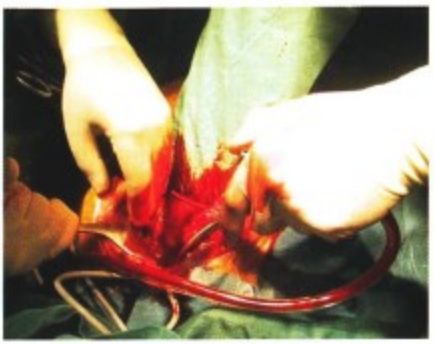
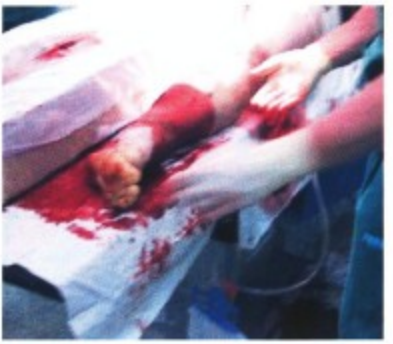
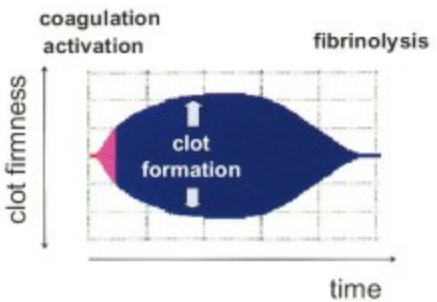
ROTEM® Analysis

Targeted Treatment of Acute Haemostatic Disorders

Andreas Calatzis[1], Michael Spannagl[1], Matthias Vorweg [2]







[1] Department for haemostasis and transfusion medicine
University Clinic, Ludwig-Maximilians University

[2] Clinic for Anaesthesiology
Hospital Cologne-Merheim
Institute for Anaesthesiology II of the University
Witten/Herdecke

thromboelastometry
ROTEM®
by pentapharm

Introduction

In this text the basis of ROTEM® analysis is described together with its use during the management of acute bleeding.

The management of acute bleeding is a complex challenge. Little that is done in this area is fulfilling the hard criteria of evidence based medicine. The recommendations in this compendium are based on the experience of the authors and on the discussion with centres, which use the ROTEM® system in clinical routine. However these recommendations have not yet been prospectively validated.

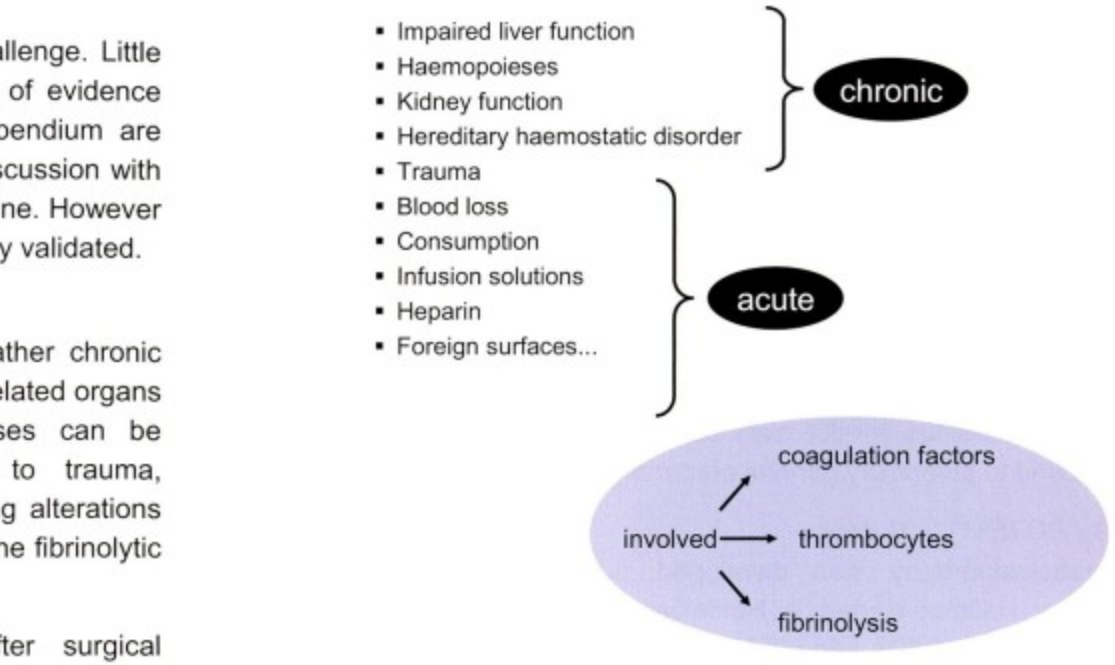
Causes of Haemostasis Disorders

Haemostasis disorders can have several causes. Rather chronic processes, such as comorbidities of the haemostasis-related organs liver – kidney – bone marrow, hereditary diseases can be differentiated from more acute alterations due to trauma, haemodilution and the current treatment. The resulting alterations affect the plasmatic coagulation factors, platelets and the fibrinolytic system.

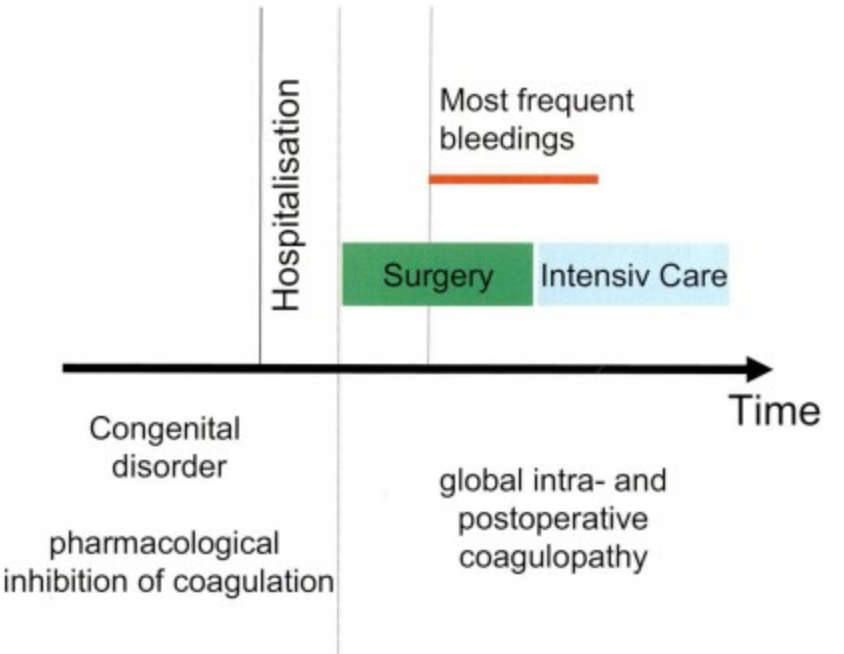
Bleeding most frequently occurs during and after surgical interventions or traumas, i.e. in situations where trauma and secondary alterations (e.g. due to haemodilution) are added to the disposition of the patient. During such complex haemostasis disorders the predictivity of the routine parameters PT, aPTT and platelet count is rather weak. This leads to the interest in laboratory methods, which better reflect haemostasis during these complex processes.

A. Calatzis, W. Schramm, M. Spannagl. Management of Bleeding in Surgery and Intensive Care. I. Scharrer / W. Schramm (Ed.), 31 st Hemophilia Symposium Hamburg 2000, Springer Verlag Berlin Heidelberg 2002.

