

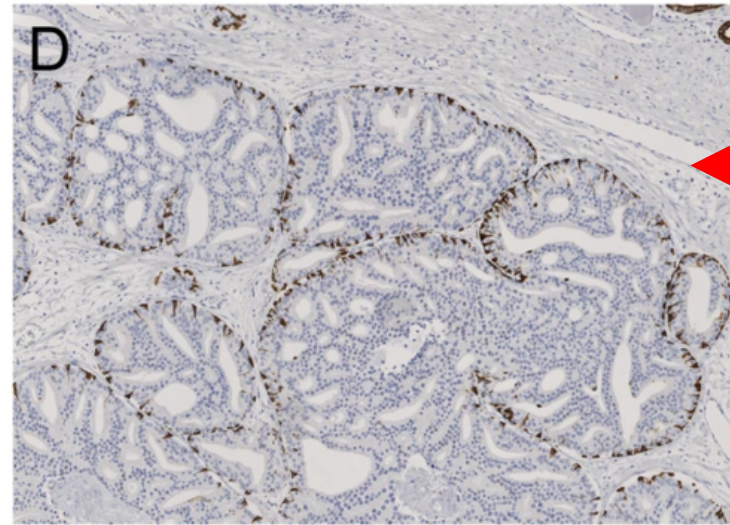
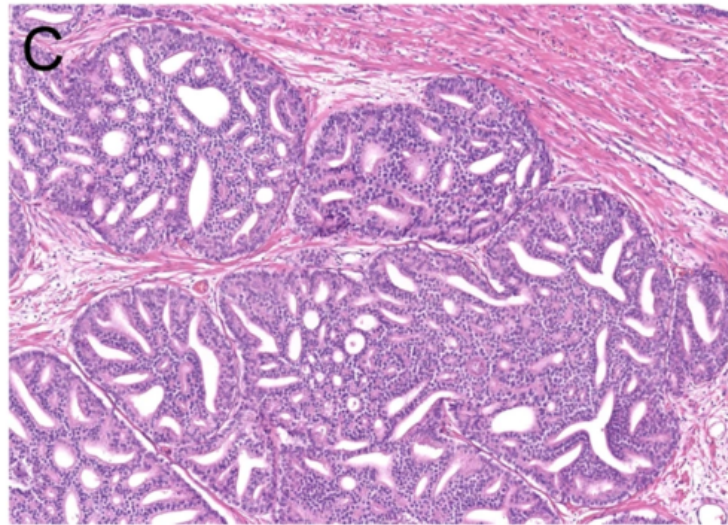
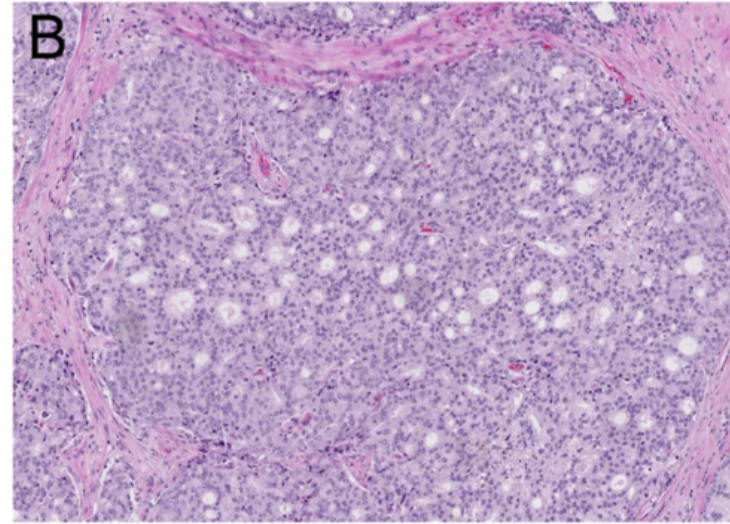
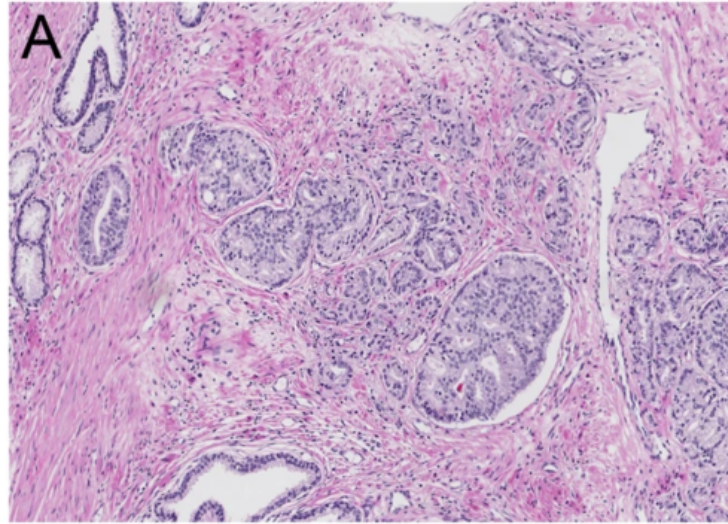
(PD48-08) The IsoPSA Assay is Sensitive for Biopsy-Identified Cribriform Pattern 4 Glands and Intraductal Carcinoma of the Prostate

