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Understanding Disease

Poster Abstracts

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KEY

Ⓟ = Presenter

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P1

An Unusual Presentation of Fatal Pulmonary Embolism

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Venous thromboembolism is a commonly encountered problem, and not an infrequent finding at post mortem. They are classically associated with increased age, obesity, immobility, cancer etc. We present a case report of a 52 year old, previously fit and healthy male, who presented with vague leg pain and a negative ultra sound who subsequently developed progressive severe cardiorespiratory compromise over the follow 4 days. While the initial Doppler ultra sound scan was negative, a CTPA the day prior to death showed multiple pulmonary emboli. His wife requested a hospital post mortem to understand/identify the cause of the pulmonary emboli.

Findings: At post mortem the significant findings were of a 20mm pale polypoid lesion in his lower oesophagus and a pericardial effusion. Histology and cytology was taken and showed disseminated micrometastases from a poorly differentiated oesophageal adenocarcinoma.

Discussion: While malignancy is a recognised risk factor for thromboembolic disease the primary lesion in this patient was small and pT1, despite which there was diffuse and disseminated metastatic disease. It is a timely reminder that small, low stage tumours, especially of the upper gastrointestinal tract can still disseminate widely and early. The repercussions of which may become the presenting complaint.

P2

Medical Student's Perceptions of Forensic Pathology

Ⓟ KL Iles

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Forensic pathology is an important sub-specialty of pathology which requires a variety skills that are relevant and transferable to many other areas of medicine. Despite this, it does not feature in the undergraduate curriculum of most medical schools meaning that knowledge specific to forensic medicine such as wound terminology may not be taught. A lack of formal teaching and an ever increasing dramatised presence of the specialty in the media may lead to a misrepresentation of the role of forensic pathologists. As a result this study aimed to examine final year medical student's perceptions of the role of the forensic pathologists and their confidence in knowledge of important aspects of forensic medicine.

An online survey was developed to assess these areas which was distributed to final year medical students at a UK institution via email.

From the respondents, the overall perception of the job role was correct, however there appeared to be some misconceptions regarding the role of a forensic scientist, or crime scene investigator in comparison to a forensic pathologist. The study also highlighted that students did not feel confident in differentiating between wound types using the correct terminology. This is important as injuries are common presentations in many clinical areas, and incorrect terminology may have mediocolegal implications. This study has highlighted the need for clarification of the job role of the forensic pathologist.

There is a greater need for forensic pathology in the undergraduate curriculum, which should focus on description and terminology of wounds and injuries.

P3

Changes in Diagnostic Practice of Metastatic Lung Cancer over a 12-Year Period in a UK Tertiary Referral Centre

Ⓟ YZ Zhang; F Mauri; A Sandison; N Gupta

Imperial College Healthcare NHS Trust, London, UK

Purpose of the study: Over the last decade there has been a rapid evolution of tumour immunoprofiling and molecular analysis, now becoming routine practice in the histopathological diagnosis of metastatic lung cancer. This coincides with the advent of targeted therapy and their pivotal role in its management. Our study aim was to investigate the influence on local practice of histopathological diagnosis of metastatic lung cancer over the last 12 years.

Methods: Retrospective observational study. 338 patients between 2004 and 2016 were included. Exclusion criterion was metastatic disease found at the time of resection. Demographic information, histopathological diagnosis and results of molecular analysis (EGFR, ALK, BRAF, KRAS, NRAS, PIK3CA) were retrieved from our electronic database.

Summary of results: Median age was 65 years, with male preponderance (58%). Cancer of Unknown Primary (CUP) represented 17% of all cases. There is a 46% increase in annual case load comparing pre- and post-2011 periods. Common metastatic sites are lymph nodes, pleura, brain, bone and liver. The majority of cases were adenocarcinoma (239/338, 71%). TTF-1/CK7 was the most commonly used positive marker panel (71%). The sensitivities of TTF-1/CK7/Napsin A were 91.2%/99.1%/74.5% respectively. There has been a steady increase in molecular testing since 2011, initially with EGFR while ALK/BRAF/KRAS/PIK3CA caught up after 2013. Amongst all adenocarcinoma cases, the overall EGFR test rate was 25% and the incidence of EGFR mutation was 15%.

Conclusions: Since 2011 we have witnessed a major increase in case load and the utilisation of molecular analysis as part of the histopathological diagnosis of metastatic lung cancer. As more molecular markers and therapeutic options are being made available, this complex diagnostic paradigm with its logistic and financial consequence will increasingly impact upon the development of an optimal treatment pathway.

P4

Are Levels Really Necessary in Assessment of Endobronchial Ultrasound Guided (EBUS) Transbronchial Nodal Biopsies?

Ⓟ MC O'Riordan; DA Moore; CJ Richards

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Purpose of study: Molecular testing of biopsies showing non-small cell lung carcinoma is increasingly required to inform patient management. As such, small biopsy specimens require careful handling in order to preserve tissue. Currently three levels are carried out as standard on all EBUS biopsy samples received in our laboratory at the initial sectioning stage. This audit was performed to determine whether levels were necessary and to determine whether the additional tissue sections and trimming affected the ability to perform downstream molecular tests.

Method: A SNOMED search was carried out for all EBUS specimens from September 2015-August 2016. 100 cases in which the final diagnosis was malignant were reviewed by a thoracic pathologist, blinded to the original report and to the second and third levels, to determine whether the diagnosis could have been made on the first level. The current referral adequacy rate for EGFR and ALK testing, and the rate of NSCLC-unclassified diagnoses were also examined to provide benchmarks for future review.

Results: Levels were found to helpful in securing a diagnosis of malignancy in less than 10% of the cases reviewed. The NSCLC-unclassified rate was around 12%.

Conclusion: In the majority of cases, a diagnosis of non-small cell lung cancer matching the original report could be made with only the first level available, indicating levels are not necessary in all cases. The current NSCLC-unclassified rate suggests there may be scope to reduce the number of levels at initial section and changes to laboratory practice are therefore being considered.

P5

Non-Small Cell Lung Carcinoma (Not Otherwise Specified) Rates are not Solely Influenced by Pathologists' Decisions on the Use of Immunohistochemistry

Ⓟ GB Chapman[1]; DA Dorward[2]; CD Lucas[2]; WA Wallace[2]

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With increasing focus on the molecular classification of non-small cell lung cancers (NSCLC) correct application of appropriate diagnostic tools is paramount. The majority of small biopsy and cytology specimens are subtyped using morphology and/or immunohistochemistry (IHC). Despite this approach there remains a small proportion in which further classification is not possible due to a 'null' IHC phenotype or where there is insufficient material for IHC. The category 'not-otherwise specified' (NSCLC-NOS) therefore remains valid. National standards state that NOS rates should be <10% of all NSCLC. The recent 'LungPath' project identified inter-departmental differences in NOS rates with variable use of IHC but did not define the reasons for this variation. This study evaluated whether, in a regional centre, designation of a case as 'NOS' was the result of failure by the pathologist to request IHC, non-informative IHC or whether insufficient material prevented IHC being performed.

All cases of NSCLC-NOS diagnosed in 2012-14 were identified using the South East Scotland Cancer Network database. These were reviewed to identify specimen type(s), use of IHC and, if not used, the reason. In total, 121 cases of NSCLC-NOS were identified (5.3% of all NSCLC cases). IHC was performed in 76% of cases. The 24% with no IHC were all cytology samples. These had either insufficient material for a cell block or the prepared block was acellular or contained no malignant cells. No cases were identified where suitable material was available but IHC was not performed.

This audit shows IHC rates cannot be taken in isolation as a marker of a pathology department's performance. Guidelines and proposed mandatory audits should acknowledge that variation in IHC rates is likely, particularly when some centres have greater numbers of cytology samples for primary diagnosis. Audits are essential to improve performance but recognition of factors beyond the pathologist's control is also necessary.

P6

Histological Markers Associated with Radiosensitivity in Non-Small Cell Lung Cancer

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Lung cancer is the main cause of cancer mortality in the United Kingdom. Over 85% of these lesions are categorized as non-small cell lung cancer (NSCLC), which includes adenocarcinoma, squamous cell carcinoma and large-cell carcinoma. Patients with lung cancer receive different treatments depending on their detailed clinical-pathological context. However, over 50% of patients are treated with radiotherapy, which is of varying efficacy. Rather surprisingly, no biomarkers are currently used to predict tumour response and to aid with radiotherapy dosing or regimen.

The aim of this study is to identify histopathological features which predict tumour radiosensitivity in patients with NSCLC. We have identified a set of 129 NSCLC cases for which pre-treatment archival tissue is available, there is a history of radical radiotherapy, and CT imaging follow-up from the period 2009 to 2014. Digital images of archival diagnostic tissue sections were examined to derive morphological measures with the potential to predict radiosensitivity. Quantitative radiological measures of response up to 24 months after radiotherapy were derived by specialist radiological examination of imaging. All of these data are tabulated in order to identify associations between the changes in tumour size and morphological features.

Although the cohort of patients with complete data is at an early stage (n=37), significant associations are emerging. For example, there is a significant correlation between the reduction of the tumour size after the radiotherapy and the presence of atypical mitoses (e.g. lag chromosomes, bridge chromosomes, catastrophic mitoses) (p=0.03). In conclusion, the presence of atypical mitoses such might be a useful histological marker to predict the radiosensitivity in NSCLC. Other emerging markers and a regression model of radiosensitivity will be discussed.

This research was supported by a Path Soc grant

P7

First Case of Death from Cardiac Rupture in a Patient with Methyl Malonic Acidemia

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Introduction: Methyl malonic acidaemia (MMA) is an autosomal recessive metabolic disorder, leading to accumulation of amino acid metabolites such as methyl malonic acid in blood and urine. Complete enzyme deficiency progresses to death within days after birth if not treated. Late onset disease may affect different organ systems.

Materials and methods: A 35-year-old Caucasian female patient was diagnosed with non-cobalamin responsive Methyl malonic aciduria (MMA) (Mut0) nine days after birth and the treatment has begun soon after the diagnosis. However, she has had learning disabilities, feeding difficulties, optic nerve atrophy and renal failure. She suddenly collapsed at home and died. Post mortem examination was performed.

Results: The predominant finding upon autopsy was haemopericardium, composed of about 300ml of blood. Leading to that there was a rupture, on the posterior wall of the ascending aorta, just above the aortic valve.

Conclusion: To our knowledge this is the first case of aortic rupture observed in a patient with MMA. Whether this was a co-incidental finding or truly associated with the metabolic condition is yet to be determined.

P8

An Audit on the Use of Immuno-Histochemistry for the Diagnosis and Classification of Non-Small Cell Lung Carcinoma

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Immunohistochemistry (IHC) is only required for classification of non-small cell lung cancer (NSCLC) into adenocarcinoma or squamous cell carcinoma if there is no or unclear morphological evidence of either, or if there is a question regarding the primary site.

The Royal College of Pathologists dataset guidance (2016) suggests that a morphological diagnosis should be reached in 50-60% of cases. The Dataset also states that immunohistochemistry should consist of a maximum panel of four stains (CK7, TTF-1, CK5/6 and p63).

This audit assessed the use of immunohistochemistry in a combined total of 69 lung and bronchial biopsies, showing non small cell lung cancer, received between January and December 2015 at a District General Hospital. Results showed a total of 32 adenocarcinomas and 30 squamous cell carcinomas of which there were 14 (44%) and 9 (30%) morphologically diagnosed cases respectively.

Immunohistochemistry was performed on the remaining cases but was incorrectly used on 5 morphologically described adenocarcinomas and 2 morphologically described squamous cell carcinomas. In addition, only 15 of the cases correctly used the staining panel suggested by the Royal College of Pathologists dataset. The others utilised additional non-necessary cytokeratin markers e.g. CK8/18, whilst others used markers to assist in determining primary site origin.

In conclusion, these findings suggest that the use of immunohistochemistry needs to be re-assessed in the department to prevent the routine excess staining of biopsy specimens, the over-use of laboratory resources and the unnecessary loss of tissue, which is crucial for molecular testing.

P9

Pleuroparenchymal Fibroelastosis: A Review of Histopathological Features

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Purpose of the study: Pleuroparenchymal Fibroelastosis (PPFE) is a rare disease recognised in the revised 2013 ATS/ERS classification of idiopathic interstitial pneumonias, with major histopathological features being predominantly subpleural intra-alveolar fibrosis and elastosis (IAFE), and visceral pleural fibrosis. This recognition has led to a significant increase in cases presenting at our institution and we have therefore reviewed this cohort to assess proposed histological criteria (IAFE and visceral pleural fibrosis), as well the incidence of coexistent individual histological features and patterns.
Methods: 41 cases of PPFE were reviewed, 12 cases having been previously reported. Each case was scored semi-quantitatively as (mild (% cases)/moderate (% cases)/ severe (% cases)) for IAFE, visceral pleural fibrosis, vascular changes, inflammation and fibroblastic proliferation, and present/absent for granulomas. Coexistent histological patterns were also documented.
Summary of results: All cases showed IAFE (17%/27%/56%), associated inflammation (14%/54%/32%) and fibroblastic proliferation (41%/39%/20%) with 93% showing fibro-intimal vascular thickening (17%/49%/27%) and 65% showing visceral pleural fibrosis (27%/19%/19%). Granulomas were seen in 29% of cases, with a histological pattern of hypersensitivity pneumonitis seen in 15% and a pattern of usual interstitial pneumonia in 10%. One aspergilloma and one case of coexistent Wegener's granulomatosis were also seen.
Conclusions: Whilst IAFE, associated inflammation and fibroblastic proliferation were always present in PPFE, visceral pleural fibrosis was less frequently seen. Vascular changes are prominent and there is wide variation in the extent of all of these features, which may reflect potential aetiologies and could provide prognostic data. Coexistent histologic patterns are also not uncommon.

