Belfast Pathology 2017
Poster Abstracts

10th Joint Meeting of the British Division of the International Academy of Pathology and the Pathological Society of Great Britain & Ireland

20 – 23 June 2017

Hosted by

Northern Ireland Molecular Pathology Laboratory
Centre for Cancer Research and Cell Biology
Queen's University Belfast ▪ Department of Tissue Pathology
Belfast Health and Social Care Trust

Venue

Belfast Waterfront, 2 Lanyon Place, Belfast BT1 3WH

Companion Sessions

AIDPATH ▪ Association of Clinical Electron Microscopists
British Association of Cytopathology
British Association of Gynaecological Pathology
British Association of Urological Pathologists
Dutch Irish English (DIE) Cardiac Group ▪ Renal EQA
Renal Transplant EQA ▪ 100,000 Genomes Project

KEY

Ⓟ = Presenter

PRESENTER'S INDEX

To be found at the end of this document, after the abstract listings.

ABSTRACT REVIEWERS

Prof MJ Arends, Edinburgh

Dr EW Benbow, Manchester

Prof DM Berney, London

Dr C Boyd, Belfast

Dr T Brenn, Edinburgh

Dr L Burke, Cork

Prof SS Cross, Sheffield

Prof MQ Du, Cambridge

Prof RM Feakins, London

Prof S Fleming, Dundee

Prof AJ Freemont, Manchester

Prof CS Herrington, Edinburgh

Dr J Houghton, Belfast

Dr O Houghton, Belfast

Dr TS Jacques, London

Prof E Kay, Dublin

Dr P Kelly, Belfast

Dr M Khan, Nottingham

Dr B Loftus, Dublin

Dr M Loughrey, Belfast

Dr P Maxwell, Belfast

Prof WG McCluggage, Belfast

Dr C McGalie, Belfast

Dr S McQuaid, Belfast

Prof GI Murray, Aberdeen

Dr S Napier, Belfast

Prof AG Nicholson, London

Dr M Osborn, London

Dr D Poller, Portsmouth

Prof E Rakha, Nottingham

Prof ISD Roberts, Oxford

Prof G Thomas, Southampton

Dr D Treanor, Leeds

Prof P van der Valk, Amsterdam

Dr L Venkatraman, Belfast

Prof KP West, Leicester

PROGRAMME ACKNOWLEDGEMENTS

This Programme is published jointly by the British Division of the International Academy of Pathology and the Pathological Society of Great Britain & Ireland.

This publication was designed and produced in England by Byte & Type Limited, Birmingham (Tel: 0333 666 4321).

COVER PHOTOGRAPHS

Front — Top: Belfast City Hall [1] **Middle:** Queens University Belfast [2] **Bottom:** The Titanic Centre [1]

The publishers wish to thank the following for granting permission to use their photographs:
[1] Northern Ireland Tourist Board [2] Queen's University Belfast [3] Belfast Waterfront

P1

How the Application of Micro-CT, for the Differentiation Between Serrated and Non-Serrated Blades, in the Infliction of Stab Wounds Varies in Different Tissue Types

Ⓟ SA Stanley

East Midlands Forensic Pathology Unit, University of Leicester, Leicester, UK

Stabbing is the most common method of homicide in the UK. Kitchen knives are commonly used and may be serrated. Individual serration points can leave markings (striations) in stabbed tissues. The proportion of serrated blade stab wounds showing striations in cartilage has been shown to fall following decomposition.
Traditional methods (physical casting and photography) of documenting striations also have limitations. Micro-CT has therefore been trialled in cartilage to *"virtually cast"* stab wounds and show striations. This project has quantitatively investigated the effects of taphonomic alteration and documentation methods on striations in skin.
Stab wounds inflicted in porcine skin were excised immediately or following aquatic and terrestrial decomposition, mummification or burning. The wounds were imaged using photography, stereo-optical microscopy and micro-CT. Independent analysts reviewed the images and their responses were used to calculate the proportion of striations in each taphonomic group. The proportion of striations decreased with time left to decompose, including in water. Striations persisted to some extent however, visibility decreased until the proportion was significantly lower than that seen in fresh samples. Mummified and burnt tissues showed a constant striation rate however, misinterpretation of tissue artefacts could have caused this. The optimum imaging technique was stereo-optical microscopy although photography was also acceptable. Micro-CT showed potential however, the use of constant imaging parameters between knife groups limited striation visualisation. Evidence of striations persisting after taphonomic processes strengthens their application for blade identification. Determining an optimum documentation technique enables their use as evidence in court.

P2

From Serrations to Striations – An Inter-Observer Study of Tool Mark Analysis of Serrated Blade Stab Wounds in Porcine Skin

Ⓟ TA Calderbank[1]; SV Hainsworth[2]; GN Rutty[3]

[1]University of Leicester, Leicester, UK; [2]Department of Engineering, University of Leicester, Leicester, UK; [3]East Midlands Forensic Pathology Unit, University of Leicester, Leicester, UK

Knife crime is a significant problem in the UK. Serrated blades leave a characteristic tool mark pattern (striations) in cartilage and porcine skin, however there is no statistical validation for the methods used in striation identification. This study aims to provide benchmark data on the incidence of striation production in wounds made by serrated blades, and to evaluate whether it is possible to use stab wound striation patterns to distinguish between different knives.
Two different serrated blades and a flat blade were used to produce stab wounds in porcine skin. Each wound tract was opened completely and the two halves imaged using stereomicroscopy. The images were randomised and shown to a group of three individuals who were asked to decide if a sample showed striations, and whether it was made with a coarsely serrated blade, a finely serrated blade or a flat blade.
Inter-observer analysis was performed using R. Striations were identified in 89% of samples produced by a serrated blade, with good agreement within the observer group. Flat blade samples showed more variable tool marks, with little agreement between observers. The wounds produced by serrated blades were correctly identified on average 62.5% of the time, whereas flat bladed samples were correctly identified only in 32% of cases.
This study provides further evidence for the use of tool mark analysis in skin, and that may be possible to distinguish between wounds made with serrated and non-serrated blades, and between knives with different serration patterns. This study has given the benchmark for other statistical studies to build upon, ultimately working towards integration into future forensic practice.

P3

Use of Post-Mortem CT as a Supplement to Autopsy in Trauma Deaths: What Does it Add?

Ⓟ JW Hamblin *(Undergraduate)*[1]; L Winter[1]; A Shavick *(Undergraduate)*[1]; ZC Traill[2]; RE Benamore[2]; J McMaster[3]; ISD Roberts[1]

[1]Department of Cellular Pathology, John Radcliffe Hospital, Oxford, Oxford, UK; [2]Department of Radiology, Churchill Hospital, Oxford, Oxford, UK; [3]Department of Trauma and Orthopaedic Surgery, John Radcliffe Hospital, Oxford, Oxford, UK

Post-mortem CT (PMCT) is used in few UK centres to supplement autopsy in the investigation of deaths from injuries. Here we review trauma deaths analysed by a Digital Autopsy Service in order to determine the added value of PMCT.
In 22 trauma deaths, PMCT was followed by full autopsy. The severity of the injuries detected by CT and dissection were separately quantified using the Abbreviated Injury Severity score (AIS, a value of severity for each injury) and the Injury Severity Score (ISS, a value of the overall severity of injury in terms of survivability), in order to determine how effective these two methods were in detecting clinically relevant injuries.
Causes of death were: multiple injuries due to road traffic collision (15), severe head injury (5) and cervical spine injury (2). PMCT exclusively detected 28 injuries: 17 vertebral fractures (5 Spinous processes, 7 transverse processes, and 5 vertebral body), 2 tonsillar herniations, 1 base of skull fracture and 7 pelvic fractures. Open autopsy exclusively detected 15 injuries: 2 mesenteric tears, 2 aortic tears, 5 cortical brain contusions, 4 pulmonary contusions, 1 liver contusion and 1 caecal perforation. The average ISS score was 43.5 based on CT alone, 44 based on dissection alone and 45.8 based on both investigations. The AIS was greater based on dissection alone in 6 cases vs 3 based on CT alone.
PMCT is excellent for detecting fractures that are missed by dissection, particularly vertebral injuries, but poor for detecting many soft-tissue injuries. PMCT is therefore a useful supplement to dissection, providing information of clinical relevance that cannot be gained from open autopsy alone.

P4

Specialist Referral Centre Retrospective Report on 161 Cases of Sudden Cardiac Death in the Community

Ⓟ *MB Cotter[1]; N Nolan[1]; K Heverin[2]; M Fitzgibbon[2]; C McGorrian[3]; J Galvin[3]; D Ward[4]; A Fabre[1]*

[1]Histopathology Department, St Vincent's University Hospital, Dublin, Ireland; [2]Department of Clinical Biochemistry, Mater Misericordiae University Hospital, Dublin, Ireland; [3]Family Heart Screening, Heart House, The Mater Foundation, Dublin, Ireland; [4]Centre for Cardiovascular Risk in Younger Persons, Adelaide and Meath Hospital, Dublin, Ireland

Purpose: Non-atherosclerotic causes of sudden cardiac death (SCD) are increasingly recognised at autopsy. Some causes are hereditary and preventable with cardiac screening and appropriate treatment. St Vincent's University Hospital provides a national specialist referral service for cardiac cases requiring expert pathology opinion. We performed the first retrospective review of all nationally referred cardiac autopsy cases to our institution for expert pathology opinion.
Methods: We retrospectively identified and reviewed all referred cases between 2013–first trimester of 2017 including those who have had tissue samples taken for genetic testing at the time of autopsy. Patient age, sex, weight, height, heart weight, thickness of left and right ventricles, toxicology results and diagnosis were recorded together with results from molecular analysis.
Summary of results: 161 cases were collated, including 116 males (72%) and 45 females (28%), age range 5 weeks-79 years. 44 cases had biocollection performed (29.9%). Males predominated in both age groups (≤35 years, >35 years). 34.8% of the hearts were structurally normal (n=56). Cardiomyopathies represented 23% (n=37), non-atherosclerotic coronary artery abnormalities 8.7% (n=14), valvular abnormalities 0.6% (n=1), metabolic diseases 11.8% (n=19), inflammatory conditions 7.5% (n=12), vascular abnormalities 4.3% (n=7), and other 9.3% (n=15). 25 families in this cohort have been referred to specialised cardiac services to date and molecular studies have been performed on 7 probands, of which clinically important cardiac-associated gene mutations were identified in two families.
Conclusions: Increased awareness of this specialist service, together with vigilant collection of tissue samples by pathologists at autopsy (including for molecular studies), is key in the earlier detection and prevention of heritable cardiac conditions associated with lethal cardiac arrhythmias, thereby reducing overall SCD rates in Ireland.

P5

Acute Respiratory Failure in Multiple Myeloma due to Pulmonary Calciphylaxis and Organising Pneumonia: A Case Report

Ⓟ A McCarthy; J Nolan; K Murphy; A McNicholl; A Fabre

St. Vincent's University Hospital, Dublin, Ireland

We report a rare case of fatal pulmonary calciphylaxis with organising pneumonia in a 68 year old lady with known COPD who had been diagnosed 4 months previously with Kappa-light chain restricted multiple myeloma and had received 3 cycles of CyBorD regimen. On the day of presentation to the emergency department the deceased was on day 11 of cycle 1 of dendamustine.

She presented with increased anxiety and paranoia. Investigations showed an elevated CRP, white cell count, neutrophil count and calcium level. A chest xray showed multiple, new, ill-defined opacities in the left upper, right middle and right lower lobes of lung. The clinical impression was of psychosis secondary to infection. Intravenous antibiotics were commenced. After transfer to ICU for respiratory failure, there was worsening of respiratory function with subtotal right middle and lower lobe pulmonary collapse/consolidation with bronchiectasis, stable complete left lower lobe collapse and multifocal pneumonia within both upper lobes. Imaging showed extensive mixed lytic and sclerotic lesions consistent with the patient's history of multiple myeloma.

A sputum sample showed a pure growth of stenotrophomonas maltophilia. Despite resuscitation measures, the patient passed away.

At post-mortem examination, there were ill-defined, firm/solid areas replacing the lower zones of both lungs. Histology showed COPD with extensive pulmonary alveolar calciphylaxis located in alveolar spaces and in alveolar septae, with organising pneumonia. Calcifications also involved blood vessels. There was no evidence of acute inflammation/acute penumonia. Calcium deposition was also observed in other organs (heart, kidney, liver vessel walls). There was bone marrow hypercellularity with a diffuse infiltrate of malignant plasma cells, in keeping with myeloma Pulmonary calcification/ calciphylaxis is a rare complication of myeloma-related hypercalcaemia and has been reported to cause fatal respiratory failure.

P6

Colloid Adenocarcinoma of the Lung: A Case Report and Review of the Literature

Ⓟ O Wise; LE Donovan; A Bille; E Mclean

St Thomas' Hospital, London, UK

Primary mucinous (colloid) adenocarcinoma of the lung is an uncommon tumour, of which fewer than 100 cases have been published in the literature. We present a case of colloid adenocarcinoma of the lung in a 73-year-old woman. Macroscopically, the tumour was a uniloculated cyst containing thick mucus. On microscopic examination, the cyst was lined partly by atypical mucinous epithelium, and partly by benign ciliated columnar epithelium.

The most important issue for the pathologist is to distinguish whether these tumours represent a primary mucin-rich pulmonary neoplasm or a metastasis. The sites where similar tumours can arise include the gastrointestinal tract, ovary, pancreas and breast. Immunohistochemical staining of colloid adenocarcinoma is variable and may not be discriminatory. Therefore, clinical and radiological correlation remains vital in the management of such patients.

P7

Maximising the Diagnostic Yield and Utility of Pleural Fluid Specimens

AS Goodchild; Ⓟ R Gillibrand

North Middlesex University Hospital, London, UK

Purpose of the study: Clot preparations have become increasingly used in our department as an adjunct to standard cytological preparation. They are now made routinely for all pleural fluid specimens. The purpose of this study is to examine the role of the introduction of routine clot preparations in addition to standard preparations in the analysis of pleural fluid samples with respect to diagnostic yield, confidence, and suitability for ancillary testing.

Methods: Searches were performed of our cellular pathology reporting system using 'Cognos' software to identify all pleural fluid samples received in the last 6 years. The samples were identified using SNOMED codes which are routinely applied to all specimens on reporting. The resulting data was analysed with respect to method of preparation (i.e. with or without clot), diagnostic utility, and the use of ancillary tests including immunocytochemistry and additional specialist testing including mutation analysis.

Summary of results: Comparison of data from 2010 and 2016 shows the number of cases of pleural cytology increasing 4-fold from 48 per annum to 201. In 2010, 11 clots were made (23% of cases) whereas these were made for all cases in 2016. Immunocytochemistry was performed on 6 cases (13%) in 2010 increasing to 65 cases (32%) in 2016. The percentage diagnosed as malignant increased from 6% in 2010 to 25% in 2016. Nine cases had molecular testing in 2016, of which 3 were insufficient for analysis.

Conclusions: The introduction of clot preparations as a routine for pleural fluid analysis has increased the diagnostic utility of the sample.

The availability of material suitable for reliable immunocytochemistry has enabled more confident and reliable diagnosis with frequent confirmation of tumour subtype in malignant effusions. In addition, this material has also been shown to be suitable for additional specialist testing, an area which is of increasing importance in cancer therapy.

P8

An Audit of Endobronchial Ultrasound-Guided Transbronchial Needle Biopsy, St. Vincent's University Hospital

Ⓟ SC Prendergast; A Fabre

St Vincents's University Hospital, Dublin, Ireland

Purpose of the Study: Endobronchial ultrasound (EBUS) has good diagnostic accuracy for the investigation of mediastinal and hilar lymphadenopathy, both in malignant and non-malignant disease processes. We sought to review our numbers performed, the use of rapid on-site evaluation (ROSE), adequacy rates, and correlation with histology where appropriate over a one year period in a tertiary referral centre.

Methods: A retrospective audit was performed of all EBUS guided samples collected between January 2015 and December 2015.

Summary of Results: One hundred and sixty-eight (168) EBUS were performed on 83 female and 84 male patients (49.70% and 49.30%), a 44.83% increase since 2012 (116 patients), with 221 nodes in total sampled. ROSE was performed in 83.23% of cases. Adequacy was improved with ROSE (inadequacy 5.07% with ROSE, 7.14% without). In cases performed in the setting of suspected sarcoidosis (44) one was inadequate (2.27%), and 29 overall showed granulomas. In cases performed query malignancy (114) 7 were inadequate (6.14%), with 62 overall carried out for both diagnosis and staging (55.65%). Malignancy was diagnosed in 58 cases (34.73%) (primary lung adenocarcinoma 12%, primary squamous cell carcinoma 7.8%, small cell carcinoma 7.2%, non-small cell lung carcinoma NOS 1.8%, mixed small cell and squamous carcinoma 0.6%, extrapulmonary malignancy 5.4%) Fourteen cases went for molecular testing and 5 epidermal growth factor receptor (EGFR) mutations were detected. Twelve patients subsequently underwent mediastinoscopy of the same node, and/or lobectomy, with overall final histological of concordance was 71.43%.

Conclusions: EBUS is an efficient and well tolerated procedure that provides good diagnostic yield for sarcoidosis and suspected lung cancer, with increasing numbers being performed in our centre each year. It provides excellent adequacy rates particularly with the use of ROSE, and can provide sufficient material to allow for molecular testing.

P9

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

NJ O'Farrell; M Redmond; C Gulmann; Ⓟ CM Ryan

Beaumont Hospital, Dublin, Ireland

Purpose of the study: To assess the difference in adequacy and diagnostic rates between EBUS specimens with and without on site evaluation and to evaluate whether direct smears performed at ROSE added any diagnostic value to rinsed specimens(eg liquid based preparations and cell blocks).
Methods: A retrospective review was carried out on all EBUS transbronchial needle aspirates(TBNAs) during 2016. Reports were reviewed and all slides for aspirates in which granulomatous lymphadenopathy was suspected clinically were evaluated for the presence of lymph node content and granulomas, noting whether these were present on the direct smear, liquid-based preparation or cell block.
Summary of results: 44 TBNAs were performed for assessment of granulomatous lymphadenopathy with ROSE employed in 86% of cases (n=38). 77% of all aspirates were adequate for diagnosis(n=34), defined as the presence of lymph node content or granulomas. 84% of EBUS with ROSE were adequate, compared to 33% (2 of 6) in those without (p=0.0179). Diagnostic rates, defined by the presence of granulomas, were 17% without ROSE and 68% with ROSE (p=0.0254). Granulomas were identified in 66% of ROSE aspirates (n=25). In 11 of these, granulomas were not present at the time of ROSE on direct smears; rather they were identified later on rinsed specimens. In the remaining 14 cases granulomas were present on both direct smears and rinsed specimens.
Conclusions: ROSE appears to improve adequacy and diagnostic rates in EBUS TBNA although our study numbers were small and could not take account of potential confounding variables such as operator proficiency. However, while direct smears at ROSE allow adequacy assessment, they ultimately added no extra diagnostic information as all cases with granulomas on direct smear also contained granulomas within rinsed specimens. This suggests that the role of ROSE may become less important with increased operator proficiency as rinsed specimens provide all diagnostic information.

P10

How Much Influence Does Intra-Operative Frozen Section Core Biopsy Results Have on the Surgeon's Decision to Proceed with Lung Resection?

Ⓟ J Lai; A Alzetani; S Jogai

University Hospital Southampton, Southampton, UK

Purpose of study: Lung cancer is the third most common cancer in the UK with the incidence increasing over the last decade. With the advances of CT scanning, detection of lung nodules have been increasing. These lung nodules can either be benign or malignant. Tissue diagnosis on many occasions cannot be obtained except through intraoperative frozen sections (FS) core biopsies due to their small size or deep location and the information given by the pathologist will guide further surgical management (malignant: lobectomy; non-malignant: wedge resection). The objective of this audit is to examine the influence of FS core biopsies of suspicious lung lesions on the surgical decision to proceed to formal resection.
Methods: Reports of all resections coded under 'lung' and 'frozen section' from 2014 to 2015 in a tertiary hospital. FS of wedge excisions, mediastinal masses, lymph nodes, resection margins, paediatric cases, and cases with no FS reports recorded were excluded. The reports for FS of lung biopsies were then compared to the subsequent decision to proceed to a resection and if so the formal histology report of the resected specimens.
Summary of results: A total of 136 FS lung biopsies were examined. Of 25 FS biopsies reported as non-malignant, 22 (88%) cases proceeded to lobectomies, and 3 (12%) to wedge resections. In subsequent specimens, 16/22 (73%) lobectomies and 1/3 (33%) wedge resections had cancer. In total, 17 cases (68%) of biopsies reported as non-malignant had cancer in the subsequent resection. The sensitivity was 85%, specificity: 89%, positive predictive value: 99%, and negative predictive value: 32%.
Conclusion: Despite negative FS results, 88% of cases proceeded to lobectomies, indicating management was driven by strong clinical suspicion. Frozen section is a good technique, but we see from this audit that it serves mainly as a guide rather than a diagnostic tool for the surgeons

P11

An Audit of Histologically Diagnosed Malignant Mesotheliomas in Northern Ireland, 2012–2016

Ⓟ SM Hegarty; N Anderson

Royal Victoria Hospital, Belfast, UK

Northern Ireland has a history of heavy industry including ship-building and this may have a role in the ongoing numbers of malignant mesothelioma cases diagnosed. We present an audit of mesothelioma cases diagnosed by histology in the Royal Victoria Hospital, Belfast, the tertiary referral centre for thoracic surgery in Northern Ireland during the period 2012–2016.
Method: SNOMED codes for mesothelioma and its subtypes were used to search the pathology database to identify cases. The database was then searched for prior diagnostic cytology specimen details and the Electronic Care Record (ECR) yielded clinical information.
Results: 96 cases of malignant mesothelioma were diagnosed during the time period; 66 of these cases had prior cytology. More recently diagnosed mesotheliomas are less likely to have a pre-existing malignant diagnosis on cytology. The majority of cases were described as epithelioid with smaller numbers of biphasic and sarcomatoid subtypes. There were 17 female and 79 males patients with an age range between 54 and 91 years of age at the time of diagnosis. There was a documented history of asbestos exposure in 67 patients; 15 had no documented exposure while in 14 it was not possible to access this information from ECR. The majority of cases originated in the Greater Belfast area, probably reflecting the site of heavy industry.
Conclusion: Newly diagnosed cases of malignant mesothelioma appear to remain relatively consistent in our centre. The cases diagnosed histologically more recently are less likely to have a cytological diagnosis. We postulate that this is a reflection of increasing familiarity and confidence in cytology together with increasing use of liquid based techniques and immunocytochemistry as an adjunct to diagnosis. The demographic profile and history of asbestos exposure in our cohort is consistent with the expected for this malignancy.

P12

Invasive Micropapillary Carcinoma of the Breast Displaying Immunohistchemical Envidence of Epithelial-Mesenchyimal Transition

Ⓟ KU Adoke

Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

Purpose of study: Invasive micopapillary carcinoma of the breast is a morphologically distinctive form of ductal carcinoma in which the tumour cells are arranged in morule-like cluster. The reported age ranges from 36-81 years. The tumour cells are arranged in small clusters that may have a serrated outer border, a central lumen is usually present. Invasive micropapillary carcinoma of the breast display tendency towards lymphovascular invasion and lymph node metastasis hence imparts a poor prognosis compared to other breast cancers. These finding are in keeping with micropapillary carcinomas reported in other organs like the ovary, endometrium and bladder. Epithelial mesenchymal transition (EMT) can occur in some carcinomas in which carcinoma cells downregulate certain epithelial markers eg E- cadherin and upregulate certain mesenchymal markers eg vimentin and smooth muscle actin (SMA) which is believed to favour metastasis. We present a 46 year old female who presented with right breast swelling for a year with histological diagnosis of invasive micropapillary carcinoma of the breast and evidence of EMT.
Methods: Seven immunohistochemical markers based on Genemed Biotechnology Protocol was adopted. The antibodies used include (ER, PR, HER2, EMA, CYTOKERATIN, EPITHELIAL MEMBRANE ANTIGEN, E-CADHERIN and VIMENTIN).
Summary of results: Immunoreactivity was present in ER (65%), PR (50%) and HER2 (35%). Immunohistochemical stain for EMA stained the cell membrane of the tumour clusters and border of the lumen. Loss of E-cadherin expression is seen in some clusters of invasive micropapillary carcinoma with decrease expression of AE1/AE3 in some clusters of cells. Vimentin is however expressed in numerous clusters of cells.
Conclusion: This case has demonstrated that invasive micropapillary carcinoma of the breast like other micropapillary carcinomas elsewhere that exhibit increased rate of lymphovascular invasion and nodal metastasis may be using EMT mechanism.

P13

Invasive Lobular Carcinoma (ILC) Typing by E-Cadherin Immunohistochemistry (IHC) in Non-Operative Breast Needle Core Biopsy — A Service Evaluation Study of 89 Cases from the Breast Unit, Belfast City Hospital, Belfast Health and Social Care Trust

Ⓟ A Ben-Mussa; T Lioe

Belfast Health and Social Care Trust, Belfast City Hospital, Belfast, UK

Introduction: Needle core biopsy (NCB) with or without fine needle aspiration cytology is the non-operative breast cancer diagnostic standard prior to definitive surgical or neo-adjuvant treatment. In our centre a NCB diagnosis of ILC triages most patients for MRI scanning to precisely determine tumour size, multifocality and contralaterality which may influence patient surgical management. Although accurate tumour typing based on H&E alone is mostly achievable, however, not infrequently some overlap of ductal and lobular features is encountered and thus E-Cad IHC is employed to confirm a lobular phenotype. This study investigates E-Cad utility for tumour typing and follow-up of surgical outcomes while bearing in mind reported aberrant staining by Canas-Marques and Schnitt (2016).
Method: All NCBs of breast cancers performed in 2014 with E-Cad IHC requested for lobular variant confirmation were retrieved from our records.
Results: 89 NCBs had E-Cad IHC. 40/89 (44.9%) had typical lobular features and of those 39/40 (97.5%) were E-Cad negative. Of those who had primary excision 15/30 (50%) had a total mastectomy as first treatment. The single E-Cad positive ILC NCB turned out to be a mixed ductal and lobular carcinoma (MDLC) on excision. 46/89 (51.7%) were designated as mixed ductal and lobular features (MDLF) and only 4/46 (8.7%) were E-Cad negative. Of those who had primary excision 15/41 (36.6%) had a total mastectomy. Of the E-Cad negative NCBs diagnosed as MDLF, three turned out to be MDLC on excision and one was not suitable for surgery.
Conclusions: 97.5% of NCBs diagnosed as typical lobular on H&E were E-Cad negative. Following MRI scans, half of these patients who had surgery had a total mastectomy as first treatment. Conversely, majority of those with a NCB diagnosis of MDLF on H&E were E-Cad positive and just over 60% were amenable for initial conservative surgery.

