MP28-02
QUANTITATIVE MEASUREMENT OF PTEN LOSS IMPROVES RISK ASSESSMENT IN PROSTATE CANCER

Tamara Jamaspishvili*, Kingston, Canada; Palak Patel, Kingston, Canada; Yi Niu, Dalian, China; People’s Republic of; Thiago Vidotto, Isabelle Caven, Rachel Livergant, Winnie Fu, Kingston, Canada; Veronica Ouellet, Montreal, Canada; Clarissa Picanço, São Paulo, Brazil; Madhuri Koti, Nathan How, Kingston, Canada; Fred Saad, Anne-Marie Mes-Masson, Montreal, Canada; Tamara Lotan, Baltimore, MD; Jeremy Squire, São Paulo, Brazil; Yingwei Peng, David Berman, Kingston, Canada; Rodolfo Reis, São Paulo, Brazil

INTRODUCTION AND OBJECTIVES: Loss of the PTEN tumor suppressor is a powerful prognostic biomarker in prostate cancer. However, the significance of tumor heterogeneity and partial loss is not clearly defined, nor are interactions between PTEN loss and the TMPRSS2-ERG fusions, the most common genetic aberration found in prostate cancer. Taking into account TMPRSS2-ERG status, we aimed to define and quantify patterns of PTEN loss that best account for the risk of recurrence in low and intermediate-risk prostate cancer patients who underwent radical prostatectomy.

METHODS: Tissue microarrays comprising a training (n=410) and validation (n=272) cohorts were constructed and PTEN protein levels were measured using automated clinical grade immunohistochemistry assays. PTEN loss was quantified per cancer cell and per cancer core using digital and visual scoring. Thresholds for PTEN loss were determined by log-rank statistics and Kaplan-Meier survival estimator. Cox’s proportional hazards models were used to determine the prognostic significance of selected cut-offs of PTEN loss along with multiple pathological and clinical variables.

RESULTS: PTEN loss in >65% of cancer cells (digital scoring)/per case or >50% of TMA cancer cores/per case (visual scoring) were associated with a 50% reduction in recurrence free survival (RFS) (% cancers, HR=4.22, p<0.001 and % cores, HR=2.75, p=0.002 in multivariate analysis, respectively). Median RFS was 10.2 yrs for any PTEN loss (p<0.001) vs 5.4 yrs for >65% cells with PTEN loss (p<0.001) in Kaplan-Meier analysis. Cases with PTEN loss but without TMPRSS2-ERG fusion had the shortest RFS (4.1 yrs) compared to cases with TMPRSS2-ERG fusion (10 yrs; p=0.001). Finally, PTEN loss was found almost exclusively in dominant tumor foci (50/54 cases).

CONCLUSIONS: Degree of PTEN protein loss is strongly associated with disease progression. PTEN loss is independently associated with increased risk of disease progression regardless ERG status. Its high level of intra-focal heterogeneity and strong association with dominant foci indicates that PTEN assessment is vulnerable to sampling error and might influence on prognostic assessment of biopsy samples. Any PTEN loss may not be a “red flag” for poor prognosis. Quantitative assessment of PTEN loss may improve risk stratification of patients with localized prostate cancer.

Source of Funding: Work by T.J., P.P. and D.M.B. was awarded by Prostate Cancer Canada (PCC) and is proudly funded by the Movember Foundation-Grant #T2014-01. T.J. was supported by a Translative Pathology Fellowship funded by the Ontario Institute for Cancer Research (OICR) through funding provided by the Government of Ontario. P.P. was supported by Terry Fox Transdisciplinary Fellowship. V.O., A.-M.M.-M and F.S. are researchers of the Centre de recherche du Centre hospitalier de l’Université Montréal which receives support from the FRQS. Biobanking was done in collaboration with the Réseau de Recherche sur le cancer of the Fonds de Recherche Québec - Santé (FRQS) that is affiliated with the Canadian Tumor Repository Network (CTRNet). TMA construction was supported by the Terry Fox Research Institute. F. Saad holds the Montreal University Research Chair in Prostate Cancer. J.A.S. and T.V. are supported by FAPESP grant no. 2015/09111-5. J.S. by CNPq Bolsa Produtividade em Pesquisa - Nível PQ-1B grant no. 306864/2014-2. M.K. is supported by funding from Prostate Cancer Foundation, Terry Fox Research Institute-Canadian Prostate Cancer Biomarker Network and Canadian Institutes for Health Research.

MP28-03
DO ELDERLY MEN (>75) HARBOR MORE AGGRESSIVE PROSTATE CANCER? COMPARISON OF DECIPHER AND PAM50 TESTS AMONG DIFFERENT AGE GROUPS

Hanan Goldberg*, Jaime Omar Herrera Cáceres, Toronto, Canada; Maria Santiago-Jimenez, Nick Fishbaen, Elai Davicioni, Vancouver, Canada; Zachary Klaassen, Thenappan Chandrasekar, Christopher Wallis, Dixon Woon, Robert Hamilton, Girish Kulkarni, Alejandro Berlin, Neil Fleshner, Toronto, Canada

INTRODUCTION AND OBJECTIVES: Age is an important prognostic factor in oncology. Over 20% of men diagnosed with prostate cancer (PC) are > 75 years old. In the growing elderly population, objective methods for predicting outcomes beyond chronologic age are necessary in order minimize the likelihood of withholding curative treatment when warranted. Herein, we describe and analyze age-related differences in clinico-genomic prognostic indices of aggressiveness in localized PC.

METHODS: Clinical and genomic data for 8355 patients from the Decipher Genomic Resource Information Database (GRID; NCT02609269) was obtained. Conventional and genomic prognostic indices including Decipher GC scores, PAM50 molecular subtypes (e.g. luminal A/B or basal) NCCN risk groups and Gleason groups (GG) were stratified by age using multivariable logistic regression analyses (MLRA).

RESULTS: With increasing decile of age, we observed a higher proportion of high GG and higher Decipher scores compared to patients <70 years old. Overall, there was a statistically significant increase in the proportion of patients with high Decipher scores with increasing age among GG1 and GG2 (<55 to 10.2%, 30.7%; 55-60 to 15.4%, 25.6%; 60-65 to 15.9%, 29.7%, 65-70 to 16.9%, 28.2%, 70-75 to 17.9%, 30%, and >75 to 20.3%, 37.3%, respectively). Furthermore, the prevalence of the PAM50 luminal B subtype (associated with worse prognosis) increased with age among GG1 and GG2 (<60 to 22.4%, 40%, 60-65 to 29.1%, 41.7%, 65-70 to 28.2%, 39.2%, 70-75 to 30%, 43.4%, 75-80 to 33.5%, 44.3%, >80 to 34.2%, 52%, respectively). Among higher grade tumors (GG 3-5), no statistically significant differences between the different age groups were observed. MLRA demonstrated that in addition to higher T stage, PSA and GG, each age decile entailed a 20% increased risk for a high Decipher score (OR 1.2, 95% C.I 1.11-1.3, p < 0.001).

CONCLUSIONS: Older men with lower grade tumors, as opposed to higher grade tumors, harbored worse disease based on genomic risk models. The accepted paradigm of elderly PC patients being treated conservatively based solely on chronologic age, needs to be changed. We provide evidence suggesting the utility of clinical-