Transcriptome wide analysis of MRI-targeted biopsy and matching surgical specimens from high-risk prostate cancer patients treated with radical prostatectomy

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Background: The index lesion defined as the most suspicious lesion on multiparametric MRI (PIRADS) may be representative of final pathology and could be amenable to focal therapy. To what extent this lesion and other foci with potentially lethal cancer subclones contribute to cancer progression is one of the key questions in current research. Here we connect prostate imaging with high-precision spatial annotation of prostate biopsies and transcriptome-wide molecular characterization of intratumoral heterogeneity.

Methods: This study includes 11 patients diagnosed with high-risk prostate cancer on MRI-targeted biopsy (Bx) and treated with radical prostatectomy (RP) at the University of Heidelberg. Five tissue specimens were collected for each patient: index tumor RP based on highest Gleason grade, index tumor prostate Bx, 2 benign tissue biopsies (adjacent to and far away from the index tumor), and a second tumor focus on Bx if available. Whole transcriptome RNA expression was profiled for each sample. Genomic prostate cancer signatures from the Decipher Genomic Resource Information Database (GRID) were used to compare the genomic signal in MRI invisible foci vs MRI visible tumors using Pearson's correlation. GRID signatures were also used to assess intratumoral genomic heterogeneity using hierarchical clustering.

Results: Ten RP and 23 Bx samples passed quality control measures. Gene expression between RP and index Bx, but not adjacent benign samples was highly correlated. The distribution of low and high PIRADS samples in the analysis was 10 and 11 respectively. The genomics of all 10 low PIRADS samples resembled benign tissue and 10 of the 11 high PIRADS samples resembled prostate cancer tissue as determined by the tumor vs normal classifier. A strong association was observed between PIRADS v2 and Decipher ($r = 0.805$, $p < 0.001$) as well as the genomic Gleason grade classifier score ($r = 0.813$, $p < 0.001$) which predicts patients with high grade disease. When clustering high PIRADS samples by GRID signature scores, most samples clustered tightly by patient. One patient showed unique tumor biology in the index vs secondary lesion suggesting the presence of intrapatient heterogeneity.

Conclusions: MRI-targeted Bx genomics show excellent correlation with RP-genomics and confirm the information captured by PIRADS. Genomics also allow exploration of intratumoral heterogeneity suggesting utility in profiling multiple foci identified by MRI.

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