A BONE SCAN INDEX TO QUANTIFY THE EXTENT OF SKELETAL INVOLVEMENT BY TUMOR CAN BE USED TO PREDICT SURVIVAL IN PROSTATE CANCER PATIENTS

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Introduction: Current diagnostic methods are insufficient when predicting survival in patients diagnosed with aggressive and/or generalized prostate cancer (PCa). Bone Scan Index (BSI) estimates the fraction of the skeleton that is involved by tumor, as well as the regional distribution of the metastases in the bones. BSI have previously been proven to be an additional parameter for patients with a large tumor burden. However, the current manual method is heavily time consuming and acquires special training. The objective of this retrospective study was to evaluate the prognostic power of BSI, obtained from a recently developed automated method, in relation and combination with digital rectal examination (DRE) and Prostate Specific Antigen (PSA).

	Univariate			Adjusted for PSA			Adjusted for PSA and clinical stage		
	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value
Overall (N=314; 57 events)									
BSI			<0.001			<0.001			<0.001
0	Ref	Ref		Ref	Ref		Ref	Ref	
0.01 to 0.05	3.08	1.33, 7.11		3.05	1.32, 7.05		2.95	1.27, 6.82	
0.06 to 1.00	7.68	3.81, 15.5		7.02	3.46, 14.2		5.99	2.95, 12.2	
> 1.0	54.9	25.7, 117		24.9	8.95, 69.1		29.1	11.3, 75.2	
Positive BSI at diagnosis (N=105; 43 events)									
BSI			<0.001			<0.001			<0.001
0.01 to 0.05	Ref	Ref		Ref	Ref		Ref	Ref	
0.06 to 1.00	2.51	1.13, 5.61		2.37	1.06, 5.32		2.02	0.90, 4.53	
> 1.0	18.4	7.66, 44.0		10.3	3.36, 31.5		11.2	3.98, 31.5	

Table 2. Univariate and multivariable Cox proportional hazards regression to evaluate the association between BSI and prostate cancer specific mortality. PSA was entered into the models with log transformed values, and clinical stage was categorized as ≤ T2 vs ≥ T3.

Model	Overall (N=314; 57 events)	Positive BSI at diagnosis (N=105; 43 events)
PSA	0.754	0.753
PSA + BSI	0.824	0.792
PSA + clinical stage	0.810	0.789
PSA + clinical stage + BSI	0.853	0.828

Table 3. Concordance index for various prediction models of prostate cancer specific mortality, with correction for overfit.

Material and method: The Malmö Preventive Medicine (MPP) and the Malmö Diet and Cancer Study (MDCS) are two large population studies that were conducted between 1974 – 1986 and 1991- 1996, respectively. Men born 1921, 1923-1946, 1948-1949 were invited. 26,656 men participated in either one or both of the studies. Up to December 31st 2006, 1809 men were diagnosed with PCa. 75% patient charts were retrieved. 550 patients had a bone scan obtained < 3 month from date of diagnosis. 450/550 of the scans were eligible for automated BSI analysis. A PSA test within <3 month from the date of bone scan were retrieved for 314/450 patients. Death due to PCa (n=57) was determined by review of patient charts. Univariate and multivariable Cox proportional hazards regression was used to evaluate the association between BSI and prostate cancer specific mortality. Kaplan-Meier was applied in order to estimate Pca specific survival. The predictive accuracy for different models was assessed by the concordance index (c-index).

	Entire cohort N=450	Subgroup with PSA < 3 months of BSI N=314
PSA	--	12.0 (6.63, 33.1)
Clinical T Stage		
T1	108 (24%)	81 (26%)
T2	173 (39%)	119 (38%)
T3	147 (33%)	99 (32%)
T4	20 (4%)	13 (4%)
Year of BSI		
1996-2000	257 (57%)	193 (61%)
2001-2006	193 (43%)	121 (39%)
BSI		
0	295 (66%)	209 (67%)
0.01 to 0.05	64 (14%)	44 (14%)
0.05 to 1.00	66 (15%)	43 (14%)
1.01 to 2.00	7 (2%)	6 (2%)
2.01 to 3.00	8 (2%)	4 (1%)
3.01 to 5.50	10 (2%)	8 (3%)
Therapy		
Anti-Androgen	66 (15%)	48 (15%)
GNRH	190 (42%)	120 (38%)
Radiation	30 (7%)	1 (0.3%)
Radical Prostatectomy	145 (32%)	117 (37%)
Anti-Androgen or GNRH before BSI	73 (16%)	25 (8%)

Table 1. Descriptive summary of the entire cohort and of the subgroup with PSA measured within 3 months of BSI. Data are given as median (interquartile range) or frequency (percentage)

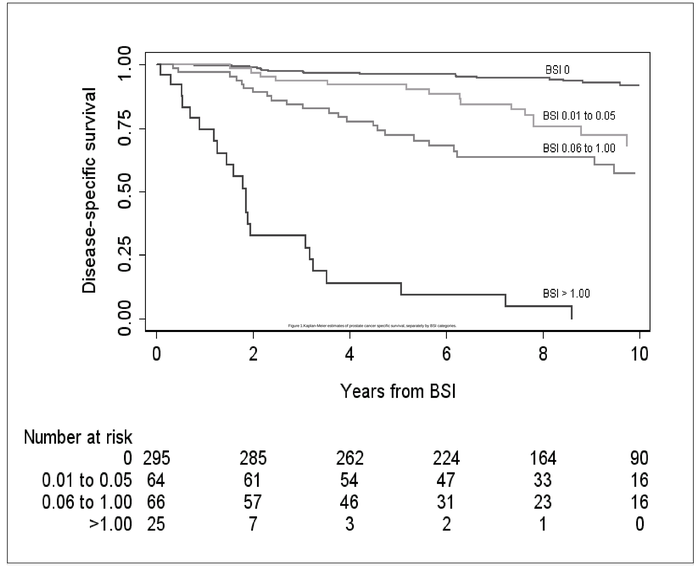

Figure 1.Kaplan-Meier estimates of prostate cancer specific survival, separately by BSI categories.

Conclusion: Our investigation shows that an automated BSI obtained at diagnosis is an independent predictor of PCa death. Adding a BSI to common diagnostic staging parameters (PSA and DRE) importantly enhances prognostic disease information. Our current results strongly suggest that automated BSI should be included as a parameter in clinical practice.