WINTER MEETING
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Let’s Talk Precision Pathology!

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Abstracts

Hosted by
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Dept of Molecular and Clinical Cancer Medicine,
Faculty of Health and Life Sciences,
University of Liverpool

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### PHOTOGRAPHS

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- (top centre and top right): Dr Carlos de Figueiredo, a post-doctoral researcher in Melanoma at LOORG (www.loorg.org), University of Liverpool.
- (lower left): Dr Anne Herrmann, a post-doctoral researcher at the University of Liverpool, investigating GFP-labelled neuroblastoma cells in chick embryo model.
- (lower right): Dr Mateus Milani, a post-doctoral researcher at the University of Liverpool, working on proteins involved in mitochondrial fission.

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Invited Speaker
Abstracts
S1

Personalised Molecular Neuropathology — Challenges and Opportunities

P. CG. Eberhart
Johns Hopkins University, Baltimore, USA

Pathological diagnosis of brain tumours has become increasingly dependent on the molecular characteristics of each case. In the 2016 WHO CNS Tumour Classification, key molecular changes were formally incorporated as defining features of some diagnostic entities for the first time. Designations such as Diffuse midline glioma, H3K27M mutant and Medulloblastoma, SHH activated, TP53 mutated embody this new diagnostic reality. While the incorporation of molecular data allows for greater precision, issues with implementing the current classification scheme on a day to day basis, as well as accounting for the rapid ongoing changes in molecular understanding, pose significant challenges. The goal of this presentation is to summarize these recent changes, to review emerging disruptive technologies such as methylation profile based tumour classification, and to introduce new international efforts such as the cIMPACT-NOW consortium which seek to provide ongoing guidance.

S2

Very Early Diagnosis of Hepatocellular Carcinoma: Serological Approaches

P. PJ. Johnson
University of Liverpool, Liverpool, UK

Hepatocellular carcinoma (HCC) is the most rapidly rising cause of cancer-related death in the Western hemisphere. Early diagnosis offers the potential for curative therapy. At present this is attempted by radiological methods, specifically ultrasound screening of high risk groups such as those with chronic liver disease and cirrhosis. In Japan, a country with a very high incidence of HCC three serological markers — alpha-fetoprotein (AFP), the L-3 isoform of AFP (AFP-L3) and Descarboxyprothrombin (DCP) have been used routinely as an adjunct to ultrasound surveillance. We have measured these in the UK, several other international populations and have built a statistical model, known as GALAD (Gender, Age, L-3, AFP and DCP) that is highly effective in diagnosing HCC. Recent studies from the USA have even suggested that the model might more effective than ultrasound. Using very large datasets from Japan, where these three biomarkers have been used for several decades, we have had the opportunity to investigate changes in the GALAD score before HCC is detected within a rigorous screening programme. Preliminary analysis suggests that there may be a long “pre-radiological” stage of HCC, during which the GALAD score rises. Patients detected in this situation may be worthy of intensive surveillance.

S3

Seeing Patterns: The Value of Studying Hereditary Cancer

P. IM. Frayling
Institute of Medical Genetics, University Hospital of Wales, Cardiff, UK

The human brain is a pattern recognition device par excellence. The value in looking for and observing patterns is obvious to all pathologists regardless of their discipline. However, while there is value in individual observations, seeing patterns across many observations can add considerably to our understanding and thus benefit patients. It is also fascinating and enjoyable. The particular value in studying those individuals who are especially prone to cancer will be discussed and illustrated with examples, to show how patterns in such patients tell us about both them and cancer in general. Evolutionary patterns in proteins are also a mainstay in the interpretation of potentially pathogenic variation in genes. And patterns can even be seen in the external quality assurance of immunohistochemistry, which, like the patterns in cancer and proteins, also fit with the Darwinian theory (or should that be law?) of evolution.

S4

This abstract has been withdrawn
S5

Imaging Life’s Complexity with Precision Pathology: Imaging MS at Work

RMA Heeren
Maastricht University, Maastricht, NL

A comprehensive understanding of molecular patterns of health and disease is needed to pave the way for personalized medicine and tissue regeneration. Pathology plays a crucial role in this diagnostic procedure. Detailed, local molecular information can aid in making pathology more precise, but is not routinely available. The objective of this lecture is to demonstrate how innovative molecular pathology imaging technologies, based on mass spectrometry, can be deployed for accurate tissue classification. These technologies offer a new insight into life’s molecular complexity. The ability to unravel this molecular complexity allows researchers in pathology to establish comprehensive and isolated biomolecular molecular patterns of health and disease. This is a key element needed to pave the way for personalized medicine and tissue regeneration. Innovations in mass spectrometry-based chemical microscopes are described that have now firmly established themselves in translational pathology research. One key aspect of translational success is the ability to obtain this molecular information on thousands of molecules in a diagnostic relevant timescale. Modern mass microscopes can now acquire images of metabolites lipids, peptides and proteins in 10-20 minutes, depending on the spatial resolution chosen. High molecular resolution techniques can reveal the role of structural isomers in maintaining cellular organization. Combined they offer a truly precision pathology approach that reveals a disease’s complexity.

Key References
1. Artificial Intelligence - The Third Revolution in Pathology. Salto-Tellez M

S6

The Future of Pathology: Considerations for Technology Adoption and Training

M Salto-Tellez

Pathology has experienced 3 key transformations in the last 40 years: immunohistochemistry (IHC), molecular diagnostics and artificial intelligence, with different degrees of adoption and success [1]. How pathologists adapt to these new paradigms dictate in many ways the future of our specialty. The purpose of this lecture [2] is to: (a) analyse the changes in diagnostic tissue pathology over the last 15 years, since molecular diagnostics / personalized medicine and digital pathology / artificial intelligence have become prominent; (b) understand how this is transforming the way pathology should be practiced; and (c) present potential training models for integrated morpho-molecular pathologists.

Key References

S7

Digital Health: Its Application Now in Medicine

AE Blandford

UCL, London, UK

As it becomes possible to gather, manage and rapidly analyse large bodies of data, new kinds of discovery are becoming possible and clinical practices and patient experiences are being transformed. In this talk, I will present a health data lifecycle that links the individual, the social group and the population. I will draw on examples from ongoing research that is exploiting digital technologies to transform healthcare research and delivery, and will identify facilitators and barriers for the future of effective and appropriate digital health solutions.

S8

Precision Medicine

M Pirmohamed

University of Liverpool, Liverpool, UK

Precision or Personalised medicine represents the overall concept of how treatments (including drugs) can be better targeted to individuals or groups of individuals to improve efficacy of the treatment, and minimize any safety issues, thereby improving the benefit-risk profile of the therapy. In order to achieve this goal, many different technologies will need to be utilised which includes all the omics technologies, drug pharmacokinetics and pharmacodynamics, and the use of wearable sensors, to name a few. While there has been a lot of emphasis on all omics technologies, genomics has had the greatest impact. Personalised or precision medicine approaches can be applied to chemical entities, cell therapies and nucleic acid-based therapies. For example, with respect to the latter, advances in gene therapy are beginning to produce real benefits in inherited diseases such as haemophilia, while antisense therapies are being utilised in a number of CNS conditions including spinal muscular atrophy and Huntington’s disease. Targeted therapies developed on the basis of the identification of somatic driver mutations are now the norm rather than the exception in cancer medicine, with combinations of treatments including targeted and immune therapies promising tractable responses in previously untreatable malignancies. Pharmacogenomics is also gaining traction with different approaches being used including pre-emptive genotyping where genetic data is available at the point of prescribing, much like the availability of liver and renal function tests. It is important that future generations of healthcare professional are trained in the area of precision medicine, as the complexity of new drugs increases, the therapy choices available increase and our ability to delve deeper into making the right therapeutic choices for patients improves.
S9
Sexual Dimorphism in Cancer Biology and Treatment: An Oncologist’s View
D Wagner
Lausanne University Hospital, Lausanne, Switzerland

Despite accumulating evidence that an individual’s sex is one of the most important factors influencing disease risk and response to treatment, the patient’s sex is usually not taken into account in clinical decision making. This is surprising given the increasing interest in precision medicine (1). In cardiovascular medicine, the impact of sex on clinical manifestations, patient management and outcomes has been extensively investigated. In addition to sex differences in response to anticancer drugs, evidence from large epidemiological studies clearly indicate significant sex differences in cancer susceptibility and survival, with men having an increased risk and poorer outcomes compared to women in a wide range of cancer types (2). Sex hormones exert pleiotropic effects on multiple extraglandular tissues. Furthermore, sex-biased gene expression signatures in clinically actionable genes have been detected in different types of cancers (3). Finally, immune responses show significant differences between males and females, pointing altogether to multiple potential differences in the biology of cancers arising in men and women (4).

Aims and objectives of this presentation are: (a) to summarize recent evidence for a sexual dimorphism in cancer; (b) to increase the awareness about potential sex differences in cancer biology; (c) to introduce the concept of gender-specific medicine.


S10
Precision Dermatology
CEM Griffiths
University of Manchester, Manchester, UK

Precision or stratified medicine has traditionally been used to signify the move away from the current construct of trial and error prescribing to a targeted approach. This has been expanded to more accurately represent the concept that wellness or disease prevention is as important as disease treatment encompassed by P4 medicine or P4 health meaning Prevention, Prediction, Personalised and Participatory. This transformation is being made possible by the rise of systems medicine and big data on the patient. One area where this has been applied is psoriasis, and for detection of minimal residual disease after initial definitive treatment. Or new resistance mechanisms. The disintegration of cancer is driven by genomic alterations, and can evolve in response to selective pressures. Sampling of tumor material however is a limiting factor for both diagnostics and research. Blood plasma contains cell-free fragments of circulating tumor DNA (“ctDNA”) that can be collected non-invasively. Analyzed with advanced genomic techniques this becomes an effective source of information. All types of somatic genomic alterations originating from solid tumors can be detected, quantified, and tracked in plasma using next-generation sequencing assays, ranging from very deep sequencing of defined regions to shallow whole genome sequencing. Serially-collected plasma samples can be used to monitor response to treatment, cancer progression and emergence of known or new resistance mechanisms. Methods are constantly being improved to detect trace amounts of tumor DNA present in body fluids. These are applied to study early-stage cancer, and for detection of minimal residual disease after initial definitive treatment. In parallel, the accumulating information allows us to learn more about the biology of cell-free DNA. In the clinical setting, “liquid biopsy” assays for non-invasive molecular stratification of advanced cancers are now being adopted to guide targeted therapy and clinical trials.

S11
The Use of 3D Printed Resources and Virtual Reality in Medical and Biomedical Teaching
PG McMenamin
Monash University, Melbourne, Australia

As a means of supplementing our cadaver-based resources for teaching anatomy to medical, biomedical science and allied health students we recently developed the concept of capturing 3D data from human cadaveric prosections and human radiographic data and converting them into coloured very accurate high fidelity 3D replicas of anatomy. These have been proven to be effective in teaching human anatomy but we have identified some limitations. These include costs, lack of haptic realism and getting exposure of the 3D prints to a global audience of students many of whom may not have access to any cadaver material during their studies. To this end we have explored ways of building a Virtual Reality (VR) anatomy laboratory. This presentation will explain the journey of an educator moving from teaching with conventional cadaver resources to developing alternative educational materials that support effective teaching – an issue still in constant debate. We have also recently commenced scanning archived pathological specimens for 3D printing.


S12
Liquid Biopsies: Monitoring Cancer and its Genome with Circulating Tumour
N Rosenfeld
Cancer Research UK, Cambridge Institute, Cambridge, UK

Cancer is driven by genomic alterations, and can evolve in response to selective pressures. Sampling of tumor material however is a limiting factor for both diagnostics and research. Blood plasma contains cell-free fragments of circulating tumor DNA (“ctDNA”) that can be collected non-invasively. Analyzed with advanced genomic techniques this becomes an effective source of information. All types of somatic genomic alterations originating from solid tumors can be detected, quantified, and tracked in plasma using next-generation sequencing assays, ranging from very deep sequencing of defined regions to shallow whole genome sequencing. Serially-collected plasma samples can be used to monitor response to treatment, cancer progression and emergence of known or new resistance mechanisms. Methods are constantly being improved to detect trace amounts of tumor DNA present in body fluids. These are applied to study early-stage cancer, and for detection of minimal residual disease after initial definitive treatment. In parallel, the accumulating information allows us to learn more about the biology of cell-free DNA. In the clinical setting, “liquid biopsy” assays for non-invasive molecular stratification of advanced cancers are now being adopted to guide targeted therapy and clinical trials.
Plenary Oral Abstracts
**PL1**

**An Innovative Technology for Breast Cancer Death Prevention in the Developing World: A Global Cancer Care Perspective**

*S Sreehari; S Pillai*

NMC Healthcare, Abu Dhabi, United Arab Emirates

**Purpose of the study:** Breast-cancer is curable if detected early, as well proven by the UK National Breast Cancer Screening Programme. How to get this outcome in countries of the world where organised Breast cancer screening programs are not available, where Breast cancer incidence is rising and as per latest IARC report 50% are dying due to it.

**Methods:** Using smartphone technology for early detection of breast cancer through the BREXA Mobile App. The app has the following features: (1) To find out if the woman is potentially at high risk of getting breast cancer. (2) Women who use BREXA are prompted every month to do self breast check for cancer. The app provides video guidance on doing this in the correct way. (3) If the breast examination is abnormal, it guides the women to do the next step (4) Information about the different tests used in breast cancer diagnosis is available in the app. (5) Once the woman crosses 40 years of age, the app automatically advises to start mammogram testing every year. (6) If the app detects high risk women, such women are given advice to further consult by expert panel of doctors. (7) Users can also book appointments with doctors and laboratories through the app and avail discounts on mammography (8) Even after diagnosis, guidance and information is available in the app, making it a comprehensive cancer solution. BREXA is now available in English and some regional languages. BREXA is completely free and can be downloaded from Google playstore and Appstore. It is designed as if a doctor companion is always with the woman giving guidance. With effective use of BREXA App, women world over can be saved from Breast cancer deaths, usually caused due to late detection.

**Results and Conclusion:** Now with nearly 30000 downloads since 1 year after its launch, BREXA App has successfully had a great impact in Kerala, India where major media channels have covered it and took it to the population resulting in detection of 104 cancers.

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**PL2**

**Quantifying the Clonal Expansion of Gastric Intestinal Metaplasia in vivo at Single Cell Resolution**

*W Waddingham; WCH Cross; G Metcalf; S Sekine; M Jansen*

1UCL Cancer Institute, London, UK; 2Barts Cancer Institute, London, UK; 3National Cancer Centre Hospital, Tokyo, Japan

**Purpose of the Study:** Over 35% of the UK population is chronically infected with Helicobacter Pylori, the main risk factor for gastric cancer (GC). Chronic infection provokes a carcinogenic cascade involving glandular atrophy and extensive metaplasic remodelling of the gastric mucosa. Although gastric intestinal metaplasia (GIM) is a pre-cursor lesion to GC, its origin and evolution remain unclear. An understanding of the clonal dynamics and genetic diversity of GIM may allow us to target surveillance to patients with chronic atrophic gastritis at increased risk of progression to GC. Our objective was to develop a quantitative model of the initiation, expansion and clonal diversity of GIM in the chronically inflamed stomach.

**Methods:** We developed a workflow to trace the clonal initiation and expansion of GIM in vivo. Analysis of an e face embedded gastric mucosa from gastrectomy specimens reveals a patchwork of islands of GIM. Using patch size dynamics, 3D modelling, and in vivo. Analysis of en face embedded gastric mucosa from gastrectomy specimens is available in the developing world: a global cancer care perspective.

**Summary of Results:** We reveal for the first time that GIM originates from a single cell of GIM.

**Conclusion:** Whole exome sequencing (WES) we quantify the clonal expansion and genetic diversity reveals a patchwork of islands of GIM. Using patch size dynamics, 3D modelling, and in vivo. Analysis of en face embedded gastric mucosa from gastrectomy specimens is available in the developing world: a global cancer care perspective.

