ORAL PRESENTATION 5B
COLORECTAL 2

0156 COMPUTER TOMOGRAPHY DEFINED BODY COMPOSITION ANALYSIS AND ITS RELATIONSHIP TO THE SYSTEMIC INFLAMMATORY RESPONSE IN PATIENTS UNDERGOING COLORECTAL CANCER SURGERY
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Introduction
Loss of lean muscle mass and weight loss are recognised as poor indicators in patients with cancer but the underlying mechanisms remain unclear. The aim of the present study was to examine the relationships between CT defined body composition (BC) parameters and the systemic inflammatory response in patients with primary operable colorectal cancer (CRC).

Methods
Data from 454 consecutive patients diagnosed with CRC undergoing elective resection between 2006 and 2011 were included. Image analysis of CT scans determined total fat, subcutaneous fat, visceral fat index and skeletal muscle area (cm²) after normalisation for stature (cm²/m²). Cut-offs for low muscularity normalised for stature were based on previous CT-based studies. The systemic inflammatory response was represented by pre-operative neutrophil: lymphocyte ratio (NLR) and albumin levels.

Results
There was a significant difference between low skeletal muscle index and both NLR (p=0.006) and serum albumin (p=0.004). Analysis showed a significant correlation between the skeletal muscle index and NLR (r=-0.115; p=0.038) and serum albumin (r=0.200; p<0.001). There were no relationships between any fat parameter of the BC analysis and serum albumin or NLR.

Conclusion
These results highlight a relationship between low skeletal muscle level and the systemic inflammatory response in patients with primary operable colorectal cancer. Understanding what factors contribute to BC alterations may produce novel and more effective interventions that optimise body composition and metabolism, ultimately improving clinical and metabolic outcomes in cancer patients both in the perioperative period and in the long term.

Take-home message
Low muscle mass in patients with CRC is an occult condition that can be identified using CT and its association with the systemic inflammatory response may contribute in improving clinical and metabolic outcomes.

0157 PREDICTIVE VALIDITY OF OBJECTIVE TECHNICAL ASSESSMENT WITHIN THE NATIONAL TRAINING PROGRAMME FOR LAPAROSCOPIC COLORECTAL SURGERY
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Introduction
The use of technical skills assessment aims to improve surgical outcomes. A summative, sign-off, assessment was introduced into the National Training Programme (NTP) for laparoscopic colorectal surgery to ensure a safe standard of technical skill prior to independent practice. This involves evaluation of a right and left sided case using a laparoscopic Competency Assessment Tool (CAT), by blinded assessors. The aim of the study was to assess the predictive validity of the CAT using clinical outcomes.

Methods
All sign-off cases submitted between August 2008 and October 2012 were analysed. The clinical outcomes of those cases with a high CAT score (>2.7) were compared with those with a low score (<2.7).

Results
A total of 370 sign-off submissions were made during the study period. Of these 296 (80%) had a high CAT (>2.7) score. The trainees who scored highly on the CAT form
performed significantly more training cases within the programme (16.1 vs 10.6, p<0.001). There was no significant difference in clinical outcomes in right sided cases with a high and low CAT score. However left sided cases with a high score had significantly fewer surgical complications (22.0% vs 7.8%, p=0.011) and had a significantly greater lymph node harvest (13.4 vs 17.3, p=0.010) and resection margin (2.9cm vs 4.1cm, p=0.011).

**Conclusions**
This is the first study to ascertain the predictive validity of a technical competency assessment tool. The findings indicate that increased training within the NTP improves CAT performance and leads to a concomitant benefit in patient outcomes.

**Take-home message**
Training within the National Training Programme for Laparoscopic Colorectal Surgery improves technical skill. The improvement can be assessed and measured and leads to improved clinical outcomes.

**O158 DEREGULATED STROMAL MICRORNA-21 PROMOTES METASTATIC PROGRESSION IN COLORECTAL CANCER**

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**Introduction**
The aim of the present study is to determine the identity and function of deregulated microRNAs in colorectal cancer (CRC) associated stroma, and to dissect out epigenetic mechanisms promoting CRC progression in the tumour microenvironment.

