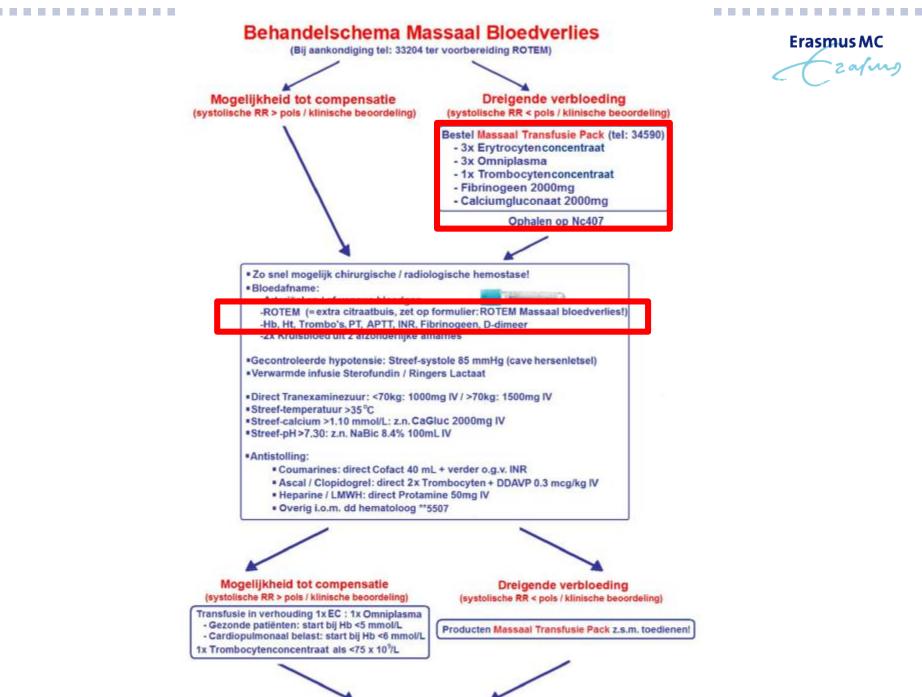


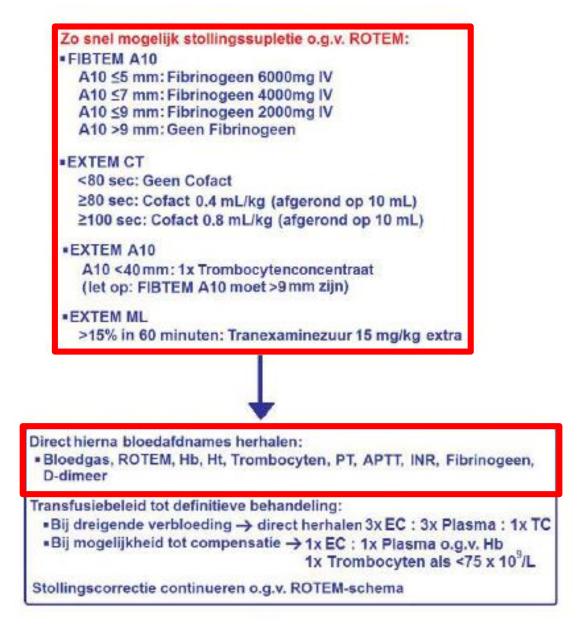
# Is there a need to measure ROTEM/TEG?

Moniek de Maat Hematologie

ECAT participant meeting, 2018







## **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)

#### Erasmus MC



## **ROTEM** at the Hemostasis Laboratory Erasmus MC





## **Dangerous:**

# I understand all about coagulation, because I looked at the ROTEM

## Limitations

#### platelet inhibitors:

- no detection of Aspirin®
- no detection of clopidogrel/Plavix®
- no detection of von Willebrand syndrome
- 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

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**Erasmus MC** 

#### External quality Control for Assays and Tests

With a focus on Thrombosis and Haemostasis

#### REPORT



SURVEY 2017-M3 ROTEM/TEG Labcode 246

> Copyright © 2017 ECAT Foundation





External quality Control for Assays and Tests With a focus on Thrombosis and Haemostasis Survey: 2017-M3 Page 3 of 10 10-oktober-2017 Labcode: 246