P14

Continuation Audit of Hormone Receptor Status in Breast Cancer Cases: Comparison of Immunohistochemistry Versus Oncotype Dx Results, January to June 2015

Ⓟ R McGrath[1]; Y McCartney[2]; M Kennedy[2]; S Conlon[2]

[1]Beaumont Hospital, Dublin, Ireland; [2]Mater Misericordiae University Hospital, Dublin, Ireland

Purpose of the Study: For cases of primary breast carcinoma diagnosed in our institution and referred for Oncotype DX testing from January to June 2015, the aim of this audit was to:
1. Determine the concordance between ER, PR, and Her-2 status as determined by:
a. Immunohistochemistry +/- in situ hybridisation (IHC/ISH), and
b. Oncotype DX testing
2. Compare the above concordance rates with those demonstrated in a previous 2013 audit in our institution.
Methods: The study included all 49 cases of primary breast carcinoma diagnosed in our institution from January to June 2015 that underwent Oncotype DX testing. The ER, PR, and Her-2 status of each as determined by both IHC/ISH and by Oncotype DX testing were recorded and compared.
Results: Our study demonstrates concordance rates of 98.0%, 83.7%, and 100% respectively for ER, PR, and Her-2 status as determined by IHC/ISH versus Oncotype DX testing. Comparing these concordance rates with those found in the previous 2013 audit in our institution (96.5%, 90%, and 98.5% for ER, PR, and Her-2 status respectively) reveals similar figures for ER and Her-2 concordance. A decrease in PR concordance is seen in this study compared to the 2013 study. Concordance rates reported to date in the literature for ER range from 91 – 99%, for PR range from 88 – 94%, and for Her-2 range from 97 – 99%. Our ER and Her-2 concordance rates are slightly higher than this range, and our PR concordance rates slightly below this range for the period of January to June 2015.
Conclusions: In our institution, high concordance rates were found when using IHC/ISH versus Oncotype DX testing to determine ER, PR, and Her-2 expression within breast carcinoma cells. ER and Her-2 concordance rates were slightly higher than published figures, while our PR concordances rates were slightly less than published figures. This may relate to sample size.

P15

Collision Tumour of Primary Breast Carcinoma and Metastatic Pulmonary Adenocarcinoma: A Unique Case

Ⓟ N Tchrakian; J Crown; A Fabre; C D'Arcy

St. Vincent's University Hospital, Dublin, Ireland

Extra-mammary metastasis to the breast is rare, and fewer than forty cases of pulmonary metastasis to this site have been reported in the literature. We describe the first case, to our knowledge, of a 'collision tumour' between a primary breast cancer and a metastatic adenocarcinoma of primary lung origin.
A 77 year old woman presented to the symptomatic breast service in our institution in July 2016. Imaging revealed two discrete lesions in the left breast, 13mm and 4mm in size, less than 10mm apart. Core biopsies showed two tumours; the first (larger), a grade 2 invasive ductal carcinoma with conventional morphology, oestrogen receptor (OR) positive, HER-2 negative. The second (5mm) was a grade 1-2 adenocarcinoma, OR, progesterone receptor (PR), HER-2 negative, and was considered to show apocrine/histiocytoid morphology, possibly representing a special variant of basal-type triple-negative breast cancer. A wide local excision confirmed both tumours - the larger was associated with ductal carcinoma in situ (DCIS), while the smaller was not. A diagnosis of invasive ductal carcinoma, grade 2 was assigned, pathological stage pT2 (m) N0 (sn). The case was discussed at multidisciplinary team (MDT) meeting; no further clinical information or imaging outside the breast was available at this time.
After a traumatic fall four months later, a CT scan revealed a 4.1cm left upper lobe lung mass, in addition to multiple smaller bilateral pulmonary nodules, several soft tissue and bone lesions, and a hepatic metastasis. Immunohistochemistry was then performed on the smaller breast tumour, which was strongly TTF-1 and Napsin positive. On review, this was felt to represent a pulmonary metastasis to the breast.
This case demonstrates a rare example of a metastasis to the breast situated adjacent to a true primary breast carcinoma. Herein we discuss the challenges and pitfalls in the unusual setting of extra-mammary metastases to the breast.

P16

The Relationship of HER2 Copy Number Evaluated by Brightfield Dual In Situ Hybridisation DNA Assay and Pathologic Response to Neoadjuvant Treatment in HER2 Positive Breast Cancer

Ⓟ G Neville; L Feeley; MW Bennett; S O'Reilly; M Corrigan; F O'Connell; TJ Browne

Cork University Hospital, Cork, Ireland

In HER2 positive breast cancer data on whether tumour response to neoadjuvant treatment correlates with HER2 copy number is limited. This study aims to evaluate the relationship between HER2 copy number assessed by Brightfield Dual in situ hybridization DNA assay (DISH) and response to neoadjuvant treatment in a HER2 positive breast cancer cohort.
Neoadjuvant treated breast cancer cases were identified over a 62 month period. Hormone receptor and HER2 status were obtained for each case. Testing was using Ventana 4B5 immunohistochemical (IHC) assay and DISH using Ventana Inform Assay. Average HER2 copy number was categorized as low (<6 copies per cell), intermediate (6-12) and high (>12). Pathologic response to treatment was evaluated and residual cancer burden (RCB) class (complete pathologic response (pCR), RCB1, RCB2 and RCB3) generated using an online tool (MD Anderson Cancer Centre algorithm).
123 cases were identified. Biomarker profiles were as follows: Hormone positive, HER2 negative: 52.8%; Hormone positive, HER2 positive: 19.5%; Hormone negative, HER2 positive: 14.6%; Triple negative: 13%. Cases were categorised as pCR (14.6%), RCB1 (6.9%), RCB2 (36.9%) and RCB3 (41.5%). Results for combined pCR and RCB1 groups were: Hormone positive, HER2 negative: 10.8%; Hormone positive, HER2 positive: 33.3%; Hormone negative, HER2 positive: 44.4%; Triple negative: 18.8%. In addition to IHC, DISH for HER2 was available for 39 of the HER2 positive group (including IHC equivocal (2+) and positive (3+) cases). Of these HER2 positive cases, 15 showed pCR or RCB class I. Breakdown for HER2 copy number was high (n=7; 46.6%), intermediate (n=6; 40%), low (n=2; 13.3%); Tumour response in 24 cases was classified as RCB2 or RCB3. Breakdown for HER2 copy number was high (n=12; 50%), intermediate (n=8; 33.3%) and low (n=4; 16.7%).
In this study HER2 positivity correlates with highest frequency of complete or near complete pathologic response however HER2 copy number does not appear to correlate with extent of pathologic response.

P17

Primary Mesenchymal Breast Tumours: A Diagnostic Spectrum

Ⓟ G Neville; L Feeley; MW Bennett; F O'Connell; N Relihan; A Ashraf; TJ Browne

Cork University Hospital, Cork, Ireland

Mesenchymal tumours of the breast parenchyma are a rare and diverse group and may be diagnostically challenging on core needle biopsies (CNB). The aim of this study was to evaluate clininopathologic parameters of malignant primary breast mesenchymal tumours and their mimics.
Methods: The database at a single large academic centre with a large subspecialised screening and symptomatic breast practice (> 600 primary breast cancer diagnoses annually) was searched for all spindle cell tumours diagnosed on (CNB) with a corresponding excision performed in the same institution over a 5 year period. Morphologic features and immunohistochemical profile were evaluated for each case.
Results: Benign primary breast mesenchymal neoplasms included as follows: nodular fasciitis (3), deep fibrous histiocytoma (1), myofibroblastoma (1), desmoid fibromatosis (3), granular cell tumor (4), neurofibroma (2) leiomyoma (1) and benign (15) and borderline phyllodes (4). There were 24 cases with a diagnosis of malignant spindle cell tumour identified over this time period. Definitive diagnosis was achieved on excision in all cases. Malignant diagnoses included 4 angiosarcomas (all radiation- associated), 1 pleomorphic sarcoma (NOS), 1 leiomyosarcoma, 5 high grade phyllodes tumours (4/5 with liposarcoma), 13 metaplastic carcinomas (5/14 matrix producing, 5/14 with malignant heterologous elements). Mean age for malignant spindle cell tumours was 54.4 years (range 32-82), average tumour size 3.9cm (range 0.7cm-11cm). 13/24 received chemotherapy. Average follow up was 31.3 months (range 6-72 months). 6/24 died of disease including 2 angiosarcoma, 1 leiomyosarcoma, 3 metaplastic carcinomas (2 cases with 2 malignant heterologous elements and 1 case with SCC).
This study evaluates the clinicopathologic features, differential diagnosis and morphologic spectrum of a series of primary malignant spindle cell neoplasms of breast in large academic breast pathology practice.

P18

BRCA1 Immunohistochemistry in Invasive Breast Carcinoma in a Cohort with Known BRCA Germline Mutational Status

Ⓟ GJ Neville; D Power; TJ Browne

Cork University Hospital, Cork, Ireland

BRCA1 and BRCA2 dysfunction resulting from germline mutations, somatic mutations and promoter methylation are known to occur frequently in breast and ovarian cancers. Identification of tumours with BRCA defects has therapeutic and prognostic implications. Our goal was to assess whether immunohistochemical analysis (IHC) for BRCA1 is an effective method for the detection of BRCA1 dysfunction. 21 patients whose germline BRCA status had been assessed met our inclusion criteria. 37 specimens from this cohort were evaluated histopathologically and with BRCA1 immunohistochemistry by two pathologists blinded to germline BRCA status. Presence of retained BRCA staining was considered normal whereas the other patterns (equivocal or loss of staining) was considered abnormal. The pathologists agreed 81.1% (30 of 37 cases) of the time. All discordant results were between equivocaland positive/negative. The 7 discordant cases were then reviewed by the pathologists and consensus was reached. BRAC1 patients; mean age 44.24, 100% Grade 3, Predictive markers: 86.67% triple negative, 6.67%triple positive, 6.67%ER pos/Her2 neg. BRAC2 patients: mean age 51.15, 61.5% Grade 3, Predictive markers: 15.4% triple negative, 15.4% triple positive, 46.1% ER pos/ Her2 neg. BRAC Neg patients: mean age 42.9, 44.4% Grade 3, Predictive markers: 22.2 % triple negative, 77.8% ER pos/Her2 neg. Of 15 cases with a known BRCA1 germline mutation, 5 showed normal (retained) staining and 10 showed abnormal staining (8 lost, 2 equivocal). Of 13 cases with a known BRCA2 germline mutation, 10 were retained and 3 showed abnormal staining (2 lost, 1 equivocal).
Of 9 BRCA negative cases, 6 were retained and 3 were lost. Retention of BRCA1 staining in 33.33% of cases with confirmed BRCA1 germline mutation suggests this stain may not be sufficiently sensitive to detect all BRCA1 mutations. Its loss in 4 cases that did not have a germline mutation for BRCA1 may be due to somatic or promoter methylation changes

P19

BRCA1/2 Testing and/or Further Genetic Assessment Scoring Sheet: A Useful Clinical Tool

Ⓟ RF Abduljabbar

Azadi Teaching Hospital, Duhok, Iraq

Purpose of the study: Genetic assessment including testing for BRCA1/2 is an integral part of the management of Breast Cancer and other malignancies including ovarian, pancreatic, and prostatic cancers. The NCCN guidelines outlined the indications for the BRCA testing/further genetic assessment in its publication (Breast Cancer Risk Reduction v1 16 December 2016). The indications are not easily memorisable. We aimed at re-organising these indications in a scoresheet that clinicians can better comprehend and apply it in practice.
Methods: The indications are categorised into three levels. Points are assigned to each indication so that a total score of 10 or more indicating further genetics assessment.
Summary of the Results: The scoresheet has two main compartments. One for patients with cancer and one for those without.
In the first compartment, ovarian cancer, male breast cancer and BRCA1/2 mutation by tumour profiling as assigned 10 points each and are indications for the test on their own (Level 1 indication). Sub-indications for other tumours were assigned 5 points each (Level 2 indication). In such scenario, Female BC has 5 points and the age of <45 of the patient has further 5 points so any BC patient under the age of 45 will be required to test for BRCA1/2 mutation. If Level 2 indication has further requirements (Level 3 indications) then further details are given 5 points each. E.g BC patient's age is less than 50 and has a close blood relative with a BC at any age.
Conclusion: The BRCA1/2 testing scoring sheet is an easy clinical tool that can be utilised to direct the patients to the required genetic assessment if it is necessary.

P20

Optimising Our 2+ / FISH Rate in HER2 Testing in Breast Cancer: A Prospective Audit

Ⓟ K Quiohilag; JF Loane

Western General Hospital, Edinburgh, UK

Assessment of human epidermal growth factor 2 (HER2) status is mandatory in all cases of invasive breast cancer as overexpression of HER2 is associated with a poor prognosis, but also with response to targeted anti-HER2 therapy. Immunohistochemistry (IHC), the first line test, can be challenging to interpret.
In our department we use fluorescent in-situ hybridisation (FISH) in the ~22% cases equivocal (2+) on IHC. One pathologist prospectively allocated his HER2 2+ cases into likely negative (2neg), equivocal (2equiv), and likely positive (2pos) groups, between mid-July 2014 and mid-January 2016, following which these groups were audited, their IHC characteristics critically reviewed and their results compared to the outcomes on FISH testing. Over this 18 month period 233 HER2 2+ cases were allocated, 115 (49.4%) into the 2neg group, 70 (30%) to the 2equiv group and 48 (20.6%) to the 2pos categories. 109 cases (94.8%) in the 2neg group were negative on FISH. Of the cases in this group which were amplified on FISH all were in the borderline positive range (ratio <2.2). 41/48 cases (85.4%) of cases in the 2pos group were positive on FISH testing. Of the 70 cases in the 2equiv group 53 (75.7%) were negative by FISH, while 17 (24.3%) were positive. We detail the IHC expression characteristics associated with each of the three groups and predict that at FISH rate of between 12 and 15% of cases is achievable based on the results of this prospective audit.

P21

Malignant Adenomyoepithelioma of the Breast with Lung Metastases and an Unusual Immunophenotype

TJ Kueh; Ⓟ GM Laing; ID Miller; KM Kerr; Y Masannat; K Buchan; E Husain

Aberdeen Royal Infirmary, Aberdeen, UK

Adenomyoepithelioma of the breast is a rare tumour characterised by a biphasic proliferation of epithelial and myoepithelial cells and is usually benign. Malignant transformation is uncommon and can be attributed to one or both components. Metastatic potential is considered low and usually follows a haematogenous route with a predilection for the lungs. A 35 year old woman presented with pain and swelling of her right breast associated with nipple discharge. Examination revealed a tender indurated area. An ultrasound scan showed an indeterminate lesion with a small satellite nodule and cytology revealed malignant epithelial cells. Core biopsy showed sheets of atypical cells surrounded by hyalinised fibrous tissue and focal fibroblastic stroma. Immunohistochemistry suggested a dual cell population of epithelial and myoepithelial cells, and due to the high mitotic count, was suspicious of malignancy. Excisional biopsy revealed a partly solid and cystic lesion. Histologically the tumour was composed of a dual population of atypical cells arranged in sheets and cords set in a fibroblastic stroma. Mitotic figures were readily identified and there were areas of necrosis. Immunohistochemistry was unusual. The epithelial and myoepithelial cells stained conventionally with CAM5.2 and basal cell markers respectively. However CK5/6 and CK14 exhibited a heterogeneous staining pattern. Focally staining was inverted with epithelial cells showing positivity and myoepithelial cells apparently negative. A diagnosis of malignant adenomyoepithelioma was made which was fully excised. A CT scan showed right lung nodules which were resected and exhibited similar features, including this unusual immunophenotype. Malignant adenomyoepithelioma of the breast is a rare tumour with poorly understood biological behaviour. Our case highlights important variations in immunophenotype compared to previously described cases, acting as a reminder of the heterogeneous nature of this neoplasm.

P22

Activated p38 MAPK and its Downstream Molecule p-ATF-2 are Associated with Good Prognosis in Breast Cancer

DAJ Ahmad; Ⓟ A Ammar; MA Aleskandarany; C Nolan; M Deiz-Rodriguez; IO Ellis; E Rakha

University of Nottingham, Nottingham, UK

Purpose of the study: Limited information is available regarding the prognostic significance of total versus activated forms of p38 expression and its relationship with its downstream mediator ATF-2. Expression of total and phosphorylated (p-) p38 and p-ATF-2 in the different molecular classes of breast cancer (BC) and their prognostic significance are addressed.
Methods: 1335 primary invasive BC samples from patient treated in Nottingham University Hospital (1989-1998), were stained with pan-p38, p-p38 and p-ATF-2 antibodies using immunohistochemistry. Associations between protein expression and different clinicopathological variables and patients' outcomes were investigated with P<0.05 defining statistical significance.
Summary of results: Cytoplasmic pan-p38, cytoplasmic/nuclear p-p38 and nuclear p-ATF-2 were observed in invasive BC tissues. Pan-p38/nuclear p-p38 were negatively associated with tumour size, grade, stage, mitosis, Ki67, while positively associated with ER/PgR status, and the luminal subtype. Pan-p38 was also associated with Her-4 and p53 mutations. p-ATF-2 was associated with pan-p38/p-p38, grade, mitosis, NPI, ER/PgR/Her-2 status and molecular subtypes. In luminal BC, nuclear p-p38 expression maintained significant associations with age, grade, nodal stage, mitosis, VI, Her-4 and Ki67. In Her-2 positive tumours, nuclear p-p38 was significantly associated with ER/PgR status. High p-p38 and high p-ATF-2 prognosticated prolonged BC specific survival with only p-ATF-2 being independent of other factors (P=0.004, HR=0.695, 95%CI=541-0.891). Only high p-ATF-2 was an independent predictor of prolonged distant metastasis free survival, (P=0.002, HR=0.694, 95%CI=0.549-0.877). Neither pan-p38 nor p-p38 showed prognostic significance in any of the molecular subtypes.
Conclusion: High p-p38 and p-ATF-2 in primary BC associate with hormone receptor status and good prognosis. Activation of p-38/p-ATF-2 in BC molecular classes requires further investigation

P23

The Impact of Heterogeneity on Risk Stratification in DCIS

Ⓟ PT Elliott[1]; LJ Jones[1]; P Makhija[2]

[1]Barts Cancer Institute, London, UK; [2]Royal London Hospital, London, UK

Introduction: The LORIS trial seeks to compare surgery versus monitoring by yearly mammograms for "low-risk" ductal carcinoma in situ (DCIS). This audit reviewed biopsy cases suitable for inclusion into LORIS, and the corresponding diagnosis on excision, to determine accuracy of biopsy diagnosis.
Aims: To determine the number of cases suitable for entry into the LORIS trial over 5 years at Barts NHS Trust. To correlate biopsy diagnosis with diagnosis at excision, and to determine the number of cases with higher grade of DCIS or invasive carcinoma on excision.
Methodology: A search for all biopsy cases coded with a diagnosis of B5a was performed at Barts NHS Trust covering a period of 5 years. Manual review of the pathology report was conducted to exclude the following:
1. Cases defined as "high-risk" DCIS by the LORIS trial entry criteria.
2. Specimen errors: miscoding (B4, B5b), lymphnode biopsy, non-biopsy cases etc.
3. Cases of paired biopsies where one biopsy had a "high-risk" or invasive diagnosis.
Slides for all cases were reviewed by two consultant pathologists to verify diagnosis. The corresponding excision specimen pathology reports were reviewed and correlated to biopsy diagnosis, with excision specimens categorised as: Downgraded (no DCIS seen), Same Grade (low-risk DCIS), Upgraded (high-risk DCIS or invasion), or No Follow Up (no excision specimen found).
Results: 101 biopsies meeting the criteria were identified. 17 were excluded. 12 had No Follow Up. Of the remaining 63, 6 (9.5%) were downgraded, 25 (39.7%) had the same grade, 32 (50.8%) were upgraded (14 (22.2%) to High risk DCIS, 1 (1.6%) microinvasion, and 17 (27%) invasive cancer).
Conclusions: Over half of the biopsies assessed were upgraded on excision, with 18 (27.6%) having a focus of invasive cancer. This suggests that methods for risk stratification of DCIS within the context of the LORIS trial are inadequate.

P24

Breast FNAC Practice in South West London Pathology — A Review

Ⓟ R Haria; C Beggan

St Georges Healthcare NHS Trust, London, UK

Background: Breast cancer is the most common cancer in females in the UK accounting for approximately 15% of all new cancer cases. The pathologic diagnostic assessment of breast lesions involves Fine needle aspiration cytology (FNAC) and/or Core needle biopsy (CNB). The benefits of FNAC over CNB include lower cost, quicker turn-around times, a less invasive procedure and a lower complication rate. We audited Breast FNAC practice in our institution over a single year. We aimed to examine the diagnostic rates with comparison to nationally acceptable standards and implement changes in practice if our results were at variance with these standards.
Method: A retrospective review of Breast FNACs performed over period of one year was undertaken. The National 'Guidelines for non-operative diagnostic procedures and reporting in breast cancer screening' were used as a standard.
Results: A total of 331 cases were included in our study. In 22% CNB was also performed on the same day. 'C' category distribution was as follows: C1 39%, C2 36%, C5 and C4 6%. Follow-up histology was available for 120 allowing calculation of diagnostic accuracy in these cases (97.5% negative predictive value for C2, 4.5% false negative rate for C2, 100% positive predictive value for C5).
Conclusion: FNAC has a role to play in the triple assessment of breast lesions. 66% of the cases were diagnostic by FNAC and, where data was available; there was good concordance between FNAC and CNB/ surgical excision. Our institutional inadequate rate is high overall, however, when adjusted to account for cystic aspirations and aspirations converted to core biopsy, is within the acceptable minimum range. Audit of clinical outcomes in these C1 cases is warranted.

P25

Clinicopathological Characteristics of Triple Negative-Basal Breast Cancer: A Comparative Study Between Egyptian and British Patients

RAA Mohammed[1]; H EL-Deek Mohamed[2]; A Green[3]; Ⓟ MA Aleskandarany[3]; IO Ellis[3]; E Rakha[3]

[1]Department of Pathology, Faculty of Medicine, Assiut University and Taibah University, KSA, Assiut, Egypt; [2]Department of Pathology, Faculty of Medicine, Assiut University, Assiut, Egypt; [3]Academic Pathology, Division of Cancer and Stem Cells, School of Medicine, University of Nottingham, Nottingham, UK

Purpose of the study: Triple negative-basal breast cancer (TN-Basal BC) in Western and European women have been extensively studied. Comparatively, less is known about those tumours in patients from the North African region. The aim of this study was to compare clinicopathological characteristics between Egyptian and British patients.
Methods: Tissue microarray blocks were constructed from invasive primary breast cancer from 836 patients [336 Egyptian (age ranged from 20 to 90, mean 48 year) and 500 British (age ranged from 18 to 72, mean 54 year)]. Sections were stained immunohistochemically with oestrogen receptor (ER), progesterone receptor (PR), HER2, CK19, CK14, EGFR1, CK5/6, P53 and Ki67 following the standard protocols. TN-Basal phenotype was identified by lacking of staining for ER, PR, HER2 and positive staining for any of the CK14, CK5/6 and/or EGFR1.
Summary of results: TN-Basal BC rate was higher in Egyptian cohort (22%) compared to 13% in the British cohort. TN-Basal tumours from both Egyptian and British patients were significantly associated with tumours of larger size (P=0.035 and P=0.005), higher histopathological grade (P<0.001 and P<0.001), higher proliferation rate (P<0.001 and P=0.001), and higher rate of P53 expression (P<0.001 and <0.001) respectively. Both groups did not show significant association with the presence of lymph node (LN) metastasis, tumour stage or presence of vascular invasion (VI). Compared with the British tumours, TN-Basal tumours from Egyptian women were significantly associated with younger patient age (P=0.002), larger size (P<0.001), higher rate of LN metastasis (P<0.001) and are of more advanced clinical stage(P<0.001).
Conclusions: TN-Basal BC is more frequent in Egyptian patients compared with British women and are characterised by unfavourable biological features. These warrant further studies to unravel the genetic background of TN-BC in non-white population for the importance of identification of this tumour subtype.

P26

Impact of Molecular Screening by Next Generation Sequencing on Management of Patients with Thyroid Nodules

Ⓟ S Bouri; M Le Mercier; L Lebrun; I Salmon; N D'Haene

Erasme Hospital, Université libre de Bruxelles, Brussels, Belgium

Background: Managing thyroid nodules is a common clinical problem. Fine needle aspiration (FNA) followed by cytological assessment is the predominant method used to differentiate benign nodules from malignant nodules. However, 10 to 26% of the nodules are classified as indeterminate. Currently, as this category is associated with a 20% to 30% incidence of malignancy, patients are referred for surgery. We previously developed a grading system for indeterminate FNA diagnosis associated with an increased risk of malignancy (RM) (G1 to G3 with a RM of 7.7 to 45.7%). In recent years, some studies have shown that detecting genetic alterations in FNA samples improves the cytological diagnosis and could avoid unnecessary surgeries. In the present study, we evaluated the impact of clinical data and molecular data obtained by targeted next generation sequencing (NGS) on the management of patients with indeterminate cytology.
Methods: We retrospectively analysed 158 patients with an indeterminate FNA for which surgical resection was performed. DNA obtained from smears or cell blocks was subjected to an NGS panel targeting mutations in 50 cancer-related genes. In addition, clinical data and US features were collected.
Results: The RM in this series of indeterminate FNA is 31%. Three variables are associated with an increased risk of malignancy: 1) the presence of anti-thyroid antibodies in the serum (RM=48%, p=0.02), 2) a G3 cytological diagnosis (RM= 76.9%, p=0.0009), and 3) a positive molecular test (RM=54.8%, p=0.00003).
Conclusion: Molecular screening by NGS increases the diagnostic accuracy of indeterminate FNA and could be integrated into the management of patients with a thyroid nodule.

P27

This abstract has been withdrawn

P28

The Comparison of DNA Quality and Integrity Between PAXgene and Formalin Fixed, Paraffin Embedded Tissues

Ⓟ R Lees; E Shaw; SJ Reilly; K Bodey; M Machado; M Ashton-Key

University Hospital Southampton NHS Foundation Trust, Southampton, UK

Purpose of the study: The STRATFix consortium is an Innovate UK funded academic and industrial collaborative project between Qiagen and NHS pathology based teams in Southampton, Birmingham, London (St Thomas' and University College London/ Stanmore), Glasgow, Papworth and Belfast. A major aim of the project is to determine what improvements in the preservation of nucleic acids can be obtained using the PAXgene Tissue system, a formalin-free fixative, in comparison to formalin fixation.
Methods: DNA was extracted from 18 paired tumour samples, of PAXgene fixed (PFPE) and formalin fixed (FFPE), paraffin embedded tissue. DNA purity and concentration in ng/µl was assessed using the NanoDrop® ND-1000. Double stranded DNA was quantified in ng/µl, using the Qubit® 3.0 fluorometer. Results were assessed with the paired student's t-test. DNA fragmentation was assessed using the BIOMED-2 control gene PCR protocol with an additional custom 600bp primer. The PCR results were analysed with Applied Biosystems GeneMapper® 4.1 and semi-quantified, peaks being scored as strong, weak or no signal present.
Summary of results: There was no significant difference in Nanodrop DNA concentrations. Qubit analysis demonstrated a significant difference indicating improved dsDNA nucleic acid preservation. PFPE samples provide superior preservation of DNA with strong signals for all samples for primers up to 400bp, at 600bp 10/18 showed a strong and 8/18 a weak signal. In comparison, FFPE samples only provided a strong signal for all samples up to 300bp; at 400bp primer 5/18 gave a strong signal, 7/18 a weak signal and 6/18 no signal; 600bp primer demonstrated a weak signal for 1 case and no signal in 17.
Conclusions: PAXgene provides superior DNA preservation compared to formalin fixation. This is could provide improved molecular diagnostics in downstream applications. Further investigations include the assessment of PFPE in next generation sequencing as part of the 100,000 Genomes Project.

