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Invited Speaker Abstracts

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KEY

Ⓟ = Presenter

PRESENTER'S INDEX

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S1

Typing and Terminology – Tips on Key Diagnoses in Ovary, Fallopian Tube and Endometrium

WG McCluggage

Belfast Health and Social Care Trust, Belfast, UK

The pathologist is playing a pivotal role in the identification of patients with familial gynaecological cancer syndromes even when there is no personal or family history of neoplasia. This is because the tumour types which occur in the various syndromes are generally fairly constant and predictable. Familial cancer syndromes in which neoplasms may occur in the female genital tract include BRCA1/2, Lynch syndrome (hereditary non-polyposis colorectal cancer syndrome), Peutz-Jeghers syndrome, DICER1 syndrome and hereditary leiomyomatosis and renal cell carcinoma syndrome. Given the close association between genotype and phenotype, the pathologist has a key role in raising the possibility of an underlying cancer syndrome and accurate diagnosis is essential to this end. In the uterine corpus, carcinomas associated with Lynch syndrome tend to be endometrioid rather than non-endometrioid in type and a proportion of these neoplasms are difficult to categorise. It is probable that only high grade serous carcinomas (which in most cases arise from the fallopian tube fimbria rather than the ovary) are associated with BRCA1/ BRCA2 germline mutations. Rarely, other ovarian tumours occur in patients with germline BRCA1/ 2 mutation but these may be coincidental or may represent misclassified high grade serous carcinoma. A scenario can be envisaged whereby all patients with ovarian/ tubal high grade serous carcinoma undergo BRCA testing and all patients with ovarian endometrioid or clear cell carcinoma undergo testing for Lynch syndrome. As such, pathologists need to provide accurate diagnosis. The role of WT1 and p53 in distinguishing between high grade serous carcinomas and endometrioid, low grade serous or clear cell carcinoma in problematic cases is stressed, as is the fact that mixed carcinomas in the ovary are very uncommon.

S2

Identifying Hereditary Predisposition in Patients Presenting with Gynaecological Malignancies – An Update on Non-BRCA Non-Lynch Hereditary Gynaecological Cancer Syndromes

BA Clarke

Toronto General Hospital, Toronto, Canada

Large cohort studies and next-generation sequencing studies have significantly advanced our understanding of hereditary gynaecological cancer syndromes, highlighting robust genotype-phenotype correlations. Tumour subtype designation by pathologists conveys genetic (both somatic and germline), prognostic and therapeutic information. Criteria for cancer genetic consultation referral include tumor type in combination with genealogy based criteria and sometimes tumour type alone (histology based criteria). Pathologists are playing an increasingly pivotal role in identifying hereditary predisposition in cancer patients. It behoves us to be aware of such associations and to advocate for genetic consultation referral when reporting appropriate cases. Furthermore, such genetic alteration may be of predictive value, influencing therapy selection and may also provide meaningful quality assurance of histologic assessment. Regarding gynaecological malignancies, the phenotype of DICER 1 syndrome is now known to include ovarian sex cord-stromal tumours, uterine cervix embryonal rhabdomyosarcoma and primitive neuroectodermal tumor in addition to pleuropulmonary blastoma, cystic nephroma, and multinodular goitre. Recent identification of SMARCA4 somatic and germline mutation in small cell carcinoma of the ovary, hypercalcemic type, has facilitated accurate diagnosis and genetic counselling as well as prompting reconsideration of tumour nosology. Other important syndromes in which histologic tumour assessment can be critical are Hereditary leiomyomatosis/ renal cell carcinoma syndrome and Peutz-Jeghers syndrome with its associated sex cord tumor with annular tubules, Sertoli cell tumour and adenoma malignum/ gastric type endocervical adenocarcinoma. Despite the vicarious nature of the patient-pathologist relationship, pathologists are crucial in the recognition and management of hereditary cancer syndromes

S3

Identifying Lynch Syndrome in Patients with Gynaecological Malignancies: Implementation of Reflex Testing and its Implications

BA Clarke

Toronto General Hospital, Toronto, Canada

Patients with Lynch syndrome (LS) are at significantly elevated lifetime risk for several cancers including ovarian and endometrial (EC) carcinoma. A gynaecological malignancy will be the sentinel cancer in the majority of women with LS. Identification of LS accrues advantages to the patient, kin and the health care system. MMR is also a prognostic (TCGA) and possibly predictive marker (immunotherapy.) Predicated on poor performance of genealogy and morphology schemas, reflex testing of gynaecologic cancer specimens with mismatch repair immunohistochemistry (MMR-IHC) has been proposed. Based on a prospective study showing MMR-IHC to be the superior screening strategy to identify LS in women with EC, we have adopted reflex screening of all patients with EC using MMR-IHC. Adoption of reflex testing using MMR-IHC has resolved some abiding contentions and raised new requirements to be addressed. It is recognised that MMR-IHC loss for MSH2/ MSH6 may result from somatic mutation, dismissing debate that MMR-IHC is akin to germline testing. Laboratories need to engage in quality assurance programs of performance and interpretation of MMR-IHC. Audits are required to ensure that tumours from all eligible patients are indeed tested with MMR-IHC with appropriate subsequent referral to genetic counsellors. Pathologists need to be cognizant of pitfalls in IHC staining and interpretation. Reporting must be standardized. Education is required to ensure the clinicians understand reports and respond appropriately. Finally the "circle of care" has to integrate the multidisciplinary team: pathologists, clinicians, family doctors, genetic counsellors and medical geneticists with sharing of information. Since the laboratory investigation of an individual patient may occur at different sites, is iterative and may involve both germline and somatic testing of MMR genes, access to genetic information by pathologists is imperative for quality assurance and comprehensive patient management.

S4

A Mainstreamed Oncogenetic Pathway Delivers Fast, Affordable Routine BRCA Testing for Ovarian Cancer (OC) Patients

Ⓟ AJ George[1]; D Riddell[2]; V Cloke[2]; M Gore[1]; S Bannerjee[1]; H Hanson[1]; N Rahman[2]

[1]Royal Marsden Hospital, London, UK; [2]Institute of Cancer Research, London, UK

The development of targeted agents such as PARP-I has made germline BRCA mutation status vital for optimal OC patient (pt) management. Over 15% of OC pt carry a BRCA mutation, exceeding the NICE testing threshold, yet few are tested. We implemented a mainstreamed 'Oncogenetic' pathway to make BRCA testing standard for OC pt. Initially, pt with serous/endometroid OC <65 yrs at diagnosis were offered BRCA gene testing in their Oncology appt by clinicians who had completed a 30 minute online training package; this later extended to all non-mucinous OC pt. Test results were returned by Genetics to the pt; mutation carriers were reviewed in Genetics to arrange other screening and family testing. Patients could contact Genetics at any time, or be referred at the discretion of the clinicician. We tested 119 pt in the first 6 months; 85% had serous tumours. Pt were tested in first line (27%), relapse (38%) or follow-up (35%); mean turnaround was 25 days. 20/119 had a mutation — 8 BRCA1 and 12 BRCA2, 12 had no family history of BC or OC. OC treatment immediately changed in 45% of carriers. All pt were sent a questionnaire to assess the protocol. 100% were happy to have had testing, all within oncology. All understood implications for them and their family. All clinicians agreed BRCA testing was important, and felt confident in offering it. The Oncogenetic model of testing allows flexible, patient-centred, equitable, high throughput gene testing with considerable time and cost savings compared to model of referral to Genetics. It identified a number of patients with mutations who would not have been identified using standard referral criteria, and has resulted in alterations in clinical management. It is now the standard pathway for BRCA testing in OC pts at Royal Marsden and has been adopted by multiple other centres.

S5

Intraoperative Diagnosis

Ⓟ CM Corbishley

St George's Healthcare NHS Trust, London, UK

The use of frozen section diagnosis has decreased in recent years but it still has its' uses. The only indication for an intraoperative consultation is when the outcome will make a difference to the current operative procedure. The pathologist and surgeon need to be aware of the pitfalls and limitations of the technique and the pathologist needs to be both decisive and safe. The talk will specifically cover the use of frozen sections in the field of cancer diagnosis including risk assessment and how to approach the frozen section cases in the final FRCPath Practical examination.

S6

Macroscopic Examination

Ⓟ M Sheehan

Galway University Hospital, Galway, Ireland

This talk will focus on how to approach the macroscopic pathology component of the FRCPath part 2 practical exam. It will also briefly look at how to approach the OSPE stations in this exam section.
The aim is to translate from the exam experience back to day to day bench experience with which the exam candidate is very familiar. The application of this day to day knowledge in a focused approach will ensure the candidate answers all the required questions competently.
For the macroscopic cases, focus will be on overall description, block sample and compliance with minimum datasets.
For the OSPEs, focus will be on a template of key issues/components which must be included in the addressing and discussing the OSPE scenario.
The talk will conclude looking at key overall challenges of exam time management, answer construction, clear thinking processes and clear communication of the candidates knowledge for maximum achievement in the exam.

