EMPoweRx conference

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Stirred, Not Shaken: Utility of Viscoelastic Testing for Monitoring Coagulation in Critically Ill Populations

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Learning Objectives

Discuss coagulation and risk factors for coagulopathy

Describe the use of viscoelastic tests in critically ill emergency department (ED) patients

Disclosures

Research funding from Spero Pharmaceutics*

Advisory board for Harm Reduction Therapeutics*

*The relevant financial relationship listed for this individual has been mitigated

Patient Case

MS is a 45-year-old male with past medical history of non-ischemic cardiomyopathy status-post left ventricular assist device placement on warfarin who presents to the ED with subdural hematoma measuring 2.6 × 3.5 × 3.1 centimeters. His physical examine is within normal limits except a scalp hematoma and altered mental status. All labs were normal except INR was 3.6 and serum creatinine was 1.52 mg/dL.

Am J Emerg Med. 2021; 41: 265.e5-265.e8.

Coagulopathy in Acute Illness

- Very common
- Predictive of poor outcomes
- Difficult to recognize & treat

Crit Care Med. 2010; 38(10):1939-46.
Emerg Med Clin N Am. 2014; 32: 797–810.

Risk Factors for Coagulopathy

Trauma

Liver disease

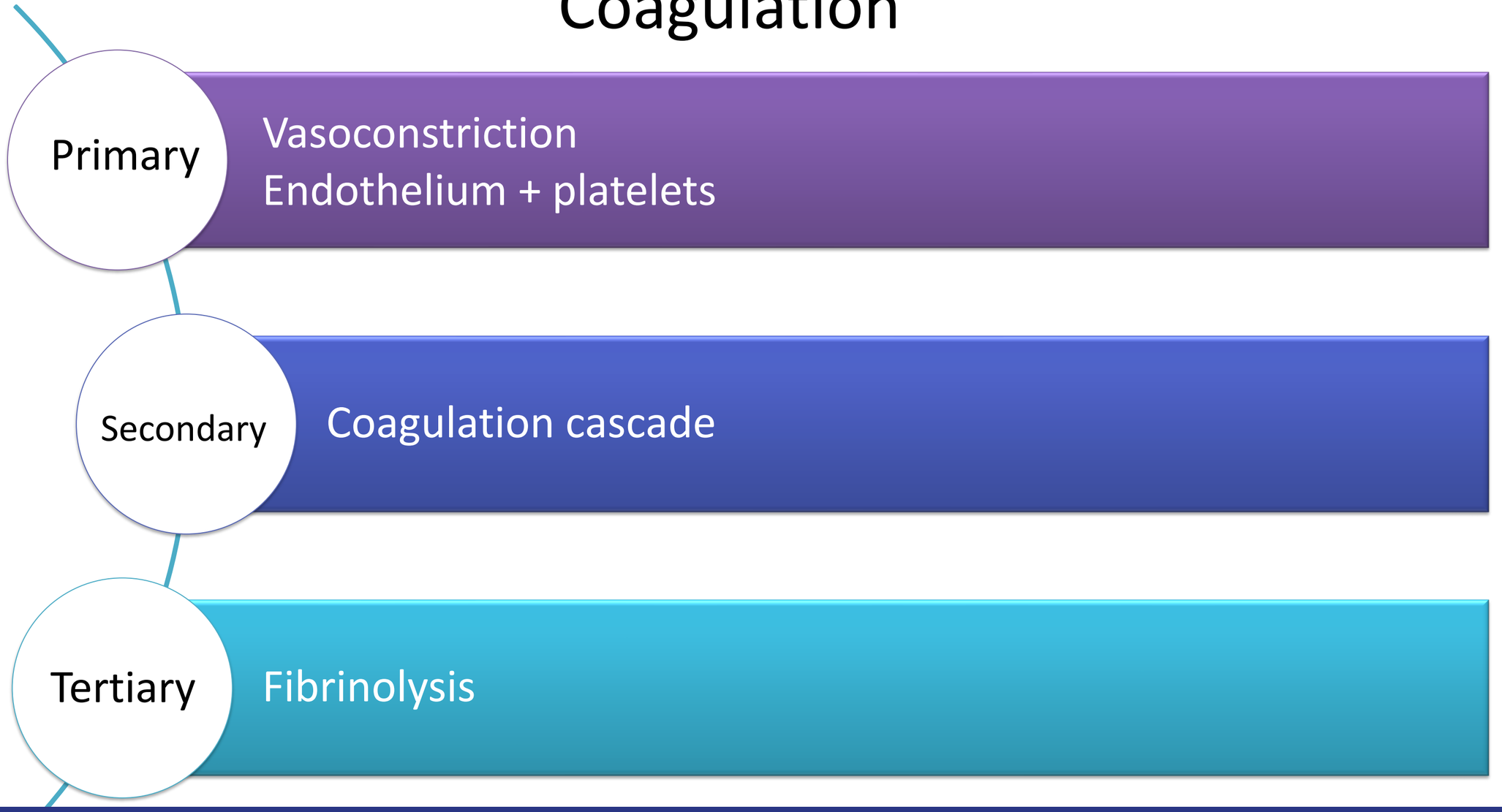
Medications

Active bleeding

Hypothermia

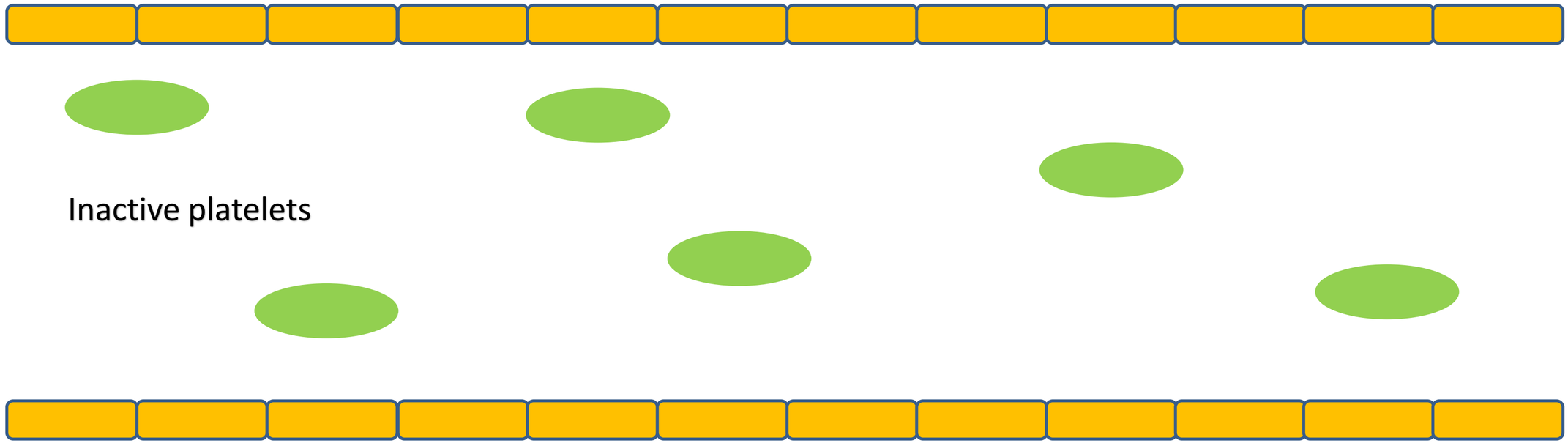
Emerg Med Clin N Am. 2014; 32: 797–810.
Anesthesiology. 2010 Nov;113(5):1205-19.

Coagulation



West J Emerg Med. 2019;20(5)770-783.

Coagulation



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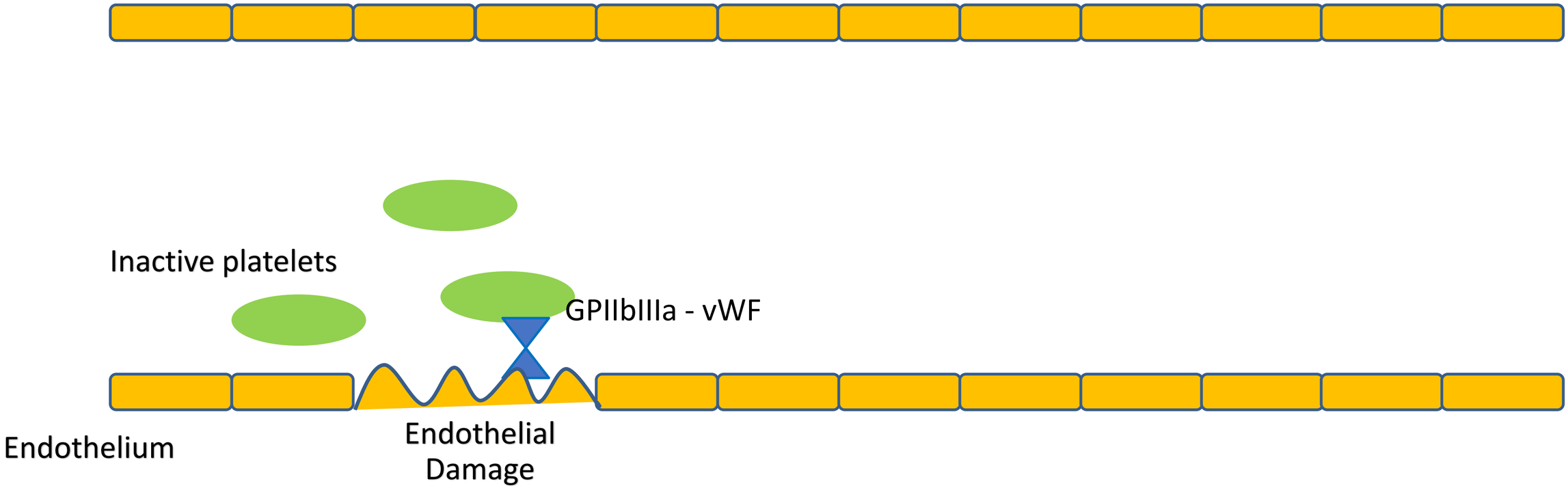

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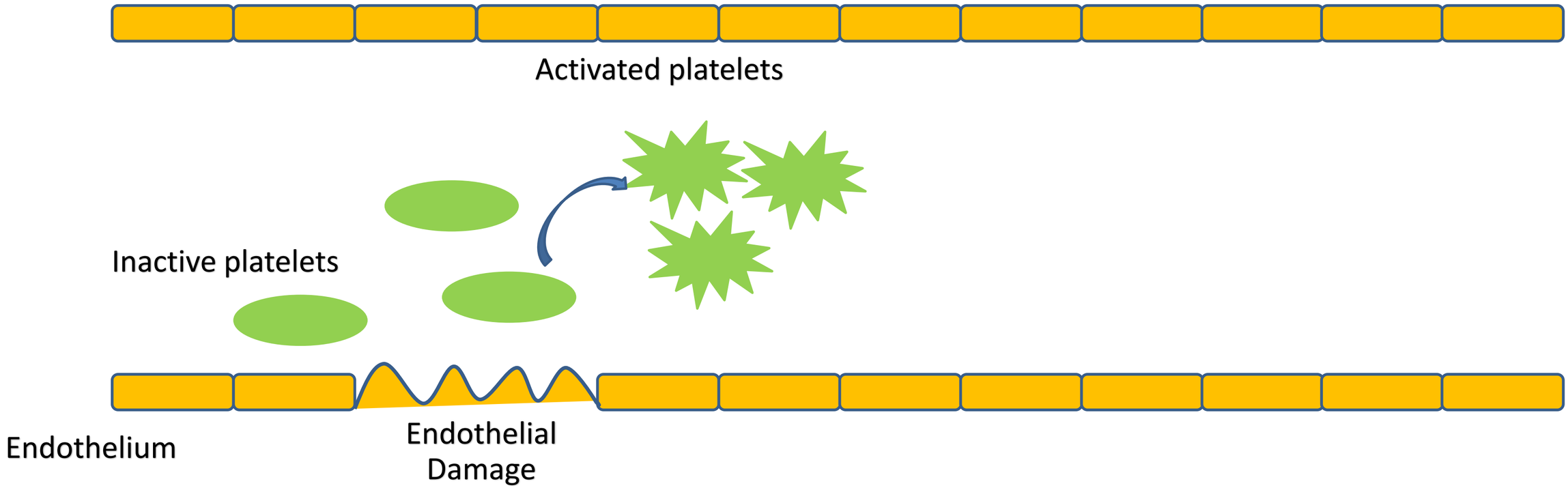