P29

Cten May Stimulates Cell Motility and Tumour Metastasis Through ROCK1 Signaling in Colorectal Cancer

Ⓟ A Asiri; M Ilyas

Division of Pathology, School of Medicine, University of Nottingham, Nottingham, UK

Objectives: C-terminal Tensin-like (Cten) is an oncogene which promotes cell motility and colony formation in colorectal cancer (CRC). It is a focal adhesion protein that play important roles in signal transduction and cytoskeletal reorganization. Rho-associated kinase 1 (ROCK1) is a protein serine/threonine kinase which regulates the actomyosin cytoskeleton and participates in several biological events cell motility, epithelial-to-mesenchymal transition (EMT) and tumour metastasis. Cten have been shown to directly interact with DLC1, a known tumour suppressor that regulates cell adhesion and actin stress fibre assembly through downstream inactivation of RhoA and ROCK. We hypothesized that Cten may induces cell motility and tumour metastasis through ROCK1 signaling.
Methods: Cten was forcibly expressed and knocked-down in the CRC cell lines HCT116, SW620, and SW620ΔCten respectively. In addition, ROCK1 was knocked-down following Cten forced expression. The functional effect of Cten/ROCK1 modulation was then investigated.
Results: Through forced expression of Cten and knockdown of Cten/ROCK1 in HCT116, SW620, and SW620ΔCten, we showed that Cten could regulate ROCK1 signaling pathway. Functionally, forced expression of Cten levels were significantly induced both cell motility and colony formation, whereas knockdown of ROCK1 after Cten forced expression inhibited both cell motility and colony formation in CRC cells, thereby demonstrating that the Cten-ROCK1 interaction was functionally relevant.
Conclusion: We are the first study identifying a novel Cten-ROCK1 signaling pathways which induces cell motility, EMT and may contributes tumour metastasis in CRC.

P30

Detection of Mutant Circulating Free DNA as a Biomarker of Colorectal Cancer

Ⓟ AA Asiri; JH Hassall; HHK Ham-Karim; HE Ebili; WF Fadhil; ON Ng; PF Fardouly; AA Acheson; MI Ilyas

University of Nottingham, Queens Medical Centre, Nottingham, UK

Introduction: Tumour cells release cellular contents into the bloodstream as a consequence of necrosis and apoptosis. These circulating free (cf) contents have potential as cancer biomarkers. High resolution melting (HRM) is relatively simple and sensitive screening method used to detect the variations within the nucleic acid sequences. We aimed to develop a robust methodology to screen for mutant tumour-derived cfDNA as a noninvasive diagnostic marker for colorectal cancer.
Methods: Blood from 25 patients with colorectal cancer was collected immediately pre-operation and daily post-operation (until discharge). The cfDNA was extracted within 1 hour of venesection. A protocol for COLD-HRM (a combination of COLD-PCR and HRM) was optimized for exon 2 of KRAS (which contains the hotspots of codon12 and 13) and used to screen the cfDNA for mutations. Subsequently, tumour DNA was obtained from the matched formalin-fixed paraffin embedded resection specimen and screened for KRAS exon 2 mutation. Mutations were validated by Sanger.
Results: The optimised COLD-HRM protocol resulted in a limit of detection of 0.75% frequency of mutant alleles. Screening analysis of the cfDNA revealed mutations in 12 (48%) cases and whilst 9 (36%) of the matched tumours were found to harbour mutations. As expected, mutations occurred in codon G12D and G13D and the mutations in cfDNA matched the mutations in the resections. In three cases, KRAS mutation detected in cfDNA could not be detected in matched FFPE tumour. Overall, the concordance in cfDNA and matched tumour samples of mutations was 75% (9/12) with sensitivity (100%) and specificity (81%).
Conclusion: Detection of mutations in cfDNA is a good means of non-invasive screening for colorectal cancer and COLD-HRM is a sensitive method of detection. A panel of genes would be required to increase the sensitivity of the this test.

P31

Alk Immunohistochemistry in Epithelioid Fibrous Histiocytoma — Our Experiences of this Recently Reported Finding

Ⓟ SH Irwin[1]; SM Casey[1]; P Maxwell[2]; S McQuaid[2]; J James[2]; M Salto-Tellez[2]; DT McManus[1]

[1]Belfast City Hospital, Belfast, UK; [2]Northern Ireland Molecular Pathology Laboratory, Belfast, UK

Epithelioid fibrous histiocytoma (epithelioid dermatofibroma) is a well-recognised but relatively rare variant of benign fibrous histiocytoma (dermatofibroma), which has recently been reported to show ALK expression on immunohistochemistry and ALK gene rearrangements on FISH and next generation sequencing. This profile suggests that this could be a unique entity, phenotypically and genotypically distinct from its more common counterpart.
We report our observations in two cases with the typical histological features of an epithelioid fibrous histiocytoma. These cases both showed only focal, weak, patchy immunohistochemical staining for ALK-1 with the Leica Bond-III platform but strong diffuse staining using the ALK D5F3 clone using the Ventana platform. In one of these cases ALK gene rearrangement was detected on subsequent FISH.
To date there is limited evidence examining which ALK clone is best suited to aid identification of these rare lesions on immunohistochemistry. Our observation is that in these two cases immunohistochemistry for the ALK D5F3 clone proved more definitive than testing with the ALK-1 clone. This finding suggests that choice of antibody clone may play a crucial role in identifying these lesions from other entities.

P32

Evaluation of Nucleic Acid Performance and Preservation in Formalin-Free PAXGene Tissue Fixative: A Comparison to Formalin

Ⓟ AJ Meecham[1]; G Gerrard[1]; H Costa[1]; F Berisha[2]; AM Flanagan[3]; M Rodriguez-Justo[1]

[1]UCL, London, UK; [2]NHS Royal National Orthopaedic Hospital, London, UK; [3]UCL / NHS Royal National Orthopaedic Hospital, London, UK

Purpose: Damage caused to nucleic acids in the fixation process by formalin limits application of molecular techniques. PAXGene tissue fixative is a methanol-based fixative aimed at preserving these nucleic acids. The aim of this work is to compare the quality of DNA and RNA from paired formalin-fixed paraffin embedded (FFPE) and PAXGene fixed paraffin embedded (PFPE) samples.
Methods: Paired tumour samples were fixed in formalin and PAXgene, routinely processed overnight, and paraffin embedded. DNA and RNA was extracted from 17 paired samples (11 colorectal(CRC)), 2 Oesophageal, 2 Lymph Nodes, 1 Lung, and 1 Ovary) using QIAGEN kits. DNA and RNA were assessed for yield (Thermofisher Qubit3 Fluorometric quantification), purity (Nanodrop 1000 spectrophotometer) and fragmentation (Agilent 2200 Tapestation). Qualitative PCR (using Illumina FFPE QC kit) was performed on the DNA. RT-qPCR and subsequent gene expression analysis (TaqMan assay (ThermoFisher)) of GUSB was performed on the RNA (11 pairs).
Results: DNA:No differences in yield (97.7ng/µl PFPE vs 97.6 ng/µl FFPE),or purity (260/280 ratio 2.03 PFPE vs 1.98 FFPE) were found. Fragment length and DNA integrity were significantly greater in PFPE ($p<0.001$), mean 24328 bp vs 6556 bp and DIN 7.4 vs 5.8 respectively. PFPE DNA was more amplifiable in n=16 cases (mean CT 15.8 v 17.7, $p=0.004$). RNA:No significant differences in yield (156ng/µl PFPE vs 153ng/µl FFPE), integrity (3.33 RIN PFPE vs 3.31 RIN FFPE), or purity (260/280 ratio 2.22 PFPE vs 2.02 FFPE) were found. GUSB expression from cDNA were significantly higher in PFPE ($p<0.01$). Eight FFPE samples failed to amplify. All 11 PFPE samples amplified.
Conclusions: Despite no significant differences in yield or purity, DNA fragment length was significantly improved with PAXGene fixative and was of higher amplifiable quality. RNA yield and purity from PFPE was comparable to FFPE, however superior quality was demonstrated following RT-qPCR and quantification of gene expression.

P33

A Molecular Survey of the Temporal and Spatial Patterns of Tumour Evolution in Chondrosarcoma

Ⓟ M Gupta[1]; P Lombard[1]; L Perez-Casanova[2]; A Meecham[1]; C Steele[1]; T Forshew[1]; F Amary[2]; R Tirabosco[2]; S Behjati[3]; PJ Campbell[3]; N Pillay[1]; AM Flanagan[1]

[1]University College London, Research Deptartment of Pathology, London, UK; [2]Royal National Orthopaedic Hospital, Stanmore, UK; [3]Wellcome Trust Sanger Institute, Cambridge, UK

Chondrosarcoma is the second most common primary bone cancer. Treatment decisions are based on histopathological grading system which is subjective. High grade tumours (GII, GIII and dedifferentiated) undergo radical surgery with significant morbidity whilst low grade tumours (enchondroma and GI) undergo intra-lesional curettage. There is an emerging role for "targeted" therapies, however a comprehensive repertoire of mutations has not been established in large sample cohorts. Biomarkers for predicting metastases are also lacking. This is clinically relevant as only 50% of GII tumours metastasise. The aims of this study were to validate the known and identify novel chondrosarcoma driver gene mutations, and markers predictive of metastases.
Methodology: Targeted next generation sequencing of 400 cancer genes was undertaken on 365 tumour samples (multi-site and multi-time point) from 95 patients. These included: GI=16, GII=148, GIII=62, dedifferentiated=128 and primary tumours=228, local recurrence=92 and metastasis=45. 72 patients had >1 sample sequenced, 18 with more than a single grade represented. 13 patients had samples studied at a minimum of two time-points.
Results: Mutations in (i) *IDH1/2* were present in 53 patients (56%), (ii) *COL2A1* in 50% cases occurring in all grades, (iii) *TP53* and *CDKN2A* (13% and 7% patients) only in higher grade samples (GII: 11% and 12%; GIII: 19% and 2%; dedifferentiated: 42% and 7%, respectively). Synovial chondromatosis had a *FN1-ACVR2A* gene fusion. Novel pathways involved, in addition to RB1 (10%) and Indian Hedgehog (12.3%), were MAPK/ERK pathway (22% cases) and chromatin remodelling genes (11% cases).
Conclusion: Mutations in *TP53* and *CDKN2A*, when present, can be used to distinguish low grade from high grade cartilaginous tumours. *FN1-ACVR2A* gene fusion is a recurrent alteration in synovial chondromatosis. Novel alterations in the MAPK/ERK pathway and SWI/SNF signalling pathways were identified opening new avenues for potential therapies.

P34

Implementation of Formalin-Free PAXGene Tissue Fixative into Routine Use: Evaluation of H&E Morphology, IHC and FISH

Ⓟ AJ Meecham[1]; G Gerrard[1]; H Costa[1]; AJ Resende-Alves[1]; N Guppy[1]; C Thom[2]; H Ye[2]; F Berisha[2]; AM Flanagan[3]; M Rodriguez-Justo[1]

[1]UCL, London, UK; [2]NHS Royal National Orthopaedic Hospital, London, UK; [3]UCL / NHS Royal National Orthopaedic Hospital, London, UK

Purpose: Formalin is the standard method of fixation; applications of formalin-fixed paraffin-embedded (FFPE) tissue such as immunohistochemistry (IHC) and FISH are optimised for this material. However formalin is damaging to nucleic acids, precluding application of molecular techniques. PAXGene fixative is designed to preserve nucleic acids, yielding higher quality DNA/RNA. We aim to evaluate the performance of PAXGene-fixed paraffin-embedded (PFPE) tissue in routine histological techniques.
Methods: Fifty paired tumour samples were fixed in Formalin and PAXgene, processed overnight and embedded in paraffin (25 colorectal (CRC), 18 prostate, 3 oesophageal, 2 lymph node, 1 lung and 1 ovary). H&E stained slides of 17 cases were scored for the quality of the nuclear, cytoplasmic and cell membrane components (max score 12). IHC was undertaken on 17 CRC cases for mismatch repair proteins (MMR), p53 and HER2. FISH, using EGFR and CDKN2A probes, was performed on 17 paired cases. An optimised protocol was used for PFPE samples consisting of a 24 hour step in formalin. All assessments were blinded to fixation methods.
Results: Morphological assessment of the H&Es from FFPE and PFPE were comparable (mean score 10.82 vs 11 respectively). No differences were observed by tissue type or by cellular component. Interpretation of IHC was concordant for all cases for HER2 and MMR proteins. One discordant pair was observed in p53, and 2 were inconclusive (1 FFPE, 1 PFPE). p53 immunoreactivity in PFPE samples was variable and suboptimal for diagnosis. Following optimisation, all 17 cases for both FISH assays were considered adequate for diagnosis, however signals from FFPE were stronger than PFPE.
Conclusions: PFPE tissue performed comparably to FFPE tissue in blinded scoring of morphology. IHC for MMR proteins and HER2 was successful; however immunoreactivity for p53 is variable. FISH performance for both fixation methods was also comparable, following optimisation of the protocol.

P35

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

Ⓟ JD Baena; CJ Talbot; JPC Le Quesne

University of Leicester, Leicester, UK

Lung cancer is the main cause of cancer mortality in the UK. 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 followup from the period 2009 to 2014. Digital images of archival diagnostic tissue sections were examined to derive morphological measures with the potential to predict readiosensitivity. Quantitative radiological measures of response at three different intervals of time 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=25), significant associations are emerging. For example, there is a significant correlation between the increase of the tumour size after the radiotherapy and the presence of atypical mitoses (e.g. multipolar mitoses) (p=0.025). In conclusion, the presence of atypical mitoses such might be a useful histological marker to predict the radio-sensitivity in NSCLC. Other emerging markers and a regression model of radiosensitivity will be discussed.
This research was supported by a PathSoc grant.

P36

Natural Killer-Like Signature Observed Post Therapy in Locally Advanced Rectal Cancer is a Determinant of Pathological Response and Improved Survival

Ⓟ M Alderdice[1]; P Dunne[2]; AJ Cole[2]; PG O'Reilly[2]; DG McArt[2]; V Bingham[1]; M Fuchs[1]; S McQuaid[1]; MB Loughrey[3]; GI Murray[4]; LM Samuel[5]; M Lawler[2]; RH Wilson[2]; M Salto-Tellez[1]; VM Coyle[2]

[1]Northern Ireland Molecular Pathology Laboratory, Centre for Cancer Research and Cell Biology, Queens University Belfast, Belfast, UK; [2]Centre for Cancer Research and Cell Biology, Queens University Belfast, Belfast, UK; [3]Department of Tissue Pathology, Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast, UK; [4]Pathology, School of Medicine, Medical Sciences and Nutrition, University of Aberdeen, Aberdeen, UK; [5]Department of Clinical Oncology, Aberdeen Royal Infirmary, NHS Grampian, Aberdeen, UK

Purpose of the study: Around 12–15% of patients with locally advanced rectal cancer (LARC) undergo a pathologically complete response (Tumour Regression Grade 4 - TRG4) to long course preoperative chemoradiotherapy (LCPCRT); the remainder exhibit a spectrum of tumour regression (TRG1–3). Understanding therapy-related transcriptional alterations may enable better prediction of response as measured by progression-free and overall survival, in addition to aiding the development of improved strategies based on the underlying biology of the disease.
Methods: To this end we performed high-throughput gene expression profiling in 40 pairs of formalin fixed paraffin embedded (FFPE) rectal cancer biopsies and matched resections following LCPCRT (discovery cohort). Differential gene expression analysis was performed contrasting TRGs. Enumeration of the tumour microenvironment cell population was undertaken using *in silico* analysis of the transcriptional data, and real-time PCR validation of NCR1 undertaken. Immunohistochemistry (IHC) and survival analysis was employed to measure CD56+ cell populations in an independent cohort (n=150).
Summary of results: Gene expression traits observed following LCPCRT in the discovery cohort suggested an increased abundance of natural killer cells (NKCs) in tumours that displayed a clinical response to CRT in a TRG-dependent manner. CD56+ NK cell populations were measured by IHC and found to be significantly higher in TRG3 patients compared to TRG1-2 in the validation cohort. Furthermore, it was observed that patients positive for CD56 cells after therapy had a better overall survival (HR=0.282, 95%CI=0.109-0.729, $\chi 2=7.854$, p=.005).
Conclusion: we have identified a novel post-therapeutic NK-like gene signature in patients responding to LCPCRT. Furthermore, patients with a higher abundance of CD56 positive NKCs post-LCPCRT had better overall survival. Therefore, harnessing an NK-like response after therapy may improve LARC patient outcomes.

P37

This abstract has been withdrawn

P38

The Light at the End of the Tunnel? Fluorometry Application for Diagnosing Early Invasive Adenocarcinoma in Colonic Polyps with High Grade Dysplasia on Histological Sections

Ⓟ YS Korneva[1]; VS Maryakhina[2]; AE Dorosevich[1]

[1]Smolensk Regional Institute of Pathology, Smolensk Medical University, Smolensk, Russian Federation; [2]Orenburg State University, Orenburg, Russian Federation

Purpose of the study: Currently there is no objective method to distinguish the early onset of invasive adenocarcinoma within adenomatous colonic polyps with high grade dysplasia. Hence, this study aims to create an objective method for this purpose on histological sections based upon biochemical changes in the tissues caused by the invasive malignant transformation.
Methods: Histopathologically diagnosed colonic biopsies were obtained, 11 with invasive adenocarcinomas (AC), 50 adenomas with various grades of dysplasia (33 low grade and 17 high grade), among them 40 tubular and 10 tubulovilllous, and 13 with normal colonic mucosa. Spectra of autofluorescence excitation from unstained histological sections of our sample groups were measured after dewaxing on a spectrofluorometer (SOLAR CM-2203). The wavelength of registration was 410 nm after its excitation in the UV region.
Results: Two maxima are to be expected based upon our previous study (Korneva et al, 2017), the first was 260–270 nm and the second 330–340 nm. Both maxima measured depend upon the underlying pathological process, the first maximum is defined by the presence of tryptophan-containing peptides, and the second by the presence of collagen. The progression towards adenocarcinoma would increase NADH concentration which would impact the second maximum. The intensity ratio of both maxima were calculated for our sample groups, and this was more than 1.46 for normal mucosa, 1.35–1.45 and 1.26–1.35 for tubular and tubulovillous adenoma respectively, and the lowest ratio value was for invasive AC, 1.13–1.25.
Conclusion: Fluorimetry might be a useful tool that could be used to objectify the diagnosis of early invasive colonic adenocarcinoma on histological sections.

P39

Validation of an Open Source Digital Image Analysis Platform for the Systematic Scoring of Immunohistochemically-Stained Tumour Tissue Microarrays

Ⓟ RS Hagan[1]; S Craig[1]; PD Dunne[1]; M Salto-Tellez[1]; MB Loughrey[2]

[1]Queen's University Belfast, Belfast, UK; [2]Royal Victoria Hospital / Queen's University Belfast, Belfast, UK

Purpose of the study: The use of predictive and prognostic biomarkers has the potential to provide a comprehensive understanding of cancer. Traditional research methods of scoring biomarkers stained by immunohistochemistry (IHC) involve manual assessment of tissue microarrays (TMA) by pathologists, which is both labour intensive and time-consuming. These methods can be confounded by variation in results due to intra- and inter-observer assessment. Digital pathology image analysis may alleviate this critical bottleneck in tissue biomarker analysis, speeding up the process whilst providing robust and reproducible results. This study aims to test new, open-source digital image analysis software, QuPath, compared to traditional manual immunoscoring analysis of selected biomarkers in a cohort of colorectal cancer (CRC) TMAs.
Methods: We analysed expression of three biomarkers (CD3, CD8 and p53) in a large population-based CRC cohort (n=740), using manual and digital image analysis (QuPath) methods. Manual and digital scores were assembled and statistical analysis on the prognostic value of each biomarker was assessed. Additionally, resulting scores obtained using the same raw digital images from multiple independent observers with varying experience in pathology and computational biology were analysed.
Summary of results: Our results demonstrate the ability of QuPath to generate comparable data to manual scoring as well as significant intra-observer comparability, regardless of user expertise. Statistical analysis of the prognostic relevance of biomarkers showed high concordance between users, validating the utility of QuPath.
Conclusions: Data presented here highlight the utility of digital pathology image analysis software in providing robust biomarker immunoexpression data. These results provide an exciting glimpse into some of the potential applications of QuPath and show evidence that tissue-based biomarker analysis in cancer pathology can be aided by digital analysis.

P40

Correlation of Core Biopsy and Lymph Node Resection Diagnosis in Lymphoma

Ⓟ H Fadlelseed; D Gibbons

St Vincent's University Hospital, Dublin, Ireland

Background: Lymph node excisional biopsy is regarded as the gold standard for the diagnosis of lymphoma but needle core biopsy provides a possible alternative. The primary aim of this study is to evaluate concordance between the core biopsy and the lymph node resection diagnoses where both procedures were carried out. A secondary aim is to establish the sensitivity of the lymph node core biopsy in the cases identified
Methodology: All lymphoma reports in the two year period from January 2014 to December 2015 were retrieved from Laboratory Information System. All reports were reviewed and concordance between core and excisional biopsies assessed.
Results: 78 reports on lymphoma were issued. Of these cases, 47 were core biopsies, 44 were lymph node resections and both procedures were carried out in 13 cases. Of these 13 cases concordance between core biopsy diagnosis and the subsequent lymph node resection was found in 10 cases. Two cases on core biopsy were composed of necrosis only and nondiagnostic. One case was negative for lymphoma on biopsy and positive on excision. In our study the sensitivity of the lymph node core biopsy for the diagnosis of lymphoma and for the subtype of lymphoma were both 90.9%. There were three grading of follicular lymphoma discrepancies which were considered minor discordances.
Conclusion: Our study shows good concordance between core biopsies and subsequent lymph node resections, with high sensitivity of core biopsies in diagnosing and subtyping lymphoma.

P41

Audit on the Diagnostic Yield of Cell Blocks in Systemic Cytology

Ⓟ DS Johal; S Sah

University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK

Background: Cell blocks (CBs) are increasingly being used as an adjunct to smears to improve the diagnostic accuracy of systemic cytology material. Our institution employs two different methods of cell block; the Cytology Cell Block (CCB) and the Plasma-Thrombin Cell Block (PTCB). No previous studies have compared the diagnostic yield of PTCB and CCB.
Purpose of study: To assess if the diagnostic yield of systemic cytology is increased by using CBs and if one method of CB is superior to the other.
Methods: A retrospective review of systemic cytology cases with routine liquid based cytology (LBC) smears that had CBs performed over a one year period was undertaken. The result of cytology was compared to the final histological diagnosis where available to assess the overall sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).
Results: Cell blocks were available in a total of 354 cases and no false positive results were reported. The diagnostic yield of LBC smears increased with use of CCB and PTCB by 10.21% and 17.26% respectively. Overall, the diagnostic yield was 7.05% greater with the use of PTCB compared to the use of CCB. Both methods of CB were associated with a decreased false negative rate, increased true positive rate, increased sensitivity and increased NPV.
Conclusions: Our data has shown that cell blocks increase the diagnostic yield of systemic cytology and that the PTCB is superior to the CCB reflecting the better cellularity and architectural features achieved with PTCB. Cell blocks provide material for performing a variety of ancillary studies such as immunocytochemistry and molecular testing.

P42

Malignancy within Proximal Femoral Fractures at Southampton General Hospital

Ⓟ JR Rickwood[1]; C Tilley[2]

[1]University of Southampton, Southampton, UK; [2]University Hospital Southampton, Southampton, UK

Purpose of the study: To evaluate the information around proximal femoral fracture (PFF) specimens, received into the histopathology department of a major trauma centre. The evaluation includes: a) identifying the percentage of PFF cases that have tissue sent for histopathological assessment; b) identifying the proportion of specimens which contain malignancy; c) identifying the proportion of malignant cases which have immunohistochemistry performed; d) identifying the proportion of malignant cases where there is a known clinical history of malignancy; e) assessing the femoral tissue types sent for histopathological analysis.
Method: This seven year retrospective audit identified the total number of admissions to a major trauma centre with proximal femoral fracture, by searching the orthopaedic database. The local pathology database was interrogated to identify the number of PFF specimens sent to the histopathology department over the same period. Each case was inputted into a spreadsheet, where the clinical details, diagnoses and other relevant information were recorded. The auditing standards were generated from a similar study carried out at a regional hospital.
Results: 4128 admissions for PFF within the seven year period. 6.3% of all PFFs (262 cases) were sent for histopathological assessment. 15% (39 cases) of the examined cases contained malignancy. Immunohistochemistry was performed on 72% of the malignant cases. There is a greater proportion of malignancy in patients with a known clinical history of malignancy. A greater proportion of femoral reaming specimens contain malignancy compared to femoral head specimens.
Conclusion: There is a higher incidence of malignancy in proximal femoral fracture specimens than anecdotally expected. It appears that patients with a known history of malignancy are more likely to have malignancy identified in their PFF specimen. Overall the audit results from the major trauma centre are similar to the identified audit standards.

P43

The Use of Royal College of Pathologists Dataset Guidelines in the Reporting of Oesophageal and Gastric Malignancies

Ⓟ I Gurung[1]; NJ Carr[2]; J Horne[2]

[1]University of Southampton, Southampton, UK; [2]University Hospital Southampton NHS Foundation Trust, Southampton, UK

Background: Surgical resection is a common treatment option for oesophageal and gastric cancer. Pathological assessment of resection specimens is crucial for prognosis and patient management. The Royal College of Pathologists (RCPath) published guidelines in 2007 for oesophageal and gastric malignancies to ensure that accurate, concise and consistent information is reported. However, there is a limited amount of medical literature investigating the level of adherence to these guidelines.
Purpose of the study: An audit was conducted to assess whether pathology reports in Southampton adhere to the RCPath dataset guidelines, and if not, it was investigated why.
Methods: 443 pathology reports (241 oesophageal and 202 gastric) of patients who had their gastro-oesophageal cancer resected between April 2007 and March 2016 at University Hospital Southampton were compared against the RCPath datasets guidelines. Individual parameters were classified under 'information provided' or 'information missing'.
Summary of results: Proforma based reports were ≤90% complete in 93% of gastric cases (83/89) and 98% of oesophageal cases (103/105). Freeform text reports were ≤90% complete in 3% of gastric cases (3/89) and 28% of oesophageal cases (28/99). Best practice was achieved in 19% gastric and 18% oesophageal cancer reports. Distance of tumour from the Circumferential Resection Margin (CRM) was the most poorly reported clinically prognostic information. It was reported in 42.6% of gastric and 70.8% of oesophageal cases.
Conclusions: The content and consistency of prognostic information in freeform text reports in Southampton is unsatisfactory when compared to proforma based reporting. Action should be taken to improve the quality of histopathology reports by ensuring widespread adherence to a proforma template, based on the dataset guidelines provided by the RCPath.

P44

Use of a Socratic Circle to Engage Students in Pathology in a Resource Limited Curriculum

Ⓟ A Dallmann[1]; D Parker[1]; B Bowman[1]; DF Griffiths[2]

[1]UHW, Cardiff, UK; [2]Cardiff University, Cardiff, UK

Lack of resources to deliver a modern medical curriculum leads to a reduction in tutor/student ratio. It is difficult to engage students in tutorials with 25 or more students. A scheme was designed to engage 25 year 3 students in which the tutees were divided into 5 groups of 5 students, in the first part of the tutorial each group was tasked with preparing answers to pre-determined questions. The topic was largely material they had covered in year 1 (the pathology of ischaemic heart disease) with one new topic requiring deduction. Questions emphasised the link between pathology, pathophysiology, symptoms, signs and clinical management. *All* groups had to prepare answers to *all* questions.
In the second part of the session the tutor would randomly select a topic for each group to presentation to the whole 25. The tutor provided feedback, filled in any gaps and gave further explanations. Students were not asked to prepare prior to the tutorial, nor were they allowed any resources (textbooks or internet access) during the tutorial.
The tutorials were assessed at structured meetings with the tutors and by an open ended feedback sheet for the students to complete at the end of the tutorials.
Tutors reported that students demonstrated anxiety and dismay at the beginning of the tutorial at not being asked to prepare and being disconnected from online resources. As the session progressed the small groups were almost always able, by collaboration, to complete the questions and presentations and usually answered the questions correctly and fully. Students surprised themselves at how much they knew or could work out, although a few would have preferred to be given the opportunity to prepare. Almost all students gave positive comments about the format and had more confidence in their understand of the topic.
The scheme is an efficient way of engaging students, conforms to educational theory, and can be adapted to unfamiliar topics if students are asked to prepare.