#### **ROTEM/TEG**

#### ROTEM

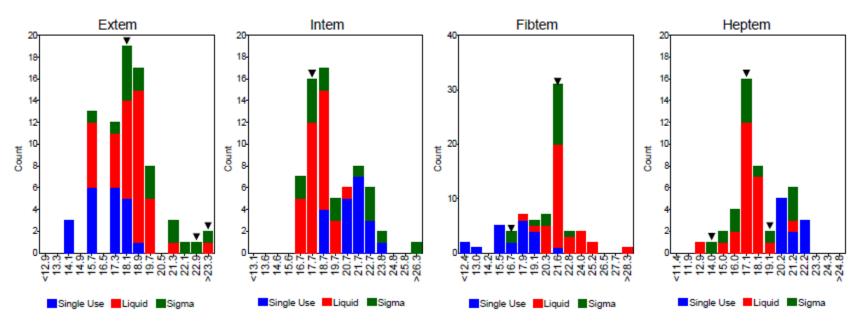
Sample No

17.132

Sample Details

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

#### MCF (mm)



#### **Erasmus MC**

ing

#### Limitations



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

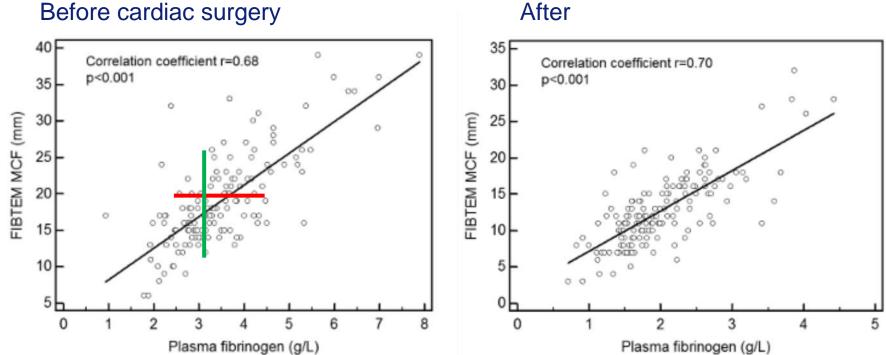
(costs >10x more than combination PT-APTT-fibrinogen)

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**



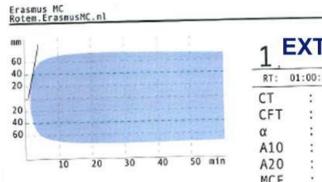
#### After

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

**Erasmus** MC

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#### **Casus** I

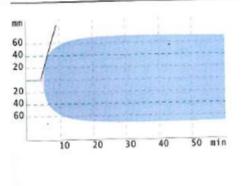


| RT: | 01:00:0 | 01  | ST: | 2018 | 8-02-06 | T16 | :55:20 | ×. |
|-----|---------|-----|-----|------|---------|-----|--------|----|
| ст  | :       | 67  | s   | [    | 38      | -   | 79]    |    |
| CFT | :       | 37  | s   | [    | 34      | -   | 159]   |    |
| α   | :       | 83  | ٥   | [    | 63      | -   | 83]    |    |
| A10 |         | 72  | mm  | ]    | 43      | -   | 65]    |    |
| A20 |         | 75  | mm  | [    | 50      | -   | 71]    |    |
| MCF |         | 75  | mm  | ]    | 50      | -   | 72]    |    |
| ML  |         | * 3 | %   | 1    | 0       | -   | 15]    |    |

ROIEM A

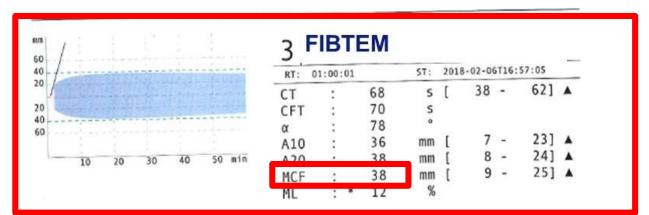
**Erasmus MC** 

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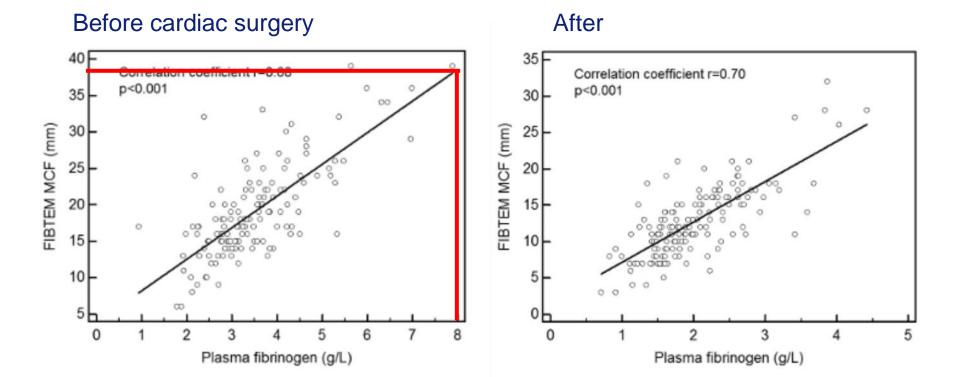


| 2   | IN |     | EM  | ST: | 201 | 8-02-06 | 5716 | :56:07 |  |
|-----|----|-----|-----|-----|-----|---------|------|--------|--|
| CT  |    | .00 | 267 | S   | 1   | 100     | -    | 240]   |  |
| CFT | :  |     | 57  | s   | i   | 30      | -    | 110]   |  |
| α   |    |     | 79  | 0   | ĩ   | 70      | -    | 83]    |  |
| A10 |    |     | 66  | mm  | ī   | 44      | -    | 66]    |  |
| A20 |    |     | 71  | mm  | ĺ.  | 50      | -    | 71]    |  |
| MCF |    |     | 72  | mm  | ]   | 50      | -    | 72]    |  |
| ML  | :  | *   | 2   | %   | ]   | 0       | -    | 15]    |  |

