

## Peer Review File

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### Reviewer A:

This is a very nicely written summary on pediatric brain tumors and well researched literature.

- *I feel that novel developments with regard to molecular genetics and immunohistochemistry classification of brain tumors could be emphasized more as the edition plans to be “An Updated Practical Guide”. It would be good to include and focus more on the possible future changes expected by next year which are currently outline in the cIMPACT-NOW articles (i.e, glioblastoma IDH wild type will not exist in the future). Also, it should be mentioned which mutation harbors a better or worse prognosis. I think a table would be useful here).*

### Response:

Thank you for your positive comments and suggestions.

We have included one brief section about the expected future changes based on the *cIMPACT-NOW* articles, as suggested.

We have also included a brief paragraph for each tumor discussed in the manuscript regarding possible differential diagnoses.

- *I don't think that the discussion on advanced imaging techniques is extensive enough to be useful (I.e., ASL). Similarly, the section on cancer predisposition. Maybe better to include specific findings (e.g., in pilocytic astrocytoma) under the tumor category or recommend some articles for further reading). Overall, the quality of images needs to be improved.*

### Response:

We have adjusted the paper by removing the sub-topics "Advanced techniques" and "Cancer predisposing." However, we did include some information about these topics when it would help in diagnosis of particular tumors.

- *Line 99: “multiple cranial abnormalities” - what do you mean? Cranial nerves?*

### Response:

We have removed this sentence and included a detailed sentence as follows: “Cortical tumors typically manifest in focal neurological deficits, while brainstem gliomas might present with hydrocephalus and headache, fatigue, ataxia, visual changes, facial weakness, and gagging.”

- *Line 145: “Pilocytic astrocytomas frequently have BRAF alterations and usually do not present 146 IDH and TP53 mutations, as do other pediatric low-grade gliomas (20).” Would move this before the imaging discussion of the specific tumour.*

**Response:**

We have adjusted according to your request.

- *Line 262: “Presence of necrosis is not expected in the first stages of the disease or before treatment.” This definitely happens, especially in areas of low T2 signal as shown in your figure 3. These low T2, restricted diffusion and possible enhancing lesions not rarely seen in DIPG need to be mentioned here (Patay et al.).*

**Response:**

We have adjusted and included this sentence according to your request.

- *Line 1102: “left cerebellar hemisphere” it is right*

**Response:**

Thank you for your detailed observation. We have corrected the figure legend.

**Reviewer B:**

- *“ Although the topic of this paper is very interesting, I missed clarity when finishing the review article. Many entities are discussed, in my opinion without much coherence. In some parts, there is emphasis on the molecular diagnostics whereas in other parts, the imaging features are emphasized. The description of the imaging features is done in a general way, without emphasis on the differential diagnosis. Overview tables would have been good.”*

**Response:**

The authors appreciate the reviewer's comments. When determining the organization of our paper, in order to offer more coherence to the reader, we subdivided the tumors based on general overview, molecular features, imaging features, and differential diagnosis.

- *The paper is too elaborate and is not “basic” anymore. I do not see the use of adding a section of advanced imaging techniques. This is a topic in itself and adding this in an already elaborate paper reinforces the “loss of focus”.*

**Response:**

The authors agree that the paper had become too elaborate. To adjust this “loss of focus” the authors have removed the subtopics “advanced imaging techniques” and “syndromic cancer predispositions,” maintaining only selected information on these topics for particular tumors when necessary for diagnosis.

- *Authors claim the WHO 2016 classification was the basis of the paper but there are entities were mentioned, not integrated in the WHO classification and other recent advances were added. Some recent papers with significant consequences on the therapy of pediatric brain tumours were not mentioned (e.g. Mondal et al. Acta Neuropathol 2020)*
- *Furthermore, there are mistakes in the figure legends and figures are not well annotated.*
- *The overall use of the English language was mediocre with multiple spelling and grammatical errors. The first part was less well written compared to the middle and last part.*

**Response:**

The authors agree with the important observation highlighted. We have adjusted the manuscript by removing the tumors not included in 2016 WHO classification. We have included the important reference suggested and also a small discussion of potential changes based on cIMPACT-NOW, as suggested by Reviewer 1. The images, legends, and overall English content of the paper have been reviewed, including editorial support from a Medical science writer.

**Reviewer C**

*Comments to the authors:*

*Nice review of pediatric brain tumors.*