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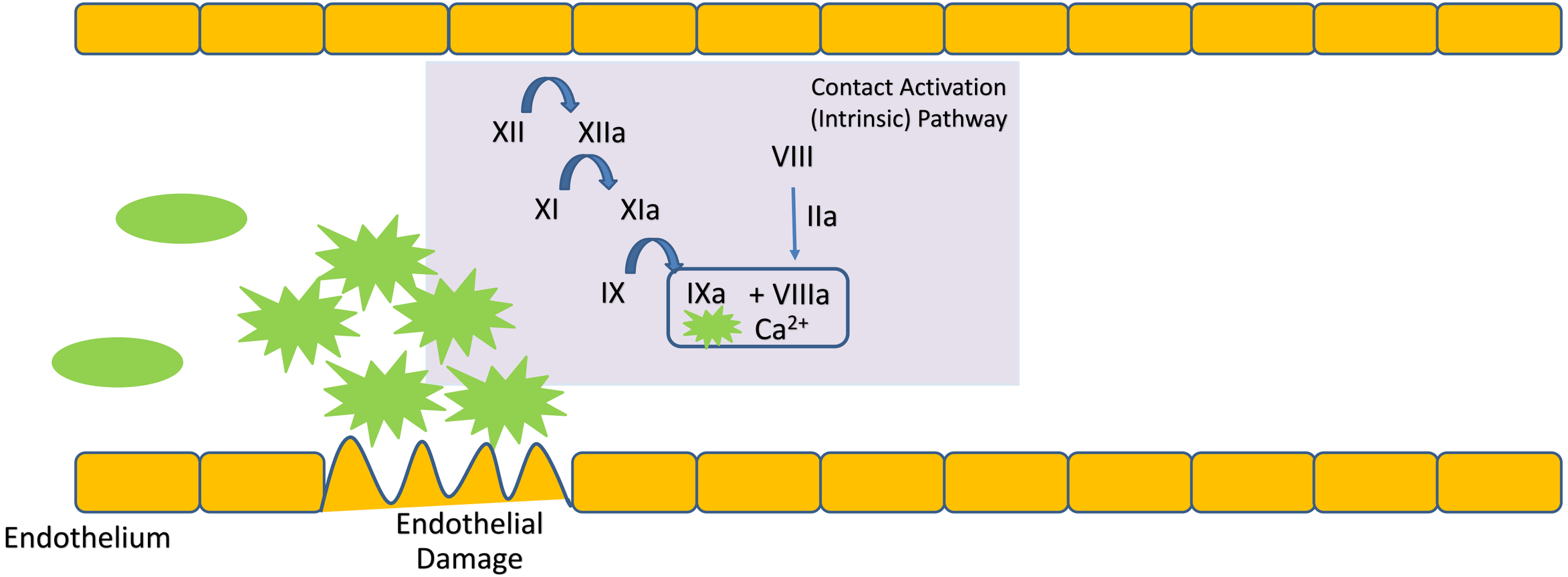

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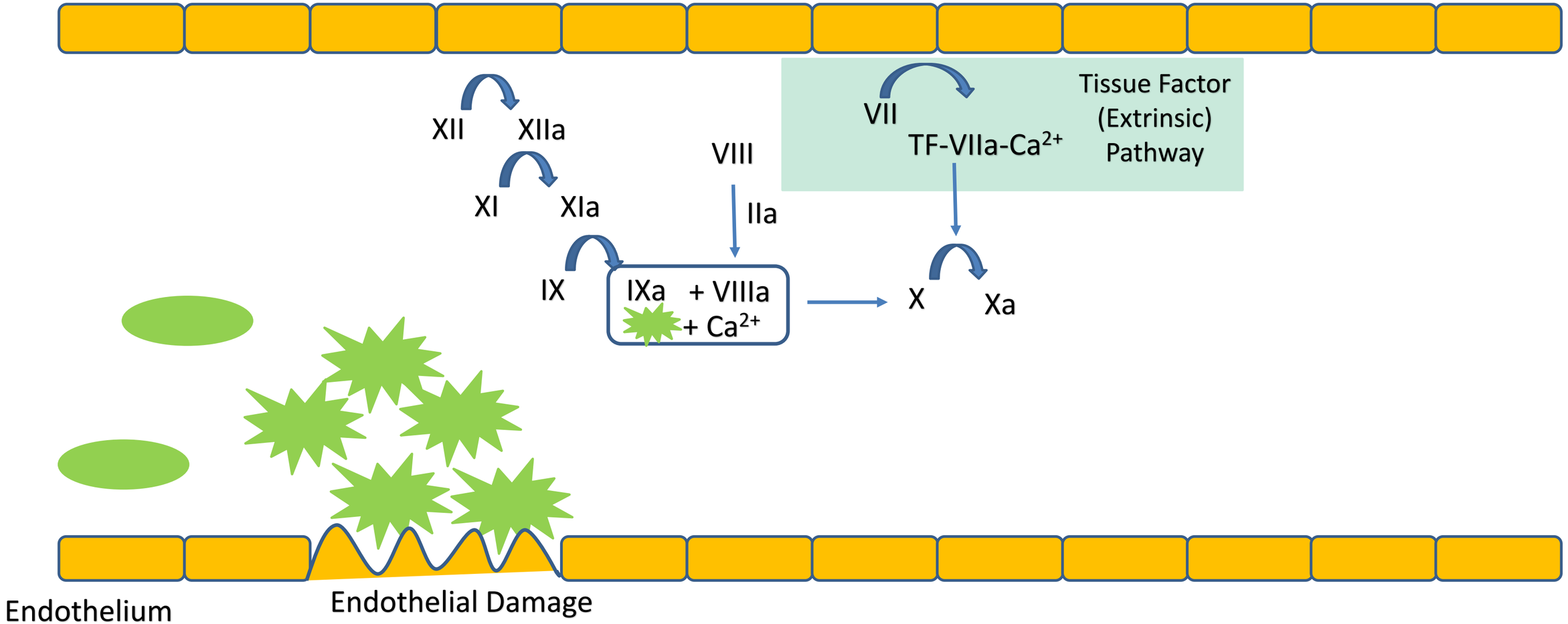

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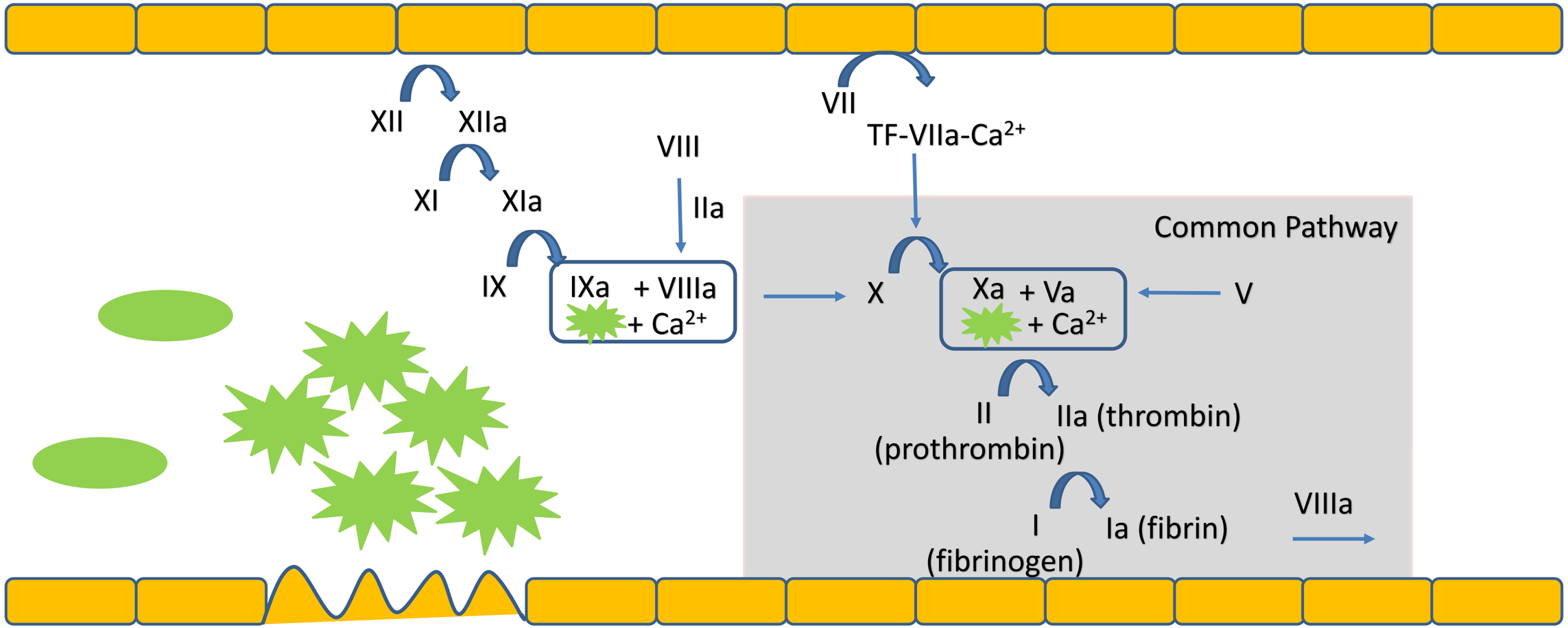

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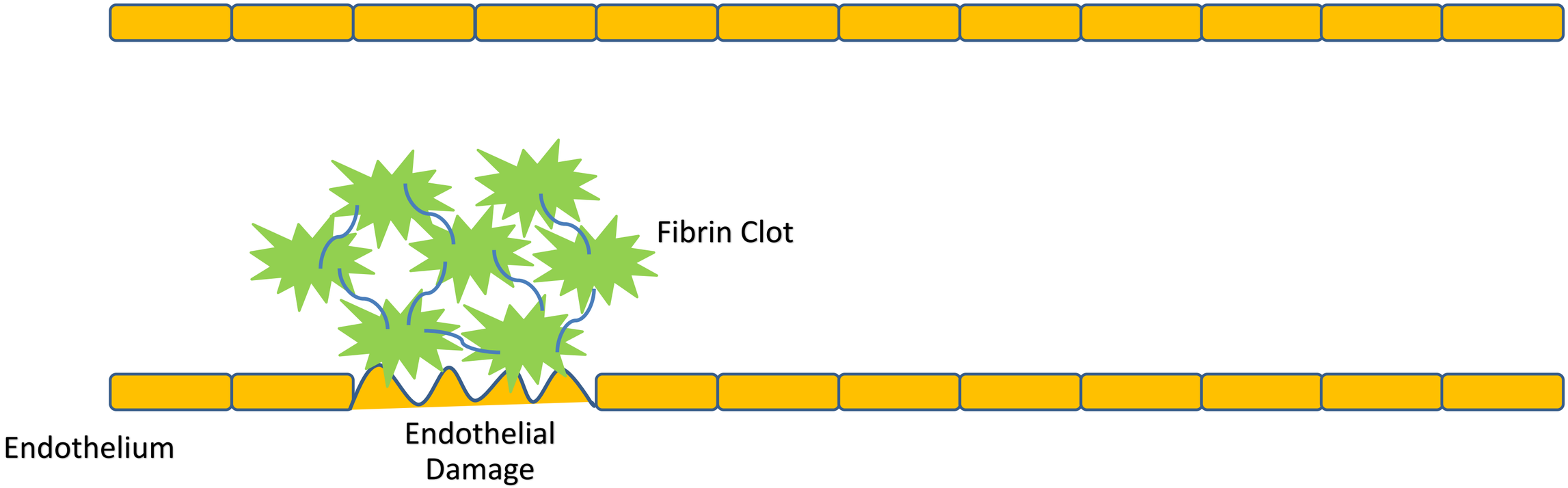

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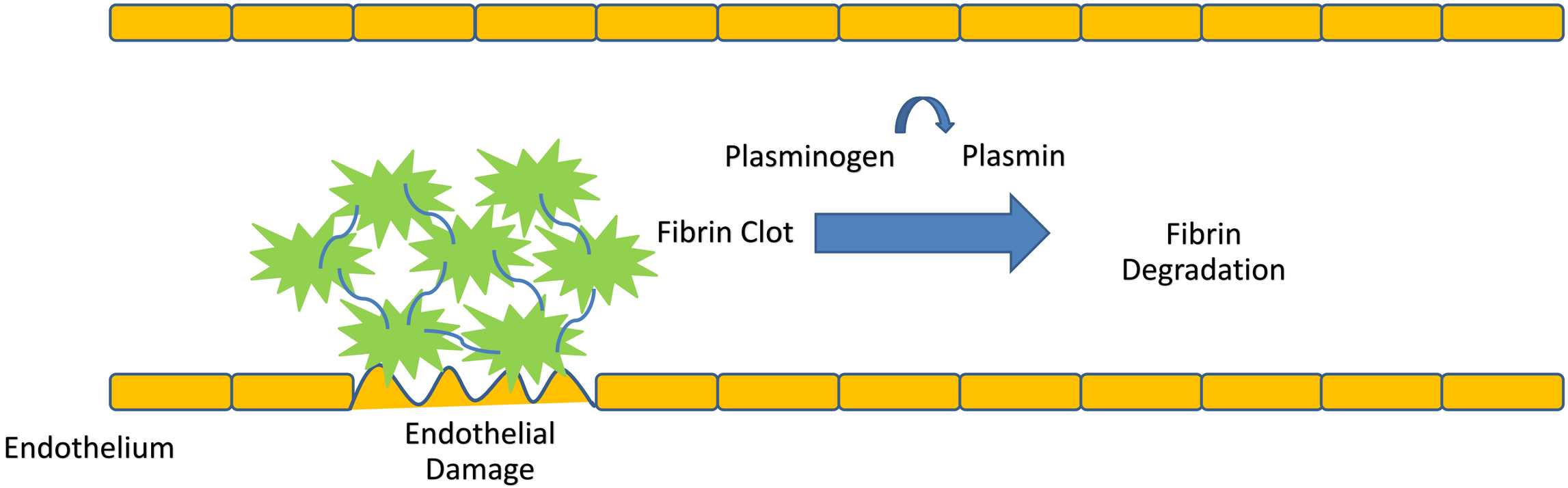


What Could Go Wrong?

