



Detection of Aggressive Prostate Cancer using [-2]proPSA and the Prostate Health Index

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Introduction

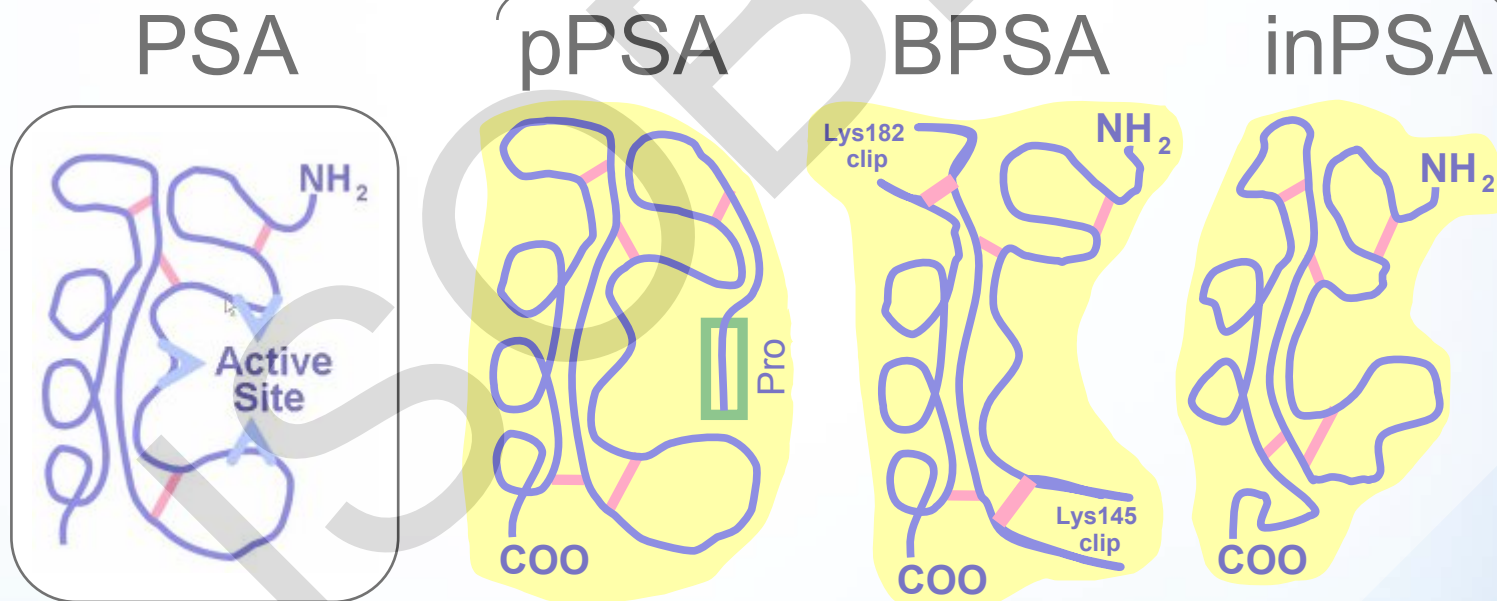
- Biomarkers challenges in PCa detection
 - ✓ Reduce number of negative biopsies
 - increase clinical specificity
 - ✓ Reduce over diagnosis
 - limit detection of indolent PCa
 - Increase detection of aggressive PCa
- %[-2]proPSA[†] improves PCa detection for men with tPSA 2 – 10ng/mL
 - Catalona et al., J Urology 2003;170:2181.
 - Catalona et al., J Urology 2004;171:2239.
 - Mikolajczyk et al., Clinical Chemistry 2004;50:1017.
 - Sokol et al., Urology 2008;180:539.
- %[-2]proPSA[†] is correlated with PCa aggressiveness
 - Catalona et al., J Urology 2004;171:2239.
 - Stephan et al., Prostate 2009;69:168.
 - Makarov et al., Clinical Cancer Research 2009;15:7316.
 - Sokol et al., Cancer Epi Biomarkers Prev 2010;19:1193.