S7

Soft Tissue Cutaneous Tumours

Ⓟ MB Leader

Beaumont, Dublin, Ireland

This presentation will discuss the approach to the diagnosis of cutaneous soft tissue sarcomas. It will discuss spindle cell tumours, myxoid tumours, epithelioid tumours and fatty tumours. Particular emphasis will be given to the differential diagnoses of these lesions and to practical advice on achieving a diagnosis. The commonest cutaneous spindle cell sarcoma of atypical fibro Xanthema will be discussed and the clinical behaviour and morphology will be contrasted with pleomorphic dermal sarcoma, leiomyosarcoma, spindle cell carcinoma and spindle cell melanoma. Three particularly difficult myxoid tumours will be highlighted including myxoinflammatory fibroblastic sarcoma, myxofibrosarcoma and fibromyxoid sarcoma. The differential of myxoma and nodular fasciitis and malignant fibroma histiocytoma will be compared and contrasted. Newer markers (immunohistochemical and molecular) will be discussed. The talk will briefly touch on lipoma like liposarcoma subtle sarcomas such as synovial sarcoma, epitheloid sarcoma and clear cell sarcoma will be demonstrated. Finally, the pitfall of pseudosarcomas with hints of how to avoid these pitfalls will be discussed.

S8

Primary Bone Tumours: Guiding Treatment Using Histology and Molecular Genetic Alterations

Ⓟ AM Flanagan

UCL Cancer Institute, London, UK

Reaching a diagnosis of a primary bone tumour is facilitated by using genetic alterations which are characteristic of such lesions. However, the pathologist's interpretation of the histology in the context of the radiology is still required for choosing the relevant tests to help arrive at a diagnosis. Benign osteoclast-rich tumours include giant cell tumour of bone, chondroblastoma and aneurysmal bone cyst and these must be distinguished from an osteoclast-rich osteosarcoma and clear cell chondrosarcoma. Over 90% of giant cell tumour of bone and chondroblastoma harbour a recurrent H3F3A and H3F3B substitution: approximately 70% of aneurysmal bone cyst harbours a USP6 rearrangement: this alteration is also found in 90% nodular fasciitis. However, ~1% of high grade osteosarcoma also harbours a H3F3 substitution: copy number change can distinguish these osteosarcomas from giant cell tumour of bone and chondroblastoma. Approximately 50% of conventional central chondrosarcoma, the most common adult primary bone tumour, harbours an isocitrate dehydrogenase (IDH) substitution (94% IDH1, 6% IDH2) but this does not help in determining tumour grade. CDKN2A and or TP53 alterations only occur in high grade tumours. An IDH alteration is particularly useful in distinguishing dedifferentiation chondrosarcoma from an osteosarcoma and is clinically relevant as the treatment is different. A GRM1 rearrangement in chondromyxoid fibroma is helpful in distinguishing this tumour from chondrosarcoma. Low grade fibrous tumours in bone include low grade osteosarcoma (central and parosteal) and fibrous dysplasia and the treatment for these differ: MDM2 amplification is found in the former and GNAS alterations in the latter: they are mutually exclusive. Development of multiplexing technology will make the delivery of these tests more efficient but the interpretation of the molecular data in the context of the histology, and clinical information will remain central to good clinical practice.

S9

Toxicology: Interpretation for the Pathologist

Ⓟ SP Elliott

ROAR Forensics, Malvern, UK

Toxicology concerns the study of the effects, nature and detection of drugs and poisons and their dose. The involvement of drugs or poisons may not always be immediately obvious to Pathologists. Even in instances where there is significant evidence to suggest the ingestion of drugs has occurred, the exact drug (or more usually drugs) may not be known. Furthermore, even if a drug has been detected, the interpretation of its presence or amount can depend on many factors. Not least the type, nature and actions of the drugs themselves. It is also important to be aware of the wider issues that impact on toxicology, including; appropriate sample collection, analysis, drug stability and possible endogenous production of compounds.

There are a number of considerations for toxicology interpretation namely; there is no fatal range for all drugs - some overlap with therapeutic range, drug tolerance, pharmacogenomics, drug combinations, drug stability, post-mortem production and importantly, post-mortem redistribution (which also means in life data does not equate to post-mortem data). The Pathologist should be aware of these factors in order to consider the potential role of drugs in a death in conjunction with the findings at autopsy and the case circumstances.

Whilst appropriate interpretation is a constant challenge for all drugs, something of significant pertinence to modern toxicological casework is the rise of so-called "legal highs". This has become a particular issue within the last decade and it is a major challenge to keep up with this either analytically (i.e. actually detecting such drugs) or interpretatively (i.e. what is the significance of the presence or concentration of a drug when little is known about it?).

Overall, there are many factors that have to be considered to enable valid and appropriate interpretation of toxicology findings and Pathologists should bear in mind that rigid toxicology "ranges" do not exist.

S10

Diagnosis of Infection, Sepsis and SIRS at Autopsy

Ⓟ SB Lucas

St Thomas' Hospital, London, UK

Problems arise in interpretation of systemic aspects of sepsis (systemic inflammatory response syndrome — SIRS) and its large differential diagnosis. The end result of severe sepsis always involves a haemophagocytic syndrome (HPS) = macrophage activation syndrome = haemophagocytic lymphohistiocytosis. The causes of HPS are genetic (inherited) and reactive (acquired) forms: Inherited genetic defects of perforin gene on chr 9q21, the MUNC13-4 gene on chr 17q25, or mutations in syntaxin 11 gene on chr 6q24. Infections: viruses such as EBV and influenza; HHV8 infection in HIV disease; numerous bacteria (eg group A Strep and Staphylococcus — toxic shock syndromes), M.tuberculosis; leishmaniasis. Autoimmmune disorders: eg adult onset Still's disease and vasculitis. Lymphomas: B-cell, T-cell and Hodgkin lymphomas can all present with HPS, even when the tumour volume is low (or occult); Common to all are the following generic features: haemophagocytosis of blood cells: these are optimally seen using macrophage immmunohistochemistry (IHC: CD68, PGM-1) where the macrophages are increased in number and size, containing engulfed cells in addition to their nucleus; seen in marrow, liver, spleen and nodes; upregulation of intercellular adhesion molecule-1 (visualised with CD54 IHC), seen best in lung vessels; acute lung injury; the spleen may be small with white pulp atrophy, or enlarged in other presentations including HHV8-associated multicentric Castleman disease HPS; the kidney may show disseminated intravascular coagulation, as part of a coagulopathy.

S11

Minimally Invasive Coroner's Autopsy – The Present and (Near) Future

Ⓟ ISD Roberts

John Radcliffe Hospital, Oxford, UK

The role of post mortem imaging is changing. In the past it was used only as a supplement to dissection in forensic practice, to reveal details of fractures and identify foreign bodies. In the last 20 years, cross-sectional imaging has been increasingly used as a replacement to standard coroner's autopsy, for those cases in which the family object to invasive examination. Early services lacked both evidence base and governance. Recent research has defined the strengths and weaknesses of post mortem imaging, optimised imaging protocols and led to technical improvements, most notably the development angiographic techniques. It is now possible to accurately identify those cases for which imaging alone is sufficient to diagnose the cause of death. CT scan is generally superior to MRI for the investigation of sudden adult deaths; using CT with angiography, three quarters can be diagnosed without the need for an invasive procedure. Furthermore, imaging is superior to dissection in identifying certain types of injuries and thus facilitates the recognition of unnatural deaths that might have been missed using traditional autopsy. In the UK, there are currently 6 centres that provide post mortem imaging services, performing several hundred cases annually. There are plans to open a further 16 CT units nationally, dedicated for post mortem work, and it is possible that post mortem CT will soon be used in the majority of coronial cases. Pathologists must become familiar with the application of imaging techniques if they are to be involved in the decision making process, and in particular the selection of cases for which an invasive autopsy is required.

S12

From Research Bench to Patient – Impact and Future of Molecular Diagnostic Developments on Lung Cancer Pathology Practice

Ⓟ S Lantuejoul

CHU A Michallon and J Fourier University, Grenoble, France

Lung cancer is the second most frequent type of cancer but by far the most frequent cause of cancer-related deaths. Up to 60% of lung adenocarcinoma and up to 50-80% of squamous cell carcinoma have known oncogenic driver mutations or translocations, most frequently leading to permanent tyrosine kinase activations targeted by specific drugs (tyrosine kinase inhibitors TKI); the pathologists are now not only expected to provide precise diagnoses whatever the size of the specimen but are also involved in the management of those specimens and the identification of new targeted genetic or molecular abnormalities; among them, EGFR mutations occur in 10% of adenocarcinoma and are detected by most platforms; with the development of NGS technologies, large panels of genes, including KRAS, BRAF, PIK3CA, ERBB2, PTEN, NRAS, STK11, DDR2, MET, FGFR3, FGFR1, will be investigated in all lung cancers; ALK and ROS1 rearrangements are detected in nearly 5% of adenocarcinoma by FISH/ immunohistochemistry by most platforms, but pathologists will be soon asked to detect new translocations (RET, NTRK1,..) and new protein overexpressions involved in secondary TKI resistance (C-MET hyperexpression/ amplifications, Axl expression,..). In addition, pathologists will likely participate to the selection of good responders to anti PD1/PD-L1 immunotherapies using PD-L1 immunohistochemistry.