> Alterations of Haemostasis: Causes



> Trauma + Coagulopathy as Cause of Bleeding



Targeted Treatment of Bleeding Events

During acute bleeding a multitude of different therapeutic options is at disposition to the physician. The difficulty is to chose the right medication at the right time and to evaluate, how much respectively how often the respective therapeutic option has to be applied. Typically only the right therapy will stop the bleeding. It will be of little use to the patient, if he is transfused with FFP while he is bleeding because of a thrombocytopenia or a hyperfibrinolysis. Although this sounds self-evident, in the clinical everyday routine often a "blind" therapy is applied. This means that different medication and blood products are administered consecutively until the bleeding stops. If the cause of the bleeding is not the most obvious, unnecessary medication and blood products are administered. Thus unnecessary costs are created and the patient is exposed to potentially harmful preparations.

TEG / ROTEM® – History

Thrombelastography was developed during world war II by professor Hellmut Hartert in Heidelberg. Following a quite broad application in the 50's and 60's the interested in TEG decreased in the 70's. In the 80's it came to a renaissance of TEG especially in the united states because of the application in anaesthesia for the management of acute bleeding. The ROTEM® system is an enhancement of thrombelastography and was developed during 1995-1997 in Munich. The instrument includes four measurement channels for simultaneous determinations, a connected laptop for automatic analysis and an electronic pipette for interactive test operation.

Note: The term "TEG" was introduced by Hartert in his first publication on thromboelastography in 1948. Surprisingly in 1993 an American company obtained a trade mark on this term in the USA, after 45 years of it use a generic medical term. In order to achieve a global uniformity of the name, the manufacturer of the ROTEM® system (Pentapharm GmbH, Munich) has renamed its instrument from "ROTEG" into "ROTEM" and the tests accordingly from "EXTEG" into "EXTEM", "INTEG" into "INTEM" etc. in 2003. "TEM" thereby stands for "thromboelastometry" (analogous to the term "thromboelastography"), thus the plotting of the clot firmness.

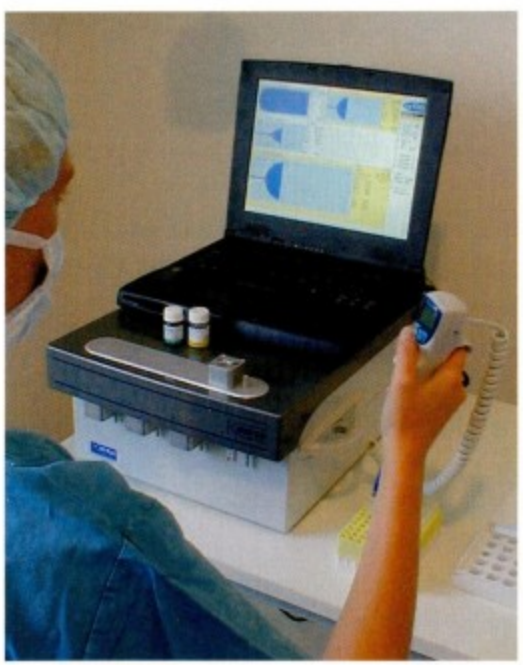
> Bleeding: Therapeutical Options

- DDAVP (Minirin®)
- antifibrinolytics
- protamin
  - after heparin exposition
- local / surgical procedure
- blood products
  - thrombocytes
  - FFP
  - fibrinogen
  - PCC
  - FVIII / FIX / FXIII
- recombinant factors
  - rVIIa
  - FVIII, FIX

? what, how much

? when, how long

As a rule, only the appropriate therapy will stop the bleeding



ROTEM®-System

- 4 channels for simultaneous assays
- electronic pipetting facilitates the use outside of established laboratories

Detection method of the ROTEM® system

In the ROTEM® system the sample is placed into a cuvette and a cylindrical pin is immersed. Between pin and cuvette remains a gap of 1mm , which is bridged by the blood, respective the blood clot. The pin is rotated by a spring alternating to the right and the left. As long as the blood is liquid, this movement is unrestricted. As soon as the blood clots, the clot restricts the rotation of the pin, increasingly with rising clot firmness. Thus, the rotation of the pin is inverse proportional to the clot firmness. It is detected optically. A laptop computer connected to the instrument calculates the ROTEM® curve as well as its numerical parameters.

In contrast, in the TEG according to Hartert the cuvette is rotated. The pin is suspended freely from a thin wire and does not move until a clot forms. Because of this free suspension of the pin the TEG according to Hartert is quite susceptible to vibration and mechanical shocks.

Due to the mechanical measurement principle of ROTEM analysis, blood or plasma can be analysed likewise. This is advantageous for the point-of-care application, as a centrifugation of the sample is omitted.

The parameters of ROTEM® analysis

For historical reasons the curve is plotted two-sided expressed in mm.

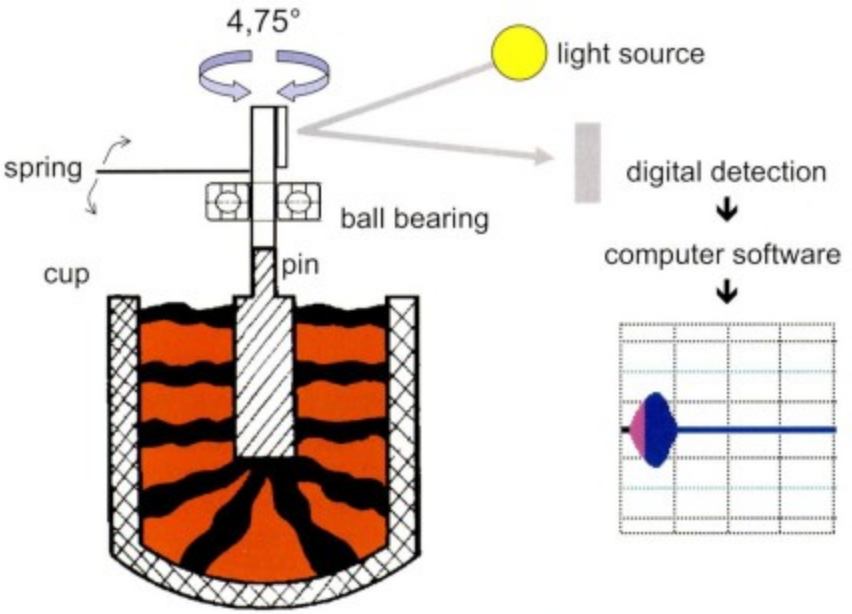
CT (clotting time): time from start of the measurement until initiation of clotting → **initiation of clotting, thrombin formation, start of clot polymerisation**

CFT (clot formation time): time from initiation of clotting until a clot firmness of 20 mm is detected → **fibrin polymerisation, stabilisation of the clot with thrombocytes and FXIII**

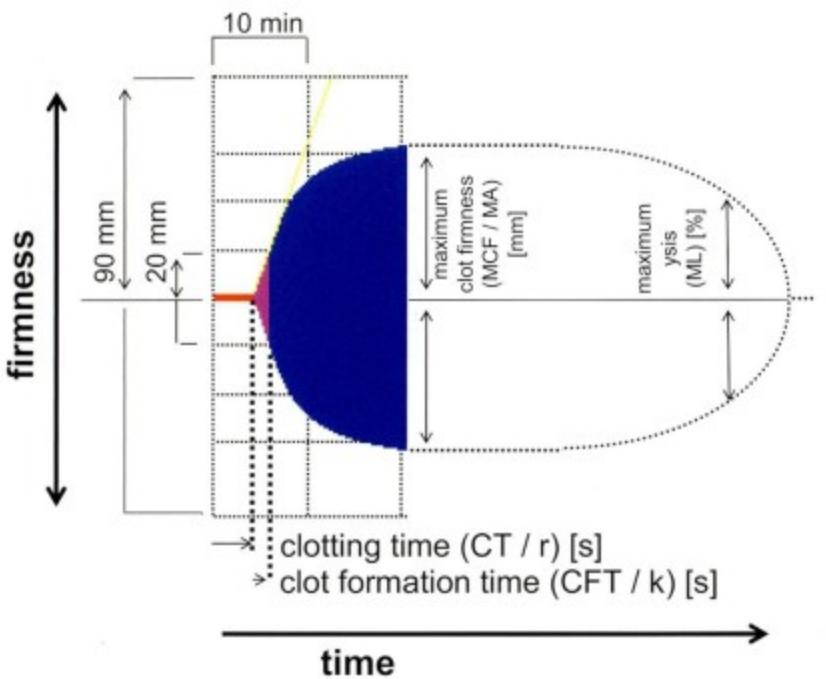
MCF (maximum clot firmness): firmness of the clot → **increasing stabilisation of the clot by the polymerised fibrin, thrombocytes as well as FXIII**

