ORAL PRESENTATION 1B
SURGICAL OUTCOMES AND BREAST

O27 SURGICAL MICRO-RETRODERMAL AXILLARY CURETTAGE (MRAC) EFFECTIVELY REDUCES AXILLARY HYPERHIDROSIS

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Introduction: Axillary hyperhidrosis affects 2% of the population. If deodorants fail, Botox injections can be considered. Micro-curettage of the retro-dermal axilla is a simple surgical techniques which may provide an alternative treatment. This study determines the outcomes of mRAC and compares them with Botox treatment for axillary hyperhidrosis.
Method: Ninety eight patients (25 male; median age 30, range 16-56 years) with localised axillary hyperhidrosis answered a questionnaire before and six weeks after mRAC (23 patients) or Botox (75 patients) treatment. The questionnaire consisted of assessments of hyperhidrosis (Hyperhidrosis Disease Severity Scale, HDSS); psychological precipitating factors and physical effects of hyperhidrosis. Non-parametric analysis between and with-in groups used the Mann Whitney U test on the SPSS V21 package.
Result: For both the mRAC and Botox treatment groups, hyperhidrosis was significantly improved when compared with pre-treatment HDSS scores (mRAC: pre 3.6, post 1.9; Botox: pre 3.3, post 1.7; $p<0.01$) and physical effects (wearing bright clothes, mRAC: pre 4.0, post 1.7; Botox: pre 4.0, post 1.9; $p<0.01$). The influence of psychological precipitating factors such as public speaking or being tense and worried were also significantly and equally improved in both groups ($p<0.05$).

Conclusion: mRAC provides a successful surgical option for the management of axillary hyperhidrosis. Longer term follow up is necessary to determine its durability.

Take-home message:
micro Retro-dermal Axillary Curettage provides a successful surgical option for axillary hyperhidrosis management.

O28 TERAHERTZ PULSED IMAGING TO DIFFERENTIATE BENIGN AND MALIGNANT BREAST TISSUE

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Introduction: This study evaluates the ability of TPI to discriminate benign from malignant breast tissue, with the aim of developing a technique for intraoperative tumour margin assessment to reduce the re-operation rate in BCS.
Method: 52 breast tissue samples (33 patients) from freshly excised breast cancer specimens were scanned using a 0-2.0 THz handheld TPI probe (REC 12-EE-0493). For each sample detailed pathology, including type of predominant tissue (tumour and tumour type, fibrous or adipose), type of background tissue, and cell density, were obtained at 0.6mm-intervals and correlated with THz data. Several parameters from the THz time and frequency domain pulses were evaluated . An AUROC analysis was performed to quantify the performance of each parameter in discriminating tumour, fibrous and adipose tissue of varying tissue cell densities. A Mann-Whitney test was performed on the best parameters to determine whether the parameter values were statistically significantly different.
Result: 17 invasive ductal carcinoma, 2 invasive lobular carcinoma, 1 invasive tubular carcinoma and 32 benign (adipose/fibrous) samples were used. 328 parameters were identified that could readily discriminate 100% adipose from tumour samples ($AUROC>=0,95$; $p<0,001$). 188 parameters were identified that could discriminate samples containing mixed adipose and fibrous tissue from tumour samples ($AUROC>=0,79$; $p<0,001$). One parameter showed promise in discriminating low tumour density samples with a fibrous background from 100% fibrous samples ($AUROC=0,76$; $p<0,005$); the biggest challenge in margin assessment.
Conclusion: TPI shows promise in discriminating benign from malignant tissue in an ex vivo setting, warranting in vivo evaluation to test the impact on BCS re-excision rates.

Take-home message:
TPI shows promise in discriminating benign from malignant tissue in an ex vivo setting, warranting in vivo evaluation to test the impact on BCS re-excision rates.

