Abstract PWE-154 Table 1

Hb quartile	Hb g/l	F < 71yrs	F > 70yrs	M < 71yrs	M > 70yrs
1	111–158	0.0% (0/35)	2.6% (1/38)	2.4% (1/42)	10.8% (7/65)
2	102–111	0.0% (0/49)	3.7% (3/81)	5.3% (1/19)	19.4% (6/31)
3	91–102	3.6% (2/55)	8.8% (6/68)	0.0% (0/13)	25.0% (11/44)
4	42–91	2.4% (1/41)	13.6% (9/66)	23.3% (7/30)	30.2% (13/43)

The prevalence of GI malignancy ranged from 0.0% in younger females with mild anaemia, to over 25% in older males with more severe anaemia. By the pre-defined criteria, the model identified subpopulations of 84 (11% of the total) at extreme low risk, and 117 (16%) at extreme high risk.

Conclusion The results confirm previous work identifying age, sex and haemoglobin concentration as variables predictive of underlying malignancy in IDA. Furthermore, the findings suggest that over a quarter of subjects with IDA can be predicted to be of extremely low or high risk on the basis of these simple and objective clinical criteria. This may be of clinical relevance for patient counselling, prioritisation of investigations and allocation of resources. Work is ongoing to validate risk prediction in a prospective study, and to refine the model by inclusion of additional variables.

Disclosure of Interest None Declared.

REFERENCE

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PWE-155 A BAD GUT FEELING: THE LONG-TERM IMPACT OF PELVIC RADIOTHERAPY ON GASTROINTESTINAL (GI) FUNCTION

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Introduction As new cancer treatments have been introduced, there have been enormous improvements in outcomes for treated patients. They are living longer and the number of survivors of cancer therapy is growing by 3% per year in the UK. 17 000 UK patients are treated annually with pelvic radiotherapy. 80% of patients who receive pelvic radiotherapy are left with chronic alteration in GI function and 50% state that this affects daily activity. There are few data on the nature of the symptoms these patients develop. This study aims to describe the symptoms troubling patients referred to a specialist Pelvic Radiation Disease clinic.

Methods A prospective service evaluation of patients treated with pelvic radiotherapy referred to our clinic was performed. Patient characteristics were recorded. Each new patient completed a modified Gastrointestinal Symptom Rating Scale and Bristol Stool Chart which described their symptoms and severity.

Results Data on the first 110 patients collected included 47 women (43%), median age, 59 (range: 37–79 years) and 63 men (57%) median age, 72 years (range: 20–83 years) treated for prostate (47%), gynaecological (27%) or anorectal cancers (17%), lymphoma (5%) and other tumours (4%). The median length of time since starting radiotherapy to presenting in clinic was 3 years 1 month; range: 0.5– 36 years.

Pelvic symptoms causing frequent or severe impact on patients daily lives were urgency (68%), diarrhoea (defined as Bristol stool chart type 6 or 7) (62%), tenesmus (55%), fatigue (51%), rectal flatulence (51%), abdominal pain (45%), faecal leakage (43%), sexual concerns (35%), problems with urination (34%), bloating (34%), borborygmi (30%), woken at night to defaecate (28%), rectal bleeding (24%), belching (20%), heartburn (15%), steatorrhoea (13%), nausea and vomiting (10%).

Women presented with a median of 12 symptoms (range: 2–17) out of a maximum of 17 recorded symptoms and men with a median of 11 (range: 2–16). The number of symptoms defined by the patients as "frequent" or "severe" was a median of 8 symptoms for women (range: 0–15) and 5 symptoms for men (range: 0–13).

Conclusion GI, sexual and urinary symptom burden is high after pelvic irradiation in new patients attending our clinic. Patients often present with multiple symptoms impacting daily activities. Symptoms clusters are complex and a systematic, multidisciplinary approach for efficient management is required. Clinicians will see increasing numbers of affected patients and may need training to deal with these patients optimally.

Disclosure of Interest None Declared.

PWE-156 GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD) SYMPTOMATOLOGY IS NOT A RELIABLE PREDICTOR OF OESOPHAGEAL ADENOCARCINOMA

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Introduction Chronic gastro-oesophageal reflux disease (GORD) is considered a risk factor for development of gastro-oesophageal junction adenocarcinoma. Our aim is to determine the prevalence of GORD symptomatology and Barrett's columnar metaplasia prior to the diagnosis of distal oesophageal, gastro-oesophageal junction (GOJ) and gastric cardia adenocarcinoma at GCDD over a 10 year period.

