Editor-in-Chief World Journal of Clinical Oncology 23 Apr 2022

Re: Our manuscript No. 76174 entitled "Simple Practical Approach for the Histomolecular Diagnosis of CNS Gliomas based on 2021 WHO Classification and EANO Guidelines"

We thank you and the respected reviewers very much for your valuable time in reviewing our MS. Your comments and critiques have been extremely valuable in guiding us in revising our MS. Accordingly, we revised our MS as suggested by the Reviewers.

For English proficiency, we sent it for English testing and correction through "Editage", one of your recommended companies. **The certificate is attached.**

Below are our responses to the comments raised by the editorial office and the reviewers (itemby-item).

Senior Editor Comments

This review presents a practical diagnostic approach for diffuse CNS gliomas and circumscribed astrocytomas using histomolecular criteria based on the WHO classification. The authors also detailed the treatment strategies for these tumors based on the European Association of Neuro-Oncology (EANO) guidelines. The theme of this article is attractive. Nevertheless, there are a number of points that may deserve some revisions. 1. The resolution of Figure 1 is not high. 2. The number of total references is few and a bit outdated, maybe a few more related references could also be cited. 3. The writing language needs to be further refined for easy reading and understanding.

Reply to the comment:

- 1. The figure 1 resolution is very high, but you need to open the image itself and not from the word document. The figure will be attached.
- 2. The number of references is not few and not outdated. We added 63 references for a challenging new topic in the literature (diffuse CNS gliomas). We compared the old classification with the new adopted ones, so for sure we should combine old and new reference. However, most of the references were between 2016-2021 (**please check**). For example: the references #3.5.6.7.8.14.16.17.20.24.25.29.34.39.49.50.58.63.
- 3. The manuscript has been refined and revised by one of your recommended language proficiency companies (Editage). **The certificate is also attached**.

Editor In-Chief Comments

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Oncology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Please be sure to use Reference Citation Analysis (RCA) when revising the manuscript. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. For details on the RCA, please visit the following web site: https://www.referencecitationanalysis.com/. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.

Reply to the comment:

- 1. We used the reference citation analysis for most of the references.
- 2. The figure 1, has been created, adjusted and structured using very advanced designing program through an expert. The figure is in high quality. We attached the figure as a JPG picture in order to pen it from the main source instead opening it from the doc word file.
- 3. The picture is original and made by us. The picture is a separate file and when we upload it into PP presentation slide, it becomes low in quality.

4. For the figure copyright, we added the sentence (Copy right© for Dr. Maher Kurdi, MD, Faculty of Medicine, Rabigh, King Abdulaziz University, 2022) at the right bottom of the picture (and NOT in PPT). The figure with high quality is attached separately.

Reviewer #1 ID 05774529

Overall, the theme of this article is attractive, but the structure of the article is not clear, which does not meet the "simple and practical" described by the author. It is suggested that the author refine and revise it for easy reading and understanding. In the context of "simple practical approach", figure 1 looks complex and inconvenient for clinical use.

Reply to the comment: Thanks for the comments. We appreciate the reviewer point of that the current approach requires revision to make it simpler and we understand the criticisms about the figure 1. **Here our response**:

- 1. The article consists of two components: the histological approach and the management approach. The histological approach describes the figure 1 in details. Using only the figures without detailed description in the test would make it very difficult to understand by the pathologist or the clinician though.
- 2. Figure 1 is very organized and simple compared to what written in WHO 5th edition and the ENO guidelines. It gives quick and simple approach how to reach the diagnosis based on the histological report written by the pathologist. It also helps the clinician, oncologist, in the diagnosis and the management approach of the case.
- 3. We had another quick revision on the manuscript. We made minor refinements to make the texts more readable, simpler, and easier for the readers.

