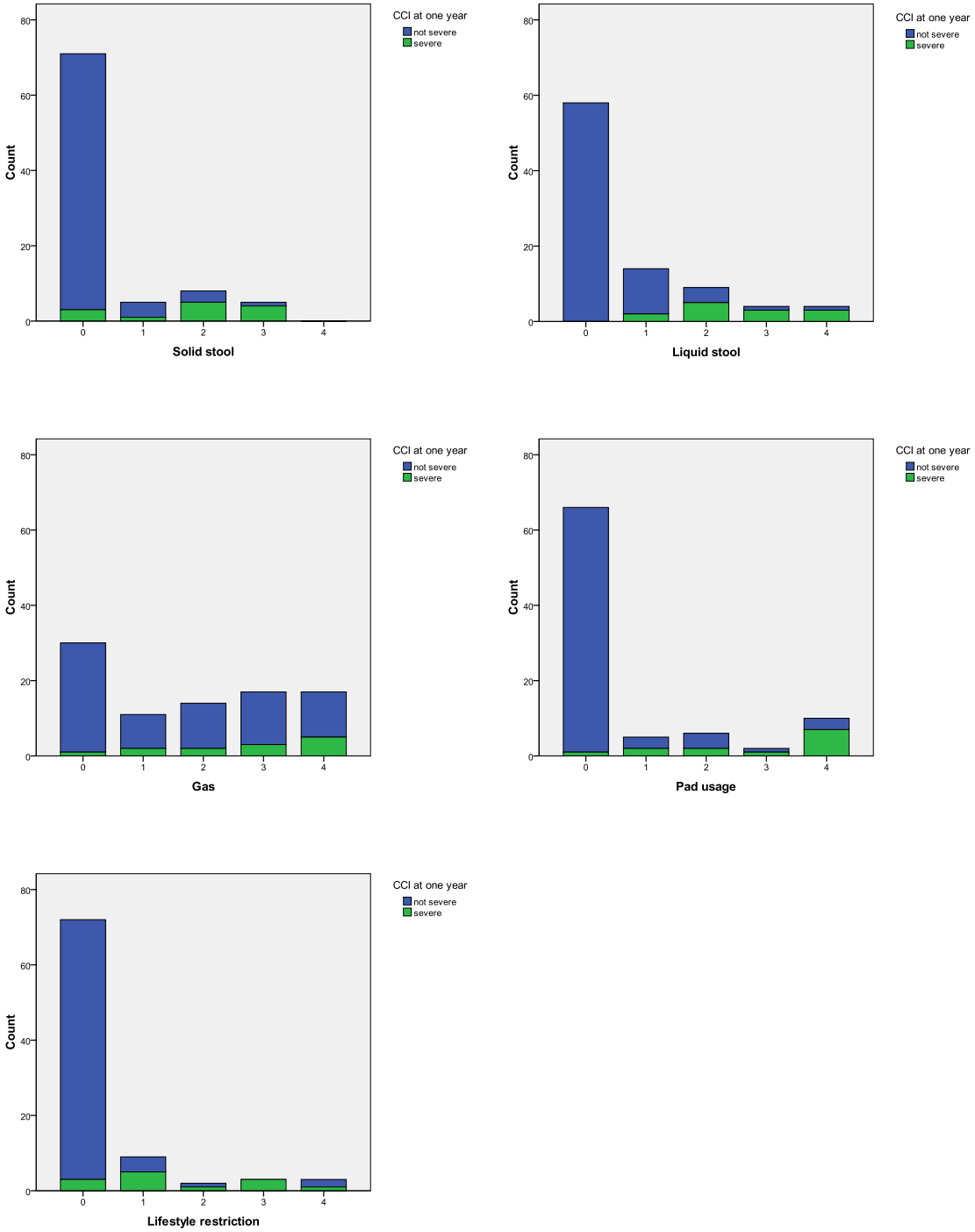
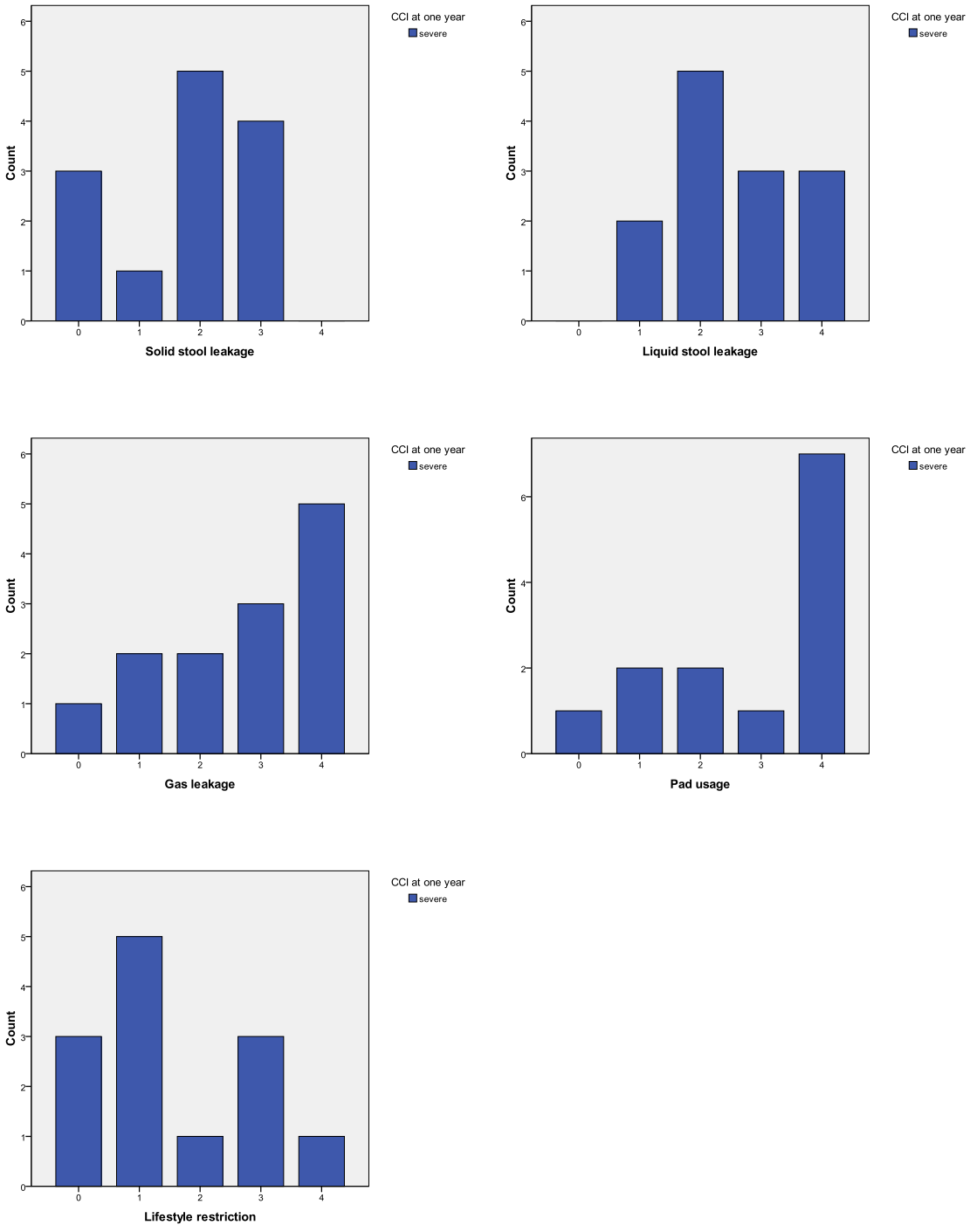


Figure 5.03.03 Components of CCI at one year in patients with severe anal incontinence (CCI >= 9)



5.3.2 **Predictive factors for severe anal incontinence at 1 year**

A Pearson Chi-squared test was used to investigate the strength of the relationship between severe CCI at baseline, 3 and 12 months. There were seven participants in the analysed group who did not have data collected at 3 months.

At baseline, 15 participants had severe anal incontinence and 4 (27%) still had severe incontinence at one year. However at one year, 11 (73%) participants had resolution of their severe incontinence. Severe incontinence developed in 9 (12%) of the participants who did not have severe incontinence at baseline (see Table 5.3.05). These differences were not significant ($p = 0.221$).

Forty-one percent of participants with severe CCI at 3 months also had severe CCI at one year and 95% of participants without severe CCI at 3 months had a good functional outcome (no severe CCI) at one year ($p < 0.01$). The sensitivity of severe CCI at 3 months for predicting a poor functional outcome (severe CCI) at one year is 75% and the specificity is 81% (Table 5.3.06). Logistic regression was used to adjust for the following factors: preoperative CCI, female gender, stoma presence and exposure to radiotherapy (Table 5.3.07). A highly significant relationship was found between severe CCI at 3 months and severe CCI at one year (B = -2.577, 95% CI: 0.015 to 0.391, P = 0.02). This relationship remained significant when adjusting for the other factors.

Table 5.3.05 Frequency Table showing Severe CCI at preoperative and one year (final)

(Missing data n = 0)

	Severe incontinence at one year	No severe incontinence at one year	Total
Severe incontinence preoperative	4 (27%)	11 (73%)	15 (100%)
No severe incontinence preoperative	9 (12%)	65 (88%)	74 (100%)
Total	13 (15%)	76 (85%)	89 (100%)

Table 5.3.06 Frequency Table showing Severe CCI at 3 months and one year (final)

(Missing data at 3 months n = 7)

	Severe incontinence at one year	No severe incontinence at one year	Total
Severe incontinence at 3 months	9 (41%)	13 (59%)	22 (100%)
No severe incontinence at 3 months	3 (5%)	57 (95%)	60 (100%)
Total	12 (15%)	70 (85%)	82 (100%)

Table 5.3.07 Relationship between severe CCI at one year and severe CCI at 3 months adjusting for female gender, exposure to radiotherapy, stoma reversal and biofeedback treatment

	B	95% Confidence Interval Lower	Upper	P
Severe CCI preoperative	-0.902	0.059	2.775	0.358
Severe CCI 3 months	-2.577	0.015	0.391	0.002
Female gender	0.914	0.440	14.142	0.302
Exposure to radiotherapy	0.664	0.306	12.324	0.481
Stoma reversal	-1.211	0.051	1.730	0.177
BFB treatment	-0.621	0.117	2.466	0.425

5.3.3 Operative details

This project was carried out when laparoscopic surgery was being introduced to Southampton General Hospital. In this series, 47 (53%) operations were carried out laparoscopically and of these 8 (17%) were converted to open. Open surgery was performed on 42 (47%) participants. There appeared to be a small advantage in favour of laparoscopic surgery in avoiding severe anal incontinence at 1 year but this was not significant (B = 0.213, 95% CI: 0.044 to 1.027, p = 0.054).

The configuration of the anastomosis was recorded in the operation note in 82 participants. It was end to end in 37 and side to end in 45. Although the odds ratio was in favour of a side to end anastomosis, this was not significant (B = 0.354, 95%CI 0.097 to 1.286, p = 0.115).

Discussion

A proportion of patients are known to have a poor functional outcome after anterior resection. In this study follow up data over the first postoperative year was available in 89 (74%) of participants recruited to a randomised trial.

Before surgery 15 (17%) participants reported severe anal incontinence. However the mean CCI for the whole group was four. Patients with rectal cancer might have a higher incontinence score due to the presence of the cancer which may alter stool consistency and rectal filling sensation. The mean CCI was worst at 3 months after surgery when it rose to 5, before returning to near baseline at 12 months. The number of participants with severe anal incontinence also peaked at 3 months (27%) before decreasing to baseline levels.

In this study, 27% of participants with severe anal incontinence at baseline still had severe incontinence at one year, but at 3 months, 41% of participants with severe anal incontinence had severe incontinence at one year.

The participants who had a poor functional outcome at one year were studied. Their preoperative incontinence scores were similar to those of participants with a good functional outcome. However the mean CCI scores at 3 months were much worse in the poor functional outcome group (CCI = 11) than in the good functional outcome group (CCI = 4). The mean difference between the two groups worsened over the first postoperative year suggesting that there is some improvement in the good function group but not in the poor function group. Severe CCI score at 3 months was the strongest predictor of a poor functional outcome after adjusting for severe CCI at baseline, female gender, stoma reversal and BFB treatment.

None of the participants reported daily leakage of solid stool after anterior resection. Uncontrolled passage of flatus was common in the groups with and without severe incontinence. A few patients scored highly in the pad usage and lifestyle restriction sections of the CCI score but did not have a total score of 9 or greater. This may represent particularly fastidious participants who wore a pad in case of a rare episode of leakage or who had relatively minor symptoms which impacted on their lifestyle excessively. In contrast three participants in the severe group did not feel that their symptoms restricted their lifestyle. It is likely that these participants were particularly well adjusted to their symptoms and were able to cope with really quite severe symptoms.

It is interesting to note that participants undergoing laparoscopic surgery had a tendency to less severe incontinence than those undergoing open surgery. A larger sample size is needed to demonstrate whether this is a significant result or not. Long-term advantages in quality of life associated with laparoscopic surgery have been difficult to demonstrate (Jayne et al., 2007), although in theory the improved view and precision of laparoscopic surgery may reduce injury to surrounding structures in the pelvis and preserve anal continence.

Anterior resection causes an acute worsening of anal incontinence. In the 3 monthly time intervals studied, this was maximal at 3 months but returned to baseline levels by one year. Although 17% reported severe anal incontinence before surgery, this rose to 27% at 3 months. One year after surgery 15% had severe anal continence.

5.4 Changes in bowel function during the first year after anterior resection

This project has focussed mainly on anal incontinence, but difficulties with rectal evacuation are also described by patients after anterior resection. In this section, changes in stool frequency, symptom severity scores and anorectal manometry over the first postoperative year are explored. Only participants who completed the study are included (n=89). In particular, groups of participants with and without severe anal incontinence (CCI >=9) and with and without constipation (EORTC-C30 Q16) are investigated.

Results

Study procedures were carried out as described in Section 4.1.

There were 13 participants with severe anal incontinence (CCI >= 9) and 76 with no severe anal incontinence (CCI < 9). There were 10 participants who complained of constipation “quite a bit” or “very much” (EORTC-C30 q16).

5.4.1 Stool frequency

The number of stools in 24 hours was recorded on question 1 of the MSKCC bowel function questionnaire as shown in Table 5.4.01. Preoperatively the mean stool frequency in 24 hours was 3.5 (SD 2.6) and this was similar in participants with and without severe anal incontinence. However significant differences were observed during the first year after surgery. There was a significant and clinically relevant difference in stool frequency between the two groups at both 3 months and 12 months. Participants with severe anal incontinence had a mean stool frequency of 5 compared to 3 in the group without severe anal incontinence ($p < 0.001$).

Table 5.4.01 showing stool frequency in 24 hours in participants with no severe anal incontinence at 1 year and participants with severe anal incontinence at 1 year

Anal incontinence at one year (CCI)		N	Mean stool in 24 hours	SD	Mean difference	Lower 95% CI	Upper 95% CI	p
Preop	**Not severe**	71	3.4	2.1	-0.89	-2.5	0.7	0.271
	Severe	12	4.3	4.6				
3 months	**Not severe**	68	3.4	2.0	-3.5	-5.0	-1.9	<0.001
	Severe	11	6.8	4.1				
6 months	**Not severe**	58	3.2	2.2	-2.6	-4.6	-0.6	0.012
	Severe	8	5.8	5.1				
9 months	**Not severe**	61	2.8	1.9	-1.8	-3.3	-0.2	0.025
	Severe	9	4.5	3.4				
12 months	**Not severe**	74	2.8	1.9	-2.4	-3.7	-1.1	<0.001
	Severe	12	5.2	2.9				

The EORTC-C30 questionnaire includes one question about constipation (question 16: “Have you been constipated?”) which is scored from 0 to 100 where zero means “not at all” and 100 means “very much”. There were 10 participants who reported “quite a bit” or “very much” in response to question 16 before surgery. Only one of these participants reported similar levels of constipation at one year after surgery. There were 10 (11%) participants who reported constipation at 12 months after surgery and 77 (89%) who did not. The mean constipation score was 15 (SD 25) before surgery and 20 (SD 29) at one year after surgery. This small difference is unlikely to be clinically relevant and was not significant (p = 0.138).

The group of participants with “quite a bit” or “very much” constipation (EORTC-C30 Q16) at 1 year was looked at in more detail. Before surgery the scores in these two groups were low (“not at all” or “a little”). After surgery there was a widening difference in constipation scores between these two groups with a mean difference of 50 and 75 at 6 and 12 months respectively (Table 5.4.02). This is a clinically relevant and

significant difference. There appears to be a group of participants who develop significant symptoms of constipation after anterior resection. Two of these participants also had severe anal incontinence at 1 year. There was no difference in 24 hour stool frequency between the group with high symptom levels of constipation at 1 year and those with low constipation scores at 1 year, using an independent T-test (mean difference 0.8, 95% CI: -0.7 to 2.3, p = 0.293).

Table 5.4.02 Comparing constipation scores (EORTC-C30 Q16) over the first year after anterior resection between participants with a high score at one year and a low score at one year

Constipation score (1year) EORTC-C30 question 16		N	Mean score Q16	SD	Mean difference	Lower 95% CI	Upper 95% CI	p
Preop	**High score**	10	30	33	17	-0.06	33	0.051
	Low score	77	13	24				
3 months	**High score**	10	40	38	27	10	43	0.002
	Low score	71	13	22				
6 months	**High score**	8	63	38	50	32	68	<0.001
	Low score	63	13	22				
9 months	**High score**	8	50	25	37	19	54	<0.001
	Low score	63	13	23				
12 months	**High score**	10	87	17	75	5	65	<0.001
	Low score	77	11	16				

The MSKCC bowel function questionnaire includes 2 questions on bowel function (question 4: “Do you feel like you have totally emptied your bowels after a bowel movement?” and question 6: “Do you have another bowel movement within 15 minutes of the last bowel movement?”). The replies are scored from 0 to 100 where zero means “always” and 100 means “never”. Because of the way these questions are phrased a high score for question 4 implies a poor outcome whereas a high score for question 6 implies a good outcome.

5.4.2 MSKCC Question 4: Bowel emptying

Small changes in bowel emptying were recorded with a mean value of 64 (SD 33) before surgery and 73 (SD 26) at 1 year after surgery. An independent T-test was used to compare mean scores of participants with high and low levels of constipation symptoms (EORTC C-30 Question 16). Data was missing from the 6 and 9 month data collection points making interpretation of the results difficult. But at 3 and 12 months significant differences were found with a mean difference in scores of 25 (Table 5.4.03).

At 12 months after surgery, the average score for bowel emptying suggests that participants in the constipation group “rarely” or “sometimes” felt as though they totally emptied their bowels after a bowel movement. Participants who did not report high levels of constipation as though like they had emptied their bowels after a bowel movement “most of the time”. However the 95% confidence intervals (8 to 42) are quite wide.

Table 5.4.03 Bowel emptying: Comparing scores for MSKCC Question 4 in participants with and without constipation (high symptom score on EORTC C30 Question 16 at 12 months after anterior resection)

Constipation score (1year) EORTC-C30 question 16		N	Mean score Q4	SD	Mean difference	Lower 95% CI	Upper 95% CI	p
Preop	**High score**	8	50	23	7	-17	32	0.565
	Low score	74	43	34				
3 months	**High score**	8	63	30	24	3	45	0.024
	Low score	72	38	28				
6 months	**High score**	7	54	30	12	-11	35	0.290
	Low score	63	41	29				
9 months	**High score**	8	50	19	13	-6	34	0.171
	Low score	61	36	28				
12 months	**High score**	10	60	24	25	8	42	0.004
	Low score	75	35	26				

Participants with severe anal incontinence at 12 months, also had worse bowel emptying (MSKCC question 4 score = 58) than those with no severe anal incontinence (MSKCC question 4 score = 35) and this difference was significant (95% CI: 8 to 38; p = 0.004).

5.4.3 MSKCC Question 6: Bowel movement within 15 minutes of last bowel movement

The scores for question 6 were 36 (SD 28) before surgery and 27 (SD 24) at 1 year after surgery. Overall there appears to be very little difference in these scores before and after surgery. Participants in the constipation group had similar scores to those not in the constipation group with a mean difference of 2 (95% CI: -17 to 22; p = 0.785).

However differences were found when the severe incontinence group was compared to the group with no severe incontinence. Using an independent T-test to compare means there was a significant difference in the scores to Question 6 at 1 year after surgery

Table 5.4.04). Participants in the severe incontinence group reported bowel movement within 15 minutes of the last bowel movement “always” or “most of the time”. Whereas, in the group with no severe anal incontinence, this symptom was reported “rarely”.

Table 5.4.04 Comparing scores for MSKCC Question 6 (“Do you have another bowel movement within 15 minutes of the last bowel movement?) for participants with and without severe anal incontinence (CCI score >= 9 at 12 months after anterior resection)

Anal incontinence (CCI)		N	Q6 score	SD	Mean difference	Lower 95% CI	Upper 95% CI	p
Preop	**Not severe**	71	70	29	14	-4	32	0.124
	Severe	12	56	32				
3 months	**Not severe**	69	63	30	21	4	38	0.017
	Severe	13	42	19				
6 months	**Not severe**	62	68	26	15	6	35	0.155
	Severe	7	54	17				
9 months	**Not severe**	60	69	24	22	5	40	0.014
	Severe	8	47	21				
12 months	**Not severe**	74	74	26	30	15	45	<0.001
	Severe	13	44	18				

5.4.4 Anorectal manometry

Maximum tolerable rectal volume was compared at baseline to values at 3 months and 12 months after anterior resection. A mean difference of 37ml and 19ml was found at 3 and 12 months respectively (p = 0.013) (Table 5.4.05). Maximum tolerable rectal volume falls after anterior resection and this may result in a more hypersensitive rectum with a smaller capacity. Although the values for maximum tolerable rectal volume are reduced after anterior resection, they do not fall into an abnormal range.

Table 5.4.05 Showing changes in maximal tolerable rectal volume after anterior resection

Maximum tolerable rectal volume	N	Mean volume (ml)	SD	Mean difference (ml)	Lower 95% CI	Upper 95% CI	p
Baseline	66	138	60	37	23	51	<0.001
3 months	66	101	55				
Baseline	72	135	61	19	4	33	0.013
12 months	72	116	66				

Maximal tolerable rectal volume was compared in participants with and without severe anal incontinence at one year. Those with severe anal incontinence had a tendency to lower maximal tolerable rectal volumes but this did not reach statistical significance (Table 5.4.06).

Table 5.4.06 comparing maximum tolerable rectal volume in participants with and without severe anal incontinence at one year

Anal incontinence CCI at one year		N	Mean volume (ml)	SD	Mean difference (ml)	Lower 95% CI	Upper 95% CI	p
Baseline	**Severe**	13	108	31	-31	-67	5	0.093
	Not severe	76	139	64				
3 months	**Severe**	10	73	42	-33	-70	3	0.074
	Not severe	56	106	55				
1 year	**Severe**	12	83	38	-40	-81	0.3	0.052
	Not severe	60	123	68				

Participants with constipation (EORTC-C30 Q16) at one year were assessed for differences in maximum tolerable rectal volume over the first postoperative year. Before surgery, the volumes were similar. The mean difference was greatest at 3 months (39ml, 95%CI: -0.77 to 80, p = 0.054).

There were 76 participants with an intact RAIR before surgery and 11 with no RAIR. Amongst the participants with preoperative RAIR, 17 (22%) had preserved RAIR at both 3 and 12 months after surgery, 10 (13%) had an absent RAIR at 3 and 12 months, 16 (21%) had return of RAIR at 12 months and 13 (17%) were equivocal. The relationship between severe incontinence (CCI>=9) and constipation (EORTC-C30 Q16) at 12 months after surgery and the presence of RAIR at 3 and 12 months after surgery was explored using logistic regression. No significant relationships were found as summarised in Tables 5.4.07 and 5.4.08.

Table 5.4.07 Relationship between severe incontinence (CCI>=9) and constipation (EORTC-C30 Q16) at 12 months after surgery and the presence of RAIR at 3 months

		RAIR at 3 months		OR (95% CI)	p
		absent	present		
Severe CCI	**no**	25	33	0.504 (0.125 to 2.029)	0.335
	yes	6	4		
Constipation	**no**	26	33	0.506 (0.100 to 2.550)	0.409
	yes	5	4		

Table 5.4.08 Relationship between severe incontinence (CCI>=9) and constipation (EORTC-C30 Q16) at 12 months after surgery and the presence of RAIR at 12 months

		RAIR at 12 months		OR (95% CI)	p
		absent	present		
Severe CCI	**no**	25	34	1.781 (0.408 to 7.777)	0.443
	yes	5	7		
Constipation	**no**	26	38	0.474 (0.094 to 2.389)	0.366
	yes	4	3		

The relationship between severe anal incontinence and the location of the anastomosis relative to the peritoneal reflection was explored. Logistic regression indicates that an anastomosis below the peritoneal reflection (p = 0.048) is a strong predictor of severe anal incontinence (OR= 8.2, 95% CI: 1.0 to 66.9). The odds of severe anal incontinence in participants with a rectal anastomosis is 8 times as great as participants with a higher anastomosis. The position of the anastomosis relative to the peritoneal reflection was not a predictor of constipation (EORTC-C30 Q16). Table 5.4.9 shows the relationships between presence or absence of a rectal anastomosis and severe anal incontinence and constipation.

Table 5.4.9 Exploring the relationship between severe anal incontinence (CCI>=9) or constipation (EORTC-C30 Q16) and rectal anastomosis (peritoneal reflection included in pathology specimen)

		Anastomosis		OR (95% CI)	p
		above	below		
Severe CCI	**no**	31	45	8.267 (1.022 to 66.880)	0.048
	yes	1	12		
Constipation	**no**	26	53	0.327 (0.085 to 1.261)	0.105
	yes	6	4		

There were significant differences in anal manometry before and after surgery. Mean resting pressure was lower after surgery (p < 0.001) (Table 5.4.10) but mean squeeze pressure was not altered.

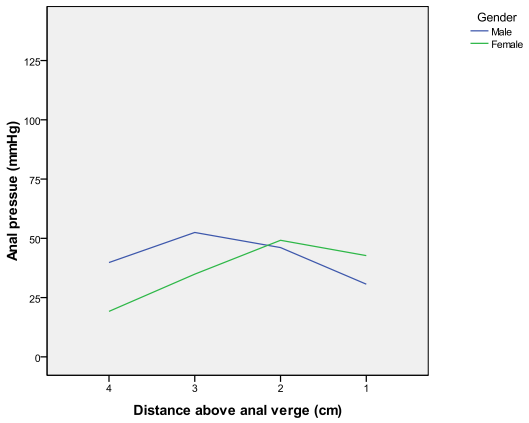
Table 5.4.10 Changes in resting pressures within the anal canal after anterior resection at 3 and 12 months

		n	Mean	SD	Mean difference	95% CI Lower	Upper	p
Max MRP	Preop	68	60	20	13	8.7	17.8	<0.001
	3 months		47	17				
Max MRP	Preop	72	60	21	16	12.1	20.9	<0.001
	12 months		43	17				
Mean MRP	Preop	68	40	15	10	7.1	13.9	<0.001
	3 months		30	12				
Mean MRP	Preop	72	40	14	12	8.6	15.0	<0.001
	12 months		28	11				

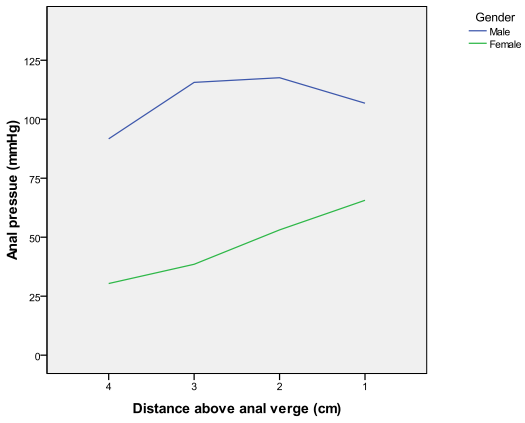
Mean resting pressure profiles along the first 4cm of the anal sphincter are different in men and women (Figure 5.4.01). In women the peak in anal pressures is at 2cm whereas in men it is at 3cm. After surgery the male profile looks more like the female one with the peak in mean resting pressures at 2cm.