Deranged hemostasis

- Consumptive
- Blood loss
- Decreased production

Hyper-fibrinolysis

- Liver disease
- Inherited disorder
- Acquired condition

Secondary causes

- Hypothermia
- Acidosis
- Hypocalcemia

Br J Haematol. 2016;175(1):12-23.

Question 1

Which of the following is a risk factor for coagulopathy?

a) Trauma
b) Hypothermia
c) End stage liver disease
d) Sepsis
e) All of the above

Measurements of Coagulation

Traditional Coagulation Tests

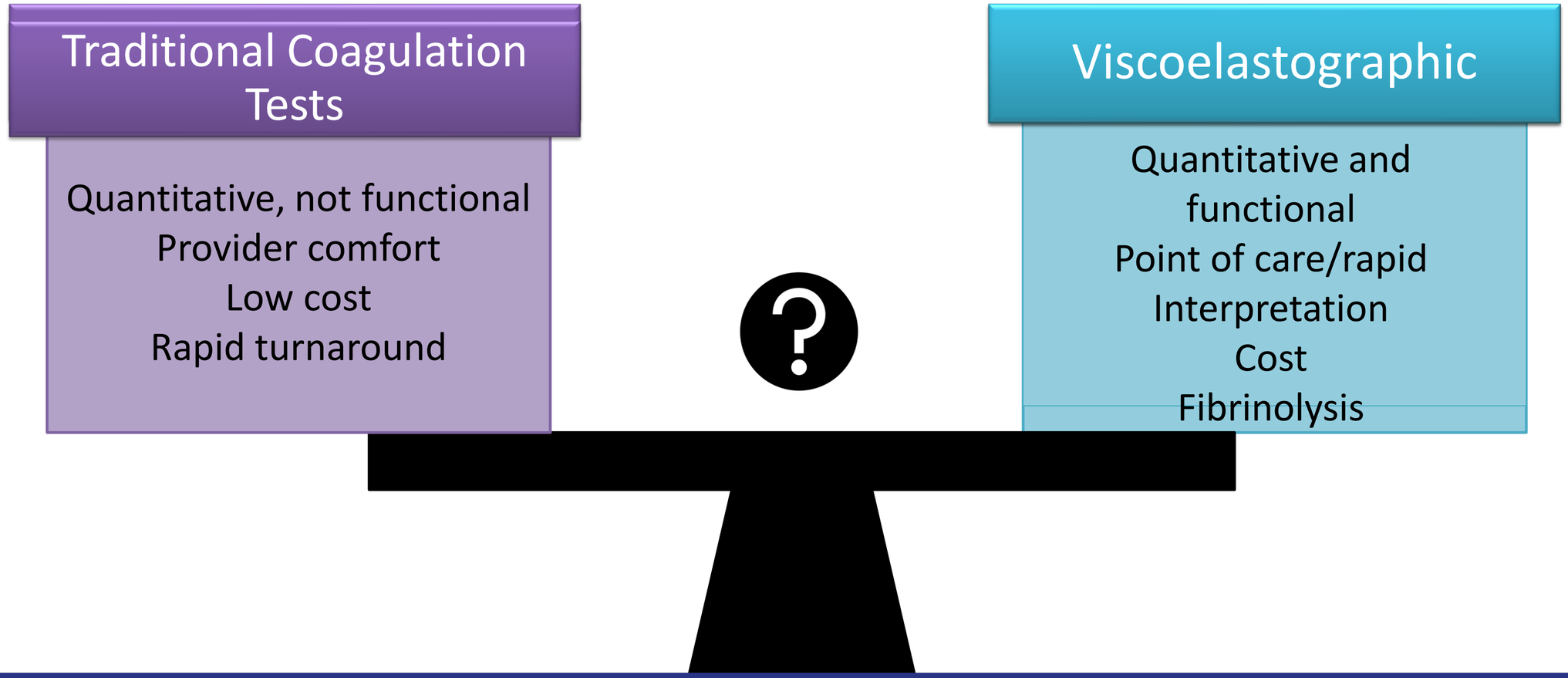
- International normalized ratio (INR)
- Prothrombin time (PT)
- Partial thromboplastin time (aPTT)
- Complete blood count (CBC)
- D-dimer

Viscoelastographic Tests

- Thromboelastography (TEG®)
- Rotational thromboelastometry (ROTEM®)

J Emerg Med. 2020 Aug;59(2):201-215.

Weighing the Options



J Emerg Med. 2020 Aug;59(2):201-215.

Old Test, New Applications

1948
- Developed by Dr. Hellmut Hartert

1970s
- First clinical application during Vietnam War

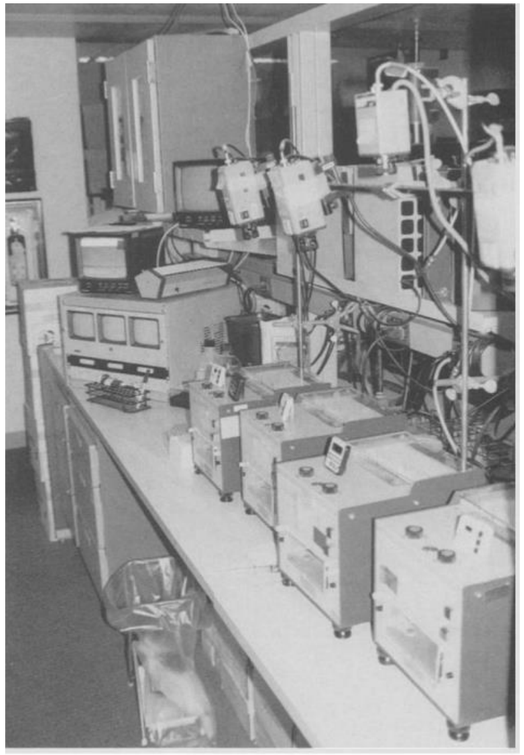
1980s
- Liver transplantation

1990s
- Cardiovascular surgery
- Trauma

Current Drug Targets. 2016, 17, 954-970

Devices

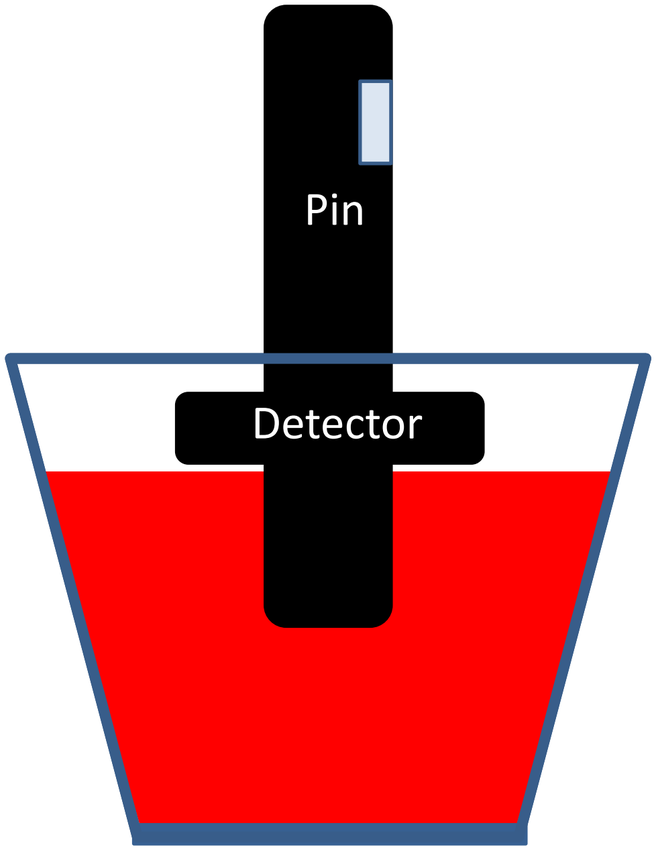
How it Started…



How it’s Going...

TEG® hemostasis analyzer photos, operational schematics and tracing images used by permission of Haemonetics Corporation®

What is Viscoelastography (VE)?



Clin Appl Thromb Hemost. 2018; 24(8):1199-1207.

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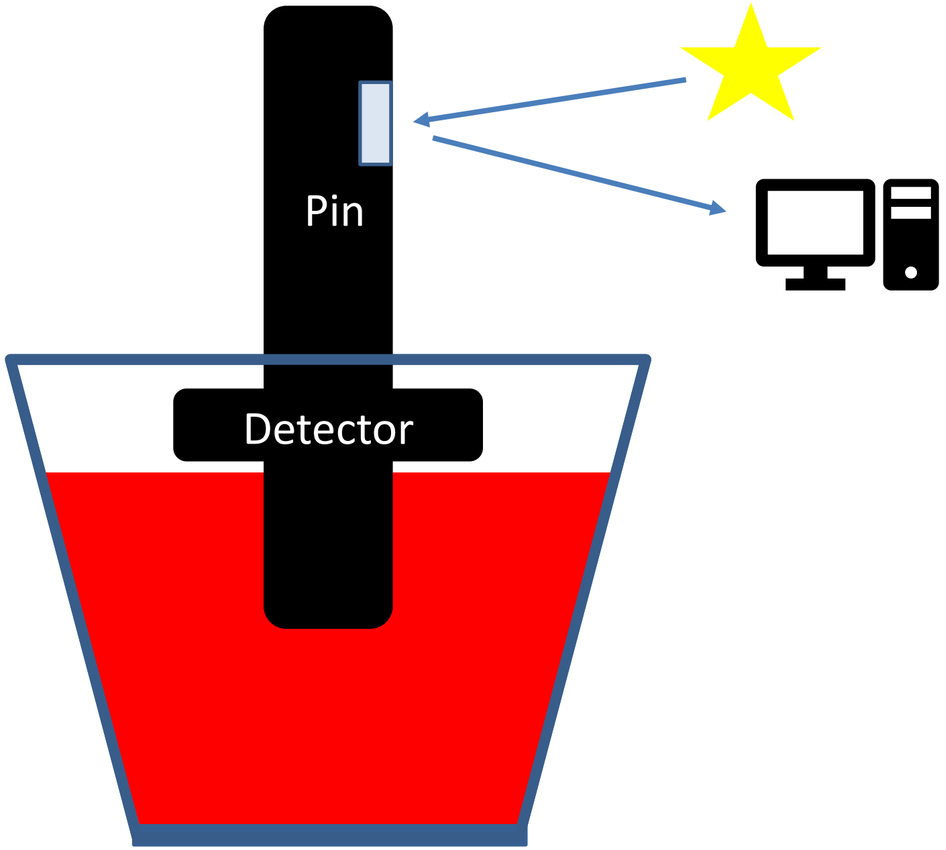

