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The New Automated Algorithm to Evaluate Ki67 in pNET. The Five "W" law: Who, When, Where, What, and Why

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Context Ki67 index (Ki67-I), is the percentage Ki67 immunoreactive cells, expressing tumor proliferation, with important clinical relevance in pancreatic neuroendocrine tumors (pNET) and to standardize its evaluation is extremely important. The pNET guideline indicate to evaluate at list 2 mm^2 of tissue or 2,000 tumor cells. However, this type of evaluation is currently done by subjective opinion of pathologist concerning the area of interest (AI). **Objective** We elaborated a new algorithm of analysis able to catch all tumor cells present in the selected area according to the pathologist's criteria. **Methods** The program (D-Sight, 2.0, Menarini, Florence, Italy) catch all color intensity on the tissue surface, to understand whether which type of sensitivity to immunohistochemistry could match with the Ki67-I. The system returns automatically the number of both total and stained cells. **Results** The first attempts made on the samples previously evaluated (15 cases with the oldest algorithm) showed an improvement of two important parameters: 1) a better evaluation of total tumor cells present in AI; and 2) a good evaluation of nuclei aggregation. These two data showed a better Ki67-I in pNET, very close to the pathologist's interpretation. **Conclusion** The possibility to standardize a fully automated methodology to evaluate Ki67 value can improve both pathological evaluation (i.e., grading of the tumor) and clinical management of pancreatic neuroendocrine patients. This application could open also the new analytical evaluations of other protein markers involved in clinical outcome of oncologic patients.