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**PL3**

**Angioimmunoblastic T-cell Lymphoma Contains Multiple Clonal T-cell Populations Derived from a Common Progenitor Cell Carrying TET2 Mutations**

*WQ Yao; F Wu; W Zhang; JS Thompson; SW Zhang; A Clipson; M Wang; H Liu; H Bibawi; JW Grant; P Wright; H El-Daly; L Rádo-Barrett; L Farkas; Z Gao; SS Chuang; M Ashton-Key; W Liu; B MQ Du*

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**Angioimmunoblastic T-cell lymphoma (AITL) is a neoplastic proliferation of T follicular helper cells with clinical and histological presentations suggesting a role of antigenic drive in its development. Genetically, it is characterized by a step-wise acquisition of somatic mutations, with early mutations involving epigenetic regulators (TET2, DNMT3A) and occurring in haematopoietic stem cells, while subsequent changes involving signaling molecules (RHOA, VAV1, PLCG1, C2DB, CTLA4-CD28, ITKSYK and VAV1-STAT2 fusion) critical for T-cell biology. To search for evidence of potential oncogenic cooperation between genetic changes and intrinsic TCR signaling, we investigated somatic mutations in 8 lymphoma genes and T-cell receptor (TRB) rearrangement in 78 AITL, 23 peripheral T-cell lymphomas with T follicular helper phenotype (PTCL-TFH) and 39 PTCL-ND by Fluidigm PCR and Illumina MiSeq sequencing. We confirmed frequent TET2, DNMT3A and RHOA mutations in AITL (77%, 30%, 45%) and PTCL-TFH (57%, 26%, 22%) and showed multiple TET2 mutations (2-3) in 62% of the involved cases. Clonal TRB rearrangement was seen in 62 cases with multiple functional rearrangements (2-4) in 19 cases (30%), which were higher in cases with multiple than those with single TET2 mutation albeit not statistically significant. In a representative case, we confirmed bi-clonal T-cell populations and demonstrated the presence of TET2 mutations in both T-cell populations by BaseScope in situ hybridization. Finally, in comparison with tonsillar TFF1 cells, both AITL and PTCL-TFH showed a significant over-representation of several TRB variable family members, particularly TRBV19. Our findings demonstrate the presence of more than one clonal T-cell population in a high proportion of AITL and PTCL-TFH. The biased TRBV usage in this lymphomas suggests that the intrinsic properties of TCR may play an important role in predilection of T-cells to clonal expansion and malignant transformation.

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**PL4**

**The Molecular Landscape of Malignant Peripheral Nerve Sheath Tumour (MPNST)**

*D Lindsay; E Hookway; C Steele; P Lombard; M Gupta; F Farrow; R Tirabosco; H Ye; A Strobi; N Pillay; AM Flanagan*

1Royal National Orthopaedic Hospital, London, UK; 2University College London, London, UK

**Purpose of the study:** MPNST is a rare aggressive soft tissue sarcoma. In 45% of patients it is associated with Neurofibromatosis type-1 caused by germline mutations in NF1. 45% occur in a sporadic setting, and 10% are radiation-induced. This study takes an integrated approach to the analyses of the heritable/somatic mutational landscape, and methylation of 46 MPNST.

**Methods:** Whole exome sequencing was undertaken on 46 MPNSTs with matched normal tissue. A total of 67 MPNSTs were analysed on the 450K Illumina methylation array, and compared with the methylation profiles of 67 undifferentiated sarcomas (USARC) and 170 soft tissue tumours from an independent cohort. Stochastic Neighbour Embedding (t-SNE) analysis was undertaken to assess how closely these tumours are related at an epigenetic level.

**Summary of results:** 18 tumours showed bi-allicic somatic alterations in NF1 and an additional 14 patients had germline mutations in NF1. Whole genome sequencing would be required for complete assessment of NF1 alterations. Epigenetically, MPNST formed three distinct clusters; cluster 1 overlapped with USARC, and the second only contained paraspinal MPNST. Cluster 3 showed loss of expression H3K27me3 (a marker of histone H3L Repressive Complex 2 (PRC-2) activity) on immunohistochemistry. The genomic loci in cluster 3, which represent those that are normally subject to repression by an intact PRC-2, are significantly hypermethylated compared to those in cluster 1. Patients in cluster 3 had a shorter survival than those in cluster 1 (p<0.0008).

**Conclusions:** We have identified 2 groups of MPNST defined by their DNA methylation profiles which provides prognostic information for patients with this disease. It also demonstrates that DNA sequencing provides more accurate diagnostic classification of soft tissue sarcomas.
Relationship of BRAF Mutation Status with Clinical and Pathological Features in Primary and Metastatic Melanomas

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1North Bristol NHS Trust, Bristol, UK; 2Cheltenham General Hospital, Cheltenham, UK

Purpose of study: BRAF mutation in metastatic melanomas predict response to BRAF and MEK inhibitor therapy. This study investigated the relationship between clinicopathological characteristics of primary and metastatic melanomas with BRAF-mutation status in samples sent for clinical testing over a 2 year period at our institute.

Methods: A total of 312 patients (316 samples) were identified. Patient age, gender and melanoma dataset items were gathered from the histology report. Each variable was analysed against BRAF mutation status.

Summary of results: 64% of patients were male and 36% were female. 48% of specimens were primary tumours and 52% were metastases. BRAF mutation rate was similar in males and females (31% in males vs 35% in females). Commonest mutations detected were p.Val600Glu (76%) and p.Val600Lys (19%). The rate of BRAF mutation was significantly associated with age groups (p<0.0001), with patients over the age of 80 less likely to show a mutation. Mutation rates between primary and metastatic melanomas were similar (29.5% vs 34% respectively) and were not associated with type of mutation detected. The majority of primary tumours were superficial spreading and nodular melanomas (accounting for 43% and 39.5% respectively). BRAF mutations were more common in superficial spreading than nodular melanomas (42% vs 18%) (p=0.3). BRAF mutation was not associated with Breslow thickness (no tumours <1mm were tested). The presence of ulceration was not associated with BRAF mutation status (p=0.0641). Metastatic site was significantly associated with BRAF status (p=0.0277), with the highest rate of BRAF mutation seen in the brain (7/9 cases).

Conclusion: BRAF-mutation status is affected by age, tumour subtype and location of metastasis. Ulceration did not significantly affect rate of mutation. Brain metastases showed an extremely high BRAF mutation rate, the reason for this is unclear and further detailed mutational profile studies are required.
Poster Abstracts
P1 Has the Quality and Readability of Online Information Contributed to the Decline in Hospital Autopsy Rates?

**Purpose:** The aim of this retrospective study was to compare the number of traumatic injuries reported in outpatient and inpatient cases. The incidence of fatal abnormalities following successful CPR was evaluated.

**Methods:** Over 2 years, 169 patients received CPR, of which 89.3% received manual CPR and 10.7% received LUCAS CPR. There was no significant difference in the number of patients who received manual CPR and LUCAS CPR (p = 0.0002). There were a statistically significant increase in rib fractures in those who received LUCAS CPR (94%) over manual CPR (48%) (p = 0.0002).

**Conclusions:** Although there were occasional high quality web articles containing autopsy information, these were diluted by irrelevant and low quality sites, set at an inappropriately high reading level. Given the paucity of high quality articles, healthcare providers should familiarize themselves with the best resources and direct the public accordingly.

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P2 Does LUCAS CPR Cause More Injuries Than Manual CPR?

**Purpose:** The goal of this retrospective study was to compare the number of traumatic injuries associated with CPR using the LUCAS device versus manual CPR, using hospital post-mortem reports from 2016 and 2017. Traumatic injuries included in this study were rib fractures and major organ haemorrhage found at post-mortem examination.

**Methods:** A total of 169 patients received CPR, of which 89.3% received manual CPR and 10.7% received LUCAS CPR. There was a significant difference in the incidence of major organ haemorrhage, including spleen and liver haemorrhage, haemotomas, and haemoperitoneum, between the two groups. There was a significant increase in rib fractures in those who received LUCAS CPR (94%) over manual CPR (48%) (p = 0.0002).

**Conclusions:** Although there was no difference in the number of patients who received manual CPR and LUCAS CPR (p = 0.0002), there was a statistically significant increase in rib fractures in those who received LUCAS CPR (94%) over manual CPR (48%).

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P3 Post-Mortem MRI Comparison with Traditional Post-Mortem Examination: Lessons Learned from the First Year in Practice

**Background:** The number of consented autopsies has been decreasing over the last ten years. Previous studies have shown that declining numbers are largely secondary to parental refusal. Studies show that MRI with ancillary testing had a 94.9% concordance rate with conventional autopsy in the foetal group. Since March 2017 post-mortem MRI has been performed on all autopsy cases > 500 grams or >24 weeks clinical gestation. One year on we review these cases.

**Methodology:** Autopsies performed with MRI between March 2017 and March 2018 were reviewed. 18 cases were divided into those with a known antenatal diagnosis of a congenital anomaly or not. MRI and post-mortem findings were compared.

**Results:** The presence or absence of structural abnormality reported at MRI was confirmed at autopsy examination in all 18 cases. (100% concordance) However in some cases there were additional findings at post-mortem which had not been reported in the MRI. These were significant in two cases with complex cardiac anomalies. This represents a false negative rate of 11.1%.

**Conclusions:** This study helps establish there is concordance of 100% when identifying structural abnormalities between post-mortem MRI and autopsy examination. At post-mortem additional significant structural anomalies were identified in two cases with cardiac anomalies, for which prenatal echocardiography is the gold standard. MRI with detailed placental examination may be a reasonable alternative to traditional post-mortem examination where resources are limited or due to parental objection to invasive examination.

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P4 Rapid On-Site Specimen Evaluation (ROSE) at Endobronchial Ultrasound (EBUS): Role in Assessment of Mediastinal Lymphadenopathy for Suspected Granulomatous Lymphadenitis

**Introduction:** The role of ROSE in mediastinal nodal sampling for sarcoidosis is unclear. This audit aimed to evaluate its usefulness in suspected granulomatous lymphadenitis.

**Materials and Methods:** Data were compiled on all EBUS performed in our hospital (2015–2016). Cases in which sarcoidosis was suspected clinically, were evaluated for the presence of node content and granulomas, noting their presence on the MGG stained direct smear or in liquid-based preparations (liquid-based cytology [LBC] +/- cell block [CB]).

**Results:** Eight cases were investigated for sarcoid, 100% having ROSE. Granulomatous lymphadenitis was present in 71% (n=57). Granulomas were absent, excluding sarcoidosis, in 18% (n=14). Inadequate nodal sampling was reported in 11% (n=9). There was no difference in the number of passes (1–6; median 3) needed to assess for granulomas or to render a procedure non-diagnostic (p=0.856). 93% of MGGs had adequate nodal sampling on the first two passes. Diagnostic accuracy was increased in LBC (78%) compared to MGGs (63%) (p<0.0001). In confirmed sarcoidosis cases, sensitivities of MGGs, LBCs and CBs for granulomas were 74%, 86% and 88%, respectively. LBC and CB combined, increased the sensitivity to 98%. In 36% no granulomas were seen on MGG and diagnostic proficiency for detecting granulomas was significantly decreased in MGGs compared to LBC (p=0.001).

**Conclusion:** ROSE had little impact in suspected sarcoidosis. In most, adequate sampling was achieved in the first 2 passes, typically performed prior to arrival of the cytopathologist. LBC and CB were better in detecting granulomas. Our outcomes have altered our practice, with ROSE now performed on a selective basis for suspected sarcoidosis and these results are being prospectively audited.
P5 Cellular Pathology in Uganda

Mbarara University of Science and Technology, Mbarara, Uganda; 2Massachusetts General Hospital, Boston, USA

For demographic reasons Sub-Saharan Africa is experiencing a rapid increase in the numbers of cancers; facilities and skills to cope with this increase in cancers are not available. Cellular pathology services, essential for accurate diagnosis, guiding treatment and quality control is, in most centres, inadequate. Uganda, with a population of 40m, has 30 qualified pathologists on the medical register, of these less than 10 full time equivalents are dedicated to the public cellular pathology service. Three of the authors (experienced cellular pathologists) have spent in excess of 6 months volunteering in a university department of cellular pathology in southern Uganda. One of only 3 only public laboratories and with a catchment population of 4 million it receives only 1000 surgical specimens and 600 cytological specimen per annum. It has outsourced equipment, inadequate funding for consumables and no IT. Nevertheless it is, thanks to donations, the only publicly funded laboratory in Uganda to carry out ER and PR predictive markers. The hospital has just one adult oncologist in post and there are no formal patient pathways or MDMs. In addition perverse incentives, together with unreliable service from the University department, encourages patients to send specimens to the private sector, where if the fee cannot be afforded the specimen may be discarded. Although a centre for training pathologists the number and nature of specimens is barely sufficient to train a cellular pathologist. The MMEd Program, a 3 yr post graduate study to train as pathologist, expects the trainee to examine 1000 specimens over 3 years under supervision in contrast to 5000. The number and nature of specimens is barely sufficient to train a cellular pathologist.

P6 Lung Cancer and Immunotherapy: How Good Are We in Selecting the Right Patients to Treat? An Audit on PD-L1 Immunohistochemistry Scoring System On Cytology Samples

Mbarara University of Science and Technology, Mbarara, Uganda; 2Massachusetts General Hospital, Boston, USA

Amongst newly diagnosed lung cancer patients 80% are inoperable and cytology is the only material available for decisions on chemotherapy options. Although the 5-years survival is generally poor for advance stage disease, immunotherapy is a new option given to patients whose tumours express a novel biomarker called Program Death Ligand 1 (PD-L1). Expression of PD-L1 can routinely be detected by immunohistochemistry, however several antibodies with different cut-off are currently available generating confusion and need for harmonisation amongst pathologists. In addition, the normal immune cells can express this marker, making assessment on cytology samples even more difficult. We assessed the concordance amongst cytopathologists who routinely report PD-L1 immunohistochemistry. Three cytopathologists from our department assessed internal agreement on scoring PD-L1. Of the three, two have Ventana training to score PD-L1. We blindly reviewed a set of 45 consecutive cell blocks from cytology samples stained with PD-L1 (Ventana assay SP263). 37 (82.2%) cases had 100% of agreement at three different cut-offs (<1%, >1 to <50% and >50% PD-L1 positive tumour cells) whilst in only two (4.4%) cases with a cut-off of more than 50% and therefore eligible for treatment, there was discordance. The degree of agreement in classification over that which would be expected by chance measured by Fleiss’ kappa was 0.73 indicating substantial agreement. In the era of personalised therapy, the role of the pathologist is becoming essential not only for diagnosis but accurate evaluation of biomarkers driving patient treatment and management. Our work demonstrates that it can be achieved with specific training, team working and internal quality control audit measures.

P7 Axillary Node Fine Needle Aspiration Cytology in NHSBSP - Is it a Useful Adjunct? Correlation with Histology and Outcomes

Mbarara University of Science and Technology, Mbarara, Uganda; 2Massachusetts General Hospital, Boston, USA

Breast cancer patients in the NHS Breast Screening Programme (NHSBSP) are subjected to fine needle aspiration (FNA) of suspicious lymph nodes found by ultrasound. This is typically performed by Radiologists as per guidelines in the NHSBSP. We wanted to look at the sensitivity, specificity and positive predictive value of cytology by looking at the final histology of the nodes and clinical outcomes, especially focusing on the inadequate samples. To do this, we retrieved all the axillary aspirate samples in one year (from April 2017 to March 2018) and looked at the final outcomes. We had 115 samples, of which 16 were inadequate, 65 reactive, 4 suspicious for malignancy and 30 showed metastatic carcinoma. Final histology was available for 68/115 patients. Of these, 31 had metastatic involvement (9 cases only showed chemotherapy effect, complete response) and 37 were reactive on histology. The sensitivity was 80.56% and specificity was 100%. The positive predictive value was calculated at 81%. These values compare favourably with the existing literature. In the 16 cases that were non-diagnostic on cytology, a possibility of human error and equipment was raised, as most cases had the same operator. An interesting feature was 9 cases of positive cytology, which had neoadjuvant chemotherapy in the interval between FNA and surgery which were negative on histology. Complete response was noted on histology, which raised an interesting question for our analysis - should these be classified as negative or positive on histology? This potentially confounds statistical analysis. As there was clear indication of therapy effect, we decided to keep them in the metastatic involvement category.