P10

Lymphangioleiomyomatosis: A Case Report

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Introduction: Lymphangioleiomyomatosis (LAM) is a rare disorder, which can affect multiple organ systems, that occurs mostly in young women. Cases of LAM can occur sporadically or in association with tuber-ous sclerosis. Due to the significant morbidity associated with LAM an early, accurate diagnosis is required to ensure appropriate treatment can be initiated.
Clinical Report: A 36 year old lady was referred to tertiary care for treatment of a persistent spontaneous pneumo-thorax. She had no significant past medical history. The pre-operative CT scan demonstrated mul-tiple bilateral cysts. She underwent VATS procedure and talc pleurodesis, at which time tissue was taken for histological assessment.
Histology and Immunohistochemistry: The H&E sections demonstrated the presence of multiple cysts of varying sizes, some of which were lined by proliferation of spindle shaped myoid cells. Immunohistochemistry demonstrated immunoreactivity for SMA and HMB-45 and patchy staining for ER.
Treatment and Follow Up: Post operatively she had serial chest radiographs which demonstrated resolution of the pneumo-thorax. She was discharged with a follow up appointment.
Discussion: Histological characteristics of LAM have been reported as cysts and a multifocal nodular prolifera-tion of immature smooth muscle and perivascular epithelioid cells. Immunohistochemistry can be used as an adjunct and shows immunoreactivity for SMA, desmin and HMB-45. LAM presents normally with breathlessness, repeated pneumothoraces, chylorus effusions and pulmonary hem-orrhage. Significant morbidity and mortality has been associated with LAM, the median time to MRC grade 3 dyspnoea has been reported as 9.3 years. Various treatments are used in the UK for LAM including mTOR inhibitors and transplantation. Therefore, to ensure accurate monitoring and treatment, there should be dissemination of confirmed cases to allow for greater knowledge of this disorder.

P11

Formin-Like Protein 1: A New Drug Target in Breast Cancer

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Introduction: Formin-like protein 1 (FMNL1) is a key driver of the actin reorganisation underpinning cell motility and invasiveness, and thus metastasis. While normally expressed in leukocytes, neo-expression of FMNL1 has recently been detected in solid tumours, including a particularly aggressive form of breast cancer.
One in eight British women will be diagnosed with breast cancer during their lifetime; this disease touches almost every family in the UK. 6,500 of the women diagnosed each year will not survive five years. Preventative measures, early diagnosis, and more effective therapy are needed. Here, FMNL1 was investigated as a possible target for the latter.
Methods: FMNL1 expression in a breast adenocarcinoma cell line, as well as its knockdown using siRNA, was confirmed by western blot. MTS proliferation, wound healing and Boyden chamber membrane invasion assays were performed. The effects of knockdown on cell shape, size and motility patterns were also analysed.
*Results*Knockdowns showed significantly lower proliferation (p=0.025*) and wound healing (p=0.044*). Boyden chamber assays showed a large but statistically unconfirmed difference in membrane invasion (control:knockdown - 1:0.55, 1:0.88, 1:0.61; p=0.114).
Conclusions: Wound healing and MTS results indicate that FMNL1 knockdown reduced two-dimensional motility and proliferation, and thus invasiveness. A reduction in three-dimensional invasiveness was grossly evident in Boyden chamber assays, but further repeats are needed to confirm this.
FMNL1 represents a novel chemotherapeutic target in a subset of solid tumours. In vitro and animal model studies of small-molecule inhibitors of formin-mediated actin assembly are needed to validate the viability of this target further.
Acknowledgements: Thanks to the Wellcome Trust and Academy of Medical Sciences' INSPIRE fund, as well as the Rothley Trust, for funding this research.

P12

Digistain: A Novel Biomarker Imaging Platform for Grading DCIS Cases Using Routinely Processed Paraffin Sections

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Introduction: "Digistain" is a new and validated imaging technology that enables the quantification of a newly conceived biomarker that is present in routinely processed, and unstained FFPE sections. By using a unique optical signature to analyse the chemical make-up of the biopsy quantitatively, the technique circumvents the subjectivity inherent in grading. Within minutes of loading a slide it yields a highly reproducible and user independent numerical score reflecting the Nuclear: Cytoplasmic ratio. We term this the Digistain Index (DI).
Method: In a double-blinded study, 29 breast DCIS biopsies were reviewed and graded by an experienced breast pathologist. A new section was cut from each block, left unstained and loaded into the Digistain instrument. A region of interest (ROI) defined by the pathologist was analysed to generate a DI for each case.
Results: A positive correlation is seen between DI score and histological grade (as assessed by the pathologist) with P=0.04, thus validating this index as a viable indicator of histological grade.
Conclusion: We believe the new Digistain approach provides for the first time, a cost effective, reproducible and quantitative measure of breast DCIS grade. This technique can be further developed to deliver an effective assessment of prognosis and recurrence risk that reaches beyond traditional qualitative measures based on H & E staining.

P13

Concurrent Giant Tumoral Pseudoangiomatous Stromal Hyperplasia Necessitating Bilateral Mastectomy

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Background: Pseudoangiomatous stromal hyperplasia (PASH) is an uncommon benign mesenchymal tumour of the breast and majority occur as diffuse lesions. Diagnosis is often incidental or made in a background of other breast pathology. Bilaterality with multiple tumoral masses in giant breasts is a rarity.
Case presentation: We report a 34years old non lactating female with 2 years history of progressive painless bilateral enlargement of the breasts, back pain and dragging sensation. A year prior to presentation, she had excisional biopsies from both breasts at a peripheral hospital for possible fibroadenoma though no histolopathologic diagnosis was made. Accelerated enlargement was noticed post-surgery with pressure ulcers on both posterior lateral breast surfaces and bilateral peau d'orange. No other palpable masses or lymph nodes. A clinical assessment of bilateral benign mammary hypertrophy, gigantomasia was made. She opted for bilateral mastectomy. Grossly, the right and left breasts weighed 10kg and 9kg respectively, with numerous discreet grey white nodules and gelatinous areas on the cut surfaces. H&E stained tissue microscopy revealed numerous anastomosing slit pseudoglandular spaces lined by spindle cells and separated by thick hyalinised collagen bundles. The spindle cells showed positive immunohistochemical reactivity for CD34 and Vimentin and were non-reactive for S100.
Discussion: Diffuse multiple lesions with incomplete excision are associated with rapid growth and giant PASH as seen in this case may require mastectomy despite its benign nature.

P14

Lympho-Vascular Invasion (LVI) Supervised Transcriptomic Study Disclosed Clusters of Genes with Significant Prognostic Importance in Invasive Breast Carcinoma

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Introduction: Defining the particular molecular mechanism of LVI in BC is challenging. In this study, we have inspected the transcriptomic data of differentially expressed genes along with their corresponding gene copy number alterations (CNA) in METABRIC breast cancer (BC) cohort.
Methods: Precisely defined subcategories of BC cases with definite (LVI+/-) status were derived from METABRIC BC cohort (n=1980) using morphological assessment and Immunohistochemistry, (n=172). Profiles of mRNA expression and CNA for each probe were generated by utilising Illumina Bead-Array microarray technology. Statistical analysis of gene expression data was performed using Linear Model for Microarray (LIMMA) software package, and SPSS for descriptive and bivariate statistics. Optimisation of Immunohistochemistry (IHC) protocol for selected targets is currently underway.
Results: The total valid probes with mRNA and CNA data was (n= 24,368). Probes with perfect matching sequence to reverse strand, statistically significant with LVI+/-, positive Log-Fc and average expression values were exclusively selected, (n=273). Then, the probes were divided into two lists according to LVI status (upregulated when LVI+, n= 20) and (upregulated when LVI-, n= 22). Promising results were initiated by the upregulated *SEC14L1*, which demonstrates positive association with LVI+ (p-value $\leq$ 0.004), CN gains (p-value $\leq$ 0.000), lymph node stage (p-value $\leq$ 0.000), tumour size (p-value $\leq$ 0.002), tumour grade (p-value $\leq$ 0.000), and BC-specific survival (p-value $\leq$ 0.000).
Conclusions: The results obtained from this study encourage the concept of LVI is driven by several genes and redundant pathways. Further integrated functional studies are essential to decipher the molecular mechanisms of LVI.
AM supported by NIHR and grant from the Academy of Medical Sciences.

P15

Zinc Finger Protein 22: a Potential Metastatic Progression Biomarker in Invasive Breast Cancer

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Purpose of the study: Metastatic progression in breast cancer (BC) occurs through the integration of multiple molecular factors/pathways. Moreover, biomarkers associated with adverse clinical outcome in breast cancer, in particular development of metastatic disease, are diversely expressed in different BC molecular subtypes. This study aims at mining for novel biomarkers associated with distant recurrence (DR) in early invasive BC.
Method: Supervised artificial neuronal network (ANN) analysis of gene expression data from 128 frozen BC samples was analysed to identify differentially expressed genes/transcripts with respect to DR. Based on selection error and significant association with DR, ZNF22 gene transcript was one of the top differentially expressed genes. ZNF22 protein expression was assessed in a large series of invasive BC (n =1377) with long-term clinical follow-up using tissue microarray and immunohistochemistry (IHC).
Summary of results: Over-expression of ZNF22 as assessed by IHC was associated with features of aggressive behaviour including higher tumour grade, advanced nodal stage, larger tumour size and definite lymphovascular invasion. Over-expression was significantly associated with shorter BC-specific survival (log rank, LR = 11.450, p = 0.001), and metastasis-free survival (LR = 11.198, p = 0.001).
Conclusions: This observational study demonstrates ZNF22 as a novel marker associated with BC progression and poor patients' outcome. Functional experiments are warranted to reveal mechanistic insights pertaining to the specific roles played by ZNF22 in BC progression.

P16

Challenging Routine Assessment of Progesterone Receptor Status in Breast Cancer

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Purpose of the study: The role of routine assessment of Progesterone Receptor status in breast cancer remains controversial with NICE guidance discouraging it and The Royal College of Pathologists defining it as optional.
The aim of this study is to quantify the percentages of different ER/PR receptor status combinations, in particular ER-/PR+, and to assess if any clinical decisions to start adjuvant therapies were made on PR receptor status alone.
Methods: A retrospective case study evaluating the ER/PR receptor statuses of all primary breast cancer biopsies between 2010 and 2011 at Kettering General Hospital, as well as assessing the MDT notes of any cancer identified as ER-/PR+ to see if any decision to start adjuvant therapy was made.
Results: 450 cases were identified and, similarly to national audit data, 71.11% of primary breast cancers were ER+/PR+, 13.33% were ER+/PR-, 14.89% were ER-/PR- and 0.67% were ER-/PR+. MDT case notes revealed that the ER-/PR+ cancers were treated in the same way as ER-/PR- cancers and adjuvant therapies were not commenced.
Conclusions: These results show that Progesterone Receptor status played no role in MDT decision-making with regards to the commencement of adjuvant breast cancer therapies. Given the time and monetary costs, it was recommended that routine PR receptor testing be discontinued. It was noted that PR receptor status might play a role in determining cancer recurrence risk and response to adjuvant therapies. As such, it is highlighted that blocks are still available for PR receptor testing at a later date, should a clinician feel it necessary. Following presentation of these results and recommendations, routine PR receptor testing has been discontinued at Kettering General Hospital with a predicted saving of £5327.96 per year.

P17

Breast Implant Associated Anaplastic Large Cell Lymphoma: A Distinct Clinico-Pathological Entity

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Purpose of the study: Primary breast anaplastic large cell lymphoma (ALCL) is rare but is being more commonly seen in patients with breast implants. Fewer than 50 cases of breast implant-associated ALCL have been reported in the English literature. The patients either present with effusion around the implant capsule or rarely with a solid mass.
Methods: A 40 year old lady presented with slight swelling around the capsule of breast implant. There was no significant past medical history and no systemic disease. Histology of the implant showed chronically inflamed fibrous capsule covered on the internal surface by fibrinous exudate. Admixed with the exudate there were a few large pleomorphic lymphoid cells with prominent nuclei. Immunohistochemical stains were applied.
Summary of results: These cells were immunopositive for CD30, CD2, CD4, CD56, EMA with a variable expression of granzyme B. They were immunonegative for ALK-1, CD3, CD5, CD7, CD8, CD20, CD15, CD68, AE1/3, CK7, ER and Melan A. Their proliferation index was around 80%. The morphological and immunohistochemical appearances were consistent with an implant-associated anaplastic large cell lymphoma after the MDT discussion and exclusion of any systemic involvement.
Conclusion: Implant-associated anaplastic large cell lymphoma is rare. Any involvement by systemic or cutaneous lymphoma needs to be excluded before making this diagnosis. The patients presenting with capsular effusion usually have an indolent course and can achieve complete remission after excision of the capsule. Those presenting with a mass may have a worse prognosis and may require chemotherapy / radiotherapy in addition to excision of the capsule.

