

Patient Blood Management Uniklinik Balgrist 9. 6. 2011

## Gerinnungsmanagement in der Orthopädie

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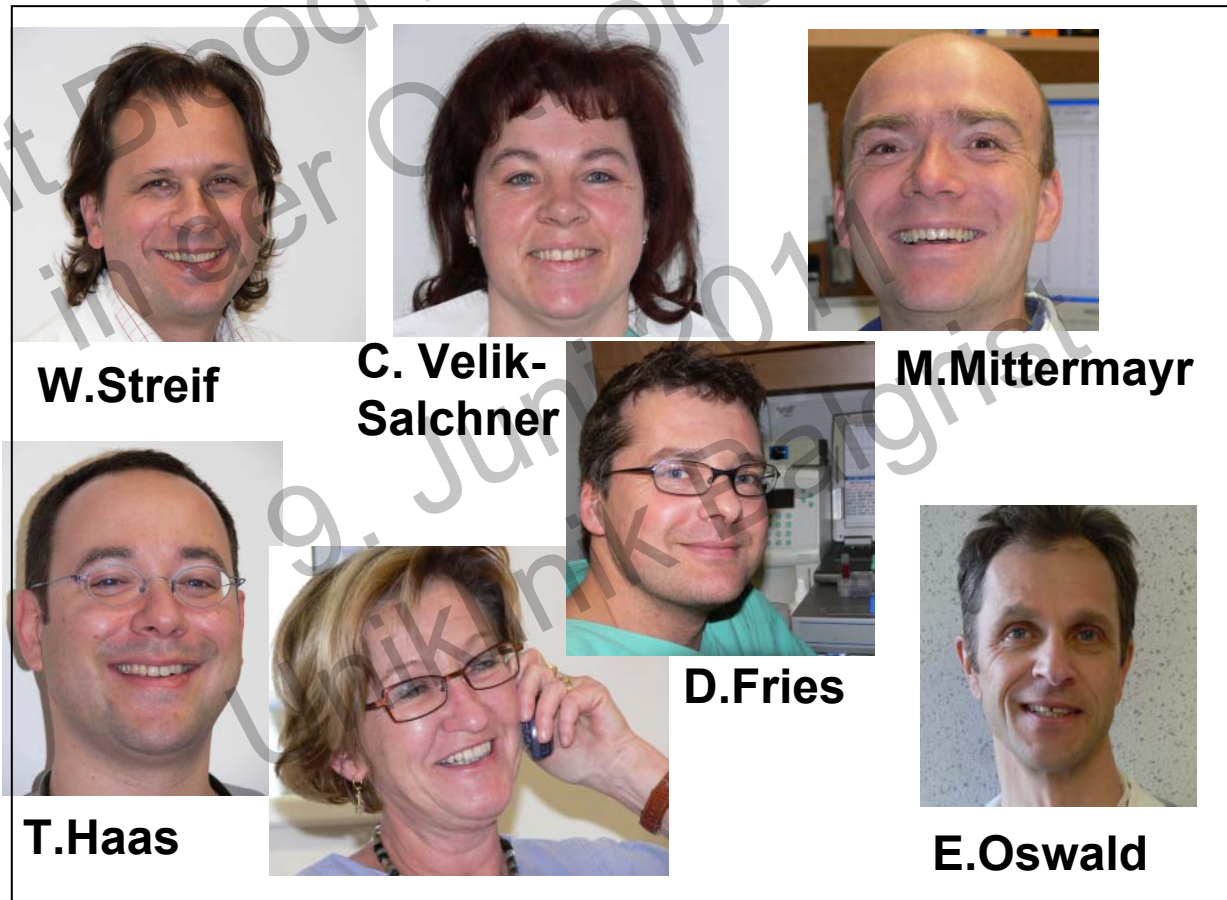


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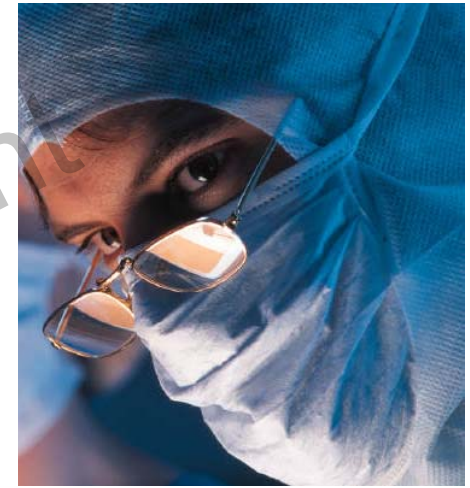
## Financial disclosure:

Baxter, Braun, CSL Behring, Fresenius,  
NovoNordisk, Octapharm, Tem Innovations

### Clotwork Research Group



# Gerinnungstherapie und Orthopädie ?



Ausgedehntes Weichteiltrauma  
Spongiosa –konstante Blutung  
OP Dauer

Unterschiedliches Patientengut

junge Patienten – hypokoagulabel

geriatr. Patienten- hyperkoaguabel

- begrenzte Kompensation

- Anämie, Medikationen



Gerinnung ist furchtbar kompliziert.....

ja/nein

Die Infusionen sind schuld.....