Figure 5.4.01 Longitudinal mean anal canal pressures before surgery, and at 3 & 12 months after surgery

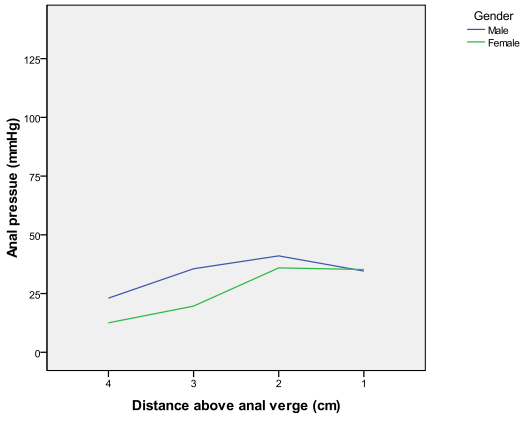
Mean resting pressure before surgery



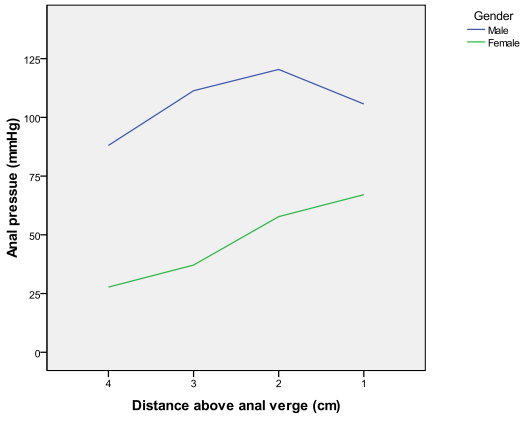
Mean squeeze pressure before surgery



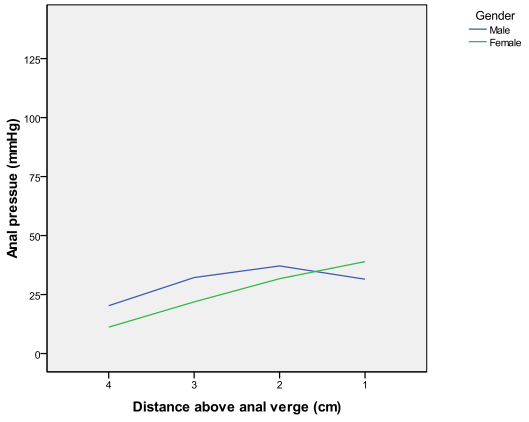
Mean resting pressure at 3 months



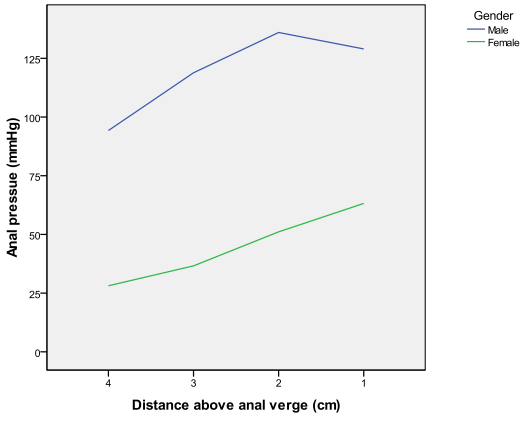
Mean squeeze pressure at 3 months



Mean resting pressure at 12 months



Mean squeeze pressure at 12 months



Discussion

The present study has focussed mainly on faecal incontinence after anterior resection, however the evidence in this chapter is that a significant group of participants also complained of difficulty with "constipation". There were 10 (11%) participants who complained of constipation ("quite a bit" or "very much") on EORTC-C30 Q16 at one year. This group of participants had a similar constipation score before surgery to those who did not complain of constipation at one year. This suggests that these participants developed constipation after their surgery rather than it being a pre-existing condition.

The definition of severe anal incontinence as CCI>=9 has been previously validated (Rothbarth, et al., 2001). Although extensively validated, the EORTC-C30 Q16 is rather ambiguous. It asks "Have you been constipated?" The term "constipation" is often used to describe a wide spectrum of symptoms including infrequent stools, hard stools, difficulty with rectal evacuation and sensation of incomplete emptying. Further information on symptoms relating to constipation could have been gathered by the addition of constipation specific questionnaires such as PAC-SYM (Frank, Kleinman, Farup, Taylor, & Miner, 1999) and PAC-QOL (Marquis, De La Loge, Dubois, McDermott, & Chassany, 2005). In the present study, data on rectal evacuation was collected in the MSKCC bowel function questionnaire. This is quite a difficult questionnaire for people to use as the questions are not phrased consistently. For example a high score on Q4 implies a poor outcome whereas a high score for Q6 implies a good outcome. This was observed to lead to confusion for some participants completing the questionnaire and may result in inconsistent results.

Participants with severe anal incontinence had a higher stool frequency than those without severe anal incontinence but there was no difference in stool frequency between those with and without constipation at one year. Bowel emptying was assessed by the MSKCC Q4 but only small changes were recorded after surgery and a larger sample size would be needed to determine if there was clinically relevant difference.

At 12 months after surgery, the average score for bowel emptying suggests that participants in the constipation group "rarely" or "sometimes" felt as though they totally emptied their bowels after a bowel movement. Participants who did not report high levels of constipation felt as though like they had emptied their bowels after a bowel movement "most of the time". Participants in the constipation group did not have lower stool frequency but did report incomplete evacuation to a greater degree.

However the 95% confidence intervals (8 to 42) are quite wide and more data are needed to determine whether the mean difference really is large enough to be clinically relevant.

There was a significant and clinically relevant difference in MSKCC Q6 scores (Do you have another bowel movement within 15 minutes of your last bowel movement?) between participants with and without severe anal incontinence Participants with severe anal incontinence reported return trips to the toilet within 15 minutes of a bowel movement “always” or “most of the time”. In contrast, participants without severe anal incontinence reported this symptom rarely.

Maximum tolerable rectal volume was compared at baseline to values at 3 months and 12 months after anterior resection. A mean difference of 37ml and 19ml was found at 3 and 12 months respectively ($p = 0.013$).

Maximum tolerable rectal volume falls after anterior resection ($p = 0.013$) and this may result in a more hypersensitive rectum with a smaller capacity. Although the values for maximum tolerable rectal volume are reduced after anterior resection, they do not fall into an abnormal range. However the confidence intervals are quite wide for the mean difference between preoperative and postoperative values. If the mean difference did fall at the upper limit of the 95% confidence intervals then it would be clinically relevant with values outside the normal range.

Participants with severe anal continence had lower maximal tolerable rectal volumes after surgery but this did not reach statistical significance. In this study an intact RAIR was not essential for anal continence. Anastomosis below the peritoneal reflection was found to be associated with a worse outcome for severe incontinence but not for constipation.

Surgery had a marked effect on lowering resting pressures but squeeze pressures were not affected. Serial pressure profiles of the anal canal showed a peak in resting pressures at 3cm in men but at 2 cm in women. After surgery the resting pressure profiles of the men looked more like the profile in women with the peak in pressures at 2cm. The squeeze pressure in men was significantly higher than in women, but there was no obvious change with surgery.

After anterior resection a significant group of participants complained of a change in their bowel habit with severe anal incontinence in 15% and constipation in 11% at one year. These patients can be investigated further with anorectal manometry and proctography to identify why this may be occurring and to target further treatment.

5.5 Estimating anastomotic height from tumour height and resection margin

The height of the anastomosis from the anal verge may be an important predictor of functional outcome after anterior resection. Previous studies have shown that a low anastomosis is associated with a worse functional outcome (Lee & Park, 1998; Lewis et al., 1995).

In Southampton, anastomotic height is not routinely measured during the surgical procedure, so limited data were available on measured anastomotic height (M height). As it may be an important predictor of functional outcome, a method for estimating anastomotic height was investigated. Length of bowel resected (R length), distal resection margin (R margin) and inclusion of peritoneal reflection are all recorded in the pathology report. Height of pathology (T height) was recorded preoperatively.

It was hypothesised that subtracting the length of the distal resection margin from the tumour height, would give an estimate of anastomotic height. In addition to the length of bowel below the tumour (distal resection margin) some additional bowel is removed in the stapling device. There is also some shrinkage of the specimen during the fixative process prior to histopathological reporting.

Results

Study procedures were carried out as described in Section 4.1.

Height of the tumour above the anal verge was recorded preoperatively in all participants. Length of bowel resected (R length) and distal resection margin (R margin) was extracted from the pathology report (Table 5.5.01). Anastomotic height measured at the time of surgery (M height) was recorded in 33 participants but only 29 of these also had the distal resection margin recorded on pathology. These 29 participants were studied further to estimate height of anastomosis (Table 5.5.02 and 5.5.03).

Table 5.5.01 Measurements for anastomotic height

	n	Distance in cm	Range
Tumour height (T height)	120	15	4 - 30
Distal resection margin on pathology report (R margin)	103	2.8	0 - 10
Measured anastomotic height (M height)	33	8.8	3 - 20
Resection length (R length)	117	19.5	8.5 - 62

Table 5.5.02: Raw data from anastomotic height estimation ordered by measured height of anastomosis

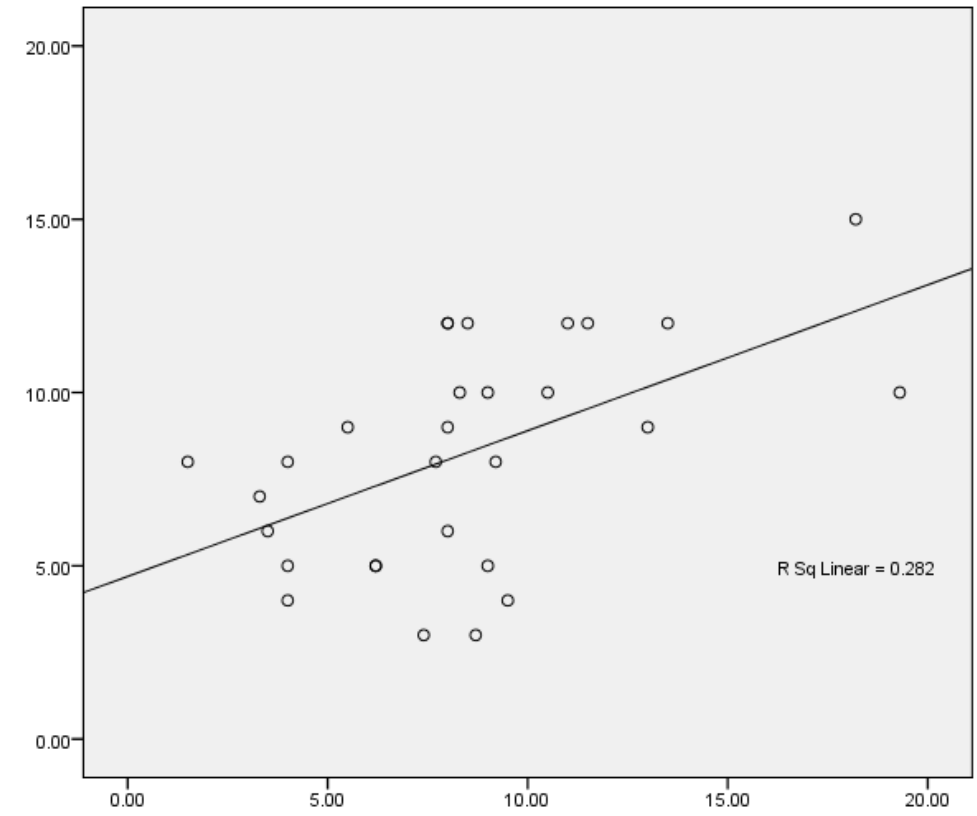
ID	Tumour height	Distal resection margin on pathology report	Measured height of anastomosis	Resection length
1	10	1.3	3	10
120	8	0.6	3	19
21	5	1	4	15
67	12	2.5	4	17
89	7	3	5	19
117	7	0.8	5	12
119	7	0.8	5	24
124	10	1	5	15
86	10	2	6	19
115	4	0.5	6	20
116	5	1.7	7	15.5
87	8	4	8	19
93	8	0.3	8	23
94	8	6.5	8	29
118	10	0.8	8	18
61	15	2	9	18
90	10	4.5	9	19
108	10	2	9	32
45	20	0.7	10	13
75	12	1.5	10	19
92	10	1	10	22
110	10	1.7	10	19
47	15	4	12	10
54	15	3.5	12	12
73	12	3.5	12	12
91	12	4	12	21
95	10	2	12	20
126	15	1.5	12	22
65	20	1.8	15	16

Table 5.5.03 Anastomotic height measurement and estimation in 29 participants

	Distance in cm	SD	Range
Tumour height (T height)	11	4.0	4 - 20
Distal resection margin on pathology report (R height)	2.1	1.5	0.3 – 6.5
Resection length (R length)	19.5	1.7	8.5 - 62
Measured anastomotic height (M height)	8.0	3.2	3 - 15
Estimated anastomotic height (E height)	8.2	4.1	5.3 – 12.8

The relationship between predicted anastomotic height (T height – R margin) and measured anastomotic height (M height) was explored (See Figure 5.5.01).

Figure 5.5.01 Scatter diagram showing estimated anastomotic height (height of pathology (T height) – distal resection height (R height)) plotted against measured height

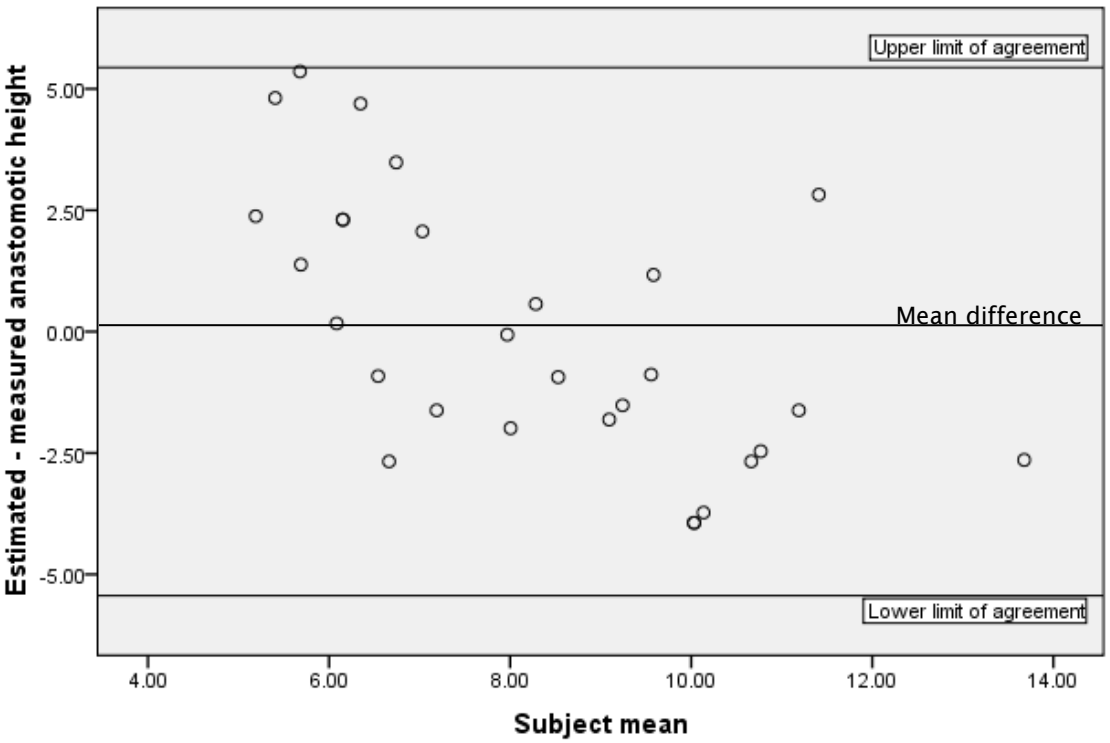


Simple linear regression indicates that there is a positive linear relationship (b=0.421, P=0.003, 95% CI: 0.156 to 0.686) between estimated anastomotic height and M height, which is described by the following equation:

Estimated anastomotic height = 4.7 + 0.4 (T height – R height)

The mean difference is close to zero. The 95% limits of agreement are shown in Figure 5.5.02. The estimated height is expected to be between 5.44cm above or below the measured height for 95% of patients, assuming the distribution of differences is approximately Normal.

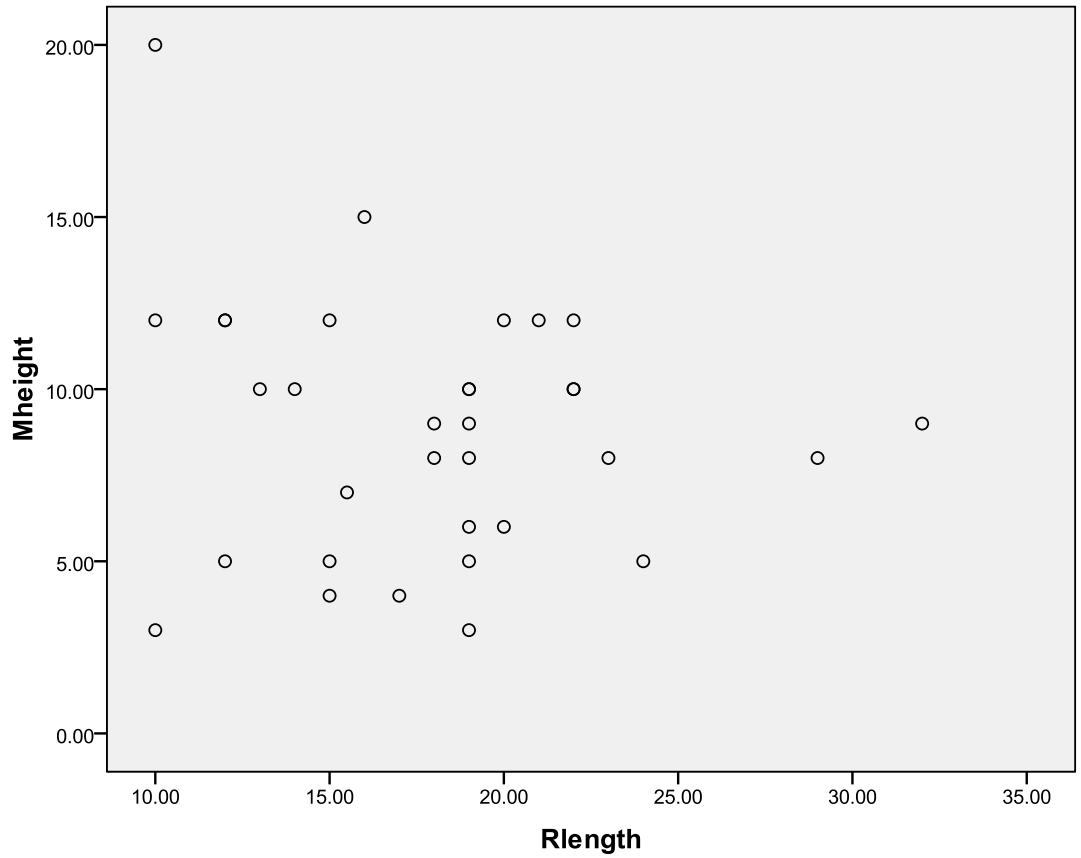
Figure 5.5.02 Bland-Altman Plot showing difference between estimated and measured height plotted against their mean



A test of significance using the correlation coefficient shows that there seems to be a relationship between the difference and mean (r = 0.53, P = 0.003). However this apparent negative trend is driven by a few key points and may be due to these influential observations rather than a true relationship.

The length of bowel resected is independent of the anastomosis height as shown in the scatter plot Figure 5.5.03.

Figure 5.5.03 Scatter plot showing length of bowel resected against measured height of anastomosis (n=29)



Discussion

On the basis of these data, it cannot be concluded that estimated height is a reliable surrogate to replace measured height. The estimated height is expected to be between 5.44cm above or below the measured height most patients. A method for estimating anastomotic height would need a greater accuracy than this as it is important to classify how much of the rectum remains after surgery. In particular the estimation of anastomotic height should be able to locate which third of the rectum it is sited in, that is lower third (first 5cm), mid third (5 to 10 cm) or upper third (10 to 15cm from anal verge).

Measurement of height of pathology is noted for its inaccuracy. It is extremely difficult to measure the length of a stretchy tube of bowel within the bony pelvis in a reliable and accurate manner. Likewise measuring the anastomotic height is also difficult. Looking at the raw data in Table 5.5.02, these difficulties are well-illustrated with several examples of measured anastomotic height being the same as the measured tumour height. Looking at the distal resection margin it is clear that this was not the case. Either measured height of the tumour or height of the anastomosis is inaccurate, or there may be errors with both.

The average length of bowel resected was 19.5cm (range 8.5 to 62cm). The amount of bowel removed is dependent on intraoperative factors. The main priority is to get below the tumour without having to remove the anal sphincter. The amount of distal bowel removed depends largely on the blood supply to the remaining bowel and trying to achieve sufficient length to form a tension-free anastomosis. The finding that the length of bowel resected is not related to height of anastomosis is expected.

For this project, the position of the anastomotic height will be measured from the anal verge where available in the participants who completed follow up (n = 22). Where the resected specimen does not contain peritoneal reflection, the participant will be classified as having a high anastomosis (n = 32) and a correlation with length of resection will be carried out. In a further 57 patients the peritoneal reflection was included in the resection specimen and therefore they must have a rectal anastomosis.

5.6 Barium versus MR Proctography

After anterior resection a considerable number of patients have disordered defaecation as a result of their surgery. Imaging of these patients during simulated rectal evacuation may distinguish between structural and functional causes. However, all measures whether using radiological techniques or an expulsion test, only simulate rectal evacuation. The natural process of defaecation is more complicated and involves coordination of colonic propulsion waves with abdominal and diaphragmatic effort in addition to the final event of rectal emptying.

A Japanese study carried out on 62 patients who had undergone rectal resection, found that barium proctography was useful in evaluating defaecatory disorders (Morihiro, et al., 2008). They studied 62 patients who had undergone anterior resection and found that participants who were able to evacuate over 55% of the rectal contrast had a significantly lower CCI score, less soiling and less urgency.

Results

Several imaging techniques are available for assessing rectal evacuation. This study aims to compare Barium (BaP) and MR proctography to identify whether there are any differences between the findings from these two techniques for assessing simulated defaecation. The most appropriate test will be recommended for investigating patients with abnormal defaecation after anterior resection.

This study was carried out as described in the Methods Section 4.2. Summary data from the 42 study participants is presented in Appendix XVI.

5.6.1 Participant recruitment

Between 8 May 2008 and 11 December 2009, this study invited 216 patients (202 female and 14 male) to participate (Figure 5.6.01). At the appointment for Barium proctography, 71 participants were recruited and 42 of these completed the study by attending for MR proctography. The remaining 29 patients withdrew from the study. Participant characteristics are shown in Table 5.6.01

Figure 5.6.01 Flow Chart showing participant recruitment and completion of the study

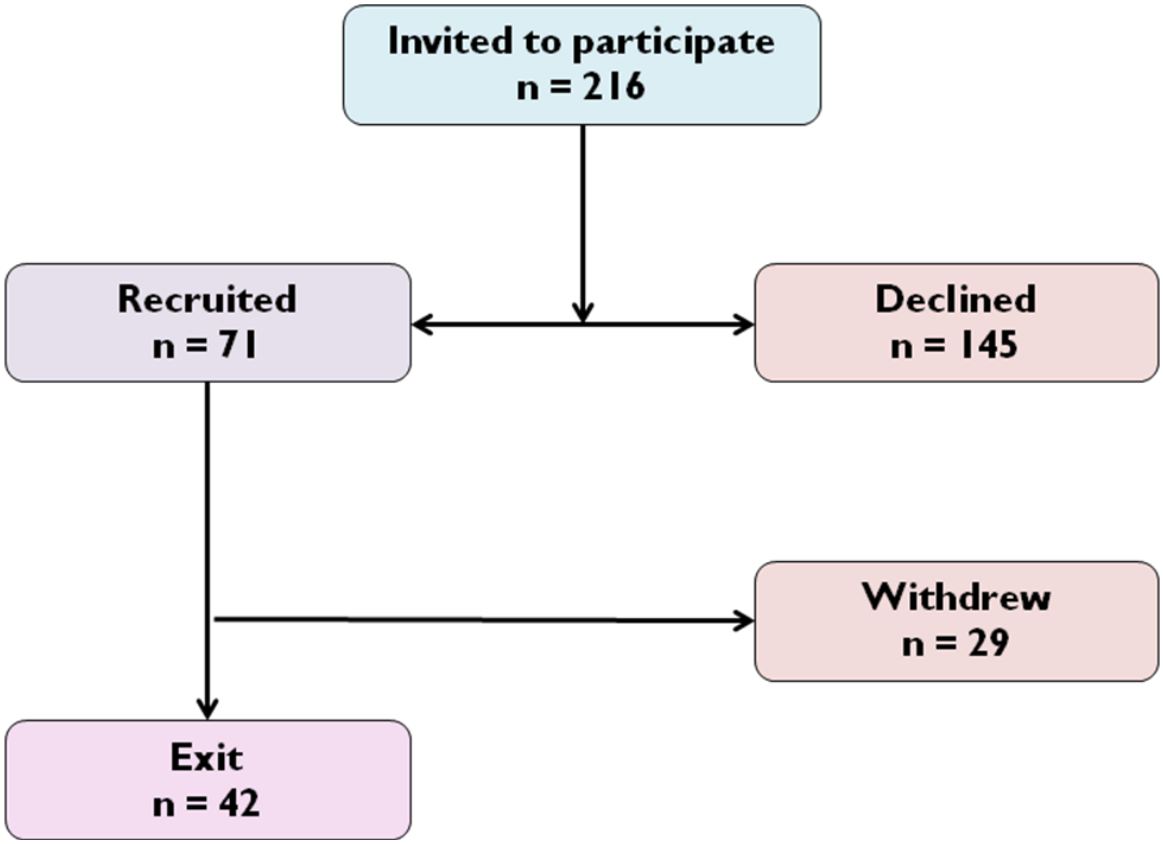


Table 5.6.01: Participant characteristics

Mean Age (range) years	59 (37 – 76)
Sex ratio FEMALE : MALE	38 : 4

5.6.2 Proctogram results

Rectoceles were extremely common and present in almost all participants on both BaP and MR proctography. The measure of agreement on presence of rectocele was substantial (Kappa 0.690) (Table 5.6.02). Rectocele length ranged up to 5.95cm on BaP and 6.20cm on MR proctography. The mean rectocele length was 3.10cm (SD 1.44) on BaP and 2.90cm (SD 1.60) on MR proctography.

