7A FUTURE PROJECTS 2

O153 IMPACT OF PHYSIOLOGICAL FACTORS ON BREATH TESTING IN PATIENTS WITH OESOPAHGO-GASTRIC CANCER

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Introduction: Oesophago-gastric cancer is one of the commonest causes of cancer related death in England and Wales. A diagnostic model for the early detection of oesophago-gastric cancer using specific volatile organic compounds (VOCs) identified as biomarkers in breath has been developed. However the effects of physiological factors such as exercise on these VOCs is unknown.

Method: Breath samples were taken using a ReCIVA (Owlstone Ltd, UK) breath sampling device from 7 oesophago-gastric cancer patients and 10 healthy controls. Samples were taken at rest and at specified intervals following a standardized aerobic exercise regime. The samples were analysed using gas-chromatography mass spectroscopy, and the compound peak areas measured.

Result: Three VOCs (octanal, nonanal and decanal) previously identified as biomarkers of oesophago-gastric cancer and two abundant VOCs (acetone and isoprene) known to be altered by exercise were studied. For the control cohort octanal was significantly lower 5 minutes following exercise ($p < 0.05$) and isoprene was significantly lower 10 minutes following exercise ($p<0.05$). Nonanal, decanal and acetone were not altered by exercise. For the cancer cohort there were no statistically significant differences between baseline and post-exercise VOC peak areas. Isoprene and acetone levels were altered by exercise but did not reach statistical significance.

Conclusion: These results suggest that VOCs significant in oesophago-gastric cancer are not altered by exercise. The variation in abundant VOCs with exercise provides validation for the methodology used. Further assessment with a larger study is required but these results suggest that exercise does not alter VOCs important in oesophago-gastric cancer.

Take-home message:

Aerobic exercise does not impact on the VOC profile of breath samples in oesophago-gastric cancer patients. This supports efforts to useVOC breath testing is a screening tool in the community setting.

O154 THE ROLE OF HYPERMETHYLATION IN RADIOSENSITIVITY OF COLORECTAL CANCER-AN IN VITRO MODEL

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Introduction: Extramural vascular invasion (EMVI) in rectal tumours is an important risk factor for disease recurrence and death. Recent studies have demonstrated CpG island hypermethylation to be an independent risk factor for developing EMVI and may modify radiotherapy responses. This study aims to investigate the cellular processes linking hypermethylation with EMVI by developing in vitro models of rectal cancer. Study Design. Hypermethylated DLD-1 human colorectal cancer cells were cultured for three days and treated daily with demethylating agents 5-azacytidine or 5-aza-2-deoxycytidine across a dose range (0.5μM to 5μM). Treated cells were subjected to a 500μm gel-insert scratch migration assay. Video microscopy was used to record time-to-convergence (TC). Relative population doubling (RPD) and tryptan blue tests of molecular cytotoxicity were also performed at each dose. Pilot Data. 5-azacytidine and 5-aza-2-deoxycytidine both demonstrated >50% RPD cytotoxicity at a dose of 2μM, with a linear dose-dependent increase in toxicity from 0.1μM to 1.0μM. Tryptan blue test also demonstrated linear increase in cytotoxicity for both agents up to 2μM. Mean TC was 38hrs +/- 2hrs for control, solvent control (DMSO), and 0.5μM AZA. Mean TC for 1.0μM and 2.0μM was 52hrs +/- 3hrs and 91hrs +/- 4hrs, respectively ($p=<0.001$). Forward Planning. We plan to refine the model and study novel demethylating compounds with simultaneous application of an in vitro ionizing radiation to study their radiosensitising effects. CpG island methylation will be quantified with methylation-specific PCR. Elucidation of DNA damage response pathways related to methylome modification will also be explored.

Take-home message:

Methylation is an important genetic process affecting rectal tumour development and behaviour. Methylation may be manipulated to therapeutic effect although in vitro models are currently poorly developed.

O155 A MULTICENTRE DOUBLE BLIND PLACEBO CONTROLLED TRIAL INVESTIGATING THE USE OF PROPHYLACTIC TAMSULOSIN IN THE PREVENTION OF URINE RETENTION FOLLOWING PROCTECTOMY

