Monitoring and Point of Care Diagnostics Tools

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SHC – 28th november 2013

No Disclosures

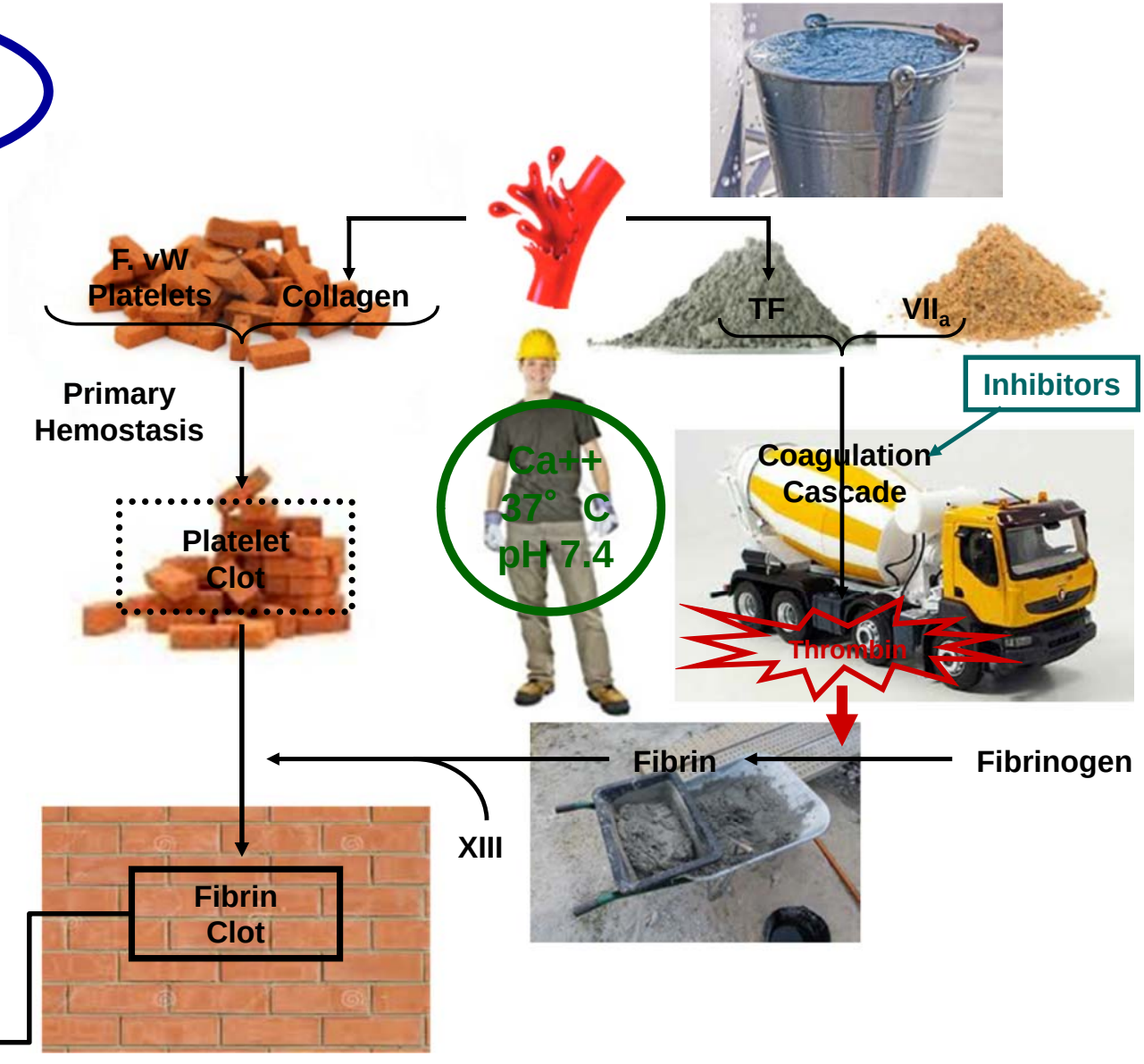
Introduction

POCT in Massive Bleedings

Conventional Assays

New Assays

Introduction



Conventional Assays

Bleeding Patient

Emergency
Operating Theater
ICU

Pitfall 1
Process

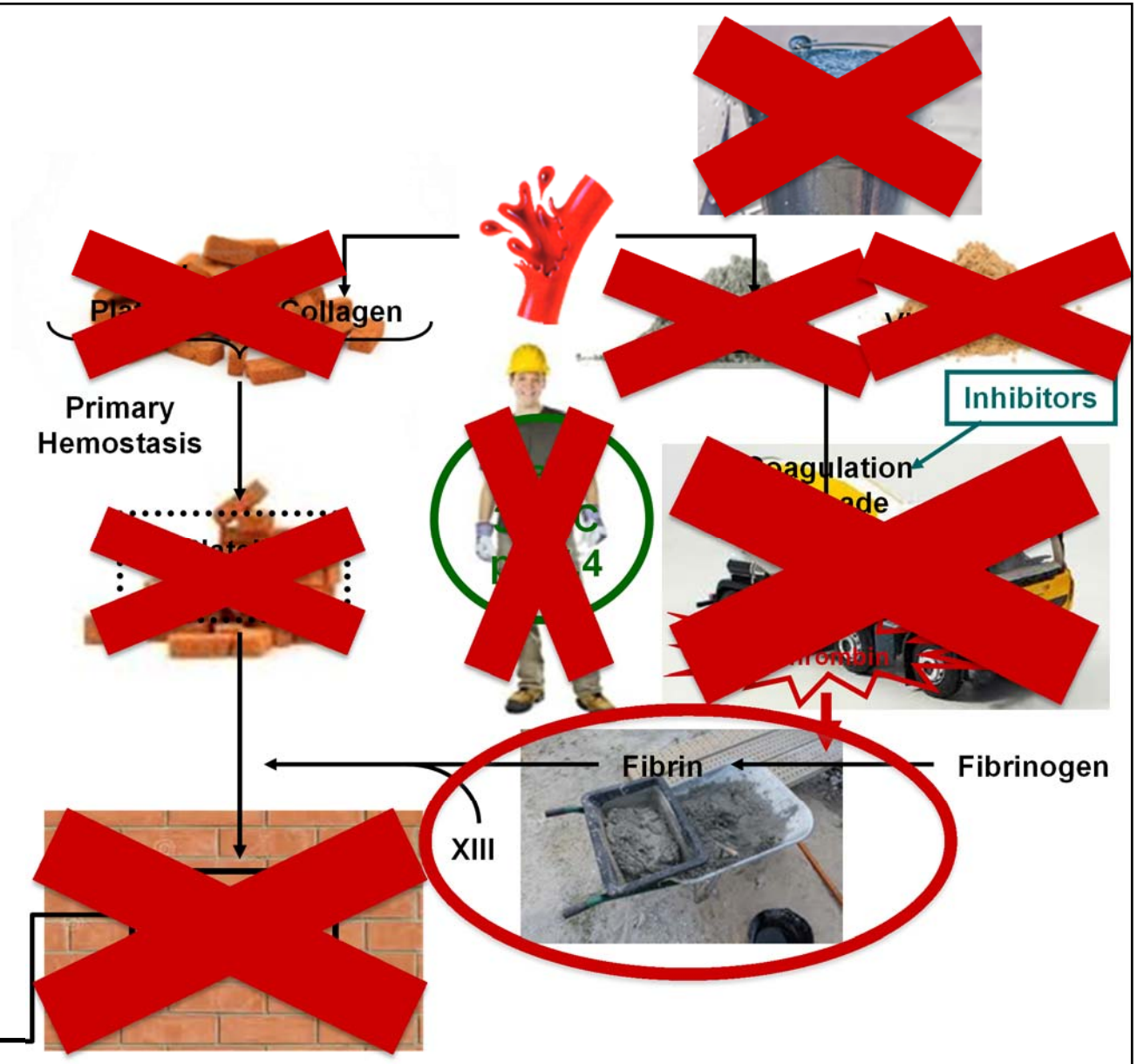
Blood Sampling	2 min	19 min
Lab transport	2 min	
Reception and introduction	5 min	
Centrifugation	10 min	