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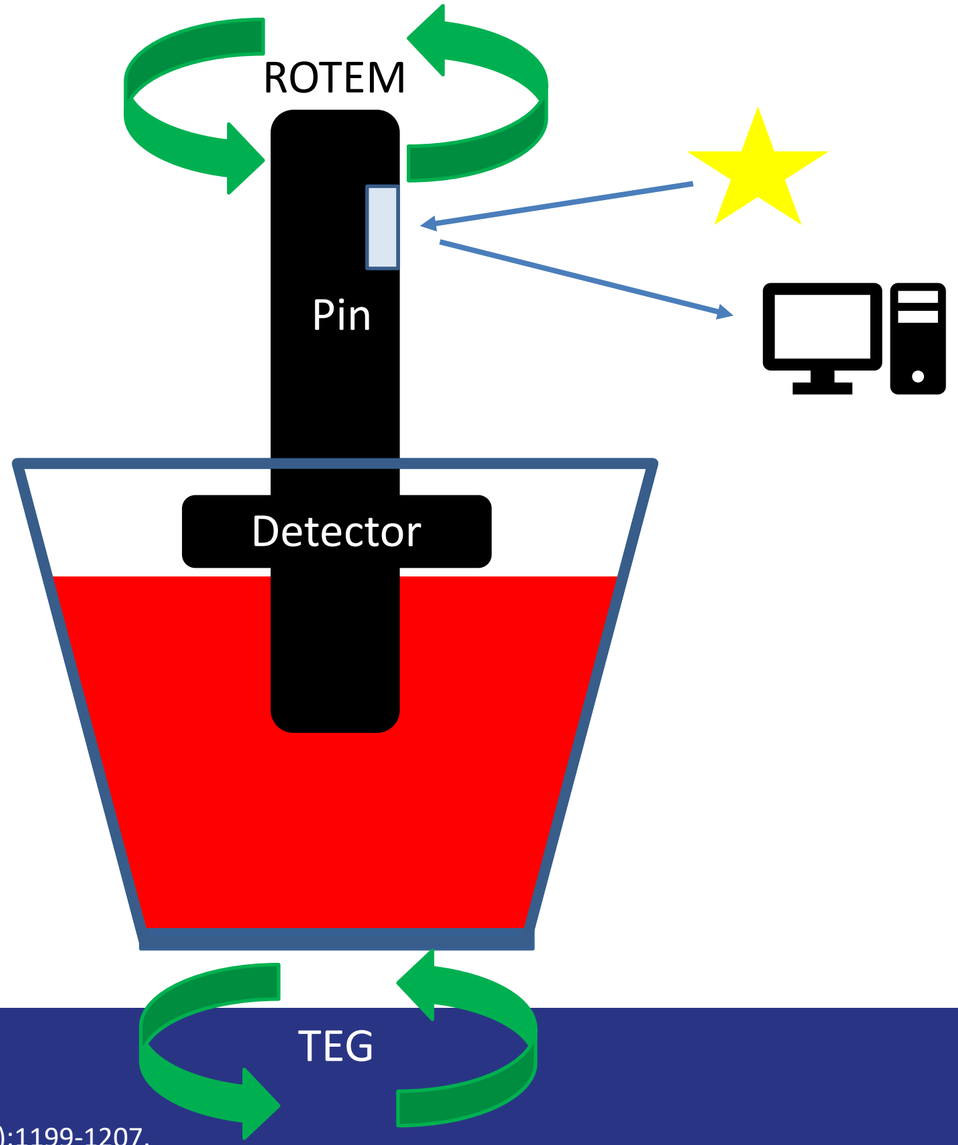

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Comparing TEG and ROTEM

TEG

- 2 samples simultaneously
  - Kaolin/tissue factor
  - HTEG
- Platelet mapping, fibrin function capabilities

ROTEM

- 4 samples simultaneously
  - INTEM
  - EXTEM
  - HEPTEM
  - FIBTEM

Results NOT Interchangeable

J Emerg Med. 2020 Aug;59(2):201-215.

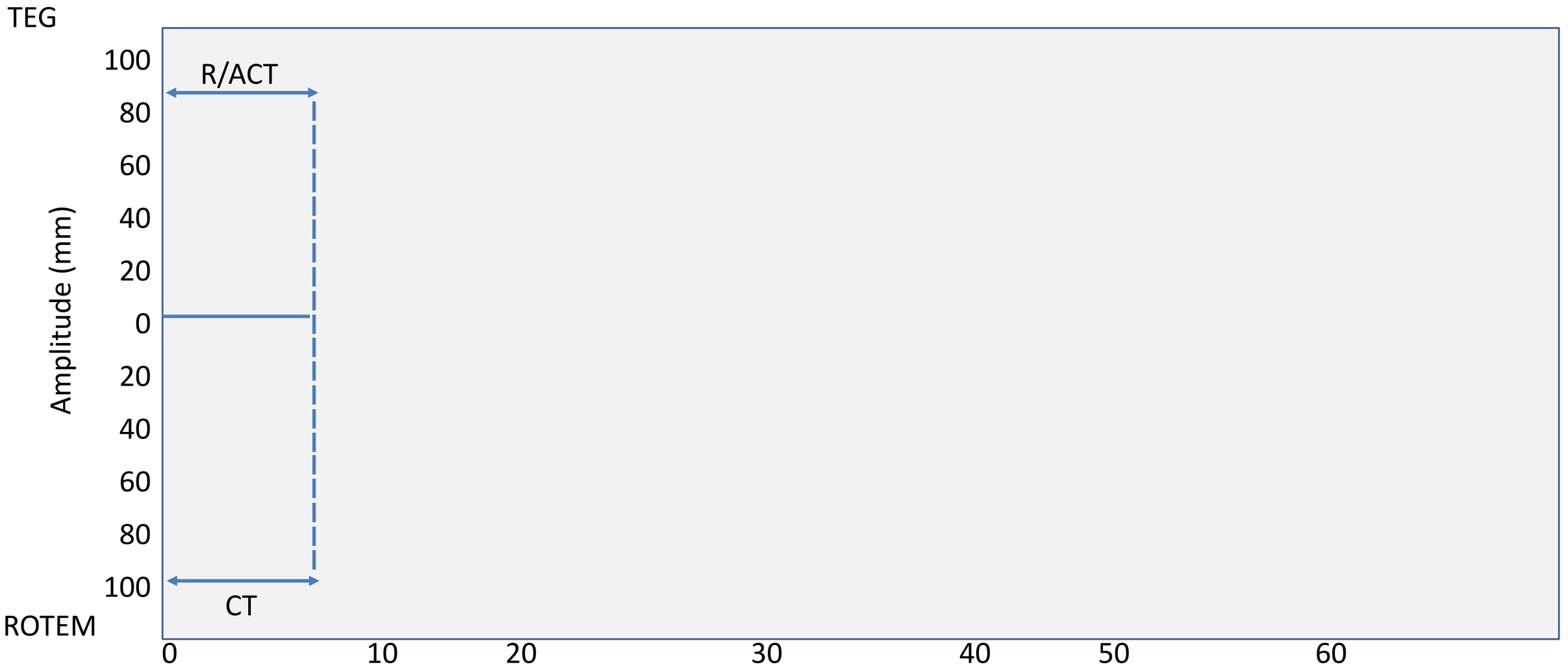
VE Parameters

Term	TEG	ROTEM	Normal Value	Clinical Measurement
R= Reaction Time	+	-	3.8 – 9.8 minutes	Time from start to clot initiation
ACT= activated clotting time	+*		86 – 118 seconds	
CT= Clotting Time	-	+	42 – 74 seconds	

*rTEG only

J Emerg Med. 2020 Aug;59(2):201-215.

Tracing the Lines



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K=Kinetic	+	-	0.7 – 3.4 minutes	Clotting factors + fibrinogen, platelets, factor VIII activity
CFT= Clot Formation Time	-	+	46 – 148 seconds	

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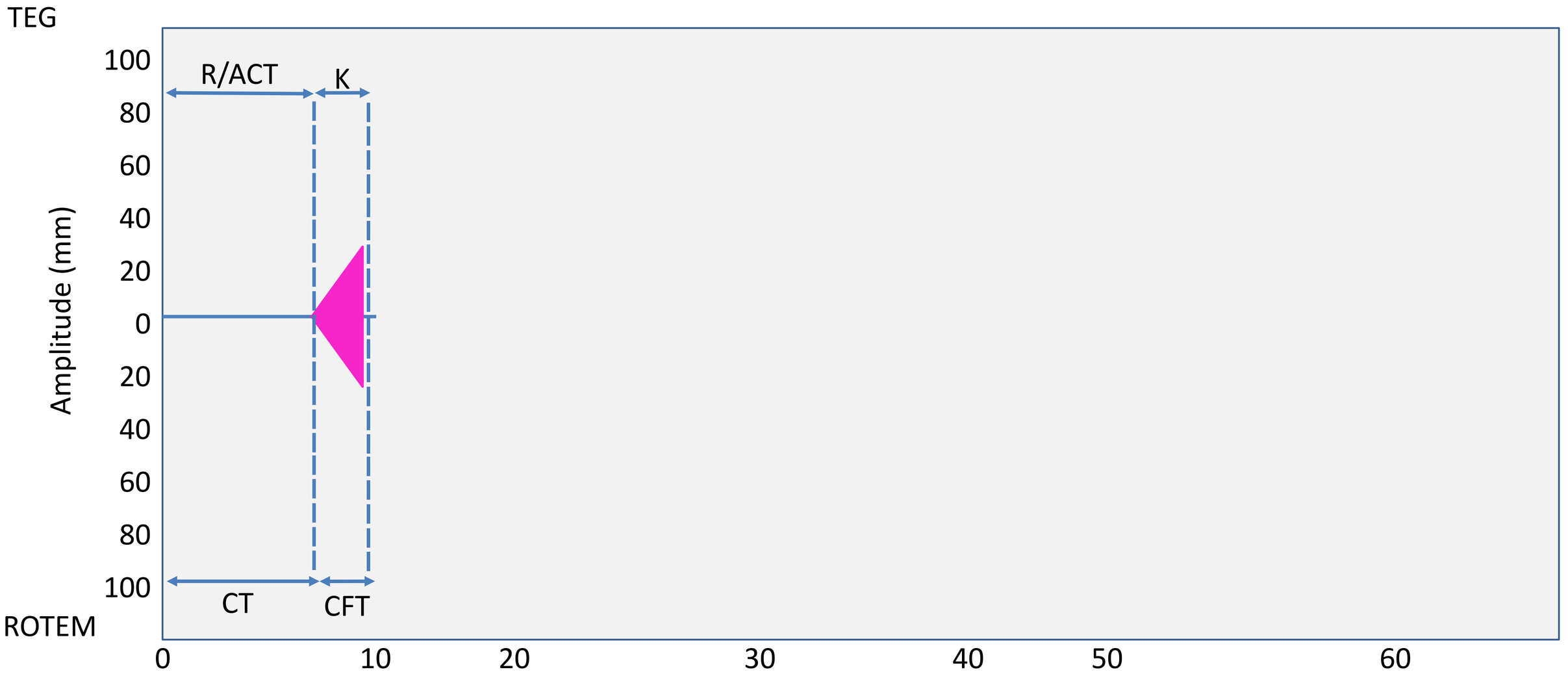

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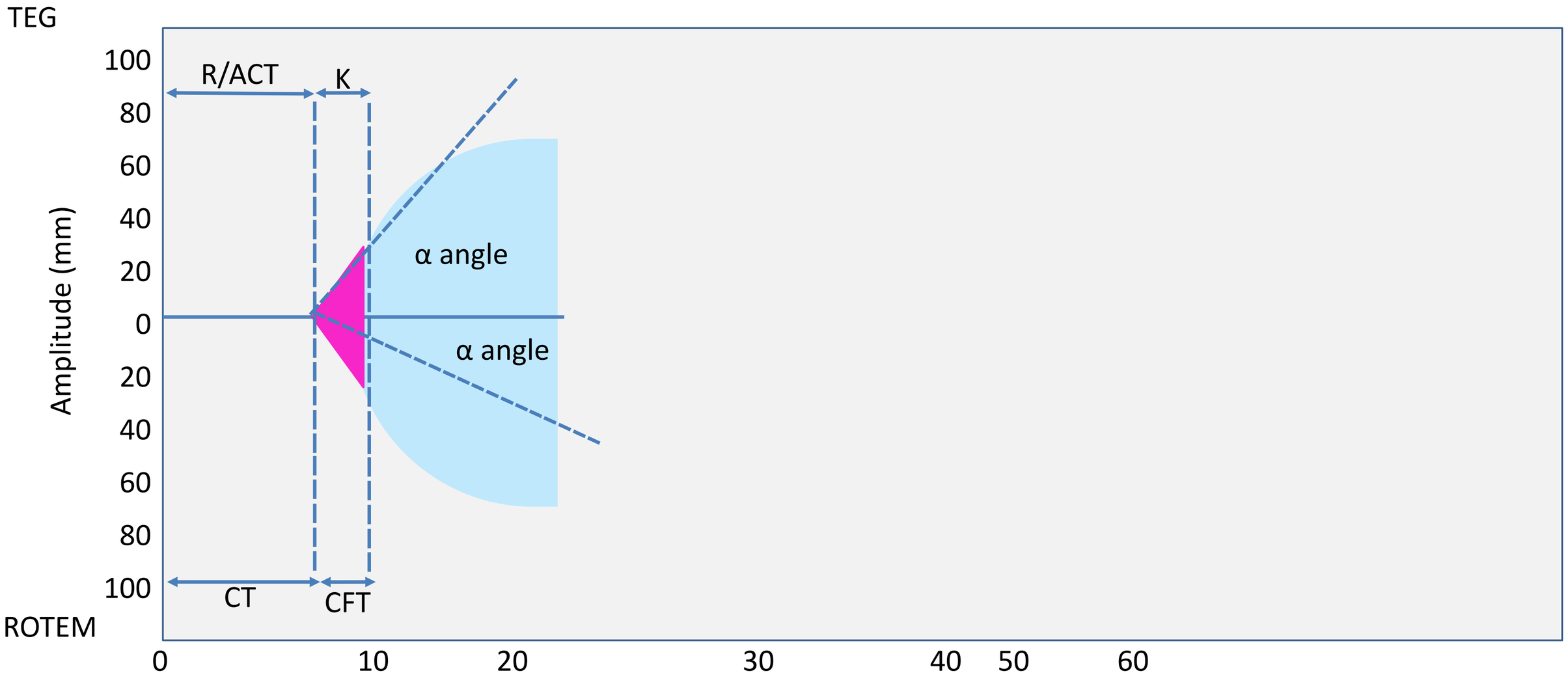

