Open Loop TCI
How to manage the induction

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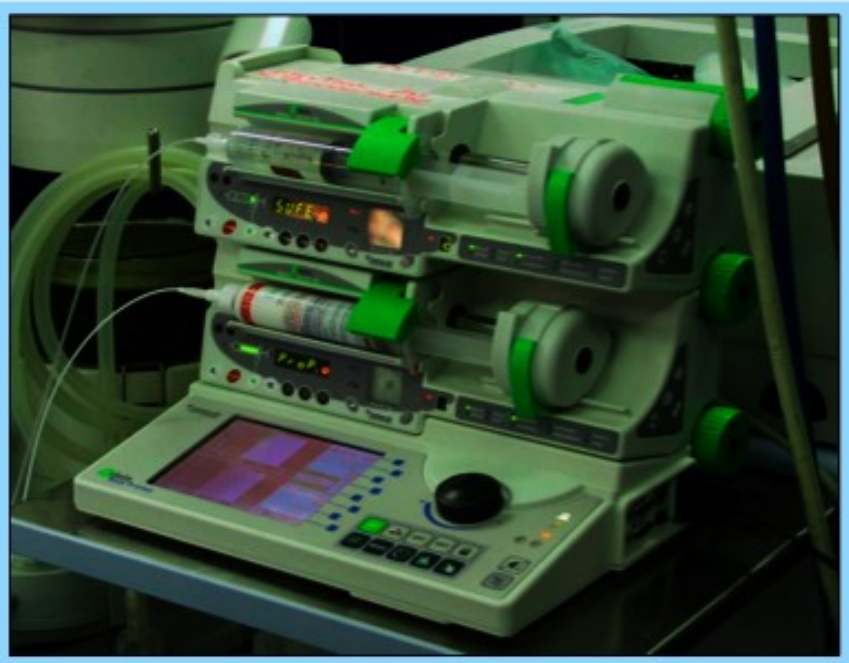
Anaesthetic for PLASTIC Surgery CHRU Lille France

SCATA/ESTAIC Meeting, London 21- 23 Nov. 2007

Modular systems CE Mark



Base Primea (Fresenius Vial)

"Including pharmacokinetic models :

• (16< Age<100 years old ; weight < 150kg)

"**Propofol:** Marsh, Schnider model (BMI<42 M <35F)

".**Remifentanil:** Minto model (BMI<42 M; <35 F). .