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Introduction: Urinary retention frequently occurs following proctectomy due to pelvic autonomic nerve damage and adrenergic over-stimulation of bladder neck and prostate smooth muscle, leading to prolonged hospital stay and increased morbidity. The aim of this study is to determine if the prophylactic use of Tamsulosin, an alpha-1 adrenergic antagonist prevents urine retention following proctectomy.
Study design: This study will be a multicentre, double blind, placebo controlled randomised-trial on 80

males over age 50 undergoing proctectomy. The test group will receive Tamsulosin 0.4mg one day pre-operatively, on the day of surgery and for 2 days post-operatively. The control group will receive a placebo in an identical manner. All patients will have a transurethral urinary catheter placed at the time of anaesthetic induction which will be removed on post-operative day 2. The primary endpoint is the number of patients requiring re-catherisation due to clinical signs of urinary retention. Pilot Data: Based on our meta-analysis of inguinal hernia literature, prophylactic alpha-blockade reduces urine retention from 18.1% in controls, to 4.2% in those receiving an alpha-blocker (OR: 0.179, 95% CI: 0.043-0.747, p: 0.018). Assuming a similar margin following proctectomy, 80 patients are required for an 80% chance of detecting (significant at the 5% level) a decrease in urine retention from 30.8% in the control group to 7.1% in the experimental group. Forward Plan: If Tamsulosin demonstrates efficacy in the prevention of urine retention following proctectomy, it is anticipated it will be incorporated into enhanced recovery protocols enabling reduced length of stay and decreased morbidity.

Take-home message:

If Tamsulosin demonstrates efficacy in the prevention of urine retention following rectal resection, it is anticipated it will be incorporated into enhanced recovery protocols enabling reduced length of stay, decreased burden on urology services and decreased morbidity.

O156 SUB-TOTAL VS. TOTAL PARATHYROIDECTOMY IN RENAL HYPERPARATHYROIDISM – A MULTI-CENTRE PERSPECTIVE

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Introduction: Tertiary hyperparathyroidism is a common, complex problem in patients with advanced chronic kidney disease. Parathyroidectomy is indicated when patients have failed MM however there is no consensus as to whether ST or T parathyroidectomy is most effective in this cohort. There has been little similar research in the UK since 1996. Study Design Retrospective and prospective reviews of ST and T parathyroidectomies for renal hyperparathyroidism in two tertiary referral centres from 2000 to present. All modalities of renal replacement therapy to be included. Data collected pre-operatively: period/potency of MM, severity of hypercalcaemia and hyperparathyroidism. Post-operatively: surgical complications, LOS, 12-month survival, severity of hypocalcaemia and recurrence rate. Pilot Data 28 T and 16 ST cases were identified. Median age at surgery was T = 49 (range 20-68) and ST = 55 (range 38-70). Median duration of pre-op MM was 15 (T) and 11 (ST) months. Median LOS was 6.5 (T) and 3 (ST) days. T group required post-operative IV calcium for longer than ST (median 2 vs. 0 days). Recurrence rate was 2/28 (7.1%, median 32.5 months) in T and 2/16 (12.5%, median 21.5 months) in ST. No haematomas / 1 neuropraxia occurred with combined 12-month survival 97.9%. Forward Plan We have an established, comprehensive, joint care protocol with the renal physicians and have begun collaboration with a second centre to combine cases and establish a large UK cohort. We aim to publish our joint, multi-centre outcomes in 2017. ST (sub-total) T (total) MM (medical management) LOS (length of stay)

Take-home message:

Large meta-analyses have failed to conclude whether sub-total or total parathyroidectomy is favourable in renal hyperparathyroidism, a multi-centre collaboration between two tertiary referral centres will generate new data to help answer this important clinical question and may shape future best-practice guidelines for managing this complex condition.

O157 DEVELOPING AN OBJECTIVE OUTCOME SCORE FOR THE COSMETIC APPEARANCE AFTER BREAST CONSERVING THERAPY FOR RESEARCH AND QUALITY ASSURANCE USE

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Introduction: In breast cancer surgery we lack an objective outcome tool to quantify aesthetic outcome. The aim of this work is to use three dimensional surface imaging (3D-SI) to develop an objective score for breast conserving therapy based on measurable parameters. Study design Ethical approval has been obtained for two independent reviewers to take measurements from 3D images obtained for a previous study. These will include volume and shape symmetry between operated and non-operated breast, (see pilot data), breast projection, nipple height difference, inframammary fold height difference and volume of any focal deficits (to be done). The results will be used in a multivariate analysis of factors associated with the dependent variable which is the score given by a panel of clinicians using the Harvard 4-point scoring system. Pilot data 200 women have participated. Mean age was 60 years (SD11.1). Mean time from surgery was 35.5 months (SD17.8). Panel scores for the 200 patients were 6%, 23%, 45% and 27% for poor, fair, good and excellent respectively. Median score for 'Satisfaction with breasts' from the BREAST-Q questionnaire was 68 (IQR55-80). Median volume symmetry was 87% (IQR78-93) and shape symmetry was 5.87mm (IQR4.23-7.95). We are continuing to calculate the measurements from the 3D images. Forward plan Our aim is to develop an automated objective score for cosmetic outcome after BCT to replace costly and time-consuming panel assessment.

This may be used in clinical research when evaluating new surgical techniques or for audit of breast surgical units as a quality assurance tool.

Take-home message:

Our aim is to develop an automated objective score for cosmetic outcome after BCT using three dimensional surface imaging. This may be used in clinical research and quality assurance.

