following diagnosis and 109 (19.2%) following surgery. There were improved survival times following diagnosis for patients prescribed a statin with OC overall (HR = 0.71, 95% CI = 0.64–0.79, p < 0.001) and specifically OAC (HR = 0.58, 95% CI = 0.43–0.78, p < 0.001). Furthermore, statin use post-oesophagectomy was associated with improved survival in those with OC overall (HR = 0.66, 95% CI = 0.48–0.91, p = 0.013) and those with OAC specifically (HR = 0.58, 95% CI = 0.30–1.10, p = 0.096) with borderline significance. There were no significant effects between statin use and survival in patients with OSCC. Associations between statin use and overall survival were very similar to their effect on disease-specific survival.

Conclusion Statin use in patients with OC either after diagnosis or post-oesophagectomy is associated with improved survival. This data suggests a need for randomised controlled trials of statins in patients with OC.

Disclosure of Interest None Declared

OC-029 RADIOFREQUENCY ABLATION (RFA) CONFERS SUSTAINED BENEFIT FOR SQUAMOUS HIGH GRADE DYSPLASIA (HGD) AND EARLY SQUAMOUS CELL CARCINOMA (SCC) IN PATIENTS WHO DO NOT PROGRESS FOLLOWING FIRST TREATMENT

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Introduction Oesphageal SCC carries a poor prognosis. Squamous HGD is the precursor lesion to SCC. Risk of progression to SCC with HGD can be 65% at 5 years. RFA is a minimally invasive technique with proven efficacy for early neoplasia arising in Barrett's oesophagus. We present prospective data from 10 centres in the United Kingdom (UK) HALO registry.

Methods Superficial lesions were removed by endoscopic mucosal resection (EMR) before RFA. Treatment consisted of a single ablation at 12J/cm2. Patients were followed up 3 months after treatment with biopsies. Those with residual dysplasia underwent further RFA until 12 months when they were assessed for treatment success or failure. Recurrent dysplasia was retreated with EMR/RFA. Primary outcomes were reversal of dysplasia (CR-D) at 12 months.

Results 26 patients had RFA. Mean length mucosa ablated was 5.3 cm (1–14). 7/26 (27%) had EMR before RFA. Prior EMR did not confer benefit to outcome, nor did baseline disease length. Following first RFA, 6/26 patients (23%) progressed to invasive disease. Only one more patient progressed later in treatment course. CR-D was achieved in 50% at protocol end, mean 1.7 RFA treatments (1–4). 10/13 (77%) with successful RFA at 12 months remain disease free at most recent follow up (median 21 months). Kaplan Meier statistics show 2 years post treatment 68% patients are likely to remain in remission from dysplasia for those with successful outcome at 12 months. 5 patients (19%) required dilatations for oesophageal stricturing.

Conclusion Squamous HGD & CIS are aggressive pathologies as evidenced by the fact that 23% patients in our cohort progressed to invasive disease despite RFA. However the majority who do not progress early (13/19 patients) achieve benefit & are more likely to have a successful & durable outcome. There is limited experience in the UK with RFA in these patients. Pre RFA EMR for visible lesions is limited in our series. As a result some patients may be under staged prior to RFA which may account for the high rate of progression after first treatment.

Disclosure of Interest None Declared

OC-030 BARRETT'S EPITHELIUM SHOWS EVIDENCE OF GASTRIC AND INTESTINAL DIFFERENTIATION PROGRAMMES BUT PRESERVES THE PROLIFERATIVE AND STEM CELL ARCHITECTURE OF GASTRIC GLANDS

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Introduction The origin and development of Barrett's oesophagus has long been discussed, with three main proposals for the origin of metaplasia: from oesophageal squamous epithelium, from upward migration of cardiac glands, or from submucosal glands.

Methods In Barrett's glands we have studied the distribution of proliferative activity using Ki67 and the migration of cells in Barrett's glands from patients infused with iododeoxyuridine 7 and 11 days pre-oesophagectomy. We have localised gene expression of mucins using immunohistochemistry (IHC) and trefoil family factor (TFF) peptides using IHC and *in situ* hybridization (ISH) and the stem cell marker Lgr5 using ISH, combining this with analysis of the clonal architecture of Barrett's glands using mitochondrial DNA (mtDNA) as a clonal marker.

