Topic 001 - UltraSensitive PSA Testing – One Example

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.***"

Topic 001.1 - UltraSensitive PSA Testing Example – The Pre-Surgical History
Topic 001.2 - Pre-Surgery PSADT Estimated by Exponential Curve Fit
Topic 001.3 - UltraSensitive PSA Testing – The Basics
Topic 001.4 - Post-Treatment PSADT Initial Estimate by Exponential Curve Fit
Topic 001.5 - Post-Treatment PSADT Estimated w/o Nadir
Topic 001.6 - Estimating the True Nadir – Intercept of Decay and Growth Curves
Topic 001.7 - Post-Treatment PSADT Estimate Improved Using Estimated Nadir
Topic 001.8 - UltraSensitive PSA Testing – Remission Protocol Performance
Topic 001.9 - UltraSensitive PSA Testing – Protocol Performance vs. PSA Estimate w/o Intervention @ 12 Months
Topic 001.10 - UltraSensitive PSA Testing – Protocol Performance vs. PSA Estimate w/o Intervention @ 16 Months
Topic 001.11 - UltraSensitive PSA Testing – Protocol Performance vs. PSA Estimate w/o Intervention @ Two Years
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.

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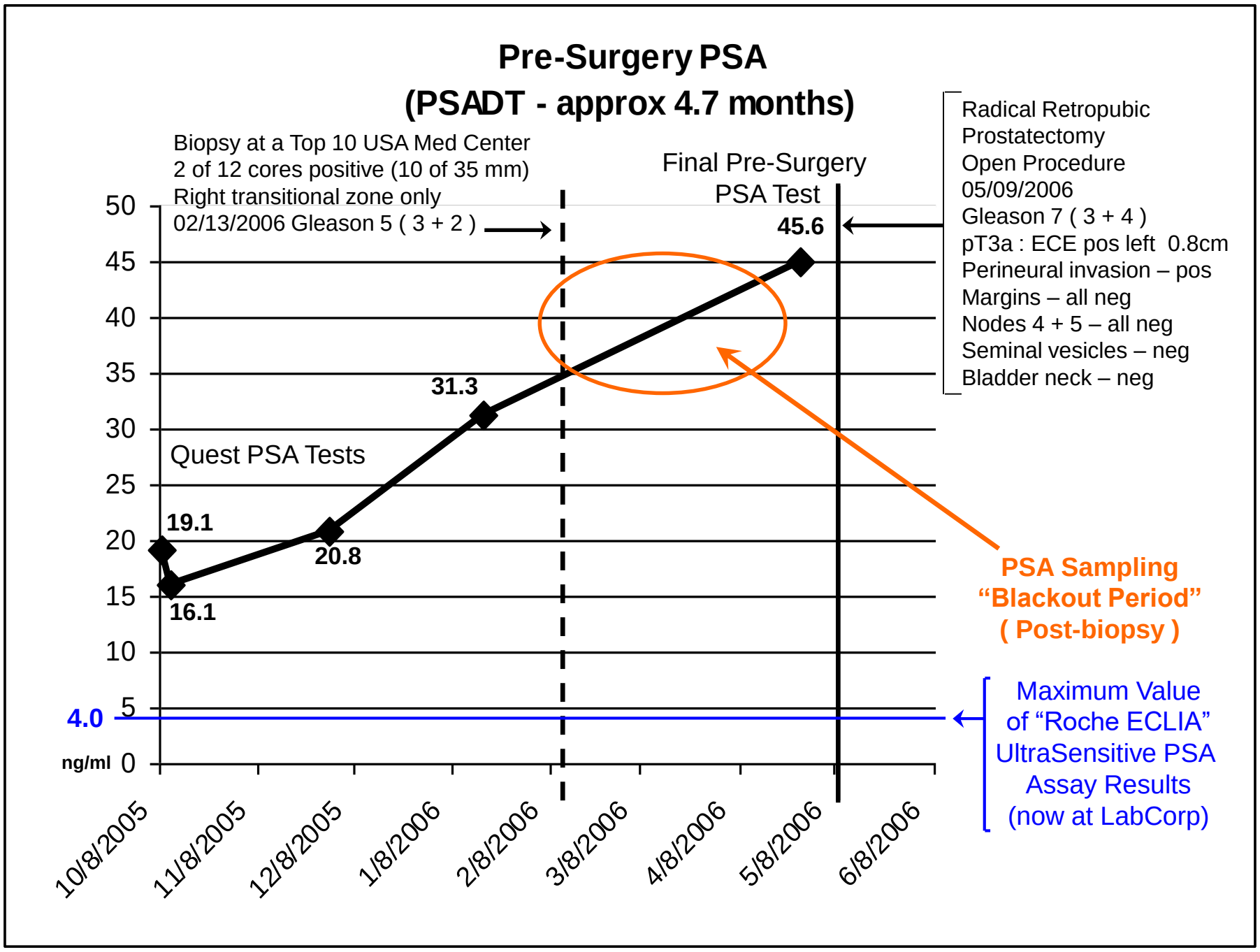
Topic 001.1 - UltraSensitive PSA Testing Example – The Pre-Surgical History