Reviewer #2 ID 06090125

My Comments and Suggestions to Authors: 1- The abstract is not convincing and is disorganized, it should be refined to precisely illustrate what authors have done in this paper within 200 words. 2- In my opinion, the abstract is too cumbersome and is hard to catch the key point. The keywords need to be more detailed. 3- The contributions presented in this paper are not sufficient for possible publication in this journal. I highly suggest authors to clearly define the contributions. 4- The literature has to be strongly updated with some relevant and recent papers focused on the fields dealt with the manuscript. 5- There are no citations for many sentences in this manuscript. Why? Please check. 6- Many details are missing and others unclear. 7- The conclusions in this manuscript are primitive. Write your conclusions. 8- References aren't formatted according to rules. 9- The manuscript is hard to be understood and words should be improved. 10. Finally, authors are suggested to revise and improve the quality of manuscript

Reply to the comment: Thanks for the comments. **Here is our response**:

- 1. I agree in this point. However, we refined the abstract again to make it more focused on the main idea of the review. We left the detail later in the text. The changes highlighted with "YELLOW".
- 2. Please see the reply comment #1. We refined the "abstract" to make it clear and focused on the idea. Unfortunately, we only have 200 words for the abstract, so we tried to summarize the concept shortly to be into the point. Generally, the idea of the review is about the recent changes of 5th edition classification of CNS gliomas using histological and newly identified and explored molecular signatures.
- 3. I'm not sure what does the review means about "the contributions". If reviewer refers to the scientific information contributed to the review, I can say that the added contribution for sure would help the neuropathologist and neuro-oncologist in the diagnosis and the management of CNS diffuse gliomas. Newley molecular defined entities and golden information about the new classification and diagnosis of high-grade gliomas were also incorporated. On the other hand, if the reviewer refers the contribution to "authors contribution", we actually included neurosurgeons, radiation neurooncologist, and Neuroradiologist, who actually contributed to the text very hard.
- 4. I disagree with the reviewer in this point. The current review is following the recent update of 5th edition of WHO classification of CNS tumours and the EANO guidelines with incorporation of previous recent articles between 2015-2021. Check references#3.5.6.7.8.8.14.16.17.20.24.25.29.34.39.49.50.58.63
- 5. Can you please mention the sentences in the text without reference?! We cited a reference to every paragraph taken from other references. However, not every sentence in the text is necessarily to have a reference. It may be written or reformed by us based on literature and our experience.
- 6. Those have been refined and corrected.
- 7. Conclusion has been revised and edited to make the informed text into the point.
- 8. Sorry, that is not right. We followed the journals rules strictly. The rules say: Style for journal references For authors' names, the name of the first author should be typed in bold letters; the family (sur)name of all authors should be typed with the first letter capitalized, followed by their abbreviated first and middle initials. For example, an article by Lian-Sheng Ma and Bo-Rong Pan will be written as Ma LS and Pan BR. The title of the cited article will be written in sentence case. The journal title will be written in its abbreviated form (as shown in PubMed) in italics and followed by the article publication information (not italicized), including the publication date, volume number (in bold numbers), and start page through end page (separated by a hyphen, with no space). The PMID and DOI will follow this information and be written as [PMID: 11819634 DOI: 10.3748/wjg.13.5396].
- 9. This is general comment. The manuscript has been written, reviewed by other authors very well, formatted again, edited using language editing proficiency team, and also finalized.
- 10. The manuscript has been revised again and few improvements were done.

Reviewer #3 ID 03731081

The histomolecular classification of CNS neoplasms based on morphology is not modern. New classifications based on genetic criteria are needed. In modern classifications it is necessary to use known mutations (single nucleotide polymorphisms). The manuscript meets these requirements. This manuscript is recommended for publication.

Reply to the comment: Thanks. Appreciated

Again, we thank you and Reviewers for your valuable time. The comments and critiques have proven to be extremely useful for us to revise the MS. We have addressed every single issue raised by the Reviewers and revised the MS accordingly.

Thank you for your consideration of our revised MS.

Yours sincerely,

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