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



#### **Clauss versus FIBTEM-MCF**



## Casus I

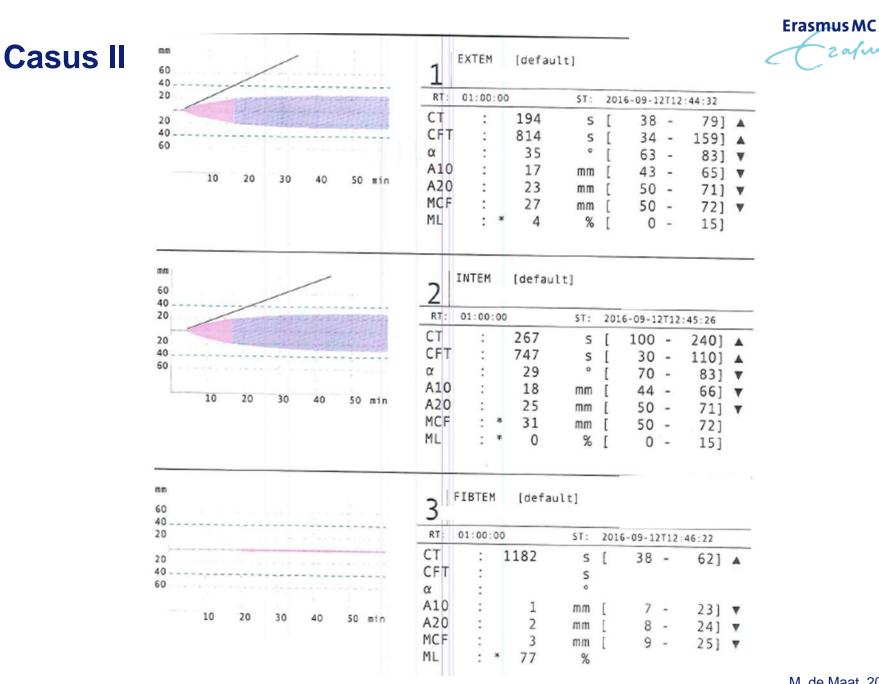


- Man, 49 years old
- Essential thrombocytosis (low risk) with in this context acquired VWD
- Malignant thymome, treated with chemotherapy
- Platelet count: 1084 10<sup>9</sup>/L
- PT: 13.3 sec
- APTT: 27 sec
- Fibrinogen: 2.3 g/L
- VWF: Ag: 0.91 (U/mL)
- VWF:act: 0.69 (U/mL)

## 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.



#### M. de Maat. 2016

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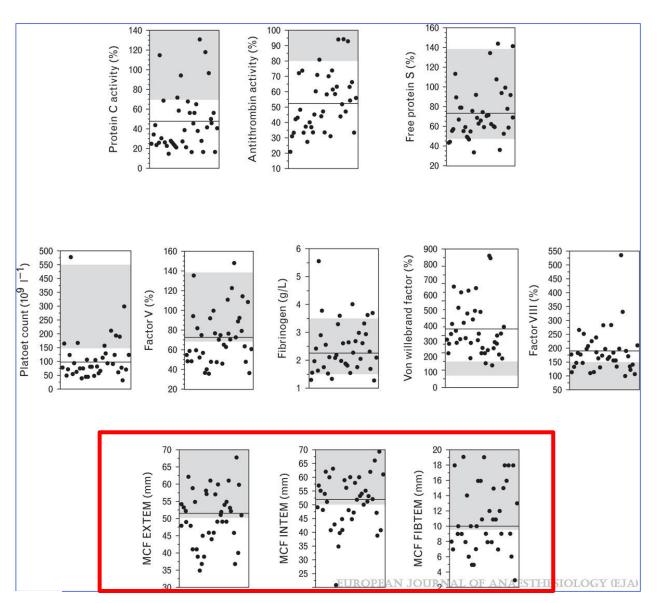
| Hemoglobine  | BL | mmol/L  | 5.1 | 5.1 <sub>L</sub>  | 5.1 | 5.2 <sub>L</sub>   | 6.1 | 5.2 <sub>L</sub>  |                   |
|--------------|----|---------|-----|-------------------|-----|--------------------|-----|-------------------|-------------------|
| Hematocriet  | BL | L/L     |     | 0.23 <sub>L</sub> |     |                    |     | 0.23 <sub>L</sub> |                   |
| Erytrocyten  | BL | 10^12/L |     |                   |     |                    |     | 2.46 <sub>L</sub> |                   |
| MCV          | BL | fL      |     | 96                |     | 96                 |     | 95                |                   |
| RDW          | BL | %       |     | 17.2 <sup>H</sup> |     | 17.3 <sup>H</sup>  |     | 17.3 <sup>H</sup> |                   |
| Trombocyten  | BL | 10^9/L  |     | 24 <sub>L!</sub>  |     | 24 <sub>L!</sub>   |     | 21 <sub>L!</sub>  |                   |
| Leukocyten   | BL | 10^9/L  |     | 8.6               |     | 7.9                |     | 9.2               |                   |
| A1antitryps. | BL | g/L     |     |                   |     |                    |     |                   |                   |
| Ceruloplasm. | BL | g/L     |     |                   |     |                    |     |                   |                   |
| lgG4         | BL | g/L     |     |                   |     |                    |     |                   |                   |
| Bloedgroep   | BL |         |     |                   |     |                    |     |                   |                   |
| IRR. Anti st | BL |         |     |                   |     |                    |     |                   |                   |
| Kruisbloed   | BL |         |     |                   |     |                    |     |                   |                   |
| TSH          | BL | mU/L    |     |                   |     |                    |     |                   |                   |
| APTT         | BL | sec     |     |                   |     | 52 <sup>H</sup>    |     |                   | 48 <sup>H</sup>   |
| APTT ratio   | BL |         |     |                   |     |                    |     |                   |                   |
| РТ           | BL | sec     |     |                   |     | 28.1 <sup>H</sup>  |     |                   | 28.2 <sup>H</sup> |
| PT INR       | BL |         |     |                   |     | 2.5                |     |                   | 2.5               |
| Fibrinogeen  | BL | g/L     |     |                   | u   | 1.5                |     | l                 | 1.4 <sub>L</sub>  |
| Factor V     | BL | U/mL    |     |                   |     |                    |     |                   |                   |
| Antitrombine | BL | U/mL    |     |                   |     | 0.31 <sub>L</sub>  |     |                   |                   |
| Antiplasmine | BL | U/mL    |     |                   |     | 0.35 <sub>L</sub>  |     |                   |                   |
| D-dimeren    | BL | mg/L    |     |                   |     | 10.90 <sup>H</sup> |     |                   |                   |