Table 5.6.02 Agreement between presence of rectocele on BaP and MR proctography

	No rectocele (MR proctogram)	**Rectocele** (MR proctogram)	**Total**
No rectocele (BaP)	4	0	**4**
Rectocele (BaP)	3	35	**35**
Total	**7**	**38**	**42**

The mean difference in rectocele length measured on BaP and MR proctography was 0.20 (95% CI: -0.23, 0.63; p = 0.35). This difference is not clinically relevant. Figure 5.6.02 is a scatter plot showing rectocele length on BaP and MR proctography with a line of equivalence. To show the mean difference in rectocele length (BaP - MR proctography) against their mean for 38 participants, a Bland-Altman Plot was constructed (Figure 5.6.03). The mean difference was 0.2cm with standard deviation 1.3cm. The Bland-Altman plot shows that 95% of the differences in rectocele length measured on BaP and MP lie between 2.8 and -2.4cm (mean +/- 2 x standard deviation). The difference for an individual would be between -2.4 and 2.8cm.

Figure 5.6.02 Scatter plot showing rectocele length on BaP (B R length) and MR proctography (M R length) with line of equivalence

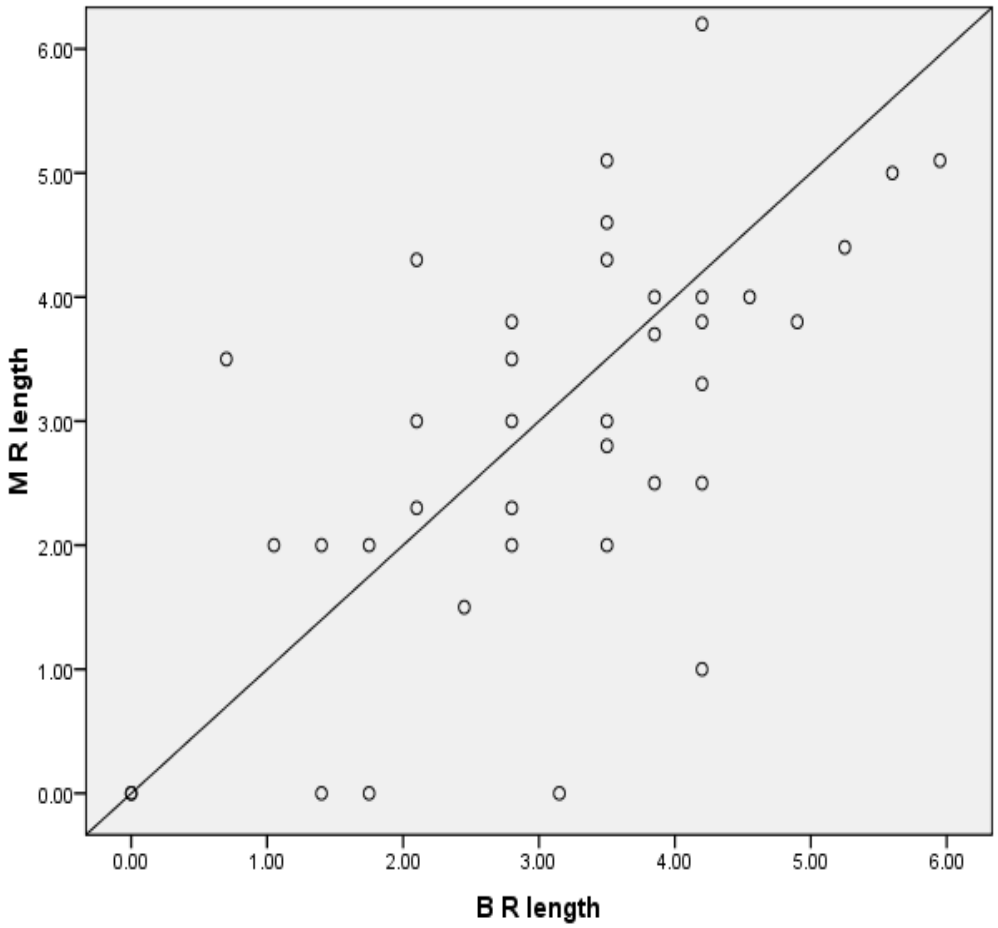
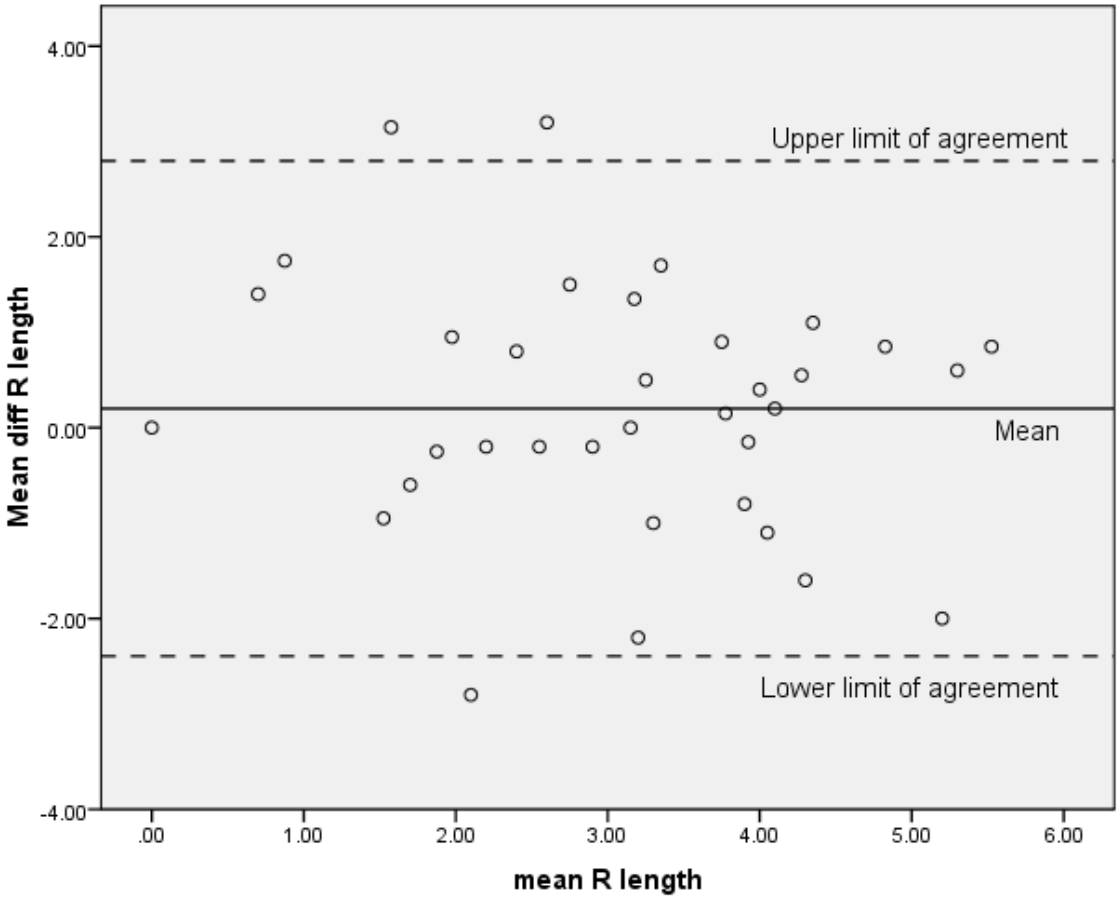
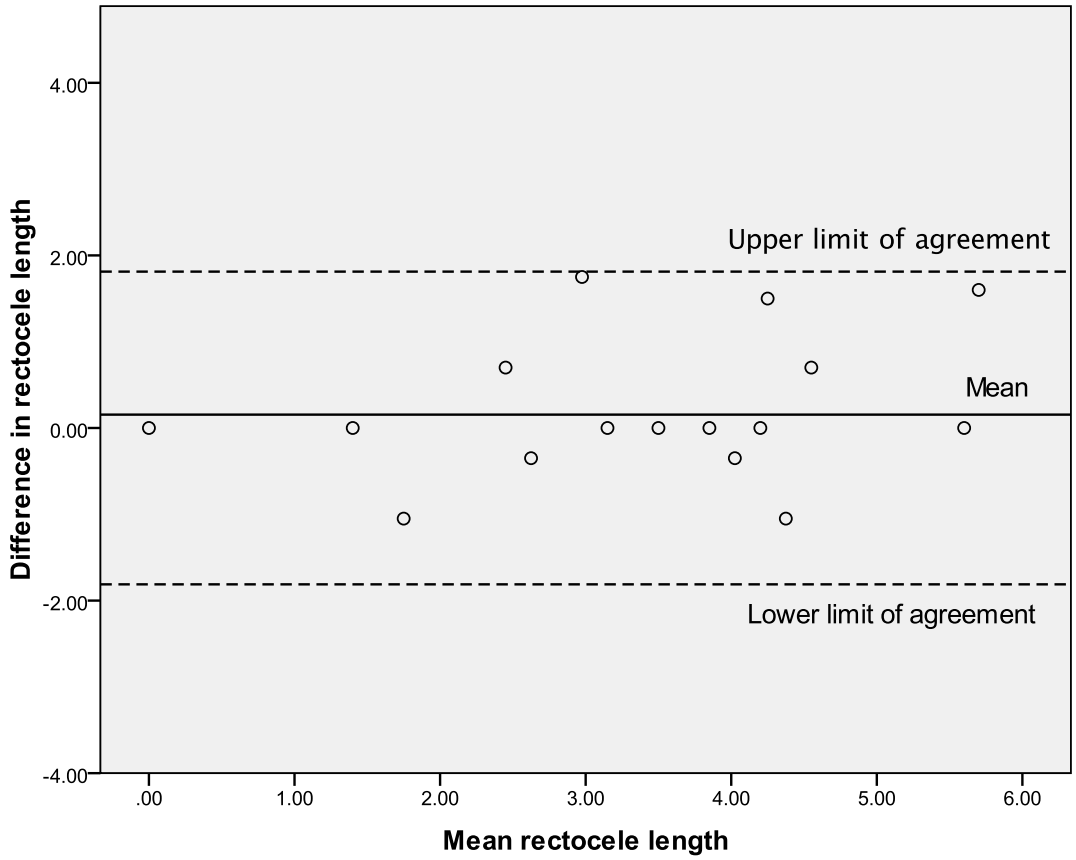


Figure 5.6.03 Bland-Altman Plot showing difference between rectocele length on BaP and MR proctography (BaP – MP) plotted against their mean (n=38)



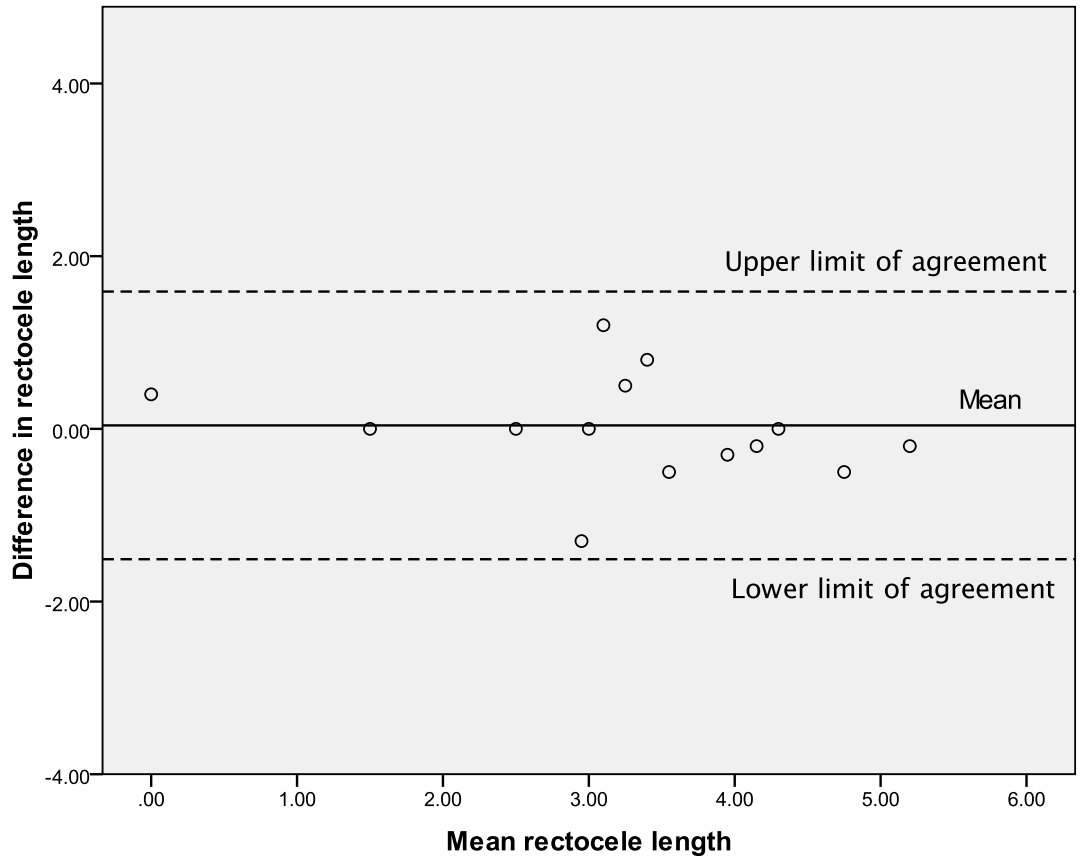
To assess intra-observer reliability for measuring the size of rectoceles, the last 20 Barium proctograms were reported again by the same reporter (DT) 12 months after the last participant was recruited. This was a considerable time gap to ensure that the reporter was not remembering the previous measurement. The mean difference in measuring length of rectocele was 0.16cm with standard deviation 0.91cm. The Bland-Altman plot in Figure 5.6.04, shows that 95% of the differences in rectocele length measured on BaP and MR proctography lie between 1.96 and -1.66cm (mean +/- 2 x standard deviation). The difference for an individual would be between -1.66 and 1.96cm.

Figure 5.6.04 Intra-observer reliability: Bland-Altman Plot showing difference between rectocele length on BaP measured by the same reporter on 2 different occasions plotted against their mean (n=20)



Inter-observer variability was assessed by comparing the measurement of rectocele length on MR proctography by one reporter (CT) with a second measurement by the other reporter (DT). The mean difference between the two measurements was 0.04cm and the standard deviation was 0.78cm. Figure 5.6.05 show the Bland-Altman plot for this data.

Figure 5.6.05 Inter-observer reliability: Bland-Altman Plot showing difference between rectocele length on MR proctogram reported by two different observers (n=20)



Agreement between findings on BaP and MR proctography are shown in Table 5.6.03. Complete rectal emptying was observed in 29% (12/42) on BaP and in 2% (1/42) on MR proctography. Anismus was reported in 18 (43%) cases on MP and in 12 (29%) cases on BaP. The measure of agreement between presence of anismus was moderate (Kappa = 0.493). There was complete agreement in 10 of the participants but an additional 8 cases were reported on MR proctography alone compared to an additional 2 cases on BaP. The measurement of agreement between BaP and MR proctography for rectal intussusception was fair (Kappa 0.209). However MR proctography missed 31% (11/35) cases detected on BaP compared with 8% (2/26) missed by BaP. The measure of agreement between Oxford Grade of Rectal Intussusception was fair (Kappa 0.260). MR proctography underestimated the grade of rectal intussusception in 21 cases and in 13 of these the difference was at least 2 grades (Table 5.6.4). There was substantial agreement between the presence of an enterocele on BaP and MR proctography (Kappa = 0.690). However the number of cases was small (n = 7) and BaP found 3 (43%) cases that were missed by MR proctography. Cystoceles and uterovaginal prolapse were not seen on BaP. MR proctography identified 21 cystoceles and 2 cases of uterovaginal prolapse.

Table 5.6.03 Comparison of findings on BaP and MR proctography (n=42)
Raw data can be found in Appendix XVI

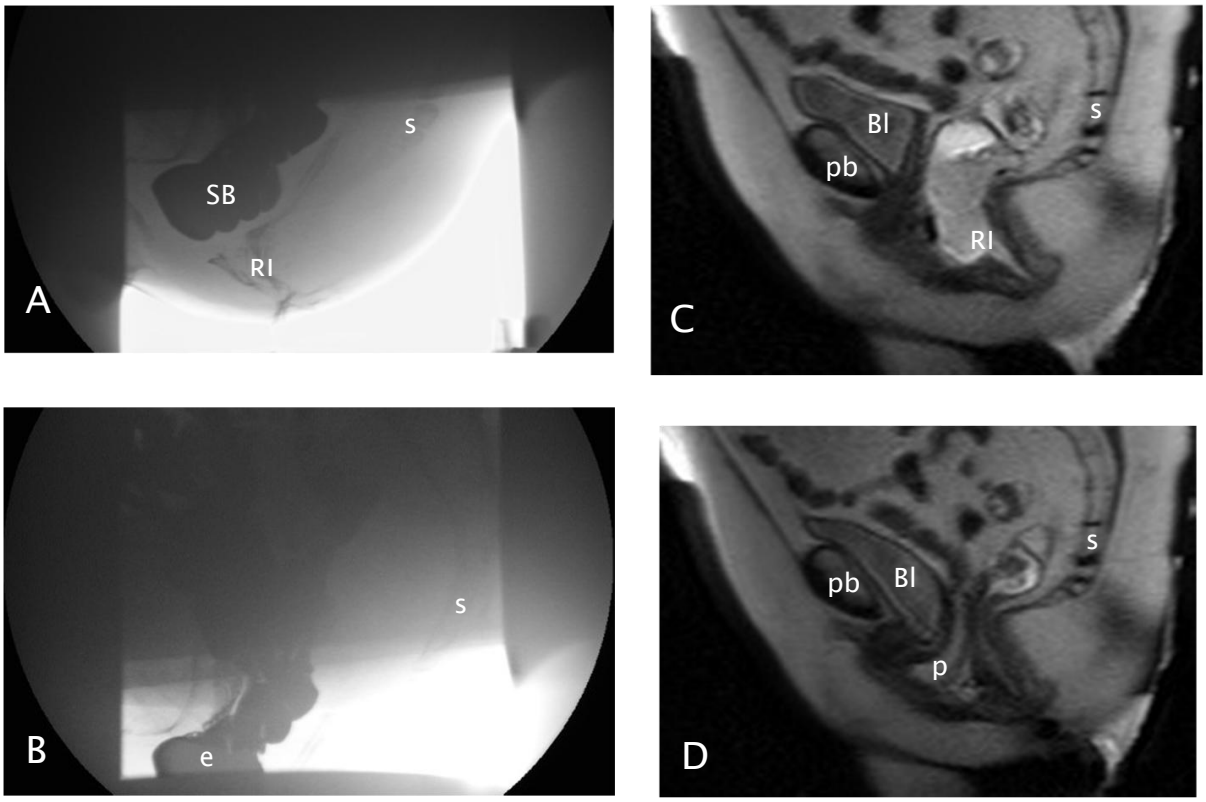
COUNT	BaP	MR proctography	Kappa
Rectocele	38	35	0.690
Rectocele emptying	11	6	0.120
Complete rectal emptying	12	1	NA
Anismus	12	18	0.493
Rectal intussusception	35	26	0.209
Enterocele	7	4	0.690

Table 5.6.04 Agreement between Oxford Grade of Rectal Intussusception on BaP and MR proctography

		MR Proctography					
		0	1	2	3	4	Total
Ba Proctography	0	5	1	0	0	1	7
	1	2	0	1	0	0	3
	2	6	1	6	0	0	13
	3	3	1	4	4	2	14
	4	0	1	2	1	1	5
	Total	16	4	13	5	4	42

An example of the different appearances on BaP and MR proctography in the same participant is shown in Figure 5.6.06. Both proctograms showed Grade 3 rectal intussusception (Figure 5.6.06 A and C). During the BaP, oral contrast in the small bowel can be seen in 5.6.06A. As the participant strains to evacuate the rectum this can be seen as an enterocele in Figure 5.6.06B. However on MR proctography an empty peritoneocele is seen on attempting to evacuate (Figure 5.6.06D). Although representative images have been selected, the dynamic sequence of images is easier to interpret.

Figure 5.6.06 Comparing BaP (A and B) and MR proctogram (C and D) on the same participant (ID 12).
Small bowel (SB), rectal intussusception (RI), enterocele (e), peritoneocele (p), sacrum (s), pubic bone (pb) and bladder (Bl) have been marked.



The changes in ARA from resting to contracting and evacuating during both BaP and MR proctography are shown in Table 5.6.05. During contraction, mean ARA decreased by 8° (95% CI: 4, 13) and 11° (95% CI: 6, 16) on BaP and MR proctography respectively. During evacuation, mean ARA increased by 18° (95% CI: 11, 25) and 22° (95% CI: 13, 29) respectively. These changes were highly significant ($p<0.001$) (Figure 5.6.07 and Table 5.6.06). Using a paired T-test, no significant difference between ARA measured on BaP and MR proctography was found.

Table 5.6.05 Descriptive statistics for anorectal angle measurements (ARA) on BaP and MR proctography during rest, contraction and evacuation in degrees

		Mean angle in degrees	Standard deviation
Resting ARA	**BaP**	109	24
	MR proctogram	105	16
Contracting ARA	**BaP**	101	27
	MR proctogram	94	17
Evacuating ARA	**BaP**	128	27
	MR proctogram	127	22

Figure 5.6.07 Box and whisker plot showing anorectal angle (ARA) in degrees during rest, contraction and evacuation on BaP and MR proctography

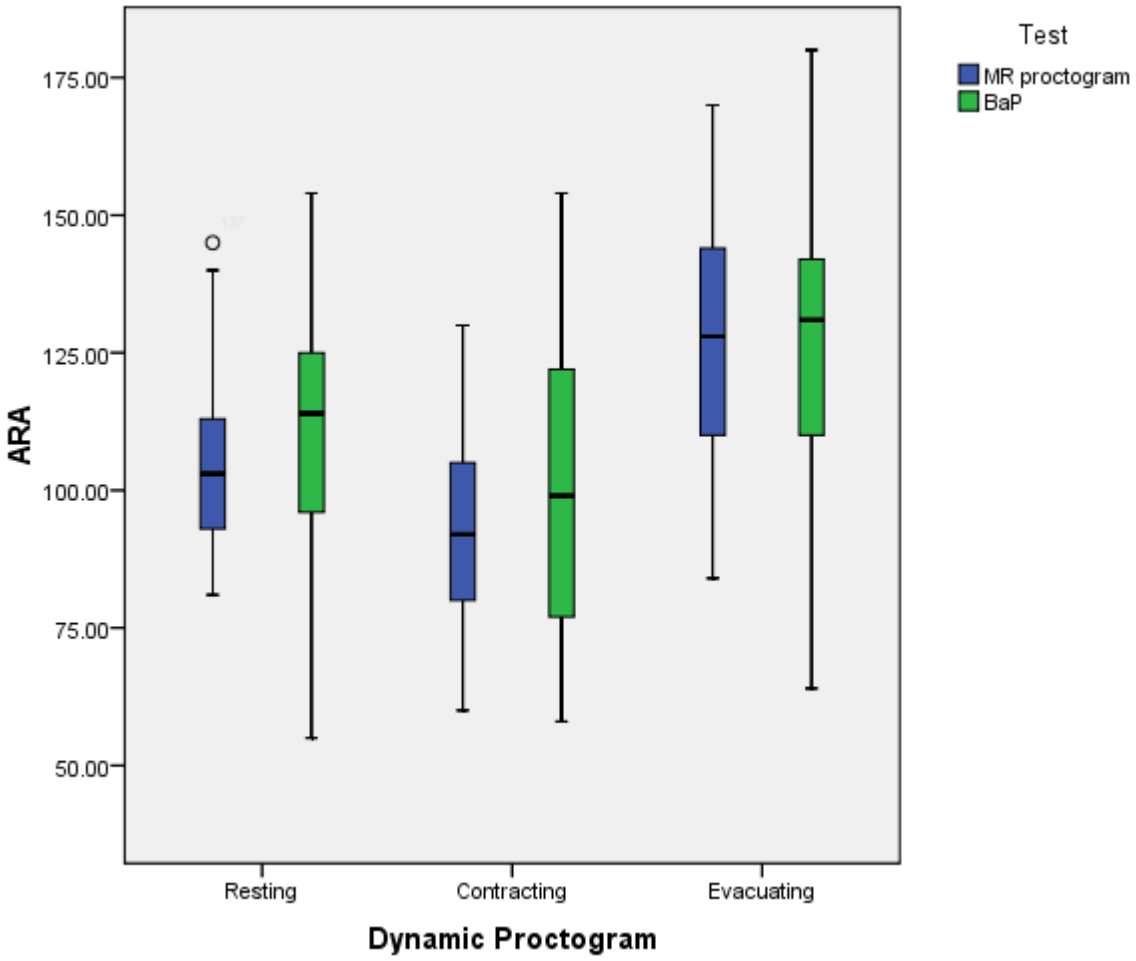


Table 5.6.06 Paired samples T test for changes in ARA during contraction and evacuation on BaP (B) and MR proctography (M) in degrees

		Mean	Lower limit 95% confidence interval	Upper limit 95% confidence interval	P value
BaP	**ARA rest – ARA contracting**	8.4	4.1	13	<0.001
	ARA rest – ARA evacuating	-18	-25	-11	<0.001
MR proctogram	**ARA rest – ARA contracting**	11	5.8	16	<0.001
	ARA rest – ARA evacuating	-22	-29	-14	<0.001

Measurements of ARJ on BaP and MR proctography are not directly comparable (Table 5.6.07). It was not possible to identify the pubic symphysis on BaP without increasing the radiation exposure to the participant. This did not have ethical approval. Therefore measurements were taken from the sacral prominence to the ARJ on BaP. MR proctography did identify the pubic symphysis so measurements were taken from the PCL to the ARJ.

Table 5.6.07 Descriptive statistics for anorectal junction measurement (ARJ) on BaP and MR proctography during rest, contraction and evacuation in cm

		Mean	Standard Deviation
Rest	**BaP ARJ**	14.7	2.1
	MR proctogram ARJ	2.3	1.5
Contracting	**BaP ARJ**	13.9	2.1
	MR proctogram ARJ	1.8	1.6
Evacuating	**BaP ARJ**	16.9	2.6
	MR proctogram ARJ	5.7	1.7

The difference in ARJ measurements associated with contraction and evacuation are similar on BaP and MR proctography despite being measured differently (Table 5.6.08).

Table 5.6.08 Paired samples T test for changes in ARJ measurement during contraction and evacuation on BaP (B) and MR proctography (M) in cm

		Mean	Lower limit 95% confidence interval	Upper limit 95% confidence interval	P value
BaP	**ARJ rest – ARJ contracting**	0.74	0.55	0.92	0.000
	ARJ rest – ARJ evacuating	-2.2	-2.7	-1.6	0.000
MR proctography	**ARJ rest – ARJ contracting**	0.58	0.23	0.93	0.001
	ARJ rest – ARJ evacuating	-3.3	-3.8	-2.8	0.000

5.6.3 Participant preference questionnaire

The patient questionnaire was administered to 42 participants and 25 participants completed it for both BaP and MR proctography. In the group of participants who answered questionnaires for both tests, 13 (52%) felt that they opened their bowels as usual during both tests, 4 (16%) felt that they opened their bowels as usual during BaP only, 3(12%) felt that they opened their bowels as usual during MR proctography only and 5 (20%) felt that they did not open their bowels as usual during either test (Table 5.6.09). There were 8 participants who only answered the questionnaire after BaP and 9 who only answered after MR proctography.

Table 5.6.09 Participant questionnaire Q1: Do you feel that you opened your bowels as **usual during the test today?**

		Q1 answer after MR proctography			
		Yes	**No**	**No reply**	**Total**
Q1 answer after BaP	**Yes**	13	4	4	**21**
	No	3	5	4	**12**
	No reply	4	5	0	**9**
	Total	**20**	**14**	**8**	**42**

All participants who completed the questionnaire for both tests agreed to have either test repeated if necessary except for one participant who did not want the MR proctogram repeated (Table 5.6.10). This participant felt that the BaP was performed in a more "respectful" manner than the MR proctography.