teilweise

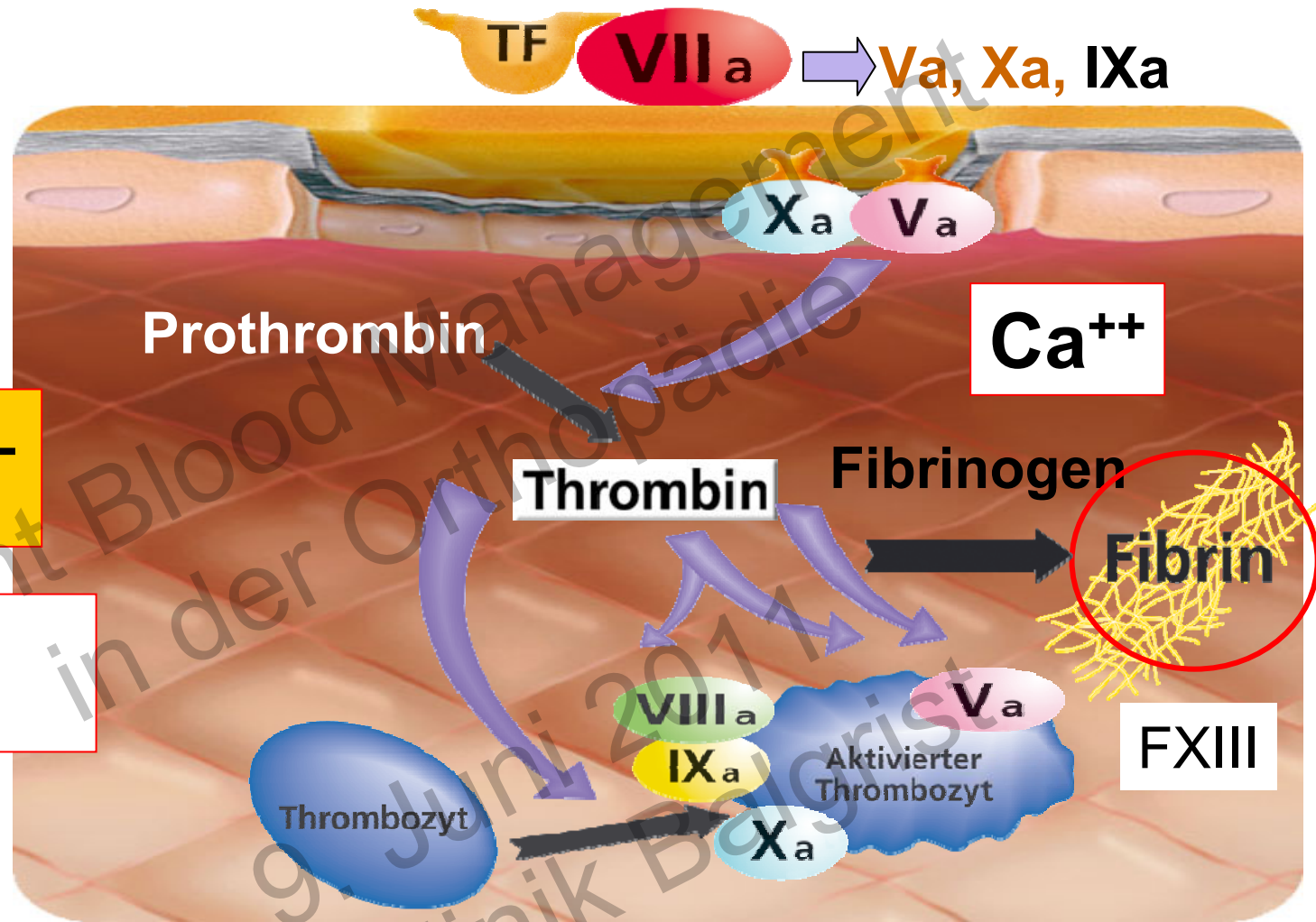
PT, aPTT, TZ .....dann weiß man mehr

nicht wirklich

FFP sind immer gut.....

sehr fraglich

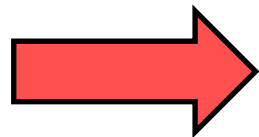
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**GF mg/L**

**Fibrinogen g/L**  
**FXIII >60%**

**TZ**  
**50-100 000/μl**



Chirurgisches Problem  
Thrombinmangel  
Substratmangel  
Fibrinolyse

## Angeborene Koagulopathie

## Erworbene Koagulopathie

**Gerinnungsfaktoren**

•Einzelfaktor

•mehrere

**Thrombin**

•vermindert

•unterschiedlich

**Fibrinogenkonz.**

•normal

•vermindert

**Fibrinpolymerisation**

•normal

•gestört

**TZ**

•normal

•vermindert

**Gewebetrauma**

•nein

•ja

**Dilution**

•nein

•ja

**Fibrinolyse**

•nein

•möglich

**Dynamik**

•nein

•ja

**Diagnostik**

**PT/aPTT....**

**Funktionelle Messung**

# Acquired bleeding states

Blood loss  
Dilution  
Consumption

decreased CF

INR

decreased fibrinogen conc./polym.

