ISSP 2020
Abstracts book

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ISSP

IRISH SOCIETY OF SURGICAL PATHOLOGY

The Irish Society of Surgical Pathology
Virtual Online Meeting 2020
Final Programme

Day /Time	Session
Thursday 15th	
14:00-14:15	Welcome, Opening Address
14:15-14:45	**Tissue Pathology and COVID-19: A catalyst for change?** Prof. Manuel Salto Tellez, Professor of Molecular Pathology and Director of the Precision Medicine Centre at Queen's University Belfast
14:45-15:00	**Partner Presentation**
15:00-15:30	**Artificial Intelligence/Machine learning** Prof. Jeroen van der Laak, Professor in Computational Pathology at the Department of Pathology of the Radboud University Medical Center in Nijmegen, The Netherlands.
15:30-16:00	Break/Poster Session
16:00-16:30	**Molecular Pathology in everyday practice** Prof. Aurelie Fabre, Clinical Professor at UCD School of Medicine and Consultant Pathologist, St. Vincents Hospital Dublin
16:30-16:45	**Partner Presentation**
16:45-17:15	**Digital Pathology for Daily Diagnostic Challenges** Dr. Maurice Loughrey, Consultant Pathologist and Senior lecturer, Queen's University Belfast.
17:15-17:30	**Round Table Discussion session.** British Division of the International Academy of Pathology (BDIAP)
Friday 16th	
09:00-09:15	Welcome
09:15-09:30	Trainee presentation #1 North Dublin – Dr G Galambosi
09:30-09:45	Trainee presentation #2 South Dublin – Dr K Dineen
09:45-10:00	Trainee presentation #3 Belfast/NI – Dr G Baker
10:00-10:15	Trainee presentation #4 Cork/Munster – Dr N Al Julandani
10:15-10:30	Trainee presentation #5 Galway – Dr E O'Connor
10.15-11.00	Undergraduate presentation- Carol Rizkalla
11.00-11:15	**Partner Presentation**
11:15-11:45	**Covid related Pathology** Prof Michael Osborn, Imperial College London, Incoming President of the Royal College of Pathologists , UK
11:45-12.00	Questions
12:00- 12:15	Close and announcement of winners, presentations, posters
12:15-13.00	**Annual General meeting of the ISSP**

ORAL PRESENTATION **Unusual BRAF mutations in malignant melanoma: A challenge in molecular pathology**

Gréta Galambosi, Owen MacEneaney, Robert Cummins, Brendan Doyle
Beaumont University Hospital

Mutations of BRAF, NRAS and KIT have been implicated in melanomagenesis. BRAF mutations are of clinical interest as targets of directed therapy. Vemurafenib, an inhibitor of V600 BRAF mutations, improves survival in metastatic melanoma. Non-V600 BRAF mutations have been reported to occur in 5-12% of melanomas1, however, their prognostic and therapeutic significance are unclear. To date, small-scale trials have reported partial response to BRAF- and MEK-inhibition in patients with melanoma harbouring non-V600 mutations2.

Our laboratory transitioned to Next Generation Sequencing for solid tumours in 2018. This platform allowed a greater number of non-V600 BRAF mutations to be detected. The aim of this study was to determine the nature and frequency of non-V600 BRAF mutations at our institution.

All reported cases of malignant melanoma with genomic analysis at our laboratory between 01/01/2018 to 01/09/2020 were extracted from the WinPath database and evaluated (n=242). A subset of patients (n=8) were identified with non-V600 BRAF mutations (e.g.: BRAF D594N, F468S or G466E), representing 3.3% of cases. None of the cases involved harboured a concurrent V600 mutation.

BRAF- and MEK-inhibitors are currently licensed only for use in patients with V600 BRAF mutations. Thus, when non-V600 BRAF mutations are identified, it is challenging to navigate both the reporting of the mutation itself and potential changes to treatment. Our report shows that these mutations, although uncommon, are detected several times per year. The lack of evidence regarding their clinical utility warrants further study to determine if targeted therapies would be beneficial in this sub-group of patients.

1 Parmar A, Feilotter H, Baetz T. Non-classical BRAF melanoma: A retrospective review of disease characteristics and prognostic implication. Journal of Clinical Oncology, 2017;35(15). DOI: 10.1200/JCO.2017.35.15_suppl.e21060 Journal of Clinical Oncology 35, no. 15_suppl

2 Arkenau HT, Kefford R, Long GV. Targeting BRAF for patients with melanoma. Br J Cancer. 2011;104(3):392-398. doi:10.1038/sj.bjc.6606030

ORAL PRESENTATION **Identification and Prognostic Utility of Cancer Stem Cells in Gastroesophageal Junction Adenocarcinoma**

Kate Dinneen1,2, Anne-Marie Baird1, Shane Brennan1,2, Julie McFadden2, Belinda Hernandez1, Marie Reidy2, Paul Smyth3, Paul Nevins Selvadurai4, John Greene4, Ciara Ryan2, Orla Sheils1

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2. Department of Histopathology, St James' Hospital, Dublin
3. Cancer Molecular Diagnostics Laboratory, St James' Hospital, Dublin
4. Department of Oncology, St James' Hospital, Dublin

Gastroesophageal junction adenocarcinomas (GEJA) have increased in incidence in the Western world over the last 50 years, a trend largely attributed to lifestyle factors including obesity and gastroesophageal reflux disease. Their prognosis is poor, and treatment is often complicated by resistance to conventional anti-cancer therapies.

Current research suggests that epithelial-mesenchymal transition (EMT), whereby epithelial cells lose their adhesive properties and acquire a mesenchymal cell phenotype, may lead to development of cancer stem cells (CSC). CSCs are a sub-population of tumour cells associated with tumorigenesis, metastasis and drug resistance.

This study sought to investigate the role of EMT and CSCs in GEJA as they de-differentiate, becoming high grade and aggressive. Two distinct areas were sampled from each tumour, defined as 'higher grade' or 'lower grade' based on histological appearances. We hypothesized that 'higher grade' areas of tumour would exhibit a molecular pattern in keeping with CSC and mesenchymal phenotypes, and that these markers would correlate with clinical outcomes including treatment resistance and survival.

We investigated mRNA, miRNA and protein expression in a panel of GEJAs using RT-PCR and IHC. Biological expression patterns were correlated with clinicopathological data for each patient.

Our molecular studies identified a range biomarkers expressed in GEJA which were significantly associated with adverse clinical outcomes. These biomarkers showed potential for use individually, or as part of a combined predictive model.

Biomarkers of EMT and CSCs hold great promise in GEJA as prognostic aids and in development of targeted drug therapies.