S13

Role of Cytopathology in the 2015 Molecular Era

Ⓟ J McCarthy

Cork University Hospital, Cork, Ireland

Cytopathologists and Histopathologists are most challenged when the sample is small, the cells are few and the differential diagnosis is wide. As diagnostic techniques become less invasive, tissue on which to diagnosis and sub-classify thoracic malignancy becomes less abundant and we as pathologists are being asked to do more with less. EBUS can sample a variety of pathologies in addition to primary lung carcinoma including lymphoma and melanoma that may also require molecular testing. The "Molecular era" brings with it therefore the challenge to offer an accurate diagnosis in addition to the reservation of sufficient material on which to perform molecular tests, affording the opportunity to target mutations specific to individual cancers. In our institution; cytology samples account for 46% of samples tested for EGFR mutatation in Lung cancer and yield 43% of the mutations detected in our tested cohort. There is no statistically significant difference between cytology and histology samples in terms of adequacy of material for EGFR testing. At the same time, the concordance rate for sub typing of Lung cancer between histology and cytology samples is 100%. Achieving this balance requires a combination of curtailed immunostains, co-ordinated handling of separately submitted histology and cytology samples, attempting molecular tests on samples not previously considered worth testing, and for the future, looking at techniques that may purify malignant cells to enhance a molecular signal above background noise. The Pathologist needs to be ready to embrace this era, preferably to be on site for targeting lesions with fine needle aspiration, and ideally situated in close proximity to the molecular testing laboratory to maximise the potential of each individual sample. This may be particularly challenging in institutions without dedicated Cytopathology or in those receiving material from external sites.

S14

Challenges of the New WHO Classification in the Diagnosis of Adenocarcinoma

Ⓟ KM Kerr

Aberdeen University Medical School, Aberdeen, UK

The new WHO classification of adenocarcinoma (ADCA) follows directly from the IASLC/ATS/ERS publication of 2011 in establishing a more clinically relevant, multidisciplinary approach to lung ADCA. The classification includes pre-invasive disease and establishes a category of in-situ (AIS) and minimally invasive (MIA) ADCA, whilst removing the diagnosis of bronchioloalveolar carcinoma. Several variants of ADCA are removed, some remain, sometimes under a new name, and resected tumours are now principally classified according to their predominant histological patterns. An important addition is guidance and nomenclature for ADCA diagnosis in small biopsy and cytology samples. Finally, efforts have been made to make the classification relevant to the radiological diagnosis of this disease as well as the molecular characterisation of tumours for the purposes of selecting patients for targeted therapy.

Whilst resolving several problematic issues with the 2004 classification, several challenges either remain or have emerged. The diagnosis of pre-invasive disease (atypical adenomatous hyperplasia or AIS) is difficult since lesions are uncommon and criteria quite subjective. The identification of invasion is frequently problematic. Accurate identification of a predominant pattern in invasive tumours, and especially the enumeration of other patterns present, is sometimes quite challenging and a pragmatic approach is needed.

Immunohistochemistry (IHC) has emerged as a crucial tool is diagnosis. Not only is it now part of the definition of solid pattern ADCA in resected cases, it is pivotal in accurate small sample diagnosis. Molecular characterisation of ADCA is now a routine standard of care. With this comes the need for technically consistent IHC, careful tissue handling to ensure IHC and molecular testing are possible, and complex workflows designed to ensure the complete diagnosis required for patient management.

S15

Staging / Classification of Thymic Epithelial Tumours

Ⓟ A Marx

University Medical Centre Mannheim Universty of Heidelberg, Mannheim, Germany

Staging of thymomas has not changed significantly since Masaoka and Koga proposed their stage I-IVb scheme. Although not validated for thymic carcinomas (TCs) it has ever since been applied to them, despite the very different propensity of thymic epithelial tumours (TETs) for lymphogenous and haematogenous metastasis (that is frequent only in TCs). Nevertheless, the International Association for the Study of Lung Cancer (IASLC) and the International Thymic Malignancy Interest Group (ITMIG) have jointly proposed an evidence-based TNM staging system that is founded on the analysis of >8.000 clinically annotated cases, is applicable to thymomas and TCs and awaits approval by UICC/AJCC. This new staging system will be presented. The 4th edition of the WHO Classification of thoracic tumours was published in March 2015. It puts emphasis on an interdisciplinary perspective on thymic tumours by depicting state-of-the-art CT or PET/CT images and incorporating cytology. Epidemiological and prognostic data were updated by mining the world-wide, retrospective database of the ITMIG that compiles over 6000 case of thymic tumors. The refinement of morphological criteria mainly addresses the "borderlands" between type A and AB thymomas, between type B1-3 thymomas and between type B3 thymoma and thymic squamous cell carcinoma, aiming to improve reproducibility and clinical relevance. For the first time immunohistochemical criteria are suggested for the diagnosis of difficult-to-classify cases and a new "atypical type A thymoma variant" is introduced to reflect the realization that histological features (like comedo-type necrosis) may be associated with the rare occurrence of advanced tumor stage, including metastasis, in type A (and AB) thymomas. The lecture will detail the differences between the 3rd and 4th edition of the WHO classification of thymic epithelial tumors.

S16

Approach to the Diagnosis of Rare and Unusual Lung Tumours

Ⓟ AG Nicholson

Royal Brompton and Harefield NHS Foundation Trust, London, UK

Any primary tumour arising in the lung apart from carcinomas and carcinoids falls under the umbrella term of a "rare lung tumour". This therefore includes other epithelial tumours, soft tissue tumours, lymphomas and even teratomas and melanomas. These have recently been updated in the WHO 2015 classification, with the last ten years seeing greater understanding of the histogenesis of certain rare neoplasms, such as sclerosing haemangioma being definitively identified as a low-grade epithelial neoplasm. New tumours with specific genetic abnormalities have also been identified such as pulmonary myxoid sarcoma with EWSR1-CREB1 translocation, and entities such as lymphangioleiomyomatosis (LAM) and Langerhans cell histiocytosis are now also classified as neoplasms. It is useful therefore to have a uniform approach to a potential neoplasm that does not look like a common entity. My approach to these tumours is to use the WHO 2015 classification as a template, then to correlate this with its morphological (e.g clear cell, spindle cell etc.) and immunohistochemical profile to see whether the proposed diagnosis is consistent with these data. I then review the case again in relation whether the presentation of the tumour is appropriate for my proposed diagnosis (benign/low-grade versus malignant cytology, tumour location, solid/cystic, local/diffuse) and finally reviewing it once more in the context of whether tumour might be a secondary process or even a reactive process. In this way, even the rarest tumour should be able to be correctly classified.

S17

The Management of B3 Lesions with Emphasis on Lobular Neoplasia

Ⓟ AM Shaaban

Queen Elizabeth Hospital Birmingham, Birmingham, UK

B3 lesions are a heterogeneous group of different pathological diagnoses including those with and without atypia. They comprise flat epithelial atypia (FEA); atypical intraductal proliferation (AIDP); in-situ lobular neoplasia (ISLN); papillomas, radial scars, fibroepithelial lesions and other. Approximately 20-25% of all B3 lesions are upgraded to cancer on further tissue. examination and the upgrade rate is higher in the presence of atypia across all B3 lesions.

The management of B3 lesions has traditionally been via diagnostic surgical excision biopsy. However, it is becoming increasingly recognised that at least some of the B3 subtypes may only be associated with a low risk of malignancy and therefore surgical excision for all may represent over-treatment.

The introduction of vacuum assisted biopsy (VAB) offers an alternative option to surgery in the management of such B3 lesions. VAB can yield up to 3.6g of tissue providing a robust method for thoroughly sampling B3 lesions diagnosed on needle core. Therefore, patients could avoid unnecessary surgery if there is confidence that the lesion has adequately been sampled by second line VAB and the diagnosis has not been upgraded to malignancy. VAB is also advantageous if it confirms a malignant diagnosis as the patient can progress straight to therapeutic surgery.

Currently, there is lack of consistency in the management of those lesions across screening centres in the UK. Guidelines are therefore being developed. Current and future management plans will be discussed in detail with emphasis on ISLN.

S18

Update from The Sloane Project

Ⓟ JS Thomas

Western General Hospital, Edinburgh, UK

The Sloane Project has closed to new cases of DCIS and data consolidation is complete for the 12,500 cases entered between 2004 and 2012 with over 90% of patients having a complete four-specialty (radiology, surgery, pathology and radiotherapy) data set. Over the period of case acquisition the Steering Group published eight peer-reviewed papers on radiological diagnosis and pathological correlation, the surgical management of DCIS particularly in relation to the axilla and variation in practice around the UK in the assessment of oestrogen receptors, radiological lesion size estimation, pathological evaluation of specimens, mastectomy rates, particularly for small lesions, and treatment with radiotherapy. In the second phase of the Project we are continuing to acquire patients with ADH and lobular neoplasia but are shifting our emphasis away from audit *per se* towards the biology of the disease. With a median of five years follow up to date we have data on over 750 recurrences/events in our patient cohort and are looking at the dataset for features associated with these events. We also have ethical approval and funding to support an examination of tissue from Sloane Project cases to look for biological markers associated with outcome measures. We are also collaborating closely with the organisers of the LORIS Trial evaluating the role of non-surgical intervention for low risk DCIS.