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Kyle Ericson, Scott Lundy, Shannon Wu, Lewis Thomas, Jesse McKenney, Mark Stovsky, Arnon Chait, Eric Klein



Cribriform carcinoma is a subtype of Gleason pattern 4 carcinoma



← Intraductal Carcinoma

Kweldam C, et al. *Modern Pathology* (2019)

Background

Study Design

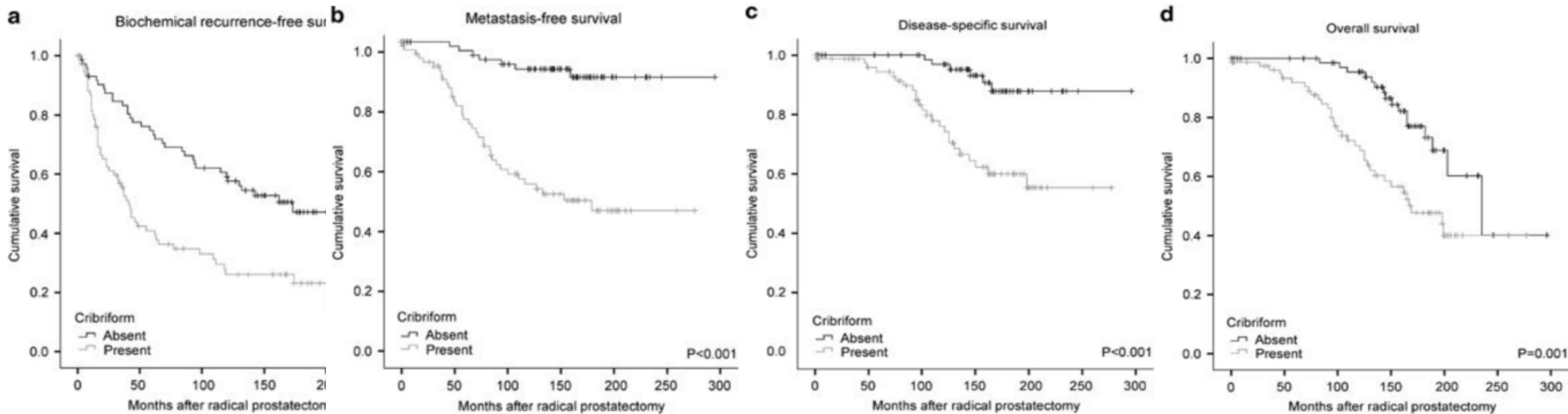
Results

Conclusions



Biochemical recurrence, metastasis, cancer-specific, and overall survival after prostatectomy in Gleason 7

- 56 men metastases or cancer-specific death, 112 matched controls
- All Gleason 7



