Liquid Biopsy in elderly men with Prostate Cancer

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AgeCare

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Prostata cancer

- I USA and Sweden the most significant cancer
- I DK around 4500 new cases per year
- 75% is between 60 and 80 year of age
- Prevalence at autopsy is between 33 and 50% at men aged more than 80 years
- 10% in family
- Latent (70-90% of the cancers)





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Impact of Screening on Incidence of Metastatic Cancer at Initial Diagnosis: Prostate vs Breast Cancers



Incidence of Cancer That Was Metastatic at First Presentation, United States, 1975-2012.

Data are for breast cancer (SEER historic stage distant) among women 40 years of age or older and prostate cancer (American Joint Committee Stage IV) among men 40 years of age or older.



781 men screened for Pr CA27 men treatedOne saved from dying of PrCA

Prof Fritz H Schröder, MD - for the ERSPC Investigators. Screening and prostate cancer mortality: results of the European Randomised Study of Screening for Prostate Cancer (ERSPC) at 13 years of follow-up. The Lancet, Volume 384, 6 December 2014

Gleason grade of prostate cancer



Normal

Cancer









Low differentiated (gleason grad 5)

Middle differentiated (gleason grad 3)

Prostate Biomarkers

The main challenge is to :

 maintain the benefit of early diagnosis and effective treatment of lethal prostate cancer

While:

- Reducing the number of unecessary biopsies
- Minimizing the diagnosis of non-lethal cancers which is:
 - Costly and results in almost 50% delayed treatment
 - Create anxiety
 - Has unproven long-term value
- Reducing the overall cost of diagnosis and treatment of PCa





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Prostate Biomarkers

Standard Prostate TRUS Guided vs Image-Guided Prostate Biopsies

TRUS Prostate Biopsy











Lucky Strike

- TRUS biopsies are performed randomly
- random biopsies are inaccurate





Risks when performing a biopsy

- Bleeding, prostatitis, sepsis, acute retention
- Mortality < 0.2 % < 61 year of age
 2.5 % at elderly > 70 year of age



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Developing Blood/Urine Liquid Biopsy for Detecting High-Grade Prostate Cancer

Plasma is separated from whole blood

Amicon Ultra-15

All voided urine (60-80ml) is concentrated to 1 ml in an Amicon Ultra-15 Centrifugal Filter Unit.





1 ml of plasma or concentrated urine is loaded onto the NucliSENS easyMAG instrument for extraction

Combined Urine and Plasma Biomarkers are Highly Accurate for Predicting High Grade Prostate Cancer



Multi-Center Prospective Study of 489 Patients



Larger AUC = better accuracy for predicting aggressive prostate cancer

AUC of other tests when applied to aggressive disease

> PHI = 0.70, 0.67^{2,3} PCA3 = 0.68⁴

	Cut-off	Sensetivity		Specificity		NPV		PPV		Total
		≥3+4	≥4+3	≥3+4	≥4+3	≥3+4	≥4+3	≥3+4	≥4+3	Missed
Actual										
Dradictad	Low	86%	96%	57%	59%	90%	98%	46%	46%	21 (4.3%)
Predicted	Standard	91%	97%	51%	44%	93%	98%	44%	52%	13 (2.7%)
positive	High	97%	99%	36%	37%	97%	99%	40%	40%	4 (0.8%)

Predicting Prostatectomy Findings

<u>Objective:</u> Clinical validation of the Urine/Plasma test using Prostatectomy data

Age (Median, Min-Max)	61 (36-77)		
Prostate size (gm) (Median, Min-Max)	34 (9.22-160)		
Gleason			
3+3	90 (29.4%)		
3+4	122 (39.8%)		
4+3	50 (16.3%)		
3+5, 4+4, 4+5, 5+4	44 (14.4%)	Stage	
sPSA (ng/ml) (Median, Min-Max)		T1	90 (29%)
≤4	62 (20%)	T1a	50 (16%)
4 to 10	198 (65%)	T1b	20 (7%)
>10	46 (15%)	T1c	122 (40%)
Race		T2	1 (0.3%)
Caucasian	246 (80.4%)	T2	E (29/)
African American	50 (16.3%)	12a	5 (2%)
Hispanic	1 (0.3%)	126	14 (5%)
Asian	1 (0.0.3%)	T2c	4 (1%)
Missing	8 (2.6%)	Bx performed by	
DRE		Ultrasound	304 (99%)
Normal	202 (66%)	MRI	2 (1%)
Abnormal	64 (21%)	Prostate sizedetermined by	
Unknown	40 (13%)	TRUS-Ultrasound	293 (96%)
Family Hx	-		
No	188 (61.4%)	MRI	10 (3%)
Yes	93 (30.3%	Unknown	3 (1%)
Uknown	25 (8.2%)		
Stage			

NeoLAB Liquid Biopsy Test is More Accurate Than Biopsy in Predicting Prostatectomy Results

Urine/Plasma Test in Predicting Biopsy Findings

	High sensetivity			Standard sensetivity			Low sensetivity		
		Lower	Upper		Lower	Upper		Lower	Upper
	Value	Limit	Limit	Value	Limit	Limit	Value	Limit	Limit
Sensitivity	95%	91%	98%	92%	87%	95%	88%	83%	92%
PPV	71%	65%	76%	70%	65%	76%	70%	64%	75%
NPV	29%	10%	58%	28%	13%	50%	22%	10%	40%

Urine/Plasma Test in Predicting Prostatectomy Findings

	High sensetivity			Standard sensetivity			Low sensetivity		
		Lower	Upper		Lower	Upper		Lower	Upper
	Value	Limit	Limit	Value	Limit	Limit	Value	Limit	Limit
Sensitivity	97%	94%	99%	94%	90%	96%	92%	87%	95%
PPV	87%	82%	90%	87%	83%	91%	87%	83%	91%
NPV	43%	19%	70%	36%	19%	57%	31%	17%	50%

Discrepancy Between Biopsy and Prostatectomy

Upgraded		Downdraded				
Gleason Score	No (%)	Gleason Score	No (%)			
3+3 to 3+4	49 (16%)	3+4 to 3+3	11 (4%)			
3+3 to 4+3	9 (3%)	4+3 to 3+3	1 (0.3%)			
3+4 to 4+3	14 (5%)	4+4 to 3+3	1(0.3%)			
3+4 to 4+4	2 (1%)	4+4 to 3+4	2 (0.7%)			
3+4 to 4+5	2 (1%)	4+4 to 4+3	11 (4%)			
4+3 to 4+4	3 (1%)	4+5 to 4+3	8 (3%)			
4+3 to 5+4	1 (0.3%)	5+4 to 4+5	1 (0.3%)			
4+4 to 4+5	1 (0.3%)	5+5 to 4+5	1 (0.3%)			
4+5 to 5+4	1 (0.3%)					
Total	<mark>82 (27%)</mark>	Total	<mark>36 (12%)</mark>			

Sensitivity and Specificity of Prostate **Biopsy in Predicting Prostatectomy** Findings

	Estimated	95% Confidence Interval			
	Value	Lower Limit	Upper Limit		
Sensitivity	78%	72%	83%		
Specificity	71%	55%	83%		
PPV	94%	90%	97%		
NPV	36%	26%	46%		

Conclusions Biomarkers In Prostate Cancer Serum and urine biomarkers

- Biomarkers are essential in modern Medicine
- Biomarkers play a significant role in diagnosis, prognosis and predicting clinical behavior
- Can help identify patients more likely to have positive MRI Pirad 4 or 5 to reduce the cost and burden

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- Non invasive
- Can be repeated over time
- Should be made widely available and affordable AgeCare
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