Quantitative tumor heterogeneity assessment on a nuclear population basis - DTU Orbit
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Quantitative tumor heterogeneity assessment on a nuclear population basis

Immunohistochemistry (IHC) Ki-67 stain is widely used for visualizing cell proliferation. The common method for scoring the proliferation is to manually select and score a hot spot. This method is time-consuming and will often not give reproducible results due to subjective selection of the hotspots and subjective scoring. An automatic hotspot detection and proliferative index scoring would be time-saving, make the determination of the Ki-67 score easier and minimize the uncertainty of the score by introducing a more objective and standardized score.

Tissue Micro Array (TMA) cores stained for Ki-67 and their neighbor slide stained for Pan Cytokeratin (PCK) were aligned and Ki-67 positive and negative nuclei were identified inside tumor regions. A heatmap was calculated based on these and illustrates the distribution of the heterogenous response of Ki-67 positive nuclei in the tumor tissue. An automatic hot spot detection was developed and the Ki-67 score was calculated. All scores were compared with scores provided by a pathologist using linear regression models.

No significant difference was found between the Ki-67 scores guided by the developed heatmap and the scores provided by a pathologist. For comparison, scores were also calculated at a random place outside the hot spot and these scores were found to be significantly different from the pathologist scores.

A heatmap visualizing the heterogeneity in tumor tissue expressed by Ki-67 was developed and used for an automatic identification of hot spots in which a Ki-67 score was calculated. The Ki-67 scores did not differ significantly from scores provided by a pathologist.

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