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Erasmus MC Cafing M. de Maat, 2016

#### **ROTEM tests in patients with cirrhosis**

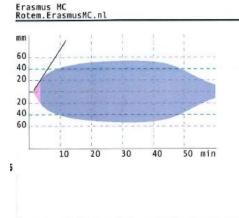


Erasmus MC 2 afmg

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

## **Fibrinolysis**





|     |          |     |     |     |        | _    | _      | 3080 |
|-----|----------|-----|-----|-----|--------|------|--------|------|
| 1   | EXT      | EM  |     |     |        |      |        |      |
| RT: | 01:00:00 |     | ST: | 201 | 8-10-2 | 5T15 | :56:03 |      |
| СТ  | :        | 96  | s   | [   | 38     | -    | 79]    |      |
| CFT | :        | 125 | s   | [   | 34     | -    | 159]   |      |
| α   | :        | 66  | 0   | [   | 63     | -    | 83]    |      |
| A10 | :        | 44  | mm  | [   | 43     | -    | 65]    |      |
| A20 | :        | 52  | mm  | [   | 50     | -    | 71]    |      |

mm [

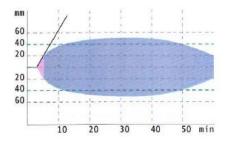
% [

ROTEM Analyser, Tem Innovations.

50 -

0 -

72] 15]



| 2 | INT | ΞM |
|---|-----|----|

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• \*

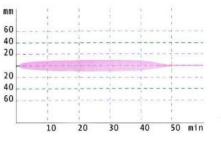
54

78

MCF

ML

| RT: | 01:00 | :00 |     | ST: | 201 | 18-10-25 | 5T15 | :56:38 |   |
|-----|-------|-----|-----|-----|-----|----------|------|--------|---|
| СТ  | 1     |     | 201 | S   | [   | 100      | -    | 240]   |   |
| CFT | :     |     | 123 | s   | [   | 30       | -    | 110]   |   |
| α   | :     |     | 67  | 0   | [   | 70       | -    | 83]    | - |
| A10 | :     |     | 43  | mm  | [   | 44       | -    | 66]    | W |
| A20 | :     |     | 50  | mm  | [   | 50       | -    | 71]    |   |
| MCF | :     |     | 51  | mm  | ]   | 50       | -    | 72]    |   |
| ML  | 0     | *   | 62  | %   | [   | 0        | -    | 15]    |   |



| 3   | FIBT     | EM  |     |     |        |       |                 |  |
|-----|----------|-----|-----|-----|--------|-------|-----------------|--|
| RT: | 01:00:01 |     | ST: | 201 | 8-10-2 | 5T15: | 57:17           |  |
| СТ  | :        | 81  | S   | [   | 38     | -     | 62]             |  |
| CFT | :        |     | s   |     |        |       |                 |  |
| α   | :        |     | 0   |     |        |       |                 |  |
| A10 | :        | 9   | mm  | [   | 7      | -     | 23]             |  |
| A20 | :        | 10  | mm  | [   | 8      | -     | 24]             |  |
| MCF | :        | 10  | mm  | [   | 9      | -     | 25]             |  |
| ML  | :        | 100 | %   |     |        |       | 3. <del>.</del> |  |