† Not intended as off-label promotion of any Beckman Coulter product



Molecular Forms of PSA

free PSA



Amino Acids 237
Complex yes
Disease *

239-244
no
Cancer

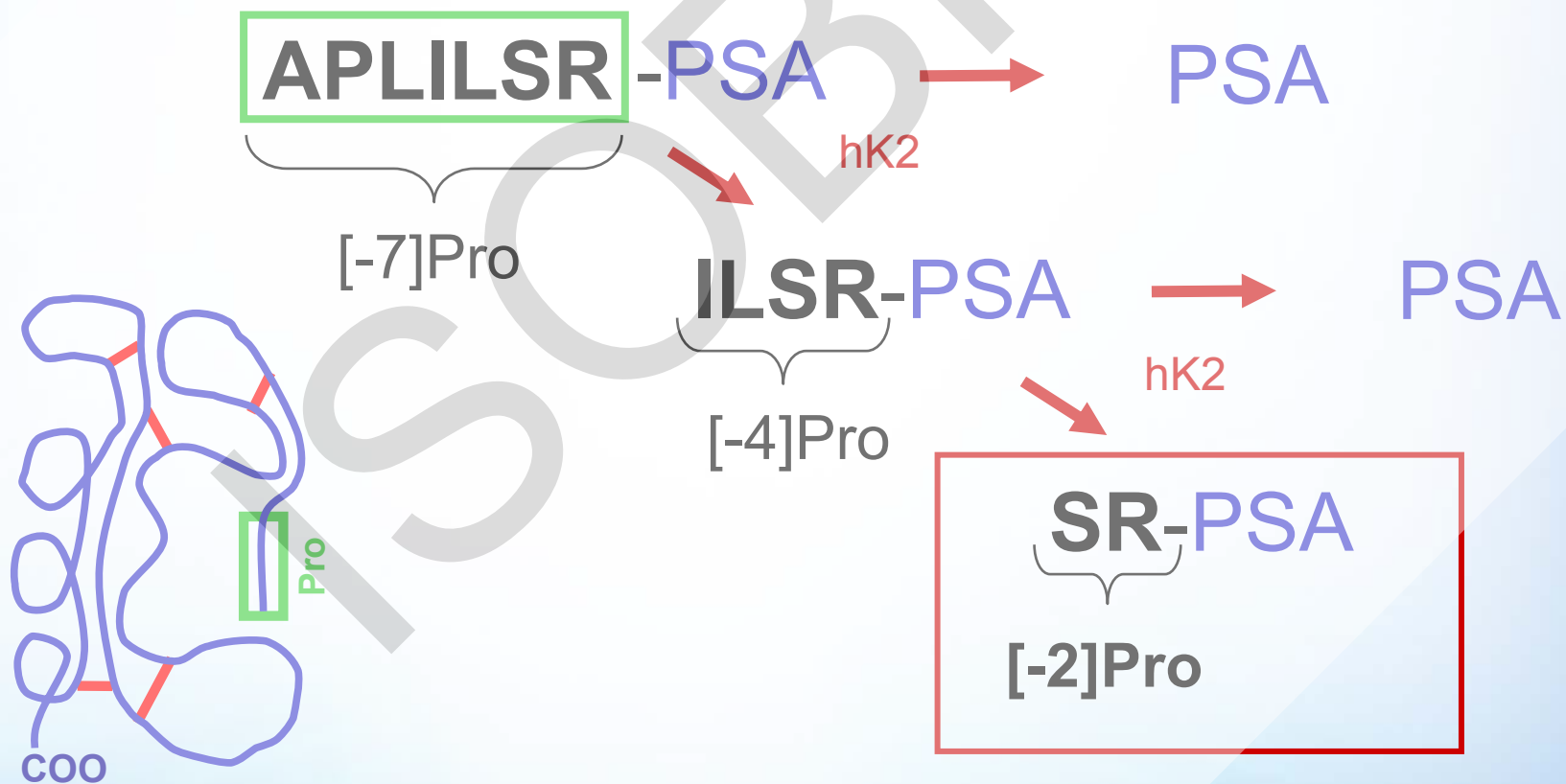
237
no
BPH

232-237?
no
?

