Diagnostiek bij massaal bloedverlies – Wanneer is de patiënt de sigaar?

Moniek de Maat
Hematologie

Sanquin, 13 november 2019

Behandelschema Massaal Bloedverlies

(Bij aankondiging tel: 33204 ter voorbereiding ROTEM)

Mogelijkheid tot compensatie
(systolische RR > pols / klinische beoordeling)

Dreigende verbloeding
(systolische RR < pols / klinische beoordeling)

Bestel Massaal Transfusie Pack (tel: 34590)
- 3x Erytrocytenconcentraat
- 3x Omniplasma
- 1x Trombocytenconcentraat
- Fibrinogeen 2000mg
- Calciumgluconaat 2000mg

Ophalen op Nc407

- Zo snel mogelijk chirurgische / radiologische hemostase!
- Bloedafname:
  - -ROTEM (= extra citraatbuis, zet op formulier: ROTEM Massaal bloedverlies!)
  - -Hb, Ht, Trombo's, PT, APTT, INR, Fibrinogeen, D-dimeer
  - -2x Kruisbloed uit 2 afzonderlijke afnames
- Gecontroleerde hypotensie: Streef-systole 85 mmHg (cave hersenletsel)
- Verwarmde infusie Sterofundin / Ringers Lactaat
- Direct Tranexaminezuur: <70kg: 1000mg IV / >70kg: 1500mg IV
- Streef-temperatuur >35 °C
- Streef-calcium >1.10 mmol/L: z.n. CaGluc 2000mg IV
- Streef-pH >7.30: z.n. NaBic 8.4% 100mL IV
- Antistolling:
  - Coumarines: direct Cofact 40 mL + verder o.g.v. INR
  - Ascal / Clopidogrel: direct 2x Trombocyten + DDAVP 0.3 mcg/kg IV
  - Heparine / LMWH: direct Protamine 50mg IV
  - Overig i.o.m. dd hematoloog **5507

Mogelijkheid tot compensatie
(systolische RR > pols / klinische beoordeling)

Transfusie in verhouding 1x EC : 1x Omniplasma
- Gezonde patiënten: start bij Hb <5 mmol/L
- Cardiopulmonaal belast: start bij Hb <6 mmol/L

1x Trombocytenconcentraat als <75 x 10^9/L

Dreigende verbloeding
(systolische RR < pols / klinische beoordeling)

Producten Massaal Transfusie Pack z.s.m. toedienen!

Erasmus MC

Zo snel mogelijk stollingssupletie o.g.v. ROTEM:

- **FIBTEM A10**
  - A10 ≤5 mm: Fibrinogeen 6000mg IV
  - A10 ≤7 mm: Fibrinogeen 4000mg IV
  - A10 ≤9 mm: Fibrinogeen 2000mg IV
  - A10 >9 mm: Geen Fibrinogeen
- **EXTEM CT**
  - <80 sec: Geen Cofact
  - ≥80 sec: Cofact 0.4 mL/kg (afgerond op 10 mL)
  - ≥100 sec: Cofact 0.8 mL/kg (afgerond op 10 mL)
- **EXTEM A10**
  - A10 <40 mm: 1x Trombocytenconcentraat
  - (let op: FIBTEM A10 moet >9 mm zijn)
- **EXTEM ML**
  - >15% in 60 minuten: Tranexaminezuur 15 mg/kg extra

↓

Direct hierna bloedafdnames herhalen:

- Bloedgas, ROTEM, Hb, Ht, Trombocyten, PT, APTT, INR, Fibrinogeen, D-dimeer

Transfusiebeleid tot definitieve behandeling:

- Bij dreigende verbloeding → direct herhalen 3x EC : 3x Plasma : 1x TC
- Bij mogelijkheid tot compensatie → 1x EC : 1x Plasma o.g.v. Hb
  1x Trombocyten als <75 x 10^9/L

Stollingscorrectie continueren o.g.v. ROTEM-schema

ROTEM in the Erasmus MC

- Historically TEG was used
- Now ROTEM, especially because of available literature
- Start: ROTEM at the departments
  - Turned out that technicians are better at using ROTEM
  - Often no maintenance done
  - Cleaning of the instrument not optimal
  - Results not in the patient file
- Therefore we moved ROTEM to the laboratory with the use of the connectivity kit (LIVE viewing for everybody, using PID nr patient)
- Everybody is positive!
- Now we use 3 ROTEM Delta and 1 ROTEM Sigma (validation)

