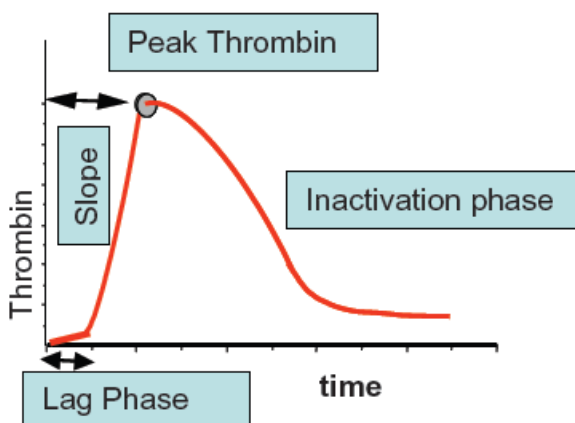
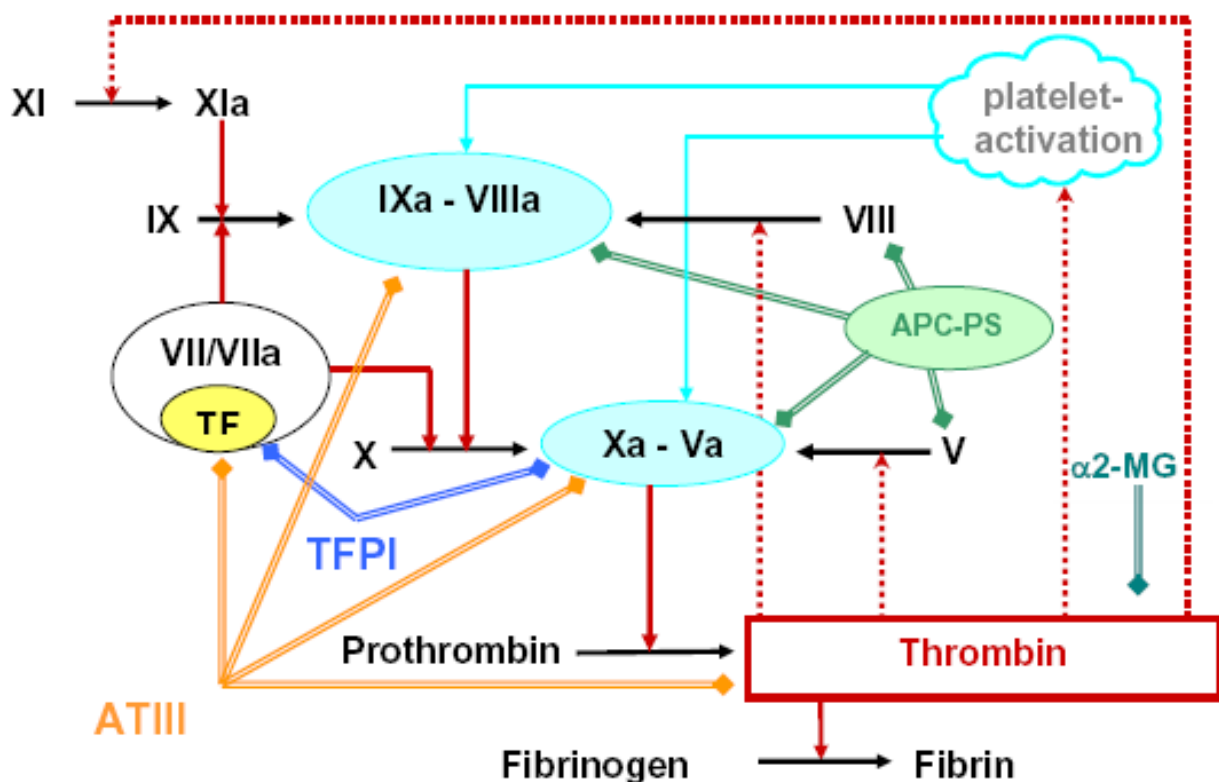


NEW! TECHNOTHROMBIN® TGA

TECHNOTHROMBIN® TGA is a **thrombin generation assay (TGA)** based on monitoring the formation of thrombin by means of a fluorogenic substrate upon activation of the coagulation cascade by tissue factor. This assay can be used to monitor hemophiliacs during inhibitor bypassing therapy, to monitor anticoagulation therapy and to determine states of thrombophilia.



The use of TECHNOTHROMBIN® TGA for such diverse applications is made possible because TECHNOTHROMBIN® TGA allows to measure the whole kinetics of thrombin generation not only during the initiation phase of thrombin formation with the end point fibrin formation, but also during the phase of down regulation of thrombin formation and inactivation of the formed thrombin. TECHNOTHROMBIN® TGA is therefore a universal tool for analysis and monitoring of the haemostatic system on an individual basis.