P18

An Audit on the Reflex Testing of ER/PR on Breast Core Biopsies

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The assessment oestrogen and progesterone receptor (ER/PR) status is essential for all invasive breast carcinomas. ER/PR immunohistochemistry are often requested following a diagnosis of invasive carcinoma and results are often issued as supplementary reports. Cases awaiting ER/PR status are often re-discussed at multi-disciplinary meetings (MDM). A trial of reflex testing for ER/PR at the time of biomedical scientist cut-up on breast core biopsies with a history E4 or 5, M4 or 5 and U4 or 5 breast lesions was introduced. The purpose of this audit is to determine the appropriateness of reflex testing for ER/PR on these cases and to determine the number of cases with benign and malignant diagnoses with a history of M4/5, U4/5, E4/5 lesions, and its impact on turnaround times.
Data was collected retrospectively on all breast core biopsies from Maidstone, Dartford and Medway hospitals with a history of M4/5, U4/5, E4/5 breast lesions from 12th August to 9th September 2016. Data was also collected on whether or not reflex testing of ER/PR was done, the final histological diagnosis and the length of time taken for specimen from laboratory to pathologist.
The total number of cases with M4/5, U4/5, E4/5 lesions was 77. Sixty-one (79%) cases had a diagnosis of B5b (invasive carcinoma), 5 (6%) had B5a (in-situ lesion) and 11(14%) had B2-3 (benign lesions). On average, there was a delay of one day (24 hours) for the specimen to reach the pathologist from the laboratory.
Out of 77 cases, 61 cases with invasive malignancy were justified in having reflex ER/PR testing whilst 11 benign lesions did not require ER/PR. Reflex testing of ER/PR led to reduction in supplementary reports and re-discussion of cases at the MDM. The main limitation of the audit is its small sample size. The recommendation was to continue reflex testing of ER/PR and to re-audit after 3 months to further assess its overall impact on the cost, turnaround time and breast core biopsy reporting.

P19

Bilateral Neurofibromas of the Nipple-Areola Complexes: A Case Report

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Introduction: Neurofibromatosis type 1 is an autosomal dominant condition causing neurofibromas to develop within subcutaneous tissue. Neurofibromas of the breast are rare among patients with neurofibromatosis type 1, occurring predominantly on the nipple-areola complex. Frequency increases with age with a greater susceptibility in women. Very few cases of nipple neurofibromas have been reported. This report describes a rare case of bilateral nipple neurofibromas diagnosed in a patient with known neurofibromatosis type 1.
Case Presentation: A 30 year old woman presented to the breast team with bilateral fleshy skin tags of the nipple-areola complexes on physical examination. She underwent bilateral diagnostic excision of the lesions. Macroscopically both nipple specimens displayed mucoid polypoid lesions with the right specimen measuring 35mm in diameter and left specimen 25mm in diameter. Histological examination showed both specimens to have similar appearances comprising skin with underlying dermal proliferation of spindle shaped cells with wavy nuclei. Large amounts of smooth muscle bundles, confirmed by smooth muscle immunohistochemistry, were admixed among the spindle shaped cells with no atypia or mitoses. Immunohistochemistry confirmed the spindle cell proliferation to be neural in origin (positive for S100 and neurofilament.) Appearance and immunohistochemical profile confirmed the diagnosis of bilateral neurofibromas.
Conclusion: This case demonstrates that although rare, benign neurofibromas of the nipple-areola complex can present in patients with neurofibromatosis type 1. The associated smooth muscle proliferation is unusual and may have been caused by irritation from the long standing neurofibromas. This report considers differential diagnoses of spindle cell proliferation within breast tissue and examines the literature surrounding breast neurofibromas.

P20

Central Pathology Review with Two-Stage Quality Assurance for Pathological Response After Neoadjuvant Chemotherapy in the ARTemis Trial

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Purpose of study: The ARTemis Trial tested standard neoadjuvant chemotherapy (NAC)+/- Bevacizumab (Bev) in the treatment of HER2 negative early breast cancer. We compare data from central pathology review with report-review and also the reporting behaviour of the two central pathologists.
Patients and Methods: 800 women with HER2-negative early invasive breast cancer were recruited. Response to NAC+/- Bev was assessed from local pathology reports for pathological complete response (pCR) in breast and axillary nodes. In-parallel all tissue sections from the original core biopsy and surgical excision were centrally reviewed by one of two trial pathologists blinded to the local pathology reports. Pathologists recorded the response to chemotherapy descriptively and also calculated residual cancer burden (RCB). 10% of cases were double-reported to compare the central pathologists' reporting behaviour.
Results: Full sample retrieval was obtained for 681 of the 781 patients (87%) who underwent surgery within the trial and were evaluable for pCR. 483 (71%) were assessed by JT, and 198 (29%) were assessed by EP. There were no significant differences in the broad reporting metrics of the two pathologists as assessed by a 65-patient crossover study. No difference was demonstrated in the trial outcome as assessed by report-review or central review of pathology. For pCR report-review was as good as central pathology review but for minimal residual disease report-review overestimated the extent of residual disease.
Conclusions: In this trial central pathology review was unnecessary for the determination of pCR but had a role in evaluating low levels of residual disease. Calculation of RCB proved to be a simple and reproducible method of quantifying response to NAC as demonstrated by performance comparison of the two pathologists. Report-review was hampered by lack of a standardised reporting format locally. Addressing this will enable more robust QA of future neoadjuvant clinical trials.

P21

Ultrasound Guided Fine Needle Aspiration of Axillary Lymph Nodes is Safe and Accurate in Axillary Lymph Node Staging of Breast Carcinoma

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Axillary staging in breast carcinoma is relevant to the immediate management of patients and to informing choices of treatment. The ability to do this accurately at the time of diagnosis has clear advantages. Collaboration between pathologists and radiologists using ultrasound guided fine needle aspiration (USGFNA) has potential merit. This retrospective audit looked at the accuracy and clinical value of USGFNA in a one-stop setting in detecting axillary lymph node metastases in breast cancer patients. USGFNA was carried out together by radiologists and pathologists, the former localising nodes, the latter placing the needle, aspirating and reporting in the clinic. USGFNA allows sampling of the subcaspular cortical area with high quality imaging. Usually, 1 Diff-Quik and 1 Papanicolaou stained direct smears were made. We compared USGFNA and subsequent node histology findings to derive sensitivity and specificity for the test in this sample. During 2015, we carried out 142 axillary USGFNAs, 89 in patients with a diagnosis of breast cancer. In 1 case only, sampling was unsatisfactory. 62 patients had later lymph node histology, 27 did not. In biopsied cases sensitivity was 95% and specificity 100% with positive and negative predictive values (PPV/NPV) for USGFNA of 100% and 92%. Of the 27, 19 positive USGFNA patients had no further surgery; 3 of 7 negatives had positive sentinel node biopsy. Overall sensitivity was 92%, specificity 100%, PPV 100% and NPV 84%. We conclude USGFNA is an accurate and safe way to investigate the axillary nodal status of breast cancer patients. Our results compare favourably with the breast cancer staging literature. Immediate assessment allows re-aspiration reducing non diagnostic specimen rates. We ascribe accuracy and value to collaborative working by radiologists and pathologist in USGFNA to provide useful immediate information for patient management.

P22

Mixed Exocrine – Endocrine Carcinoma of Parathyroid Gland: an Index Case Report

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Parathyroid carcinoma is one of the rare causes of primary hyperparathyroidism accounting for less than 1% of all cases. Amphicrine(Mixed endocrine-exocrine) carcinoma is a peculiar tumour in which the cells have both exocrine and neuroendocrine differentiation, with mucus and neuroendocrine granules within the cytoplasm. These tumours display variable quantitative extent of the two components ranging from single scattered neuroendocrine cells to a well-defined neuroendocrine tumour cell population. These are extremely rare tumours, with only scattered case reports in the pancreas, liver and stomach. In Mixed exocrine endocrine carcinomas, usually the most aggressive cell population drives the clinical behaviour. Conversely, adenocarcinoma with neuroendocrine differentiation generally does not show a different clinical outcome, compared to the corresponding conventional forms. These are grey zone tumours and attempts to classify them correctly as well as to define their biologic behaviour and treatment have been the subject of several studies. We present the unique case of an aggressive 'endocrine-exocrine' or 'amphicrine' carcinoma of the parathyroid gland, with associated hypercalcaemia, resulting in acute necrotising pancreatitis. To the best of our knowledge and extensive literature study we have not found parathyroid carcinoma with both exocrine and endocrine components and would like to report this as an index case.

P23

Mutation Signatures Linked to Polymerase Epsilon Defects and APOBEC Cytidine Deaminase Activity Occur Early in a Range of Cancer Types

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Over 30 signatures of aberrant mutation processes have been reported in human cancers. Against this background, over 200 driver genes have been identified across cancers, most of which are specific to three cancer types or fewer. The extent to which variation in mutation signatures can explain variation in driver mutations is unknown. In particular, the timing of mutation signatures is, in many cases, unknown, as is the degree to which these mutation processes promote carcinogenesis by causing key driver mutations. Here, we analysed associations between mutation signature activity and the presence of key driver mutations in 10,188 tumour samples across 22 major cancer types. For each recurrent driver mutation in each cancer type, we tested for a difference in the relative activity of each mutation signature in samples harbouring the recurrent mutation compared to those without the mutation.

We identified 770 associations between mutation signatures and the presence of mutations in specific driver genes, and 68 associations between mutation signatures and the presence of specific amino acid changes within those genes. The results suggest that signature 10, linked to defects in polymerase epsilon, occurs as an early, possibly initiating, event, in colorectal cancer. We also present evidence that signatures 2 and 13, linked to APOBEC, frequently occur as early events in bladder cancer, and that Signature 14, of unknown aetiology, can occur as an early event that causes driver mutations in uterine carcinoma. Multiple positive associations between mutation signature activity and the presence of mutations in the PIK3CA gene suggest that this gene has an unusual capacity to drive clonal expansions when mutated by single-nucleotide alterations. Taken together, these results highlight the interplay of intrinsic and extrinsic factors that lead to key driver mutations and promote carcinogenesis, and suggest mutation signatures that may be of particular clinical relevance.

P24

Optimising Technical Protocols to Detect AID Expression in Archived FFPE Samples of Patients with Follicular Lymphoma

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The B-cell mutator, activation induced cytidine deaminase (AID), induces genomic alterations required for immunoglobulin SHM and CSR in normal B cells. The mutagenic effects of AID may also contribute to genomic instability in B-cell malignancies. Measuring AID in B-cell malignancies is hampered by technical difficulties in obtaining good quantity and quality of RNA and protein in FFPE tissues. The aim of our study was to optimize test conditions for the detection of AID mRNA and protein levels in FFPE lymph nodes from 87 patients with FL.

By comparing different RNA extraction kits, we found that the Qiagen RNeasy FFPE kit produced the highest yield of RNA using the smallest amount of FFPE tissue. RNAs prepared from 60 of the 87 FFPE samples that had RNA integrity number (RIN) ≥2.1, were successfully used to quantify AID expression in RT-qPCR with primers targeting a 90-bp sequence.

We used IHC and a standard scoring system to quantify AID protein expression in FFPE tissue sections from all of the 87 patients. Staining was scored by two independent observers. A significantly positive correlation between the mRNA and protein expression was observed, (r=0.36, p=0.005; Pearson correlation).

To investigate AID subcellular localization, we found that the Hoechst stain with IF produced the best images with confocal microscopy. We used Image J software, and improved the program's ability to make a clear nuclear-cytoplasmic distinction and automatically measure subcellular AID in a large number of cells.

We demonstrated a significantly higher proportion of nuclear AID in 20 patients with high total AID protein by IHC (r=0.54, p=0.013; Pearson correlation).

In summary, we have successfully optimized methods for quantification of AID mRNA, as well as total and nuclear proportion of AID protein in archived FFPE samples from patients with FL. These protocols are applicable to measure expression of other genes from FFPE tissues in any disease.