ORAL PRESENTATION **The Molecular Aspects of Aberrant Negative P53 Immunohistochemistry in Barrett's Oesophagus: A Pilot Study**

Dr Gavin Baker, Mark Catherwood, Paul Kelly
Belfast Trust Health and Social Care Trust

Purpose: p53 immunohistochemistry is an adjunct in the histological diagnosis of dysplasia in Barrett's oesophagus (BO). Previously p53 immunohistochemistry assessment was binary with recognition of aberrant positive or normal staining. Currently an aberrant negative/null staining pattern is also recognised, which results in total loss of staining and may carry a greater risk of progression to adenocarcinoma. This pilot study aims to determine the molecular biology of aberrant negative p53 BO-related dysplasia using Next Generation sequencing (NGS) in endoscopic biopsies and assess if mutations can also be detected in non-dysplastic BO.
Methods: Biopsies showing BO-related dysplasia with aberrant negative p53 immunostaining were identified from archives and reviewed for suitability. Tissue was macrodissected from annotated sections, with separate dissection of dysplastic and non-dysplastic tissue. DNA was extracted and analysed using NGS and Sanger sequencing.
Results: 12 cases were identified for this pilot. 3 cases provided separate samples of dysplastic and non-dysplastic areas. 44 TP53 mutations were detected in 9/12 dysplastic samples and 3/3 non-dysplastic samples. The most common mutations seen were missense (61%) with exon 4 most frequently affected (61%). Sanger sequencing on 4 cases did not detect any mutations.
Conclusions: NGS has characterised TP53 mutations in biopsies showing BO-related dysplasia associated with aberrant negative p53 immunostaining and may be more sensitive than Sanger sequencing. No single defining mutation was identified but missense mutations in exon 4 were most frequent. NGS also identified mutations in separate non-dysplastic BO. Further studies may help to establish a role for NGS in future surveillance strategies.

ORAL PRESENTATION **Rates of high grade dysplasia and villousness in colorectal adenomas: the impact of subspecialisation**

Nabila Al-Julandani, Brian Hayes
Department of Histopathology, Cork University Hospital

Reporting of high grade dysplasia(HGD) and tubulovillous/villous architecture(TVA/VA) in colorectal adenomas is poorly reproducible. At CUH three BowelScreen pathologists(BSP) report proportionally more adenomas than the twelve non-BSP consultants. We aimed to assess rates of HGD and TVA/VA architecture, compare with accepted standards, and compare rates between BSPs and non-BSPs.
Reports of colorectal endoscopic cases SNOMED-coded as tubular adenoma, TVA, VA or “dysplasia” from January-March 2018 were reviewed. Polyps with invasive carcinoma and serrated adenomas were excluded. Mode of presentation, reporting consultant and microscopic features were recorded for each adenoma. Categorical variables were compared using Fisher’s exact test with a two-tailed p-value.
741 adenomas were identified (from 467 cases), 24.7% screen-detected and 75.3% symptomatic. Architecture was recorded for 671 adenomas(90.55%): 80.77% tubular, 18.62% TVA, 0.59% VA. BSPs reported 48.3% of all adenomas and reported more TVA/VA architecture than non-BSPs(22.6%-15.3%,p=0.0184). 4.7% of adenomas had HGD, with no significant difference between BSPs and non-BSPs (6.1%-3.4%,p=0.0831). TVA/VA architecture did not vary between screen-detected and symptomatic adenomas overall (20.2%-18.9%), but BSPs reported more TVA/VA architecture than non-BSPs in symptomatic adenomas (25.2%-15.4%,p=0.0110). There was no significant difference between rates of HGD in screen-detected and symptomatic adenomas (3.8 %-5%).
Colorectal adenomas reported at CUH achieve the BowelScreen standard of less than 10% with HGD. This series also meets the NHS BCSP standard of less than 25% of adenomas reported with TVA/VA architecture. Our greater rate of TVA/VA architecture reported by BSPs underlines the importance of subspecialisation in assessment of subjective microscopic features

ORAL PRESENTATION **Molecular and PD-L1 Expression Profiles of Metastatic Non-Small Cell Carcinoma (NSCC) Samples derived from Endobronchial Ultrasound-Guided (EBUS) Aspirates by Standard of Care Testing in the West of Ireland.**

E. O'Connor, AM Quinn

Treatment of NSCC has transformed with the identification of molecular alterations with differing responses to targeted therapies. Characterise the spectrum of molecular and PD-L1 expression profiles of positive thoracic EBUS lymph node aspirates.

EBUS reports of NSCC over a 60-month consecutive period were analysed to identify PD-L1 and mutation status. 306 cases of NSCC were analysed. Mutation analysis was successful on 176 of 187 cases (94%). Oncogenic mutations were identified in 42 (23.9%) cases (M:F=24:18, mean age=65.5). EGFR (10.8%) and ALK (6.3%) were the most common mutations. ALK positive cases had a younger age distribution (mean age=55.3) than non-ALK cases (P=0.001).

PD-L1 analysis was successful on 121 of 143 cases. 58.7% of metastatic squamous carcinomas had PD-L1 expression <1% and 19.5% had PD-L1 expression >50%. 36.7% of metastatic adenocarcinomas had PD-L1 expression <1% and 32% had expression >50%.The frequency of ALK positive NSCC is high. ALK translocations are normally seen in 3-5% of NSCC [1,2]. ALK translocations were identified in 12% of 2019 cases and 11% of 2018 cases in this study.

The sensitising mutations exon 21 L858R and exon 19 deletions accounted for 80% of single EGFR mutations. 3 of the 4 cases with additional mutations on retesting were exon 20 Thr 790 Met mutations. This is the commonest EGFR kinase inhibitor resistance mutation [3]. PD-L1 expression status is an important predictor of response to immunotherapy. Previous studies have shown that PD-L1 expression was significantly higher in squamous carcinoma than adenocarcinoma [4]. In our study the opposite was true.

[1] Auliac JB, Monnet I, Dubos-Arvis C, et al. Non-Small-Cell Lung Cancer (NSCLC) Harboring ALK Translocations: Clinical Characteristics and Management in a Real-Life Setting: a French Retrospective Analysis (GFPC 02-14 Study). Target Oncol. 2017;12(6):833-838. doi:10.1007/s11523-017-0520-7.

[2] Garber, K. (2010) 'Article Navigation ALK, Lung Cancer, and Personalized Therapy: Portent of the Future?', Journal of the National Cancer Institute, 102(10), pp. 672-675 [Online]. Available at: https://academic.oup.com/jnci/article/102/10/672/2516226 (Accessed: 01/09/2020).

[3] Mok, T.S., Carbone, D.P., Hirsch, F.R., et al. (2017) IASLC ATLAS OF EGFR TESTING IN LUNG CANCER, Available at: https://www.iaslc.org/Portals/0/egfr_atlas_lo-res.pdf?ver=2019-06-06-153729-323 (Accessed: 03/08/2020).

[4] Lee, S.E., Kim, Y.J., Sung, M., et al. (2019) 'Association with PD-L1 Expression and Clinicopathological Features in 1000 Lung Cancers: A Large Single-Institution Study of Surgically Resected Lung Cancers with a High Prevalence of EGFR Mutation', International Journal of Molecular Sciences, 20(19), pp. 4794 [Online]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6801455/ (Accessed: 03/08/2020).