Analyser

Fibrinogen
TT
PT
aPTT

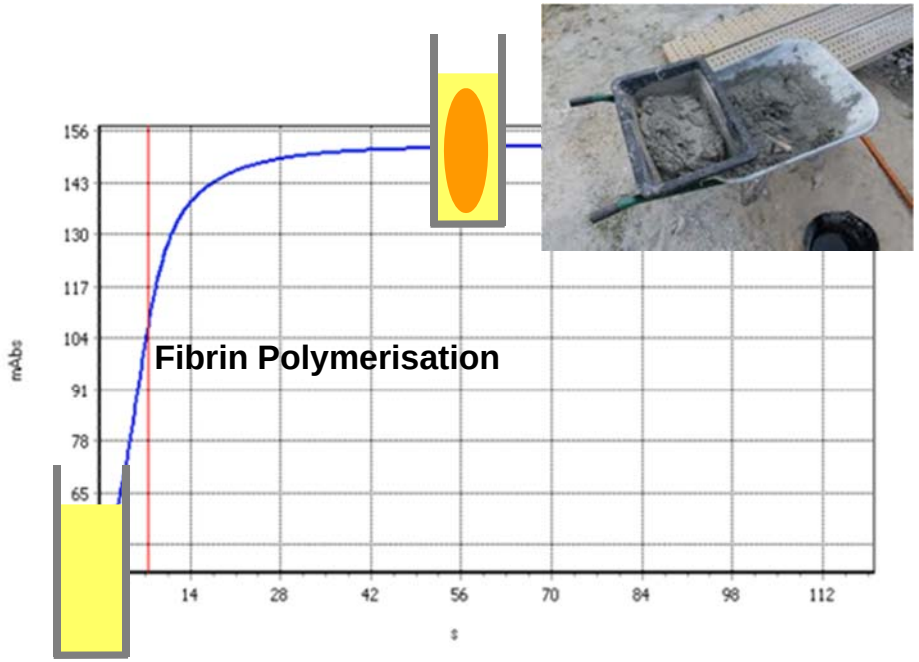
Conventional Assays

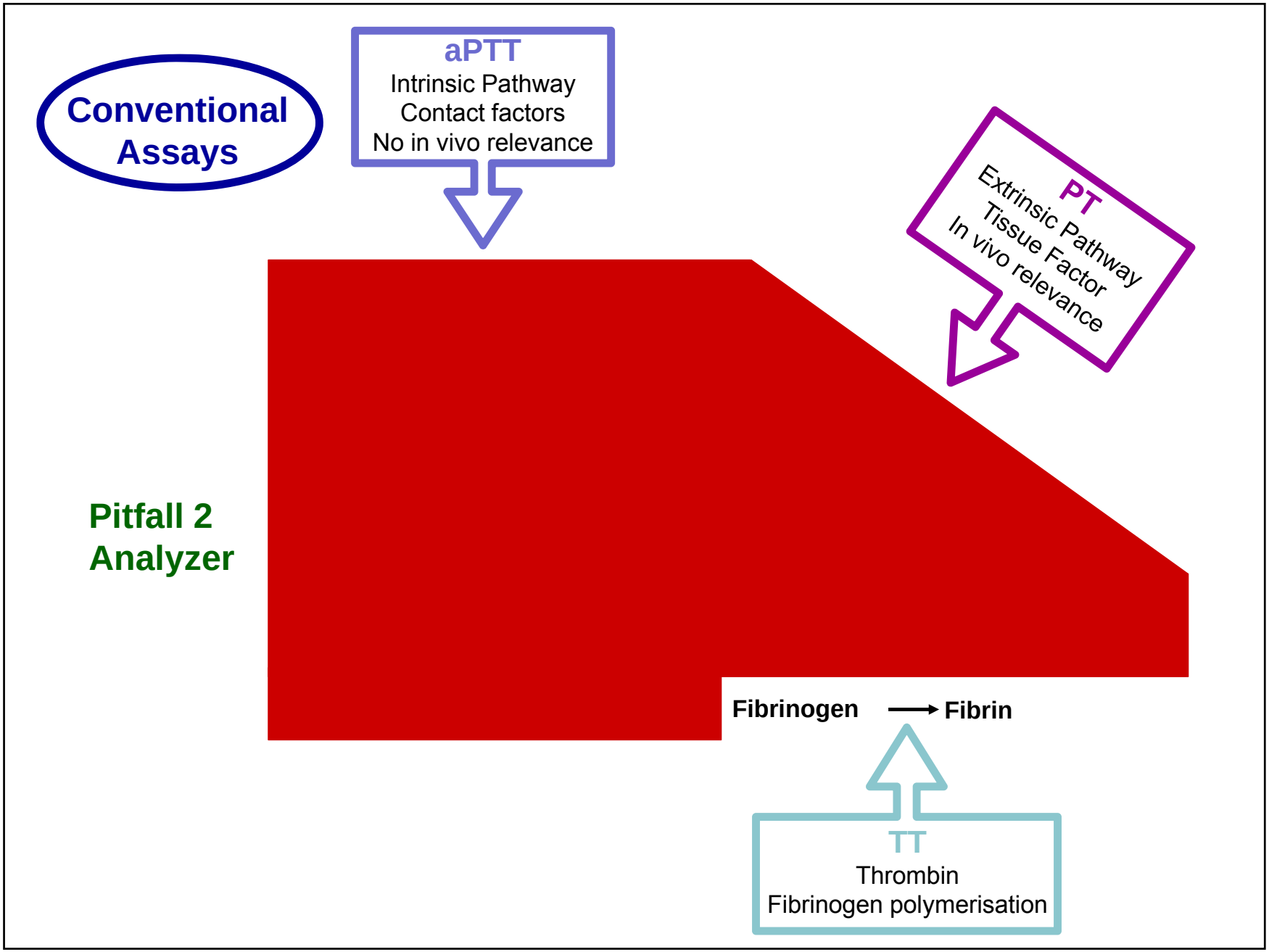
Pitfall 2 Steps analysed with CCT



Conventional Assays

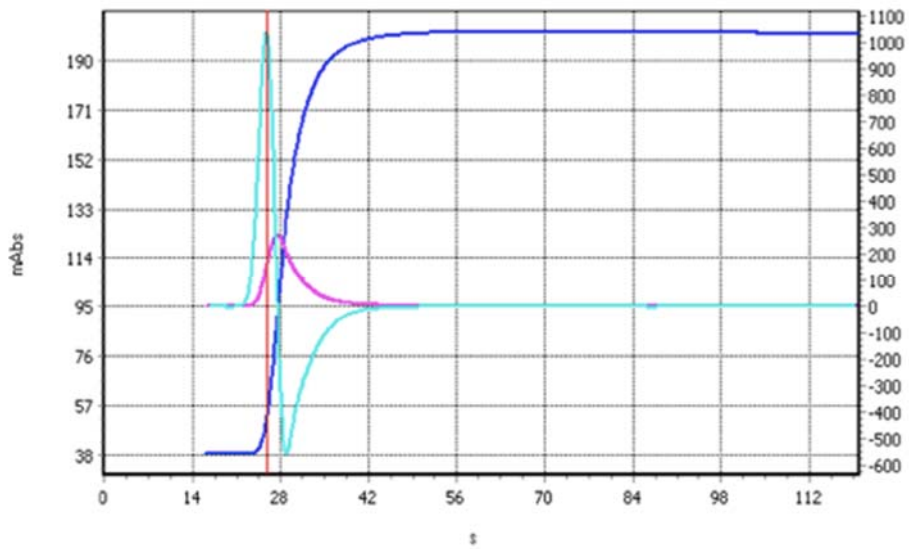
Pitfall 2 Analyser




Conventional Assays
aPTT
Intrinsic Pathway
Contact factors
No in vivo relevance
PT
Extrinsic Pathway
Tissue Factor
In vivo relevance
Pitfall 2
Analyzer
Fibrinogen
Fibrin
TT
Thrombin
Fibrinogen polymerisation