Results In Barrett's glands proliferation is seen mainly in the middle part of the gland and diminishes towards the surface and the base of the gland. Cells migrate in a bidirectional manner. MUC5AC and TFF1 expression are found superficially, while MUC6 and TFF2 are found at the bases of the glands, similar to the distribution seen in antral gastric glands: MUC2, staining goblet cells and columnar cells, is concentrated superficially. *Lgr5* mRNA is also found in the middle part of the glands, indicating the location of the stem cell niche. Barrett's glands are clonal, indicating derivation from a single cell, and suggesting that Barrett's stem cells have dual differentiation capacity. Gastric intestinal metaplasia, on the other hand, shows basal *Lgr5* mRNA localisation with a distribution of proliferative activity similar to intestinal crypts.

Conclusion We conclude that Barrett's glands show the proliferative and stem cell architecture, and preserve patterns of gene expression of pyloric-type gastric glands, but are maintained by unique stem cells with both gastric and intestinal differentiation capacity: we propose that Barrett's glands originate as gastric glands and that subsequent intestinal differentiation advances with time, strongly supporting an origin from the proximal cardiac mucosa.

Disclosure of Interest None Declared

OC-031 USING GENOME-WIDE STUDIES TO IDENTIFY NOVEL FOXM1 TRANSCRIPTION FACTOR TARGET GENES IN OESOPHAGEAL CANCER

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Introduction The prognosis of oesophageal cancer remains poor with < 10% 5-year survival. Delineating the molecular pathogenesis of oesophageal cancer could inform future research into targeted therapies and may uncover novel biomarkers to aid management decisions. As a transcription factor with important roles in the control of cell cycle transcription, FOXM1 regulates cellular proliferation and chromosome stability. FOXM1 is frequently overexpressed in human cancers and this aberrant expression has been implicated in cancer initiation, progression and resistance to chemotherapy. Overexpression of FOXM1 mRNA and protein has recently been described in oesophageal adenocarcinoma (OAC) tissues. We aim to identify novel gene targets of FOXM1 to better understand the molecular pathogenesis of OAC.
Methods Chromatin immunoprecipitation (ChIP) followed by deep sequencing (ChIP-seq) of FOXM1 binding sites was performed in OE33 OAC cells. FOXM1 binding at target gene promoters was confirmed with ChIP-qPCR studies. Target gene expression in OE33 cells after siRNA-mediated FOXM1 depletion was examined using qRT-PCR and western blotting. Target gene expression in OAC tissues was examined by analysis of microarray gene expression data. Statistical significance (p)in knockdown studies was calculated by Student's t-test. The Pearson correlation coefficient (r) was used to measure strength of correlation of gene expression.
Results Putative novel FOXM1 targets identified from an existing FOXM1 ChIP-seq dataset in U2OS osteosarcoma cells were validated by ChIP-seq in OE33 cells. A large overlap between the genes bound by FOXM1 in both cell types was observed. Genes with FOXM1 binding in both cell types whose expression was highly correlated with FOXM1 in OAC tissues such as *ETV4*, *SKA2* and *NUCKS1* (r = 0.83, 0.84 and 0.72) were analysed further with ChIP-qPCR and FOXM1 knockdown gene expression studies. OE33 cells demonstrated significant FOXM1 binding at the *ETV4* promoter and a reduction in *ETV4* mRNA in FOXM1 depleted cells was observed compared to control ($p = 0.0006$). However, despite highly significant FOXM1 binding at the *SKA2* and *NUCKS1* promoters the reduction in *SKA2/NUCKS1* mRNA following FOXM1 knockdown was modest and not significant.
Conclusion We have identified *ETV4* as a novel FOXM1 target in oesophageal cancer. We found strong correlation with FOXM1 expression in clinical tissues, *in vivo* FOXM1 binding to its regulatory regions and evidence of regulation by FOXM1 in OE33 cells. Our studies also highlight the importance of validating ChIP-seq data with gene expression analysis since transcription factor binding at gene promoters does not always correlate with transcriptional regulation by that transcription factor.
Disclosure of Interest None Declared