## Fibrinolysis



| nm<br>50<br>10                       | 1  | EX            |   | 1  |           |   |  |     |
|--------------------------------------|--|---------------|---|--|-----------|---|--|-----|
| 20<br>20<br>50<br>10 20 30 40 50 min | RT:<br>CFT<br>α<br>A10<br>A20<br>MCF<br>ML | :             | 71<br>109<br>71<br>46<br>7<br>47<br>100 | s<br>s<br>mm<br>mm<br>mm<br>%            |           | 8 -<br>4 -<br>3 -<br>3 -<br>0 -<br>0 -<br>0 - | 79]<br>159]<br>83]<br>65]<br>71]<br>72]<br>15] | **  |
| m<br>50<br>10                        |  | IN7           | EM                                      | ST:                                      | 2018-0    | -0671   | 4:25:48  |     |
| 10                                   | CT   | :             | 299                                     | s  |           | 0 - 0   | 240]   |     |
| 0                                    | CFT  | :             | 167                                     | S  | - A-1 - C | - 0   | 110]   |     |
| 0                                    | α  | :             | 59                                      | ٥  |           | 0 -   | 83]  | ۷   |
|                                      | A10  |               | 33                                      | mm                                       | 1 4       | 4 -   | 66]<br>711                                     |     |
| 10 20 30 40 50 min                   | 420  |               |   | #15.000                                  | r r       |   |  |     |
| 10 20 30 40 50 m1n                   | A20<br>MCE                                 | :             | 3                                       | mm                                       |           | 0 -   |  | ÷   |
| 10 20 30 40 50 min                   | A20<br>MCF<br>ML                           | :             | 33<br>100                               | mm<br>mm<br>%                            |           | 0 -<br>0 -                                    | 72]<br>15]                                     | *   |
| n<br>0                               | MCF  | FIE           | 33                                      | mm<br>%                                  | i :       | 0 -   | 72]  | *   |
| o                                    | MCF<br>ML                                  | :<br>:<br>FIE | 33<br>100<br>BTEN                       | mm<br>%                                  | [         | 0 -   | 72]  | *   |
|                                      | MCF<br>ML<br>3<br>RT:<br>CT                |               | 33<br>100<br>BTEN                       | тт<br>%<br>Л                             | 2018-02   | 0 -   | 72]<br>15]                                     | *   |
|                                      | MCF<br>ML<br>3<br>RT:<br>CT<br>CFT         |               | 33<br>100<br>BTEN<br>62                 | mm<br>%<br>A<br>st:<br>s<br>s            | 2018-02   | 0 -<br>0 -                                    | 72]<br>15]<br>4:26:28                          | *   |
|                                      | MCF<br>ML<br>3<br>RT:<br>CT<br>CFT<br>α    |               | 33<br>100<br>BTEN<br>62<br>70           | mm<br>%<br>A<br>st:<br>s<br>s            | 2018-02   | 0 -<br>0 -                                    | 72]<br>15]<br>4:26:28<br>62]                   | *   |
|                                      | MCF<br>ML<br>3<br>RT:<br>CT<br>CFT<br>A10  |               | 33<br>100<br>BTEN<br>62<br>70<br>12     | mm<br>%<br>A<br>st:<br>s<br>s<br>s<br>mm | 2018-02   |   | 72]<br>15]<br>4:26:28<br>62]<br>23]            | *** |
|                                      | MCF<br>ML<br>3<br>RT:<br>CT<br>CFT<br>α    |               | 33<br>100<br>BTEN<br>62<br>70           | mm<br>%<br>A<br>st:<br>s<br>s            | 2018-02   | 0 -<br>0 -                                    | 72]<br>15]<br>4:26:28<br>62]                   | *   |



| Test         | Materiaal | 24-05-2016<br>10:21 | 24-05-2016<br>10:30 | 24-05-2016<br>12:48 | 25-05-2016<br>06:59 | 27-05-2016<br>06:28 | ■<br>06-02-2018<br>14:47<br>Hoek | ■<br>06-02-2018<br>15:00 | ■<br>06-02-2018<br>15:06 | Eenheid |
|--------------|-----------|---------------------|---------------------|---------------------|---------------------|---------------------|----------------------------------|--------------------------|--------------------------|---------|
| APTT         | Bloed     |                     |                     |                     |                     |                     | 54                               | -                        |                          | sec     |
| D 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                          |                          |                          |         |

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## 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

