Dear editor and reviewer,

I am glad to receive your letter. Thank you very much for your hard work and kind suggestions. I have read the comments carefully and revised the manuscript according to your suggestions. Thanks again for your excellent work.

If you have any questions, please don't hesitate to contact me.

With best regards,

Sincerely yours

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Response to Editor and Reviewer:

Thanks for your valuable comments and suggestions which have led to significant improvement in the presentation and quality of this paper. The following are point-by-point responses to your concerns. And we shall detail the changes we have made on the paper.

1. The content of the article is reflected in its title.

Reply: Many thanks for your kind comments.

2. Abstract has to be improved. There is unusual term used "data learning". As well, "prognostic prediction" (can prediction be un-prognostic?)

Reply: Thank you for your advice. Sorry for the wrong usage of these phrases. According to your advice, the phrase "data learning and processing" has been replaced with" analysis of complex medical data", the phrase "prognostic prediction" has been replaced with "prognostic estimation", which refers to the estimation of treatment efficacy of certain disease in the long-term.

3. "automatically learning feature information" are strange.

Reply: Thank you for your reminder. Sorry for the misunderstanding usage of the phrase. We have revised and replaced it with "extracting key features and building mathematical models by computers".

4. There is a statement where the "automation" in building models found in machine learning is contradicted to direct programming. It is a too intense simplification. This ML "automation" can be achieved by coding the software.

Reply: Thank you for your clear explanation. Sorry for the misunderstanding simplification regarding "automation". We have revised the statement.

5. There is also unsupported statement (that is also not proved in the remaining part of the article): "Current evidence demonstrates that machine learning models can yield better performance than human clinicians."

Reply: Thanks for your reminders. We have changed this statement into "increasingly achieved expert-level performance" and added the supported reference.

6. Key words are adequately applied.

Reply: Many thanks for your kind comments.

7. There are two Sections "Introduction" and "Machine learning" that serve as an introduction. They refer to the articles about the medical application of ML. Probably that has caused several problems with these sections. Referring the definitions of AI, ML, discussing the issues of inputting data to the IT literature would be much more precise. AI arisen from ML. ML is not a branch of AI.

Reply: Thanks for your kind reminders. Following your suggestions, we have incorporated "Machine Learning" into "Introduction" and made a more precise description of AI and ML.

8. "Increasing the data size for a specific database" sounds strange and it is doubtful.

Reply: Thanks for your reminders. Sorry for the unclear expression. We have revised this statement into "accumulating enough data."

9. Even a "mini-review" - if it deals with ML - should be introduced with any simple classification of the tools. Especially the tools used by the authors of the referenced articles should be somehow classified and described more.

Reply: Thanks for your kind reminders. Following your suggestions, we have added the classification and description of the characteristic machine learning tools.

10. There is also unsupported statement: "Currently, better-performed algorithms typically belong to supervised learning".

Reply: Thanks for your kind reminders. We have revised the statement and added the support reference.

11. Validating or testing is not repeatedly adjusting the statistical model as stated at the end of ML section.

Reply: Thank you for your correction. We have deleted this statement.

12. MRI is not explained.

Reply: Many thanks for your kind comments. We have added the explanation of MRI, that is "magnetic resonance imaging", an imaging technique mainly used for the examination of soft tissue, including temporomandibular joint disc.

13. The aricle - the minireview - for its nature does not bring any new knowledge or results. In section "Maxillofacial malignant tumors" AUC, NPC, PET/CT are used and not explained.

Reply: Thanks for your kind reminders. We have added the explanations of AUC, NPC, and PET/CT in the manuscript.

14. There is unsupported statement at the end of this section "ML techniques have been shown to outperform the traditional statistical methods in early screening and prognosis evaluation of maxillofacial malignant tumors." Very good results of ML application are presented but not compared to other methods.

Reply: Thanks for your reminders. Sorry for the inaccurate expression. We have already revised it and added the reference.

15. I don't know who are "normal people" mentioned in section "Maxillofacial bone defects reconstruction".

Reply: Thanks for your reminders. According to the study of Jie et al., the phrase "normal people" can be understood as normal and healthy adults.

16. In section "Orthognathic surgery" the following three sentences are close together, but their meaning is not understandable to me: " However, extensive manual input is still required. Hence, the applications of ML in orthognathic surgery is promising. Shin et al. [50] extracted the features from posteroanterior and lateral cephalogram and evaluated the necessity for orthognathic surgery using DL networks."

Reply: Thanks for your reminders. Sorry for the misunderstanding expression. We have revised these sentences.

17. The use of the phrase "existing algorithms may be unsatisfied" (used in Problems and Solutions section) can be a true one but it needs a proof (an argument, or example, or reference). The phrase "has been shown little effect on the real clinical decision-making" is not understandable.

Reply: Thanks for your reminders. I'm sorry for the unsupported and inaccurate statements. We have revised the statement and added the supported reference.

18. Why it is stated that the privacy issue is important specifically in ML? Is it not important in statistical approaches?

Reply: Thanks for your suggestion. Sorry for the incorrect statement. Indeed, the privacy issue is important both in ML and statistical approaches. We have revised the statement.

19. The conclusion section (2 sentences in 5 lines) is definitely too short. What is the aim of the article, if the authors can conclude it in two sentences. It seems that the article suffer from lack of co-authoring of IT specialist experienced in ML.

Reply: Thanks for your reminders. After the consultation of the IT specialist, we have added more points in the conclusion section.

20. Some misunderstandings of these advanced methods (ML, DL, issues of data) can be found in the article. It certainly needs to be supplemented.

Reply: Thanks for your suggestions. We have supplemented more introduction of these advanced methods.

21. Also the proof reading is necessary. Even Word has found mistakes as "ethetics", "recontruction", "apperance", "contructed"...

Reply: Thanks for your reminders. Sorry for the wrong usage of these words. According to your advice, we have revised these words.

22. The scope and number of articles illustrating the application of ML in the medicine areas on subject is high.

Reply: Many thanks for your kind comments.