O158 A POTENTIAL ROLE FOR STATINS IN IMPROVING THE SURVIVAL OF LOWER LIMB ARTHROPLASTY

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Introduction: Joint replacement (arthroplasty) is the gold-standard intervention in end stage OA. Arthroplasties have a finite life span with a 10-year revision rate of 3.76% in TKA and 6.87% in THA. The most common indications for revision arthroplasty are aseptic loosening, pain, dislocation and particulate wear debris reaction. As the life-expectancy of the population increases the likelihood of patients out-living their prosthesis is increasing. Statins have recently been associated with a reduced risk of arthroplasty revision in a Danish national cohort study. Study Design Retrospective population based cohort study undertaken via the CPRD. Analysis of TKA and THA for primary OA in the CPRD database (08/1997 – 06/2016). Cox regression models will be used to compare the estimated risk of revision of arthroplasty in participants exposed/unexposed to statins. Confounding factors to be addressed via propensity score analysis. Pilot Data A review of the current literature suggests various recognised biological mechanisms underpinning the theory that Statins may have a role in reducing the risk of failure in arthroplasty. The main hypothesis is that statins inhibit periprosthetic osteolysis and subsequently reduce aseptic loosening. There has been no such study undertaken in a UK cohort to date. Forward Plan Funding from John Charnley Trust for the CPRD component of the study has been granted. If there is a significant effect noted in the retrospective study a randomised controlled trial may be warranted to investigate this effect further. OA – Osteoarthritis TKA – Total Knee Arthroplasty THA – Total Hip Arthroplasty CPRD – Clinical Practice Research Datalink

Take-home message:

An ever ageing population is likely to result in increased numbers of revision arthroplasties which are often complex and challenging, identifying novel ways to improve the survival of prosthetic joints is crucial for future treatment of osteoarthritis in the UK.

O159 A NATIONWIDE STUDY OF CLINICAL VARIATION IN THE MANAGEMENT AND OUTCOMES OF SYMPTOMATIC COMMON BILE DUCT STONES

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Introduction: Biliary disease, and gallstone disease in particular, continues to be one of the most commonly managed conditions by general surgeons and physicians. Common bile duct (CBD) stones are present in 10-18% of patients at the time of cholecystectomy. Several options for clearance of the CBD exist. These include open or laparoscopic CBD exploration and endoscopic retrograde cholangiopancreatography (ERCP) either in isolation or combined with cholecystectomy. A Cochrane review in 2013 identified open CBD exploration as superior to ERCP for CBD clearance, and laparoscopic CBD exploration comparable with ERCP. The included trials were deemed to be at high risk of bias. Management of common bile duct stones is subject to wide loco-regional variation in practice due to resource availability and capacity. Study design. The study will take the form of a population-based cross-sectional study. It will be piloted by the Northern Ireland Surgical Research Collaborative during November 2016. Following the pilot, extension of the study to other UK centres through the National Research Collaborative network is planned. Data collection will be performed over a two-month period in 2017. The study will be performed by trainee-led research collaboratives. The study data will be recorded using a standardised database at each centre. Pilot data. No pilot data is yet available. Forward plan. Regional pilot is planned for November 2016, with a national study planned for 2017. Recruitment of nationwide centres will commence in January 2017. This will guide policy planning and future interventions aimed at improving patient care and outcomes.

Take-home message:

This study aims to determine management and outcomes of symptomatic common bile duct stones across the UK and will be delivered using a trainee research collaborative model.

O160 FIRST USE OF 3D PRINTING IN COMPLEX PAEDIATRIC TRANSPLANTATION

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Introduction: There are increased challenges in transplanting small children (<20kg) with significant vascular abnormalities where feasibility is uncertain based on reviewing conventional imaging. We

assessed the use of 3D printing as a preplanning tool to facilitate complex paediatric transplantation. Study Design Adult living donor kidneys and their respective paediatric abdomens were 3D printed in 4 complex cases using Mimics software from data extracted from CT/MR. 3D models of the adult donor kidney and paediatric abdomen were produced by a Stratys Object500Connex Printer. We assessed their utility using pre and post operative questionnaires and geometric validation studies. Pilot Data All models were independently confirmed to be useful for preoperative planning and consenting facilitating transplantation which in some cases were initially uncertain with respect to feasibility. All models showed geometric consistency with pre-printed designs and intraoperative anatomical correlation within surgical acceptance for critical decision making. Forward plan Our pilot study demonstrates clinical translation of these models into the operating theatre providing 3D haptic spatial appreciation for decision making - in particular locating anastomoses sites and graft placement. We aim to do more cases to evaluate further benefit and use in paediatric liver transplantation.

Take-home message:

3D printing is a useful and promising tool in facilitating complex paediatric transplantation in cases where feasibility is uncertain on conventional imaging. To our knowledge this is a world first.