ORAL PRESENTATION **(undergraduate) COVID-19: a disease of the endothelium?**

Carol Rizkalla

The recent emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the subsequent pandemic has resulted in a healthcare emergency of unmatched magnitude. Recent evidence suggests coronavirus disease 2019 (COVID-19) is associated with significant risk of thrombotic sequelae. The evidence to date supports the mechanism being due to the ability of SARS-CoV-2 to downregulate ACE- 2 present on endothelial cells, resulting in oxidative damage and subsequently thrombosis. As such, individuals with higher baseline levels of oxidative stress are at greatest risk of complications. D- dimers (measure of coagulation cascade activation) and thrombomodulin have emerged as prognostic markers in COVID- 19. As the thrombotic consequences have led to high mortality rate, strategies to prevent thrombosis have been proposed and trialled: heparin, anti-platelet therapy and many more unconventional therapies (ie. Ivermectin). The striking overlap between risk factors for severe COVID-19 and vitamin D deficiency, including obesity, older age, and Black or Asian ethnic origin, has led some researchers to hypothesise that vitamin D supplementation could hold promise as a preventive or therapeutic agent for COVID-19. Currently, there is much we do not know about this novel virus, however, every day we are witnessing a myriad of new studies- the aim being an approved efficacious treatment modality.

Precise Morphomolecular Analysis for Molecular Pathology

May Almezen, Dr. Allan O'Keeffe, Sinead Conneely, Professor Grace Callagy, Dr. Sean O. Hynes
Dept of Histopathology, NUI Galway and UH Galway

Morphological analysis is vital for accurate quantification of tumour DNA in histopathology samples in order to assess their suitability for different molecular testing platforms. For example, single gene testing requires 10% tumour nuclear content and NGS requires 20-30% depending on copy variant analysis. The aim of our study was to manually and accurately assess cell numbers and tumour content across multiple histological levels in order to mathematically model tumour content.

Four anonymized colorectal cancer cases had 12 sections cut over a span of 36 microns. Sections were stained for H&E at levels 1, 4, 8 and 12 to assess for changes in tumour content. Numbers of cells were counted precisely using manual methods. Volumes of cells and DNA content of cells was estimated based on data from the literature. A report by Gillooly et al., showed that an averaged lymphocyte holds 7.1 picograms of DNA.

We have shown quantitatively that tumour nuclear content can change significantly within 12 microns. In one case the percentage change between levels 1 and 4 were shown to change by 33%. Other cases for example Case 3, which was mucinous, changed by only 1% between levels.

CONCLUSIONS: Our study has shown quantitatively that tumour DNA content can significantly change within 12 microns. This is a standard extraction procedure for tumour DNA for molecular assessment. Therefore, precise quantification of tumour nuclear content is vitally important as a 33% change can result in a below threshold assessment which can have implications for false negative molecular results with regard variant expression.

References

Gillooly, James F et al. "Nuclear DNA Content Varies with Cell Size across Human Cell Types." Cold Spring Harbor perspectives in biology vol. 7,7 a019091. 1 Jul. 2015, doi:10.1101/cshperspect.a019091

CONSERVATION OF PREDICTED T-CELL EPITOPES ACROSS THE HUMAN CORONAVIRUSES

J. Cronin[1] , D. Farrell[2]
[1]UCD School of Medicine, [2]UCD School of Veterinary Medicine

As the COVID-19 pandemic continues to dominate the globe and causes significant mortality and morbidity, new research has put the spotlight on the T-cell response to SARS-cov-2. With particular scrutiny being placed on the suggested cross-reactivity of memory T-cells specific to common-cold coronaviruses having heterologous immunity to SARS-cov-2. A recent paper by Mateus et al[3] demonstrates this experimentally[3].

Using epitope prediction software, NetMHCIIpan, a list of the potential epitopes for CD4 T-cell 15-mer epitopes was predicted, for the 8 most common human HLA alleles. To simplify our analysis we concentrated on the SARS-cov-2 spike protein. Additionally, a sequence alignment of the spike protein genome for these viruses was performed to manually assess for conservation of each epitope we identified in the spike sequence and a literature review of relevant papers on T-cell cross-reactivity were performed.

Out of 92 SARS-cov-2 epitope predictions, 2 predicted peptides were conserved with >70% identity in all 6 coronaviruses and 8 epitopes had varying degrees of conservation with different combinations of the 6 coronaviruses.

These conserved epitopes across the human coronavirus family are significant in that they contribute to the growing body of evidence of human coronavirus memory T-cells displaying heterologous immunity to SARS-cov-2. The results underscore the need for further research, but also these results and how they fit in with the previous literature, informs the understanding of the immune response to COVID-19 and future therapeutic designs, and offers a possible explanation for the variability of COVID-19 symptoms[4].

References:

3. Mateus, Jose, et al. 'Selective and Cross-Reactive SARS-CoV-2 T Cell Epitopes in Unexposed Humans'. Science, Aug. 2020. science.sciencemag.org, doi:10.1126/science.abd3871.

4. Sekine, Takuya, et al. 'Robust T Cell Immunity in Convalescent Individuals with Asymptomatic or Mild COVID-19'. BioRxiv, June 2020, p. 2020.06.29.174888. www.biorxiv.org, doi:10.1101/2020.06.29.174888.

Adenxal Mass in Pregnancy

Dr. Caroline Hannigan,

Waterford University Hospital

Incidence of adnexal mass in pregnancy is between 0.05% to 2.4% and approximately 1% to 6% of these masses are malignant . Resection of the ovarian neoplasm for pathologic examination is the only method to confirm diagnosis. Some benign ovarian masses such as functional cysts and mature teratomas display distinctive features on ultrasound to rule out the need for additional surgical exploration. Most cases worldwide are diagnosed using routine ultrasound at first trimester. Age range in child-bearing women means most cases are benign and will resolve by early second trimester. Awareness and management are critical for early diagnosis and treatment to avoid complications to mother and baby.

There were 64 cases of adnexal masses diagnosed in pregnancy at the Rotunda Hospital between 2006 – 2016. Some cases involved multiple tumours with 6 patients having >1 tumour and 1 patient with 3 tumours. Incidence was 0.0629% of deliveries. 30 benign cystic teratomas (40%), 28 benign cystadenomas (37%), 13 functional cysts (17%) and 2 borderline cystadenomas (2%) were found. The majority of masses (67%) were diagnosed incidentally at delivery.

As the majority of cases identified were benign adnexal masses with known distinctive sonographic features, it is plausible these cases could have been diagnosed earlier than delivery. Incidences of adnexal masses in pregnancy doubled in Ireland in 2015 with a relative high incidence still in 2016. Ultrasound surveillance throughout pregnancy with resection post-delivery is the standard treatment in non-enlarging, asymptomatic masses. Laparoscopy is standard where the mass is enlarging, symptomatic or poses a danger to the pregnancy.

THINK OUTSIDE THE BLACK BOX

DR. DAWN BAYNES, SHO HISTOPATHOLOGY, GALWAY UNIVERSITY HOSPITAL
DR. SEÁN HYNES, CONSULTANT HISTOPATHOLOGIST, GALWAY UNIVERSITY HOSPITAL

Pathology training and medical education in general, has had to make changes to ensure delivery of information continues during COVID-19. The introduction of digital whole slide images (WSI) is a likely transition in the pathology world. Familiarity with the promising technology would be beneficial to trainees in their future careers.