P25

Adequacy of Endoscopic and Endobronchial Ultrasound-Guided Fine Needle Aspiration Material for Diagnosis, Immunohistochemical and Molecular Testing at a Tertiary Hospital

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Background: Endoscopic ultrasound-guided (EUS) fine needle aspiration (FNA) and endobronchial ultrasound-guided transbronchial (EBUS)-FNA are established minimally invasive techniques to obtain samples for microscopic examination. However, there is considerable variation in the published diagnostic adequacy of EUS-/EBUS-FNA. The aim of this study was to determine the adequacy of EBUS-/EUS-FNA obtained material for diagnosis, immunohistochemistry (IHC) and molecular testing in our centre.
Methods: All patients who underwent EUS- or EBUS-FNA between November 2014 and April 2016 were retrospectively reviewed. Patient demographics, sample source, diagnosis and adequacy of IHC and molecular tests were recorded. In our hospital, there are 3 and 2 operators for EUS- and EBUS-FNAs respectively which are collected without rapid onsite cytopathological evaluation (ROSE) using multiple passes with a 22g needle. Samples are processed according to our previously published protocol aimed at maximising material available for histological examination with all material processed into formalin for cell block preparation and only serial slides 1, 5, and 10 H&E stained for histological assessment.
Results: The median age at procedure was 41 (range 19-89). 47% of patients were female. There were a total of 495 cases amounting to 550 (505 EUS, 45 EBUS) individual samples. 88% of all samples were diagnostically adequate (34% benign, 49% malignant, 18% atypia/suspicious). 97% and 90% of samples were adequate for IHC (178/183 samples) and molecular testing (18/20 samples) respectively.
Conclusion: Our results show that EUS-/EBUS-FNA is a high yield diagnostic technique with material available for IHC/molecular testing in a high proportion of cases. The concentration and development of operator experience/technique in sample acquisition and optimising sample preparation using our protocol confirms our previous recommendation that ROSE is not required to achieve these results.

P26

Significant Variation in the Use of Immunohistochemistry in the Sub-Classification of Non-Small Cell Lung Cancer: A Multi-Centre Service Evaluation

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Aims: The conservation of tissue has become a major priority when subtyping non-small cell lung cancers (NSCLCs) in small lung biopsies to ensure enough tissue is available for clinically significant molecular testing to be performed. Currently, there is a paucity of information regarding the use of IHC in this subtyping process. Therefore, this study aimed to determine whether current use of IHC at multiple centres in the south of England adhered to the current Royal College of Pathologists (RCPath) guidance on this issue.
Methods: Small lung biopsies with a diagnosis of any of the subtypes of NSCLC received between September 2015 and May 2016 were identified, including 30 cases from a central reviewing hospital and 40 cases from 11 external referral hospitals. All of the cases were prospectively reviewed at the central reviewing hospital at the weekly 'pre-MDM' meeting by the four resident Consultant Pathologists to determine whether the use of IHC adhered to RCPath guidance.
Results: The overall proportion of external referral cases with IHC deemed to be non-adherent to RCPath guidance was 52.5% compared to 3.2% at the reviewing centre.
Conclusion: This study highlights a significant lack of adherence to RCPath guidance and a significant variation in practice between multiple centres, when using IHC to sub-classify NSCLCs. As the demand for molecular testing increases, it is likely that a stricter adherence to the RCPath guidance will be required, to prevent tissue run-out, ensuring patients receive optimal molecular work-up for novel targeted therapies.

P27

A Diagnosis of Endometrial Hyperplasia: Where Are We Now?

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Purpose: Endometrial hyperplasia (EH) is an 'umbrella-term' depicting a heterogeneous collection of morphologically abnormal endometrial lesions. When cytological atypia is present there is substantial risk of endometrioid endometrial cancer development. In 2014, the WHO endorsed the Endometrial Intraepithelial Neoplasia (EIN) system of EH classification. Although predominantly a morphological classification, it recognises the importance of unopposed oestrogen stimulation in EH development, distinguishing it from a mutationally activated premalignant clone (EIN) developing in an oestrogen stimulated background. Utilising EIN criteria has been shown to increase diagnostic reproducibility and aligns well with clinical treatments, more so than the preceding WHO94 classification.
Methods: Pathology reports coded as EH using WHO94 diagnostic criteria within NHS Lothian were retrospectively evaluated from 2004-2009. The index diagnostic sections (n=127) underwent blinded expert gynae-path review to: 1) verify WHO94 diagnosis and 2) reclassify using EIN criteria. FFPE sections were obtained from the cohort (LREC:15/ES/0094) and immunohistochemistry performed (PTEN, PAX2, ARID1A, HAND2, p53) for characterisation of molecular features.
Results: Agreement between initial WHO94 diagnosis and expert review WHO94 diagnosis was 52% (n=66). The largest inconsistency was within the WHO94 complex EH category, where only 38.5% (10/26) of review diagnoses agreed with the original. The cohort contained 44 EIN and 83 non-EIN cases. Of note, PTEN-null gland expression was found in 56.8% (25/44) of EIN cases, including 38.6% (17/44) where the entire EIN lesion was PTEN-null.
Conclusions: Our study highlights problematic interobserver differences encountered using WHO94, which remains a familiar system in gynaecological practice, thus creating potential for under/overtreatment of EH. Work continues to fully elucidate the molecular features of EH/EIN and unravel underlying neoplastic mechanisms.

P28

The Accuracy of the Endometrial Cancer Grading between the Pre-operative Endometrial Sampling and the Subsequent Hysterectomy at Edinburgh Pathology Directorate

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Introduction: The grade of the tumour is a well-known prognostic factor for women with endometrial carcinoma that correlates with the final staging and affects the subsequent management.
Objectives: To compare preoperative grading (%) of endometrial cancers with the final grading.
Material and Methods: A total of 156 patients (from 2000–2010) were retrospectively reviewed.
Results: (1) the total accuracy rate is 60.41%. (2) The accuracy rate of grade 1 is 76.74%; 18.60% and 4.65 % were upgraded to grade 2 and 3 respectively. (3) The accuracy rate of grade 2 is 76.74%; 19.60% and 3.92% were downgraded or upgraded to grade 1 and 3 respectively. (4) The accuracy rate of grade 3 is 65.21%; 30.43% and 4.34% were downgraded to grade 2 and 1 respectively. (5) 16 cases were diagnosed as atypical complex hyperplasia, most of these finally upgraded to grade 1 and one case to grade 2. 6). In 11 cases, no grading was given on the preoperative biopsies. (7) 18.80% of cases had lymphovascular space invasion, and 11.80% had cervical stromal involvement and 9.02% had endocervical surface implant.
Conclusion: Our total accuracy rate is quite good. The accuracy rate of grade 1, 2 and 3 were 76.74%, 76.47% and 65.21% respectively.

P29

An Audit of Cervical Loop Histopathology Reporting After Proforma Introduction

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Objectives: This audit's objective was to determine whether large loop excisions of transformation zone (LLETZ) reporting was consistent with the minimum dataset according to the Royal College of Pathologists Guideline "Tissue pathways for gynaecological pathology (Jan 2015)" section 4.16. A proforma for reporting had been introduced to the trust in 2012.
Method: Histological reports of LLETZ procedures over a 12 month period were identified using colposcopy department records. The reports were then compared to the reporting recommendations in the above guidelines using the following headings:
– Macroscopic description of sample
– Reporting of features that impair interpretation
– CIN Grade
– Reporting of invasion
– Margins (if CIN found)
– Provisional FIGO stage (where invasive disease found)
– Presence of pathological features (i.e. inflammation or HPV related changes)
– Crypt involvement
Results: Reporting was variable. Indicators on the proforma such as grade, macroscopic features and margins were reported in 100% of cases. Other indicators such as the presence of pathological features or crypt involvement - which were not on the proforma - were reported inconsistently (28% and 17% respectively).
Conclusion: The use of a proforma introduced extremely high levels of accuracy and consistency with reporting. However any criteria not on the proforma were very poorly reported. Thus proformas must be regularly updated. The proforma will be amended and re-audited.

P30

Borderline Mucinous Tumour of the Ovary with Luteinised 'Leydig Like' Cells in the Stroma; Physiology or Oncology: A Diagnostic Dilemma

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Introduction: Ovarian neoplasms are known to show various histological variants involving the glandular and the stromal components. This is furthermore complicated by the various physiological states like pregnancy and histological changes encountered in them. We present a case which highlights the confusion caused by such physiological states. Stained slides and paraffin blocks of an ovarian mass in a 20 year old woman were referred to us by the surgical oncologist at our centre. Microscopy revealed a borderline mucinous tumour and the stroma showed clusters of round to polygonal cells with voluminous, intensely eosinophilic cytoplasm and bland nuclei, resembling Leydig cells. IHC showed expression of CK7 and CA125 by the epithelial cells. The stromal cells expressed Inhibin. Based on these morphologic and IHC findings, two possibilities were considered. First was a borderline mucinous tumour developing as a heterologous element in a Sertoli-Leydig cell tumour.
The other possibility considered was that of a borderline mucinous tumour with luteinized stromal cells, and accordingly, the surgical oncologist was requested to provide a detailed clinical history. It was then discovered that the review material from the ovarian mass was actually obtained during a Caeserean section performed elsewhere. The patient had also undergone an ovarian cystectomy one year prior to the Caeserean section and underwent another surgery at our centre for recurrence, 3 months after the Caesarean Section. In both the instances, microscopy revealed a borderline mucinous tumour without any luteinized stromal cells, reiterating the fact that the appearance and disappearance of these cells was purely a gestation related phenomenon.
Conclusion: This case illustrates the need to understand the various histological changes during pregnancy and the need to obtain a detailed clinical history in every case, which is imperative in preventing an over-diagnosis of a much more sinister pathology.

P31

Microscopic Heterotopic Extra-Ovarian Sex-Cord Proliferations: Expanding the Histological Spectrum

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Purpose of the Study: Microscopic, heterotopic extra-ovarian sex-cord proliferations have only recently been reported in the literature. We describe the largest series to date, of 30 cases of microscopic, incidentally-detected, heterotopic extra-ovarian sex-cord proliferations.
Methods: Thirty cases of heterotopic, extra-ovarian sex-cord proliferations were identified by gynecological pathologists over an 18-month period between July 2014 and December 2015. All were incidental findings, noted during routine histological examination of gynaecological specimens in women aged between 25 – 79 years who had undergone surgery for a range of benign and malignant gynaecological conditions. The proliferations were identified in standard haematoxylin and eosin (H&E)-stained sections, and the site, size and morphology of the heterotopic extra-ovarian proliferations were recorded. Owing to the small size of the proliferations we succeeded in immunolabelling only 11 cases for the sex cord-stromal markers calretinin, inhibin and CD56. In some cases immunolabelling was also performed for WT1, Ber-Ep4 and epithelial membrane antigen (EMA).
Summary of Results: In 14 patients the foci of proliferation comprised ovarian cortical stroma, in some cases with an ovarian fibroma-like appearance. 10 cases of adenofibroma and cystadenofibroma were also identified, including one Brenner adenofibroma; 2 cases comprised both ovarian cortical stroma and serous cystadenofibroma; 4 cases showed sex cord proliferation resembling microscopic granulosa cell tumours. Immunohistochemistry, where possible, confirmed the sex cord nature of the heterotopic proliferations. The foci of proliferation were <1 – 7 mm, and most were at the fimbrial end of the fallopian tube.
Conclusions: We report the largest series of microscopic, extra-ovarian sex cord-stromal proliferations, and extend the morphological spectrum to include proliferation of ovarian cortical stromal tissue (in some cases resembling ovarian fibroma), adenofibromas and cystadenofibromas, including a benign Brenner adenofibroma. Although such lesions have been postulated to represent non-neoplastic embryological remnants, the predominance of such lesions in the fimbrial end of the fallopian tube raises the possibility that at least some of these lesions result from the incorporation of exposed ovarian parenchymal tissue at the time of ovulation. These proliferations are likely to be encountered with increasing frequency as we sample the adnexa more extensively.

P32

Audit on Adequacy of LLETZ Pathology Reports at Betsi Caldwaladr University Health Board

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Introduction: Histopathology reporting plays a key role in the NHS Cervical Screening Programme (NHSCSP).Biopsy reports are a 'gold standard', against which findings from cytology and colposcopy are correlated. Therefore high standard of pathology reports are essential to link together various components of the programme and in multidisciplinary working. It is also an indicator of quality, and is used to audit and monitor the effectiveness of each part of the service.
Aim of the study: (1) To assess the completeness of histopathology reports of LLETZ samples. (2) To obtain uniformity in reporting practice.
Materials and methods: Pathology reports of LLETZ samples in the Department of Histopathology at Glan Clwyd hospital were reviewed over a period from 1/01/2015 to 30/06/2015.The total number of pathology reports reviewed were180. No slides were reviewed. These reports were compared against a proforma based on standards set by NHSCSP.
Discussion and conclusions: The audit showed that there is a wide variation in reporting patterns of LLETZ pathology reports. A proforma based reporting brings uniformity,adds clarity to report and ensure inclusion of minimum data necessary for clinical management. We recommended that the Pathologists must have access to cytology report while reporting histology to allow correlation between cytology and histology. We also recommended introduction of proforma and distribution to all consultants including Locums and a re-audit against same standards after six months.