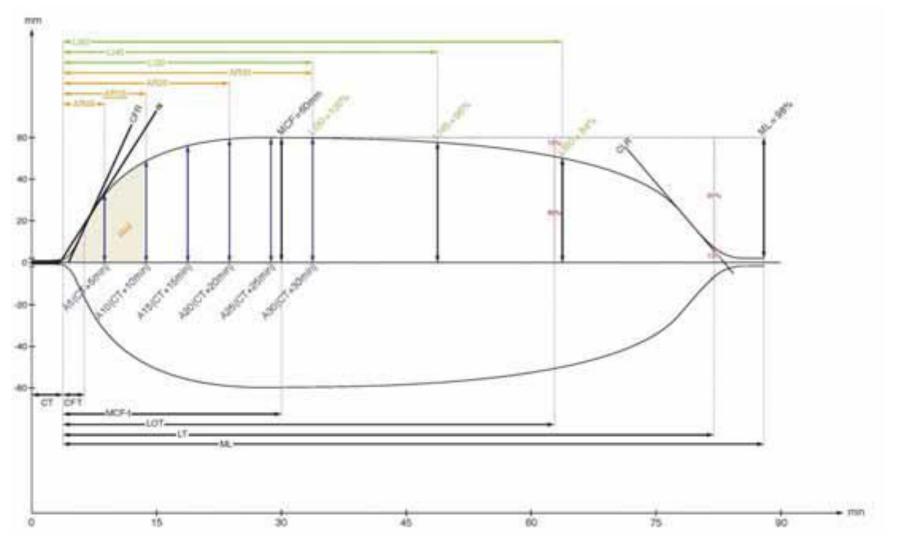


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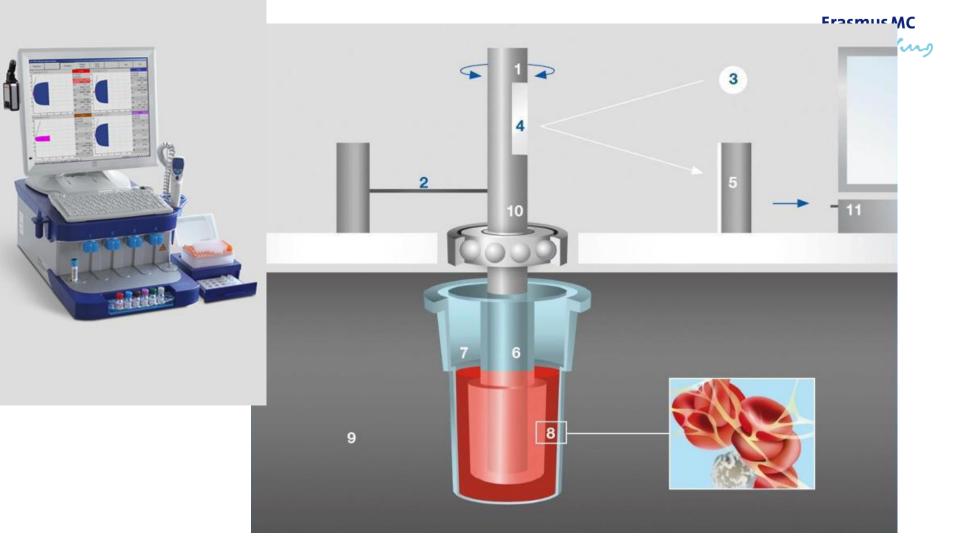
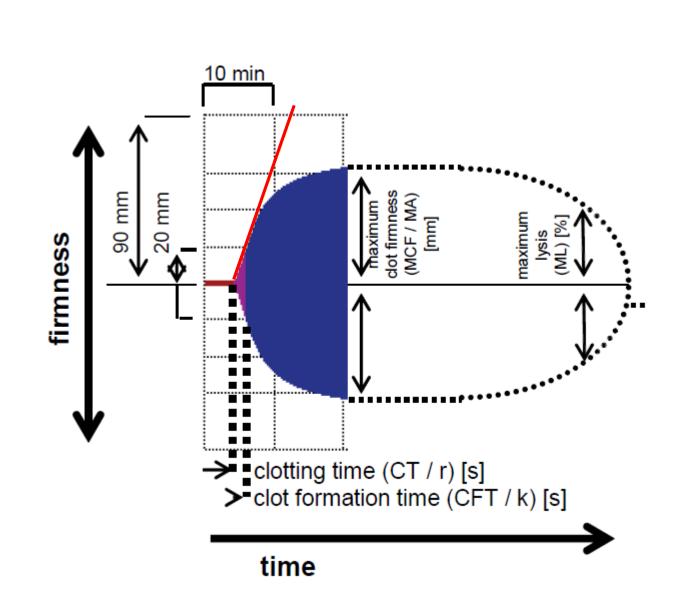


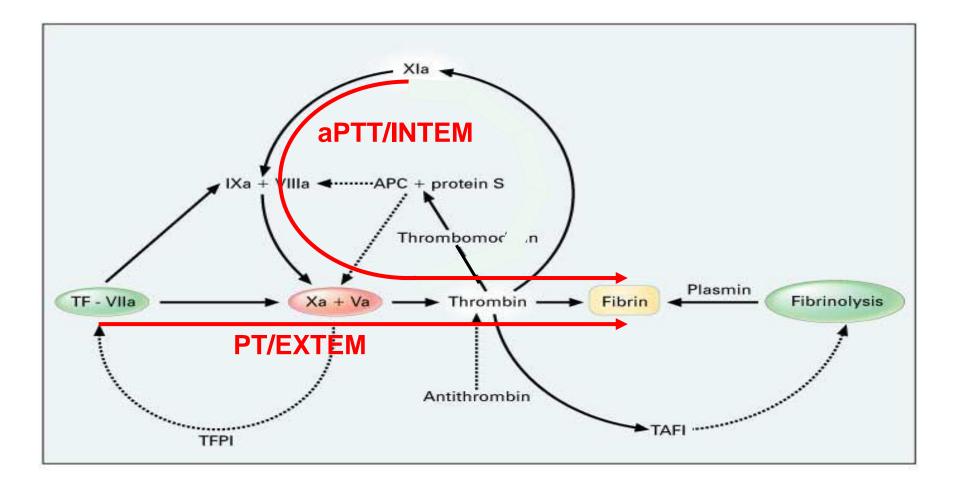
Figure 4-1: Principle of thromboelastometry with ROTEM® delta1 Axis (~4.75 °)7 Cup filled with blood2 Spring8 Fibrin fibres and thrombocyteaggregate9 Heated cup holder3 Light source/diode9 Heated cup holder4 Mirror10 Ball bearings5 Detection device (electric camera)11 Data processing6 Sensor pin11



Erasmus MC 2 afrag

#### **PT and APTT**





## EXTEM



- Activator: tissue factor
- **Principle**: mild extrinsic coagulation activation
- **Application**: Global analysis of coagulation, largely heparin insensitive
- 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</p>
  - May show pathological values caused by very high heparin levels

## INTEM

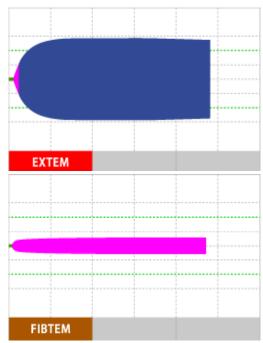


- Activator: Partial thromboplastin phospholipid made of rabbit brain (chloroform extract), ellagic acid
- Principle: mild intrinsic coagulation activation
- Application : Global analysis of coagulation
- *Limitations*:
  - Insensitive to milde coagulation factor deficiencies
  - Insensitive to defects of primary hemostasis (VWD and platelet aggregation

