Thrombo-elastografie en orale antistolling

SKS 30 oktober 2008

am

Stollingsonderzoek: nieuwe ontwikkelingen ?!

Blutgerinnungsstudien mit den Thrombo-elastographie, einem neuen untersuchungsverfahren
Hartert, H. Klin. Wochenschrift 1948

Thromboelastographic study of 76 patients on long-term anticoagulant therapy with coumadin-type drugs
Am. Heart Journal 1962

Haemoscope TEG
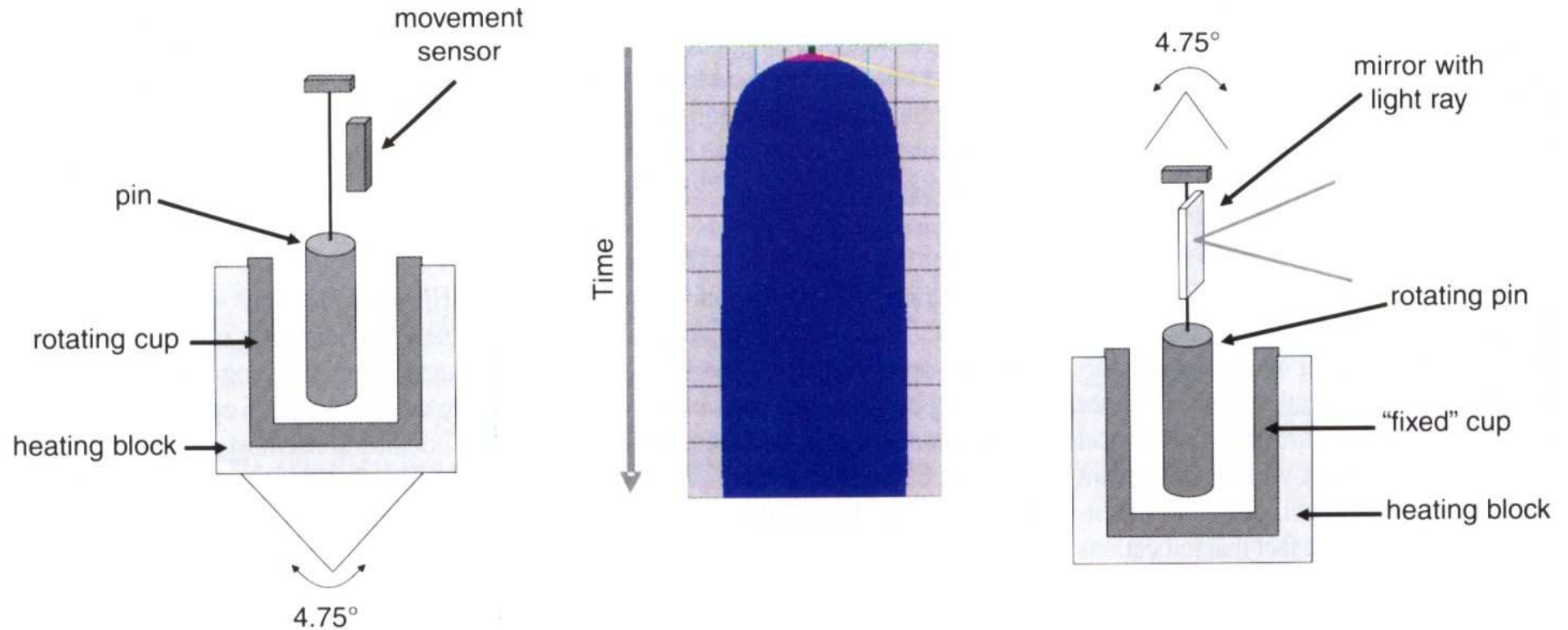
Pentapharm Rotem delta

De techniek

Globale stollingstest uitgevoerd in vol bloed:

- stollingsfactoren
- stollingsremmers
- fibrinolyse
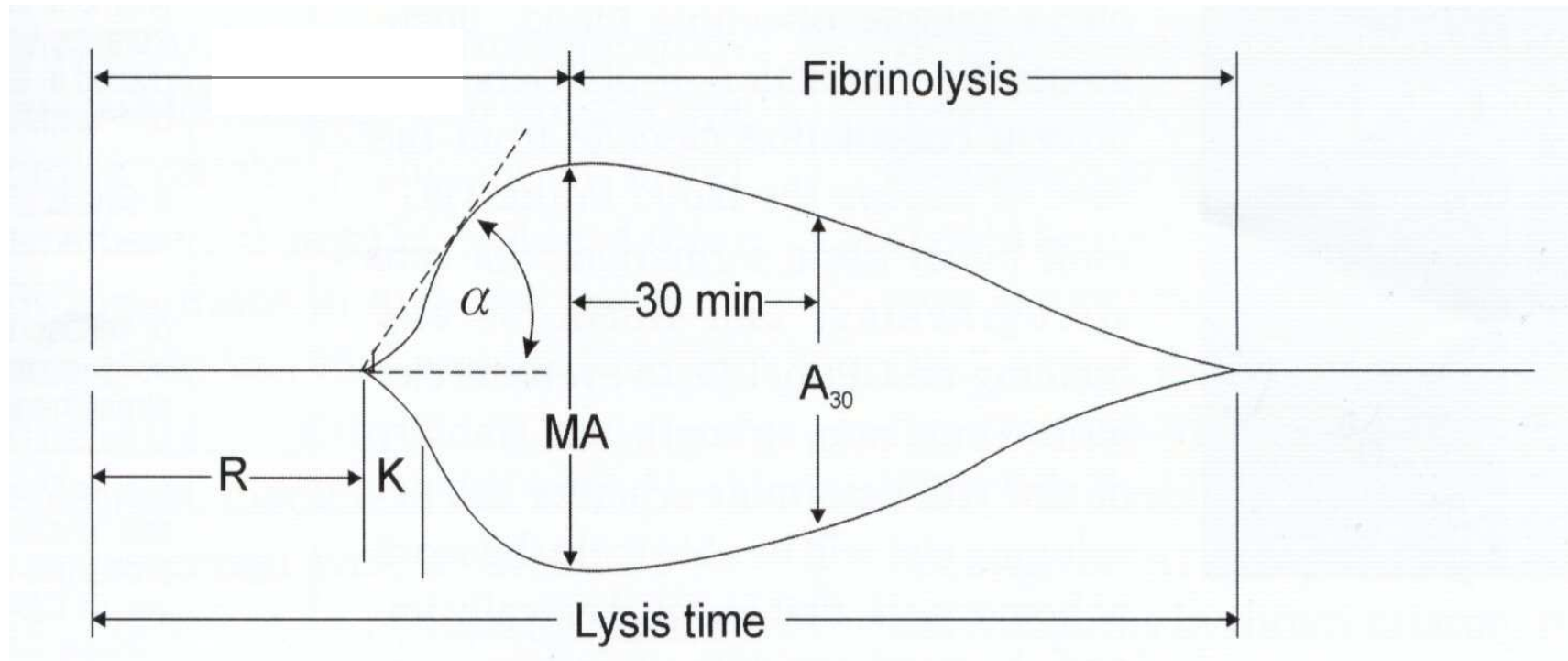- trombocyten
- erythrocyten e.a.