ML (maximum lysis): reduction of clot firmness after MCF in relation to MCF → **stability of the clot (if < 15%) or fibrinolysis (if > 15%)**

> ROTEM® Detection Method



> Parameters and Scaling



ROTEM® tests

In the past "the thrombelastogram" was analysed using freshly drawn blood without the addition of any citrate/calcium and without any activators. The measurements were therefore very time consuming (45-60 min) and quite unspecific.

With the ROTEM® usually activated determinations are performed. As in the laboratory coagulation analysis, various activators or inhibitors are added to the sample, in order to represent different processes of haemostasis. For the analysis usually citrated blood is used.

In **EXTEM,** coagulation is activated by a small amount of tissue thromboplastin (tissue factor). This typically leads to the initiation of clot formation within 70's. Thus; clot formation can be assessed within 10 minutes.

In **INTEM,** coagulation is activated via the contact phase (as in the aPTT and ACT). The INTEM is therefore sensitive for factor deficiencies of the intrinsic system (e.g. FVIII) and for the presence of heparin in the sample.

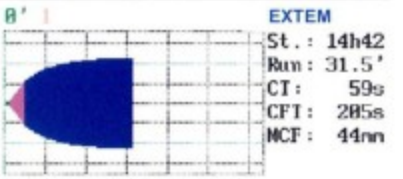
In **FIBTEM,** coagulation is activated as in EXTEM. By the addition of cytochalasin D the thrombocytes are blocked. The resulting clot is therefore only depending on fibrin formation and fibrin polymerisation.

In **APTEM,** coagulation is also activated as in EXTEM. By the addition of aprotinin in the reagent, fibrinolytic processes are inhibited in vitro. The comparison of EXTEM and APTEM allows for a rapid detection of hyperfibrinolysis. Furthermore, APTEM enables the estimation, if aprotinin therapy alone normalises the coagulation or if additional measures have to be taken (e.g. administration of fibrinogen).

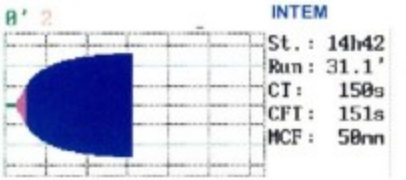
In **HEPTEM,** coagulation is activated as in INTEM. The addition of heparinase in the reagent degrades heparin present in the sample and therefore allows the ROTEM® analysis in heparinised samples.

> ROTEM-tests

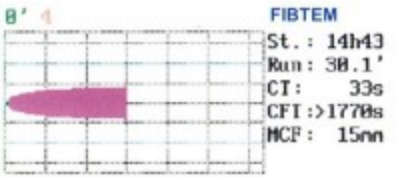
EXTEM: activation of clot formation by thromboplastin (tissue factor). Assessment of the factors: VII, X, V, II, I, platelets, fibrinolysis



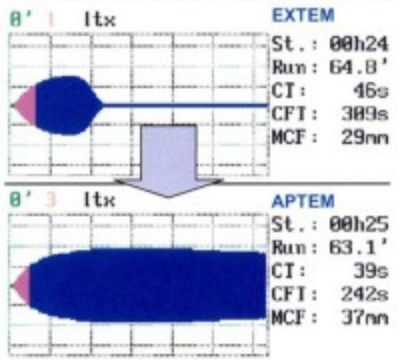
INTEM: activation of clot formation via the contact phase. Assessment of the factors : XII, XI, IX, VIII, X, V, II, I, platelets, fibrinolysis



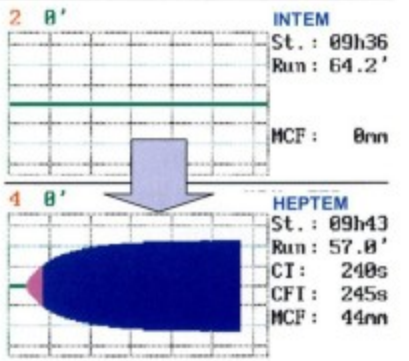
FIBTEM: activation as in EXTEM with addition of cytochalasin D, a platelet-blocking substance. In the FIBTEM assay fibrinogen levels and fibrin polymerisation can be assessed in a functional way.



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.



HEPTEM: activation as in INTEM with the addition of heparinase. Heparinase degrades heparin. When HEPTEM results are compared to INTEM heparin related coagulation disturbances can be specifically detected.



Expected values

On the opposite page typical ROTEM values are shown, which are found when healthy patients without coagulation disorders are analysed. Depending on the examined population these values can vary (for example when healthy younger persons are assessed lower MCF values are found, due to the lower fibrinogen concentration and higher hematocrit in this population). It is therefore recommended at introduction of ROTEM® to analyse some patients without pathological findings in order to establish respective 'local' reference ranges.

Interpretation of HEPTEM / APTEM / FIBTEM

In HEPTEM and APTEM the comparison with INTEM respectively EXTEM is important for the interpretation. A shortening of the clotting time in HEPTEM as compared to INTEM indicates a heparin effect. A better clot formation (shorter CFT, greater MCF) in APTEM than in EXTEM indicates fibrinolysis.

A reduced MCF in FIBTEM indicates a reduced fibrinogen level and / or a clot polymerisation inhibition. Discrepancies between FIBTEM and the fibrinogen determination in the laboratory are frequently found, as FIBTEM is much more sensitive to clot polymerisation disorders when compared to the conventional laboratory assays.

Classification of the ROTEM® results

The bottom table shows an orientating classification of the ROTEM® results based on our clinical experiences.

Depending on the situation and possible comorbidities of the patient, different target ranges will be aimed for the MCF, respectively CFT. During surgery we typically aim for an MCF value of at least 40 mm and a CFT of maximal 300 s. In persistent bleeding situations an almost normalisation of the ROTEM® findings will be aimed for.

Fibrinolysis (lysis of the clot in vitro) is always pathological and can be treated with aprotinin or tranexamic acid. Nevertheless, hyperfibrinolysis can be self-limiting, which can be controlled by repeated determinations without any preceding therapy.