- **Cribriform/Intraductal associated with poor outcomes irrespective of Gleason score**

Kweldam et al. *Modern Path* (2017)



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Any biomarker used for the early detection of prostate cancer must not miss these biologically aggressive tumors



Background

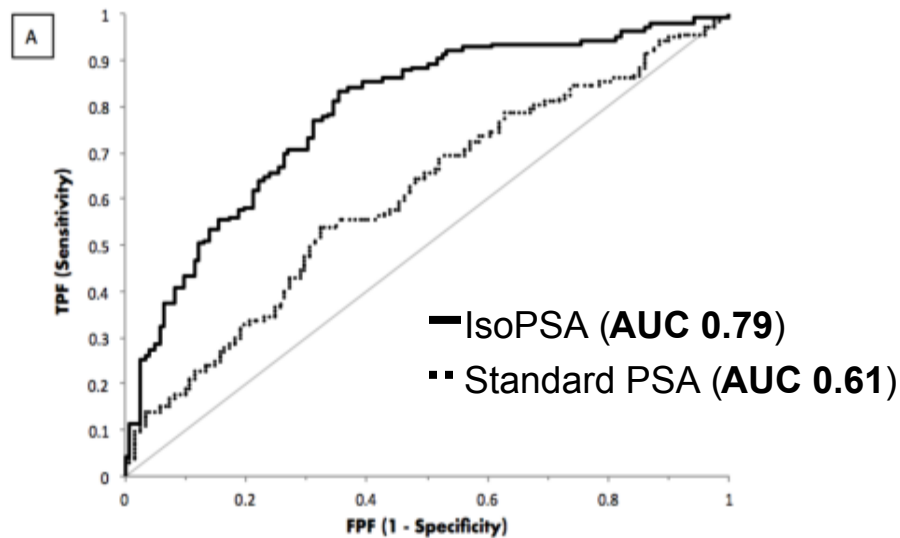
Study Design

Results

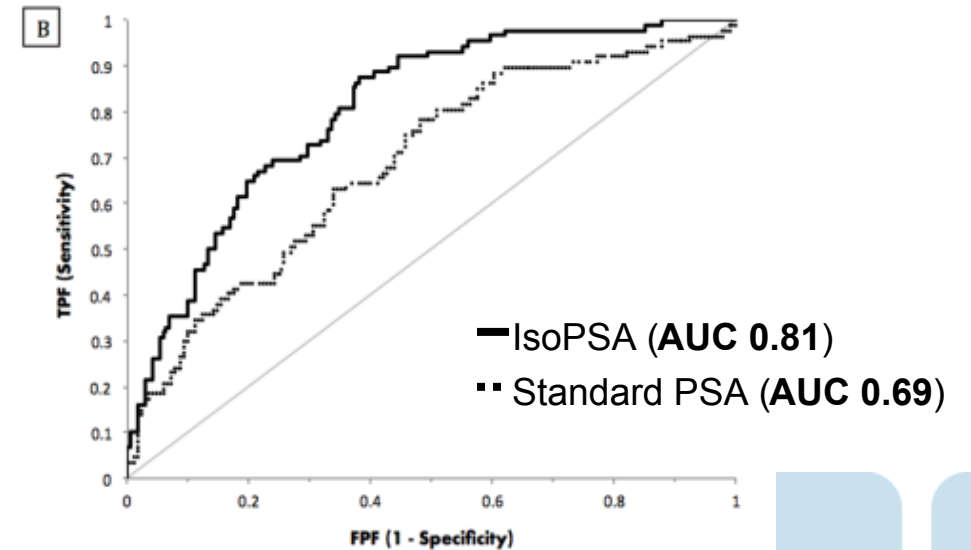
Conclusions

IsoPSA™ is a serum-based assay that detects relative concentration of PSA isoforms altered by dysregulated cellular processes

- Readout is IsoPSA K



Cancer vs No Cancer



High-Grade Cancer vs Low-Grade or No Cancer

Klein E et al. *Eur Urol* (2017); Stovsky et al. *J Urol* (2019)



