

## FACTORS INFLUENCING KI67 CALCULATION IN NEUROENDOCRINE TUMORS

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We selected 70 patients with NET and NET- like tumors, who came to the Institute between 2007 and 2013. One pathologist and a pathology assistant performed a manual count of Ki67 in more than 2000 cells by case; three pathologists (JS, CG & LC) performed an eyeball Ki67 evaluation and pathology assistant run the advanced version of immunoratio software in tumor hotspot pictures. Most common primary tumor was intestinal (18.5%), female genital (15.7%), pancreas (14.3%), liver & gallbladder (12.9%), esophagus & stomach (11.4%), lung & thymus (8.6%), head & neck (7.1%) and urinary system (7.1%). Manual count of ki67 is accepted as the standard methodology and found that 58.6% cases had larger ki67 than 20%, 22.9% had 3- 20% and 18.6% had less than 3%. Incorrect assessment of Ki67 by CG resulted in 23 cases (32%) of upgradation; and incorrect assessment of Ki67 by JS resulted in 4 (4.2%) cases of upgradation and 4 cases (5.7%) of downgradation; and incorrect assessment of Ki67 by LC resulted in 3 (13.6%) of upgradation and 3 (13.6%) of downgradation. Ki67 by immunoratio score resulted in 12 cases (17.14%) of upgradation and 6 (8.57%) cases of downgradation. We evaluated factors related to variation of Ki67 evaluation and better concordance between eyeball and manual count when the Ki67-labeling index was <3% ( $-0.88 \pm 0.74$  JS,  $-1.88 \pm 5.30$  and  $0.66 \pm 0.78$  CG), and poorest concordance when the Ki67-labeling index was in the range of 3% to 20% ( $1.81 \pm 5.27$  JS,  $-0.07 \pm 4.57$  and  $6.06 \pm 3.29$  CG) and >20% ( $-6.13 \pm 16.0$  JS,  $-3.13 \pm 17.4$  and  $12.85 \pm 15.0$  CG). We evaluated if level of tumoral fibrosis, quality of ki67 staining, quality of sample, biopsy/ resection, cellularity, level of intratumoral lymphocyte and level of intratumoral neutrophile infiltration influence variation between eyeball and manual Ki67 count but we did not find association ( $p = 0.120- 0.862$ ,  $p = 0.094- 0.873$ ,  $p = 0.099- 0.731$ ,  $p = 0.099- 0.731$ ,  $p = 0.054- 0.882$ ,  $p = 0.013- 0.803$ ,  $p = 0.583- 0.841$ ,  $p = 0.102- 0.842$ , respectively). Finally, we evaluated if the same factors influence variation between immunoratio and manual Ki67 but we didn't find association ( $p = 0.586$ ,  $p = 0.496$ ,  $p = 0.071$ ,  $p = 0.271$ ,  $p = 0.071$ ,  $p = 0.284$ ,  $p = 0.574$ ,  $p = 0.216$ , respectively). Conclusion: We found that there is a difference range of Ki67 among pathologist and even for immunoratio software. Better concordance is found among pathologists when Ki67 is lower than 4%.