Table 5.6.10 Participant questionnaire Q2: Would you have this test repeated if it was necessary for your treatment?

		Q2 answer after MR proctogram			
		Yes	**No**	**No reply**	**Total**
Q2 answer after BaP	**Yes**	25	1	7	**33**
	No	0	0	0	**0**
	No reply	9	0	0	**9**
	Total	**34**	**1**	**7**	**42**

Question 3 asked patients to give a preference for BaP or MR proctography. There were 8 participants who did not answer this question and they have not been included in the results. The tests were reported as equal in 2(6%) participants. A preference was reported in 32(94%) participants. MR proctography was the preferred test for 21(62%) participants and BaP was the preferred test for 11(32%) participants (Table 5.6.11).

Table 5.6.11 Participant questionnaire Q3: Which test did you prefer?

	Count
MRP	21
BaP	11
No data	8
No preference	2
Total	**42**

The second part of question 3 referred to the reason why the participant preferred one test or the other (Table 5.6.12). The most frequently chosen reason for test preference was “less embarrassing” and this was given as a reason by 22 (69%) participants. In all participants who preferred MR proctography, it was thought to be less embarrassing than BaP. Participants who preferred BaP (n=11) reported that the position was better, n=10 (91%), and that it was easier to empty n=7 (64%) but only 1 (9%) participant reported that it was less embarrassing than MR proctography.

Table 5.6.12 Participant questionnaire Q3 reason: Reasons given for test **preference**

	BaP n=11	**MR proctography n=21**	**Total n=32**
Less embarrassing	1 (9%)	21 (100%)	22
Less uncomfortable	5 (45%)	8 (38%)	13
Better position	10 (91%)	6 (29%)	16
Easier to empty	7 (64%)	5 (24%)	12
Preferred staff	0	2 (10%)	2

Discussion

Studies investigating rectal evacuation are difficult to carry out not least due to the embarrassing nature of the tests and the reluctance of participants to volunteer. This is reflected in the current study. Although 216 patients were invited to participate, the number recruited was 71 (33% recruitment) and 29 withdrew (41% dropout rate). This still leaves 42 participants which is a meaningful group to study.

All patients in the study group were being investigated for pelvic floor disorders. There is likely to be a higher degree of abnormality within the study group than the general population and measurements taken will not reflect normal ranges. However the aim of this study was to investigate whether there are measurable differences between the two techniques. All proctograms are at best simulated defaecation and the degree to which this reflects events occurring in the privacy of the patients own toilet is debatable.

Rectoceles were extremely common in the study group and were diagnosed on both BaP and MR proctography in 83% of participants. There was substantial agreement between BaP and MR proctography on presence of rectocele. BaP did not miss any rectoceles that were evident on MR proctography, but MR proctography missed 3 cases of rectocele. Rectocele emptying occurred more frequently on BaP. There was poor agreement between BaP and MR proctography (Kappa 0.12). The mean rectocele size was 3.10cm (SD 1.44) on BaP and 2.90cm (SD 1.60) on MR proctography. The mean difference in rectocele length was 0.2cm. This is not a clinically relevant difference and was not significant ($p = 0.345$). However the 95% CI demonstrates that the actual difference is probably between -0.2 and 0.6cm. A difference of 0.5cm might be clinically significant. A larger sample size would be necessary to assess whether the difference really is this large on average.

The Bland-Altman plot (Figure 5.6.03) shows that 95% of the differences in rectocele length measured on BaP and MR proctography lie between 2.8 and -2.4cm. The maximum likely difference between rectoceles measured on BaP and MR proctography for an individual is approximately 2.6cm (standard deviation x 2). A difference this large would be clinically significant, therefore it cannot be concluded from this data that the two methods are comparable for assessing rectocele size.

Intra-observer reliability for rectocele length on BaP was good. Figure 5.6.04 shows that 95% of the difference in rectocele length measurement lies between -1.66 and 1.96cm. This is considerably better than the difference in rectocele length between BaP and MR proctography. Inter-observer reliability for rectocele length on MR

proctography was also good as shown in Figure 5.6.05. The observed differences in rectocele size between BaP and MR proctography are therefore unlikely to be due to observer reliability alone.

Participants seemed to have difficulty emptying the rectum when lying in the MRI scanner. Complete rectal emptying only occurred in 2% MR proctograms compared to 29% BaP. This is a problem because other pathology such as rectal intussusception will be missed if the patient is unable to evacuate. Another explanation is that the ultrasound gel coats the rectum and is more difficult to completely expel. However the increased presence of anismus (8 additional cases on MR proctography) is more in keeping with participants having difficulty evacuating.

Rectal intussusception was found on both BaP and MR proctography in 57% of participants (83% BaP). Shorvon's study on normal subjects found rectal intussusception in 50% of men and women (Shorvon, et al., 1989). The higher rate of detection of rectal intussusception in the present study may be due to the case mix which was entirely pelvic floor patients. The confirmation of rectal intussusception on proctography is important for the management of patients with obstructive defaecation who may be candidates for the Stapled Transanal Rectal Resection (STARR) procedure (Boccasanta et al., 2004; Meurette, Wong, Frampas, Regenet, & Lehur, 2010; Pechlivanides et al., 2007; Vermeulen, Lange, Sikkenk, & van der Harst, 2005). The results of the current study suggest that BaP detects more cases of rectal intussusception with only 8% missed on BaP compared to 31% on MR proctography. Symptoms are also important in patient selection for the STARR procedure and the proctogram findings must not be used in isolation. If the cases of rectal intussusception that were missed on MR proctography were asymptomatic or those that had a poor outcome after STARR, then perhaps missing them would not make a clinically significant difference. Symptoms at presentation and surgical outcome were not assessed in this project so we can only assume that MR proctography may miss a significant amount of rectal intussusception that might be treatable. In addition MR proctography underestimated the Oxford Grade of Intussusception in 50% of cases and in 31% of cases this underestimation was by at least 2 grades. A relative contraindication to STARR is the finding of an enterocele. Enteroceles were rare in this study with only 7 cases. Importantly MR proctography missed 3 of the cases. Larger numbers of participants are needed to determine whether MR proctograms do miss in the region of 40 to 50% of rectal intussusception or not. Mucosal prolapse tends to be a clinical diagnosis and was poorly appreciated on either BaP or MR proctography.

Participant 12 shown in Figure 5.6.06, is a good example of agreement between the proctograms on Grade of rectal intussusception. However towards the end of evacuation an enterocele is clearly demonstrated on BaP, whereas the MR proctogram shows an empty peritoneocele. This could simply be within the margins of reproducibility due to the effort exerted by the individual during the two tests. Alternatively, it may be due to the horizontal position of the participant during MR proctography and this study did find that the MR proctograms reported less rectal emptying which could also be positional. Although representative static images have been included in Figure 5.6.06, some information is lost and the dynamic sequence is easier to interpret.

Structures in the anterior compartment such as cystoceles and uterovaginal prolapse are not seen on BaP. Use of vaginal contrast allows some assessment of the anterior compartment to be made. In contrast, MR proctography does visualize the anterior compartment. During MR proctography, 21 cystoceles and 2 uterovaginal prolapses were seen. These conditions tend to be treated by gynaecologists rather than colorectal surgeons. In addition they can be diagnosed with a high degree of accuracy on physical examination.

The dynamics of normal rectal evacuation are not clearly defined. Good proctographic studies in normal subjects are difficult to carry out. Even determining what comprises a “normal” subject is difficult. The present study has been performed on a group of patients who are undergoing investigation for pelvic floor disorders and is therefore unlikely to include a large proportion of normal subjects. Shorvon (Shorvon, et al., 1989) performed a proctogram series in “normal” individuals in 1989. No significant differences were found between men and women. In agreement with the present study, ARA was found to decrease during squeeze and increase on evacuation (Table 5.6.13). The more acute angles recorded Shorvon’s subjects may reflect the younger age group studied. The mean age was 21 years compared with 59 years in the current study.

Table 5.6.13: ARA in normal subjects (Shorvon) compared with the current participants on BaP and MR proctography in degrees

	Rest (SD)	Contracting (SD)	Evacuating (SD)
Men (Shorvon 1989)	96 (17)	80 (16)	98 (19)
Women (Shorvon 1989)	95 (16)	71 (12)	103 (15)
BaP	109 (24)	101 (27)	128 (27)
MR proctography	105 (16)	94 (17)	127 (22)

Mean pelvic floor descent during evacuation was estimated by subtracting ARJ length during evacuation from resting length. It was 2.2cm on BaP and 3.3cm on MR proctography. Different techniques were used to make these measurements and they are not directly comparable. However, Shorvon's study found a similar value for descent of 2cm in both sexes.

Reproducibility with repeated proctograms on the same individual was not investigated in this study or previous studies. It is unlikely that ethical approval would be given for repeated BaP on the same individual but MR proctography could be performed more than once on the same individual to assess repeatability. Some of the changes observed may be within the normal variation of repeated testing.

Proctograms aim to simulate events occurring during defaecation. This study supports the use of proctograms as most patients felt that they were able to open their bowels as usual during the test. Only 20% of patients felt that they could not open their bowels as usual during either BaP or MR proctography. Most patients (52%) reported that they opened their bowels as usual during both tests, although 16% felt that they opened their bowel as usual during BaP only, compared with 12% during MR proctography only. Reduced embarrassment associated with the test was the most frequently given reason for choice of test (69%) suggesting that for most participants this was their biggest concern. MR proctography was consistently found to be less embarrassing than BaP and consequently was reported as the preferred test. However patients who reported a preference for BaP seemed to be less concerned about embarrassment than how they performed during the test and reported that the position was better and that it was easier to empty. It is not clear from this study whether patients would chose the least embarrassing test instead of the test that gave the most helpful results. It is certainly

possible that patients would chose the most useful test even if it was also the most embarrassing. However this question was not specifically addressed.

If repeating this investigation, asking the patient to score each of the 5 main reasons for test preference at the time of the test as well as inviting free comments would give more useful comparative data. In an ideal experiment the participant would be randomly assigned to receive either the BaP or MR proctogram as the first test. In the present study participants underwent BaP first followed by MR proctography. Their expectations of the test may have been altered by their experience on the first occasion leading to a selection bias.

This is an important study investigating two methods of dynamic pelvic floor imaging in pelvic floor patients. BaP reproduced rectal emptying and demonstrated structural abnormalities to a greater extent than MR proctography. If using proctography to investigate disorders of rectal evacuation after anterior resection, this study suggests that BaP would be the best test to use.

5.7 The role of biofeedback in improving continence after anterior resection

Incorporation of routine biofeedback training into the management of patients with rectal cancer who are undergoing anterior resection may result in improved anal continence when compared with standard management.

Results

The following trial was performed as described in Section 4.1. A table of the raw data is included in Appendix XIV.

5.7.1 The Trial

Figure 5.7.01 shows the trial profile. Between 27 November 2006 and 18 August 2008 (21 months), 61 participants were randomly assigned to biofeedback training and 60 participants were assigned to the control group. Follow up was completed on 13 May 2010 with complete follow-up data available for 89 (74%) of 121 participants. All participants received the intended treatment and 89 completed the follow-up to 1 year and were analysed for primary outcome (final CCI). One participant withdrew immediately after randomisation. Randomisation was stratified for preoperative radiotherapy exposure. No postoperative radiotherapy was given. One participant in the radiotherapy group was allocated a randomization number in the no radiotherapy group. During the analysis this participant was included in the radiotherapy exposure group. Table 5.7.01 summarises participant follow up for all participants recruited.

The overall dropout rate after randomisation was 26% (n=32). This includes a small number of participants who withdrew from the study (n=10) and 22 who were not followed up for other reasons (Table 5.7.02).

Thirteen participants were scheduled to have an anterior resection but were either inoperable (n=2) or had a non-restorative resection (abdominoperineal excision n=4, Hartmann's Procedure n=7). Two of these participants initially had an anterior resection but this was followed by an anastomotic leak necessitating end colostomy formation during their index admission. The other Hartmann's Procedures (n=5) were performed for technical reasons encountered during the operation. The possibility of APE and inoperability was discussed at the MDT meeting in these cases, but the consensus opinion was that there was a chance of restorative surgery so the patients were recruited to the study.

One participant in the control group developed a large rectovaginal fistula at 6 months as a complication of her surgery. She had significant faecal leakage associated with the fistula and therefore was withdrawn from the study. It was impossible to determine if leakage was due to poor sphincter function or to the fistula. Three participants were lost to follow up because they were too medically unfit to undergo further general anaesthesia for reversal of ileostomy.

There were 5 deaths in the study. Postoperative anastomotic leak and subsequent sepsis was the cause of death in 3 participants who died at 8, 16 and 73 days after surgery. One participant died from metastatic disease at 161 days after surgery and one participant had a myocardial infarction at home at 156 days after surgery. They were reported as serious adverse events but none of these deaths could be causally linked to the research project. More participants in the control group died (n=4) compared to the BFB group (n=1). The death in the biofeedback group was due to anastomotic leak.

The main diagnosis based on postoperative histology, was cancer in 88% (n=106) of the study group. There were 14 diagnoses of benign disease including 7 large tubulovillous adenomas and 7 diverticular strictures. The two intervention groups were fairly similar in their baseline demographic and clinical characteristics, as shown in Table 5.7.03. There were 50 (41%) women and 71 (59%) men. Participants were aged 60 years or greater in 78% of the randomised group and aged 70 years or greater in 47% of the randomised group. There were proportionally more men (n=38, 62%) in the BFB group than in the control group (n=33, 55%).

A total of 89 participants completed the study with follow-up to 1 year and were included in the ITT analysis. There were 43 participants in the control group and 46 participants in the BFB group. Baseline characteristics were similar again (Table 5.7.04). There were 29 (63%) men in the BFB group compared to 21 (49%) in the control group.

There were 43 temporary ileostomies in the total study group. The mean number of days before ileostomy closure was 168 (range 24 to 722). Only 5 participants with temporary ileostomies did not complete the trial and 2 of these were in the biofeedback group. In the BFB arm of the analysed group, there were 22 (47%) participants with a temporary ileostomy compared to 16 (35%) in the control group.

There were 17 participants who requested telephone follow up. They were equally distributed between the control (n=9) and biofeedback groups (n=8) and did not have anorectal physiology testing at one year. After the first session which all participants

attended, 17 participants declined further ARP testing. Eight of these participants were in the biofeedback group and therefore did not have the rectal catheter inserted for subsequent BFB sessions. Subjectively the rest of the information given to the participants was the same whether the participant was having a telephone or clinic follow up.

Figure 5.7.01 CONSORT 2010 Flow Diagram to show trial profile
Randomised trial to investigate biofeedback after anterior resection

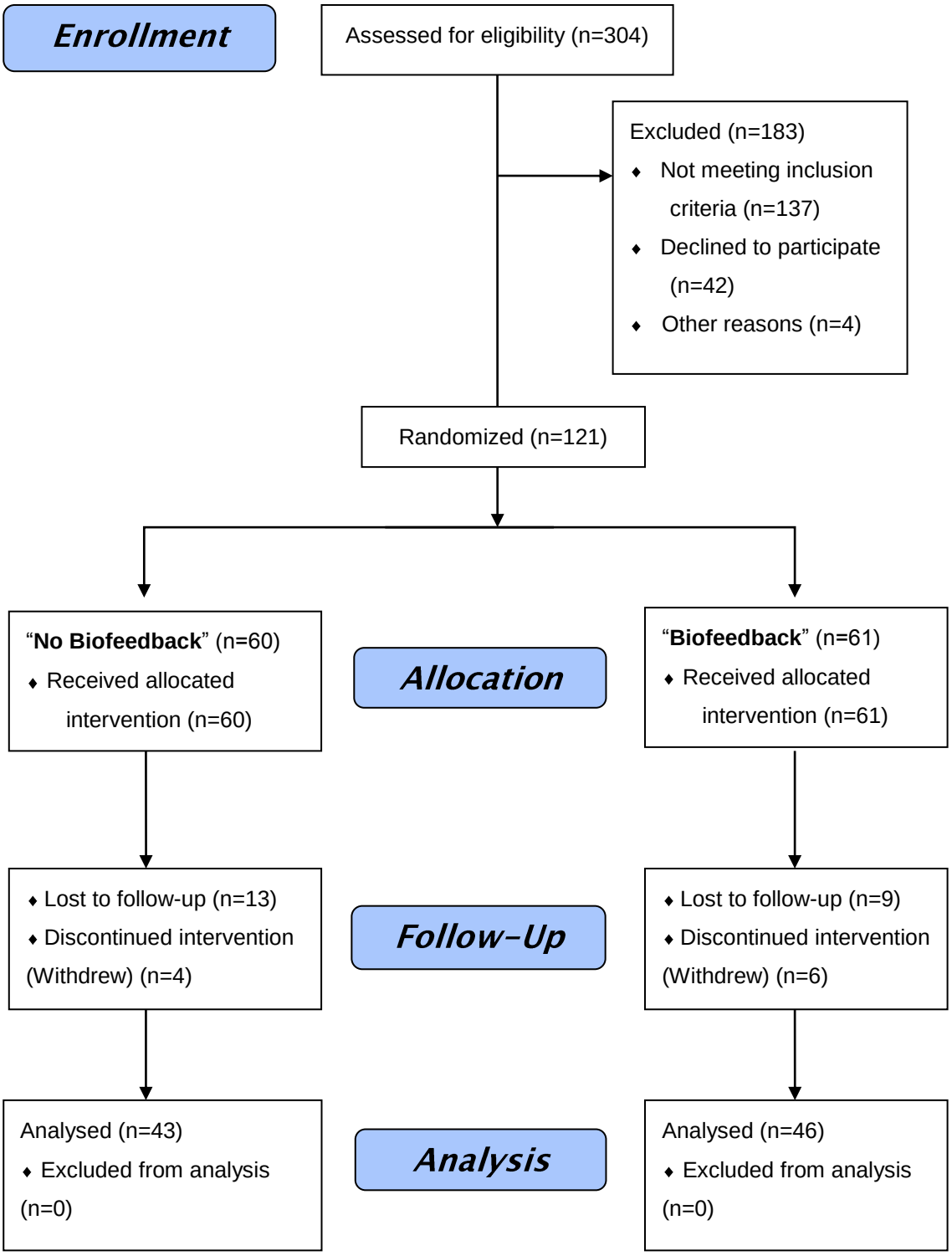


Table 5.7.01 Participant follow up

		Treatment Arm		
		No Biofeedback	**Biofeedback**	**Total**
Follow up	**Analysed**	43 (72%)	46 (75%)	89 (74%)
	Lost	13(22%)	9 (15%)	22 (18%)
	Withdrew	4 (7%)	6 (10%)	10 (8%)
	Total	60	61	121

Table 5.7.02 Reasons for lost to follow up
(excluding 10 participants who withdrew from the study)

	Treatment Arm		
	No Biofeedback	**Biofeedback**	**Total**
Hartmann's Procedure	4	3	7
Died	4	1	5
APE	2	2	4
Ileostomy not reversed	1	2	3
Inoperable	1	1	2
Rectovaginal fistula	1	0	1
Total	**13**	**9**	**22**

Table 5.7.03 Baseline characteristics in randomised participants

		No BFB (n=60)	BFB (n=61)	Total (n=121)
Gender	**Male**	33 (55%)	38 (62%)	71 (59%)
	Female	27 (45%)	23 (38%)	50 (41%)
Radiotherapy	**No DXT**	43 (72%)	42 (69%)	85 (70%)
	Short course	9 (15%)	10(16%)	19 (16%)
	Long course	8 (13%)	9 (15%)	17 (14%)
Temporary	**No stoma**	41 (68%)	32 (52%)	73 (60%)
ileostomy	**Stoma**	19 (32%)	29 (48%)	48 (40%)
Geography	**Southampton**	52 (87%)	55 (90%)	107 (88%)
	Jersey	6 (10%)	5 (8%)	11 (9%)
	Winchester	2 (3%)	1 (2%)	3 (2%)
Cancer	**Benign**	8 (13%)	7 (11%)	15 (13%)
	Cancer	52 (87%)	54 (89%)	105 (87%)
Age	**Years (SD)**	66 (9)	69 (10)	
Incontinence	**CCI (SD)**	4 (5)	4 (5)	
EORTC C30	**Q29 (SD)**	5 (1)	5 (1)	
	Q30 (SD)	6 (1)	5 (1)	
Physiology	**MRP (SD)**	43 (15)	41 (15)	
	MSP (SD)	83 (49)	84 (50)	
	maxMRP (SD)	61 (21)	59 (21)	
	maxMSP (SD)	110 (54)	114 (60)	

Table 5.7.04 Baseline characteristics in the analysed participants

		No BFB (n=43)	BFB (n=46)	Total (n=89)
Gender	**Male**	21 (49%)	29 (63%)	50 (56%)
	Female	22 (51%)	17 (37%)	39 (44%)
Radiotherapy	**No DXT**	33 (77%)	36 (78%)	69 (78%)
	Short course	6 (14%)	4 (9%)	10 (11%)
	Long course	4 (9%)	6 (13%)	10 (11%)
Temporary ileostomy	**No stoma**	27 (63%)	25 (54%)	52 (58%)
	Stoma	16 (37%)	21 (46%)	37 (42%)
Geography	**Southampton**	36 (84%)	42 (91%)	78 (88%)
	Jersey	5 (12%)	3 (7%)	8 (9%)
	Winchester	2 (4%)	1 (2%)	3 (3%)
Cancer	**Benign**	6 (14%)	7 (15%)	13 (15%)
	Cancer	37 (86%)	39 (85%)	76 (85%)
Incontinence score	**Mean CCI (SD)**	4 (5)	3 (4)	
Age	**Years (SD)**	66 (9)	69 (10)	
Incontinence	**CCI (SD)**	4 (5)	3 (5)	
EORTC C30	**Q29 (SD)**	6 (1)	5 (1)	
	Q30 (SD)	6 (1)	5 (1)	
Physiology mmHg	**MRP (SD)**	40 (13)	40 (15)	
	MSP (SD)	76 (44)	87 (49)	
	maxMRP (SD)	60 (19)	58 (21)	
	maxMSP (SD)	102 (49)	117 (61)	

5.7.2 Incontinence Score at one year

The mean CCI score at 1 year was 4 in both groups (see Table 5.7.05). The adjusted CCI score at 1 year is calculated by subtracting baseline CCI from final CCI. A negative value for adjusted CCI reflects a better outcome for the participant because their anal continence has improved compared to baseline CCI. Although there was a slightly better outcome in the control group after adjusting for baseline CCI, this difference was not significant.

Table 5.7.05 Mean CCI score at 1 year

	Mean CCI (SD) Control	Mean CCI (SD) BFB	Mean difference	P	95% CI
CCI final	3.7 (3.5)	4.2 (4.2)	-0.5	0.549	-2.1 to 1.1
Adjusted CCI final	-0.7 (5.5)	1.2 (6.0)	-1.9	0.129	-4.3 to 0.6

The effect of BFB, baseline CCI, female gender, temporary stoma and radiotherapy exposure on final CCI was investigated to determine whether baseline CCI, temporary stoma and radiotherapy exposure are confounders in the relationship between BFB and final CCI.

Simple linear regression indicated that BFB is not a predictor of final CCI (b=0.496, p=0.549, 95%CI -2.1 to 1.1). Using multiple linear regression to control for baseline CCI, gender, temporary stoma, radiotherapy exposure and baseline anal canal pressures (mean and maximal MSP) there was no significant relationship between final CCI and BFB as shown in Table 5.7.06

Table 5.7.06 Multiple linear regression for anal incontinence at one year (final CCI)

	Beta coefficient	95% Confidence Interval	
		Lower limit	Upper limit	P
BFB treatment	-0.539	-2.209	1.132	0.523
Female gender	0.945	-1.275	3.164	0.400
Exposure to radiotherapy	-1.727	-4.267	0.813	0.180
Temporary stoma	-0.960	-3.086	1.165	0.371
Baseline CCI	0.062	-0.124	0.248	0.509
Baseline mean MSP	-0.012	-0.072	0.048	0.689
Baseline maximal MSP	-0.001	-0.050	0.047	0.952

Final CCI was converted to a binary variable where CCI score greater than or equal to 9 was coded as 1 and CCI score less than 9 was coded as 0. Univariate logistic regression indicated that BFB (p=0.401) is not a strong predictor of severe anal incontinence (OR = 0.571, 95%CI: 0.155 to 2.110). Adjusted odds ratio shows that BFB is not a predictor of final CCI as shown in Table 5.7.07. Preoperative CCI greater than or equal to 9 was a predictor of final CCI at one year.

Table 5.7.07 Adjusted logistic regression for anal incontinence at one year (final CCI)

	OR	95% Confidence Interval	
		Lower	Upper
BFB treatment	0.392	0.083	1.862	0.239
Female gender	5.745	0.383	86.216	0.206
Age	0.990	0.897	1.093	0.843
Exposure to radiotherapy	1.462	0.229	9.328	0.688
Temporary stoma	0.316	0.049	2.047	0.227
Mean MRP	0.995	0.895	1.107	0.933
Mean MSP	1.039	0.965	1.118	0.313
Maximal MRP	1.027	0.953	1.107	0.488
Maximal MSP	0.960	0.903	1.020	0.187
Baseline CCI>9	0.080	0.007	.961	0.046

Although there was no difference in CCI between control and BFB groups or even a slightly improved outcome in the control group if baseline CCI is accounted for, the BFB group had more patients with temporary stomas.

The CCI score at one year in participants who had a temporary stoma was on average 2 units worse than those who did not have a temporary stoma and this difference was significant (P = 0.019; 95% CI: 0.3 to 4) (Table 5.7.08). But there was a similar difference in baseline CCI and when this was adjusted for there was no relevant or significant difference between stoma and no stoma groups.