decreased platelets

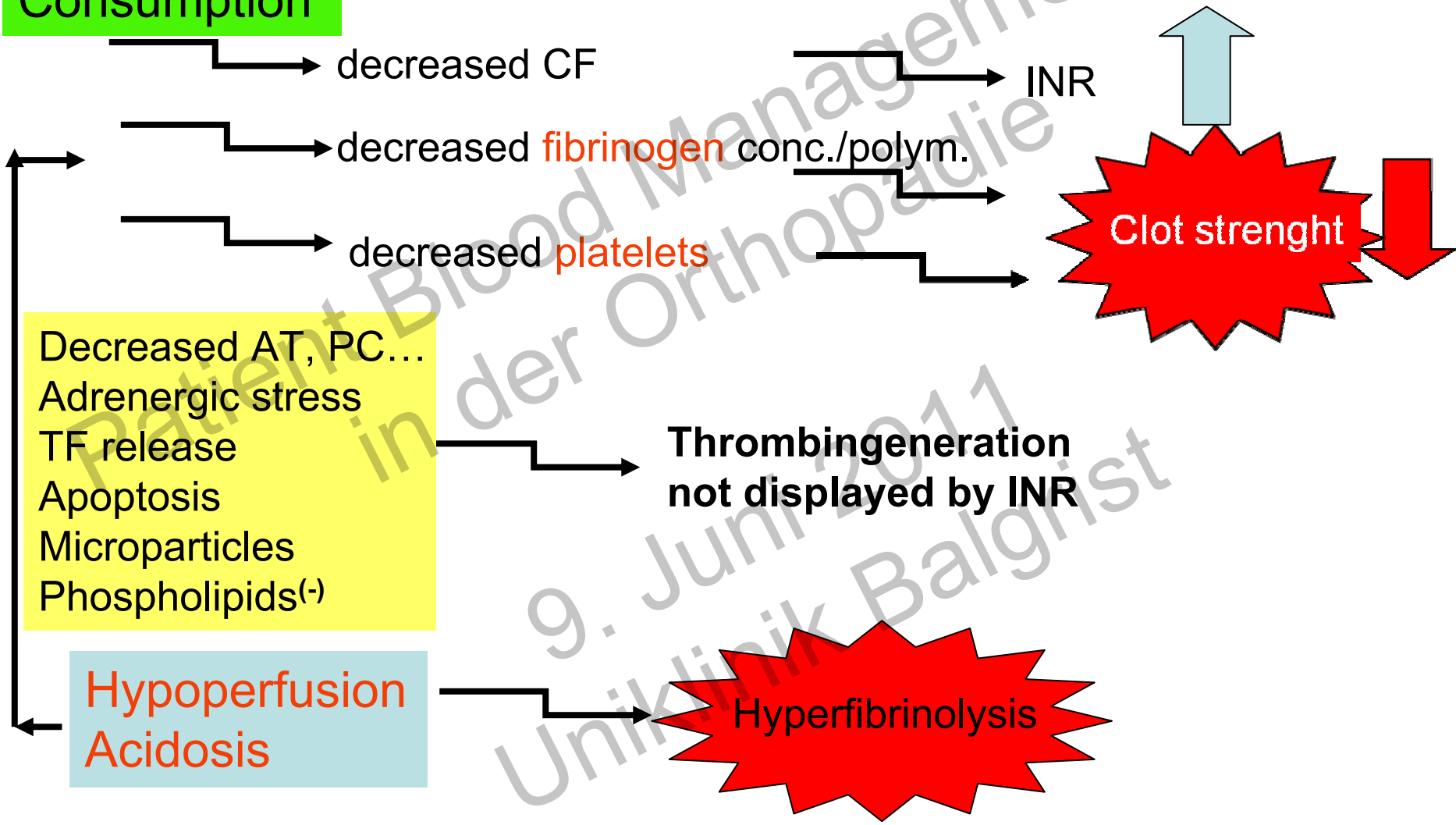
Clot strenght

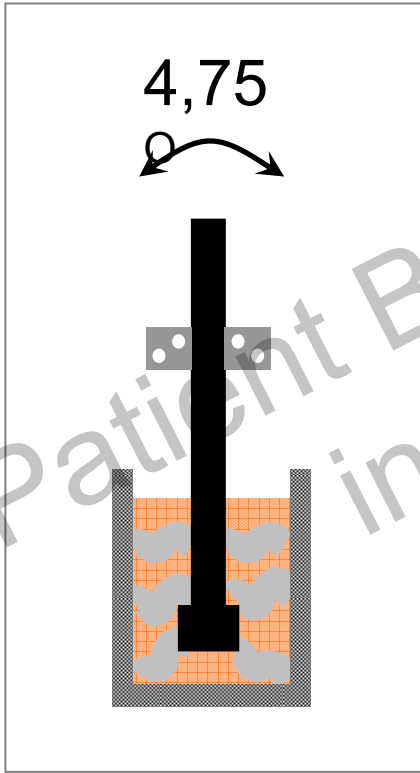
Decreased AT, PC...  
Adrenergic stress  
TF release  
Apoptosis  
Microparticles  
Phospholipids(-)

Thrombination  
not displayed by INR

Hypoperfusion  
Acidosis

Hyperfibrinolysis

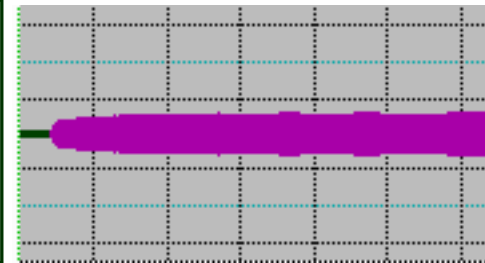




EXTEM

+ TZ- Blockade =

FIBTEM



MCF: >9mm



### 3 Parameter

#### *CT (GF, Inhibitoren)*

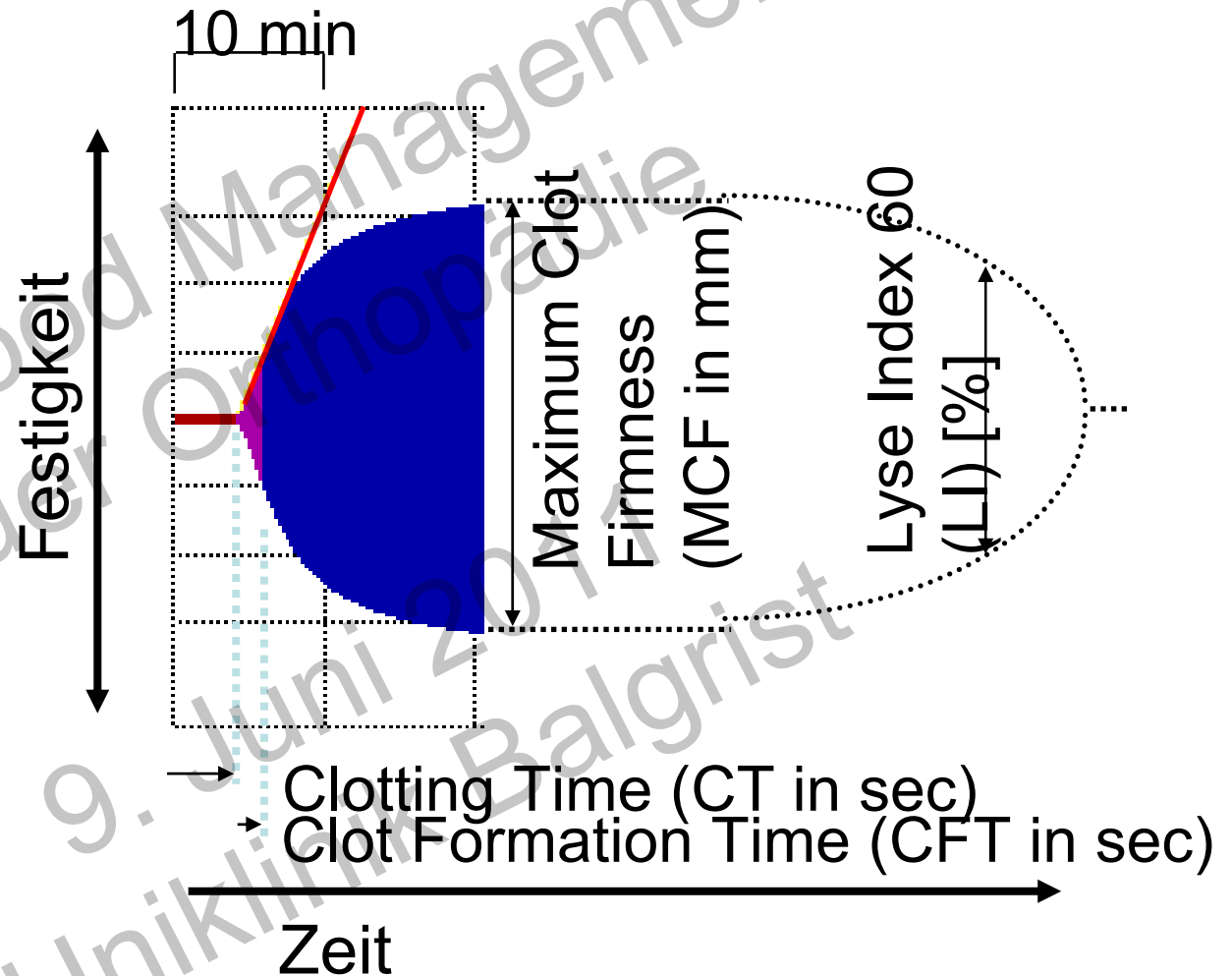
Zugabe des Aktivators bis Beginn der Gerinnungsbildung

#### *MCF (TZ, Fib, FXIII)*

Maximale Amplitude der TEM-Kurve

#### *LI 30 und 60*

% noch vorhandener MCF



## Kristalloide

## Kolloide

Verteilung PV und IF

Volumeneffekt 25% (1:4)

KOD

interst. Compl.