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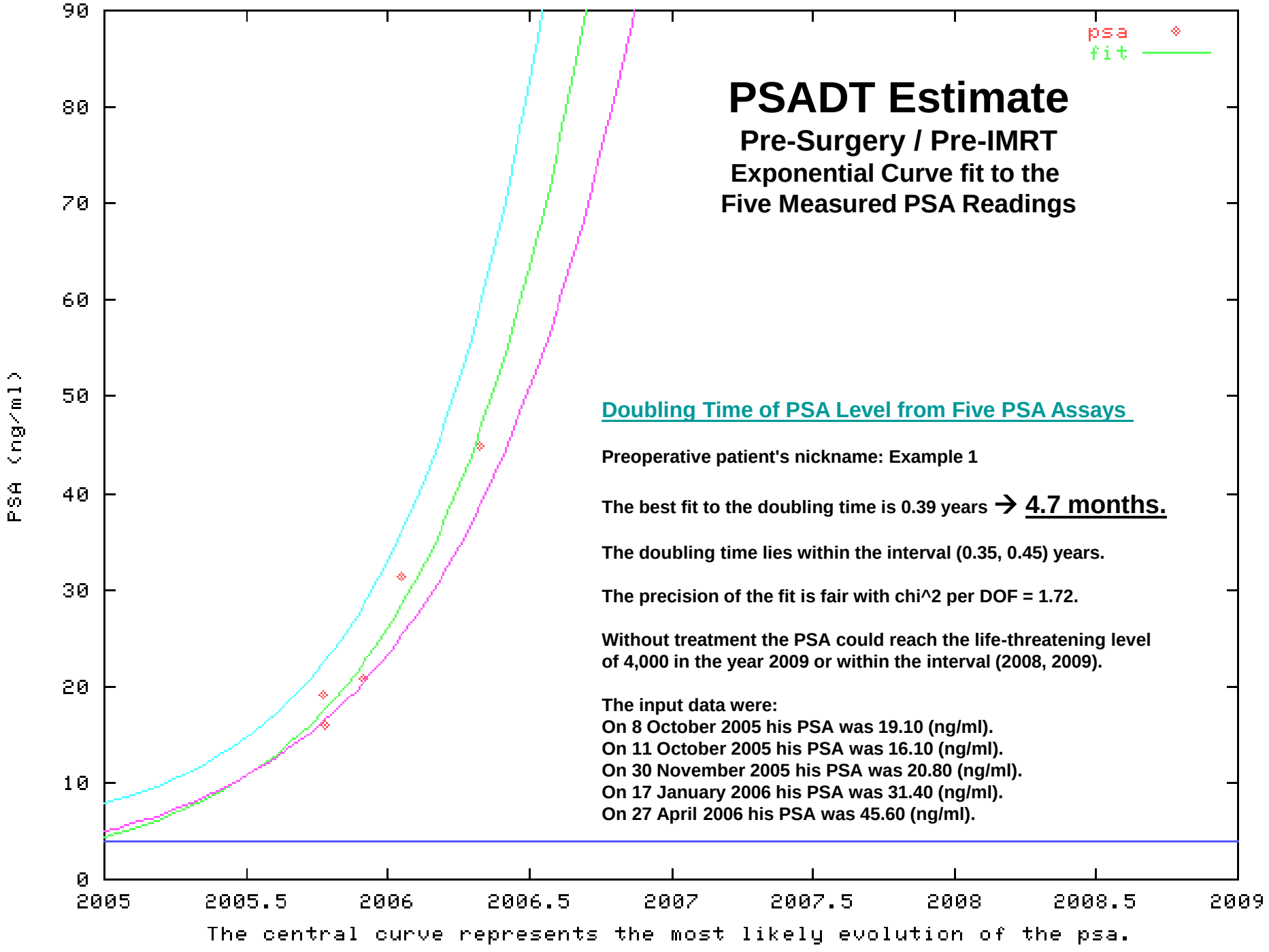
Topic 001.2 - Pre-Surgery PSADT Estimated by Exponential Curve Fit



PSADT Estimate

Pre-Surgery / Pre-IMRT
Exponential Curve fit to the
Five Measured PSA Readings

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).

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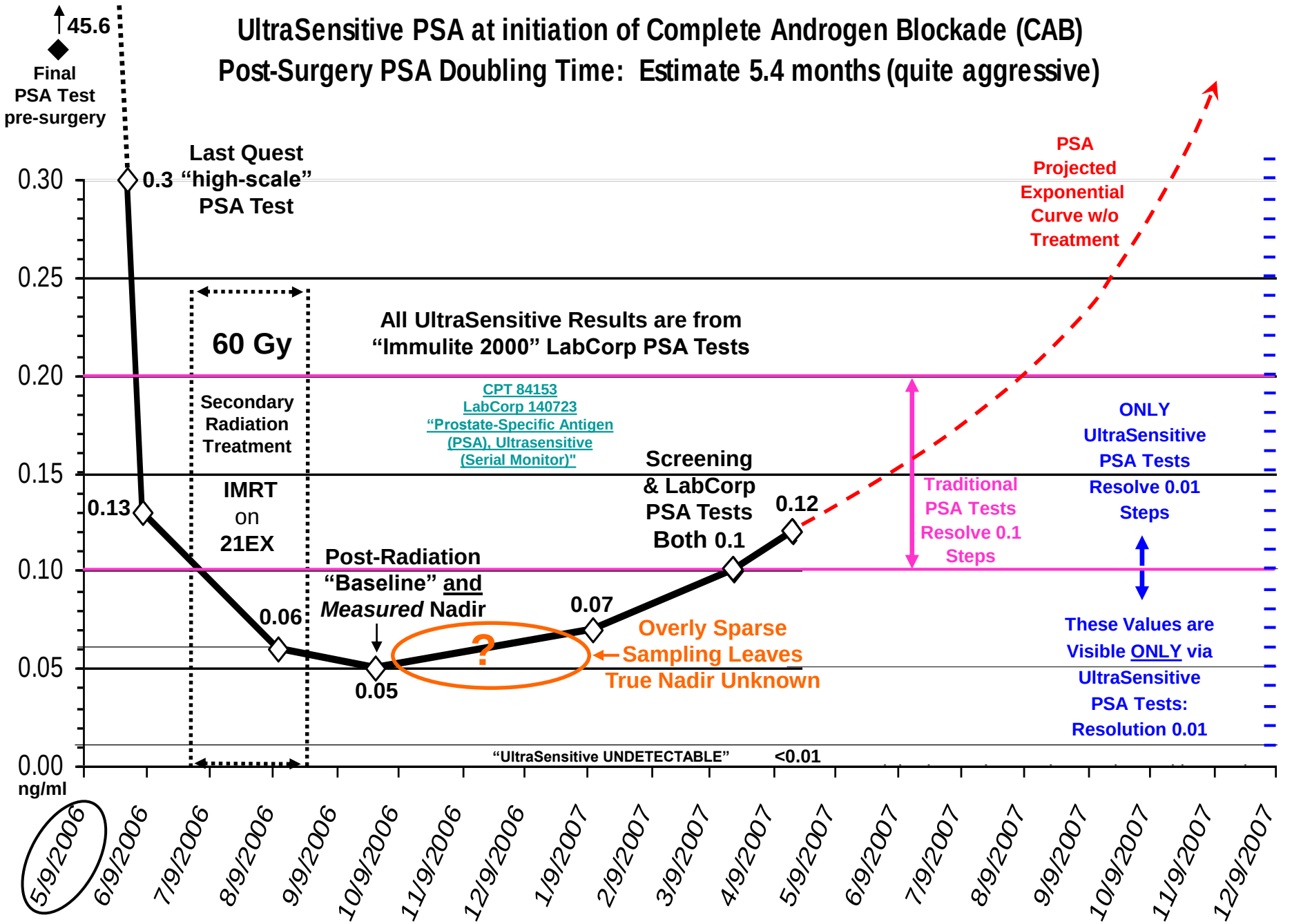
Topic 001.3 - UltraSensitive PSA Testing – The Basics



