ORAL PRESENTATIONS 7
FUTURE PROJECTS (3)

O153 THE PROOF-OF-CONCEPT PROJECT TO DEVELOP AN EX-VIVO PERFUSION MODEL, TO STUDY THE REAL-TIME MOLECULAR CHANGES AND THERAPEUTIC METHODS OF COLORECTAL LIVER METASTASES (CRLM).

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Introduction: Cell-culture and animal-models are being used to study real-time molecular changes and treatment of cancer. However, these models have limited translational value due to the limitations in extrapolating results to the human setting1. The viability of transplant organs can be enhanced and extended by machine-perfusion2,3. We are developing an ex-vivo perfusion model to keep resected, cancer bearing human organs and animal organs viable for up to 24 hours to study the above molecular changes and effects of therapeutic methods.

Method: In this proof-of-concept research, porcine livers and human CRLM bearing surgical specimens are used. Haemodynamics of the system will be optimised by experimenting on porcine livers. The flow rate to keep livers viable with optimum tissue oxygenation and minimum damage to parenchyma is being investigated and will be used for our future perfusion experiments. The induction of HIF1α (Hypoxia-inducible-factor) and changes of 34 proteins related to other cancer pathways in response to progressive hypoxia will be studied in CRLM using immunohistochemistry, Western-blot/Rt-PCR analysis, and Collaborative-Enzyme- Enhanced-Reactive-immunoassay (CEER®) respectively. This model will be used to study effects of ablative therapy on liver. Progress • Induction patterns of HIF1α and its downstream markers have been studied in CRLM. • Preliminary CEER results have shown the response of cancer pathways in response to chemotherapy and portal vein embolization in CRLM and normal liver. • An effective ex-vivo perfusion system to keep organs viable has been developed. • Preliminary experiments have shown the possibility of using this system to study the effects of ablative therapy on ex-vivo perfused porcine livers.

Take-home message:
Ex-vivo perfused organ systems; a potential model for cancer research.

O154 INTRAOPERATIVE ASSESSMENT OF ABDOMINAL MICROVASCULAR VISCERAL PERFUSION USING CONTRAST ENHANCED ULTRASOUND

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Introduction: Mean arterial pressure (MAP) and cardiac output (CO) monitoring are used to help guide organ perfusion and measure global blood flow. We have previously demonstrated poor correlation between MAP and microvascular visceral blood flow in healthy volunteers. Meta-analyses suggest goal directed therapy reduces surgical morbidity. This study aims to track changes in MVBF across a range of MAP and CO in anaesthetised patients undergoing bowel resectional surgery. Contrast-enhanced ultrasound (CEUS) was used to provide a validated measure of MVBF.

Study Design: Following ethical approval, 32 healthy male volunteers will be recruited. Heart rate and non-invasive blood pressure was recorded and stroke volume measured using ODM (CardioQ™). 5-95% Rise Time (RT) in the kidney and liver was determined using CEUS with contrast bolus doses of Sonovue® (Sulphur-hexa-fluoride microbubbles). Measurements were taken at three time points during the operation. Data was extracted using Qlab (Philips). Data was assessed for normality and analysed using ANOVA with Tukey post-hoc analysis; correlation assessed via Pearson rank. Pilot data Interim data of 7 patients shows intraoperative CEUS to be well tolerated with no complications noted. Good image acquisition was achieved at all time points. Measurement of MVBF did not significantly affect surgical duration. Forward Plan This work in progress suggests CEUS to be a well-tolerated technique for the intraoperative measurement of MVBF. Correlation analysis between MAP, CO and MVBF of the completed study may provide insight into the use of surrogate markers of visceral perfusion and provide future end points for haemodynamic goal directed therapy.

Take-home message:
Bolus contrast enhanced ultrasound can provide real-time intraoperative assessment of abdominal visceral microvascular perfusion and may provide a future end point for goal directed therapy.

O155 THE ROLE OF GFAP, NEUROGRANIN AND BDNF AS NOVEL MARKERS OF MICROEMBOLIC NEUROLOGICAL DAMAGE FOLLOWING ENDOVASCULAR AORTIC ANEURYSM REPAIR - A PILOT STUDY