At an IsoPSA K cutoff of ≥ 8.5 and PSA ≥ 4 :

| | <u>IsoPSA</u> | <u>PSA</u> |
|---------------------------|---------------|------------|
| Sensitivity | 93 - 96% | 93 - 94% |
| Specificity | 40 - 43% | 18 - 22% |
| Positive Predictive Value | 39 - 46% | 34 - 36% |
| Negative Predictive Value | 93 - 95% | 83 - 89% |

Klein E et al. *Eur Urol* (2017); Stovsky et al. *J Urol* (2019)

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Question:

How well does IsoPSA capture these biologically aggressive forms of prostate cancer?

Objective:

Characterize the diagnostic accuracy of IsoPSA for cribriform and intraductal carcinoma



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Design: Retrospective review of men enrolled in validation study (Stovsky et al. *J Urol* [2019])

- Cleveland Clinic cohort

Patients: Men scheduled for biopsy for routine indications (ie abnormal DRE or concerning PSA) were prospectively enrolled

Lab: IsoPSA drawn prior to biopsy

Pathology: Biopsy specimens re-reviewed for presence of cribriform pattern 4 carcinoma and intraductal carcinoma



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Primary Outcome

- Sensitivity of IsoPSA at pre-designated cutoff of ≥ 8.5 for cribriform and intraductal carcinoma (CC/IDC)

Secondary Outcome:

- Diagnostic performance of IsoPSA compared to standard PSA by receiver operating characteristic (ROC) curve analysis



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172 patients biopsied in Cleveland Clinic cohort

101 (58.7%) with prostate adenocarcinoma

32/101 men (31.7%) with biopsy-identified
CC/IDC



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Baseline characteristics of 172 men biopsied

| | Benign Biopsy n = 71 | Cancer+, CC/IDC- n = 69 | Cancer+, CC/IDC+ n = 32 | p |
|------------------------|-------------------------|----------------------------|----------------------------|-------------------|
| Age, median (IQR) | 64 (59 – 68) | 63 (59 - 67) | 64 (59 - 70) | 0.49 |
| PSA, median (IQR) | 5.97 (4.00 – 9.48) | 5.49 (4.01 – 7.12) | 7.18 (5.61 – 12.98) | 0.001 |
| PSAD, median (IQR) | 0.11 (0.08 – 0.17) | 0.12 (0.07 – 0.19) | 0.20 (0.14-0.31) | < 0.001 |
| IsoPSA K, median (IQR) | 9.1 (6.9 – 11.6) | 11.9 (8.4 – 14.9) | 16.9 (11.6 – 21.5) | < 0.001 |
| Biopsy GGG, n (%) | | | | < 0.001 |
| 1 | 0 | 45 (65) | 1 (3) | |
| 2 | 0 | 18 (26) | 18 (56) | |
| 3 | 0 | 4 (6) | 6 (19) | |
| 4/5 | 0 | 1 (1) | 7 (22) | |



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Primary Outcome

Sensitivity of IsoPSA $K \geq 8.5$ for CC/IDC: 100%

- No patients with CC/IDC would have been missed by IsoPSA screening
 - 32/32 CC/IDC+ tumors had an IsoPSA $K > 8.5$
-
- Specificity: 26.2%
 - PPV: 22.9%
 - NPV: 100%