Aims:

- To assess opinions on importance of a range of activities and their impact on learning
- To evaluate preference of virtual and digital slides for black box sessions

Interesting cases were chosen for routine Black box session. They were anonymised and scanned using the Ventana DP 200 Roche slide scanner. The cases were built on UPath software (Roche). Trainees were given the access details and asked to complete a SurveyMonkey®.

Out of 10 participants, all (100%) had experience using digital pathology in the past. For preference of black box delivery, 50% of trainees preferred a mix of both digital and manual slides, 40% preferred fully manual slides and 10% preferred fully digital. Comparing the mean scores on a scale of 1 to 5 relating to both manual and digital slides, manual scored higher for both ease of use (4.4-3.6), quality of slides(4.5-3.9) and ease of interpretation(4.3-3.7). Conversely, digital slide had a significantly higher mean score of 4.6 compared to 3.7 for manual. Reasons for manual slide preference were morphological clarity and better image quality. Reasons for digital slide preference were convenience and availability.

Black box was seen as an important contribution to training. Fully digital black box delivery was the least preferred option. Although considered the most convenient option, digital infrastructure issues were highlighted as the main hindrance in optimal delivery of digital slides for educational training.

Case Report - Extra mammary Paget's Disease of penis.

Dr. Caroline Hannigan,
Waterford University Hospital

Carcinoma of the penis is rare in industrialized countries, accounting for less than 1 percent of cancers in men. Penile cancer is typically a disease of older men with the mean age at diagnosis being 60 years. Extramammary Paget disease is an adenocarcinoma of apocrine gland-bearing skin. It often presents as a slow-growing, eczematous, well-demarcated patch. Histologically, tumour cells are large with pleomorphic nuclei, clear or eosinophhilic cytoplasm and occasional mitoses. Invasion is usually limited to the epidermis but in rare cases can extend to the dermis. Mucinous Paget cells can be identified with Alcian Blue and periodic acid-Schiff (PAS) stains. Immunohistochemically, they stain positively with
cytokeratins CK7 and CK20, EMA and carcinoembryonic antigen (CEA). A 79-year-old man presented with a non-healing penile ulcer. He had a history of radiotherapy for prostate cancer. A biopsy showed malignant extra mammary Pagets
Disease of the penis at the glans margin. He underwent wide local excision and graft repair with complete excision achieved. Histological examination showed a typical pagetoid scatter of large epithelial cells distributed singly and in small clusters between normal keratinocytes with occasional mitoses in the epidermis. These cells were positive for multiple stains including CK7 and CEA as well as focally positive for CK20.
This rare case of extramammary Pagets disease highlights its propensity for the anogenital region. The slow-growth pattern characteristic of this disease often leads to late presentation with ulceration. Macroscopically it can appear similar to squamous cell carcinoma and is truly only diagnosed with microscopic examination and immunohistochemical staining.

Morphological characterisation of putative circulating tumour cells in prostate cancer

Leon Seow1 , Carol Ng2 , Dhruv Kapoor3 , Marvin Lim3,4 , John Green3 , Anne-Marie Baird1 , Orla Sheils1 , Ray McDermott4,5 , Brian Hayes6 , Stephen Finn1, 7
1 School of Medicine, Trinity Translational Medicine Institute, Trinity College Dublin 2 School of Medicine, National University of Ireland, Galway 3Dept. Histopathology and Morbid Anatomy, Trinity Translational Medicine Institute, Trinity College Dublin 4Dept. of Medical Oncology, Tallaght University Hospital 5Dept. of Medical Oncology, St. Vincent's Hospital 6Dept. of Histopathology, Cork University Hospital 7Dept. of Histopathology, St. James's Hospital

No ideal technique exists for the identification of circulating tumour cells (CTCs). However, ScreenCell®, a size-based microfiltration device, enables the selection of CTCs irrespective of surface markers. Nevertheless, little data exists describing putative CTC morphology using this technique.
This study aimed to evaluate the morphological features of putative CTCs isolated using ScreenCell®, in a series of clinical trial samples.
Thirteen samples were randomly selected from a prostate cancer clinical trial. ScreenCell® filters were stained with May Grunwald-Giemsa and examined microscopically. A number of morphological features of putative single CTC nuclei and cytoplasm, and of CTC clusters, were recorded.
Overall, 192 single CTCs and 49 CTC clusters were identified. Single CTCs overlapped a filtration pore, had a well-defined dark blue/purple nuclei at least 2 pore diameters (PD) in maximum dimension, with 76% lacking cytoplasm. However, cytoplasm was evident in 81.6% of CTC clusters. Nuclei were more commonly oval vs. circular in single and clustered CTCs. Most single CTCs had nuclear indentations (82.8%), but these were rare in clusters. Clusters with cytoplasm had more heterogenous cell populations, generally paler nuclei, and were more often of irregular shape (40%), with adherent platelets visible in 22.5%.
Nuclei in single CTCs are more often indented than those in clusters. Morphology varies in CTC clusters depending on the presence of cytoplasm. Further analysis is required to determine whether some of these cells may represent non-CTC elements.

The use of Digital Pathology to assess percent of stenosis in post-mortem samples with known cardiac related causes of death.

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Digital Pathology through the incorporation of image analysis allows for a more standardised approach of coronary artery stenosis assessment at post-mortem in determining the final cause of death, however it has yet to be extensively researched for utilisation routinely in post-mortem evaluation of coronary artery stenosis. The aim of this study was to assess whether the use of digital pathology in combination with image analysis (ImageJ analysis and Cellsens analysis) in post-mortem assessment of coronary arteries agrees with the current visual estimation that is used. This was a cross sectional study of 99 arterial sections involving 33 post-mortem cases taken from the Division of Anatomic Pathology, University Hospital Galway (UCHG). The analysis of digital pathology assessment with the values reported at time of post-mortem assessment revealed no statistically significant difference (95% confidence interval). The use of the two digital pathology/image analysis programs (ImageJ analysis and Cellsens analysis) yielded similar results to that in the original pathology report. We would therefore conclude that no statistically significant difference exists between the digital pathology approach compared to the traditional approach of measuring for the determination of percent stenosis; therefore, the digital pathology approach has potential to assess coronary artery stenosis in a more standardised fashion.

2019 audit of Endobronchial Ultrasound-Guided Transbronchial Needle Aspirates (EBUS-TBNA) in St Vincent's University Hospital.

