3-D Nuclear chromatin texture analysis of prostate tissue using confocal laser scanning microscopy

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The transformation of a normal cell into a malignant cell is associated with genetic alterations that often result in abnormal chromosome sets ("aneuploidy") and changes in the distribution of chromatin inside the nucleus. These changes are often subtle and are mostly referred to as "malignancy associated changes" (MACs). Unfortunately, these changes cannot easily be detected through the microscope and can also be found in morphologically benign cells. To correctly discriminate between normal and (potentially) malignant cells these changes are therefore best not merely visually assessed but also mathematically quantified by image cytometry as "texture features". The aim of this study was to develop methods for quantification of the nuclear chromatin architecture by means of analysis of 3-D texture features as a potential aid in future tissue diagnosis and prognosis assessment of prostate cancer. TO-PRO-3 (a stoichiometric dye) for staining of the tissue specimens was used[1]. After applying the staining procedure, 3-D image stacks were acquired with a confocal microscope. To obtain ploidy and texture feature measurements for single nuclei, a segmentation procedure was applied on the images. Thirty-five features thoughtfully chosen from 4 categories of (3-D) texture features were used. In a pilot study we used the 3-D texture feature analyses to discriminate between benign and malignant prostate nuclei[2]. For each patient, a pathologist selected benign regions and malignant regions, and from those two regions at most 300 nuclei were segmented. Together with the texture feature analysis, ploidy measurements were performed on the segmented nuclei from the 3-D image stack. The best results to discriminate between benign and malignant cell nuclei were obtained when multivariate statistics using Linear Discriminant Analysis was employed instead of ROC analysis. We have shown that we are able to successfully discriminate between benign and malignant nuclei in 89% of the cases[3]. In the successive studies that were performed, the many technical difficulties to obtain clinically useful analysis of 3-D nuclear chromatin distributions in prostate tissue have been overcome. It is now possible to successfully perform such analysis, although expensive equipment is required and throughput is low. Therefore, by incorporating the sensitivity of nuclear texture features to detect small nuclear chromatin differences an earlier diagnosis can possibly be made.

References

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