**Dilutionsazidose**

Leukozytenaktivierung

O<sub>2</sub> Radikale, Apoptose

endotheliale Dysfunktion

hypertone Lösungen ?

Verteilung PV (IF)

Volumeneffekt 100% (1:1)

KOD

interst. p<sub>onk</sub>



**Fibrinogenpolymerisation**

Anaphylaxie

Nierenversagen

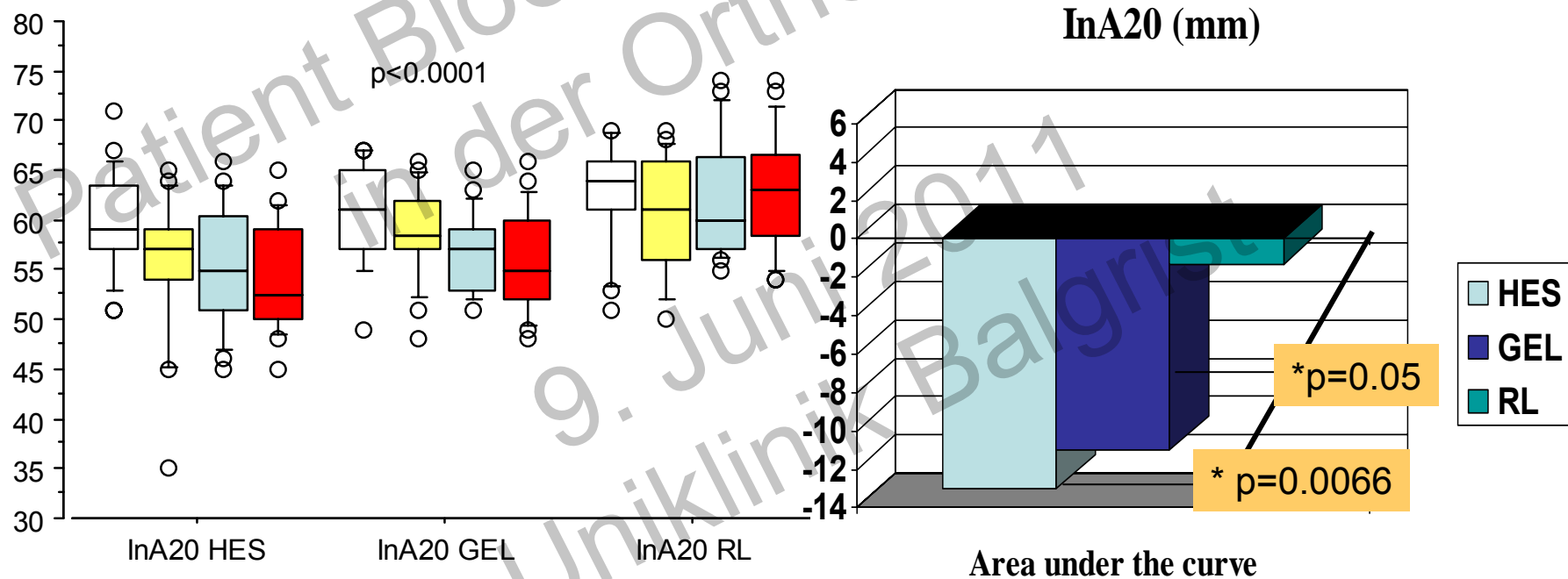
Viskosität- Mikrozirkulation ?

**Ödem**

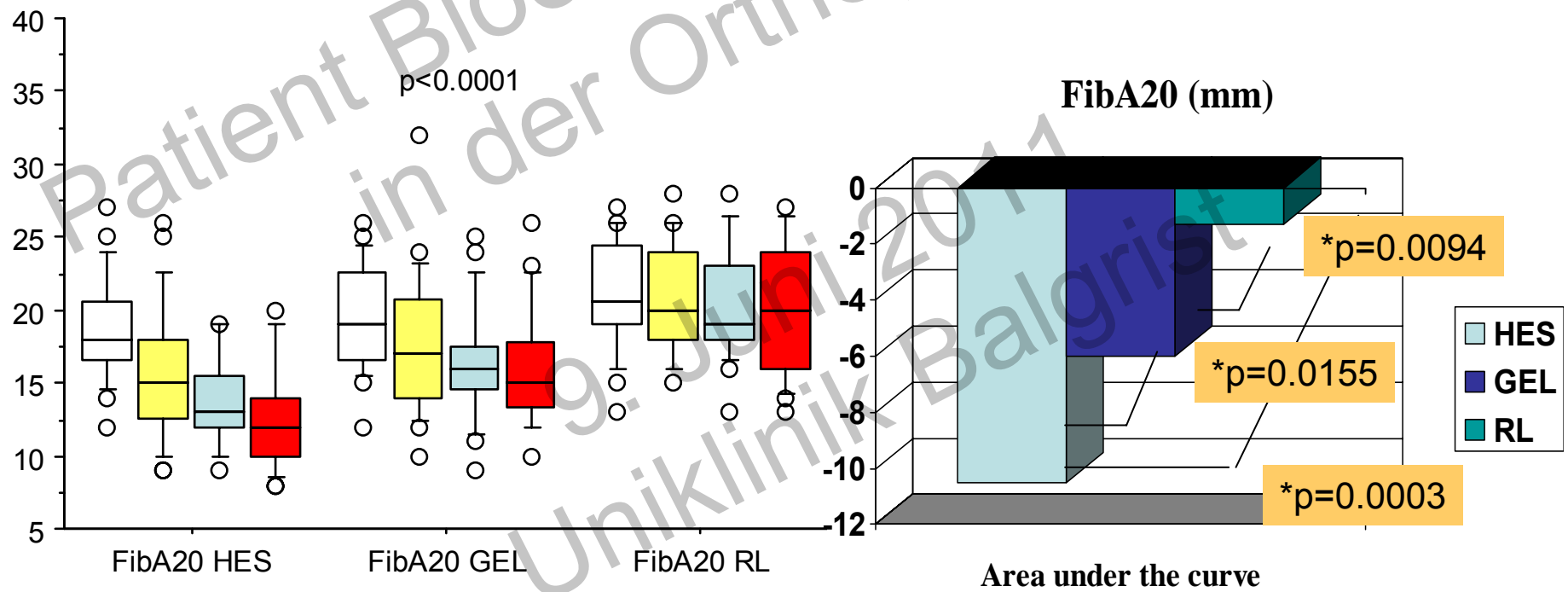
**Gerinnungsstörung**

# The effects of perioperatively administered colloids and crystalloids on primary platelet-mediated hemostasis and clot formation.

