#### **ORDERING INFORMATION**

Cat. Nº	Product
HC-T2-F	Thrombodynamics Analyser System T2-F (fibrin registration only)
HC-T2-T	Thrombodynamics Analyser System T2-T (fibrin and thrombin registration)
HC-TDX-10	Reagents kit for 10 fibrin measurements
HC-PLS-10	Reagents kit for 10 fibrin and thrombin measurements

The product was launched in the European market as a RUO device at the beginning of 2014.

Thrombodynamics Analyser System is sold in Russia from the end of 2012. Thrombodynamics assay has already been approved for clinical use in Russian Federation.

We help clinicians to succeed, providing clear and reliable estimation of patients coagulation state, thus giving an ability to prevent thrombotic or bleeding comlications.



Switzerland **ENDOTELL AG** info@endotell.ch

www.endotell.ch

**Benelux** 

NODIA info@nodia.com www.nodia.com

**UK and Channel Islands** Quadratech Diagnostics Ltd quadratech@btinternet.com www.quadratech.co.uk

**Austria and Germany** CoaChrom Diagnostica GmbH info@coachrom.com www.coachrom.com

Don't find your local distributor? Do not hesitate to contact us: mail@hemacore.com



www.thrombodynamics.com www.hemacore.com/en/





## **HEMOSTASIS & THROMBOSIS BEYOND BIOCHEMISTRY NEW GLOBAL VIEW**



## **THROMBODYNAMICS ASSAY**

SPATIAL DYNAMICS OF FIBRIN CLOT GROWTH



# THROMBODYNAMICS-4D

**ASSAY** 



SPATIAL DYNAMICS OF THROMBIN GENERATION & FIBRIN CLOT GROWTH

Research Use Only. Not for use in diagnostic procedures.

#### SPATIAL DYNAMICS OF COAGULATION

Thrombodynamics is the only laboratory test with adequate physiological model based on the up-to-date understanding of the spatial aspects of in vivo coagulation process.

Thrombodynamics imitates in vitro physiological and pathophysiological processes that occur in vivo during hemostatic plug formation or thrombosis.

Unlike other routine coagulation assays the fibrin clot growth process in thrombodynamics assay develops in space and time rather than only in time.

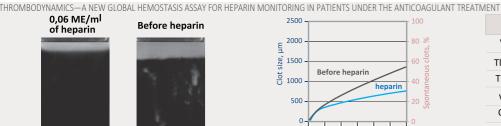
The fibrin clot starts to form, growing from the tissue factor bearing surface, but then propagates into the bulk of the plasma sample without interaction with activator.

Thromb Res. 2015

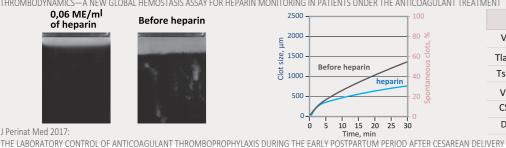
HEMOSTASIS AND THROMBOSIS BEYOND BIOCHEMISTRY: ROLES OF GEOMETRY, FLOW AND DIFFUSION

#### **EFFECT OF ANTICOAGULANTS**

Thrombodynamics is sensitive to all types of anticoagulants. Thrombodynamics is more sensitive to heparin than APTT, comparable to anti-Xa and higher than that of TGT and TEG.

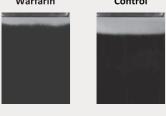


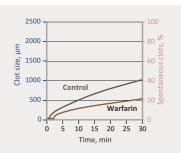






Warfarin Control





	Warfarin	Control
V	12	24
Tlag	2,7	1,1
Tsp	None	None
Vi	26,9	42,1
CS	543	995
D	18 102	31 955

Result: 30 min

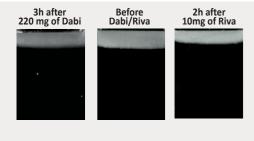
V [um/min], Growth rate

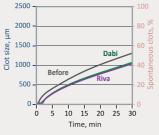
Tsp [min], Spontanous clots formation time

Talanta 2018:

CS [um], Clot size

TF-coated





	3h after 220 mg of Dabi	Before Dabi/Riva	2h after 10mg of Riva
V	29,8	31,5	27,5
Tlag	2,2	1,1	1,8
Tsp	None	None	None
Vi	45,7	57,8	44,1
CS	1 075	1 284	1 042
D	31 251	32 826	30 426

#### **COAGULATION STATES AND FIBRINOLYSIS**

Thrombodynamics is both a qualitative and quantitative evaluation of the coagulation status and fibrinolysis. Clot formation/lisys process is registred by a CCD camera and then calculated.