"**Sufentanil:** Gepts

Asena PK *(Alaris)*

Propofol: Marsh,.
Paedfusor pharmacokinetic model
.Remifentanil:Minto

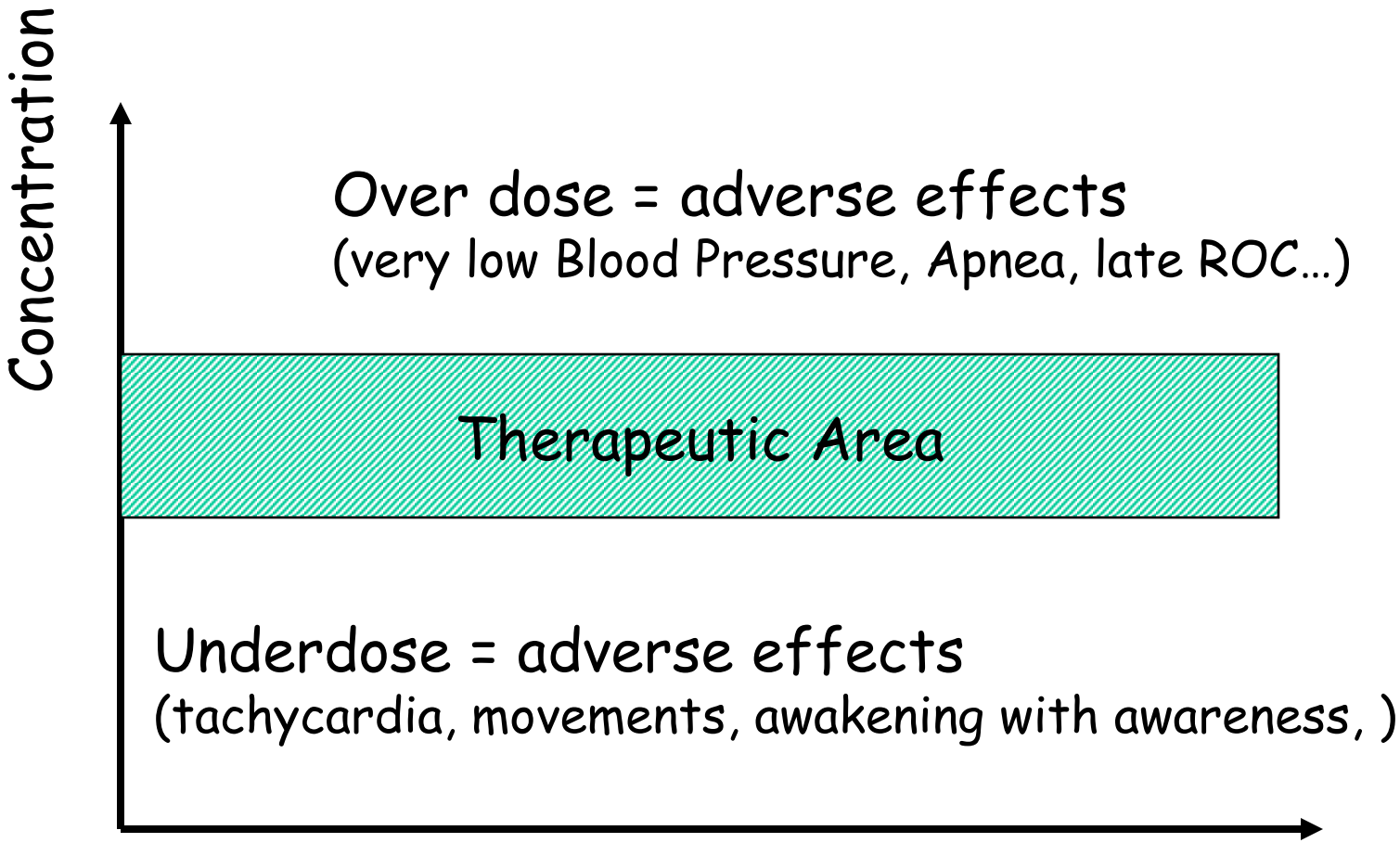
TCI for Sedation

simple, safe

For ASA III elderly patients
Ec P < 0.9µg.ml^{-1}

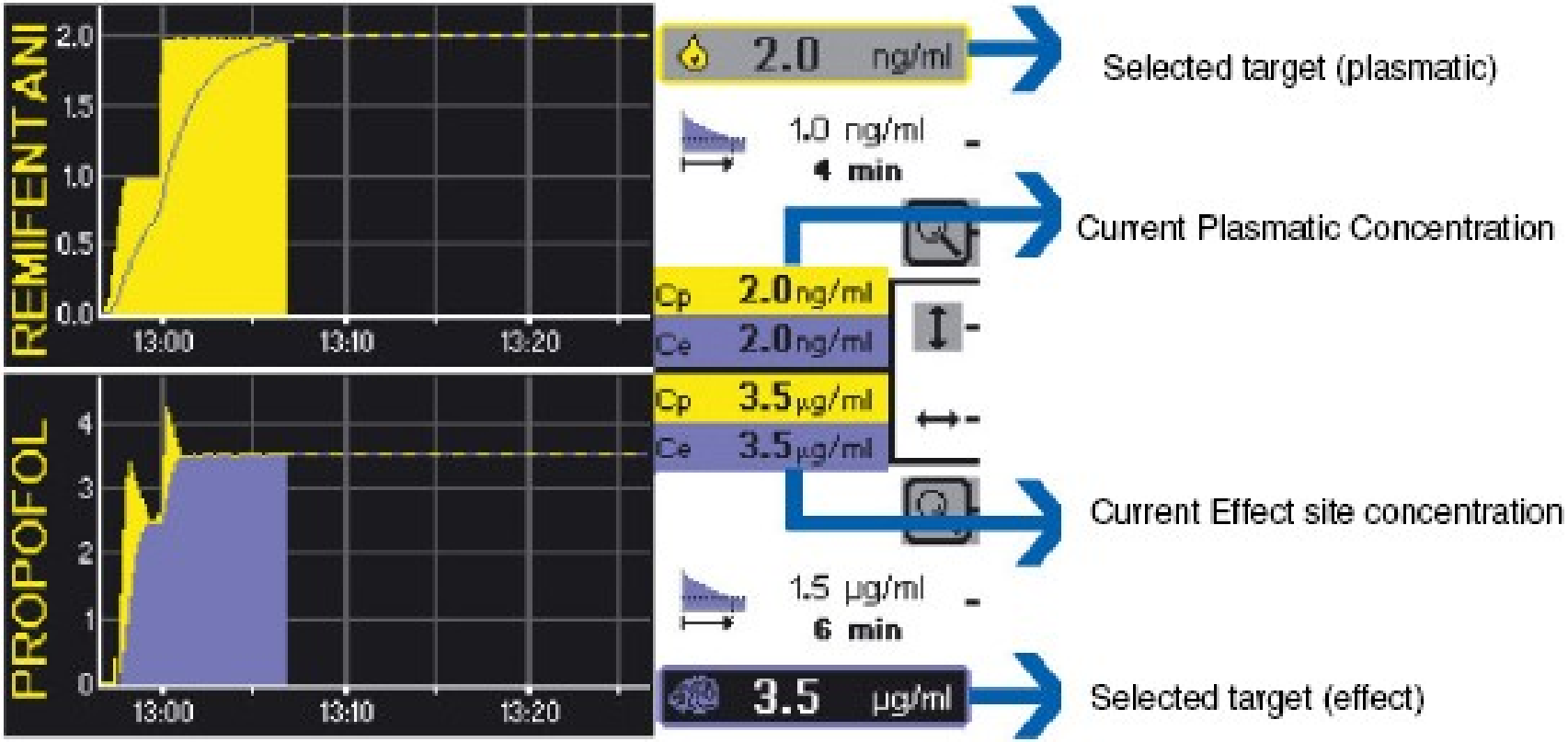
Villeret I Ann Fr An Rea 2003;22:196-201