Table 5.7.08 Difference in mean CCI score for participants with a temporary stoma and with no stoma (n=37)

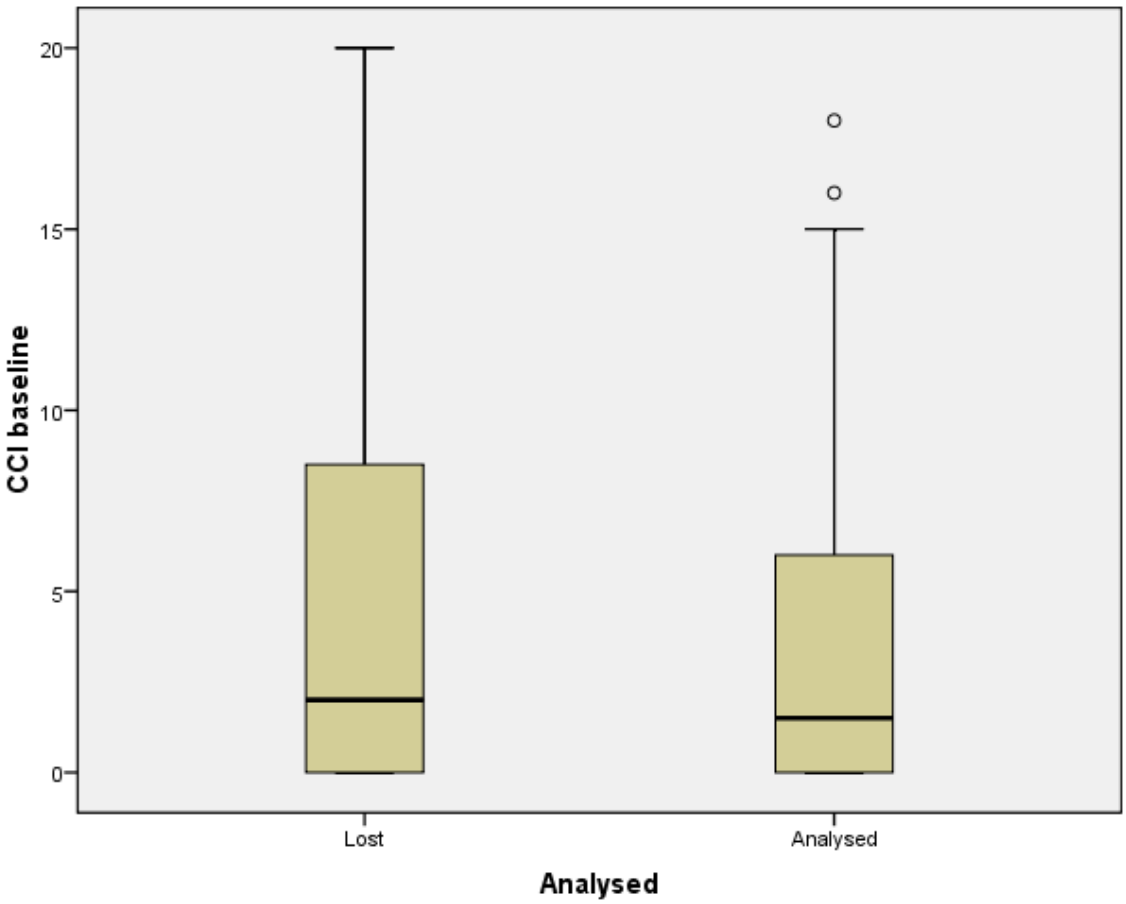
				95% Confidence Interval		
	No stoma (SD)	Stoma (SD)	Mean difference	Upper limit	Lower limit	p
CCI final	3.17 (3.45)	5.11 (4.20)	-1.94	-3.55	-0.32	0.019
CCI preop	3.27 (4.44)	5.25 (6.42)	-2.49	-3.93	-0.22	0.048
CCI final (adjusted)	0.38 (4.39)	0.36 (7.43)	-0.02	-2.49	2.53	0.985

5.7.3 Comparing lost and analysed participants

Slightly more participants withdrew from the BFB group (n=6) than the control group (n=4). As shown in Table 5.7.01, more participants dropped out in the control group and this was due to more participants dying or undergoing Hartmann's Procedure than in the BFB group (Table 5.7.02).

Figure 5.7.02 displays the mean baseline CCI for participants who were analysed (n=89) and lost to follow up (n=31). The mean baseline CCI was 3.7 (SD 4.9) in the analysed group and 5.1 (SD 6.6) in the lost to follow up group.

Figure 5.7.02 Box and whisker plot showing preoperative CCI for analysed and lost groups



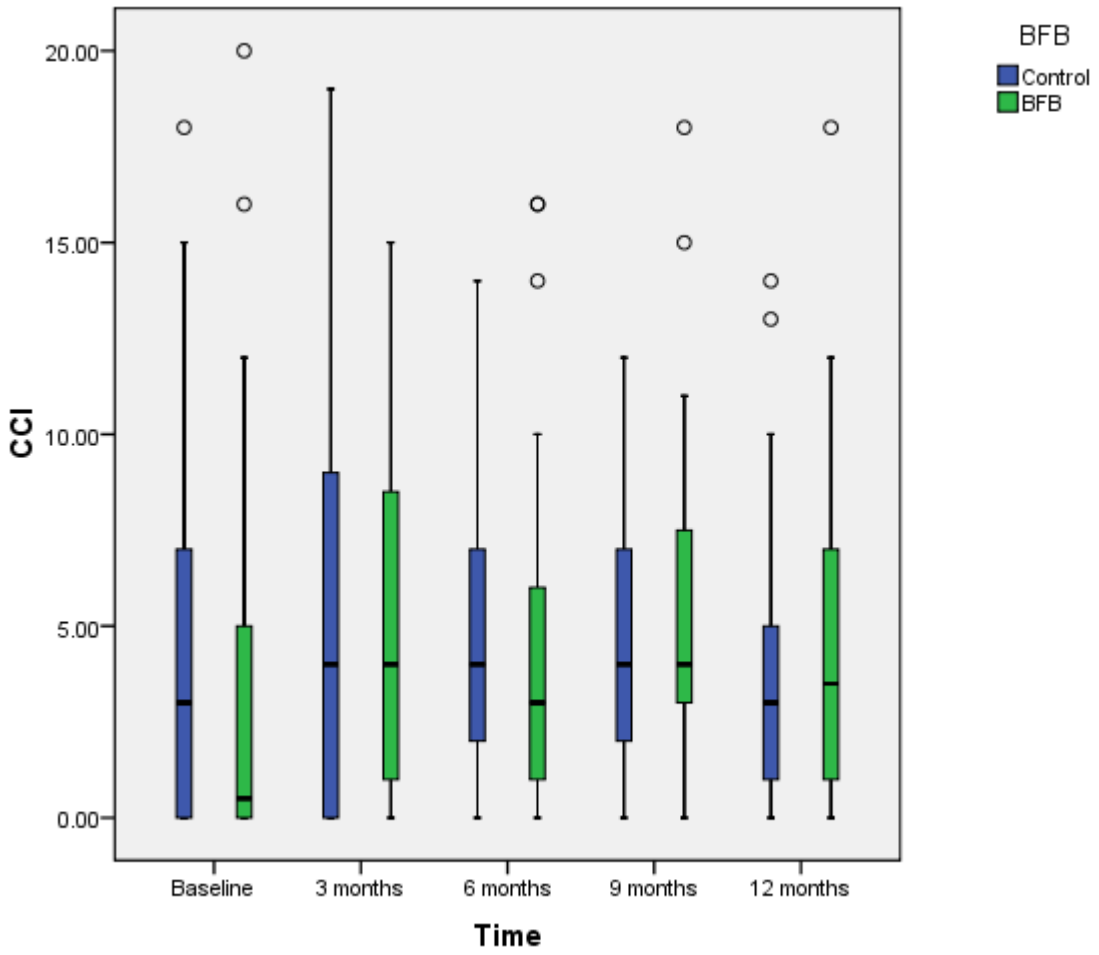
5.7.4 Secondary objective outcome analysis

Table 5.7.09 and Figure 5.7.03 show the postoperative changes in CCI during the first year after anterior resection. The mean CCI gets a little worse at 3 months and then improves. There are no large differences between the biofeedback and the control groups.

Table 5.7.09 Changes in CCI scores over one year in the analysed participants

		N	Mean (SD)
Baseline	**Control**	43	4.4 (5.2)
	BFB	46	3.0 (4.6)
3 months	**Control**	39	5.1 (5.1)
	BFB	43	5.4 (4.8)
6 months	**Control**	37	4.7 (4.0)
	BFB	37	4.5 (4.5)
9 months	**Control**	35	4.6 (3.4)
	BFB	36	5.2 (4.1)
12 months	**Control**	43	3.7 (3.5)
	BFB	46	4.2 (4.2)

Figure 5.7.03 Box and whisker plot showing changes in CCI over first year in analysed participants in control and BFB groups



At one year after surgery, biofeedback treatment did not influence the scores for MSKCC Q1 (stool frequency in 24 hours), 4 (bowel emptying) and 6 (Need to pass stool within 15 minutes of last bowel movement) (Table 5.7.10).

Table 5.7.10 Assessing the effect of biofeedback on bowel function (MSKCC questionnaire) at one year

BFB		N	Mean score	SD	Mean difference	Lower 95% CI	Upper 95% CI	p
Q1	**BFB**	45	3.2	2.2	0.3	-0.7	1.5	0.538
	No BFB	41	2.9	2.2				
Q4	**BFB**	46	35	25	-5.9	-17	5.6	0.309
	No BFB	40	41	29				
Q6	**BFB**	46	72	27	4	-7.7	16	0.496
	No BFB	41	68	28				

Biofeedback did not influence maximum tolerable rectal volume (mean difference at one year -16ml, 95%CI: -47 to 15ml; p = 0.306)

5.7.5 Excluded patients

Although 304 patients were assessed for eligibility at 82 consecutive MDT meetings, 137 (45%) did not meet the inclusion criteria. The reasons for this are given in Table 5.7.11. Almost one third of these patients had metastatic disease and therefore were treated palliatively without surgery. One quarter of patients were undergoing abdominoperineal resection with formation of a permanent colostomy. It was not possible to include patients who were admitted acutely and had emergency surgery (n=19, 14%) because they were discussed at the MDT after surgical intervention. Patients with significant psychological problems or who were thought to be unable to cope with the study were excluded after advice from the colorectal nurse specialists. This resulted in only 8 (6%) exclusions and therefore is unlikely to have introduced significant bias in the selection process. Forty-two patients declined to participate although they were eligible and the reasons they gave for not taking part are given in Table 5.7.12.

Table 5.7.10 Patients with left sided colorectal cancer who were excluded from the study because they did not fit inclusion criteria

Reason	N = 137 (%)
Palliative care due to metastatic disease	42 (31%)
Abdominoperineal resection with permanent colostomy	36 (26%)
Emergency surgery	19 (14%)
Declined to have surgery or were too unfit	13 (9%)
Surgery at a private hospital	10 (7%)
Psychological problems	8 (6%)
Other colorectal resection	5 (4%)
Hartmann's Procedure with permanent colostomy	2 (1%)
Died	2 (1%)

Table 5.7.11 Patients who were eligible to take part but declined

Reason	N = 42 (%)
No reason given	14 (33%)
Time constraints	8 (19%)
Felt too anxious	6 (14%)
Didn't want to travel	4 (10%)
Felt too old	2 (5%)
Carer for relative	2 (5%)
Didn't want additional rectal examination	2 (5%)
Felt too unwell	2 (5%)
Embarrassed	1 (2%)
Didn't like look of equipment	1 (2%)

Participant recruitment to the trial was slower to accrue than had been predicted so recruitment was extended from 12 to 21 months. Recruitment was terminated when 121 participants had been recruited.

Discussion

Anal incontinence and excessive stool frequency after anterior resection can be troublesome for some patients and difficult to treat. Symptoms usually improve with time and anti-diarrhoeal agents are frequently used for symptomatic control. Biofeedback is useful for the treatment of these types of symptoms and is widely used in different clinical contexts. There is some evidence to suggest that biofeedback treatment may be effective after anterior resection (Ho, et al., 1996). However in this study, routine biofeedback did not result in any measureable difference in incontinence scores between patients who received biofeedback training and those who did not.

The study participants were typical for patients with rectal cancer. Rectal cancer is more common in men than in women (3:2) and is predominantly a disease of the elderly with 71% of patients presenting with rectal cancer aged 60 years or older and 53% aged 70 years or older. The results from this study are similar, with 58% men and 42% women. Participants were aged 60 years or greater in 78% of the randomised group and aged 70 years or greater in 47% of the randomised group. The main diagnosis was cancer in 87% of the randomised group.

The two treatment allocation groups were well matched in their baseline characteristics, although in the BFB group 29 (48%) participants had a temporary ileostomy compared with 19 (32%) in the control group. Participants with a temporary stoma have a period of about 3 months after their surgery before the stoma is reversed and intestinal continuity restored. Although a considerable amount of research demonstrates the negative effect of an ileostomy on quality of life, little has been done to investigate whether the functional outcome is worse after a stoma is reversed compared to patients who do not have a stoma. It is generally thought that function after stoma reversal is worse than in patients who never had a stoma. It is difficult to know whether this effect is due to the presence of a low anastomosis which usually accompanies the formation of a defunctioning ileostomy. The larger number of patients with an ileostomy in the BFB group might bias the results if indeed patients have a worse outcome after a temporary stoma. However in the analysed group, there was less of a difference with 21 (46%) participants in the BFB group having an ileostomy compared to 16 (37%) in the control group.

In this study participants who had a temporary stoma did have a worse outcome than those who did not have a stoma. But this difference disappeared when the baseline CCI was taken into account. Biofeedback was not associated with improved final CCI in patients who had a stoma.

Stoma nurses routinely see all patients prior to anterior resection because the need for an ileostomy is unpredictable before surgery. Part of the advice given by the stoma nurses before surgery includes information about pelvic floor and anal sphincter muscle exercises to improve anal sphincter function after reversal of ileostomy. Forty percent of the participants had an ileostomy and are likely to have been encouraged by their stoma nurse to do exercises. Many patients in the control group would have received advice about exercises to improve anal continence. This effect was not controlled for and it would have been unethical to attempt to stop the stoma nurses from giving this information to the control group. However this may have resulted in dilution of the biofeedback effect.

It was not possible to stratify randomisation for stoma formation as this was a largely unpredictable event decided by the surgeon at the time of surgery. Surgery took place after randomisation and after the first intervention. In addition the sample size was only large enough for stratification of one factor and radiotherapy exposure is thought to have a significant impact on functional outcome after anterior resection.

Slightly more participants withdrew from the BFB group (n=6) than the control group (n=4). The numbers are very small but it is possible that the BFB participants withdrew because they didn't want to do the BFB exercises any more. Overall more participants dropped out in the control group and this was due to more participants dying or undergoing Hartmann's Procedure than in the BFB group.

All participants were recruited through the colorectal MDT meetings. Other studies have included "biopsy-proven adenocarcinoma of the rectum" judged resectable for cure with an abdominal procedure (Holm, Singnomklao, Rutqvist, & Cedermark, 1996) as part of the eligibility criteria. In the current trial, all participants had biopsy-proven or suspicious radiological imaging for cancer. In addition they had been judged resectable by the colorectal MDT process.

Three hundred and four patients with a colorectal cancer within 30cm of the anal verge presented and were discussed at the colorectal MDT during the 21 month study period. At the MDT meeting they were deemed suitable for primary resection with anastomosis (with or without a covering ileostomy) and curative intent. Despite this robust recruitment process, there was an overall dropout rate of 26% and the most frequent reason for this was that a different operation was performed.

There was an apparent failure of the MDT meeting to predict the suitability for primary resection in 11 cases, as shown in Table 5.7.02. The three reasons for this were APE, inoperable tumour and Hartmann's Procedure.

No lower limit was set for height of tumour above the anal verge. Occasionally it becomes evident during surgery that the cancer is too low to preserve the sphincter and an abdominoperineal resection is performed. This occurred in 4 cases in this trial. The possibility of non-restorative surgery was discussed at the MDT meeting and with the patient prior to surgery. Perhaps these 4 patients should not have been recruited to the trial. However, there was a chance of restorative surgery so it was deemed reasonable to recruit them. The number of patients who had a possible similar outcome but had restorative surgery was not recorded. If a lower limit had been set for height of tumour above the anal verge, these participants would not have been recruited. But some participants with low tumours would have been excluded although they did undergo anterior resection. This wide inclusion policy allowed us to recruit patients with low cancers. Sphincter function is likely to be poorer in patients who have very low anastomoses so they were an important group to include in this trial.

Most patients with inoperable cancer were excluded from the trial but inoperable disease was discovered at laparotomy in 2 participants despite full imaging workup and MDT discussion. There were 7 participants who underwent Hartmann's Procedure with end colostomy formation. The reasons for this were technical difficulties encountered during the surgery or due to anastomotic leak postoperatively with return to theatre. These are unpredictable events and it would not be possible to identify and exclude these participants before randomization.

It is very unlikely that a clinical trial will have no dropouts but any dropout is associated with introduction of potential bias into the results. One way of trying to account for missing data is to use imputation. However a dropout rate of 26% is acceptable for a clinical trial of this nature. The baseline CCI was slightly worse in the participants who were lost to follow up (CCI=5) compared with those in the analysed group (CCI=4).

The study was powered to detect a difference in CCI of 30% with 80% power. A difference of this order of magnitude was not found. The difference in CCI between the two groups was very small and would not be clinically relevant. Before concluding that biofeedback is of no use in improving outcome after anterior resection and accepting the null hypothesis it is necessary to critically assess the trial design for any features that may lead to a Type II error. The trial was adequately powered (80%) and sufficient

participants were recruited and contributed to the final analysis as demanded by the sample size calculation. Other possible explanations for this result include: primary outcome tool (CCI) was too blunt to detect changes, participant compliance with the biofeedback exercise was not consistent between the two groups and participants were not blinded to treatment group.

The Cleveland Clinic Incontinence score (CCI) is a widely used score of anal incontinence. It is easy to understand and use but when compared with the reproducibility of other scoring systems it does not perform so well. CCI was used as the primary outcome measure but may not be sensitive enough to detect differences in anal continence between the two intervention groups.

Outcome from biofeedback training is known to be highly dependent on participant motivation. Participants in the biofeedback group received a phone call every 3 months to remind them about doing the exercises, but compliance was low. The participant questionnaire suggests that participants did find doing the exercises helpful. Although in general participants had low levels of incontinence, biofeedback did not seem to improve anal continence.

With a clinical trial such as this one, it is impossible to blind the participants to the intervention they are receiving. Although the information sheet clearly stated that BFB training after anterior resection was experimental and that it was not known whether BFB improved anal continence or not, some patients not randomised to BFB may have tried to do exercises in the hope of improving their outcome. A cohort study of patients not included in the trial time course could be studied for comparison to see if the information given to the participants altered their expectations and final continence scores as a direct result of taking part in the study. Pilates are a popular form of exercise in women and some of the women in the study continued to do pilates irrespective of which group they were randomised to. If repeating this study it would be useful to record information about exercises (pilates or as advised by the stoma nurses) already performed by the participants and whether they continued these for the duration of the study.

The biofeedback sessions were carried out by an experienced GI nurse specialist. However there was no quality control of the information provided to the participants. Audio-taping of the consultation would have been a useful method for gaining further information about the uniformity and quality of the BFB sessions.

This study does not support a role for the routine use of focussed biofeedback in patients undergoing anterior resection to improve anal incontinence as measured by CCI. It is possible that the involvement of other nursing specialists including stoma nurses, who routinely recommend sphincter exercises, may have diluted the effect of biofeedback in the study group.

There may be a place for selective biofeedback training in patients who have symptoms of anterior resection syndrome and further research would be useful in this area. Preliminary studies suggest that there may be a role for neuromodulation in these patients (Ratto et al., 2005) and again this would be a very interesting area for further research.

6 Summary

Although routine biofeedback for all patients undergoing anterior resection is an attractive option to reduce anal incontinence (Ho, et al., 1996), this randomised trial does not show any added advantage when compared with standard treatment. Participants in the control and treatment arms of the trial both received preoperative advice about exercises for the anal sphincter from the stoma nurses. The extent of this advice and how rigorously it was adhered to by the participants was not assessed but may have resulted in bias. A useful addition to this trial would have been to record whether participants were performing any kind of regular pelvic floor or sphincter exercises.

In this project, 15% of participants had a poor functional outcome at one year after major rectal resectional surgery. This impacted on their quality of life and symptom severity scoring. These participants were characterised by having a CCI greater than or equal to 9. “Anterior resection syndrome” can be defined as CCI greater or equal to 9 at one year after surgery.

There may be a place for selective biofeedback training in patients who have symptoms of anterior resection syndrome and further research would be useful in this area. A significant proportion of participants with severe anal incontinence at 3 months had a poor functional outcome at one year and this would be a good group to target for biofeedback. Preliminary studies suggest that there may be a role for neuromodulation in patients with a poor functional outcome after anterior resection (Ratto, et al., 2005). Data from the current trial report that 41% (9/22) of the study group with severe incontinence at 3 months will still have severe incontinence at one year. A randomised trial to compare BFB versus neuromodulation for patients with severe anal incontinence at 3 months would demonstrate whether there was any advantage to BFB or neuromodulation in this group. The main outcome measure would be anal incontinence at one year as assessed with CCI. It would be interesting to include the Bristol Stool Form Chart (Heaton, et al., 1991; Heaton, et al., 1992; O'Donnell, et al., 1990) in the outcome measures.

There is a significant increase in severe anal incontinence after anterior resection at 3 months. This is accompanied by changes in anorectal physiology. Before surgery, 17% of participants reported severe anal incontinence. Although the prevalence of severe incontinence at one year was similar to that before surgery, the majority of affected individuals (69%) did not have severe incontinence before surgery. There appears to be a shift in anal incontinence after anterior resection with 73% of individuals with severe

incontinence before surgery no longer reporting severe incontinence, and 12% of individuals developing new severe anal incontinence which had not resolved at one year.

Anastomotic height is an important factor for rectal function after anterior resection. Tumour height and length of bowel resection cannot be used as a surrogate for measuring anastomotic height. Therefore it is important to assess anastomotic height with rigid sigmoidoscopy. This is best achieved immediately after surgery when the patient is still in a modified lithotomy position. The integrity of the anastomosis can be checked and the height measured under reproducible conditions.

Barium proctography is superior to MR proctography for assessing anatomical abnormalities associated with rectal dysfunction. Further investigation is warranted to see if this is a useful investigation in patients with anterior resection syndrome.

Quality of life and functional outcome are not major contributors to the MDT process at present (Emmertsen & Laurberg, 2008). Tailoring of surgery, radiotherapy and chemotherapy with a view to optimising survival whilst minimising poor functional outcome, is important and would be facilitated by the inclusion of routine health-related quality of life and symptom assessment (Wilson, et al., 2006).

This is an important trial which documents functional outcome and quality of life after anterior resection. No added advantage was found when routine biofeedback was added to standard management. A significant group of participants had a poor functional outcome that had not resolved 12 months after surgery.

Appendix I Participant information sheet (BFB)

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PATIENT INFORMATION SHEET
Ethics Committee Number: 06/Q1704/84

ROLE OF BIOFEEDBACK IN IMPROVING CONTINENCE AFTER ANTERIOR RESECTION

Introduction
You are being invited to take part in a research study, which aims to find out whether biofeedback improves how the bowels work after surgery for rectal and sigmoid colon abnormalities. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

What is the purpose of the study?
Faecal incontinence can be a complication of major surgery for rectal and sigmoid colon abnormalities. Although biofeedback has been shown to improve faecal incontinence, its use after surgery has not been looked at in detail. The purpose of the trial is to show if biofeedback reduces the occurrence of incontinence after surgery when compared directly with another group of patients who have not had biofeedback. Patients enrolled to the study will be followed up for one year after their surgery as part of the research.

Why have I been chosen?
All patients who are having major bowel surgery for rectal and sigmoid colon abnormalities are potentially able to take part in the study and we hope to include 110 people.

Do I have to take part?
No. It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

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What will happen to me if I take part and what do I have to do?
We would like you to agree to take part in this study. We would like to see you before your surgery and then 3-monthly for one year. You will be asked to complete a patient quality of life questionnaire and will be asked about your normal bowel habit. Special tests involving ultrasound scanning and pressure measurements will be carried out on the muscles at the anus that are responsible for preventing bowel leakage. In addition 50% of patients enrolled on to the study will receive a course of biofeedback. This will involve four 30-minute sessions with the research specialist during which you will be taught how to empty the bowel efficiently and given some exercises for the anal muscles.

Why is a trial necessary?
The only reliable way of comparing one treatment with another is to carry out a randomised trial. In such a trial, people will be put into groups and compared. The groups are selected by a computer, with no information about the individual – i.e. by chance. Patients in each group then have different treatment and these are compared. This is ethically and scientifically important when no one knows which is the better treatment to opt for.

Expenses
Car-parking expenses for additional visits will be paid.

Will my taking part in the study be kept confidential?
Yes. All the information about your participation in this study will be kept completely confidential and will not be disclosed to anyone, not even other members of your family or your Doctor. We will inform your Doctor that you have been enrolled in the study.

What are the risks involved?
Biofeedback is a specific method for re-training the body to open the bowels more efficiently. At present it is not routinely used for patients who have had a bowel resection, but it may be beneficial. The method is safe, painless, well-tolerated and does not preclude further alternative treatment if unsuccessful.

What are the possible benefits of taking part?
We hope that the information we get from this study will help us to treat future patients who are having major rectal and sigmoid colon surgery and improve their outcome with respect to their bowel habit and risk of bowel leakage.

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What if something goes wrong?
If you find participating in the study makes your symptoms worse, you will be seen by your nurse specialist or consultant to discuss further treatment options. Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. If you have a concern about any aspect of this study, you should speak with the researchers who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

What will happen to the results of the research study?
The results will be submitted for publication in a medical journal. A summary sheet will be sent to participants with the key findings of the research project. Individual participants will not be identified in any report or publication.

Who has reviewed the study?
This study was given a favourable ethical opinion for conduct in the NHS by the Southampton and South West Hampshire Research and Ethics Committees

If I have any questions, whom do I ask?
The Research Doctor is: Sophie Pilkington

The Surgical Consultant is: Miss KP Nugent

University Surgical Unit
Southampton General Hospital
Southampton SO16 6YD

TELEPHONE NUMBER: 023 8079 6145

(VERSION 4: 16.10.2007)

Appendix II Consent form (BFB)

CONSENT FORM

Ethics Committee Number: 06/Q1704/84

Patient Identification Number for this trial:

Study Title: THE ROLE OF BIOFEEDBACK IN IMPROVING CONTINENCE AFTER ANTERIOR RESECTION: A RANDOMISED CONTROLLED TRIAL

Name of Researcher: S. Pilkington

Please initial box

1.	I confirm that I have read the information sheet dated 31.07.2008 (version 5) for the above study and have had the opportunity to ask questions.	☐
2.	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐
3.	I understand that sections of any of my medical notes may be looked at by responsible individuals or from regulatory authorities where it is relevant to my taking part in the research. I give permission for these individuals to have access to my records.	☐
4.	I agree to take part in the above study.	☐

NAME OF PATIENT	DATE	SIGNATURE
NAME OF PERSON TAKING CONSENT (IF DIFFERENT TO RESEARCHER)	DATE	SIGNATURE
RESEARCHER	DATE	SIGNATURE

1 for patient; 1 for researcher; 1 to be kept with hospital notes

(VERSION 5: 31.07.2008)

Appendix III GP letter (BFB)

Ethics Committee Number: 06/Q1704/84

Study Title: THE ROLE OF BIOFEEDBACK IN IMPROVING CONTINENCE AFTER ANTERIOR RESECTION: A RANDOMISED CONTROLLED TRIAL

Dear Dr

We are carrying out a study to test the hypothesis that biofeedback in the peri-operative period improves the continence of patients who have had anterior resection. Your patient has agreed to take part in this single blind prospective randomised trial.

If you have any enquiries about this study or in the event of an emergency please contact us at Southampton General Hospital, contact telephone number: 023 8079 6145

I enclose a copy of the patient information sheet. This study has been reviewed by the Southampton and SW Hampshire Research Ethics Committee, who gave a favourable opinion.