O29 COORDINATING PERIOPERATIVE CARE FOR THE HIGH RISK GENERAL SURGICAL PATIENT USING RISK PREDICTION SCORING

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Introduction: Identifying High Risk (>5%) emergency general surgical patients early, allows appropriate peri-operative care to be allocated by securing critical care beds and ensuring the presence of senior surgeons and senior anaesthetists intra-operatively. Scoring systems can be used to predict perioperative risk and coordinate resources peri-operatively. Currently it is unclear which estimate of risk correlates with current resource deployment.
Method: A retrospective study was undertaken assessing the relationship between deployment of perioperative resources; senior surgeon, senior anaesthetist and critical care bed with three different measures of high risk (PPOSSUM Score, Pearse Criteria, HES data) in 100 consecutive emergency laparotomies at Salford Royal Foundation Trust. Data was analysed using Mann Whitney U and Fisher Exact tests.
Result: Senior surgeons attended 94% of the emergency cases, in particular those with high PPOSSUM morbidity/mortality scores. Patients with higher operative severity and morbidity scores were allocated HDU/ICU beds postoperatively. No correlation existed between the HES and Pearse criteria and presence of senior surgeons intra-operatively. Senior anaesthetists attended 73% of the cases but no association existed between any scoring system and their presence intra-operatively.
Conclusion: Almost all High Risk patients with high PPOSSUM mortality and morbidity scores had a consultant senior surgeon present intra-operatively. Critically unwell patients with higher operative severity and perioperative morbidity scores received higher care (HDU/ICU) beds postoperatively, ensuring they receive appropriate care if they deteriorate. Therefore PPOSSUM scoring should be utilized peri-operatively in emergency cases to coordinate appropriate perioperative care for high risk general surgical patients.

Take-home message:
Amongst the various risk prediction scoring systems that exist, the PPOSSUM score is an effective perioperative risk stratification tool that can be used to deploy and coordinate appropriate perioperative care for high risk emergency general surgical patients.

O30 THE USE OF ONESTEP NUCLEIC ACID AMPLIFICATION (OSNA) AND TUMOUR RELATED FACTORS IN THE TREATMENT OF AXILLARY BREAST CANCER: A PREDICTIVE MODEL

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Introduction: The effectiveness of CK 19 m RNA copy number and tumour related factors in predicting non-sentinel axillary nodal involvement was investigated, in order to facilitate the formulation of local treatment guidelines for axillary clearance (ANC) following intra-operative analysis of the sentinel node biopsy (SNB) using one-step nucleic acid amplification (OSNA).
Method: Patients due to have (SNB) for breast cancer as well as patients with high-grade ductal carcinoma in situ with pre-operative negative assessment of the axilla were included. Alternate slices of each node were sent for assessment by either OSNA or Histopathology. Immediate ANC was performed if OSNA was positive. The CK19 m RNA nodal copy number, the total tumour load (TTL) measured by summation of m RNA copy numbers of all positive nodes, the total nodal status at ANC and tumour characteristics for each patient was recorded. A model of risk probability was constructed using TTL and tumour related factors.
Result: 664 nodes were analysed from 425 patients who had SNB performed. 105 ANC were performed. The concordance was 91.4%, positive predictive value , negative predictive value was 77% and 97% respectively.TTL ($p<0.01$), and presence of LVI ($p<0.05$) predicted additional nodal involvement. Patients with TTL less than 1400 did not have additional non sentinel lymph node involvement. All patients with 2 or more positive nodes were identified by the model. CONCLUSION: Patients deemed high risk may be offered ANC using risk model based on risk stratification.

Take-home message:
ANC need only be performed in patients identified as high risk by the probability model using OSNA and tumour related factors at sentinel node biopsy with most patients avoiding axillary nodal clearance.

O31 ASSESSING ARGONAUTE-2 AS A BIOMARKER FOR BREAST CANCER

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Introduction: While many advances have been made in terms of our molecular understanding of breast cancer, further research is required to discover and validate novel biomarkers for this disease. Argonaute-2 (Ago2) forms an essential component of the RNA-induced silencing complex, enabling the gene silencing phenomenon RNA interference. While gene expression studies have implicated aberrant Ago2 in tumorigenesis, the role of Ago2 protein in breast cancer remains to be elucidated. This study aimed to assess Ago2 in the further molecular characterisation of breast cancer.
Method: Using immunohistochemical staining, a tissue microarray of 391 breast cancer specimens was

assessed for Ago2 protein expression and subcellular localization. Ago2 staining pattern and intensity were then correlated with patient clinicopathological details.

Result: A significant inverse association was identified between Ago2 protein and Luminal A breast cancer, with strongest staining seen in triple negative breast cancer. A significant inverse association was identified between Ago2 and the presence of oestrogen and progesterone receptors. Finally, Ago2 protein was significantly associated with metastasis. To assess functionality, Ago2 protein levels were characterised in cell lines representing distinct molecular subtypes of breast cancer. Cell lines with endogenously low Ago2 expression were transfected with GFP-tagged Ago2. The effect of this Ago2 over-expression was seen to stimulate cell proliferation, supporting a pro-oncogenic role for Ago-2.
Conclusion : Investigating the role of Ago2 will provide insights into basic molecular differences between breast cancer subtypes. Furthermore, Ago2 may potentially serve as an additional prognostic or predictive biomarker for breast cancer, facilitating treatment optimization and individualization.