Methods A prospective pilot study collected data from patients diagnosed with adenocarcinomas arising from the distal oesophagus, GOJ and cardia in one year. A standardised proforma was designed to capture demographics, clinico-pathological and endoscopic data including the relationship of tumour epicentre with the distal end of the tubular oesophagus, the presence or absence of Barrett's oesophagus; history of recurrent heartburn or regurgitation. To avoid reversed causality, we disregarded symptoms that occurred less than five years prior to cancer diagnosis.

Results 37 patients were diagnosed with adenocarcinoma of lower oesophagus and cardia between January and December 2011. 73.5% of patients were male and the age at diagnosis ranged between 45 and 97 years. Only 32% of diagnosed cancers were referred through 'Urgent suspected cancer' pathway. 43% of patients were smokers and 28% were ex-smokers; 55% drank alcohol regularly. Only 6 out of 37 patients had chronic symptoms (more than 5 years duration) suggestive of reflux including nausea, heartburn and sore tongue. 62% of these patients were on proton pump inhibitors or Histamine blockers at the time of diagnosis. 20% of the endoscopies showed a large hiatus hernia at index endoscopy and 20% showed evidence of Barrett's (length between 6 and 11cm). Only 30% of patients were treated with curative intervention and the rest were managed by palliative means. 63.8% of diagnosed patients were not alive at one year of follow up out of which one patient had treatment with curative intent, Correlation testing between GORD and diagnosis of GOJ adenocarcinoma using regression analysis did not reach statistical significance.

Conclusion This interim report did not reveal a significant correlation between chronic reflux and development of gastrointestinal adenocarcinoma. The number is too small to permit a firm conclusion and we will report further results upon completion of the 10 years.

Disclosure of Interest None Declared.

PWE-157 TWO DIMENSIONAL MAPPING OF MUTANT CLONES IN HUMAN COLONIC CRYPTS REVEAL STEM CELL DYNAMICS AND MIGRATION PATTERNS

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Park Hospital, Harrow, London; [3]Cancer Research UK; [4]Department of Histopathology, University College London Hospitals, London, UK; [5]Centre for Evolution and Cancer, University of California San Francisco, San Francisco, United States

Introduction Deficiency in the enzyme cytochrome C oxidase (CCO) has proven to be a versatile marker of clonal population in human tissues. CCO is encoded entirely by the mitochondrial DNA (mtDNA) and deficiency in CCO expression is usually attributable to mutation in the mtDNA. CCO-deficient cells are easily detectable by two-colour enzyme histochemistry. This staining provides means to identify clonal patches of CCO-deficient cells. Subsequent sequencing of mtDNA from individual cells within the patch and revealing the same somatic mutation in each cell confirms the clonality of a patch.

In the human intestine, crypts are composed of a population of a contiguous CCO-deficient mtDNA-mutated cells, and also non-mutant CCO-proficient cells are frequently observed: from the small clones occupying only a few cell positions on the crypt circumference (partially-mutated crypts), to crypts composed only CCO-deficient cells (wholly-mutated crypts). Patches of adjacent and clonal CCO-deficient crypts are also observed. Larger patches are more common in older patients indicating that CCO-deficient crypts continue to divide in the ageing colon.

Methods To study stem cells dynamics within intestinal crypts, we aim to characterise the shape and the size of clones in partially CCO-deficient crypts, by combining the two-colour enzyme histochemical staining with image analysis and computer reconstruction.

Multiple serial sections in the transverse plain were taken through frozen samples. Digital images were then taken of each serial section and used to create a 'crypt map' using in-house analytical software. A crypt map is a representation of the whole 3D tubular crypt unfurled and laid flat with colour enhancement post-processing.

Results Our results in normal and diseased human colon show that clone size can be approximated by the percentage of the crypt circumference measured from crypt transverse sections and occupied by a CCO-deficient clone.

Conclusion We envisage that analysis of such clonal distributions in the context of a branching process model could be used to determine the patterns of stem cell division within the human colon.

Disclosure of Interest None Declared.