Yours sincerely,

Miss SA Pilkington (Specialist Registrar in Surgery) and Miss KP Nugent (Consultant Colorectal Surgeon)

(Version 4: 16.10.2007)

Appendix IV Case Report Form (BFB)

CASE REPORT FORM (*VERSION 1: 10.06.2006*)

Study Title: THE ROLE OF BIOFEEDBACK IN IMPROVING CONTINENCE AFTER ANTERIOR RESECTION: A RANDOMISED CONTROLLED TRIAL

NAME:
DOB:
Hospital Number:
Address:

MDT Date:
Information sheet given to patient? YES / NO Date:

INCLULSION CRITERIA

- Patient knows diagnosis of rectal cancer
- Patient is awaiting anterior resection
- Patient is aged 18 years or older
- Patient has given written informed consent to participate in the trial **Date:**

EXCLUSION CRITERIA

- Patient deemed mentally incompetent
- Pregnant and nursing mothers

Clinical height of tumour:

MRI height of tumour:

MRI date: **CT date:**

Staging: **Staging:**

Preoperative radiotherapy / chemo:

Date of preassessment:

Date of admission:

Date of surgery: **Date of discharge:**

Date of closure of ileostomy:

Letter sent to GP: YES / NO **Date:**

Presenting complaint

Profession Weight Height

PMH Diabetes

Past surgical history

Anorectal history PR blood Incontinence Pain Fissure

Perianal ops: Haemorrhoidectomy Lateral sphincterotomy I&D abscess

Obstetric history: Children Heaviest: Episiotomy/Forceps/Stitiches

Medications & laxatives

OPERATION

DATE OF SURGERY:

OPERATION TITLE:

HEIGHT OF ANASTOMOSIS:

ANASTOMOSIS: **end to end** **side to end** **J-pouch**

DEFUNCTIONING STOMA: **NO** **YES**

Reason for stoma:

Surgeon **Consultant** **SPR**

ASA:

Complications

HISTOLOGY **T** **N** **M**

DUKES' STAGE

ONCOLOGY

PREOP RADIOTHERAPY: **SHORT** **LONG** **NONE**

POSTOP RADIOTHERAPY:

POSTOP CHEMOTHERAPY:

Appendix V Symptom specific questionnaires: CCI and MSKCC

Incontinence Score

Please indicate on average how often in the last month you experienced the following:

	Never	Rarely Less than once a month	Sometimes Less than once a week	Usually Less than once a day	Always Everyday
Solid stool leakage	☐	☐	☐	☐	☐
Liquid stool leakage	☐	☐	☐	☐	☐
Gas leakage	☐	☐	☐	☐	☐
Pad use	☐	☐	☐	☐	☐
Lifestyle restriction	☐	☐	☐	☐	☐

Table 5.
MSKCC Bowel Function Instrument – Draft 1 [a]

1.	Over the last 4 weeks, how many bowel movements do you generally have in 24 hours?	_____ bowel movement/24 hours				
	Over the last 4 weeks	Always	Most of the time	Sometimes	Rarely	Never
2.	Do certain solid foods increase the number of bowel movements in a day?	☐	☐	☐	☐	☐
3.	Do certain liquids that you drink increase the number of bowel movements in a day?	☐	☐	☐	☐	☐
4.	Do you feel like you have totally emptied your bowels after a bowel movement?	☐	☐	☐	☐	☐
5.	Do you get to the toilet on time?	☐	☐	☐	☐	☐
6.	Do you have another bowel movement within 15 minutes of your last bowel movement?	☐	☐	☐	☐	☐
7.	Do you know the difference between having to pass gas (air) and needing to have a bowel movement?	☐	☐	☐	☐	☐
8.	Have you used medicines to decrease the number of bowel movements (drugs like Imodium®, Lomotil®)?	☐	☐	☐	☐	☐
9.	Have you had diarrhea (no form, watery stool)?	☐	☐	☐	☐	☐
10.	Have you had loose stool (slight form, but mushy)?	☐	☐	☐	☐	☐
11.	Have you been able to wait 15 minutes to get to the toilet when you feel like you are going to have a bowel movement?	☐	☐	☐	☐	☐
12.	Have you been able to control the passage of gas (air)?	☐	☐	☐	☐	☐
13.	Have you limited the types of solid foods you eat to control your bowel movements?	☐	☐	☐	☐	☐
14.	Have you limited the types of liquids you drink to control you bowel movements?	☐	☐	☐	☐	☐
15.	Have you had soilage (leakage of stool) of your undergarments during the day?	☐	☐	☐	☐	☐
16.	Have you used a tissue, napkin, and/or pad in your undergarments during the day in case of stool leakage?	☐	☐	☐	☐	☐
17.	Have you had soilage (leakage of stool) of your undergarments when you go to bed?	☐	☐	☐	☐	☐
18.	Have you had to alter your activities because of your bowel function?	☐	☐	☐	☐	☐

MSKCC = Memorial Sloan-Kettering Cancer Center.

Appendix VI Quality of life questionnaires:

EORTC QLQ-C30

ENGLISH

EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials: _____

Your birthdate (Day, Month, Year): _____

Today's date (Day, Month, Year): 31 _____

		Not at All	A Little	Quite a Bit	Very Much
1.	Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2.	Do you have any trouble taking a long walk?	1	2	3	4
3.	Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4.	Do you need to stay in bed or a chair during the day?	1	2	3	4
5.	Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:		Not at All	A Little	Quite a Bit	Very Much
6.	Were you limited in doing either your work or other daily activities?	1	2	3	4
7.	Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8.	Were you short of breath?	1	2	3	4
9.	Have you had pain?	1	2	3	4
10.	Did you need to rest?	1	2	3	4
11.	Have you had trouble sleeping?	1	2	3	4
12.	Have you felt weak?	1	2	3	4
13.	Have you lacked appetite?	1	2	3	4
14.	Have you felt nauseated?	1	2	3	4
15.	Have you vomited?	1	2	3	4
16.	Have you been constipated?	1	2	3	4

Please go on to the next page

ENGLISH

During the past week:	Not at All	A Little	Quite a Bit	Very Much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

EORTC QLQ-CR29

ENGLISH

EORTC QLQ – CR29

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

During the past week:	Not at All	A Little	Quite a Bit	Very Much
31. Did you urinate frequently during the day?	1	2	3	4
32. Did you urinate frequently during the night?	1	2	3	4
33. Have you had any unintentional release (leakage) of urine?	1	2	3	4
34. Did you have pain when you urinated?	1	2	3	4
35. Did you have abdominal pain?	1	2	3	4
36. Did you have pain in your buttocks/anal area/rectum?	1	2	3	4
37. Did you have a bloated feeling in your abdomen?	1	2	3	4
38. Have you had blood in your stools?	1	2	3	4
39. Have you had mucus in your stools?	1	2	3	4

During the past week:	Not at All	A Little	Quite a Bit	Very Much
40. Did you have a dry mouth?	1	2	3	4
41. Have you lost hair as a result of your treatment?	1	2	3	4
42. Have you had problems with your sense of taste?	1	2	3	4
43. Were you worried about your health in the future?	1	2	3	4
44. Have you worried about your weight?	1	2	3	4
45. Have you felt physically less attractive as a result of your disease or treatment?	1	2	3	4
46. Have you been feeling less feminine/masculine as a result of your disease or treatment?	1	2	3	4
47. Have you been dissatisfied with your body?	1	2	3	4
48. Do you have a stoma bag (colostomy/ileostomy)? (please circle the correct answer)	Yes		No	

Please go on to the next page

ENGLISH

During the past week:	Not at All	A Little	Quite a Bit	Very Much
Answer these questions ONLY IF YOU HAVE A STOMA BAG, if not please continue below:				
49. Have you had unintentional release of gas/flatulence from your stoma bag?	1	2	3	4
50. Have you had leakage of stools from your stoma bag?	1	2	3	4
51. Have you had sore skin around your stoma?	1	2	3	4
52. Did frequent bag changes occur during the day?	1	2	3	4
53. Did frequent bag changes occur during the night?	1	2	3	4
54. Did you feel embarrassed because of your stoma?	1	2	3	4
55. Did you have problems caring for your stoma?	1	2	3	4

Answer these questions ONLY IF YOU DO NOT HAVE A STOMA BAG:				
49. Have you had unintentional release of gas/flatulence from your back passage?	1	2	3	4
50. Have you had leakage of stools from your back passage?	1	2	3	4
51. Have you had sore skin around your anal area?	1	2	3	4
52. Did frequent bowel movements occur during the day?	1	2	3	4
53. Did frequent bowel movements occur during the night?	1	2	3	4
54. Did you feel embarrassed because of your bowel movement?	1	2	3	4

During the past 4 weeks:	Not at All	A Little	Quite a Bit	Very Much
For men only:				
56. To what extent were you interested in sex?	1	2	3	4
57. Did you have difficulty getting or maintaining an erection?	1	2	3	4

For women only:				
58. To what extent were you interested in sex?	1	2	3	4
59. Did you have pain or discomfort during intercourse?	1	2	3	4

FIQL (Fecal Incontinence Quality of Life Instrument)

Fecal Incontinence Quality of Life Instrument

Q 1: In general, would you say your health is:

1 □ Excellent
2 □ Very Good
3 □ Good
4 □ Fair
5 □ Poor

Q 2: For each of the items, please indicate how much of the time the issue is a concern for you due to accidental bowel leakage.

Q2. Due to accidental bowel leakage:	Most of the Time	Some of The Time	A Little of the Time	None of the Time
a. I am afraid to go out	1	2	3	4
b. I avoid visiting friends	1	2	3	4
c. I avoid staying overnight away from home	1	2	3	4
d. It is difficult for me to get out and do things like going to a movie or to church	1	2	3	4
e. I cut down on how much I eat before I go out	1	2	3	4
f. Whenever I am away from home, I try to stay near a restroom as much as possible	1	2	3	4
g. It is important to plan my schedule (daily activities) around my bowel pattern	1	2	3	4
h. I avoid traveling	1	2	3	4
i. I worry about not being able to get to the toilet in time	1	2	3	4
j. I feel I have no control over my bowels	1	2	3	4
k. I can't hold my bowel movement long enough to get to the bathroom	1	2	3	4
l. I leak stool without even knowing it	1	2	3	4
m. I try to prevent bowel accidents by staying very near a bathroom	1	2	3	4

Q 3: Due to accidental bowel leakage, indicate the extent to which you AGREE or DISAGREE with each of the following items.

Q3. Due to accidental bowel leakage:	Strongly Agree	Somewhat Agree	Somewhat Disagree	Strongly Disagree
a. I feel ashamed	1	2	3	4
b. I can not do many of things I want to do	1	2	3	4
c. I worry about bowel accidents	1	2	3	4
d. I feel depressed	1	2	3	4
e. I worry about others smelling stool on me	1	2	3	4
f. I feel like I am not a healthy person	1	2	3	4
g. I enjoy life less	1	2	3	4
h. I have sex less often than I would like to	1	2	3	4
i. I feel different from other people	1	2	3	4
j. The possibility of bowel accidents is always on my mind	1	2	3	4
k. I am afraid to have sex	1	2	3	4
l. I avoid traveling by plane or train	1	2	3	4
m. I avoid going out to eat	1	2	3	4
n. Whenever I go someplace new, I specifically locate where the bathrooms are	1	2	3	4

Q 4: During the past month, have you felt so sad, discouraged, hopeless, or had so many problems that you wondered if anything was worthwhile?

1 □ Extremely So - To the point that I have just about given up
2 □ Very Much So
3 □ Quite a Bit
4 □ Some - Enough to bother me
5 □ A Little Bit
6 □ Not At All

Scale Scoring

Scales range from 1 to 4; with a 1 indicating a lower functional status of quality of life. Scales scores are the average (mean) response to all items in the scale (e.g. add the responses to all questions in a scale together and then divide by the number of items in the scale). (Not apply is coded as a missing value in the analysis for all questions.)

Scale 1. Lifestyle, ten items.

Q2A Q2B Q2C Q2D Q2E Q2G Q2H Q3B Q3L Q3M

Scale 2. Coping/Behavior, nine items.

Q2F Q2I Q2J Q2K Q2M Q3C Q3H Q3J Q3N

Scale 3. Depression/Self Perception, seven items.

Q1 Q3D Q3F Q3G Q3I Q3K Q4, (Question 1 is reverse coded.)

Scale 4. Embarrassment, three items.

Q2L Q3A Q3E

Appendix VII Protocol 5, 31/07/2008 (BFB)

CLINICAL STUDY PROTOCOL

CONFIDENTIAL

THE ROLE OF BIOFEEDBACK IN IMPROVING CONTINENCE AFTER ANTERIOR RESECTION:

A RANDOMISED CONTROLLED TRIAL

Lead Investigator: Miss SA Pilkington

Specialist Registrar, Wessex Surgical Rotation

Supervisor: Miss KP Nugent

Consultant Colorectal Surgeon, University Surgical Unit

Southampton General Hospital

Date this version written 03.09.2005

Revised 31.03.2006
10.06.2006
11.05.2007
16.10.2007
31.07.2008

REC Reference Number: 06/Q1704/84

VERSION 5: 31.07.2008

PROTOCOL SUMMARY

THE ROLE OF BIOFEEDBACK IN IMPROVING CONTINENCE AFTER ANTERIOR RESECTION: A RANDOMISED CONTROLLED TRIAL

OBJECTIVES
To compare the changes in faecal continence of patients after anterior resection using treatment with biofeedback or no biofeedback by carrying out a clinical trial.

DESIGN
Single blind prospective randomised controlled trial to investigate whether biofeedback is of benefit to patients undergoing anterior resection.

SAMPLE SIZE
A total of 120 patients will be recruited to the study. Patients will be randomised to either no biofeedback (group A: control) or biofeedback (group B: biofeedback) in a ratio of 1:1, so that 60 patients will receive biofeedback and 60 will not.

INTERVENTIONS
Group A (control) will have assessment of anal sphincter function preoperatively and postoperatively at 3 and 12 months.
Group B (biofeedback group) will receive five 30-minute biofeedback sessions: one pre-operative session and post-operative sessions at 3 monthly intervals. This will be in addition to assessment of anal sphincter function preoperatively and postoperatively at 3 and 12 months postoperatively.

METHODOLOGY
Patients will be identified as potential participants for this trial at the colorectal clinics at Southampton General Hospital. Computer randomisation will take place with the patients' consent and they will be allocated to no biofeedback (group A) or biofeedback (group B). The investigators will be blinded to the randomisation process and will carry out assessment of anal sphincter function preoperatively and postoperatively at 3 and 12 months postoperatively. Anal sphincter function will be assessed in four modalities: Cleveland Clinic incontinence score, Quality of Life Questionnaire, anorectal physiology and anorectal ultrasound.

DURATION OF SUBJECT PARTICIPATION
After entering the study, patients will participate in the study for one year.

INVASIVE PROCEDURES
Rectal examination with anorectal ultrasound will be performed preoperatively and postoperatively at 3 months. Anorectal physiology will be performed preoperatively and postoperatively at 3 and 12 months.

PROTOCOL

THE ROLE OF BIOFEEDBACK IN IMPROVING CONTINENCE AFTER ANTERIOR RESECTION: A RANDOMISED CONTROLLED TRIAL

INTRODUCTION

Faecal incontinence is one of the most debilitating complications of surgery for rectal cancer. The most commonly used endpoint of surgical treatment for rectal cancer is survival. Much emphasis is directed towards achieving a complete surgical excision and reducing cancer recurrence rates[1] to improve survival. However, the functional outcome of the neorectum is also a significant factor for patients[2].

The treatment of choice for most patients with rectal carcinoma is sphincter-preserving surgery with total mesorectal excision[3;4]. Although continuity is preserved, up to 50% of these patients may experience the 'anterior resection syndrome' of faecal leakage, urgency and frequency[2]. Such symptoms are distressing to the patient and adversely affect their quality of life[5]. Changes detected with anorectal ultrasound and physiological studies of the internal anal sphincter have been shown to correlate with recovery of continence after surgery[6;7]. Other patients with pathology within 30cm of the anal verge also undergo anterior resection and these patients will be included in this study. The same operation is performed and patients suffer from the same post operative complications.

Biofeedback is a specific form of behavioural modification. It has been shown to be beneficial in the treatment of faecal incontinence with an overall efficacy of up to 80%[8]. However, there is a lack of high quality randomised controlled trials that address the role of biofeedback in treating faecal incontinence[9]. The use of biofeedback specifically in postoperative patients after surgery for rectal cancer has not been studied in detail. Only one study has looked at the role of biofeedback in symptomatic patients with excessive stool frequency or incontinence following anterior resection or total colectomy[10]. The number of patients in this study was small but biofeedback was found to be safe and effective. Ten out of 13 patients treated had at least 90% reduction in their incontinence episodes. Biofeedback programs are variable. The method in use at Southampton General Hospital involves 30-minute sessions. During the biofeedback sessions the patient is advised about methods of efficient defaecation and given a series of exercises to practise to improve sphincter function. A rectal balloon with visual feedback display is used to demonstrate to the patient whether they are managing to produce an adequate squeeze pressure.

Despite the lack of high quality randomised trials, biofeedback programs have emerged as a popular and successful treatment for faecal incontinence with reported success rates of between 50 and 92%[11] and a clinical improvement

lasting at least 2 years. The method is safe, painless, well tolerated and does not preclude further treatment if it is unsuccessful.

Rectal function is difficult to quantify. In this trial, four modalities will be used to assess changes in rectal function:

1. Cleveland Clinic incontinence score
2. Condition specific quality of life questionnaire
3. Anorectal physiology
4. Anorectal ultrasound

The Cleveland Clinic incontinence score is an incontinence severity score. It is easy to use and gives the patient a score of 0 to 20, where 0 equates to no incontinence. It is already in use in the anorectal physiology laboratory in Southampton General Hospital. It was first proposed by Wexner *et al*[12] and is widely used as a tool to measure the severity of faecal incontinence[13;14].

There are many quality of life questionnaires published, but little consensus about the optimal instrument to use. Generic assessment tools, such as SF-36, are unlikely to be specific enough to detect the changes in quality of life in our group of patients. Condition specific quality of life instruments such as the Faecal Incontinence Quality of Life Scale (FIQL)[15], EORTC CRC38[16] and Manchester Health Questionnaire[17] are more likely to be sensitive to the effects of a given health problem, such as faecal incontinence. These examples have been validated and tested for reliability. For this study the Faecal Incontinence Quality of Life Scale (FIQL)[15] and EORTC CRC38[16] will be used to compare quality of life in the two groups.

Initial anorectal physiology and ultrasound investigations will be used to look for underlying causes of faecal incontinence existing prior to surgery. Postoperative assessment will investigate whether surgery has altered the structure or function of the anal sphincter. Improvements in resting pressure have been found to correlate with biofeedback[14]. Both anorectal physiology and ultrasound will be used to follow changes occurring after surgery and to compare the control and biofeedback groups.

The proposed study will be the first to investigate the routine use of biofeedback in improving rectal function after anterior resection. At present there is a lack of robust evidence[9] for this potentially extremely useful treatment option for patients with faecal incontinence. Patients undergoing anterior resection are a key group of patients in whom to assess the effectiveness of an established biofeedback program, as is proposed in this trial.

The results of the proposed trial will be used in clinical decision-making to determine whether patients undergoing anterior resection would benefit from routine biofeedback in terms of improved faecal continence postoperatively. The results will also improve our understanding of the mechanisms of faecal incontinence after anterior resection.

OBJECTIVES

The primary outcome is anal sphincter function at one year after anterior resection with and without biofeedback as assessed by the Cleveland Clinic Incontinence Score. Anal sphincter function will also be assessed by quality of life questionnaire, anorectal ultrasound and anorectal physiology.

Secondary objectives will be:

- To compare changes in anorectal ultrasound before and after surgery and to look at the effect of radiotherapy
- To compare changes in Cleveland Clinic Incontinence Score at 3, 6 and 9 months postoperatively with and without biofeedback and to see if this correlates with quality of life assessments
- To compare changes in quality of life 3, 6 and 9 months postoperatively with and without biofeedback.
- To compare safety and tolerability of the biofeedback program with no biofeedback.
- To determine compliance with treatment and dropout rates in the two study groups

HYPOTHESIS

Biofeedback in the perioperative period improves rectal function and continence of patients who have had anterior resection.

STUDY DESIGN

The study is designed as a single blind prospective randomised controlled trial to compare anal sphincter function in participants receiving no biofeedback (group A: control) or biofeedback (group B) after anterior resection for rectal cancer.

Patients who are undergoing anterior resection for pathology within 30cm of the anal verge and fulfil the inclusion criteria will be recruited to the study from the colorectal clinics at Southampton General Hospital. In addition to assessing anal sphincter function, patients in the biofeedback group (B) will receive three monthly biofeedback sessions. The first of these sessions will be conducted preoperatively and subsequent sessions will be 3 monthly postoperatively for one year.

Anal sphincter function of all participants will be assessed preoperatively (baseline) and postoperatively at 3 and 12 months with the Cleveland Clinic Incontinence Score, anorectal physiology and quality of life questionnaires. In addition the Cleveland Clinic Incontinence score and quality of life questionnaires will be completed at 6 and 9 months postoperatively. Anorectal ultrasound will be carried out preoperatively and postoperatively to look for underlying sphincter damage or changes associated with surgery.

SAMPLE SIZE

A total of 120 patients will be recruited to the study. Participants will be randomised to either no biofeedback or biofeedback in a ratio of 1:1, so that 60 participants will receive no biofeedback and 60 will receive biofeedback.

Using a standard deviation of 10 [13], an analysable sample size of 45 patients in each arm will be needed to detect a 30%[11] difference in Cleveland Clinic incontinence scores. In a recent study of 239 patients treated with biofeedback for faecal incontinence, 11% failed to start treatment and a further 6% failed to complete treatment[8]. Assuming that a dropout rate of 30% is encountered, 120 patients would need recruiting to ensure that a final sample size of 42 per treatment arm was achieved. Assuming a common SD of 5 and 80% power, a difference of 3 in Cleveland Clinic incontinence score could be detected. This would be clinically significant.

POPULATION TO BE DRAWN FROM

A total of 120 patients will be recruited from colorectal clinics in Southampton. They must satisfy all inclusion and exclusion criteria.

Inclusion Criteria

- Patients with a diagnosis of colorectal cancer who are going to have an anterior resection
- Patients aged 18 years or older
- Patients who have given written informed consent to participate in the trial

Exclusion Criteria

- Patients deemed mentally incompetent
- Pregnant and nursing mothers
- Patients considered by their physician as being unlikely to comply with the protocol

INTERVENTIONS

Patients in group A will receive no biofeedback. Patients in group B will receive biofeedback sessions with Sister S. Gilbert (GI physiology nurse specialist). Each session lasts approximately 30 minutes. The first session will be preoperatively. Subsequent sessions will be at 3 monthly intervals for one year and will start 3 months after surgery. Patients who have had a defunctioning ileostomy will begin their biofeedback sessions 3 months after closure of their ileostomy.

During the biofeedback sessions the patient will be advised about methods of efficient defaecation and given a series of exercises to practise to improve

sphincter function. The nurse specialist will also demonstrate how the patient can most efficiently produce an adequate squeeze pressure for continence using a rectal probe with visual feedback display.

DATA REQUIRED TO SATISFY OBJECTIVES

Anal sphincter function will be assessed preoperatively and postoperatively at 3 and 12 months. It will be measured in three modalities: Cleveland Clinic Incontinence Score, quality of life questionnaire and anorectal physiology. In addition, Cleveland Clinic Incontinence Score and quality of life questionnaries will be completed at 6 and 9 months. Anorectal ultrasound will be carried out preoperatively and postoperatively. The research doctor assessing anorectal physiology and the radiologist performing endoanal ultrasound will both be blinded to the treatment groups. Additional information will also be collected including operative details, histology and adjuvant chemoradiotherapytherapy (see case report form). All adverse events will be recorded.

STUDY PROCEDURE

Patients who are scheduled for anterior resection will be identified at the colorectal clinics at Southampton General Hospital. Once all inclusion/exclusion criteria have been met, the patient will be given the information sheet (SEE APPENDIX I) and invited to join the study. Patients will be given at least two days to decide if they wish to take part. All patients willing to participate in the trial will be asked to sign the consent form (SEE APPENDIX II). A letter will be sent to the patient's GP to inform the GP about the recruitment of the patient to the trial (SEE APPENDIX III). Computer randomisation will then take place and will be operated by the trial statistician (Scott Harris, Medical Statistician) to ensure that the research assessors of functional outcome are blinded to the randomisation process.

Anal sphincter function will be assessed preoperatively and postoperatively at 3 and 12 months. It will be measured in three modalities: Cleveland Clinic Incontinence Score, quality of life questionnaire and anorectal physiology. In addition, Cleveland Clinic Incontinence Score and quality of life questionnaries will be completed at 6 and 9 months. Anorectal ultrasound will be carried out preoperatively and postoperatively. Patients who have had a defunctioning ileostomy will not start assessment until 3 months after closure of their ileostomy. Anorectal ultrasound will be performed by Dr Dewbury (Consultant Radiologist) and anorectal physiology will be conducted by Miss Nugent (Consultant colorectal surgeon) and Miss Pilkington (research SpR). All of these researchers will be blinded to the treatment groups and will not be involved in the biofeedback sessions.

In addition, patients in group B will also receive 30-minute sessions of biofeedback with Sister Gilbert. The first session will be pre-operatively. Subsequent sessions will be every three months postoperatively for one year.

Patients who have had a defunctioning stoma will receive the first postoperative session 3 months after closure of their stoma.

A full register of patients recruited to the study will be kept. The case report form will be kept in the patient file until they have met the endpoint criteria.

STUDY MEDICATION

None

DURATION OF SUBJECT PARTICIPATION

After entering the study, all patients will be given an initial assessment of anal sphincter function to establish the baseline for each patient. After surgery they will be seen every three months for one year and repeat assessment of anal sphincter function will be performed.

INVASIVE PROCEDURES

Rectal examination with anorectal physiology will be performed at the initial appointment and postoperatively at 3 and 12 months. Anorectal ultrasound will be performed pre and postoperatively.

ADVERSE EVENT REPORTING

All adverse events that occur during the investigation (ie after the patient has given informed consent) will be documented in the Case Report Form. Postoperative complications such as chest infection, wound infection, cardiorespiratory problems, thromboembolism and anastomotic leak resulting in further surgery or death will be recorded in the case report form. SUHT Research related SAE/SUSAR initial reporting form will be completed for all deaths and for adverse events such as complete anal incontinence or intolerability of biofeedback but will not be completed for common post-operative complications such as wound infection, chest infection, cardiorespiratory problems, thromboembolism and anastomotic leak. The investigator will make an assessment of severity and causality. Each patient's GP will be notified of the patient's participation in the trial (SEE APPENDIX III). The patient will be encouraged to phone directly the principal investigator or their GP if they experience a problem.

WITHDRAWALS AND DROPOUTS

The patient may choose to withdraw from the study at any time and for any reason. Completion of the study will be at one-year post surgery. A patient lost to follow up is defined as a patient who was recruited to the study but did not turn up for follow-up visits. These patients will be sent a letter with another appointment and will be contacted by telephone to ascertain the reason for their non-attendance (eg patient withdrawal of consent).

ETHICAL CONSIDERATIONS

This study has been reviewed by the Southampton and SW Hampshire Ethics Committee and no objections where raised on ethical grounds. Informed consent will be sought from potential participants in the trial. Information will be in both written and oral form. See appendices for information sheet and patient consent form.

DATA ANALYSIS PLAN

Advice has been sought from Dr Steven George (Epidemiologist) and Mr Scott Harris (Medical Statistician) regarding statistical analysis.

The primary outcome measure is sphincter function as measured by the Cleveland Clinic incontinence score at one year compared to baseline function. The one-year Cleveland Clinic incontinence score will be examined in a linear regression model adjusted for the baseline level. A comparison of treatment groups will be conducted and presented with its 95% confidence interval. This primary comparison will be conducted on an intention to treat (ITT) basis.

Secondary analyses will include changes in sphincter function in the four modalities in the two groups over the first postoperative year. These secondary analyses will be carried out using similar regression models. Other efficacy criteria will be to compare safety and tolerability of the biofeedback program with no biofeedback and to determine compliance with treatment and dropout rates in the two study groups.

APPENDICES

I Patient Information Sheet
II Patient Consent Form
III Letter to GP (will include copy of Patient Information Sheet)
IV Case report form
V Symptom Scores
VI Patient Quality of Life Questionnaires

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Appendix VIII Patient information sheet (BaP vs MR proctogram)

Radiology Department
Poole Hospital NHS Trust
35 Parkstone Road
Poole
BH15 2NG

Tel 01202 442313

Patient Information Sheet

VERSION 4
31/03/2008

Barium and MR proctography

Introduction
You are being invited to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?
The purpose of this study is to compare two tests for investigating why some people have difficulty emptying their bowels and to determine which is best. In addition we will compare which test the patient finds least troublesome. The two tests are a barium proctogram which is done in Poole Hospital and an MR proctogram which is done in Dorchester Hospital. If you do take part in this study you will have an extra proctogram test as well as your routine one.