In summary, our study shows that axillary FNA is a useful adjunct with good sensitivity and excellent specificity. Regular cytology-histology correlation is helpful to audit FNA processes. Neo-adjuvant chemotherapy can raise difficulties for analysis of cyto-histo correlation.

P8 Student Authored E-Learning in Pathology Teaching: Widening Participation in Pathology Learning Among Clinical Students

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There is increasing awareness of the role of e-learning in medical education, and the advantages of e-learning are well established. Preliminary e-learning modules received excellent student feedback, but required a significant amount of faculty members’ time to produce. Student authored faculty-supervised e-learning was suggested as an alternative.

Aim: Determine the efficacy of e-learning modules, as opposed to traditional resources, as aids to lecture-based clinical pathology teaching. Explore the potential benefits of e-learning authorship for students.

Methods: Two e-learning modules were created by year 5 medical students using Xerte software under the supervision of a specialist consultant. The modules were published on the VLE to accompany pathology teaching as pre- and post-lecture activities. Student feedback was collected using survey-monkey software and usage statistics were generated by our VLE.

Results: Students became skilled in the use of e-authoring software and had an opportunity to learn about an area of pathology in detail. Usage statistics showed a significant increase in the numbers of users accessing material compared to the previous year. 34/34 students providing feedback rated the pre-session e-learning as being highly educational and 85% of this cohort indicated a preference for e-learning over traditional reading resources.

Conclusion: We found that this student led e-learning out-performed traditional supplementary reading resources and suggest that the student-led aspect offers additional benefits both to the authors and the wider student community and increases student engagement with pathology.
P9
Honours Student’s Professional Competencies Improved Significantly by Organizing a Full Day Programme at an International Pathology Meeting

The abstract has been withdrawn.

P10
This abstract has been withdrawn.

P11
Specialist Biobanking: What Do We Really Think? A Qualitative Exploration in to the Opinions and Experiences of Pathologists and Scientists in the UK

P12
Near Real-time Stratification of PI3KCA Mutant Breast Cancers Using the iKnife
null
P17
Lobular Neoplasia in an Intra-Ductal Papilloma of the Breast
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Background: Classical lobular neoplasia (LN), previously termed Lobular Carcinoma In Situ (LCIS), is defined by a lobulo-centric proliferation of small uniform cells which fill and distend most of the acini in the lobule. Pagetoid spread of LCIS into duct-like structures is well known but other patterns of extension into pre-existing ducts are also described. LN can colonise radial scars and scarring adenosin mimicking an invasive carcinoma. Equally it can be seen in a papilloma and be misdiagnosed as Ductal Carcinoma In Situ (DCIS). Here we present a case observed in a re-excision margin. Case History: 54 year old female with a recent history of Grade 2 invasive ductal carcinoma with Low grade DCIS and LN, underwent re-excision of margins.
Pathology: There was no residual invasive carcinoma but there was a dilated duct containing an intraductal papilloma close to the new resection margin. The papilloma was unusualy cellular because of a population of small sized, uniform cells suggesting low grade ductal carcinoma in situ (DCIS). The cells showed negative staining for e-cadherin and positive staining for P120 leading to a diagnosis of LN colonising an intraductal papilloma.
Discussion: LN can lead to diagnostic confusion with other conditions. For example, when the breast contains an invasive ductal carcinoma with DCIS, like in the current case, the papilloma could be interpreted as harbouring DCIS rather than LN leading to an over diagnosis which requires further surgical excision for clear margins. Equally an under diagnosis cannot be ruled out if the pagetoid spread of LN cells underlying the luminal epithelium of the papilloma are interpreted as myoepithelial cells.
Conclusion: This case highlights that pathologists need to be aware of possible under and over diagnosis when reporting intraductal papillomas in re-excision or margins of breast cancers.

P18
Targeting TBX2-KDM1A Addiction to More Effectively Treat Poor Outcome Breast Cancer
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Breast cancer is a prevalent disease worldwide and is a leading cause of death in the developed world. A subset of poor outcome breast cancers are known to possess amplification of a region of chromosome 17 (17q23), which contains the transcriptional repressor oncogene T-box2 (TBX2). Our group previously identified the epigenetic modifier, KDM1A/LSD1, as a novel interactor of TBX2. KDM1A siRNA knockdowns were shown to prevent the repressive action of TBX2, leading to the upregulation of TBX2 targets (such as the tumour suppressor genes CST6 and NDRG1) and the induction of cell senescence. This study aimed to investigate the TBX2-KDM1A complex in breast cancer cells, its role in senescence-bypass and the possibility of using KDM1A inhibition to target TBX2 overexpression and develop novel therapies. Multiple in vitro techniques were used to investigate the effect of candidate KDM1A inhibitors on cancer cell growth and on key cellular targets. One KDM1A inhibitor in particular, HCl-2509, showed clear anti-tumourigenic effects through the re-expression of tumour suppressors. The cell viability of all cell lines reduced to ≤50% after treatment with HCl-2509, demonstrating its anti-tumourigenic effect and dramatically increased the mRNA expression of CST6 and NDRG1 (9-fold increase, P<0.05, and 4-fold increase, P<0.01, respectively, in MCF7 cell line), demonstrating its ability to enable transcriptional de-repression of TBX2 targets. HCl-2509 was shown to prevent cell cycle progression and enable senescence, with a 5-fold increase in senescent cells and a reduction in CDK1 protein. Unlike other KDM1A inhibitors, HCl-2509 did not produce a consistent upregulation in H3K4 methylation, suggesting that it does not target the catalytic activity of KDM1A. In summary, this study has profound clinical implications and proposes that a chromatin modification complex containing TBX2 and KDM1A could be successfully targeted to improve patient survival in poor outcome breast cancer.

P19
Characterising the Effects of Extracellular Annexin A1 on Macrophage Phenotype and Epithelial Cell Function in Lung Adenocarcinoma
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Purpose of the study: In lung adenocarcinoma increased AnnexinA1 (ANXA1) expression within tumour cells is associated with metastatic spread and poor prognosis. Present both as an intracellular and secreted factor, its potentially pleiotropic roles in influencing the tumour microenvironment are poorly characterised. Tumour-associated macrophages (TAMs) contribute towards tumour growth and metastasis through their pro-resolution phenotype. ANXA1 accelerates inflammation resolution but its role in tumour progression is less well understood. We hypothesised that extracellular ANXA1 released by lung adenocarcinoma cells would drive TAMs towards a pro-resolution phenotype as well as influencing epithelial cell function. These could therefore serve as potential mechanisms by which the detrimental effects of ANXA1 are mediated.
Methods: Monocytederived macrophage (MDMs) were generated and cultured from peripheral blood of healthy human volunteers before treatment with ANXA1. Effects on macrophage surface marker expression and phagocytic capacity of apoptotic cells as well as lung epithelial cell proliferation and migration were examined.
Results: Within the parameters of the in vitro systems used, we were unable to demonstrate any effect of extracellular ANXA1 on macrophage surface marker expression or phagocytic capacity. Additionally, ANXA1 inhibited both epithelial cell proliferation and migration in a concentration-dependent manner.
Conclusions: Further work, including characterisation of other aspects of macrophage function, are required to confirm whether ANXA1 plays a role in altering macrophage phenotype. The observation that exogenous ANXA1 inhibits epithelial cell proliferation and migration suggests that if ANXA1 directly contributes to tumour progression it may be through intracellular interactions rather than extracellular ANXA1 binding to surface receptors.
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P20
Audit of Expression of PD-L1 Immunohistochemical Using Dako 22C3 Kit
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Objective: To assess the proportion of PD-L1 expression in clinical cases using Dako 22C3 kit.
Introduction: Pembrozilumab was approved by Scottish Medicines Consortium in July 2017 for treatment in patients with advanced non-small cell lung cancer with tumour proportion score >50% with no EGFR and ALK tumour mutations. This decision is reflected in clinical practice with the introduction of PD-L1 IHC staining.
Method: Clinical cases reported from this institute were identified using SNOMED code. A total of 416 cases was identified (326 biopsies and 90 cytology cases). PD-L1 expression and histologic features of the cases were recorded.
Result: Only data from biopsied samples were used to make comparisons against KEYNOTE-001, 010 and 024. This cohort showed that 144 cases (44.2%) of cases were negative for PD-L1 expression (<1%), 67 cases (21.4%) showed low expression (1-49%) and 115 cases (34.9%) showed high expression (>49%). This cohort had similar proportion of negative expression with KEYNOTE-001 (39.2%). Different proportion were seen when comparing all three levels of expression with KEYNOTE-010. Similar expression is seen in strong expression (30.2%) in KEYNOTE-024. In term of histologic features, this cohort showed similar proportion of non-squamous cell lung carcinoma (84.4% vs 81.0%) and squamous cell carcinoma (14.4% vs 17.2%) when compared to KEYNOTE-001, similar proportion of non-squamous (70.3% vs 70.1%) when compared to KEYNOTE-010 but different proportion of both squamous (7.8% vs 18.4%) and non-squamous lung carcinoma (92.2% vs 81.6%) when compared with KEYNOTE-024.
Conclusion: It is difficult to compare proportion of PD-L1 expression with trials due to differences in morphology reported. Hence, benchmarking is not possible before more data is available from clinical cases. The audit will be repeated internally to ensure similar proportion is achieved in future cases.
P21

Investigating the Molecular Mechanisms of Congenital Pulmonary Airway Malformation (CPAM)

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Purpose of study: Congenital Pulmonary Airway Malformation (CPAM) is an abnormality of lung development, resulting in cyst formation in utero that is associated with neonatal respiratory distress, recurrent childhood pulmonary infection and, without resection, malignant potential. Thyroid Transcription Factor-1 (TTF-1), Retinaldehyde dehydrogenase 1 (RALDH1) and SRY-box 2 (SOX2) have been identified as genes critical to lung development. The products of these genes were identified by immunohistochemical (IHC) staining of CPAM and normal adult lung tissue and their localisation compared.

Methods: Normal adult, resected adult CPAM and embryonic human lung tissue sections were analysed by light microscopy following IHC staining for TTF-1, RALDH1 and SOX2. Digital images were obtained and staining location quantitatively compared.

Summary of results: Staining of CPAM sections differed compared to normal adult sections, more closely resembling localisation observed in embryonic sections. Normal adult TTF-1 expression was most prominent in type II pneumocytes, whilst in embryonic sections TTF-1 was expressed in all epithelial cells of the developing airways as expected. CPAM TTF-1 expression in cyst-lining epithelial cells resembled embryonic epithelial expression, suggesting that these cells retain a less mature phenotype. Similarly, Sox2 expression in cyst-lining epithelial cells of CPAM sections was up-regulated compared to normal adult, more closely resembling embryonic Sox2 expression observed in the proximal airway epithelium. RALDH1 expression was of low-intensity with variable localisation in CPAM, absent in normal adult and present in all epithelial cells in embryonic sections.

Conclusions: Localisation of 3 factors critical to lung development differ between normal and CPAM adult lung sections, demonstrating expression similar to that observed in embryonic sections. These results support the hypothesis that CPAM arises from localised arrest of lung development.

P22

PD-L1 Expression in Histological and Cytological Specimens and Outcomes Following Immunotherapy in Non-Small-Cell Lung Cancer

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Purpose of study: In non-small-cell lung cancer (NSCLC), immunotherapy manipulates a checkpoint involving programmed death receptor 1 (PD-1) and programmed death ligand 1 (PD-L1). Response to PD-1 inhibitors may be predicted by PD-L1 expression of neoplastic cells. In the UK pembrolizumab (PD-1 inhibitor) is used to treat EGFR and ALK negative NSCLC based on PD-L1 expression. We stratified NSCLC patients using PD-L1 expression. Current PD-L1 assays are validated for histologic specimens only, we aimed to evaluate expression in cytological specimens also.

Methods: Classification of NSCLC patients tested for PD-L1 within The Royal Devon and Exeter NHS Trust using Dako PD-L1 1HC2/CT7 pharmDX by percentage of tumour cells positive for PD-L1. Pathology reports revealed NSCLC subtype and type of specimen. Case notes and radiology reports revealed clinical response in a cohort receiving immunotherapy.

Results: In 2017 161 PD-L1 assays were performed in 158 NSCLC patients, 42 (26%) showed PD-L1 expression ≥50% and 112 showed expression ≤4%. 101 assays on histological specimens found 25 with ≥50% PD-L1 expression (24.8%), 72 with ≤49% (71.3%), and 4 insufficient samples (3.9%). The 60 cytological samples were comparable; 17 showing ≥50% (28.4%), 40 showing ≤49% (66.6%), and 3 insufficient samples (5%). 22 patients received immunotherapy as of November 2017, 16 had ≥50% expression, 6 patients showed expression between 5-49%, 9 patients demonstrated disease reduction, 4 stable disease, 8 no response, 1 awaits follow-up.

Conclusions: The Keynote-024 trial demonstrated that in NSCLC patients with PD-L1 expression ≥50%, pembrolizumab led to longer progression-free and overall survival compared to chemotherapy. Current assays are not validated for use on cytological samples. Studies with paired comparison of PD-L1 expression on cytological and histological specimens indicate that assessment is feasible on cytological material alone. This is supported by our own experience.

P23

Neuroendocrine Tumours of the Lung: What Factors Could Predict Behaviour

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Well differentiated lung neuroendocrine tumours (WD lung NETs) are generally regarded as comparatively indolent when compared to the poorly differentiated neuroendocrine carcinomas. Despite this assumption, WD lung NETs can become metastatic, exhibit carcinoid syndrome and lead to mortality. Carcinoid syndrome is well documented as a poor prognostic complication but it remains unclear what predisposes to the development of the syndrome in WD lung NETs. This study used data collected from 176 patients diagnosed with WD lung NETs at a specialist Oncology Centre. SHIAA, a metabolite of Serotonin, was elevated in 48 patients with 10 developing carcinoid syndrome. The patients with persistently raised SHIAA levels, with or without symptoms, were most likely to be metastatic at presentation or become metastatic over time. While high SHIAA levels were seen equally in male and females, carcinoid syndrome was seen 4 times more commonly in male patients. A higher tumour proliferation index (Ki67) was more common in tumours developing carcinoid syndrome. Tumours associated with carcinoid syndrome were less likely to express TTF1.

Conclusion: Male sex, expression of tumour TTF1 and high Ki-67 index were associated with high SHIAA levels and predicted a biologically more aggressive tumour with greater likelihood of metastatic potential. The study supports the need for a larger multi-centre larger study to validate these findings as this syndrome remains a poorly understood condition.

P24

PD-L1 Expression Heterogeneity in NSCLC: Accuracy and Reliability of Using Primary Lung Tumour Versus Metastatic Lymph Node Deposits

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Purpose: Assessing expression of PD-L1 on tumour cell membranes by immunohistochemistry is an important complementary or crucial companion diagnostic test to guide the use of immune modulating drugs (IMs) in the treatment of non-small-cell lung cancer (NSCLC). Difficulties in ascertaining an accurate and precise PD-L1 score are due in part to the heterogeneity of PD-L1 expression and questions over suitability of specimens for testing. Primary tumour tissue and metastatic tissue reflect different tumour microenvironments, and the question of which may provide a more reliable and accurate substrate for PD-L1 analysis is an area of ongoing debate.

Methods: 61 cases of resected NSCLC had PD-L1 expression assessed on two blocks of matched primary tumour and 35 cases of resected NSCLC had multiple matched nodal deposits of tumour assessed for PD-L1 using the Roche-ventana SP263 antibody and expressed as the tumour proportion score (TPS%). 122 blocks of primary tumour and 85 blocks of involved nodes were assessed.

Results: Of the 61 matched primary cases, 6 (10%) showed a discrepancy of PD-L1 score based on a clinical threshold cut-off of TPS ≥25% or ≥50%. Of the 35 matched nodal deposit cases, 4 were N1 and the remainder were N2. Of these, 6 (17%) showed a discrepancy of PD-L1 score based on clinical thresholds of TPS at ≥1%, ≥25% or ≥50%.

Discussion: Difficulties in ascertaining a precise PD-L1 score due to expression heterogeneity is compounded by the use of small specimens that do not provide accurate representation of the entire tumour/nodal deposit. Primary blocks of tumour show less intra-tumoural variation than cases comparing matched metastatic deposits, but the amount of tissue required for fair representation is far greater. Therefore, small specimens from lymph node deposits may, relative to overall metastases, provide a more reliable and accurate assessment of PD-L1 expression.