ROTEM at the Hemostasis Laboratory Erasmus MC

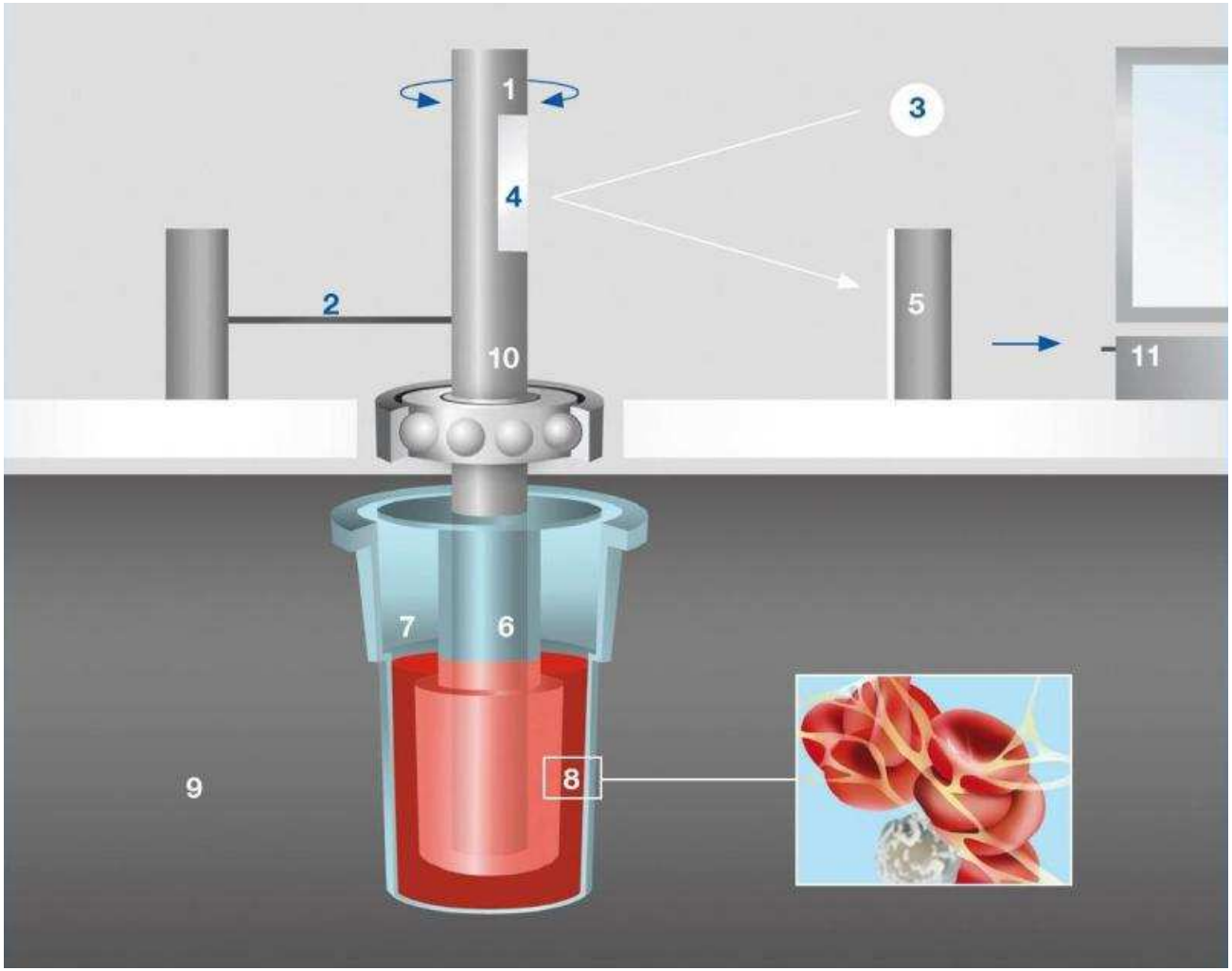
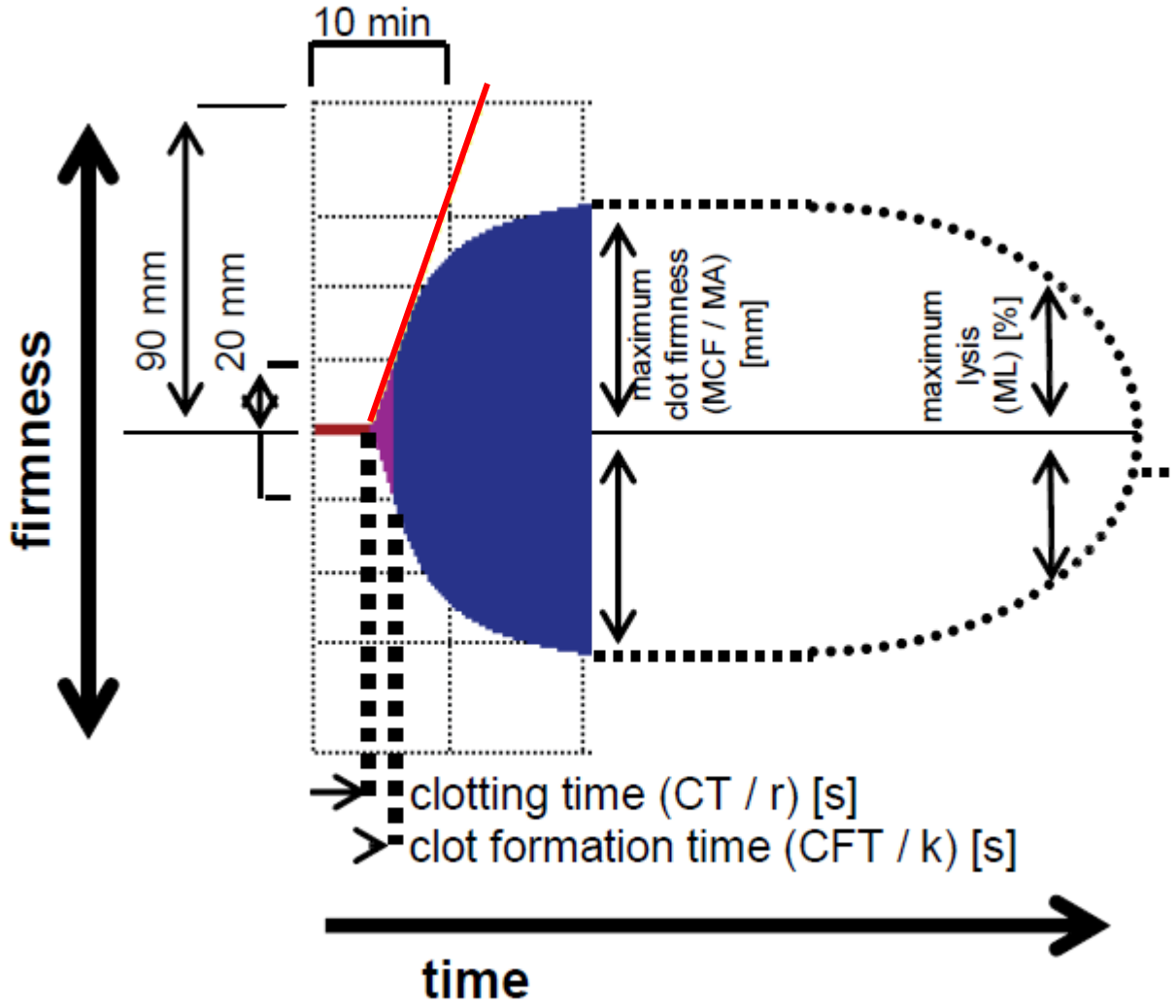
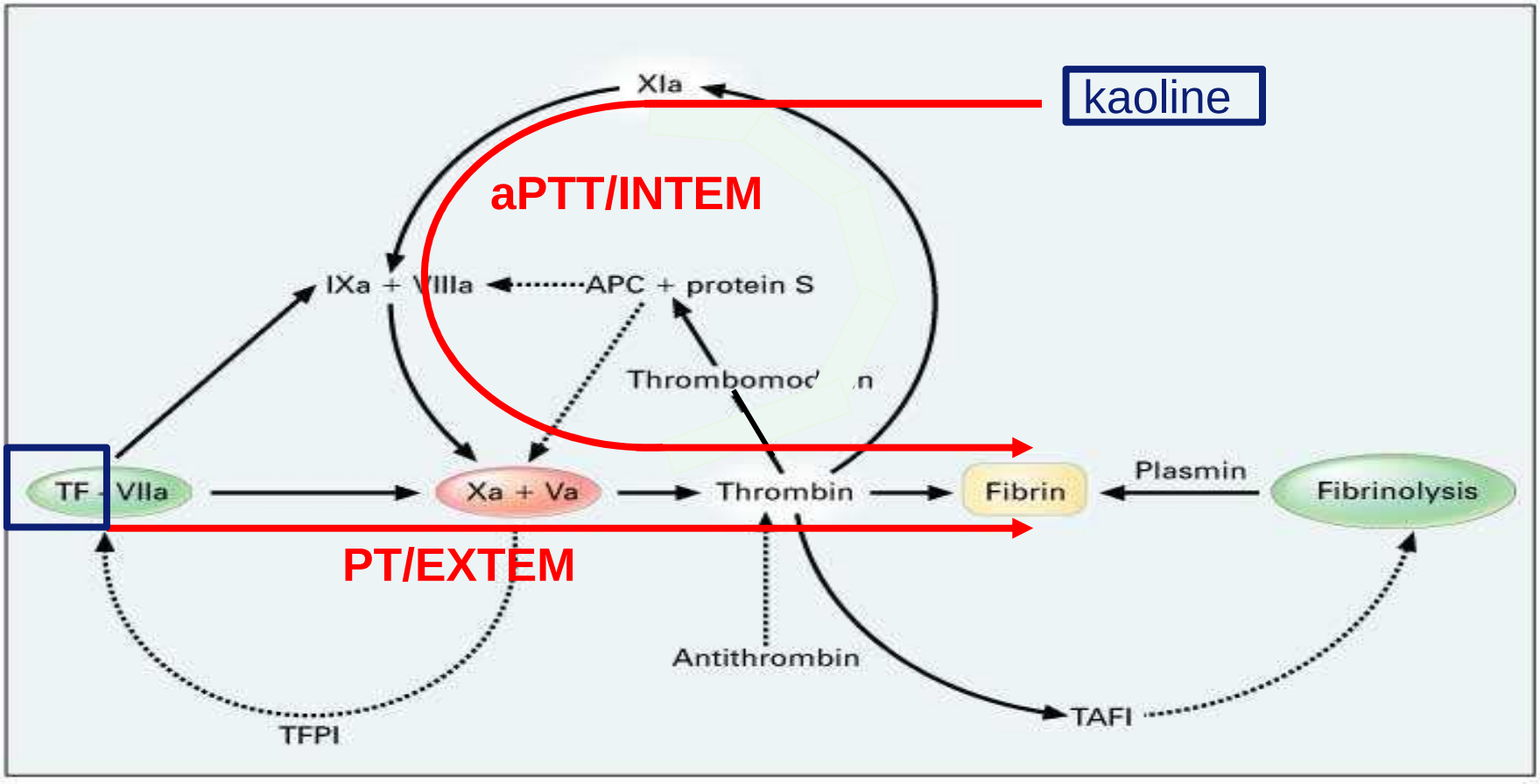