Conventional Assays

Pitfall 2
Analyzer



Errors and warnings

No errors

		Replicate 1	Replicate 2	Mean
Measured	**s**	25.8		25.8
	s	25.8		25.8

Conventional Assays

Pitfall 3
Fibrinogen after haemorrhage

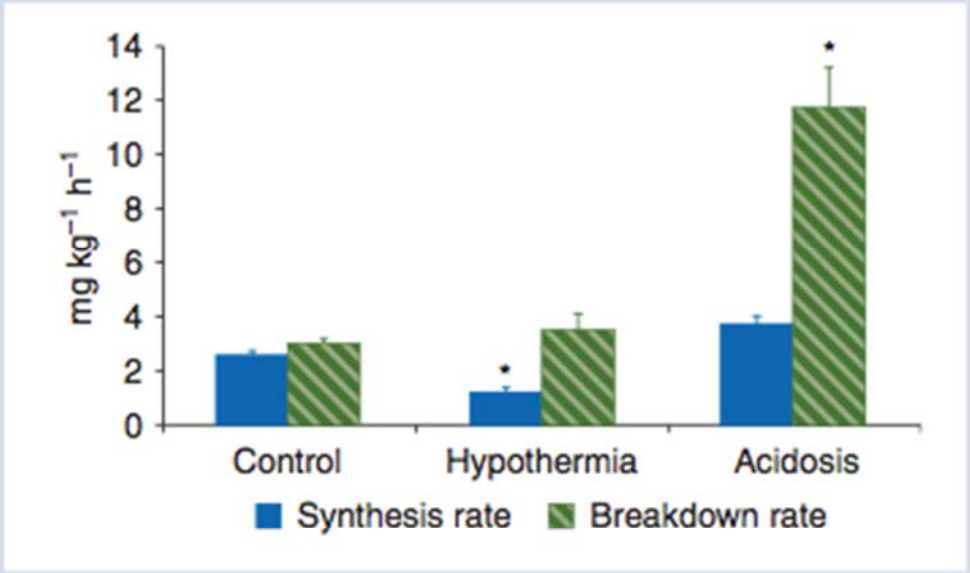


Fig 1 Changes in fibrinogen synthesis and breakdown in pigs after haemorrhage, hypothermia, and acidosis. Data from Martini and colleagues[17] and Martini and Holcomb.[18] *$P<0.05$ compared with control values.

