

### **Our response to the first reviewer:**

We would like to thank the reviewer for the time spent reviewing our work and for the valuable and thorough feedback. Below we provide our responses to the reviewer's comments in a point-by-point manner:

- i. (1) The opportunities of AI applications were not extensively discussed. There were a lot of bullets on opportunities. However, there is no connections to previous literatures discussed earlier. These sections should be discussed in more details since it is one of the major focuses of this article. Moreover, in section 4 and 5, there is so much information about previous literatures. The authors should summarize them into tables, which will give the highest benefits to readers.: **Our response:** We thank the reviewer for drawing our attention to these omissions on our end. Per the reviewer's suggestions, we have now organized the studies regarding the AI applications into 8 different tables. The knowledge provided to the readers has now been expanded to include information regarding the parameters employed by each model, the AI classifiers used, the size of the training and validation cohorts in each study, the specific outcome(s) of each study, and the performance of each study including specifically the accuracy, c-index, sensitivity, and specificity in the training, internal validation, and external validation cohorts. We hope that the reviewer shares our opinion that these tables significantly improve the readability of our paper by providing valuable information for the reader in a condensed manner. We understand the reviewer's spirit regarding the comment that opportunities have not been elaborated enough. In our minds,

the opportunities are demonstrated through the applications of these models. Nevertheless, to make this clear, we have now elaborated on our sections regarding the opportunities that arise from AI/ML applications. In addition, regarding each opportunity that arises from AI applications, we now mention the current efforts that correspond to that opportunity while appropriately citing the relevant studies to provide a connection between the two sections as recommended by the reviewer.

- ii. [2.1] In section 3, the author stated that ANN is a supervised ML ANN is just another name of neural network and can be used for both supervised and unsupervised learning: **Our response:** We thank the reviewer for raising this semantic error on our part. As per the reviewer's suggestion, we have revised the sentence accordingly. **The sentence reads:** "An artificial neural network (ANN) is an ML model inspired by the human brain's neuronal connections that consist of an input layer, an output layer, and a hidden layer between them <sup>[18]</sup>. ANNs are applied both in supervised and unsupervised ML <sup>[24]</sup>."
  
- iii. [2.2] The authors separately mentioned Deep Learning (DL) and Deep Neural Network (DNN). In fact, they are very much the same. I would suggest using only one term to avoid confusion. Otherwise, the authors should clearly state their differences: **Our response:** We thank the reviewer for raising this semantic error on our part. As per the reviewer's suggestion, we have revised the sentence accordingly. **The sentence reads:** "When multiple hidden layers

are inserted between the input and output layers, and the network's architecture becomes more complex with multiple interconnections, the concept of deep neural networks (DNN) emerges <sup>[24,25]</sup>.”

- iv. [3.3] The last sentence of section 3 is a bit confusing because of the terms "before been fed to the CNN". Normally, the convolutional process is an integral part of CNN. So far, I really enjoy reading section 6 the most. However, in section 6.2, I cannot really relate cybersecurity in the second paragraph to specific AI applications: **Our response:** We thank the reviewer for drawing our attention to this semantic error on our end. We have now revised the sentence accordingly. **The sentence reads:** “During the CNN model development, the images are preprocessed using multiple filters, and multiple feature maps are created in a process called convolution <sup>[26]</sup>.” Finally, we thank the reviewer regarding the comment about the second paragraph of section 6.2, and we apologize for this omission on our end. As per the reviewer’s recommendation, we have added an example where deep learning was used in a study to attack a healthcare facility to trick radiologists and a state-of-the-art AI model by introducing and removing lung cancer tumors from CT scans. **The sentence reads:** “In a recent study, the authors demonstrated how attackers could use DL to add or remove lung cancer tumors in CT scans <sup>[174]</sup>. This study demonstrated how both a group of radiologists and a state-of-the-art deep AI model were particularly susceptible to the attack <sup>[174]</sup>. How could we, therefore, be confident that the AI/ML

model has not been compromised?” In addition, we have revised the previous sentence to make clear that it explicitly refers to cybersecurity concerns regarding AI. **The sentence reads:** “Data could be introduced malevolently in the algorithms to manipulate the developed AI/ML models into making wrong decisions with currently unknown ramifications to patient outcomes [173].”