Figure 4-1: Principle of thromboelastometry with ROTEM® *delta*

1 Axis (~4.75 °)
2 Spring
aggregate
3 Light source/diode
4 Mirror
5 Detection device (electric camera)
6 Sensor pin
7 Cup filled with blood
8 Fibrin fibres and thrombocyte
9 Heated cup holder
10 Ball bearings
11 Data processing

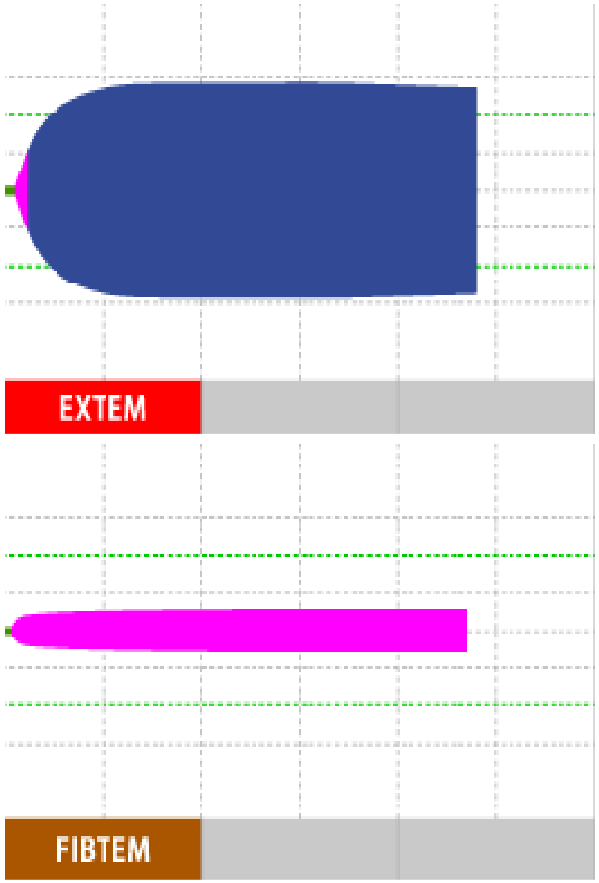

10 min
90 mm
20 mm
firmness
maximum clot firmness (MCF / MA) [mm]
maximum lysis (ML) [%]
clotting time (CT / r) [s]
clot formation time (CFT / k) [s]
time

PT/EXTEM and APTT/INTEM



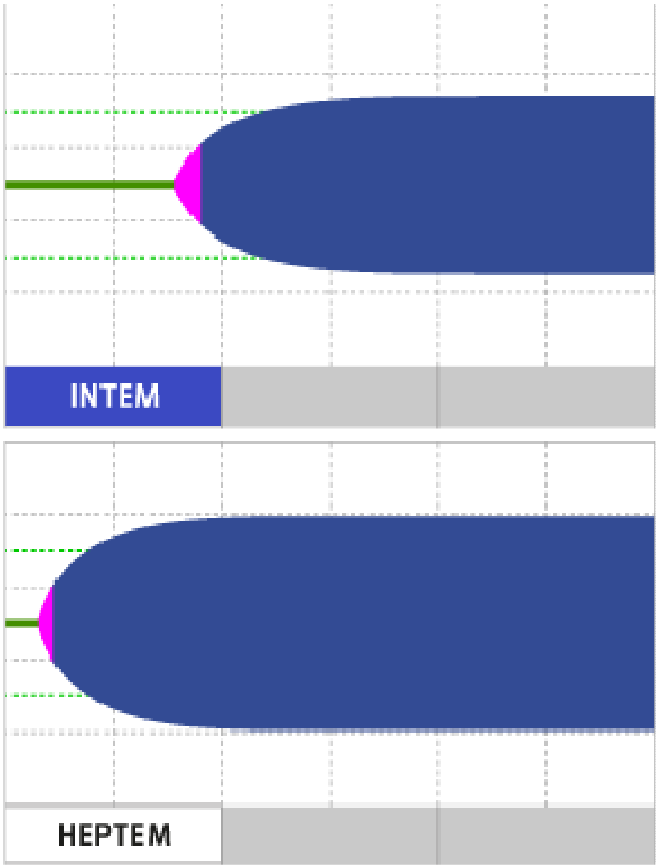
FIBTEM

- **Activator**: Cytochalasin D, recombinant tissue factor and phospholipids, $CaCl_2$



HEPTEM

- **Activator**: Heparinase, partial thromboplastin phospholipid made of rabbit brain, ellagic acid



Dangerous:

I understand all about coagulation,

because I looked at the ROTEM

Limitations

- Insensitive to milde coagulation factor deficiencies
- Insensitive to defects of primary hemostasis (VWD and platelet aggregation
- May still be normal when INR is <3-4
- no detection of von Willebrand syndrome

platelet inhibitors:

- no detection of Aspirin®
- no detection of clopidogrel/Plavix®
- poor sensitivity to Reopro®

anticoagulants:

- poor sensitivity to low molecular weight heparin, Orgaran® and pentasaccharide
- poor sensitivity to oral anticoagulants (coumarins Warfarin®, etc.) and DOACs