TEST PRINCIPLE

TECHNOTHROMBIN[®] TGA is based on monitoring the fluorescence generated by thrombin cleavage of a fluorogenic substrate over time upon activation of the coagulation cascade by different concentrations of tissue factor (RA, RB, RC Low and RC High*) and negatively charged phospholipids in plasma. From the changes in fluorescence over time, the concentration of thrombin (nM) in the sample can be calculated using the respective thrombin calibration curve (only one calibration has to be done for each lot). The rate of increase in thrombin concentration over time then allows to calculate generation of thrombin in the sample per minute and to plot this value over time for the whole coagulation process. This then results in the visualization of the different phases of clot formation.

The TECHNOTHROMBIN[®] TGA Kit 3x16 T. [REF](#) 5006010 contains :

mL	reagent	description
3 x 1.5	TGA substrate	Fluorogenic substrate 1 mM Z-G-G-R-AMC, 15 mM CaCl ₂
1 x 3	TGA buffer	Hepes-NaCl-buffer containing 1% bovine serum albumin
1 x 0.5	TGA thrombin calibrator	~1.000 nM thrombin in buffer with BSA
1 x 0.5	TGA reagent B (RB)	Low conc. of phospholipid micelles containing 17.9 pM rhTF in Tris-Hepes-NaCl buffer
1 x 0.5	TGA reagent C Low (RC Low)	Low conc. of phospholipid micelles containing 71.6 pM rhTF in Tris-Hepes-NaCl buffer
1 x 0.5	TGA reagent C High (RC High)	High conc. of phospholipid micelles containing 71.6 pM rhTF in Tris-Hepes-NaCl buffer
1 x 1	TGA control 1 (C1)	Normal human plasma, lyo.
1 x 1	TGA control 2 (C2)	Human plasma with increased thrombin generation, lyo.
1 x 1	TGA control 3 (C3)	Human plasma with decreased thrombin generation, lyo.

* TGA Reagents RA, RB, RC Low and RC High are particularly suitable for:

TGA RA = measuring circulating micro particles
TGA RB = monitoring F VIII inhibitor therapy (FEIBA)
TGA RC Low = measurement of thrombophilia and monitoring of F VIII inhibitor therapy (rFVIIa)
TGA RC High = monitoring anti-coagulant therapy

QUANTITATIVE MEASUREMENT OF THROMBIN GENERATION

Fluorescence Reader

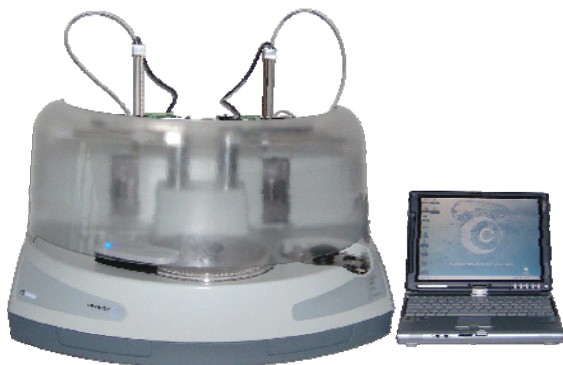
For assaying thrombin generation using TECHNOTHROMBIN[®] TGA you need a fluorescence reader equipped with filters ~360 nm and ~460 nm (excitation/emission) as the BioTek[®] FLx 800[™] TC ([REF](#) 9810010) with an * adapted software for TECHNOTHROMBIN[®] TGA.

Applications are available for:

BioTek[®] FLx 800[™] TC *
BMG Labtech FLUOstar OPTIMA
Molecular Devices Gemini / SpectraMax
Perkin Elmer[®] Victor Wallac
TECAN Genios
Thermo Fluoroskan

CEVERON[®] alpha

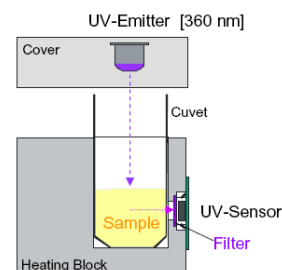
The new automated analyser CEVERON[®] alpha ([REF](#) 9820010) is equipped with a fluorescence measurement module and thus suitable for assays such as TECHNOTHROMBIN[®] TGA. With CEVERON[®] alpha, standard clotting tests and thrombin generation assays can be performed in parallel or up to 48 samples (plasma or whole blood) can be analyzed for thrombin generation simultaneously.



Thrombin Generation is measured with a special adapted TGA fluorimetric module which is placed over the cuvette rotor (Fig.1). With an UV emitter (360 nm) placed in the module, thrombin generation can then be measured (Fig. 2).



