Background: Biomarkers that can identify which active surveillance (AS) prostate patients are likely to progress would have clinical utility.

Methods: Using a DNA specific stain (Feulgen-Thionin) and deep learning based segmentation to identify/delineate every nucleus in prostate needle biopsies with an accuracy comparable to human annotation even in areas of overlapping nuclei. Further quantifying the distribution of the DNA within these nuclei one can automatically define different tumour, immune and stromal cell categories. Within these cell categories one can identify subsets that construct classifiers that differentiate between AS patients that progress (35 cases, poor outcome) from those that do not (69 cases, good outcome). Approximately 5.4% cells across all cases were used to build these classifiers and they were tested on the remaining 94.6% of cells.

Results: Across the 126 needle biopsies, ~1.5 million nuclei were segmented by the deep learning algorithm (>90% accuracy of correct segmentation upon visual examination). Classifier training involved 78,271 of these nuclei, leaving 1.4 million nuclei as test set. The frequency of immune like cells, density of tumour nuclei and subsets of tumour cells and stroma cells were found to be predictive of progression or non-progression. A combination of these cell frequencies defined risk groups that predict future behavior (See figure 1). Cases with a high frequency of immune like nuclei were predicted to have good outcome even if the features of the tumour cells predominately are predicted poor outcome. Examining the distribution of these immune cells within a prostate needle biopsies with spatial distinct tumour nuclei predicting poor outcomes and good outcomes it was interesting to observe that the immune cell density was much higher in the areas of tumour nuclei predicting poor outcomes. Suggesting that the immune system was also recognizing the aggressive poor outcome predicting cells and dealing with them as these patients did not progress. This also suggests that potentiating tumour immune cell interactions could potentially affect prostate patient outcomes.

Conclusions: Deep Learning segmentation paired with a DNA specific stain can identify/delineate cell nuclei with high accuracy and quantitative measures of the DNA distribution within these nuclei can be predictive of AS patient outcome. Immune cell frequency identified in this fashion is predictive of patient outcomes.

Ethics Approval: Ethics approval was obtained from the UBC-BC Cancer Research Ethics Board. The number of the ethics approval is H1301398.