total PSA

infinosis™

total (free + complexed) PSA - Prostate-specific Antigen (FIA)

REF: IN067702 Σ 25

Please note
The measured tPSA value of a patient's sample can vary depending on the testing procedure used. The laboratory finding must therefore always contain a statement on the tPSA assay method used. tPSA values determined on patient samples by different testing procedures cannot be directly compared with one another and could be the cause of erroneous medical interpretations. If there is a change in the tPSA assay procedure used while monitoring therapy, then the tPSA values obtained upon changing over to the new procedure must be confirmed by parallel measurements with both methods.

Intended use
The infinosis™ total PSA is a fluorescence immunoassay for the in vitro quantitative determination of total (free+complexed) prostate-specific antigen in Human Serum or Plasma.

Summary
Prostate−specific antigen (PSA) is a glycoprotein (molecular weight 30000−34000 daltons) having a close structural relationship to the glandular kallikreins. It has the function of a serine proteinase.[1]
The proteolytic activity of PSA in blood is inhibited by the irreversible formation of complexes with protease inhibitors such as alpha−1−antichymotrypsin, alpha−2−macroglobulin, and other acute phase proteins.[2] Beside these complexes, about 30 % of the PSA present in blood occurs in the free form, but is proteolytically inactive.[3,4,5]
Elevated concentrations of PSA in serum are generally indicative of a pathologic condition of the prostate (prostatitis, benign hyperplasia or carcinoma).[6,7]
As PSA is also present in para−urethral and anal glands, as well as in breast tissue or with breast cancer, low levels of PSA can also be detected in sera from women. PSA may still be detectable even after radical prostatectomy.
The main areas in which PSA determinations are employed are the monitoring of progress and efficiency of therapy in patients with prostate carcinoma or receiving hormonal therapy. The steepness of the rate of fall in PSA down to no−longer detectable levels following radiotherapy, hormonal therapy or radical surgical removal of the prostate provides information on the success of therapy.[8]
An inflammation or trauma of the prostate (e.g. in cases of urinary retention or following rectal examination, cystoscopy, coloscopy, transurethral biopsy, laser treatment or ergometry) can lead to PSA elevations of varying duration and magnitude.

Test principle
Sandwich principle. Total duration of assay: **15 minutes**
Sample is added to the sample well of the test, then the fluorescence-labeled detector anti-PSA antibody binds to PSA antigen in blood specimen. As the sample mixture migrates on the nitrocellulose matrix of test strip by capillary action, the complexes of detector antibody and PSA are captured to anti-PSA antibody that has been immobilized on test strip.
More antigens in the sample will form more antigen-antibody complexes which lead to stronger fluorescence signal by detector antibodies, which is processed by instrument for infinosis™ tests to show PSA concentration in the sample.

Reagents
Materials provided
- **Test Cartridge**, 25 pcs, individually packaged
- **ID Chip**, 1 pcs
- **Sample Buffer,** 25 tubes
- **IFU**, 1 copy

Materials required (but not provided)
- Infinosis™ 2020 FIA analyzer
- Single use disposable lancing device
- Transfer pipette set (100 µL size)
- Alcohol pads
- Timer

Precautions and warnings
- For in vitro diagnostic use only.
- Carefully follow the instructions and procedures described in this instructions before testing.
- The Test cartridge should remain in its original sealed pouch until ready to use. Do not use it if the pouch is damaged or the seal is broken.
- Do not use reagents beyond the labeled expiry date.
- Do not mix or use components from kits with different Lots.
- Don't use Test cartridge if its Lot does not match with ID Chip that is inserted onto the instrument.
- The Infinosis™ PSA assay should be used only in conjunction with the instrument for infinosis™ tests.
- The tests should be applied by professionally trained staff working in certified laboratories at some remove from the patient and clinic at which the sample is taken by qualified medical personnel.
- infinosis™ PSA assay is single use only. Do not re-use it.
- The Test cartridge and Analyzer should be used away from vibration and magnetic field. During normal usage, the Test cartridge may introduce minute vibration, which should be regarded as normal.
- Use separate clean pipette tips and detector buffer vials for different specimens. The pipette tips and detector buffer vials should be used for one specimen only.
- Do not smoke, eat, or drink in areas in which specimens or kit reagents are handled.
- Blood specimens, used Test cartridges, pipette tips and detector buffer vials are potentially infectious. Proper laboratory safety techniques, handing and disposal methods should be followed in accordance with standard procedures and relevant regulations observed by microbiological hazard materials.
- The results should be interpreted by the physician along with clinical findings and other laboratory test results.