## **FIBTEM**



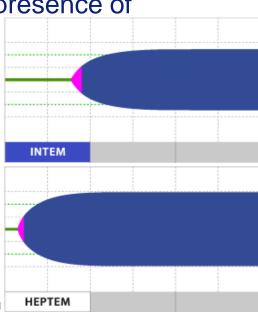
- Activator: Cytochalasin D, recombinant tissue factor and phospholipids, CaCl<sub>2</sub>
- Principle: mild intrinsic coagulation activation in the presence of a platelet inhibitor
- Application:
  - Detection of fibrinogen deficiency and fibrin polymerisation disorders
  - Compared to EXTEM: indirect determinantion
    - of the platelet component
  - Largely heparin insensitive
- Limitations:
  - May be influenced by very high heparin levels
  - Represents only the fibrin component



## HEPTEM

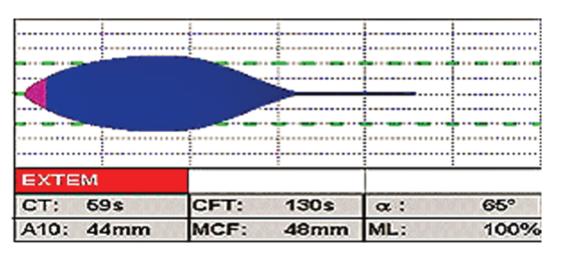


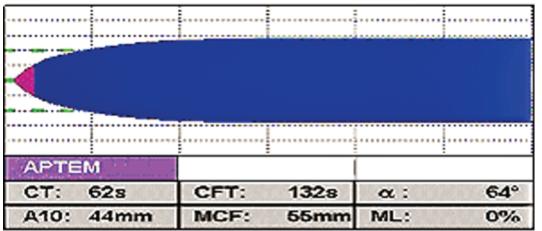
- Activator: Heparinase, partial thromboplastin phospholipid made of rabbit brain, ellagic acid
- Principle: mild intrinsic coagulation activation in the presence of heparin degradation
- Application:
  - Global analysis of coagulation after the elimination of the influence of heparin
  - In comparison to INTEM: qulitative assay for the presence of heparin.
- Limitations:
  - Insensitive to milde coagulation factor deficiencies
  - Insensitive to defects of primary hemostasis (VWD and platelet aggregation



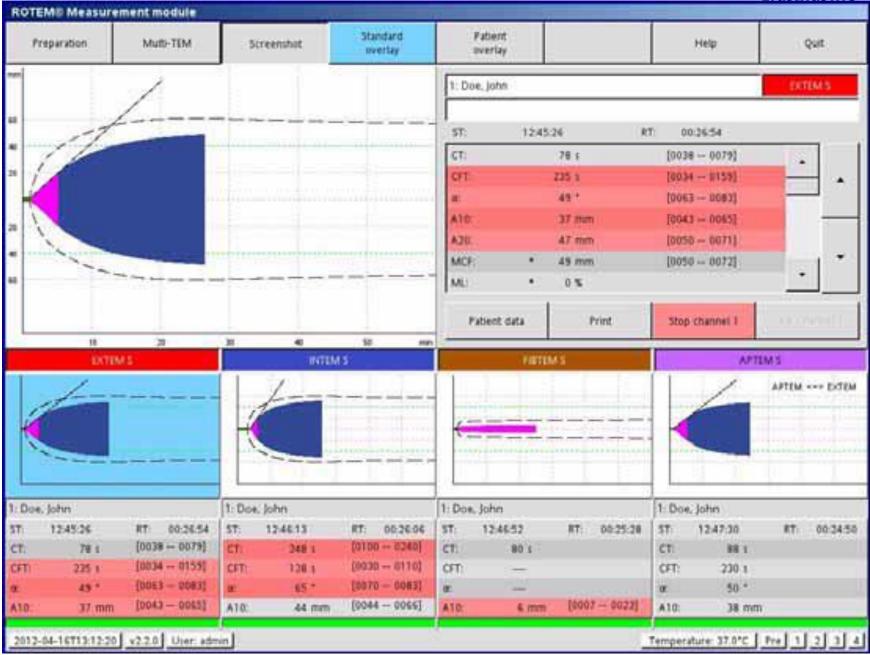
**APTEM:** activation as in EXTEM with addition of aprotinin, a fibrinolysis inhibitor. In an assay comparing APTEM to EXTEM massive hyperfibrinolysis can be recognised within 10 - 20 minutes.