> Expected Values: Patients w/o Pathological Findings

	CT	CFT	MCF	ML
	clotting time [s]	*clot formation time* [s]	*maximum clot firmness* [mm]	*maximum lysis* [% of MCF]
EXTEM	35-80	35-160	53-72	< 15
INTEM	100-240	35-110	53-72	< 15
HEPTEM	100-240	35-110	53-72	< 15
	A significantly shortened CT in HEPTEM as compared to INTEM is indicative of a heparin effect			
APTEM	35-80	35-160	53-72	< 15
	An improved clotting (shortening of CFT, higher MCF) in the APTEM assay as compared to EXTEM is a sign for hyperfibrinolysis			
FIBTEM			8-20	
	MCF < 8 mm → reduced fibrinogen level or impaired polymerisation. Therapy: infusion of fibrinogen (or larger quantities of FFP). *MCF > 20 mm → increased fibrinogen level. This may lead to normal clot formation in EXTEM or INTEM in spite of thrombocytopenia.*			

> INTEM/EXTEM Results – Clinical Interpretation

MCF

MCF > 72 mm: enhanced haemostatic reserve
MCF 53-72 mm: normal range
MCF 46-52 mm: usually unimpaired haemostasis with reduced reserve
MCF 45-40 mm: bleeding risk
MCF 39-30 mm: high bleeding risk
MCF < 30 mm: usually no effective haemostasis

CFT

CFT 35-160 s: normal range
CFT 160-220 s: usually unimpaired haemostasis with reduced reserve
CFT 220-300 s: bleeding risk
CFT 300-400 s: high bleeding risk
CFT > 400 s: usually no effective haemostasis

Fibrinolysis

Lysis of the clot within 20 minutes (fulminant lysis):
usually acute bleeding
Lysis of the clot within 20-40 minutes:
high bleeding risk
Lysis of the clot after more than 40 minutes:
frequently clinically insignificant, may however raise to fulminant lysis

Assessment of the ROTEM® analysis

The ROTEM® analysis covers the whole process of whole blood coagulation, from the formation of the first fibrin strands over the maximum firmness of the clot until its lysis.

The assessment of the ROTEM® analysis is carried out along the time axis (from left to right): A *disturbed activation of coagulation* is indicated by a prolonged clotting time. As causes a factor deficiency or a heparin effect have to be considered. The comparison of INTEM and HEPTEM allows for a specific detection of a heparin effect.

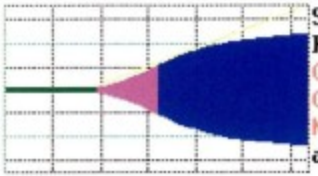
An *abnormal clot formation* is indicated by a prolonged clot formation time (CFT) and/or a reduced clot firmness (MCF). The CFT is thereby influenced stronger by a clot polymerisation disorder than the MCF. A prolonged CFT with at the same time normal MCF indicates therefore a polymerisation disorder, whereas a reduced MCF with a normal CFT rather indicates a deficiency of clottable substrate (fibrinogen and / or platelets).

A *fibrinolysis* is detected by the lysis of the clot (ML > 15%) or by the finding of a better clot formation (shorter CFT, greater MCF) in APTEM as compared to EXTEM. Several centres use in massive bleeding already a shortening of the CT in APTEM as compared to EXTEM as a trigger for aprotinin administration.

Limitations

In the interpretation of ROTEM® analysis it is important to know and consider the limitations of the method. The ROTEM® is not sensitive to the effect of the platelet inhibitors aspirin, clopidogrel and reopro (only in supra-therapeutic doses). Also, the effect of the von Willebrand factor is not detected. Furthermore, a normal ROTEM® analysis dose not exclude the anticoagulants orgaran, pentasaccharide, low-molecular-weight heparin as well as warfarin. For analysis of these factors other diagnostic tests have to be employed.

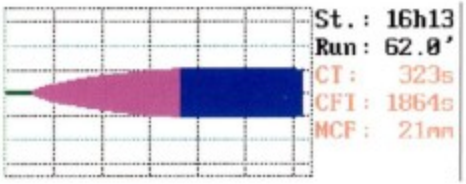
> ROTEM: Detection and Therapy



Activation of coagulation

→ *protamin, FFP or PPSB*

→ *differentiation by HEPTEM*



Clot formation

→ *infusion of thrombocytes and / or fibrinogen / FFP*

→ *differentiation by FIBTEM*

Fibrinolysis

→ *Infusion of aprotinin or tranexamic acid*

→ *more rapid detection by the combination of APTEM – EXTEM*

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, marcumar®, etc.)

Consequence:

1.Combine with other methods where required

2.Consider limitations for interpretation!

Performance of ROTEM® analysis

As in all diagnostic tests, correct pre-analytics a correct performance of the assay are essential for meaningful results.

As ROTEM® is run directly with citrated whole blood, a specific sample preparation is not necessary. "Correct sampling" means: Complete filling of the sampling tube (in order to ensure the correct citrate-blood ratio), during sampling from catheters the assurance that no contamination with heparin or other anticoagulants occurs, and the avoidance of haemolysis during sampling (use of a needle with sufficiently wide diameter). We typically aim for an analysis of the sample within 2 hours from the sampling of the blood (if required up to four hours). The analysis of samples that have been transported by a tube system is usually possible. As a precaution this should be verified (split the sample and analyse with/without transport by the tube system).

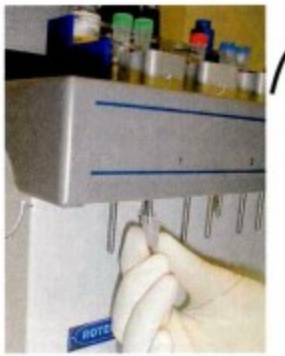
The steps to be performed for ROTEM® analysis are shown on the right. The test operation is generally simple - also for staff without any laboratory experience. Nevertheless, a certain familiarisation period and motivation are necessary.

Apart from the correct performance of the analysis – as in every laboratory test – the plausibility control of the analysis is important. Measurements with irregular shapes (steep rise of fall of the clot firmness, noised curves, and start of the clot formation in less than 20 seconds) should be controlled.

During pipetting of the liquids it has to be controlled optically, if the liquid was actually aspirated. A typical source of error is that the pipette tip has not been immersed into the liquid.

The regular analysis of the control materials allows for the check-up of the correct function of the instrument and of the reagents.

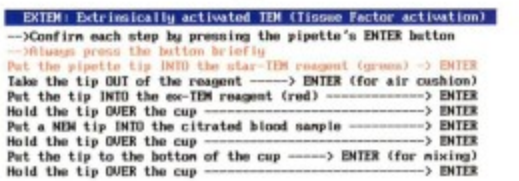
> Performing A Test



1. properly attach pin

2. insert cup and bring to position using the MC rod

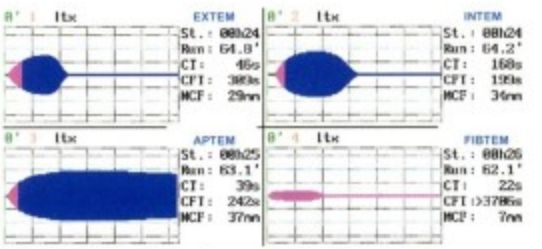
3. select test



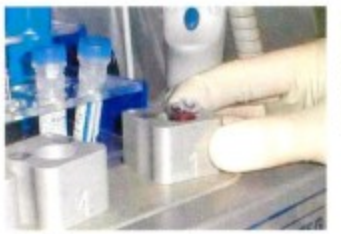
4. pipetting steps are displayed on the screen

5. pipetting of reagents and blood

6. insert cup holder in measurement position after mixing of reagents and sample



7. on screen display of TEMograms and numeric parameters



8. discard used cup and pin

Interpretation of ROTEM®- analysis: examples

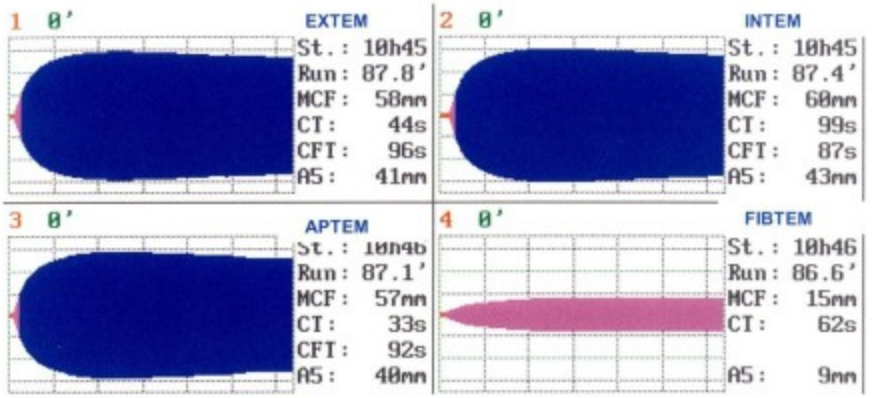
On each of the next three double pages three typical combinations of ROTEM® tests are shown. The figures are displayed exactly as on the screen of the ROTEM® system. With each measurement you see the respective test name above of the parameters. In each case the figures represent 1-4 measurements of one sample. The measurements are not commented on the right hand page. This shall give the reader the opportunity to reflect the interpretation and therapy on his own.