P45

Phaeochromocytomas and Extra Adrenal Paragangliomas: A Retrospective Study of 24 Cases

Ⓟ A Rajapakse; S Cummins; T Worthington; IN Bagwan

Royal Surrey County Hospital, Guildford, Surrey, UK

Introduction: Phaeochromocytomas and extra adrenal paraganglioma are tumours derived from endocrine cells of neural crest. Malignant phaeochromocytoma account for 10% of total incidence and tend to be larger. Adrenal gland Scaled Score (PASS) was developed to identify malignant potential. PASS score of >4 is associated with a higher probability of malignancy. Paragangliomas may develop wherever sympathetic nerve cells are present and their common site of origin is in the abdomen.
Aim: Retrospective analysis of phaeochromocytoma and extra adrenal paragangliomas encountered in tertiary cancer centre over a period of 7 years.
Materials and methods: Winpath pathology database was searched from 2009 to 2016 to identify cases of phaeochromocytoma and paraganglioma. Available clinical records and histopathology slides were reviewed for various parameters.
Results: 10 phaeochromocytoma cases included 1 male and 9 female patients indicating a female predominance. 2 cases with a PASS score of >4 occurred in patients >70 years of age. Cases with PASS score <4 showed an age range of 41–70 years. Average weight of cases with PASS >4 was 127g and PASS <4 was 44.7g. The age range for paraganglioma was 39–55 years, with carotid body being the most common site, followed by retroperitoneum and duodenum.
Conclusion: Phaeochromocytoma was more common in females. PASS score of >4 occurred in older age group (>70 years). with larger tumour size. Carotid body was the most common site of origin for paraganglioma followed by retroperitoneum and duodenum.

P46

Evaluation of Efficacy of Endoscopic Mucosal Resection in Treating Early Oesophageal Cancers: A Retrospective Study of 51 Cases

H Patel[1]; Ⓟ TN Warusavithana[1]; S Beeslaar[2]; M Bahhadi- Hardo[2]; S Woodrow[2]; IN Bagwan[1]

[1]Royal Surrey County Hospital, Guildford, UK; [2]Frimley Park Hospital, Frimley, UK

Introduction: Endoscopic mucosal resection (EMR) is an endoscopic alternative to surgery in resecting polypoid mucosal neoplasms, submucosal neoplastic lesions and intramucosal carcinomas (IMC). Although high cure rates are achieved with oesophagectomy, there is significant treatment-related morbidity and mortality. Patients who are hemodynamically unstable might not tolerate the anaesthesia and surgery itself. The incidence of superficial oesophageal carcinomas is increasing, while the incidence of lymph node metastasis has been negligible in high grade dysplasia and IMC, the demand for endoscopic approach has led to the creation of ablative techniques and EMR.
Aim: Retrospective clinicopathological analysis of the EMR specimens received in the pathology department over a period of 7 years.
Materials and methods: Winpath pathology database was searched from 2009 to 2016 for oesophageal EMR specimens. Histology reports and medical records were assessed for various clinicopathological parameters.
Results: The 2 main indications for EMR were Barrett's with dysplasia (21/51) and early carcinoma on biopsy (19/51). Following histological examination, 33/51 (64.7%) cases demonstrated carcinoma (54.5% being intramucosal). 59% (30/51) were incomplete excisions and on follow up 33% (10/30) showed no dysplasia, 30% (9/30) required major surgery and 16% (5/30) developed Barrett's oesophagus with dysplasia. Of the 41% (21/51) cases with complete excision, on follow up, 76% showed no dysplasia and 19% developed Barrett's with dysplasia. Only one of 33 carcinoma cases demonstrated lymph node metastasis in oesophagectomy specimen.
Conclusion: EMR is a useful procedure and potentially curative in the early mucosal and submucosal oesophageal tumours, avoiding major surgery.

P47

The Perceptions of Nigerian Pathologists About the TSL-WADIAP External Quality Assessment (EQA) Scheme

Ⓟ MO Odubanjo[1]; UO Igbokwe[2]; de Obaseki[3]; GO Ogun[4]; DB Olusina[5]; SA Ahmed[6]; AT Atanda[7]; CO Ukah[8]; CC Okani[9]; EK Abudu[10]; Y Iliyasy[6]; FB Abdulkareem[1]; AAF Banjo[1]

[1]Lagos University Teaching Hospital, Lagos, Nigeria; [2]Queen's Hospital, Romford, London, UK; [3]University of Benin Teaching Hospital, Benin, Nigeria; [4]University College Hospital, Ibadan, Nigeria; [5]University Of Nigeria Teaching Hospital, Enugu, Nigeria; [6]Ahmadu Bello University Teaching Hospital, Zaria, Nigeria; [7]Aminu Kano University Teaching Hospital, Kano, Nigeria; [8]Nnamdi Azikwe University Teaching Hospital, Nnewi, Nigeria; [9]Anambra State University Teaching Hospital, Awka, Nigeria; [10]University of Uyo Teaching Hospital, Uyo, Nigeria

Introduction: The principal function of an EQA scheme is educational. 1, 2, 3 Nigeria's first and only Diagnostic Histopathology External Quality Assurance Scheme (EQAS), the TSL-WADIAP (TSLW) EQAS was launched in November 2011. Slides are circulated to Nigerian pathologists every 6 months, and cases discussed at workshops in May and November. The theme varies with each circulation including either Breast or GIT, one other sub-specialty and a few cases teaching Immunohistochemistry. Participation is voluntary.
Purpose of the study: To test the effectiveness of the TSLW EQAS and to assess participation in the scheme for the round ending in May 2014.
Methods: Questionnaires were administered. Full participation was taken as submission of responses ± any other related activity such as the personal review of the slides for the EQAS and or the attendance of the workshop at which the cases were discussed.
Results: 111 questionnaires were completed. 46 were excluded, from residents less than 3 completed years in training and not adequately familiar with the concept of EQAS. Sixty-five (65) were analyzed. 73.8% of the 65 questionnaires were completed at the TSLW workshop of May 2014 and 26.2% between May and November 2014 at various conferences attracting Nigerian Pathologists. 78.5% participated in the scheme for May 2014, all present at the workshop; 41.5% fully participated; 24.6% reviewed the slides and attended the workshops; and 12.4% only attended the workshops. 93.8% of respondents do not participate in any other EQAS. 95.4% agree that EQA is a valid tool for identifying poor performance among Nigerian pathologists, and 96.9% agree that the cases on the TSL-WADIAP EQAS are of educational value. 89.2% believe the EQAS should be mandatory.
Conclusions: Full participation may not improve significantly until the scheme becomes mandatory, possibly for renewal of annual practicing licence by the Medical and Dental Council of Nigeria.

P48

Assessing the Effect of Preoperative Treatment on Specimen Quality and Lymph Nodes in Advanced Rectal Cancer

Ⓟ SJ Betterton; HM Wood; P Quirke; NP West

Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, UK

Rectal cancer is treated by surgical resection, which may be preceded by chemotherapy and/or radiotherapy in advanced disease. Resection should occur in the mesorectal plane (MRP) to ensure optimum outcomes. However, preoperative therapy creates fibrosis, leading to more challenging surgery. It also reduces lymph node size making them more difficult to find. This study aims to determine the effect of preoperative therapy on surgical quality and lymph nodes. Plane of mesorectal surgery and lymph node yield/size were compared across three groups: no preoperative therapy (controls, n=661), preoperative chemoradiotherapy (CRT, n=111), and preoperative chemotherapy (CT, n=10). Mesorectal planes and nodal yield were determined from the pathology reports. Node size was assessed on a subset by measuring the cross sectional area on scanned H&E slides using Aperio ImageScope. MRP was observed more frequently in the CRT group when compared to controls (64.5% vs. 45.3%, p=0.0002). In the CRT group, abdominoperineal excisions (APE) were inferior to anterior resections (AR) (55.6% vs. 73.6%, p=0.051). Nodal yield was greater in the treated groups (CT 19.6 [mean] ± 5.5 [SD], CRT 16.5 ± 8.5, control 13.6 ± 7.9). Node size was smaller in the treated groups (CT 5.5 ± 8.5mm^2, CRT 6.2 ± 7.5mm^2, control 11.8 ± 13.3mm^2). Surgical quality was better after CRT over controls, contrary to our hypothesis. This likely reflects surgical advances between the control (1998-2005) and CRT (2012-2017) studies. In line with previous reports, AR is associated with better planes when compared to APE after CRT. It was surprising that more nodes were found in the CRT group when compared to controls. This probably reflects improvements in pathology evidenced by the fact that the nodes were smaller. In conclusion, this study has shown that improvements in surgical and pathological quality over time have had a greater effect on the mesorectal plane and nodal yields than the effect of preoperative therapy.

P49

Intraoperative Colon Cancer Fluorescence Using 5-Aminolevulinic Acid: A Quantitative Histopathological Analysis of Fluorescent and Non-Fluorescent Tumours

Ⓟ MA Goldsworthy[1]; E Tinkler-Hundal[2]; TI Maisey[1]; N Corrigan[3]; NP West[2]; G Gossedge[1]; H Andrew[1]; GW Taylor[1]; DG Jayne[1]

[1]Leeds Institute of Biomedical and Clinical Sciences, Leeds, UK; [2]Leeds Institute of Cancer and Pathology, Leeds, UK; [3]Leeds Institute of Clinical Trials Research, Leeds, UK

Purpose of the study: 5-aminolevulinic acid (5-ALA) selectively accumulates in cancer cells, where it is metabolised to the fluorophore protoporphyrin IX. Our recent multicentre study investigated the feasibility of using 5-ALA as an intraoperative fluorescent probe for the identification of colon cancer and lymph node metastases. However, only 13 of 39 cancers showed fluorescence, suggesting a fundamental difference between fluorescent and non-fluorescent tumours. The aim of this study was to use a quantitative histopathological approach to investigate whether differences in fluorescence could be explained by differences in tumour composition, which may hold prognostic significance.
Methods: Primary tumour tissue was available from 30 trial participants. Tumour cell density and tumour vascularity were quantified by point counting using digitally scanned tissue sections. The presence of a T cell-mediated inflammatory response was determined by staining for CD3 with immunohistochemistry. Staining was quantified using microscopic spectral imaging.
Summary of results: For fluorescent vs. non-fluorescent tumours, median tumour cell density was 34.6% vs. 34.2%, median vessel density was 1.7% vs. 1.6%, and median T cell infiltration in high-density fields at the invasive margin was 2.1% vs. 4.3%. On logistic regression analysis, none of these variables emerged as significant predictors of tumour fluorescence (P>0.05).
Conclusions: The results indicate that fluorescent and non-fluorescent tumours were similar with respect to tumour cell density, vascularity and inflammatory response. We therefore propose that cellular uptake and metabolism of 5-ALA is a more likely explanation for differential fluorescence. Fluorescent probes that avoid the need for tumour metabolism should be used in future studies in this setting.

P50

The Quality of UK Colon Cancer Specimens from the Multicentre FOxTROT Trial Compared to Published Gold Standards

Ⓟ ER Price[1]; P Quirke[1]; D Morton[2]; NP West[1]

[1]University of Leeds, Leeds, UK; [2]University of Birmingham, Birmingham, UK

Around 41,000 new UK colorectal cancers are diagnosed each year of which two thirds occur in the colon. High quality rectal cancer surgery is known to improve outcomes. There is now good evidence that high quality colon cancer surgery is also important. Complete mesocolic excision with central vascular ligation (CME) has been proposed as the optimal operation. We aimed to assess the quality of UK colon cancer specimens and compare these to published data. 150 cases operated on for advanced colon cancer were identified from the FOxTROT trial between 2008 and 2010. Of these, 55 had photos that were assessable (46 fixed, 9 fresh). Quality was assessed by tissue morphometry using Aperio ImageScope and included the distance between the tumour and high tie (THT), length of large bowel (LLB) and area of mesentery (AOM). Lymph node yields were available for 145 cases. The cases were compared to a published series of Danish CME (n=93) and Danish conventional surgery (n=170). UK surgery was associated with a lower THT distance when compared to Danish CME in both right sided (72 vs 89mm) and left sided (51 vs 69mm) fixed specimens, and lower than the Danish conventional cases (R: 79, L: 59). The LLB was similar to CME but greater than Danish conventional (R: 250 vs 254 vs 215mm, L: 225 vs 227 vs 203mm). The AOM was significantly smaller in UK specimens compared to CME (R: 6944 vs 9967mm^2, L: 6150 vs 7292mm^2). Danish conventional surgery had a greater AOM on the right (8896mm^2) but lesser on the left (5596mm^2). The median lymph node yield was 22 which was lower than Danish CME (28) but greater than Danish conventional surgery (18). We have shown that recent UK colon cancer surgery in a large clinical trial does not meet the oncological principles of CME when judged by tissue morphometry and lymph node yields. Failure to resect sufficient tissue between the tumour and high tie leaves lymph nodes and blood vessels behind that may harbour occult metastases leading to recurrence

P51

The Degree and Number of Lymph Nodes with Tumour Regression Predicts Survival in Patients with Oesophageal Cancer Treated with Pre-Operative Chemoradiotherapy

Ⓟ W Koemans[1]; R Larue[2]; L Heij[1]; R Riedl[3]; M Sosef[4]; HI Grabsch[1]

[1]Department of Pathology, Maastricht University Medical Center, Maastricht, Netherlands; [2]Department of Radiotherapy, MAASTRO clinic, Maastricht, Netherlands; [3]Department of Pathology, Zuyderland Medical Center, Heerlen, Netherlands; [4]Department of Surgery, Zuyderland Medical Center, Heerlen, Netherlands

Introduction: The pathological TNM stage is the only clinical tool to predict survival in oesophageal cancer (OeC) patient (pts) after neoadjuvant chemoradiotherapy (nCRT). Location of lymph node metastases (LNmet) and tumour regression (TRG) in LNmet have been suggested as new prognostic markers in OeC. We hypothesised that the degree of TRG in LNmet in combination with LNmet location and LN number predicts survival.
Methods: Haematoxylin/Eosin stained slides from 123 OeC resections after nCRT were reviewed. TRG of every LNmet was classified according to Romano et al as (A) no tumour, (B) tumour without regression, (C) tumour with regression, (D) complete tumour regression. Relationships between TRG in LNmet, location of LNmets and number of LNmets weighted by the LN TRG (LNscore) and survival were analyzed. LNscore was calculated as (nB*2+nC*1.5+nD*1.25)/(nB+nC+nD).
Results: Median (range) LN number/patient was 17 (6-51). 69 (55%) pts were 'true N0' (class A), 23 (19%) pts had LNmets in class B, 19 (15%) pts had LNmets in class C and 14 (11%) pts had a complete LNmet response (class D). Class A and class D pts showed similar survival which was significantly better than that of class B and C pts, p=0.005. The more LNmets/pts showed TRG, the better the survival (p=0.008). Pts with LNmets below the diaphragm had a better survival than pts with LNmets above the diaphragm, or patients with LNmets above and below the diaphragm (p=0.001).
Conclusions: Our results confirm that TRG in LNmets predicts survival in OeC pts treated with nCRT. Patient stratification can be further refined using a combination of number of LNmets and TRG. Due to overall small number of LNmet, subgrouping by LN station was not possible. A larger samples size is needed to created a nomogram using TNM stage in combination with primary TRG, LNmet TRG and LNmet location to predict survival.

P52

Neo-Adjuvant Chemotherapy Improves Outcome in Patients with Oesophageal Mucinous Adenocarcinoma

Ⓟ LN Spaans[1]; Y Saito[2]; N Davarazani[1]; D Cunningham[3]; W Allum[3]; RE Langley[4]; EC Smyth[4]; HI Grabsch[5]

[1]GROW School for Oncology and Developmental Biology, Maastricht University Medical, Maastricht, Netherlands; [2]Dept of Thoracic Surgery, Saitama Cardiovascular and Respiratory Center, Saitama, Japan; [3]Department of Gastrointestinal Oncology and Lymphoma, Royal Marsden Hospital, London, UK; [4]Medical Research Council Clinical Trials Unit at UCL, London, UK; [5]Section of Pathology and Tumor Biology, Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, UK

Background: Survival of patients with locally advanced oesophageal cancer (OeC) is poor despite multimodal treatment. Patients with gastric mucinous adenocarcinoma (mucAd) have the poorest survival and do not benefit from pre-operative chemotherapy. Patients with OeC mucAD may favour from preoperative chemoradiation. The survival of OeC patients with mucAd and their response to chemotherapy is currently unknown.
Purpose: We hypothesized that OeC patients with mucAd have a poorer survival after chemotherapy than OeC patients with non-mucinous adenocarcinomas (non-mucAd).
Methods: Haematoxylin and eosin (H&E) slides from 351 oesophageal adenocarcinoma resections (181 treated with chemotherapy and surgery (CS), 170 with surgery alone (S)) from the OE02 trial were centrally reviewed and classified as either mucAd or non-mucAd by two independent observers. The histological phenotype was related to clinical pathological data, overall survival (OS) was compared between treatment groups.
Results: 17 (9.4%) OeC were classified as mucAd in the CS groups versus 12 (7.1%) in the S group. 79% patients with mucAd were male, 83% had stage III disease. In the S group, patients with mucAd had poorer OS, p=0.004. In the CS group, OS was similar between patients with and without mucAd, p=0.546. When comparing treatment arms, OS of patients with mucAd was significantly longer in the CS group compared to the S group (p=0.005).
Conclusions: This is the first study to suggest that OeC patients with mucAd from the OE02 trial benefit from pre-operative 5-Fluoruracil/cisplatin based chemotherapy. Our results appear similar to those in OeC treated with preoperative chemoradiation but is in contrast to reports from gastric mucAd. The clinical pathological characteristics of oesophageal mucAd were similar to gastric mucAd. Our results require validation in a second larger OeC series before considering the presence of mucAd as biomarker for chemotherapy benefit.

P53

No Epstein-Barr Virus Infection and Extremely Rare Mismatch Repair Deficiency in Oesophageal Cancer

Ⓟ LC Hewitt[1]; IZ Inam[2]; T Yoshikawa[3]; A Quaas[4]; A Hoelscher[5]; Y Saito[1]; G Fazzi[1]; V Melotte[1]; RE Langley[6]; D Cunningham[7]; W Allum[8]; GG Hutchins[2]; HI Grabsch[1]

[1]Maastricht University Medical Center, Maastricht, Netherlands; [2]Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, UK; [3]Kanagawa Cancer Center, Yokohama, Japan; [4]Institute for Pathology, University Hospital Cologne, Cologne, Germany; [5]University Hospital Cologne, Cologne, Germany; [6]Medical Research Council Clinical Trials Unit at University College London,, London, UK; [7]The Royal Marsden Hospital NHS Foundation Trust, London, UK; [8]Royal Marsden National Health Services Foundation Trust, London, UK

Purpose of the study: Patients with oesophageal (OeC) or gastric (GC) cancer have poor survival and very limited targeted therapy options. Immune-targeting therapy has shown promising results in other cancer types and mismatch repair (MMR) deficiency has been used as a biomarker to predict response to programmed cell death protein 1 (PD1) in colorectal cancer. Epstein Barr virus (EBV) infection has been proposed as a potential marker for response to PD1/PDL1 inhibitors in GC. The aim of this study was to establish the frequency of EBV infection and MMR deficiency as potential biomarker in OeC.
Methods: 988 OeC resection specimens (OE02 trial: n=443 (45%), Leeds Teaching Hospitals (LTH) UK: n=223 (23%), University Hospital Cologne, Germany n=322 (33%)) were investigated for the presence of EBV infection by RNA in situ hybridization and loss of expression of MMR proteins MLH1, MSH2, MSH6 and PMS2 by immunohistochemistry (IHC). In a subset of OE02 trial cancers (n=419), we also performed microsatellite instability (MSI) testing. OeC results were compared to results from 1015 GC from LTH (n=763, 75%) and Kanagawa Cancer Center Hospital, Japan (n=252, 25%).
Summary of results: The frequency of MMR deficiency was 0.8% in OeC (5 adenocarcinoma, 2 squamous cell carcinoma) which was similar to the frequency of MSI-High (0.6%). Concordance between MMR IHC and MSI was 99%. None of the OeC was EBER positive. In GC, EBER positivity was 4% and 10% showed MMR deficiency.
Conclusions: This is the largest OeC study to date demonstrating that, in contrast to GC, EBV does not play a role in OeC carcinogenesis. Furthermore, the very low frequency of MMR deficiency in OeC makes MMR testing to screen for eligibility for immune-targeting therapies unfeasible. Future studies need to explore whether there are other potential biomarkers in OeC patients that could be used to identify patients potentially benefitting from immune-targeting therapy.

P54

Optimising the Sampling Strategy to Determine the Tumour Proportion in the Diagnostic Endoscopic Biopsy in Oesophageal Cancer

Ⓟ N Davarzani[1]; MD Hale[2]; S Jolani[3]; LC Hewitt[1]; G Fazzi[1]; GA Hutchins[2]; HI Grabsch[1]

[1]GROW School for Oncology and Developmental Biology, Maastricht University Medical Center, Maastricht, Netherlands; [2]Section of Pathology and Tumour Biology, Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, UK; [3]Department of Methodology and Statistics, CAPHRI, Maastricht University, Maastricht, Netherlands

Background: We recently showed that proportion of tumour (PoT) in the biopsy of oesophageal cancer patients predicts benefit from pre-operative chemotherapy. Originally, we sampled up to 600 points per biopsy piece irrespective of the size of the tissue or tumour density which was a very time consuming process. Accurate estimation of PoT is essential as patient treatment may depend on it.
Purpose of the study: To optimise the sampling process in order to avoid unnecessary counting without compromising the accuracy of the result.
Methods: We tested a stepwise sampling strategy ('pre'-sampling measurement points (MP) – calculating PoT and re-sampling depending on PoT) to determine the optimal final number of MPs needed. In a simulation study, 10 Mio artificially generated 'biopsies' were used to compare different possible pre-sampling re-sampling strategies. The pre-sampling re-sampling approach was evaluated using existing data from 574 biopsy pieces (258300 points from 281 patients). The difference in PoT between the original approach and the new pre-sampling re-sampling method was used to determine the best sampling strategy.
Results: Pre-sampling with 50 MPs appears optimal. When calculating the final number of MPs needed, the desired absolute precision of the result can be included in the calculations. Our simulation showed, that the final number of MP is highly dependent on PoT and highest when PoT is 50%. Applying this new sampling strategy on our existing dataset, only 103966 (40.2%) of the originally measured 258300 points are necessary to estimate PoT with an error < 0.05.
Conclusions: Using existing data and mathmatical modelling to optimise the sampling strategy avoids over- and undercounting and thus saves time without compromising the accuracy of the result. Validation of the sampling method in the OE02 trial biopsies demonstrated that the optimised sampling approach will safe time making this measurement much more feasible in routine pathology laboratories.

P55

Comparing Gene Copy Number Status of Receptor Tyrosine Kinase and Downstream Signalling Genes Between Oesophageal and Gastric Cancer

Ⓟ HL Slaney[1]; LC Hewitt[2]; A Silva[1]; C Wickstone[1]; N Davarzani[2]; P Quirke[1]; GA Hutchins[1]; HI Grabsch[2]

[1]Section of Pathology and Tumour Biology, Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, UK; [2]GROW School for Oncology and Developmental Biology, Maastricht University Medical Center, Maastricht, Netherlands

Background: The survival of patients with gastric (GC) or oesophageal (OeC) is poor. Patients with GC or OeC are currently treated with the same regimens. Gene copy number alterations can influence protein expression and activity of signalling pathways. The aim of this study was to compare DNA copy number changes of receptor tyrosine kinase genes (RTKs: EGFR, HER2, FGFR2, MET) and downstream signalling genes (DSS: PIK3CA, KRAS, MYC and CCNE1) between GC and OeC.
Methods: A previously established multiplex ligation dependent probe amplification assay (MLPA) was used to determine the frequency of RTK and DSS gene copy number changes in DNA extracted from resection specimens (OeC n=380, GC n=523). A ratio > 2 was defined as high amplification. Frequency of gene copy number and relationship to clinicopathological data was compared between OeC and GC.
Results: Frequency of high amplification was different between OeC and GC for PIK3CA (1% vs 13%), MYC (16% vs 28%), KRAS (19% vs 5%), FGFR2 (0% vs 8%) and HER2 (15% vs 24%), but not for EGFR (8% vs 8%), MET (5% vs 4%), CCNE (7% vs 11%). In OeC, METamp and CCNE1amp were more frequent in higher TNM stage (p<0.001, p=0.012). Whereas in GC, MYCamp and HER2amp were more frequent in higher pT (p=0.005) and higher pN (p=0.022). No other relationship with clinicopathological variables seen.
Conclusion: This is the first study to compare gene copy number status of RTKs and DSS between OeC and GC using the same methodology. Our results suggest that in contrast to the current treatment with the same cytotoxic chemotherapy regimen, patients with OeC and GC are potential candidates for different targeted therapy approaches. Furthermore, resistance mechanisms related to RTK downstream signalling amplification, appears to be different in OeC and GC. Validation of our results in a second study is warranted.
This study was funded by Yorkshire Cancer Research.

P56

Epithelial Cytoplasmic HMGB1, Epithelial Nuclear RUNX3 and Dynamic Stromal Lymphocytic Phenotype are Associated with Oesophageal Neoplastic Progression

Ⓟ RJ Porter[1]; DP Brice[1]; GI Murray[1]; RD Petty[2]; MH McLean[1]

[1]University of Aberdeen, Aberdeen, UK; [2]University of Dundee, Dundee, UK

Introduction: Barrett's oesophagus (BO) is a pre-malignant lesion for oesophageal adenocarcinoma (OAC). HMGB1 impacts genomic stability, influences epithelial cell behaviour and immune responses. We previously reported loss of nuclear and emergence of cytoplasmic epithelial HMGB1 in BO. Our aim was to define expression of HMGB1 in upper GI malignancy, assess expression of HMGB1 downstream effector proteins p53 and RUNX3 and characterise lymphocytic infiltrate in oesophageal neoplastic progression.
Methods: Tissue was sourced from the Grampian Biorepository (n=241 total). Intensity of epithelial nuclear and cytoplasmic expression of target proteins were assessed immunohistochemically in a tissue microarray representing 150 upper gastrointestinal cancers (58 OAC, 9 oesophageal squamous cancer, 83 gastric adenocarcinoma), 15 normal oesophageal mucosa, 24 normal gastric mucosa and 14 BO mucosa adjacent to OAC. Expression of p53, RUNX3 and lymphocytic inflammatory cell infiltrate was also assessed in 78 and 13 biopsies of non-dysplastic or dysplastic BO.
Results: There was loss of nuclear HMGB1 across all cancer phenotypes. Epithelial cytoplasmic HMGB1 expression was associated with OAC compared to normal epithelium (p<0.001), but with weaker intensity to non-dysplastic (p=0.001) or dysplastic BO (p=0.002). Dysplastic BO expressed strong nuclear p53 (p<0.001 versus normal mucosa) and this was lost on malignant transformation (p<0.001). Epithelial nuclear RUNX3 was associated with dysplastic BO (p=0.004). Dysplastic BO is associated with increased Foxp3+ regulatory T cells (p<0.002) and non-dysplastic BO with reduced CD20+ B cell (p<0.001), CD4+ (p<0.001) and CD8+ (p<0.001) T cell infiltrate.
Conclusion: This study offers new insight into the pathogenesis of oesophageal neoplastic progression and the biological significance of this data warrants further investigation.
This work was supported by a Pathology Society Bursary awarded to an undergraduate medical student (RJP).