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UCD School of Medicine

EBUS is a minimally invasive yet sensitive diagnostic tool for the investigation of mediastinal and hilar lymphadenopathy.
This is a retrospective yearly audit of EBUS performed in 2019 in a large teaching hospital, to assess diagnostic yield, adequacy, and use of rapid on-site evaluation (R.O.S.E.).
Overall, 158 patients underwent EBUS procedure (44.9% women, 55.1% men) with a mean age of 60.9yrs.
The overall inadequacy rate was 9.5% .
Rapid on-site evaluation (ROSE) was performed in 84.8% with a positive yield in 123/134.
A total of 187 lymph nodes were sampled 80.2% were N2 lymph nodes stations (2, 4, 7); 22.4% were N1 stations 10,11,12 lymph nodes. In 19% cases, 2 nodes or more where sampled.
Overall, 61.4% showed benign cytology, of which granulomas were identified in 26.6% .
Sarcoidosis suspected in 43 patients and EBUS TBNA was performed in 49 lymph nodes. Positive results were obtained in 34 patients (79.1%).
Of the 111 EBUS performed for suspected malignancy, 38.7% for pulmonary and extra-pulmonary malignancies; 7 showed granulomas (6.31%).
Overall malignancy was confirmed in 27.22% of cases: metastatic small cell carcinoma in 27.9%, pulmonary adenocarcinoma in 23.2% , squamous cell carcinoma in 11.6% ; 7% NSCLC NOS). In cases an extra-pulmonary malignancy was diagnosed, metastatic breast carcinoma was the commonest (23.26%).
EBUS is a good tool for the diagnosis of both malignant and non-malignant causes of hilar and mediastinal lymphadenopathy, with 79.1% yield for sarcoidosis and overall inadequacy rate of 9.45%. These samples can be used to assess for molecular targets.

Assessment of PD-L1 expression in triple-negative breast carcinoma

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Triple-negative breast cancer (TNBC) (diminished expression of ER, PR and absent HER2/neu (ERBB2) gene amplification), is an aggressive disease with a high metastatic and low survival rate unaided by limited treatment options. The upregulation of an immune inhibitory signal protein, programmed death-ligand 1 (PD-L1), by tumour cells and tumour-infiltrating immune cells allowed approval of combined Atezolizumab (TECENTRIQ©), a monoclonal antibody against PD-L1, and nab-paclitaxel chemotherapy by the U.S. FDA for the treatment of locally advanced or metastatic TNBC.

The VENTANA PD-L1 (SP142) assay was used to assess the expression of PD-L1 in eighteen separate cases of TNBC, scored internally, where ≥1% tumour-infiltrating immune cells are considered positive for PD-L1 expression, by four individual Pathologists; and referred to the Poundary Cancer Institute, Dorchester for assessment. Separately, the NordiQC Companion external quality assessment module of PD-L1 TECENTRIQ® was performed.

9/18 case results showed complete concordance between all four Pathologists and the Poundary Cancer Institute. 9/18 had some element of discordance between either the Pathologists or the Poundary Cancer Institute. Internal assessment was completely concordant with the NordiQC reference data in all submitted cases.

This is one of the first PD-L1 scoring assessments to be performed on TNBC in Ireland. Significant reasons for discordance included the low cut off point for positivity (1%), lack of accompanying H&E slide and definition of the tumour area. Continued practice and assessment is required to ensure valid PD-L1 results and access to novel therapies.

An Analysis of BRAF V600 Mutations in Melanoma Identified using Next Generation Sequencing in Beaumont Hospital from 2017 to 2020

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Introduction: Melanomas frequently display activating mutations in the V600 codon of BRAF, and it has been reported that V600E mutations account for 80-90% of these. Other less commonly seen mutations include V600K, V600R and V600D. Patients with V600 mutations are eligible for targeted therapy with BRAF inhibitors.
Aims: This audit was performed to investigate the frequency and range of V600 mutations identified in Beaumont Hospital, from 29/11/2017 to 07/08/2020.
Methods: NGS data input at the time of testing was compiled and analysed to calculate the frequency and range of V600 mutations.
Results: 242 melanomas were sequenced, with a V600 mutation rate of 23.1% (56).
92.9% (52) of V600 mutations identified were V600E, with the remaining 7.1% (4) V600K.
Discussion: Beaumont Hospital uses Next Generation Sequencing to identify all mutations at the V600 codon. Other widely used approaches to the identification of BRAF mutations in melanoma include real-time PCR (rtPCR) and immunohistochemistry. All of these approaches come with associated advantages and disadvantages. rtPCR will identify rare V600 mutations but not non-V600 mutations. Immunohistochemistry is readily available and is highly sensitive and specific for V600E mutations but may not detect less common V600 mutations. In our series 7.1% of cases with V600 mutations had non-V600E mutations. This highlights an advantage of NGS in detecting potentially actionable BRAF mutations that may not be detected by immunohistochemistry. The rate of V600 mutations in our series was 23.1%, which is lower than internationally reported figures of 50%, but in keeping with previous studies on Irish populations.

MEDIASTINAL PRIMARY AND METASTATIC GERM CELL TUMOURS WITH TERATOMATOUS COMPONENT - A CASE SERIES

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Mediastinal primary germ cell tumours (GCTs) are rare but represent a cause of anterior mediastinal masses in 10 - 15% of adults, the most common site for extra-gonadal GCTs.

This case series is a review of eight patient cases of mediastinal germ cell tumours with teratomatous component, aged 16-62 years at the time of presentation.

Four of the cases had an uncomplicated postoperative course and histology showed no malignant change, and have been followed up with no evidence of recurrence.

One case had initial relapse of malignant disease, however is now in prolonged remission following surgical resection and chemotherapy.

Two cases describe initially malignant GCTs which were converted to benign histology by chemotherapy. One underwent resection without recurrence, and the other was found to have two benign metastatic thoracic deposits in addition to the primary, which were also resected without recurrence.

One patient developed a mediastinal metastatic deposit from a testicular primary.

Seven of the cases were extragonadal primaries, one had a primary origin in the testis. Six of the seven extragonadal cases had mediastinal primaries, one had an abdominal primary.

The purpose of this case series is to discuss the rarer presentation of GCTs in the mediastinum, and to demonstrate that histology of GCTs is predictive of behaviour, with mature teratomas having the best prognosis when compared with mixed or non-seminomatous germ cell tumours.

Metastatic disease to the mediastinum from a gonadal primary carries a worse prognosis and outcomes. Chemotherapy of malignant extra-gonadal GCTs pre-surgery carries a good prognosis.

Multilocular Peritoneal Inclusion Cyst – A Case Study and Review

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A 30 year old lady presented to services with abdominal discomfort and heavy menstrual bleeding and was diagnosed with a retroperitoneal tumour on imaging. She underwent surgical resection of the mass, which revealed an intact oval multilocular complex cystic mass measuring 15cm in maximum dimension and weighing 500g. Macroscopic sectioning revealed a multilocular cystic lesion, the cystic spaces containing clear fluid.

On microscopy, the cystic spaces are lined by bland flattened or low cuboidal mesothelium. The mesothelial cells stained positive for AE1/AE3, calretinin and D2-40, and stained negative for HMB45, CD31and desmin. No infiltrative component or cytological atypia was seen. A diagnosis was made of a multilocular peritoneal inclusion cyst (MPIC).