*active PSA not present in serum



ProPSA Molecules





The Prostate Health Index (*phi*)[‡]

For men with tPSA between 2 – 10 ng/mL
and non-suspicious DRE for PCa

tPSA

fPSA

[-2]proPSA



$$([\text{-2]proPSA/fPSA}) * \sqrt{\text{tPSA}}$$

phi

[‡] Not Available in the United States



phi Improves PCa Detection in Patients with tPSA 1.6 – 8.0ng/mL*

Patients (n)	250
Diagnosis (n)	
NoPCa	107
PCa	143

Test	Area ROC	95% CI	p
tPSA (µg/L)	0.53	0.46 to 0.61	-
%fPSA	0.58	0.51 to 0.65	0.3063*
%[-2]proPSA	0.72	0.66 to 0.79	0.0004**
<i>phi</i>	0.72	0.66 to 0.79	<0.0001**

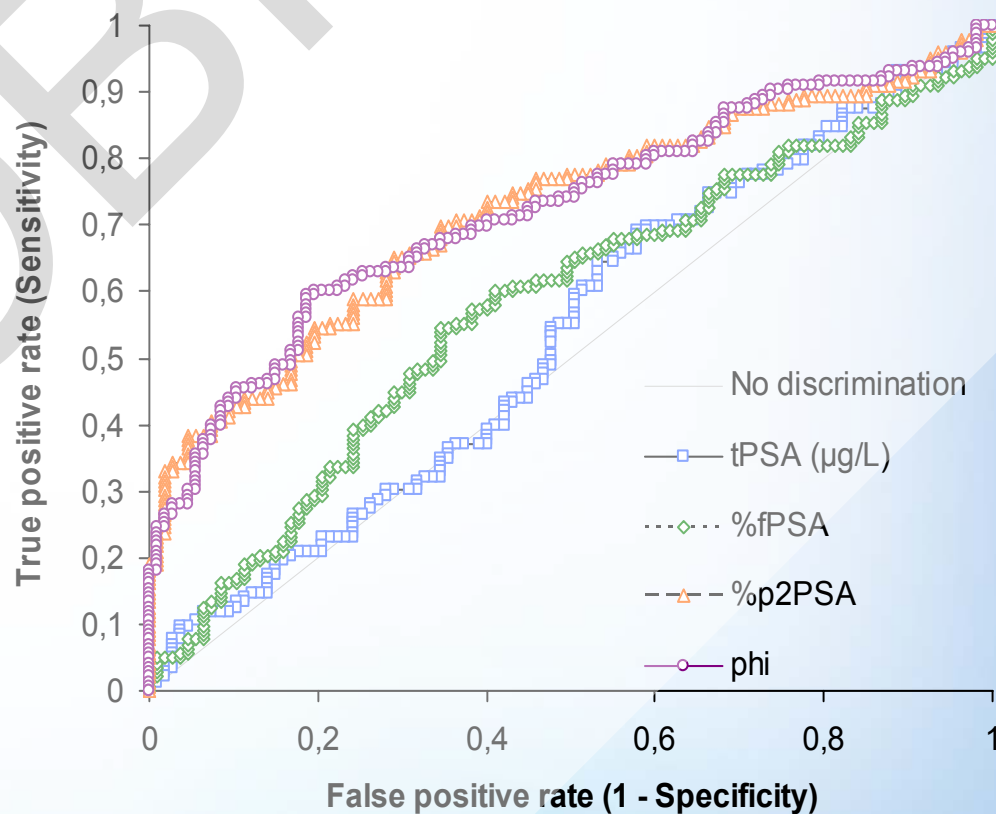
Mann-Whitney Test

* %fPSA vs tPSA

** %fPSA vs %proPSA

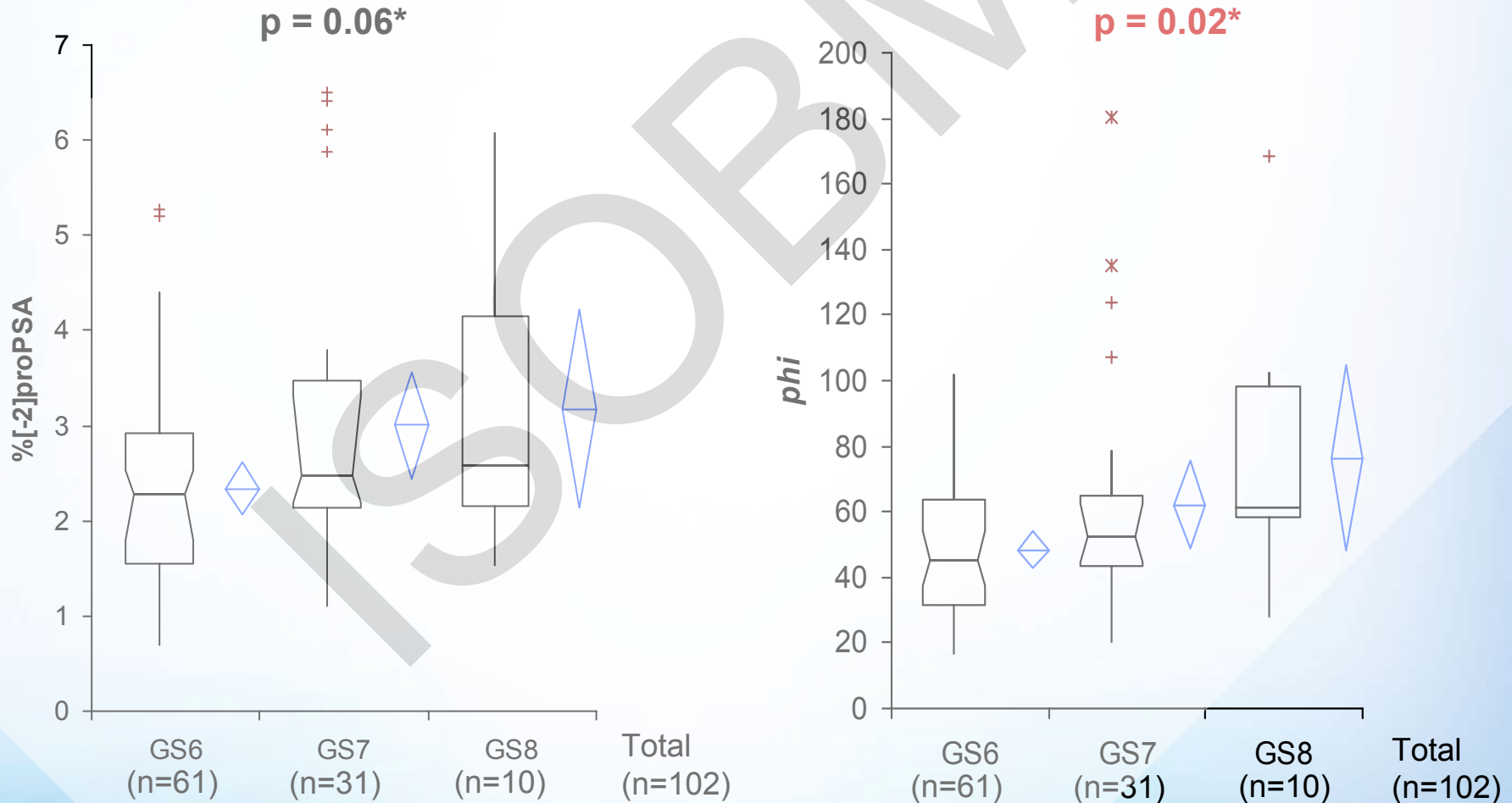
** %fPSA vs phi

* WHO calibration





Relationship with Gleason Score



* : Kruskal-Wallis test