Uitslag snel beschikbaar

Kan als POCT; evt mogelijkheid "remote viewing"
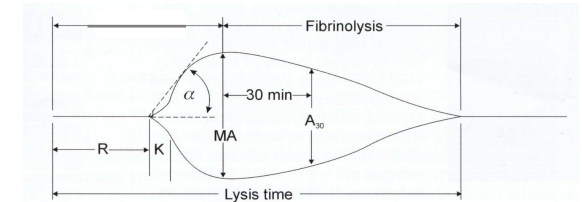
Meetprincipe

Uitslagformat / parameters

Parameters

TEG / ROTEM	
R / CT	min / s
k / CFT	min / s
α / α	gr / gr
A_x / A_x	mm / mm
MA / MCF	mm / mm
lysis	lysis

Reagentia

	TEG	**ROTEM**
Activator	kaoline	ellaginezuur (Intem) tromboplastine (Extem)
	$CaCl_2$	$CaCl_2$
Reagens	heparinase	heparinase (Heptem)
	Funct. fibrinogen	Fibtem
Overig	Platelet mapping	Aptem

Uitvoering

TEG	ROTEM
CaCl$_2$ (20 μL)	CaCl$_2$ (20 μL)* Activator (20 μL)*
Bloed (1 mL) in kaoline buis $\rightarrow$ 340 μL	Bloed (300 μL)*

*Geïntegreerde pipet.

Voorbeeld
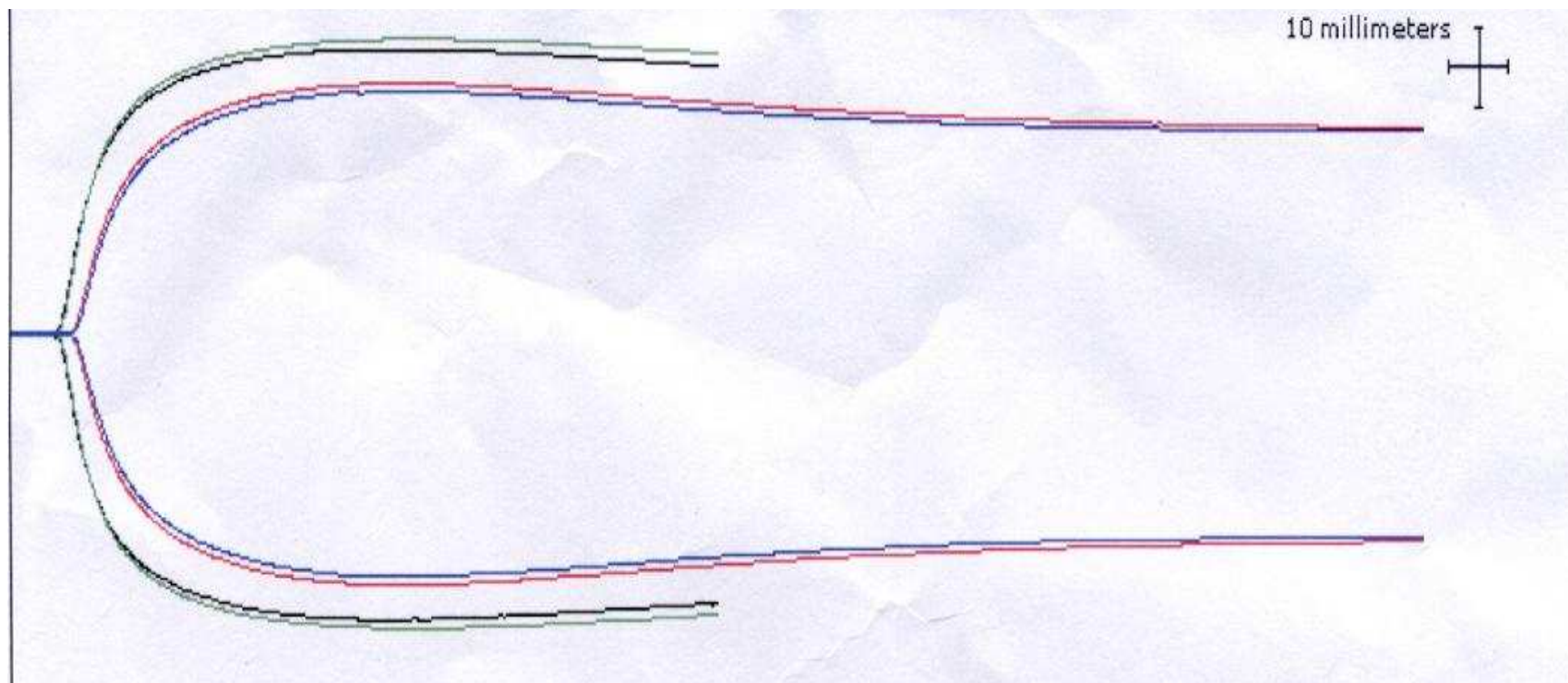
Imprecisietesten

	Intem*	Extem*
CT	2.6 - 5.2	4.0 - 7.8
CFT	5.5 - 6.6	4.3 - 11.2
α	0.7 - 1.7	0.9 - 1.8
MCF	0.9 - 3.4	2.7 - 3.8

*VC (%; 3 series in citraat bloed, n=8 per serie).

Imprecisietest (Intem)

	Within run	Total
CT	5.8	8.1
CFT	11.1	17.6
α	0.6	1.5
MCF	2.1	3.2

*VC (%; verkort EP5 protocol: 10 dagen; controlemateriaal PRP)