MPIC (previously known as benign cystic mesothelioma) is an uncommon and often incidental finding. They are benign lesions with usual incidence in the 3rd-4th decade. They are more common in the pelvic organs, but can occur in the upper abdominal cavity, and less commonly still in the retroperitoneum as in this case. MPIC are often linked to pelvic inflammation, for example with pre-existing Pelvic Inflammatory Disease, surgery/adhesions or Endometriosis. They can measure up to 15cm, and have an excellent prognosis with complete surgical resection, however tend to recur with incomplete excision. The typical microscopic appearance is of simple inclusion cysts lined by single-layered cuboidal/flat mesothelial cells, with bands of loose connective tissue/fibrous septa, and can rarely have cribiform pattern, squamous metaplasia or papillae. Top differentials to exclude are cystic malignant mesothelioma and multilocular cystic lymphangiomas.

AUDIT OF ACUTE ALLOGRAFT CELLULAR REJECTION POST LIVER TRANSPLANT

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To analyse the patient-specific factors and histological variance of liver explant and post-transplant biopsies of a cohort of transplant patients diagnosed with cellular rejection between 2017 and 2019 in the St Vincent's Histopathology Department.
268 liver transplant biopsy and liver explant specimens from 64 patients were audited between January 2017 and December 2019.
We also reviewed the concordance between primary disease on the diagnostic biopsy and explanted liver.
Cellular rejection diagnosed on histology was assessed using various histological items, including the BANFF rejection score. Other features such as chronic rejection, ductopaenia, phenotypic change, changes relating to a drug reaction or mechanical/ischaemic effect, and recurrence of primary disease were assessed.
30 men (46.88%), 34 women (53.13%) were included. The mean age at first transplantation was 46.92 years.
There was a 90% concordance rate in histology on biopsy and explant and the most common liver disease was cirrhosis secondary to Primary Sclerosing Cholangitis.
50.79% biopsies showed acute cellular rejection with BANFF score varying between 3 and 9, (mean score 4.6). Rejection rates were equal in men and women. Drug reactions were uncommon (1.05%).
Less than 25% developed chronic rejection, 18.32% showed ductopaenia.
Disease recurrence in that period was rare, and found on second- or third-time explants only in 1.3% of cases and the commonest recurring disease was PSC.
20% required a second transplant, 1.5% required a third.
These finding from the National Transplant centre are in line with published data and the majority of acute cellular rejection was mild-moderate.

Adequacy rates of molecular testing in endobronchial ultrasound-guided transbronchial needle biopsies

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Molecular testing of EGFR and ALK mutations are used to guide targeted oncologic treatments in non-small cell lung cancer. Occasionally, there is not enough tissue remaining for such testing after diagnosis and ancillary techniques. The invasive nature of tissue sampling precipitates the need for optimisation of sample taking and laboratory processing procedures.
To assess the adequacy of tissue sampling in endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for molecular testing in lung adenocarcinoma in a single-centre retrospective study and to compare the rate of adequacy with previous local studies and rates from other centres.
We collated a database of EBUS-TBNA specimens from 2019 in UCH Galway using data from respective pathology reports, highlighting the presence of cancer, cancer type, decision to perform testing and adequacy of the sample for testing. The rates of various findings in molecular studies such as EGFR mutation, KRAS mutation and ALK translocation were examined. This data will be added to annual results of similar audits to compare adequacy rates.
Of the 209 cases observed, 30 (14.3%) were found to be primary lung adenocarcinoma. 26 of the 28 (92.8%) primary adenocarcinoma biopsies that had been tested for genetic mutations contained sufficient tissue. The overall percentage of adequate samples matched the findings of similar single-centre retrospective studies and larger systematic reviews.
Current methods of obtaining and processing EBUS-TBNA tissue in Galway are adequate compared to other international studies.

Re-audit of B3 & B4 diagnoses in the Symptomatic Breast Service 2017-2018

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This is a re-audit of B3 and B4 diagnoses in the symptomatic breast service (SBS). A previous audit was performed on cases from January 2008-March 2009. The aim is to study a series of B3 (uncertain malignant potential) and B4 (suspicious for malignancy) needle core biopsies (NCB) in SBS to establish outcomes and calculate positive predictive values (PPVs) for malignancy.
The audit population was biopsies from the SBS with pathology codes B3 and B4 over 2017 and 2018. Cases were extracted from the Dendrite clinical information system and results were compared with the previous audit.
There were 1997 breast biopsies in total, 70 of which had a B3/ B4 diagnosis. B3 biopsies (n=64) were uncommon, comprising 3.2% of all biopsies. The major B3 categories comprised atypical intraductal epithelial proliferations, fibroepithelial lesions, lobular neoplasia, papillary lesions and radial scars. B4 biopsies (n=6) were rare, comprising 0.6% of all biopsies. B3 lesions had a PPV of 24% in 2017/18 compared to 14% in 2008/09. B4 lesions had a PPV of 100% in 2017/18 whilst PPV for B4 lesions (n=2) in the 2008/09 audit was 50%.
B3 lesions are a heterogenous group, encompassing a wide spectrum of entities with varying prognoses. B4 diagnoses are rare. All B3/B4 cases should be discussed at multidisciplinary meetings.

A Quality Improvement Project of the Investigation and Management of Hyponatraemia at Royal Blackburn Hospital

Dr Kim Pramanik

Hyponatraemia is present in 15-20% of non-selected emergency admissions to hospital and is associated with increased length of hospital stay and morbidity. A closed loop audit based on the Royal College of Pathologists guideline on the investigation and management of hyponatraemia was completed, using cases of severe hyponatraemia at Royal Blackburn Hospital at separate periods during 2018 to 2020. Changes implemented included launching a trust-wide hyponatraemia protocol, and grand round presentation to raise awareness.

An initial audit was performed using retrospective case notes analysis of medical and surgical admissions, aged 16 or over, with sodium <120mmol/L from August 2018 to January 2019 (n=24). This was re-audited from April to May 2020 (n=27) following protocol implementation.

Following initial audit recommendations, the proportion of patients with documented admission sodium increased from 87.5% (n=21) to 96.3% (n=26), and those with a plan for hyponatraemia management increased from 33.3% (n=8) to 70.4% (n=19). Aspects which remained similar in both audits were volume status assessment (45% vs 44.4% n=12), urine osmolality measured and paired with plasma osmolality (33.3% n=8 vs 30.0% n=8).

Successful management of hyponatraemia relies critically on timely sampling and information assimilation, as delays in these results in misdiagnosis, and subsequent mismanagement. We conclude from these audits that some aspects of documentation and management plan formation could be improved. This suggests the need for increased awareness of the existing protocol, and supports the consensus that the inpatient assessment of severe hyponatraemia could be further optimised from specialty admission.

AUDIT: CORRELATION OF B4 DIAGNOSIS ON NEEDLE BIOPSY WITH DIAGNOSIS ON BREAST RESECTION

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DR. CAROLINE BRODIE, CONSULTANT PATHOLOGIST, GALWAY UNIVERSITY HOSPITAL
DR. AIDEEN LARKE, CLINICAL DIRECTOR AND LEAD CONSULTANT RADIOLOGIST, BREASTCHECK WEST

Ultrasound guided core needle biopsy is the gold standard procedure in preoperative diagnosis of breast carcinomas. The aim of this audit was to screen B4 diagnoses on breast needle core biopsies and compare them to the diagnosis on excisional biopsy/mastectomy.