S19

Genetics of Cardiomyopathies

Ⓟ ER Behr

St George's University of London, London, UK

The presentation will describe the current state of genetic knowledge in relation to cardiomyopathy. It will primarily focus upon the sub-phenotypes of hypertrophic, arrhythmogenic and dilated cardiomyopathies. Current issues with 'genetic noise' will be addressed and the role for genetic testing on a clinical basis will be further discussed. Genetic variation in cardiomyopathy genes associated with unexplained sudden death and the Brugada syndrome will also be explored.

S20

Clinico-Pathological Correlations on Vasculitis

Ⓟ A Fabre; Ⓟ E Molloy

St Vincent's University Hospital, Dublin, Ireland

This lecture provide four examples on different patterns of small and large vessels vasculitis as well as their underlying etiologic factors, to assess the clinic-pathological correlation. All cases discussed with have clinical and radiological data and the discussion will emphasis on tissue sampling, histological patterns and differential diagnoses, both by microscopy and clinically, including autoimmunue associations and drug related changes. This will provide an opportunity to bring the clinical aspects of vasculitis into the histopathological evaluation of vascular changes in light of improved imaging available to clinicians.

S21

Sudden Cardiac Death in Athletes

Ⓟ S Sharma

St George's University of London, London, UK

The benefits of regular exercise on the cardiovascular system are established; therefore the sudden death of an athlete from a cardiac cause sends shockwaves through the lay community. Over 80% of all non-traumatic deaths in athletes are attributable to abnormalities of the heart. The prevalence of sudden cardiac death (SCD) in athletes is generally in the range of 1 in 50,000. Over 90% of SCDs affect males. Athletes of African or Afro-Caribbean origin are at greater risk compared with Caucasians. Deaths are most common in dynamic sports of a start-stop nature such as soccer and basketball. Hypertrophic cardiomyopathy is the commonest cause of SCD worldwide, whereas arrhythmogenic right ventricular cardiomyopathy is the leading cause in Italian athletes. There is emerging data from US athletes and soldiers and from a tertiary UK center that these diseases may account for up to 30% of all deaths. Pre-participation screening to identify athletes at risk of SCD is recommended by learned scientific communities. ECG screening is effective at detecting high risk ion channel diseases and congenital accessory pathways. ECG screening is also helpful for raising suspicion of the cardiomyopathies. A 25 year old prospective ECG screening programme in Italian athletes revealed a 90% reduction in the prevalence of SCD in athletes from 3.6/100,000 to 0.4/100,000. ECG screening is associated with high incidence of false positive results and is ineffective for detecting coronary artery disease. Furthermore deaths from acquired conditions such as myocarditis, heat injury and electrolyte disturbances cannot be predicted, therefore the availability of personnel trained in cardiopulmonary resuscitation and automated external defibrillators (AEDs) at sporting arenas is prudent. Data from high schools with AEDs and mass participation events shows that early CPR and use of AEDs has a survival to discharge of up to 65%.

S22

Update of the Classification of Renal Carcinomas

Ⓟ S Fleming

University of Dundee, Dundee, UK

The classification of renal cell carcinoma has been based on the underlying genetic changes since pioneering work in the early 1990s. As new genetic alterations are identified and corresponding morphological criteria developed the classification is regularly updated through the work of the ISUP and WHO consensus meetings and publications. The latest version of the WHO Classification (Version 4) is due to be published shortly. It recognises several lesions described since the 2004 classification and further emerging entities which require further characterisation. It is now recognised that there exists a family of renal tumours exhibiting translocations involving the MiT family of transcription factors, most commonly TFE3 on Xp11 but others involving TFE B on chromosome 6 are now well described. Tubulocystic carcinomas have a typical morphology and behaviour, previously classified as low grade collecting duct carcinoma they have now been re-classified. Mutation of the fumarate hydratase gene encoding a member of the mitochondrial electron transport chainis seen in the hereditary leiomyomatosis and renal cll carcinoma syndrome (HLRCC). RCC formation is accompanied by loss of the wild type allele and gives rise to a morphologically recognisable tumour type. A second mitochondrial gene, succinate dehydrogenase B is also seen in a morphologically distinct form of RCC. These several new tumour types will be presented.

S23

Update in Penile Pathology: The new Dataset and Diagnostic Pitfalls

Ⓟ CM Corbishley

St George's Healthcare NHS Trust, London, UK

Penile tumours are rare with only 600 cases of cancer and precancer diagnosed in the UK per year. The last 12 years have seen a major change in the way that these tumours are dealt with surgically with increasing subspecialisation and the formation of cancer supranetworks which are well developed in England and Wales. Over the last 14 years at St George's in London we have seen over 1100 new cases of penile, scrotal and distal urethral cancer and have pioneered the use of sentinel node evaluation and penile preserving surgery.

2015 sees the publication of the new WHO blue book on Urological cancers and the new Royal College of Pathologists Cancer dataset for reporting of Penile and Distal Urethral cancers. Much has changed since the previous 2006 dataset edition. The terminology of precancerous lesions is now encompassed by the term PeIN (Penile Intraepithelial Neoplasia) and the entity differentiated PeIN has been described.

New subtypes of penile cancers have been identified and the association of some tumours with HPV subtypes, particularly type 16, is well established. Sentinel node evaluation has been shown to be reliable and prevents unnecessary debilitating groin dissections. Penile preserving surgical techniques, such as glansectomy and glans resurfacing with plastic reconstruction, are used wherever possible to avoid formal penectomy and give good cancer control.

The major pitfalls in penile cancer pathology include difficulties in diagnosing PeIN subtypes and accurate invasive tumour grading and subtyping. The anatomy of the penis is complex and accurate staging requres a detailed knowledge of anatomy. Some of the well differentiated variants, verrucous carcinomas and pseudohyperplastic carcinomas, are difficult to diagnose especially in small biopsies.

As with other rare tumours, consistency of reporting is improved with experience and the opportunity to report significant numbers of cases within a specialist multidisciplinary team.

S24

Updates in Bladder Cancer Including the RCPath Dataset, Subtypes of Bladder Cancer and Molecular Developments

Ⓟ JH Shanks

The Christie NHS Foundation Trust, Manchester, UK

One controversy in preparing the RCPath "Dataset for tumours of the urinary collecting system [2nd edition])", April 2013 was which WHO grading scheme (1973 or 2004) to use for urothelial carcinoma. Since there is a split within grade 2 (1973) between low grade & high grade, use of both schemes in parallel was recommended. This has the advantage of better indicating where a particular patient lies in the grading continuum & minimises the consequences of 'grading error' for cases close to the threshold between low & high grade in the 2004 scheme, (a critical distinction for management if 2004 WHO grading is used in isolation). The 2015 NICE guidance on bladder cancer (http://www.nice.org.uk/guidance/ng2) incorporates risk stratification tables for Ta/T1 bladder cancer utilizing this parallel WHO grading recommendation in a multiparameter formula that also considers tumour size, pT classification and the presence/absence of CIS or aggressive subtype(s).

Amongst the more aggressive bladder cancer subtypes is invasive micropapillary urothelial carcinoma and the nested variant. A bladder origin can be difficult to recognise at metastatic sites, especially for micropapillary and discohesive/ plasmacytoid subtypes. Uroplakin II has recently become available, is more sensitive than uroplakin III & may assist within a panel. Spindle cell lesions of the bladder are often difficult & loss of cytokeratin expression is common in sarcomatoid carcinoma. There is potential to mistake inflammatory myofibroblastic tumour for a malignant tumour.

Two molecular pathways for bladder cancer are recognised. *FGFR3* at 4p16 is the most frequently mutated oncogene in bladder cancer & is prevalent in low grade papillary tumours. *p53* loss of function mutations and loss of RB1 are prevalent in CIS. No prognostic molecular test is currently validated for clinical use in bladder cancer, though some (e.g. FISH) are in use as an adjunct in diagnosis.

S25

'New' Observations About Old Entities in Testicular Pathology

Ⓟ TM Ulbright

Indiana University School of Medicine, Indianapolis, USA

Some dogmas in testicular pathology do not hold up to scrutiny. The belief that all pure, postpubertal teratomas are malignant is invalid. Within this group there is a small subset that is benign; these may be divided into dermoid and non-dermoid types that, however, share features that distinguish them from the usual teratoma of adults. These include absence of: atypia, regressive parenchymal changes, intratubular germ cell neoplasia, and i(12p). Also they usually show organoid arrangements, and prominence of ciliated epithelium, squamous cysts and smooth muscle. Patients do not need further intervention beyond excision sufficient to establish the diagnosis.
Cases often interpreted as isolated testicular polyarteritis nodosa because of the presence of fibrinoid vascular necrosis are mostly attributable to chronic, intermittent torsion. They usually present as pain-associated, palpable or ultrasound-detected masses, with the "mass" corresponding to infarct and/or hemorrhage. There are associated chronic vascular changes, with frequent marked intimal hyperplasia of arteries, mural fibrosis of veins, dilated venules and arteriolar hyalinization, consistent with torsion-induced venous outflow obstruction and secondary arterial hypertension. These patients do not develop systemic vasculitis on follow-up.
Many "sarcomas" in patients with germ cell tumours, especially after chemotherapy, are more correctly regarded as sarcomatoid yolk sac tumours. They are reactive for cytokeratin and glypican 3. They often show characteristic features: nodular growth, myxoid and fibrous stroma, spindled and epithelioid cells, abrupt changes in cellularity, and tumor "ringlets." Most are high grade and aggressive.
Most regressed germ cell tumours can be recognized through a combination of findings, although the only diagnostic ones are a scar with coarse intratubular calcifications or with intratubular germ cell neoplasia.

