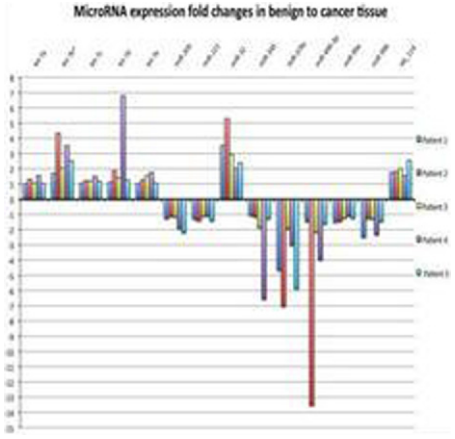
METHODS: RNA was extracted from foci of prostate cancer as well as areas of benign glandular architecture from paraffin embedded radical prostatectomy specimens from 5 patients using the "Recover-All™ Total Nucleic Acit Isolation Kit for Formalin- Fixed Paraffin Embedded Tissues" (Applied Biosystems, Carlsbad, CA). Foci of prostate cancer were outlined during secondary review by a uropathologist. Subsequently, miRNA profiles were analyzed using an Illumina miRNA microarray profiling assay, and levels of expression were analyzed and compared using the associated GenomeStudio software platform with internal controls for all reported miRNAs with p-values <0.05 (Illumina, San Diego, CA).

RESULTS: Of the 5 patients in the study, age ranging from 49 to 68 years, all had preoperative PSA$>$5.4 and pathologic Gleason sum of 7. Analysis of differential expression revealed 7 miRNAs that were consistently upregulated and 7 miRNAs consistently downregulated in cancer foci compared to non-cancerous areas in all 5 patients. Figure#1 displays the fold change in miRNA expression for these 14 miRNAs of interest for each patient analyzed.

CONCLUSIONS: We have identified 14 specific miRNAs for which expression varies consistently from areas of cancerous glands compared to benign glands in patients with prostate cancer. These miRNA "signatures" found in this pilot study will be further investigated in an effort to better define miRNA significant in prostate cancer, not only to serve as a potential biomarker but possibly as a route to better understand the genetic and epigenetic roles of carcinogenesis in these patients.



Source of Funding: None

Prostate Cancer: Localized

Moderated Poster 41

Monday, May 16, 2011 **3:30 PM-5:30 PM**

1292
PROSTATE MRI FINDINGS PRIOR TO COMMENCING ACTIVE SURVEILLANCE AMONG MEN WITH LOW RISK PROSTATE CANCER

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INTRODUCTION AND OBJECTIVES: Increasing evidence suggests that early failures among men on active surveillance (AS) are due to under appreciation of the amount of disease at baseline. The role of MRI prior to AS has not been established. We report our experience with prostate MRI among unselected consecutive men with low risk prostate cancer (PCa).

METHODS: We prospectively enrolled men with low-grade, low risk, localized PCa (clinical stage T1c-T2a, Gleason score $\leq$6, no Gleason pattern 4, serum PSA $\leq$ ng/mL). After enrolment and consent, all patients underwent multiparametric endorectal coil MRI scanning. Patients with troubling discrepant findings (TDFs) between MRI and initial biopsy were offered a second confirmatory biopsy (MRI guided). The primary outcome was the percentage of patients by a screening MRI who had TDFs evidenced by more apparent disease than that found at biopsy. We further aimed to recognize clinical parameters (such as age, prostate volume, PSA, PSA density, number of cores positive and percent of cancer in core) associated with TDFs. The study population was stratified into 3 groups: Group 1- No cancer detected on MRI; Group 2-cancer characteristics on MRI concordant with initial biopsy; Group 3- cancer characteristics on MRI demonstrating TDF. We performed a univariate analysis using one way ANOVA to assess the differences in clinical parameters between the groups.

RESULTS: The study cohort consisted of 60 consecutive patients. Of these, MRI did not detect any cancer in 23 patients (38%) while MRI and initial biopsy were concordant in 24 patients (40%). TDF was detected among 13 patients (22%) with 10/12 of these findings confirmed on biopsy (one patient refused biopsy). The average unidimentional size of these TDF¡¯s was 1.5 cm (range 0.5–3.2 cm), and 50% had Gleason sum upgrading. Zonal distribution of these lesions were: anterior (55%), peripheral (25%) and transition zone (20%).On univariate analyses, only PSA density was significantly elevated among those patients upstaged by MRI compared to those with no cancer on MRI (0.19$\pm$.15 vs. 0.09$\pm$.06 ng/ml/cc, respectively p$=$0.021).