Conclusion: Accessing expression of PD-L1 on tumour cell membranes by immunohistochemistry is an important complementary or crucial companion diagnostic test to guide the use of immune modulating drugs (IMs) in the treatment of non-small cell lung cancer (NSCLC). Difficulties in ascertaining an accurate and precise PD-L1 score are due in part to the heterogeneity of PD-L1 expression and questions over suitability of specimens for testing. Primary tumour tissue and metastatic tissue reflect different tumour microenvironments, and the question of which may provide a more reliable and accurate substrate for PD-L1 analysis is an area of ongoing debate.
P25
The Importance of Mutational Analysis in Lung Cancers Presenting as Multiple Ground Glass Opacities: A Case Series
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Purpose of the study: Multiple lung nodules clinically can represent synchronous adenocarcinomas or intrapulmonary metastasis. Radiologically they are referred as ground glass opacity (GGO). Therefore, staging, treatment selection and prognosis varies significantly and is therefore critically important to distinguish them. However, it is not always possible by imaging based on size or shape and by pathology based on histological patterns. We report three cases in which the final diagnosis was achieved integrating the histological diagnosis with the molecular profile. This highlights the importance of integrated diagnosis.

Material and methods: Three patients each with two GGOs underwent surgical resection. Although not all histological criteria were met, the tumours were all diagnosed as synchronous tumours and material sent for molecular studies. All cases were analysed with Next generation sequencing with 50 panel genes. Mutations in EGRF, KRAS, BRAF and PIK3CA genes were reported.

Results: All adenocarcinomas showed lepidic as predominant histological pattern. All three cases showed KRAS mutations in at least one of the two lesions. The second lesion in two cases showed BRAF mutation and EGFR in the last.

Conclusion: The presence of different driver mutations in two simultaneously resected lung tumours showing similar histological pattern suggests that these GGOs have arisen independently and therefore are best regarded as synchronous tumours rather than intrapulmonary metastasis. We propose that mutational analysis becomes part of the pathology report for tumours presenting as multiple lesions as this is the most reliable way of classifying them as synchronous primary or metastatic.

P26
T-cell Prolymphocytic Leukaemia in a Patient with Chronic Myeloid Leukaemia Receiving Nilotinib: First Documented Report
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Introduction: Since the introduction of imatinib, the first oral tyrosine kinase inhibitor targeting the Philadelphia (Ph) Chromosome, the prognosis in chronic myelogenous leukaemia (CML) has dramatically improved, however there have been concerns about the use of second generation TKIs, especially T/NK cell monoclonal lymphocytosis with the use of dasatinib. Herein, we report the first case of T-cell prolymphocytic leukaemia (T-PLL) occurring in a patient with CML in sustained deep molecular response after treatment with nilotinib.

Case Report: This 64-year old lady was diagnosed with chronic phase (CP) CML in 2008. The karyotype at diagnosis showed the classic Ph chromosome (46,XX,t(9;22) (q34;q11)). She received first line nilotinib 400 mg BD and achieved an optimal response. Nine years after the initial diagnosis of CML, she developed an expansion of post-thymic CD4+ T-cells with the following immunophenotype: CD3 (weak), CD2 (weak), CD5, CD7 (strong), CD4, CD25 (weak), CD26, CD28 (strong), CD52 and CD30 (weak). They were negative for CD8, CD1a, TdT and B-cell and NK cell markers. T-cell receptor rearrangement studies detected clonality in the TCR gamma gene. Interphase FISH showed a 14q11 (TCRA/D) rearrangement, gain of one copy of RUNX1T1 at 8q24 (p<0.05). All four biomarkers were found to demonstrate a strong positive correlation consistent with maturity of T-cell lineage markers.

Conclusion: Modulating immune checkpoints such as ICOS could provide therapeutic potential for patients with lung adenocarcinoma. The association identified between increased ICOS expression and survival has been demonstrated in other cancer types, supporting further investigation into other lung cancers such as squamous cell carcinoma of the lung to confirm the prognostic capacity of this biomarker in NSCLC.

P27
ICOS Predictive of Patient Survival in the Immune Landscape of Lung Adenocarcinomas
AP Douglas; SG Craig; MP Humphries; V Bingham; S McQuaid; JA James; M Salto-Tellez
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Purpose of study: Lung cancer has a poor prognosis, with an average 5 year survival of around 11%, with non-small cell lung cancer (NSCLC) representing the majority of cases. The significance of the host-tumour immune response is becoming increasingly recognised, with tumour infiltration by CD8+CD45RO+ T-cells conferring a survival advantage in lung adenocarcinoma. We wished to further characterise the immune contexture of lung adenocarcinoma and explore the relationships between the adjuvant immune response and patient survival.

Methods: Lung adenocarcinomas from 89 patients were assessed in tissue microarray format for six biomarkers representing adaptive immunity and immune checkpoints. All biomarkers were assessed by digital image analysis using open source software (QuPath). Biomarker densities were dichotomised using ROC curves for survival analysis. All statistical analysis was performed using R.

Summary of results: The immune landscape was extensively assessed using digital image analysis in lung adenocarcinoma. Improved patient survival was associated with ICOS, CD4, CD8 and CD45RO (p<0.05). All four biomarkers were found to demonstrate a strong positive correlation consistent with maturity of T-cell lineage markers.

Conclusions: Modulating immune checkpoints such as ICOS could provide therapeutic potential for patients with lung adenocarcinoma. The association identified between increased ICOS expression and survival has been demonstrated in other cancer types, supporting further investigation into other lung cancers such as squamous cell carcinoma of the lung to confirm the prognostic capacity of this biomarker in NSCLC.

P28
Evaluation of Effectiveness of an Online Training Tool for Scoring Programmed Death-Ligand 1 (PD-L1) Diagnostic Tests for Lung and Urothelial Cancer
R Diezko; G Bänfer; B Jasani; R Fish; W Waelput; Y Sucdaet; C Barker; J Whiteley; J Walker; R Hovelink; B Jasani; R Diezko; G Bænfer

Introduction: Since the introduction of immunohistochemistry (IHC) diagnostic tests for PD-L1 detection are approved for various cancers including non-small cell lung cancer (NSCLC) and urothelial cancer (UC). Consistent classification of patients relies on accurate and reproducible scoring of PD-L1 expression on tumour cells (TCs) and/or infiltrating immune cells (ICs). Appropriate training of pathologists is vital to ensure consistency of scoring in clinical laboratories.

Methods: An online digital library was created from scanned PD-L1-stained UC or NSCLC tumour sections. Slides were stained with the VENTANA PD-L1 (SP263) assay for UC, and with VENTANA PD-L1 (SP263), PD-L1 IHC pharmDx 22C3 or PD-L1 IHC pharmDx 28-8 assays for NSCLC. For each indication, representative cases encompassing a range of complexity and expression levels were selected and annotated by two expert pathologists and served as a training and validation set for instructor-led, computer-based, training. After training, participants scored a set of scanned reference slides and the overall percentage agreement (OPA) was assessed between their registered scores and the reference consensus scores across 18 cases in NSCLC (cut offs: TC ≥1%, ≥25% or ≥50%) and/or 18 UC cases (algorithm: TC/IC ≥25%).

Results: Total 52 pathologists received training in NSCLC and 38 in UC scoring. OPA for PD-L1-stained NSCLC was 95% for TC≥1%, 87% for TC≥25% and 85% for TC≥50%. In UC, OPA for TC and IC scores at 25% cut off was 92% vs 77%, respectively.

Conclusions: High agreement between pathologists for PD-L1 expression levels in TCs was obtained in NSCLC and UC following training using a digital approach. The results for IC reproducibility are promising, given the complexity of IC scoring. Overall, online training tool offers a means for standardised training of pathologists in a clinical setting. Further optimisation of the approach is however warranted to deliver higher levels (>85%) of inter-reader reproducibility for IC scoring in UC.
has identified genes, miRNAs and functional pathways dysregulated in UM which are
EIF4 signalling; whilst EIF2 signalling was downregulated. Transcriptomic analysis
function and highly-upregulated canonical pathways in HR UM, included mTOR and
concordance with microarray data. IPA identified cancer as the main biological
downregulated and associated with LR included: PDE3A, SPP1, CHL1, hsa-miR-509-3p,
with HR included: HTR2B, ADAM23, RAB31, hsa-miR-371b-5p, hsa-miR-572; whilst those
the HR c.f LR group. The most differentially upregulated genes and miRNAs associated
expressed with fold change >2; 56 miRNAs were upregulated and 93 downregulated in
expressed genes (fold change >2, P<0.05), with 372 genes upregulated and 523
using PCR and Sanger sequencing. Transcriptomic analysis identified 895 differentially
expressed with chromosome 3, can stratify patients into low (LR) or high (HR) metastatic risk groups. In
half of all UM patients develop metastases, usually to the liver, which are often fatal <2
years following diagnosis. Chromosomal aberrations, in particular loss of one copy of
3, can stratify patients into low (LR) or high (HR) metastatic risk groups. In
this study, we used transcriptomics to define gene and miRNA signatures unique to LR
and HR UM patients and to identify signalling pathways, which can be exploited in the
development of treatment strategies for metastatic disease. Total RNA was extracted
from 20 UM patients; 10 LR and 10 HR, which was then hybridised to human Affymetrix
microarrays. DNA and RNA (Oncomine-Thermo-Fisher) molecular analysis of the
carcinoma showed a BRAF-V600E mutation and the presence of ETVG-NTRK3 fusion
gene. The latter has been reported in radiation induced differentiated thyroid
carcinoma and primary secretory carcinoma of thyroid but is uncommon. Under
supervision of the medical oncology team, this gentleman was commenced on clinical trial of Larotrectinib, a novel oral TRK-inhibitor. He developed pulmonary metastases and
Larotrectinib was discontinued. A combination of Dabrafenib and Trametinib (BRAF
inhibitors) was thereafter initiated. Recent imaging 17 months post initial diagnosis
reported no further pulmonary or distant metastases.
In conclusion, this case demonstrates that advances in molecular pathology and the
ability to identify multiple molecular aberrations using both DNA and RNA from the
same sample are relevant for predictive therapeutic decisions and access to clinical
trials. This case underscores an extremely rare occurrence of 2 known driver mutations in a single tumour, once again highlighting the impact of tumour heterogeneity and its
clinical relevance.

Using Transcriptomics to Define Metastatic Risk in Uveal Melanoma
K Aughton; SL Lake; H Kalirai; SE Coupland
University of Liverpool, Liverpool, UK
Uveal melanoma (UM) is the most common primary intraocular tumour in adults. About
half of all UM patients develop metastases, usually to the liver, which are often fatal <2
years following diagnosis. Chromosomal aberrations, in particular loss of one copy of
chromosome 3, can stratify patients into low (LR) or high (HR) metastatic risk groups. In
this study, we used transcriptomics to define gene and miRNA signatures unique to LR
and HR UM patients and to identify signalling pathways, which can be exploited in the
development of treatment strategies for metastatic disease. Total RNA was extracted
from 20 UM patients; 10 LR and 10 HR, which was then hybridised to human Affymetrix
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carcinoma showed a BRAF-V600E mutation and the presence of ETVG-NTRK3 fusion
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supervision of the medical oncology team, this gentleman was commenced on clinical trial of Larotrectinib, a novel oral TRK-inhibitor. He developed pulmonary metastases and
Larotrectinib was discontinued. A combination of Dabrafenib and Trametinib (BRAF
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In conclusion, this case demonstrates that advances in molecular pathology and the
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same sample are relevant for predictive therapeutic decisions and access to clinical
trials. This case underscores an extremely rare occurrence of 2 known driver mutations in a single tumour, once again highlighting the impact of tumour heterogeneity and its
clinical relevance.

MLH1 Promoter Hypermethylation: Development and Validation of a Methylation-Specific High Resolution Melt Curve Analysis (MS-HRM) Assay for use in a Lynch Syndrome Pre-Screen Pathway
D Pelka; S Hansel; D Moore; P Bennett; G Gerrard
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Lynch Syndrome (LS) is associated with germline mismatch repair deficiency (dMMR)
and microsatellite instability (MSI). These also arise somatically through MLH1 promoter
methylation, which in colorectal cancer is associated with BRAFVal600Glu mutation. We
sought to develop and validate an MS-HRM MLH1 promoter methylation assay for
clinical use, using kits from MethylDetect ApS and Qiagen. Paired tumour/normal DNA
was extracted from 26 FFPE samples: 16 colorectal, 10 non-colorectal. Thirteen samples
were MSI-H, 13 MSI-stable (MSI); 6 were dMMR, 3 MMR-normal; 6 were BRAFVal600Glu,
11 BRAFmut; 1 known LS, 3 suspected LS. DNA (20µL SnpEff version 3.2a and Integrative Genomics Viewer.

The mutation rate was similar to previous studies. Patients were able to be stratified
into survival groups based on specific combinations of copy number changes and
mutations.
Conclusion: Our data shows that it is possible to develop a custom-designed NGS panel to detect CNV and mutations in UM.
**P33**

Clinical Diagnostic Validation of the Promega MSI v1.2 System for Microsatellite Instability Testing in Solid Tumours and Early-Access Evaluation of Improved PCR Mastermix and Workflow

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Microsatellite instability (MSI) analysis provides an assessment of DNA mismatch repair (MMR) status for use in Lynch Syndrome (LS) screening and stratifying cancer patients for checkpoint-inhibitor immunotherapy. The Promega MSI v1.2 system contains a mastermix and fluorescently-labelled primers, which we sought to validate for clinical-diagnostic use. Additionally, we obtained early-access to an improved Promega fast-PCR mastermix for parallel evaluation. Twenty-one MSI-characterised tumour-normal samples from Addenbrooke's Hospital (18 colorectal, 2 endometrial, 1 ovarian) were blinded-tested, along with 12 paired-samples from our diagnostic service: 10 colorectal, 1 bladder, 1 endometrial. Seven had MMR status (2 normal, 5 deficient (dMMR)) and 1 suspected LS. Three of the colorectal were BRAF(V600E) positive. All external samples were concordant (11 MSI-High (MSI-H); 10 MSI-stable (MSI-S)). Of the 12 in-house samples, 9 were MSI-H and 3 were MSS. All 7 known MMR samples were concordant: 2 MMR-normal were MSS; 5 dMMR samples were MSI-H. The 3 BRAF(V600E) positives and the suspected LS sample were all MSI-H. Of the 5 samples with no pre-characterisation, 2 were MSS and 3 were MSI-H. The early-access mastermix and workflow performed equally well to the standard. This assay is now on-scene as a diagnostic service. The early-access mastermix performed equally well, with an improved workflow.

**P35**

Whole Genome Sequencing (WGS) in Cancer: Why Fresh Frozen Tissue Provides the Patient with Improved Genomic Results

**SN Hing; J Moorhead; S Henderson; L Jones; C Craig; A Sosinsky; S Deans; S Hill**


Formalin fixation is universally used by histopathology laboratories to preserve tissue for subsequent diagnostic analysis such as haematoxylin and eosin (H&E) staining and immunohistochemistry (IHC) tests. It is known that formalin preserves tissue by forming protein-protein cross links which prevents DNases, RNases and proteinases digesting the tissues. As a result any DNA extracted from such tissues requires harsh pre-treatment prior to extraction to reverse the cross linking, resulting in fragmented and degraded DNA. This is sub-optimal for downstream genomic testing. Early results from the 100,000 Genomes project for cancer demonstrated marked differences in the quality of data obtained from DNA extracted from fresh frozen (FF) and formalin-fixed paraffin-embedded (FFPE) tissue taken from the same prostate tumour. FFPE samples gave sub-optimal results including AT and CG dropout and unevenness of coverage. As a result national sample handling guidance was introduced to prioritise the implementation of formalin free pathways. Other guidance included upstream handling of fresh tissue including the use of refrigeration to preserve tissue as well as vacuum packing. However it was recognised that in some circumstances fresh tissue was not an option therefore an optimized DNA extraction from FFPE tissue protocol was provided which included recommendations such as controlled processing schedules and fixation. Protocols for DNA extraction were recommended including time and temperature for reversing cross links. Some improvement in the DNA quality was observed from routine FFPE processed samples but there was still inflation in likely artefactual somatic calls. The WGS results from fresh tissue clearly demonstrated the superior quality of WGS results with the lack of background noise. This benefits the patients by minimising inaccurate calling of variants, copy number and structural variants providing a more accurate, reliable WGS service which can aid patient care.