S26

Dying for a Drink – The Problem with Alchohol (and Some Solutions)

Ⓟ FE Murray

Royal College of Physicians of Ireland, Dublin, Ireland

Alcohol consumption has doubled in Ireland and the UK in the last 60 years. The causes of this increase include increased affordability of alcohol and its widespread availability. As a consequence, the health harms associated with alcohol have dramatically increased. Binge drinking and alcohol consumption among by women have risen especially dramatically. For example, the mortality from cirrhosis has doubled in the last 20 years in both men and women. In response to this, the medical profession on both islands have led informal and later formal campaigns to encourage policy change regarding alcohol at a national level. In Ireland, this was driven by RCPI. The involvement of the medical profession has had a powerful influence, as doctors do not have a conflict of interest in this matter, in contrast to the alcohol industry. The policy changes advocated include particularly Minimum Unit Pricing (MUP), which has been shown to be effective in reducing alcohol consumption, alcohol-related admission to hospital and crime in Canada. Modelling of the data suggests it would have similar benefits in UK and Ireland. This is regarded as the single most important first step. Other steps which will help include actions around alcohol labelling, availability and breaking the link between alcohol and sports and leisure promotion. Turning off the tap of cheap alcohol will hopefully soon reduce alcohol health harms in UK and Ireland

S27

Barrett's Oesophagus: An Evolving Challenge for the Gastroenterologist

Ⓟ DOT O'Toole

St James's Hospital & St Vincent's University Hospital & Trinity College Dublin, Dublin, Ireland

Cost-effective surveillance programmes for Barrett's oesophagus (BO) needs to be focused at risk groups. It is not only a question of identifying more individuals with BO (initial screening) but screening and subsequent surveillance has to identify at-risk individuals with BO who can benefit most from surveillance or therapy. Advances in endoscopic imaging (high resolution endoscopy ([HRE] with dye-based chromoendoscopy, electronic chromoendoscopy, and autofluorescence,...) certainly prove beneficial in better detecting dysplasia within known BO and can guide sampling and subsequent therapy. Dysplasia can be patchy and easily missed during routine biopsy sampling of BO and adequate training with high resolution instruments is needed to increase detection rates. Once dysplasia is detected, endoscopic ablation is recommended. Until recently, the standard treatment for HGD was oesophagectomy but endoscopic resection and ablation techniques are now available to eradicate dysplasia and mucosal adenocarcinomas. Resecting visible lesions (using endoscopic mucosal resection [EMR] or endoscopic submucosal dissection techniques) allows full pathological T staging. When invasive cancer is eliminated at multidisciplinary review (i.e., purely mucosal neoplasia confirmed with a nodal risk <2%), further endotherapy to ablate residual metaplasia in BO can be performed using radiofrequency ablation (RAF). In a tertiary centre use of staging EMR is frequently necessary (>60%) in patients referred for endotherapy and expert endoscopy is required to ensure safe and complete oncological resection. Conversely pT1 submucosal cancers detected following EMR are confidently triaged for oesophagectomy. Combination of EMR and RFA in expert groups exceeds >95% for eradication of neoplasia and metaplasia. Adverse events are quite low (stricture form healing, 4%; self-limited haemorrhage, very rare perforations ...) and recurrence of BO is also low (<10% at 5 years). Careful follow-up endoscopies is necessary at 3 to 6 months initially; intervals theerafter probably yearly.

S28

The Pathologist's Role in the Diagnosis and Management of Neoplasia in Barrett's Oesophagus

Ⓟ C Muldoon

St. James's Hospital, Dublin, Ireland

The last decade has seen a revolution in the management of neoplasia in Barrett's oesophagus. More detailed biopsy protocols, along with the advent of sophisticated local resection and ablation techniques, have radically altered the management of this expanding cohort of patients. These new treatment modalities, coupled with a massive increase in the numbers of cases of Barrett's being diagnosed, have significantly altered the demands placed upon pathologists involved in this area.
These changes have presented pathologists with an opportunity to challenge our existing practices, to improve the reproducibility of our analysis and to increase the clinical relevance of the way in which we report neoplasia in this setting, where the pathologist plays a critical role in the multidisciplinary management approach.
This talk aims to outline a practical approach to the handling of these specimens and to provide clear guidelines as to how to report them in the most clinically useful way.

S29

Modern Management in IBD

Ⓟ MWR Vieth[1]; H Neumann[2]

[1]*Klinikum Bayreuth, Pathology, Bayreuth, Germany;* [2]*University Hospital Erlangen, Medical Clinic I, Erlangen, Germany*

Ulcerative colitis and Crohn's make a distinct histological picture. Around 80% of an IBD diagnosis is the clinical information and about 20% derives from histology, only. For routine purposes it is recommendable in case of a first manifestation of an IBD to make a diagnosis such as: "picture of ulcerative colitis or picture of crohn's disease" and to recommend a follow-up endoscopy with biopsies not prior to 8 weeks after the first endoscopy and than confirm the diagnosis later to exclude mimickers of IBD. In Crohn's disease it is helpful to take biopsies from the upper GI-tract to get further hints of Crohn's disease. In case of neoplasia, the guidelines leave some room for local endoscopic treatment of low grade dysplasia whereas high grade dysplasia is still seen as an indication for operation since there is a high probability of detecting a carcinoma in the operation specimen afterwards. Operation means on normal complete proctocolectomy. This has been indivdually questioned in the last time.
There are exceptions for discussing the indication of an operation in IBD: cases with numerous pseudopolyps that cannot be searched for neoplasia, low grade lesions that cannot be completely removed, multiple neoplastic lesions and unresponsiveness to medical treatment.Operation and endoscopic specimen in IBD need a subtile search for neoplastic lesions. A microscope with reverse light may help to identify suspicous lesions and may help to decide where exactely to cut a specimen.
In conclusion a tight cooperation between clinical and histopathological partners is recommended to reach a high standard for patient care. Second opinions may help to achieve and fuel the own learning process esp. in an institution with a lower number of IBD patients during the year.

S30

The Pathology of Colorectal Cancer Screening

Ⓟ MB Loughrey

Royal Victoria Hospital, Belfast, UK

Colorectal or bowel cancer screening (BCS) is commonplace and organised national screening programmes have been developed in many countries, most notably in western Europe. Traditionally, faecal occult blood (FOB) detection has been the screening method of choice, those testing positive being selected for subsequent colonoscopy, but this is changing, with alternative or additional screening tests gaining favour. Most of the problems in BCS pathology practice are particularly related to FOB-based screening programmes, as these are enriched for large, bleeding sigmoid adenomas, in comparison to programmes utilising endoscopy as the primary screening modality. Experience within the closely related UK BCS programmes to date has yielded several recurring problems: the diagnosis of stage pT1 or 'polyp' cancers, in particular distinguishing common epithelial misplacement from 'true' invasion; the management of stage pT1 cancers, in relation to indications for surgical intervention after such a diagnosis; and the minimum criteria for a biopsy diagnosis of colorectal adenocarcinoma. These issues will be discussed with illustrative examples, along with the somewhat more mundane but highly important practical issue of measuring various parameters related to BCS pathology. The importance of quality assurance measures to ensure high standards within BCS pathology is emphasised.

S31

Predicting Lymph Node Metastatic Disease in pT1 Polyp Cancers

Ⓟ ID Nagtegaal

Radboud UMC, Nijmegen, Netherlands

With the introduction of colorectal cancer screening in various countries of the EU there is a sharp increase in the incidence of early colorectal cancer. A significant part of these early tumours presents in a pedunculated polyp. In most cases, these carcinomas are already completely removed by polypectomy. Classic risk factors that suggest a high risk for lymph node metastases include Haggitt level 4, positive resection margins, poor differentiation and lymphatic or vascular invasion. However, the evidence is rather thin. Most pT1 studies are performed on sessile polyps. Risk factors are more firmly established and include differentiation grade, lymphatic invasion, Kikuchi level sm3 or the presence of budding. However, for a clinical useful decision model, we will need an integrated approach, and both specificity and sensitivity of the various factors should be taken into account. Radical surgery seems overtreatment for a large number of polyp cancers.

S32

Colorectal Cancer: Updated Royal College of Pathologists' Guidelines

Ⓟ P Quirke

Leeds University, Leeds, UK

Minimum datasets have changed cancer reporting. This talk will explain the decision making processes behind the latest datasets both for cancer reporting and bowel cancer screening. It will also look at where we may be going in the future for staging and molecular reporting.

S33

Infective Pathology in the Intestines

Ⓟ MR Novelli

UCL, London, UK

The intestines play host to a broad spectrum of infective organisms ranging from viruses, through bacteria , fungi and unicellular parasites to worms. The spectrum of infections seen varies with geographical location, due to socioeconomic factors and due to changes in human behaviour. Immunocompromisation due to infections (in particular HIV), malignancy (especially haematological tumours) and the use of immunosuppressive drugs also has an important role in determining the infections commonly seen in the GI tract. The typical pathological features of intestinal infections will be discussed together with suggestions on how to optimise the diagnosis of such pathologies.