Fries et al., Br J Anaesth 2010

Conventional Assays

Pitfall 3
Fibrinogen after haemorrhage

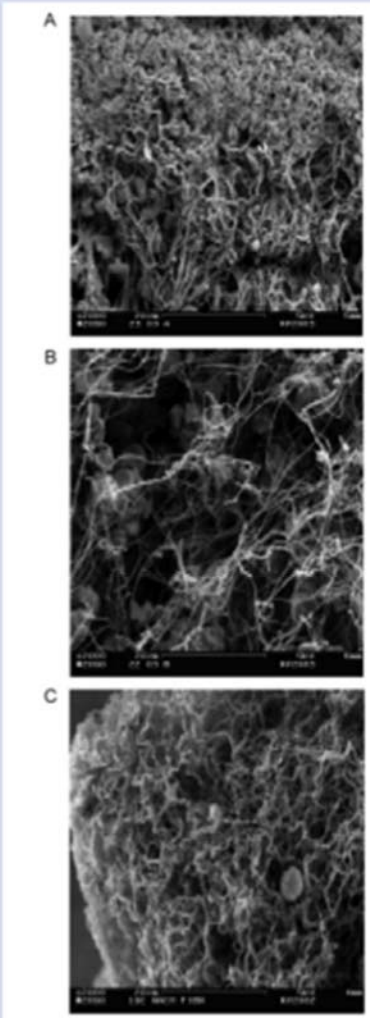


Fig 3 Electron microscopic scan of a ×2000 magnified blood clot in a non-diluted state (a), after 65% haemodilution with gelatin (b), and after administration of fibrinogen concentrate to compensate dilutional coagulopathy (c). The administration of fibrinogen was able to compact the rarefied fibrin network again.[21]

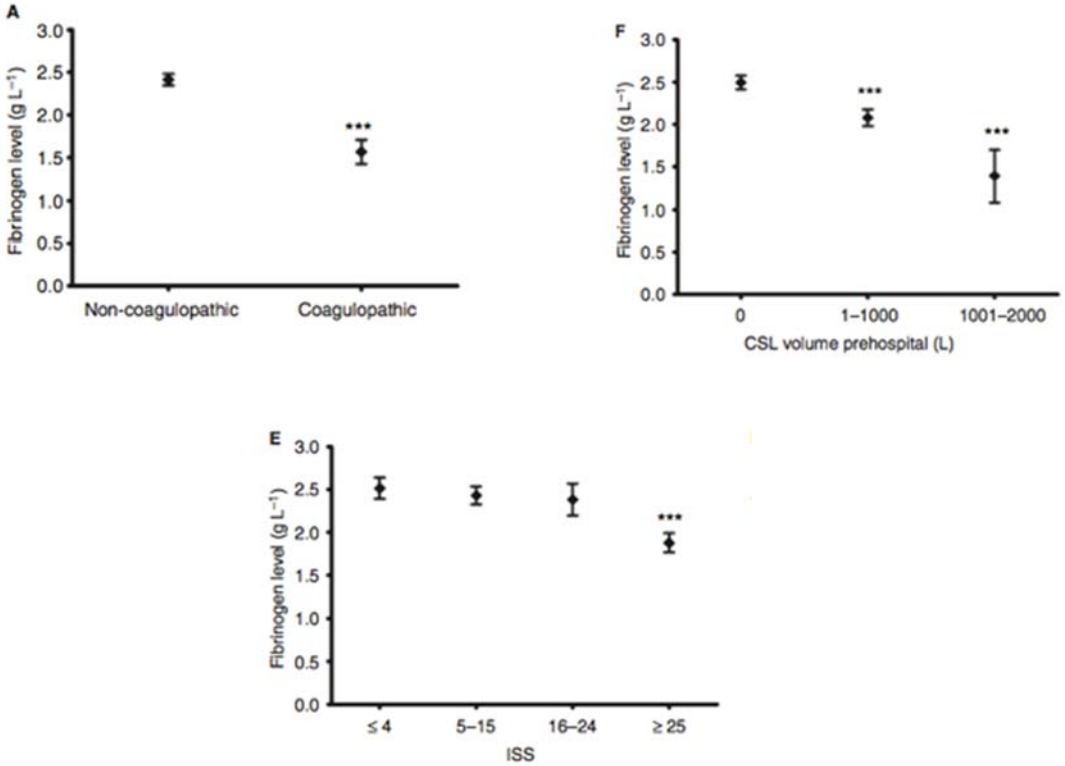
Fries et al., Br J Anaesth 2010

Conventional Assays

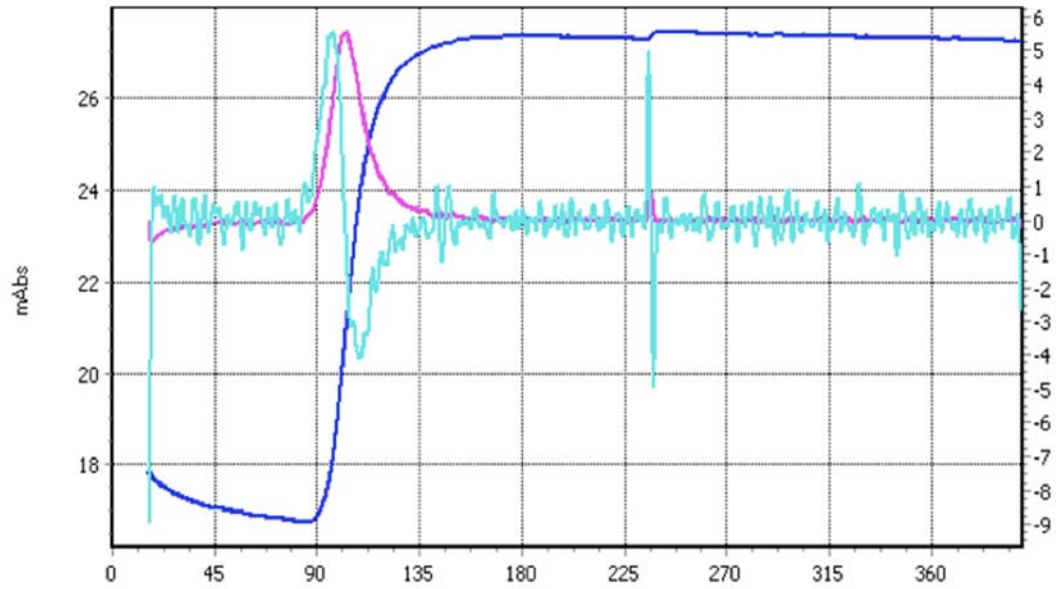
Fibrinogen levels during trauma hemorrhage, response to replacement therapy, and association with patients outcomes
Rourhe C, Curry N, Khan S, Taylor R, Raza I, Davenport R, Stanworth S, Brohi K
J Throm Haemost 2012