1. Fluorimetric module

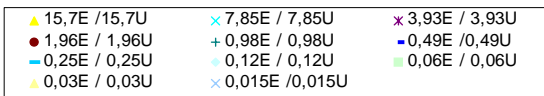
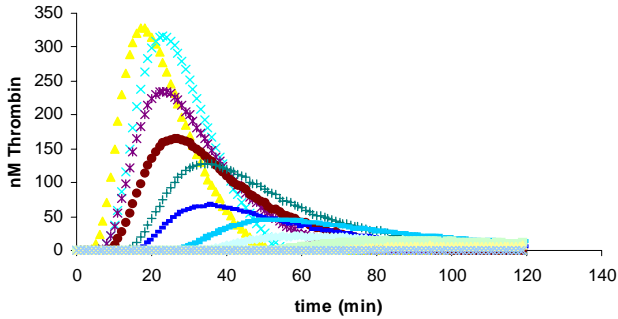


2. Measuring principle of the TGA module

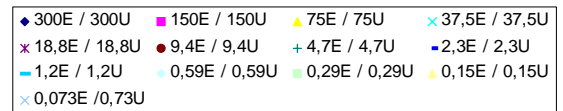
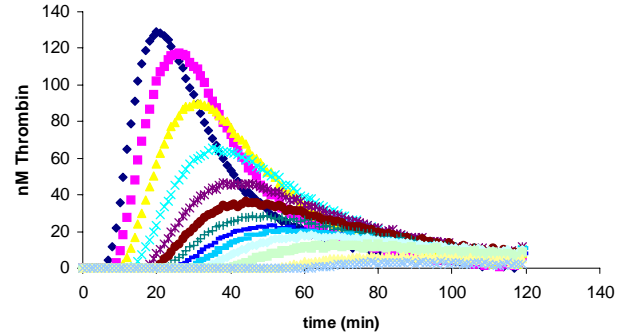
FACTOR VIII INHIBITOR THERAPY

Dose dependent reconstitution of thrombin generation potential in Factor VIII inhibitor plasma after addition of FEIBA (Factor Eight Inhibitor Bypassing Activity) or rFVIIa (NovoSeven®).

TECHNOTHROMBIN TGA RB / FEIBA
FVIII INH 3O31000 [58,4BU/ml]



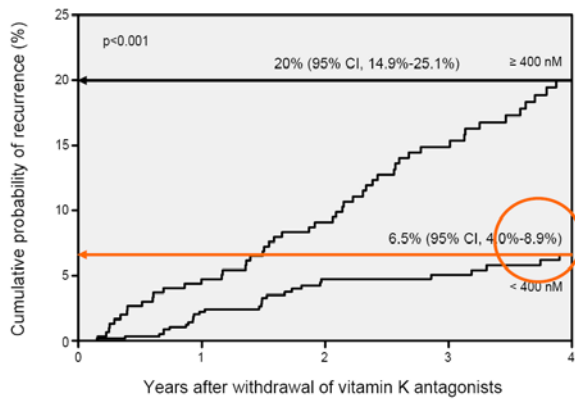
TECHNOTHROMBIN TGA RC LOW / Novo Seven
FVIII INH 3O31000 [58.4 BU/ml]



ASSAYING THROMBOPHILIC TENDENCY

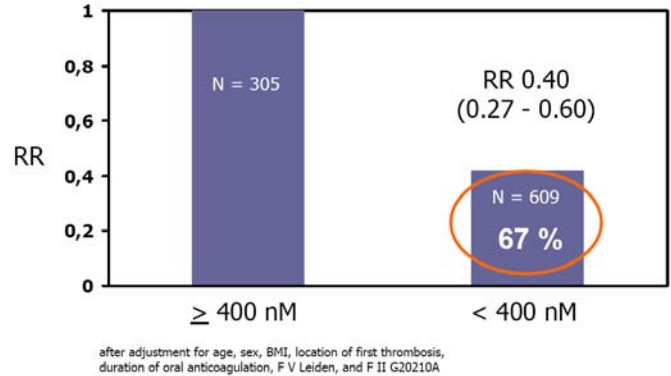
In some forms of thrombophilia, such as deficiencies of ATIII, Protein C, or Protein S tissue factor triggered clotting produces a larger amount of thrombin than in normals. Such thrombophilic states can be detected by assaying thrombin generation in platelet poor plasma.

Peak thrombin - Probability of Recurrent VTE



Hron G. et al., JAMA, July 26, 2006 – Vol 296, No. 4, 397-402

Peak thrombin - Relative Risk of Recurrence



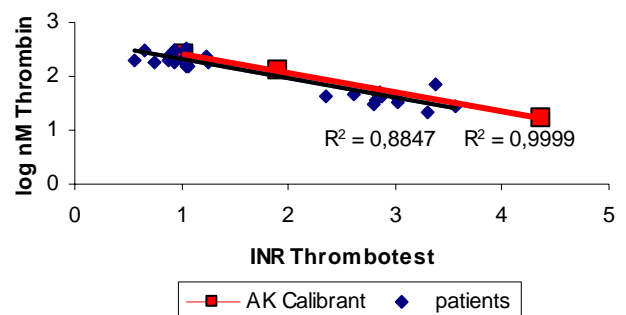
MONITORING OF ANTI-COAGULATION THERAPY

All forms of anti-coagulant therapies such as heparin therapy, direct thrombin inhibitors or oral anti-coagulants can be monitored using TECHNOTHROMBIN® TGA. TECHNOTHROMBIN® TGA is also suitable for determination of INR values.

