Molecular dissection of magnetic resonance imaging visible and invisible prostate cancer: Biological insights and therapeutic implications

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Background: While multiparametric magnetic resonance imaging (mpMRI) of the prostate has improved disease detection, up to 20% of patients with negative mpMRI harbor high grade prostate cancer (PCa). In this study, we sought to characterize and compare the molecular profiles of mpMRI visible and invisible PCa.

Methods: Patients who underwent mpMRI prior to radical prostatectomy were identified for this IRB-approved study. mpMRI for each patient was reviewed by a radiologist with expertise in prostate mpMRI and histopathology reviewed by a genitourinary pathologist. Whole-mount histopathology was co-registered with axial mpMRI images. DNA and RNA were co-isolated from all tumor foci pre-identified on formalin-fixed paraffin-embedded specimens. High depth, targeted DNA and RNA next generation sequencing was performed to characterize the molecular profile of each tumor focus using the Oncomine Comprehensive Panel (DNA sequencing) and a custom targeted RNAseq panel assessing PCa relevant genes.

Results: A total of 26 primary tumor foci from 10 patients were analyzed. The median number of PCa foci was 3. Of the 14 (54%) invisible lesions on mpMRI, 5 (36%) were Gleason 3+4=7. We detected high-confidence prioritized genetic mutations in 54% (14/26) of tumor foci, 43% (6/14) of which were in mpMRI-invisible lesions. Additionally, 64% (9/14) of lesions exhibiting prioritized mutations were Gleason 7. Notable point mutations were in *APC, AR, ARID1B, ATM, ATRX, BRCA2, FAT1, MAP3K1, NF1, SPEN, SPOP, TP53,* and a frameshift mutation was detected in *SOX2.* The expression profile of mpMRI visible and invisible lesions were similar.

Conclusions: We found no significant difference in the molecular profile of visible and invisible cancer foci on mpMRI. However, 36% of mpMRI invisible lesions exhibited biologically significant mutations. More work is needed to further characterize the molecular basis for mpMRI prostate cancer visibility.

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