Multicenter validation study of a urine-based molecular biomarker algorithm to predict high-grade prostate cancer.

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BACKGROUND
The major challenge in prostate cancer (PCa) diagnostics is to improve the early detection of high-grade PCa. Ideally, PCa-specific biomarkers could be obtained non-invasively, for example derived from urine. Recently, a promising urinary mRNA biomarker combination was identified8,9, that predicts high-grade PCa upon biopsy.

OBJECTIVES
To develop a model combining HOXC6-DLX1 mRNA expression levels and traditional risk factors to accurately predict high-grade PCa upon prostate biopsy. To assure robustness of the proposed risk score the model was validated in an independent cohort.

MATERIAL & METHODS
Two prospective multicenter studies
- Cohort A: n=492 (41% PCa of which 51% GSz7)
- Cohort B: n=371 (47% PCa of which 50% GSz7)

Men scheduled for prostate biopsy
- PSA >3.0 ng/ml / abnormal DRE / family history
- Urine collection first-void, post-DRE
- Biomarker mRNA levels were measured using RT-qPCR.
- Quantification of the mRNA using the Delta Delta Ct (ΔΔCt).
- Development of the high-grade PCa risk score in training Cohort A and validation in Cohort B.

RESULTS
HOXC6-DLX1 scores in relation to biopsy Gleason scores
- The HOXC6-DLX1 score was significant positively associated with the Gleason score upon biopsy.

Performance of the HOXC6-DLX1 score in the PSA ‘grey zone’ (4-10 ng/ml)
- Consistent performance of the HOXC6-DLX1 score in patients with low PSA values.

CONCLUSION
HOXC6-DLX1 score urine test combined with traditional clinical risk factors:
- Prediction of high-grade PCa upon prostate biopsy.
- Positive association with higher Gleason score.
- Consistent diagnostic performance in PSA ‘grey zone’.

Using the HOXC6-DLX1 risk score: non-invasive solution to select patients for prostate biopsy, and to reduce the amount of unnecessary biopsies.