Dear editor,

Please find attached our proposal of modifications in response to the constructive remarks of your reviewer. Thank you for the opportunity to submit our work again.

You will find below a point by point response to the remarks. Our modifications are highlighted in red in the attached document.

1/ ADC usually originate in the olfactory cleft: reference?
The references are added

2/ 10% in a multicentric GETTEC study: reference?
The reference is added

3/ The statistical analysis software is not mentioned.
The following sentence was added:
SAS 9.2 was used for the analysis.

4/ Results of the evaluation of the relationship with each anatomical barrier are partially explained in the text.
One of the major problems of this study is that the criteria used to assess the stage of the tumor (d1, d2, d3,...) are not explained. It is especially important for the difference between d3b and d4 (tumor lysed the bone with an imprint onto the adjacent organ and the tumor was invading the adjacent organ). It is the hardest point to define when we evaluate a tumor’s stage.

We agree with your remarks. To avoid redundances, we wanted to develop (and discuss) the criteria used in the discussion. This is why we propose to add - in the method section - the following sentence with three references:
"For the differenciation between d3b and d4a stages, we used the criteria developed by Eisen and Kraus (7-9), which are presented in the discussion."
and further explanations are provided in the discussion (please refer to the response to point 8)

Please notify us if this change is not sufficient.
5/ In the table 1 shows that relationship of the tumor with the ethmoidal roof is quite difficult to establish. This is not mentioned in the text neither in the discussion whereas the relationship with the anterior wall of the sphenoid is well discussed. This should be modified before publication.

This point is now briefly discussed:
"Due to the site of onset of these tumors, the integrity of the ethmoidal roof is generally well preserved in early stage adenocarcinomas. Though, the presence of inflammation or retention in ethmoidal cells may be misleading: in these cases, the association of CT-scan and MRI is helpful. In advanced stages, the lysis usually begins on the medial side, in the olfactory groove. As the ethmoidal roof is thicker than the olfactory cleft, lysis is better identified."

6/ It could be interesting, in another study (?), to compare histological reports to results of the grid.

We totally agree with this remark. Though, this is better evaluated in prospective studies and we could not provide a precise response in this study. Another study is mandatory.

7/ The discussion should be modified as mentioned above.
We modified the discussion, and hope that the above modifications will help in clarifying the study.

8/ The discussion of the imaging criteria chosen to assess or not the invasion of adjacent organ should also be discuss before to recommend any MRI sequences.
We modified the paragraph as follows:
"Assessing the invasion of the adjacent organ may be challenging, so that MRI is usually necessary. Because of its protection by the middle turbinate, the invasion of the orbit generally begins anteriorly (behind the frontal process of the maxillar, at the level of the lamina papyracea) or posteriorly (orbital apex). Once the bone destroyed, the periorbita acts like a barrier to tumor spread: a regular displacement of the orbital content is usually associated with the respect of the orbital content, while a nodular aspect is highly suspect, even if this sign is not completely specific (18). The disparition of the orbital fat - because of its invasion - is well seen on MRI (T1 weighted coronal sequences), as an enlargement, abnormal signal or abnormal enhancement of the extra-ocular muscles (T1 with gadolinium and T2 weighted coronal sequences), which are very specific signs of orbital invasion (18). Though, this differentenciation was not really problematic in our study (K=0.8). As for the dura mater, a thickening of more than 5 mm in length, with nodular or irregular aspect must be considered highly suspect, especially if there is association with thickening of the leptomeninges (19). Assessing the invasion of the cerebral cortex may be difficult when the tumor already reaches the dura mater (K=0.5). As adenocarcinomas have a low ability to invade adjacent tissues, it seems that as long as the cortex remains visible in MRI (T1 or T2), the risk of cerebral involvement is low. The cerebral invasion may be suspected when enhancement of the brain cortex is present, especially with adjacent oedematous reaction in the parenchyma, better seen on MRI (fig 2E)."
9/ The last part of the discussion (about surgery of the orbital content) is not in the subject I think.
The paragraph is suppressed

10/ There is a typing error on the address of Université de Lorraine: Avenue de la Forêt.
This error is cleared: Université de Lorraine: Avenue de la forêt de Haye

11/ There is a typing error in the abstract: Methods: We
This error is cleared

12/ Figure 1 title is too long, should be less than 15 words
The title is modified
Figure 1: Coronal CT-scan (bone window) with normal anatomy of the olfactory cleft.

We hope that these modifications will help in clarifying the manuscript.
Sincerely yours,

Dr Patrice GALLETT