Limitations

- ROTEM is not really POCT
- Assays with ROTEM are expensive

  (costs >10x more than combination PT-APTT-fibrinogen)
- Differences between ROTEM equipment and reagent

ECAT FOUNDATION

External quality Control for Assays and Tests

With a focus on Thrombosis and Haemostasis

Erasmus MC

REPORT

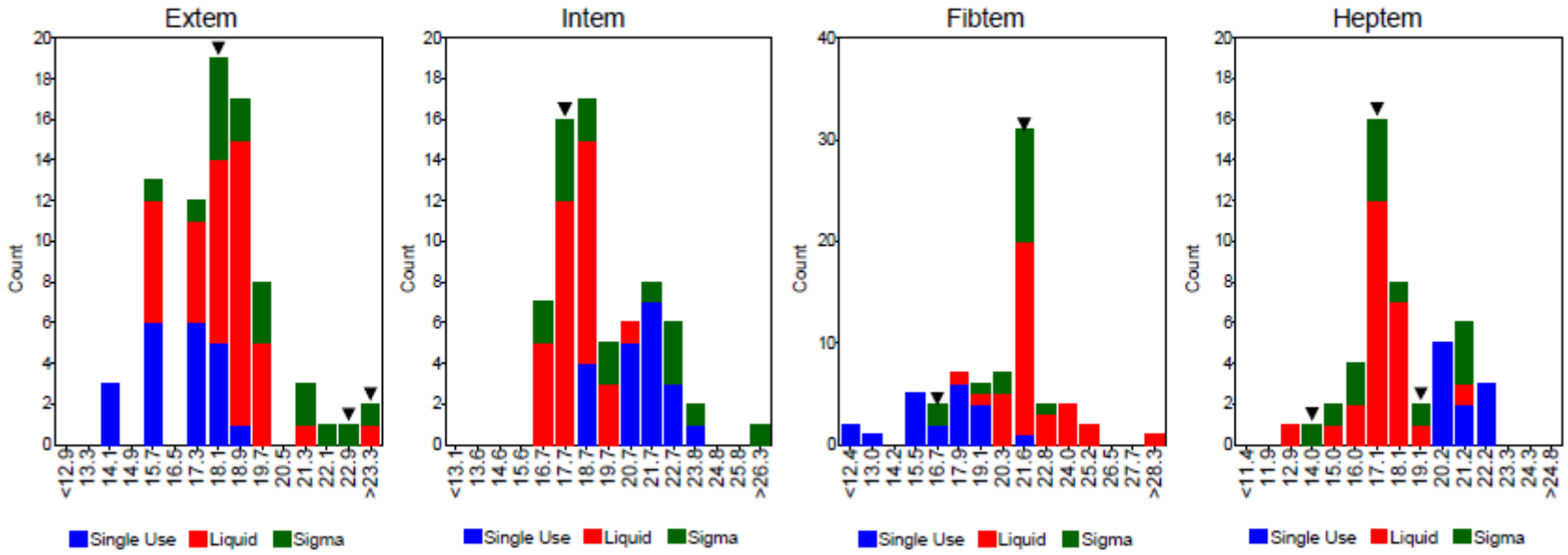
SURVEY 2017-M3
ROTEM/TEG
Labcode 246

ROTEM/TEG	ROTEM

Sample No 17.132

Sample Details Plasma with an UFH level of approx. 0.25 IU/mL

MCF (mm)



Limitations

- ROTEM is not really POCT
- Assays with ROTEM are expensive

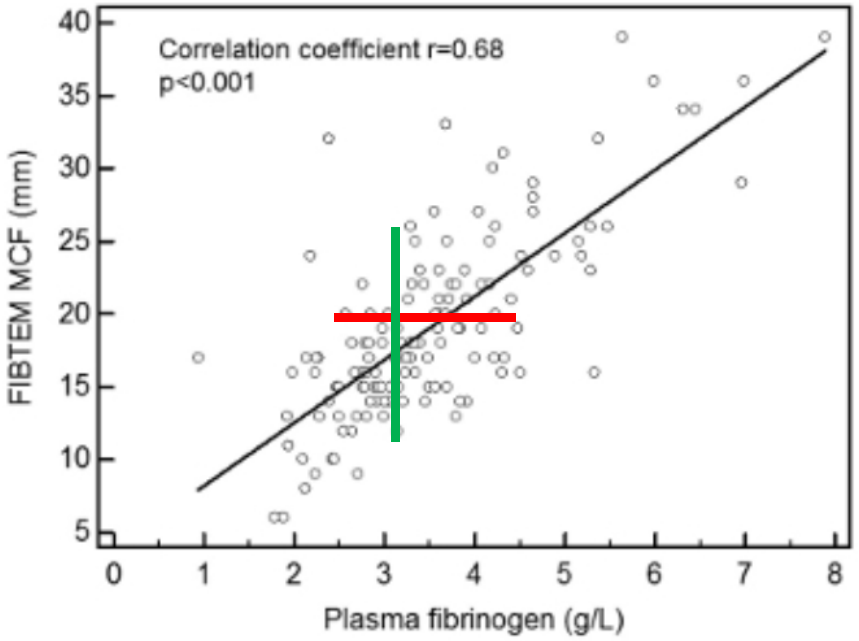
  (costs >10x more than combination PT-APTT-fibrinogen)
- Differences between equipment and reagent

Advantage

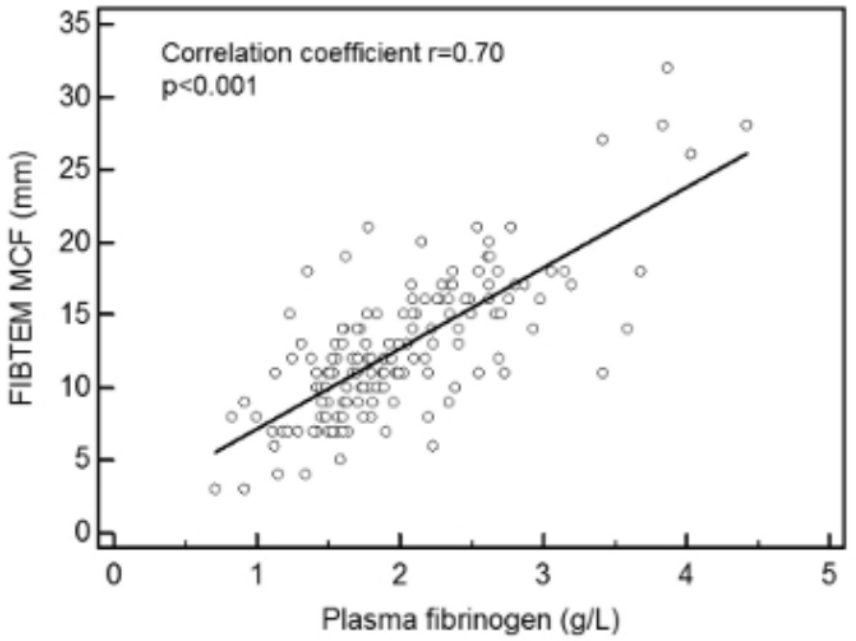
- Fast indication of coagulation
- Fast assay for fibrinogen levels