— 95% CI Notched Outlier Boxplot

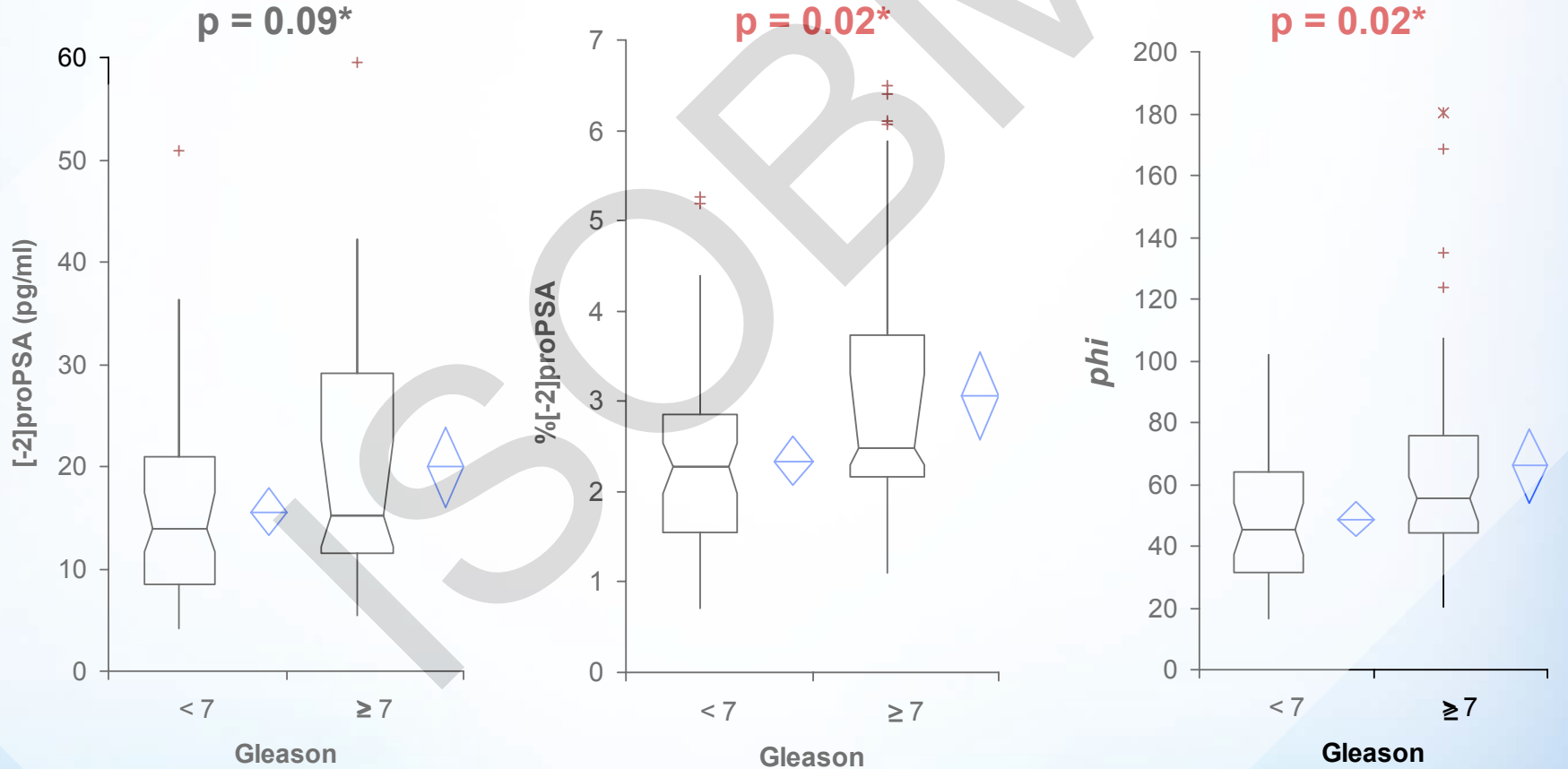
+ Outliers > 1.5 and < 3IQR

— 95% CI Mean Diamond

* Outliers > 3IQR



Relationship with Gleason Score



* : Mann-Whitney test

Gleason ≥ 7 (n=41)

Gleason < 7 (n=61)

— 95% CI Notched Outlier Boxplot

+ Outliers > 1.5 and < 3IQR

— 95% CI Mean Diamond

* Outliers > 3IQR



Relationship with Gleason Score

Median Values (n=102)