Why have I been chosen?
We are hoping to include 60 patients in this study. All patients who are having a proctogram as part of their routine investigation may be invited to take part in the study. However, if you have a pacemaker it will not be possible to include you in this study.

Do I have to take part?
It is up to you to decide. We will describe the study and go through this information sheet, which we will give to you. We will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

What will happen to me if I take part?
If you agree to take part, you will be offered an extra proctogram test. You will be asked about your patient experience and which of the two tests you preferred.

What do I have to do?
If you agree to take part in this study, it is very important that you attend the extra proctogram test in addition to your routine test. It will be possible to rearrange the appointment to suit you. The study does not involve taking any drugs and you should continue taking your regular medication. The standard information sheets from Poole (Having a Proctogram: A Guide to the Test) and Dorchester Hospitals (MR-Proctography) about the two types of proctogram are included with this information sheet. Please read these information sheets carefully.

What are the possible disadvantages and risks of taking part?
You will be asked to undergo one additional proctogram test. You will therefore need to attend both Poole and Dorchester radiology departments. You will have free car parking for the extra proctogram and you will be reimbursed for £12 towards your travel costs.

What are the possible benefits of taking part?
We cannot promise that the study will help you but the information we get might help improve the investigation and treatment of people with difficulty emptying their bowels.

What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak with the research doctors who will do their best to answer your questions (See contact numbers at the end of this information sheet). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

In the event that something does go wrong and you are harmed during the research study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

Will my taking part in the study be kept confidential?
Yes. All the information about your participation in this study will be kept confidential. All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you which leaves the hospital will have your name and address removed so that you cannot be recognised from it.

We will inform your doctor that you have been enrolled in the study. However the information that you give will be completely confidential and will not be disclosed to your doctor.

What if relevant new information becomes available?
Sometimes during the course of a research project, new information becomes available about the investigation or treatment that is being studied. If this happens, your research doctor will tell you about it and discuss whether you want to or should continue in the study. If you decide not to carry on, your research doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an updated consent form.

Also, on receiving new information your research doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

If the study is stopped for any other reason, you will be told why and your continuing care will be arranged.

Will any genetic tests be done? No

What will happen to the results of the research study?
The results of the study will be submitted for publication in a medical journal. A summary sheet will be sent to all the participants with the key findings of the research project. Individual participants will not be identified in any report or publication unless they have consented to release such information.

Who is organising and funding the research?
The research doctor (Sophie Pilkington) is funded by the Royal College of Surgeons Joint Dunhill Medical Trust. This work is being undertaken as part of an educational qualification for an MD thesis. A Research Bursary from the Bowel Disease Research Foundation has been awarded for the project.

Who has reviewed the study?
This study was given a favourable ethical opinion for conduct in the NHS by the Dorset Research Ethics Committee.
REC Reference Number: Dorset REC 07/H0201/154

How can I get more information?
If you would like more information please contact the research doctor, Sophie Pilkington
Telephone number: 023 8079 6145

Alternatively you could contact:

Dr Tarver (Consultant Radiologist, Poole Hospital) 01202 442313

Dr Thomas (Consultant Radiologist, Dorchester Hospital) 01305 254422

Thank you for reading this patient information sheet

Appendix IX Consent form (BaP vs MR proctogram)

Radiology Department
Poole Hospital NHS Trust
35 Parkstone Road
Poole
BH15 2NG

Tel 01202 442313

Patient Identification Number: ☐

CONSENT FORM
Version 4: 31.03.2008

Title of Project: Barium proctography versus dynamic magnetic resonance proctography for pelvic floor disorders: A comparative study

Name of Researchers: Miss S. Pilkington, Dr C. Thomas & Dr D. Tarver

Please initial box

1. I confirm that I have read and understand the information sheet dated: 31.03.2008 (version 4) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that relevant sections of any of my medical notes and data collected during the study, may be looked at by responsible individuals from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
4. I agree to my GP being informed of my participation in the study. ☐
5. I agree to take part in the above study. ☐

Name of Patient	Date	Signature
Name of Person taking consent	Date	Signature

When completed, 1 for patient; 1 for researcher site file; 1 (original) to be kept in medical notes

Appendix X GP letter (BaP vs MR proctogram)

Radiology Department
Poole Hospital NHS Trust
35 Parkstone Road
Poole
BH15 2NG

Tel 01202 442313

Ethics Committee Number: Dorset REC 07/H0201/154

Study Title: Barium proctography versus dynamic magnetic resonance proctography for pelvic floor disorders: A comparative study

Short title: Barium and MR proctography
Version 2: 16/10/2007

Dear Dr

Your patient _____
has agreed to take part in the above study. This study has been reviewed by the Dorset Research Ethics Committee, who raised no objections on ethical grounds.

Please find enclosed a patient information sheet, which gives more information about the research study.

If you have any further questions about this study, please contact us at Poole Hospital, contact telephone number: 01202 442313.

Yours sincerely,

Miss SA Pilkington (Specialist Registrar in Surgery, Southampton)
Dr C Thomas (Consultant Radiologist, Dorchester)
Dr D Tarver (Consultant Radiologist, Poole)

Appendix XI Case Report Form (BaP vs MR proctogram)

SHORT TITLE: Barium and MRI proctography
Case Report Form Version 2 (16/10/2007)

Patient Name:

Date of Birth:

Hospital Number:

SHORT TITLE: Barium and MRI proctography
Case Report Form Version 2 (16/10/2007)

Date: Barium ☐ MR ☐ Reported by: DT ☐ CT ☐
Report date:

Pubococcygeal Line (PCL)
(inferior symphysis pubis to last coccygeal joint)

- Anorectal junction distance to PCL (cm)
  resting contracting evacuating
- Anorectal angle (ARA) at intersection between line along posterior wall rectum and line along central axis anal canal
  resting contracting evacuating

Evidence for:

Complete rectal emptying	N	Y		
Anismus	N	Y		
Mucosal prolapse	N	Y		
Rectal intussusception	N	Y	Grade (Oxford):	
Uterovaginal prolapse	N	Y		
Peritoneocele	N	Y		
Sigmoidocele	N	Y		
Cystocele	N	Y	Cystocele size (cm):	
Enterocele	N	Y	Max AP length (cm):	

Distance from sacral promontory to lower margin of enterocele:

PCL to lower margin of enterocele at 90°:

Rectocele	N	Y
Empties	N	Y

Length from extended anterior wall anal canal (cm):

Comments:

Table 1: Oxford radiological grading of rectal intussusception

Grade of intussusception	Radiological characteristics of intussusceptum
I (high rectal)	Descends no lower than proximal limit of the rectocele
II (low rectal)	Descends into the level of the rectocele, but not onto sphincter/anal canal
III (high anal)	Descends onto sphincter/anal canal
IV (low anal)	Descends into sphincter/anal canal
V (overt rectal prolapse)	Protrudes from anus

Appendix XII Questionnaire (BaP vs MR proctogram)

SHORT TITLE: Barium and MRI proctography
Debriefing Questionnaire Version 2
16/10/2007

Patient Name:

Date of Birth:

Hospital Number:

Date: ☐ Barium ☐ MR ☐

1. Do you feel that you opened your bowels as usual during the test today?

Yes No

2. Would you have this test repeated if necessary for your treatment?

Yes No

3. Any other comments?

If this is your second test, please complete questions 4 and 5.

4. Which test did you prefer? (please tick) Barium ☐ MR ☐

5. Why? Less embarrassing
Less uncomfortable
Better position
Easier to empty bowels during the test
Preferred the staff/nurse/doctor/radiographer/hospital
Other reason, please explain:

Thank you very much for taking part in this study.

Appendix XIII Protocol 4, 31/03/2008 (BaP vs MR proctogram)

Barium proctography versus dynamic magnetic resonance proctography for pelvic floor disorders: A comparative study

SHORT TITLE: Barium and MR proctography

Protocol Version 4

31/03/2008

Sponsor: University of Southampton

Dorset REC number: 07/H0201/154

Chief Investigator: Miss SA Pilkington, Surgical Research SpR

University Surgical Unit, Southampton General Hospital, Tremona Road,

Southampton, SO15 5JF

02380 796145

07969 164 874

Other Investigators:

Dr D Tarver, Consultant Radiologist Tel 01202 442313

Poole Hospital, Longfleet Road, Poole, Dorset, BH15 2JB

Dr C Thomas, Consultant Radiologist Tel 01305 254422

Dorset County Hospital, Dorchester, Dorset. DT1 2JY

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Background

Accurate and reliable imaging of pelvic floor dynamics is important for determining treatment options for patients with obstructive defaecation and pelvic organ prolapse[1]. Estimates suggest that one in every nine women will undergo surgery for pelvic floor disorders during their lifetime and that 30% of these will require additional surgery for the same condition[2].

Dynamic pelvic imaging has a central role to play in selecting which patients are likely to benefit from surgery. Until recently, evacuating barium proctography was the gold standard for investigating such patients[3;4]. During this investigation, the rectum is filled with barium paste and the vagina and small bowel are opacified with contrast medium. The patient is seated on a radiolucent commode and fluoroscopic images are taken in the sagittal plane at rest, during straining and during defaecation. However, barium proctography is associated radiation exposure to the pelvic organs. The mean effective dose equivalent has been estimated at between 3.6 and 6.5mSv, which is approximately 360 chest radiographs[5].

Recent advances in magnetic resonance imaging technology have made it possible to perform dynamic MR studies of the pelvic organs during defaecation[6]. In a conventional closed coil MRI system, the patient is positioned supine during scanning[6] with a support for the feet so that the knees and hips are flexed.

Ultrasound gel is placed in the rectum with a bladder syringe and tubing. Twenty T2-weighted single midsagittal sections each 5mm thick are taken at 2 second intervals to build-up a dynamic sequence as the patient bears down and evacuates the rectum. For this study a 1Tesla magnet (Phillips Intera) will be used. The rectal wall and neighbouring soft tissue structures are clearly visualised allowing the diagnosis of rectocele, cystocele, enterocele, uterovaginal prolapse or rectal intussusception to be made. The patient is not in a physiological position for defaecation and this may limit the relevance of this investigation in some cases. The development of open configuration MRI scanners has allowed MRI scanning to be carried out with the patient in an upright position during defaecation[7]. A suspension of gadolinium is placed in the rectum and T-1 weighted images are taken during defaecation. One study has compared these two MRI techniques using patients who presented with stress urinary incontinence and/or symptoms of pelvic prolapse[8]. Although they report that all rectal intussusception was missed on supine MRI, only 3 patients in the study group of 38 patients had rectal intussusception and there was no information as to whether these patients were symptomatic or not. In addition, although MRI during straining was carried out in the closed coil scanner, images were not acquired during defaecation due to restrictions imposed by the institution guidelines.

Studies that report poor performance of MR proctography when compared to barium proctography, frequently fail to include MRI scans acquired during

defaecation, whereas this is always part of the barium study protocol[9;10]. When dynamic MRI scans do involve simulated defaecation, rectal intussusception can be detected[6]. In addition, although MRI scanning in the supine position may not simulate exactly the same mechanisms taking place in the squatting or seated position usually adopted for defaecation, it may provide useful information about the structures that will be encountered when the patient is supine on the operating table. This is likely to be particularly important when planning stapled transanal rectal resection (STARR) operations for rectal intussusception where there is a risk of forming an enterorectal fistula if the stapling device is fired through an adjacent enterocele.

Although some hospitals are using dynamic MR proctography as a substitute for barium proctography because no radiation is involved[11], it is still not clear whether the results of these two investigations are comparable[12].

The normal process of defaecation with associated movement of pelvic organs is poorly understood and the boundaries between normal and pathological movement are difficult to define[13-15]. In addition the precise definitions of the lines and angles measured vary between different studies. For the purposes of quantitative research it is useful to measure the change in position of the pelvic organs during defaecation with respect to their neighbouring bony and soft tissue structures. The pubococcygeal line (PCL) which connects the inferior aspect of the symphysis pubis with the last coccygeal joint[7], is an important landmark for

assessing pelvic floor movement. At rest in a normal patient the base of the bladder, the upper third of the vagina and the peritoneal cavity (including small bowel and sigmoid colon) are usually situated superior to the PCL[16]. The anorectal junction (ARJ) is the point at which a line along the posterior border of the rectum transects a line along the central axis of the anal canal. This point is usually situated within 3cm of the PCL.

Several methods for quantifying rectoceles on imaging have been described. A reference line may be drawn along the anterior wall of the anal canal and extended[3], or the maximum distension of the rectocele beyond the predicted margin of the anterior rectal wall is measured[3;17;18]. Mellgren *et al* classified rectocele size into three groups according to the maximum distension. In addition to grading the size of the rectocele, the presence of post-defaecatory trapping can be demonstrated. Invagination of the rectal wall, known as rectal intussusception, frequently co-exists with rectocele. Rectal intussusception may be anterior, posterior or circumferential. The intussusception may be contained within the rectal ampulla or it may extend into the anal canal or beyond, where it is known as a rectal prolapse.

At Poole Hospital 115 barium proctograms were performed between 16/07/2006 and 17/07/2007. Poole Hospital has carried out barium proctography for patients who are seen at Dorchester Hospital and require proctography. However the

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pelvic floor service in Dorchester has the facilities to perform dynamic closed coil MR proctography.

This project will carry out barium and MR proctography on a cohort of 60 consecutive patients presenting to the pelvic floor service in Poole and Dorchester. Barium proctography will be performed in Poole by Dr D. Tarver and MR proctography will be carried out in Dorchester by Dr C. Thomas. Each proctogram will be reported by the consultant performing the investigation according to a standard proforma. In addition each proctogram will be reported by the other radiologist, blinded to the first report. In cases where a significant discrepancy is found, the proctograms will be discussed at the Southern Pelvic Floor MDT to determine whether the discrepancy has any clinical relevance for the management of the patient. If during the extra proctogram another condition emerges, the consultant who referred the patient for the routine proctogram will be informed and the case will be discussed at the Southern Pelvic Floor MDT. Follow-up will be arranged as would be normal routine practice. Often this involves a pelvic ultrasound scan which would be organised via the patient's consultant. It is not anticipated that additional conditions will be found very often because we are not collecting volumetric data through the pelvis but just one slice in a dynamic sequence.

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Aims and Objectives

The purpose of the study is non-commercial and will contribute to an MD thesis.

The primary objective is to determine whether there are measureable differences between barium and MR proctogram findings. In particular, the size of rectocele demonstrated on erect barium proctography and supine MR proctography will be compared.

The secondary objectives include:

- A comparison of proctogram measurements including anorectal descent, change in anorectal angle and enterocele size
- Comparison of presence of complete rectal emptying, anismus, mucosal prolapse, rectal intussusception, uterovaginal prolapse, peritocele, sigmoidocele, cystocele, enterocele, rectocele and rectocele emptying between the two proctograms
- Agreement between the two reports on each barium proctogram and each MR proctogram
- Determine tolerability and patient preference for the two procedures
- Determine whether differences between the two investigations have any clinical significance.

Study Design

This is a cohort study comparing barium and MR proctography on 60 consecutive patients. The proctograms will be reported by two consultant radiologists who specialise in pelvic floor disorders and are blinded to the results of the other investigation.

All patients in the study group will be undergoing proctography as part of their routine NHS care. Patients who fulfil the inclusion/exclusion criteria will be offered an additional appointment at Dorchester Hospital for MR proctography. MR proctography is similar to barium proctography in that the patient has contrast placed in the rectum. However unlike barium proctography no contrast is placed in the vagina or small bowel. The MR sequence is usually recorded over a 30 second time period during which the patient evacuates the rectum whilst lying in the scanner. MR proctography does not involve ionising radiation.

The study involves one additional non-ionising investigation on each patient and there is no follow-up. The study would be discontinued if patients found the procedures intolerable or if there was overwhelming evidence that one investigation was significantly superior to the other.

Subject selection

The potential subjects will be those attending Poole and Dorchester Radiology Departments for proctography. These patients will have been seen at the

colorectal and gynaecology clinics at Poole and Dorchester Hospitals as part of the pelvic floor service. This is an appropriate group of patients because they have been referred for proctography already as part of their NHS management.

Inclusion Criteria

- Referred for proctography as part of routine NHS management
- Patient gives informed consent
- Aged greater than 18 years old

Exclusion Criteria

- Patient incompetent to give informed consent
- Claustrophobia or unable to tolerate MRI
- Contraindications to MRI such as pacemaker, high BMI
- Patient unable to lie flat

Subject recruitment

The patient invitation letter and information sheet will be posted to the patient so that it is received a minimum of 2 days before the proctogram. At the appointment in the radiology department in Poole Hospital, the study will be explained to the potential participant by a senior radiographer (Jane Brenner) and consultant radiologist (Dr Tarver). A consent form (see appendix) will be signed to document informed consent for all participants to the study. An

appointment for an MR proctogram will be arranged at Dorchester Hospital for participants. Free car-parking at Dorchester Hospital will be provided. Patients will be reimbursed with £12 as a contribution towards their travel expenses.

Subject compliance and withdrawal

Patients who do not attend the MR proctogram after informed consent will be contacted by telephone to determine whether they have withdrawn from the study or not. One further appointment for an MR proctogram in Dorchester will be arranged if the patient has not withdrawn consent.

Sample size

This is an exploratory study. There is inadequate previous data to base a sample size calculation on. Statistical advice on sample size has being sought from Scott Harris, Medical Statistician at Southampton University Hospitals Trust.

An analysable sample of 60 patients is proposed based on feasibility in the given time frame of one year. Assuming a dropout rate after recruitment of 20% we would need to recruit 75 patients. Between 16/07/2006 and 17/07/2007 a total of 115 barium proctograms were carried out in Poole Hospital. If the recruitment rate is 70%, we would recruit the proposed sample size of 75 patients in 11-12 months.

With a sample size of 60 and standard 80% power, allowing for a maximum difference in rectocele size of 0.5 cm, we could pick up a standard deviation of

1.5, at most. This is a clinically relevant difference to detect. An interim analysis after recruitment of 20 patients will be performed to inform further sample size/power calculation.

Data collection

A case report form (See appendix) will be used to collect the data. Each of the 60 barium proctograms in this project will be reported by 2 consultant radiologist resulting in 120 barium reports. Each of the 60 MR proctograms will be reported by 2 consultant radiologists resulting in 120 MR reports. All reports will take the standardised format on the case report form (See appendix).

Data handling and record keeping

Sophie Pilkington, Jane Brenner, David Tarver and Cen Thomas will be responsible for data collection, recording and quality. Source data will be stored in the radiology departments at Poole and Dorchester Hospitals for 5 years. The Data Protection Act 1998 will be adhered to. A screening and recruitment log will be maintained.

Statistical analysis

All participants who attend both proctograms will be included in the analysis. Statistical advice has being sought from Scott Harris, Medical Statistician at Southampton University Hospitals Trust. Results in all participants will be compared using the Pearson parametric statistic to determine any correlation

between measurements (eg rectocele size) made on each barium and MR proctogram. A paired T-test will be used to look at difference with a 95% confidence interval and 0.5cm equivalence. Bland and Altman plots will be used to assess agreement between the measurements of anorectal junction descent and anorectal angle change on straining or rectal emptying made using each barium and MR proctogram.

Safety Assessments

All adverse events will be reported according to the hospital R&D guidelines.

Stopping / discontinuation rules

The study will be completed when 60 patients have undergone barium and MR proctography or 1 year after recruitment begins if 60 patients have not been recruited by this time.

Research Governance, Monitoring and Ethics & R&D approval

The study will be conducted in compliance with the Research Governance Framework for Health and Social Care and Good Clinical Practice (GCP).

Finance

A Research Bursary has been awarded by the Bowel Disease Research Foundation to support the running costs of this project. Patients will be

reimbursed with £12 as a contribution towards their travel expenses. Free car-parking at Dorchester Hospital will be provided for the additional proctogram.

Indemnity

The University of Southampton will act as sponsor for this project.

Reporting and dissemination

Once the study has been completed, all patients will be sent a layman's summary of the findings. The results will be submitted for publication in a peer review journal.

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Appendix XIV Participant Raw Data: BFB Project

Case Number	BFB =1	Analysed = 1	Age (years)	Female =1	Cancer = 1	Short DXT=1	Stoma =1	Stoma delay (days)	Laparoscopic =1	Tumour height above anal verge (cm)	Resection included peritoneal reflection=1	1=sidetoend anastomosis	Outcome	CCI baseline	CCI final
1	0	1	63	1	1	0	0		1	10	1	1	completed	0	0
2	1	0	62	1	1	0	1		0	12	1	1	APE	0	na
3	1	1	82	0	1	0	1	231	0	18	1	1	completed	0	0
4	0	0	84	0	1	0	0		0	5	1	0	leak died	0	na
5	0	1	65	1	1	0	1	722	0	15	1	0	completed	13	10
6	0	0	73	0	1	0	1		0	8	1	na	APE	5	na
7	1	1	76	0	1	0	1	188	0	10	1	0	completed	0	10
8	1	0	85	1	1	0	0		0	12	1	1	leak died	13	na
9	1	1	75	0	1	0	1	269	0	15	0	0	completed	0	2
10	0	1	74	1	1	0	0		0	18	1	0	completed	11	2
11	1	1	74	0	1	0	0		0	18	1	0	completed	4	4
12	0	0	66	0	1	0	0		0	35	0	1	died	0	na
13	1	1	71	1	1	0	0		0	10	1	1	completed	4	4
14	0	0	67	1	1	0	0		0	10	none	na	inoperable	20	na
15	1	1	75	0	1 polyp cancer	0	0		0	22	0	1	completed	0	0
16	0	1	65	0	1	0	1	56	0	18	1	0	completed	8	0
17	1	1	57	1	1	0	1	101	0	17	1	0	completed	16	3
18	0	1	50	1	1	0	0		0	20	0	0	completed	0	5
19	0	1	53	0	1	0	1	287	0	25	0	0	completed	3	0
20	1	1	75	0	1	0	0		0	15	1	1	completed	0	0
21	0	1	69	1	1	0	1	77	0	5	1	1	completed	0	2
22	1	1	50	1	TVA	0	0		0	14	1	1	completed	0	2

Appendix XIV Participant Raw Data : BFB Project (continued)

Case Number	BFB =1	Analysed = 1	Age (years)	Female =1	Cancer = 1	Short DXT=1	Stoma =1	Stoma delay (days)	Laparoscopic =1	Tumour height above anal verge (cm)	Resection included peritoneal reflection=1	1=sidetoend anastomosis	Outcome	CCI baseline	CCI final
23	1	1	81	0	1	0	1	119	0	18	1	0	completed	0	0
24	0	1	74	1	1	0	0		0	16	1	1	completed	3	0
25	1	1	69	0	1	0	0		0	20	0	0	completed	5	1
26	0	1	73	0	1	0	0		0	30	0	0	completed	3	2
27	0	1	56	1	1	0	0		0	30	0	1	completed	0	3
28	1	1	69	0	1	0	1	164	0	12	1	0	completed	0	10
29	0	0	54	1	Diverticular stricture	0	0		0	25	1	0	died	4	na
30	0	1	82	0	1	0	0		0	27	0	0	completed	5	3
31	1	1	56	0	TVA	0	0		0	16	0	0	completed	5	4
32	1	1	72	1	1	0	1	279	0	8	1	0	completed	0	5
33	1	1	86	1	1	0	1	146	0	12	1	1	completed	5	0
34	0	1	74	0	1	0	0		0	15	1	1	completed	0	8
35	0	1	64	1	TVA	0	0		0	15	1	?	completed	6	6
36	0	1	58	1	1	0	0		0	18	0	0	completed	0	3
37	1	1	82	1	1	0	0		0	15	0	1	completed	7	1
38	1	1	71	1	TVA	0	0		0	18	1	1	completed	3	3
39	1	0	74	0	1	0	0		0	14	1	na	hartmann	9	na
40	0	0	51	1	1	0	1	58	0	13	1	0	xdeclined	0	na
41	0	1	71	0	1	0	1	102	0	10	1	1	completed	8	4
42	1	1	69	0	1	0	0		0	13	0	0	completed	3	0
43	0	1	75	1	1	0	0		0	15	1	0	completed	3	3
44	0	0	50	1	1	0	0		0		0	0	xdeclined	0	2
45	1	1	59	0	1	0	0		0	20	0	1	completed	0	0
46	1	1	60	1	TVA	0	0		0	16	1	1	completed	7	8

Appendix XIV Participant Raw Data : BFB Project (continued)

Case Number	BFB =1	Analysed = 1	Age (years)	Female =1	Cancer = 1	Short DXT=1	Stoma =1	Stoma delay (days)	Laparoscopic =1	Tumour height above anal verge (cm)	Resection included peritoneal reflection=1	1=sidetoend anastomosis	Outcome	CCI baseline	CCI final
47	1	1	55	1	1	0	0		0	15	0	1	completed	0	4
48	1	1	62	0	Diverticular stricture	0	0		0	20	0	1	completed	9	1
49	0	1	69	1	1	0	0		0	25	0	1	completed	9	1
50	0	1	78	1	Diverticular stricture	0	0		0	30	0	0	completed	4	2
51	1	1	70	0	1	2	1	64	0	10	1	0	completed	1	7
52	0	1	46	0	Diverticular stricture	0	0		0	20	0	0	completed	0	8
53	1	1	68	0	1	0	0		0	15	1	0	completed	0	10
54	0	1	64	1	1	0	0		0	15	1	1	completed	4	4
55	0	1	78	0	1	0	0		0	25	0	0	completed	0	1
56	1	0	91	1	1	0	0		0	17	none	na	inoperable	17	na
57	0	0	52	0	Diverticular stricture	0	0		0	20	0	0	died	0	na
58	1	1	57	1	1	0	1	413	0	15	1	1	completed	0	4
59	0	1	63	0	1	0	1	341	0	10	0	?	completed	2	6
60	1	1	57	0	Diverticular stricture	0	0		0	25	0	1	completed	9	4
61	1	1	63	1	1	0	0		0	15	1	1	completed	12	18
62	0	1	79	0	1	0	0		0	15	1	1	completed	4	0
63	0	1	64	0	1	0	0		0	25	1	?	completed	2	1
64	1	1	67	0	1	0	0		0	25	1	1	completed	1	4
65	0	1	71	1	1	0	0		0	20	0	1	completed	7	4
66	1	1	75	0	1	0	0		0	20	1	1	completed	0	0

Appendix XIV Participant Raw Data : BFB Project (continued)