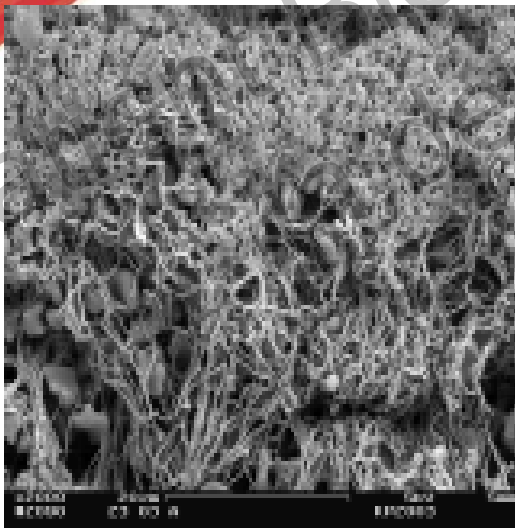
Innerhofer P, Fries D et al. *Anesth Analg* 2002;95:858-65



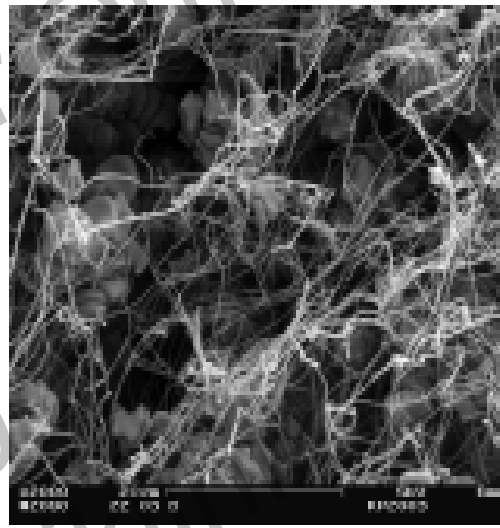
## Fibrinogen component of the clot (Fib A20)



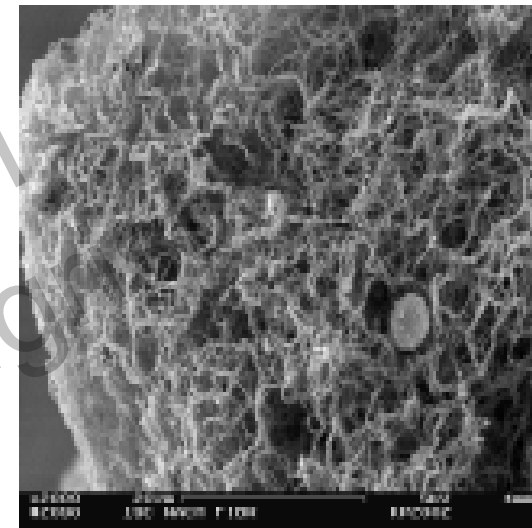
# Elektronenmikroskopie



baseline



dilution



fibrinogen

A microscopic image showing a dense, interconnected network of purple fibrin fibers. Several red blood cells, appearing as bright red, biconcave discs, are trapped within the mesh. The background is dark, highlighting the intricate structure of the fibrin and the presence of the cells.

Fibrinogenkonzentration

≠

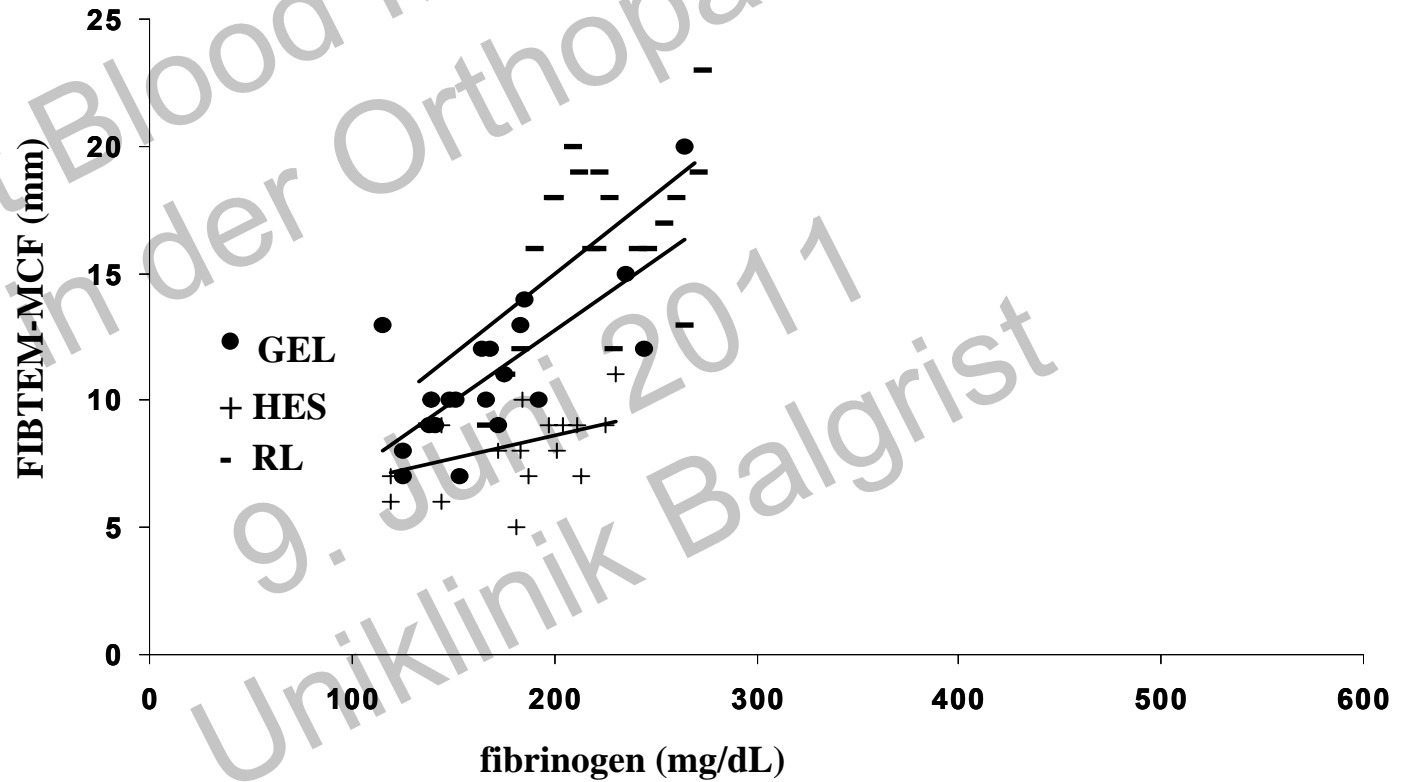
Fibrinpolymerisation

Konzentration  
Thrombin  
FXIII  
Fibrinolyse  
Fluids (HES)

