

## Peer Review File

**Article information:** <http://dx.doi.org/10.21037/tlcr-20-591>.

### Reviewer 1

#### Comments to the authors:

**Comment 1:** The authors report an overview of digital pathology and artificial intelligence focusing on lung cancer. This is a very nice and complete overview on the applicability of Digital Pathology and Artificial Intelligence for routine pathologists and clinicians

➤ **Reply 1:** We would like to thank the reviewer for a positive evaluation of our work.

I have some minor comments.

**Comment 2:** Can the authors provide more details about whole slide imaging technology

The needs, organization in the lab and limitations in few sentences for AI to explain the reluctance from some pathologists. Which lab can do that.... How many cases are necessary for accuracy, the quality and extent of the database.

➤ **Reply 2:** It turned out that our manuscript in its present form is barely fit to the word count limit offered by the journal; therefore, expanding any section beyond 2-3 additional sentences is likely impossible. We understand an interest of the reviewer to get more information about whole-slide imaging (both as technology and diagnostic tool). A possible excuse is that our list of references contains the most notable publications relevant to this topic, including CAP/DPA guidelines (#5), and studies on implementation and validation of digital pathology (##1-5, #12-16). The issue of AI adoption is described in detail in the section “Barriers to clinical translation of AI” (p.21-25).

**Comment 3:** Can also the authors provide more details on multiplex image analysis discussing the limitations for clinical applicability

➤ **Reply 3:** Added sentence short note to explain multiplex IHC at page 20, line 481.

### Reviewer 2

#### Comments to the authors:

**Comment 4:** The paper provides an overview of the development of digital pathology and AI, and covers most of state-of-the-art aspects in the field.

The paper is overall well-written and largely well supported by decent references. In its current shape the paper will be very useful for pathologists and/or biomedical researchers. Because there is a need in such papers, I evaluated the article as ‘top 10% of importance’.

➤ **Reply 4:** We appreciate this high evaluation of our study by the reviewer.

**Comment 5:** However, if the main reader in MD, oncologist or biologist, the technical details need to be explained on different level. On another hand, for non-pathologists, the real needs are not clearly explained also. Why metastases in lymph nodes are important? Why histological subtype is important and what it is? Etc.

➤ **Reply 5:** Added as requested, page 17, line 393 and page 18, line 415 with one reference.

I have also several more specific comments.

**Comment 6:** Figure legends need to be improved. In most of cases the legends are descriptive enough. For example, Fig 9D: – it is not really explained what does it mean ‘Pathologists + AI’, what does the diagonal line on the graph mean; there is ‘trend of overestimation’ mentioned in the legend text but it is not shown.

➤ **Reply 6:** Added sentence to explain more about Figure 9D at page 42, line 996-999, and added circle suggesting areas overestimated by pathologists on the Figure 9D, page 42, line 1000.

**Comment 7:** Figure 2 – **if possible** for the publication in international journal one could consider providing images with English labeling. Resolution is very low in current version.

➤ **Reply 7:** Our idea was to show an overwhelming complexity of integrated clinical, pathological, and beyond (radiologic and molecular) data which is needed to establish precise diagnosis in difficult cases. We didn’t aim to make all lines readable (and, therefore) disclose actual information of the patient.

**Comment 8:** Certain paragraphs are not specific enough. For example, page 13, lines 291 to 305. Many long sentences without providing clear references. It would fit for introduction but not for main text.

**Comment 9:** On another hand, there is a number of references without proper explanation. I believe text can be re-written to provide more useful information with the same work count.

- **Reply 8:** In fact, this paragraph is an introduction to third section “APPLICATION OF DEEP LEARNING IN PATHOLOGY”.
- **Reply 9:** Added one reference.

**Comment 10:** There is a number of typos.

- **Reply 10:** Additional proofreading has been done by the native speaker (and coauthor) and, if the reviewer wishes to point out to the specific typos, we will be happy to fix those.

### **Reviewer 3**

#### **Comments to the authors:**

**Comment 11:** Line 79: Handouts?

- **Reply 11:** Thank you for picking up this typo. We actually use Google Meet, therefore the sentence has been changed accordingly.

**Comment 12:** Line 247: Possible incorrect reference to figure 5.

- **Reply 12:** Thank you for pointing out this mistake. Indeed, we referred to Figure 4C, which now has been corrected.