FIBTEM is not a measurement of Fibrinogen concentration
Clauss versus FIBTEM-MCF

Before cardiac surgery

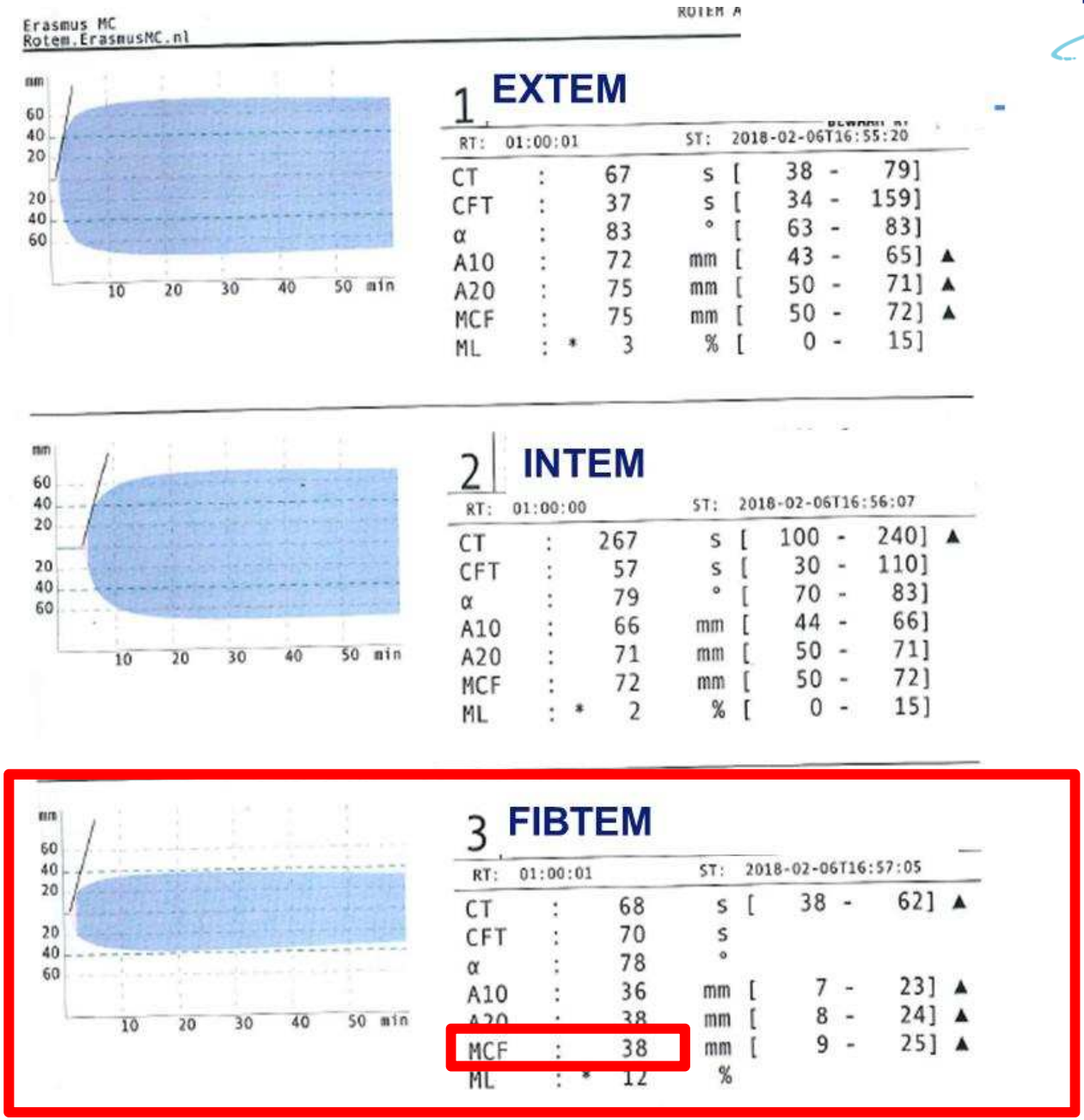


After



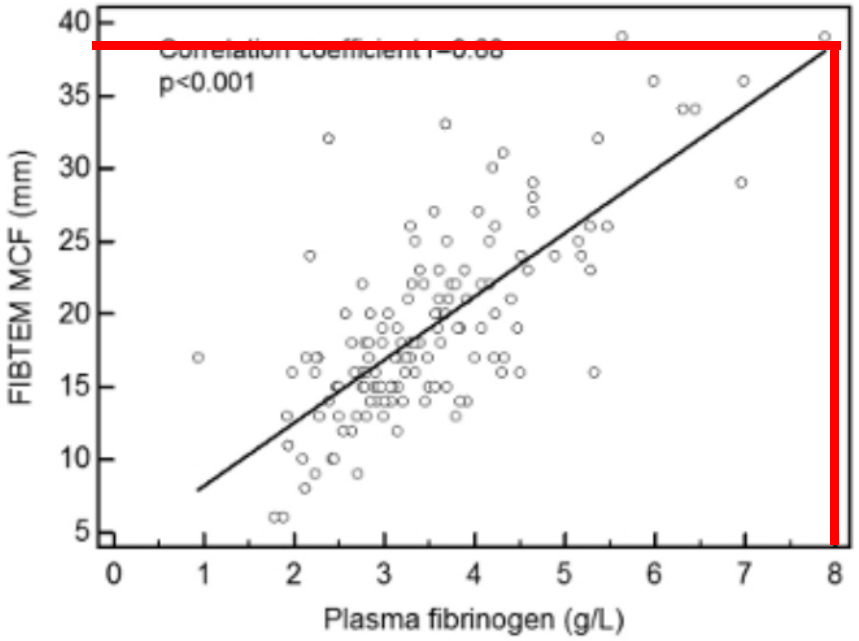
Solomon et al. Blood Transfus 2013; 11: 412-8