Take-home message:
Ago2 may provide further molecular stratification of breast cancer subtypes, enabling the development targeted therapies for personalised breast cancer management.

O32 TRAFFIC LIGHT SYSTEM AT SURGICAL ASSESSMENT UNIT

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Introduction: The acute surgical patients often require complex management and delay in review worsens outcomes. In this study we assigned the patients colour categories and set targets for these patients to be seen by the junior and senior doctors. These targets were then monitored.
Method: This study was prospective collection of data from the patients coming to surgical assessment unit. Red colour was given to patients with early warning score of more than 5. Orange colour was given to score of 3-4 or pain score of 3 whilst green colour was given to score 1-2 or and pain score 1-2. The targets set to get a senior review was 15 min for red, 30min for orange and 4 hours for green.
Result: There were a total of 249 patients in three months study period. Majority were general surgical patients (67.5%) followed by urology (9%) and Medicine (5.2%). Green category was the commonest (87.2%) followed by orange (12%) and red (0.8%). Mean time taken by the senior doctors to see the patient was 119 min (target 15 min) for red, 176 min for orange (target 120 min) and 180 min for green (target 240 min). 30% of all the patients were seen after four hours in almost all the specialities.
Conclusion: The adoption of an escalation strategy which incorporates defined time-points and the early involvement of senior staff when necessary are strongly advised. As we are behind targets in terms of doctor's review especially seniors, a re-audit is in process.

Take-home message:
Trastuzumab has changed the economic landscape of breast cancer treatment entirely. However, little has been done to determine the economic impact of the newer applications of the drug.This study hopes to shed some light on this area.

O33 VARIATIONS IN SURVIVAL AND OUTCOMES BETWEEN HER2 +VE BREAST CANCER SUBTYPES FOLLOWING THE INTRODUCTION OF TRASTUZUMAB

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Introduction: It is established that breast cancer subtype influences treatment options, outcomes and survival. The aim of this study was to assess the patterns of Her2 +ve breast cancer subtypes (Her2 over-expressing and Luminal B), with specific emphasis on relapse patterns prior to and following the introduction of trastuzumab.
Method: Analysis of 469 patients with Her2-positive breast cancer treated at a tertiary referral unit from 1992–2014. Differences between the two subtypes in overall survival (OS), disease free survival (DFS) and patterns of relapse were investigated.
Result: 61.2% of tumours were Luminal B and 38.8% HER2-overexpressing. Univariate analysis found no significant difference between the subtypes in DFS or 5yrs OS. However, multivariate analysis of Luminal B relative to Her2 determined the estimated hazard ratio of DFS & OS was 0.6 and 0.67 respectively. Comparing outcomes following the introduction of trastuzumab, a greater reduction was seen in Luminal B cancers (46.7% to 8.8% $p<0.001$) than HER2 over-expressing (30.9% to 17.7% $p=0.107$). Examining recurrence type, a significant reduction of locoregional recurrence was seen in the Luminal B cancers only (14.3% to 1.6% $p<0.001$; HER2 over-expressing 14.7% to 10.6% $p=0.473$). Importantly, a significant reduction in distant metastasis was seen in both groups. However a greater reduction was seen in the Luminal B cancers (33.3% to 7.1% $p<0.001$ vs HER2 over-expressing: 26.5% to 11.5% $p=0.032$).
Conclusion: Her2 positive breast cancer exhibit distinct patterns of recurrence according to subtype. Our study demonstrates Luminal B cancers exhibit a greater response following trastuzumab treatment.

Take-home message:
The two HER2 receptor positive breast cancer subtypes differ in response to treatment with trastuzumab. A greater response is seen in the Luminal B cancers.