Sample 1: normal coagulation in the ROTEM®. EXTEM and INTEM show a normal coagulation activation (CT normal), normal clot formation (CFT and MCF normal) as well as a stable clot (no lysis of the clot, respectively no better clot formation in APTEM as compared to EXTEM). The FIBTEM shows a normal fibrin clot.
Should the patient bleed clinically, the following causes have to be considered: surgical cause of bleeding, warfarin therapy (low sensitivity of EXTEM), aspirin, clopidogrel, von Willebrand syndrome (for these medications respectively pathologies ROTEM® shows low sensitivity) as well as errors (e.g. sample mix-up).

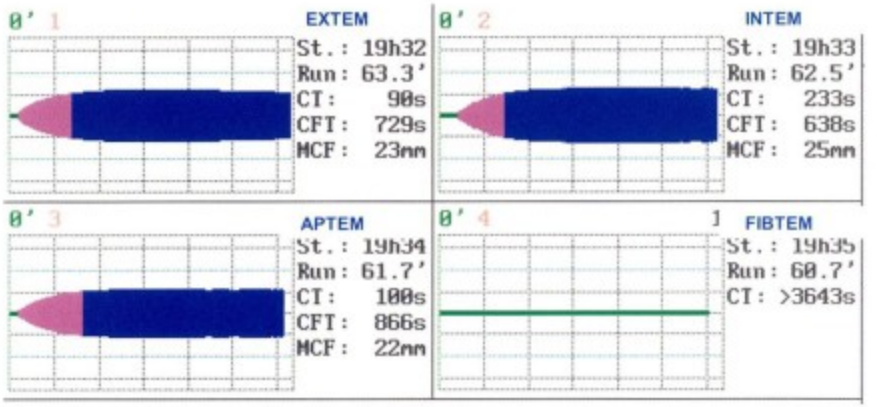
Sample 2: strongly prolonged clot formation time (CFT), strongly reduced clot firmness (MCF) in EXTEM and INTEM show a strongly reduced haemostatic capacity. The zero line in FIBTEM (no clotting) shows a strongly reduced fibrinogen level and/or a disturbed fibrin polymerisation. The first line treatment would be a highly dosed administration of fibrinogen concentrate (2-6 g) or cryoprecipitate or a larger amount of FFP (5-15 units). In cases of massive bleeding it would be considered to concomitantly transfuse platelets..

Sample 3: fibrinolysis (lysis of the clot in EXTEM, INTEM and FIBTEM) with an at the same time borderline acceptability of MCF (MCF = 43 mm) in APTEM. Good fibrin clot in FIBTEM. Therapy would be aprotinin (e.g. 1 mio KIE bolus) or tranexamic acid. In cases of persisting bleeding an administration of platelets would be suggested (for correction of the clot formation).

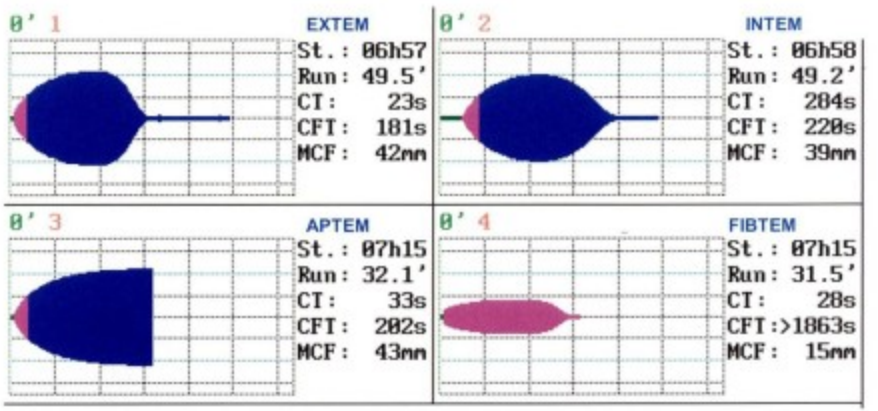
Constellations on ROTEM: 1



Constellations on ROTEM: 2



Constellations on ROTEM: 3

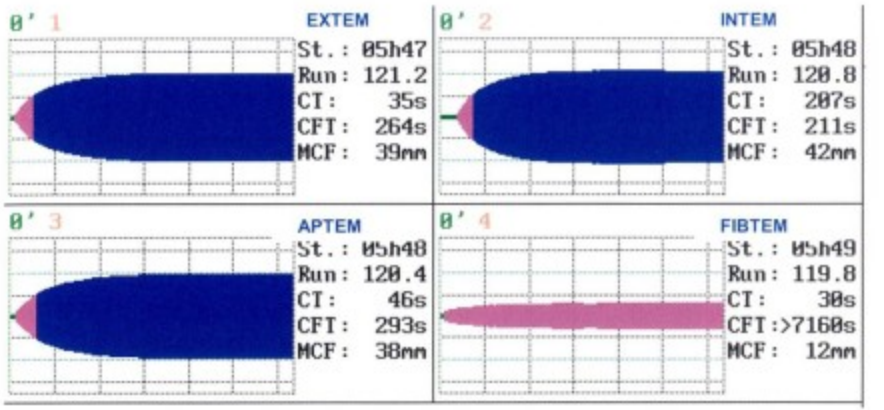


Sample 4: borderline acceptability of clot firmness in INTEM and EXTEM. No evidence of a hyperfibrinolysis. Normal fibrin clot in FIBTEM. Comparable results are sometimes found with or without clinical bleeding. First line therapy for improvement of clot formation would be the administration of platelets. In any case, the patient has typically only a poor haemostatic reserve at further haemodilution. Depending on the situation (further surgical blood loss expected or not) a correction of coagulation can be considered also without the occurrence of acute bleeding.

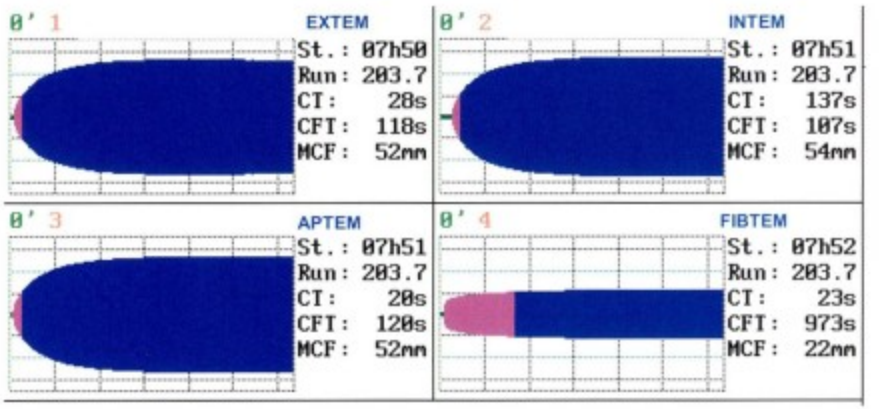
Sample 5: just abnormal / still normal clot formation in EXTEM and INTEM (depending on the investigated reference population). The relatively high clot firmness in FIBTEM (MCF = 22 mm) can lead to a normal whole blood coagulation, also when thrombocytopenia is present. Therefore a blood count should be determined in this situation (in order to assess platelet count directly), and the coagulation in course of further haemodilution should be controlled. Patients with high fibrinogen levels usually tolerate a thrombocytopenia better than patients with normal or reduced fibrinogen levels. Nevertheless, it is reasonable to keep an eye on the blood count in these situations.