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Cerebral microembolisation caused by wire manipulation around the aortic arch has been reported following endovascular aortic aneurysm surgery (EVAR) and linked to post-operative cognitive decline (POCD). POCD is associated with significant patient morbidity and mortality. A pilot study was designed to determine if levels of three novel serum biomarkers of subclinical brain damage could identify patients at greatest risk of neuronal damage due to peri-operative micro-emboli. Transcranial Doppler was used to quantify micro-embolic counts (MEC) via the left middle cerebral artery in 14 patients undergoing EVAR. Serum levels of glial fibrillary acidic protein (GFAP), Neurogranin and brain-derived neurotrophic factor (BDNF) were measured before surgery, in recovery, and on days 1 and 3. Mean serum GFAP levels were highest at day 1 (baseline 0.05 ± 0.18, recovery 0.05 ± 0.18, day 1 0.12 ± 0.26, day 3 0.07 ± 0.21). Differences between those in the lowest and highest MEC group approached significance (0 vs 11-20 p=0.69 95% CI -1.76-0.28). Neurogranin demonstrated highest mean levels in recovery (Day 1 0.13 ± 0.25, recovery 0.37 ± 0.60, day 1 0.20 ± 0.42, day 3 0.28 ± 0.55) but no correlation with MEC. There was no correlation between BDNF and time-point or MEC. GFAP demonstrates the earliest promise as a marker of MEC associated neurological injury in a small patient cohort. Ongoing work includes linking these results to incidence of POCD in a larger cohort. Earlier risk stratification will allow implementation of risk reducing strategies such as carotid protection devices and increased support post-operatively.

Take-home message:

Endovascular aneurysm repair causes micro-embolic brain damage with links to post-operative cognitive decline. GFAP shows early promise as a marker of degree of neurological injury due to peri-operative micro-embolic volume.

O156 MULTI-CENTRE BLIND VALIDATION DIAGNOSTIC STUDY OF NON-INVASIVE EXHALED BREATH ANALYSIS FOR THE PREDICTION OF OESOPHAGO-GASTRIC CANCER

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Introduction: Early diagnosis is a key strategy to improve oesophago-gastric cancer (OGC) survival but early disease has non-specific symptoms that are very common while the warning clinical picture often indicates advanced disease. The aim of this research is to validate a breath test to predict OGC therefore allowing earlier diagnosis and introduction of treatment.

Study design: The study will include 325 patients and be conducted across four OGC centres in London, UK. This research will utilise selected ion flow-tube mass spectrometry exhaled breath analysis, for comparison of predicted cancer risk based upon the previously developed volatile organic compound (VOC) exhaled breath model, with endoscopic findings and histology biopsies in a blinded fashion. This will be determine the overall diagnostic accuracy for non-invasive breath testing for the diagnosis of OGC. NRES committee approval has been gained (14/LO/1136), and the study has been registered on the National Institute for Health Research clinical trials portfolio (UKCRN 18063). Pilot data: In a cohort of 220 patients we developed a model based upon the analysis of twelve VOCs from exhaled breath, with a sensitivity of 84.6% and specificity of 76.1%, for the prediction of oesophago-gastric adenocarcinoma. Further work undertaken over the past year in a follow-up cohort of 60 patients has further refined this diagnostic VOC breath model to nine VOCs from two chemical groups (sensitivity 95% and specificity 69%). Forward plan: External validation of this VOC breath model in a large multi-centre study will provide this risk-stratification tool that triages patient to have endoscopy.

Take-home message:

The aim of this present study is to determine the diagnostic accuracy of an exhaled breath test in the prediction of oesophago-gastric cancer in a multi-centre blind validation study.

O157 A PROSPECTIVE, MULTICENTRE STUDY ON THE USE OF EPIDERMAL GRAFT TO OPTIMISE OUTPATIENT WOUND MANAGEMENT

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Introduction: Current wound management with the use of split thickness skingrafts often requires hospital admission, a period of immobility, attentive donor site wound care and pain management. This study evaluates the feasibility of using a novel epidermal graft harvesting device (CelluTome) which allows pain-free epidermal skin grafting in the outpatient clinic setting.

Method: A prospective series of 35 patients was performed in 2 centres, involving 10 acute and 25 chronic wounds. All patients were subjected to epidermal grafting in the outpatient specialist clinic, without the use of anaesthesia, and allowed to return home after the procedure.

Result: Completely healed wounds were noted in 22 patients (62.9%).The overall mean time for 50% and 100% reduction in wound size was 3.31±2.33 weeks and 5.91±3.48 weeks respectively. There was no significant difference in healing times between the acute and chronic wounds (50% reduction in wound size; acute 2.20±0.91 weeks versus chronic 3.73±2.63 weeks, p=0.171. 100% reduction in wound size; acute 4.80±1.61 weeks versus chronic 6.83±4.47 weeks, p=0.183). The mean time for donor site healing was 5.49±1.48 days. The mean pain score during graft harvest was 1.42±0.95 and the donor site Vancouver Scar Scale was 0 for all cases at 6 weeks. CONCLUSION This device offers skin

harvesting in the outpatient setting with minimal or no pain and a scarfree donor site. It has the potential to save NHS resources by eliminating the need for theatre space and a hospital bed, while at the same time benefiting patient care.

Take-home message:

Epidermal Grafting allows for pain free autologous grafting in the outpatient setting and can be a useful tool in the management of acute and chronic wounds.