Casus I

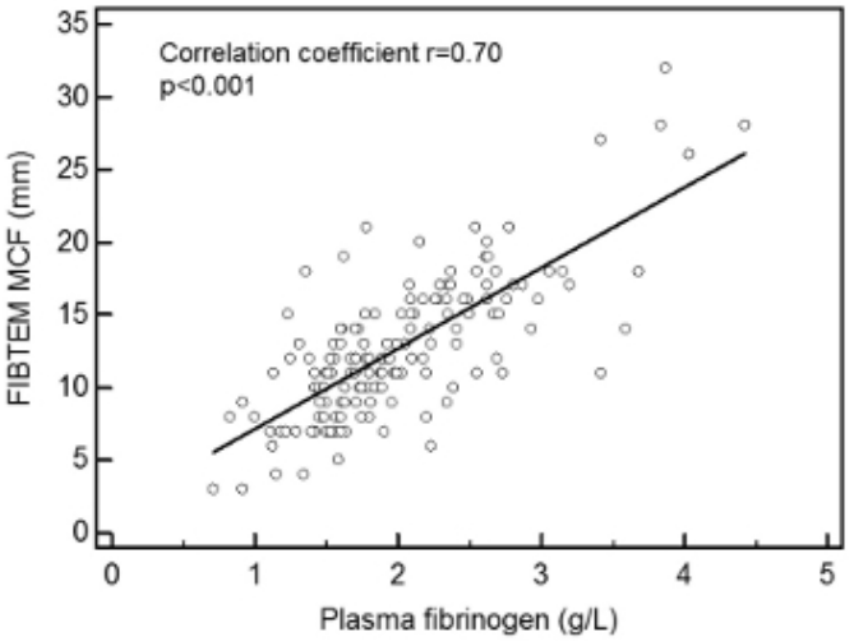

Erasmus MC
Rotem.ErasmusMC.nl
ROTEM A
1 EXTEM
RT: 01:00:01
ST: 2018-02-06T16:55:20
CT : 67 s [38 - 79]
CFT : 37 s [34 - 159]
α : 83 ° [63 - 83]
A10 : 72 mm [43 - 65] ▲
A20 : 75 mm [50 - 71] ▲
MCF : 75 mm [50 - 72] ▲
ML : * 3 % [0 - 15]
2 INTEM
RT: 01:00:00
ST: 2018-02-06T16:56:07
CT : 267 s [100 - 240] ▲
CFT : 57 s [30 - 110]
α : 79 ° [70 - 83]
A10 : 66 mm [44 - 66]
A20 : 71 mm [50 - 71]
MCF : 72 mm [50 - 72]
ML : * 2 % [0 - 15]
3 FIBTEM
RT: 01:00:01
ST: 2018-02-06T16:57:05
CT : 68 s [38 - 62] ▲
CFT : 70 s
α : 78 °
A10 : 36 mm [7 - 23] ▲
A20 : 38 mm [8 - 24] ▲
MCF : 38 mm [9 - 25] ▲
ML : * 12 %
mm
60
40
20
20
40
60
10 20 30 40 50 min

Clauss versus FIBTEM-MCF

Before cardiac surgery



After



Solomon et al. Blood Transfus 2013; 11: 412-8

Casus I

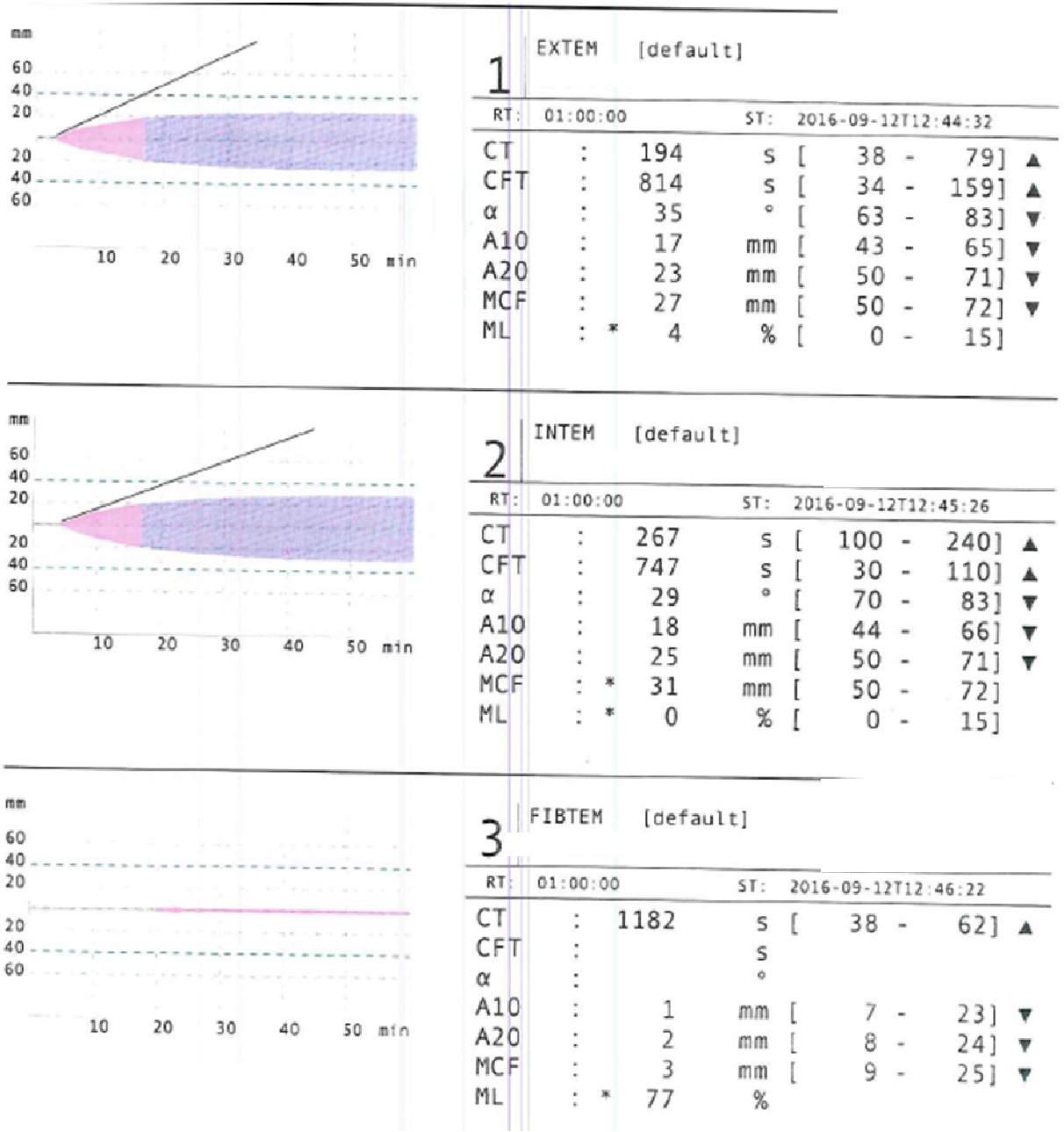
- Man, 49 years old
- Essential thrombocytosis (low risk) with in this context acquired VWD
- Malignant thymome, treated with chemotherapy

- Platelet count: 1084 10^9/L
- PT: 13.3 sec
- APTT: 27 sec
- Fibrinogen: 2.3 g/L
- VWF: Ag: 0.91 (U/mL)
- VWF:act: 0.69 (U/mL)

Casus II

- Man, born in 1949 (67 jaar)
- 2006 Cryptogenic liver cirrhosis, unexplained (viral, AIH, hemochromatosis, PSC negative)
- 2014 Start of billirubin increase, decrease albumin and prolonged clotting tests
- 2016 Progressive decrease of liver function, accompanied by kidney insufficience, decompensation and coagulation abnormalities.