CONCLUSIONS: MRI appears to discover underappreciated large volume disease in up to 22% of patients with low risk prostate cancer who undergo AS. This number is consistent with early ¡°progression¡± rates and likely explains many of these cases. MRI prior AS should be strongly considered as part of standard patient care and especially among patient with elevated PSA density.

Source of Funding: Prostate Cancer Canada

1293
PREVIOUSLY DEVELOPED SYSTEMS-BASED BIOPSY MODEL (PROSTATE PX+) IDENTIFIES FAVORABLE-RISK PROSTATE CANCER FOR MEN ENROLLED IN AN ACTIVE SURVEILLANCE PROGRAM

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INTRODUCTION AND OBJECTIVES: We previously developed two independent pre-treatment prostate cancer risk assessment (systems) models (Prostate Px+) using the patient's own prostate needle biopsy (PNB) specimen and 8-year median outcome data post radical prostatectomy. We sought to determine the performance of these disease progression models on predicting which patients enrolled in an active surveillance (AS) program are most likely to remain on AS or be treated, by evaluating predictors of disease progression including subsequent biopsy Gleason grade (GG) upgrading and time from AS enrollment to definitive treatment.

METHODS: 100 AS patients (median age 71 years, 92% cT1–T2a, 85% $<=$GS6, median PSA 6.2 ng/mL), with overall 8-year median follow up and available diagnostic PNB specimens were evaluated with our systems pathology platform as previously reported. Disease progression models predicting either GG upgrading on a subsequent biopsy or time to definitive treatment were evaluated. The AUC/concordance index (CI), PPV, NPV, and hazard ratio with p-value were used to assess models performance.

RESULTS: Utilizing existing model thresholds now applied to clinical endpoints of upgrading and treatment, the Prostate Px+ models were able to accurately identify which AS patients are most likely to not have a Gleason upgrade on a subsequent biopsy (AUC 0.73, NPV 0.86, PPV 0.60). In addition, we were able to predict with good

accuracy which patients are at risk for requiring therapy while on AS (hazard ratio 3.4, p value 0.006). The correlation of Gleason rise with treatment had a chi-square of 16.45, $p<0.001$.

CONCLUSIONS: Prognostic systems-based models using the patient's own prostate NB specimen are able to accurately identify AS patients at risk for Gleason upgrading and / or requiring treatment while on protocol. Identifying such patients may enhance the primary treatment decision process.

Source of Funding: None

1294

ACCEPTANCE AND DURABILITY OF SURVEILLANCE AS A MANAGEMENT CHOICE IN MEN WITH SCREEN-DETECTED, LOW-RISK PROSTATE CANCER: IMPROVED OUTCOMES WITH STRINGENT ENROLLMENT CRITERIA

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INTRODUCTION AND OBJECTIVES: To analyze the acceptance rate and durability of surveillance among contemporary men with low-risk prostate cancer managed at a large, U.S. academic institution.

METHODS: Patients with low-risk parameters on initial and repeat biopsy were offered surveillance regardless of age. Regular clinical evaluation and repeat prostate biopsy were recommended every 1–2 years, and intervention was recommended based on adverse clinical and pathologic parameters on follow-up. Acceptance rate of active surveillance, freedom from intervention, and freedom from recommended intervention were measured.

RESULTS: Of 202 low-risk patients, 86 (43%) chose immediate treatment and 116 (57%) underwent repeat biopsy for consideration of surveillance. Intervention was recommended after initial repeat biopsy in 27 (23%) men due to higher risk features, leaving a total of 89 men on surveillance. Over a median follow-up of 33 months, 16 men were ultimately treated and 8 were recommended to undergo treatment due to adverse clinical features on subsequent evaluations. Of the men on surveillance, the 3-year freedom from intervention and freedom from recommended intervention was 87% (95% CI, 78–93) and 93% (95% CI, 85–97),respectively.

CONCLUSIONS: Acceptance of surveillance (57%) in low-risk patients in this series is substantially higher than previous reports, and approximately one-third of these patients are ultimately managed by surveillance using stringent criteria. The risk of re-classification to a more aggressive cancer over short-term follow-up in appropriately selected patients is low.

Source of Funding: None

1295

ANDROGEN DEPRIVATION THERAPY AND MORBID OBESITY: DO THEY SHARE CARDIOVASCULAR RISK THROUGH METABOLIC SYNDROME?