Case Number	BFB =1	Analysed = 1	Age (years)	Female =1	Cancer = 1	Short DXT=1	Stoma =1	Stoma delay (days)	Laparoscopic =1	Tumour height above anal verge (cm)	Resection included peritoneal reflection=1	1=sidetoend anastomosis	Outcome	CCI baseline	CCI final
67	1	0	90	0	1	0	1		0	12	1	1	no reversal	8	na
68	0	1	64	1	TVA	0	0		0	30	0	0	completed	0	4
69	1	1	88	0	1	0	1	76	0	10	1	1	completed	6	2
70	0	0	93	0	1	0	0		0	8	1	0	xdeclined	0	na
71	1	1	81	1	1	0	0		0	30	1	1	completed	2	2
72	0	1	61	0	Diverticular stricture	0	0		0	20	0	1	completed	0	4
73	0	1	81	0	1	0	0		0	12	1	1	completed	0	5
74	1	1	78	0	1	0	0		0	22	0	1	completed	0	3
75	1	0	79	0	1	0	1		0	12	1	1	no reversal	0	na
76	1	1	86	0	1	0	0		0	20	0	1	completed	0	0
77	0	0	70	0	1	0	0		0	25	1	0	xdeclined	2	na
78	0	1	67	0	TVA	0	0		0	12	1	1	completed	0	6
79	0	0	61	0	1	0	0		0	25	0	1	xdeclined	0	na
80	1	1	67	1	1	0	0		0	17	0	0	completed	0	12
81	0	1	65	1	1	0	0		0	20	0	1	completed	6	0
82	1	1	72	1	1	0	0		0	15	1	0	completed	0	1
83	1	1	71	0	1	0	1	24	0	10	1	0	completed	2	12
84	0	1	69	0	1	0	0		0	27	0	0	completed	0	0
85	0	1	78	1	1	0	0		0	25	0	0	completed	7	2
86	1	1	70	0	1	0	1	195	0	10	1	1	completed	0	0
87	0	0	75	1	1	2	1		0	8	1	0	no reversal ileostomy	16	na
88	1	1	78	0	1	2	1	179	0	8	1	0	completed	4	9
89	0	1	60	1	1	1	1	203	0	7	1	1	completed	13	14
90	1	1	73	0	1	1	1	137	0	10	1	0	completed	1	7

Appendix XIV Participant Raw Data : BFB Project (continued)

Case Number	BFB =1	Analysed = 1	Age (years)	Female =1	Cancer = 1	Short DXT=1	Stoma =1	Stoma delay (days)	Laparoscopic =1	Tumour height above anal verge (cm)	Resection included peritoneal reflection=1	1=sidetoend anastomosis	Outcome	CCI baseline	CCI final
91	0	1	68	0	1	1	1	241	0	12	1	1	completed	6	2
92	1	0	75	0	1	1	1		0	10	1	0	leak hartmann	11	na
93	0	1	61	0	1	1	1	144	0	8	1	0	completed	0	10
94	1	1	63	1	1	1	1	98	0	8	1	1	completed	20	0
95	1	0	60	1	1	1	0		0	10	1	0	xdeclined	4	na
101	1	1	70	1	1	2	1	158	0	15	1	0	completed	99	3
102	0	0	73	0	1	2	1		0	5	1	na	hartmann	0	na
103	1	1	77	1	1	1	0		0	10	1	1	completed	0	0
104	0	0	48	0	1	2	1		0	8	1	na	hartmann	0	na
105	1	1	56	0	1	2	1	150	0	6	1	0	completed	0	7
106	0	1	73	0	1	2	1	239	0	7	1	1	completed	0	1
107	0	0	71	1	1	1	1	175	0	8	1	1	early exit	0	na
108	1	1	59	1	1	2	1	70	0	10	0	0	completed	10	4
109	0	1	78	0	1	1	1	243	0	10	1	0	completed	18	13
110	1	1	55	0	1	2	1	112	0	10	1	1	completed	0	4
111	1	0	65	0	1	2	0		0	11	0	?	xdeclined	2	na
112	0	0	64	0	1	2	1		0	15	1	na	hartmann	0	na
113	0	0	68	0	1	1	1		0	7	1	na	APE	0	na
114	1	0	48	1	1	1	1		0	4	1	na	APE	14	na
115	0	1	57	0	1	2	1	113	0	4	1	1	completed	0	9
116	1	0	62	0	1	1	1	194	0	5	1	1	xdeclined	4	na
117	0	1	55	1	1	2	1	89	0	7	1	1	completed	0	1
118	1	0	55	0	1	2	1	203	0	10	1	1	xdeclined	5	na
119	1	1	70	0	1	1	1	96	0	7	1	1	completed	0	12
120	0	1	74	0	1	1	1	108	0	8	1	1	completed	15	4

Appendix XIV Participant Raw Data : BFB Project (continued)

Case Number	BFB =1	Analysed = 1	Age (years)	Female =1	Cancer = 1	Short DXT=1	Stoma =1	Stoma delay (days)	Laparoscopic =1	Tumour height above anal verge (cm)	Resection included peritoneal reflection=1	1=sidetoend anastomosis	Outcome	CCI baseline	CCI final
121	0	0	67	0	1	1	1		0	12	1	na	leak hartmann	0	na
122	0	1	81	1	1	1	1	147	0	10	0	0	completed	15	2
123	1	1	70	0	1	1	1	91	0	13	1	0	completed	4	7
124	1	0	44	0	1	1	1	40	0	10	0	1	xdeclined	3	na
125	1	0	52	0	1	2	1		0	6	1	na	hartmann	4	na
126	0	1	52	1	1	2	1	72	0	15	1	1	completed	15	3

KEY to Appendix XIV Table

BFB = 1	Participant was randomized to receive biofeedback training
Analysed = 1	Participant completed follow up to 1 year after surgery and was included in the analysed sample (n = 89)
Short DXT = 0	No radiotherapy
Short DXT = 1	Short course preoperative radiotherapy
Short DXT = 2	Long course preoperative chemoradiotherapy
Stoma delay	Days following surgery before stoma reversal
Anastomosis	0 = side to side anastomosis
	1 = end to side anastomosis
CCI baseline	Cleveland Clinic Incontinence score at baseline
CCI final	Cleveland Clinic Incontinence score at 1 year after surgery

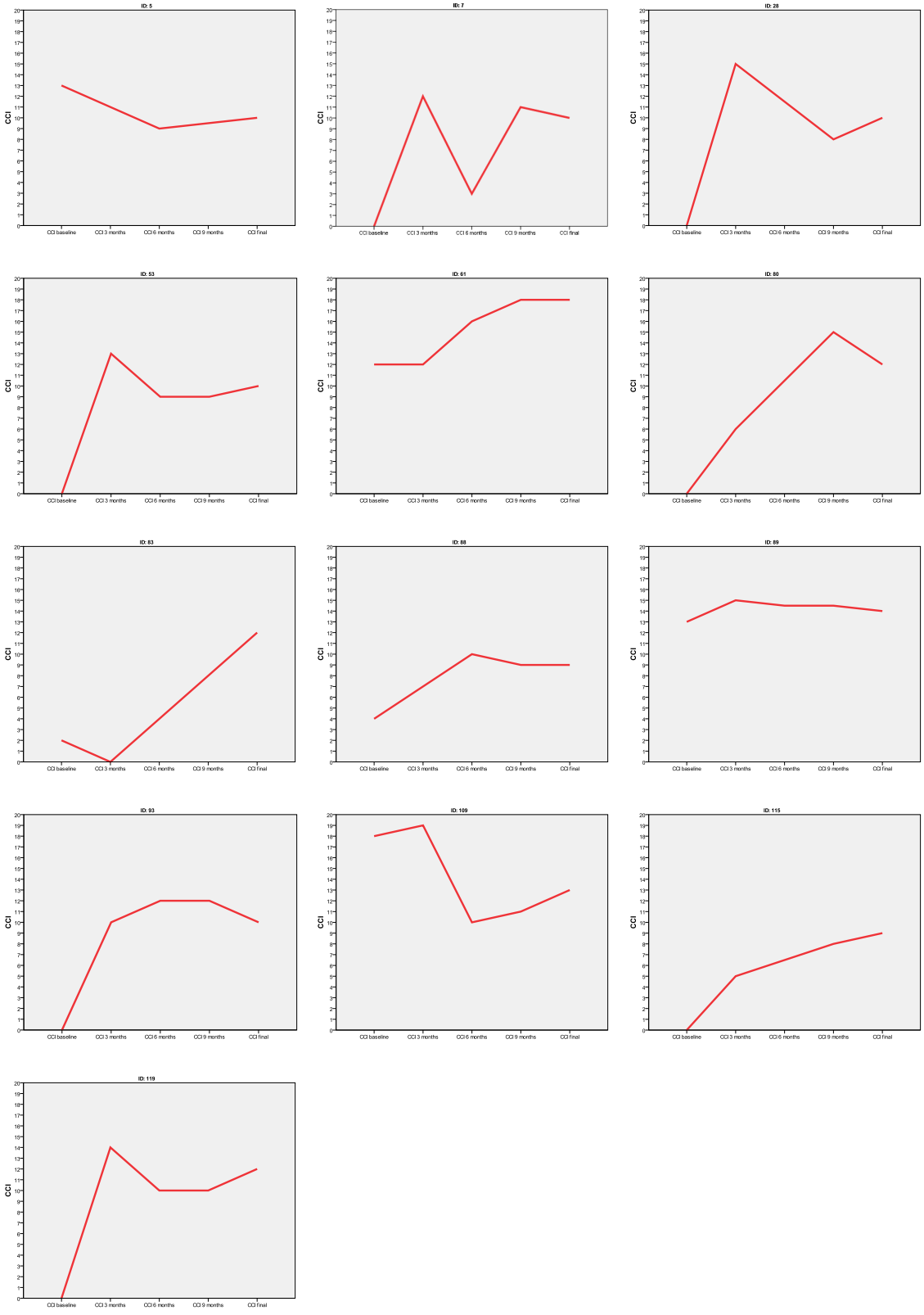
Appendix XV Temporal changes in CCI after anterior resection in analysed participants

N = 89

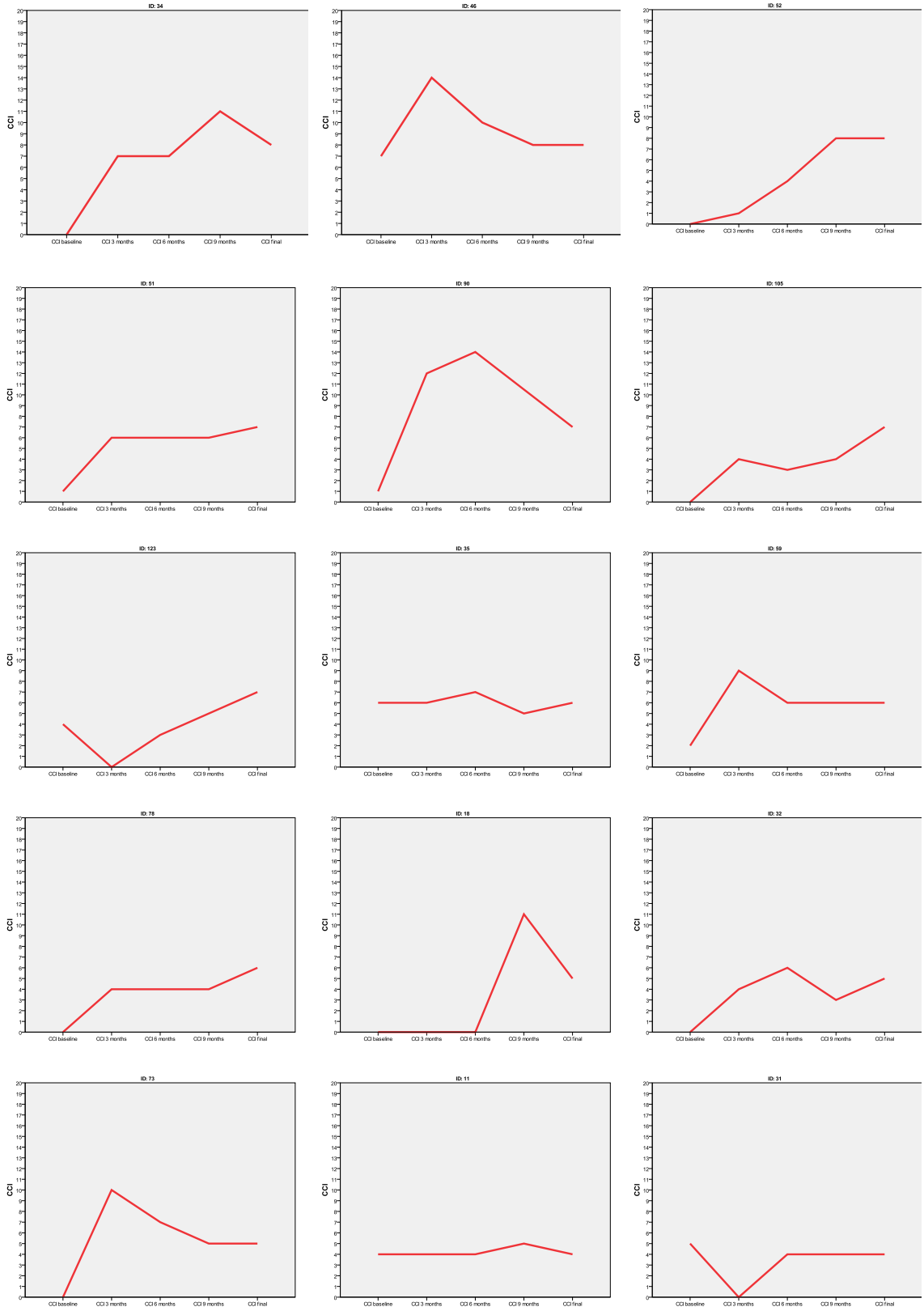
Appendix XVa Participants with severe anal incontinence at one year (CCI >= 9)
N = 13

Appendix XVb Participants with no severe anal incontinence at one year (CCI <9) ordered from worst highest CCI score at one year (final) to lowest CCI score at one year
N = 76

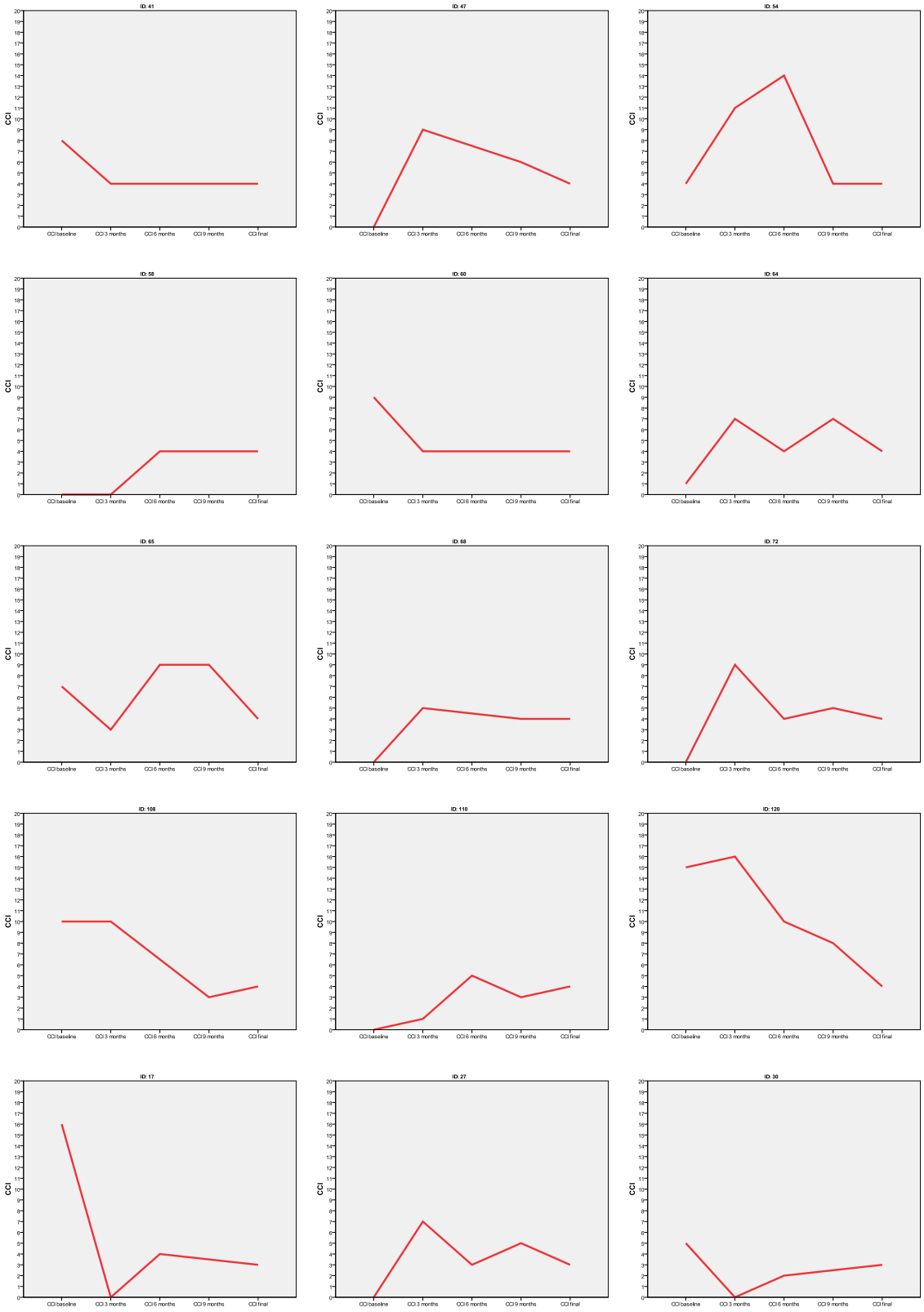
Appendix XVa Participants with severe anal incontinence at one year (CCI >= 9)



Appendix XVb Participants with no severe anal incontinence at one year (CCI <9) ordered from worst highest CCI score at one year (final) to lowest CCI score at one year



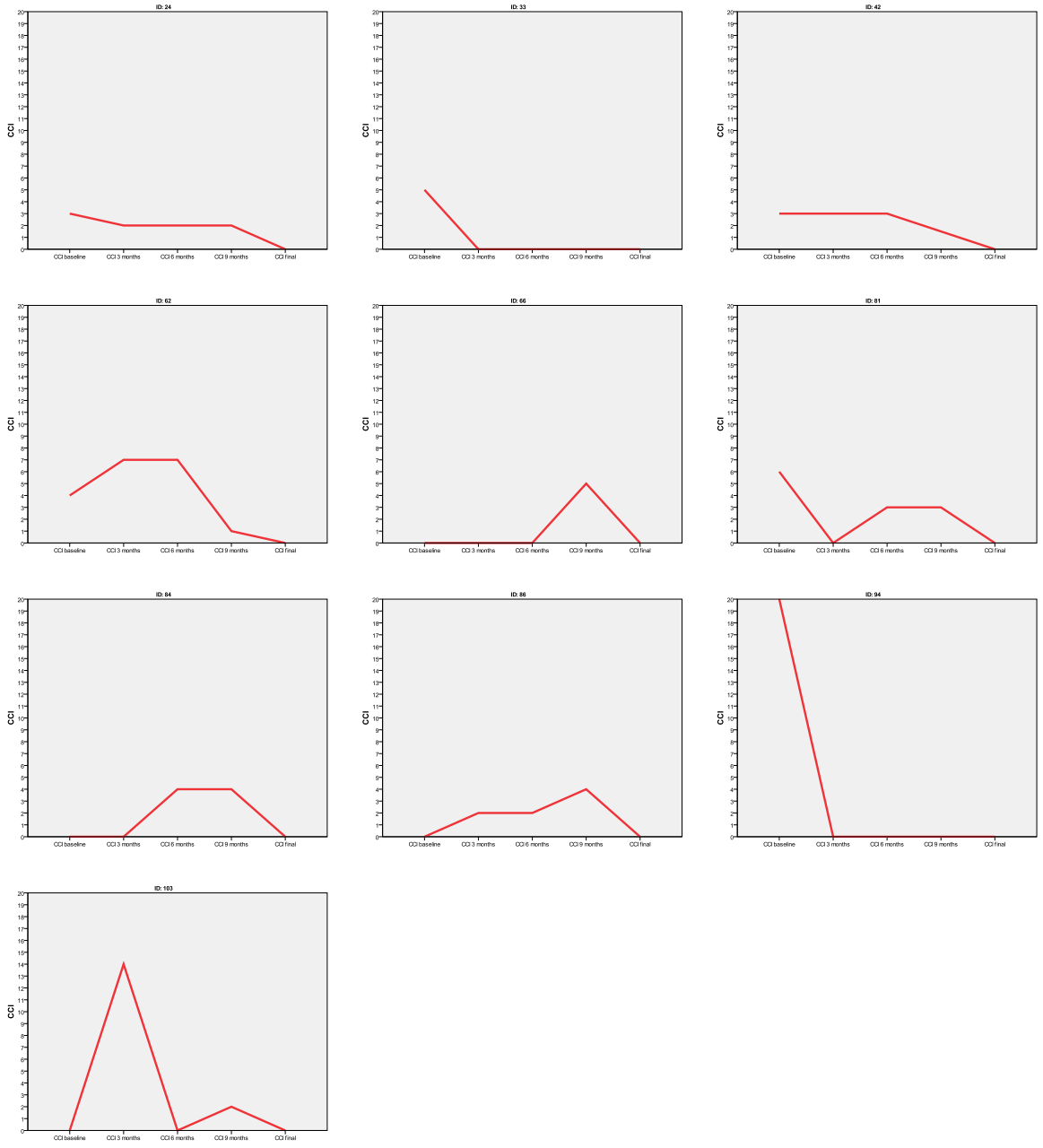
Appendix XVb (continued)



Appendix XVb (continued)

Appendix XVb (continued)

Appendix XVb (continued)



Participants 1, 3, 15, 45 and 76 reported CCI = 0 at all 5 time points over the first year after anterior resection

Appendix XVI Participant Raw Data: Proctogram Project:

Appendix XVIa Barium Proctography Raw Data

Appendix XVIb MR Proctography Raw Data

Appendix XVIa Barium Proctography Raw Data

(RI: rectal intussusception) (Rectocele size is corrected for radiological magnification)

ID	Age years	Female = 1	Rectocele = 1	Rectocele empties = 1	Rectocele length (cm)	Enterocele = 1	Complete rectal emptying = 1	Anismus = 1	RI = 1	RI grade
1	40	1	1	0	3.5	0	0	1	1	2
3	66	1	1	1	1.1	0	0	1	0	0
4	62	1	1	1	3.5	1	1	0	1	2
5	72	1	1	1	2.1	1	1	0	1	4
6	48	1	1	0	4.6	0	1	1	1	2
7	65	1	1	1	3.5	0	1	0	1	3
9	73	1	1	0	6.0	0	0	0	1	2
10	64	1	1	0	4.2	1	0	0	1	4
11	61	1	1	1	2.8	1	1	0	1	3
12	76	1	1	1	2.8	1	1	0	1	3
13	72	1	1	1	2.1	0	1	0	1	4
14	50	1	1	0	4.2	0	0	0	1	2
17	69	1	1	1	1.8	0	1	0	0	0
20	50	1	1	0	1.4	0	0	1	1	1
21	70	1	1	1	2.8	0	1	0	1	3

Appendix XVIa Barium Proctography Raw Data (continued)

ID	Age years	Female = 1	Rectocele = 1	Rectocele empties = 1	Rectocele length (cm)	Enterocele = 1	Complete rectal emptying = 1	Anismus = 1	RI = 1	RI grade
23	47	1	1	0	3.5	0	0	0	1	2
25	61	0	0	NA	0.0	0	0	0	1	3
27	47	1	1	0	5.3	0	0	0	1	3
29	49	1	1	0	4.2	0	0	0	1	1
30	53	1	1	0	4.2	0	0	0	1	3
31	44	1	1	0	2.1	0	0	0	1	3
32	64	0	0	NA	0.0	0	0	1	0	0
33	56	1	1	0	2.5	0	0	1	1	3
34	57	1	1	0	5.6	0	0	0	1	4
37	69	1	1	0	0.7	1	0	0	1	4
38	50	1	1	0	3.9	0	0	0	1	2
40	56	1	1	1	0.0	0	1	0	0	0
42	72	1	1	0	0.0	0	0	0	1	2
45	54	1	1	0	4.2	1	0	0	1	3
46	58	0	0	0	0.0	0	0	1	1	2
47	37	1	1	1	2.8	0	0	1	1	3
51	69	1	1	1	4.2	0	0	0	1	3

Appendix XVIa Barium Proctography Raw Data (continued)

ID	Age years	Female = 1	Rectocele = 1	Rectocele empties = 1	Rectocele length (cm)	Enterocele = 1	Complete rectal emptying = 1	Anismus = 1	RI = 1	RI grade
52	49	1	1	0	3.9	0	1	0	1	3
55	64	1	1	0	3.5	0	0	0	1	2
56	60	1	1	1	2.8	0	0	1	1	2
57	42	1	1	0	3.2	0	0	1	0	0
58	54	1	1	0	3.9	0	0	0	0	0
59	58	1	1	0	4.9	0	0	1	1	1
63	74	1	1	0	1.4	0	0	1	1	2
65	76	0	0	NA	0.0	0	0	0	0	0
68	64	1	1	0	1.8	0	1	0	1	2
71	64	1	1	0	3.5	0	0	0	1	3

Appendix XVIb MR Proctography Raw Data

(RI: rectal intussusception)

ID	Age years	Female = 1	Rectocele = 1	Rectocele empties = 1	Rectocele length (cm)	Enterocele = 1	Complete rectal emptying = 1	Anismus = 1	RI = 1	RI grade
1	40	1	1	0	3	0	0	1	1	1
3	66	1	1	0	2	0	0	1	0	0
4	62	1	1	0	4.6	1	0	0	1	2
5	72	1	1	1	4.3	1	0	0	1	4
6	48	1	1	0	4	0	0	1	0	0
7	65	1	1	0	2.8	0	0	0	1	2
9	73	1	1	0	5.1	0	0	0	1	2
10	64	1	1	0	6.2	0	0	0	1	2
11	61	1	1	1	3	1	0	0	1	3
12	76	1	1	0	2	0	0	0	1	3
13	72	1	1	1	3	0	0	0	1	3
14	50	1	1	0	4	0	0	1	1	2
17	69	1	0	0	0	0	0	0	0	0
20	50	1	1	0	2	0	0	1	0	0

Appendix XVIb MR Proctography Raw Data (continued)

ID	Age years	Female = 1	Rectocele = 1	Rectocele empties = 1	Rectocele length (cm)	Enterocele = 1	Complete rectal emptying = 1	Anismus = 1	RI = 1	RI grade
21	70	1	1	0	3.5	0	0	0	1	3
23	47	1	1	NA	2	0	0	1	0	0
25	61	0	0	0	NA	0	0	0	0	0
27	47	1	1	0	4.4	0	0	0	1	2
29	49	1	1	0	1	0	0	1	0	0
30	53	1	1	0	2.5	0	0	1	0	0
31	44	1	1	NA	2.3	0	0	0	1	1
32	64	0	0	0	0	0	0	1	0	0
33	56	1	1	NA	1.5	0	0	0	1	2
34	57	1	1	0	5	0	0	0	1	1
37	69	1	1	1	3.5	1	0	0	1	2
38	50	1	1	NA	2.5	0	0	1	0	0
40	56	1	1	1	3	0	0	0	1	4
42	72	1	1	0	4.3	0	0	0	1	2
45	54	1	1	0	3.3	0	0	0	1	2
46	58	0	0	NA	0	0	0	1	0	0
47	37	1	1	0	3.8	0	0	1	0	0

Appendix XVIb MR Proctography Raw Data (continued)

ID	Age years	Female = 1	Rectocele = 1	Rectocele empties = 1	Rectocele length (cm)	Enterocele = 1	Complete rectal emptying = 1	Anismus = 1	RI = 1	RI grade
51	69	1	1	1	3.8	0	1	0	1	3
52	49	1	1	1	3.7	0	0	0	1	4
55	64	1	1	0	4.3	0	0	1	1	2
56	60	1	1	0	2.3	0	0	0	1	2
57	42	1	0	NA	NA	0	0	1	0	0
58	54	1	1	0	4	0	0	1	1	1
59	58	1	1	0	3.8	0	0	1	1	2
63	74	1	0	0	0	0	0	1	0	0
65	76	0	0	NA	NA	0	0	0	0	0
68	64	1	1	0	2	0	0	1	0	0
71	64	1	1	0	5.1	0	0	0	1	4

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