HROMBODYNAMICS, A NEW GLOBAL COAGULATION TEST: MEASUREMENT OF HEPARIN EFFICIENCY

In addition to the fibrin clot growth thrombodynamics allows quantifying the clot lysis process in presence of plasminogen activators. Lysis process follows clot propagation and starts inside the formed clot. Further coagulation propagation is simultaneous with the lysis process.

In progress: 30 min Result: 60 min LOT [ min ] Lysis onset time LP [ %/min ], Lysis progretion

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#### MAIN PARAMETERS AND INTERPRETATION

Tlag, [min] - Lag-time - time between contact of plasma sample with activator and start of clot growth. This parameter is sensitive to the initial stage of blood coagulation and reactions of the extrinsic pathway. Prolongation of this parameter is caused by hypocoagulation of differing nature: deficiency of factors VII and X, (direct thrombin or factor Xa inhibitors, vitamin K antagonists). Shortening is rarely observed, and can be due to different causes of hypercoagulation.

Vi, [um/min] - Initial rate of clot growth - calculated on the interval 2-6 minutes after the beginning of clot growth, also describes initial stages of clot growth but it is spatial elongation rather than local increase of thrombin concentration. A low Vi indicates differing hypocoagulation states (factors VII or X deficiency, anticoagulant agents – factor Xa inhibitors, thrombin inhibitors, vitamin K-antagonists, UFH and LMWH). A high Vi indicates differing hypercoagulation states.

Vst, [um/min] - Rate of clot growth - is the average rate of clot growth calculated on the interval 15-25 min after the beginning of clot growth. If there are no spontaneous clots Vst and V are equal. In the presence of active spontaneous clotting Vst is not calculated. This parameter characterizes the propagation stage of blood coagulation and it is sensitive to all coagulation cascade reactions, including the contact pathway and excluding the initiation reactions of the extrinsic pathway. Decreased Vst indicates various different hypocoagulation states (factors V, VIII, IX, X, XI or thrombin deficiency; anticoagulant agents – vitamin K antagonists, UFH and LMWH). Increased Vst value indicates different hypercoagulation states.

Tsp. [min] - Spontaneous clots - formation time - is the time that spontaneous clots appear in the sample volume which had no initial contact with the activating insert, characterizes clotting independent of the activator surface. Under normal condition, no spontaneous clotting is observed. Spontaneous clotting is induced by circulating activators, active coagulation factors and microparticles. Indicates a high pro-thrombotic tendency.

CS, [um] - Clot size - at the 30th minute of measurement. It is sensitive to all major components and processes of blood coagulation, because it is defined by both Tlag and rate of clot growth.

D. [a.u.] - Clot density - parameter reflects firmness and structure of a formed clot. It reflects quantity and biological activity of fibrinogen, but cannot replace direct measurement of fibrinogen concentration. Sensitive to fibrinogen (concentration and polymerization ability) and factor XIII activity.

Ast, [Activity Unit/L] - Stationary amplitude of thrombin peak - as thrombin generation propagates in space as a moving peak (Dashkevich et al, Biophys J 2012), height of this peak is calculated as a maximal activity of thrombin in the fibrin formation zone which moves from the activator while clot grows. The parameter characterizes the propagation stage of blood coagulation.

Vt, [um/min] - Rate of thrombin peak propagation - characterizes the propagation stage of blood coagulation, sensitive to changes in intrinsic pathway of blood coagulation; factors VIII, IX, XI, V, X and thrombin concentration and also to phospholipid vesicles concentration in plasma.

ETP ATG, [AU\*min/L] - Thrombin potential, Cmax ATG, [AU/L] - Maximum concentration, Tmax ATG, [min] - Time to thrombin peak - are calculated on the activating surface and similar to homogeneous Thrombin Generation Test parameters.

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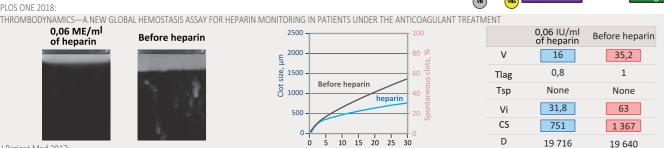
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Thromb Res. 2015:

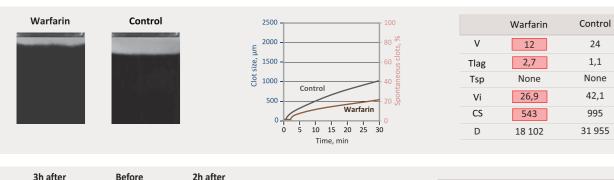
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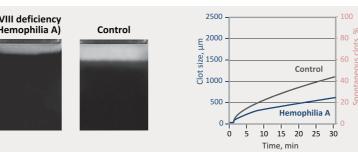


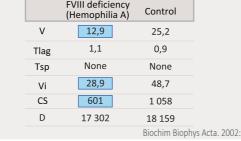
PERINAT MED 2017:
THE LABORATORY CONTROL OF ANTICOAGULANT THROMBOPROPHYLAXIS DURING THE EARLY POSTPARTUM PERIOD AFTER CESAREAN DELIVERY



#### **COAGULATION FACTOR DEFICIENCIES**

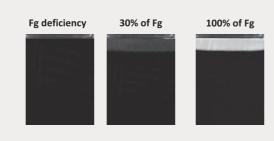
In cases of hemophilia, i.e. deficiency of fVIII or IX, the intrinsic tenase does not work normally impairing propagation of the clot.





HEMOPHILIA A AND B ARE ASSOCIATED WITH ABNORMAL SPATIAL DYNAMICS OF CLOT GROWTH

The Thrombodynamics results for fibrinogen deficient plasma which was spiked with different concentrations of fibrinogen are shown below. In the case of deficiency no clot is observed, increases of fibrinogen concentration result in increases of clot density.



V [um/min], Growth rate

CS [um], Clot size

27,5

1,8

1 042

30 426

2,2

31 251

32 826

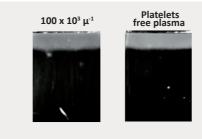
Tsp [min], Spontanous clots formation time

D 0 8 000 28 500		Fg deficiency	30% of Fg	100% of Fg
	D	0	8 000	28 500

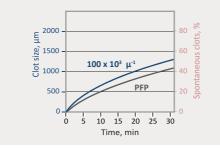
#### **PHOSPHOLIPID SURFACE AND PLATELETS**

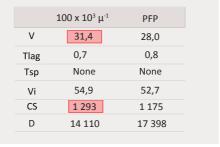
In the thrombodynamics assay platelet free plasma is used with no phospholipids added. But for some application it is possible to introduce additional phospholipid surfaces. For example artificial phospholipid vesicles or platelets.





The vesicle composition is: PS:PC:PE = 20:20:60 molar ratio





26.6

0,9

None

58,8

1 161

20 622

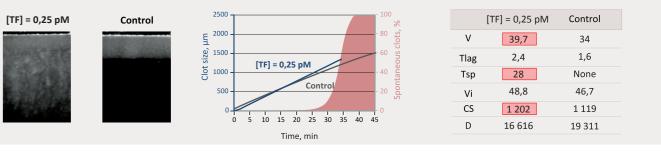
71,3

1 525

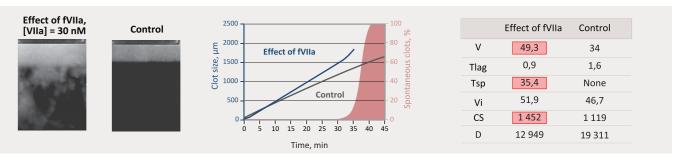
16 120

#### PROCOAGULANT AGENTS

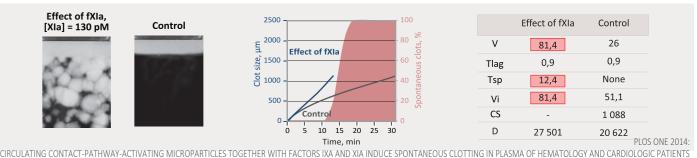
The presence of TF in plasma increases clot growth rate and can result in he formation of spontaneous clots in the plasma.

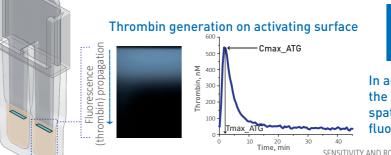


Factor VIIa is used as a bypassing agent in hemophilia treatment. It causes changes in clot formation similar to TF.



If fXIa is present the clot growth rate is increased and spontaneous clot formation is observed.





### **THROMBIN GENERATION**

In addition to the registration of spatial fibrin clot growth from the TF-bearing surface Thrombodynamics-4D allows monitoring spatial dynamics of thrombin generation using an AMC-based fluorogenic substrate.

SENSITIVITY AND ROBUSTNESS OF SPATIALLY DEPENDENT THROMBIN GENERATION AND FIBRIN CLOT PROPAGATION