**P34**

Investigating the Role of Grp94/Endoplasmin/HSP90B1 in the Life Cycle of the Vaccinia Virus

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Poxviridae are the largest mammalian viruses, comprising a double-stranded DNA genome in a virion surrounded by an inner and outer membrane. Variola Virus, the most notorious Poxivirus, is the causative agent of Smallpox causing millions of deaths throughout history. The disease was deemed eradicated by the World Health Organisation in 1979, through an immunisation programme utilising Vaccinia Virus (VACV). However, the recently identified cases of monkeypox in the UK have highlighted the need to continue studying and developing an understanding of Poxvirus infections to combat future epidemics, bioterrorism and evolution. The role of Grp94/HSP90B1/Endoplasmin was investigated in Poxvirus infection using a VACV model. Preliminary data showed that Grp94 was phosphorylated by Viral Kinase B1 hypothesising the requirement of the protein in the VACV life cycle. The key experimental approach involved using a Grp94 inhibitor BEP800. We observed the effects of inhibition in 24-hour mature virion yield plaque assays. This then prompted further investigation of the mechanism of action of Grp94, utilising Immunofluorescence (IF) and Flow Cytometry experiments. Our results in the plaque assay showed that the inhibition of Grp94 significantly inhibited the replication of vaccinia virus. This was visualised through IF, where treatment with BEP800 reduced the visible number of replication sites. We then went on to show that Grp94 was particularly necessary for VACV Late Gene transcription or translation through Flow Cytometry measured gene expression data. Our results, therefore, suggest that Grp94 is phosphorylated by the VACV and necessary for (viral) physiological replication site formation through a mechanism involving the correct production and processing of Late Gene transcripts.

**P36**

The Preliminary Results from the 100,000 Genomes Project: The Genomic Landscape of Colorectal Cancer

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The remit of the 100,000 Genomes England Project is to develop a new genomics service for the NHS, while facilitating the research of a large number of human conditions, including more than 20 types of cancer. Here, we present the preliminary analysis of 1000 colorectal cancer genomes which represents the most comprehensive dataset of it’s kind in the world. Methods: We performed bioinformatic processing and analysis using a wide variety of tools: the Illumina ISAAC workflow was used in combination with Strelka, Starling and Sequenza to obtain somatic and germline mutational calls. The Ensembl variant effect predictor (VEP) was used to score and annotate mutations and we referred to the TCGA, COSMIC and other sources to identify known driver mutations and compare our results with those published so far. Summary of results: The cohort comprises 1077 patients with 400 detailed clinical annotations and at least 120X whole genome sequencing of each primary and normal pair. Hierarchical clustering of the mutations present in 264 known driver genes revealed a multitude of differing genotypes, including clusters dominated by several rarer wnt signalling disruptions and SMAD4, BRCA1 and PIK3CA, and several genes with as yet unknown etiology in colorectal cancer. Notably, although the canonical genes APC, KRAS and TP53 were the most frequently mutated, only a minor fraction of cancers possessed mutations in all three. Analysis of the genotypes underlying these mutations revealed the presence of a core set of copy number aberrations. Karyotypes also fit into several subtypes including mostly diploid, those containing chromothripsis, and those with genome doubling which represents around 40% of non-MSI CRCs. Conclusions: Colorectal cancers can be driven by hugely varied drivers and karyotypic states and in these preliminary results we point to several new features that are only made obvious through en masse analysis of whole genomes.
P37
Clonal Evolution of Alternative Splicing in Colorectal Cancer at Single Gland Resolution

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Recent research has revealed frequent and recurrent post-transcriptional modifications in driver genes across many cancer types. These modifications, such as intronic polyadenylation and alternative splicing, can produce mRNA transcripts (and therefore proteins) of differing lengths, affecting gene function. However, it is unclear how these recurrent modifications arise and whether they are heritable and therefore able to drive tumour evolution. Matched whole genome sequencing (WGS) and RNA-seq was performed on multiple regions of colorectal cancers. A mixture of bulk samples and glands (approximately 10,000 recently clonally derived cells) were analysed. A custom bioinformatics pipeline was used to call somatic mutations and derive copy number profiles from the WGS and compare it to gene expression profiles and alternative splicing patterns from the RNA-seq. Analysis of alternative splicing revealed heritable splicing patterns within tumours. Evolutionary relationships between individual glands are concordant when inferred from genetic mutations, copy number profiles or alternative splicing. Sub-clonal copy number aberrations match changes in gene expression, but this does not necessarily translate to functional effects. Meanwhile, alternative splicing events in tumour suppressor genes (TSGs) are more common and more frequently result in shorter isoforms in comparison to non-TSGs, analogous to alternative splicing events in tumour suppressor genes (TSGs). Evolutionary relationships between individual glands are concordant when inferred from genetic mutations, copy number profiles or alternative splicing. Sub-clonal copy number aberrations match changes in gene expression, but this does not necessarily translate to functional effects. Meanwhile, alternative splicing events in tumour suppressor genes (TSGs) are more common and more frequently result in shorter isoforms in comparison to non-TSGs, analogous to alternative splicing events in tumour suppressor genes (TSGs).

P39
This abstract has been withdrawn

P38
SDHC Epimутant GIST: Experience from the UK National Paediatric and Adolescent Wild Type and Syndromic (PAWS)-GIST Clinic

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Background: Gastrointestinal stromal tumours (GIST) have an incidence of 1.3-155x10\textsuperscript{5} in the UK. 85% of GIST harbour somatic KIT and PDGFRA mutations which can be treated with small molecule kinase inhibitors (TKIs). The remaining 15% harbour germline variants or epimutations involving genes encoding for the SDH protein complex (SDHx), neurofibrin (NF1) and other rare mutation. SDH deficient (dSDH) GIST account for up to 7.5% of gastric GISTs and mainly affect individuals below the age of 40. Up to 20% of these GIST show a loss of function of the SDH complex related to silencing of the SDHC gene by promoter hypermethylation. Diagnosis of tumours with SDHC promoter methylation is not established in routine diagnostic. dSDH GIST do not respond to TKIs. We have validated a test which reliably identifies SDHC epimutant GIST.

Methods: Patients with tumours which showed a loss of SDHB by immunohistochemistry and lack identifiable germline variants in SDHx were further assessed for SDHC epimutations. Therefore DNA and RNA from tumour and adjacent normal tissue were extracted from FFPE material. SDHC promoter methylation analysis was performed by pyrosequencing. SDHC mRNA levels were assessed by qRT-PCR.

Results: We have identified six patients with SDHC epimutations: all showed SDHC promoter hypermethylation and concurrent SDHC down regulation. Conclusions: We propose SDHB immunohistochemistry to be performed on every tumour with a poor prognosis.

Discussion: Colorectal rhabdoid carcinomas are reported to have aggressive biological behaviour with poor response to conventional therapeutic modalities. Previous case studies describe that molecular analysis detects a number of genetic mutations, such as loss of nuclear SMARCB1 protein and CIMP+ phenotype. This may suggest a genetic pathway of rhabdoid differentiation, which could aid the development of more specific and effective treatments.

Conclusion: The presented cases illustrate the aggressive behaviour of the rhabdoid phenotype. Highlighted is the importance of histologically recognising this very rare subtype of colorectal tumours, and the difficulties of treatment with current therapeutic modalities.
P41

Plexiform Angiomyxoid Myofibroblastic Tumour (PAMT) of the Stomach: A Rare Incidental Tumour

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Introduction: Gastricplexiform angiomyxoid myofibroblastic tumour (PAMT) represents a rare benign mesenchymal tumour of the stomach, typically occurring in the antrum with only 42 cases being described in the English literature so far. We present a rare example of gastric antral PAMT discovered as an incidental finding during the resection of GOJ adenocarcinoma.

Case report: A 52-year male with a complex surgical history presented with a 6-week history of nausea, abdominal distention and cramping. OGD revealed a 4cm GOJ tumour confirmed on biopsy as adenocarcinoma. Following 3 cycles of neo-adjuvant chemotherapy a total gastrectomy was performed as a second incidental lesion was identified in the antrum during surgery. Radiological final pre-treatment staging T3N1M0.

Histology: The GOJ tumour was confirmed as a poorly differentiated adenocarcinoma, ypT3N0M0. The cut surface of the antral tumour showed a circumscribed tumour measuring 48mm with gelatinous areas admixed with foci of cystic degeneration. Histology revealed irregular tumour nodules dissecting through the muscularis propria onto the serosa and was composed of bland spindle cells in a richly vascular myxoid stroma with low mitotic activity without necrosis. The neoplastic cells were focally positive for S100, SMA and CD34 and negative for cytokeratins, p63, DOG1, CD117, Melan-A, HMB-45, CD31 and desmin. DNA sequencing revealed no pathogenic mutations of the KIT or PDGF alpha genes.

Discussion: Gastric PAMT exhibits favourable outcome and distinct morphological characteristics.

P42

This abstract has been withdrawn

P43

A Benign Neoplasm With PDGFRA Mutation: Inflammatory Fibroid Polyp

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We present a case of an inflammatory fibroid tumour in a gastric polyp, in a 56 year old female patient who was symptomatic with abdominal pain. Histology revealed a bland submucosal tumour, composed of bland spindle cells and characteristic onion skinning fibrosis around the vessels. This was associated with mixed inflammatory cells and granulation like stroma. Immunohistochemistry was performed and the lesion showed strong diffuse positivity for CD34. The lesion showed negative immunoreactivity for CD117, DOG1, SMA, desmin and S100. This immunohistochemistry panel was supportive of a diagnosis of an inflammatory fibroid tumour. Inflammatory fibroid polyps are relatively uncommon, polyloid submucosal masses with CD34+ spindle cells and granulation tissue, usually in distal stomach or terminal ileum. They can present as an obstructive mass or cause intussusception. They are now regarded as neoplasms with a benign behaviour, usually with PDGFRA mutation. Surgical excision is usually curative. We present this interesting case and discuss the histological features and patterns of an inflammatory fibroid polyp. We also discuss the differential diagnosis of spindle cell lesions within the stomach and how immunohistochemistry can assist in the diagnostic algorithm.

P44

Is There A Significant Stage Benefit In Colorectal Cancer Detected in the BCSP?

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Background: The bowel cancer screening programme (BCSP) has shown to decrease incidence and mortality from colorectal carcinoma. However, this improvement in disease stage at diagnosis in BCSP patients in comparison to those identified through symptomatic presentation (non-BCSP) has not been demonstrated within the local service.

Aims: The primary objective of this study was to compare BCSP patients and non-BCSP patients to determine whether there is a stage benefit with BCSP.

Methods: In this retrospective audit, all colorectal specimens received in 2016 from both BCSP (n=39) and non-BCSP (n=237) patients were reviewed. Follow up for all patients was also analysed.

Results: All BCSP patients managed with local colorectal excisions in the form of polypectomies and endoscopic mucosal resections (EMR) showed only stage 1 disease. In contrast, 3 of the non-BCSP cases managed with local excision developed stage 4 disease with distant metastases at 2 year follow up. BCSP patients managed with colorectal resections showed a higher percentage of stage 1 (25% vs 15%) and stage 3 (33% vs 32%) tumours when compared to the non-BCSP group. In both BCSP and non-BCSP groups, 37% of patients had stage 2 disease. The non-BCSP group showed a much higher percentage of stage 4 disease (16% vs 3%).

Conclusion: This study demonstrated colorectal carcinomas detected through the BCSP were associated with an improvement in disease stage at time of diagnosis/surgical resection.
P45
A Quality Improvement Project Demonstrating Improved Staging and Recognition of Renal Sinus Involvement in Renal Cell Carcinoma

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Purpose: Renal sinus involvement is an important factor in the staging and prognosis of renal cell carcinoma, increasing tumour stage to pT3a irrespective of tumour size. Renal sinus invasion is considered the principal route of extra renal extension of the tumour as it contains the lymphovascular supply of the kidney. The International Society of Urological Pathology (ISUP) 2013 consensus guidelines define renal sinus involvement as the presence of tumour within sinus fat, loose connective tissue and smaller vessels of the sinus. In an important study, Bosniak found that >90% of >70mm clear cell RCCs invaded the renal sinus.

Methods: Initial retrospective audit in 2014-15 showed that 53% of tumours >70mm in size were reported as pT3a and only 16% as showing renal sinus involvement; much lower than expected compared to published data. Presentation of this data in 2016 heightened awareness of the ISUP criteria for diagnosis and the importance of renal sinus sampling by pathologists to demonstrate sinus involvement. Subsequent analysis of our 2016–17 data found 16 cases of tumours >70 mm, 14 of which were staged as pT3a, equating to 88% of cases. Reasons for pT3 upstaging were reported as: sinus vascular involvement in 4 cases, sinus fat or connective tissue involvement in 5 cases, or a combination of pT3 criteria in 3 cases. The remaining 2 cases showed perinephric fat extension only without sinus involvement. Ten tumours measuring 70mm or less were also staged as pT3a; 5 demonstrated sinus involvement, 2 each revealed sinus fat involvement and peri-renal fat extension and 1 a combination of pT3 criteria.

There were no reported tumours of stage pT3b or above.

Conclusion: Our project demonstrates significant quality improvement as a direct result of regular service evaluation of consultant reports. We have demonstrated an increase in recognition and reporting of sinus involvement in renal cell carcinoma resection cases, improving accuracy of tumour staging.

P46
Disease Distribution Pattern of Bone Metastasis of Prostatic Cancer Over 10 Years

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Introduction: Being the second commonest cancer in UK, incidence of bone involvement of advanced prostatic cancer is high and the 5 year survival rate is only 25% with bone metastases.

Materials and methods: In this retrospective study, histopathology data base was analysed to identify patients with metastatic prostate cancer to bone during 2009-2018 period at tertiary cancer centre. Clinical history, site of metastasis and the pattern of Gleason were recorded from medical records and histology reports.

Results: 16/30 patients were >80 years of age. 12/30(40%) patients with bone metastases did not have any prior history of prostate cancer. The common sites of bone metastasis were vertebral-10 (33%) and pelvic bone-10(33%) followed by femur-9 cases (30%).Histological examination of bone metastatic deposits revealed Gleason pattern 5 being the most common pattern(63%) followed by Gleason pattern 4- 33%. Neuroendocrine differentiation was identified in only one case.

Conclusion: A good proportion of patients can have bone metastases occurring as the initial presentation of prostatic cancer, especially in elderly age group, with high Gleason pattern. Sequential analysis of PSA in the community would have been beneficial in early detection of prostatic cancer. However this data was not available during the study to consider this hypothesis.

P47
Use of Transperineal Template Prostate Biopsy in a Tertiary Referral Centre in an Unresourced Setting

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Purpose of the study: To assess the clinical utility and laboratory impact of transperineal template prostate biopsy, without accompanying histopathology reviewing.

Methods: A retrospective review of transperineal template prostate biopsies from January 2016 to December 2017 with respect to clinical indications, diagnostic yield and turnaround times.

Summary of results: 86 of 136 transperineal template prostate biopsies (63.2%) were positive for prostatic adenocarcinoma. Only 45 patients had more than 1 prior negative transrectal (TRUS) biopsy. Of 86 positive biopsies, 39 were a first diagnosis of prostatic adenocarcinoma, of which 48.3% were Gleason score 7. 59 cases were active surveillance patients. In the active surveillance group, Gleason score (GS) is as follows: GS0 (18.6%), GS 6 (49.2%), GS 7 (32.2%). GS increased in 17/59 (28.8%) of active surveillance cases. Anterior prostatic adenocarcinoma alone was detected in only 13 of 39 primary diagnosis cases. 12 patients had an anterior lesion on MRI, 2 had prior biopsies following TRUS and 2 were unable to tolerate TRUS. Mean no. of cores per transperineal template prostate biopsy = 30. There was a 30% increase in total cores processed and turnaround time deteriorated to 40% signout at 5 days.

