Meeting Summary

61st Annual Meeting of the
Canadian Association of Neuropathologists
Association canadienne des neuropathologistes
(CANP-ACNP)

Meeting Abstracts

October 14–16, 2021

Canadian Association
of Neuropathologists
Association canadienne
des neuropathologistes

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The Canadian Association of Neuropathologist – Association canadienne des neuropathologistes (CANP-ACNP) held their 61st annual meeting via Zoom from October 14th to 16th, 2021, under the leadership of Dr. Peter Gould, President of the CANP-ACNP, Dr. Peter Schutz, Secretary Treasurer of the CANP-ACNP, and with technical support from CANP administrators Heather Dow and Colleen Fifield.

The academic program comprised 17 scientific abstracts, 8 unknown cases, the Presidential symposium on Epilepsy and Neoplasms, and a Neuropathology in Practice session on the implementation of the new WHO classification of CNS neoplasms in Canada. Digital pathology images from the 8 unknown cases are available for viewing online (www.canp.ca). The unknown case sessions were moderated by Dr. Andrew Gao.

The Presidential Symposium 2021 on Epilepsy and Neoplasms featured the David Robertson Lecture given by Dr. Eleonora Aronica entitled *Evolving classification of epilepsy-associated tumors: Understanding epileptogenesis,* the Gordon Mathieson Lecture delivered by Dr. Harvey Sarnat on *Why are some cerebral malformations more epileptogenic than others? Clues from developmental neuropathology,* and the Jerzy Olszewsky Lecture presented by Dr. Maria Thom on *Neuropathology in sudden and unexpected death in epilepsy and future directions.* The program was completed Dr. George Ibrahim's lecture on *Epilepsy as a network disorder*.

The Mary Tom Award for best clinical science presentation by a trainee went to Dr. Suzy Kosteniuk (Supervisor Dr. S. Das), and the Morrison H. Finlayson Award for best basic science presentation by a trainee was won by Dr. Nicole Schwab (Supervisor Dr. L.N. Hazrati).

The following abstracts were presented at the 61st annual meeting of the Canadian Association of Neuropathologists – Association candienne des neuropathologistes (CANP-ACNP) in October 2021.

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Abstract 1

Meeting Abstract

Histologic and clinical spectrum of brain tumours harbouring FGFR3-TACC3 fusions

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Fibroblast growth factor receptor (FGFR) gene family alterations, including point mutations and fusions, have been described in brain tumours as oncogenic drivers (NG 2013; 45(6): 602–612). FGFR3-TACC3 fusions were initially described in IDH wildtype glioblastomas (Science 2012; 337:1231–1235) and are most frequently seen in morphologic or molecular GBM although occasional WHO grade 2 astrocytomas may harbour this alteration. The significance of this alteration as a single driver in low-grade glioma is unclear. In order to better understand the clinical implications of finding this alteration, a series of low-grade gliomas underwent molecular testing at Sick-Kids. The series includes six samples of diffuse low-grade gliomas, with a mean age of 24.8 years (range 1 to 44 years), three males and three females. Five out of six tumours are localized in the supratentorial region, and one in the spinal cord. Three patients presented with seizures, one was asymptomatic. Morphologic appearance showed different aspects, from cells with oligo-like features in a neuropil-rich stroma to spindle cells with fibrillary cytoplasm in a loose microcystic background. Single nucleotide polymorphism (SNP) array was performed on two samples and one of them shows the gain of chromosome 7 and loss of chromosome 10, indicating a molecular profile of high grade glioma. Follow-up was available for four patients, all are alive without progressive disease with follow-up ranging from six months to two years. Longer follow-up will be required to determine the significance of this alteration in low grade glioma.

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Abstract 2

Ganglion cell maturational markers in peripheral neuroblastic tumours of children

Harvey B. Sarnat[1]

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Peripheral neuroblastic tumours of neural crest origin are the most frequent solid neoplasms outside the CNS in children. Neuroblastoma/ganglioneuroblastoma have a natural evolution of histological differentiation over time. Together with mitosis-karyorrhexis index and patient age (International Neuroblastoma Pathology Classification criteria), ganglion cell maturation determines grading and prognosis. Maturation presently is assessed only by H&E histology.