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INTRODUCTION AND OBJECTIVES: Although the use of androgen deprivation therapy (ADT) has resulted in improved survival in men with advanced prostate cancer, the resulting hypogonadism is associated with profound adverse effects comparable to those found in morbid obesity, being cardiovascular risk among the most lethal. Evaluate metabolic syndrome, metabolic abnormalities and cardiovascular risk in patients with prostate cancer under ADT, not under ADT and morbid obese men.

METHODS: This is a cross-sectional study that involves 79 men presenting prostate cancer, of whom 54 under ADT and 25 not under ADT and 91 morbidly obese patients paired by sex and age. To define metabolic syndrome, we used the International Diabetes Federation (IDF) criteria. Metabolic abnormalities, metabolic markers and Framingham score to predict the ten year coronary heart disease risk were compared among patients under ADT, not under ADT and morbid obese.

RESULTS: Patients under ADT presented significantly greater occurrence of diabetes and central obesity and higher levels of total cholesterol and low density lipoprotein (LDL) compared to eugonadal men (Table 1). The mean cardiovascular risk was significantly higher in patients under ADT (39.97 $\pm$ 12.53% vs. 26.09 $\pm$ 14.80%, $p = 0.021$). Morbidly obese and prostate cancer patients under ADT had comparable ten year coronary heart risk disease ($p = 0.054$).

CONCLUSIONS: This study suggests that patients under ADT show higher prevalence of metabolic abnormalities and cardiovascular risk similar to those found in morbidly obese subjects. It is possible that both process share cardiovascular risk through metabolic syndrome.

Table 1 γÇô Metabolic abnormalities and metabolic markers between prostate cancer patients under and not under androgen deprivation therapy

	Under ADT (n = 54)	Not Under ADT (n = 25)	p value
Metabolic Abnormalities			
Hypertension*	39 (72.2%)	16 (64.0%)	0.335
Metabolic Syndrome	29 (53.7%)	6 (24.0%)	0.052
Diabetes	14 (25.9%)	3 (12%)	0.043
Hypertrigliceridemia**	17 (31.4%)	7 (28%)	0.782
Central Obesity***	38 (70.3%)	9 (36.0%)	0.008
Metabolic Markers			
Age (years)	73.06 > 7.57	73.76 > 8.16	0.742
Gleason score	7.25 > 1.27	6.60 > 0.54	0.064
BMI (kg/m²)	25.55 > 4.27	24.79 > 3.08	0.490
Cholesterol (mg/dL)	216.37 > 47.24	193.57 > 51.43	0.049
LDL (mg/dL)	124.58 > 34.26	105.92 > 37.07	0.038
VLDL (mg/dL)	30.50 > 16.68	25.76 > 11.62	0.073
HDL (mg/dL)	61.81 > 21.24	56.78 > 12.78	0.295
Triglicerides (mg/dL)	159.86 > 97.17	179.64 > 195.59	0.562
Fasting glucose (mg/dL)	101.76 > 23.40	103.78 > 18.97	0.747
Abdominal waist (cm)	97.48 > 8.39	91.23 > 21.40	0.031
Systolic pressure (mmHg)	130.18 > 13.93	131.20 > 15.36	0.773
Diastolic pressure (mmHg)	83.98 > 14.45	88.00 > 9.12	0.139

*: defined as systolic pressure γëÑ 140 mmHg or diastolic pressure γëÑ 90 mmHg; **: defined as triglycerides γëÑ 150 mg/dL; ***: defined as abdominal waist γëÑ 94 cm

Source of Funding: None

1296

LOGISTIC REGRESSION MODELING OF FACTORS AFFECTING RATES OF HIGH GRADE PROSTATE CANCER IN THE REDUCTION BY DUTASTERIDE OF PROSTATE CANCER EVENTS (REDUCE) STUDY

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INTRODUCTION AND OBJECTIVES: In the REDUCE study, dutasteride (DUT) compared with placebo (PBO) reduced the risk of biopsy-detectable prostate cancer (PCa) by 23% in men at increased risk of PCa. However, there was no significant difference in the incidence of Gleason 7–10 PCa (6.7% DUT, 6.8% PBO). We developed a multivariate logistic model to evaluate the effect of baseline and post-baseline variables on the incidence of high grade tumors (HGTs) in REDUCE.

METHODS: REDUCE was an international randomized, double-blind, PBO-controlled study. Men received daily DUT (0.5 mg) or PBO for 4 yrs. Eligible subjects included men 50–75 yrs, with prostate specific antigen (PSA) level 2.5–10 ng/ml and a single negative prostate biopsy (6–12 cores) within 6 months of enrollment. Biopsies (10