P33

Prognostic Significance of Vascular Endothelial Growth Factor-A in Endometrial Cancer

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Purpose: Endometrial cancers (ECs) are typically categorised into Types I and II. The latter commonly share adverse prognostic features and include uterine serous carcinomas, carcinosarcomas and high grade endometrioid carcinomas (Grade 3). This study profiled VEGF-A levels in the tumour microenvironment across Type I and II ECs and assessed its value as a prognostic marker in an independent retrospective cohort.
Methods: VEGF-A was measured in fresh frozen endometrial tissue lysates (n=38 normal, 25 hyperplastic and 97 malignant; 46 Type I/51 Type II) as part of a multiplex immunoassay panel. Expression was evaluated by immunohistochemistry in tissue microarrays from a retrospective cohort with long term follow up (n=419; 252 Type I/167 Type II) using a 1-3 scale to evaluate staining intensity. Tissue VEGF-A levels were compared using Kruskall-Wallis followed by Dunn's post hoc tests and corrected for multiple comparisons using the False Discovery Rate. Prognostic significance was determined using Kapplan-Meier and Cox Proportional Hazards analyses.
Results: VEGF-A levels were significantly increased in both Type I and II ECs compared to normal endometrium (P<0.05). However, VEGF-A levels did not differ significantly between Type I and Type II ECs. Applying a cutoff of ≥2.5 (mean score of valid cores) to all cases, high VEGF-A expression was associated with worse disease free survival (DFS; HR: 1.51, P=0.02) but not overall survival (OS). Subgroup analysis revealed that high VEGF-A associated with both worse OS (HR: 1.80, P=0.028) and DFS (HR:2.15, P=0.002) in Type I ECs but did not associate with outcome in Type II ECs. High VEGF-A remained an independent indicator of worse DFS in Type I ECs (HR: 1.77, P=0.031) after adjusting for age, stage and the presence of lymphovascular invasion.
Conclusions: VEGF-A is an independent prognostic indicator in Type I ECs but has no prognostic significance in their Type II counterparts.

P34

Classification, Immunohistochemical and Molecular Testing of Non-Small Cell Lung Cancer

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Background and Aim: With the increasing use of targeted therapy for lung cancer, the histological subtyping and molecular testing of non-small cell lung cancer (NSCLC) has important clinical implications. The aim of this audit was to reassess our performance in NSCLC classification following our centre's participation in the *LungPath* study.
Methods: All new cases of NSCLC diagnosed at Queen Elizabeth Hospital Birmingham between 2013 and 2015 were identified using our hospital's cancer registry (*n*=566). The frequency of diagnostic subtypes was determined. A subset of cases (*n*=55) was selected for more detailed analysis and included approximately equal numbers of adenocarcinoma, squamous cell carcinoma, adenosquamous carcinoma, neuroendocrine carcinoma and NSCLC-NOS (not otherwise specified).
Results: Over 80% of cases were diagnosed as either adenocarcinoma or squamous cell carcinoma. The diagnostic rate of NSCLC-NOS was low at 4.8%, and represented an improvement of 1.3% compared to our performance in the *LungPath* study.
Of the 55 selected cases, there were 41 biopsies and 14 cytology specimens. Immunohistochemistry (IHC) was performed in 54/55 cases with an average of 8 immunostains per case. TTF-1, CK7, napsin A, CK5/6 and p63 were the most commonly used markers. Additionally, 48/55 cases were tested for EGFR mutations with a success rate of 85% and 33/55 cases were tested for ALK translocations (IHC) with a success rate of 100%. There were 4 EGFR mutations detected; no ALK translocations were detected.
Conclusions: The low rate of NSCLC-NOS diagnosed at our centre is likely due to our regular use of IHC, which is particularly helpful in establishing the diagnosis in cases where the primary site is unknown. Our use of IHC does not appear to affect the success of subsequent molecular testing, probably because our protocol of cutting multiple unstained spare tissue sections for all lung biopsies during initial processing helps to preserve tissue.

P35

The Role of the Pathologist in Malignancy of Unknown Origin: A Multicentre Trainee-Led Service Evaluation

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Purpose of the study: Carcinoma of unknown primary (CUP) and malignancy of unknown origin (MUO) present challenges to pathologists and clinicians alike. We sought to evaluate the journey of these specimens through the histopathology department with a focus on the use of immunohistochemistry.
Methods: This was a retrospective cohort study of patients with suspected CUP/ MUO referred to the relevant multidisciplinary team (MDT) at four tertiary referral departments in 2015-16. Notes, clinic letters, radiology and laboratory results were reviewed.
Summary of results: 131 adult patients (50% male) were referred to the relevant MDT. Of these 124 (95%) were diagnosed with malignancy, either on histology or clinicoradiologically. 78 (60%) of the cases were classifiable as MUO or CUP, and a biopsy was taken in 67 of these cases. Adenocarcinoma accounted for 30 cases. 2 cases were obscured by necrosis. Other morphological findings included epithelioid (n=11) and squamous cell (n=8). The median number of immunohistochemical tests used was 9 (range 0-34) per case. The median number of positives was 3 (range 0-11) per case and the median number of negatives was 5 (range 0-29). Multiple immunohistochemistry rounds were needed in 34 cases. In 2 cases, repeat biopsies were required as there was insufficient tissue for a confident diagnosis.
Conclusions: We have shown the feasibility of a trainee-led collaborative audit project. Patients with CUP or MUO represent a significant volume of work for the pathology laboratory. The diagnostic yield from immunohistochemistry is low overall and there is a risk of patients requiring additional biopsies if tissue is not used prudently.

P36

ASAP and HGPIN: Should We Be Concerned?

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Purpose of the study: Atypical small acinar proliferation (ASAP) and high-grade prostatic intraepithelial neoplasia (HGPIN) are widely considered precancerous.
The objectives of this study are:
Primary: To measure the rate of repeat biopsy and adenocarcinoma in patients with ASAP and HGPIN
Secondary: To identify any clinico-pathologic parameters at diagnosis of ASAP/ HGPIN that are predictive of adenocarcinoma
Methods: Patients with a diagnosis of ASAP/ HGPIN with no previous or concomitant cancer were identified from a prospective pathological database. An electronic clinical database was reviewed retrospectively for data. PSA and/ or MRI changes were monitored. Patients were re-biopsied at the clinician's discretion.
Summary of results: 19 were diagnosed with ASAP and 17 with HGPIN. 7 patients with ASAP (37%) and 6 with HGPIN (35%) underwent re-biopsy. 3 (16%) patients with ASAP and 5 with HGPIN (29%) were diagnosed with adenocarcinoma. The difference in cancer detection rates between ASAP and HGPIN was not significant (p=0.35). 5 patients (14%) in total required definitive therapy for adenocarcinoma. 64% did not undergo repeat biopsy. A range of clinico-pathologic parameters at diagnosis of HGPIN and ASAP, including PSA, prostate volume, PSA density and the number and proportion of positive cores, were compared between the cancer and non-cancer cohorts with none found to be predictive of adenocarcinoma.
Conclusions: The relationship between ASAP/ HGPIN and adenocarcinoma is unclear. By monitoring PSA and/or MRI changes, we managed to spare two-thirds of our patients the morbidity of prostate biopsy. Further evaluation is necessary to characterise the malignant potential of these lesions.

P37

Testicular Metastasis from Bladder Urothelial Carcinoma with Prostatic Invasion

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Secondary testicular tumours are rare, accounting for 2.4% of all testicular tumours in one study. The commonest primary site is the prostate while origin from the bladder is rare. A literature search found 16 cases of metastatic urothelial carcinoma to the testis, 10 of these were from the bladder. We report a case of testicular metastasis of recurrent bladder urothelial carcinoma with prostatic stromal invasion in an 81 year old man presenting with a left testicular swelling. This case illustrates the importance of considering a urothelial origin of a poorly differentiated testicular tumour in a patient with history of urothelial carcinoma.

P38

An Interesting Case of Simultaneous Presentation of Primary Mucoepidermoid Carcinoma of the Prepuce Along with High Grade Transitional Cell Carcinoma of the Bladder

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Mucoepidermoid carcinoma is more common in the salivary glands but primary involvement of the penis is very rare. Only five cases have been reported so far in literature. Hence the prognostic implications of this disease are yet to be explored. Most of the reported cases had extensive disease with either inguinal or pelvic lymphadenopathy and aggressive treatment such as partial or total resection of penis with or without lymphadenectomy was undertaken. Although local recurrence was being reported, the follow up period for the cases were not long enough to predict outcome.

We hereby report an interesting case whereby an eighty-year-old gentleman who initially presented with haematuria underwent a cystoscopy which revealed a large necrotic mass in the bladder. A transurethral resection of the tumour was performed and histology showed a high grade (Grade 3) Transitional cell carcinoma of the bladder. Subsequently, a Computed Tomography was performed which showed T3 disease with involvement of perivesical fat. No pelvic lymphadenopathy was identified and he was therefore treated with palliative radiotherapy. However simultaneously, a papillary lesion was noticed in the prepuce and this was also excised at the same time as that of the transurethral resection of bladder tumour. Histology from this penile lesion interestingly supported features of mucoepidermoid carcinoma with presence of mucin vacuoles that was also confirmed by Alcian blue. Immunohistochemistry performed revealed strong positivity for Epithelial Membrane Antigen and Cytokeratin8/18. Cutaneous metastasis of transitional cell carcinoma to the prepuce was considered but mucoepidermoid carcinoma was favoured due to its distinct morphology, identification of an in situ component in the prepuce and the lack of lymphovascular invasion. The tumour in the prepuce was completely excised in our patient and there had been no evidence of local recurrence yet, though the follow up period is limited.

P39

Granulomatous Prostatitis after BCG Therapy for Urothelial Carcinoma of the Bladder – Histopathological Observations and Clinical Correlation

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Purpose of study: Granulomatous prostatitis after intravesical bacillus Calmette-Guerin (BCG) therapy for early-stage urothelial carcinoma of the bladder is a well-recognised phenomenon and is usually observed in prostate biopsy specimens. What are not as well-documented are the distribution and qualitative information about the histomorphology of BCG granulomas. We aimed to study BCG granulomatous prostatitis and to identify any potential patterns of inflammation with the goal of adding to the wider understanding of prostatic inflammation.

Method: We retrospectively reviewed whole mount blocks of prostates from cystoprostatectomy cases for urothelial carcinoma that had previously been treated with intravesical BCG between 2012 and 2015. Findings documented included inflammation type, granuloma morphology, and their number, zonal distribution and relationship to ducts and glands.

Results: 28 cases were identified for review. 23 (82%) showed granulomatous inflammation, 17 of which included necrotising granulomas. The predominant pattern observed was lymphocytic and granulomatous cuffing around one or more prostatic ducts, leading to a wedge-shaped area of classical BCG-type necrotising granulomatous inflammation. 15 of the 23 cases (65%) showed predominant peripheral zone involvement; the rest showed mixed zonal involvement. No definite correlation between BCG instillation regime and inflammation type could be found.

Conclusion: The pattern and distribution of post-BCG granulomatous prostatitis implies that it probably develops as a result of reflux along prostatic ducts. They are in keeping with the theory that the peripheral zone is more prone to intraprostatic ductal reflux of urine (and therefore potential carcinogens), perhaps because the ducts join at less obtuse angles than those in other zones. Our findings add to the understanding of prostatic inflammation in general and ultimately, perhaps, some processes that might be involved in prostatic carcinogenesis.

P40

An Audit on the Lengths of Prostate Core Biopsies Performed at a Tertiary Hospital, and the Impact on Cancer Diagnosis

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Purpose of the study: Previous studies have shown that longer prostate core biopsies have an improved diagnostic rate of cancer, with an optimal mean length of >12 – 13mm. The aim of the audit was to analyse the lengths of prostate cores received. We also compared the lengths of transrectal ultrasound (TRUS) guided biopsies with transperineal template (TPT) biopsies.

Methods: All prostate core biopses performed over a one year period (September 2014 – August 2015) were analysed. For each case, the number of cores received, the lengths of each core (either from the macroscopy report or measured on the sections), the presence of cancer and the lengths of cancer were recorded.

Summary of results: There were prostate cores from 519 patients, with a total of 7229 cores, 486 cases of TRUS biopsies (6492 cores) and 33 of TPT biopsies (737 cores). 27% of TRUS cores contained prostatic adenocarcinoma; while 11% of TPT biopsies contained cancer. For TRUS biopsies, the average lengths of positive cores was 14.4mm, average lengths of negative cores were 13.3 mm ($p<0.01$, unpaired t-test). Overall, 79% of the cores were >=10mm and 63% of cores were >=13mm. There was an increased cancer diagnosis rate with longer core lengths: 20% positive in cores <10mm, 26% in cores 10-15mm, and 32% in cores >15mm. No difference on core lengths were found between TRUS and TPT biopsies ($p<0.01$, unpaired t-test), although the sample size of TPT biopsies was small.