517/555 enrolled patients
Exclusion criteria: < 2000 mL of fluid before hospital arrival
ACT defined on Rotem results

Pitfall 3 Fibrinogen during trauma haemorrhage



Conventional Assays



Pitfall 3
Analyzer

Errors and warnings

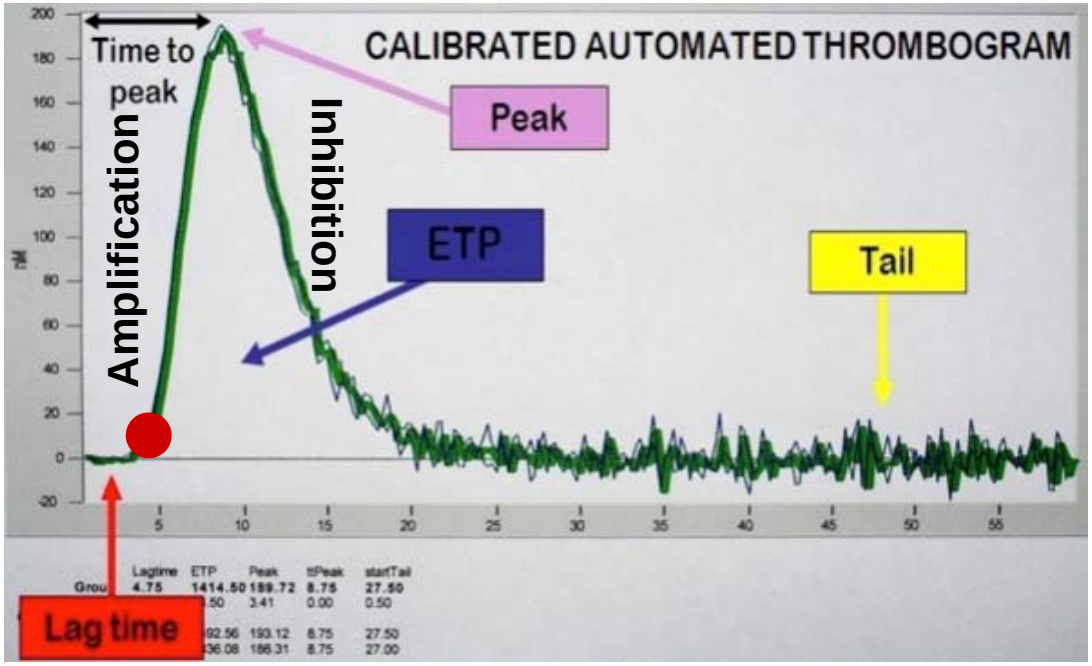
		Replicate 1
		Measured (s)
CE	5071	(Coag) First derivative peak not found
		Unit 1 (s)
RE	5100	Measured result failed

Validation rules
Rerun: modified fibrinogen, FibLow…

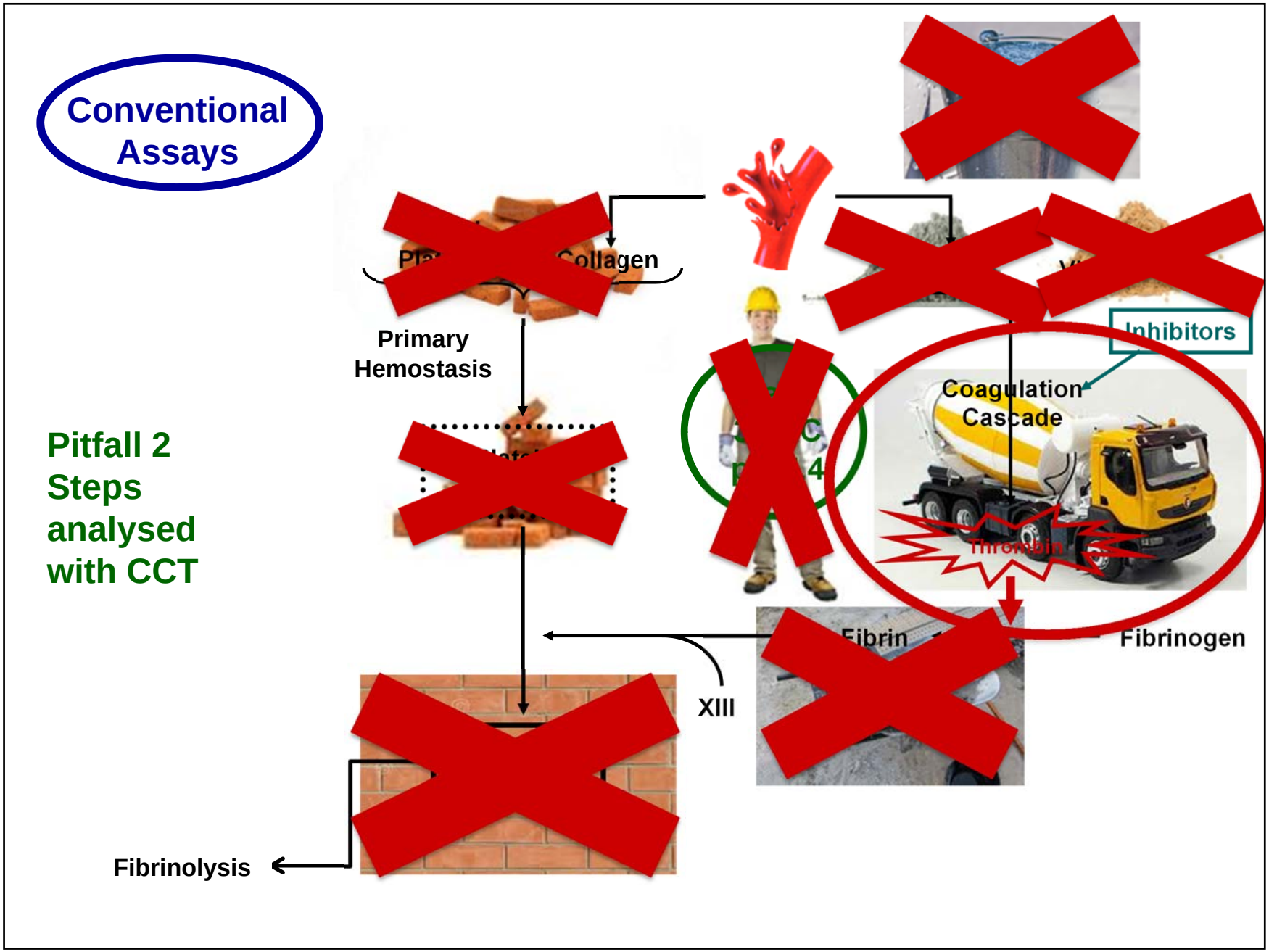
Coagulation results obtained after at least 45 min