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

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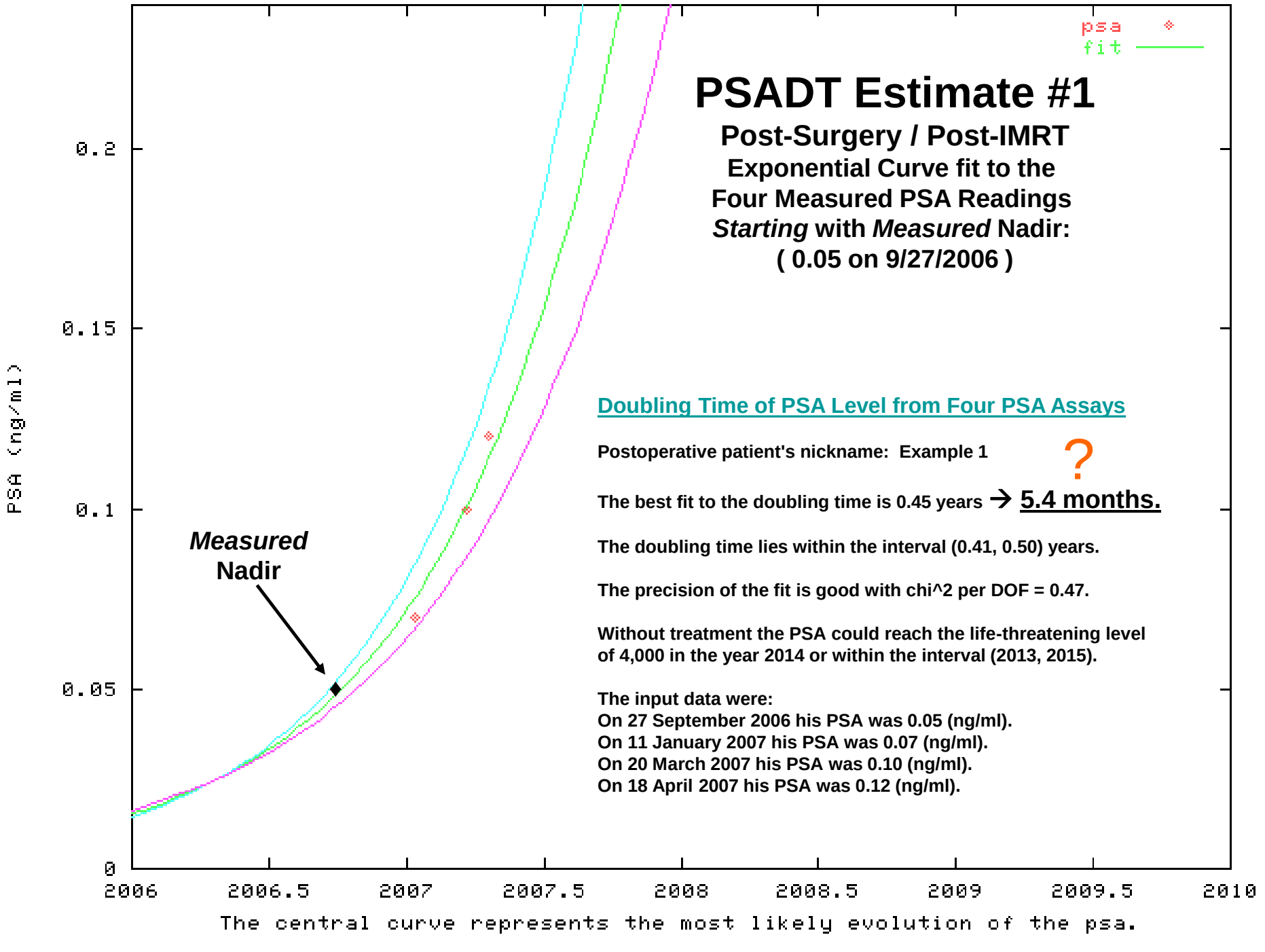
Topic 001.4 - Post-Treatment PSADT Initial Estimate by Exponential Curve Fit



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 → 5.4 months.