Praktijkvoorbeeld UFH
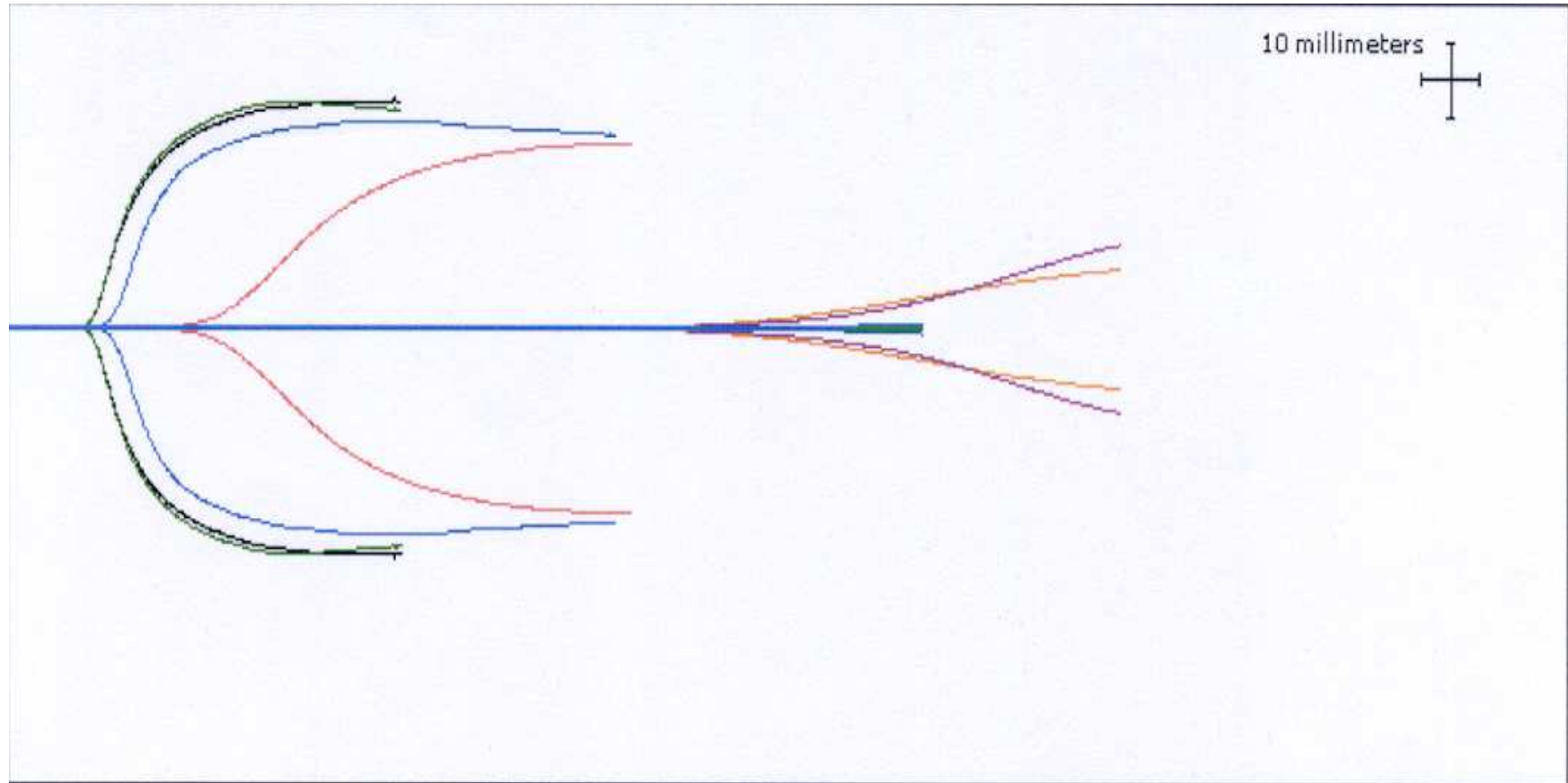
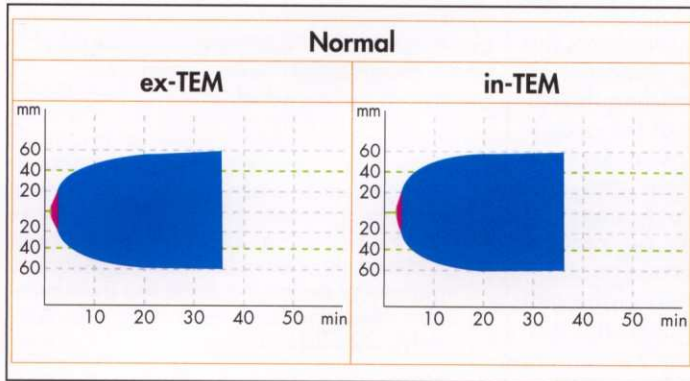# Praktijkvoorbeeld UFH
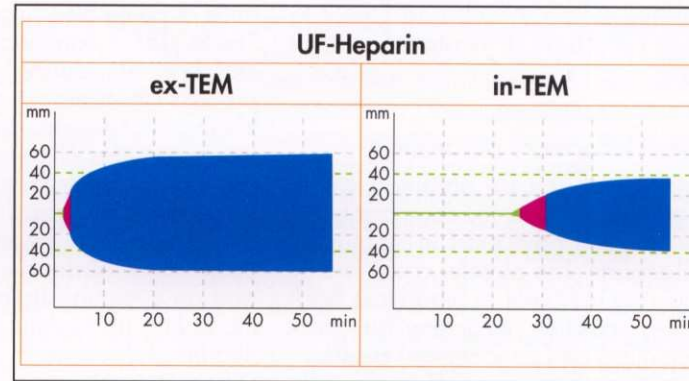## (+ heparinase)

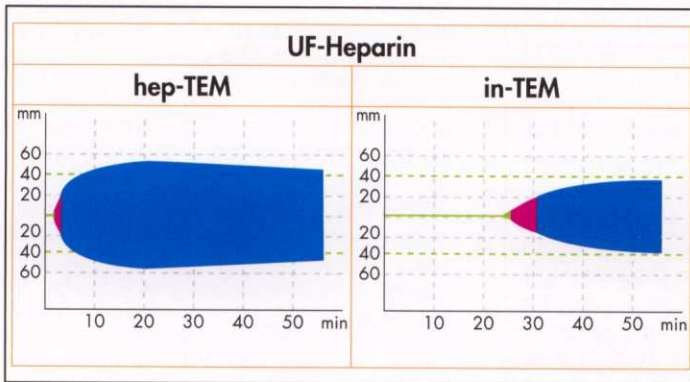10 millimeters
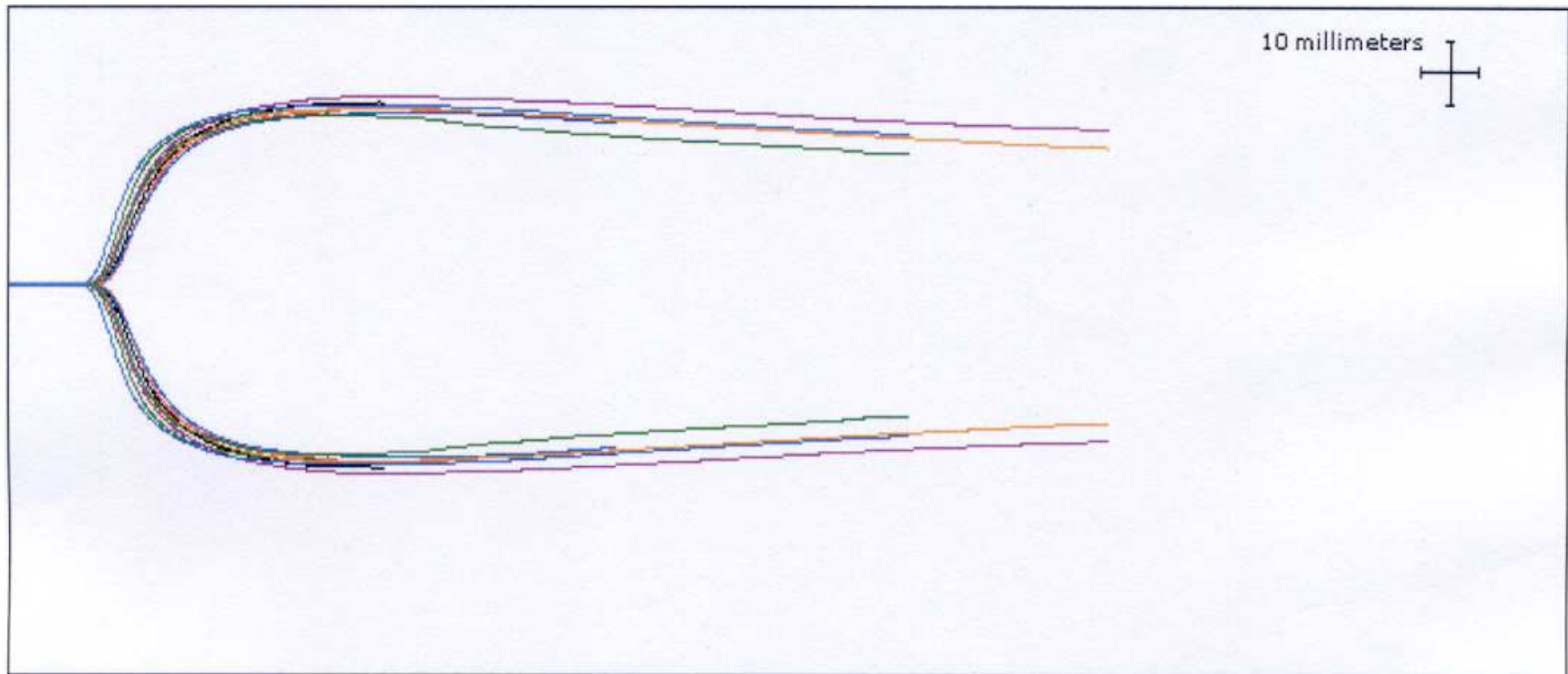
Illustration III