# Hemostatic changes following crystalloid or colloid fluid administration during major orthopaedic surgery: role of fibrinogen administration. [M. Mittermayr Anesth Analg 2007](#)



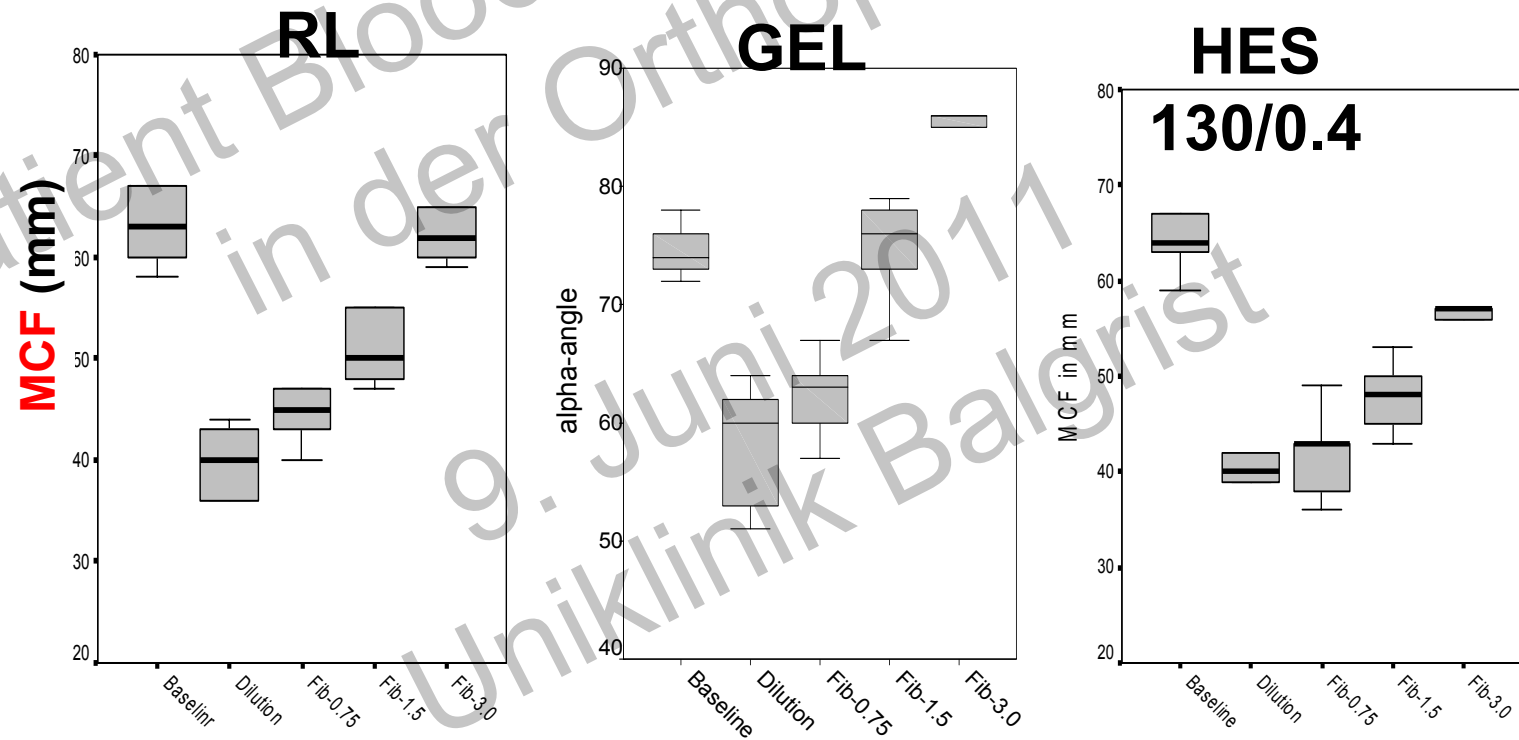
C



# The effect of fibrinogen substitution on reversal of dilutional coagulopathy: an in vitro model.

D. Fries BJA 2006

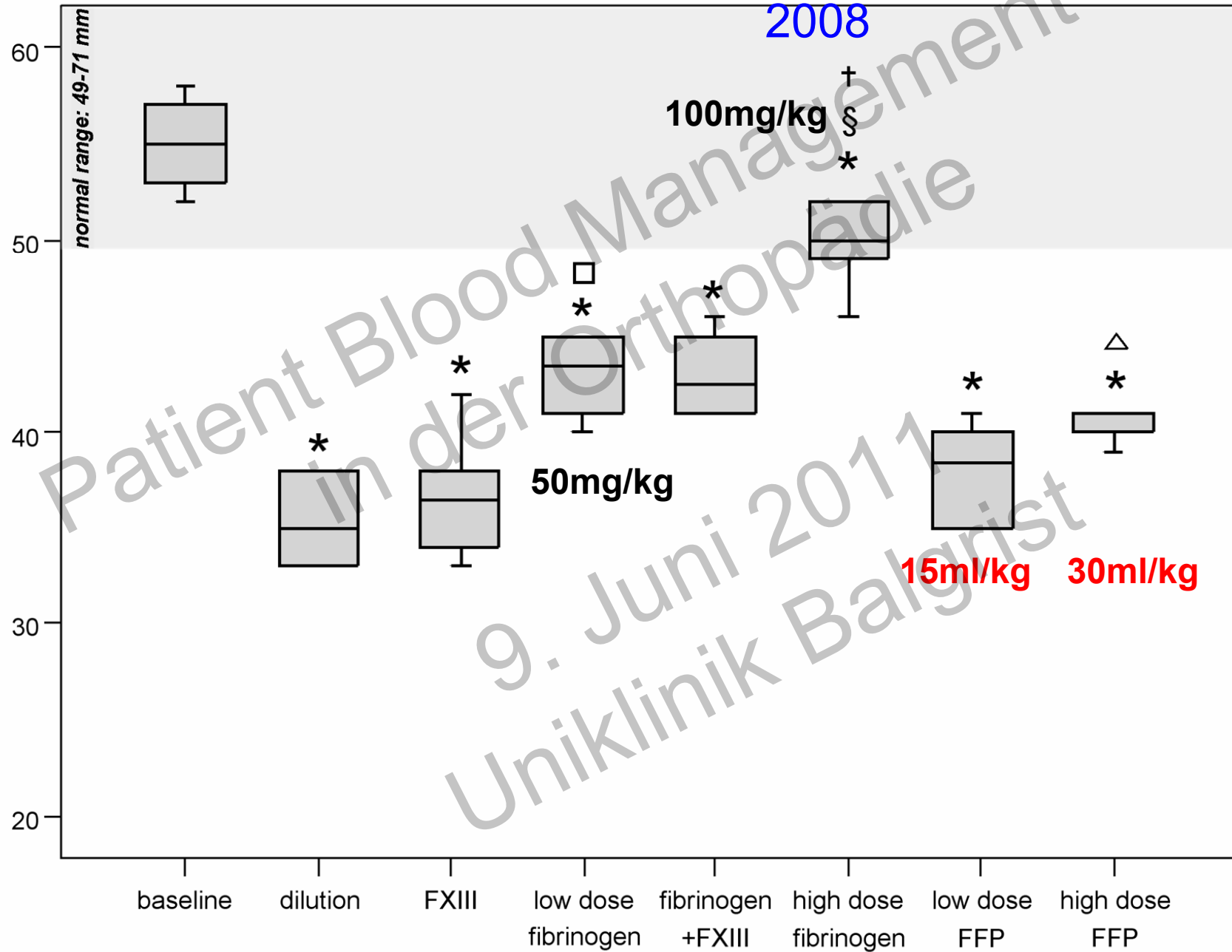
BL- Dilution + **Fib 0.75-1.5-3.0**





MCF [mm]

T. Haas Anest Analg  
2008

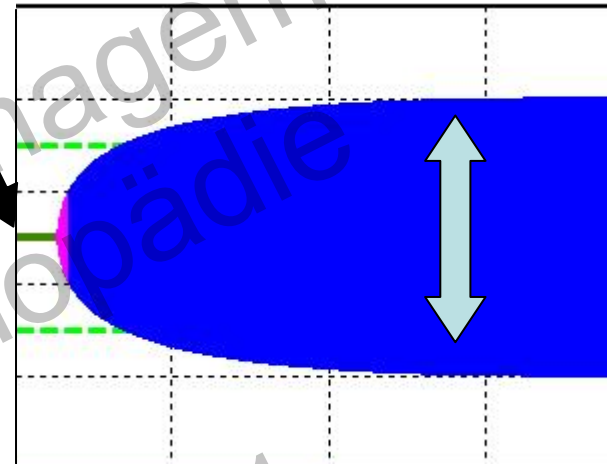


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15ml/kg 30ml/kg

# Dilution und TEG®/ROTEM®

Mardel  
Mortier  
Egli  
Jamnicki  
Petroianou  
Niemi  
Entholzer  
Ruttmann  
Ruttmann  
Fries  
Innerhofer  
Fenger-Eriksen  
Mittermayr  
Haas



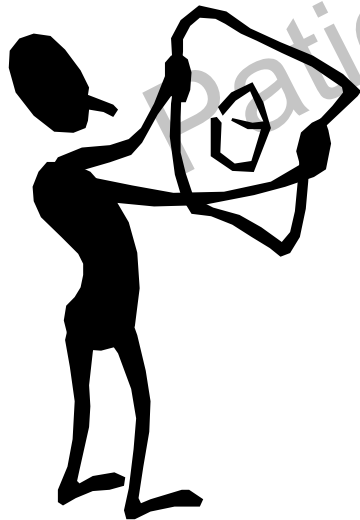
↓ Clotbildung (Fibrinogenpolymerisation)

↑ CT-Zeit (>60% Dilution, ca. 200% BV)

Kolloide > Kristalloide: HES > GEL > ALB

- British Committee BJH 2004; Update 2006
- ASA Guidelines Anesthesiology 1996; Update 2006
- European Guidelines Crit Care Med 2007; Update 2009
- German Guidelines 2009

- FFP for „surgical bleeding“ (INR, aPTT, **TEG**)
- Fibrinogen critical: <150-200 mg/dl ?
  - Cryoprecipitate
  - **Fibrinogen concentrate 50mg/kg** (D, EU)
- PCC for OAC reversal (D, UK)
- PCC may be necessary (<40%, D)
- Platelets below  $50 \times 10^9/L$
- **rFVIIa**



## FFP- effektiv ?

- Is FFP clinically effective ?

A systematic review of randomized trials.

