PROSTATE CANCER

Nuclear irregularity is a predictor of clinical outcome

Nuclear roundness variance (NRV) is better able to identify aggressive phenotypes of prostate cancer than Gleason score, according to a team at Johns Hopkins University School of Medicine.

The progression to malignancy within prostate tissue is associated with an increase in irregularity of the nuclear border. This is owing to changes in nuclear structure and DNA content, especially in chromatin organization, via activation of oncogenes and chromatin remodeling genes. Thus, NRV acts as a measure of pleiomorphism, which reflects heterogeneity in nuclear shapes—a well-known feature of malignancy.

The team, led by Robert Veltri, at the James Buchanan Brady Urological Institute, determined the prognostic value of NRV for prostate cancer progression, metastasis and prostate cancer-specific death-free survival in a cohort of 116 men followed up for a mean of 17 years. Using tissue collected during radical prostatectomies performed between 1975

and 1991, they calculated the NRV of 150 randomly selected nuclei in each patient sample, and evaluated how accurately NRV was able to predict all three clinical outcomes compared to Gleason score, currently the most commonly used predictor of prostate cancer progression.

Their studies showed that NRV values were significantly higher in patients with prostate cancer progression, metastasis and prostate cancer-specific death, whilst Gleason score was significantly higher only in patients with disease progression. The predictive accuracy of NRV (measured as change in concordance index) increased from progression, through metastasis, to prostate cancer-specific death-free survival. In addition, the concordance index for NRV was significantly greater than that of Gleason score for metastasis and prostate cancer-specific death survival predictions, indicating that NRV is a more accurate predictor of these clinical outcomes than Gleason score.

Despite several studies in the 1980s demonstrating the potential prognostic utility of assessing nuclear morphology in a variety of tumor types, this technique has fallen out of favor. It is time-consuming, and the cell morphology measurement system used for cell tracing has been unavailable commercially since 1993.

The team's conclusions could spark renewed interest in a prognostic marker which appears valuable in assessing the aggression of prostate cancer phenotypes. They are currently collaborating in the development of an automated high-resolution imaging system, to bring the use of NRV as a prognostic factor back into pathology workups.

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Original article Veltri, R. W. *et al.* Nuclear roundness variance predicts prostate cancer progression, metastasis and death: a prospective evaluation with up to 25 years of follow-up after radical prostatectomy. *Prostate* **70**, 1333–1339 (2010)