UltraSensitive PSA assays (blood tests) are capable of both higher resolution and lower thresholds of detection than standard PSA “screening tests.” Although multiple laboratories have offered UltraSensitive PSA “monitoring tests” for years, both Prostate Cancer (PC) specialists and policy makers at major medical centers do not universally embrace UltraSensitive PSA testing for post treatment monitoring of PC patients following their initial surgery and/or radiation.

Significant confusion today is found among PC patients resulting from this ongoing dispute within the PC industry.

PC physicians and patients do not always speak the same language. There is no better example than discussions regarding the UltraSensitive PSA test. Physicians frequently are quoted as saying “there is NO clinical significance in the use of the UltraSensitive PSA test.” It is important for patients to realize that this physician-assertion actually translates as “at our institution, we would not make treatment decisions differently based on results of PSA UltraSensitive testing.”

Some physicians falsely imply to patients that the UltraSensitive test is somehow “not a valid assay.” Some go so far as to assert that “there is no science supporting the use of UltraSensitive PSA Testing.” Such assertions are purely uninformed.

This dispute is not really over the validity of UltraSensitive PSA testing, but instead, this is a dispute among physicians over which disease model should be used for prostate cancer. Physicians who do not support the use of UltraSensitive PSA testing, by definition, simply do not themselves believe that recurrent prostate cancer CAN be forced into remission IF treated APPROPRIATELY AND treated EARLY ENOUGH. These physicians are actually saying that “this test is not important because early detection of residual disease is not important because early treatment is not important.”

Several notable PC Oncologists believe that prostate cancer does follow normal “cancer rules” and that UltraSensitive PSA testing is critical to early detection which increases their success in obtaining durable remissions through “early treatment.”

Reference: Clinical Significance of UltraSensitive PSA Test Results in Post Operative Monitoring
Reference: Using UltraSensitive PSA Testing To Potentially Gain Years of Earlier Warning of Recurrence
Reference: Rising PSA in Nonmetastatic Prostate Cancer - Judd Moul and Stephen Freedland

This example demonstrates the use of UltraSensitive PSA testing in early recurrence PC detection and intervention.
Pre-Surgery PSA
(PSADT - approx 4.7 months)

Biopsy at a Top 10 USA Med Center
2 of 12 cores positive (10 of 35 mm)
Right transitional zone only
02/13/2006 Gleason 5 (3 + 2)

Final Pre-Surgery PSA Test
45.6

Quest PSA Tests
20.8
19.1
16.1

Maximum Value of “Roche ECLIA” UltraSensitive PSA Assay Results
(now at LabCorp)

PSA Sampling “Blackout Period” (Post-biopsy)

Radical Retropubic Prostatectomy
Open Procedure
05/09/2006
Gleason 7 (3 + 4)
pT3a: ECE pos left 0.8 cm
Perineural invasion – pos
Margins – all neg
Nodes 4 + 5 – all neg
Seminal vesicles – neg
Bladder neck – neg

Topic 001.1 - UltraSensitive PSA Testing Example – The Pre-Surgical History

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**Doubling Time of PSA Level from Five PSA Assays**

Preoperative patient’s nickname: Example 1

The best fit to the doubling time is 0.39 years → 4.7 months.

The doubling time lies within the interval (0.35, 0.45) years.

The precision of the fit is fair with chi^2 per DOF = 1.72.

Without treatment the PSA could reach the life-threatening level of 4,000 in the year 2009 or within the interval (2008, 2009).

The input data were:
On 8 October 2005 his PSA was 19.10 (ng/ml).
On 11 October 2005 his PSA was 16.10 (ng/ml).
On 30 November 2005 his PSA was 20.80 (ng/ml).
On 17 January 2006 his PSA was 31.40 (ng/ml).
On 27 April 2006 his PSA was 45.60 (ng/ml).
UltraSensitive PSA at initiation of Complete Androgen Blockade (CAB)
Post-Surgery PSA Doubling Time: Estimate 5.4 months (quite aggressive)

Last Quest
0.3 “high-scale” PSA Test

60 Gy
Secondary Radiation Treatment

IMRT on 21EX

CPT 84153
LabCorp 140723
“Prostate-Specific Antigen (PSA), UltraSensitive (Serial Monitor)”

Screening & LabCorp PSA Tests
Both 0.1

Post-Radiation “Baseline” and Measured Nadir
0.06

0.05

0.07

0.12

Overly Sparse Sampling Leaves True Nadir Unknown

“UltraSensitive UNDETECTABLE” <0.01

Example Graph Showing Necessity of UltraSensitive PSA Testing – From Surgery / IMRT through first 6 months of recurrence

Surgery
Doubling Time of PSA Level from Four PSA Assays

Postoperative patient’s nickname: Example 1

The best fit to the doubling time is 0.45 years \( \rightarrow 5.4 \text{ months}. \)

The doubling time lies within the interval (0.41, 0.50) years.

The precision of the fit is good with \( \chi^2 \text{ per DOF} = 0.47. \)

Without treatment the PSA could reach the life-threatening level of 4,000 in the year 2014 or within the interval (2013, 2015).

The input data were:
On 27 September 2006 his PSA was 0.05 (ng/ml).
On 11 January 2007 his PSA was 0.07 (ng/ml).
On 20 March 2007 his PSA was 0.10 (ng/ml).
On 18 April 2007 his PSA was 0.12 (ng/ml).
PSADT Estimate #2

Post-Surgery / Post-IMRT
Exponential Curve fit to the
Three Measured PSA Readings
Recorded After but
Excluding the Measured Nadir:
(0.05 on 9/27/2006)

Doubling Time of PSA Level from Three PSA Assays

Postoperative patient’s nickname: Example 1

The best fit to the doubling time is 0.35 years → 4.2 months.

