

## PEER-REVIEW REPORT

**Name of journal:** Artificial Intelligence in Gastroenterology

**Manuscript NO:** 57853

**Title:** Artificial Intelligence for the study of colorectal cancer tissue slides

**Reviewer's code:** 05355683

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2020-06-29

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-06-30 15:01

**Reviewer performed review:** 2020-07-01 02:22

**Review time:** 11 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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## **SPECIFIC COMMENTS TO AUTHORS**

Formica presented a short but interesting review topic specifically focused on AI application in analyzing colorectal cancer tissue slides. Detailed descriptions of machine learning application should be provided in some of the examples instead of simply mentioning that ML was applied. More examples in each section should be provided if available as most sections only provided one example. Citations are missing in multiple places. Scientific writing of a review paper and summary of literature can be further improved. Please refer to my specific comments below.

1. Citations are required: "Early studies were based on the analysis of specific slide regions, such as the tumor center, margins, stroma or others."
2. Citations are required: "More recently, with the ability of the computational analysis of higher digital dimension, automated analysis of whole HE-stained tumor tissue slides has been possible."
3. A figure presentation is recommended to better explain machine learning detection of "hand-crafted" features of the cells.
4. Citations are required: "Shape and orientation of cancer cells are among the most commonly assessed variables to predict patient outcome."
5. Full terminology of TP1 has to be provided.
6. There is only one example in "Assessment of shape and organization of cancer cells" and more examples should be given if more literature support can be found to make this section solid.
7. In the section of "Assessment of tumor infiltrating lymphocytes", citations in several sentences are missing. In most examples, the authors simply mentioned the use of machine learning such as "automated AI classifier" and "ML-based". More details of machine learning application should be discussed instead of focusing on the outcome as the readers to this review are more likely to be interested of how machine learning approaches were designed and applied.
8. In the section of "AI for identification of peculiar molecular subgroups", citations in several sentences are missing. The trained features of Resnet18 should be discussed instead of simply describing "very large cohort of gastrointestinal cancer".



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More examples should be included in this section if available. 9. In the section of “AI for the quantification of stromal tissue”, how deep learning was used? How training was performed? What is “TCGA”? What do you mean “similar results”? It is quite hard to understand the only example in this section and more details should be included. More examples and literature support should be included if available. 10. In the section of “Biology-agnostic machine learning”, the CNN example is very interesting, but the authors should improve the descriptions and writing to make the entire section easier to understand. For example, what is “biological background”? Why no biological background was fed? Why was “DoMore-v1-CRC” used and how it related to CNN? How was “non-distinct outcome” defined? More examples should be given if available.

## PEER-REVIEW REPORT

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**Manuscript NO:** 57853

**Title:** Artificial Intelligence for the study of colorectal cancer tissue slides

**Reviewer's code:** 05418778

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Professor

**Reviewer's Country/Territory:** India

**Author's Country/Territory:** Italy

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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#### **SPECIFIC COMMENTS TO AUTHORS**

1. Abstract needs major modification. Considerable information not given. 2. Introduction need proper structure. 3. Methodology not clear for the technologies mentioned here regarding AI. 4. A review paper should have challenges, their solutions and future directions. But I do not know what authors wants to review. 5. References is also very low.