Conclusions: The rate of primary detection of prostate cancer by transperineal biopsy (28%), and of upgrade in Gleason score in active surveillance patients, does not exceed that of transrectal biopsy at our institution. Anterior cancer was only detected in 1 patient without MR evidence of anterior disease: the other anterior cancers (12) had MR evidence of anterior lesions. Transperineal biopsy is only warranted in highly selected patients, with prior biopsies or MR evidence of anterior tumour, in an un-resourced setting, in order to avoid significant deterioration in turnaround time.

P48
Merkel Cell Carcinoma (MCC) in an Irish Renal Transplant Population: Report from a Database Spanning 54 Years

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Background: Merkel cell carcinoma (MCC) is a rare, aggressive cutaneous neuro-endocrine carcinoma. Its prevalence is ten times greater in patients with solid organ transplants than in the general population. Transplant recipients who develop MCC have a worse prognosis. The aims of this study were to determine the prevalence and behaviour of MCC in an Irish renal transplant population.

Methods: The renal transplant database in Ireland was reviewed for recorded episodes of MCC occurring in the renal transplant population from 31/1/1964 to 01/04/2018. Follow up was censored at death or 01/04/2018. The renal transplant database was cross referenced with the National Cancer Registry of Ireland (NCRI) for cases of MCC occurring in any renal transplant recipient. Follow up for NCRI data began on 1/1/1994 and finished on 31/12/2014.

Results: In total, 5108 patients received renal transplants in Ireland between 1964 and 2018. Of these, 12 developed MCC. The patients were all male. The causes of end stage kidney disease and immunosuppressive medications were varied. Where details were available the median age at time of diagnosis was 67 (range 49–86 years). The most common primary site of MCC was the head and neck. Treatment options included surgery, radiation, chemotherapy and palliation. The five year survival from time of diagnosis was 25%. The latency period to the development of MCC post transplant ranged from 4.6 to 31 years.

Discussion: This Irish transplant review was compared to 2 other similar reviews (Cincinnati and Finnish databases). The Irish database has the highest prevalence of MCC and the longest clinical follow up period. It also shows the longest latency period from the time of transplantation to the development of MCC. These results highlight the importance of screening for this aggressive malignancy in renal transplant recipients.
P49
An Audit of Medical Renal Biopsies Weighed Against Compliance of RCPath Standard of Tissue Pathway

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Renal biopsies are a common specimen received in our lab. It has been agreed nationally to audit compliance against RCPath standards of tissue pathway for medical renal biopsies. We wished to verify that we were receiving appropriate specimens, with the audit being used to feedback to the nephrology department so that their team could clinically benefit from the biopsy results. The RCPath guidance sets out a guideline giving specific criteria of how to assess a renal specimen which includes the requirement to link the gross and microscopic description. We adopted the RCPath guidelines, guidelines which state that if there is evidence-based minimum workload, a sample has to be assessed in each of the 6 categories. We conducted the audit on self-assessed reports and identified 74 specimens for the 2017 period. All were audited against the standard.

Results: Out of the 74 specimens, only 34% of the reports had all 6 categories completed. Given the limited range of recommended indications for histopathological examination all the renal specimens had a valid indication in all 6 categories. It was imperative that the inclusion of SNOLED codes within reports usually have a standard that 95% of reports that have T and M codes. The reports at James Cook had a 100% standard.

Conclusion: Renal biopsies have been identified by national guidance issued by the Royal College of Pathologists as a specimen of limited clinical value. The RCPath guidelines state regarding staffing and workload that an evidence-based minimum workload is, as yet, not clearly identified. However, pathologists must bear in mind their diagnostic experience, ongoing CPD activity and EQA outcomes in assessing their ability to maintain an acceptable level of reporting expertise. Our medical renal biopsies were 74 biopsies for the calendar year January 2017 to December 2017. We do not consider our numbers so low that they need to be sent away to a larger unit.

P51
Positive AKT Expression is a Predictive Marker for Tumour Recurrence in Epithelial Ovarian Cancer

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Ovarian cancer (OC) is the third most common gynaecological cancer among women worldwide and it is associated with the highest mortality rate among gynaecologic malignancies. A major reason for the lack of success in effectively eradicating OC can be due to the complex interconnected signalling networks coupled with the distinctive tumour microenvironment. There is an urgent need to refine classification of ovarian cancer and identify novel targeted therapies. The PI3K/AKT/mTOR pathway is an intracellular signalling pathway important in regulating the cell cycle. Therefore, it is directly related to cellular quiescence, proliferation and cancer. We aimed to investigate the prognostic role of AKT in ovarian cancer.

Methods: Investigation of the expression of AKT in ovarian epithelial cancer was carried out on tissue microarrays of 525 consecutive ovarian epithelial cancer cases treated at Nottingham University Hospitals (NUH) between 1997 and 2010 and their expression was correlated to clinicopathological outcomes as well as to recurrence free survival (RFS).

Results: High cytoplasmic AKT expression was significantly associated with serous type of tumour (p = 0.042) and poor outcome in terms of recurrence Free Survival (RFS) (P=0.034). Moreover, by selecting only stage one disease high AKT expression was significantly correlated with worse recurrence outcome (P=0.038) and higher chance of residual tumour following surgery (P=0.049). In Mucinous tumour subtype, a higher chance of resistance to platinum chemotherapy was in borderline significance with high AKT expression (P=0.062). In addition in Endometroid tumours, high AKT expression showed a significant higher chance of residual tumour following surgery (P=0.045).

Conclusion: AKT protein is a prospectively valuable recurrence predictive biomarker of epithelial ovarian cancer. Furthermore, it could be used as a future target in OC management.

P50
Predictive, Prognostic and Therapeutic Significance of Human Ligases (I, III and IV) in Epithelial Ovarian Cancers

Nottingham University Hospitals, Nottingham, UK

Ovarian cancer (OC) is the third most common gynaecological malignancy. Development of biomarkers and therapeutic targets is a high priority. The human DNA ligases I, III and IV play critical roles in maintaining genomic integrity. Ligases join DNA breaks generated during replication and recombination in an ATP-dependent manner. We have conducted the first comprehensive clinical study of ligase I, III and IV in epithelial ovarian cancers.

Methods: Ligase I, III and IV expression was investigated in 525 ovarian cancer patients treated at Nottingham University Hospitals (NUH) between 1997 and 2010. Ligases expression was correlated to clinicopathological features, Progression free survival (PFS) and ovarian cancer specific survival (OCSS). Pre-clinical mechanistic studies were conducted in Ligase I knock down (KD) A2780 (platinum sensitive) and A2780cis (platinum resistant) ovarian cancer cell lines.

Results: High nuclear Ligase I was significantly associated with aggressive features including higher grade, high FIGO stage, sub-optimal de-bulking, platinum resistance and poor survival (all p values ≤ 0.01). High cytoplasmic Ligase III level was also linked to aggressive ovarian cancers (all p values <0.05). Interestingly, high nuclear ligase IV associated with platinum sensitivity and favourable clinical outcome (p <0.05). In Cox multivariate model, Ligase I independently associated with PFS (p=0.001) and OCSS (p=0.029). Pre-clinically, Ligase I KD substantially increased platinum sensitivity. Increased cytotoxicity was associated with DNA double strand break accumulation, G2M cell cycle arrest and increased apoptosis.

Conclusions: We provide the first clinical evidence that Ligases are important predictive and prognostic biomarkers in ovarian cancer. Importantly, the data shown here supports the development of Ligase I inhibitors for personalized ovarian cancer therapy.

P52
An Audit of Placental Specimens, Their Clinical Indications and Suitability for Assessment

James Cook University Hospital, Middlesbrough, UK

Renal biopsies have been identified by national guidance issued by the Royal College of Pathologists as a specimen of limited clinical value. The RCPath guidelines guidelines which state regarding staffing and workload that an evidence-based minimum workload is, as yet, not clearly identified. However, pathologists must bear in mind their diagnostic experience, ongoing CPD activity and EQA outcomes in assessing their ability to maintain an acceptable level of reporting expertise. Our medical renal biopsies were 74 biopsies for the calendar year January 2017 to December 2017. We do not consider our numbers so low that they need to be sent away to a larger unit.
P53

Chronic Ulcerative Vulvar Herpes Virus Infection Mimicking Carcinoma

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Purpose of the study: Genital herpes simplex virus (HSV) infections characteristically present as painful vesicles, pustules or crops of erosions. Unusual clinical presentations such as hypertrophic, condyloma-like, nodular, ulcerative and tumour-like nodules or plaques have been documented mainly in patients with HIV and have rarely been documented in immunosuppressed patients secondary to either an underlying medical condition or a systemic therapy.

Methods: We report a case of multiple ulcerated vulvar HSV infection simulating neoplasia in a patient receiving immunosuppressive therapy for rheumatoid arthritis.

Summary of results: An 82-year old woman with a history of rheumatoid arthritis presented with a six-week history of sore, weeping lumps on both labia. Examination revealed ulcerated lesions on the labia, measuring up to 25mm. An MRI scan revealed a 19mm lesion of the right introitus with suspicious involvement of the posterior distal urethra. She underwent wide local excisions of bilateral vulval lesions with mapping biopsies. Histology of the bilateral vulval excisions revealed inflamed ulcerated lesions with abrupt margins. The residual epithelium showed pseudopitheliomatous hyperplasia and contained multinucleated epithelial cells with ground glass inclusions which on immunohistochemistry for HSV was positive. CMV immunostaining was negative. She remained asymptomatic during 14 months follow-up at vulval disorders clinic.

Conclusions: Vulval HSV infection presents a diagnostic challenge for pathologists and clinicians because of its unusual clinicopathological features mimicking neoplasia and its rarity, often leading to a delayed diagnosis. Eliciting a history of immunosuppression forms an important clinicopathological clue to the diagnosis of this rare mimic.

P54

Dermatofibrosarcoma Protruberans of the Vulva: A Case Report

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Purpose of the study: Dermatofibrosarcoma protruberans (DFSP) is a low grade sarcoma of the dermis with a high rate of local recurrence and a low propensity for metastasis. It usually involves the trunk and extremities. DFSPs arising in the vulva are unusual, with only approximately 54 cases reported in the English-language literature.

Methods: A 48 year old woman presented with a few-weeks history of a painless unilateral vulval lump, appearing as a 2cm area of high diffusion signal in the right posterior labia on MRI scan. A radical wide local excision of vulval lesion with lotus petal flap reconstruction was performed following a biopsy diagnosis of DFSP.

Summary of results: Vulvectomy contained an irregular firm lesion measuring 30x25x15mm. The tumour had infiltrative margin involving deep subcutaneous fat, measured approximately 55mm microscopically and was composed of interwoven bundles of uniform spindle cells with occasional admixed multinucleated giant cells, intermingled collagen and scattered mitoses. Immunohistochemically the tumour was positive for CD34, BCL2 and negative for SMA, S100, desmin, CD117, DOG1, EMA, PAX8, ER and PR. The patient remains recurrence-free 14 months after surgery.

Conclusions: DFSP frequently invades the vulva; however correct diagnosis is important because of the potential for local recurrence even after apparent complete excision. The morphological features in combination with a characteristic immunohistochemical phenotype, particularly diffuse CD34 positivity, should enable distinction from other vulval spindle cell lesions.

P55

Rare Benign Tumours of the Uterus: Report of Two Cases

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Purpose of the study: Lipomatous uterine tumours are uncommon benign neoplasms, with an incidence ranging from 0.03% to 0.2%. This includes mixed lipoma and pure lipoma of uterus, the latter being exceptionally rare. Adenomymetroid tumour is an uncommon benign tumour of mesothelial origin that has been described in female genital tract. Only 7 cases of the leiomyoadenomatoid variant, which features a prominent smooth muscle component, have been reported in the English literature.

Methods: We report 2 rare benign uterine tumours (pure lipoma and leiomyoadenomatoid tumour) which were discovered incidentally.

Summary of results: Case 1: A 77 year old female underwent hysterectomy with bilateral salpingo-oophorectomy for a left ovarian serous cystadenoma. The myometrium contained a circumscribed 33 mm circumscribed bright yellow nodule which, on microscopy, was confirmed to be a pure uterine lipoma showing no mitotic activity, pleomorphism or necrosis.

Case 2: A 47 year female underwent staging hysterectomy following a diagnosis of a right ovarian borderline mucinous tumour. Multiple firm, pale myometrial lesions were seen, measuring up to 20mm. Microscopy demonstrated circumscribed lesions containing smooth muscle interspersed with vascular-like spaces that were lined by flattened to cuboidal cells. The lining cells were positive for AE1/3, calretinin and WT1 and negative for BerEP4, ER, PR, CD34 and CD31. SMA and desmin highlighted the smooth muscle component.

Conclusions: These rare benign uterine tumours typically present incidentally in uteri removed for other causes. Because of their morphological overlap with leiomyomas, they are frequently undersampled or misdiagnosed, potentially resulting in underestimation of their true incidence. Awareness of the histological characteristics of these entities and generous sampling of suspected leiomyomata showing unusual macroscopic features is likely to enable accurate diagnosis of these rare tumours.

P56

Multiple Cutaneous and Uterine Leiomyomatosis / Hereditary Leiomyomatosis and Renal Cell Carcinoma: A Case Report

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Introduction: Multiple cutaneous and uterine leiomyomatosis (MCUL) is an autosomal dominant condition caused by a heterozygous mutation in the Fumarate Hydratase (FH) gene. A small number of cases are associated with aggressive renal cell carcinomas whereby this condition is known as Hereditary leiomyomatosis and renal cell carcinoma (HLRCC). A 40 year old Para1+1 presented with a 4 month history of abdominal distension and bulky abdomen. A CT scan demonstrated multiple large solid and cystic leiomyomata in the abdominal cavity. She underwent total abdominal hysterectomy, myomectomy and salpingo-oophorectomy. Past history included a large vulval cutaneous leiomyoma.

Pathology: Macroscopically, multiple lesions ranging in size from 85mm to 205mm were received. Histologically, the largest was a smooth muscle tumour of uncertain malignant potential (STUMP) and the remainder were benign leiomyomata.

Follow up and management: This unusual presentation raised the suspicion of MCUL / HLRCC. She was referred to clinical genetics and was found to have two first-degree relatives with similar history. FH gene mutation was not demonstrated on testing but follow-up with yearly MRI was recommended for early detection of renal lesions.

Discussion: MCUL is characterised by multiple cutaneous and uterine leiomyomatas. Uterine lesions tend to be larger and present earlier than in the general population. At least 73 different mutations have been found in the FH gene. Consequently, a mutation may not always be easily detected. Renal tumours in HLRCC tend to be more aggressive and metastasise early. Therefore, it is important to identify this condition to ensure adequate monitoring and follow up.
P57
Uterine Carcinosarcoma: A Retrospective Comparison of Morphology with Other Prognostic Factors
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Purpose of the study: Uterine carcinosarcoma is a rare neoplasm that carries a poor prognosis. Prognostic factors include tumour stage, size and depth of myometrial invasion. The significance of heterologous elements in prognostication is a controversial topic, which the Royal College of Pathologists recognises. The recommendation is to specify the epithelial and mesenchymal components with the respective subtypes. Our aim is to correlate the morphological features with other prognostic factors.

Methods: A single centre retrospective study over 8 years was conducted to examine carcinosarcoma cases that underwent primary surgical staging identified using a WinPath database. The tumour stage, lymphovascular invasion, metastases, and histologic subtypes of carcinomatous and sarcomatous components, including presence of heterologous elements, were recorded.

Summary of results: A total of 35 hysterectomies for carcinosarcoma were conducted. Of the cases with stated epithelial components, 43% showed high grade serous carcinoma (n=15), 20% endometroid adenocarcinoma, one showed both morphologies and the remaining were unlisted. 60% showed heterogeneous elements (n=21). PT1a was the most common stage regardless of sarcomatous morphology. 63% of all cases showed lymphovascular invasion (LV1) but there was no significant difference between the incidence of LV1 in carcinosarcoma with heterogeneous (n=10) and homologous elements (n=8), with proportions of 61% and 57% respectively. Of the 6 patients with metastatic lymph node, all but one had heterologous components.