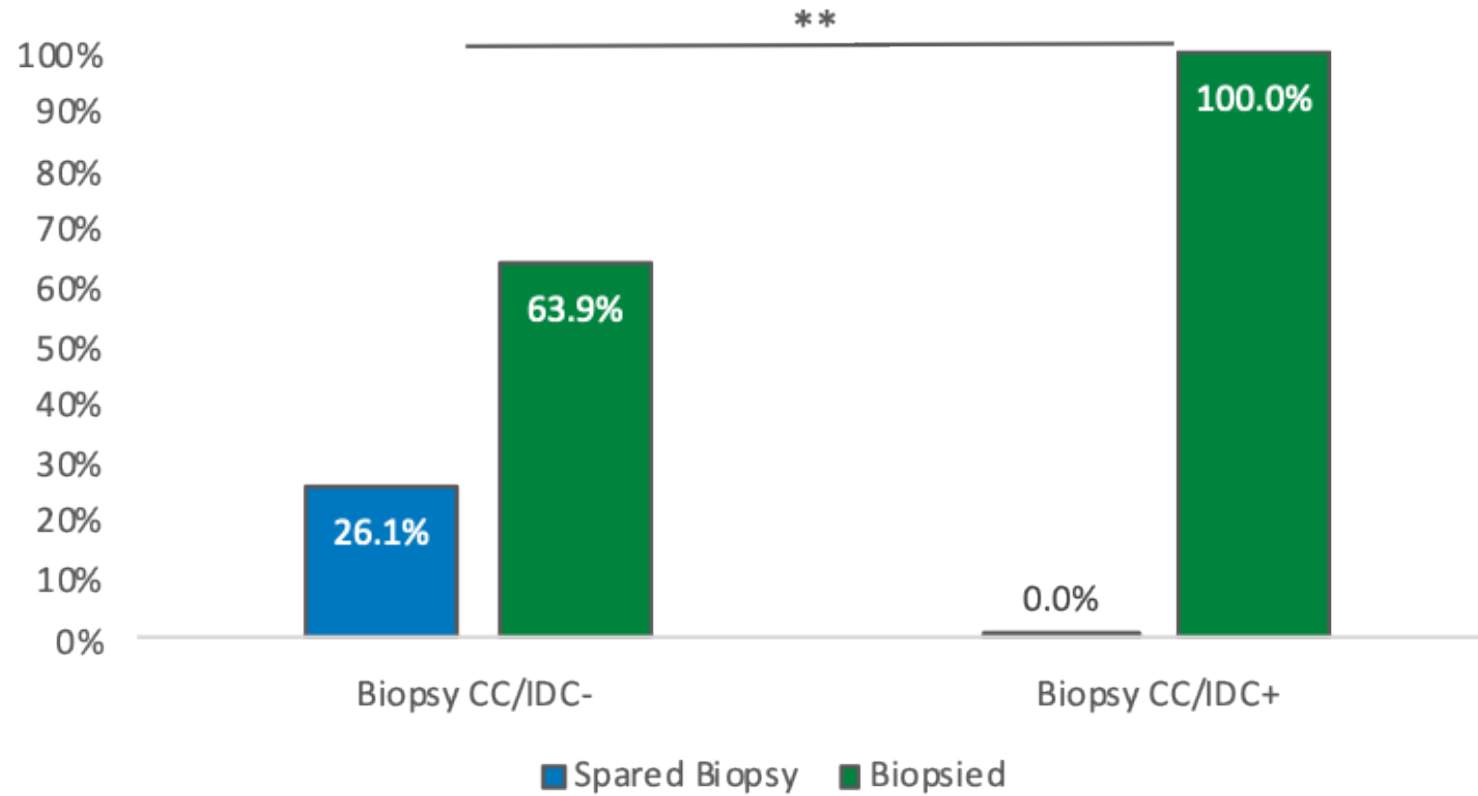
Background

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Decision to Biopsy by IsoPSA Early Detection