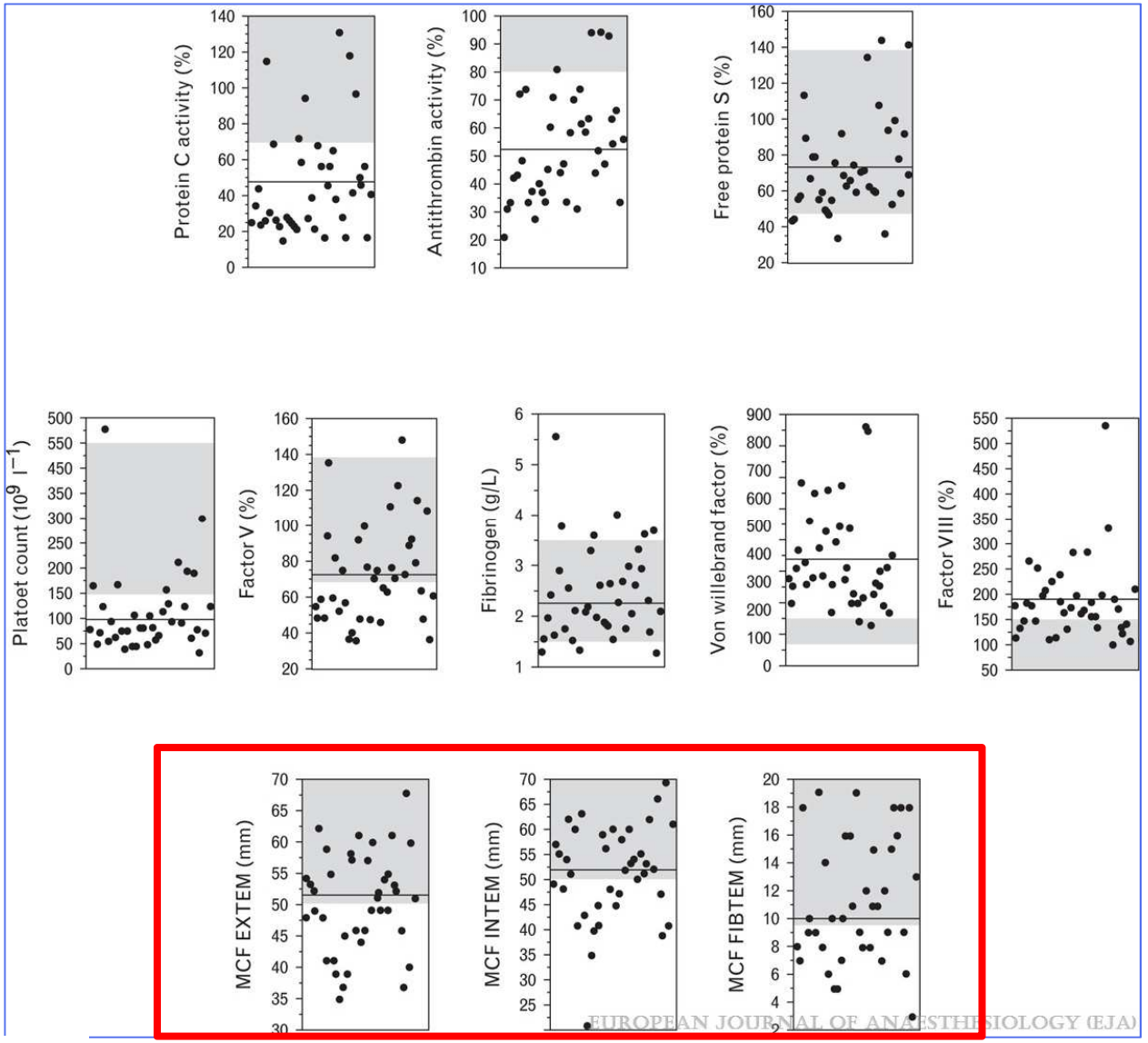
Casus II



M. de Maat, 2016

Hemoglobine	BL	mmol/L	5.1	5.1$_{L}$		5.1	5.2$_{L}$	6.1	5.2$_{L}$	
Hematocriet	BL	L/L		0.23$_{L}$					0.23$_{L}$	
Erytrocyten	BL	10^12/L							2.46$_{L}$	
MCV	BL	fL		96			96		95	
RDW	BL	%		17.2^{H}			17.3^{H}		17.3^{H}	
Trombocyten	BL	10^9/L		24$_{L!}$			24$_{L}$		21$_{L!}$	
Leukocyten	BL	10^9/L		8.6			7.9		9.2	
A1antitryps.	BL	g/L								
Ceruloplasm.	BL	g/L								
IgG4	BL	g/L								
Bloedgroep	BL									
IRR. Anti st	BL									
Kruisbloed	BL									
TSH	BL	mU/L								
APTT	BL	sec					52^{H}			48^{H}
APTT ratio	BL									
PT	BL	sec					28.1^{H}			28.2^{H}
PT INR	BL						2.5			2.5
Fibrinogeen	BL	g/L					u 1.5			u 1.4$_{L}$
Factor V	BL	U/mL								
Antitrombine	BL	U/mL					0.31$_{L}$			
Antiplasmine	BL	U/mL					0.35$_{L}$			
D-dimeren	BL	mg/L					10.90^{H}			

ROTEM tests in patients with cirrhosis



Lentschener. et al. European Journal of Anaesthesiology 2016; 33(2):126-133

ROTEM tests in patients with cirrhosis

Age (years)	61 ± 11
Sex ratio (male/female)	34/8
BMI ($kg\,m^{-2}$)	23 ± 4
Cause of cirrhosis	
Alcoholic liver disease	12
Hepatitis C virus	6
Hepatitis B virus	8
Nonalcoholic steatohepatitis	6
Alcoholic liver disease and nonalcoholic steatohepatitis	8
Aspartate aminotransferase ($IU\,l^{-1}$) [reference range 10 to 45]	85 (25 to 234)
Alanine aminotransferase ($IU\,l^{-1}$) [reference range 10 to 45]	52 (8 to 148)
Alkaline phosphatase ($IU\,l^{-1}$) [reference range 35 to 120]	156 ± 77
Bilirubin ($mg\,dl^{-1}$) [reference range 3 to 17]	63 (8 to 368)
Albumin ($g\,l^{-1}$) [reference range 35 to 52]	30 ± 6
Haemoglobin ($g\,dl^{-1}$)	11.6 ± 2.2
Creatinine ($\mu mol\,l^{-1}$) [reference range 55 to 110]	76 ± 28
Model for end-stage liver disease score	13 (7 to 25)