New Assays

Thrombin Generation Assay (TGA)



Initiation


Conventional Assays
Pitfall 2 Steps analysed with CCT
Collagen
Primary Hemostasis
Inhibitors
Coagulation Cascade
Thrombin
Fibrin
Fibrinogen
XIII
Fibrinolysis

Conventional Assays

Thrombin Generation Assay (TGA)

TGA and Massive Bleeding

Little data in human
No POCT
Requires trained staff
Indepedent of fibrinogen level
No transfusion chart described
In vitro studies
Mainly studies on animal trauma models

TGA and Resuscitation Fluids

Altered TGA with HES but not with other fluids
Correction with PCC or cryoprecipitate
Weak improvement with Novoseven
No correction with fibrinogen

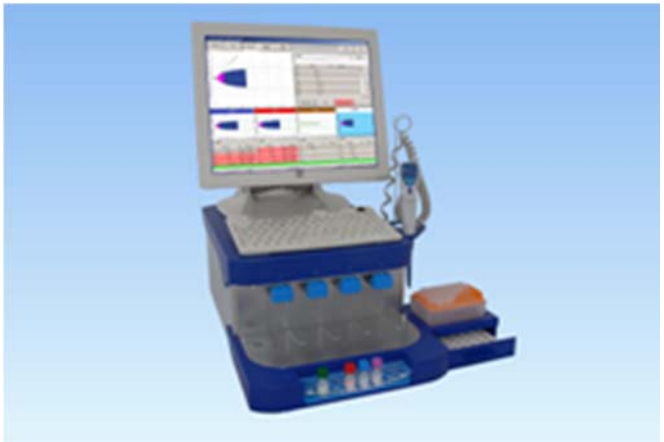
TGA and Acidosis

Pig trauma model
Induced acidosis
Reduction of the ETP and thrombin peak

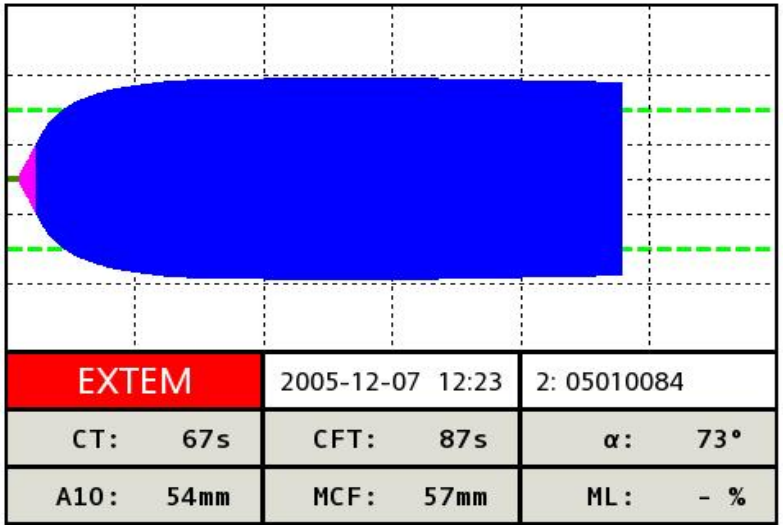
Caballo et coll, Bllod Transfu 2012
Darlington et coll, J Trauma 2011