P57

Audit of Lymph Node Yield from Colorectal Cancer Resections: 2005 to 2016

Ⓟ MM Davie; GI Murray

Aberdeen Royal Infirmary, Aberdeen, UK

The Royal College of Pathologists' dataset for colorectal cancer (CRC) states that a median number of 12 lymph nodes (LNs) should be examined per specimen. Scottish CRC Quality Performance indicators state that this target should be achieved in 80% of cases. The presence of LN metastases is one of the most important prognostic factors in CRC. An adequate LN yield is required to ensure precise staging, and accurate detection of LN metastases is vital in determining whether adjuvant treatment is required. The purpose of this audit was to analyse LN yield from CRC resections in our centre, and compare against current standards. A retrospective analysis of a database containing anonymised data from all CRC resections reported by a regional cancer centre over an eleven year period (2005 to 2016 inclusive) was performed. 3126 cases were analysed. 15% of cases were screen-detected. A fifth of cases received neoadjuvant therapy, the majority of these being rectal tumours. 42% of tumours were located in the proximal colon, 30% in the distal colon, and 27% in the rectum. Most cases were staged as Dukes B (42%) or Dukes C (41%). Median LN yield by year ranged from 14 to 23. LN yield improved over time, with a median yield of 20 or above achieved since 2012. 69% to 97% of cases produced 12 or more LNs, and this target was satisfied in over 80% of cases since 2008. In 2016, median LN yield was 21, and 95% of cases harvested 12 or more LNs. LN yield was highest for proximal tumours. A higher LN yield was generally seen in higher stage tumours, and in cases with extramural venous invasion. This audit demonstrates that our centre has consistently achieved a median LN yield of 12 or more for the past 11 years. Since 2008 this target has been achieved in over 80% of cases. Furthermore, we demonstrate that a much higher median LN yield can be achieved in routine practice, with a median yield of 20 or above for the past 5 years.

P58

Complete Pathological Response to Neoadjuvant Chemotherapy in EBV Positive Gastric Adenocarcinoma

Ⓟ JL Taylor[1]; D Spence[1]; R Kennedy[1]; E Napier[1]; R Turkington[2]; M Eatock[1]; WDB Clements[1]; DT McManus[1]

[1]Belfast HSC Trust, Belfast, UK; [2]Belfast HSC Trust and Queen's University, Belfast, UK

Recent data from the Cancer Genome Atlas network have proposed a molecular classification of gastric carcinoma into 4 subtypes; the Epstein-Barr virus positive subtype is thought to represent between 5 and 10% of cases worldwide and may have an improved prognosis. In the UK, approximately 50% of patients with gastric carcinoma, undergo perioperative chemotherapy. This report describes 3 patients with gastric adenocarcinoma, positive with EBER ISH on endoscopic biopsy who underwent neoadjuvant chemotherapy followed by gastrectomy /subtotal gastrectomy and who showed a complete pathological response. All 3 were elderly males, smokers or ex-smokers and had ulcerating tumours in the body of the stomach. Two of the resections had a macroscopically visible scarred tumour bed and in one of these, a separate incidental type1 grade I carcinoid was detected. In the third patient, there was no definite tumour bed but several enlarged lymph nodes showed scarring suggestive of complete regression of nodal metastasis. Two of the endoscopic biopsies showed a "lacey" pattern, associated with EBV positive cases. Tumour classification systems aim to identify tumour subtypes which are biologically distinct, the recognition of which is of clinical value. Complete pathological response to perioperative chemotherapy is comparatively rare in gastric adenocarcinoma and only a single case report describes complete pathological response in EBV positive gastric carcinoma. While this represents an anecdotal mini case series, EBER in situ hybridisation is available in most histopathology laboratories and could be included in a panel with HER2, p53, MMRIHC and E cadherin to allow prospective molecular classification in an attempt to select patients with gastric adenocarcinoma who are more likely to respond to chemotherapy.

P59

This Case Report Describes Metastasis of Breast Carcinoma to the Colon Where it Mimicked a Primary Colonic Neuroendocrine Tumour

Ⓟ KA Elliott[1]; DT McManus[2]

[1]Royal Victoria Hospital, Belfast, UK; [2]Belfast City Hospital, Belfast, UK

This case report describes metastasis of a breast carcinoma to the colon where it mimicked a primary colonic neuroendocrine tumour. There was a history of grade 3 infiltrating duct breast carcinoma 5 years previously. The CT also showed thickening of the proximal descending colon and omental metastasis. The findings suggested a colonic neoplasm with omental and pulmonary metastases and she was referred for colonoscopy where a colonic tumour was not detected but a 2 mm diameter sessile polyp was noted in the hepatic flexure of the colon. Histological examination showed a tumour centred on the submucosa composed of plasmacytoid cells that appeared relatively monotonous. The appearances did not suggest primary colonic adenocarcinoma but a primary colonic neuroendocrine tumour was considered. The tumour cells stained strongly for synaptophysin but were negative for CD56. CK7 was positive whereas CK 20 and CDX2 were both negative. The tumour cells were strongly positive for ER and GATA 3. The original breast cancer was obtained from file. There were areas showing a papillary growth pattern and immunohistochemistry showed strong synaptophysin staining in much of the tumour. It was concluded that the tumour in the colon represented metastasis from the breast carcinoma. Colonic neuroendocrine tumours (NET) are rare, representing less than 10% of all Gastroenteropancreatic neuroendocrine tumours (GE markedly different from that of metastatic ductal carcinoma of the breast. The current case of metastatic breast carcinoma mimicking a neuroendocrine tumour of the colon further highlights the importance of accurate pathological diagnosis due to the diversity in management based on histology

P60

HPV-Associated Lymphoepithelioma-Like Carcinoma of the Anal Canal: A Rare Variant of Squamous Cell Carcinoma with Potential for Misdiagnosis

Ⓟ K Scott[1]; G McVeigh[1]; JM Trainor[1]; J Jamison[2]; MB Loughrey[1]; WG McCluggage[1]; PJ Kelly[1]

[1]Royal Victoria Hospital, Belfast, UK; [2]Antrim Area Hospital, Antrim, UK

Purpose of study: Lymphoepithelioma-like carcinoma (LELC) occurs at a variety of sites and at some considered to be an uncommon variant of squamous cell carcinoma (SCC). These tumours are frequently associated with Epstein-Barr virus (EBV) but more rarely there is an association with human papilloma virus (HPV), particularly in the uterine cervix. Other cases reports have described this occurrence in the penis and breast. We present a case of HPV associated LELC of the anal canal, to our knowledge the first case described at this site, and highlight the potential for misdiagnosis.
Method and results: A 68 year-old male underwent biopsy of a rectal polyp. This showed non-dysplastic rectal mucosa containing foci of poorly differentiated carcinoma with a solid cohesive or syncytial growth pattern and prominent tumour infiltrating lymphocytes, morphologically suggestive of a rectal medullary-type carcinoma. The tumour showed intact normal nuclear immunoreactivity for MLH1, PMS2, MSH2 and MSH6 but was positive for p63 and CK5/6. BerEP4, neuroendocrine markers and mucin stains were negative. A diagnosis of LELC was made, a variant of SCC. Subsequent anorectal biopsies showed tumour and adjacent dysplastic surface anal squamous mucosa (AIN III). In situ hybridization for EBV-encoded RNA was negative but p16 showed aberrant "block" positivity, suggesting high risk HPV infection. Molecular studies confirmed the presence of HPV type 16.
Conclusions: In summary, we present the first case of HPV-associated LELC of the anal canal. Immunohistochemistry was required to establish the diagnosis and exclude the main initial differential diagnosis of rectal medullary carcinoma, a tumour with similar morphology but requiring different management.

P61

Microscopic Colitis: A Single Centre Experience Over an Eight Year Period, with Clinical Follow-Up

Ⓟ M Moore; PJ Kelly; MB Loughrey

Department of Histopathology, Royal Victoria Hospital, Belfast Health and Social Care Trust, Belfast, UK

Purpose of the study: Microscopic colitis is an increasingly common chronic inflammatory disorder of the colon. We report our single centre experience of this condition over an eight year period.
Method: The histopathology laboratory system within Belfast Trust was interrogated for cases coded as collagenous colitis or lymphocytic colitis between 2008 and 2016. The study only included cases diagnosed by specialist gastrointestinal pathologists. Information was collected from electronic records on patient age, gender, endoscopic and histological features, associated autoimmune disorders, medication history, treatment and outcome.
Results: 141 patients with collagenous colitis (CC) and 50 patients with lymphocytic colitis (LC) were identified. Both CC and LC predominantly involved females in the seventh decade. 15% demonstrated mild endoscopic abnormalities. Endoscopic sampling protocols varied widely. 67 (47%) of CC and 16 (32%) of LC cases were diagnosed on a single set of random colonic biopsies. 43 (30%) of CC and 16 (32%) of LC cases had separate specimens taken from right and left colon. Right and left sided biopsies were concordant in 40 (93%) and 14 (87%) of these cases respectively. In the remainder, the sampled left colon was normal or near normal. 18% of CC and 40% of LC cases had recognised associated autoimmune diseases. 80 (57%) CC and 32 (64%) LC patients were taking a recognised potentially causative drug at diagnosis. Of the total 191 cases, only one (of LC) was refractory to treatment. The rest exhibited clinical response to therapeutic drugs, causative drug withdrawal or no treatment. 27 CC patients and eight LC patients had follow-up biopsies, three of each showing persistent disease histologically.
Conclusion: Overall, CC and LC are benign conditions with similar demographics, clinical associations, management and outcomes, with only subtle differences. Sampling of right colon at colonoscopy will avoid potentially missing 10% of cases.

P62

HER-2 Over-Expression in Gastric Carcinomas in Lagos University Teaching Hospital (LUTH): A 5-Year Retrospective Study

Ⓟ VI Onyekwelu[1]; KB Badmos[2]; NA Awolola[2]; FB Abdulkareem[2]

[1]Clina-Lancet Laboratories, Lagos, Nigeria; [2]Lagos University Teaching Hospital, Lagos, Nigeria

Introduction: Gastric carcinoma is the second most common digestive tract cancer and the third leading cause of cancer death worldwide. In Nigeria, it is a major contributor to cancer mortality. Recently, there is interest in studying targeted therapy in its management using anti-HER-2 monoclonal antibody to achieve a better prognosis.
Objectives: To determine the frequency of HER-2 over-expression in gastric carcinomas in LUTH, comparing it with known pathologic and prognostic factors.
Methods: This was a retrospective study of 54 cases of gastric carcinoma in LUTH. H&E slides were made from the patients' FFPE blocks and were reviewed to confirm diagnosis and pathological parameters. HER-2 over-expression was assessed by staining with anti-HER-2 antibody. The data was analysed using SPSS 16 to correlate HER-2 over-expression and the pathological features of the carcinomas.
Results: Of the 54 cases, 42 were biopsies and 12 were gastrectomies. The mean age was 55.96 years. The male to female ratio was 3.2:1. Majority of the carcinomas were of intestinal type (83.3%), with diffuse, mixed and indeterminate types accounting for 13%, 1.9% and 1.9% respectively. Almost half of the cases (44%) were of the moderately differentiated grade and patients who had gastrectomies presented mostly with stage T3 disease (75%). HER-2 was over-expressed in 13% of cases, with one equivocal case. There were no statistically significant associations between the variables tested (histotype, grade, stage), although most cases over-expressing HER-2 were of the intestinal type.
Conclusion: HER-2 over-expression occurs in a small percentage of gastric carcinomas in our patients and is independent of most of the pathological parameters, although most of the cases with HER-2 over-expression are of the intestinal histotype. Further work, with larger cohort, is needed to better characterize the possible prognostic benefits of targeted anti-HER-2 therapy in gastric carcinomas.

P63

Colorectal Carcinoma Reporting in Lagos: A 5-Year Audit

Ⓟ KB Badmos[1]; AO Osinowo[1]; AO Lawal[1]; MY Habeebu[1]; O Rotimi[2]; FB Abdulkareem[1]

[1]Lagos University Teaching Hospital, Lagos, Nigeria; [2]St. James's Hospital, Leeds, UK

Purpose of study: The aim of the study is to audit colorectal cancer histopathology reporting in Lagos between 2011 and 2015 before the adoption of the Nigerian Gastroenterology proforma reporting method in 2016.
Method: All resected colorectal carcinoma cases were identified from the Histopathology record of our Department and that of a private Laboratory in Lagos. The dataset as contained in the proforma was extracted from the reports and analysed using SPSS 16.
Result: A total of 92 colorectal resections were received during the 5 year period consisting of 90 colonic and 2 rectal tumours. In 14.1% of these cases, the tumour sites were not recorded. The maximum tumour diameter was stated in 82 (89.1%) cases while tumour distance to the nearest margin was mentioned in 70 (76.1%) cases. The presence/absence of tumour perforation was stated in 68 (73.9%) cases. The record on tumour differentiation was complete in 89 (96.7%) cases. The involvement of longitudinal margins or otherwise was stated in 76 (82.6%) cases. The total number of lymph nodes was stated in 77 (83.7%) cases while lymph node status was stated in 85 (92.4%) cases. The level of venous invasion and maximum tumour distance beyond muscularis propria were unstated in 72 (78.3%) and 86 (93.5%) cases respectively. The presence/absence of separate abnormalities was mentioned in 72 (78.3%) cases only. Distant metastasis was reported in 9 (9.8%) cases, unknown in 80 (87%) cases and unstated in 3 (3.3%) cases. The extent of primary tumour (pT) was complete in 84 (91.3%) cases. Of the 2 rectal tumours resected, plane of mesorectal excision was unstated in the 2 cases while tumour relation to peritoneal reflection was stated in a case. TNM staging was complete in 84 (91.3%) cases.
Conclusion: None of the data item was 100% complete. The use of free text reporting means not all cases can be properly staged. Proforma reporting should improve complete reporting of parameters, better staging and management of cases

P64

An Audit to Assess Immunohistochemical Testing for Cytomegalovirus Infection within the Gastrointestinal Tract

Ⓟ J Horne; B Green

University Hospital Southampton, Southampton, UK

Purpose of the study: We performed an audit of immunohistochemical testing for gastrointestinal tract cytomegalovirus (CMV) infection.
Methods: The records of 369 patient requests that included the term 'CMV', received over a five-year period were reviewed.
Summary of results: CMV immunohistochemistry was reported in 301 patient requests. In 2014–2015 there was a 94% increase in CMV immunohistochemistry requests. Over the five-year period there was a two-fold increase in requests in lower GI biopsies, but a 38% decrease in requests in upper GI biopsies. Inflammatory bowel disease (IBD) was the underlying pathology in 49% of patient requests. In 43% of cases, immunohistochemistry was performed due to pathologist suspicion of CMV infection, whilst in 35% the clinician requested testing. There was a ten-fold increase in clinician requested testing (6-65 requests). Immunohistochemistry detected CMV in 5% of requests. In 63% of patient requests, virological testing was also performed when immunohistochemistry was requested by the clinician. In 75% of requests, immunohistochemistry and virology both detected CMV. In 36% of requests, immunohistochemistry was negative whilst virological testing detected CMV.
Conclusions: The diagnostic prevalence of CMV detected by immunohistochemistry is low. There has been a marked step change in the number of requests for immunohistochemical testing, especially clinician requesting. This correlates with a marked increase in the use of monoclonal antibodies to treat IBD. Virological testing is often requested alongside immunohistochemistry, and it may detect the virus when immunohistochemistry fails. Immunohistochemistry is good at identifying true positives and true negatives, but it also gives a high number of false negatives. The use of immunohistochemistry should be questioned, when virology is available. This could improve diagnostic accuracy, whilst also delivering cost savings for pathology.

P65

Markers of Apoptosis and Autophagy are Predictive of Survival in Oesophageal Adenocarcinoma

Ⓟ S El Mashad[1]; T O'Donovan[2]; E Kay[3]; T O'Grady[3]; D McManus[4]; S McQuaid[5]; R Turkington[6]; S McKenna[2]

[1]Beaumont Hospital, Dublin, Ireland; [2]CCRC, Cork, Ireland; [3]Beaumont Hospital and RCSI, Dublin, Ireland; [4]Belfast City Hospital, Belfast, UK; [5]Northern Ireland Biobank, Belfast, UK; [6]Centre for Cancer Research and Cell Biology, Belfast, UK

Background: Less than 20% of patients with advanced oesophageal carcinoma benefit from receiving neo-adjuvant therapy. Studies using oesophageal cancer cell lines have shown that drug sensitive tumour cells undergo apoptosis in response to drug treatment, whereas resistant cells induce autophagy and can recover following withdrawal of drug. In this study, we evaluated markers of apoptosis (cleaved/activated caspase 3) and autophagy (LC3B) to establish whether these markers are predictive of clinical response post neoadjuvant therapy.
Aim of the study: To evaluate markers of autophagy (LC3B) and apoptosis (active caspase 3) to establish whether these markers can be predictive of clinical response in oesophageal adenocarcinoma.
Methods: Oesophageal adenocarcinoma tumour tissue from the Northern Ireland Biobank at Queens University Belfast was examined retrospectively. Tumours from 144 patients post neoadjuvant therapy were assembled into tissue microarrays prior to immunohistochemical analysis. Kaplan-Meier survival curves and log-rank tests were used to assess the impact of active caspase 3 and LC3B expression on survival. Cox regression was used to examine association with clinical risk factors.
Results: In patients who received neo-adjuvant chemotherapy 38.9% had high LC3B expression, which correlated with poor overall survival (P=0.017). Conversely high levels of active caspase 3 were found in 14.6% of patients and this correlated with a significantly better prognosis (P=0.027). A distinct globular pattern of LC3B expression was found to be predictive of overall survival (p<0.001).
Conclusions: The activation of caspase 3 and elevation of LC3B can provide pharmacodynamic markers of cellular response (apoptosis or autophagy) and outcome following neo-adjuvant treatment. In addition, a distinct globular LC3B staining pattern was observed as a highly predictive poor prognostic marker.

P66

Colorectal Serrated Neoplasia — A Retrospective Review

Ⓟ AJ McCarthy; S O'Reilly; J Shanley; E Ryan; G Cullen; K Sheahan

St. Vincent's University Hospital, Dublin, Ireland

Background: Colorectal cancer is a heterogeneous disorder that arises via multiple distinct pathways, including the serrated pathway, in which serrated polyps are the precursor lesions. As such, serrated polyps of the colorectum, including sessile serrated lesions/polyps (SSL/Ps) and traditional serrated adenomas (TSAs), have gained increased recognition in recent years.
Aim: To characterize a series of serrated colorectal polyps, focusing on the clinicopathological features of SSL/Ps and TSAs. Methods: A search was performed using the laboratory information system to identify all colorectal polyps assigned a 'serrated adenoma' SNOMED code between 01/01/2004 and 31/12/2015. All available and suitable slides were reviewed by 1 pathologist, who was blinded to the original diagnosis and the site of the polyp. Subsequently discordant cases, SSL/Ps with dysplasia and all TSAs were reviewed by a second pathologist.
Results: Over 144 months, 577 polyps were assigned a 'serrated adenoma' SNOMED code, with 560 (from 441 patients) available for review. 10% of these polyps were reclassified following review by 2 pathologists, with the majority of these changes being from SSL/P to hyperplastic polyp (Hyp) (40/56). There were 438 SSL/Ps (91.8%) and 35 TSAs (7.3%). 85.2% of SSL/Ps were in the right colon and 65.5% were small (<1cm). 5% of SSL/Ps exhibited dysplasia. 13/438 SSL/Ps were downgraded from SSL/P with dysplasia to SSL/P without dysplasia. Detection of SSL/Ps peaked in the most recent years reviewed (85.2% reported between 2013 and 2015, inclusive), coinciding with the introduction of 'BowelScreen' (the Irish colorectal cancer screening programme). 85.7% of TSAs were in the left colon and 77.3% were large (>/=1cm).
Conclusion: It can be challenging to distinguish SSL/Ps from Hyps, as there are often only subtle differences. As the malignant potential of SSL/Ps and TSAs has been clearly demonstrated, it is important that serrated polyps are identified and correctly classified histologically. A low rate of SSL/Ps with dysplasia is confirmed (5%).

P67

Bariatric Surgery and an Unexpected Inflammatory Fibroid Polyp of the Oesophagus: A Case Report

Ⓟ J Cunningham[1]; A Rendek[1]; B Sgromo[2]; E Williamsom[2]; R Gillies,[2]; S Antonowicz[2]; Z Orosz[1]

[1]Department of Cellular Pathology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [2]Department of Surgery, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

Introduction: Inflammatory fibroid polyp (IFP) first described by Vanek in 1946 is a rare entity found in the gastrointestinal tract, usually in the stomach and small intestine. The aetiology is unknown and it is considered a reactive pseudotumour. We present a case located in the oesophagus diagnosed incidentally prior to bariatric surgery.
Case Report: A 36 year old overweight, asymptomatic female (BMI 57) referred for bariatric surgery. During surgical work-up an endoscopy was performed revealing an incidental lesion in the lower oesophagus. The biopsy findings raised the possibility of an IFP with a differential diagnosis including polypoid eosinophilic oesophagitis and GIST.
An endoscopic mucosal resection was attempted but this was abandoned due to the sessile nature of the polyp. The surgical team then undertook a laparoscopic intragastric resection to remove the polyp. The morphology and immunohistochemistry (CD34 positive, c-kit, S100, DOG1 and desmin negative) were consistent with an IFP. The patient had no post-operative complications and was discharged home after two days. She is now awaiting bariatric surgery.
Discussion: IFP in the oesophagus is rare with only 18 cases reported in the literature. They are considered benign with many cases shown to harbour platelet derived growth factor receptor alpha (PDGFRA) activating mutation suggesting they may be neoplastic/clonal lesions. This case is significant because it demonstrates both the benefit of pre-operative endoscopy, a controversial issue in work up to bariatric surgery, and the laparoscopic technique used which would be impossible if bariatric surgery had taken place, reducing the size of the stomach. It demonstrates how using a minimally invasive technique such as laparoscopic surgery can result in swift recovery and early discharge.

P68

Adequacy of Duodenal Biopsies

Ⓟ L McKenna; B Newell

St George's Hospital, London, UK

Duodenal biopsies are a very common histological specimen with over 2500 duodenal biopsies received per year in this department. It has been noted that some of the specimens received are inadequate due to small biopsy size. In addition, there is often insufficient clinical information received. Small sample sizes and inadequate clinical information can lead to difficulties diagnosing and interpreting findings.
The indications for duodenal biopsies include the evaluation of malabsorption, investigation of iron deficiency anaemia, diagnosis and monitoring of coeliac disease, investigation of diarrhoea and diagnosis of neoplasia or ulceration. Therefore, accurate and clinical information is essential to allow for appropriate assessment of the biopsy. The RCPath tissue pathway has stated that for a duodenal biopsy to be considered adequate at least 4 biopsies should be obtained. This retrospective looked at the sample size and clinical information received for a 3 month period over the last year.
Results: Of the 599 biopsies received over that period, an indication was received for 89.3% of biopsies. 21% of biopsies were received for diagnosis of coeliac disease while 19.5% were received for iron deficiency anaemia. Medical history was present on 40.1% of request cards. In this audit it was found that only 29.7% of specimens contained at least four pieces of tissue. Of the 599 biopsies, 5.2% (31) were reported as inadequate and only 2.2% confirmed coeliac disease.
Conclusion: As the recommended tissue is not being received for pathological diagnosis, it may be that diagnostic features are not being sampled. In addition, medical information was only received in a minority of patients. The paucity of medical information puts the pathologist at a disadvantage as there is no clinical context. Previous biopsy results would allow pathologists to place the current biopsy into the context of previous results.

P69

This abstract has been withdrawn

P70

Feasibility of Transcriptional Profiling of Formalin-Fixed Paraffin Embedded (FFPE) Pancreatic Ductal Adenocarcinoma Resection (PDAC) Specimens

Ⓟ PJ Kelly[1]; SM Walker[2]; RC Turkington[3]; RD Kennedy[4]

[1]Royal Victoria Hospital, Belfast, UK; [2]Almac Diagnostics Ltd, Craigavon, UK; [3]Centre for Cancer Research and Cell Biology, Queen's Univeristy of Belfast, Belfast, UK; [4]Centre for Cancer Research and Cell Biology, Queen's University of Belfast and Almac Diagnostics Ltd, Belfast, UK

Purpose of study: PDAC is the fifth commonest cause of cancer-related death in the UK. Recent studies have revealed novel subgroups of PDAC to which treatment may be targeted but have relied upon fresh frozen tissue, limiting the datasets which may be used for biomarker discovery. We sought to explore the feasibility of obtaining whole transcriptome data from FFPE PDAC resection specimens.
Methods: Transcriptional profiling of 29 formalin FFPE samples (17 PDAC, 12 normal pancreas) taken from 13 patients was performed using the Almac Diagnostics XceITM array, a cDNA microarray-based technology optimized for archival FFPE tissue. All PDAC specimens were obtained by Whipple's resection at the Belfast Trust between 2008 and 2013 and cases divided into good (relapse-free survival (RFS)> 12 months) and poor (RFS ≤12 months) prognosis groups. Principal components analysis, unsupervised hierarchical clustering, differential gene expression and functional enrichment were performed and prognosis was assessed by Kaplan-Meier survival analysis.
Results: All samples underwent successful RNA extraction and transcriptional profiling. There were no significant differences in age, sex, performance status, tumour site, post-operative TNM staging or resection margin involvement between good/poor prognosis groups. Principal components analysis demonstrated a biological split between tumour and normal samples and good and poor prognosis cases. Unsupervised hierarchical clustering successfully separated the normal and tumour samples and demonstrated differences in gene expression within the tumour group. Differential gene expression between the good and poor prognosis samples identified significant biological pathways involved in cell division and proliferation.
Conclusion: Our feasibility study has demonstrated our ability to obtain high quality microarray data from archive FFPE PDAC resection specimens and provides a platform for novel biomarker discovery.

P71

Granulomatous Variant of Type 2 Autoimmune Pancreatitis: A Report of Two Cases

Ⓟ JM Trainor; MB Loughrey; PJ Kelly

Royal Victoria Hospital, Belfast, UK

We present two cases of granulomatous inflammation in the pancreas associated with features of type 2 autoimmune pancreatitis (AIP). Granulomatous inflammation has not been described before in type 2 AIP.
Patient 1 was a 53 year old male and patient 2 a 44 year old male. Both presented with obstructive jaundice and a pancreatic head mass on imaging, clinically suspicious of malignancy. Both had a history of ulcerative colitis (UC). Both patients had negative biliary cytology but underwent a Whipple's procedure on the basis of clinical and radiological suspicion of malignancy. Histology showed features typical of type 2 AIP: dense lymphoplasmacytic periductal inflammation, granulocytic – epithelial lesions and patchy lobular inflammation. In addition numerous non-caseating granulomata were evident. IgG4-positive plasma cells were only focally encountered; obliterative phlebitis was not a feature. Granulomas were also identified in the duodenum, particularly within Brunner glands, and in the gastric mucosa. Granulomatous inflammation in the pancreas is extremely rare but has been described in association with infections, foreign bodies, diabetes mellitus, sarcoidosis and in a case of Crohn's disease (CD). Here we describe two cases of suspected pancreatic malignancy subsequently found histologically to have granulomatous inflammation in the pancreas along with other typical features of type 2 AIP. Type 2 AIP is associated with inflammatory bowel disease, particularly UC, in approximately 30% of cases. We suggest that our cases reflect a granulomatous variant of Type 2 AIP, which has not been described before. Both cases had gastroduodenal granulomas raising the possibility of CD rather than UC. A single case report of granulomatous pancreatitis associated with Crohn's disease was described in 1995. This may have been an example of granulomatous variant of type 2 AIP based on clinicopathological features described therein.

