KiNet: A Novel Imaging Informatics Tool for Pancreatic Neuroendocrine Tumors

ABSTRACT

Background: Neuroendocrine tumors (NETs) are one heterogeneous type of cancer affecting most organ systems. NETs must be correctly graded to ensure proper treatment and patient management. The proliferation index, as measured by Ki67 nuclear staining, is required for gastrointestinal (GI) and pancreatic NET grading per the criteria of the World Health Organization (WHO). Measuring the Ki67 labeling index (Ki67 LI) from pathology images requires accurate quantification of immunopositive tumor, immunonegative tumor and non-tumor cells. This process is an essential procedure in basic, translational and clinical research and in routine clinical practice. However, current Ki67 image analysis tools have a number of drawbacks: 1) Ki67 LI assessment is still mainly achieved with manual or semi-automated methods, leading to increased labor costs, awkward workflows, low-throughput image analysis and significant potential inter- and intra-observer variability; 2) computer-aided Ki67 counting is error-prone due to the multi-stage image processing design, where each stage itself is a very challenging task; 3) current algorithm design does not take into consideration the characteristics of Ki67 images such that it has technical difficulty in classifying different types of cells in Ki67 stained images. Therefore, it has a need of better computational methods for automated Ki67 LI assessment.

Experimental Approach: In one of our current projects, we have developed and disseminated a novel deep learning-based imaging informatics system, KiNeT, specifically for better automated Ki67 LI measurement in GI and pancreatic NETs. KiNet takes advantage of cutting-edge artificial intelligence/deep learning algorithms, deep fully convolutional networks (FCNs), to develop an end-to-end, pixel-to-pixel model for single-stage Ki67 LI assessment. We first formulate Ki67 counting as a cell identification problem and solve it using class-aware structured regression modeling within a novel FCN network. This network is able to simultaneously detect and classify immunopositive tumor, immunonegative tumor and non-tumor cells. Next, we further enhance cell identification with another related task, extraction of regions of interest (ROIs), which differentiates tumor from non-tumor regions by taking Ki67 image characteristics into consideration. These two tasks have been unified into one single neural network and jointly learned to benefit both cell identification and region classification for Ki67 counting in NETs.

Results: KiNet has provided very promising performance for automated Ki67 LI assessment and has outperformed other recent computerized methods in cell identification [Xing et al. IEEE Trans Biomed Eng 66(11), 2019] [Zhang et al. JCO Clin Cancer Inform 4, 2020]. It has also demonstrated the feasibility of AI-based computational methods for automated, efficient and effective Ki67 counting. In addition, KiNet has introduced a completely different single-stage Ki67 counting strategy and would provide a new perspective for Ki67 image quantification. The source codes of KiNet have been recently released in GitHub: https://github.com/exhh/KiNet.

Conclusions: Compared to manual counting and current Ki67 image analysis methods, KiNet can significantly improve the objectivity, consistency, reliability, reproducibility and efficiency. Meanwhile, it would release NET researchers and pathologists from doing daily, routine and boring work such as individual cell counting and labeling. In the future, we will further improve KiNet by using the latest advances in AI/deep learning algorithms to consider contextual information within input images for enhanced cell identification and to address dataset shifts between image data from different institutions for transferable Ki67 counting. The improved KiNet will accelerate Ki67 score computation across different datasets to facilitate early diagnosis and improved therapies for pancreatic NETs.