Oral anti-coagulation therapy

When using calibrated plasmas (AK-Calibrant) TECHNOTHROMBIN® TGA can be used for direct determination of INR. There is a highly significant correlation between INR values that are determined using TECHNOTHROMBIN® TGA and those that result from assays using different thromboplastin preparations, e.g. Thrombotest®.

Peak TECHNOTHROMBIN TGA (RC) / INR
Thrombotest

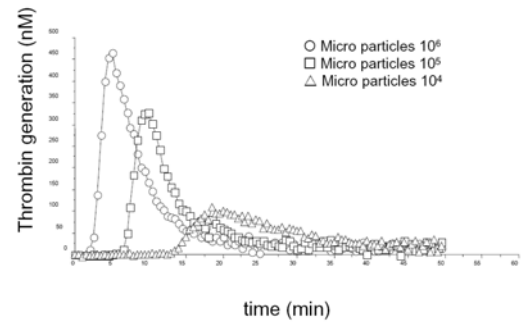


THROMBIN GENERATION BY MICRO PARTICLES

Thrombin generation induced by micro particles can be measured by the TECHNOTHROMBIN® TGA assay.

The amount of thrombin generated is dependent on the number of micro particles present in the sample.

Micro particle induced thrombin generation / TGA RA



SUMMARY

Reagent	Purpose
TGA RA	- to monitor the activity of circulating micro particles contained in platelet poor plasma
TGA RB	- to monitor inhibitor bypass therapy with FEIBA in hemophiliacs with Factor VIII inhibitors
TGA RC Low	- measurement of thrombophilia tendency (preferentially in standard PPP plasma) -to monitor inhibitor bypass therapy with rFVIIa in hemophiliacs with Factor VIII inhibitors
TGA RC High	- monitoring anticoagulation therapy

ORDERING INFORMATION

Complete reagent kit:

REF 5006010 TECHNOTHROMBIN® TGA Kit



Modular reagents:

REF 5006205	TECHNOTHROMBIN® TGA RA	5 x 0.5 mL
REF 5006206	TECHNOTHROMBIN® TGA RA	50 x 0.5 mL
REF 5006209	TECHNOTHROMBIN® TGA RB	5 x 0.5 mL
REF 5006210	TECHNOTHROMBIN® TGA RB	50 x 0.5 mL
REF 5006212	TECHNOTHROMBIN® TGA RC Low	5 x 0.5 mL
REF 5006213	TECHNOTHROMBIN® TGA RC Low	50 x 0.5 mL
REF 5006214	TECHNOTHROMBIN® TGA RC High	5 x 0.5 mL
REF 5006216	TECHNOTHROMBIN® TGA RC High	50 x 0.5 mL
REF 5006235	TECHNOTHROMBIN® TGA SUB	5 x 1.5 mL
REF 5006230	TECHNOTHROMBIN® TGA SUB	50 x 1.5 mL

Additional Control:

REF 5006350	TECHNOTHROMBIN® TGA MFC (microparticle free control)	5 x 0.5 mL
REF 5006310	TECHNOTHROMBIN® TGA C1	5 x 1 mL
REF 5006320	TECHNOTHROMBIN® TGA C2	5 x 1 mL
REF 5006330	TECHNOTHROMBIN® TGA C3	5 x 1 mL
REF 5006345	TECHNOTHROMBIN® TGA CAL Set	1 Set

Machines:

REF 9820010	Ceveron® alpha with TGA module	pc.
REF 9810010	BioTek® FLx 800™ TC Fluorometer	pc.

Black plates for the TGA determination on the fluorescence reader are available on request.

Technoclone GmbH
Brunner Str. 59/5
1230 Vienna, Austria
Tel: +43 1 86373-10
Fax: +43 1 86373-44

Technoclone Deutschland GmbH
Hans Bunte Str. 8-10
69123 Heidelberg, Germany
Tel: +49 6221 830 441
Fax: +49 6221 830 437

Technoclone Ltd.
Eclipse House 7, Curtis Road,
Dorking/Surrey RH4 1EJ
Tel: +44 1306 888 777
Fax: +44 1306 883 883



sales@technoclone.com <http://www.technoclone.com>

TGA001E.011
10/2006