S34

Unusual Colitides

Ⓟ P Demetter

Erasme University Hospital, Brussels, Belgium

Pathologists are confronted with different types of colitis, most commonly infectious colitis and inflammatory bowel disease (IBD) followed by microscopic colitis and ischaemic colitis. Several other forms of colitis, however, exist and might be underrecognised; these diseases include segmental colitis associated with diverticulosis, diversion colitis, eosinophilic colitis and Behcet's colitis. Clinical presentations of these rare types of colitis vary, and laboratory data are often non-specific; mucosal biopsy is essential in establishing the diagnosis. Segmental colitis associated with diverticulosis (SCAD) is mainly characterised by the involvement of the sigmoid colon with sparing of the rectum and proximal colon. SCAD often mimics IBD at endoscopic and histological examination; since SCAD has a self-limited course that resolves without further recurrence or need for treatment, the implications of an inaccurate diagnosis are obvious. Diversion colitis is a non-specific colonic inflammation following surgical diversion of the faecal stream. Is is characterised by a chronic lymphoplasmacytic infiltrate, and the existence of lymphoid follicular hyperplasia is considered to be a hallmark feature. The development of diversion colitis is attributed to a lack of short chain fatty acids. Eosinophilic colitis is etiologically obscure and can be associated with involvement of other sections of the gastrointestinal tract. An infiltrate of eosinophilic granulocytes is found to varying degrees in all wall layers. A history of food intolerance or allergy is present in most of the patients, and peripheral eosinophilia is present in 80% of cases. Gastrointestinal involvement has been reported in up to 25% of patients with Behcet's disease. In cases with ileocolonic involvement, it is often difficult to distinguish Behcet's disease from other inflammatory bowel diseases. The diagnosis, therefore, often depends on clinical manifestations and intestinal ulcerative lesions.

S35

How to Write a Paper and Get it Published

Ⓟ CS Herrington[1]; Ⓟ DM Berney[2]

[1]University of Edinburgh, Edinburgh, UK; [2]Barts Health NHS Trust, London, UK

Scientific papers have a predetermined structure, and writing in this way requires practice. Most Journals accept only a small fraction of submitted papers and it is important that any paper has something specific to say; and says it in a clear and concise way that can be understood by editors, reviewers and readers, all of whom play a role in assessment of its contribution. Editors look for novelty and significance in the context of the aims and scope of their Journal; and scientific rigour, which expert reviewers help them to assess. Writing a paper and having it assessed by a Journal is an iterative process. During the writing phase, the scientific rigour of the argument can be refined; and following submission and peer review, reviewers and editors often make constructive comments that help to improve it still further. The peer review process therefore acts not only as a quality filter but also as a mechanism for quality improvement. Writing papers and submitting them for publication is therefore generally a positive experience, particularly if one remembers that the process is iterative and (inevitably) not all papers will be accepted for publication by the first Journal that they are sent to.

S36

Large-Scale Routine Diagnostics Using Whole-Slide Imaging in Sweden – the Linköping Experience

Ⓟ C Lundström

CMIV, Linköping University, Linköping, Sweden

This presentation will describe the large-scale routine usage of WSI at Linköping University Hospital, Sweden. Since 2011 all histology slides are scanned, amounting to more than half a million slides to date. To a significant extent the digital images are used for primary review. The initial implementation led to several of the benefits foreseen with digital pathology, but it could also be concluded that further development was needed to unlock the full potential, in particular within the IT solutions. Therefore, a consortium led by CMIV, Linköping University was formed in 2012 to create innovations for a new generation of digital pathology. This triple helix consortium also includes industry and more than half of Sweden's health care providers, an engagement that reflects the dominating view in Swedish pathology that large-scale adoption of WSI practice is possible and desirable.
This talk covers the experiences made during the initial digitization, including laboratory process adjustments, and the later additions to the digital pathology toolbox accomplished by the ongoing innovation project. Apart from obvious targets such as the pathologists' workstation, the developments also touch upon other areas including grossing and enterprise image management.

S37

Digital Pathology – Are We There Yet?

Ⓟ SM Hewitt

National Cancer Institute, Bethesda, Maryland, USA

The implementation of whole slide imaging for diagnostic histopathology is far more complex than connecting an instrument to a server, and placing a computer on a pathologist's desk. The technology is additive to the histology workflow, with additional cost beyond the current practice of review with a microscope. The adoption of Digital Pathology for histomorphologic diagnosis requires the restructuring of the workflow, additional technology advances beyond the imaging instrument, and development of new tools to assist the pathologist. The end goal is to improve pathologist's productivity and provide additional diagnostic information. Digital Pathology, to succeed must become a value-added proposition. The adoption of Digital Pathology requires: 1)Improvements in scanner performance as measured by defined quality metrics. 2)Advancement in server and networks to distribute images to the desktop efficiently. 3)Software to facilitate review and diagnosis, beyond presenting only and image of the slide. Evolution of the current technologies is required to provide an economic impetus for widespread adoption and use of Digital Pathology in the diagnostic setting.

S38

Benign versus Malignant Melanocytic Lesions: Lesional Symmetry, Maturation and Ascent

Ⓟ WJ Mooi

VU Medical Centre, Amsterdam, Netherlands

To a significant extent, the distinction between melanocytic naevi and malignant melanomas is based on tissue architecture. Amongst the best known architectural features pointing to malignancy are absence of lesional symmetry and maturation, and presence of melanocyte ascent. However, each of these three features has significant pitfalls. As a rule, naevi are 'roughly symmetrical' and melanomas are not, but there are asymmetrical naevi (traumatized naevi, most larger congenital naevi; some combined naevi; some large acral and genital naevi) and symmetrical melanomas (including many small melanomas, especially small nodular melanomas; some spitzoid melanomas). In addition, it is not always clear whether a lesion should be considered 'roughly symmetrical' or not. I suspect that not uncommonly, a diagnosis is reached first, and the verdict regarding symmetry is adjusted according to that diagnosis. Similar caveats relate to absence of maturation as an indicator of malignancy. It is seen in blue naevi and all its variants; deep penetrating naevi; some BAP1 naevi. Melanomas not uncommonly feature smaller cells in their deeper parts, or there may be an underlying naevus remnant with smaller cells. Naevi with ascent include many Spitz naevi; Reed naevi; some naevi in early infancy; traumatized naevi; naevi of acral skin. Over-interpretation of ascent may result from inexperience with Melan-A and some other immune stains. Melanomas devoid of ascending melanoma cells comprise a wide variety of subtypes including, desmoplastic melanomas and, vexingly, some spitzoid melanomas. These architectural features must, therefore, be evaluated in the context of all other findings, and with a 'splitter's' mind set, taking into account the individual characteristics of the specific naevus and melanoma variants that are of relevance to the case under study.

S39

Melanoma Variants

Ⓟ JE Calonje

St John's Institute of Dermatology, London, UK

Most melanomas are fairly easy to diagnose on histological grounds. However, melanoma is a tumour that can histologically mimic almost any other tumour including epithelial and mesenchymal neoplasms. Pathologists need to familiarize with the wide histological appearances of melanoma to avoid serious misdiagnoses. Of crucial importance is the knowledge that a number of melanomas can closely mimic benign naevi. Some variants of melanoma represent distinctive clinicopathological entities and these include desmoplastic melanoma, "malignant" blue naevus, pigment synthethizing melanoma, naevoid melanoma, spitzoid melanoma and epidermotropic metastatic melanoma. Tumoral melanosis refers to complete regression of a melanoma, a diagnosis that it is often missed because of the absence of tumour cells within the regressed area. A small percentage of melanomas display focal or extensive histological changes that closely mimic other neoplasms and often a combination of histological features with immunohistochemistry is necessary to arrive to the correct diagnosis. Microscopic variants of melanoma include adenoid (pseudoglandular), angiotropic and angiomatoid, signet ring cell, balloon cell, clear cell, rhabdoid and follicular (with exclusive involvement of hair follicles). Some melanomas display heterologous differentiation also known as transdifferentiation. The latter should not be confused with the so-called collision tumour in which a melanoma co-exists with a neoplasm of different lineage. A wide variety of heterologous differentiation has been described in melanoma including osteosarcomatous and chondrosarcomatous (mainly seen in acral melanomas), meiomysarcomatous, rhabdomyosarcomatous, neuroendocrine, ganglioneuromatous and even epithelial. Except for desmoplastic and pigment synthetizing melanoma, all other variants of the tumour have the same behaviour as ordinary melanomas.

S40

Spitzoid Tumours

Ⓟ T Brenn

WGH, Edinburgh, UK

Melanocytic tumours with Spitzoid features represent one of the most challenging and controversial areas in Dermatopathology. What is currently known as Spitz naevus was initially reported as "juvenile melanoma" by Sophie Spitz on 1948. She recognized the relatively indolent but somewhat unpredictable behaviour of these distinctive melanocytic lesions that are particularly common in young children. Over the years, the histological spectrum of these tumours was expanded, and it has become clear that classical Spitz naevi follow an entirely indolent disease course. The prognosis of tumours with atypical histological features remains somewhat unpredictable. This presentation will give an overview of the morphological spectrum of Spitzoid melanocytic tumours, their behaviour and recent advances of their molecular characteristics.

