Image Analysis in Neuropathology: Hue-Saturation-Intensity vs. Colour Deconvolution

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As image analysis expands into clinical and basic applications it is important that users be aware of opportunities and limitations. A common image analysis workflow involves the digitization of stained tissue sections into a red-green-blue (RGB) colour model for quantitative interpretation. Upstream of the digital image, quality and variability can be degraded at each step (tissue handling, fixation, sectioning, staining, image acquisition). Digital image analysis presents additional steps where variables can affect data quality. Image analysis platforms are not uniform. Aside from interface preferences, some introduce unintended variability due to their processing architecture that may not be obvious to the end-user. One important component of this is colour space representation: hue-saturation-intensity (HSI) vs. colour deconvolution (CD). A potential weakness of analyses within the HSI colour space is the mis-identification of darkly stained pixels, particularly when more than one stain is present. We were interested to discover whether HSI or CD provided greater fidelity in a typical immunoperoxidase/hematoxylin dataset.

Fifty-nine samples were processed using HSI- and CD-based analyses. Processed image pairs were compared with the original sample to determine which processed image provided a more accurate representation. CD proved superior to HSI in 94.9% of the analyzed image pairs. Where the option exists, CD-based image analysis is strongly recommended.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. To describe differences between HSI and CD colour spaces
2. To explain limitations in the use of HSI-based analyses
3. To be aware of recent developments in CD-based platforms

SESSION 3: Tumour neuropathology

NTRK2 Fusion Driven Pediatric Glioblastoma: Identification of key molecular drivers by personalized oncology

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We describe the case of an 11-month-old girl with a rare cerebellar glioblastoma driven by a *NACC2-NTRK2* (Nucleus Accumbens Associated Protein 2-Neurotrophic Receptor Tyrosine Kinase 2) fusion. Initial workup of our case demonstrated homozygous *CDKN2A* deletion, but immunohistochemistry for other driver mutations, including IDH1 R132H, BRAF V600E, and H3F3A K27M were negative, and ATRX was retained. Tissue was subsequently submitted for personalized oncogenomic analysis, including whole genome and whole transcriptome sequencing, which demonstrated an activating *NTRK2* fusion, as well as high PD-L1 expression, which was subsequently confirmed by immunohistochemistry. Furthermore, *H3* and *IDH* demonstrated wildtype status. These findings suggested the possibility of treatment with either NTRK- or immune checkpoint- inhibitors through active clinical trials. Ultimately, the family pursued standard treatment that involved Head Start III chemotherapy and proton radiotherapy. Notably, at most recent follow upapproximately two years from initial diagnosis, the patient is in disease remission and thriving, suggesting favorable biology despite histologic malignancy. This case illustrates the value of personalized oncogenomics, as the molecular profiling revealed two actionable changes that would not have been apparent through routine diagnostics. *NTRK* fusions are known oncogenic drivers in a range of cancer types, but this is the first report of a *NACC2-NTRK2* fusion in a glioblastoma.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Explore the current molecular landscape of pediatric high grade gliomas
2. Recognize the value of personalized oncogenomic analysis, particularly in rare and/or aggressive tumors
3. Discuss the current status of NTRK inhibitor clinical trials

Update on the national survey on molecular diagnostics in CNS tumors

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There have been significant changes in the diagnostic criteria for diffuse gliomas in the 2016 WHO CNS tumor classification, with the incorporation of molecular criteria into a number of definitions. This has placed a greater emphasis on the availability of key immunohistochemical and molecular tests. In order to determine the effect that these changes have had on