Illustration IV

Illustration V
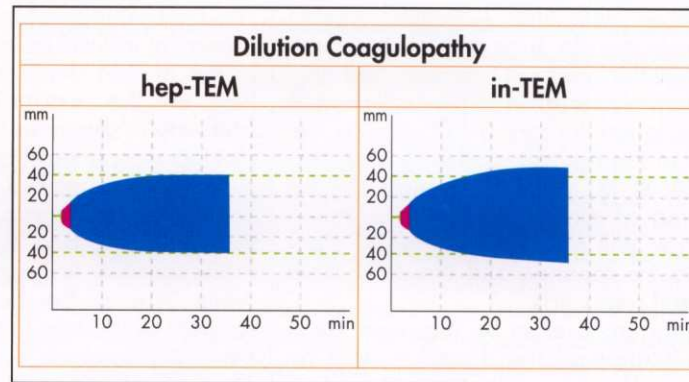
Illustration VI
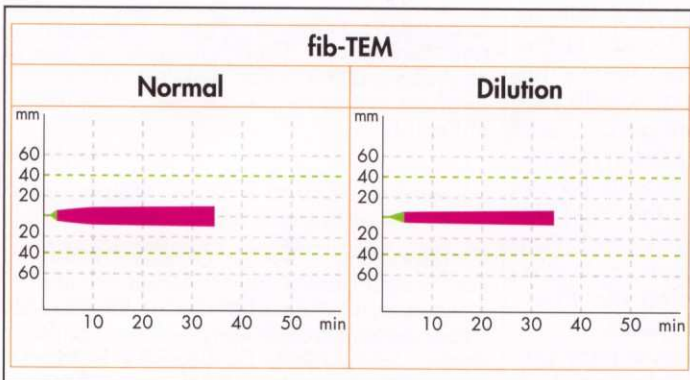
Illustration VII
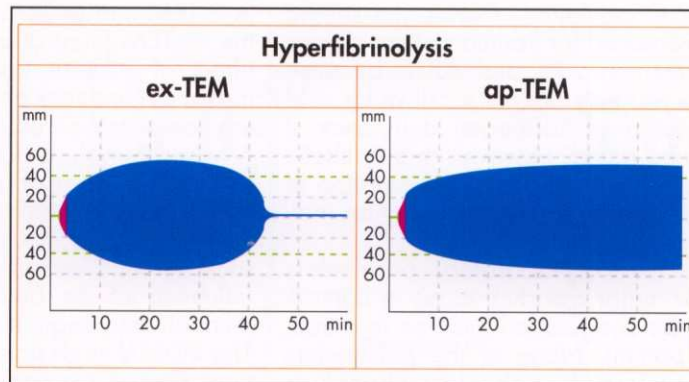
Illustration VIII

Mogelijke voordelen thromboelastografie/metrie

- Snelle diagnose bij bloedingsproblemen
- Meer gerichte therapie
- Effect van therapie snel te meten
- Optimaal gebruik van bloedproducten
- Verkorting totale opnameduur

Klinische toepassing

- Cardiochirurgie
- Levertransplantatie
- Traumatologie
- Post partum bloedingen
- Hypercoagubiliteit
- Neonaten

- Monitoren behandeling met F VIII$_c$, PPSB, F VII$_a$
- Orale antistolling?

POC Coagulation Management during Liver Transplantation

K. Goerlinger: Coagulation management during liver transplantation. Hämostaseologie 2006; 26 (3a): S64-75

ROTEM® Management of cardiac surgical patients

Result and Action

Anaesthesia

INTEM   EXTEM

1. Only TREAT if the patient is BLEEDING
2. Abnormal results + NOT bleeding: Observe patient; repeat tests
3. Some institutions advise a higher FIBTEM target in the bleeding patient (e.g. 12 or greater) and especially in presence of dual anti-platelet therapy
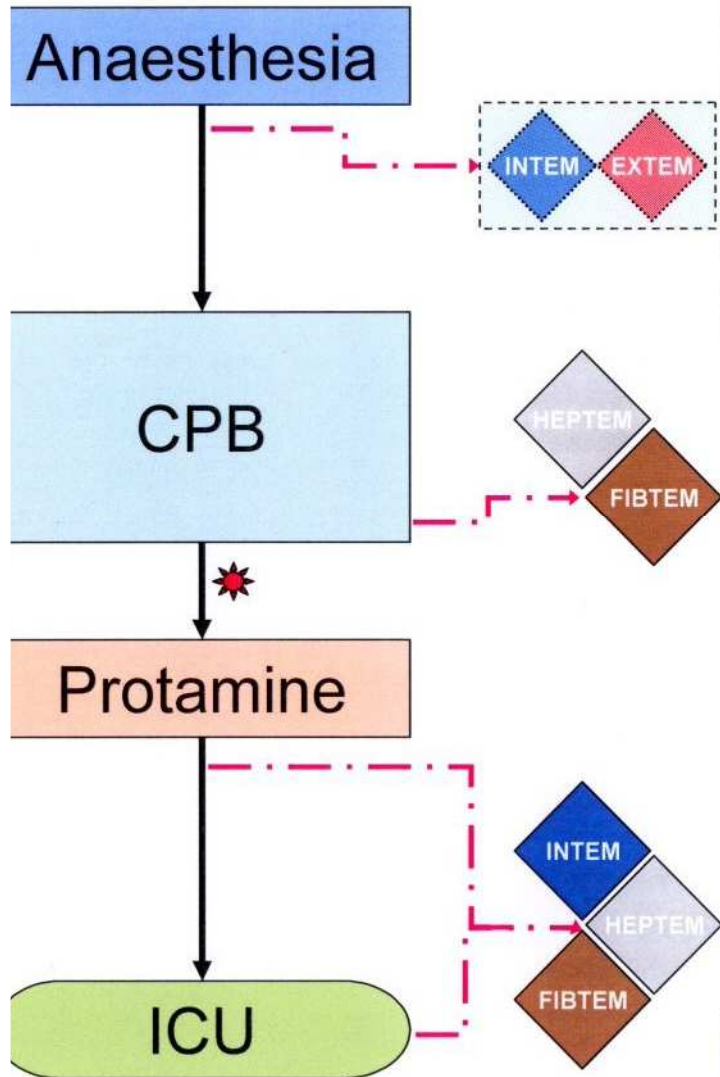4. Aprotinin therapy increases CT_{INTEM}: therefore use EXTEM instead
5. Some clinicians give DDAVP (0.3-0.4µg/kg) in patients on aspirin - there are mixed reports of efficacy (and complications) in the literature
6. Indications for Factor rVII are not established: but efficacy relies on first optimizing pH, temperature, Ca^{++}, fibrinogen (FIBTEM >8), platelet number (>20,000), and hematocrit (Hct)

CPB

HEPTEM   FIBTEM

HEPTEM A10 < 35: *consider* obtaining **PLATELETS**

FIBTEM A10 < 8: *consider* obtaining **FIBRINOGEN** (Cryoppt/FFP)

Ensure satisfactory pH (>7.25), temperature (>35°C),Ca^{++}
The bleeding patient may benefit from target Hct >25%

Protamine

INTEM   HEPTEM   FIBTEM

$CT_{INTEM} \gg CT_{HEPTEM}$: *circulation has excess heparin* - **PROTAMINE**

FIBTEM A10 < 8: *low fibrinogen, likely < 1g/L* - **FIBRINOGEN** (or Cryoppt or FFP)
- Some institutions aim for FIBTEM ≥10

INTEM A10 < 35: *assuming satisfactory fibrinogen, FIBTEM A10 > 8* - **PLATELETS**
- Some institutions aim for FIBTEM ≥10 before considering platelets

$CT_{INTEM} \leq CT_{HEPTEM}$ **AND > 300 s**: *may also check EXTEM (>100s)* - **FFP or PCC**
- But correct FIBTEM first; low fibrinogen prolongs CT

ICU

Near-normal result or high bleeding rate: *unlikely to be coagulopathy* - **RESTERNOTOMY**

- Otherwise, consider platelets +/- aprotinin if recent antiplatelet therapy

Klinische toepassing

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- Monitoren behandeling met F $VIII_c$, PPSB, F VII_a
- Orale antistolling?