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

The precision of the fit is good with chi^2 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).

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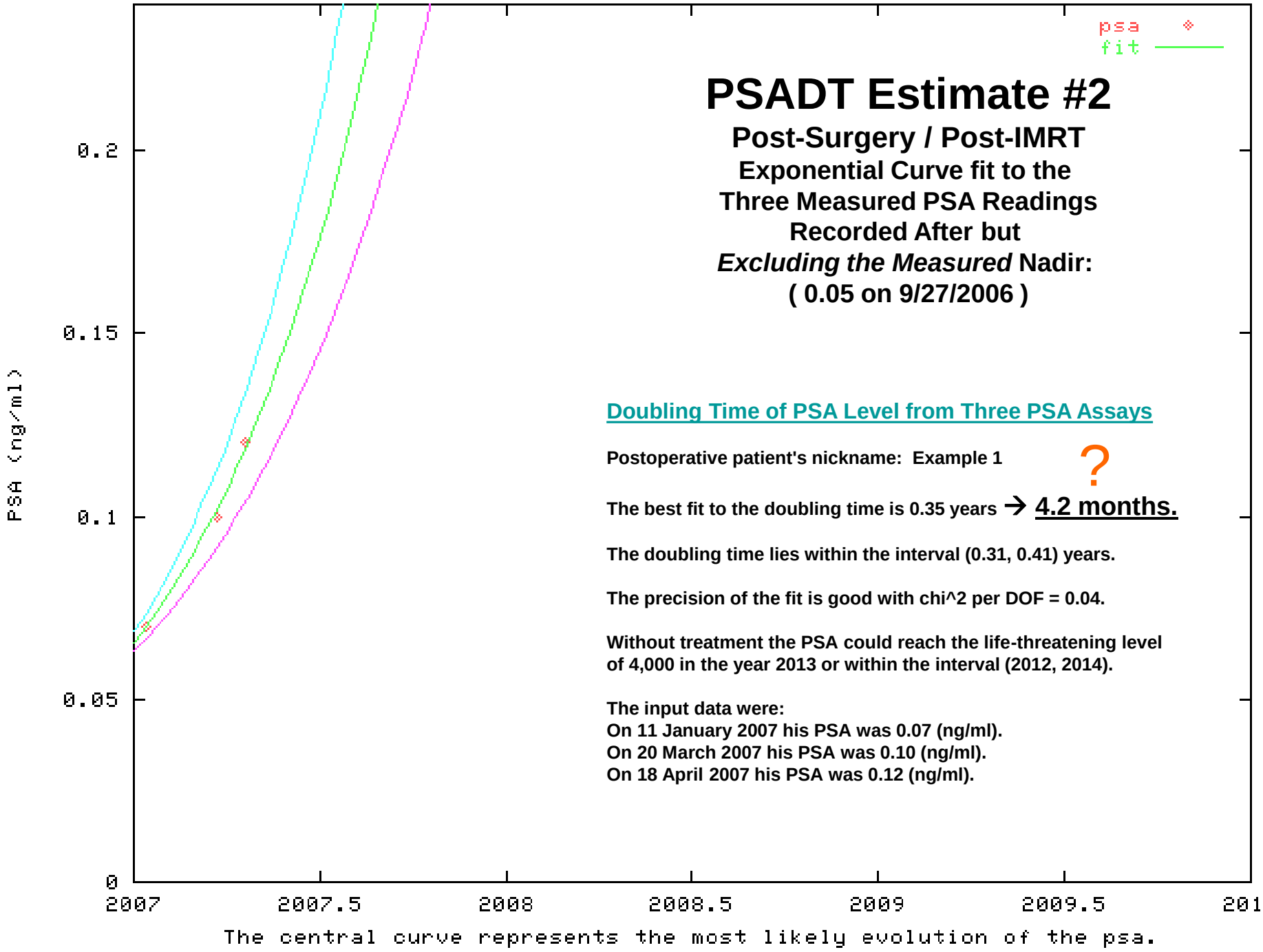
Topic 001.5 - Post-Treatment PSADT Estimated w/o Nadir



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).