Methods: Immunocytochemical markers of neuroblast maturation in fetal CNS were applied to peripheral neuroblastic tumours arising in adrenal medulla or sympathetic chain. Resected tumours of 4 toddlers were examined using antibodies demonstrating neuronal identity and maturation: MAP2; synaptophysin; chromogranin-A; NeuN; keratan sulfate (KS); glutamate receptor antibody (GluR2). Others: Ki67; S-100β protein; vimentin; nestin; α-B-crystallin; neuroblastoma marker PHOX2B.

Results: Degrees of neuroblastic maturation were demonstrated by MAP2, chromogranin, synaptophysin, KS and GluR2; NeuN was negative consistent with sympathetic neural crest lineage. KS was sparsely distributed within the tumours adherent to somata and proximal neuritic trunks. PHOX2B did not distinguish maturational stages. Ki67 was expressed in scattered primitive cells that also expressed vimentin and nestin, but not in differentiated neoplastic neurons. S-100β protein and α-B-crystallin labeled Schwann cells, especially Schwannian ganglioneuroma.

Conclusions: Immunocytochemical markers of neuroblast maturation in fetal brain also are useful in peripheral neuroblastic tumours, providing greater precision than histology alone. The most practical are MAP2 and synaptophysin. Prognosis and choice of treatment including chemotherapy might be influenced.

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Abstract 3

Long term disease-free survival after surgical resection only: Malignant IDH-mutated astrocytoma versus ganglioglioma

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Gangliogliomas are important to distinguish from anaplastic astrocytoma and glioblastoma multiforme, to avoid potentially damaging radiation and for accurate prognostication. Two patients with a seizure presentation at age 31 and 30 had large, well demarcated brain tumors each 4.3 cm with no suggestion of diffuse glioma on imaging. Both patients requested tumor resection. The first patient intra-operatively was found to have the tumor in close proximity to the motor cortex, and resection was thus incomplete, leaving residual tumor in situ. The second patient had a gross total resection. An initial diagnosis of ganglioglioma, was changed to malignant astrocytoma based on IDH1 mutation, loss of ATRX, abundant mitoses and a high Ki67 labelling index. Conventional histology revealed glial, neuronal and intermediate forms in both tumors. Both patients declined treatment following neurosurgery and remain without tumor growth on neuroimaging at 6 and 3 years later, respectively. The findings illustrate the conundrum of tumors diagnosed as malignant astrocytomas based on molecular profile, but showing no growth after no treatment, as well as the superiority of resection over needle biopsy, as the first tumor was called a diffuse astrocytoma on a needle biopsy prior to resection. Without diffuse astrocytoma appearing on long-term follow-up in the absence of radiochemotherapy, a diagnosis of diffuse, malignant astrocytoma is increasingly untenable as years pass. Both patients and their clinicians question the malignant diagnosis. Gangliogliomas have been reported with IDH mutation (Brain Pathol 2011; 21: 564-574). Ganglioglioma versus diffuse astrocytoma remains a difficult differential diagnosis in neuropathology.

Abstract 4

Diagnostic challenges in unusual high-grade gliomas

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Diagnosis of most of adult high-grade gliomas is largely based on morphology and immunohistochemistry, with an increasing role of molecular studies to aid proper classification (IDH wildtype and IDH-mutant gliomas, H3K27M mutant diffuse midline glioma). On occasions, despite all the work-up, the results do not allow for a definite diagnosis that are established in the most recent WHO classification. Some glial tumor shows dedifferentiation and looses GFAP expression. In these cases, methylation profiling is a power tool in establishing the diagnosis. Therefore, it is very important that the tissue should be utilized optimally and carefully especially when the biopsies are very small and extensive work may be required. On rare occasions, definitive diagnosis can be challenging despite complete histological and molecular characterization. Some variants of glioblastoma may show epithelial or primitive neuronal differentiation and some variants may have increased predilection for CSF metastasis and therefore it is important to subclassify these variants. These challenges will be discussed with some examples of high-grade gliomas that we received in our institution at Health Sciences Center, University of Manitoba.