S41

A Research Career in Pathology

Ⓟ NP West

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

The number of pathologists actively engaging in research has risen again over recent years following the introduction of a defined academic training pathway and the support of bodies like the Pathological Society. A research career is exceptionally rewarding and offers the chance to undertake potentially ground breaking research alongside clinical practice.

An interest in pathology research can begin as an undergraduate and a number of opportunities now exist to allow students to explore a research career and embed themselves within academic pathology groups at an early stage. Most medical schools offer special study modules where students can apply to do a piece of research in an area of interest. Several students also opt to undertake research placements during the summer holidays. This can be taken further with a full year out from a medical degree to intercalate a BSc/MRes, or even undertake a three year Doctoral degree.

Following university, academic foundation placements allow for a four month period of research and lead into specialist training pathways where further experience can be gained as an academic clinical fellow (ACF) with up to 25% of time spent in research. This is usually followed by three years out of clinical training to complete a higher degree and leads into a clinical lectureship (CL) where 50% of time is spent undertaking research at an increasingly independent level. ACF and CL opportunities are advertised across the UK in centres of academic excellence. On completion of clinical training, a senior lectureship allows continuation of academic activities at a senior level alongside working as a consultant.

A research career is stimulating and varied and offers the chance to undertake research in a world class environment. You get the opportunity to travel widely and experience pathology practice across the world as well as present your work to the scientific community. It is a career path highly recommended by the speaker!

S42

This abstract is not available before the meeting

S43

Student Perception of Optimisation Compared with the Evidence of Optimisation in Paediatric Radiography Case Studies

Ⓟ J Doyle; K Matthews; A McGee

University College Dublin, Dublin, Ireland

Optimisation is a core tenet in radiography and involves the radiographer ensuring that images of diagnostic quality are produced with minimum radiation dose burden to patient and staff [1,2]. In paediatric practice this is particularly important due to the more radiosensitive nature of the child [1]. In alignment with the ISRRT 2013 World Radiography Day theme 'Radiographers Optimise Dose', radiography students in an institution submitted clinical case study coursework that focused on paediatric radiation dose optimisation.

The purpose of the current study was to analyse these case studies as examples of prevailing radiographic practice and to compare students' perception of optimisation with the evidence within each case. The evidence of optimisation was established through independent and objective image analysis along with thematic analysis of the case commentaries.

The case study evidence demonstrated that optimised techniques were generally well implemented. The exception was collimation, which was sub-optimal in 84% (n=31) of the examinations, and on average irradiating an area 27% larger than necessary. Students were generally able to correctly identify techniques as optimal or not. However, when appraising exposure, positioning and collimation, between 9% and 33% of students were inaccurate in their assessment of what is optimal.

Overall the study reflects positively on current Irish paediatric radiography with regard to dose optimisation, although more accurate collimation needs to be practised. Similarly student perceptions show good understanding of optimal techniques, although appreciation of exposure, positioning and collimation errors could be improved.

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1. Matthews K, Brennan P. Optimisation of X-ray examinations: General principles and an Irish perspective. Radiography. 2008:15:262-268.
2. Willis CE. Optimizing digital radiography in children. European Journal of Radiology.2009:72:266

S44

Design of a Paediatric Immobilisation Device for use in Radiographic Examinations

Ⓟ JPM Murtagh[1]; MD Davis[2]; EOC O'Cearbhaill[3]; JG Grehan[2]

[1]UCD School of Medicine, Dublin, Ireland; [2]UCD School of Health Sciences, Dublin, Ireland; [3]UCD School of Engineering, Dublin, Ireland

The aim of this project was to design and prototype immobilisation devices for children who are unable to independently maintain upright sitting posture during radiographic investigations. While current market devices exist, they are seldom used by radiographers - particularly in Europe as their methods of restraint have been deemed 'culturally unacceptable' with some claiming that they are in violation of the human rights of the child [1]. The design challenge was to create devices that were functional (fit for purpose [2], radio-lucent, compliant with infection control and easy to use) while minimising discomfort and intimidation. A search of the literature, prior art, patent landscape and current market devices was performed in order to identify product requirements. TRIZ methodologies - a problem solving, analysis and forecasting tool derived from the study of patterns of invention in the global patent literature were used to identify the physical contradictions underlying the design challenge and generate potential solutions. Eight unique concept designs were identified from these methods. These were then evaluated using Pugh Criteria — a ranking system of the relative merits of each concept based on design requirements identified. Four of the eight concepts were chosen to be prototyped: a 3-D printed seat, a swing based template, an acrylic-based support and an adaptable wheelchair. The prototypes were made in collaboration with the UCD School of Engineering and tested using paediatric phantoms in UCD Radiography department. The final prototypes will be trialled in Crumlin Children's Hospital with a view to future use and development.

References: 1. Hardy M. Holding Children Still! Synergy- January. 2004:16-19.
2. European Commission. European guidelines on quality criteria for diagnostic radiographic images in paediatrics. Publication EUR 16261 EN Brussels, Belgium: European Commission, 1996.

S45

Thrombotic Microangiopathy and the Kidney

Ⓟ AM Dorman

Beaumont/RCSI, Dublin, Ireland

Thrombotic microangiopathy (TMA) is a pathology that results in thrombosis of capillaries and arterioles due to endothelial injury. It is usually characterized by an atypical haemolytic syndrome (aHUS) or thrombotic thrombocytopaenic purpura (TTP). TMA is considered to be caused by infections, drugs, autoimmunity, tumours, pregnancy, transplants and inherited abnormalities involving the alternate complement pathway. This presentation describes the pathology of TMA. It includes a retrospective 15 year study (1999 - 2013) of all renal biopsies reported by one pathologist. All renal biopsy request forms and reports, where cases included light (LM), fluorescence(FM) and electron microscopy(EM), were reviewed. Cases without all 3 modalitles (LM, FM, and EM) were excluded. 6639 biopsies were reported in the study period (328 in 1999 to 629 IN 2013). 2105 were transplant biopsies. 284 biopsies were insufficient (LM, FM and EM all not possible. This resulted in 4250 native renal biopsies as the study group. Following review of the reports 641 cases were reported as TMA. 66 were associated with thin membrane nephropathy, 41 with minimal change disease and 24 with plasma cell dyscrasia/ B cell malignancy. This resulted in 510 cases with TMA as the only pathology reported which represents 12% of all adequate native medical renal biopsies. Clinical indications included proteinuria in 73%, nephrotic syndrome in 15%, increased creatinine in 43%, increased blood pressure in 55% and haematuria in 43% of the cases. Acute renal failure was described in 10% and HUS in just 1% of the cases. Pathological changes were predominently arteriolar sclerosis and glomerular double contours on LM with chronic subendothelial injury on EM. The conclusions of this presentation are 1. TMA is overwhelmingly a chronic lesion as seen in renal biopsy pathology. 2. It is a very common pattern of injury. 3. It is not usually associated with clinical HUS or TTP features at presentation

S46

Next Generation Sequencing: What Will it Mean for the Pathologist?

Ⓟ CL Corless

Oregon Health & Science University, Portland, Oregon, USA

The era of targeted cancer therapeutics has brought forth new challenges for molecular diagnostic laboratories. The list of genes, and indeed specific mutations, that predict drug responses keeps growing, and with it grows the demand for molecular sub-classification of tumors. In colorectal carcinoma, for example, recent studies support expanding testing beyond KRAS to include NRAS and BRAF in predicting resistance to EGFR-targeted therapies. Similarly, in non-small cell lung carcinoma standard screening for EGFR mutations and ALK gene fusions may be insufficient when actionable alterations involving ROS1, RET, HER2, MET, BRAF and other genes are being targeted (successfully) in ongoing clinical trials. Fortunately, the introduction of next-generation sequencing (NGS) into the clinical laboratory is meeting the demand. Due to its quantitative output, NGS not only provides precise mutant allele ratios, but it can also be used to detect gene gains and losses. Furthermore, when applied to RNA, NGS supports the detection of gene fusions and serves in assessing gene expression levels. While NGS is a powerful tool for molecularly characterizing solid tumors, the quality of the results in large part rests on the selection of appropriate input material; therefore, review by a pathologist prior to testing remains a cornerstone to success. Other growing uses of NGS include monitoring minimal residual disease in the setting of hematologic malignancies, and in the detection of targetable mutations in cell-free DNA within the plasma.

S47

Next Generation Sequencing in Muscle Disease – A Tale of Two Cities

Ⓟ AR Foley

National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, USA

The advent of next generation sequencing has ushered in an era of tremendous potential for identifying the molecular causation of simple and complex disorders, both rare and common. The successes of next generation sequencing reflect the combined interpretive skills of geneticists, bioinformaticians and clinicians working in close collaboration.

In the realm of muscle disease, we have witnessed both the strengths and the weaknesses of next generation sequencing technologies. The use of exome sequencing in patients with rare muscle disease who have been carefully phenotyped has proven to be a successful strategy for identifying causative variants in new genes as well as in known genes. In fact, exome sequencing has significantly expanded both the clinical and the histological phenotypic spectra of muscle conditions associated with causative variants in known genes. In the absence of careful phenotyping or large genetic reference data sets for identifying variants of interest, causative variants may be missed, however. The use of RNA sequencing- using RNA extracted from muscle biopsy specimens- has proven to be a powerful tool for finding causative variants affecting gene splicing or expression, which may be missed with next generation sequencing.