TCI Anaesthesia
Titration : Therapeutic Area



Titrate Plasma or Effect Site Target

Kabi



Induction time is shorter with Effect TCI than Plasmatic TCI
Without causing more hypotension

Struys et al, Anesthesiology, 2000; 92:399-406

Effect Site Concentration depends on pharmacokinetic model

For the same Ec Target, Time to induction is shorter With Schnider than with Marsh Model

Propofol Schnider

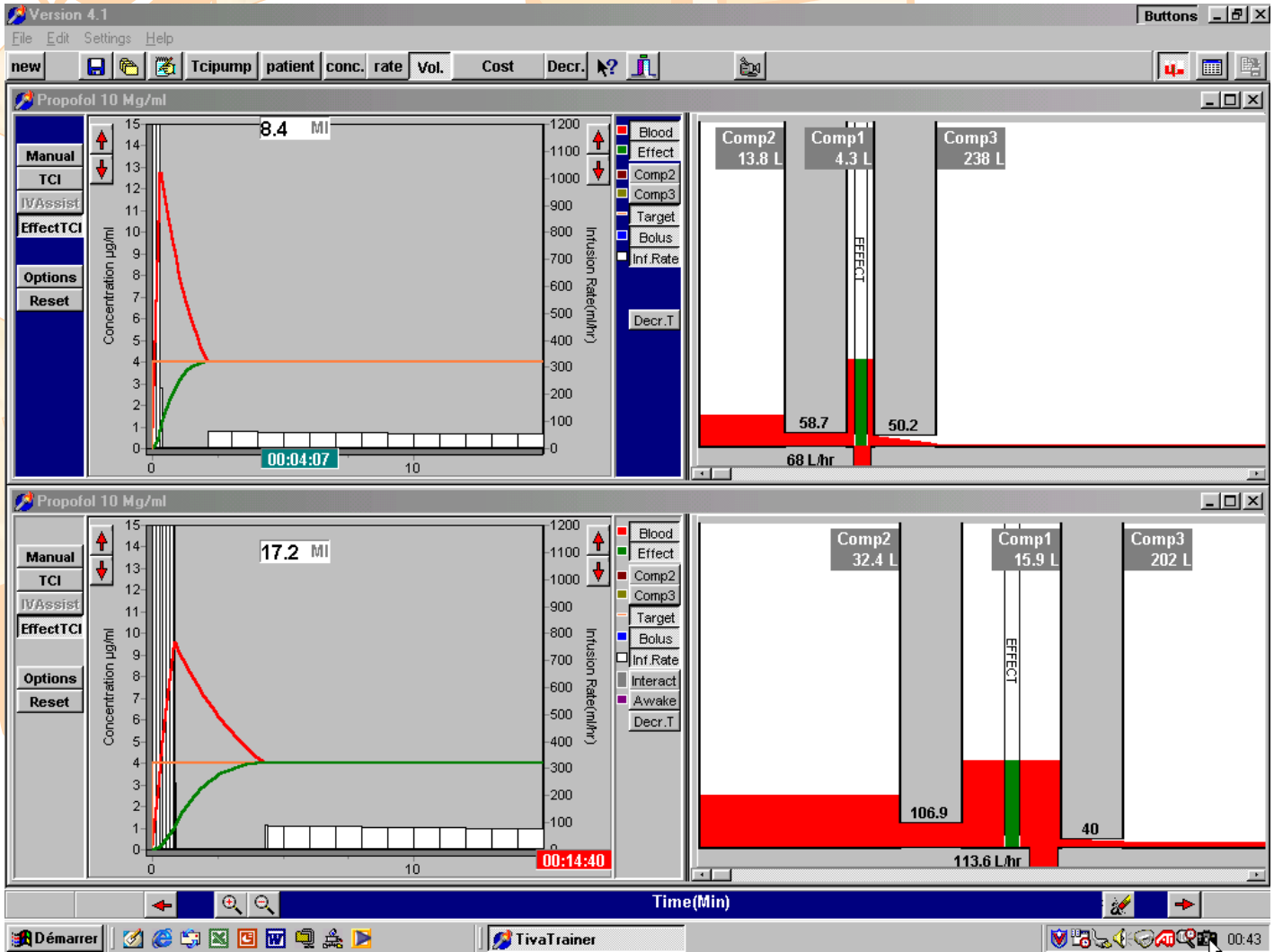
T1/2 k_{eo} = 1.8 min

K_{eo} = 0.485 min^{-1}