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Abstract 5

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Meeting Abstract

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Regional variability of α-synuclein inclusion size in multiple system atrophy

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Relevance: Multiple system atrophy (MSA) patients show variable duration of illness and distinct constellation of clinical symptoms suggestive of different pathological α-synuclein strains.

Objective: Based on this, our aim is to investigate whether the seeding and aggregation process of α-synuclein are different in MSA brains, leading to variability of size and detectability of oligodendrocytic inclusions using different anti-α-synuclein antibodies.

Methods: The putamen and cerebellum of 6 MSA cases were immunostained using nitrated, truncated, phosphorylated and disease-specific α-synuclein (clone 5G4) antibodies. Sections were scanned using TissuescopeTM and images were processed using Photoshop (v.21.0.3). 5G4-immunoreactive oligodendrocytes with visible nucleus were optically dissected and inclusion sizes were evaluated using algorithms that we developed using the software Image J.

Results: The size of 5G4-reactive inclusions were significantly larger in the cerebellum than in the putamen in 4 out of 6 cases. In one case, the inclusion size was significantly larger in the putamen than in the cerebellum, while a single case showed similar sizes. In addition, case-wise comparison revealed significant variability between the size of inclusions in both regions. In addition, substantial differences were noted between the number of inclusions stained by the different α-synuclein antibodies.

Conclusions: We developed a novel computer-based method to measure the size and number of α-synuclein inclusions in MSA. Our observations on the variability of size and number of inclusions, detected by different α-synuclein epitopes between brain regions and cases, support the notion of distinct subtypes of disease. Our study further provides a first step to developing AI-based evaluation strategies for large scale comparative studies.

Abstract 6

Cognitive resilience in individuals with severe Alzheimer's disease neuropathology

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We sought to identify demographic, clinical, genetic, and neuropathological features associated with cognitive resilience in subjects with severe Alzheimer's disease (AD) neuropathology. Data for this study was obtained from a National Alzheimer's Coordinating Centre (NACC) dataset. Study inclusion criteria are as follows: severe AD pathology, i.e., frequent neuritic plaques and Braak & Braak stage V/VI pathology, interval between last visit and death ≤ 2 years, and absence of other primary neuropathology diagnoses. Cognition was assessed by the Mini-Mental Status Examination (MMSE) score. A total of 654 cases met our criteria. Of these, 59 (9%) persons had MMSE scores ≥24 at their last visit and were categorized as cognitively resilient. First, bivariate analysis was done to compare resilient with non-resilient groups. Then, variables with significant results were entered into the multivariable model. Based on our binary logistic regression model, resilient subjects were older (odds ratio [OR]=1.03; 95% confidence interval [CI]=1–1.07), had more years of education (OR=1.16; 95% CI=1.04-1.29), had lower BMI (OR=0.91; 95% CI=0.85-0.99), were more likely to be a smoker (OR=2.78; 95% CI=1.45-5.34), and were more likely to use an anticoagulant/antiplatelet at last visit compared with subjects with impaired cognition (OR=1.87; 95% CI=1.01-3.48). In addition to expected protective factors such as higher education and lower BMI, our results showed that more smoking and frequent use of an anticoagulant/antiplatelet at last visit could also be possibly associated with resilience to clinical expression of AD severe pathology. Pharmacological approaches that mimic the effects of nicotine may be useful in amelioration of AD symptoms.

Abstract 7

Linking iron homeostasis to vulnerability patterns in progressive supranuclear palsy

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Progressive Supranuclear Palsy (PSP) is a 4-repeat tauopathy in which pathology starts in select subcortical areas including the globus pallidus (GP) and the substantia nigra (SN), regions also associated with age-related iron accumulation. Toxic iron burden in these regions of PSP brains have been examined but given the differences in cellular iron homeostasis across cell types and the heterogeneity in PSP tau cytopathology, we aim to examine the possible role of iron accumulation on the cellular selective vulnerability of tau pathology in the vulnerable anatomical regions of PSP brains. Using human post-mortem brain tissue of the early-affected PSP brain regions (GP, SN, and putamen), we visualized iron deposition in the neurons, astroglia, oligodendrocytes, and microglia using a combination of DAB-enhanced Perl's (ferric) and Turnbull (ferrous) iron staining with immunohistochemistry of cell type-specific markers. Iron deposition was also examined in relation to their tau cytopathologies using AT8-immunohistochemistry. In all three regions, astrocytes and microglia were seen to predominantly accumulate both species of iron. Moreover, tau-positive astrocytes showed the highest frequency of cellular iron deposition compared to neurofibrillary tangles and oligodendroglial coiled bodies. On the other hand, association of iron burden with different cellular tau pathologies was species-specific in the same regions, suggesting iron functions in PSP tau cytopathology may be distinct by species. Our mapping of cellular iron burden in relation to pathology in PSP brains suggests a selective cellular vulnerability to iron deposition in diseased brains, and further supports the role of pathological iron in the early pathogenesis of PSP.

