European Radiology (2022) 32:7778–7779
https://doi.org/10.1007/s00330-022-09098-3

EDITORIAL COMMENT

Editorial comment: "Diffuse glioma, not otherwise specified: imaging-based risk stratification achieves histomolecular-level prognostication"

Takayuki Yamamoto [1] · Thomas Tourdias [1,2,3]

Received: 6 July 2022 / Revised: 6 July 2022 / Accepted: 23 July 2022 / Published online: 13 September 2022

Adult-type diffuse gliomas are the most common tumors of the central nervous system. Depending on the subtype, survival rates range from over 80% for low-grade gliomas to less than 20% for high-grade gliomas [1]. Over the 2016 and 2021 revisions of the World Health Organization (WHO) classification, the molecular profile has become increasingly important because specific genetic changes have been found to have essential prognostic implications. Currently, the diagnosis of adult-type glioma involves more than the presence of isocitrate dehydrogenase (IDH) and 1p/19q codeletion. However, it is acknowledged that some centers may not have the ability to carry out genetic testing or fluorescence in situ hybridization (FISH). Therefore, NOS (not otherwise specified) suffix is reserved for cases where a diagnostic test cannot be performed, or the results are inconclusive [2]. Tumors with histological grades 2 or 3 are a mixture of tumor types with different prognoses: oligodendroglioma, IDH-mutant and 1p/19q-codeleted; astrocytoma, IDH-mutant; glioblastoma, IDH wildtype. Lower grade gliomas, NOS can include all of these; hence, clinicians are struggling to manage them.

Imaging meets an impetus to predict molecular markers to guide therapy and prognostication non-invasively. It allows a qualitative or quantitative assessment of the tumor burden before and after the treatment. Various signs have been identified that can help to predict the molecular status of glioma in the daily clinical setting. For example, the famous T2/FLAIR mismatch sign — showing low sensitivity but high specificity for IDH-mutant astrocytoma [3] — has been proven to be a reliable marker. Prior to the present, differentiation and prognostic analysis of high-grade glioma from low-grade glioma were the major topics of research. However, in light of the heterogeneity of gliomas, more attention is being paid to the diagnosis of lower grade gliomas [4, 5].

In this article published in *European Radiology*, Jang EB et al [6] investigated the diagnostic performances to prognosticate grade 2 or 3 gliomas with unknown molecular features in a total of 220 patients by using imaging-based risk type, designed to comply with WHO classification. The proposed imaging criteria relied only on conventional images with the following findings: location, margin, T2/FLAIR mismatch, calcification on CT, multifocality, and enhancement. Such an approach was proposed to facilitate reproducibly at any facility.

The diagnostic performance in terms of prediction of the prognosis was measured by Cox proportional hazards regression models and receiver operating characteristic (ROC) analysis. The curves of progression-free survival (PFS) and overall survival (OS) of each risk type were clearly separated ($p < 0.001$). The area under the curves with 10-fold cross-validation showed a good performance for both PFS and OS (0.772, 0.806, and 0.790 for PFS at 1-, 3-, and 5-years post-surgery; 0.650, 0.793, and 0.812 for OS at 1-, 3-, and 5-years post-surgery, respectively). In the multivariable analysis, imaging-based risk type was shown to be an independent factor (HR = 1.54–2.48, $p < 0.001$), following to histological grading (HR = 1.51–3.12, $p < 0.001$).

This research provides an encouraging piece of data for prognostication inferred from the tumor subtype without the use of any advanced imaging techniques such as perfusion imaging, diffusion-weighted imaging, spectroscopy, chemical exchange saturation transfer, or positron emission tomography. However, since genetic information was not determined,

This comment refers to the article available at https://doi.org/10.1007/s00330-022-08850-z

✉ Takayuki Yamamoto
t@kayuki.jp

[1] Institut de Bio-imagerie IBIO, Université de Bordeaux, 146 rue Léo saignat 33076, F-33000 Bordeaux, France

[2] Centre Hospitalier Universitaire (CHU) de Bordeaux, Neuroimagerie Diagnostique et Thérapeutique, F-33000 Bordeaux, France

[3] INSERM, Neurocentre Magendie, Université de Bordeaux, U1215, F-33000 Bordeaux, France

one of the limitations of this study is that there is no way to identify the underlying reason when imaging-based risk classification does not work. To illustrate, glioma with CDKN2A/B homozygous deletion — classified as grade 4 currently regardless of any histologic grade — can be diagnosed as grade 2 or 3 by imaging. Although there is already extensive knowledge of the finding of glioma, the situation is not perfect for patient management. More accurate characterization of tumors may provide insight into novel imaging phenotypes, given the unprecedented demand for genetic properties. With the availability of datasets such as The Cancer Genome Atlas Low Grade Glioma (TCGA-LGG), it is now possible to perform large-scale analyses that are not restricted to one institution [7]. While machine learning methods such as radiomics and deep learning can be expected to provide more accurate diagnostic outcomes than conventional analyses that rely on the human eye, it is still challenging to translate these methods into indicators that can be easily applied in clinical practice. It is hoped that reviews such as this study will be updated pending further consolidation of knowledge.

Funding The authors state that this work has not received any funding.

Declarations

Guarantor The scientific guarantor of this publication is Thomas Tourdias.

Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was not required for this study because it is an Editorial Comment.

Ethical approval Ethical approval was not required for this study because it is an Editorial Comment.

Methodology
• Editorial comment

References

1. Ostrom QT, Cioffi G, Waite K et al (2021) CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2014-2018. Neuro Oncol 23:iii1–iii105
2. Louis DN, Wesseling P, Paulus W et al (2018) cIMPACT-NOW update 1: not otherwise specified (NOS) and not elsewhere classified (NEC). Acta Neuropathol 135:481–484
3. Do YA, Cho SJ, Choi BS et al (2022) Predictive accuracy of T2-FLAIR mismatch sign for the IDH-mutant, 1p/19q noncodeleted low-grade glioma: an updated systematic review and meta-analysis. Neurooncol Adv 4:vdac010
4. Lasocki A, Buckland ME, Drummond KJ et al (2022) Conventional MRI features can predict the molecular subtype of adult grade 2-3 intracranial diffuse gliomas. Neuroradiology. https://doi.org/10.1007/s00234-022-02975-0
5. Wu W, Wang Y, Xiang J et al (2022) A novel multi-omics analysis model for diagnosis and survival prediction of lower-grade glioma patients. Front Oncol 12:729002
6. Jang EB, Kim HS, Park JE et al (2022) Diffuse glioma, not otherwise specified: imaging-based risk stratification achieves histomolecular-level prognostication. Eur Radiol. https://doi.org/10.1007/s00330-022-08850-z
7. Liu X-P, Jin X, Ahmadian SS et al (2022) Clinical significance and molecular annotation of cellular morphometric subtypes in lower grade gliomas discovered by machine learning. Neuro Oncol. https://doi.org/10.1093/neuonc/noac154