Conclusions: We found that prostate core biopsy length is associated with increased detection rate of prostate cancer. In our practice, a mean core length of 13 mm for cancer detection is achieved, with more than 10mm in >75% of cores. Initial analysis of TPT samples suggest no inferiority of core lengths measured. A further audit is recommended to assess more fully the diagnostic impact of TPT biopsy lengths.

P41

The Value of Grading Dysplasia in Mucinous Neoplasms of Appendix

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Purpose of study: A recent consensus for reporting appendiceal mucinous neoplasia (AMN) recommended that "cystadenoma" should not be used and introduced a new term 'high grade appendiceal neoplasm (HAMN)'. We investigate our reporting practice and the spectrum of histological features of AMN in Oxford.
Method: 16,340 appendices from 2008-2015 received in Oxford, including those from right hemicolectomies and gynae-oncological resection specimens, were reviewed. All the cases with the clinical diagnosis of pseudomyxoma peritonii were excluded.
Summary of results: Forty-nine appendices showed AMN (2.3%, F:M 34:15). 30 patients were aged over 50. 22 were clinically suspicious pre-operatively. Diagnostic term 'low grade appendiceal mucinous neoplasm (LAMN)' was used in 37 (71%) cases. Those termed as mucinous cystadenoma (9) and mucocele (3) were reclassified as LAMN on review. 16% cases showed unequivocal focal high grade cytological dysplasia and hence renamed as high grade appendiceal mucinous neoplasm (HAMN) and rest were allocated as low grade appendiceal mucinous neoplasm (LAMN).
In 38 cases (including LAMN and HAMN) with effaced muscularis propria, 71% and 36% had extra-appendiceal mucin and dysplastic epithelium identified respectively. Remaining 11 cases with obliterated muscularis mucosae did not show extra-appendiceal mucin or epithelium. Thirteen had dystrophic calcification. Seven had associated acute appendicitis and 3 had serrated sessile polyp. 2 cases showed endometriosis and one of the case had a well differentiated neuroendocrine tumour at the tip of the appendix. None of the cases of both HAMN and LAMN showed any evidence of recurrences on the follow-up.
Conclusion: Both HAMN and LAMN cases showed no difference in clinical presentations and histological findings. Therefore in the absence of clinical pseudomyxoma peritonii and a clear separate clinical management guideline for HAMN and LAMN, the use of this sub classification should be discouraged.

P42

A Local Service Evaluation: Reporting Practices of Colorectal Lesions with Serrated Morphology

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Background: Colonoscopy commonly identifies premalignant adenomas and benign hyperplastic polyps (HP). The less common sessile serrated lesion (SSL) is recognised as a premalignant lesion showing morphological overlap with HP. This and varying minimum diagnostic criteria may be contributing to poor interobserver agreement when categorising lesions with serrated morphology. The aims were to determine if the local frequency of HP and SSL reflected that of the literature and assess concordance between lower gastrointestinal reporting pathologists categorising lesions with serrated morphology.
Methods: One month of polypectomy cases were reviewed to assess the frequency of HP, SSL, other lesions with serrated morphology and adenomas. Twelve cases with serrated morphology were selected and reviewed blindly by five lower gastrointestinal reporting pathologists. A multi-header review of cases followed to reach a consensus agreement on case diagnosis and future reporting practices.
Results: 34% of cases reviewed showed serrated morphology (n=135), of which 11% were SSL and 87% were HP. In 3 cases diagnosed as HP, a SSL could not be ruled out. Concordance between reporting pathologists, using clinically relevant categories, showed substantial interobserver agreement (Fleiss' Kappa = 0.6864). At a multi-header review a consensus diagnosis was agreed in all but one case, based on morphology alone.
Discussion: Overlapping features between benign HP and premalignant SSL remains a diagnostic challenge. Maturation of normal colonic epithelium results in the accumulation of cytokeratin 20 (CK20) at the apex of crypts. Dysmaturation is one feature of a SSL that has been reported to be demonstrable with CK20 immunohistochemistry. The equivocal "HP with features raising the possibility of a SSL" reviewed at the multi-header session, showed abnormal CK20 positive staining in the crypt base, supportive of a diagnosis of SSL. Selective use of CK20 may help differentiate an equivocal SSL from a HP.

P43

Plexiform Fibromyxoma of Stomach: A Case Report

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Introduction: Plexiform fibromyxoma is a rare and newly discovered gastric tumour with a peculiar plexiform pattern, bland spindle cells and a myxoid stroma rich in arborizing blood vessels.
Method: Here we describe a case of 52 year old man who was admitted with a 2 year history of iron deficiency anaemia and night sweats. Endoscopy revealed an 8 x 5mm submucosal lesion which was resected endoscopically.
Results and Conclusion: A diagnosis of plexiform fibromyxoma was made on histopathological and immunohistochemical examination. The post operative period was uneventful.

P44

A Retrospective Audit of the Diagnosis of Barrett's Oesophagus in a Tertiary Care Hospital

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Purpose of the study: • At least 50 cases of Barrett's oesophagus to be examined retrospectively. • Endoscopy documentation and histopathology reports to be assessed for adherence to minimum standards set by The British Society of Gastroenterology. • If minimum standards are not being met to investigate the cause and make intervention to improve this.
Methods: (1) A search was performed using PATHNET to find relevant patients. (2) Cases were examined from 1/1/2015 to 10/5/2016. 81 cases were found and 23 cases were excluded leaving 58 cases. (3) Endoscopy reports and histology reports reviewed using 'Electronic Patient Record'. (4) Microsoft Excel was used to collate and analyse data.
Summary of results: • Age range: 25 years – 87 years (mean 61 year); 36 males (62%), 22 females (38%). • Barrett's oesophagus was seen at endoscopy in 48/58 cases (83%); Barrett's was diagnosed in histology report in 55/58 cases (95%). • Biopsy location was given in endoscopy report in 36/58 (62%) cases. • The BSG definition of Barrett's oesophagus was not adhered to in 28/55 cases (51%) due to unclear biopsy sites and/or an absence of Barrett's mucosa seen at endoscopy.
Conclusions: • In four cases Barrett's oesophagus was not seen at endoscopy, but a diagnosis was made based on histology and the patient was placed on surveillance.
• Minimum required information from endoscopy is not reaching pathologists.
• This audit unexpectedly revealed weakness in the transfer of information from clinician to pathologist; this impacts our management of patients in this very common condition.
• It has prompted discussion between Gastroenterologists and Pathologists at our hospital to attain consensus on how to improve the Barrett's oesophagus diagnostic pathway.
• This highlights the value of audit in assessing and improving clinical practice.
• It has also highlighted how careful interpretation of guidelines is paramount in allowing them to achieve their objective of better patient care.

P45

Pathology of Polyps Identified in the Bowel Scope Programme

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Background: The bowel scope programme is a new addition to NHS bowel cancer screening which offers adults aged 55 a flexible sigmoidoscopy to remove polyps found in the left side of the colon, with the aim of reducing the incidence of invasive colorectal adenocarcinoma and facilitate early detection of existing cancers. Patients are stratified into low medium and high risk groups following the procedure, which determines the nature and frequency of future surveillance and treatment.
Method: This audit looks at all the histopathological submissions made under the programme between August 2015 and July 2016. It examines the number and nature of all polyps (or biopsies) removed, the severity of any dysplasia identified and the presence of invasive adenocarcinoma.
Results: 283 patients had tissue submitted for histopathology, with a total of 510 polyps removed. Of these 510 polyps, 234 were adenomas (2 villous, 89 tubulovillous, 143 tubular). 5 were found to contain high grade dysplasia and the remaining 229 were low grade. In addition, 206 serrated lesions were identified (194 hyperplastic polyps, 2 traditional serrated adenomas and 11 sessile serrated lesions, of which 1 contained conventional dysplasia). One adenocarcinoma was diagnosed. 2 lesions were carcinoid tumours and the remainder non-neoplastic.
Conclusion: Tubulovillous adenomas made up 38% of conventional adenomas, which is higher that that found at full colonoscopy, with tubular adenomas 60% and villous adenomas less than 1%. The proportion or high grade dysplasia found in conventional adenomas was 2%, which is somewhat lower than that found during full colonoscopy as part of the BCSP. The percentage of sessile lesions approached 50% of polyps removed, compared to around 25% of those from full colonoscopy. There was a high proportion of hyperplastic polyps amongst the serrated lesions examined (94%).

P46

International Tumour Budding Consensus Conference (ITBCC 2016) Recommendations on Assessment and Reporting in Colorectal Cancer

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Background: Tumour budding is an independent prognostic factor in colorectal cancer (CRC). However, its implementation has failed due to the lack of a standardized scoring method. Therefore, an international tumour budding consensus conference (ITBCC) was held to agree a scoring system for tumour budding in CRC.
Design: In April 2016 the consensus group of 23 GI expert voting members from eleven different countries met. Prior to the meeting, a systematic search of the literature was performed, forming the basis of the initial statements proposed by the steering committee. The Grading of Recommendation Assessment, Development and Evaluation (GRADE) approach was used to assess the strength of recommendation and quality of evidence.
Results: Consensus statements include the following: • Tumour budding is defined as a single tumour cell or a cell cluster consisting of 4 cells or less. • Tumour budding is an independent predictor of lymph node metastases in CRC and an independent predictor of survival in Stage II CRC. • Intratumoral budding exists in CRC and has been shown to be related to lymph node metastases. • Tumour budding and grade are not the same. • Tumour budding is counted on H&E and assessed in the hotspot (0.785mm2) at the invasive front. A 3-tier system should be reported together with the budding count. • Tumour budding should be taken into account with other clinico-pathological features in a multidisciplinary setting. • Tumour budding should be included in guidelines for CRC reporting.
Conclusion: Tumour budding is an independent prognostic parameter in CRC, strongly affects the management of stage I and stage II CRC patients and should be therefore included in CRC reporting, guidelines and staging systems.

P47

Characterising the Gastrointestinal Microbiome in Comorbid Inflammatory Bowel Disease and Irritable Bowel Syndrome

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Introduction: Many inflammatory bowel disease (IBD) patients experience apparent irritable bowel syndrome (IBS) without evidence of IBD activity, though whether this is truly IBS is disputed. These patients do not have a quality of life significantly different from those with active IBD. IBD and IBS are associated with gastrointestinal dysbiosis, but no studies have examined this in comorbid IBD and IBS. The presence of dysbiosis would suggest that this is true IBS, and could indicate that microbiome modulation would be effective in its management. Additionally, few studies have sought to compare the gastrointestinal microbiomes of those with Crohn's disease (CD) and ulcerative colitis (UC), which could improve knowledge of their pathologies.
Methods: Stool samples were taken from outpatients with CD (n=150) and UC (n=120). Faecal calprotectin levels, clinical IBD activity indices, and the presence or absence of IBS symptoms were used to define four disease status groups - 'active IBD', 'quiescent IBD', 'occult mucosal inflammation' and 'true IBS'. Microbiome analysis was performed using next-generation sequencing of the V4 region of the 16S rRNA gene. This work was supported by a PathSoc grant.
Results: Marked inter-subject microbiome variability was seen. Minor, statistically significant variation was found between the disease status groups. In CD, there was a lower abundance of Faecalibacterium (3.46% versus 6.97%; p<0.001), lower alpha diversity (p<0.001), and greater within-group beta diversity (p=0.010) compared to UC.
Conclusions: The lack of marked dysbiosis in the 'true IBS' patients may indicate that the gut flora does not play a role in their symptoms, although the presence of small differences between the groups suggests that targeted interventions may be beneficial. Previously described features of dysbiosis were observed in CD relative UC, suggesting that dysbiosis may be more exaggerated in CD. Future studies would benefit from adjusting for confounders.

P48

Comparison of Three Different Tumour Budding Methods to Evaluate the Prediction of Lymph Node Metastasis in pT1 Colorectal Carcinomas

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Purpose of the study: Prediction of lymph node metastasis (LNM) in early colorectal cancer (CRC) is poor. Tumour budding (TB) is reported to be linked to adverse prognosis in CRC. We compared three different budding methods (Ueno 2004, Lugli 2013, Ueno 2002/Kirsch 2012) and established the optimal threshold for "high grade tumour budding" in our cohort and their ability to predict LNM.
Methods: Our cohort of 206 pT1 CRC cases comprises patients with and without LNM (Toh 2015). The area with maximum TB was selected for all three methods and the different fields sizes marked and counted. An additional nine fields with hot spots for TB were also separately evaluated (Lugli 2013). Associations between categorical data and LNM were performed using the $\chi 2$ test and Fisher exact tests. A modified receiver operating characteristic (ROC) curve was generated to determine the cut-off values for optimum prediction of tumour budding.
Summary of results: The modified ROC curve led to a cut off of 2 and 0.2 for the average of ten fields (Lugli 2013). Only the budding method of Ueno 2002/Kirsch 2012 with a threshold of 10 showed a significant correlation with LNM (p=0.009; 5/19; 26.3%) in our cohort. With our established threshold of 2 and 0.2 we could identify 16/19 (84.21%) patients for all three methods. To achieve this high resection rate we had to recommend resection of 110 of 206 patients (53.39%). The field diameter of Ueno 2002/Kirsch 2012 (0.385mm2) with our established threshold of 2 showed in our cohort the most significant p-value with 0.007(110/206; 53.39%) in comparison with Lugli 2013 (p-value=0.014,116/206;56.31%) and Ueno 2004 (p=0.008,114/206; 55.34%).
Conclusions: With the established threshold of TB in our cohort 2 and 0.2 all field diameters were significantly correlated with LNM and detected 16/19 (84.21%) LNM. Performing the most effectively as the field diameter of 0.385mm2. Further work and re-evaluation in a bigger cohort of the threshold of TB is needed.