(a)

(b)

(c)

(a)
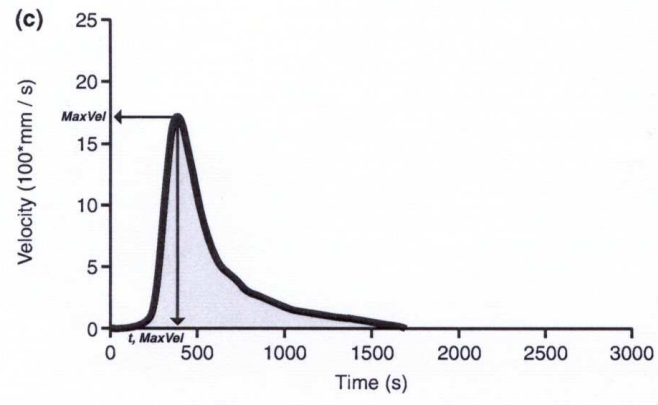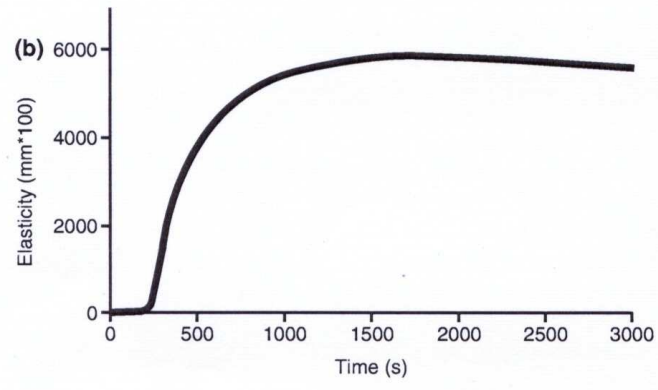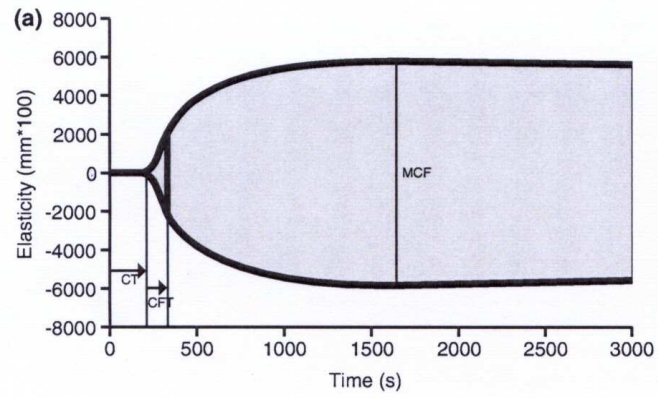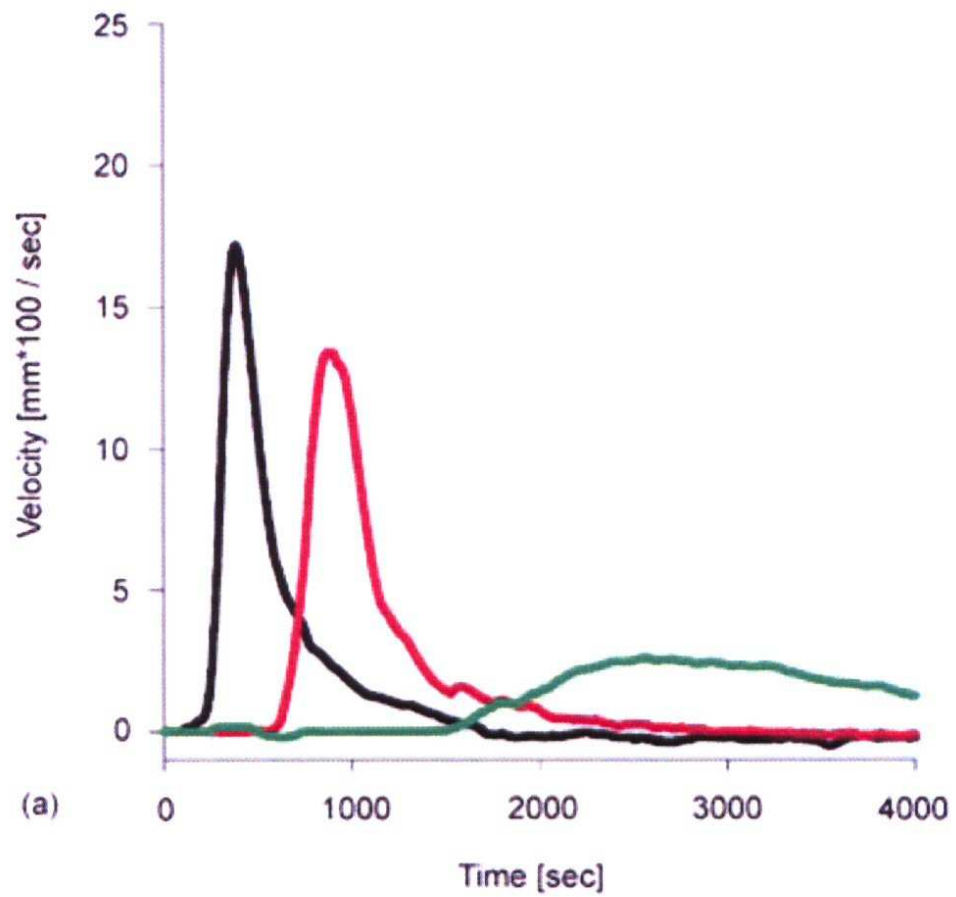
Tromboelastografie/metrie en orale antistolling

- Theoretisch
- Praktisch
  - Niet geautomatiseerd / tijdrovend
  - Onvoldoende gestandaardiseerd
  - "Standaard" uitvoering relatief ongevoelig
  - Kosten
  - Self-management patiënten
  - Enz.