PWE-158 THYMOSIN BETA 4 AS A PUTATIVE MARKER IN NEUROENDOCRINE TUMOURS

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Introduction Neuroendocrine tumours (NETS) arise from the diffuse endocrine system which produce biogenic amines and peptides that could be potential biomarkers. We previously analysed proteomes secreted by NET cell lines and identified mac2BP as putative marker which was also elevated in patients compared to healthy controls

Methods 3 Cell Lines BON-1, NCI-H727, and SHP-77 cells were grown in serum-free media overnight, which was then fractionated and the secreted 3–10kDa polypeptides were identified using Tandem Mass spectrometry. One of the small proteins, Thymosin β4 was measured in serum samples of patients and controls using ELISA. Mac2BP & chromogranin A was also measured

Results 70 proteins were secreted by all three lines, including 20 small proteins of which 3 were thymosins α1, β4 & β10. Serum samples were analysed in 34 patients and 24 healthy controls. Thymosin β4 was elevated in the serum of NET patients compared with healthy controls ($p < 0.002$). The area under the curve was 0.84 following ROC analysis.

Conclusion Mass spectrometry of the secretomes of 3 NET cell lines offers a novel way of identifying potential biomarkers. Thymosin β4 could be such a biomarker but further examination of tissue and other cell lines is necessary. A further analysis of serum from larger groups of patients both pre and post therapy is needed.

Disclosure of Interest None Declared.

PWE-159 HIF-1ALPHA-DEPENDENT GASTRIN GENE EXPRESSION MEDIATES RESISTANCE TO HYPOXIA-INDUCIBLE APOPTOSIS IN A HUMAN COLORECTAL CANCER CELL LINE

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Introduction Understanding the molecular processes mediating colorectal cancer (CRC) tumorigenesis will enable the development of targeted therapies that selectively disrupt the pathways responsible for tumour growth. The gastrin family of growth factors promote CRC growth, invasion and angiogenesis. Hypoxic microenvironments, caused by tumours outgrowing their local blood supply, stimulate aggressive tumour behaviour. However, the effect of hypoxia on gastrin expression in CRC is unknown.

Methods Expression of the gastrin gene in the CRC cell line LoVo was examined under conditions of normoxia and hypoxia. The effect of inhibiting expression of HIF-1α (the transcriptional master regulator of cellular responses to hypoxia) and of deleting HIF-binding sites in the gastrin promoter was investigated. The effect of inhibiting gastrin expression on CRC cell behaviour *in vitro* and on tumorigenesis in mouse xenografts was analysed.

Results Gastrin gene expression in CRC cells is stimulated by hypoxia by HIF-1α binding to the gastrin promoter. The viability of hypoxic (1% O_2) gastrin knockdown cells *in vitro* is diminished due to loss of resistance against hypoxia-inducible apoptosis. In xenografts in mice exposed to hypoxia (10% O_2) for 21 days, apoptosis is significantly increased by knocking down gastrin expression.

Conclusion This work provides evidence that gastrin expression is involved in the adaptation of CRCs to hypoxic microenvironments through resistance to apoptosis. Shrinkage of CRC liver metastases by the angiogenesis inhibitor bevacizumab is dependent on hypoxia-induced apoptosis. Therapies that target gastrin may enhance the therapeutic efficacy of bevacizumab and increase secondary resectability rates in patients with CRC liver metastases.

Disclosure of Interest None Declared.

PWE-160 INTERFERON ALPHA THERAPY FOR METASTATIC NEUROENDOCRINE TUMOURS: A RETROSPECTIVE STUDY

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Introduction Interferon alpha has been used in the management of NETs for over 20 years. It has generally not been popular due to perceived lack of efficacy and due to toxicity profile. Currently molecular targeted medical therapies such as mTOR inhibitors and tyrosine kinase inhibitors are promoted but studies demonstrate only modest anti-tumour effect and time to progression (TTP) with not insignificant toxicity.

Aim To perform a retrospective analysis of Interferon alpha (IFNα) in patients with metastatic NET and assess efficacy and toxicity.

Methods We identified 37 patients treated with IFNα 3 – 5 million units x 3 per week between 2000–2012. Mean age 58.6 (24–88) years; 26:11 male:female; 21 midgut primary, 7 pancreatic, 1 hindgut, 1 bronchial, 1 thymic and 6 unknown. Histology: G1 49%; G2 41%; G3 5%: unknown 5%. 76% were also on somatostatin analogue. 65% had recorded progressive disease at disease