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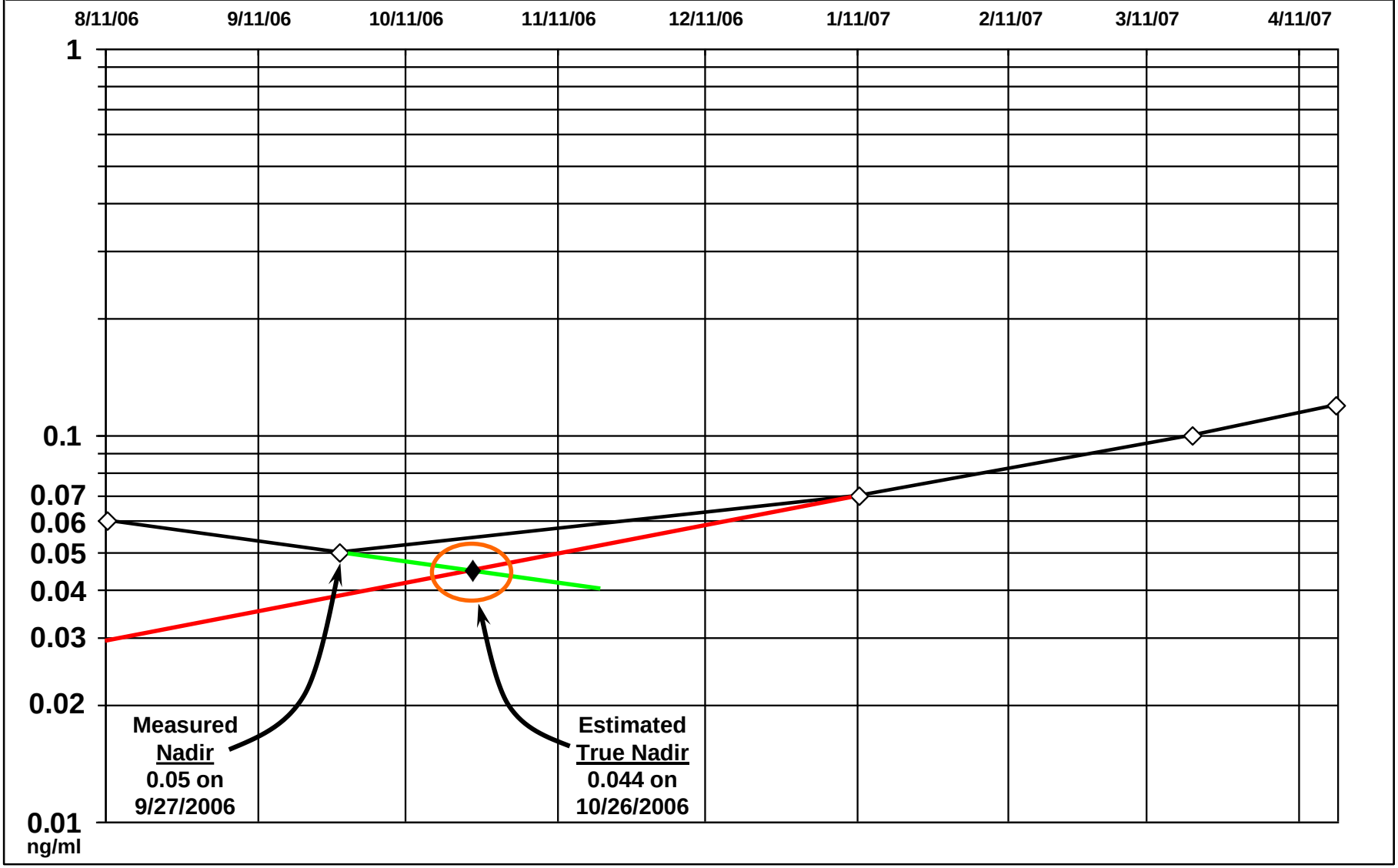
Topic 001.6 - Estimating the True Nadir – Intercept of Decay and Growth Curves

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**



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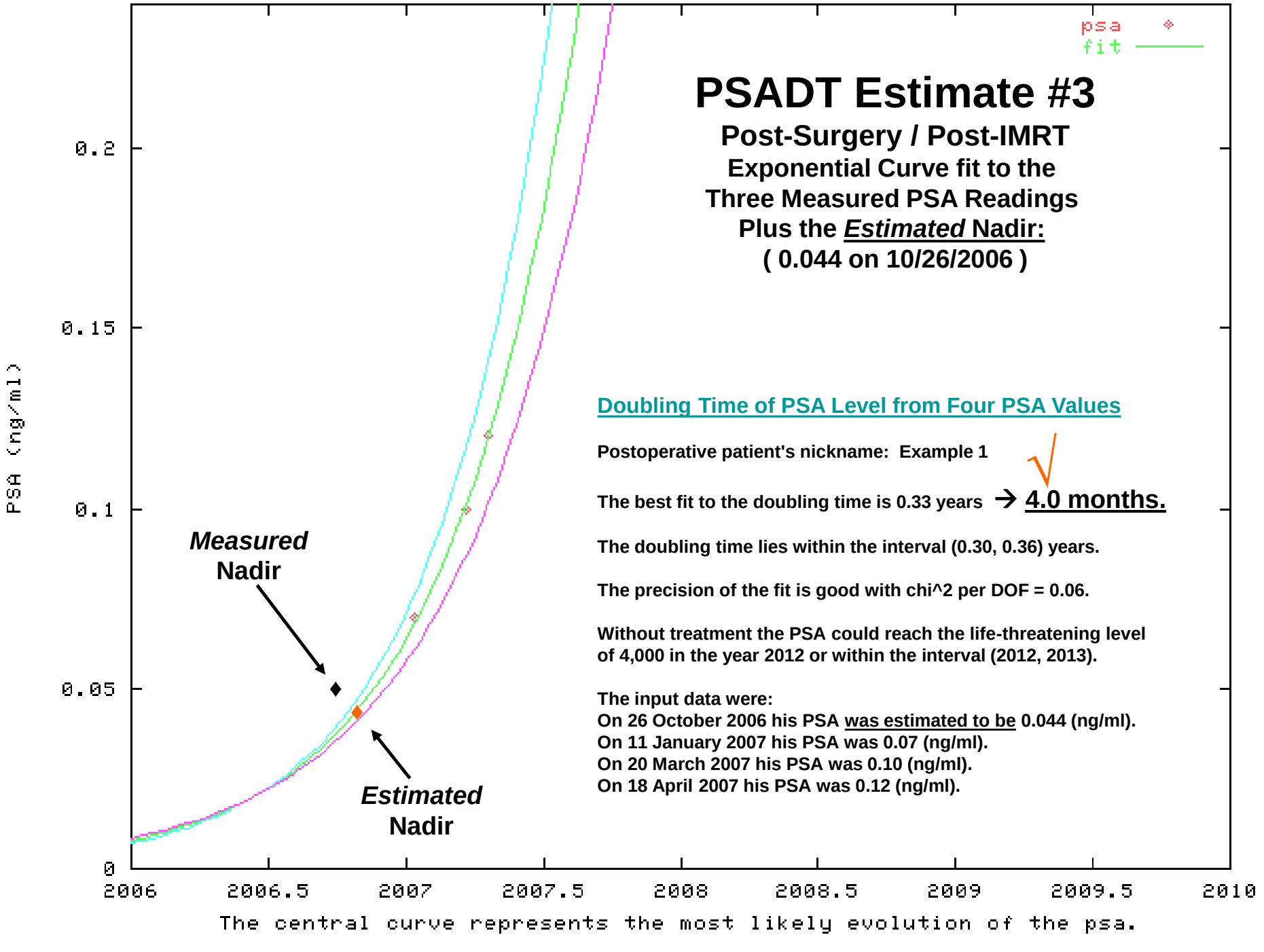
Topic 001.7 - Post-Treatment PSADT Estimate Improved Using *Estimated* Nadir



