

Reviewer #1:

Specific Comments to Authors: This editorial has reviewed and discussed the application of ML and DL on the analysis of radiological and histological images, as well as multi-omics data in precision oncology. I have the following comments for the revision.

Author's Response: Thank you for the comments.

1. Concerning the applications on radiological and histological images, the information is relatively sufficient. However, the paragraphs for multiomic data are quite brief for such a big topic. Some enrichment may be necessary.

Author's Response: The following paragraphs for multi-omics data have been added to the revised manuscript.

DL algorithms for analysis of omics data have been demonstrated to facilitate classification and detection of cancer as well as stratification of risk in patients with cancer. Using a DL approach, termed Stacked Denoising Autoencoder (SDAE), to extract features from RNA sequencing (RNA-seq) expression in The Cancer Genome Atlas (TCGA) database, breast tissues can be classified into cancer or non-cancer and the involved genes can be identified as potential cancer biomarkers [Danaee et al, 2017]^[24]. By application of CNN for analysis of RNA-seq data in Pan-Cancer Atlas, tissue samples have been classified with accuracy into 33 different types of cancer [Lyu and Haque, 2018]^[25]. Besides gene expression data, DL analysis of epigenetics data particularly DNA methylation in the context of CpG islands has also been shown to classify cancer types. A deep neural network (DNN) was developed to extract the deep features of DNA methylation data, and this method can differentiate patients with breast cancer from healthy individuals [Si et al, 2016]^[26]. Similarly, a CNN-based DL model can classify different types of cancer by analysis of the patterns of DNA methylation [Chatterjee et al, 2018]^[27]. Furthermore, an advanced DNN-based model, DeepGene, was developed to analyze somatic point mutation data, and it was demonstrated to improve classification of 12 selected types of cancer [Yuan et al, 2016]^[28]. Recently, the power of DL and traditional ML methods in cancer classification using TCGA datasets was compared, and results of the study indicate that the DL method, termed Multi-Layer Perceptions (MLPs), outperforms the other approaches in discrimination of samples with cancer from non-cancer [Yu et al, 2019]^[29].

In addition to classification of cancer types, DL and ML have been exploited to predict patient prognosis and investigate gene regulation. By DL-based analysis of multi-omics data, including RNA-seq, microRNA sequencing (miRNA-seq), and DNA methylation data, patients with hepatocellular carcinoma can be classified into subgroups with difference in survival [Chaudhary et al, 2018]^[30]. DL autoencoder algorithm for analysis of multi-omics datasets comprising mRNA, miRNA, and DNA methylation from TCGA can also predict the survival subtypes of patients with urinary bladder cancer [Poirion et al, 2018]^[31]. Besides, ML-based integrative analysis of multi-omics data on the cloud has been demonstrated to improve the accessibility and productivity of cancer research for discovery of gene regulatory subnetwork, analysis of disease subtype, analysis of survival, prediction of clinical outcome, and visualization of multi-omics results [Oh et al, 2020]^[32]

2. Data-driven machine learning (ML) and deep learning (DL) are the main focus of this editorial. For readers that are not familiar with computer science, a few sentences to highlight the differences between these two terms may be necessary.

Author's Response: The following sentences to highlight the differences between machine learning and deep learning have been added to the Figure 1 legend in the revised manuscript. Machine learning is a branch of artificial intelligence that manually extract features from input data to create a model that categorizes the object. Neural network is a set of machine-based learning algorithms to learn labeled datasets and perform classification tasks, and it comprises an input layer, a hidden layer of interconnected nodes, and an output layer. Deep learning is a machine learning technique that uses neural network architectures, and the term "deep" refers to the number of hidden layers (more than 3) in the neural network.

3. The author has plainly described the contents of cited references. However, readers may expect more contents on the discussion of current issues, drawbacks and bottlenecks and more detailed description of the future perspectives.

Author's Response: The Conclusions and Future Perspectives section has been modified in the revised manuscript as follows.

Medical application of AI technology has been revolutionizing healthcare. ML and DL algorithms create powerful tools and opportunities for advancing translational cancer research. Accumulating evidence has begun to demonstrate the value for improving various aspects of clinical oncology such as diagnosis and treatment of cancer. In particular, advances have been made by DNN-based analysis of "big cancer data" towards the goal of precision oncology (Figure 7).

A number of hurdles will need to be resolved in order to move toward implementation of multi-modal ML in clinical practice. Limitations in radiomics may include inter-observer variability of data processing, reproducibility of radiomic features, tumor heterogeneity, and difference in radiomics approach among researchers [Lambin et al, 2017; Bodalal et al, 2019]^[47-48]. Large infrastructural networks and platforms for collection, processing, storage, sharing, and accessing medical images, histopathology, and clinical data across institutions may impose challenges [Coppola et al, 2019]^[49]. Due to access of personal information and cloud-based storage of data, ethical and regulatory issues concerning patient confidentiality and data security are non-trivial [Jobin et al, 2019; Theodorou et al, 2020; Kaissis et al, 2020]^[50-52].

However, multi-modal ML approaches that integrate large datasets, including medical images, digitalized pathology, holomics, and clinical features will continue to evolve. Emerging applications of AI in oncology involve ML in selection of treatment [Ho 2020]^[23], palliative care and hospice [Kamdar et al, 2020]^[53], and design of clinical trials [Harrer et al, 2019]^[54]. Multi-disciplinary collaboration for development and adoption of multi-modal ML is expected to accelerate healthcare evolution towards precision oncology through computer-aided clinical decision on individualized management of patients.

Reviewer #2:

Specific Comments to Authors: Very nice review of the current state of AI in precision oncology

Author's Response: Thank you for the comment.

Science editor:

The authors should provide the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an invited manuscript. The topic has not previously been published in the WJTM.

5 Issues raised:

(1) The authors should add some figures or tables in the manuscript;

Author's Response: Seven figures have been added in the revised manuscript.

(2) The authors should add the number before each reference in order;

Author's Response: The number has been added before each reference in order.

(3) The reference' number should be put in the square bracket, then make them be superscript;

Author's Response: The reference's number has been put in the square bracket as superscript.

(4) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

Author's Response: The reference list has been revised.

(5) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text.

Author's Response: The Core tip is included at the beginning of the main text.

(6) Re-Review: Required.

(7) Recommendation: Conditional acceptance.