O34 ECONOMIC IMPACT OF TRASTUZUMAB TREATMENT IN A WEST OF IRELAND PRIMARY CARE FACILITY: A COST-EFFECTIVE ANALYSIS

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Introduction: Trastuzumab was approved for adjuvant treatment in 2006 for breast cancer patients overexpressing human epidermal growth factor 2 receptors (HER2). This was after studies showed improved survival rates and subsequently demonstrated an economic benefit. It was subsequently approved for neo-adjuvant treatment but the economic impact has yet to be examined. Our aim was to determine the changing costs of breast cancer treatments, specific to the HER2-positive subtypes, in both the adjuvant and neoadjuvant setting.
Method: A database of 468 HER2-positive patients, treated at a tertiary referral unit from 1992-2014, was analysed. Demographics, survival and individual treatment regimens were recorded. The cost of treatment per individual patient was calculated, using the most recent costings.
Result: In total 468 patients were included; 268 (61%) Luminal B and 181 (39%) HER2-positive. Trastuzumab was used in 62% (254 adjuvant & 74 neo-adjuvant). In patients treated with Trastuzumab a statistically significant improvement was seen in both 5yr DFS and 5yr OS ($p<0.001$).The average cost per patient increased over time. Prior to the introduction of Trastuzumab the average cost was €35,776, increasing to €42,515 (Luminal B), and €45,633 (HER2-positive) in adjuvant treated patients, and increasing further in those receiving neo-adjuvant therapy to €48,175 (Luminal B) and €46,608 (HER2-positive).
Conclusion : Breast cancer treatments are continuing to evolve and become more targeted. These changes are affecting the economics of treating breast cancer significantly. However, study has shown that despite the increasing cost, an improved survival benefit warrants the increased spending for breast cancer treatment.

O35 1.9NM GOLD NANOPARTICLES ENHANCE X-IRRADIATION CELL KILLING OF BREAST CANCER CELLS

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Introduction: Gold Nanoparticles (GNPs) are a potential addition to increase cancer cell killing during radiotherapy (Dose Enhancement; DE). To investigate the underlying molecular mechanisms and variations observed between different model systems, which are poorly understood, we compared two breast cancer cell lines that differed in functional P53 and response to anti-oestrogen treatment for: cytotoxicity, DNA-damage and recovery from treatment.
Method: MCF-7 and MB-231 cells were exposed to 0-6Gy of 6MV X-ray irradiation; with or without GNPs. Treatment with 0-1mg/ml of 1.9nm GNPs for 24hrs was analysed with and without 3Gy 6MV X-ray irradiation. The extent of DNA-damage was measured by ICC for γH2AX foci while clonogenicity assays indicated survival after treatment; cytotoxicity was measured by LDH assay.
Result: Clonogenicity assays identified a significant negative correlation for irradiated MB-231 cells ($p=0.041$); GNP treatment produced DE ratios of 2.005 (MCF-7; 95% CI 1.350–2.755) and 2.258 (MB-231; 95% CI 1.722-2.794) above X-irradiation alone. GNPs alone were not cytotoxic for either cell line. On average 3 foci per cell were detected in MCF-7 cells and 5 per cell in MB-231 cells, GNPs had no effect on γH2AX foci levels; furthermore, no significant changes were observed in combined GNP and X-irradiation treatment, compared to X-irradiation alone.
Conclusion: Incubation with 1.9nm GNPs followed by 6MV irradiation increased cell killing in both cell lines, as indicated by clonogenicity assay, but produced no change in γH2AX foci levels. These data and the observations that GNPs were not cytotoxic support the potential use of GNPs as radiotherapy adjuvants.

Take-home message:
Incubation with 1.9nm gold nanoparticles prior to x-ray irradiation increases the cell kill but does not result in increased double strand break foci in these breast cancer cell lines.

O36 INVESTIGATION OF MEDIATORS OF LYMPHANGIOGENESIS AT A CIRCULATING AND TISSUE LEVEL IN BREAST CANCER

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Introduction: Lymph node(LN) metastasis strongly predicts breast cancer patient prognosis. The vascular endothelial growth factors VEGF-C and VEGF-D, along with the protein COX-2, are intricately

involved in lymphangiogenesis. The aim of this study was to quantify the levels of circulating VEGF-C and VEGF-D in breast cancer patients with and without LN metastases compared to healthy individuals. Expression of COX-2, VEGF-C and VEGF-D in breast tumour tissues and matched LN metastases was also analysed.
Method: Following ethical approval and informed patient consent, circulating levels of VEGF-C and VEGF-D were measured by ELISA in serum from breast cancer patients(n=58) and healthy controls(n=20). Tissue samples(n=38) were harvested from breast cancer patients, consisting of primary tumours(n=19) and matched LN metastases(n=19) from the same individuals. Tissues were homogenised, total RNA extracted, and COX-2, VEGF-C and VEGF-D expression quantified using RQ-PCR.
Result: VEGF-C and VEGF-D were detected in all serum from breast cancer patients and controls. Circulating VEGF-C levels were found to be significantly increased in breast cancer patients (5438±1270pg/ml) when compared to controls(3560±1477pg/ml, p>0.01). A trend towards increased levels of VEGF-C in patients with higher tumour grade was also found. In contrast to VEGF-C, no change in circulating VEGF-D levels was found. In the tissue samples, COX-2, VEGF-C and VEGF-D were detected in matched tumours and LN metastases, however no significant change in gene expression was detected.
Conclusion: The data presented illustrates that although VEGF-C and VEGF-D are not dysregulated at a tissue level, circulating VEGF-C may represent a potential biomarker for measuring breast cancer progression.