P72

Mucinous Cystic Neoplasm of the Liver Arising in Polycystic Liver Disease: A Case Report

Ⓟ S Venkatesan; B Haugk; J Scott; DM Manas; CH Wilson

Royal Victoria Infirmary, Newcastle Upon Tyne, UK

Mucinous cystic neoplasm (MCN) of the liver is a rare tumour with an incidence of less than 5%.They remain a diagnostic challenge radiologically with differential diagnoses ranging from inflammatory and parasitic cysts to malignant neoplasms. Accurate diagnosis is critical given the potential for malignant transformation in MCN but bearing in mind potentially devastating consequences of anaphylactic shock from echinococcal cyst aspiration/rupture.Hence definitive diagnosis is usually made on surgical excision specimens.In contrast, polycystic liver disease (PLD) as part of autosomal dominant polycystic kidney disease (ADPKD) is largely managed conservatively requiring surgical excision/liver transplant only in exceptional circumstances.We hereby report a case of MCN with classical ovarian type stroma in a known background of PLD which,to the best of our knowledge, has not been described in the literature before.
A fifty year old woman on surveillance for ADPKD presented with non-specific abdominal pain and raised CA 19-9.Cross-sectional imaging showed several small cysts dispersed throughout the liver in keeping with PLD. In addition, a 13cm complex multilocular, septated cyst was noted in the left lobe with cyst within cyst appearance,mural nodule and suspicion of mucinous cyst contents on MRI.Radiological differential diagnoses included MCN and hydatid cyst.Excision specimen showed a 11cm,unilocular cyst and multiple small cysts in the background. Histology revealed MCN with classical ovarian type stroma and columnar mucinous epithelium exhibiting low grade dysplasia.Extensive sampling did not demonstrate any high grade dysplasia or invasive carcinoma.Von-Meyenburg complexes were noted in the background in keeping with known PLD.The prognosis of non-invasive MCN is excellent but recurrences can occur when,as in this case,excision is incomplete.Multidisciplinary approach is critical in the management of cystic liver lesions as neoplastic cysts can co-exist with PLD.

P73

Genetic and Epigenetic Alterations in Biliary Tree Cancers: Combined FISH, IHC and NGS Approach

Ⓟ D Patel; R Hamoudi; S Khan; D Allen; J Edeline; J Bridgewater; M Rodriguez-Justo

UCL, London, UK

Purpose of the study: Cholangiocarcinoma (CCA) is the most common biliary tract malignancy. CCA is a heterogeneous malignancy and has been classified as intrahepatic, perihilar or extrahepatic based on the anatomical location. It is often asymptomatic until it has metastasized, treatment options are limited and it has a poor five-year overall survival. Increased incidence of CCA in the West has been seen in the last decades, partially due to more accurate classification. Increasing our knowledge of CCA (identifying novel therapeutic targets and better molecular classifications) will offer new targets for therapy and allow for more personalised treatments.
Methods: A cohort of 54 clinically well characterised CCA cases was included. Formalin-fixed-paraffin-embedded blocks were used for immunohistochemistry (mismatch-repair proteins) and FISH (amplification of FGFR1, FGFR2, HER2 and FGFR2 break-apart). DNA was extracted from the FFPE blocks and a number of genes were targeted for using NGS.
Results: The majority of tumours were MMRp (mismatch repair proficient) (92.6%). There was no evidence of FGFR1 or FGFR2 amplification whilst HER2 amplification was seen in 11.3% samples. Sequencing data revealed mutations in KRAS (24.5%), NRAS (15.1%), EGFR (13.2%) BRCA1 (13.2%), BRCA2 (7.5%) as well as in IDH1 (1.89%) and IDH2 (1.89%). No mutations were seen in BRAF. Half of the HER2 amplified cases had mutations in the genes mentioned above. FGFR2 translocations were seen in 12.7% of samples, interestingly we also saw amplification of parts of the C-terminal and N-terminal of the receptor.
Conclusions: Our results add further evidence that the EGFR pathway is a promising molecular target for CCA. Alterations in kinase receptor FGFR2 gene are targetable and might be useful in the diagnosis of the disease. The role of IDH inhibitors is being investigated in early clinical trials in tumours with mutant IDH enzymes. HER2 blockade is also promising treatment strategy for patients.

P74

EUS FNA Microcore Biopsy is Superior than Endobiliary Biopsy in the Diagnosis of Malignant Pancreaticobiliary Lesions

R Tiam; Ⓟ B Jalil; J Cooke

Hull Royal Infirmary, Hull, UK

Introduction: The ability to provide definitive and timely histological diagnosis of malignancy in suspected malignant pancreaticobiliary lesions depends on high quality tissue sampling. We conducted a study to evaluate the diagnostic utility of endobiliary biopsy versus endoscopic ultrasonography-guided fine needle aspiration (EUS FNA) microcore biopsy.
Method: We performed a retrospective search of our laboratory information management system for patients with suspected malignant pancreaticobiliary lesions who had endobiliary and EUS FNA microcore biopsies. The haematoxylin and eosin-stained slides were retrieved and reviewed, and assessed for adequacy; a biopsy is regarded as adequate if a pathological diagnosis can be rendered. All adequate biopsies are then categorised into whether a definitive diagnosis can be established (diagnostic) or not (non-diagnostic).
Results: The search yielded 94 endobiliary biopsies and 78 EUS FNA microcore biopsies. 77 out of the 94 endobiliary biopsies were deemed adequate, and out of this 54 was diagnostic of malignancy (sensitivity 57%). In 11 cases where the endobiliary biopsy was not diagnostic, subsequent EUS FNA microcore biopsies provided a malignant diagnosis in 9. 96% of EUS FNA microcore biopsies were adequate and in 62 a malignant diagnosis could be established (sensitivity 83%).
Conclusion: Our study indicates that EUS FNA microcore biopsy is more sensitive than endobiliary biopsy in the diagnosis of malignant pancreaticobiliary lesions. Because lesions are visualised, sampling is targeted and this provides high tissue yield of tumour and stroma enabling a malignant histological diagnosis to be rendered and reduces the need for repeated sampling. The tissue sample is also amenable to immunohistochemical staining which is important in characterising suspected metastases. As such, we believe that EUS FNA microcore biopsy should be the standard method of tissue sampling in suspected malignant pancreaticobiliary lesions.

P75

Plasmacytoma of the Ureter: A Case Report of an Exceedingly Rare Tumour

Ⓟ MM Davie; D McClelland

Aberdeen Royal Infirmary, Aberdeen, UK

Introduction: Plasmacytoma is a discrete tumour mass of neoplastic monoclonal plasma cells. This entity constitutes fewer than 5% of plasma cell neoplasms. These tumours occur in bone, or less commonly in soft tissue. Progression to myeloma occurs in approximately 15% of extra-osseous cases. Plasmacytomas of the genito-urinary tract are exceedingly rare. To our knowledge, only two other cases of ureteric plasmacytoma have been reported.
Case presentation: A 58 year old woman underwent CT scan following investigations for a urinary tract infection. This revealed right hydronephrosis and a tumour within the right ureter. The presumed diagnosis was urothelial cell carcinoma. Due to co-morbid disease, the surgery was delayed for 18 months. Open nephro-ureterectomy was performed, revealing a 90mm ureteric tumour. Microscopy showed plasmacytoma, and this was confirmed with positive immunostaining for CD138, with kappa light chain restriction. There was continuous extension of the tumour from the ureter to the collecting system, with a positive distal ureter margin. The renal parenchyma was uninvolved. Further work-up did not show evidence of systemic myeloma. Subsequent cystoscopy showed inflammatory changes within the bladder, and biopsy confirmed plasmacytoma of the bladder.
Discussion: Plasmacytoma of the ureter is exceedingly rare, although there are several reports of retroperitoneal plasmacytoma causing ureteric obstruction. Of the two previously reported cases, both occurred in elderly female patients with hydronephrosis. The diagnosis of plasmacytoma was unexpected in both cases. In one case the tumour was poorly differentiated, and immunohistochemistry was essential in making the diagnosis. We present a case of ureter plasmacytoma with subsequent bladder involvement. This rare tumour may mimic urothelial cell carcinoma radiologically.

P76

Case Report: Juxtaglomerular Cell Tumour, a Rare Renal Neoplasm

Ⓟ TJ Kueh; D McClelland

Pathology Department, Aberdeen Royal Infirmary, Aberdeen, UK

Introduction: Juxtaglomerular cell tumour (JGCT, also known as reninoma) is a rare benign renal neoplasm. Only approximately 100 cases have been reported in literature. Synaptophysin positivity is rarely reported.
Case Presentation: A 59 year old man was discovered to have a left renal mass whilst undergoing investigations for gastrointestinal symptoms. CT scan confirmed the presence of a Bosniak III cystic lesion. The initial date of surgery was postponed due to poorly controlled hypertension. He underwent a laparoscopic partial left nephrectomy. Macroscopic assessment revealed a 40mm solid and cystic lesion with cream, yellow and haemorrhagic cut surface. Histology showed a largely solid tumour with a thick fibrous capsule. Focally a 'leaf-like' polypoidal architecture was observed. The tumour was composed of sheets of polygonal cells with granular eosinophilic cytoplasm. Occasional spindle cells were present. Abundant thin-walled blood vessels were observed. The tumour cells stained positively with Vimentin, Smooth Muscle Actin, CD34, CD117 and Synaptophysin. They were negative with Pan-CK, CK7, CK20, S100, HMB-45, Desmin, Chromogranin and CD56. The diagnosis of JGCT was made.
Discussion: JGCT occur more frequently in women and young adults, being especially rare over the age of 40. JGCT is a rare cause of secondary hypertension and, while classified as benign, have been known to cause fatal events, primarily as a sequela to uncontrolled hypertension. Vascular invasion and distant metastases have also been reported. Most JGCT show diffuse positivity with vimentin and CD34 but definitive diagnosis is usually achieved by positive renin labelling. Synaptophysin positivity is rarely reported in JGCT – one such case was of a multicentric, recurrent and likely malignant JGCT. Complete surgical resection is generally curative for these lesions. Most cases return to normotension post-resection. In our case, the patient suffered a cerebral infarct post-operatively.

P77

An Unusual Presentation of Muir-Torre / Lynch Syndrome

Ⓟ H Jawad; N Conlon; NJ Mayer

Cork University Hospital, Cork, Ireland

Upper tract urothelial carcinoma (UC) is rare compared to its bladder counterpart and may develop as a manifestation of Muir-Torre syndrome (MTS), a phenotypic variant of Lynch syndrome (LS). LS is characterized by mutations in a number of DNA mismatch repair genes and results in microsatellite instability. We present the case of a 51 year old male who underwent nephroureterectomy for multifocal UC of renal pelvis and ureter, which immunohistochemically was MSH-2 and MSH-6 deficient, and MLH-1 and PMS2 intact. Subsequently, the patient was diagnosed with colorectal adenocarcinoma and suspected sebaceous carcinoma; both these tumours shared the same mismatch repair (MMR) immunoprofile as the UC. Subsequent genetic analysis on blood confirmed two germline mutations in the MSH2 gene (c.1915C>T and c.2211-1G>T). This case emphasises the importance of undertaking MMR testing in cases of upper tract UC, particularly in young patients, because of the clinical significance of a diagnosis of Lynch syndrome.

P78

Phyllodes Tumour of the Urinary Bladder: A Report of a Unique Case

Ⓟ N Tchrakian[1]; E Browne[1]; JH Shanks[2]; RJ Flynn[1]; S Crowther[1]

[1]The Adelaide and Meath Hospital, Dublin, Ireland; [2]The Christie NHS Foundation Trust, Manchester, UK

Phyllodes tumours (PT) of the male urogenital tract (UGT) are rare; to date, fewer than one hundred cases have been described in the prostate, and under fifteen cases are reported to have arisen in the seminal vesicle. They are histologically similar to their counterparts in the breast; namely, they are true biphasic lesions which comprise an admixture of stromal and epithelial components in varying proportions.
As with breast PTs, the histologic appearances and clinical behaviour of the male UGT neoplasms are highly variable; the lesions may be cured by surgical resection, but a large proportion exhibit local recurrence, and cases of direct invasion into adjacent organs and widespread metastasis have been reported. Although no single morphologic feature is reliably predictive of prognosis, a combination of features may be used for grading purposes and prognostication, similar to the approach used for grading PTs of the breast. Although stromal tumours of the urinary bladder (benign and malignant) have been described, primary biphasic fibroepithelial tumours have not, to our knowledge, been reported in humans. We describe the unique case of a primary PT of the urinary bladder arising in the dome of the bladder in a 54 year old man, which exhibited multiple recurrences, and which was eventually treated with partial cystectomy. The cystoscopic resection and biopsy samples received in the pathology department in the intervening years presented considerable diagnostic difficulty, and a range of diagnoses were proposed at different times, including fibroepithelial polyp, hamartomatous tumour, and polypoid/bullous cystitis. However, it was on the eventual partial cystectomy specimen that a diagnosis of PT, benign/low grade was ultimately made. We discuss the histopathological features of our case, and we address diagnostic and classification considerations specific for this site in the wider context of PTs thus far reported in the male UGT.

P79

An Audit of Prostate Biopsy Reporting Practice in an Irish University Hospital in the Year 2015

Ⓟ N Tchrakian; T Crotty

St. Vincent's University Hospital, Dublin, Ireland

Background: Prostate biopsies (PBs) constitute a high proportion of specimen accessions in most general pathology laboratories. In this audit, we assess the reporting of PBs in our institution, a major Irish University Hospital.
Objectives: 1. To assess our practices in reporting PBs and to compare them with those of the Royal College of Pathologists (RCPath) for quality assurance (QA) purposes;
2. To audit reporting trends and interobserver variability among pathologists within the department;
3. To assess concordance of Gleason Score reporting between PB and subsequent radical prostatectomy specimens.
Methods: Histology reports for PB specimens in the year 2015 were reviewed (n = 741). Clinical, demographic, macroscopic and microscopic reporting data were collected and analysed. Parameters examined were taken from the RCPath Dataset, and included the reporting of perineural and lymphovascular invasion (PNI, LVI) and extraprostatic extension, together with the use of immunohistochemistry (IHC) and intradepartmental review. In addition, reporting trends between pathologists were examined in order to assess interobserver variability. Lastly, the histology reports of subsequent prostatectomy specimens were reviewed for Gleason Score comparison (n = 33).
Results: 58% (n = 432) of a total of 741 PBs showed invasive adenocarcinoma, which were distributed between Grade Groups of 1-5, respectively, as follows: 37.3%, 22.7%, 11.8%, 16%, and 12%. Reporting parameters which differed notably between pathologists included reporting of PNI, use of IHC, and intradepartmental consultation. Comparison with radical prostatectomy specimens revealed that the Gleason Scores of 30% of resection cases were downgraded, 6% upgraded, and the remainder (64%) unchanged.
Conclusion: Auditing of PB reporting is a useful tool for the assessment and maintenance of QA, and may help to characterize reporting trends between pathologists with a view to improving reproducibility.

P80

Incidence of Primary Malignant Renal Tumours According to the 2016 WHO Classification: A 15-year Review from a Tertiary Referral Centre

Ⓟ JJ Aird; J Thorne; C Gulmann

Beaumont Hospital, Dublin, Ireland

Purpose: The WHO Classification of Tumours of the Urinary System and Male Genital Organs published in 2016 introduced new distinct subtypes of renal tumours. The incidence of these tumours is low and restricted to case reports in the literature in some instances. The aim of our study was to evaluate the incidence of the different subtypes of malignant renal tumours in our institution.
Methods: We reviewed slides from all radical and partial nephrectomy specimens over a 15 year period (31st January 2002 to 31st December 2016) and classified them according to the criteria set out by the 2016 WHO Classification. The details from all primary malignant tumours were entered into a database.
Results: 556 primary malignant tumours were identified. The most common subtype was clear cell carcinoma (81%) followed by papillary renal cell carcinoma (11.5%) and chromophobe renal cell carcinoma (3.4%). All other subtypes represented <1% each. There were six cases of multilocular cystic renal neoplasm of low malignant potential, five cases of unclassified renal cell carcinoma, four cases of translocation renal cell carcinoma, two cases of clear cell papillary renal cell carcinoma, two cases of mucinous tubular and spindle cell carcinoma, two cases of tubulocystic renal cell carcinoma, two cases of acquired cystic disease-associated renal cell carcinoma and one case of collecting duct carcinoma.
Conclusions: The incidence of the new subtypes of renal cell carcinoma is low, each representing <1% of all primary malignant renal neoplasms. The incidence of chromophobe renal cell carcinoma is lower in our institution than that reported in the literature.

P81

The Mutational Frequency of BRAF and KRAS in Low Grade Serous Testicular Neoplasms: A Case Series

Ⓟ P Gwiti[1]; Z Melegh[2]

[1]Royal United Hospital Bath, Bath, UK; [2]Southmead Hospital, Bristol, UK

Low grade serous neoplasms of the testis are rare tumours that demonstrate striking morphological similarities with the better-understood ovarian neoplasms. Although the morpho-phenotypical similarities between ovarian and testicular serous neoplasms are well recognised, the genotypic background of testicular serous neoplasm has not been extensively interrogated and the molecular aberrations associated are not established. The cell of origin and the pathogenesis of these neoplasms are still of considerable discussion. The more extensively studies low grade serous ovarian neoplasms are known to harbour mutations in the MAP-kinase pathway. We recently reported a single case of borderline serous neoplasm showing BRAF mutation which intrigued us to learn more about this rare neoplasms. Seven cases were collected, six of which were borderline serous neoplasms and one was a low-grade serous carcinoma. The morphology and immunophenotype on all cases were reviewed. Tumour DNA was extracted and testing for V600E and KRAS demonstrated BRAF and/or KRAS mutation in 3 of the 7 cases, similar to the proportions reported in low grade ovarian serous neoplasms. This supports the role of aberrant signalling of the MAP-kinase pathway in the pathogenesis of low grade serous testicular neoplasms and provides a genetic link between low grade testicular and ovarian serous tumours. The fact that low grade serous neoplasms with similar geno- and phenotype do occur in both the testis and the ovary, while high grade serous neoplasms are very rare in the testis further support the theory that low grade and high grade ovarian serous tumours likely have a completely different pathogenesis. We thus hypothetise that these neoplasms arise from Mullerian metaplasia of either paratesticular mesothelium or intratesticular mesothelial remnants. Our findings could help promote role of molecular analysis in the assessment of these rare neoplasms as accurate diagnosis has obvious management implications.

P82

Müllerianosis of the Renal Calyx: A Unique Case Report

Ⓟ AJ Byers; S Kumar

Royal Blackburn Hospital, Blackburn, UK

Müllerianosis of the urinary tract is a rare condition which mostly occurs in females of reproductive age. Müllerianosis is the proliferation of tissues derived from embryological müllerian ducts (endocervical, endometrial or endosalpinx) within organs of non-müllerian origin. In the urinary tract, the bladder is the most common site, with rare ureteric cases but no recorded cases in the renal calyx. We present a case of a 4 cm polypoidal lesion arising from the left renal calyx of a 24 year old woman who was under follow-up for recurrent urinary tract infections and bilateral reflux nephropathy. Clinically and radiologically the lesion was suspected to be a tumour, possibly a urothelial carcinoma. Initial biopsies were inconclusive. The multidisciplinary decision was to perform a percutaneous biopsy of the mass for a firm pathological diagnosis, since treatment would have been a left nephroureterectomy in a young patient who had poor renal function. Histopathological analysis of the chippings demonstrated renal calyx with underlying stroma containing scattered glandular structures, lined by low cuboidal, ciliated columnar or mucinous epithelium, and focal endometrial-type stroma. No cytological atypia was identified within glands or surface urothelium. The morphological features and immunoprofile were those of, endocervicosis, endosalpingiosis and endometriosis; diagnostic of müllerianosis of the renal calyx. To our knowledge this is the first case of müllerianosis of the renal calyx. Müllerianosis has a good prognosis but has potential for misdiagnosis as a malignant tumour. It should form part of the differential diagnosis of a urinary tract lesion.

P83

Radiological and Pathological Correlation of T3 Prostate Cancer Staging

Ⓟ JTT Lai; S Rasbridge

Royal Bournemouth Hospital, Bournemouth, UK

Purpose of study: Accurate staging of prostate carcinoma is important to determine treatment options, specifically with regards to T3 tumours where radical radiotherapy may be a possible alternative to radical prostatectomy depending on patient status. Where a possibility of radical therapy (prostatectomy or radical radiotherapy) is present, MRI staging is offered to men (or CT if MRI contraindicated).
Methods: Retrospective data collection from October 2014 to October 2016. All pre-treatment (radiological) stages of T3 were compared to the corresponding final pathological staging and final pathological T3 stages compared with the pre-treatment staging. Histology and radiology reports and/or slides were reviewed to assess extent of discrepancy where present.
Standard: Histopathological staging is the gold standard for prostate carcinoma staging.
Results and discussion: There were 44 cases of pre-treatment T3 staging over 25 months. Of these, 6 cases were excluded as there were no final pathological staging. 21 cases (55%) showed staging concordance. 10 cases (26%) were upstaged in the final pathological staging and 7 cases (18%) were downstaged in the final staging.
There were 79 cases of final pathological staging of pT3 over the same period. 8 cases were excluded due to absence of definitive MRI staging results (e.g. Pirads score and region). 24 cases (34%) showed concordance between final staging and MRI. 45 cases (63%) were upstaged in the final pathological staging compared to radiological staging. 1 case (1%) was downstaged (nodal status N1 in radiology but N0 in pathological staging). The sensitivity of MRI locally is 47%, consistent with sensitivity of 42% in studies summarised in the NICE guidance.
Conclusion and recommendation: The concordance of radiological and pathological staging is low. The factors that may explain the discrepancy between radiological and pathological staging such as size and location of extraprostatic extension will be explored.

P84

A Case Report on the Dual Presentation of Non-Invasive Transitional Cell Carcinoma and Primary Malignant Melanoma of the Bladder

Ⓟ S Venkatesan; A Mutton; A Nambiar; J Cresswell

James Cook University Hospital, Middlesbrough, UK

Transitional cell carcinoma of the bladder is a well-recognised entity but malignant melanoma of the bladder is very rare with less than thirty cases reported in the literature to date and to the best of our knowledge there is no report of these two pathologies presenting together. Although the treatment of urothelial carcinoma is well established, there is no consensus on the appropriate management for malignant melanoma of the bladder due to the limited number of cases.The prognosis for primary malignant melanoma of the bladder is very poor and hence reporting such cases is important to help in developing appropriate treatment regimes. We hereby report another example of primary malignant melanoma of the bladder but with an unusual presentation of concomitant non-invasive transitional cell carcinoma of the bladder. An 84 year old gentleman presented with gross haematuria but no other symptoms. Urine cytology was reported as suspicious for high grade Transitional cell carcinoma. Subsequent cystoscopy revealed a large bladder tumour.Histological assessment of a transurethral bladder resection sample revealed a readily recognisable non-invasive Transitional cell carcinoma along with a smaller second population of poorly differentiated cells with an epithelioid morphology and prominent nucleoli but no differentiating features.The initial impression was of a mixed low and high grade poorly differentiated Transitinal cell carcinoma.On further review and immunohistochemical assessment the poorly differentiated tumour component was found to be positive for HMB-45, Melan A and S-100 and negative for pan cytokeratin, confirming its melanocytic nature.Clinical and radiological assessment has revealed no evidence of atypical melanocytic skin lesions or involvement of other viscera thus supporting a primary bladder origin.This case re-affirms the vigilance required when reporting on bladder biopsy samples and the importance of not assuming all tumours are of urothelial origin

P85

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

Ⓟ S Venkatesan; A Husain; N Gatt; A El-Sherif

Royal Victoria Infirmary, Newcastle Upon Tyne, UK

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 eightyyear-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.

P86

Urine Cytology Atypia Rate and Attempted Reclassification Using The Paris System: 'A Yearning for Paris?'

Ⓟ BH Fergie; R Hussain

Northumbria Healthcare NHS Foundation Trust, North Shields, UK

Purpose of study: Record the results of urinary tract cytology over one year in the Trust. Compare atypia reporting with published rates. Attempt to apply The Paris System to atypical samples and correlate with histology. Compare with published outcomes from other centres.
Methods: All cases coded as urine/bladder washings over 12 months were retrospectively selected. Rates of the different outcomes were calculated (classified as inadequate, benign, atypical, suspicious or malignant). Atypical cases reviewed by the authors and reclassification by The Paris System attempted. In cases with matched histology, cytology diagnosis was correlated with histology.
Summary of results: 278 voided urine/bladder washing cytology cases were identified covering the 12 month period. Benign 183 (66%), Atypical 72 (26%), Suspicious 5 (2%), Malignant 3 (1%).
Conclusions: Nationally, rates of atypical results reportedly range from 2 to 30%, compared with 26% at our Trust. A wide interobserver variability is recognised. Classification systems have evolved and The Paris System aims to have high sensitivity and specificity for high grade urothelial carcinoma. They recommend that atypia should be diagnosed when there are rare cells, reminiscent to that of high grade urothelial carcinoma. We have additionally attempted to apply this system to local cases and compare with histology where available.

P87

Paraganglioma of the Bladder as a Rare and Significant Diagnosis During Pregnancy: A Case Report

Ⓟ J Cunningham[1]; C Verrill[2]; ISD Roberts[1]; A Rendek[1]; D Roskell[1]; J Crew[3]; C Tapping[4]; L Browning[1]

[1]Department of Cellular Pathology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [2]Nuffield Department of Surgical Sciences, University of Oxford, Oxford, UK; [3]Department of Urology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; [4]Department of Radiology, Oxford University Hospitals NHS Foundation Trust, Oxford, UK

Introduction: Paraganglioma of the urinary bladder is rare, representing 0.05% of bladder tumours. These tumours are often secretory, presenting with signs and symptoms of catecholamine excess such as hypertension. We present a case of paraganglioma of the bladder diagnosed incidentally during the second trimester of pregnancy.
Case report: A pregnant 31-year-old with no significant past medical history, was found to have a bladder mass on routine 12 week ultrasound scan. Cystoscopy and biopsy of the mass was uneventful. Histology showed benign urothelium with an unencapsulated tumour in the lamina propria composed of nests of synaptophysin and chromogranin positive polygonal cells with a delicate vascular network highlighted by CD34. There was no atypia, no mitoses, tumour necrosis or lymphovascular invasion. MIB1 proliferation rate was 1%. The diagnosis of paraganglioma was made and following MDTM discussion the patient was referred urgently to the endocrinologists and specialist obstetric physicians, with the plan to resect any remaining bladder tumour after the pregnancy. The patient delivered a healthy baby at term, and following local resection of the bladder tumour post-partum she will remain on clinical follow-up.
Discussion: Paraganglioma of the urinary bladder is rare, and published literature on these tumours occurring during pregnancy is limited to case reports. The diagnosis is significant due to the potential impact of a functioning tumour on the pregnancy. The pregnancy will also impact on the timing of further surgical management; a concern as although most are benign there is a small proportion of tumours which show malignant behaviour.