Conclusion: Current literature contains conflicting evidence on the prognostic impact of heterologous components in uterine carcinosarcoma. Our data shows that whilst there is no increased risk of lymphovascular invasion or staging, a higher incidence of metastatic lymph nodes may be possible. Future multicentric research of this rare neoplasm will help elucidate the true prognostic impact of heterologous components.

P58
Extra-Uterine Placental Site Nodule: A Case Presentation and Review of the Literature
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Placental site nodules (PSNs) are benign lesions, which comprise intermediate trophoblasts at a previous implantation site which failed to achieve complete involution. These lesions are uncommon and are usually incidental findings on histology taken for other indications. PSNs within uterine curettings have been described as early as 1997. Histologically, PSNs are composed of syncytiotrophoblasts at a previous implantation site which failed to achieve complete involution. These data show that αvβ6 expression is associated with an immunosuppressive tumour microenvironment. A systems biological analysis of HNSCC RNA sequencing data in The Cancer Genome Atlas using weighted gene network analysis showed that expression of αvβ6 correlated with TGF-β, and was located in a hypoxic/glycolytic gene expression module that was associated with immune evasion. In vivo studies using an HPV-driven tumour model showed that the overexpression of αvβ6 resulted in significantly larger tumours; containing significantly fewer cytotoxic (CD8+) T-cells and increased numbers of regulatory (FoxP3+/CD4+) T-cells. These data show that αvβ6 expression is associated with an immunosuppressive tumour microenvironment in HNSCC, and that targeting αvβ6 may be a useful adjunct to immunotherapy. This work was supported by a Pathological Society Career Development Fellowship.
P61

Re-Audit: Diagnostic Adequacy and Accuracy of Core Needle Biopsy Versus Fine Needle Aspiration Cytology in Salivary gland Tumours – Results From May 2016 to April 2017

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Purpose of study: This is a re-audit of the adequacy and accuracy of core needle biopsy (CNB) versus fine needle aspiration cytology (FNAC) for diagnosing salivary gland lesions. During this study, we compared our results (May 2016 to April 2017) with the findings of the initial audit (April 2015 to April 2016), to see if there had been a reduction in the number of inadequate samples received.

Methods: The records of patients that had fine needle aspiration and core needle biopsy for salivary gland lesions were obtained from the hospital computer system (EPIC). All cases were analysed for patient’s demographics (age, sex and tumour site) and hospital of origin. The adequacy, accuracy, sensitivity and specificity of core needle biopsy and fine needle aspiration cytology were analysed and compared to the previous audit.

Summary of results: Overall, the number of adequate FNAC and CNB received from all hospitals increased from 56% and 86% respectively in the previous audit to 91% and 97%. The accuracy of diagnosis for CNB in both benign and malignant cases was 100%. While the accuracy of diagnosis for FNAC in malignant and benign lesions was 100% and 95% respectively.

Conclusion: A key recommendation of the previous audit was to advocate the use of Cytoyl for specimen preservation. This allowed a wider range of sample preparations, analysis and ancillary tests (including immunohistochemistry). The recent audit showed 60% - 70% of FNAC samples were received in Cytoyl. This is considered to be the main factor which resulted in a significant reduction in inadequate samples.

P63

Chronic Lymphocytic Leukaemia Representing as Bilateral Enlargement of Ear Lobes with Literature Review

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A 66 year old male presented to his GP with a 9 month history of symmetrical enlargement of both ear lobes. Past history included type 2 diabetes mellitus, ischaemic heart disease and a 5 year history of B cell chronic lymphocytic leukaemia (B-CLL). On examination the left ear lobe was slightly larger than the right; measuring 3.5 cm and 3.2 cm respectively (average lobe height in adult male 1.5 - 2.2cm). There was no history of previous scarring or piercing. Punch biopsies of each ear lobe showed a dense monotonous infiltrate of small lymphocytes extending from the papillary dermis to the subcutis. There was an absence of lymphoid follicles and epidermal involvement. The infiltrate showed immunoreactivity for CD20, CD5 and CD23. Negative staining was seen with CD3, CyclinD1, CD10 and CD30. A diagnosis of ear lobe involvement by B-CLL was made. Whilst leukaemia may be associated with a variety of skin lesions including purpura, urtica, erythoderma, pyoderma gangrenosum, cutaneous vasculitis and Sweet’s syndrome, leukaemia cutis is uncommon and may present in any site. The correct diagnosis is rarely made clinically. It has a predisposition for scars especially after Herpes infections. Auricular involvement by B-CLL is extremely rare and may occur in patients with known B-CLL or may be the presenting feature of B-CLL. A review of the literature identified 3 male patients with known B-CLL who developed symmetrical ear lobe enlargement. The mean duration post diagnosis of B-CLL was 9 years (range 3 – 14 years). The mean age of the patient was 64 (range 59 – 67 years). Two patients were treated with radiotherapy and one with chemotherapy. Two additional patients also had involvement of the tip of the nose and the eyebrows in addition to ear involvement. Seven further cases of auricular involvement are also discussed where the alteration of the ears led to investigations which resulted in a diagnosis of B-CLL. The prognostic significance of leukaemia cutis in B-CLL is debated.

P62

Correlation of Salivary Gland FNA Cytopathology with Histological Outcomes and the Use of Milan System for Reporting Salivary Gland Cytopathology

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Background: Fine needle aspiration of salivary gland is a widely used diagnostic procedure guiding the management of salivary gland lesions. The aims of this study are 1. To review and correlate salivary gland FNA cytology with their histological outcomes and determine sensitivity and specificity. 2. To categorise the cytopathological diagnoses using the proposed Milan system for reporting salivary gland cytopathology, calculate the risk of malignancy for each category and establish its utility in routine practice.

Methods: This is a retrospective study of FNAs from salivary gland lesions reported over a period of 5 years (Jan 2012 - Dec 2016). The cytopathological diagnoses were correlated with their histological outcomes and were also categorised using the Milan system for reporting into 7 categories, C1: non-diagnostic C2: non-neoplastic C3: atypia of undetermined significance (AUS) C4a: benign neoplasms C4b: salivary gland neoplasm of uncertain malignant potential (SUMP) C5: suspicious for malignancy, C6: malignant. The risk of malignancy was calculated for each diagnostic category. The specificity and sensitivity were calculated including and excluding the indeterminate categories (AUS and SUMP)

Summary of results: There were a total number of 457 cases during the study period, 168 of which had histological outcomes. The sensitivity and specificity excluding the indeterminate categories were 95% and 98% and including the indeterminate categories were 95% and 84%. The risk of malignancy for C1, C2, C3, C4a (benign neoplasm), C4b (SUMP), C5 and C6 were 11%, 9%, 29% 0%, 15%, 86% and 97% respectively.

Conclusion: Salivary gland FNA is a cost effective and valuable diagnostic tool with a high sensitivity and specificity. The use of proposed Milan system of reporting is useful for risk stratification and classification of indeterminate cases.

P64

Core Needle Biopsy in the Management of Salivary Gland Tumours: A Tertiary Centre Experience

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Purpose of the study: Ultrasound-guided core needle biopsy (CNB) forms part of the pre-operative diagnostic armamentarium for salivary gland lesions. To confirm its appropriateness for delivery of patient care, this study assessed the: 1) reporting turn-around time (RTAT) against the recommendations of Royal College of Pathologists (RCPATH) and 2) concordance of CNB diagnosis with that of the corresponding surgical resection (SR)

Methods: The RTAT times of ninety-eight salivary CNB’s from 2015 to 2017 were assessed against the recommendations of RCPATH. The concordance of CNB diagnosis with that of the corresponding resection was compiled for fifty-two cases that were managed at the hospital.

Summary of results: 88% of salivary CNB’s, most of which had reflex tests were reported within 10 calendar days. 12% including inflammatory lesions and metastatic disease, among others, did not meet this criterion. The diagnostic concordance between CNB and SR diagnosis when subclassified as malignant, benign, inflammatory and non-inflammatory lesions were 97%, 93%, 100% and 100% respectively. A discordant diagnosis was observed for salivary duct carcinoma (20%), epithelial-myoid epithelial carcinoma (33%) and adenoid cystic carcinoma (50%).

Conclusions: The RTATs and diagnostic concordance for salivary CNBs at the hospital meets the recommendations for appropriate level of patient care. The sample sizes for specific tumours which yielded diagnostic discordance were small, but this serves as a reminder of the diagnostic challenges faced in salivary gland pathology.
**P65**

**Sclerosing Mucoepidermoid Carcinoma of Parotid Gland: A Challenging Diagnosis**

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**Background:** Mucoepidermoid carcinoma is one of the most common malignant tumours of the salivary gland. The sclerosing mucoepidermoid carcinoma subtype is very rare and difficult to diagnose especially on biopsy samples. There are <30 cases described to date. Here we describe a case of sclerosing mucoepidermoid carcinoma which was only recognised when the surgical specimen was available.

**Case history:** A 56-year-old female presented with nasal blockage, intermittent epistaxis and pain in the left cheek. A tumour was present in the left maxillary sinus. Histology showed a high-grade mucoepidermoid carcinoma.

**Pathology:** Surgical specimen showed an unencapsulated, poorly circumscribed lesion, which mostly comprised of hyalinised sclerotic tissue with entrapped nerve fascicles. There were scant epithelial elements with squamous-like, intermediate, clear and mucus secreting cells. The lack of encapsulation along with the entrapment of nerve fascicles favoured mucoepidermoid carcinoma.

**Discussion:** When the characteristic features of mucoepidermoid carcinoma with a combination of squamous-like, intermediate, clear and mucus secreting cells are present the diagnosis is straightforward. The sclerosing mucoepidermoid carcinoma is usually confused with a benign tumour such as involuted pleomorphic adenoma or a scarring process.

In our case the pre-operative diagnosis was not possible because of extensive fibrosis on a biopsy sample. The imaging however showed a mass with irregular outline, which was not consistent with pleomorphic adenoma and the diagnosis required review from a pathologist with an interest in salivary gland pathology.

**Conclusion:** Pathologists need to be aware of sclerosing mucoepidermoid carcinoma to avoid misdiagnosing it as a benign lesion.

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**P66**

**A Case Report: HPV-Related Carcinoma with Adenoid Cystic Like Features of the Sinonasal Tract**

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**Background:** The association of Human papillomavirus (HPV) with squamous cell carcinoma (SCC) of the oropharynx is well known, but a new subset of these carcinomas, due to HPV16/18 infection, is introduced as ‘HPV-related carcinoma with ACC-like features’. It showed a significant morphological overlap with adenoid cystic carcinoma (ACC). Here we present another case and its immunohistochemistry profile.

**Case history:** A 56-year-old female was presented with nasal blockage, intermittent bleeding and a ‘polyp’ which was biopsied.

**Pathology:** Histologically the tumour showed solid nests of basaloid cell cells mixed with some areas with bilayered glandular and cribriform structures. The basaloid component showed hyperchromatic nuclei, prominent nucleoli, brisk mitotic activity and focal evidence of keratinization. Severe dysplasia was present in the adjacent mucosa. AE1/AE3, CAM5.2, MNF116, CK7, S100, P63, CK5/6, CK14, p16, Caldesmon, P63, BCl2, CD56 and SMA was performed revealing an uneven distribution of epithelial and myoepithelial markers. Neuroendocrine and lymphoid markers were uniformly negative. p16 stained all the tumour cells with both nuclear and cytoplasmic staining.

**Discussion:** In our case the pre-operative diagnosis was not possible because of extensive fibrosis on a biopsy sample. The imaging however showed a mass with irregular outline, which was not consistent with pleomorphic adenoma and the diagnosis required review from a pathologist with an interest in salivary gland pathology.

**Conclusion:** Pathologists need to be aware of sclerosing mucoepidermoid carcinoma to avoid misdiagnosing it as a benign lesion.
P69

Argininosuccinate Synthetase (ASS1) Expression in Pancreatic Ductal Adenocarcinoma and Response to Arginine Deprivation

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Some cancers lose expression of ASS1, the penultimate enzyme in arginine synthesis that converts aspartate and citrulline into argininosuccinate, resulting in dependence on exogenous arginine. Selective targeting of these cancers by arginine deprivation therapy (ADT) is currently in clinical trials, however biomarker development is needed to guide therapy more precisely. We aimed to investigate expression of ASS1 in human and murine pancreatic ductal adenocarcinoma (PDAC) cell lines and determine how this correlates to arginine dependence. Using PDAC cell lines from a genetically engineered mouse model and human PDAC cell lines, MIA PaCa2, BxPC3, PANC-1, ASS1 expression was assessed by immunoblotting. Cells were grown in arginine-free media supplemented with citrulline, arginine and argininosuccinate accordingly, and proliferation assays performed. Differential ASS1 expression was seen in the murine PDAC cell lines; 6 out of 10 showed high expression. All murine cell lines exhibited dependence on exogenous arginine for normal proliferation, regardless of ASS1 status, and despite citrulline availability. Argininosuccinate supplementation rescued proliferation in all murine lines, indicating that the defect in ASS1-positive cells was not lack of argininosuccinate lyase activity, the final step in arginine synthesis. The human PDAC cell lines all expressed ASS1. As expected, BxPC3 was resistant to arginine deprivation and maintained normal proliferation in the presence of citrulline, suggesting functional ASS1. MIA PaCa2 and PANC-1 retained dependence on exogenous arginine for proliferation, showing a similar phenotype to the mouse cells. This is a surprising finding of sensitivity to arginine deprivation despite ASS1 expression in murine PDAC cells, and in a selection of human PDAC cell lines. We will establish whether ASS1 is mutated. By determining the basis of this metabolic defect, we may identify patients with ASS1-expressing pancreatic tumours as candidates for ADT.

P70

Histomorphological Changes and DNA Repair Protein Expression in Uveal Melanoma (UM) Following Proton Beam Therapy (PBR)

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Study aims were to examine histomorphology of enucleated eyes with UM post-PBR, and to investigate expression of ATM and XRCC1, which target DNA repair proteins involved in single strand break and complex DNA damage repair processes following irradiation.

Methods: Included were forty clinically- and genetically well-phenotyped UM treated with PBR between Jan 2005-Dec 2017. H&E sections of the enucleated eyes were examined for irradiation-induced morphological changes. 37 UM were also immunohistochemically stained and evaluated for ATM and XRCC1.

Results: The UM were morphologically classified as: 14 epithelioid, 8 spindle and 18 as mixed cell types. Diffuse tumour necrosis was seen in 5 UM (12.5%); bizarre mitotic figures in 3 (7.5%); tumour cell-ballooning in 23 (57.5%) and tumour cell ‘mummification’ in 25 (62.5%) cases. Thickening and hyalinization of intratumoral capillaries was observed in 20 (50%) and 28 (70%) UM, respectively. Prominent tumour-infiltrating lymphocytes and -macrophages were noted in 13 (32.5%) UM. Degenerative scleral changes were seen in 27 UM (73.5%), and 5 cases demonstrated intrascleral tumour cell infiltration (12.5%). 36/37 UM (97.3%) showed clear nuclear expression for XRCC1: in 26 (70.3%) a diffuse pattern was observed, whilst in 3 (8.1%) cases, it was focal only. 30/37 stained cases (81.1%) showed nuclear positivity for ATM: 6 cases (16.2%) with a diffuse pattern, and 8 (21.6%) with focal staining only.

Conclusion: UM post-PBR demonstrate typical degenerative and inflammatory changes. High expression of DNA repair proteins, XRCC1 and ATM, are present and may explain tumour radioresistance in these cases.