**Methods**
RT-PCR-based profiling of 20 laser capture microdissected colonic tissue specimens was used to identify stromal microRNAs differentially expressed in CRC compared with paired normal tissue. Candidate miRNAs were evaluated by in-situ hybridization (ISH) to determine cells of origin, and assessed for biological significance using in-vitro and 3-D organotypic functional assays.

**Results**
Eighteen microRNAs were differentially expressed between CRC stroma and paired normal colonic stroma including microRNA-21, a known oncogene. ISH reveals that microRNA-21 is expressed exclusively in cancer associated fibroblasts. Ectopic microRNA-21 expression in fibroblasts supports myofibroblast transdifferentiation, a key pro-metastatic stromal event. Conditioned medium from microRNA-21 over-expressing fibroblasts protects CRC cells from Oxaliplatin induced apoptosis and increases proliferative capacity. Furthermore, 3-D organotypic co-cultures, developed to model in-vivo circumstances, reveal that ectopic stromal microRNA-21 is associated with a 2.5-fold increased invasion of CRC epithelium into stroma (p<0.001). RECK, an inhibitor of the matrix-remodelling enzyme MMP2, is targeted by microRNA-21, and significantly downregulated by ectopic microRNA-21 in both cultured and ex-vivo human colorectal fibroblasts. Inhibition of MMP2 activity abrogates the invasion promoting effects of ectopic stromal microRNA-21.

**Conclusions**
This data which characterises a novel pro-metastatic mechanism mediated by microRNA-21 in the CRC stroma, highlights the importance of microRNA deregulation within the tumour microenvironment and identifies potential applications for stromal microRNAs as biomarkers in cancer.

**Take-home message**
Deregulation of the oncogene microRNA-21 is a stromal phenomenon and supports CRC progression through myofibroblast transdifferentiation, resistance to Oxaliplatin cytotoxicity and promotion of tumour cell invasion.

**O159 UNDER-RECOGNISED CO-EXISTENCE OF CONSTIPATION AND Faecal INCONTINENCE IN THE ADULT POPULATION: A LARGE SINGLE-CENTRE EXPERIENCE**

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Introduction
Chronic constipation (CC) and faecal incontinence (FI) are acknowledged to co-exist in paediatric and geriatric populations. We tested the hypothesis that this symptom inter-relationship is also commonly present in adults, but is under-recognised.

Methods
Analysis of prospectively collected data from adult patients (age 18 – 80) consecutively attending a specialist anorectal physiological investigation service over a 4 year period. The co-existence of CC and FI symptoms was rated using 3 methods: (1) referral letter included symptom as primary referral reason; (2) referral letter included a secondary symptom; (3) validated symptom severity scores with published cut-offs - St Marks Incontinence Score [score > 5] and Cleveland Clinic Constipation Score [score > 8].

Results
2419 patients (2056 [85%] female; mean age 52 [range 18-80]) were eligible for inclusion from 4079 referrals (by formal letter). Only 8% of patients were primarily referred with co-existent symptoms of both FI and CC, with 13% having symptoms of both recorded anywhere in the referral letter. However, 46% had significant symptoms of both FI and CC on formal scoring. Inter-rater agreements between the two main assessment methods were moderate for both CC (agreement 75% (expected 52%), kappa: 0.48 (moderate), p=0.0001); and FI (agreement 72% (expected 51%), kappa: 0.42 (moderate), p=0.0001).

Conclusions
Significant symptoms of constipation and faecal incontinence co-exist in nearly half of patients referred for specialist anorectal physiological testing, yet only 13% had both symptoms recognized by the referring clinician. This has major implications for the management of overlapping pathophysologies.

Take-home message
Significant symptoms of constipation and faecal incontinence co-exist in nearly half of patients referred with either presenting symptom. This is hugely under recognized by the referring clinician and may have implications for the management of overlapping pathophysologies.

O160 BEHAVIOURAL ANIMAL MODEL OF Fecal CONTINENCE
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Introduction
The aim of this study was to establish a behavioural model of faecal continence in the rat. While no animal can completely replicate the human situation, this model of continence is important to further investigate the pathophysiology and treatments of incontinence.

Methods
Ethical approval was granted by the appropriate authorities. Six virgin female Wistar rats were individually housed in standard cages. Each animal’s movements were monitored with a custom designed computer program, video camera and infrared lighting. Latrine boxes were secured in the corner furthermost from the food and drink and for one week the animals were trained to defaecate in these. Subsequently, faecal pellets were counted daily from the latrine and non-latrine areas. The number of pellets passed per hour spent in each area (defaecation rate) was calculated daily. The continence index was derived by dividing the defaecation rate in the latrine by the combined defaecation rate in latrine and non-latrine.