Tot slot…

- Klinische toepassing
  - bloedende patiënt
- Onvoldoende klinische validatie
- Optimaliseren apparatuur en reagentia
- Kan in POC setting

  → rol voor het laboratorium

Table of ROTEM® Parameters

Acronym	Parameter	Definition	Unit
Coagulation activation and clot polymerisation parametrs			
CT	Coagulation Time (synonym r)	The time from test start until an amplitude of 2 mm is reached.	s
CFT	Clot Formation Time (synonym k)	The time between 2 mm amplitude and 20 mm amplitude.	s
α	α-Angle	Angle between the baseline and a tangent to the clotting curve through the 2 mm point.	degree (°)
CFR	Clot Formation Rate	Angle between the baseline and the tangent at the maximum slope.	degree (°)
Clot firmness parameters			
MCF	Maximum Clot Firmness (synonym MA)	The maximum amplitude reached during the test.	mm
MCF-t	MCF-Time	The time from CT until MCF is reached.	s
ACF	Actual Clot Firmness or Last Clot Firmness	Clot firmness at the actual time point after reaction start. ACF is not a parameter in its classical sense, but it is for orientation to judge the clot firmness at the actual time point.	mm
A(x)	Amplitude (firmness) at time x		mm
A5	Firmness at time 5 minutes		
A10	Firmness at time 10 minutes		
A15	Firmness at time 15 minutes	Clot firmness (in mm amplitude) at the respective time point after CT.	
A20	Firmness at time 20 minutes		
A25	Firmness at time 25 minutes		
A30	Firmness at time 30 minutes		
MCE	Maximum Clot Elasticity $E=100*MCF/(100-A)$	MCE is a parameter calculated from MCF. The spreading (solution) of this parameter at high amplitudes is better as compared to the MCF.	
Clot lysis parameters			
ML	Maximum Lysis	Maximum lysis detected during the run time, described as the difference between MCF and the lowest amplitude after MCF, described in % of MCF	%
LI(x)	Lysis Index at time x minutes	Ratio of the amplitude and MCF at a given time point after CT.	%
LI30	Lysis Index at time 30 minutes	LI 30 at CT + 30 min calculated A/MCF*100.	%
LI45	Lysis Index at time 45 minutes	LI45 at CT + 45 min calculated A/MCF * 100.	%
LI60	Lysis Index at time 60 minutes	LI60 at CT + 60 min calculated A/MCF * 100.	%
LOT	Lysis Onset Time	The time span from CT to the start of significant lysis in s. Significant lysis is defined as a decrease of the amplitude of 15% as compared to MCF.	s
LT	Lysis Time	The time from CT until the clot firmness is decreased to 10% of the MCF during fibrinolysis.	s
CLR	Clot Lysis Rate	The strongest lysis, described by the angle between the baseline and the tangent to the declining firmness curve at the minimum of the 1st derivative.	degree (°)
Research parameters calculated from curve			
G	$G = 5000MCF/(100 - MCF)$ Shear Elastic Modulus Strength	G is a calculated parameter. It increases exponentially as compared to the amplitude. It allows a more sensitive resolution at high amplitudes.	
TPI	Thrombodynamic Potential Index $TPI = EMX/K$ $EMX = (100*MCF)/(100-MCF)$	According to Raby 1975, the Thrombodynamic Potential Index describes the patient's global coagulation.	
Research parameters for derivative curves (according to Sørensen et al. 2003)			
maxVel	Maximum velocity	The maximum of the 1st derivative of the curve	mm/min
t-maxVel	Time to maximum velocity	Time from reaction start until the maximum of the 1st derivative of the curve is reached.	s
AUC	Area under 1st derivative curve	Area under the 1st derivative curve from start of the derivative curve until MCF is reached.	mm x 100
Other research parameters			
AR(x)	Area under the curve at time x		
AR5	Area until time 5 minutes		
AR10	Area until time 10 minutes		
AR15	Area until time 15 minutes	The area under the curve from CT to the respective time point.	mm²
AR20	Area until time 20 minutes		
AR25	Area until time 25 minutes		
AR30	Area until time 30 minutes		

Important routine parameters are shaded grey

AMC

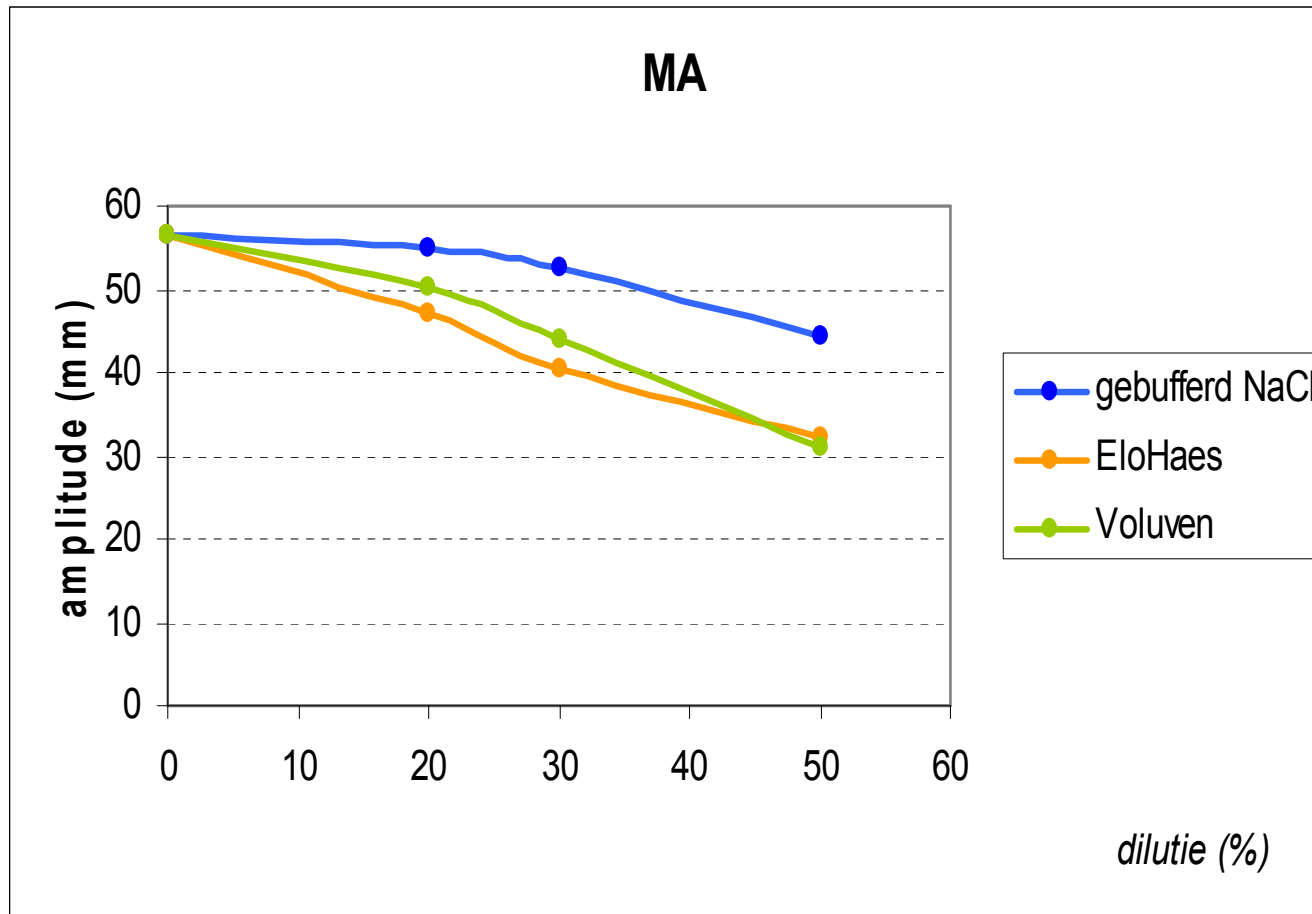In vitro en klinisch onderzoek

Klinisch:

i.s.m anaesthesiologie / traumatologie
in POC setting

Lab:

bedieningsprotocollen , training operators,
onderhoud, trouble shooting, QC, expert-kennis t.a.v.
interpretatie uitslagen , back-up apparatiuur …….
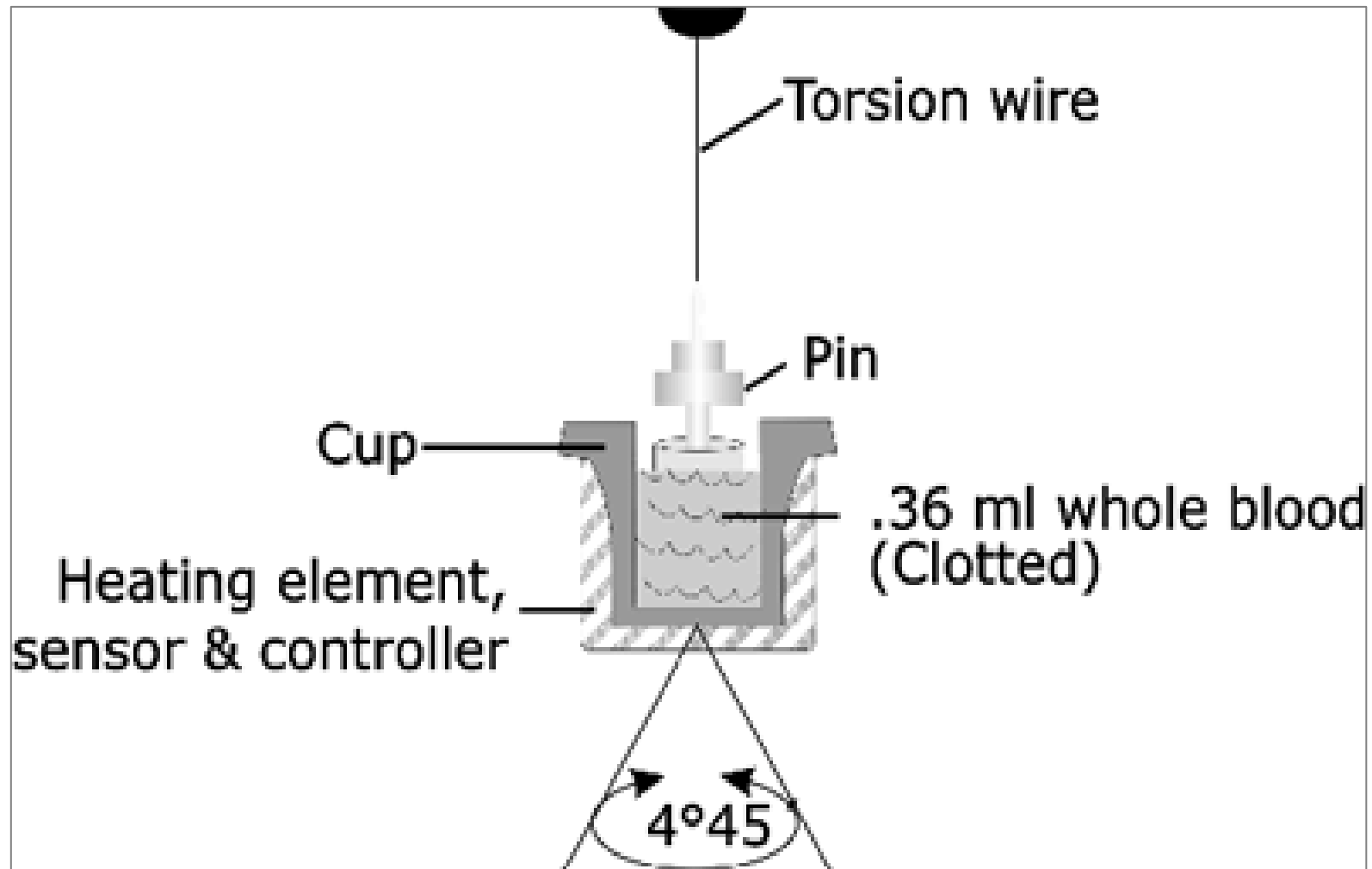
AMC

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TEG

Aantal trombocyten - TEG

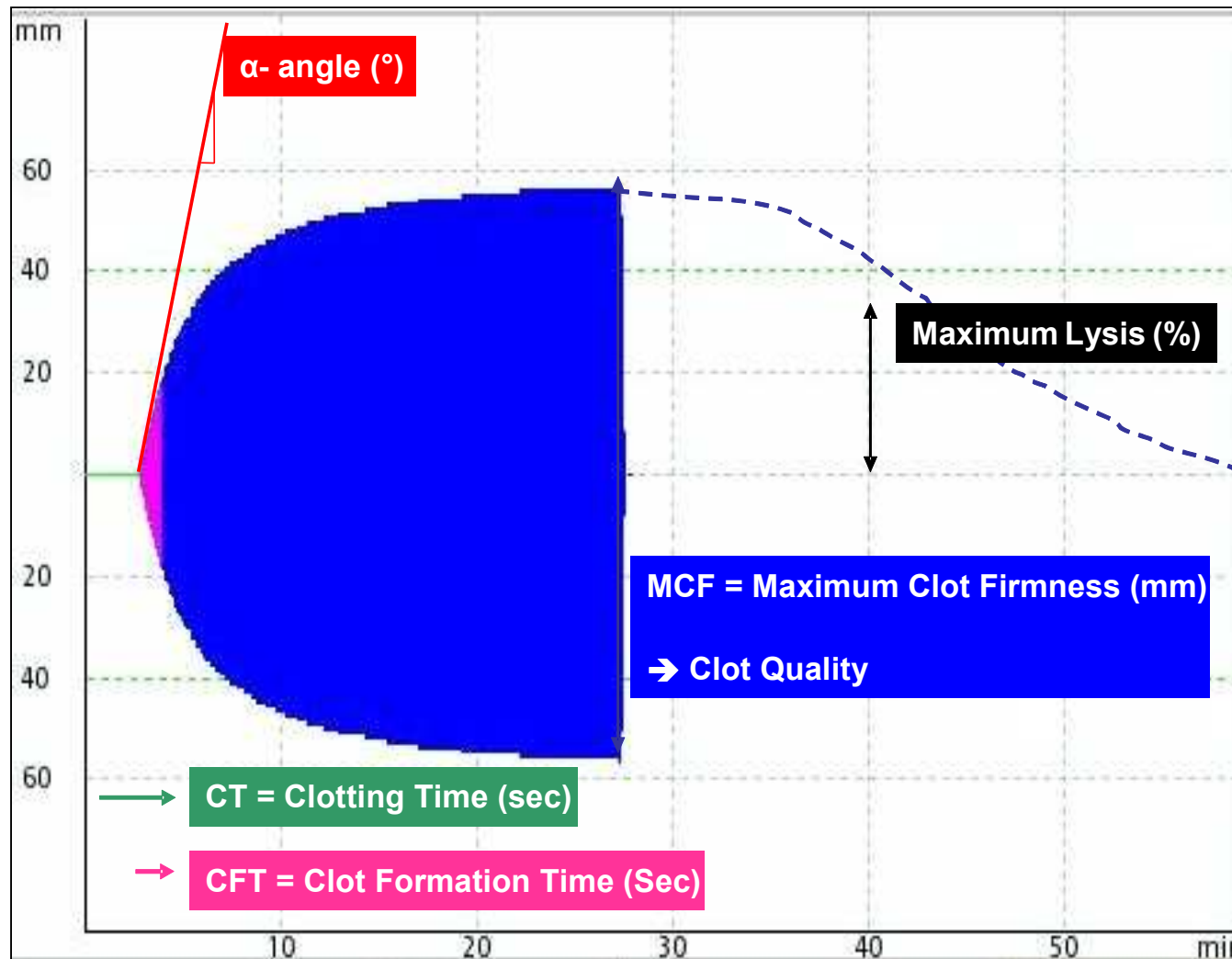| Eigen trombocyten		Donor trombocyten	
Trombo	MA	Trombo	MA
40	39	121	55
79	49	192	63
111	55	276	64
147	59	343	64