Sample 6: combined haemostasis disorder. We see a fibrinolysis (lysis of the clot in EXTEM and INTEM), a prolonged CT in INTEM (heparin effect), a strongly reduced clot firmness in APTEM (indicates a disturbance of clot formation exceeding fibrinolysis) as well as a zero line (no clotting) in FIBTEM (reduced fibrinogen and / or polymerisation disorder). This result is not compatible with clinically normal haemostasis and requires a rapid combined treatment: aprotinin or tranexamic acid for the treatment of the hyperfibrinolysis, fibrinogen or FFP (greater amount) for improvement of the clot formation. In cases of such a poor clot formation also a simultaneous platelet administration is recommended (it would however also be possible to give fibrinogen or FFP first and then control the clot formation).

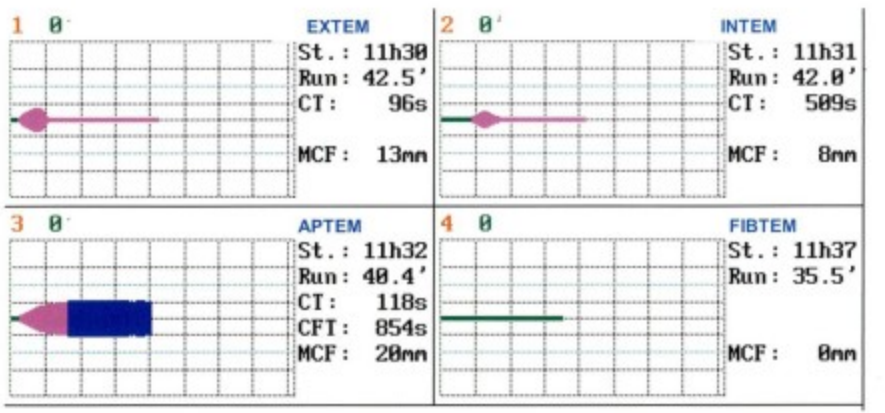
Constellations on ROTEM : 4



Constellations on ROTEM: 5



Constellations on ROTEM: 6



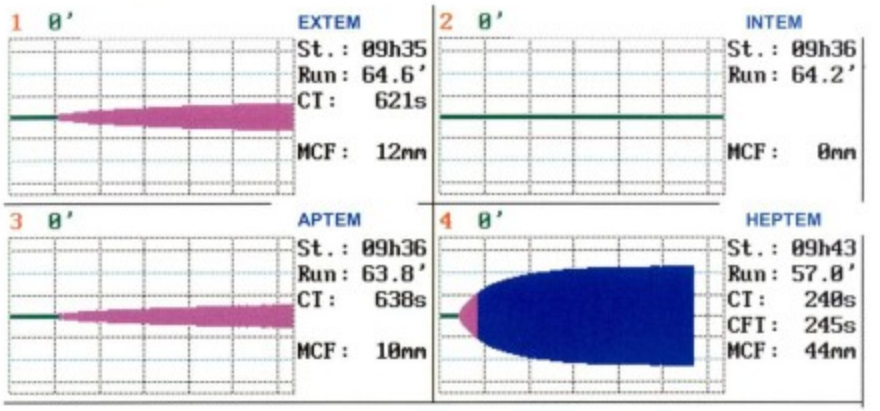
Sample 7: detection of heparin (strongly prolonged CT in INTEM, corrected in HEPTEM). In this situation one can wait (short half-life o heparin) or neutralize the heparin using protamin (during acute bleeding). As seen in HEPTEM, the clot firmness is reduced, but still within an acceptable range. Therefore one would usually neutralise the heparin first and see if bleeding stops. If bleeding continues administration of FFP, fibrinogen or platelets might be necessary.
Note: The EXTEM reagent has been modified in the meantime, resulting in a very low heparin sensitivity of EXTEM, FIBTEM and APTEM.

Sample 8: erroneous measurement. This error can occur if the pin was not attached completely onto the axis or the cup was not inserted sufficiently into the cup holder. The measurement should be stopped and started again.

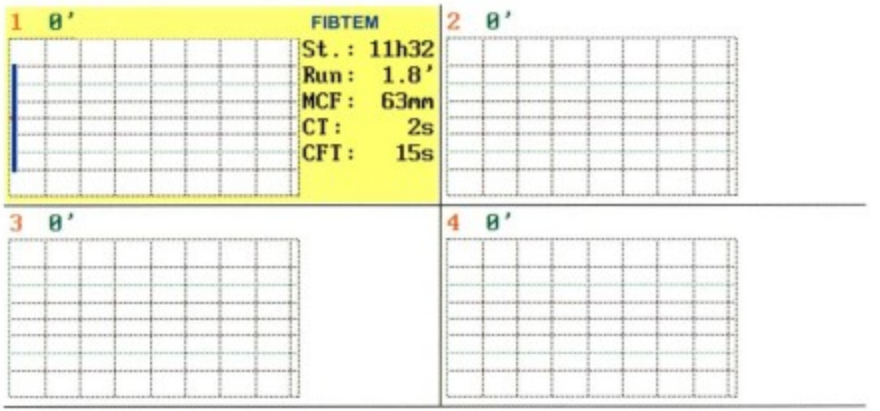
Sample 9: erroneous measurement. After MCF is reached there is after some time a further increase of the clot firmness. This is caused by a drying of the sample. A falsely-high MCF is detected. In this case it should be checked whether the cup holder is dirty at its upper surface, respectively to clean the corresponding area on the lower side of the instrument. For this a moist cloth should be used and no sprays should be applied on the instrument as this could lead to damage of the ball bearing. Should there be no contaminations, the cup holder might be damaged and need replacement.

Note: laboratory results should represent only one aspect of any therapeutic decision. Always the situation (bleeding yes - no), the plausibility of the findings, patient history, comorbidities as well as the expected (surgical) course of the case has to be taken into account. Further laboratory tests may be performed if required (PT, antithrombin, D-dimer, platelet function tests, blood count).

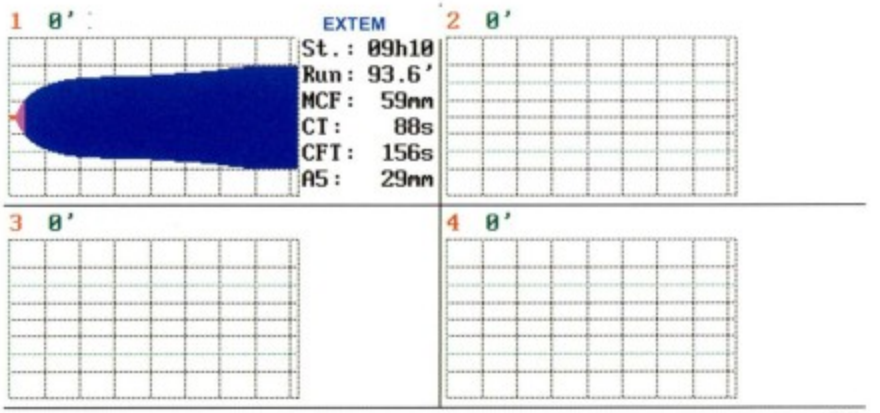
Constellations on ROTEM: 7



Constellations on ROTEM: 8



Constellations on ROTEM: 9



Clinical cases:
On the following two double pages clinical cases with the corresponding ROTEM® analyses are shown.

Case 1:

The course of whole blood coagulation during a multiple trauma treatment is shown on the right page.