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 → 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).

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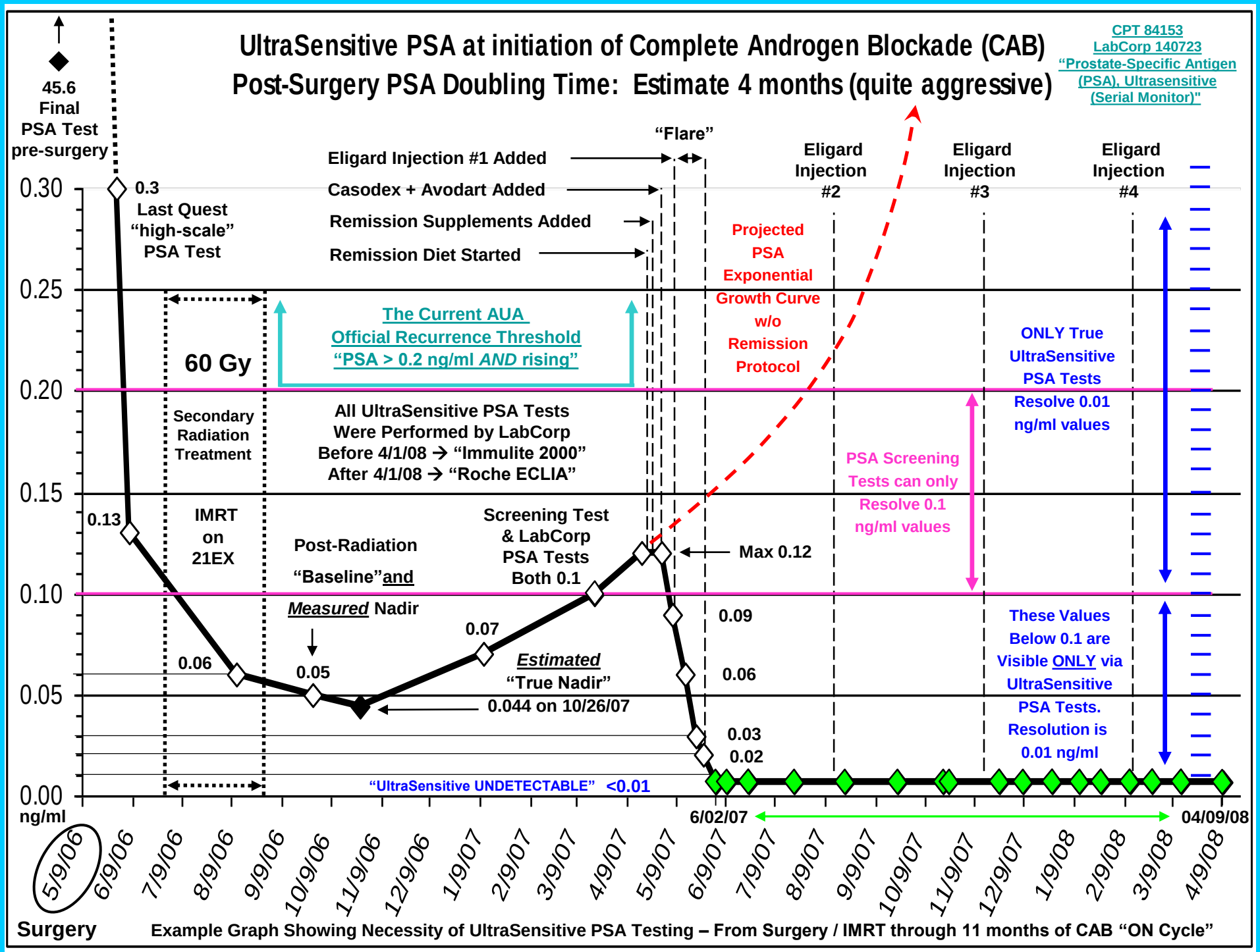
Topic 001.8 - UltraSensitive PSA Testing – Remission Protocol Performance



Example Graph Showing Necessity of UltraSensitive PSA Testing – From Surgery / IMRT through 11 months of CAB "ON Cycle"