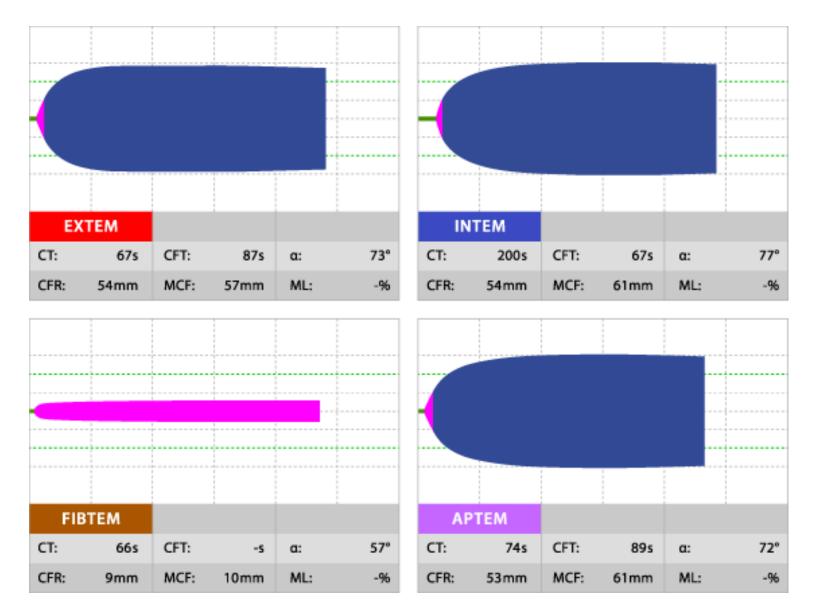


#### **Erasmus MC**



## **Normal ROTEM pattern**

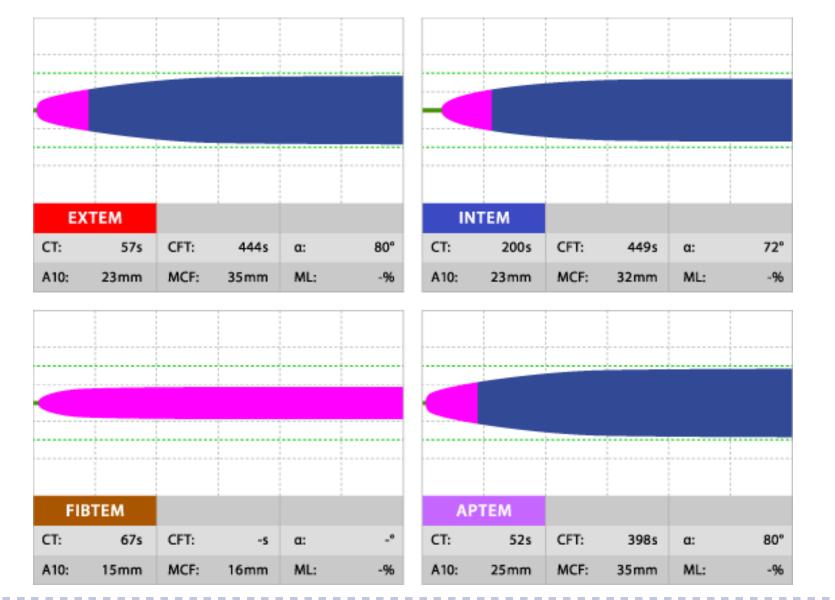




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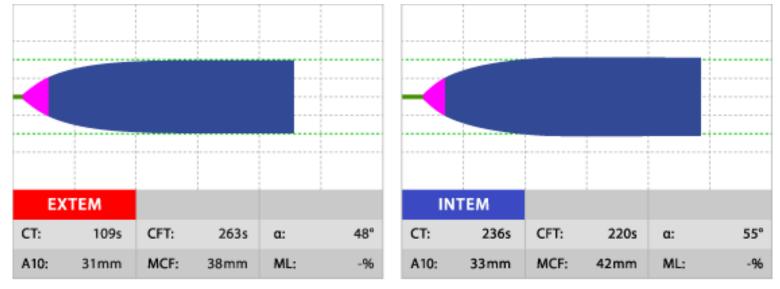
#### **Platelet deficiency**

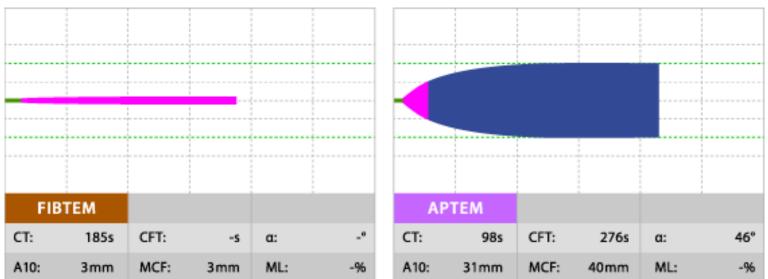


Erasmus MC Cafung

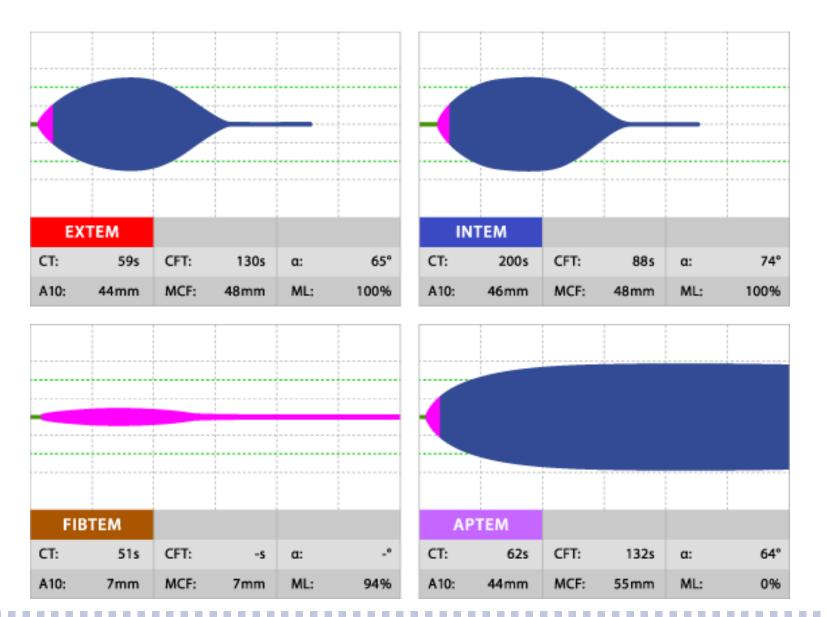
## **Fibrinogen deficiency**







## Hyperfibrinolysis





### **Heparin influence**