- **Hb = 8.6 mmol/L**

Uitslagformat / parameters
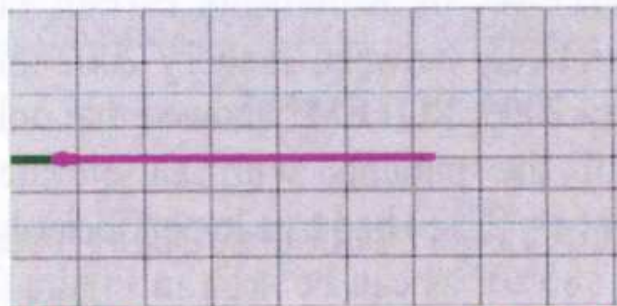
Invloed bepalingstemperatuur

- **Intem**   percentages van de waarde bij 37 C

- Temp(oC)   C T   CFT   MCF   alpha

Temp(oC)	C T	CFT	MCF	alpha
41	92.6	78.3	98.3	104.9
39	96.6	87.2	100.9	103.5
37	100	100	100	100
35	105.1	117.8	98.3	95.8
33	108.2	141.7	94.9	92.4
31	119.3	171.7	94.0	87.5

Hyperfibrinolyse

extreneky severe hyperfibrinolysis
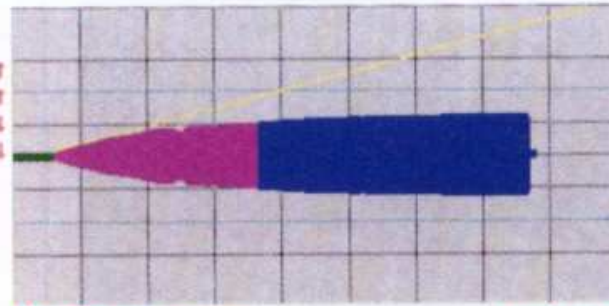
Date:	
Starttime:	
CI:	362s↑
CFI:	>3440s↑
MCF:	4mm↓
MCE:	5↓

Date:	
Starttime:	
CI:	355s
CFI:	1833s
MCF:	25nn
MCE:	33
alp:	15°
LI60:	97%

MCF: 5 mm   EXTEM

MCF: 25 mm   APTEM

plasma coagulation

PT	not measurable	AT	45%	Plt	$60 \times 10^3/\mu l$
aPTT	not measurable	Fgn	not measurable	DD	3730 µg/l

isolated heparin effect

Date:
Starttime:
CT: 354s↑
CFT: 81s
MCF: 62mm
MCE: 161
alp: 74°
LI60: 93%

CT: 354 sec.   INTEM

Date:
Starttime:
CT: 152s
CFT: 72s
MCF: 63mm
MCE: 171
alp: 72°↓
LI60: 92%

CT: 152 sec.   HEPTEM
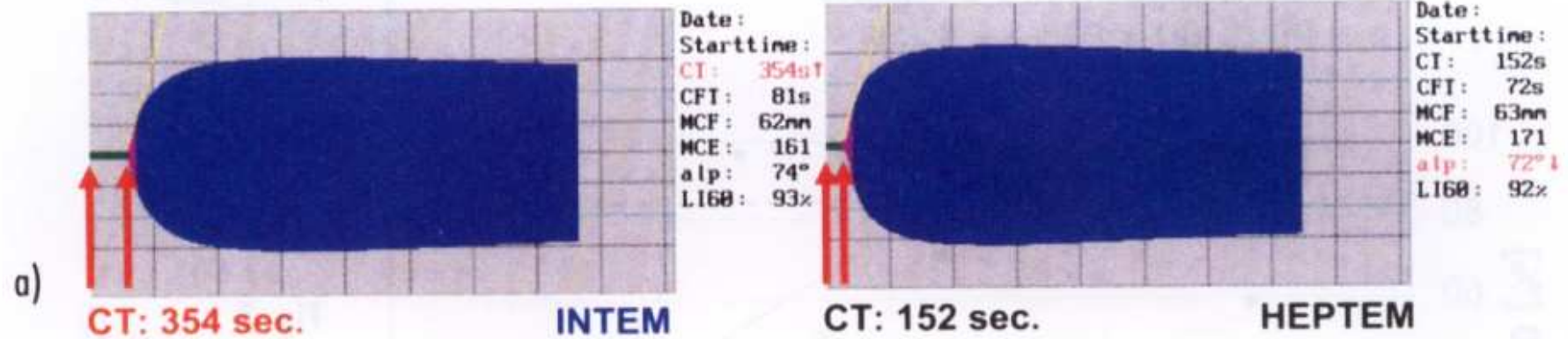
isolated endogenous factor deficiency

Date:
Starttime:
CT: 409s↑
CFT: 188s↑
MCF: 53mm↓
MCE: 112↓
alp: 56°↓
LI60: 95%

CT: 409 sec.   INTEM

Date:
Starttime:
CT: 406s↑
CFT: 230s↑
MCF: 47mm↓
MCE: 89↓
alp: 51°↓
LI60: 97%

CT: 406 sec.   HEPTEM
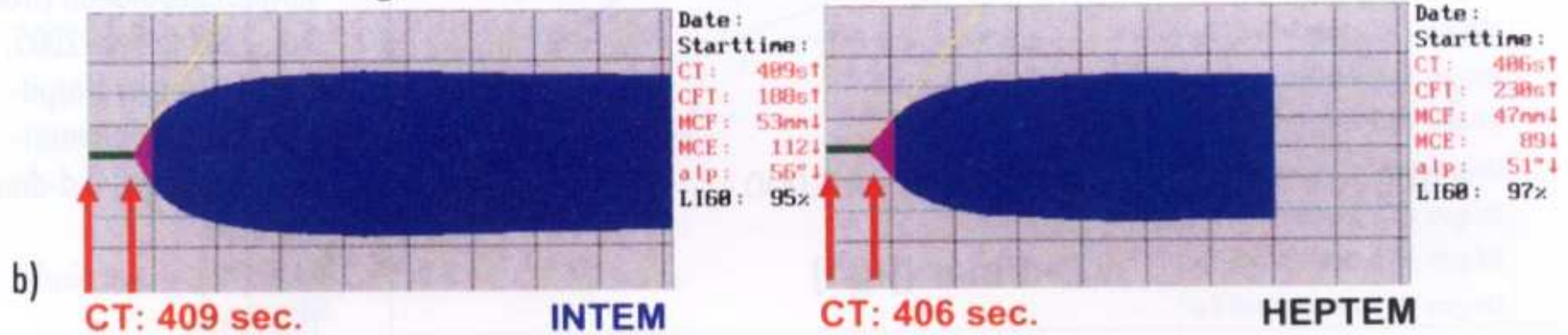
heparin effect + endogenous factor deficiency

Date:
Starttime:
CT: 475s↑
CFT: 257s↑
MCF: 46mm↓
MCE: 84↓
alp: 54°

CT: 475 sec.   INTEM

Date:
Starttime:
CT: 349s↑
CFT: 394s↑
MCF: 42mm↓
MCE: 72↓
alp: 39°↓

CT: 349 sec.   HEPTEM

Reagentia

	TEG	ROTEM
Activator	kaoline	ellaginezuur (Intem) tromboplastine (Extem)
	$CaCl_2$	$CaCl_2$
Reagens	heparinase	heparinase (Heptem)
	Funct. fibrinogen	Fibtem
Overig	Platelet mapping	Aptem