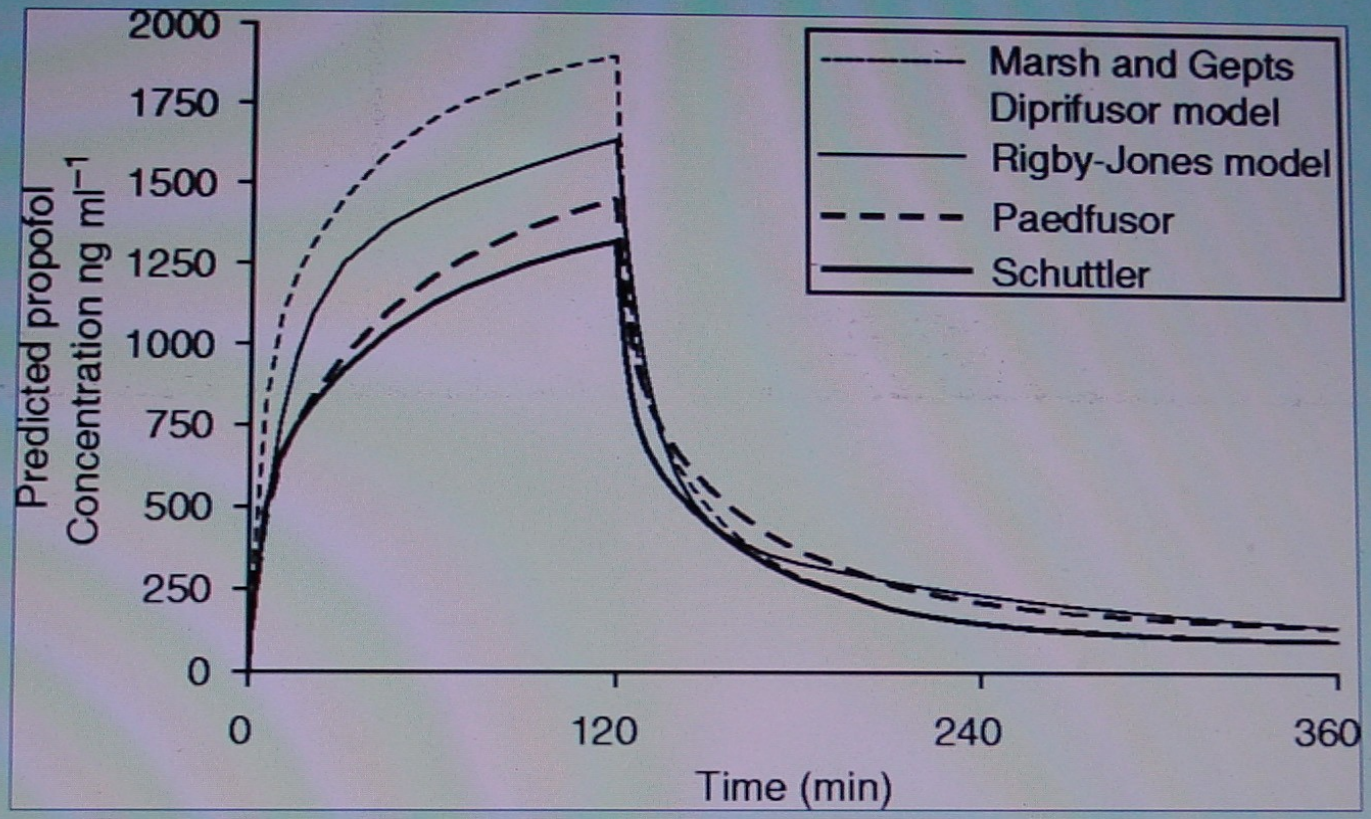
Propofol Marsh

T1/2 k_{eo} = 2.6 min

K_{eo} = 0.27 min^{-1}



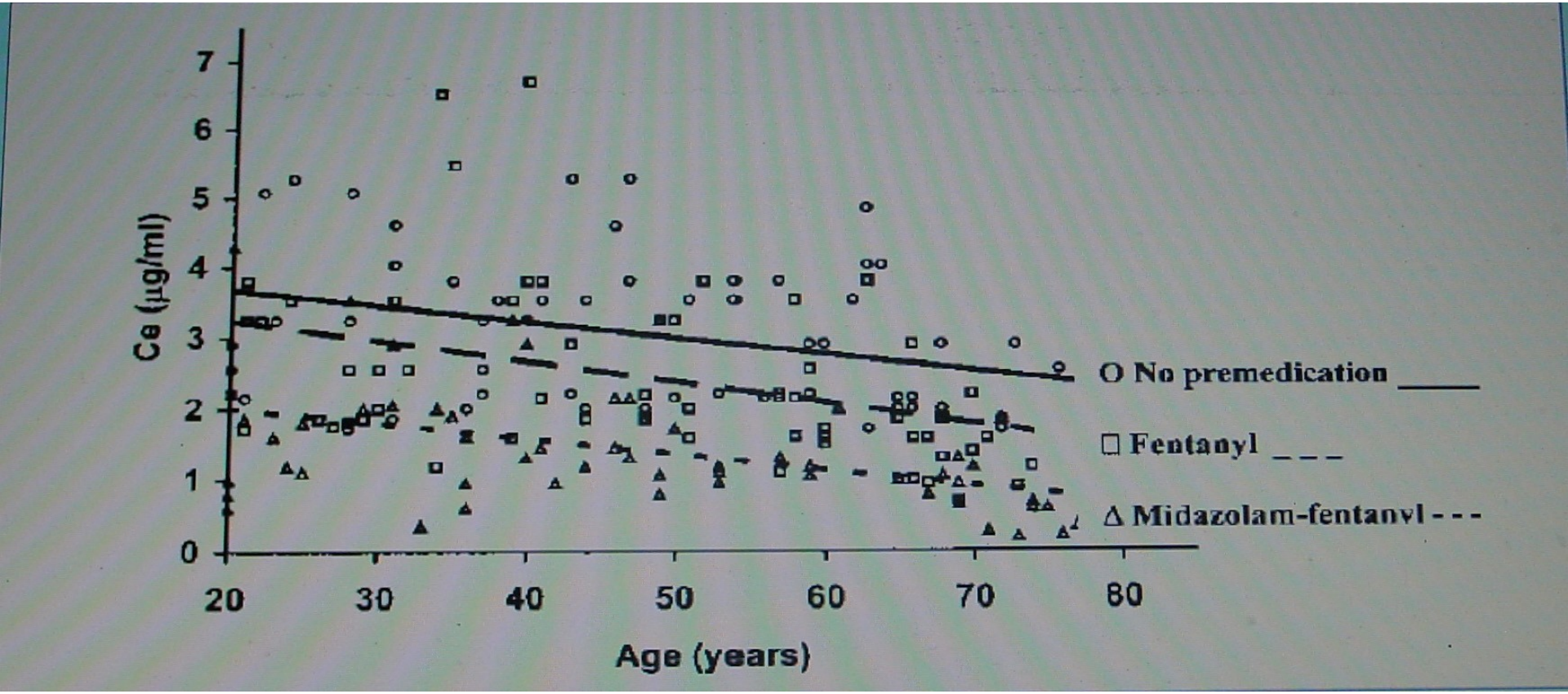
Predicted blood Propofol C into a 20 kg child aged 5 yr after 120 min infusion of propofol 4mg.kg^{-1}.h^{-1}



Predicted blood propofol concentrations after a 120 min infusion of propofol 4 mg kg^{-1} h^{-1} into a 20 kg child aged 5 yr. Four pharmacokinetic models are compared. Plots represent, from top to bottom: Marsh[61] and