Muscle pathology plays an essential role in complementing next generation sequencing. The deep phenotyping of patients with muscle disease relies heavily on muscle histological and immunohistochemical findings in combination with muscle imaging, clinical history and neuromuscular examination findings. Examples of how next generation sequencing coupled with careful clinical and histological phenotyping has uncovered causative variants in new genes as well as in known genes will be discussed in this talk.

S48

Companion Diagnostics: The Evolving Role of Diagnostic Pathology

Ⓟ MTP Padilla

Ventana Medical Systems, Inc./Roche Tissue Diagnostics Companion Diagnostics, Tucson, USA

Medicine, diagnostic pathology, technology, and diagnostic tests are evolving at an extremely rapid pace. Drug developers and diagnostic developers each face unique challenges. Companion diagnostic development is a key component of pharma drug development strategy. We will discuss the importance of companion diagnostics in the success of personalized medicine, the FDA position on companion diagnostics, and the role, advantages and disadvantages of tissue based companion diagnostics. Other technologies, such as Next Gen Sequencing, will increasingly be utilized in a complementary fashion along with traditional slide based immunohistochemical and in situ hybridization. The scope and limitations of available technologies will be reviewed. Diagnostic technologies of all types will complement each other to provide the most accurate diagnostic information for clinicians and patients.

S49

Companion Diagnostics for Haematological Malignancies

Ⓟ RJ Flavin

St. James's Hospital, Dublin, Ireland

Following the 2008 WHO classification of haematological malignancies there has been a greater emphasis on the integration of molecular information with clinical and morphological data not just for diagnostic purposes but also to help convey both prognostic and therapeutic information. This talk will concentrate on routine testing in the work-up of common haematological malignancies focusing specifically on clonality and translocation analysis in lymphoproliferations and mutational testing in BCR-ABL negative myeloproliferative neoplasms. Using case studies to illustrate common indications for testing this talk will also highlight some of the practical points and pitfalls in the interpretation of these tests.

S50

The Neuropathology Post Mortem for Trainees

Ⓟ M Farrell

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"Should I keep the brain?" is one of the most frequent questions addressed to neuropathologists by surgical pathology colleagues. Fears relating to inappropriate organ retention coupled with decreasing availability of expert neuropathology opinion and the widely held belief that advances in neuroimaging have replaced the brain autopsy, have all contributed to a decline in the post mortem study of human brain tissue. Leaving aside the critical relevance of neuropathology to forensic medicine, the vital role played by careful examination of the post mortem brain extends far beyond pathology and has contributed greatly to science and medicine. In general, prolonged retention of entire brains may be avoided. In hospital practice it is uncommon for a patient to die without brain imaging. Access to pre-mortem brain imaging will guide the surgical pathologist in careful and appropriate sampling of calvarial, dural, meningeal, vascular and parenchymal central nervous system components. Spinal cord examination requires prior experience in spinal cord removal but most post mortem technologists are expert in cord extraction. Sampling and appropriate processing of nerve and muscle requires prior experience or neuropathology advice. High quality photography obtained at all phases of post mortem brain examination including the coronally sectioned individual cerebral hemispheres, with retention of blocks from each of the brain lobes together with cerebellum, brain stem, vessels and dura — meninges will ensure that in the event of a neuropathology opinion benign required — that opinion will not be compromised. Specific issues which will be addressed will include the death of patients with epilepsy, dementia, stroke and undiagnosed neurological disease. The key learning objective will be to ensure that pathology trainees approach post mortem examination of the nervous system with interest and excitement.

S51

Approach to the Neuropathology of Brain Tumours

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Dr Kathreena Kurian is a Consultant Neuropathologist and Head of the Brain Tumour Research Group, Institute of Clinical Neurosciences, Bristol. She will present an Approach to the Neuropathological Diagnosis of Brain Tumours and update on what's new in brain tumour research. Kathreena has published widely on Brain Tumour Research and has authored the textbook An Atlas of Gross Neuropathology Kurian KM, Moss T, Camelo-Piragua A; published by Cambridge University Press. She sits on the NCRI Brain Tumour Clinical Subgroup and Novel Agents and Translational Research Subgroup, and is Associate Editor for Frontiers in Oncology and is on the Editorial Board for the Journal of Pathology. She recently launched a National Campaign with the charity Brainstrust to raise awareness among Brain Tumour Patients of the need for consent to use tissue for research .

S52

A National Framework for Quality Assurance in Cellular Pathology – The Irish Approach

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Following several high profile misdiagnoses in Ireland a national quality assurance (QA) programme for cellular pathology in 2009 was initiated with a vision of establishing a patient-centred pathologist-led framework that would enhance the quality of patient care with timely, accurate and complete pathological diagnoses and reporting. National QA guidelines were developed based on 17 key quality activities generating a total of 51 Key Quality Indicators (KQI). Examples of the quality activities include turnaround time, monitoring of amended reports, frozen section correlation and various elements of peer review. All 25 cellular pathology departments in the public state-funded hospitals participate in the programme in addition to 7 laboratories within privately-run hospitals. Each laboratory enters codes on individual cases designed to capture the relevant KQI and the anonymised encrypted QA data is then electronically extracted from the laboratory information system to a national database. This national central database is managed by a novel information technology system, the National Quality Assurance Intelligence System (NQAIS)-Histopathology, that was designed to process and display the QA data so that each individual laboratory can analyse their own data and also compare their performance to the national average for each KQI. Since 2013 complete national data has been inputted into the NQAIS system and in 2014 initial QA targets were agreed for turnaround time, frozen section correlation and rate of intra-departmental consultation (IDC). In 2015 additional targets for autopsy ICD, frozen section deferral rate and turnaround time have been added. To our knowledge this programme has enabled Ireland to be the first country to publically report national metrics on the quality of their pathology services.

S53

The Politics of EQA: The NHS England QA Review and its Consequences

Ⓟ DE Hughes

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In 2013, a review of External Quality Assessment processes was carried out on behalf of NHS England. The main recommendations of this review related to the strengthening of governance of EQA, both nationally and within pathology provider organisations. Recommendations specifically affecting Cellular Pathology were: (i) Professional bodies, led by RCPath, should develop methodologies for assessing the performance of individuals in EQA schemes. (ii) All pathologists reporting pathology results and providing clinical advice should be participate in EQA schemes relevant to their practice, should achieve levels of performance determined by the professional bodies and this performance should be noted at annual appraisal. (iii) Where a need to improve performance is identified, additional remedial training should be carried out, or practice in the area of concern should be stopped until appropriate retraining has been undertaken and revalidation achieved. This process should supported and resourced by the employing organisation, as should EQA scheme participation. (iv) Interpretative EQA schemes are designed to assess and improve individual performance, and attempts at collusion are considered matters of professional probity. The professional response to these recommendations is expected to be led by the RCPath under the guidance of a newly-established national oversight group working on behalf of NHS England and should be more clear at the time of the Pathsoc conference. A key part of this response will be to separately consider the implications of this review for technical schemes, affecting laboratories, and interpretative schemes, affecting individual practitioners.

S54

The Role of Quality Assurance in the Molecular Laboratory

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Tumour samples to guide treatment decisions have become of increasing significance. Most importantly the results of companion diagnostic testing directly influences the management of individual patients as more drugs are approved for treatment of specific molecular distinct subgroups.

Reporting suboptimal quality test results may be harmful to the patient and cause the mismanagement of a prescribed companion drug. The consequences of unsatisfactory performance and measures for improvement are the responsibility of the laboratory.

Presently, there are number of EQA schemes for molecular testing available in Europe however, their results clearly indicate the need for EQA since 10%—15% of laboratories do not carry out according to the standard set by the EQA provider or utilize standardized procedures.

Continual improvement programs, internal quality control and validation program assist laboratories however; by using standardized quality practices such as ISO 15189 and the use of external quality assurance schemes can provide essential feedback to the laboratory to assure accurate molecular testing results.

S55

How to Run a Histopathology EQA in the Digital Age

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Interpretative EQA schemes in Histopathology were first introduced in the UK in the mid-1980s, well before the advent of the Internet and high resolution digital images. In this lecture we will outline key developments, as EQA schemes have evolved into the digital era, with particular emphasis on the National Urological EQA scheme, which we have run since 2007. We will outline the main practical issues involved in running an EQA scheme and share our personal experience of the development and introduction of the web-based EQAlite software, which is being utilised by increasing numbers of schemes. We will address the pros and cons of traditional glass slide-based circulations versus virtual circulations using scanned digital images and show how the digital archive generated from old EQA circulations has become a valuable educational and teaching resource. We will also briefly explore, from an Organiser's perspective, the major issues facing EQA schemes in the future, as EQA performance becomes more embedded into revalidation and fitness to practice.

S56

Molecular Pathology: The Future?

Ⓟ CS Herrington

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Molecular pathology is already central to stratified medicine. And the ability of pathologists to understand disease phenotype is essential for interpretation of the current explosion in '-omics' data. Moreover, the future of stratified medicine will require integration of information from different sources, in the context of disease phenotype, to inform patient management: pathologists are ideally placed to lead this integration. This applies not only to data derived from *ex vivo* cells and tissues but also to molecular imaging data, which require accurate correlation with cell and tissue phenotype for accurate interpretation. Molecular pathology is key to the future of pathology; and this future extends beyond the traditional light microscope