Storage and stability
- Store the test kit at 2-30℃, the stability is up to the expiration date printed on package.
- Test cartridge and sample buffer should be used within 1 hour after opening the pack.

Specimen collection and preparation
- The test can be performed with either Serum or Plasma.
- Collect serum samples in accordance with correct medical practices.
- Using standard phlebotomy procedure, collect a venipuncture whole blood specimen using a blood collection tube. If collecting plasma use a blood collection tube containing suitable anticoagulant (EDTA recommended).
- Separate the serum/plasma from blood as soon as possible to avoid hemolysis.
- Test should be performed immediately after the specimens have been collected. Do not leave the specimens at room temperature for prolonged periods. Specimens may be stored at 2-8℃ for up to 3 days. For long-term storage, specimens should be kept below -20℃.

Calibration
The instrument automatically reads in the lot-specific calibration data from the QR code information printed on the Test cartridge, eliminating the need for calibration by the user.

Quality control
- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- The control tests should be performed immediately after opening a new test lot to ensure the test performance is not altered.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are provided on demand with infinosis™ tests. For more information regarding obtaining the control materials, contact DiaSino Laboratories Co., Ltd for assistance.

Test setup
- Ensure that the lot number of the cartridge matches that of the sample buffer, and the ID Chip.
- If the sealed cartridge and sample buffer have been stored in refrigerator, place them at room temperature (18-25 ℃) at least 30 minutes before measurement.
- Turn on the instrument for infinosis™ tests.
  Refer to the *'instrument for infinosis™ tests Operation Manual'* for the complete information and operating instructions.

Test procedure
1. Insert ID Chip into the instrument for infinosis™ tests and read ID chip information.
2. Using a pipette to transfer **50 µL** of sample (Human plasma/serum) to the **sample buffer tube** provided in the kit.
3. Close the lid of the sample mixing tube and mix the sample thoroughly for **5-10 seconds** by tapping or inverting the tube.
4. Pipette out **100 µL** of **sample mixture** and load it onto the sample well on the cartridge.
5. Leave the sample-loaded cartridge at room temperature for **15 minutes.**
6. Insert the sample-loaded cartridge into the cartridge holder of instrument for infinosis™ tests.
   Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder.
7. Press **"Test"** button on the instrument for infinosis™ tests.
8. Instrument for infinosis™ tests will start scanning the sample-loaded cartridge immediately.
9. Read the test result on the display screen of the instrument for infinosis™ tests.
10. Print out the testing results when press **"Print"** button on the instrument for infinosis™ tests.

Limitations - interference
- The assay is unaffected by icterus (bilirubin < 1000 µmol/L or < 58 mg/dL), hemolysis (Hb < 1.0 mmol/L or < 1.61 g/dL), lipemia (Intralipid < 1500 mg/dL) and biotin (< 200 nmol/L or < 49 ng/mL).
- Criterion: Recovery within ± 10 % of initial value.
- No interference was observed from rheumatoid factors up to a concentration of 1500 IU/mL.
- There is no high−dose hook effect at tPSA concentrations up to 8000 ng/mL.
- In vitro tests were performed on 28 commonly used pharmaceuticals. No interference with the assay was found.
- It is known that in rare cases PSA isoforms do exist which may be measured differently by different PSA tests. Findings of this kind have occasionally been reported for PSA tests from various manufacturers.[9,10,11]
- Patients who have received mouse monoclonal antibodies for either diagnosis or therapy can develop HAMA (human Anti- mouse antibodies). HAMA can produce either falsely high or falsely low values in immunoassays which use mouse monoclonal antibodies. Additional information may be required for diagnosis.