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α-angle	+	+	47.8 – 77.7 degrees	Fibrinogen activity
A10= Amplitude at 10 minutes	-	+	43 – 65 mm	Clot Stability

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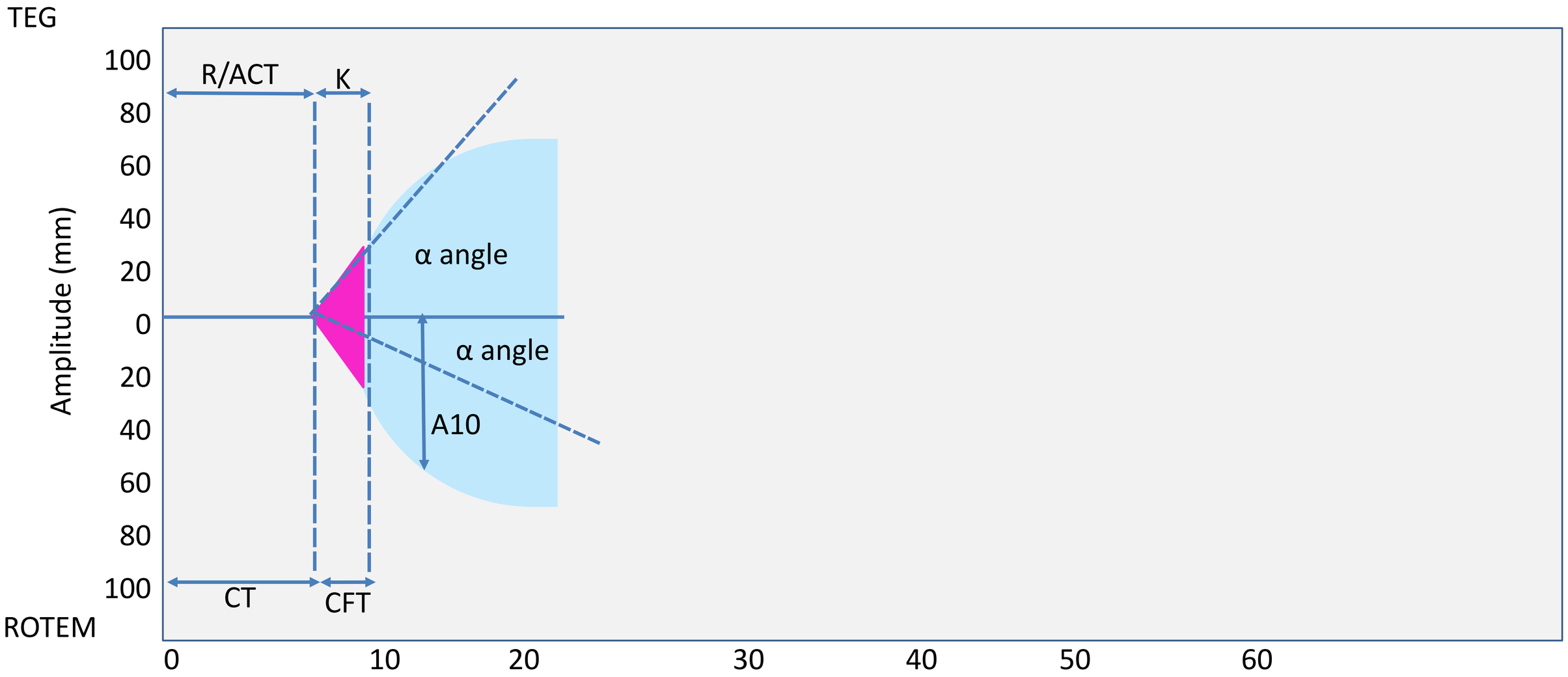

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A10= Amplitude at 10 minutes	-	+	43 – 65 mm	Clot Stability
MA= Maximum Amplitude	+	-	49.7 – 72.7 mm	Platelet count, platelet function, fibrinogen content
MCF= Maximum Clot Firmness	-	+	52 – 72 mm	

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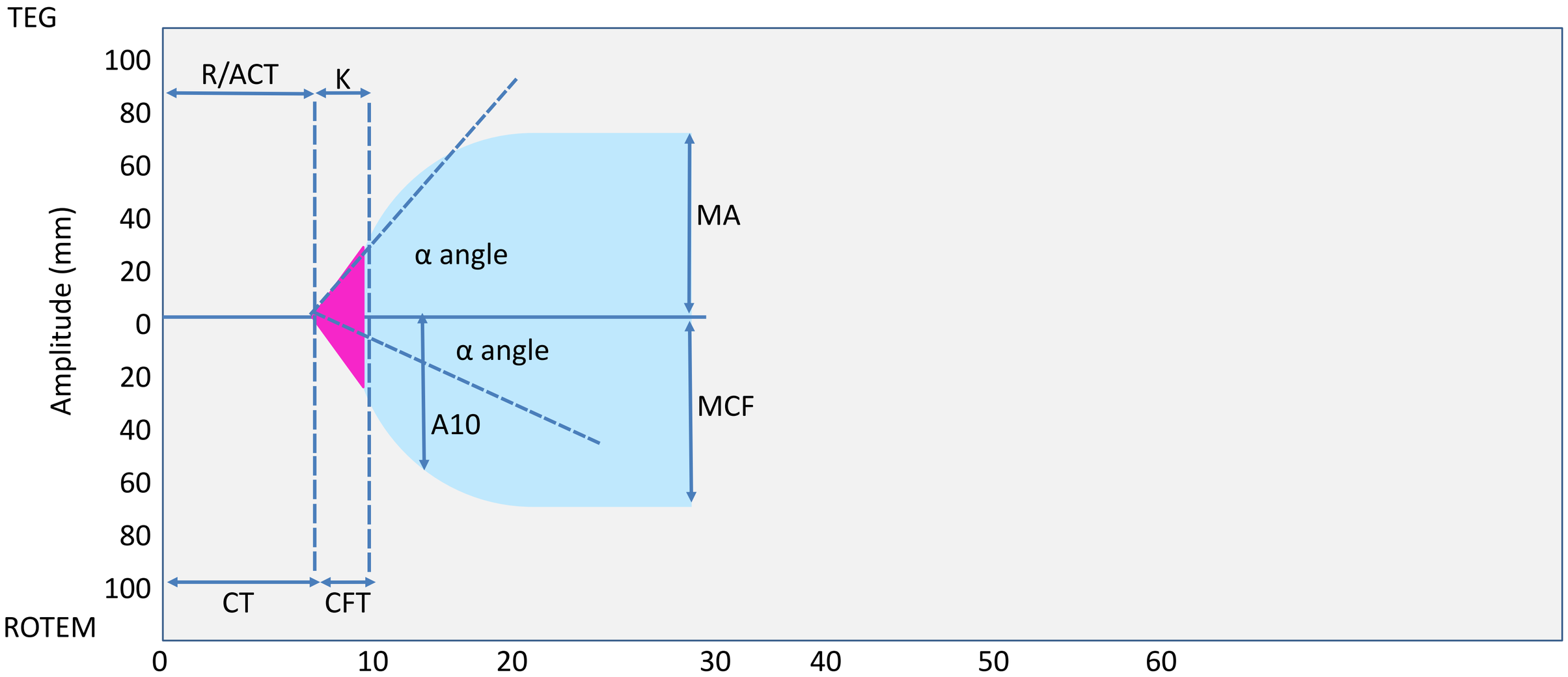

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LY30= Lysis at 30 minutes	+	-	-2.3 – 5.77%	Degree of fibrinolysis
LI30= Lysis Index at 30 minutes	-	+	94 – 100%	% drop in MCF at 30 minutes

*rTEG only

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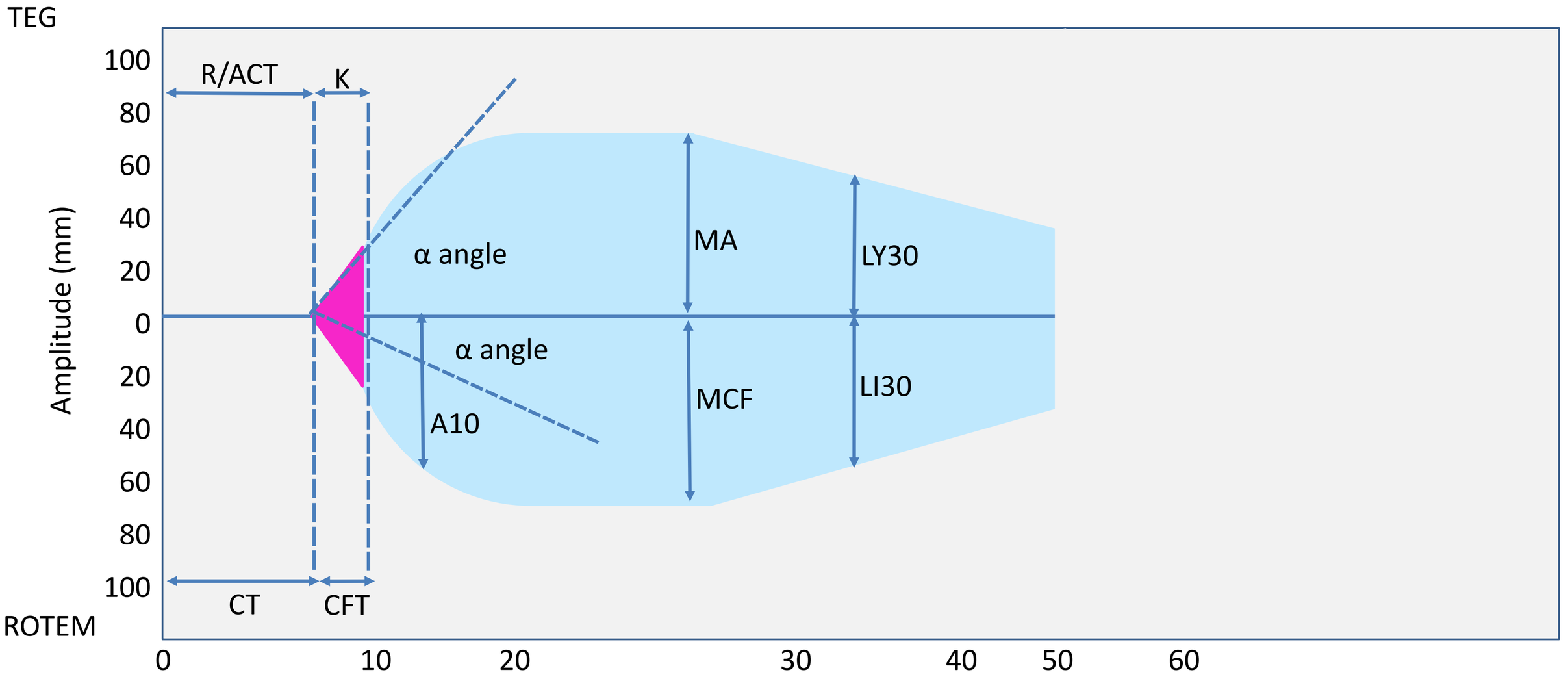

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LI30= Lysis Index at 30 minutes	-	+	94 – 100%	% drop in MCF at 30 minutes
ML= Maximum Lysis	-	+	0 – 12%	Minimum amplitude noted at end of test

