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Comparison of Manual and Automatic Methods of Ki-67 Proliferation Index For Neuroendocrine Tumors: The Development and Validation of a Novel Digital Pathology Tool (Ki67 Counter)

Janna H. Neltner, MD[1]; *Hai Su[2], MS; *Fuyong Xing[2], MS; Julie Rosser, DO[1]; Michael L. Cibull, MD[1]; Peter Nelson, MD[1]; Lowell Anthony, MD[3]; and Lin Yang, Ph.D[2]

[1]Department of Pathology, College of Medicine, University of Kentucky, Lexington, KY, 40536
[2]Division of Biomedical Informatics, Department of Biostatistics, Department of Computer Science, University of Kentucky, Lexington, KY, 40536
[3]Division of Medical Oncology, College of Medicine, University of Kentucky, Lexington, KY, 40536

Background: Ki-67 proliferation index is an increasingly important biomarker used to grade neuroendocrine tumors. Manual counting methods are laborious and subject to inter- and intra-observer variability. Digital counting methods hold promise for fast and reproducible indices, however are fraught with technical difficulties.

Method: We have developed a novel automated tool, Ki67Counter, to improve the speed, reproducibility, and accuracy of automatic Ki-67 counting. We have created digital Ki-67 slides of 46 biopsy and/or resections of pancreatic and gastrointestinal neuroendocrine tumors from the University of Kentucky.

Results: The counting results are compared with both pathologists' manual results and a commercially available image analysis platform (Aperio™ Nuclear algorithm, Image Analysis Toolbox™). We found that both digital methods were able to count much faster than the manual methods (Aperio average 6.4 minutes, KiCounter average 1.5 minutes, compared to manual average 21.6 minutes). Consistent with the literature, we also noted that the Aperio's results were consistently higher than the manual counting results, due to inclusion of non-tumor cells (particularly lymphoid infiltrates) despite reasonable efforts to exclude these populations.

Conclusion: Ki67Counter is superior to the Aperio in both analysis speed (1.5 minutes VS 6.4 minutes) and accuracy (three times more accurate than Aperio) due to Ki67Counter's excellent performance in differentiating tumor/non-tumor cells. Ki67Counter offers a novel, rapid, and reproducible method which eliminates many of the issues that have plagued automated digital pathology analysis of Ki-67 proliferation index for clinical practice.