Results
A pattern of continence was evident in 4 rats with a mean continence index of 86%. In 2 rats the mean continence index was 60%. Conclusion We have established a behavioural animal model of faecal continence which can be used in future studies investigating the mechanisms of injury resulting in faecal incontinence and their treatments.

Take-home message
This behavioural model of continence can be used in future research into the pathophysiology and treatment of incontinence.

O161 EDUCATIONAL LEVEL & COLORECTAL CANCER RISK IN DEVELOPED COUNTRIES: A SYSTEMATIC REVIEW & META ANALYSIS
Education level is a potential risk factor for colorectal cancer. This systematic review and meta-analysis aims to determine whether there are disparities in colorectal cancer risk between basic (primary school and lower) and higher educational level (university and beyond) groups.

Ovid Medline and EMBASE databases were searched for studies published between 1946 and 2013. Data were extracted and pooled analyses were undertaken using random effect, inference of variance statistical models.

Pooled analysis including 14,996 patients for colon and 9,778 for rectal cancer were carried out. Amongst males, the higher education group had a higher incidence of colon cancer compared with the basic education group (OR 1.13, CI: 1.02-1.27). Amongst females, the reverse was true (OR 0.93, CI: 0.88-0.98). For rectal cancer, females within the higher education group again had lower incidence of cancer (OR 0.91, CI:0.84-0.98) whilst there was no difference between the two education groups for males (OR 0.91, CI: 0.80-1.05).

Male patients of a higher educational background have a higher incidence of colon cancer than their less educated counterparts, while well educated females tend to have a lower risk. Rectal cancer also appears to be less predominant amongst females of a higher educational background.

Male patients of a high level of educational attainment are at increased risk of colon cancer, but not females when compared to those of lower educational level. For rectal cancer, well educated females also have a lower incidence of cancer, while there is no difference in incidence in men.

Colonic transit may be abolished by the presence of a diverting ileostomy. This suggests that clearance of the left colon alone, using an enema, may be sufficient for patients undergoing low anterior resection, thus avoiding the morbidity associated with standard bowel preparation.
Take-home message
Full mechanical bowel preparation may NOT be necessary for patients undergoing low anterior resection with a diverting loop ileostomy.

O163  HISTOLOGICAL AND MECHANICAL DIFFERENCES IN THE SKIN OF PATIENTS WITH RECTAL PROLAPSE
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Introduction
It is still an enigma why some patients develop rectal prolapse while others with similar risk factors do not. Biomechanical assessment of supports of the pelvic organs may elucidate the aetiology of this complex condition. Elastic fibres are an integral part of extracellular matrices and are critical for providing elastic recoil. Numerous human conditions result from inherited elastic fibre abnormalities; such abnormalities can be detected in the skin which has an abundant elastic fibre network.

Methods
Between January and June 2013 fresh skin specimens were obtained during consecutive laparoscopic rectopexy from 20 patients with rectal prolapse and 21 controls having laparoscopic surgery for non-prolapse conditions. Skin elastin expression was measured by Orcein staining and Image J. Tensile tests were performed using the Zwick Roell Device. For statistical analysis, Student's t-test was used.

Results
Elastic fibre density was 3.2% higher in male patients than in male controls (p=0.001) and 1.2% higher in female patients than in female controls (p=0.02). Patients with more severe prolapse (external) had a significantly (p=0.04) higher dermal elastic fibre density - 6.9% vs 6.1% than those with internal prolapse. The Youngs Modulus of patients with prolapse was lower in males (3.3 vs 2.8, p=0.05) and females (3.1 vs 2.7, p=0.04) than in controls.

Conclusion
Patients with prolapse have a higher concentration of elastin fibres in the skin confirming previous reports. These differences are reflected by changes in mechanical properties. The results suggest that the aetiology of prolapse may be associated with a disorder/polymorphism of elastic fibre assembly.

Take-home message
Rectal prolapse is still an enigma. The aetiology of prolapse may be associated with a disorder/polymorphism of elastic fibre assembly.