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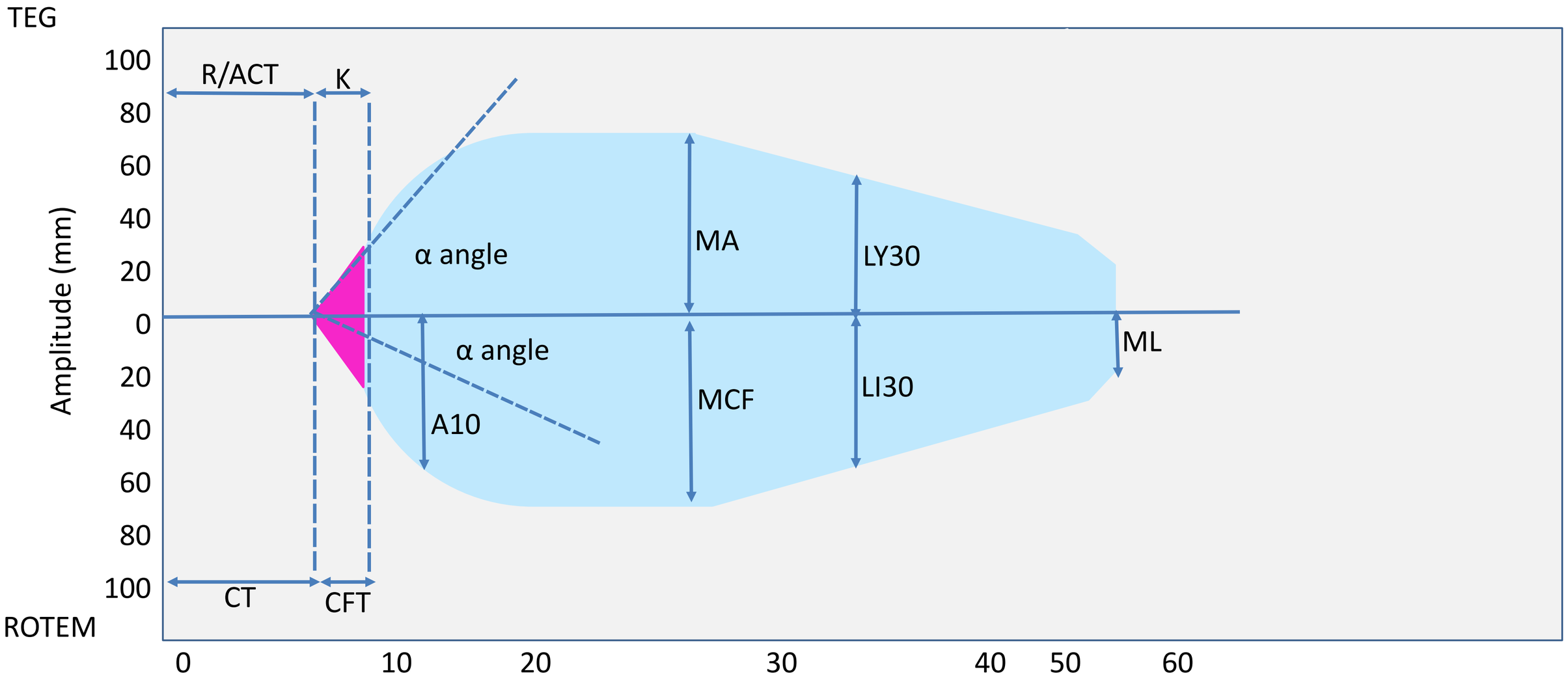

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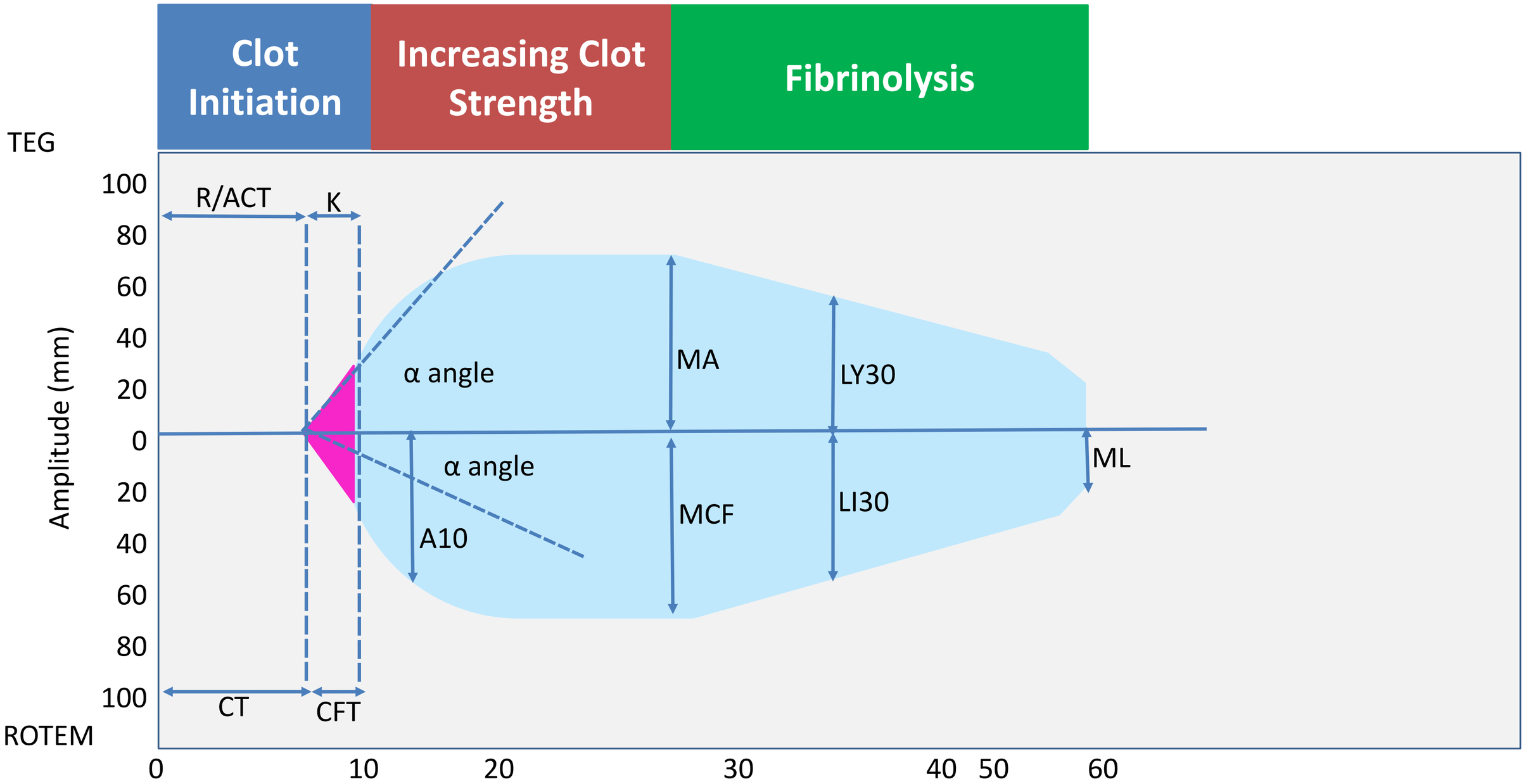

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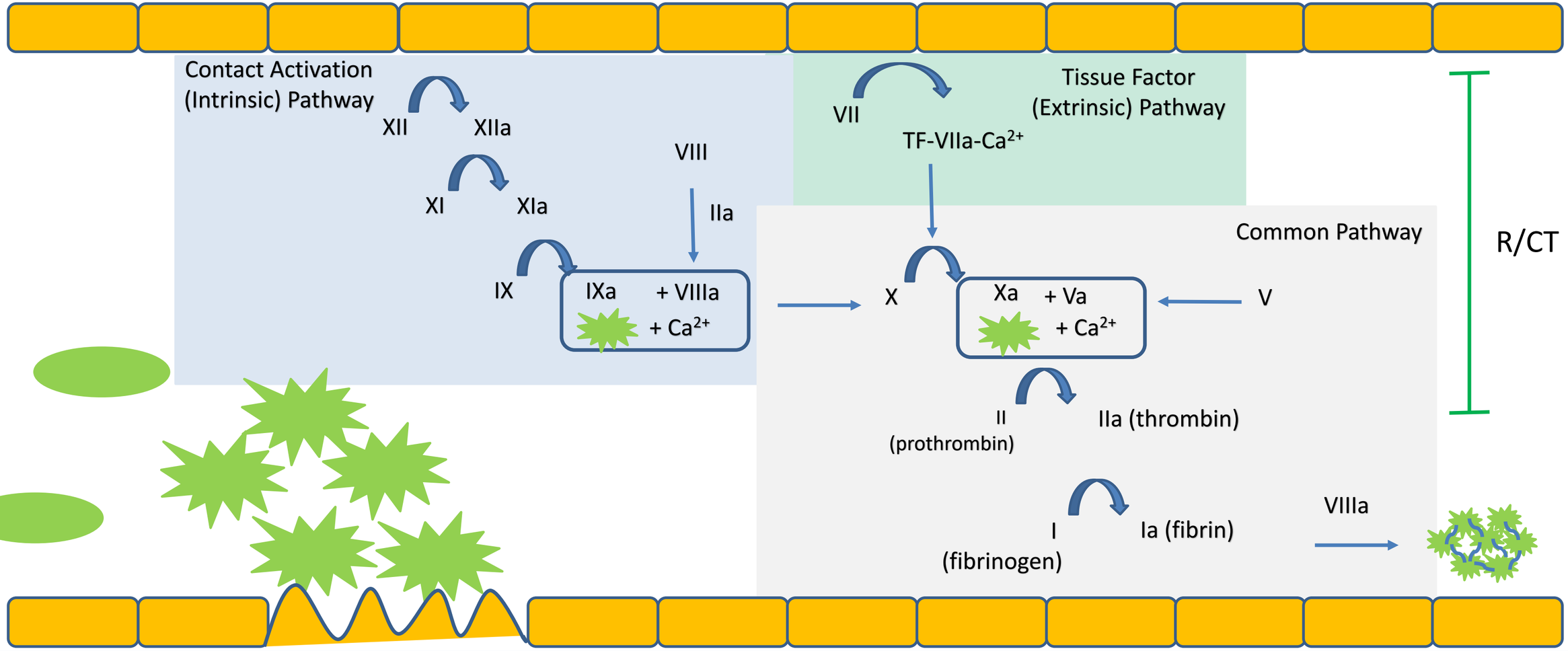
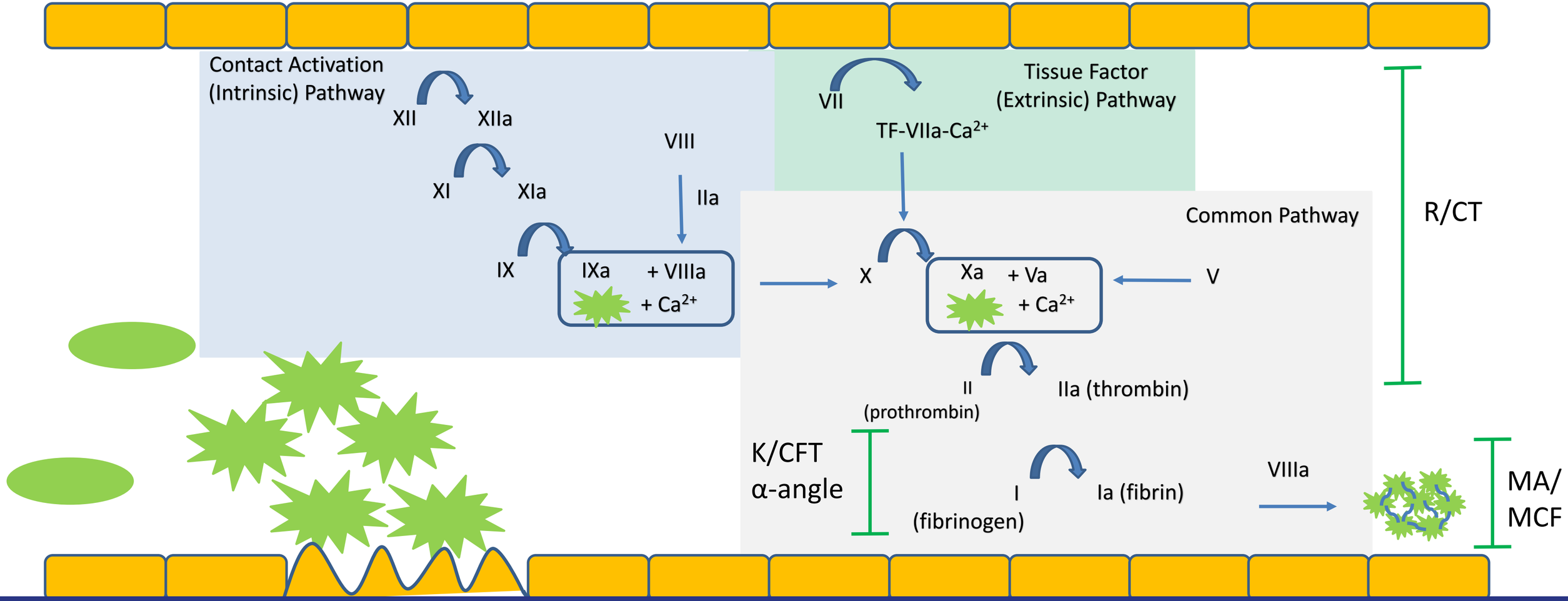
Where's VE?


