Apparent diffusion coefficient (ADC) predicts risk of disease upgrading in men on active surveillance (AS)

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Background
- No consensus on how to best monitor patients on active surveillance (AS)
- Prior studies have shown an association between apparent diffusion coefficient (ADC), a measurement of water molecule movement on diffusion-weighted mpMRI, and clinically significant prostate cancer (PCa)

OBJECTIVE: To determine if ADC on baseline MRI is associated with increased risk of upgrading to Grade Group ≥2 (Gleason Grade ≥3+4) while on AS.

Methods

COHORT
- Retrospectively identified 244 men from the Johns Hopkins AS registry with baseline prostate mpMRI (2010 – 2015) showing lesions assessed with ADC. Median time in AS prior to mpMRI was 16.5 months (IQR 7 – 51.5)

MRI REVIEW
- Due to inconsistencies in acquiring and reporting of ADC values in the original radiology reports, 2 expert radiologists reviewed all 244 cases and re-scored the original index lesions, using the mean ADC from maps generated with b-values 50 and 800, or 0 and 800

STATISTICAL ANALYSIS
- Study group characteristics at time of mpMRI were assessed and compared between upgraders (GG=1) and non-upgraders (GG ≥2)
- Association between baseline ADC and upgrading to GG ≥2 was evaluated using survival analysis and an optimal cut-off for ADC was determined using an outcome oriented method (Contal and O’Quigley)
- Association between ADC and upgrading was adjusted for age, PSA density (PSAD), and risk status (low-risk [LR] vs. very low-risk [VLR]).

Results
- Of the 244 men included in our study, 71 (27%) upgraded to GG ≥2 with a median post-MRI follow-up of 16 months (IQR 5 – 28).
- Compared to non-upgraders, upgraders had higher PSAD (median: 0.10 vs. 0.08, p = 0.002), higher proportion of low-risk cancer (51% LR vs. 38% VLR, p = 0.005), and lower ADC values on baseline mpMRI (median: 1043 vs. 1147, p = 0.01). There was no significant decrease in originally-reported ADC values (median: 861 vs. 880, p = 0.38)
- Significantly higher proportion of men with baseline ADC <1128 upgraded compared to ADC ≥1128 (39% vs. 18%, respectively, p <0.001) [Fig 1]
- Men with ADC < 1128 had significantly higher risk of upgrading compared to ADC ≥1128 (p < 0.001) [Fig 2]
- On univariate analysis ADC was significantly associated with upgrading to GG ≥2 (as categorical variable, <1128 vs. ≥1128: HR = 2.49, 95% CI = 1.5 – 4.15, p = <0.001; as continuous variable (per 100-unit decrease: HR = 1.13, 95% CI = 1.03 – 1.23, p = 0.009)
- Adjusting for age PSAD and risk-status (LR vs. VLR), baseline ADC remained significantly associated with upgrading to GG ≥2 (as categorical variable, <1128 vs. ≥1128: HR = 2.86, 95% CI = 1.66 – 4.90, p = <0.001; as continuous variable (per 100-unit decrease: HR = 1.13, 95% CI = 1.03 – 1.24, p = 0.008)

Limitations
- Retrospective study
- Excluded men who underwent MRI, but did not have an ADC value reported
- Single institution study, with more selective criteria for participation in active surveillance

Conclusions
- For men in AS, lower ADC value on baseline MRI is associated with increased risk of upgrading to GG ≥2 and thus could be a useful component of multivariable risk prediction tools
- These data suggest that a clinically relevant ADC cut-off for men who are in AS (low volume GG1) is likely to be higher than previously reported ADC cut-offs for identifying high grade cancer (750 x 10^-6 mm²/s).