Lentschener. et al. Eur J Anaesthesiol 2016; 33(2):126-133

Fibrinolysis

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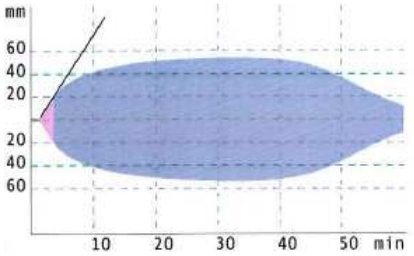
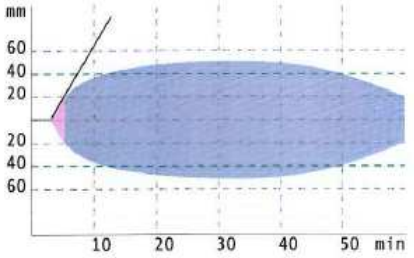
ROTEM Analyser, Tem Innovations
3080



1 EXTEM

RT: 01:00:00 ST: 2018-10-25T15:56:03

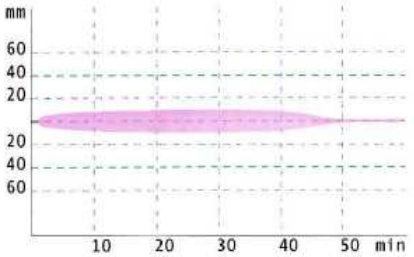
CT	:	96	s	[	38	-	79]	▲
CFT	:	125	s	[	34	-	159]	
α	:	66	°	[	63	-	83]	
A10	:	44	mm	[	43	-	65]	
A20	:	52	mm	[	50	-	71]	
MCF	:	54	mm	[	50	-	72]	
ML	: *	78	%	[	0	-	15]	



2 INTEM

RT: 01:00:00 ST: 2018-10-25T15:56:38

CT	:	201	s	[	100	-	240]	
CFT	:	123	s	[	30	-	110]	▲
α	:	67	°	[	70	-	83]	▼
A10	:	43	mm	[	44	-	66]	▼
A20	:	50	mm	[	50	-	71]	
MCF	:	51	mm	[	50	-	72]	
ML	: *	62	%	[	0	-	15]	

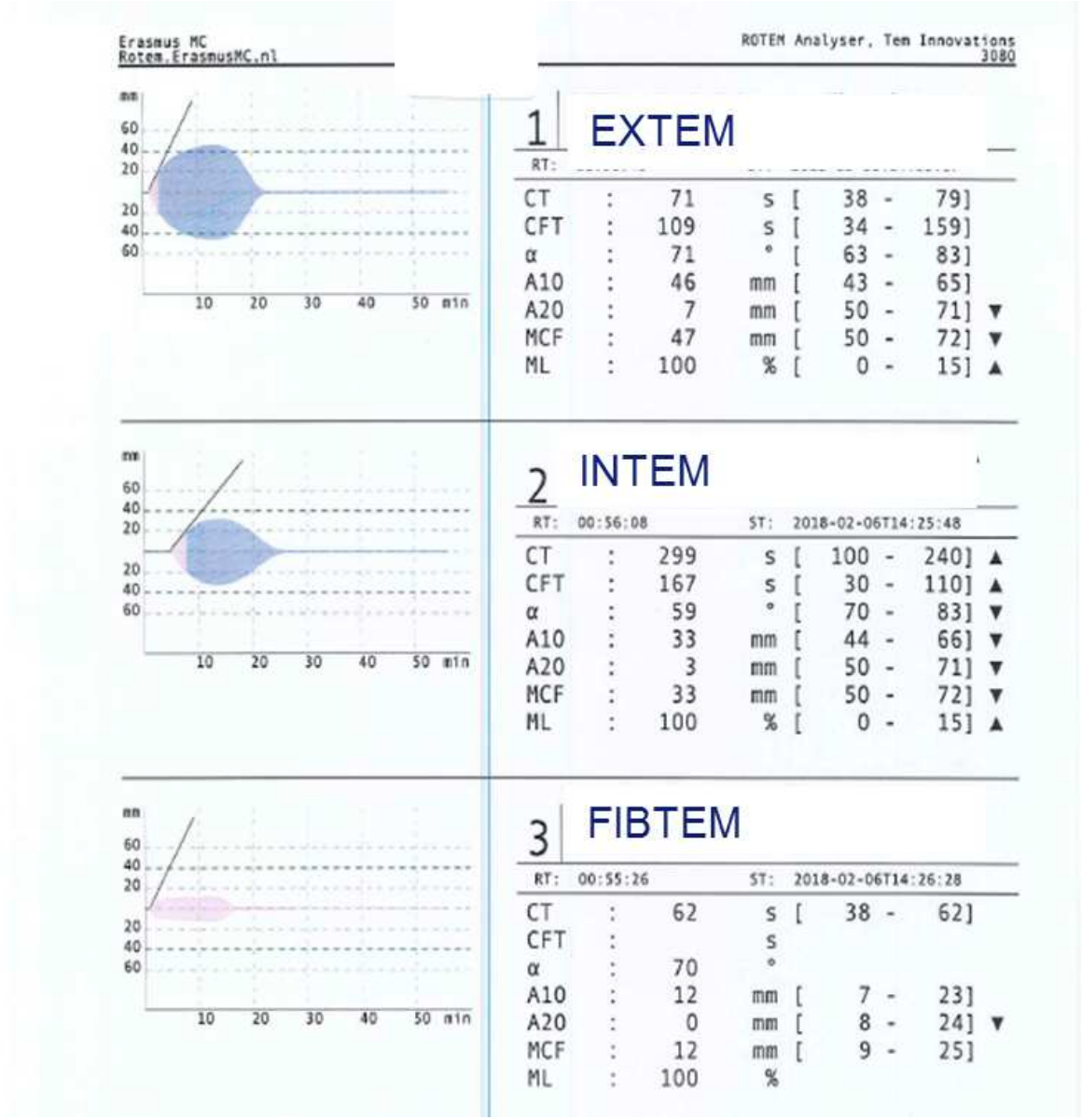


3 FIBTEM

RT: 01:00:01 ST: 2018-10-25T15:57:17

CT	:	81	s	[	38	-	62]	▲
CFT	:		s					
α	:		°					
A10	:	9	mm	[	7	-	23]	
A20	:	10	mm	[	8	-	24]	
MCF	:	10	mm	[	9	-	25]	
ML	:	100	%					

Fibrinolysis



Erasmus MC

Test	Materiaal	24-05-2016 10:21	24-05-2016 10:30	24-05-2016 12:48	25-05-2016 06:59	27-05-2016 06:28	06-02-2018 14:47 Hoek	06-02-2018 15:00	06-02-2018 15:06	Eenheid
APTT	Bloed						54			sec
PT	Bloed						15.8			sec
PT INR	Bloed						1.4			
Fibrinogeen	Bloed						2.6			g/L
D-dimeren	Bloed						61.56			mg/L
ROTEM EXTEM	Bloed						Zie-Opm			
ROTEM INTEM	Bloed						Zie-Opm			
ROTEM FIBTEM	Bloed						Zie-Opm			
ROTEM HEPTEM	Bloed						Zie-Opm			

Conclusions

- ROTEM is valuable in massive blood loss protocols, where the risk of coagulation abnormalities is small.
- Many factors are not detected using the ROTEM