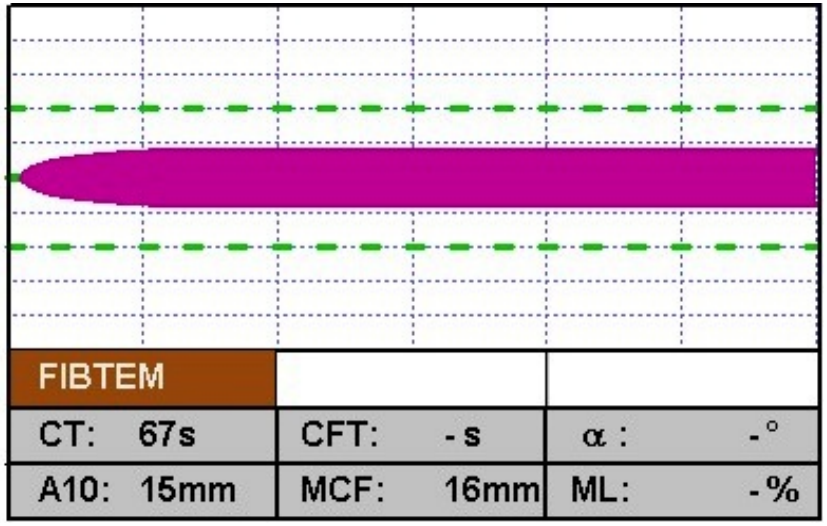
Rotem

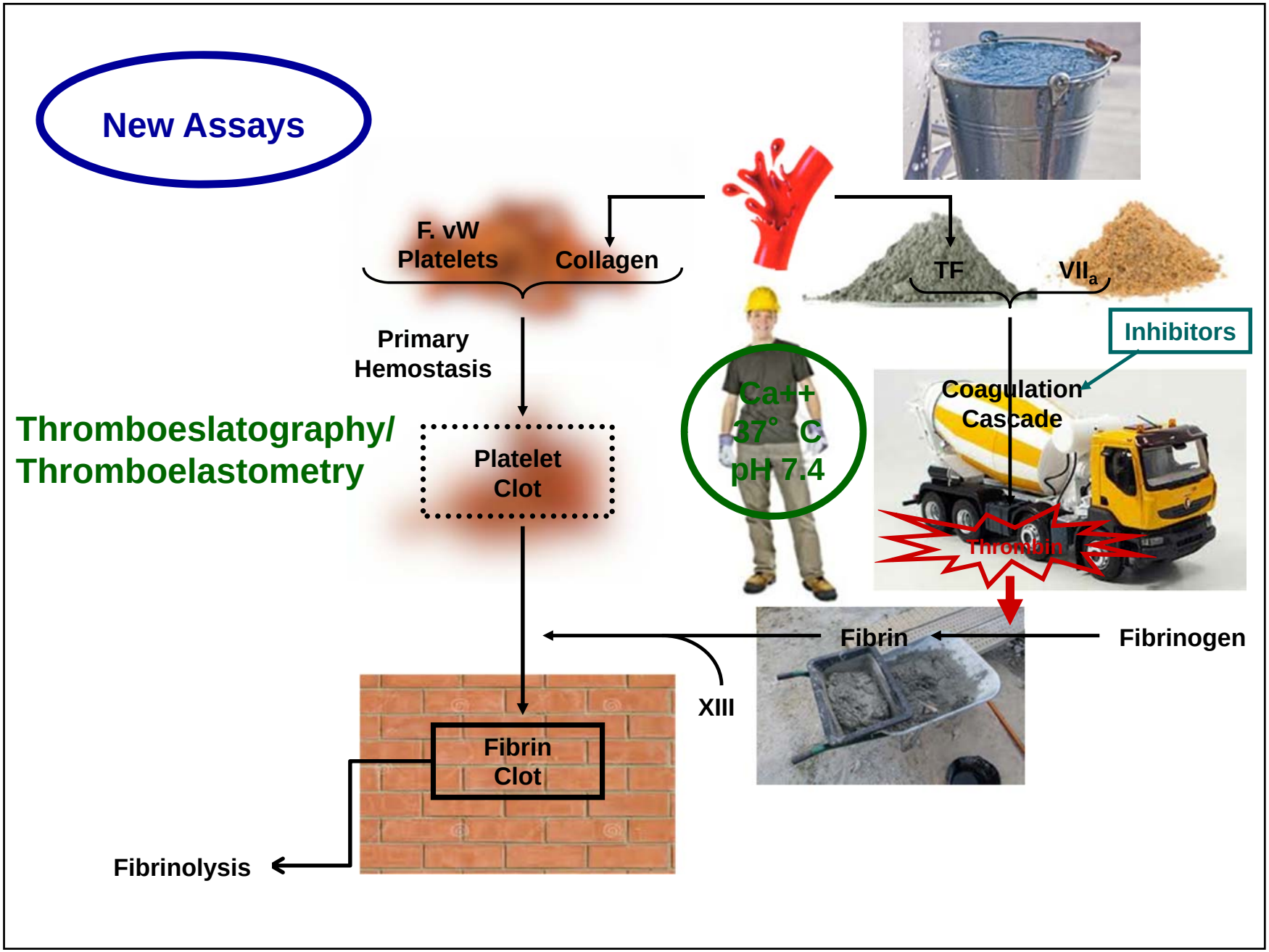
New Assays



Thromboeslatography/ Thromboelastometry






New Assays
F. vW
Platelets
Collagen
TF
VIIa
Inhibitors
Primary
Hemostasis
Thromboeslatography/
Thromboelastometry
Platelet
Clot
Ca++
37° C
pH 7.4
Coagulation
Cascade
Thrombin
Fibrin
Fibrinogen
XIII
Fibrin
Clot
Fibrinolysis

New Assays

Admission rapid thrombelastography can replace conventional coagulation tests in the emergency department: experience with 1974 consecutive trauma patients.
Holcomb J, Minei K, Scerbo M, Radwan Z, Wade C, Kozar R, Gill B, Albarado R, McNutt M, Khan S, Adams P, McCarthy J, Cotton B
Ann Surg 2012

Rotem

Patients

Memorial Hermann Hospital, Houston, Trauma Center
Deep trauma, exclusion of third-degree burns
>18 y
September 2009 – February 2011

Analysis

Immediatly at the admission
PT, aPTT, Fibrinogen
Platelets
} CCT (Conventionnal Coagulation Tests)
r-TEG

Outcomes

Correlations r-TEG-CCT (<0.3, 0.3-0.7, >0.7)
Correlations r-TEG-transfusions
Correlations CCT-transfusions

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Ann Surg 2012

Rotem

Résultats
1908 trauma patients included

Correlation of r-TEG values with CCTs (n=1974)

	PT	aPTT	INR	Platelet Count	Fibrinogen
ACT, sec	0.35	0.47	0.52	-0.15	-0.17
r-value, min	0.24	0.32	0.37	-0.14	-0.17
k-time, min	0.21	0.44	0.34	-0.25	-0.32
α-angle, degree	-0.23	-0.41	-0.33	0.34	0.53
MA, mm	-0.22	-0.35	-0.27	0.42	0.63
G-value	-0.02	-0.03	-0.03	-0.01	0.01

ACT, r-value: deficit in factors, hemodilution
k-time:deficit in fibrinogen, (deficit in factors)
α-angle, degree: deficit in fibrinogen, deficit in platelets
MA: deficit in fibrinogen, deficit in platelets
G-value: clots'strength

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Ann Surg 2012

Rotem

Multiple regression analysis

Prediction of pRBC transfusion in the first 6 hours of admission:
- Predicted: r-TEG, PT, aPTT, INR
- Non predicted: fibrinogen, platelets

Prediction of FFP and platelets transfusion
- Predicted: r-TEG, PT, aPTT, INR, platelets number
- Non predicted: fibrinogen

Massive transfusion
- Predicted: r-TEG and CCT (α angle is the more predicted)

Mortality at 6h and 30d
- Predicted: r-TEG, aPTT
- Non predicted: PT, INR, platelets number, fibrinogen

Conclusions

r-TEG is better then the 5 CCT in the management of MB
Early detection of patient with accute needs of transfusion
r-TEG at the admission could (should) replace CCT

European Recommandations: grade 2c (2010) vers grade 1c (2013)

New Assays

Rotem

Advantages

Extensive coagulation exploration
- Coagulation cascade
- Fibrino-formation
- Fibrinolysis

Whole blood
- Short TAT
- No centrifugation
- Hematocrit
- Platelets

POCT

Real-time analysis, no buffering

Transfusion protocols

Recommanded in the European guidelines

Disadvantages

Not sensitive to platelets function
- Inhibitors of platelet function
- Must be used with platelet function analyser (Verify-Now…)