**Stanworth SJ BJH 2004;126:139-152**

57 Studien: nur 6 Studien (1 Studie chirurg. Ind.)  
mögl. Benefit

- The role of prophylactic FFP in decreasing blood loss and correcting coagulopathy in cardiac surgery. A systematic review.

**Casbard AC Anaesthesia 2004;59:550-58.**

6 Studien: kein Effekt auf Blutverlust

# Changes after FFP

Hedin A and Hahn G. Clinical Science 2005;10:217-224

- 1000ml 5% albumin or autologous plasma
- without blood loss/deficiency

| Albumin  | FFP      |
|----------|----------|
| PV + 17% | PV + 21% |
| Fib -12% | Fib + 6% |
| AT -16%  | AT + 3%  |
| Tz - 7%  | Tz - 10% |
| PT ↑     | PT ⊥     |
| aPTT ↑   | aPTT ⊥   |

volume expans.+ low conc. -> difficult to correct deficiency

# Gerinnungstherapie mit FFP

## Pro

**Entsprechend Guidelines**  
**Aktivatoren+Antikoagulatoren**  
**Geringes Thromboserisiko**  
**“physiolog.” Volumenersatz**  
**kostengünstig**

## Contra

**Blutverlust minimiert ?**  
**Zeitverzögerung**  
**Wechselnde und niedrige Konz.**  
**(1g Fibrinogen=2FFP)**  
**Gezielte Korrektur unmöglich**  
**Volumenexpansion**

- Anämie, Thrombopenie
- EK und TK vermehrt nötig

**Nebenwirkungen**

- TACO, TRALI, TRIM, MOF
- Infektionen

# Alternative: Faktorenkonzentrate

## Pro

**Sofort infundierbar**  
**Definierte hohe Konz.**  
**Ohne Volumenexpansion**  
**Nachweislich effektiv**  
**Selektive Ther. möglich**  
**Kein TACO, TRALI, TRIM**  
**virusinaktiviert**