NGM free papers

OC-032 A NEW VALIDATED WHOLE GUT TRANSIT TIME (WGTT) MEASUREMENT USING MAGNETIC RESONANCE IMAGING (MRI-WGTT) TECHNIQUE

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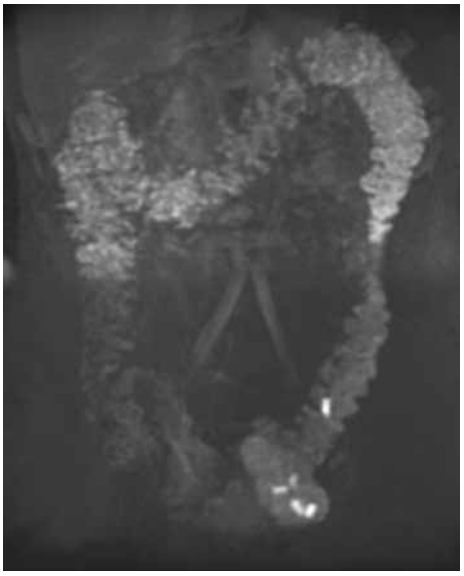
Introduction Disorders of gut transit are very common in gastroenterology clinics. Objective assessment may be useful for targeting and monitoring treatment. Current scintigraphic or radio-opaque marker techniques involve undesirable ionising radiation.
Aims

1. To validate a new MRI method for measuring WGTT against the current gold standard in which 20 radio-opaque markers (ROMs) are ingested per day on 3 consecutive days and the number retained assessed from a single abdominal x-ray on day 4.
2. To assess reproducibility of MRI-WGTT.

Methods 20 healthy volunteers (HV) ages 21–70 (12 males and 8 females) participated in the study involving 2 visits a week apart (test-retest). On each visit, each HV underwent 2 tests: (A) MRI-WGTT test for which HV swallow 5 pills, each filled with a MRI contrast agent diluted with water, 24 hours before undergoing MRI scans which precisely locate the pills in the colon. Transit of the markers was assessed by scoring each pill from its position in the colon (7 = small bowel, 6 = lower ascending 5 = upper AC, 4 = right transverse (TC), 3 = left TC, 2 = descending, 1 = rectosigmoid, 0 = expelled) and calculating an average score (Transit score TS) using an algorithm which gives a weighting inversely related to the distance from the median. (B) ROM test: the number of ROM was counted and multiplied by 1.2 to give a WGTT in hours. Spearman's correlation was used to assess the correlation between the two measurements and intra-class correlation coefficient (ICC) was used to assess the variability of each test when repeated twice.
Results The MRI images provided excellent 3D spatial resolution, allowing the gut to be viewed from all angles, hence allowing accurate location of the pills within the colon especially the sigmoid region (Figure 1). WGTT using ROM was median (SD), 27.6 (20.8) and TS was 0.9 (0.8). WGTT using ROM and TS were well correlated, Spearman's r = 0.85, $p < 0.01$. Using this we converted TS to MRI-WGTT in hours. Mean calculated MRI-WGTT was 27.6 (24.7) hours. The mean absolute difference in the MRI-WGTT on 2 separate visits was 15.3 hours (SD, 15.8) with an ICC of 0.62 ($p < 0.01$). The mean absolute difference in the WGTT for ROMS on 2 separate visits was 11.3 hours (SD, 9.7) with and ICC of 0.69 ($p < 0.01$).



Abstract OC-032 Figure 1 Maximum intensity projection, T1 weighted MRI image showing the MRI transit pills in descending and sigmoid colon.

Conclusion MRI-WGTT correlated well with the gold standard ROM WGTT but was more convenient, involving only one day of marker ingestion and no exposure to ionising radiation. This technique could be implemented easily in most NHS hospitals. Funded by: Medical Research Council and NIHR UK.
Disclosure of Interest None Declared

OC-033 IS LYMPHOCYTIC DUODENOSIS A MARKER FOR IRRITABLE BOWEL SYNDROME?

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