Moderatly sensitive to anticoagulants (heparin, …)

Performed at 37° C

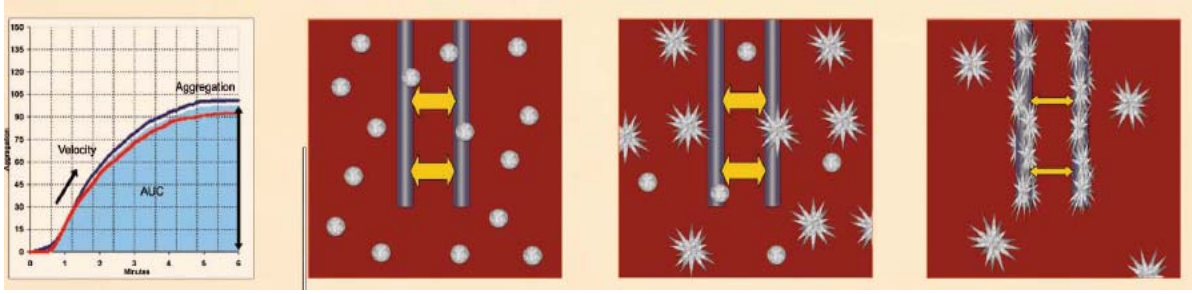
Recalcification

High concentration of TF

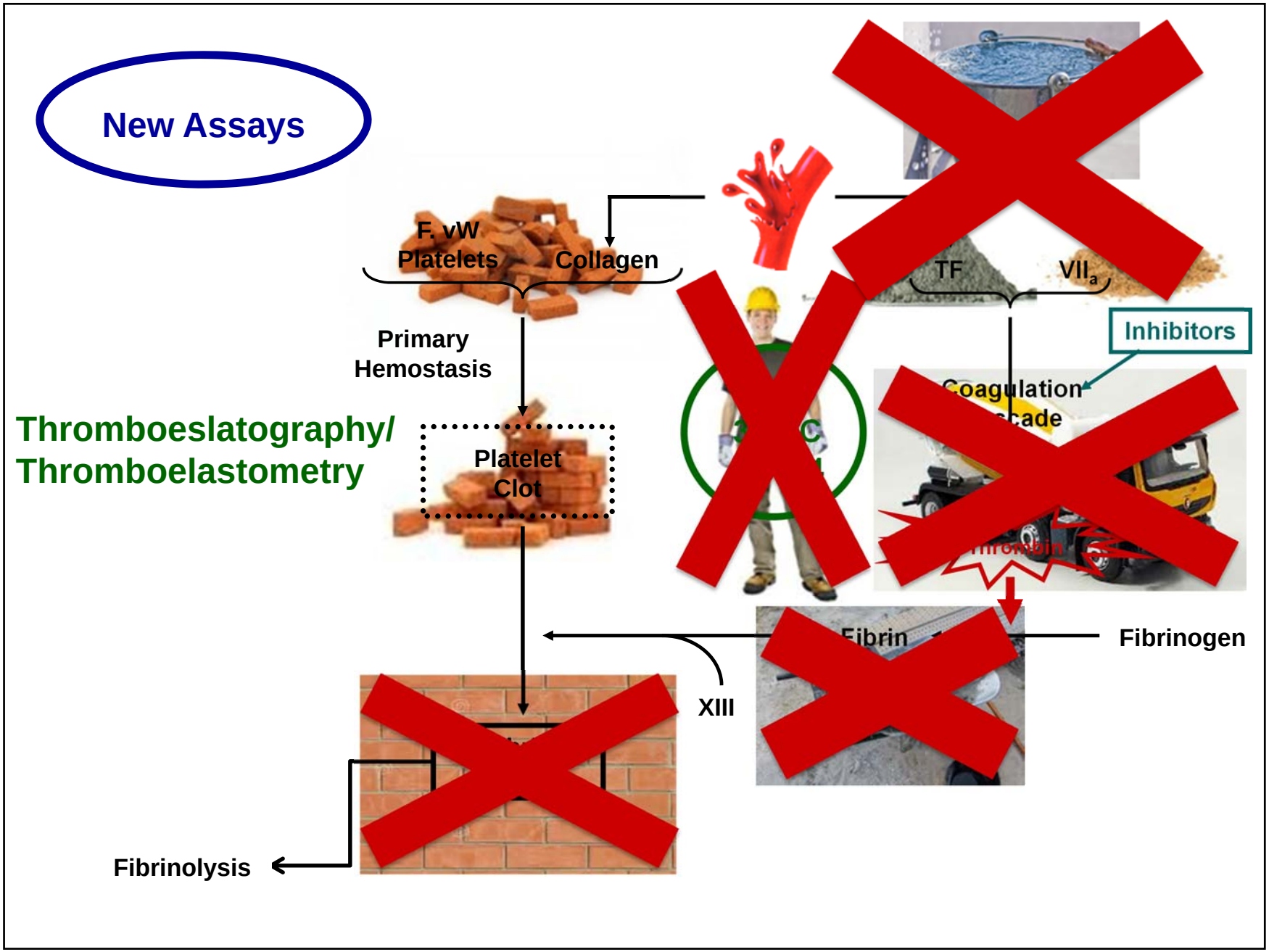
No information about the sub-endothelium functionnality

New Assays

Multiplate



Solomon et coll, Thromb Haemos 2011
Retrospective study on 163 traumas (ISS>18, 12,3% death)
ADP, COL, TRAP
ADP and TRAP: abnormal values in the non survival group
Platelet dysfunction is a sign of ACT


New Assays
F. vW
Platelets
Collagen
TF
VII$_a$
Inhibitors
Primary
Hemostasis
Thromboeslatography/
Thromboelastometry
Platelet
Clot
Coagulation
Fibrin
Fibrinogen
XIII
Fibrinolysis

POCT in Massive Bleedings

Conventional Assays

Specific assays
Slow
No transfusion protocols
Not predictive enough

Accurate
Validated
Cheap

New Assays

Global assays
Fast
Real-time results
Transfusion protocols
Predictive of blood requirement

Validation
Variability
More expensive

pRBC: 116 euros
FFP: 90 euros
Platelets: 413 euros
Fibrinogen: 350 euros