## Contra

**Kosten**

- 1g Fibkonz. 250€
- 2FFP ca. 120€

**Thromboserisiko ?**  
**Keine random. Studien**

## **Dagnosis and Treatment of Trauma Induced Coagulopathy study (DIA-TRE-TIC)**

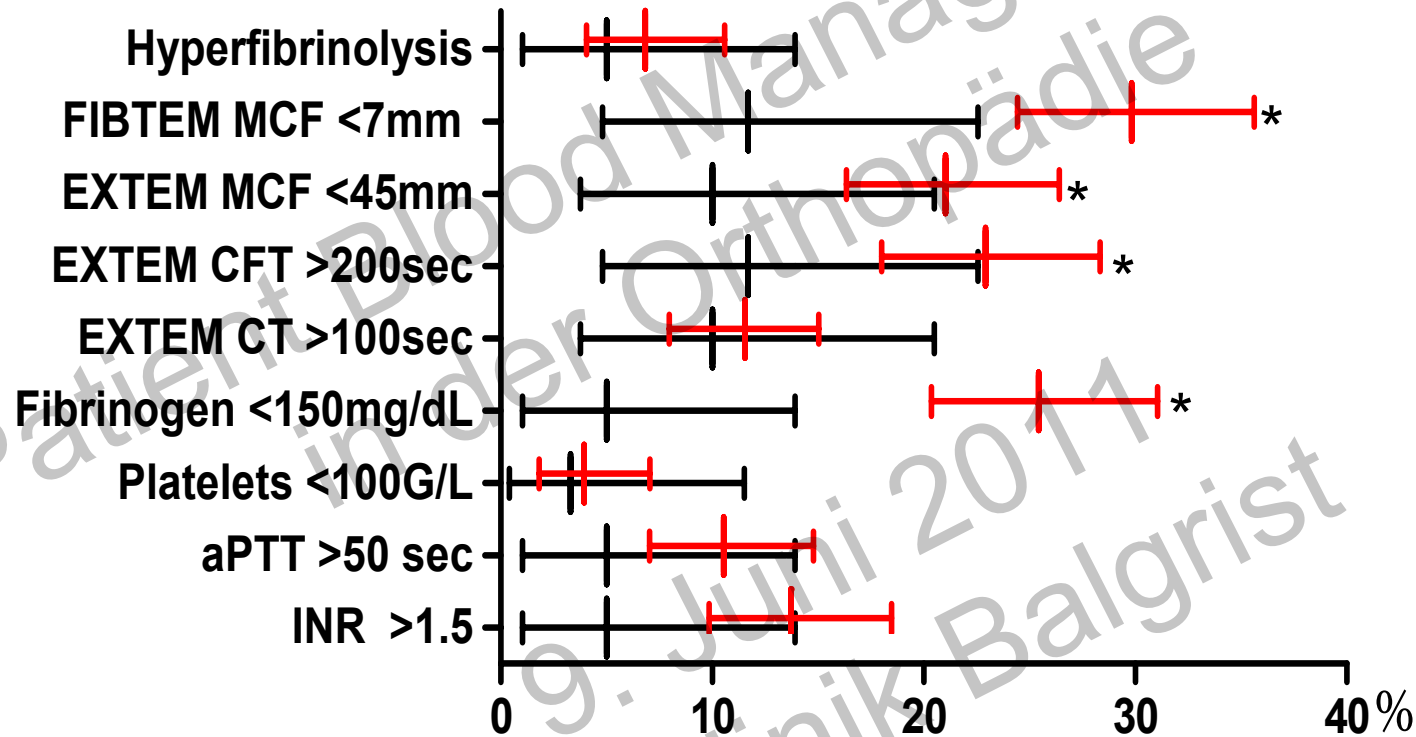
Kohortenstudie Universitätsklinik Innsbruck (2005-2008)  
334 Traumapatienten (ISS >15)

### **Fragestellungen:**

- Prevalenz und Bedeutung von Gerinnungsstörungen bei Traumapatienten (BJA 2011 in press)
- **Therapie und Outcome (n=144 Polytraumapat.)**

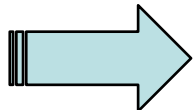


Fig 1 Prevalence of abnormal coagulation tests in patients with isolated brain injury (n=60) and multiple injuries (n=274)



# Ergebnisse Transfusionen

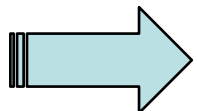
|                           | Nur Faktoren<br>(n=66) | FFP +<br>Faktoren<br>(n=78) | p value |
|---------------------------|------------------------|-----------------------------|---------|
| EK (U)                    | 2 (0, 4)               | 9 (5, 12)                   | <0.001  |
| Transfundierte Pat.(n)    | 40 (60.6)              | 76 (97.4)                   | <0.001  |
| FFP (U)                   | 0 (0, 0)               | 10 (5, 13)                  | <0.001  |
| Transfundierte Pat.(n)    | 0 (0)                  | 78 (100)                    | NT      |
| TK(U)                     | 0 (0, 0)               | 1 (0, 2)                    | <0.001  |
| Transfundierte Pat.(n)    | 3 (4.5)                | 44 (56.4)                   | <0.001  |
| Fibrinogen Konzentrat (g) | 4 (2, 4)               | 4 (2, 7)                    | 0.007   |
| Patienten behandelt(n)    | 66 (100)               | 70 (89.7)                   | 0.125   |
| PCC (IE)                  | 0 (0, 1000)            | 750 (0, 1800)               | 0.006   |
| Patienten behandelt(n)    | 23 (34.8)              | 40 (51.3)                   | 0.064   |



Große Unterschiede im Transfusionsbedarf

# Ergebnisse Outcome

|                        | Nur Faktoren<br>(n=66) | FFP +<br>Faktoren<br>(n=78) | p value      |
|------------------------|------------------------|-----------------------------|--------------|
| ICU (Tage)             | 12 (6, 24)             | 14 (7, 30)                  | 0.217        |
| KH Aufenthalt (Tage)   | 24 (12, 35)            | 29 (16, 50)                 | 0.074        |
| Sepsis (n)             | 11 (16.9)              | 28 (35.9)                   | <b>0.014</b> |
| MOF (n)                | 12 (18.2)              | 29 (37.2)                   | <b>0.015</b> |
| Mortalität 30 Tage (n) | 5 (7.6)                | 6 (7.7)                     | 0.979        |
| Thrombembolie (n)      | 6 (10.0)               | 6 (7.7)                     | 0.772        |



**Transfusionsbedingte Unterschiede ?  
Randomisierte Studie zur Klärung notwendig !**

## Take Home.....

- **Erworbene  $\neq$  angeborene Koagulopathie**
- **Fibrinpolymerisation/Gerinnselstärke vorrangig betroffen**
- **viskoelastisches Monitoring wichtig und hilfreich**
- **HES bei relevanten Blutverlusten vermeiden**
- **gezielte Faktorentherapie**
  - **Effektiv**
  - **Reduziert Transfusionen, MOF... ?**
  - **Geforderte Voraussetzungen**
    - **grundlegendes Verständnis**
    - **viskoelastisches Monitoring**

