Editorial for "Deep Learning for Noninvasive Assessment of H3 K27M Mutation Status in Diffuse Midline Gliomas Using MR Imaging"

Diffuse midline glioma, H3 K27-altered is one of the main pediatric-type, high-grade, diffuse gliomas. Its most common subtype is H3 K27-mutant glioma: a WHO grade 4 tumor, typically occurring in children and young adults in characteristic midline locations, especially thalamus, brainstem, and spinal cord.

Accurate identification of H3 K27 mutation status is fundamental for prognostic assessment, stratification for clinical trials, and potential targeted therapy. However, given the deep, midline location of this tumor type, stereotactic or surgical biopsy can be very challenging, with a significant risk of complications. Therefore, there is a strong need to identify accurate MRI-based biomarkers for a noninvasive diagnosis, which might be further supported by mini-invasive molecular biology analysis techniques, such as "liquid biopsy," in the near future.[1]

From an MRI point of view, H3 K27-mutant gliomas are remarkably variable, with a spectrum of presentations spanning between contrast-enhancing mass-forming lesions with central necrosis and infiltrative processes without contrast enhancement.[2] Apparent diffusion coefficient values of the lesion are likewise variable, but usually low to slightly low.[2] There have been some promising results with cerebral blood flow values, but data are currently limited and further research is warranted.[2]

Recent work has demonstrated the applicability of artificial intelligence (AI) techniques for improving H3 K27 mutation status definition, based on conventional MRI sequences. Most studies have used machine learning (ML) techniques, which are capable of learning complex tasks and developing predictive models through sample data.[3] In detail, Pan et al were able to generate a model that was predictive of H3 K27 mutation status with an accuracy of about 85% in a cohort of 151 patients with brainstem gliomas, by using a random forest algorithm on preselected MRI features from T1-weighted, T2-weighted, and postcontrast T1-weighted images.[4] A similar approach was used by Jung et al on 41 spinal cord glioma patients, with an accuracy of about 63% for discriminating H3 K27 mutation status.[5]

Of course, feature extraction can be automatized with unsupervised ML, for instance, using principal component-based radiomics analysis. With this approach, Li et al identified few features from T2-weighted images as useful for differentiating H3 K27-mutant vs. wild-type brain diffuse midline gliomas. Among these features, cystic formation in K27-mutant tumors was identified as the most useful biomarker.[6]

The natural evolution of these approaches was to combine principal component analysis with subsequent random forest-based model estimation, as in the work by Su et al.[7] Principal component analysis was used for extracting the radiomic features from FLAIR images of 75 patients with brain diffuse midline glioma. Then, these features were used for building 10 different models with a random forest-based ML algorithm. The final model showed an accuracy of about 86% for separating H3 K27-mutant vs. wild-type brain midline gliomas. A similar combined approach was used by Kandemirli et al on multiparametric MRI acquisitions, including T1-, T2-weighted, FLAIR, postcontrast T1-weighted, and apparent diffusion coefficient sequences.[8] The accuracy of the final model was about 73% for separating H3 K27-mutant vs. wild-type brain midline gliomas.

The following evolution of this two-step combined ML approach was to use deep learning (DL) algorithms, which offer the ability to make predictions without pre-engineered features. Liu et al developed a cascaded deep convolutional neural network (CNN) algorithm able to achieve a good tumor segmentation result in 55 brainstem gliomas and to predict H3 K27 mutation status with an accuracy of about 95%.[9]

In this issue of *JMRI*, Liu et al used a similar approach on a larger scale: 341 diffuse brain midline gliomas and, separately, 91 spinal cord diffuse gliomas acquired at multiple centers on 1.5 T and 3.0 T MRI scanners.[10] Using conventional T2-weighted images, they developed a CNN-based DL algorithm with 3D U-Net architecture, which was able to perform accurate tumor segmentation as compared with manual segmentation by experienced neuroradiologists. Furthermore, a second CNN-based DL algorithm, this time with

EfficientNet-B0 architecture, was developed, managing a high accuracy for predicting H3 K27M mutation: over 90% for brain midline gliomas and 85% for spinal cord gliomas. Interestingly, models using only T2-weighted images showed higher accuracy than those also including FLAIR and post-contrast T1-weighted images, which is an interesting topic, open for future investigations.

This study demonstrates how advanced AI techniques can achieve major breakthroughs, starting from conventional MRI sequences. Among CNS tumors, H3 K27-mutant gliomas are in urgent need for such breakthroughs, especially for an early mini-invasive diagnosis. Provided future validation, the AI-based algorithms presented by Liu et al in this issue of *JMRI* may be able to reach a noninvasive assessment of H3 K27 mutation status, potentially co-adjuvated by biological breakthroughs such as "liquid biopsy."

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