Gepts[37] Diprifusor model, mostly based on adult data; Rigby-Jones[85] model, postcardiac surgery; Paedfusor;[1] and Schuttler.[93] Thick solid line shows pooled analysis including data from healthy children.

Sneyd JR, Br J Anaesth 2004; 93: 725-736

Effect of the Ec P depends on Age and premedication



Olmos, ASA 2000

Comparison of Target, Manual Controlled Infusion and Etomidate/Desflurane

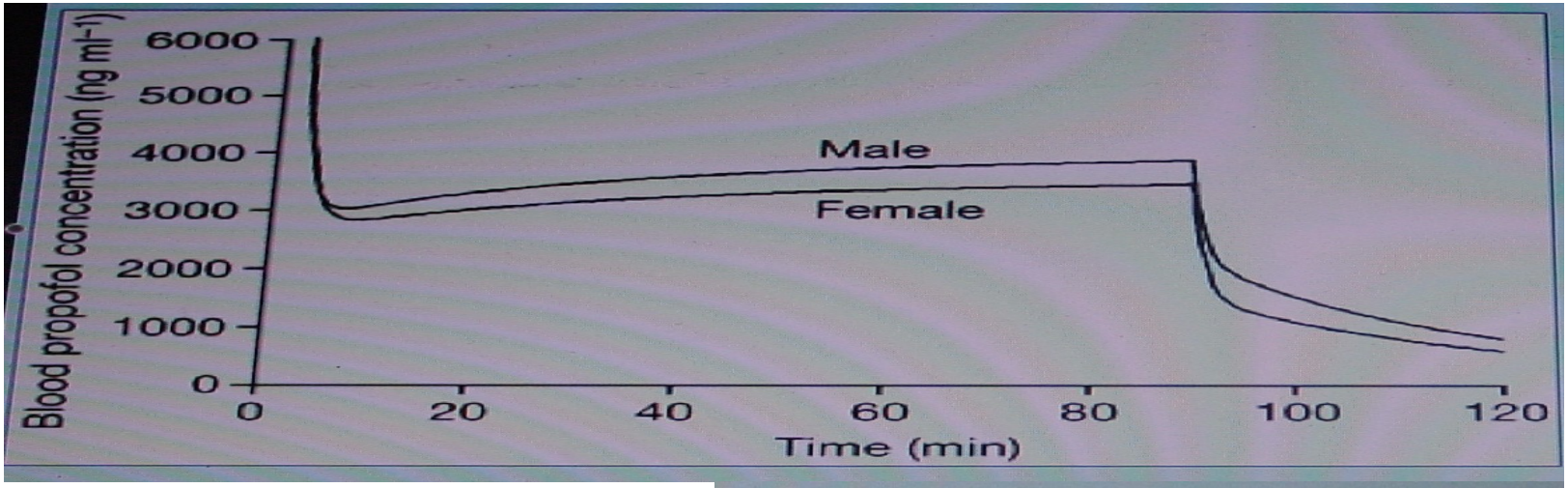
in Elderly patients undergoing Hip Facture Surgery