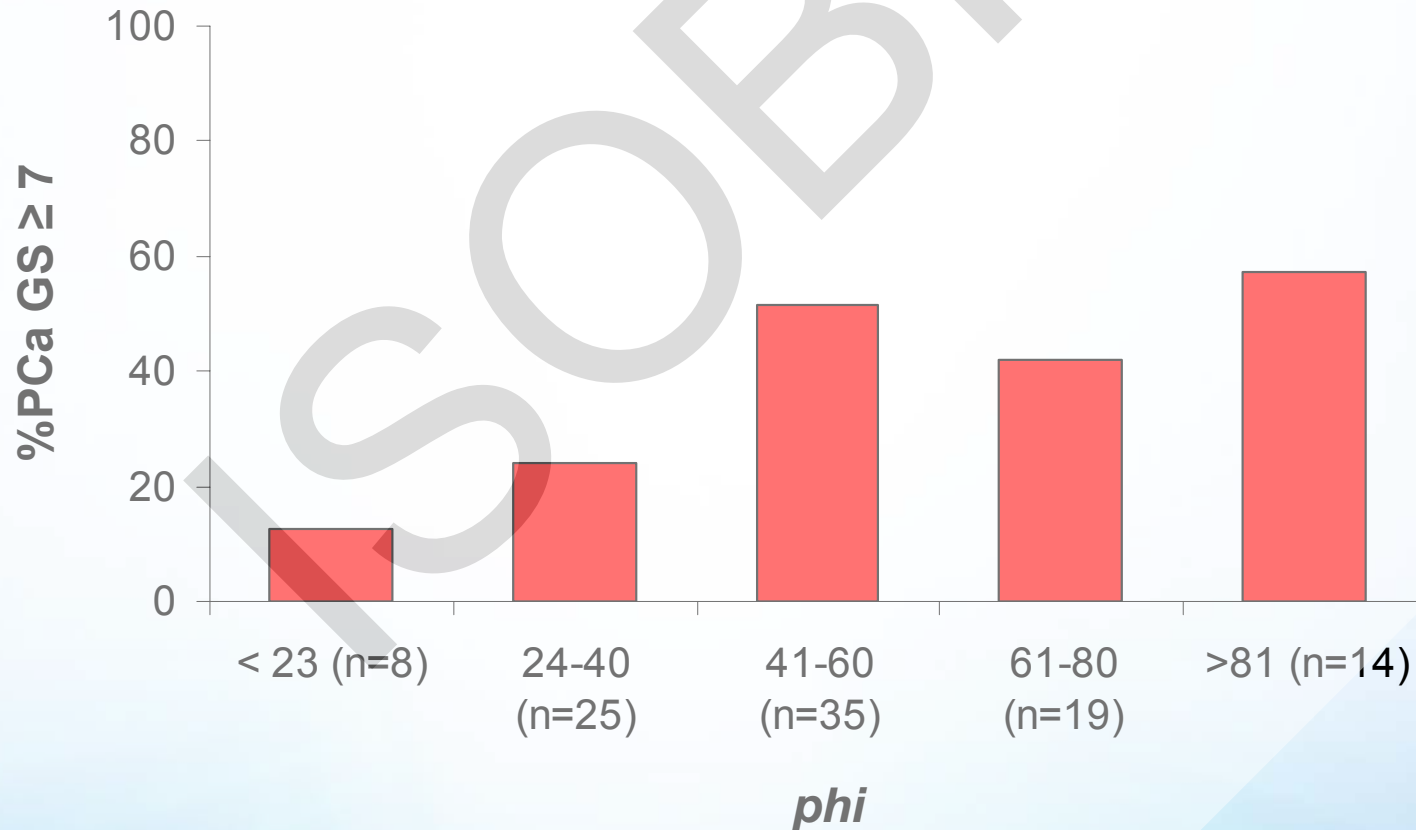
	Gleason < 7 n=61	Gleason ≥ 7** n=41	p *
tPSA	4.34	4.40	0.66
%fPSA	15.2	13.5	0.62
[-2]proPSA	13.87	15.20	0.089
%[-2]proPSA	2.29	2.49	0.02
<i>phi</i>	44.08	54.35	0.02