P71

This abstract has been withdrawn

P72

Use of the Chick Embryo Chorioallantoic Membrane (CAM) Model in Uveal Melanoma

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Uveal melanoma (UM) is the most common intraocular cancer in adults, with a mortality rate of ~50% due to metastatic disease. Despite the high success rates of primary tumour treatment, there is no effective adjuvant therapy in place for metastatic UM (mUM). We here use the chick embryo as a model to explore mUM. The chick embryo model (CEM) is an established model in developmental biology and in recent years has been used to study cancer due to the highly vascularised chorioallantoic membrane (CAM), permitting a broad spectrum of applications. The CEM is economical, accessible and effective, and as it shares significant gene conservation and early developmental homology with humans, it is an ideal model to study both primary and mUM. This study examined the ability of the MM66 UM cell line, which is derived from a metastatic liver lesion, to grow as xenografts in the CEM. GFP-labelled MM66 cells were grafted onto the CAM, and then examined for in situ nodule formation and metastasis using fluorescence microscopy. We observed a tumour nodule forming efficiency of 40% at embryonic day 14. The UM nodules and chick embryo tissues showing fluorescent signal, such as the liver, were dissected and processed for histological analysis by MelanA immunohistochemistry, a melanocytic marker. MelanA positive cells were observed in the UM nodules formed on the CAM, suggesting that the CAM is able to support MM66 cell growth. The confirmation of this models use for MM66 UM contributes to the diversity of UM cell lines available for future research into novel drug targets and treatments that could be used to improve mUM patient outcomes.

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P73
The Role of CD166/ALCAM in Uveal Melanoma Metastasis

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Purpose of the study: Uveal melanoma (UM), the most common intraocular tumour in adults is characterized by the malignant transformation of melanocytes in the uvea. CD166 is a cell adhesion molecule that is associated with aggressive tumour phenotypes in several cancers including glioblastoma, colon and cutaneous melanoma. It is also implicated as a marker of tumour initiating or cancer stem cells. In this study we examined the expression of CD166 in UM cell lines, normal choroidal melanocytes (NCM) and primary UM cells isolated from human tissue, grown in short term culture (STC).

Methods: Eight UM cell lines (derived from primary and metastatic tumours), NCM from four donors and STCs from ten UM patients were examined by flow cytometry for CD166 expression. Anoikis resistance, invasion and tumour transendothelial migration were examined using the UM cell lines.

Results: The metastatic cell lines upregulated their expression of CD166 in cells surviving anoikis (OMM1: 87.7%-95.1%), (OMM2.3: 3.7%-6.8%), (OMM2.5: 17.6%-26.4%). Expression of CD166 in MP41, a primary cell line with loss in chromosome 3 and gain in 8q was also increased (3.0%-18.2%) after anoikis resistance. CD166 expression was higher in the STCs than the NCM (mean expression 78.3% vs 18.8%). Cell lines expressing higher CD166 had a higher migration rate in the invasion assay. The CD166+ UM cells also crossed the endothelial barrier faster than the CD166− population.

Conclusion: We have shown that ALCAM promotes UM cell survival from anoikis induced death, enhances their migration and intravasation in vitro. TCGA analysis shows that higher ALCAM gene expression results in shorter overall survival for UM patients. Further functional studies including use of in vivo models are necessary to determine if these results can be recapitulated.

P74
A Rare Case of a Spinal Intradural Fibrolipomatous Hamartoma and Systematic Review of the Literature

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Introduction: A neural fibrolipoma/fibrolipomatous hamartoma is a rare benign lesion. It usually affects the appendicular nerves and intradural cases are exceptionally rare. Case report: We report the third case of a spinal Intradural Fibrolipomatous hamartoma and systematic review of the literature. Discussion: This is a benign entity, though it can lead to pressure on the adjacent neural structures. In the spinal cord, complete excision is difficult because the lesion is infiltrative. Although extremely rare, this lesion should be considered in the differential diagnosis of fat containing intradural extraaxial lesions of the spinal cord. We systematically review the previous cases of spinal neural fibrolipomas and draw notable similarities.

P75
Authors do not wish this abstract to be published

P76
The Genetic Profiling of adamantinoma

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Introduction: Adamantinoma is a rare primary bone tumour characterised by epithelial differentiation. There is evidence that in most instances it arises from osteofibrous dysplasia (OFD), a developmental bone abnormality also containing epithelial cells, but compared to adamantinoma these are extremely sparse. OFD can regress, but may progress to adamantinoma as demonstrated by greater density of epithelial cells. High grade transformation and dedifferentiation can occur.

Purpose of the study: To examine comprehensively the genomic landscape of adamantinoma and compare it with other primary bone tumours.

Methods: Whole genome sequencing was performed on fresh frozen tissue from 11 tumours with matched normal tissue. The diagnoses were confirmed as adamantinoma (classical, dedifferentiated or OFD-like) (n=7) and OFD (n=4) by. Sequencing was performed on the Illumina HiSeq 2500 platform with average tumour coverage of at least 40x and of normal DNA at least 30x. Somatic variant calling was undertaken using the Sanger Cancer genome project pipeline and copy number variation was analysed using ASCAT.

Summary of results: Non-synonymous mutations (n=72) were detected in conventional (n=3) and dedifferentiated adamantinoma (n=2). Somatic mutational burden (average 0.2 mutations/Mb) increased with higher tumour grade and cellularity. Cancer driver genes implicated in sarcoma such as TERT and BCor were mutated, but no recurrent alterations were identified. Somatic copy number variants and rearrangements were identified but no recurrent aberrations were present.

Conclusion: No recurrent genomic alterations were identified in our cohort of OFD and adamantinoma. The low neoplastic cell content present in these tumours may help to explain the low mutational burden. Tumour cell enrichment, single cell analysis and/ or targeted sequencing for genetic regions of interest may identify recurrent driver mutations in this tumour.

This work is supported by The Pathological Society
P77

Recurrent Distal Epithelioid Sarcoma with Potential Periauricular Metastatic Nodule in a Young Adult Female

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Introduction: Epithelioid sarcoma is a rare slow growing aggressive tumour of uncertain histogenesis that preferentially affect young adult males with mean age of 27 years at presentation.

Case presentation: A 19 years old female re-presented to our hospital with a 3 months history of slow growing 3x4cm left posterior auricular nodule. She first presented 3 years earlier with an 8 years history of a circumscribed re-growing painless right hand mass located between the middle and ring fingers which had previously been excised twice at a private hospital without histopathological diagnosis. The mass at presentation measured 8x8 cm in diameter, and was covered by an intact skin with healed surgical scar. A trucut biopsy was diagnosed epithelioid sarcoma based on cytomorphology of malignant epithelioid cells arrayed in nests, vague alveolar pattern with foci of pseudoangiomatous growth. Tumour was CD 34 + focally. She had 4 courses of chemotherapy and tumour enbloc excision with excision of 3rd and 4th hand digit with hand reconstruction. Tissue microscopy showed epithelioid sarcoma with resection margins involvement and was CD34 +, EMA +, S100 -, Desmin -. She did well for a year until development of the posterior auricular nodule which was morphologically similar to the hand mass. Chest x-ray and hand radiograph revealed no lesions. Discussion: Epithelioid sarcoma is a distinct clinico-pathologic tumour fraught with recurrences as seen in this female whose age of occurrence appears to be 9 years anecdotally. ES may be misdiagnosed due to nonspecific clinical symptoms, radiological and pathological findings. Distant metastasis often involve lymph nodes, lungs, scalp and bone, though posterior auricular location was seen in this case.

Conclusion: Large tumour size, recurrences, inadequate excision, and cutaneous metastasis are bad prognostic factors despite the young age and female sex of our patient.

P78

Myxoinflammatory Fibroblastic Sarcoma: A Rare Sarcoma in a Non Acral Site – Myths Re-Evaluated

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We report a case of a 20mm myxoinflammatory fibroblastic sarcoma (MIFS) which presented as an incidental finding on a knee MRI scan of a 32 year old male. Prior to surgery it was thought to represent a cyst. The laboratory received multiple fragments of tissue measuring 35x25x15mm. Microscopy showed a poorly circumscribed lesion with a predominantly inflammatory infiltrate composed of lymphocytes, plasma cells and neutrophils in loose connective tissue. Myxoid areas with histiocyte like cells, spindle cells in a reticular pattern and large cells with large nuclei and nucleoli and abundant eosinophilic cytoplasm, so called “acrocyte like” cells were present. Immunohistochemistry was non-specific and CD34 showed positive cells. Following diagnosis a wide local excision of the scar down to the deep fascia and a local perforator flap was performed. MIFS was initially described in the late 1990’s as an acral tumour. The WHO classification subsequently removed “acral” in the nomenclature. These are rare tumours. There is no gender preference, peak age of occurrence is in the 4th and 5th decades but 10% occur in patients less than 12 years and older than 75 years. Thirty percent are at non acral sites. Hands and fingers account for almost 50% of cases. Twenty percent occur in the foot, most commonly the dorsum. The trunk and head account for 3%. Almost 75% of cases have a pre-op diagnosis of a benign lesion. Although typically regarded as a low grade malignancy 3% of cases metastasise, usually to local lymph nodes, but lung metastases are also reported. Twenty two percent recur twice at a private hospital without histopathological diagnosis. The mass at presentation measured 8x8 cm in diameter, and was covered by an intact skin with healed surgical scar. A trucut biopsy was diagnosed epithelioid sarcoma based on cytomorphology of malignant epithelioid cells arrayed in nests, vague alveolar pattern with foci of pseudoangiomatous growth. Tumour was CD 34 + focally. She had 4 courses of chemotherapy and tumour enbloc excision with excision of 3rd and 4th hand digit with hand reconstruction. Tissue microscopy showed epithelioid sarcoma with resection margins involvement and was CD34 +, EMA +, S100 -, Desmin -. She did well for a year until development of the posterior auricular nodule which was morphologically similar to the hand mass. Chest x-ray and hand radiograph revealed no lesions. Discussion: Epithelioid sarcoma is a distinct clinico-pathologic tumour fraught with recurrences as seen in this female whose age of occurrence appears to be 9 years anecdotally. ES may be misdiagnosed due to nonspecific clinical symptoms, radiological and pathological findings. Distant metastasis often involve lymph nodes, lungs, scalp and bone, though posterior auricular location was seen in this case.

Conclusion: Large tumour size, recurrences, inadequate excision, and cutaneous metastasis are bad prognostic factors despite the young age and female sex of our patient.

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This abstract has been withdrawn

P80

Sentinel Node Biopsy for Malignant Melanoma: Our Experience Using a Modified EORTC Protocol

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Malignant melanoma is the 6th most common cancer in the UK with aggressive biological behaviour in a significant number of cases. Sentinel lymph node biopsy (SLNB) is a very strong prognostic determinant in melanoma. Our hospital was chosen as the designated hub for melanoma SLNBs for a regional network in 2009. The evidence base for the SLNB EORTC protocol is one of the strongest currently available for Research and Treatment of Cancer (EORTC) based. Alternative protocols are also acceptable outwith EORTC clinical trials provided there is evidence of a detection rate equivalent to that of the EORTC protocol of at least 25%. The EORTC protocol involves a combination of H&Es with multiple levels and immunohistochemistry (6 pairs of sections for H&E and 100 with 8 spares). We finalised a modified version in 2017 after various audits – 5 pairs of sections for H&E and Melan A with an S100 at L2. Present auditing has shown there has been a very significant improvement in the positive detection rates in SLNB to 27%. This is in accordance with the stated desired positive detection rate required to prove equivalence with the full EORTC protocol.
P81
This abstract has been withdrawn

P82
Bilateral Inflammatory Linear Verrucous Epidermal Nevus (B-ILVEN)

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ILVEN usually presents in childhood with unilateral psoriasisiform lesions in a Blaschko-like distribution accompanied by pruritus. The even rarer bilateral presentation may lead to misdiagnosis and prolonged patient morbidity. A 33-year-old woman was referred by surgical colleagues who had excised a lesion from her right shin and were uncertain how to interpret the histology. She complained of intense pruritus within this lesion and similar lesions on both lower legs; present since infancy and recalcitrant to years of topical psoriasis therapies. Lesions were always confined to fixed sites on the lower legs. Examination revealed curvilinear psoriasisiform plaques on both legs; a plaque on the left great toe and recurrent erythema at the excision site. Examination was otherwise normal. Further biopsies were taken from both lower legs. Histology from these demonstrated similar findings: acanthosis and psoriasiform hyperplasia of the epidermis, mild spongiosis, exocytosis and a mild perivascular chronic inflammatory infiltrate. In addition there were mounds of parakeratosis with absent underlying granular layer alternating with mounds of orthokeratosis overlying hypergranulosis. The original histology was reviewed and found to be similar. A diagnosis of bilateral ILVEN was made and she was referred for pulsed dye laser therapy. Bilateral ILVEN is extremely rare and poses a diagnostic challenge; confusion with linear psoriasis, other linear dermatoses, and co-existence with psoriasis may occur. Most ILVEN presentations are apparent by history and clinical features and histology is usually characteristic. Immunohistochemical studies may be of future value in cases of clinical and histological overlap but to date have yielded inconsistent results. Management may be difficult; topical treatments are often ineffective. Lasers, surgical shaving and cryotherapy may be useful for smaller lesions; excision may be curative but results in significant scarring.

P83
A Unique Case of a Composite Cutaneous Mycosis Fungoides and B-CLL 17 Years after Presentation with Cutaneous B-Cell Lymphocytic Lymphoma

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Composite lymphoma is a rare disease defined by the occurrence of two distinct lymphomas within a single tissue at the same time. Composite cutaneous T-cell and B-cell lymphoma is extremely rare. We present a composite lymphoma of mycosis fungoides (MF) and cutaneous small cell B cell lymphocytic lymphoma/leukaemia in the same skin biopsy in a 57-year-old man. Our patient first presented with a scalp nodule in 2001, the histology of which demonstrated a malignant infiltrate of small B lymphocytes. Haematological evaluation showed a mildly elevated B cell lymphocytosis of 3.92 (normal range 1.50-3.50). As a bone marrow evaluation was negative, a diagnosis of a cutaneous small B cell lymphocytic lymphoma (SLL) was made. The patient was treated with three cycles of CHOP and local radiotherapy with a good response. Four years later he developed a clonal B cell proliferation in peripheral blood and a diagnosis of B-CLL leukaemia was made. In 2006, the patient developed generalised plaques which were clinically consistent with, and confirmed on biopsy as, mycosis fungoides. He responded well to PUVA therapy. In 2018, he developed a new large atypical scalp nodule, which showed two distinct lymphomas: a clonal T cell infiltrate indicative of mycosis fungoides and also a separate infiltrate of B-CLL. There are only three other cases in the English literature of composite lymphomas in the skin showing mycosis fungoides and B-CLL in the same skin biopsy. However, this is the first reported case of a patient with cutaneous SLL who subsequently developed CLL leukaemia and then also developed composite MF with B-CLL. Suggested pathogenic theories for the occurrence of composite T-cell and B-cell lymphomas include a common origin of both neoplasms from a stem cell progenitor or genetic events which predispose to malignancy of both B and T cell lineage cells. Other possibilities include the co-incident occurrence of two unrelated neoplasms or immunodeficiency post chemotherapy.

P84
Recurrence Rate Associated with Histological Margins of Cutaneous Squamous Cell Carcinoma

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Introduction: Although there are guidelines for excision margins of Squamous Cell Carcinoma (SCC) there is a paucity of data relating histological margins and recurrence. As a result skin MDTs have no guidance for advice on reducing recurrence after completely but closely excised SCCs. The aim of this study is to analyse any correlation between histological margins and recurrence of completely excised cutaneous SCC at the same site within 5 years.

Methods: Retrospective data was collected for patients with SCCs treated at Queen Victoria Hospital during period of 2014–2018. The following data was analysed: histological margins of first excision, site, size, thickness, level of invasion, grade, stage and host immunosuppression.

Results: 2036 SCC were excised during the study period, with same site recurrence rate of 2.16% (44 cases) after complete excision. Mean age of patients with recurrence was 81, 73% were male, mean lesion size was 21.2 mm (SD 13.56), 70.4% of recurrences were in the head and neck and 84% were “high risk” at first excision. Mean histological margin of the recurrence group was 2.09mm deep and 4.77mm radial, compared to average of 3.9 mm deep and 5.2mm radial in the non-recurrence. 66% of recurrences had deep margin of 2.5 mm or less. Recurrence rate with deep histological margin of 2.5mm or less was 1.42% and with deep histological margin of greater than 2.5mm was 0.74% (p = 0.041). The lymphovascular and perineural invasion of the initial and the recurrent lesions were the same.

Conclusions: A deep histological margin of >2.5 mm is required to achieve a low recurrence rate. Recurrence is highest amongst elderly male with high risk head and neck lesions. This information maybe relevant in MTDS and for long term follow up of SCC patients.
ABSTRACT REVIEWERS

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