Variable	ETO/DES	TCI group by steps	MCI group Bolus P 1mg/kg
LER (min)	1.3±0.6*	4.8±3.9	2.4±1.6
Time of T. Intubation (min)	4.9±2.2*	12.1±3.9	8.5±4.5
Decrease MAP%	37.4±21.8*	44.3±7.8	49.2±8.2
Drugs dosage adjustements (n)	2(1-6)*	3(1-4)	6(2-12)
PONV (n patients)	7*	0	0

Passot S and al Anesth Analg 2005;100:1338-42

The influence of Gender on LOC with Sevoflurane or Propofol

- Women required more propofol to maintain equivalent BIS than men and awake faster (eye opening, response to verbal command)
  Gan, Anesthesiology, 99; 90:1283



CpP Male > CpP Female of 15 %

Vuyk. Br J Anaesth 2001; 86: 183-8

How to determine Ec P at LOC clinically?

- Plasma TCI:

  Ec P is better correlated to BIS

  - **At loss Verbal command**
  - Than at loss Eyelash Reflex (37% missing)
  - at yawning (47% missing)
  - at apnea (47% missing)

  (Kim DW J Clin Anesth 2002)

- Effect TCI: **EcP at loss of Eyelash reflex**

  Determines the loss of Consciousness

  (Milne SE Br J Anaesthesia 2003, 90 (2) : 127- 131)

  (Lim TA Br J Anaesthesia 2003, 91(5):730-2)

  (CrinquetteV, ESA 2003) …

Ec P at LOC may predict the Ec P at other endpoints

- **Ec P for laryngoscopy**

  Ec P laryngoscopy = 1.7+ (2x Ec P LOC)

  (Anglade D , Ann Fr Anest Réanim 2002;21:416s, R431)

- **During a stimulus**

  (Milne SE, Br J Anaesth 2003;90(2):127-31)

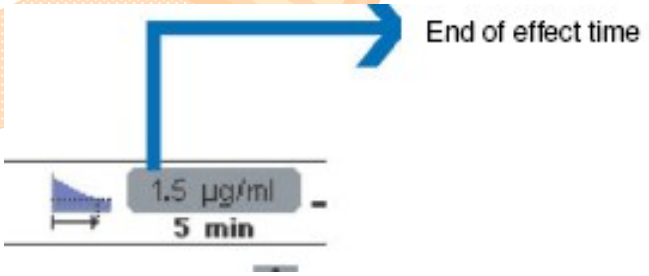
- **Ec P at LVC is near Ec P at ROC (recovery of consciousness)**

  Ec propofol: LVC = 2.0 ± 0.9 (0.7 to 4.9) ; ROC = 1.8 ± 0.7 µg/ml

  (Milne SE, Kenny GNC, Br J Anaesthesia 2003, 90 (5) : 623- 9)

  So, the software may predict the time to awake the patient when you stop the infusion if the Ec P at LVC of the patient is recorded.

- **⇒ guide TCI at different end points**



Monitoring of Hypnosis

- **Monitoring :**

	LOC	BIS	PEA
remi alone*	LVC	86,1 ± 7,1	72,4 ±4,2
P TCI P**	LER	70,9 (88-52,9)	54,3 (68,6-40)

*Alexandre F (anesthesiology Annual meeting of ASA 2001 A728
**(Milne SE Br J Anaesthesia 2003, 90 (2) : 127- 131)

-BIS, Narcotrend, Entropy are more Rapid than MAP

LOC is correlated to the different values

Useful when curarised, history of increased or decreased MAP

You don't undestand (Big doses of drugs and no sleep, low MAP with very small level of EcP