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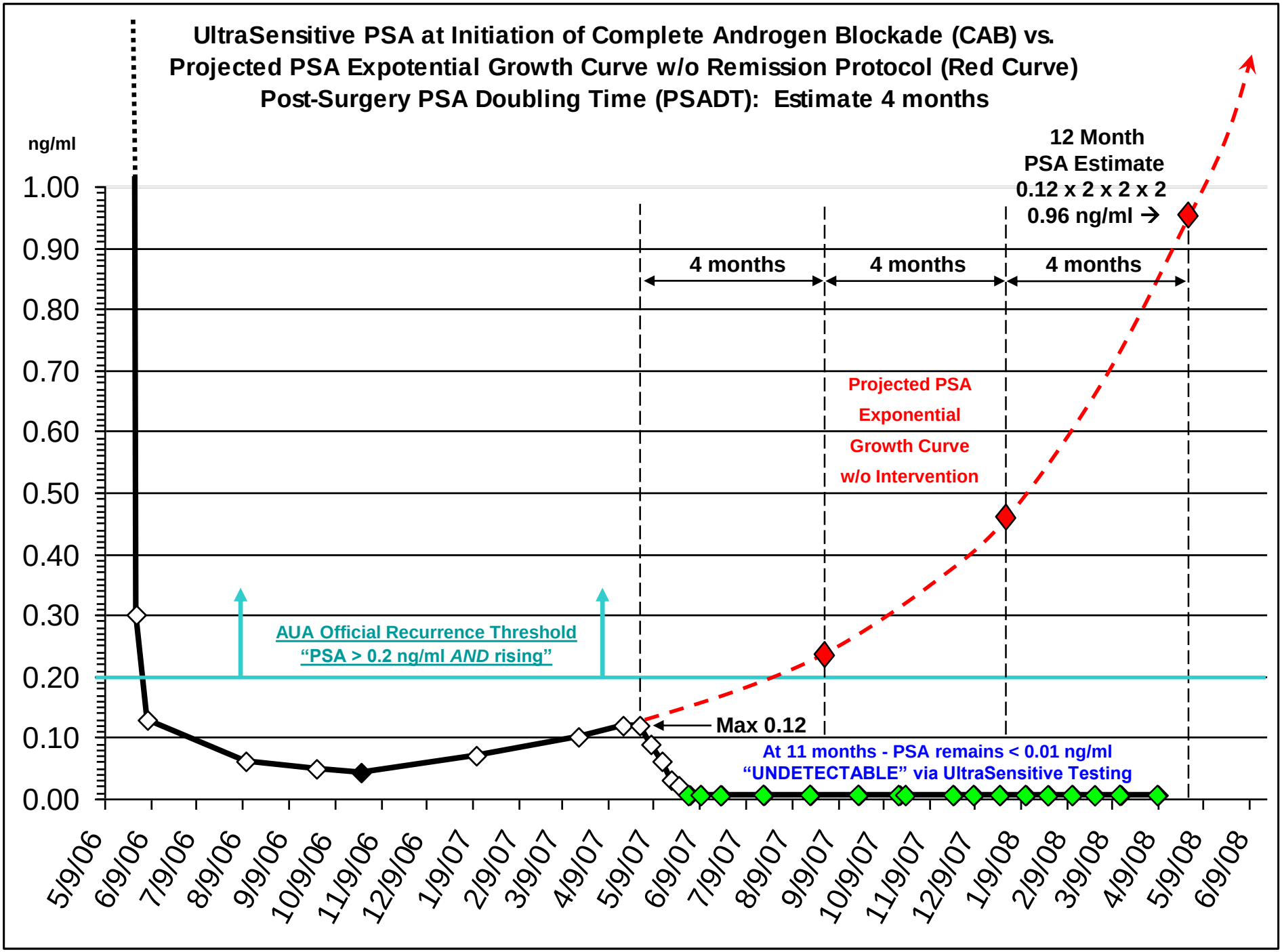
Topic 001.9 - UltraSensitive PSA Testing – Remission Protocol Performance



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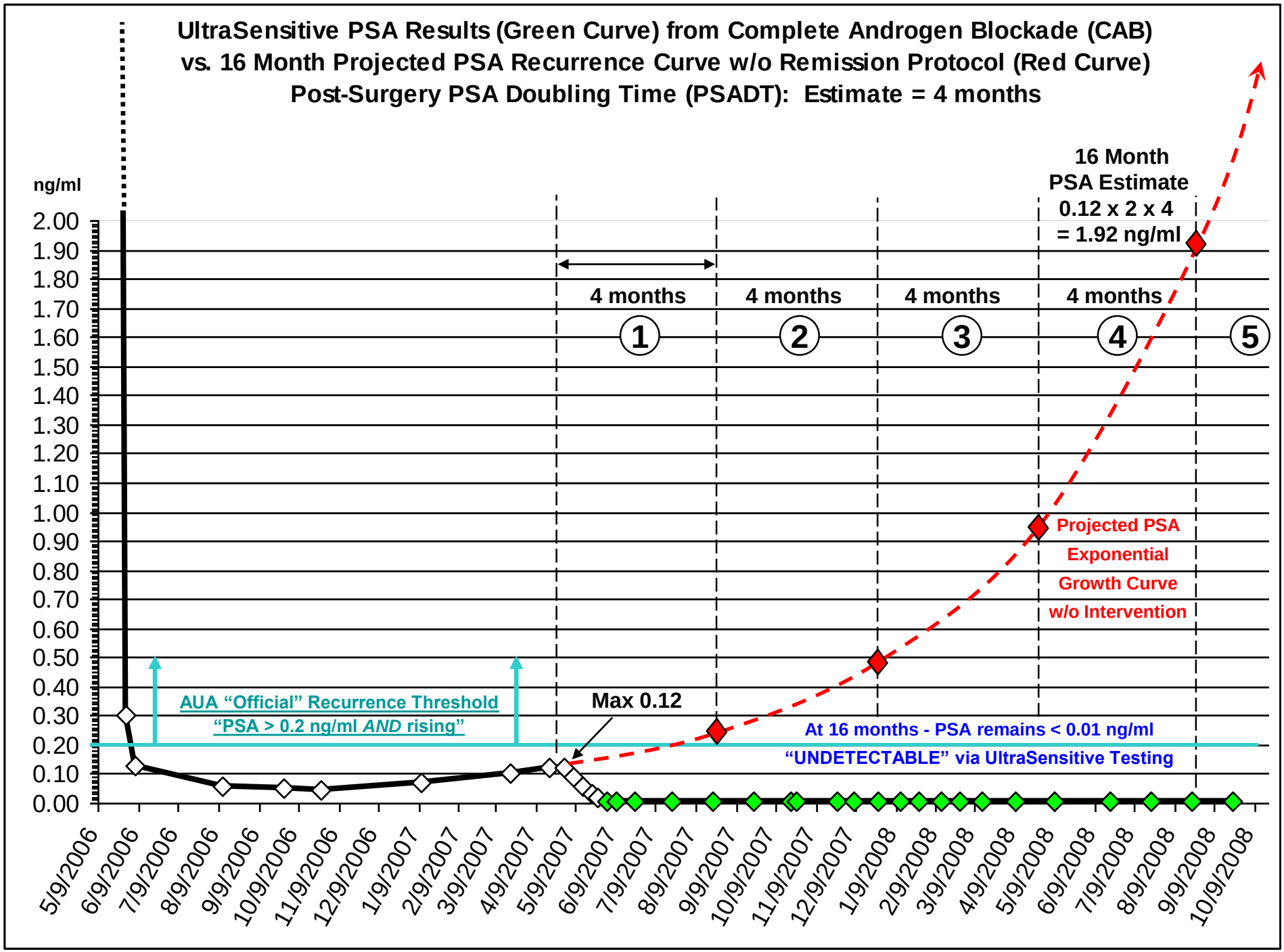
Topic 001.10 - UltraSensitive PSA Testing – Remission Protocol Performance