P49

Comparing FibroScan with Liver Biopsy for Investigating Patients with Chronic Liver Disease – a Retrospective Study of the Staging of Liver Disease in Routine Clinical Practice

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Purpose: FibroScan (FS) is a type of ultrasound used to predict liver fibrosis, enabling biopsy to be avoided in some patients. It was validated on cohorts of clinical trial patients. The purpose of this retrospective study was to compare FS with liver biopsy (LB) fibrosis stage in routine practice.
Methods: We identified patients with LB between January 2015 and March 2016 who also had FS. We recorded FS result, LB length, portal tracts (PT), diagnosis and fibrosis stage. We determined Positive Predictive Values (PPV), Negative Predictive Values (NPV) and Chi-square between groups.
Results: 66 patients had hepatitis B (HB), 108 non-alcoholic fatty liver (NAFLD) and 39 had various other pathology (not included in further analysis), reflecting current pathways for liver investigation. FS results predicted at least bridging fibrosis in 11/66 (>10.7kPa,17%) HB and 66/108 (>8.8 kPa,61%) NAFLD patients. On biopsy, 6/66 HB patients had Ishak stage 4-6, and 30/108 NAFLD had Kleiner stage 3-4. Compared with LB, the FS result had NPV of 96% and 90% and PPV of 36% and 39% for HB and NAFLD respectively. The biopsy length was 6-28mm (median 16mm). LB above median length had significantly higher fibrosis stage (p=0.017) but did not affect correlation with FS. LB contained 3-19 (median 9) PTs; PT count did not correlate with stage or affect FS correlation. The interval between LB and FS (-30 to +16 months, median -4) did not affect the correlation of LB and FS.
Conclusions: In our routine practice, a low FS has a NPV >90%, identifying patients unlikely to have significant fibrosis. However most patients with a FS result predicting bridging fibrosis did not have bridging on LB. Other clinical factors contribute to a raised FS result (e.g. activity of disease, time since meal). Shorter LB had significantly lower disease stage, consistent with understaging, emphasising need for adequate sample to determine fibrosis stage.

P50

Resection of Colorectal Liver Metastasis – What is the Significance of a Positive Resection Margin?

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Background: Resection of colorectal liver metastases (CRLM) has a 5 year survival of around 40%. Resection margin status is a significant prognostic factor. The frequency of positive margins varies from <10% to >40%. but intrahepatic recurrence at the margin seems rare. Audit of our 2012 CRLM resections showed 28.4% positive margins and 16.5% with <1mm clearance. We reviewed these patients to determine disease free survival (DFS) and site of recurrence in the liver.
Methods: All patients with CRLM resection in 2012 were included. A prospective database was retrospectively analysed for margin (<1 or >1mm), DFS and site of liver recurrence. For a subset (31 patients, 66 tumours) histological growth pattern (GP) was recorded.
Results: There were 111 patients (76 male; 65y (25-86); median follow up 38.3 months). Kaplan Meier analysis showed median DFS for >1 and <1mm margin was 38.3 and 17.7 months respectively. 22/111 (19.1%) patients had recurrence of CRLM, including 11/69 (16.1%) with >1mm and 11/42 (26.1%) with <1mm clearance. Only 5/22 of these recurrences were at the site of previous resection, of which 2/5 had a margin >1mm. Desmoplastic margin was rare overall (11/66 tumours, at least one in 8/31 patients). None of 13 tumours present at the margin were from desmoplastic tumours. For 59 tumours within 30mm of the margin, clearance was <1mm in 1/11(9.1%) desmoplastic compared with 21/48 metastases with pushing or mixed margin (p<0.05).
Conclusion: We identified intrahepatic recurrence following CRLM resection in 19.1% patients after 4 years follow up. A positive margin did not predict local recurrence at the surgical site. Patients with a positive margin had more frequent and earlier recurrence suggesting the adverse prognosis of a positive margin is more related to underlying tumour biology than technical failure. The absence of a desmoplastic margin is one factor that contributes to the positive margin.

P51

Subcellular Localisation of KLF2, RBPJ and NOTCH2

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Purpose: Splenic marginal zone lymphoma (SMZL) is a low-grade B-cell lymphoma, originating from marginal zone B-cells of the spleen. Recent studies by whole-exome sequencing have identified KLF2 mutation as the most frequent genetic change in SMZL, with the majority being frameshift indels and nonsense mutations. The mutations inactivate the ability of KLF2 to suppress NF-κB activation by TLR, BCR and BAFFR signalling and also its ability to repress RBPJ activation by the NOTCH2 intracellular domain (N2ICD); these two pathways are critical for marginal zone B-cell development. To investigate whether KLF2 directly interacts with these transcription factors, we have studied the subcellular localisation of KLF2, N2ICD and RBPJ.
Methods: HEK293 cells were transfected with HA-tagged KLF2, flag-tagged RBPJ and N2ICD, grown on poly-L-lysine-coated coverslips and subjected to immunofluorescence staining with specific primary antibodies, followed by appropriate, fluorophore-conjugated secondary antibodies. Confocal microscopy was carried out to examine the subcellular localisation of the three proteins 48 hours after transfection.
Summary of results: Single transient transfection showed expression of each construct in up to 20% of transfected cells, with each of the three proteins, namely KLF2, RBPJ and N2ICD, localised to the nucleus. Co-transfected cells with all three expression constructs showed evidence of co-localisation of these three proteins in the nucleus.
Conclusion: KLF2 co-localises with RBPJ and N2ICD to the nucleus and this may enable KLF2 to suppress the transcriptional activity of RBPJ and N2ICD. We are in the process of investigating whether KLF2 mutants show altered subcellular localisation and thus potential altered interaction with RBPJ and N2ICD.
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P52

PTEN Loss in DLBCL – Any Therapeutic Advantage?

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The tumour suppressor phosphatase PTEN (Phosphatase and Tensin homologue protein), a negative regulator of PI3-kinase signalling, is frequently mutated in cancer. Therefore, loss of PTEN may be a potential biomarker for responses to PI3K and homologous recombination targeted therapies. The incidence of PTEN negativity in relapsed Diffuse large B cell lymphoma (DLBCL) is not known. Our preliminary studies show a high incidence of PTEN loss by immunohistochemistry. We screened a large cohort of archived cases and correlated PTEN expression with clinical response to chemotherapy regimens that frequently include platinum compounds. Laboratory studies with PTEN-negative DLBCL cells will also be evaluated for their response to cytotoxic agents, targeted therapies including PI3K and PARP inhibitors, and to drug combinations. These results will help establish the role of PTEN in the pathophysiology and therapy of DLBCL.
We have screened 18 samples of DLBCL at presentation and 19 at relapse, with matched pair analysis for 13 cases. PTEN-negative samples were 28% at presentation and 63% at relapse. 5 of 11 matched pair cases showed loss of PTEN at relapse; in contrast, no PTEN-negative cases regained PTEN expression at relapse. PTEN-negative haematopoietic cells have enhanced sensitivity to Cisplatin, which is of a similar level to that seen in PTEN-negative epithelial tumours. Loss of PTEN also leads to enhanced PI3K signalling which can up regulate anti-apoptotic pathways. We found that the combination of a selective PI3K inhibitor, PIK90, and Cisplatin in PTEN negative cells led to increased cytotoxicity compared with either agent alone.
The results of this study could inform patient stratification for choice of salvage therapies in DLBCL and for entry into trials of novel agents targeted towards homologous recombination. In addition, loss of PTEN could identify patients more likely to respond to inhibitors of PI3K, several of which are in clinical trials.

P53

Comparison of Two Decalcification Protocols for Bone Marrow Trephine Biopsy Samples

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Aim: To compare two decalcification systems in histological and molecular analysis of bone marrow trephine biopsy slides.Method: Bone marrow trephine biopsy (BMT) specimens were decalcified using two protocols each, the SAKURA TDE™ 30 Decalcifier System and the Hammersmith protocol.
10 BMT specimens were cut in half and one half was decalcified using each protocol. Slides were stained using Haematoxalic and Eosin (H&E) and Reticulin stain. Sections were prepared for molecular analysis.The slides were anonymised and independently examined by two experienced pathologists. Slides were assessed on the following basis: (1) Stain quality, (2) Section quality/thickness, (3) Nuclear detail, (4) Suitability for diagnosis (suitable/borderline/unsuitable).
Results: It was noted by both reviewers that the quality of slides in all these cases was better than the routine average bone marrow section quality. Molecular analysis is still in progress.H&E: H&E stained slides showed an improvement in the section thickness for slides decalcified using the Hammersmith protocol. The nuclear detail was comparable for both methods.The Hammersmith protocol generated a greater number of slides suitable for analysis compared to slides decalcified by the SAKURA TDE™ 30 System.
Reticlin: There was an improvement in the stain quality in slides decalcified using the Reticulin staininig, Hammersmiths protocol.The slide quality/thickness for slides decalcified by both methods is comparable. Decalcification using the Hammersmith's protocol however generates a greater number of slides suitable for analysis as compared to slides decalcified by the SAKURA TDE™ 30 Decalcifier System. Conclusion (1) The quality of all slides in the analysed cases was better than the average bone marrow section quality, (2)The Hammersmith protocol generated a greater number of slides suitable for analysis by H&E and Reticulin stains than the SAKURA TDE™ 30 Decalcifier System.

P54

Determination of Human Embryonic Development Using Micro-CT Imaging

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Whilst conventional autopsy remains the gold standard for post-mortem examination, many advances are being made in the field of 'investigation after death'. These include imaging and less invasive tissue sampling with the development of novel investigations based on new laboratory techniques, such as proteomics and transcriptomics. These techniques provide a less invasive form of autopsy that are more likely to be widely accepted, can verify prenatal diagnoses, and may demonstrate additional information that could otherwise be missed by traditional autopsy alone, particularly where parents decline invasive examinations.
In this study, we used detailed imaging to determine the gestational age of an embryo case study. Micro CT was performed using a Nikon XTH225 micro-CT scanner, with images reconstructed using proprietary software, and post-processed using VG Studio MAX. Detailed assessment of internal and external morphological features, plus biometry measurement of crown-rump length (CRL), were then compared to existing normative developmental measurements and features, allowing us to accurately estimate gestational age.
We show that micro CT can give detailed age estimation of embryonic and early foetal death. The major aim of this project was to improve and develop existing imaging approaches to assist post-mortem examinations, allowing us to improve the understanding of paediatric diseases. This project was supported by bursaries from the Pathological Society and British Division of the International Academy of Pathology.

P55

A Digital Ocular Pathology Teaching Resource

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Purpose of the study: Ocular pathology is a small sub-speciality and consequently there are relatively few units within the UK which provide such specialist services, making teaching cases difficult to obtain outside of tertiary centres.
Methods: To respond to this need, we have produced a novel, freely accessible digital ocular pathology teaching resource designed for trainee pathologists. It can be found at: **http://www.virtualpathology.leeds.ac.uk/ocular/**. The resource covers over 100 cases scanned using whole slide imaging. The cases are subdivided by tissue type and cover a wide range of diseases. The images can be viewed freely on any internet connected PC using Spectrum WebScope software from Leica Microsystems (UK) Limited, or alternatively on a tablet/ phone using a Leica Microsystems mobile application, ePathViewer. The resource allows users to test their own knowledge by reviewing the virtual slide first before revealing the diagnosis and relevant explanatory information.
Results: Anonymous feedback was acquired from ten histopathology consultants and trainees at St James's University Hospital, Leeds. All users reported that the resource was a useful, user-friendly resource and would recommend it to their colleagues. Similarly, all respondents found the cases to be clear with a good range of included diseases and that the teaching resource would be useful to general histopathology trainees without access to ocular cases. Four respondents stated that the teaching resource would make them more likely to consider a career in ocular and neuropathology.
Conclusions: The feedback we received was very encouraging and highlighted that this teaching resource may be particularly useful for trainees without access to an ocular pathology specialist centre. We invite your attendees to use our digital ocular pathology teaching resource and hope that they too find it useful.