Background

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Results

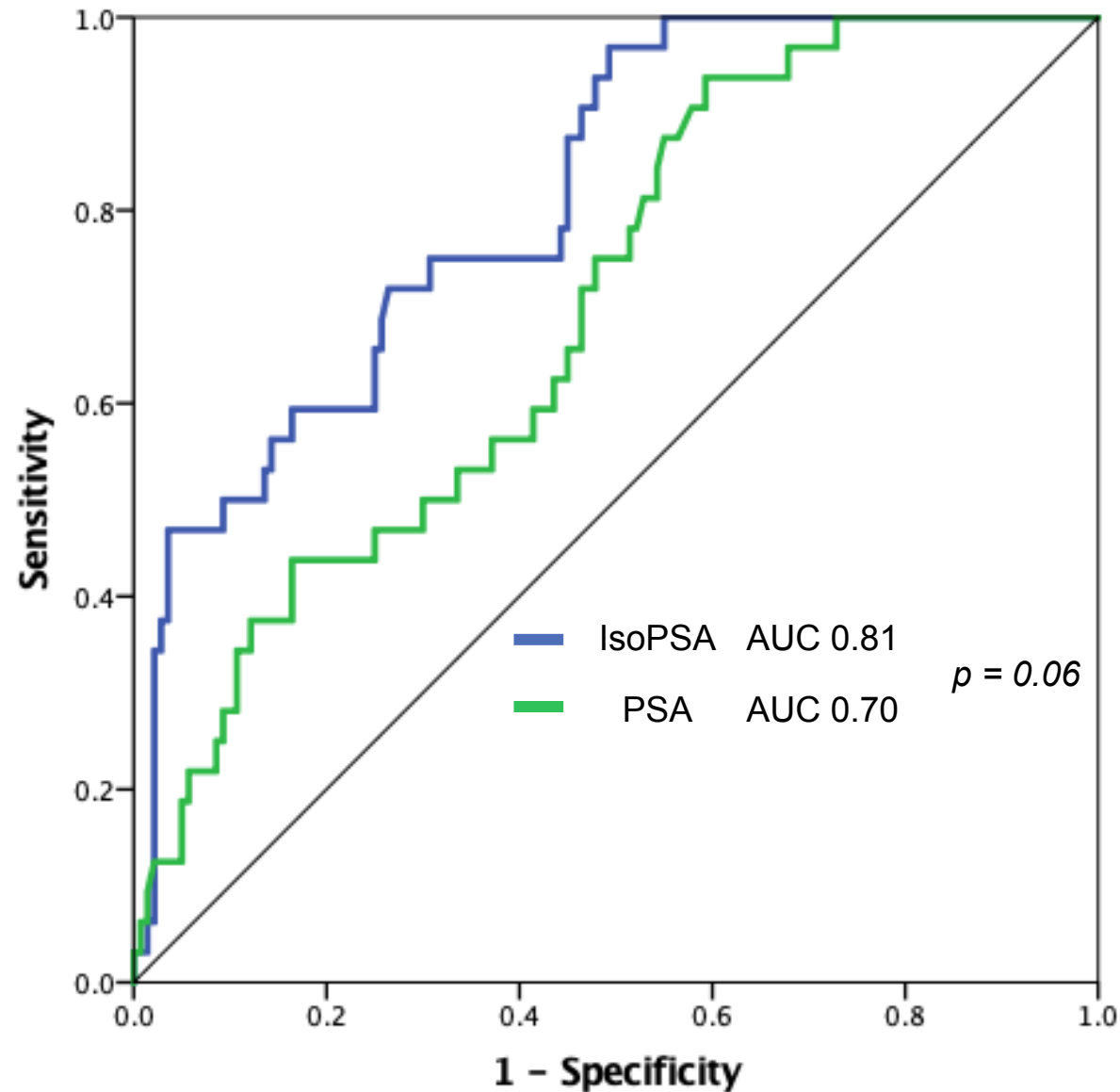
Conclusions

Of the 50 men who may have been spared a biopsy:

- 64% (32/50) did not have cancer
- 26% (13/50) had Gleason 6 tumors
- 8% (4/50) had CC/IDC negative GG2 tumors
- One patient had a GG3 prostate cancer



Receiver Operator Curve Analysis



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Limitations

- Relatively small cohort (n – 172)
- Prostatectomy specimens were not re-reviewed for the presence of CC/IDC



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1. IsoPSA is markedly sensitive for cribriform carcinoma and intraductal carcinoma

2. IsoPSA-based early detection protocols could reduce unnecessary biopsies without missing these biologically significant tumors



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Conclusions

Thank You



Cleveland Clinic

Every life deserves world class care.