Take-home message:
This study illustrates that although VEGF-C and VEGF-D are not dysregulated at a tissue level, circulating VEGF-C may represent a potential biomarker for measuring breast cancer progression.

O37 CIRCUMFERENTIAL FOCUSED ULTRASOUND IN THE TREATMENT OF BREAST FIBROADENOMATA

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Introduction: Breast fibroadenomata (FAD) are the most common breast lesions in women. Three options are available for palpable FAD: reassurance, vacuum assisted mammotomy or surgical excision. Focused ultrasound (FUS) is a minimally invasive ablative technique which has been used to treat FAD, but its utilisation is limited by long treatment times. In this prospective study, we performed circumferential FUS treatment to reduce the treatment time by isolating the FAD from its blood supply.
Method: Patients (age ≥18 years) with diagnosed, symptomatic, palpable and/or painful FAD, visible on ultrasound were eligible. In patients >25 years, a histological confirmation was required. Patients were treated under local anaesthesia with the ultrasound guided Echopulse device (Theraclion Ltd, France). Outcome measures included the reduction in treatment time, decrease in FAD volume and complication rate. This study received regional ethics approval (REC13/LO/1221).
Result: From December 2013, 45 patients (47 treatments, mean age 30.1±7.4 years) underwent circumferential FUS treatment. Mean treatment time was reduced by 30.8±15.8%. FAD volume reduced by 41.7±25.6% (n=26) at three, 53.7±28.3% (n=17) at six and 57.4±22.5% (n=13) at 12 months. Most frequent short term complications at two weeks (n=42) were ecchymosis (n=13), erythema (n=11) and skin numbness (n=3). All complications were self-limiting apart from altered skin pigmentation which was first observed at three months (7/35 patients) and persisted at six (5/25 patients) and 12 months (4/17 patients).
Conclusion: Circumferential FUS ablation of FAD is feasible with a significant reduction in treatment time and a low side effect profile. FAD – Fibroadenomata FUS – Focused ultrasound

Take-home message:
Circumferential FUS ablation of FAD is feasible with a significant reduction in treatment time and a low side effect profile.

O38 DETERMINING CHANGES IN MOLECULAR SUBTYPE OF BREAST CANCER RECURRENCE: LOCO-REGIONAL VERSES DISTANT METASTASIS

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Introduction: There are 4 main molecular subtypes of breast cancer (Luminal A or B, Her2 overexpressing and triple negative). Recently, it was determined that recurrences of breast cancer can be of a different subtype from primary cancers. However, the rate of variation is still unclear. Our aim was to assess percentage of patients who had changes in subtype between primary and breast cancer recurrences.
Method: Retrospective database of all breast cancer recurrences at a tertiary referral centre was analysed. 140 breast cancer patients had recurrent lesion biopsied, of which 40 patients had distant metastasis. 100 patients had loco-regional recurrence (LRR) and 4 patients had both. All pathology specimen reports were analysed and subtype changes recorded
Result: Of the 140 patients, we found subtype changes in 36 cases. Overall, the most common

changing subtype was Luminal B (8/21, 38.1%). Only 6/108 (5.55%) patients changed from HER2 receptor negative to positive. However, 7/36 (19.4%) HER2 receptor positive patients became negative. No difference was seen between LRR (24/100, 24%) and distant metastasis (12/44, 27.3%). For LRR, the highest change was Her2 over-expressing 5/13 (38.5%) patients (4 luminal B and 1 triple negative) and the lowest was seen in luminal A (11/55, 20%). In distant metastasis, the greatest change of subtype was to in Luminal B (5/8, 62.5%) and the lowest in Her2 (0/2, 0%).
Conclusion: Changes in breast cancer subtype following recurrence were seen in 36 patients (25.7%). This highlights the need to biopsy recurrences as changes in subtype may affect treatment regimes.

Take-home message:
This highlights the need to biopsy recurrences as changes in subtype may affect treatment regimes so larger study is needed to confirm the result