Abstract 8

Friedreich cardiomyopathy is a secondary desminopathy

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Hypertrophic cardiomyopathy with or without arrhythmia is the predominant cause of death in Friedreich ataxia (FA). The clinical and pathological phenotypes of FA are diverse. The pathogenesis of the FA-related lesions in the central and peripheral nervous systems, heart, skeleton, and endocrine pancreas is incompletely understood. The hypothesis in this research is that frataxin deficiency affects the cellular proteome in downstream mechanisms. Antibody microarrays of pooled FA heart lysates showed upregulation in several proteins, including alpha B crystallin, a desmin chaperone. Western blots of individual and pooled heart lysates revealed a prominent extra desmin band at 47 kDa that was absent or under-expressed in control samples. Mass spectrometry confirmed the origin of this band from canonical desmin (53 kDa). Co-immunoprecipitation of FA heart lysates with anti-desmin, recovery of the antigen-antibody complex with protein A-Sepharose, sodium dodecylsulfate polyacrylamide gel electrophoresis, and Western blotting confirmed the interaction of desmin and αB crystallin. Slide techniques, including immunohistochemistry and double-label immunofluorescence, disclosed desmin and alpha B crystallin aggregation near intercalated discs and Z-discs. Congo Red fluorescence microscopy did not confirm the formation of amyloid. We suggest that accumulation of a truncated desmin and aggregation with αB crystallin cause accelerated heart disease in FA.

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Abstract 9

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Meeting Abstract

Glial senescence (not tau) is the driver of post-concussive symptoms

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Mild traumatic brain injury (mTBI) leads to chronic symptoms in some patients. Pathologically, mTBI is associated with chronic traumatic encephalopathy (CTE), a neurodegenerative disease characterized by hyperphosphory-lated tau (p-tau) in neurons and astrocytes at the depths of cortical sulci. CTE has been proposed as the driver of these symptoms, despite many patients presenting with severe symptoms yet minimal pathology. It is known that low levels of p-tau are present in cognitively intact individuals, including ageing-related tau astrogliopathy (ARTAG), and that p-tau accumulates prior to a diagnosis of Alzheimer's disease. We propose that examining changes beyond p-tau is critical to understand mTBI pathology.

The objective of this study is to identify novel pathological markers of mTBI which may explain clinical symptoms and allow for the development of therapeutic targets.

Using a brain bank of former professional athletes with mTBI history we used immunohistochemistry and gene expression analysis to show cellular senescence as a mechanism driving brain dysfunction after mTBI. Compared to controls, mTBI brains show widespread DNA damage (γH2AX) and cellular senescence in ependymal cells, astrocytes, and oligodendrocytes even in cases with no neuropathology. Gene expression analysis revealed up-regulation of the senescence-associated secretory phenotype (SASP), a form of chronic low-level inflammation which has been proposed to drive cognitive dysfunction and proteinopathy. In a mouse model of mTBI, we have recapitulated these results and shown that eliminating senescent cells with senolytic therapy is beneficial.

mTBI brains are characterized by early ageing through cellular senescence, which may drive clinical symptoms and p-tau pathology.