P88

Plasmacytoid Urothelial Carcinoma — A Clinicopathological Case Series from a Tertiary Care Oncology Centre

Ⓟ S Menon; P Gajaria; G Prakash; G Bakshi; A Joshi; V Murthy; SB Desai

Tata Memorial Centre, Mumbai, India

Purpose of study: To report a clinico-pathological case series of plasmacytoid urothelial carcinoma (PUC) from our institute.
Methods: We retrospectively analysed the clinico-pathological data of cases of PUC retrieved from the electronic medical record (EMR), either primarily diagnosed and/or treated at our institute from 2011 to 2015.
Summary of results: Fourteen patients with plasmacytoid urothelial carcinoma were retrospectively reviewed and analysed. All the 14 patients in our series were males with the mean age of 57.7 years (range 46-75 years). Seven cases (50%) were pure plasmacytoid forms while the remaining 7 cases had a minor component of conventional urothelial carcinoma. The plasmacytoid tumour cells were arranged in cords and single cell pattern in all cases (100%) and in loose groups/nests in 2/14 cases (14.28%). Immunohistochemistry was performed in 9 cases and all demonstrated positivity for AE1/AE3 (100%). CK 7 was negative in only one case (11.11%). 5/ 7 cases (71.42%) showed positivity for CK 20 and 7/7 (100%) cases were positive for CD 138. Treatment data was available for 7 patients; five (71.4%) underwent surgery (radical cystoprostatectomy) and three of these also received adjuvant chemotherapy , one patient (14.28%) received intravesical BCG post Trans Urethral Resection of Bladder Tumour (TURBT) and one inoperable patient (14.28%) was given external beam radiation. Limited follow-up data was available for 6 patients with median follow up of 6 months (range 1-60 months).Only one patient was alive at 5 years follow up.
Conclusion: PUC is an aggressive variant of urothelial carcinoma with poor prognosis and hence should be recognized by the pathologist

P89

Is it Safe to Leave a Renal-Biopsy Proven Oncocytoma Alone? An Observational Cohort Study

Ⓟ V Srirangam[1]; M Moghul[2]; BP Rai[2]; A Abroaf[2]; M Hosny[2]; S Agarwal[2]; P Nathan[2]; T Lane[2]; D Hanbury[2]; N Vasdev[2]; J Adshead[2]

[1]Royal Free Hospital, London, UK; [2]Lister Hospital, Stevenage, UK

Introduction: Oncocytomas and chromophobe renal cell carcinomas (RCC), particularly eosinophillic variants, share clinical, histological and radiological similarities. Both renal oncocytomas and chromophobe RCC arise from intercalated cells of the collecting ducts.
Methods: The histological database was retrospectively reviewed for patients who had renal biopsies for suspected oncocytoma or chromophobe renal cell cancer between 2011 and 2015. Histological concordance rates between renal biopsy and partial nephrectomy specimens were evaluated. Renal biopsy-proven oncoctyoma patients who did not proceed to surgical intervention were also followed up.
Results: 16 renal biopsies were performed. The mean age was 71 years (range 53–87 years, SD +/– 8 years). The male to female ratio was 3:1. The mean tumour size on cross-sectional imaging was 28.6mm (range 13–60mm, SD +/– 12.5mm). The histological diagnoses were oncocytoma (10), chromophobe RCC (4), oncocytic papillary carcinoma (1), possible malignancy (1). Five patients were suitable for surgical treatment. Four of these patients had partial nephrectomies and one had cryoablation. One patient had metastatic disease and died before commencing treatment. The histological concordance between renal biopsies and nephrectomy specimens was 100%. Ten patients with biopsy proven oncocytomas were followed with surveillance imaging. The median follow up of these patients was 27 months (range 6–57 months). All of these patients continue to be asymptomatic. None of these patients have required re-biopsy or surgical intervention.
Conclusions: This study would suggest that active surveillance of renal biopsy proven oncocytoma in the short term may be safe. However larger studies with longer follow up are still required.

P90

Scottish Glomerulitis Concordance Survey

Ⓟ J Crosby; S Coley

Queen Elizabeth University Hospital Glasgow, Glasgow, UK

Purpose of the study: Glomerulitis is an important histological feature in the assessment of renal transplant biopsies for the presence of antibody mediated rejection. The most recent definition of glomerulits is given as: "A complete or partial occlusion of >1 glomerular capillary by leukocyte infliltration and endothelial cell enlargement" (Haas et al. *American Journal of Transplatation* 2014; 14: 272-283). In practice however, many pathologists describe that they find this a difficult area and that the agreed definition is not easily applied to 'real life' cases. The aim of this audit was to assess the degree of concordance between the Scottish renal pathologists in the scoring of glomerulitis.
Methods: All 15 consultant pathologists who report adult and/or paediatric renal biopsies in Scotland were contacted via email and sent an online survey via the surveymonkey website. The survey consisted of a series of 15 pictures of single glomeruli for each of which the participants were asked "Is glomerulitis present in this glomerulus?" with possible answers being "Yes", "No" and "Not sure". Pictures included a range of appearances, approximately half being deemed negative and half being deemed positive for glomerulitis by the authors.
Summary of results: Early results demonstrate that there is a high rate of variation between consultant pathologists when assessing glomerulitis. Only one picture was scored positive for glomerulitis by all participants. Four pictures were scored negative for glomerulitis by all participants. In the remaining 10 of the 15 included pictures there was a degree of disagreement in the participant's opinion.
Discussion: This small study highlights the difficulty experienced by many consultants in assessing glomerulitis. Further discussion and education may be beneficial in achieving higher concordance rates in this area.

P91

A Rare Renal Cause of Secondary Hypertension: Case Report and Literature Review

Ⓟ R Haria; CJ Anderson; M Gonsalves; BE Tinwell

St George's University Hospitals NHS Foundation Trust, London, UK

Introduction: More than 90% of adults with hypertension do not have an identifiable cause (primary or essential hypertension). Secondary causes of hypertension are sometimes considered in younger individuals or with resistant hypertension. Here, we present the pathology of a rare, curable cause of secondary hypertension in a young male.
Case Description: A 16 year old male with no significant past medical or family history was referred to the department of urological surgery following investigation for systemic hypertension. A computed tomography scan had showed a solitary, 47mm, enhancing mass in the lower pole of the right kidney and he subsequently underwent a robotic partial nephrectomy. The cut surface of the formalin-fixed specimen showed a well-circumscribed, thinly encapsulated tumour with tan-pink and haemorrhagic areas. Histology showed a variably cellular tumour composed of sheets of polygonal to spindle-shaped cells with moderate amounts of granular eosinophilic cytoplasm, round to ovoid nuclei with finely dispersed chromatin and inconspicuous nucleoli. Perinuclear cytoplasmic clearing was a seen. There was a variable amount of loose myxoid stroma. Occasional entrapped branching tubules and small cleft-like spaces containing broad papillae covered by bland cuboidal cells were seen. Mitotic figures were rare, and there was no high grade cytological atypia, necrosis or lymphovascular invasion. The tumour cells showed immunoreactivity for CD34, bcl-2 and Vimentin. They were negative for PAX8, CK8/18, EMA, CD117, CD56 and CD99. The specific renin antibody was not available, but the overall features were entirely consistent with those of a juxtaglomerular cell tumour ('reninoma').
Discussion: Juxtaglomerular cell tumors are rare mesenchymal renal tumours mostly commonly affect young adults, but occasionally seen in children and older individuals. Although they usually behave in a benign fashion, there are reports of angio-invasive tumours and of metastasis.

P92

Primary Ovarian Non-Hodgkin's Lymphoma: Unexpected Clinical, Radiological and Pathological Diagnosis

Ⓟ E Abdellatif; V Charan; A Ganjifrock

Royal Oldham Hospital, Manchester, UK

Primary ovarian lymphomas are rare neoplasms. It constitutes around 0.5% of Non-Hodgkin's Lymphoma (NHL) and 1.5% of ovarian tumours. Although primary NHL of the ovary is unexpected diagnosis during the work up of ovarian tumours, the involvement of the ovary by malignant lymphoma as a manifestation of disseminated NHL is not rare. In the literature, there are few cases which were reported as primary ovarian lymphomas. These tumours are usually large unilateral tumours showing either B-cell or T-cell NHL. The follow up studies of those patients after treatment showed a good prognosis. We present a case of a unilateral ovarian tumour showing severe necrotic changes. The diagnosis of a malignant lymphoma was made by the histopathological examination of the removed ovary along with immunohistochemical studies. Although this diagnosis is rare and usually unexpected clinically and radiologically, it is important to be considered in patients having huge unilateral ovarian masses and showing evidence of unexplained necrosis in the absence of disseminated disease.

P93

The Role of P57 in the Diagnosis of Hydatidiform Mole in a Resource Limited Setting

Ⓟ OA Oguntunde[1]; NA Awolola[2]; FB Abdulkareem[2]; AAF Banjo[2]; B Kaur[3]

[1]Lagos University Teaching Hospital, Lagos, Nigeria; [2]College of Medicine, University of Lagos/Lagos University Teaching Hospital, Lagos, Nigeria; [3]Hammersmith Hospital, Imperial College Healthcare NHS Trust, London, UK

Hydatidiform mole is the commonest Gestational Trophoblastic Diseases worldwide. The two types of HM bear different risk for Persistent Trophoblastic Disease.This occurs in 15–20% of patients with complete hydatidiform mole (CHM), and rare following partial hydatidiform mole (PHM).Early presentation poses diagnostic variability using morphologic features alone.This study therefore aimed at assessing the use of p57 immunohistochemistry as a proven marker to differentiate CHM from PHM. Formalin fixed paraffin embedded tissue blocks and corresponding H&E stained slides of all the cases of HM within the study period were reclassified (WHO 2012).These cases were reviewed by a referent pathologist in one of the major tertiary referral centre. Further classification using p57 antibodies was applied on all the HMs. Fifty five cases of HM were studied. CHM and PHM accounted for 96.4% and 3.6% respectively.The age range for all the molar pregnancies was 15–50 years with majority seen in the 4th decade of life. 72.7% presented at second trimester. The review by referent pathologist, using morphologic criteria, overturned the original diagnosis of PHM in 9 out of 14 (64.3%) to a definite CHM and favored CHM in other 3 cases.This was confirmed with application of p57 immunohistochemistry, and 12 out of 14 (85.7%) cases of PHM were reclassified as CHM.100% of the CHM diagnosed on morphological criteria had positive p57 expression in the stroma villus cells and cytotrophoblast. The diagnosis of HM is sometimes difficult for general pathologists and gynaecopathologists.In a low resourced setting lacking complete arsenal of ancillary tests, following steps will be useful in subtyping HMs.First, adequate knowledge and use of strict morphological criteria; Secondly, cheaper ancillary techniques especially the application of P57 and finally use of referent pathologists and systematic rereading of slides is valuable to improve the diagnosis of HMs, particularly in the first trimester

P94

Metastasis of Small Cell Carcinoma of the Cervix to the Ovary: A Case Report

KJ Griffin[1]; Ⓟ N Orsi[1]; A Thangavelu[1]; NB Wilkinson[2]

[1]Leeds Teaching Hospitals Trust, Leeds, UK; [2]University College London, London, UK

Small cell, neuroendocrine, carcinoma of the cervix is a rare and aggressive tumour which is frequently characterised by haematogenous metastasis. Dissemination to bone, liver, lung and lymph nodes is common and parallels have been made with the poor prognosis of small cell carcinoma of the lung. However, metastasis to the ovary has not been previously reported. Here we present the case of a 32-year old woman who initially presented with a two-month history of lower abdominal discomfort and vaginal bleeding. Investigations revealed a large, ulcerated cervical tumour, complex bilateral adnexal masses and peritoneal deposits. Diagnostic surgery was undertaken and histology from all sites showed morphological features of small cell carcinoma with immunohistochemistry verifying the neuroendocrine nature of this tumour. Expression of p16 was strongly positive in all samples, confirming the primary cervical origin with ovarian metastases. Here, we outline the clinicopathological features of this case in detail and summarise the current literature pertaining to this highly malignant tumour.

P95

Ovarian Dedifferentiated Endometroid Adenocarcinoma: A Rare Case Report

Ⓟ MPM Thomas; A Moulla; R Athavale; M Hocking; S Sah

University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK

Introduction: Dedifferentiated endometroid carcinoma (DDEC) represents an aggressive variant of endometroid carcinoma in which an undifferentiated carcinoma occurs concurrently with an endometrioid carcinoma usually of low grade. DDEC is mainly described in endometrium and has rarely been reported in ovary.
Case report: A 56 year old postmenopausal lady with background history of endometriosis was referred with a four month history of abdominal distension and pain. A right ovarian mass identified on ultrasound, confirmed as 17cm complex mass with 4cm solid nodule on CT scan. In 9 months her CA 125 increased from 13 to 88. She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy and appendicectomy. She subsequently underwent adjuvant chemotherapy in the form of Carboplatin/Taxol at three-weekly intervals.
Histology and immunohistochemistry: Right ovarian multilocular cyst measured 160mm with a solid area of 45mm. Histology revealed a dedifferentiated endometroid adenocarcinoma, FIGO stage IC1 due to intra-operative spillage. Cystic area showed endometriosis. The tumour consisted predominantly of grade 1 endometroid adenocarcinoma with abrupt transition to areas of undifferentiated carcinoma (35%). Immunohistochemically grade 1 component showed diffuse positivity for PAX8. ER. The undifferentiated component was positive for pancytokeratkins, but only weakly positive for PAX8 and ER. CD34 and neuroendocrine markers were negative.
Discussion: Given subtle differences in histological appearance, DDEC may be mistaken for a high-grade endometrioid carcinoma, carcinosarcoma and sarcoma. DDEC has more aggressive behaviour regardless of the amount of undifferentiated carcinoma. Therefore, it is important to accurately diagnose this neoplasm. Specific histological and immunohistochemical features should enable accurate diagnosis.

P96

Giant Endocervical Polyp: A Rare Case Report

Ⓟ MPM Thomas; S Julian; S Sah

University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK

Introduction: Cervical polyps are common benign lesions and most are less than 1cm in diameter. Giant cervical polyps with a size greater than 4cm are benign and thought to be the result of reactive changes. They are rare and so far only a few cases have been reported. We describe a case of giant cervical polyp in a perimenopausal woman with clinical suspicion of malignancy.
Case report: A 50 year old, nulligravid female was referred to Obstetrics and Gynaecology due to intermenstrual spotting, dyspareunia and vaginal discharge for several months. Pelvic ultrasound demonstrated multiple cervical cysts more than 6cm size. Pelvic examination revealed a fleshy tongue of tissue with cystic areas arising from the cervix. A subsequent pelvic MRI suggested the cystic lesion could have been vaginal in origin extending from the intraoitus to the cervix. In view of continued troublesome symptoms and clinical suspicion of malignancy, a total abdominal hysterectomy was carried out.
Histology: Biopsy performed prior to hysterectomy showed features of a benign endocervical polyp. Hysterectomy specimen demonstrated a large polypoid lesion extending through the os arising from the endocervical canal. It measured 70mm in maximum dimension and appeared multiloculated and cystic. On histology the lesion to be consisted of multiple dilated glands filled with mucin and lined by benign endocervical epithelium with stromal fibrosis and chronic inflammation. The ectocervix was unremarkable and there was no evidence of CIN, CGIN or invasive malignancy.
Discussion: Giant cervical polyps are rare and their size and clinical presentation can mimic a cervical neoplasm leading to radical surgery. Excision polypectomy is generally sufficient as definitive treatment. An awareness of this entity is important as part of clinical assessment to avoid unnecessary major surgery.

P97

A Review of BRCA Testing and STIC Rates in Prophylactic Salpingo-Oophorectomies Over a Five-Year Period in a Tertiary Referral Centre

Ⓟ SC Prendergast; D Gibbons

St Vincents's University Hospital, Dublin, Ireland

Purpose of the study: Prophylactic salpingo-oophorectomy is recommended for patients at high risk of serous tubo-ovarian carcinoma. Risk is determined by personal or family history or ideally by BRCA testing. The presence of STIC (Serous Tubal Intraepithelial Carcinoma) is reported at between 0.6% - 7% in the BRCA positive population. We sought to determine the percentage of BRCA positive patients and the STIC rate in our prophylactic cohort.
Methods: A search of our database from Jan 2012 to Jan 2017 was perfomed using SNOMED codes to identify all prophylactic salpingo-oophorectomies in this period.
Summary of results: Ninety-eight (98) prophylactic surgeries were identified. Median age was 52 years. Eighteen (18 .5%) had known BRCA mutations (5 with BRCA1, 9 with BRCA2 and 4 not specified). BRCA status was undetermined in 80 (81.5%). Those without mutations had a complex variety of family and personal histories. The number of prophylactic surgeries received in the laboratory increased each year from 5 in 2012 to 32 in 2016. The rate of all embedding of specimens also increased during this period. P53 and Ki67 immunohistochemical studies were performed in 6 cases. One case of STIC (1%), which was also associated with invasive serous carcinoma, was identified and this was in a BRCA positive patient.
Conclusions: Our rate of STIC detection in prophylactic salpingo-oophorectomy specimens is low. With increasing selection of the population by BRCA germline testing we expect to see the positive predictive value for STIC in this population increase.

P98

Gynaecologic Pathology Frozen Section Analysis in a Tertiary Referral Hospital in India: Audit of 3 years (2014 –16)

Ⓟ KK Deodhar; A Verma; B Rekhi; S Menon; R Kerkar; A Maheshwari; TS Shylasree

Tata Memorial Hospital, Mumbai, India

Purpose of the study: To analyze the distribution and accuracy of frozen section reporting in gynaecologic pathology practice in our institution over a period of 3 years (2014–2016).
Methods: During the period 2014–16, a total of 920 frozen sections (FS) were carried out pertaining to gynaecological oncology surgery. FS diagnoses and their paraffin section / final diagnoses were noted from the records. A total of 15 surgical pathologists handled this work in rotation.
Summary of results: Primary diagnosis of the adnexal mass was the commonest specimen (403 cases, 43.8%), followed by pelvic node examination for metastasis (238 cases, 25.86 %), depth of myometrial invasion and cervical involvement in endometrial adenocarcinoma (108 cases, 11.73%). Other FS requests included histopathology of deposits over omentum, sigmoid colon, urinary bladder, pelvic mass biopsy etc.
The overall agreement between FS and paraffin section was 86.1 %. (All discrepancies 128, major 103(11.2%), minor 25(2.7%)). The minor discrepancies included changes in subtypes of malignant tumour, while major discrepancies included benign or borderline ovarian tumour FS diagnosis with carcinoma diagnosis on paraffin report, change in depth of myometrial invasion in endometrial carcinoma or a metastatic lymph node reported as uninvolved in FS. Change in subtypes of benign conditions was not counted as discrepancy. The variety of discrepancies are discussed.
Conclusions: Primary diagnosis of adnexal mass is the commonest FS request in gynecologic pathology, followed by pelvic node examination and depth of myometrial invasion by endometrial carcinoma. The overall agreement between the FS and paraffin section diagnosis in a team of 15 pathologists is 86.1%.

P99

Ovarian Teratoma Associated with Anti-NMDA Receptor Encephalitis: A Report of Two Cases

Ⓟ S Kulkarni; A Faruqi

Royal London Hospital, London, UK

Encephalitis due to anti N-methyl-D-aspartate (NMDA) receptor antibodies is a rare disorder that is often associated with tumours, usually ovarian or testicular teratomas. This is a potentially fatal disease that affects both genders and can occur at any age. However it is frequently seen in young otherwise healthy patients who present with an acute onset of neuropsychiatric symptoms. Removal of the tumour may result in amelioration of some these symptoms and it is therefore important for the histopathologist to be aware of this association.
We present two cases in which the patients were young women who initially presented with psychiatric disorders and were subsequently found to have ovarian teratomas that revealed characteristic inflammatory infiltrates around blood vessels of the glial tissue within the tumours

P100

Multispectral Immunofluorescence for Simultaneous Analysis of Multiple Tumour Infiltrating Lymphoid Cells Demonstrate Positive Prognostic Significance of T-cells and FOXP3 T-Regulatory Cells

Ⓟ P Sheppard; AM Tsakiroglou; M Fergie; C West; S Astley; K Linton; R Byers;

University of Manchester, Manchester, UK

Follicular lymphoma is one of the most common forms of non-hodgkin lymphoma, accounting for approximately 20% of cases. It has been proposed for both follicular lymphoma and other cancers that the cells of the tumour microenvironment may play a significant role in disease progression and prognosis. Whilst the effect of the number of these different cells within the microenvironment, specifically tumour infiltrating lymphoid cells, has been investigated extensively, results are inconclusive and often contradictory, largely due to difficulty in enumerating several types of immune cells simultaneously. To tackle this we used 5-plex multiplex immunofluorescense for CD3, CD8, CD68, FOXP3 and PD1 in a tissue microarray of 39 patients with follicular lymphoma. Multispectral imaging with the Vectra and Inform platform (PerkinElmer) was used to enumerate cells positive for CD3, CD8, CD68, FOXP3 and PD1 in the microenvironment and the results used in Kaplan Meier survival analysis. The results showed a significant association with favourable outcome for values of FOXP3 above the median (p=0.0188), and significant association with favourable outcome for numbers of T-cells (positive for FOXP3, CD3, CD8 and PD1) above the 25th centile (p=0.0068). Additionally, higher numbers of PD1 positive cells showed a trend towards favourable outcome (p=0.054). These results show that follicular lymphoma patients with larger populations of T cells and specifically FOXP3+ Tregs in the tumour microenvironment have a better prognosis, confirming the importance of the microenvironment in the pathophysiology of follicular lymphoma and of measurement of it to predict clinical outcome and response to immunotherapy.

P101

Persistent EBV Positive Mucocutaneous Ulcer in the Rectum

Ⓟ LM Lane[1]; E Keeling[1]; D Fennelly[2]; M Leader[1]

[1]Department of Histopathology, Royal College of Surgeons, Beaumont Hospital, Dublin, Ireland; [2]Department of Medicine, The Blackrock Clinic, Co. Dublin, Ireland

EBV-positive mucocutaneous ulcer (EBVMCU) is a recently recognized B cell lymphoproliferative disorder driven by latent EBV infection[1]. It is characterised by discrete ulcerated lesions, typically in the oropharynx, but described more recently in the gastrointestinal tract and skin of immunosuppressed patients[2.] These CD30 immunoreactive lesions may mimic lymphomas. The clinical course is unclear. The majority of cases show a self-limiting indolent course, however others can experience a persistent disorder[1] as reported in this case. We present EBVMCU arising in the rectum of an 88-year-old gentleman who has two unusual features namely, an associated nodule and a persistent stricture. He had no significant past medical history of immunosuppressive illness or medications. He presented with an ulcerated 3cm rectal mass. Biopsies revealed colonic mucosa with a dense atypical polymorphous inflammatory infiltrate, comprising large atypical pleomorphic lymphoid cells. These were positive for PAX5, CD30 and EBER. CD20 and CD79a were negative. T cell markers were negative. Immunoglobulin gene rearrangements were not detected. A diagnosis of EBVCMU was subsequently made. Imaging showed no lymphadenopathy. On four year follow up he has persistent non-progressive disease requiring endoscopic rectal dilatation. Subsequent biopsies showed features similar to the original biopsy. EBVMCU is not included in the 2008 WHO Classification of Lymphoproliferative disorders. As it is a newly recognised clinicopathologic entity there are no evidence-based guidelines to guide therapy. To date, we are aware of five other published cases of EBVMCU occurring in the colon[2].

[1] Dojcinov S.D., Venkataraman G., Raffeld M., Pittaluga S., Jaffe E.J. Am J Surg Pathol 2010; 34(3): 405-417. [2] Roberts T.N., Chen X., Liao J.J. Exp Hematol Onco 2016; 5:13.

P102

The Use of MYD88 Testing in Lymphoplasmacytic Lymphoma: Our Experience

Ⓟ LC Mackintosh[1]; L Gilroy[2]; A Sproul[3]; W Al-Qsous[1]

[1]Pathology, Western General Hospital, Edinburgh, UK; [2]Haematology Malignancy Diagnostic Service (HMDS), Western General Hospital, Edinburgh, UK; [3]Western General Hospital, Edinburgh, UK

Background: MYD88 c.794T>C p.(Leu265Pro) is the most commonly identified mutation in Lymphoplasmacytic Lymphoma (LPCL) and is often used as a further diagnostic tool in small B cell lymphomas with plasmacytic differentiation that have overlapping clinicopathological features. At our centre, a CLL score is used to aid classification of small B cell lymphoproliferative disorders, and MYD88 is performed as a Reflex test on cases with a CLL score <2.
Aim: To examine the use of MYD88 mutation analysis as a further diagnostic test in LPCL and how it correlates with other investigations, and to investigate the use of CLL score and reflex testing to identify suitable cases for MYD88 testing.
Methods: The results of successful MYD88 tests from July 2014 - August 2016 (n=69) were recorded, including the source of the test request. Using ILabs and TRAK, information on paraprotein status, bone marrow aspirate and trephine results and final clinical diagnosis was collected and analysed in Excel.
Results: Of 69 tests, an MYD88 mutation was detected in 28 (40.6%). Of these, 26 (92.9%) had a bone marrow aspirate or biopsy indicating LPCL as a differential diagnosis, 23 (82.1%) had an associated IgM paraprotein and 25 (89.28%) had an LPCL diagnosis . Of 41 negative cases, 7 had a diagnosis of LPCL. 46 of the MYD88 tests were performed as Reflex testing. Of these, 23 (50%) had a detectable MYD88 mutation, constituting 82.1% of all positive MYD88 results; 21 (45.6%) had a final diagnosis of LPCL, constituting the largest single diagnosis in the Reflex test group.
Conclusions: MYD88 testing is a useful aid in the diagnosis of LPCL and should be considered in small B cell lymphomas with plasmacytic differentiation. However, the findings should always be correlated with other parameters, including the bone marrow aspirate and biopsy findings as an negative result does not necessarily exclude this diagnosis. Reflex testing can be useful in identifying suitable cases for MYD88 testing

P103

This abstract has been withdrawn

P104

Proximal Type Epitheloid Sarcoma with Hybrid Features

Ⓟ KU Adoke

Ahmadu Bello University Teaching Hospital Zaria Nigeria, Zaria, Nigeria

Purpose of study: Epitheloid sarcoma (ES) is the most common soft tissues sarcoma of distal extremities. It occurs in young adults mainly between 10-30 years of age with median age of 26 years. Male/ Female ratio of 2:1. The classic distal from of ES usually present as a small indurate ill defined dermal or subcutaneous nodule or larger variable necrotic masses involving tendon and/ or fascia. It is characterized by nodular growth pattern and is composed of mixed proliferation of epitheloid and spindle cell exhibiting slight nuclear atypia, vesicular nucleous and small nucleoli. Frequently, tumour nodules undergo central necrosis resulting in pseudogranulomatons appearance. Pseudoangiosarcomatous features can also occur. The proximal type of ES is characterized by its propensity to arise in axial location and it is more aggressive. Histologically the proximal type of ES has marked cytological atypia, vesicular nuclei and proximal nucleoli, rhabdiod features are frequently observed. We present a rare case of proximal type of ES in a 30 year old male patient with perianal mass measuring 7x11x12cm.
Methods: Specimen from the patient was fixed in 10% buffered formalin and processed and stained using routine histological techniques. Four immunohistochemical stains were performed using Genemed Biotechnology Protocol (AE1/AE3,Vimentin, CD 34 and S-100).
Summary of results: Histology shows hybrid features of both classic and proximal type i.e multinodular growth pattern of epitheloid and spindle cells having marked nuclear atypia, prominent nucleoli pseudoangiosarcomatous areas, necrosis, numerous mitosis. No rhabdoid features seen. Immunohistochemistry shows positive staining for AEI\AE3, vimentin, CD 34 and focal positively for S-100 protein.
Conclusion: Although the histiogenesis of this tumour remains obscure. Some Pathologists believe that very rare hybrid forms do exist.

P105

Case Report: Primary Cutaneous Angiomyolipoma of the Right Index Finger

Ⓟ EM O'Hare; EB Brown; T Grigor

Royal Cornwall Hospitals NHS Trust, Truro, UK

Introduction: Primary cutaneous angiomyolipoma (pcAML) is a rare neoplasm with similar histomorphology to renal AML but with key clinical and immunohistochemical differences. We describe the case of a pcAML arising in the index finger of the right dominant hand.
Case: A 62 year old male presented with a two year history of a slowly enlarging, painless 10 x 8mm swelling over the dorso-ulnar aspect of the right index finger overlying the proximal interphalangeal (PIP) joint. An excision biopsy was performed. The intraoperative impression was of a ganglion which was excised intact.
Surgical pathology: Macroscopic examination of the resection specimen revealed a nodular fragment of pale tan tissue measuring 12 x 10 x 5mm. Microscopy showed a well circumscribed, non-encapsulated triphasic nodular lesion composed of myoid spindle cells, mature adipose tissue and dysmorphic thick-walled blood vessels. There was no undue atypia or malignancy. Immunohistochemistry for human melanoma black (HMB) 45 and mirophthalmia transcription factor (MiTF) was negative in tumour cells. S-100 was negative, except in fat cells.
Discussion: The histomorphology of pcAML is that of a triphasic neoplasm, similar to renal AML. The latter is strongly associated with Tuberous Sclerosis (TS) and belongs to the perivascular epithelioid cell (PEComa) family of mesenchymal tumours. Both consist of a variable admixture of dysmorphic vessels, myoid and adipose tissue. In contrast to PEComa, pcAML lacks HMB45 expression, typically occurs sporadically, without any syndromic associations and exhibits a male predilection. Nestled in the deep dermis or subcutis surrounded by a pseudocapsule, they often "shell out" or enucleate via skin incision. Recurrence after surgical excision is exceedingly rare. To the best of our knowledge, this is the first case to be reported of pcAML originating in the index finger of the dominant hand.

