In the pursuit of glioma diagnosis – the challenges and opportunities of deep neural network augmented analyses.

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The incorporation of machine learning (ML), an application of artificial intelligence (AI) into the practice of medicine is one of the most promising areas of research and development in 21st century neuro-oncology[1,2]. This newfound interest in using ML for solving practical problems in medicine is driven by recent advances in one of its algorithms: deep learning. Among the artificial networks used by deep learning, deep neural networks (DNNs) are being applied to problems ranging from screening radiological and pathological imaging to screening for diabetic retinopathy.[3–5] DNNs consist of many layered (hence "deep") networks, mimicking the human brain, hence neural networks. Among them convolutional neural networks (CNN) are used for images and rooted on neocognitron[6], a concept based on the biological mechanisms of visual recognition of the vertebrate primary visual cortex. DNNs can automatically extract hierarchical features from high dimensional imaging in order to perform an underlying predictive task – often supervised classification. However, their ability to automatically learn features can result in seemingly accurate but actually erroneous models that do not work in practice.[7] Like many experimental techniques, DNNs must be employed and validated in a rigorous fashion to avoid confounding elements.

Differentiating pseudo-progression from progression is one of the most common diagnostic dilemmas in neuro-oncology. It is a commonly held belief that within the high dimensional data of pathology or radiology imaging there exist distinct signals corresponding to progression or pseudo-progression. The gold standard for diagnosis of pseudo-progression is surgical biopsy and pathological examination that requires both a neurosurgical operation as well as analysis by a trained neuro-pathologist. Hollon et al. in their most recent work combine the use of stimulated Raman Spectroscopy (SRH) and DNNs in order to tackle the problem of distinguishing glioma recurrence from pseudo-progression on pathological analysis.[8] Based on ten-fold cross-validated internal results, they demonstrated an average AUC of 96.2-98.7% for patient level predictions. Subsequently on an external test set, they achieve an impressive accuracy of 95.8% (sensitivity 100%, specificity 88.9%). One of the main benefits of ML is its ability to automate tasks, and one of the strongest recommendations of the work by Hollon et al. is its automation of the analysis. By using SRH to derive imaging from intraoperative tissue specimens and then automating the analysis with a DNN they bring the pathological diagnosis from the laboratory and into the operating room at the point of care.

If ML can bring the diagnosis of pseudo-progression to the OR, it raises the question as to whether it can lead to a diagnosis without surgery at all – a tissue-free diagnosis from radiological imaging. If a DNN can diagnose pseudo-progression in SRH imaging though, can it diagnose pseudo-progression on MRI? Here the results have been decidedly less impressive. As noted by the authors, non-invasive predictions of pseudo-progression using MRI including routine MRI, perfusion MRI, and magnetic resonance spectroscopy (MRS) all have had limited results in the hands of expert clinicians with AUCs ranging in the 80s to low 90s. The use of ML with radiology imaging, frequently referred to as "radiomics", has had little better results with AUCs also ranging from 80-90%.[9,10] Furthermore, all of these studies lack a rigorous external validation, and more hypothesis generating than conclusive. The pursuit of tissue-free diagnosis of pseudo-progression and other neuro-oncological diagnosis remains a promising future direction for ML in neuro-oncology as we work to incorporate technologies such as SRH driven technique into the OR.[8] In all cases we expect that DNNs and other ML techniques will be at the forefront of future pathological and radiological advances in neuro-oncology.

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