Abstract 10

Hail to astrogliosis! The unsung hero of the CNS tissue reaction to the spinal cord injury

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Spinal trauma results in a localized spinal cord injury (SCI) with an area of hemorrhage and necrosis surrounded by edema in Acute Phase that lasts 2 days followed by an Inflammatory Phase beginning on day 3 with infiltration of necrosis by inflammatory CD68+/CD163- macrophages whose numbers rapidly increase and persist at high levels for 4 weeks and then decline but are still present in low numbers at 16 weeks. This destructive inflammation is fuelled by myelin-rich necrotic debris and the macrophage activation causes ongoing damage to the surrounding spinal cord and further damaged myelin to sustain a mechanism of vicious cycle. The severity of post-SCI inflammation becomes inhibited and eliminated by a spinal cord tissue response in the 3rd Phase, Resolution. Astrogliosis is a hallmark of reaction to SCI. In the 1st week astrocytes surrounding the lesion hypertrophy and define a cavity of injury (COI) containing macrophage-rich inflammation and accumulation of water. Progression of severity of astrogliosis around the COI coincides with the reduction of numbers of macrophages and leads to formation of quiescent syrinx. While the inflammation in the COI leads to damage of blood vessel in the surrounding spinal cord resulting in vasogenic edema beyond 16 weeks post-SCI, astrocytes equipped with aquaporin-4 pass excess edema water to 4 extra-spinal spaces; (1) the sub-arachnoid, (2) the central canal, (3) the blood vessels, and (4) the COI, a novel mechanism. Astrogliosis is a beneficial element in neuroplasticity following the SCI and should not be inhibited in anti-inflammatory treatments effecting neuroprotection.

Abstract 11

Ischemic-like pathology in aberrant white matter tracts of fetal holoprosencephaly: A case series

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Holoprosencephaly (HPE) is due to defective early forebrain induction resulting in a "lack of cleavage" of the primitive prosencephalon into paired cerebral hemispheres. HPE is generally considered sporadic, although clear environmental and genetic factors have been recognized. From a genetic perspective, an autosomal dominant inheritance pattern is most commonly noted. Chromosomal abnormalities are common in HPE, seen in 25-50% of affected individuals, with Trisomy 13 being the most frequent. A number of structural chromosomal abnormalities (e.g., 21q22.3 deletion) and pathogenic copy number variations have also been described, as have syndromic associations. Pertinent biologic pathways include SHH, NODAL and BMP; in turn, several single gene mutations related to these pathways have been uncovered, including SHH, ZIC2, and SIX3. Although not frequently emphasized in neuropathologic descriptions of HPE, abnormal white matter has been reported, mainly in the form of aberrant tracts (e.g., absence of the corpus callosum and hypoplasia of the corticospinal pathway). In this study, we detail the clinicopathologic features of 8 fetal BCCH cases bearing a seemingly unique dual form of white pathology. All 8 cases demonstrated ischemic-like pathology, with 7 of 8 exhibiting such pathology in a similar location – ventral to the fused deep grey nuclei. Diffusion tensor imaging (DTI) studies suggest that the neuroanatomic substrate of this aberrant white matter is fused superior and inferior occipito-frontal fasciculi, with the resultant fibers crossing the midline. While the etiology of this ischemic-like pathology is unclear, the literature raises the possibility of a role for the SHH pathway.

Abstract 12

Brain pathology in patients with congenital heart disease

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Brain pathology in patients with congenital heart disease (CHD) are associated with neurodevelopmental delay. Imaging studies support vascular etiology for both white and gray matter lesions. In this retrospective study, we describe the pathological changes in the brains of patients with CHD. The last 20 autopsy cases in patients with CHD at our institution were retrieved and the clinical and the autopsy report were reviewed. The available H&E, special, and immunostains were evaluated and at least one section from each case was stained with GFAP, APP, and HLA-DR. Five control cases included telencephalic leukoencephalopathy (3) and no significant pathological changes (2). The following histological features were assessed: necrotic cells in cortex, hippocampus and the cerebellum; APP and GFAP staining pattern, and presence of focal lesions and amphophilic globules. Twenty patients (10 males, 10 females) were identified with age range of 2 weeks – 19 years. The pathological findings are as follows: 8 cases had changes consistent with acute global hypoperfusion, 5 cases showed features consistent with chronic global hypoperfusion, 3 cases showed focal white matter lesions (1 secondary, to septic emboli), 4 cases with only widespread gliosis, one case with only old focal neuronal loss in dentate gyrus, and one with no significant changes. Subarachnoid hemorrhages were present in 5 cases and germinal matrix hemorrhage in 3 cases. In conclusion, most of the pathological changes could be explained by cerebral hypoperfusion and better techniques to improve the cerebral perfusion are warranted in the management of these patients.

