Topography of molecularbiological micrometastases in lymph nodes of prostate cancer patients treated with radical prostatectomy and extended lymphadenectomy

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INTRODUCTION & OBJECTIVES: In the present study we sought to establish a method for molecular detection and localization of lymph node metastases that are not identified with standard histopathological examination using quantitative reverse-transcriptase (qRT)-PCR. We present results of the first 30 prostate cancer patients treated with radical prostatectomy (RP) and extended lymphadenectomy (eLAE).

MATERIAL & METHODS: All prostate cancer patients were treated with RP and eLAE. Inclusion criteria were Gleason Score $\geqslant$ 7 or PSA $\geqslant$ 10 ng/ml or clinical T-stage $\geqslant$ 2b (intermediate and high risk prostate cancer). Each lymph node (LN) was divided into two halves. One half was examined by a pathologist applying conventional histopathology. The second half was assessed by frozen section histopathology as well as prepared for RNA extraction followed by qRT-PCR. For detection of occult disseminated prostate cancer cells in LNs we established a qRT-PCR protocol with3 the markers prostate specific antigen (PSA) and prostate-specific membrane antigen (PSMA) which are expressed in prostate cancer cells but not in blood or lymph nodes. 201 LNs of 19 bladder cancer patients were used to establish a threshold for qRT-PCR results. qRT-PCR was determined positive if at least one marker (PSA and/ or PSMA) was above the threshold.

RESULTS: 717 LNs of 30 patients (median 24 LNs/ patient) were analyzed by conventional histopathology and qRT-PCR. Histopathological examination was positive (pN1) in 25 (3.5%) LNs of 6 (20%) patients. All of them were confirmed to be positive by qRT-PCR. 81 (11.7%) out of 692 histopathologically negative LNs (pN0) were positive using qRT-PCR corresponding to 14 (58.3%) out of 24 node-negative patients (pN0). All patients with Gleason score 8-10 had either histopathological positive LNs or qRT-PCR-positive LN-micrometastasis. 60% of histopathologically positive lymph nodes were located outside the obturatoric region. More than one half (56%) of qRT-PCR-positive LN-micrometastases were located outside the obturatoric region.

CONCLUSIONS: Results of our mapping study support extended lymphadenectomy in order to remove LN-micrometastases in patients with intermediate and high risk prostate cancer. Follow-up data will validate if there is a correlation between the molecular detection of occult disseminated tumor cells in LNs and biochemical recurrence.