P106

Ossifying Fibromyxoid Tumours: Two clinical Cases Demonstrating the Diagnostic Pitfalls of these Rare Neoplasms

Ⓟ C Roberts; T Crotty

St. Vincent's University Hospital, Dublin, Ireland

Ossifying fibromyxoid tumours belong to a group of tumours of intermediate malignant potential. The precise cell of origin remains a subject of debate. OFMTs were first described in 1989 by Enzinger et al. Less than 300 cases have been described worldwide. Grossly, these tumours are lobulated with a thick fibrous pseudocapsule. 75-80% of tumours are surrounded by an incomplete shell of metaplastic lamellar bone. Up to 20% of cases are non-ossifying. OFMTs mostly have a bland morphological appearance which predicts a benign clinical course, however atypical and malignant forms have been described. In extremely rare cases, the tumour has proved fatal. Here we present two cases of this rare tumour diagnosed in our institution. The first case is that of a 62 year old male with a mass in the posterior right thigh. The lesion is a well circumscribed with an incomplete bony shell. No mitoses are seen. No necrosis or LVI is present. Immunohistochemistry demonstrates positivity with vimentin. S100, AE1/3, CD34, SMA and desmin are negative. The second case is a 44 year old male with a palpable lump on the left shoulder. This lesion is composed of bland, oval cells within a hyalinized stroma. The mitotic count is 2 per 50 hpfs but no atypical features are seen. No necrosis or vascular invasion is present. No bony capsule is identified. Tumour is positive for S100. AE1/3, EMA, SMA, MelanA and CD34 are negative. Although rare, awareness of this entity is important as a minority of cases will recur and metastatic disease has been recorded. Diagnosis can be problematic and important differentials include epithelioid fibrosarcoma, malignant peripheral nerve sheath tumour, synovial sarcoma and extraskeletal myxoid chondrosarcoma. S100 is often positive in OFMTs with significant variability in other immunostains. Elucidation of the PHF1 gene rearrangements associated with both OFMTs and endometrial stromal sarcomas may aid in the identification of subtypes with malignant potential

P107

Ewing Sarcomas Highly Express Mortalin

Ⓟ SR Dundas; GI Murray

Aberdeen Royal Infirmary, Aberdeen, UK

Purpose of study: Mortalin (mitochondrial heat-shock protein 70/ mtHsp 70) is a multifunctional protein involved in regulating a wide array of cellular functions with important roles in cellular senescence and immortalisation. Mortalin over-expression is a key event in the earliest stages of neoplasia. We investigated whether mortalin could be implicated in the growth of different types of sarcoma.
Methods: A tissue microarray constructed from a well-defined series of 80 bone and 401 soft tissue sarcomas of all types linked to a patient database was immunostained for mortalin. Immunohistochemical expression levels were determined using a scoring system based on staining intensity and cellular distribution. 36 separate pre-treatment, post-chemotherapy or metastatic Ewing sarcoma samples from 26 patients were arrayed; mean age 22 years, range 1yo -59yo; 14 male: 12 female cases.
Summary of results: High expression of Mortalin was identified in Ewing sarcomas. 78% of primary and secondary Ewing sarcomas displayed either moderate or strong and diffuse positivity. Weak staining was seen only seen in two post-chemotherapy cases (5%). Levels of mortalin expression were higher in primary lesions (p=0.003) and bone tumours (p=0.003) but independent of age, sex or anatomical site.
Conclusions: Our findings suggest that mortalin may be fundamentally involved in Ewing sarcoma tumourigenesis. Drug-induced disruption of mortalin/ p53 binding induces apoptosis by modulating the Ras-Raf-MAPK and hnRNP-K pathways, and this suggests that mortalin might provide a novel potential therapeutic target for Ewing sarcoma.

P108

Digital Fibromyxoma: A Challenging and Unusual Case

Ⓟ KE Allen[1]; Ⓟ S Majeed[2]; B Mathew[1]; MJ Alemkunnapuzha[2]

[1]Leeds Teaching Hospitals NHS Trust, Leeds, UK; [2]The Mid Yorkshire Hospitals NHS Trust, Dewsbury, UK

Digital fibromyxoma is a soft tissue tumour which usually, but not always, arises in the subungual or periungual region of the digits on hands and feet. A recent study of 124 cases gives a local recurrence rate of 24%, with a mean recurrence interval of 27 months. No cases to date have been found to metastasise, and the lesion is considered benign. We present the case of a 30-year-old male patient with a lump on the left index finger nailbed. The clinician wished to exclude the possibility of a sarcoma. Macroscopically it was a firm, pale, fibrous nodule measuring 13x11x5mm, with a homogenous cut surface. Microscopically it is an unencapsulated and expansile, but relatively well-demarcated lesion. It is situated within the dermis and subcutaneous tissue, and extends to the margins. It comprises elongated spindle cells arranged in fascicles and separated by collagen strands. In places the spindle cells are accompanied by a myxoid stroma. Both thin and thick-walled vessels are seen crossing the tumour. The mitotic count is less than one per ten high power fields, and there is no pleomorphism or necrosis. Immunohistochemical staining showed the tumour to be diffusely and strongly positive with CD34, and occasional tumour cells are positive with desmin. The tumour stains negatively with AE1/AE3, MNF116, SMA, SMM, H-caldesmon and S-100. This morphological and immunohistochemical profile is of a digital fibromyxoma. Diagnosis of these lesions remains a challenge for histopathologists. We explore the clinical, histological and immunophenotypic findings of this particular case, compare them to those found within literature, and consider the important differential diagnoses.

P109

Retroperitoneal Dedifferentiated Liposarcoma with Heterologous Osteosarcomatous Differentiation and a Prominent Aneurysmal Bone Cyst-Like Morphology

Ⓟ CVH Van Haverbeke[1]; JVD Van Dorpe[1]; EL Lecoutere[1]; UF Flucke[2]; LF Ferdinande[1]; DC Creytens[1]

[1]Ghent University Hospital, Ghent, Belgium; [2]Radboud umc, Nijmegen, Netherlands

A 69-year-old woman with a medical history of recurrent dedifferentiated liposarcoma of the retroperitoneum presented with a 3-cm large hemorrhagic and multicystic left-sided retroperitoneal mass. Histopathological examination of the resected tumour revealed a heterogeneous, high-grade mesenchymal nonlipogenic tumour with areas of osteoblastic differentiation. Moreover, there were zones with aneurysmal bone cyst (ABC)-like features, with large blood-filled spaces without endothelial lining and separated by septa containing spindle cells, clusters of osteoclast-like multinucleated giant cells and thin strands of woven bone. A diagnosis of a dedifferentiated liposarcoma with heterologous osteosarcomatous differentiation and an aneurysmal bone cyst-like morphology was made, based on the morphology, the clinical presentation and the supportive immunohistochemical and molecular findings (MDM2 overexpression and amplification of the MDM2 gene, respectively). We believe that this is the first description of aneurysmal bone cyst-like morphology in dedifferentiated liposarcoma, further expanding the wide morphological spectrum of dedifferentiated liposarcoma.

P110

Role of Somatostatin Immunohistochemistry in the Diagnosis and Management of Gastroenteropancreatic Neuroendocrine Tumours

Ⓟ R O'Connor[1]; C Ryan[2]; G Tamagno[3]; D O'Shea[1]; D O'Toole[1]; J Geoghegan[1]; N Swan[1]

[1]St. Vincent's University Hospital, Dublin, Ireland; [2]St. James's Hospital, Dublin, Ireland; [3]Mater Misericordiae University Hospital, Dublin, Ireland

Purpose of the study: Gastroenteropancreatic neuroendocrine tumours (GEP NETs) are a heterogenous group of tumours with varying degrees of differentiation and grade, ranging from indolent to highly aggressive neoplasms. Currently, somatostatin receptor (SSTR) scintigraphy (using SSTR 2A) is used to assess patients' suitability for somatostatin analogue therapy. SSTR immunohistochemistry (IHC) is not in routine use for the pathological assessment of GEP NETs. The aims of our study were: to assess the expression of SSTRs in GEP NETs using IHC for SSTRs 1, 2A, 3, 4, and 5; to evaluate differences in SSTR2A expression between primary and metastatic tumours; to assess for correlation between Ki67 proliferative index staining and SSTR2A expression.
Methods: GEP NET biopsies and surgical resections were identified using SNOMED coding lists from 2002-2013. All tissue material was formalin fixed and paraffin embedded. Specimens were stained for SSTRs 1, 2A, 3, 4, and 5. The standardised semi quantitative H-score (H1- H5) was used to assess degree of staining and was positive if H≥3. Ki67 proliferative index was based on hotspot counting of a minimum of 1000 nuclei.
Summary of results: 127 cases of primary and metastatic GEP NETs were identified (primary= 84, metastatic= 43). 108 cases had all 5 SSTRs and Ki67 assessed. SSTR positivity was as follows: SSTR1= 110/123 (89.4%), SSTR2A= 114/127 (89.8%), SSTR3= 20/116 (17.2%), SSTR4=21/120 (17.5%), SSTR5= 14/127 (11%). Of the 28 cases with both primary and metastatic tumours, all had concordant H-scores. Of the 13 SSTR2A negative cases, 9 had a Ki67 ≥3% (p value <0.05, chi square).
Conclusion: SSTR1 and SSTR2A stain the majority of GEP NETs, with all primary tumours positive for at least 1 SSTR. SSTR2A staining is consistent between primary and metastatic tumours. SSTR2A expression is more likely to be absent in high grade tumours.

P111

Audit of Reporting of Thyroid Cytology Specimens Emphasising on the Number of Inadequate Samples Taken With and Without US Guidance

Ⓟ EH Hadjimichael; CS Simpson; MMK Khan

Nottingham University Hospitals, Nottingham, UK

Introduction: Fine needle aspiration cytology (FNAC) is a valuable preoperative investigation for thyroid nodules in adults. FNAC samples taken with Ultrasound (US) guidance and immediately assessed for adequacy (Rapid on-site evaluation, ROSE) have reduced rates of unsatisfactory samples. ROSE is not provided by Nottingham University Hospitals therefore an audit measuring the number of inadequate samples taken with and without US guidance was undertaken.
Aims: 1: To measure the number of inadequate samples taken with and without US guidance. 2: To determine the percentage of cases in each Thy category locally.
Method: Data from January 2015 until December 2015 were retrospectively collected from winpath and Notis. Data collected included the type of first and subsequent FNACs, if US guided or not and the correlation with any subsequent histology.
Results: 160 cases were identified from Winpath. Seven were excluded as there was no Thy category assigned. Eleven were excluded as they were undertaken in private practice and the US data were not available. 142 cases were included in the analysis. 14% of US guided FNAC and 16% of non US guided FNAC were classified as Thy1. The percentage of cases of each Thy category was similar to the ones provided by the Royal College of Pathologists (RCPATH). 33.3% of Thy1 (US and non US guided) were not investigated further.
Conclusion: Results of our local practice has shown that US guided FNAC has similar adequacy rate as palpation guided FNA. Both rates are close to the standard (15%) suggested by the (RCPATH).ROSE could facilitate further reduction but also better management of patients with Thy1 as first FNAC.

P112

Recurrent Inflammatory Pseudotumour Arising in a Lymph Node Within the Submandibular Gland: A Comparative Study

Ⓟ EB Brown[1]; EM O'Hare[1]; E Grobbelaar[2]; T Grigor[1]

[1]Department of Histopathology, Royal Cornwall Hospitals NHS Trust, Truro, UK; [2]Department of ENT Surgery, Royal Cornwall Hospitals NHS Trust, Truro, UK

Introduction: Inflammatory pseudotumour is a rare benign lesion with a usual clinical presentation and radiological appearance which mimics invasive malignancy. We describe the case of a recurrent inflammatory pseudotumour (IPT) arising in a lymph node within the submandibular gland.
Case: A 43 year old woman presented with a history of intermittent swelling in the right upper neck. Her past surgical history included a lumpectomy to the same area over 2 years previously. An excision biopsy of the node was performed. The intraoperative finding of the pathological node underneath the capsule of the right submandibular gland was highly unusual.
Surgical pathology: Macroscopic examination of the lymph node showed a discrete "fish flesh" appearance. Microscopy revealed a storiform proliferation of spindle cells, with a superimposed mixed inflammatory infiltrate, composed of aggregates of plasma cells, lymphocytes, sparse neutrophils, and occasional loose clusters of eosinophils. Classical or lacunar Reed-Sternberg cells were not seen. The immunophenotype was consistent with an IPT, and the lesional cells were negative for EBV. Anaplastic large cell lymphoma, Kaposi sarcoma, and mycobacterial spindle cell pseudotumour were considered in the differential diagnosis and excluded using special stains and a comprehensive immunopanel. Direct comparison of the serial resection specimens from the same site revealed identical morphological and immunohistochemical features.
Discussion: The natural history of an IPT is usually benign and is distinct from inflammatory myofibroblastic tumour at the same site. The recurrence of an IPT in this case is therefore intriguing, and adds further complexity to the dichotomy of malignant presentation and benign behaviour that typifies these lesions.

P113

Is Thyroid Frozen Section Diagnosis for Thy 4 Lesions Reliable?

Ⓟ DR Walsh; R Prichard; S Skehan; E Mc Dermott; D Gibbons

St Vincent's University Hospital, Dublin, Ireland

Purpose of the study: Intraoperative frozen section can be a valuable procedure to confirm the fine needle aspirate (FNA) cytological diagnosis and identify malignancy in cases with an indeterminate or inadequate cytological diagnosis. The use of thyroid frozen sections can also potentially reduce to likelihood of unnecessary extensive surgery. Our aim was to assess the reliability of thyroid frozen section diagnoses.
Methods: Using a SNOMED search of our laboratory database, we identified all thyroid fine needle aspirate cytology cases coded as Thy 4 (suspicious for malignancy) over a 7 year period from January 2009 to December 2016. All authorised reports were reviewed in order to assess the rate and outcome of thyroid frozen sections in cases where the cytological diagnosis was coded as Thy 4.
Summary of results: In total, 69 cases of thyroid aspirates coded as Thy 4 were identified. Surgical resection (total or partial) was performed in 42 of the 69 cases (60.9%). Frozen sections were performed in 6 of the 69 cases (8.7%). Of the 6 frozen sections, 5 cases were reported as malignant with 1 case deferred to permanent sections. All 5 cases of malignancy reported on frozen section were confirmed on the excision specimen, yielding a concordance rate of 100%. The deferred case was also confirmed as malignant.
Conclusions: Frozen sections performed on all cases of Thy 4-coded thyroid lesions have been highly accurate. The use of thyroid frozen sections, possibly in combination with BRAF molecular testing, may allow more definitive surgical resection ab-initio.

P114

Morphological Assessment of the Tumour Microenvironment in Squamous Cell Carcinoma

Ⓟ J Sampson; S Craig; S McQuaid; M Salto-Tellez; JA James

Queen's University Belfast, Belfast, UK

Multiple studies have highlighted the prognostic role of the tumour microenvironment (TME) in squamous cell carcinoma (SCC) of various sites. Despite this, microscopic assessment of the TME in SCCs has not been adopted into routine practice. Based on the findings of previous published studies, we assessed and scored tumour-infiltrating lymphocyte (TIL) density, stromal percentage and tumour budding in representative H&E-stained whole tumour sections from a cohort of 173 treatment-naïve, clinically annotated HPV-positive (n = 66) and HPV-negative (n = 107) oropharyngeal SCC cases. Preliminary analysis indicates a low TIL density (<50% stromal compartment occupied by lymphocytes) is associated with a worse prognosis in both HPV cohorts (HPV-positive $p = 0.0004$, HPV-negative $p = 0.04$) while high stromal percentage (≥50%) was only shown to be prognostic in HPV-positive but not the HPV-negative oropharyngeal SCC (HPV-positive $p = 0.0001$, HPV-negative $p = 0.09$); tumour budding (≥5 tumour buds per case) was not found to be associated with survival in either HPV-positive or negative oropharyngeal SCC. In conclusion, our preliminary analysis suggests that microscopic assessment of stromal percentage and TIL density may provide prognostic information in oropharyngeal SCC in an HPV dependent manner. Validation of these preliminary findings using digital-based image analysis is ongoing; we are also extending this study to include SCCs of the lung and oesophagus, incorporating a detailed assessment of other predictive/prognostic biomarkers that could underpin effective stratification of patients to receive immunotherapy.

P115

Keratoacanthoma Within a Tattoo: Case Report and Literature Review

Ⓟ H Jawad[1]; D Domeney[1]; S Ranga[2]; CC Heffron[1]

[1]Cork University Hospital, Cork, Ireland; [2]Carrigtwohill Clinic, Cork, Ireland

Tattooing is a process of implantation of permanent pigment granules in the skin. Tattoos can be decorative, medical or accidental. There has been an increase in decorative tattooing especially among the younger age groups. Many adverse side effects to tattoos have been reported including granulomatous inflammation and hypersensitivity reactions. However, the potential local and systemic carcinogenic effects of tattoos remain unclear and there is debate as to whether tumours arising in tattoos are coincidental or whether there is a causative effect. From emerging reports, the colour of the tattoo would appear to influence the type of adverse reaction that occurs and would seem to be associated in particular with the development of pseudoepitheliomatous hyperplasia and squamous cell carcinoma. It was thought that mercury salts within early red ink may have been at fault, however, its use has now been restricted and yet, tumours and tumour-like lesions are still being reported. The occurrence of keratoacanthoma in a tattoo and in particular in a red tattoo has been reported rarely. We present the case of a 36 year old male presented with a tumour on his right calf, over an area of red pigment in a professional tattoo. Histological analysis revealed a keratoacanthoma arising in an exogenously pigmented area which was completely excised. We report this case to alert the dermatopathologist that keratoacanthoma should be included in the list of cutaneous complications related to tattooing, specifically in red pigmented areas. The diagnosis can be challenging as the histological differential diagnoses include pseudoepitheliomatous hyperplasia and other forms of squamous cell carcinoma. Complete excision of the entire lesion followed by thorough histological examination is mandatory for diagnosis. This case also adds to the current literature as we try and understand the significance behind the association of tattoos and skin tumours.

P116

PDL-1 Expression and CD8+ Tumour Infiltrating Lymphocytes Correlating with Significant PD-1 Inhibitor Response in Two Cases of Recurrent Desmoplastic Melanoma

Ⓟ JP O'Neill; E Gilhooley; A Lally; G Gullo; A Fabre

St Vincent's University Hospital, Dublin, Ireland

Desmoplastic melanoma (DM) is a deceptive and rare form of melanoma comprising less than 4% of invasive melanomas, typically occurring in the head and neck region of elderly individuals. Desmoplastic melanoma is characterised histologically by amelanotic spindled melanocytes, stromal fibrosis, tumour infiltrating lymphocytes and neural invasion. Loco-regional recurrence is common, however DM has a lower metastatic potential than other melanoma subtypes. A recent study has found that DM carries amongst the highest mutation burden of any cancer and as a result may respond to immunotherapy due to high neoantigen expression. Indeed DM appears to show a greater response to anti-PD1/PD-L1 therapy than other melanoma subtypes. There is emerging data that tumoural PD-L1 expression in DM is associated with depth of invasion (>4mm) and the presence of CD8+ tumour infiltrating lymphocytes (TILs). Herein we present two cases of scalp DMs in elderly males (80 years and 76 years old), both of which were notable for multiple loco-regional disease recurrences despite repeated wide local excision and multiple courses of adjuvant radiotherapy. However a marked and sustained response has been achieved in both cases with the PD-1 inhibitor Pembrolizumab, with complete remission achieved in one instance after a single dose. Correspondingly a predominant CD8+ TIL population with PD-L1 tumour positivity was present in both cases. Depth of invasion (Breslow) was 7mm and 8mm. PD-1 inhibitor response in DM with loco-regional recurrence has not been previously reported. These findings support emerging data concerning increased responsiveness of DM to PD-1 inhibition in comparison to other melanoma subtypes, specifically in the setting of CD8+ TILs and PD-L1 positivity. This may allow better selection of patients for anti-PD-1/PD-L1 therapy in malignant melanoma cases.

P117

Granulomatous Mycosis Fungoides: A Rare Cutaneous T Cell Lymphoma Variant

Ⓟ SE Low; N Sharma; J Ellison

Whiston Hospital, Liverpool, UK

Granulomatous mycosis fungoides (GMF) is a rare histologic subtype of cutaneous T-cell lymphoma. We present the case of a 58 year old woman who has had a longstanding rash on her back (7 years duration) with a purplish hue which had spread to the legs. Clinically, differentials were of an odd sarcoid, a drug rash or cutaneous T cell lymphoma. Histology revealed small granulomas and scattered multinucleated giant cells admixed with a dermal lymphocytic infiltrate. On close examination of the lymphoid infiltrate, we noted atypia and epidermotropism of the lymphoid infiltrate. Our diagnosis of GMF was confirmed with immunohistochemistry and molecular studies. It is important to note that granuloma formation can be quite prominent and GMFs can often be initially misdiagnosed as granulomatous dermatitis. Sarcoidal granulomas are well known in nodal lymphoma but these are rarely found in primary cutaneous lymphomas (circa 2%). Epidermotropism, a clue to diagnosis in classical mycosis fungoides, may be absent in half of GMF. Sometimes, the granulomatous component may also be intense and obscures the lymphomatous component. GMFs show a therapy-resistant, slowly progressive course and have an apparently worse prognosis than classic MF. There are no distinctive clinical patterns associated with GMF unlike granulomatous slack skin (GSS) which presents with pendulous skin folds hence awareness of this entity and careful histological examination especially in the presence of granulomas and a setting of what appears to be inflammatory dermatitis is paramount to prevent misdiagnosis.

P118

One Year Audit of Adherence to RCPath Guidelines for the Histological Reporting of Primary Cutaneous Melanoma in a Tertiary Care Centre

Ⓟ H Abdelghany

Queen Elizabeth Hospital, Birmingham, UK

Aim: To assess the adherence to minimum dataset reporting for the histopathological reporting of primary cutaneous malignant melanoma as per Royal College of Pathologists' (RCPath UK) guidelines.
Methodology: A retrospective analysis of all invasive melanoma excision reports generated during the year of 2015 at Queen Elizabeth Hospital (University Hospital Birmingham). The reports were retrieved from the hospital's pathology (telepath) and clinical (portal) database systems. All reports were analyzed to see whether they met the standards as per RCPath's reporting proforma for cutaneous melanoma (Appendix D1, Version 3) published in May 2014.
Results: A total of 103 reports of primary cutaneous melanoma excision were evaluated. The number of adherent reports was 54 (52%) and non-adherent reports were 49 (48%). In these non-adherent reports, the documentation of the following parameters was sub-optimal: perineural invasion (47), ulceration (1), lympho-vascular invasion (1) Growth Phase (1).
Conclusion: A significant number of melanoma reports did not include some of the core dataset items. The most commonly omitted data item was peri-neural invasion/ neurotropism. Perineural invasion is a core data item for the National Clinical Guidelines on melanoma, and correlates with a higher local recurrence rate.

P119

Dual Genotype Oligoastrocytoma Revealed at Tumour Recurrence: A Case Report

Ⓟ L Lebrun; M Le Mercier; A Van Ham; B Melendez; I Salmon; N D'Haene

Erasme Hospital, Université libre de Bruxelles, Brussels, Belgium

According to the 2016 WHO CNS tumour classification, histology and molecular data allow classification of nearly all of the gliomas as either astrocytomas or oligodendrogliomas. There, the diagnosis of oligoastrocytoma is strongly discouraged. Despite this, true oligoastrocytomas consisting of histologically and molecularly distinct astrocytic and oligodendroglial tumour populations have been reported, albeit rarely. A 39-year-old man was admitted in 2009 following an epileptic seizure. MRI showed an expansive lesion in the right parietal lobe. Histopathological examination of the surgical resection revealed an infiltrating glioma consisting of oligodendroglial tumour cells without anaplasia. No 1p/19q codeletion was noted by fluorescence in situ hybridization (FISH). Diagnosis of an infiltrating WHO (2007) grade II oligodendroglioma was made. No adjuvant therapy was administered. In 2017, an MRI suggested a progressive tumour in the right frontal lobe. Histopathological examination revealed an infiltrating glioma with a tumour block of oligodendroglial cells and areas of astrocytic infiltrating cells, both with signs of anaplasia. The tumour showed strong positive ATRX staining and 1p19q codeletion in the oligodendroglial areas but no expression of ATRX and no 1p19q deletion in the infiltrating cells. New immunostains were performed on the 2009 sample and showed lack of ATRX expression but intense p53 staining. Targeted NGS analysis was performed on samples from 2009 and 2017; it revealed IDH2 and TP53 mutations in both samples but with different allelic frequencies for TP53 (91% in the 2009 sample and 8% in the 2017 sample). Following the 2016 WHO classification, we retained the diagnosis of grade II astrocytoma, IDH-mutant, 1p/19q-intact for the 2009 sample and the diagnosis of anaplastic oligoastrocytoma with a dual genotype for the 2017 sample. This case illustrates the difficulties of diagnosing tumours with mixed morphologies and dual genotypes.

P120

Is Whole Slide Imaging (WSI) Non-Inferior to Light Microscopy (LM) in the Assessment of Intraductal Lesions/Epithelia Atypia in Breast Cancer Screening Programme Specimens?

Ⓟ IP Wilson[1]; D Treanor[2]; BJ Williams[2]

[1]University of Leeds, Leeds, UK; [2]St James's University Hospital Leeds, Leeds, UK

Purpose of the study: There is interest in using digital pathology in the primary diagnosis of cancer screening specimens. Due to this, validation studies using digital pathology are necessary to prove diagnostic concordance between light microscopy (LM) and whole slide imaging (WSI). These studies could also increase pathologists' confidence in diagnosing breast specimens using WSI, thus potentially establishing digital pathology as the primary platform for delivering diagnosis.
Methods: Three consultant pathologists examined and reported on 50 breast screening specimens using both LM and WSI. The slides were reviewed on two separate occasions with a 'washout period' between each viewing. The pathologists completed a tick box proforma for each slide documenting the time taken for each lesion to be diagnosed on each modality and indicating how confident they were in their diagnosis.
Results: Of the 50 cases the original grading were B2 in 16, B3 in 19 and B5a in 15. A total of two trials with three participants were analysed. Data demonstrated that Pathologist A and C showed excellent concordance on glass vs. digital (kappa 0.94 and 0.82 respectively). Pathologist B demonstrated good concordance on glass vs. digital (kappa 0.63). The approximate time taken for the pathologist to diagnose each specimen was significantly different on glass vs. digital, with means of 60.91 seconds and 77.41 seconds (t=2.584 p=0.0112) respectively. Diagnostic discrepancies were most commonly found in the grading of B3 specimens.
Conclusions: Our data support the concordance of reporting breast screening pathology samples using WSI and LM. The significant difference in time taken between making diagnosis using the different modalities could be due to many factors including the fact that each sample consisted of only one slide, whereas digital imaging truly comes into its own in multi-slide cases.