Inclusion criteria were all patients presenting to the BreastCheck screening service, Western Area, with a B4 breast needle core biopsy report in a thirty month period from Nov 2016 to March 2019. The core biopsy was compared with the subsequent excision biopsy, wide local excision and/or mastectomy. The positive predictive value was calculated from a B4 report and the subsequent final diagnosis.

In the study period (November 2016 to March 2019), there were 12 B4 reports on cores from 11 lesions from10 women. One woman had two consecutive B4 diagnoses on a repeat biopsy and another woman had a B4 diagnosis on another lesion a year later. 40% (4 out of 10) women had a repeat biopsy before excision, while the other 6 women had an excisional biopsy after B4 diagnosis on the first core. 50% (6 of 12) of the B4 reports had invasive carcinoma. 25% (3 of 12) had in-situ carcinoma. 25% (3 of 12) had a final diagnosis of atypia. Nine of twelve B4 reports had a final diagnosis of malignancy; 6 B4 reports bore invasive carcinoma and 3 B4 reports bore DCIS.

The positive predictive value of a B4 diagnosis for carcinoma was high (75% in this institution).

A CASE REPORT OF AN INTRACTABLE DISSEMINATED INTRAVASCULAR COAGULOPATHY (DIC) DIAGN PRIMARILY ON SKIN PUNCH BIOPSY AND IN BOWEL RESECTION SEPECIMEN WITH ATYPICAL CLINICAL PRESENTA

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A 57 year old male, with history of coeliac disease presented to accident and emergency in our hospital with severe abdomina Exploration laparotomy was performed and a segment of small bowel with multiple perforations was removed. The patient, ther developed necrotising erythematous rash on the face, trunk and limbs, of which two lesions were biopsied and sent to our la dermatologist's impression was a probable pyoderma gangrenosum. As the punch biopsies were processed faster than the segment, the punch biopsy slides were readily available for microscopic examination before the bowel segment which required fixation. Skin biopsies revealed prominent necrosis of the epidermis and superficial dermis with prominent multiple fibrin thro dilated capillaries and small blood vessels. These findings were interpreted as disseminated intravascular coagulopathy extremely rare to be diagnosed in skin biopsy and with differential diagnosis including thrombotic thrombocytopenic purpura or w use. The histology result was promptly discussed with the dermatologist and the diagnosis was communicated to the clinica who requested coagulation profile tests. The patient's general condition deteriorated with multi-organ failure. There was high Tro that could be seen with myocardial infarction and deteriorated liver and kidney function tests. The small bowel sections wer examined and revealed similar multiple thrombosed blood vessels and necrosis. However, in addition, an advanced coeliac di modified Marsh IIIB was confirmed. Further IHC study of revealed refractory coeliac disease type II (RCDII), However, no enter associated T-cell lymphoma (EATL) was discovered. The laboratory tests excluded COVID 19, which in recent articles show association with DIC. Vasculitis screening tests were negative and immunofluorescence (IF) of skin biopsy was negative. The pa general condition deteriorated more and unfortunately, the patient died in intensive care unit.

In summary, skin biopsy was of great value in guiding the clinical diagnosis and management in this case. Skin biopsy result marked as red flag in urgent cases like this case and in certain life-threatening vesiculo-bullous dermatitis. Moreover, the link be refractory coeliac disease and DIC, may need to be explored further.

Impact of the COVID-19 Pandemic on suicide rates.

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Restrictions have been in place across Ireland since March 2020 to control the spread of COVID-19. It has been shown that secondary consequences of social distancing measures may increase the risk of suicide. Social isolation is a significant contributing factor. Consequently, the use of social distancing as a public health action is a concern for suicide prevention.

To assess the prevalence of suicide rates in our centre since the implementation of social distancing measures in March 2020 and comparison of the same time period over the previous 4 years.

A retrospective review of our autopsy logbook was carried out to identify suicides as a cause of death recorded between 15/03/20 and 31/08/20. A review of the same time period over the previous 4 years was also carried out as a control. Autopsy reports were evaluated to ascertain further details regarding circumstances of death and to extract demographics.

17 suicide cases were identified between 15/03/20 and 31/08/20 which is consistent with the suicide prevalence over the same time period for the previous 4 years. The average age of suicides in 2020 was 44yrs and the male to female ratio was 3:1 which are both in keeping with previous years.

As this audit shows, COVID-19 restrictions do not appear to have had a significant impact on suicide rates in our centre to date. However, this is an ongoing situation and should be kept under regular review.

Hernia sac histopathology – a blind alley?

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Hernia sac specimens are anecdotally reported to rarely contain findings which alter patient management, and in some institutions they are subjected to a “gross only” examination. We aimed to determine the proportion of hernia sac specimens with microscopic findings and to determine whether histological sampling can be safely omitted in some cases.

A SNOMED search was performed for specimens coded as “hernia”(M31500) at CUH from 2015-2019. Histopathology reports were reviewed and demographic, macroscopic and microscopic parameters were recorded. Comparison of means was made by the unpaired t test. Percentages in categorical variable groups were compared using Fisher’s exact test.

1011 specimens were included, 78.9% from male and 21.1% from female patients. The most common site was inguinal(58.2%). Most cases had no significant macroscopic findings(80%). 82.8% of cases were sampled in a single tissue block. Microscopic findings were recorded in 27.9%, including chronic inflammation(18%), acute inflammation(11.6%) and fibrosis(3.2%). 4.5% included a surgically-identified structure such as testis, skin or lipoma. There was no evidence of malignancy in any of the specimens. Microscopic findings were significantly more likely in female than in male specimens(42% vs 24.3%, $p<0.001$). Specimens with microscopic findings had a greater mean gross diameter(6cm vs 5.2cm, $p=0.0096$) and were sampled in a greater mean number of blocks(1.7 vs 1.19 blocks, $p<0.0001$).

Unexpected malignant disease is vanishingly rare in these specimens. Hernia sacs from female patients and large specimens are more likely to contain microscopic findings and their examination should not be limited to “gross only”.

Tuberous sclerosis complex associated papillary renal cell carcinoma, case report

Dr Brian Pierce, Dr Nick Mayer. CUH Histopathology department

Tuberous sclerosis complex (TSC), a disorder resulting from loss of function germline mutations of the tumour suppressor genes TSC-1 (hamartin, 9q34) or TSC-2 (tuberin, 16p13), is inherited in an autosomal dominant pattern in one third of cases and de novo in the remainder.

The manifestations of TSC are diverse, potentially involving multiple systems. While renal manifestations, including angiomyolipomas and polycystic kidney disease, are common overall, being present in 80-85% of cases, TSC- associated renal cell carcinoma (RCC) is rare, present in only 2-4%, and may be of several morphologies and is often multicentric.