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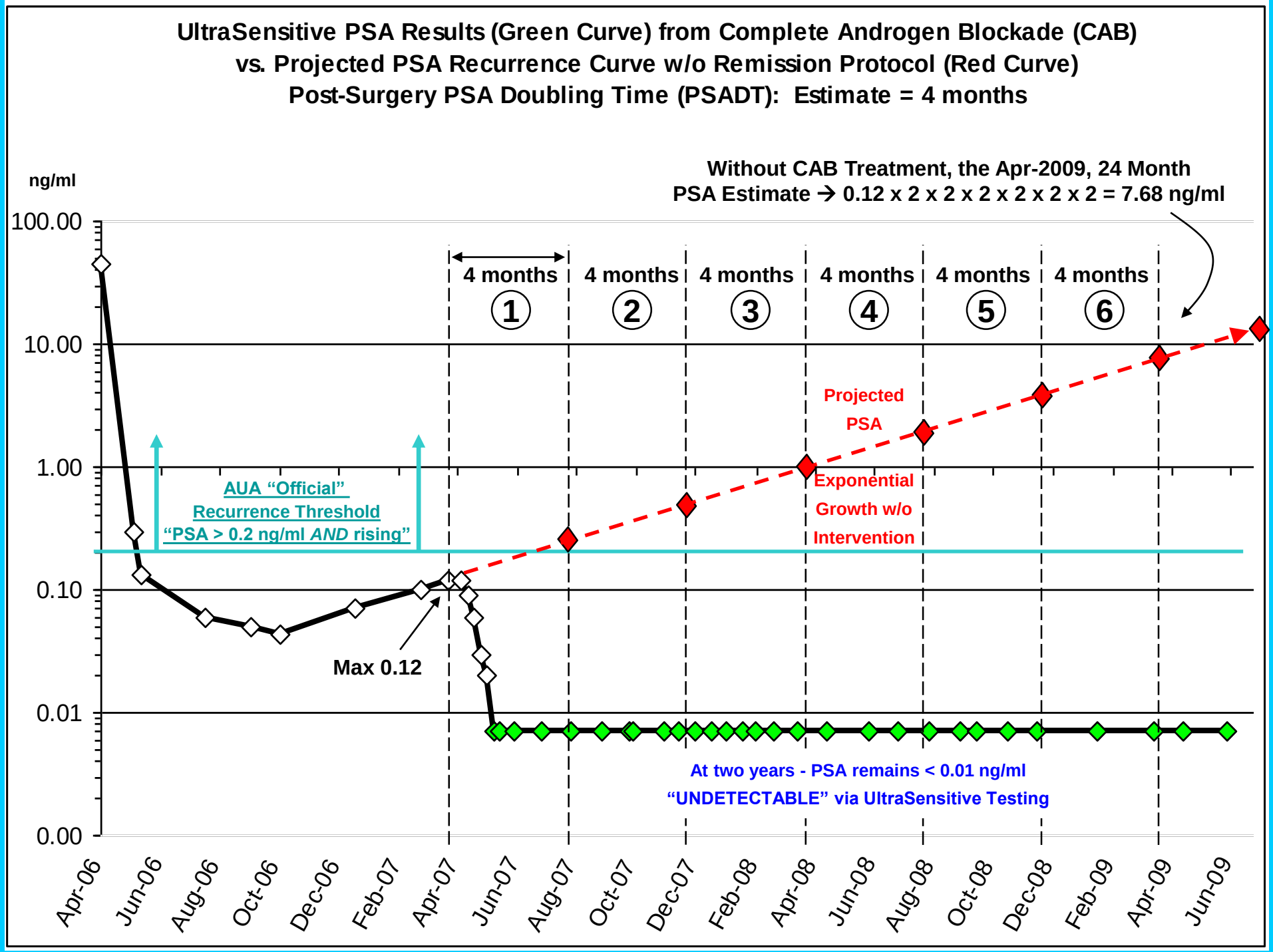
Topic 001.11 - UltraSensitive PSA Testing – Remission Protocol Performance



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