DISCUSSION OF MATHEMATICAL APPROACH OF PSA LEVEL TEST DURING PROSTATE CANCER ANALYSIS

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Abstract

The most common test for the detection of prostate cancer is based on the PSA level of blood. This inexpensive monitoring method can be repeated quite often compared to the empirical propagation velocity of the disease. The disadvantage of this test is that besides tumor other factors may also increase the PSA level (e.g. inflammation), therefore the number of false positive results is high.

Here we examine the PSA level monitoring, and establish a mathematical method to improve the PSA test results.

Introduction

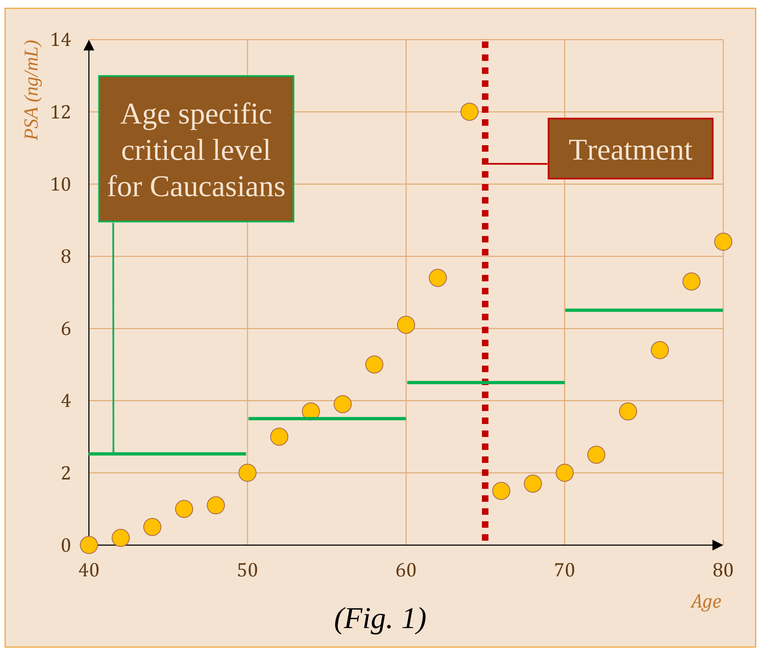
The prostate cancer is one of the most common male tumorous disease. The disease is generally indolent, plus the detection and treatment at an early stage results high proportion of cured patients or improved quality of life.

Those materials, which pointing to the existence of cancer called *tumor markers*. The tumor markers are verified by laboratory tests, or are tried to isolate the high-risk cases with screening – depending on the type of cancer.

For screening those laboratory method are suitable, which are cost-effective, easy to implement, and sufficiently sensitive and specific – that helps to distinguish the clinically significant cases from the insignificants.

The prostate cancers are often used to indicate with the following tests.

1. The **PSA level test** measures the presence of prostate-specific antigen (this antigen is a tumor marker) from blood sample. This procedure carried out cheaply (10-12 EUR), therefore currently this is the most widely used screening. The investigation has the disadvantage that beyond cancer other reasons also raise the PSA level, so the process could over diagnose - about 20% of the positive results are false-positive.
2. During the digital rectal examination (**DRE test**) the urologist checks the prostate through the rectum and looking for differences.
3. The **PCA3 level test** is a genetic test that measures the level of the PCA3 gene. This gene is only detectable in the prostate tissue and therefore the sensitivity of the process exceeds the monitoring of PSA level test. The false-positive alerts only about 10% of the total positive tests. However, the procedure is also costly (235-250 EUR).



(Fig. 1)

The task

Through a man's life in general the PSA level of blood varies according to *Fig. 1*.

The primary goals are, that after a series of PSA tests calculates sufficient estimations for the following questions:

1. What is the estimated value of the PSA level in an arbitrary time t? What t_c time reaches the estimated PSA level a predetermined critical value c?
2. What is t_d time to reach the estimated PSA levels the double of the last measured value? (In oncology the prostate cancer process is considered booted, when the PSA level doubling time is less than one year.)
3. How will change the current velocity of change of PSA level?