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Abstract 13

Characterizing the hippocampal dentate gyrus involvement in temporal lobe epilepsy

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Hippocampal sclerosis (HS) is the most common pathology finding for drug resistant temporal lobe epilepsy (TLE) and is characterized by neuronal loss and gliotic Cornu Ammonis. Nearly 20% of surgical specimens from drug-resistant TLE surgery contain "normal" populations of neurons, termed no-HS, yet still benefit from surgical resection. This observation suggests a neuropathological explanation for the epileptogenic focus in the resected tissue that is not detected through standard diagnostic practices. The goals of this project are to increase the neuropathological understanding of drug resistant TLE, and to elucidate the structural changes of HS and no-HS, focusing on the granule cell layer (GCL). In this study, 21 TLE surgical resection cases were examined, including 14 HS and 7 no-HS cases, to investigate GCL morphometry. Information on histopathological diagnosis and post-operative outcome were collected. The digital image analysis software QuPath was used to perform cell detection analysis on the GCL. Measures including Delaunay mean cell density were analyzed. HS patients show a significant increase in granule cell spacing and decrease in granule cell density within the GCL compared to no-HS patients. Regardless of the histological diagnosis, patients who achieved seizure freedom post-operatively demonstrated an increase in granule cell spacing and decrease in granule cell density in comparison to those who did not achieve seizure freedom post-operatively. HS and no-HS diagnosis groups have disease- and post-operative outcome dependent morphometry differences. The post-operative outcome dependent morphometry observed in HS and no-HS patients presents a potential additional method to evaluate post-operative prognosis for TLE surgical-resection patients.

Abstract 14

Meeting Abstract

Deep learning approaches to deciphering intra-tumoural heterogeneity in glioblastoma

Anglin Dent[1], Brian Lam[1], Kevin Faust[1], Alberto J. Leon[3], Phedias Diamandis[1]

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Background: Emerging evidence strongly implicates intra-tumoral heterogeneous biology in treatment resistance and disease progression across many cancer types (1). Using glioblastoma (GBM) as a prototype, I have aimed to leverage the computational power of Artificial Intelligence (AI) and deep learning (2) to develop an autonomous workflow for the objective definition and quantification of biologically distinct tumour subpopulations.

Objectives: I hypothesize that AI-defined tumoral clusters predict spatially distinct molecular profiles and therapeutic targets.

Methods: I apply our developed image clustering workflows (3) to quantify AI-defined subregions within a clinical cohort of 10 GBM patient tumors and use laser capture microdissection and mass spectrometry-based proteomics to address if AI-defined subregions show intra-tumoral molecular variation. Further, I leverage existing pharmacogenomic databases (4) and carry out drug sensitivity and transcriptional clustering to define biomarkers and validate their intra-tumoral expression in my clinical GBM cohort.

Results: Preliminary data shows that region-to-region heterogeneity can be found in IDH wild-type GBM using our unbiased omics approach, in addition to predicting different pharmacogenomic sensitivities.

Conclusions: This project aims to develop the first AI-driven tool to guide the routine and systematic molecular analysis of spatial morphogenomic heterogeneity. Further, this tool may have the potential to provide novel approaches for personalized care by selecting drug combinations that target a larger fraction of a tumor's true biology.

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Abstract 15

Meeting Abstract

Integrating morphologic and molecular histopathological features through whole slide image registration and deep learning

Michael K. Lee[1], Kevin Faust[2,3], Anglin Dent[1], Clare Fiala[3], Alessia Portante[1], Madhu Rabindranath[1], Noor Alsafwani[3,4], Andrew Gao[1,3], Ugljesa Djuric[5], Phedias Diamandis[1,3,5,6]

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Background and Objective: Despite recent innovations in deep learning, integrating histomorphologic and molecular information found on respective H&E and IHC-stained tissue sections still remains a challenge. While human observers can easily align these different tissue sections, routine computational approaches for image registration of giga-byte sized WSIs are still needed. Here, we aim to address this issue by incorporating another computer vision tool, scale-invariant feature transform (SIFT), to align H&E-stained sections with accompanying IHC studies for automated subclassification of gliomas.