IVD

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- For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Measuring range
0.05–100 ng/mL (defined by the lower detection limit and the maximum of the master curve). Values below the lower detection limit are reported as < 0.05 ng/mL. Values above the measuring range are reported as > 100 ng/mL.

Lower detection limit
0.05 ng/mL
The detection limit represents the lowest analyte level that can be distinguished from zero. It is calculated as the value lying two standard deviations above that of the lowest standard (master calibrator, standard 1+2 SD, repeatability study, n = 18).

Expected values
Expected values in normal healthy males
Studies in two hospitals with the total PSA assay on sera from 316 healthy men of various age groups yielded the following results:

		tPSA (ng/mL)	
Age (years)	n	Median	95th percentile
< 40	62	0.55	1.38
40-49	58	0.58	1.88
50-59	146	0.71	2.61
60-69	38	1.58	3.76
≥ 70	12	1.63	4.25

tPSA values in detection of prostate cancer

A study was performed to demonstrate the effectiveness of total PSA assay when used in conjunction with digital rectal examination (DRE) as an aid in the detection of prostate cancer in men 50 years of age or older.
A total of 951 serially accrued men 50 years of age or older participated in the study. The mean age of the cohort was 66.4 years (95 % confidence interval = 65.9 to 66.8 years).
Distribution of tPSA values by biopsy result and digital rectal examination result

Prostate biopsy result: benign

		tPSA (ng/mL)		
DRE result	n	Median	Minimum	Maximum
Normal	298	5.7	0.38	68.4
Pathological	301	4.5	0.25	23.6
Total	599	5.0	0.25	68.4

Prostate biopsy result: malignant

		tPSA (ng/mL)		
DRE result	N	Median	Minimum	Maximum
Normal	154	7.4	2.4	136.5
Pathological	198	8.0	0.55	1044.9
Total	352	7.6	0.55	1044.9

Utility of tPSA in detection of prostate cancer

As shown in the table below, within this cohort of 951 males, 352 (37.0 %) prostate cancers were detected by biopsy. Abnormal digital rectal examination (DRE) results were reported for 220 (62.5 %) of the 352 prostate cancers while tPSA results above 4 ng/mL were reported for 302 (85.7 %) cancers for DiaSino tPSA ELISA. Of the 352 men diagnosed with cancer, 337 (95.7 %) had either an abnormal DRE result or a tPSA value above 4.0 ng/mL.

The positive predictive value for the DiaSino total PSA ELISA was 0.414 using 4.0 ng/mL as a cutoff (malign prostate biopsy + tPSA > 4.0 ng/mL: n = 302 / tPSA > 4.0 ng/mL: n = 729).
Results for digital rectal examination and tPSA as referred to prostate cancers detected by biopsy in a cohort of:
951 males 50 years or older referred to an urologist for prostate evaluation.

	Total	DRE+ a)	PSA+ b)	PSA+ or DRE+	PSA+ and DRE+	PSA+ and DRE- c)	PSA- and DRE+ d)
Total number	951	521	729	899	366	370	154
No. of malignant pro-state biopsies	352	220	302	337	176	125	36
% positive biopsies	37.0%	42.2%	41.4%	37.5%	48.1%	33.8%	23.4%

a) abnormal DRE
b) tPSA value > 4 ng/mL
c) normal DRE
d) tPSA value < 4 ng/mL

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data
Representative performance data are given below. Results obtained in individual laboratories may differ.

Analytical specificity
For the monoclonal antibodies used, the following cross-reactivities were found:
PAP and ACT: none; PSA and PSA–ACT are recognized on an equimolar basis.

Functional sensitivity
0.07 ng/mL
The functional sensitivity is the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of 20 %.

Method comparison
A comparison of the Infinosis™ PSA assay (y) with the Elecsys PSA assay (x) using 171 clinical samples gave the following correlations:

Linear regression

y = 1.0321x + 0.077

r = 0.9856

References

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Symbols

IVD			REF
In vitro diagnostic medical device	Temperature limit	Consult instructions for use	Catalog number
LOT			Σ
Batch code	Date of manufacture	Use-by date	Contains sufficient for <n> tests
Manufacturer	Do not re-use	Do not use if package is damaged and consult instructions for use	

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