The doubling time lies within the interval (0.31, 0.41) years.

The precision of the fit is good with chi^2 per DOF = 0.04.

Without treatment the PSA could reach the life-threatening level of 4,000 in the year 2013 or within the interval (2012, 2014).

The input data were:
On 11 January 2007 his PSA was 0.07 (ng/ml).
On 20 March 2007 his PSA was 0.10 (ng/ml).
On 18 April 2007 his PSA was 0.12 (ng/ml).
PSADT - Estimating True Nadir During Sparse Sampling Interval

Best Estimate of the True Nadir is the Exponential Intersection of the Decay Curve with the Reemergence Growth Curve.

The graph shows a decay curve and a reemergence growth curve intersecting at a point labeled as the best estimate of the true nadir. The measured nadir was 0.05 on 9/27/2006, and the estimated true nadir is 0.044 on 10/26/2006.
**Measured Nadir**

**Estimated Nadir**

The central curve represents the most likely evolution of the PSA.

**Doubling Time of PSA Level from Four PSA Values**

**Postoperative patient’s nickname:** Example 1

The best fit to the doubling time is 0.33 years \( \rightarrow 4.0 \) months.

The doubling time lies within the interval \((0.30, 0.36)\) years.

The precision of the fit is good with \( \chi^2 \) per DOF = 0.06.

Without treatment the PSA could reach the life-threatening level of 4,000 in the year 2012 or within the interval (2012, 2013).

The input data were:

- On 26 October 2006 his PSA was estimated to be 0.044 (ng/ml).
- On 11 January 2007 his PSA was 0.07 (ng/ml).
- On 20 March 2007 his PSA was 0.10 (ng/ml).
- On 18 April 2007 his PSA was 0.12 (ng/ml).
UltraSensitive PSA at initiation of Complete Androgen Blockade (CAB)

Post-Surgery PSA Doubling Time: Estimate 4 months (quite aggressive)

The Current AUA Official Recurrence Threshold “PSA > 0.2 ng/ml AND rising”

All UltraSensitive PSA Tests Were Performed by LabCorp
Before 4/1/08 → “Immulite 2000”
After 4/1/08 → “Roche ECLIA”

Screening Test & LabCorp PSA Tests Both 0.1

Estimated “True Nadir” 0.07

Max 0.12

These Values Below 0.1 are Visible ONLY via UltraSensitive PSA Tests.

PSA Tests. Resolution is 0.01 ng/ml

“UltraSensitive UNDETECTABLE” <0.01

“Flare”

Projected PSA Exponential Growth Curve w/o Remission Protocol

Resolve 0.01 ng/ml values

Resolve 0.1 ng/ml values

ONLY True UltraSensitive PSA Tests

CPT 84153 LabCorp 140723
“Prostate-Specific Antigen (PSA), Ultrasensitive (Serial Monitor)”

Remission Diet Started

Casodex + Avodart Added

Remission Supplements Added

Eligard Injection #1 Added

0.3 Last Quest “high-scale” PSA Test

60 Gy Secondary Radiation Treatment

IMRT on 21EX

Post-Radiation “Baseline” and

0.13 0.06 0.07 Measured Nadir

0.05 0.06 0.07

0.044 on 10/26/07

0.09 0.06 0.03 0.02

6/02/07 6/07/07 9/07/07 11/07/07

Estimates “True Nadir”

0.044 on 10/26/07

0.06

0.09
UltraSensitive PSA at Initiation of Complete Androgen Blockade (CAB) vs. Projected PSA Exponential Growth Curve w/o Remission Protocol (Red Curve)

Post-Surgery PSA Doubling Time (PSADT): Estimate 4 months

12 Month PSA Estimate
0.12 x 2 x 2 x 2
0.96 ng/ml →

4 months
4 months
4 months

Projected PSA Exponential Growth Curve w/o Intervention

AUA Official Recurrence Threshold
“PSA > 0.2 ng/ml AND rising”

At 11 months - PSA remains < 0.01 ng/ml
“UNDETECTABLE” via UltraSensitive Testing

Max 0.12
UltraSensitive PSA Results (Green Curve) from Complete Androgen Blockade (CAB) vs. 16 Month Projected PSA Recurrence Curve w/o Remission Protocol (Red Curve)

Post-Surgery PSA Doubling Time (PSADT): Estimate = 4 months

16 Month PSA Estimate
0.12 x 2 x 4 = 1.92 ng/ml

AUA “Official” Recurrence Threshold
“PSA > 0.2 ng/ml AND rising”

Max 0.12

At 16 months - PSA remains < 0.01 ng/ml
“UNDETECTABLE” via UltraSensitive Testing
UltraSensitive PSA Results (Green Curve) from Complete Androgen Blockade (CAB) vs. Projected PSA Recurrence Curve w/o Remission Protocol (Red Curve)

Post-Surgery PSA Doubling Time (PSADT): Estimate = 4 months

Without CAB Treatment, the Apr-2009, 24 Month PSA Estimate → 0.12 x 2 x 2 x 2 x 2 x 2 x 2 = 7.68 ng/ml

AUA “Official” Recurrence Threshold
“PSA > 0.2 ng/ml AND rising”

Max 0.12

At two years - PSA remains < 0.01 ng/ml
“UNDETECTABLE” via UltraSensitive Testing