*: Mann-Whitney Test for difference between Gleason Groups

** : Gleason ≥ 7 = GS8 + GS7

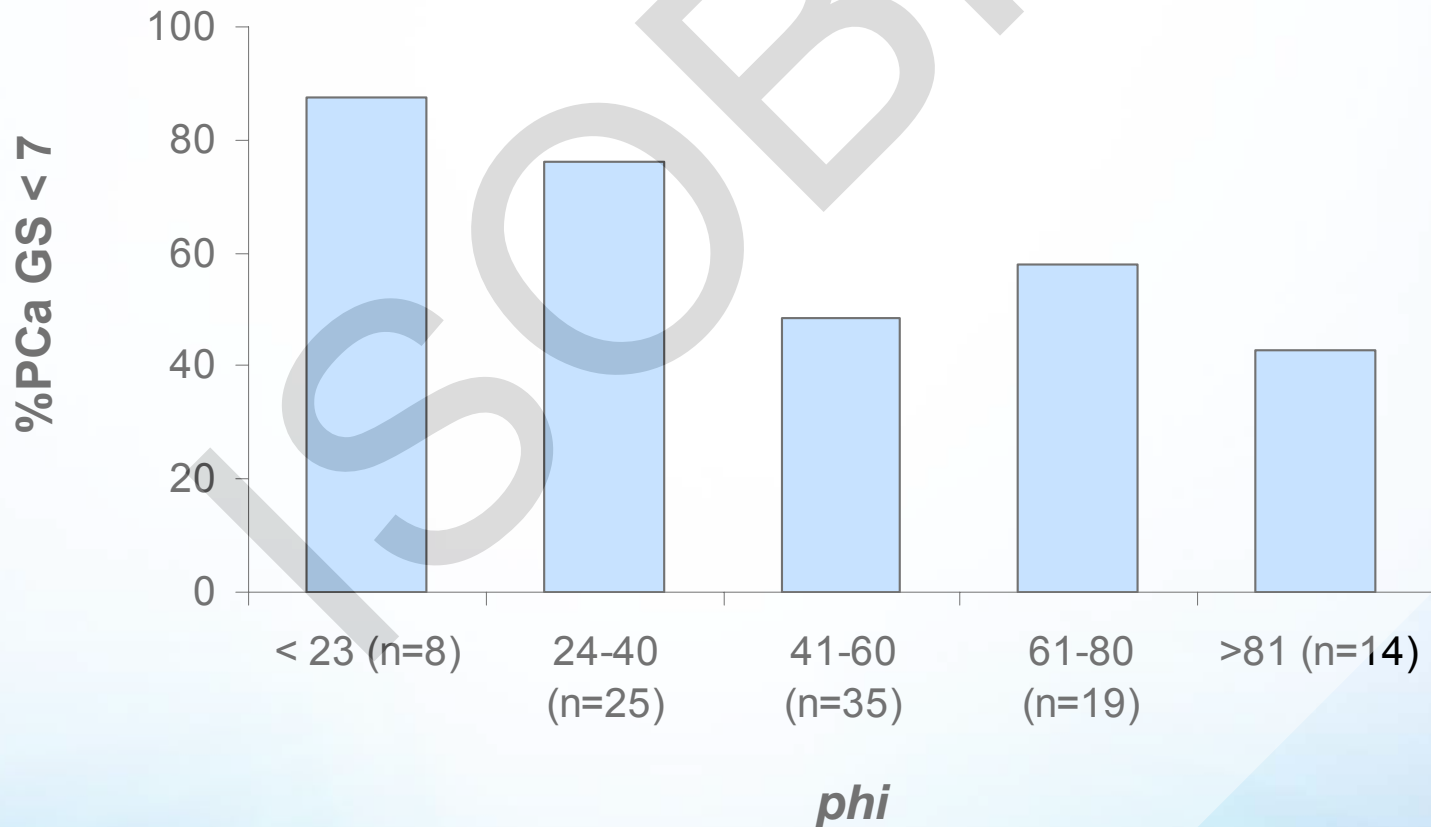


Relationship of *phi* to PCa with Gleason Score ≥ 7



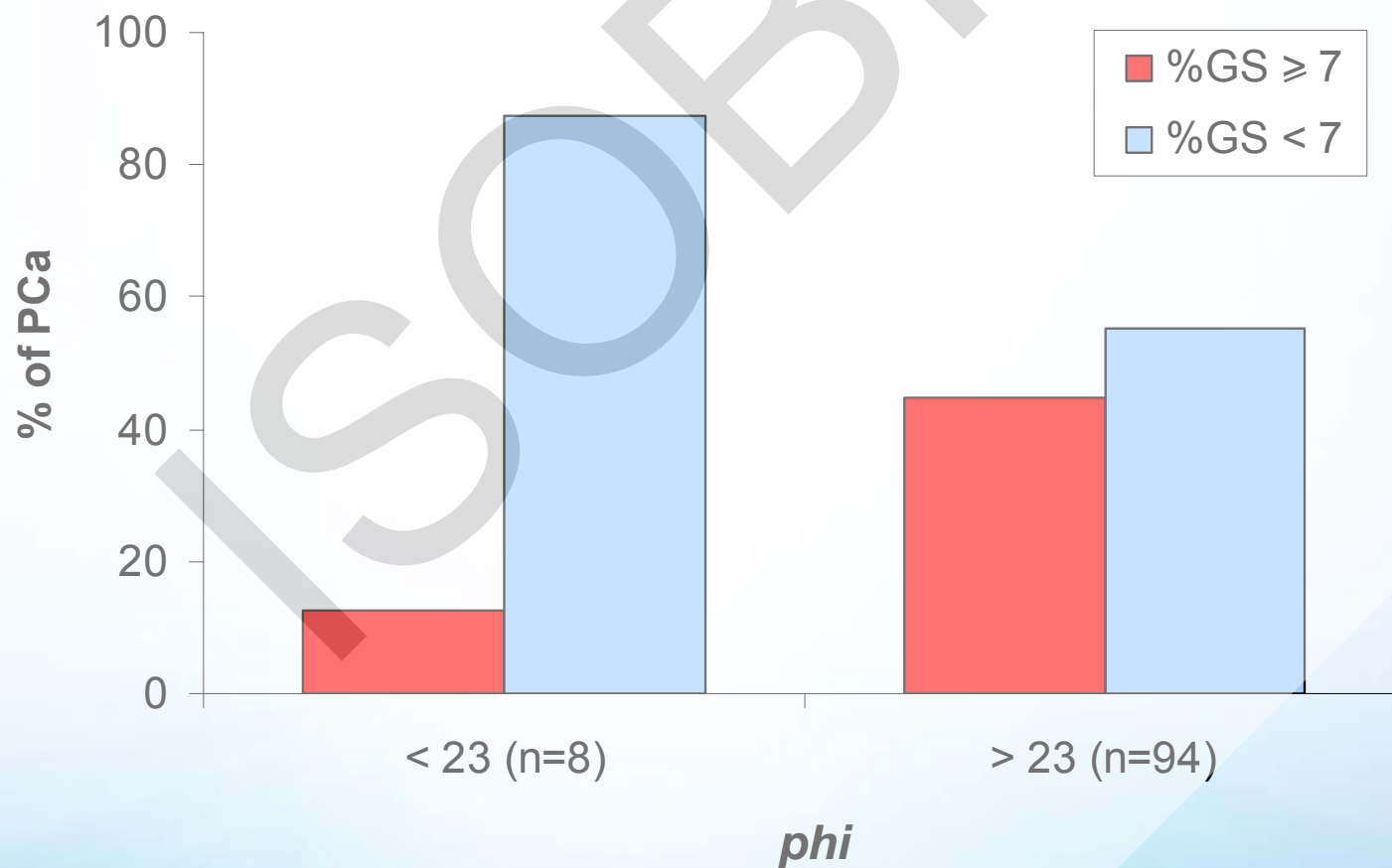


Relationship of *phi* to PCa with Gleason Score < 7





Prostate Cancer with $phi < 23$ are Mainly Gleason < 7





Conclusion

- %[-2]proPSA and *phi* improve the detection of PCa for men with tPSA 1.6 – 8.0ng/mL*
- %[-2]proPSA and *phi* correlate with the PCa biopsy Gleason score
- *phi* preferentially detects PCa with Gleason Score ≥ 7
- Prostate Cancer not detected by *phi* at 90% sensitivity are mainly Gleason Score < 7 (88% of cases)

* WHO calibration

Thank you for your attention