Further goal was to determine the accuracy of the estimations and reduce the number of false positive results of the PSA level test.

Stochastic approach

Let $t_1 < t_2 < t_n$, the date of the PSA level tests and p_1, p_2, p_n the measured PSA level for each date ($n \in IN, n \geq 3$).

Consider the PSA level as random variable which depends from the time continuously.

Let $F(t)$ is the expected value of the PSA level at a given t time. Consider the *Taylor-series* of $F(t)$

$$F(t) \approx F(0) + \frac{F'(0)}{1!}t + \frac{F"(0)}{2!}t^2$$

and name $b = F(0)$, $v = F'(t)$, $a = F"(t)$. With these rename look the

$$F(t) \approx p(t) = b + vt + \frac{a}{2}t^2$$

quadratic polynomial, which approximates $F(t)$well near t.

An estimation can be created for b, v and a using the *least square method* on (p_i, t_i) pairs $(1 \leq i \leq n)$. With the knowledge of these parameters the t_c, and t_d time countable. The current velocity of change countable with the

$$\dot{p}(t) = v + at$$

formula. Here the acceleration of the PSA level raising is described with the

$$\ddot{p}(t) = a$$

equation.

Recursive approach

Adding to the known (p_i, t_i) coordinate pairs a new (p_{n+1}, t_{n+1}) one$(1 \leq i \leq n, n \geq 3)$ recursive formulas can be used for better estimations.

For each step the b_3, b_4, …, b_n, the v_3, v_4, …, v_n, and the a_3, a_4, …, a_n coefficients can be calculated. From here a more accurate estimation can be established using the

$$\overline{b_{n+1}} = \frac{b_1 + b_2 + \cdots b_{n+1}}{n+1}$$

$$\overline{v_{n+1}} = \frac{v_1 + v_2 + \cdots v_{n+1}}{n+1}$$

$$\overline{a_{n+1}} = \frac{a_1 + a_2 + \cdots a_{n+1}}{n+1}$$

formulas $(n \in IN, n \geq 3)$. Notice, that in the stochastic approach the acceleration (parameter a) is constant, and in this recursive version it changes from time to time. This recursive approach does not fine the counted $p(t)$ values for t_1, t_2, …, t_{n+1}, but estimates better in case of $t > t_{n+1}$.

Discussion

During the estimation process the monotonic increase is required from the PSA level series. However due to test inaccuracy (or an inflammation which lifts the PSA level) there are cases, when the measured values do not give a monotonic series.

The least squares method adjusts the small deviations properly, but at higher amplitudes the method is too sensitive.

Suppose a specific n where the counted parameter $\overline{a_n} < 0$.

(In practice this is unimaginable, because in this case there must exist a t^* time, from onward the $p(t^*) < 0$, and it contradicts the fact that the PSA level always greater than zero.)

In case of $\overline{a_n} < 0$, a new PSA test is required. The test results a (p_{n+1}, t_{n+1}) pair and the new $\overline{b_{n+1}}$, $\overline{v_{n+1}}$ and $\overline{a_{n+1}}$ parameters are counted. In case of $\overline{a_{n+1}} > 0$, then the normal process goes forward.

In case of $\overline{a_{n+1}} < 0$, than consider

$$\overline{p_n} = \frac{p_1 + p_2 + \cdots p_n}{n}$$

number the constant value for $p(t)$ onward, and states the PSA stagnant until the next PSA test.

Conclusion

Based on this mathematical model a web based service is being planned under the name of PRO-FILTER, which will help doctors to evaluate the process of PSA changing and allow them to plan carefully the time of their next actions.

References

Dobó Andor: Prosztatarák terjedésének matematikai leírása, (Budapest, 03/07/2012, Manuscript)

Dr. Nagy Károly MD: A prosztata rosszindulatú betegségének rövid összefoglalása (Budapest, 03/31/2012, Manuscript)

Dobó Andor: Stagnáló PSA (Budapest, 08/11/2013, Manuscript)

Dobó Andor: Teendő $\overline{a_{n+1}}$<0 esetén (Budapest, 12/22/2013, Manuscript)