Contact Activation
(Intrinsic) Pathway
XII
XIIa
XI
XIa
VIII
IIa
IX
IXa + VIIIa
+ Ca2+
VII
TF-VIIa-Ca2+
Tissue Factor
(Extrinsic) Pathway
Common Pathway
X
Xa + Va
+ Ca2+
V
II
(prothrombin)
IIa (thrombin)
I
(fibrinogen)
Ia (fibrin)
VIIIa
R/CT

Where's VE?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K/CFT
α-angle
I
(fibrinogen)
Ia (fibrin)
VIIIa
MA/
MCF

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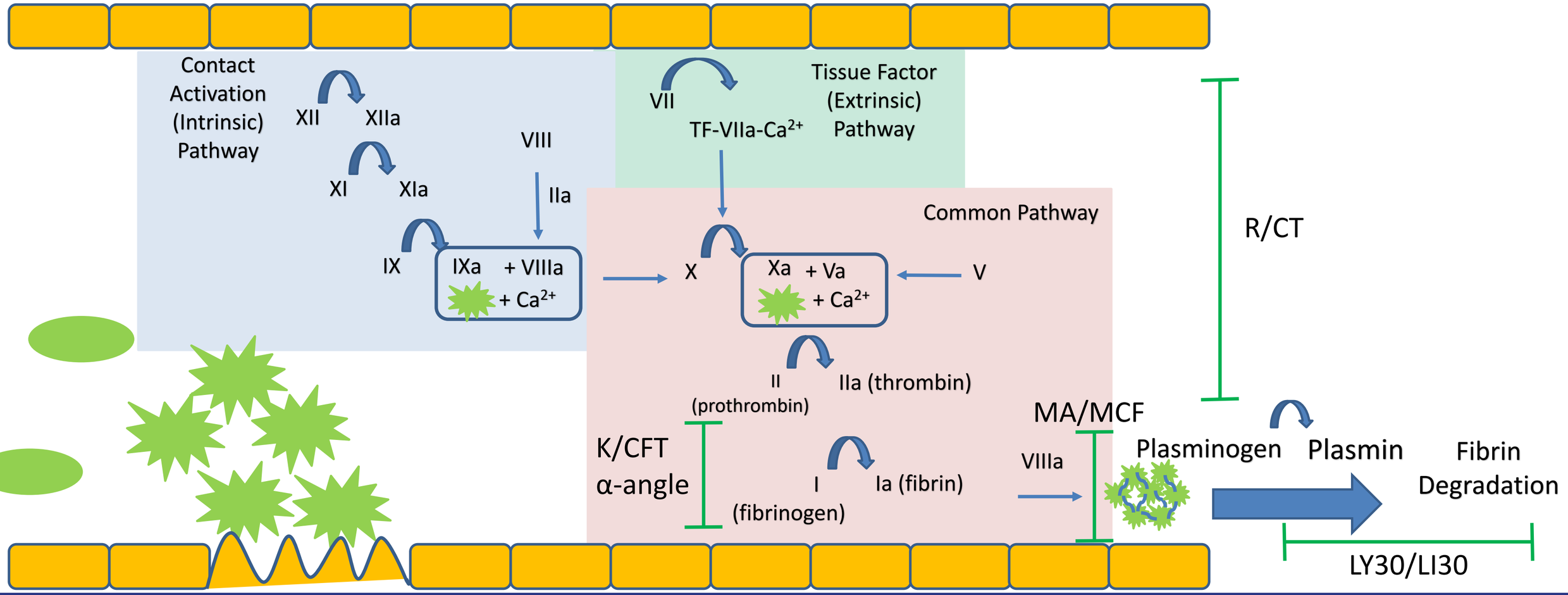
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V
II (prothrombin)
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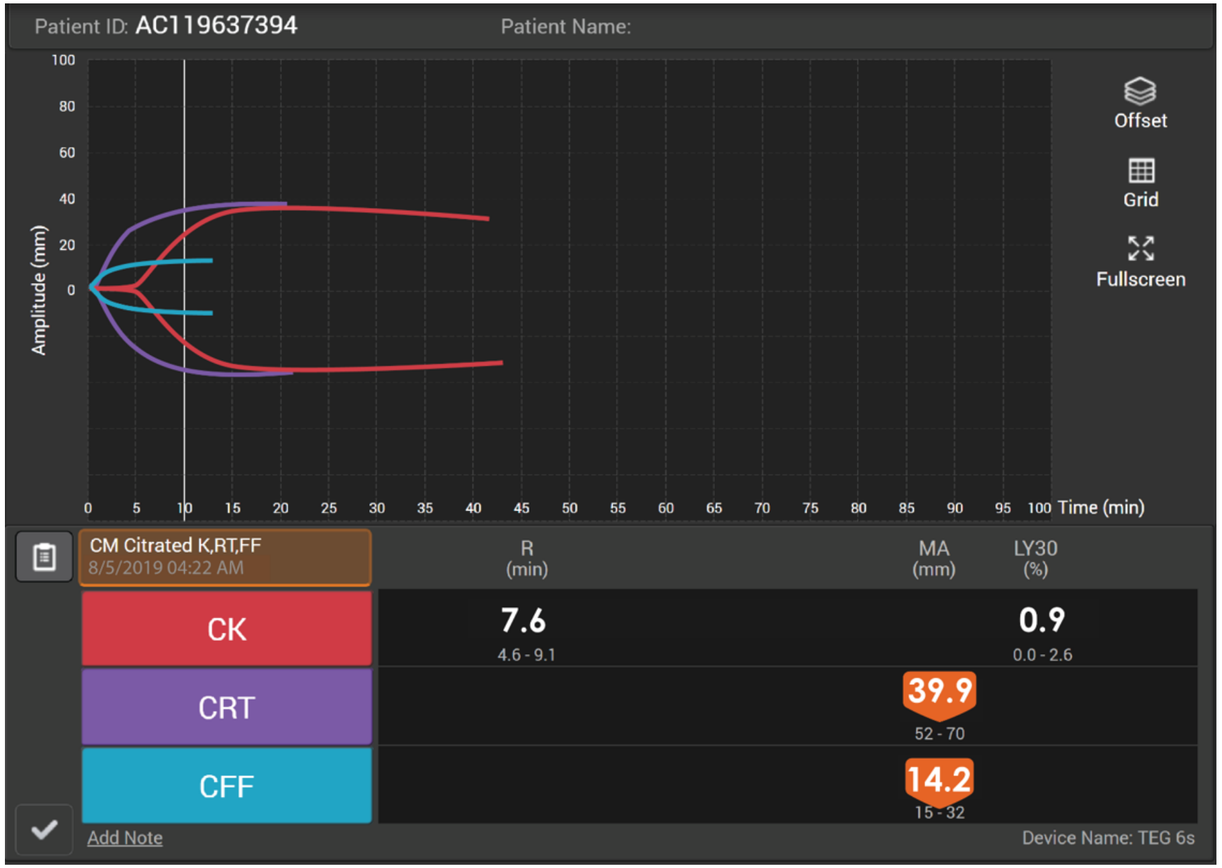
I (fibrinogen)
Ia (fibrin)
MA/MCF
VIIIa
R/CT
Plasminogen
Plasmin
Fibrin Degradation
LY30/LI30

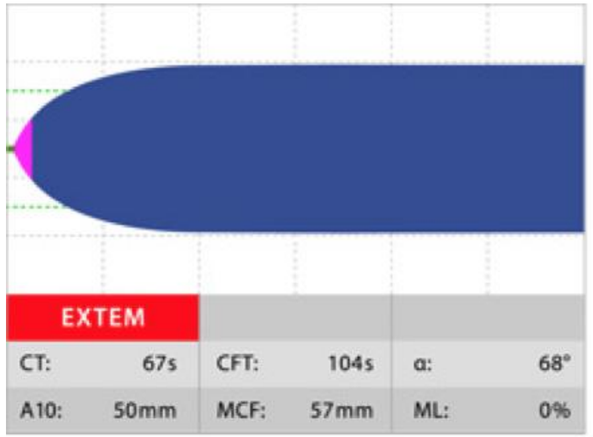
Question 2

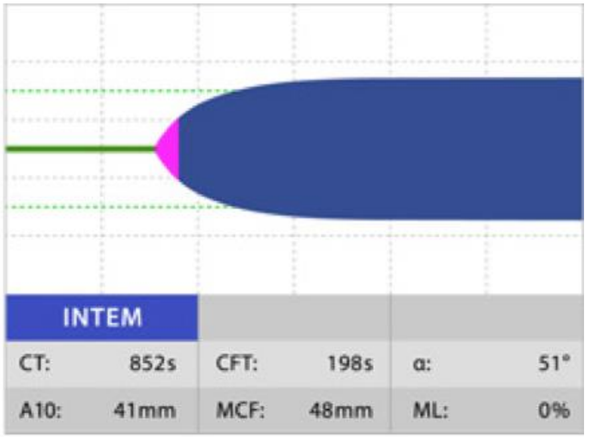
Which of the following components of viscoelastic testing determines the time to start of clot formation?

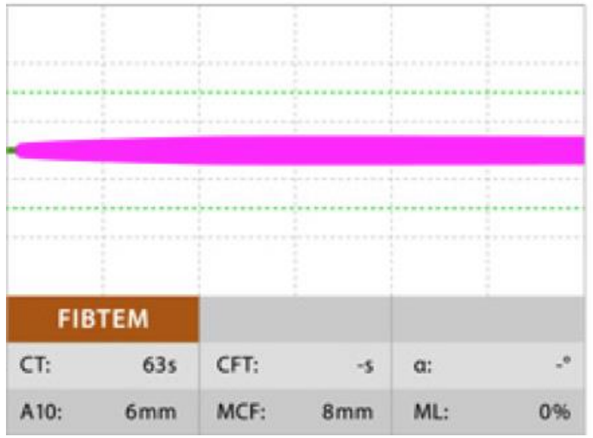
a. Maximal clot firmness
b. Reaction time
c. Alpha angle
d. Lysis 30 minutes (LY30)

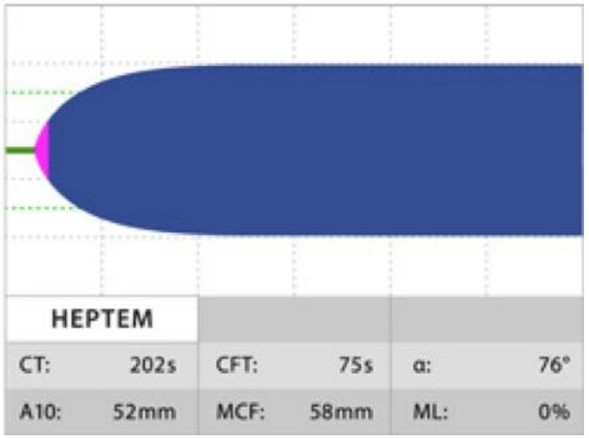
Sample Tracings









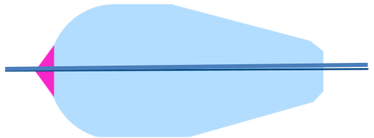


TEG® hemostasis analyzer photos, operational schematics and tracing images used by permission of Haemonetics Corporation

Application

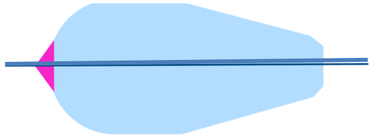
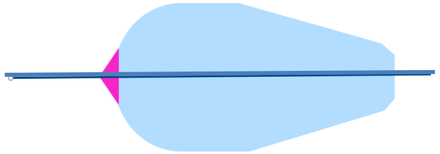
↑R/CT	Fresh frozen plasma (FFP) or prothrombin complex concentrate (PCC)
↓MA/MCF	Cryoprecipitate (if FIBTEM/fibrin function[FF]↓) Platelets (if FIBTEM/FF normal)
↑LY30/LI30	Tranexamic acid (TXA)

Shaken, Not Stirred or Stirred, Not Shaken?

