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Defining the prevalence of inherited DNA damage repair genetic variants (DDRv) in men with prostate cancer (PCa) detected by PSMA PET.

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Background: Approximately 12% of patients (pts) with metastatic PCa (mPCa) identified by conventional imaging harbor DDRv. The increased use of PSMA PET has identified a group of pts with extra-prostatic PCa which is not apparent on conventional imaging and for whom the frequency of germline DDRv testing remains unknown. **Methods:** A single-institution retrospective analysis of patients with PCa detected by PSMA PET who had also undergone germline genetic testing was undertaken. Data collected included PSA level at time of PSMA PET imaging, stage/Gleason score at diagnosis (dx), rationale for germline testing, castration status, and whether the metastatic disease identified on PSMA PET represented de novo or recurrent mPCa. Germline sequencing results were evaluated for 16 DNA damage repair genes: *ATM, ATR, BAP1, BARD1, BRCA1, BRCA2, BRIP1, CHEK2, GEN1, MSH2, MSH6, NBN, PALB2, PMS2, RAD51C,* and *RAD51D.* The frequency of DDRv was evaluated in groups defined by PSMA imaging results: localized (N0M0), Node-Positive (N+M0), metastatic (M+) PCa. **Results:** Of 795 PCa pts who underwent germline testing and 2101 PCa pts who underwent PSMA PET imaging, 386 had undergone both, and constitute the study cohort. In the study cohort the distribution of PCa extent identified by PSMA PET was: 81/386 (21.0%) N0M0; 76/386 (19.7%) N+M0; 229/386 (59.3%) M+. There were no statistically significant differences in the prevalence of DDRv with regards to age, Gleason score at dx, PSA at time of imaging, castration status at time of imaging, rationale for germline testing, or if metastatic, whether de novo or recurrent. The distribution of DDRv is shown in the table. There were no statistically significant differences between groups. **Conclusions:** The overall frequency of pathogenic germline DDRv in PCa pts who had undergone PSMA PET imaging was 4.66%, considerably lower than what has been reported in men with mPCa detected with conventional imaging. The presence or absence of extra-prostatic PCa detected by PSMA PET imaging did not appear to affect the frequency of DDRv. Validation of these findings in other cohorts will be important to guide recommendations for germline genetic testing in the growing group of PCa pts undergoing PSMA PET imaging. Research Sponsor: None.

Pts with DDRv	Total	Localized PCa (N0M0)	Any extra-prostatic PCa (N+ M0) + (M+)	Node Only (N+M0)	Any Metastasis (M+)
N	18/386	4/81	14/305	2/76	12/229
%	4.66%	4.94%	4.59%	2.63%	5.24%