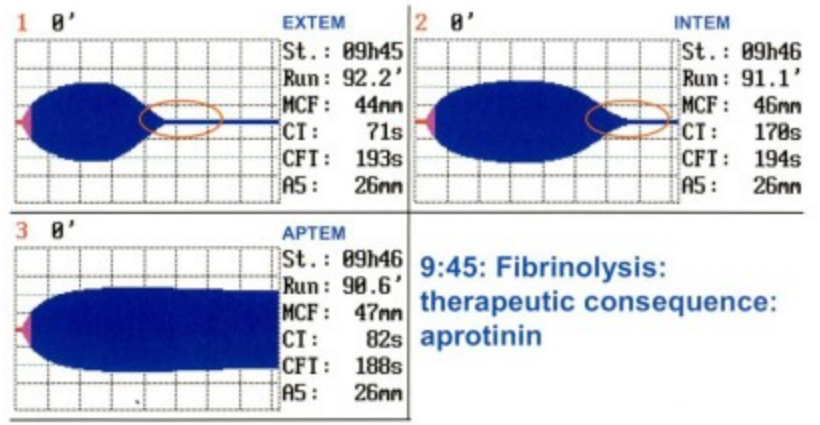
The first test timepoint shows a fibrinolysis in EXTEM and INTEM. In APTEM no lysis appears due to addition of aprotinin in the reagent.
In APTEM we see an abnormal, but still acceptable clot firmness.

The therapeutic consequence was the administration of aprotinin.

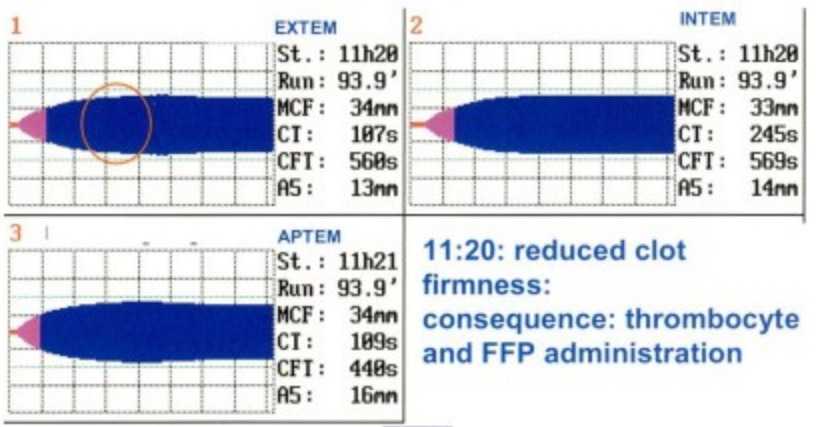
The second timepoint shows the therapeutic success of the aprotinin administration (no lysis detected any more). Nevertheless we see a strongly reduced clot firmness (MCF) as well as a strongly prolonged clot formation time (CFT), which was the indication for platelet and FFP administration.

The third timepoint represents a normal, whole blood coagulation towards the end of the surgery .

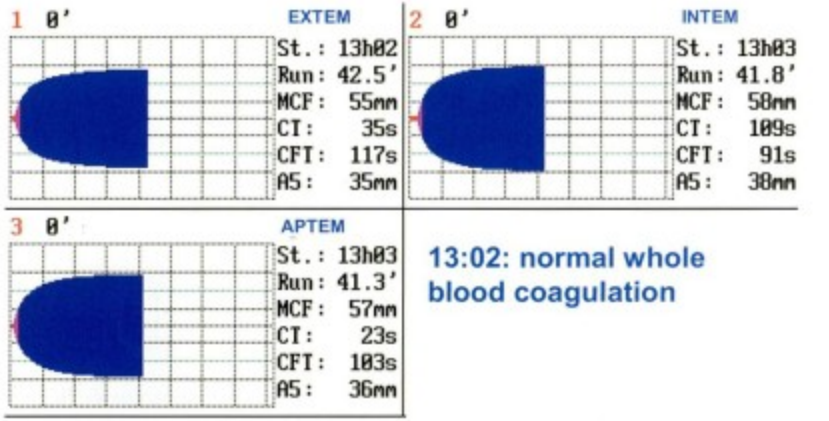
> ROTEM-Analysis in a Polytrauma Treatment



9:45: Fibrinolysis: therapeutic consequence: aprotinin



11:20: reduced clot firmness: consequence: thrombocyte and FFP administration



13:02: normal whole blood coagulation

Case example 2:

The second case example shows the therapy control with ROTEM® in a situation, in which initially therapy was guided on the basis of the routine laboratory.

We thank Dr. Georg Pfanner, consultant anaesthesist at the Department of Anaesthesia and Critical Care of the Academic Teaching Hospital Feldkirch, Austria (georg.pfanner@lkhf.at), for recording and providing us with this case.

The situation: A patient with a multiple trauma is admitted to the hospital. The patient has been already notably diluted (4 l of infusions).
The initial laboratory findings show a prolonged PT (factor deficiency), a low fibrinogen, low antithrombin and a thrombocyte count of 101.000/µl.

On the basis of these results fibrinogen, PCC and antithrombin was administered. Because of a strongly increased D-dimer result the question of an antifibrinolytic therapy aroused.

In the persistent bleeding situation a control with ROTEM® is carried out. The results show a strongly abnormal clot formation (clot firmness reduced, clot formation time prolonged) in spite of the initial therapy. In spite of an initially acceptable platelet count there is no sufficient whole blood coagulation.
After therapy with fibrinogen, platelets and PCC clinically a clear improvement of the clinical haemostasis was found together with a normalised whole blood coagulation in ROTEM®.

Initial situation:

Polytrauma → GCS 3, suspected thorax-trauma, pelvic fracture

Severe bleeding from nose, mouth, multiple wounds at the neck

Infusion therapy: HES 1000 ml, cristalloid 3500 ml

Laboratory results in hospital (65 min after arrival):

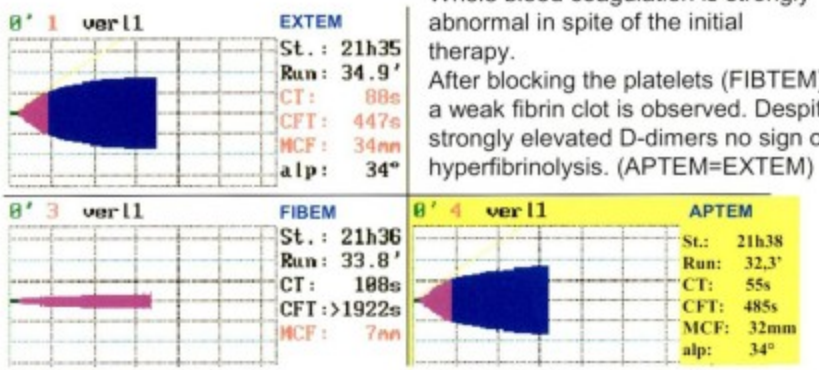
TPZ 40 %, aPTT 55.8 s, fibrinogen 0.87 g/l, AT 49%, D-dimer 39.7, thrombocytes 101.000/µl

Assessment: reduced fibrinogen level, factor levels low, antithrombin lowered (similar to TPZ), platelet count still sufficient. Fibrinolysis? (very high D-Dimer)

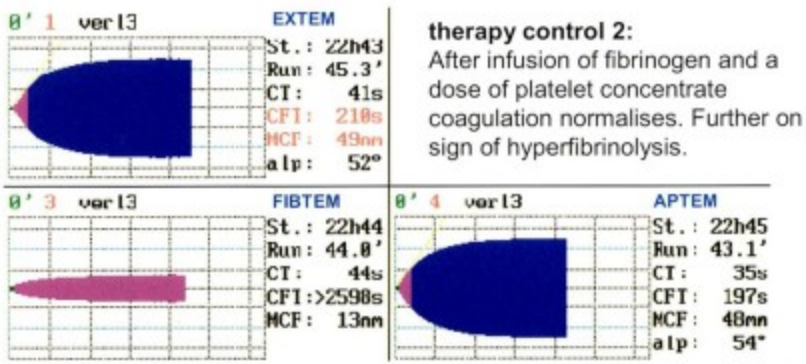
Initial therapy: 3 g fibrinogen (haemocomplettan), 4000 units PCC, 3000 units antithrombin

Therapy sufficient? Anti-fibrinolytic therapy required?

therapy control 1:
Whole blood coagulation is strongly abnormal in spite of the initial therapy.
After blocking the platelets (FIBTEM) a weak fibrin clot is observed. Despite strongly elevated D-dimers no sign of hyperfibrinolysis. (APTEM=EXTEM)



3 g fibrinogen, 1 platelet concentrate, 2000 IE PCC



therapy control 2:
After infusion of fibrinogen and a dose of platelet concentrate coagulation normalises. Further on no sign of hyperfibrinolysis.