Description	Tracing	Glass	Action
Normal			Do nothing!

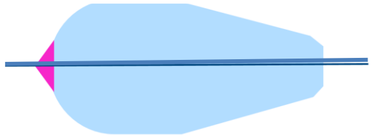
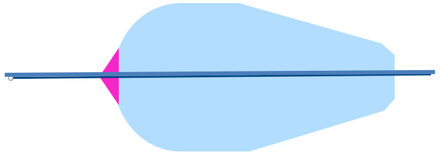
J Emerg Med. 2020 Aug;59(2):201-215.

Shaken, Not Stirred or Stirred, Not Shaken?

Description	Tracing	Glass	Action
Normal			Do nothing!
Anticoagulated Hemophilia			FFP or PCC

J Emerg Med. 2020 Aug;59(2):201-215.

Shaken, Not Stirred or Stirred, Not Shaken?

Description	Tracing	Glass	Action
Normal			Do nothing!
Anticoagulated Hemophilia			FFP or PCC
↓ Fibrinogen/ platelets			Platelets Cryoprecipitate

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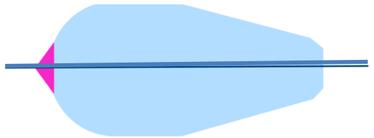
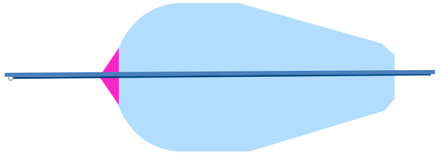
Normal			Do nothing!
Anticoagulated Hemophilia			FFP or PCC
↓ Fibrinogen/ platelets			Platelets Cryoprecipitate
Fibrinolysis			TXA

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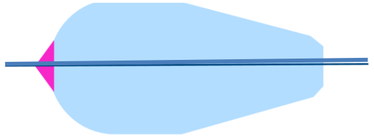
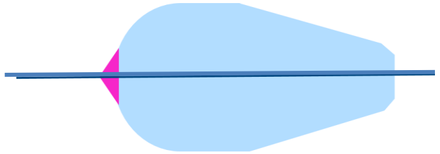
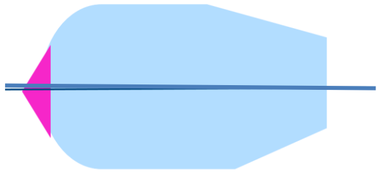
Shaken, Not Stirred or Stirred, Not Shaken?

Description	Tracing	Glass	Action
Normal			Do nothing!
Anticoagulated Hemophilia			FFP or PCC
↓ Fibrinogen/ platelets			Platelets Cryoprecipitate
Fibrinolysis			TXA
Hypercoagulability			Monitor vs. anticoagulation

J Emerg Med. 2020 Aug;59(2):201-215.
https://corp.7-eleven.com/corp-press-releases/

Why don’t we use this everywhere?

- Training & expertise
- Wide range of “normal”, not static
- Logistics & standardization
- $$$
- Data lacking

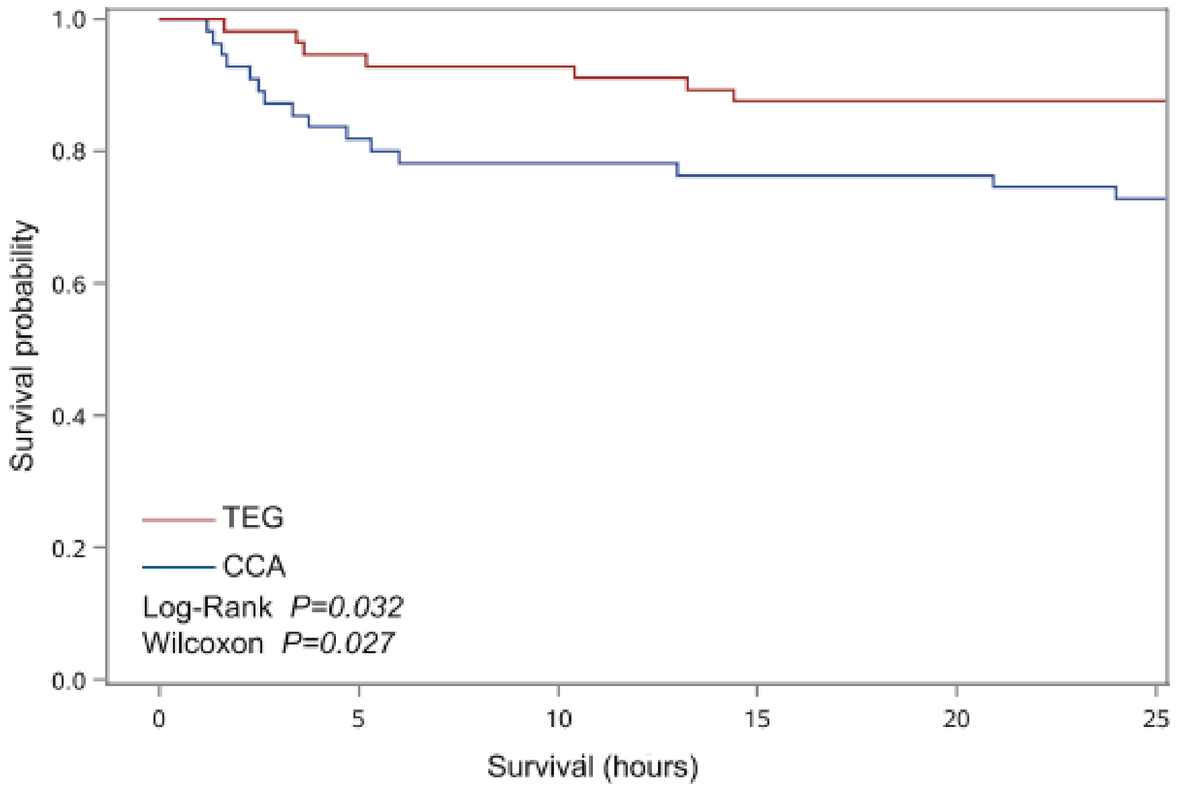
Where should we use it?

- Ischemic stroke
- Trauma
- Intracranial Hemorrhage
- Liver Disease
- Surgery (CV, liver transplant)
- Anticoagulant Monitoring*

J Emerg Med. 2020;59(2):201-215.
*Heparin/LMWH; DOACs less reliable

Goal-Directed Hemostatic Resuscitation

- Single center RCT of L1 trauma patients requiring MTP activation
- TEG (n=56) or conventional coagulation assays (CCA; n=55)
- Baseline demographics similar
  - TBI: 16% TEG vs. 21.8% CCA
- TEG group ↑ survival at 28 days
- Blood Products:
  - Similar PRBCs (4.5 units TEG vs. 5 units CCA, p=0.32)
  - ↓ FFP (0 TEG vs. 2 CCA, p=0.02)
  - ↓ platelets (0 TEG vs. 0 CCA, p=0.04)



Ann Surg 2016;263:1051–1059

Acute Ischemic Stroke

Prospective observational study of 246 mild to moderate AIS (NIHSS ≤ 14) aimed to determine if TEG on admission for predicting early neurological deterioration (END)

TEG Parameter, mean	END (n=72)	Non-END (n=174)
R	4.5±1*	4.7±1.2
K	1.3±0.4*	1.5±0.4
MA	64.3±6.1	63.5±5.7
α angle	70±4.9	68.7±5.3
LY30	95.6	95.8

After adjustment, the lower tertile of R (R ≤3.8 min) was associated with END (OR 3.556, 95% CI 1.17 -10.86)

ROC analysis demonstrated that R ≤3.45 minutes had the best predictive value for END with 87.9% sensitivity and 40.3% specificity

Cerebrovasc Dis 2018;46:125–31.

And Hemorrhagic Transformation?

205 patients with AIS s/p alteplase, TEG within 6 hours

TEG Variable	Hemorrhagic Transformation (N=28)	No Hemorrhagic Transformation (N=177)	P Value
R, minutes, mean (SD)	4.3 ± 0.8	4.7 ± 1.1	0.1
K, minutes, median (IRQ)	1.5 (1.2–1.8)	1.4 (1.2–1.7)	0.11
Alpha angle, degrees, median (IRQ)	68.4 (62.9–72.5)	69.6 (65.3–72.9)	0.26
MA, degrees, mean (SD)	61.1 ± 7.1	62.2 ± 8.7	0.54
LY30, %, median (IQ)	2.6 (0.1–6.5)	1.8 (0.4–5.4)	0.43

In multivariate logistic regression analysis, R<5 minutes was associated with hemorrhagic transformation (OR 3.215, 95% CI 1.153–8.969)

Am J Emerg Med. 2020; 38(9):1772-1777.

Intracranial Hemorrhagic

Prospective observational cohort of 64 spontaneous ICH patients vs. 57 controls

Variable, mean ± SD	Baseline ICH (n=64)	36 Hours ICH (n=27)	Controls (n=57)	Hematoma Expansion (n=11)	No Hematoma Expansion (n=38)
R	4.7±1.7*	6.5±4.4	6.1±1.8	5.7 (4.5-6.9)	4.4 (3.5-5.4)
K	2.1±1.6	2.1±2.8	2.1±0.6	3.1 (2.0-4.1)*	1.6 (0.6-2.6)
MA	64.5±14.1*	70.7±4.8*	64.4±5.8	61.7 (52.0-71.4)	61.6 (53.5-69.7)
α angle	64.4±10.8	66.4±12.3	61.3±5.8	58.0 (50.6-65.4)	62.0 (55.8-68.1)

*P<0.05 relative to control

In adjusted analysis, baseline K was longer in HE+ compared with HE- patients (median K 3.1 [2 - 4.1] vs. 1.6 [0.6 - 2.6], P=0.04)

Stroke. 2014; 45(3): 683–688.

Last but not least..

MS is a 45-year-old male with past medical history of non-ischemic cardiomyopathy status-post left ventricular assist device placement on warfarin who presents to the ED with subdural hematoma measuring 2.6 × 3.5 × 3.1 centimeters. His physical examine is within normal limits except a scalp hematoma and altered mental status. All labs were normal except INR was 3.6 and serum creatinine was 1.52 mg/dL.

30 minutes s/p 4F-PCC 2000 fIXa units IVPB and vitamin K 5 mg IVPB ROTEM:

ROTEM Parameter	Extrinsic ROTEM
Clot time (CT), seconds (reference range)	77 (43-82)
Clot formation time (CFT), seconds (reference range)	196 (48-127)
α-angle, degrees (reference range)	77 (65-80)
Amplitude at 10 minutes (A10), millimeters (reference range)	69 (46-67)
Maximum Clot Firmness (MCF), millimeters (reference range)	74 (52-70)
Lysis Index at 30 minutes (LI30), % (reference range)	100 (94-100)

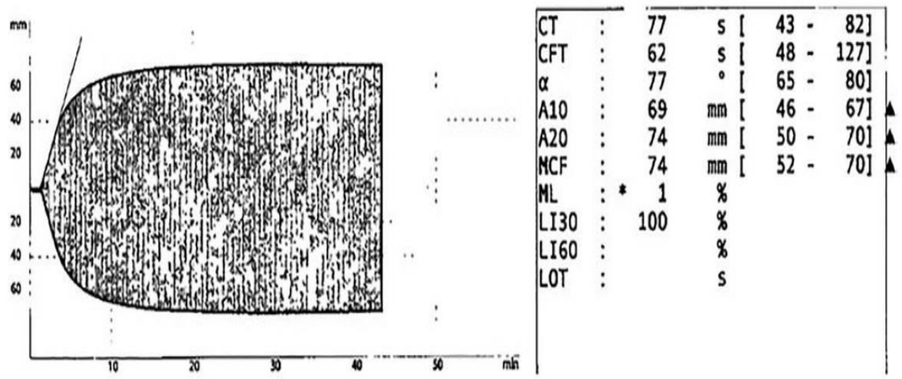


Fig. 2. Patient ROTEM® (Extrinsic).

Am J Emerg Med. 2021; 41: 265.e5-265.e8.

Question 3

Based on this ROTEM, what should we give?

a) Order additional 500 fIXa units of 4F-PCC
b) No additional factors needed
c) Order platelets
d) Order fresh frozen plasma

Conclusions

- Coagulopathy is common in critically ill patients
- VE testing is useful to guide management of coagulopathy in many patient populations
- VE has been studied across a wide range emergencies, though further research is needed to determine its role beyond a prognostic tool in most settings outside of trauma

EMPoweRx conference

A conference that is for us and by us

Stirred, Not Shaken: Utility of Viscoelastic Testing for Monitoring Coagulation in Critically Ill Populations

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Maywood, Illinois

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