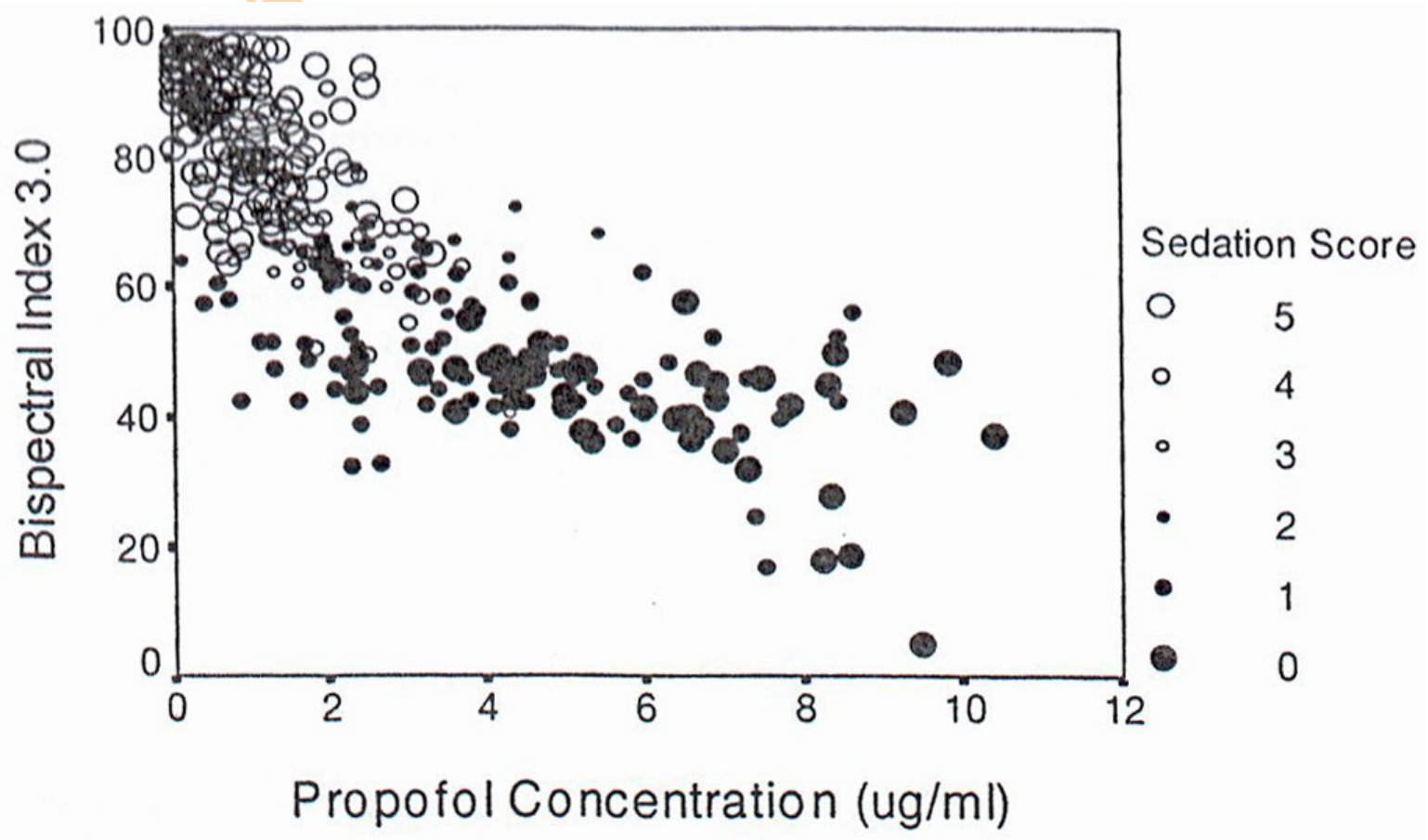
But big range of values (BIS>PEA): doubt

Artefact (EMG +, electronic cautery, hypoglycemia, hypotermia< 32°, low brain perfusion

- **Cinical and Monitoring are better:**

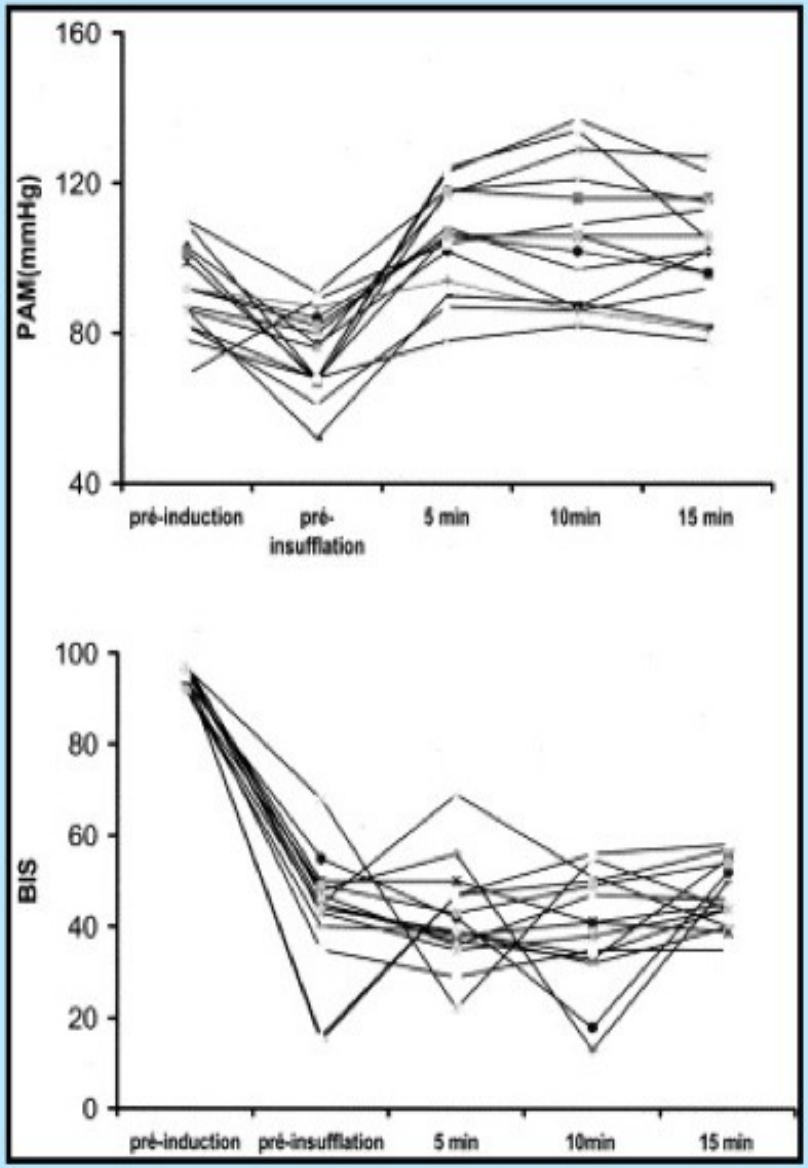
(Struys M, Anesthesiology 2003; 99:802-12)

