

Prevention of Over-diagnosis and Over-therapy of Prostate Cancer with DNA-Cytometry

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In Germany alone over 70,000 prostate cancers are newly detected every year. Mortality from this cancer is below 15%; e.g. only 13 % was reported in 2002 in the USA (SEER Cancer Statistics, 2002¹).

Currently, 53% of prostate cancer patients are subjected to radical prostatectomy in Germany (Weißbach L, 2011²). Yet, PSA screening currently renders between 30% and 50% of low-risk, i.e. clinically insignificant cancers of the prostate (Roemeling et al., 2006³; Carter et al., 2003⁴), defined as 1 - 3 small (≤ 3 mm) foci with Gleason-scores 6 or 7a. However, the interobserver reproducibility of this subjective grading is less than 50% (Burchardt et al., 2008⁵) and thus may not be sufficient. Additional markers are therefore desired that would specify the risk of tumor-progression of individual patients. It has been shown that DNA-cytometry adds significant prognostic information to the Gleason score; to date 27 scientific articles have already been published demonstrating that including DNA grading provides objective and more reproducible diagnosis (Engelhardt, 2012⁶). It has been therefore advocated that DNA-grading of malignancy should be routinely added to the Gleason score.

German S3-guidelines currently recommend Active Surveillance or Watchful Waiting to low risk prostate cancer patients as an alternative to invasive treatment. Active Surveillance includes regular PSA control, digital rectal examinations and control biopsies. Over 40% of all prostate cancers are DNA-diploid with a low proliferation fraction (Engelhardt, 2012⁶). DNA-diploid (type A) micro-carcinomas of the prostate with low proliferation fraction should be included in the Active Surveillance based strategy, whereas patients with tetraploid, x-ploid and multiploid micro-carcinomas should receive a potentially curative therapy. This strategy has been recommended by the German health insurance "Barmer-GEK". The two German pathology societies, Deutsche Gesellschaft für Pathologie (DGP) and the Bundesverband Deutscher Pathologen (BDP) already recommend that DNA-grading by cytometric investigation may be performed in addition to the Gleason-Grading in cases where Active Surveillance is a potential course of action. Currently this approach is further investigated in a prospective cohort study of 280 patients.

In addition to the presentation, a commercially available device will be demonstrated for manual and semi-automated DNA-measurements on individual cells prepared from pre-existing prostate core biopsies.

¹ seer.cancer.gov/statfacts/html/prost.html. 24.01.2012

² Weißbach L: Informationen der HAROW-Studie zur Therapie des lokal begrenzten Prostatakarzinoms. 2011; www.harow.de

³ Roemeling S, Roobol MJ, Postma R, Gosselaar C, van der Kwast T, Bangma CH, Schröder F: Management and survival of screen-detected prostate cancer patients who might have been suitable for active surveillance. *Europ Urology*. 2006; 50: 475-482

⁴ Carter CA, Donahue T, Sun L et al. : Temporarily deferred therapy (watchful waiting) for men younger than 70 years and with low risk localized prostate cancer in the prostate-specific antigen era. *J Clin Oncol*. 2003 ; 21 : 4001-4008

⁵ Burchardt M, Engers R, Müller M, Burchardt T, Willers R, Epstein JI, Ackermann R, Gabbert HE, de la Taille A, Rubin MA : Interobserver reproducibility of Gleason-grading: evaluation using prostate cancer tissue microarrays. *J Cancer Res Clin Oncol*. 2008; 134: 1071-1081

⁶ Engelhardt M: PSA-Kinetiken als Indikationsstellung zur Prostatastanziopsie. Med. Diss., Heinrich-Heine-University Düsseldorf, Germany