→ OP → minimal bleeding
→ Successful wound treatment and tamponade of the ENT injury

Differential diagnosis and therapy: algorithms

On the right hand page the differential diagnostic and therapeutic algorithm used in the Clinic Cologne-Merheim is shown (Reference: Vorweg M, Hartmann B, Knuttgen D, Jahn MC, Doehn M. Management of fulminant fibrinolysis during abdominal aortic surgery. J Cardiothorac Vasc Anesth. 2001 Dec;15(6):764-7).

This algorithm shows, how coagulation activation, clot formation and fibrinolysis are assessed starting from EXTEM and INTEM as screening tests. If no coagulopathy is found other reasons for the bleeding are evaluated: surgical bleeding / coagulopathy which is not detected by ROTEM analysis (aspirin? von Willebrand factor? warfarin?).

The combination of EXTEM and APTEM allows for a rapid detection of a fulminant fibrinolysis.

The cause for a reduced clot firmness can be differentiated by performing a FIBTEM test.

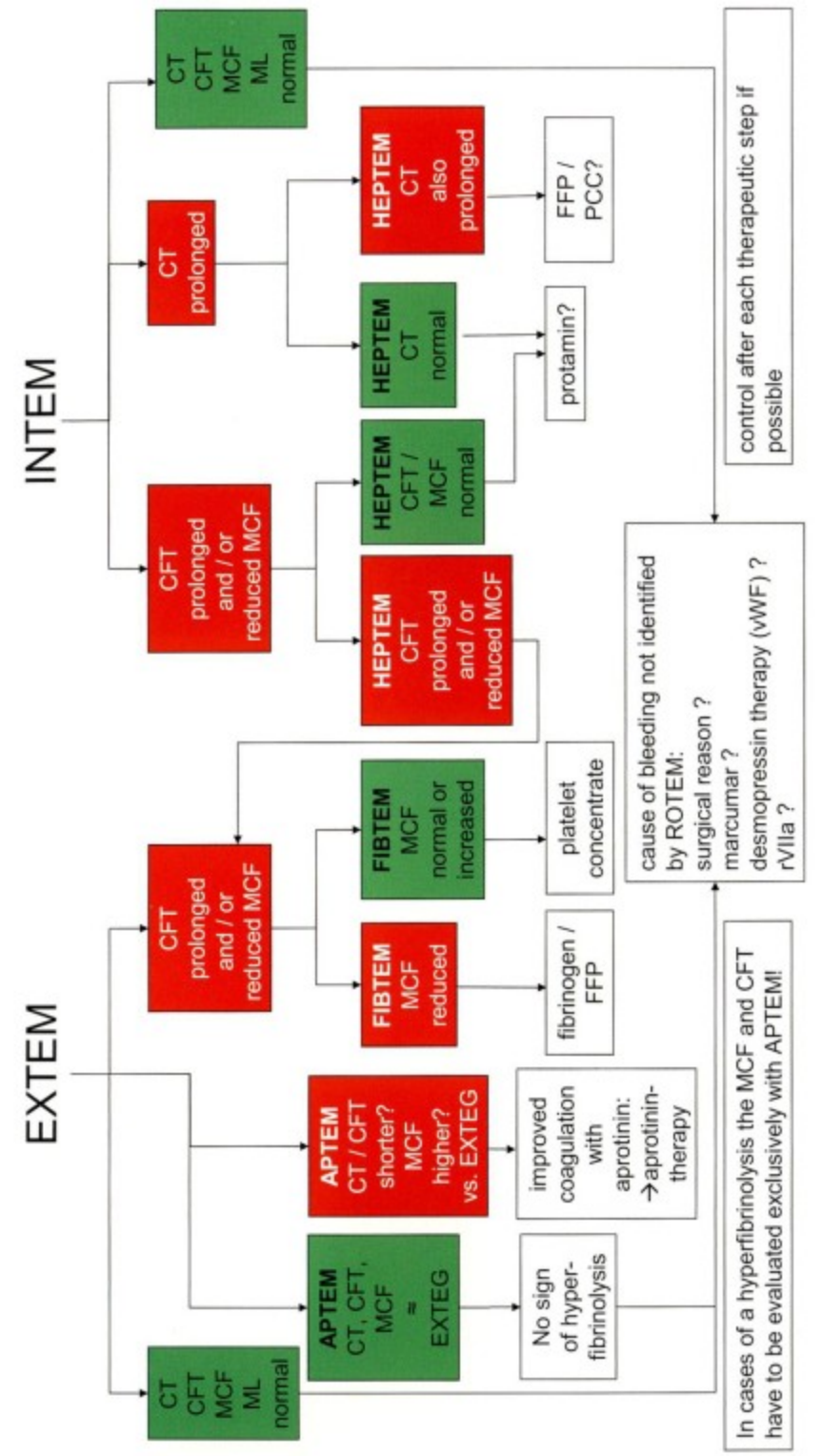
With the HEPTEM test a prolonged clotting time in INTEM can be differentiated.

Thus many causes of acute haemostasis disorders can be recognised rapidly and in consequence be treated appropriately.

Acknowledgement

The authors would like to thank very much senior physicist Dr. Herbert Schöchl from the trauma specialised Hospital Salzburg, Austria, for providing the photos on the title page, as well as the numerous ROTEM® users for their valuable discussions during the last years, which contributed to this compendium.

The authors also want to thank Dr. Meret Lakner of Pentapharm and Joanne Collings of Sysmex for the assistance with the English translation.



Dr. Andreas Calatzis, PD Dr. Michael Spannagl
Department for haemostasis and transfusion medicine
University Clinic, Ludwig-Maximilians University
Ziemssen Str. 1, 80336 Munich, Germany

Dr. Matthias Vorweg
Hospital Cologne-Merheim
Institute for Anaesthesiology II of the University Witten/Herdecke
Ostmerheimer Str. 200, 51109 Cologne, Germany

The ROTEM® system is an improvement of thromboelastography as described by Professor Hellmut Hartert. Andreas Calatzis developed the ROTEM® system in collaboration with the physicist Pablo Fritzsche. Michael Spannagl is a consultant for internal medicine and angiology. He has been working for many years on the diagnosis and management of acute and chronic disturbances of the haemostatic system. Matthias Vorweg is a consultant anaesthetist and introduced ROTEM® analysis in the Cologne-Merheim hospital more than 6 years ago. The Cologne-Merheim hospital was one of the first centres to introduce the concept of the ROTEM®-based differential diagnosis and targeted therapy in the clinical routine.

Manufacturer:
Pentapharm GmbH
Stahlgruberring 12
81829 Munich
Tel +49 (89) 454295-0
Fax +49 (89) 454295-22
rotem@pentapharm.com
www.pentapharm.de