Papillary RCCs (PRCC) associated with TSC are morphologically and immunohistochemically distinct, typically displaying papillae lined by cells with abundant, variably clear to eosinophilic cytoplasm, showing strong, diffuse staining with CK7 and CAIX and without expression of SDHB or AMACR (p504s). Also, while some morphological features of TSC-associated PRCC are shared with MiT family translocation RCCs, the former is negative on TFE3 staining.

We describe a case of TSC-associated PRCC with an unusual immunophenotype, arising on a background of multiple angiomyolipomas.

When encountering a PRCC with atypical morphological and immunohistochemical features, the possibility of TSC-associated PRCC should be considered.

Post-vasectomy semen analysis from specimens received to Galway University Hospital in 2019; a re-audit

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The Histopathology Department of Galway University Hospital receives a significant number of post-vasectomy semen specimens each year from General Practitioners throughout the West of Ireland for analysis.

Many samples are received to the laboratory after a significant interval post-collection. This delay can impede on the accuracy of analysis due to specimen degradation and microbacterial overgrowth.

Despite improvements following a 2017 re-audit, important clinical details continue to be omitted from the clinical information forms.

To evaluate the time interval between specimen collection and receipt to the laboratory.

To evaluate if adherence to the World Health Organisation and British Andrology Society guidelines are being maintained.

Reports were analysed from the internal Apex laboratory system.

42% of post-vasectomy specimens were received by the laboratory on the same day as specimen collection, representing a significant improvement from 14.1% in 2017.

Only 6 of 400 samples (1.5%) in 2019 had documented the exact date of the vasectomy.

Only 8 of 400 samples (2%) in 2019 documented that the vasectomy took place at least 16 weeks prior to specimen collection.

0 of 400 samples (0%) recorded that the specimen was collected after a minimum of 24 ejaculates were produced.

Despite collection time improvements, there continues to be poor adherence in recording essential information, as per the recommended guidelines, on the laboratory request forms.

The results will be communicated to service users along with copies of the current guidelines to encourage adherence to the recommended guidelines and improve the quality of service that our laboratory can provide.

Review of 135 lacrimal gland biopsies in an Irish cohort.

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To review the distribution of pathology in lacrimal gland biopsies performed in an Irish cohort in a retrospective review.
One hundred thirty-five lacrimal gland biopsies from 138 patients were examined.
Pathology database in The Royal Victorian eye and ear hospital in Dublin were searched for lacrimal gland biopsies performed between 1 January 2008 and 31 December 2018.
Main outcome measures: Distribution of pathology affecting the lacrimal gland; patient age and gender.
The distribution of lacrimal gland pathology was: benign inflammation conditions 45%, the majority of which is composed of no specific subtype 28%, granulomas 4%, dacryoadentitis 9% with one case of IGG4 related disease. Lymphomas 12%, other malignancies, 6%, including squamous cell carcinoma 2% and melanoma 2%. Benign cyst 6%, pleomorphic adenoma 5%, pseudotumour 4%.
Ages ranged from 2 to 98 years with the average age being 50.64 years. Sixty-five percent were females and 35% males. The average age of those diagnosed with lymphoma was 64.93 while the average age of those diagnosed with inflammatory pathologies was 49.13.
Almost half of all lacrimal gland biopsies were benign inflammatory conditions with the vast majority of those being of no specific type. The majority of malignancies were lymphomas with carcinomas accounting for 5%. This data shows that when a biopsy or FNA of lacrimal gland is received it is much more likely to be inflammatory and if malignant lymphoma is more common than primary epithelial tumour.

Succinate Dehydrogenase-Deficient Renal Cell Carcinoma- A Case Study

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A 39 year old lady presented to services with a large right sided renal mass on imaging. She underwent a right nephrectomy, which revealed a macroscopically solid tan well-circumscribed tumour in the lower pole of the right kidney (9.7cm in maximum dimension), with a pushing but not grossly infiltrative margin. Microscopic examination described cells arranged in nests with pleomorphic nuclei and occasional nucleoli and eosinophilic, flocculent cytoplasm. Immunohistochemistry was performed (Positive for PAX8 and AE1/AE3, negative for CD10, CK7, CD117, E-cadherin, RCC, chromogranin, EMA, HMB45, Melanin A, Synaptophysin and Vimentin), and was performed for SDHB, which was negative. A diagnosis was made of Succinate Dehydrogenase-Deficient Renal Cell Carcinoma, pT2a, with normal background kidney. She is currently undergoing work up for other neoplasms related to a deficiency of the enzyme Succinate Dehydrogenase (SDH).
A germline mutation in one of the four subunits of SDH (A-D) can lead to numerous distinct neuroendocrine neoplasms; Gastrointestinal Stromal Tumours (GIST), pituitary adenomas, paragangliomas, phaeochromocytomas and, included in the WHO Classification for the first time in 2016, renal cell carcinomas. For a definitive diagnosis of SDH-Deficient RCC, loss of SDH subunit B immunostaining must be present. It accounts for <0.2% of all renal carcinomas. Typical microscopic features are nests or tubules with cystic changes, cuboid cells with round nuclei and dispersed chromatin, and vacuoles/inclusions in the cytoplasm. Prognosis correlates with degree of differentiation, and long term follow up is advised, along with screening for other SDH-deficiency related neoplasms.

Molecular and Morphological Profiling of Gastro-Intestinal Stromal Tumours (GISTs) in the West of Ireland

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Introduction: GISTs are rare mesenchymal neoplasms, frequently harbouring oncogenic mutations in one of two receptor tyrosine kinases: KIT or PDGFRA.

Aims: Characterize the molecular and morphological profile of GISTs in the West of Ireland.

Methods: Histopathology reports of GISTs diagnosed from February 2010 to December 2019 were analysed for molecular and morphological data.

Results: 54 GISTs were identified over 9-years (male: female= 19:35, mean age= 64). 3.7% of GISTs occurred before age 40. GISTs were either spindle cell (81%), mixed epithelioid/spindle (11%) or epithelioid (8%) morphology. 54/54 cases were C-KIT positive. 51/51 cases analysed for DOG1 were positive. Mutation analysis attempted on 45 cases demonstrated KIT exon 11 (73%), PDGFRA (16%), KIT exon 11+13 (7%), KIT exon 9 (2%) mutations. 2% were KIT/PDGFRA wild type.

Conclusions: GISTs are uncommon in patients under age 40. Immunohistochemistry is a reliable method of confirming GISTs. The most common mutations were KIT exon 11 (73%) and PDGFRA mutations (16%). PDGFRA mutated GISTs were more likely to have epithelioid or mixed morphology (86%) compared to those with KIT mutations (5%). Acquisition of secondary KIT mutation was associated with aggressive GISTs and disease progression. All GISTs with secondary mutations were recurrent and 67% were multi-site, while only 14% of GISTs with single mutations were multi-site. All cases with secondary KIT mutation had KIT exon 13 +11 mutations. Resistance to TKIs is associated with these secondary mutations. Small intestine GISTs were larger than gastric GISTs at time of diagnosis, and 75% had a moderate/high recurrence risk, compared to 36% of gastric GISTs.