Method: To test the workflow, we first trained a VGG19 convolutional neural network (CNN) using pathologist-annotated H&E WSIs to recognize histological patterns of 16 common tissue and lesion classes. Afterwards, we optimized a different set of CNNs to recognize various IHC markers, such as IDH1-R132H and ATRX, which are relevant for molecular subclassification of gliomas. For the integrated analysis, we employed SIFT to find features for image matching which were used to align lesional regions of H&E and IHC slides.

Results: The histomorphologic classifier (CNNH&E) excelled at classification with accuracies of 100% for glioma, meningioma and metastatic carcinoma, and 93% for schwannoma (n = 125). Using the newly developed CNNH&E and SIFT-based alignment, the quantitative analysis by the IHC classifiers significantly improved for ATRX retained and IDH1-R132H positive WSIs when compared to that of unaligned WSIs.

Conclusion: SIFT can work in concert with deep learning tools to provide a pathologist-inspired workflow to help automate advanced immunohistochemically diagnostic tasks, such as subclassification of glioma.

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Abstract 16

Neuropathology of eight cases of the New Brunswick cluster of Neurological Syndrome of Unknown Cause (NSUC)

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On March 17, 2021 a press conference aired featuring a Moncton neurologist and New Brunswick's Chief Medical Health Officer, regarding a cluster of patients in New Brunswick who had symptoms reminiscent of CJD, and were claimed to have a novel neurological syndrome. The onset of the disease was between 2015 and 2021. All patients in that cluster had at that time been reported by one neurologist, although subsequently a few incidental cases were reported by other neurologists. The size of this cluster has been reported at around 50 cases. Further news publications have suggested that an environmental factor is the causative factor for this cluster.

This news has significantly disturbed the medical community. Since 2019 eight patients have died that belonged to this cluster. We report their neuropathological findings and hope this will bring some clarity.

There was one case of metastatic carcinoma, one case of FTLD-TDP43, one case of neocortical Lewy body pathology, one case of neocortical Lewy body pathology and AD, 2 cases of AD with vascular pathology, one case of mainly vascular pathology, and one case without significant pathology (consistent with the patient's previous history). In these 8 patients no evidence for a prion disease was found, nor novel pathology. We suggest that these 8 patients represent a group of misclassified clinical diagnoses.

Since June 3, 2021 the Oversight Committee was established in New Brunswick reviewing the clinical and epidemiological data of the patients in this cluster. We hope that our findings are useful to them.

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Abstract 17

Meeting Abstract

COVID-19 pandemic impact on surgical neuropathology services at London Health Sciences Centre

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The COVID-19 pandemic has had a significant impact on medical services. Many jurisdictions postponed non-urgent procedures to balance individual patient care with public health precautions. Surgical backlogs caused by the COVID-19 pandemic have been evaluated by different groups. However, the impact of this pandemic on pathology and specifically neuropathology (NP) services has received limited attention. In this study, we reviewed all surgical NP reports of our centre from March 2018 (two years before the pandemic declaration) through July 2021. Patient demographic information and pathological variables were collected. For tumours, site, type, and WHO grade were analyzed.

Within the period under study, the total number of NP samples was lowest in April 2020, corresponding to the first Ontario provincial lockdown. In comparison to the dramatic decrease in other surgical pathology subspecialties (CAMJ 2021;193(10): E343), the NP surgical specimen initially had a minimal volume reduction, with a rapid return to baseline. Among the different types of NP surgical specimens, muscle biopsy and epilepsy-related specimens showed a more significant reduction. There was a slight increase in higher-grade tumours. Interestingly, a gradual increase of brain biopsies for inflammatory conditions was noticed.

Our results show that the neuropathology service volume reduction due to the COVID-19 pandemic has not been as significant as other pathology subspecialties. Studying the variations in histopathological diagnoses in pandemic years could be helpful for future planning in both clinical and pathological sectors, especially when the data is strengthened by the experiences of other medical centers.

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