P56

Defining the Tumour Type and Location of Resected Intra-Cranial Tumour Cases Submitted for Tissue Banking Compared to Those Not Submitted

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Tissue banks are an important resource for research and tissue banking of neurosurgical specimens should be performed if there is sufficient tissue and appropriate consent. A previous service evaluation project found the operating surgeon to be an important factor in determining if tissue banking takes place. The aim of this project was to understand the effect of other factors (type of tumour and position of tumour) on the rate of tissue banking for resected intra-cranial tumours. Data was collected from a sample of adult intra-cranial tumour cases complied from neurosurgical specimens submitted for tissue banking and CNS tumour specimens on MDT lists over a 6 month period. 170 resection specimens were identified and were analysed for the type of tumour, the 2007 WHO grade and their anatomical position. Chi squared test was used to assess significance.
Of the 170 resected specimens, 104 (61%) were banked and 66 (39%) were not. A significantly higher proportion of banked specimens were glioblastomas and WHO grade 4. Conversely a significantly higher proportion of non-banked specimens were meningiomas and WHO grade 1 ($p<0.01$). With respect to tumour position, a significantly smaller proportion of non-banked tumours came from the right side and a higher proportion were midline tumours ($p<0.01$). A higher proportion of banked specimens came from temporal lobes (either side), ($p<0.05$).
Comparison of groups of banked and non-banked tumours revealed varied tumour populations. This seems to be primarily accounted for by the variable treatment of glioblastomas (81% of which were banked) compared to meningiomas (48% of which were banked). These two tumour types accounted for 50% of tumours in this sample and therefore led to significant difference in tumour type and WHO grade between the banked and non-banked specimens. There was also significant difference in the location of tumours tissue banked compared to those not banked, the cause for this requires further investigation.

P57

Tissue Clearing for Brain Tumour Research

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Purpose of the study: Current methods of analysing the phenotypical properties of tumour cells in brain tumour tissue all have significant limitations. We have used novel tissue clearing methods to perform single-cell phenotyping both in an *in vivo* glioblastoma (GBM) model and in human tumour samples. We have adapted a recently described passive tissue clearing technique to image thick sections (up to 4mm) of the murine CNS xenografted with GBM cell lines, and human surgical and autoptic tumour tissue.
Methods: We used lentiviral-mediated transduction of GFP in GBM cells. The cells were then xenografted into the caudo-striatum of NOD-SCID mice. Tumour bearing mice were culled, the brains removed and hydrogel-tissue hybrids created then rendered optically transparent. Human surgical and autopsy samples underwent the same tissue clearing process. Immunohistochemistry was performed and 3D phenotypic maps were then created with confocal fluorescence imaging.
Summary of results: Using this method of passive tissue clearing allowed us to generate 3D phenotypical information for human and xenografted tumours as well as host cells with a resolution allowing single-cell characterisation.
Conclusions: This method of tissue clearing, compatible with endogenous fluorescence and immunohistochemistry, has allowed us to interrogate the fine structural properties of and relationship between tumour cells and their host environment. We have shown the utility and applicability of this novel fluorescence imaging platform for brain tumour research. This technique allows phenotypic analysis at the single-cell level as well as at the whole-organ level without the high amount of tissue disruption that other methods entail.
This work has been funded by a grant from The Pathological Society of Great Britain and Ireland.

P58

Olfactory Neuroblastoma Presenting as Submandibular Tumour

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Purpose of the study: Olfactory Neuroblastoma is a rare, locally aggressive malignant neoplasm arising from the olfactory epithelium. The clinical presentation can be with metastasis mostly in the cervical lymph nodes but the occurrence of metastasis in the submandibular gland has not been reported yet. Here we describe such a case.
Methods: Clinical history was retrieved from discussion in Head and Neck MDT meeting and medical records. Routine macroscopic and microscopic histological examination along with appropriate immunohistochemistry was performed.
Summary of results: We present a case of left submandibular tumour in a 75 year old female who was initially diagnosed as high grade neuroendocrine carcinoma requiring further investigation for characterising it as primary or metastatic. Subsequent investigation revealed the presence of left skull base lesion which on excision was confirmed to be olfactory neuroblastoma. In addition, we include the review of literature of olfactory neuroblastoma metastatic to different sites.
Conclusion: It is important to think laterally and consider metastatic tumours when evaluating neuroendocrine lesions in the submandibular region as this can be the first manifestation.

P59

Diagnostic Adequacy and Accuracy of Core Needle Biopsy Versus Fine Needle Aspiration Cytology in Salivary Gland Tumours: Results from April 2015 to April 2016

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Purpose of the study: The aim of this study is to compare the adequacy and accuracy of core needle biopsy versus fine needle aspiration cytology for diagnosing salivary gland lesions.
Methods: Records of patients undergoing fine needle aspiration or core biopsy for a salivary gland lesion were obtained from the hospital computer system (Epic) over a 13 month period from 2015 to 2016. All the cases were analysed for patient demographics (age, sex and tumour site) and hospital of origin. Adequacy, accuracy, sensitivity and specificity of diagnosis for core biopsy and FNA were calculated and the results of the two methods were compared.
Summary of results: FNAC yielded higher non-diagnostic sample rates in comparison to CNB in 2 out of 3 centres. One case of Warthin's tumour was misinterpreted as metastatic squamous cell carcinoma. Sensitivity was 100% for core needle biopsy and 75% for FNAC which were in keeping with the published literature. Specificity was 100% for both CNB and FNA in keeping with the published literature. Accurate diagnosis was given in 85.7% of CNB and 60% of the FNAC in the limited sample studied.
Conclusion: We recommend CNB as the primary diagnostic tool for evaluating salivary gland neoplasm as it has accurate tumour sub-typing and lower non-diagnostic sample rates.

P60

Muco-Epidermoid Carcinoma Rich in IgG4+ Plasma Cells: A Case Report

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Introduction: Muco-epidermoid carcinoma (MEC) is the commonest primary malignancy in the salivary gland. IgG4-related disease is amore recently described syndrome with characteristic lymphoplasmacytic infiltrates mostly composed ofIgG4 positive plasma cells. Most cases present with an enlargedexocrine gland but in one study an association between IgG4 disease and sclerosing MEC has been described. Here we report a similar association without coexistent fibrosis.
Method: The patient is a 39 year old female presented with funny sensation in the right ear and retro mandibular pain. On investigation, MRI scan showed a 13mm tumour in the deep lobe of the right parotid. Extra capsular type of dissection of the tumour was performed.
Results: On histological examination the tumour was a 10mm, composed of squamous-like and mucous secreting cells meeting the criteria forintermediate grade muco-epidermoid carcinoma. In addition, there was a dense inflammatory infiltrate mostly composed of mature plasma cells. On immunostaining, the IgG4 positive plasma cells were about 35-40/hpf and the ratio of IgG4+/IgG+ was approximately 30-35%.
Conclusion: IgG4 disease can be seen in MEC without accompanying sclerosis. The relationship between the MEC and IgG4 + plasma cells requires further studies.

P61

There is More to Malignancy Than Meets The Eye

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Introduction: Apart from major multi-disciplinary meetings (MDM), Pathologists participate in meetings such as cancers of unknown origin in an effort to ensure every patient's cancer has been discussed in a relevant tumour board. There are SOPs to ensure Histopathology departments are able to have cases ready for local discussion or referral to relevant regional MDMs. There can be situations where in the same case needs to be considered in more than one MDM.
Methods: We report two cases which warranted discussion in more than one MDM due to morphological mimicry. The first case was a 70 year old woman with a tumour mass detected at the appendicular orifice and the biopsies showed signet ring cell adenocarcinoma. The surgical specimen showed signet ring adenocarcinoma ex goblet cell carcinoid prompting discussion firstly at the local colorectal MDT followed by referral to the regional Neuroendocrine Tumour MDM. The second case was of a 56 year old man in whom a soft tissue lump removed from the right knee region showed a malignant melanocytic neoplasm with consistent histological and immunohistochemical features. Due to the tumour topography, clear cell sarcoma and metastatic melanoma were considered and discussed at the local skin MDM and subsequent referred to Royal Marsden soft tissue MDM.
Conclusion: These two cases illustrate the importance of availing local as well as regional resources to ensure that patients are directed to the correct cancer pathways as this can impact treatment regimens and cancer audit data.

P62

Extraskeletal Osteosarcoma – Does this Rare Tumour Represent Dedifferentiated Liposarcoma or Malignant Peripheral Nerve Sheath Tumour (MPNST) with Heterologous Osteosarcomatous Differentiation? A Study of Twenty-Two Cases using *MDM2* FISH and Immunohistochemistry for H3K27me3.

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Purpose of Study: Extraskeletal osteosarcoma is an extremely rare and clinically aggressive tumour occurring in the soft tissues. Dedifferentiated liposarcomas and MPNSTs are two soft-tissue sarcomas that may undergo osteosarcomatous differentiation and therefore must be considered in the differential diagnosis. Distinction is not always possible on morphological grounds alone in biopsy specimens. We screened a series of 22 extraskeletal osteosarcomas to explore these differential diagnoses by utilising FISH for *MDM2* copy number and immunohistochemistry for H3K27me3 expression, a recently described marker the expression which is lost in the vast majority of high grade MPNST.
Methods: 22 cases of extraskeletal osteosarcoma were retrieved from the archive and reviewed to confirm the diagnosis. We performed FISH using a Vysis MDM-2/CEP 12 probe. Immunohistochemistry was performed on 20 of the cases with the antibody H3K27me3.
Summary of results: All of the cases were negative for *MDM2* amplification (17 showed polysomy of chromosome 12). Nuclear expression of H3K27me3 was seen in 17/22 cases. Two cases were equivocal and one negative.
Conclusions: The absence of *MDM2* amplification in all 22 cases, and nuclear positivity for H3K27me3 in 17 cases support that these tumours are not dedifferentiated liposarcomas or MPNSTs with osteosarcomatous differentiation respectively. The single case showing nuclear loss of H3K27me3 may represent an MPNST. Our results support the concept of extraskeletal osteosarcoma as a defined entity. Determining the molecular genetic / epigenetic profile of these tumours would be valuable for diagnosis and understanding the mechanism by which these tumours form bone in soft tissue.

P63

Audit of Breslow Thickness in Cutaneous Melanoma – Does Size Matter?

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Advanced melanoma still confers a dismal prognosis for most patients, although immunotherapy and cytotoxic agents such as Vemurafenib, Dabrafenib and ipilimumab are starting to offer increased survival times for those with advanced or metastatic disease in BRAF V600 positive melanomas. The RCPath dataset for cutaneous melanoma states "thickness is a continuous variable and the integers set in the AJCC 6th and 7th editions are arbitrary and for practical convenience." However, these are the most reliable parameters for managing patients appropriately and have widespread support from all members of the multidisciplinary team.
As the current recommendations for managing patients with melanoma relies so heavily on the Breslow thickness we wanted to assess routine clinical practice at our hospital to see how many melanomas are being correctly measured (and therefore staged) at the time of initial diagnosis.
Method and Results: We retrospectively reviewed 100 cases and compared the original Breslow measurement with a second taken at the time of review.The results showed that 95% of cases were accurately staged. More interestingly was the variable adherence to the guidelines related to recording of Breslow thickness with some consultants recording to one decimal place and others only reporting whole numbers.

P64

Sebaceous Neoplasia and Mismatch Repair Deficiency: A Review of Clinical Practice

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Background: Muir-Torre syndrome is a sub-type of Lynch syndrome characterised by the presence of one or more sebaceous tumours with a Lynch-associated visceral malignancy. It is recognised that between 26–78% of sebaceous neoplasms exhibit mismatch repair (MMR) protein deficiency on immunohistochemistry (IHC) and emerging literature suggests that MMR protein deficiency is predictive of germline MMR gene mutation in a proportion of cases. MMR gene mutation confers increased risk of malignancies including colorectal and endometrial carcinoma. However, at present there is no consensus regarding the investigation and management of patients presenting with sebaceous neoplasia.
Method: A review of all cases of sebaceous neoplasia in our department between 2005–2016 was performed to assess practice regarding: (1) MMR IHC, and; (2) referral of cases for genetic testing.
Results: 79 cases of sebaceous adenoma, carcinoma and sebaceoma were diagnosed between 2005–2016. Of these, 18 cases underwent MMR IHC of which 72% (13/18) exhibited MMR protein deficiency: ten with loss of both MSH2 and MSH6, two with loss of MLH1 and PMS2, and one with loss of MSH6. Three patients were subsequently referred to clinical genetics, none of whom underwent germline MMR mutation analysis due to lack of family history of Lynch-associated tumours. Three patients had either existing diagnoses of HNPCC syndrome, or had already been referred to clinical genetics with other Lynch-associated tumours. Three further patients had histories of Lynch-associated tumours; of these only one underwent MMR IHC.
Conclusion: Our review suggests that there is considerable variation in practice regarding the investigation of patients with sebaceous neoplasia. Further research to determine the utility of MMR IHC and both personal and family history in selecting patients for germline genetic testing would provide a more evidence-based and consistent approach for pathologists, dermatologists and clinical genetics service.

P65

This abstract has been withdrawn

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