BIS & Increased plasma Propofol concentration



Glass et al. Anesthesiology,1997;86:836.

BIS and High Blood Pressure (HTA) in coeliochirurgy



- 15 patients
- $C_{propofol}$ = 4 g.mL^{-1}

  $C_{fentanyl}$ = 2 ng.mL^{-1}
- HTA au cours de l'insufflation sans variation du BIS

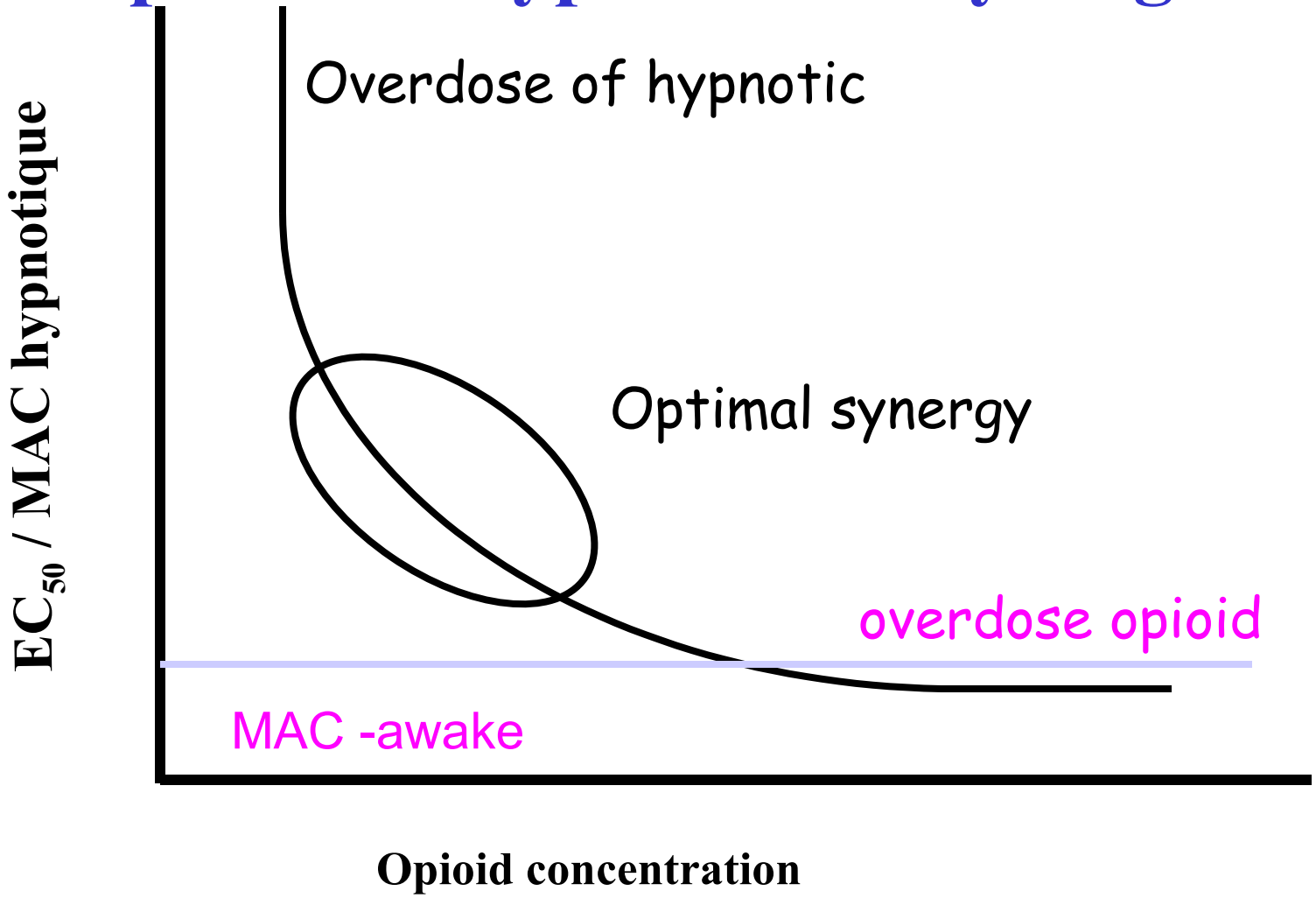
Mavoungou et al. Ann Fr Anesth Réanim 2000;19:582-7

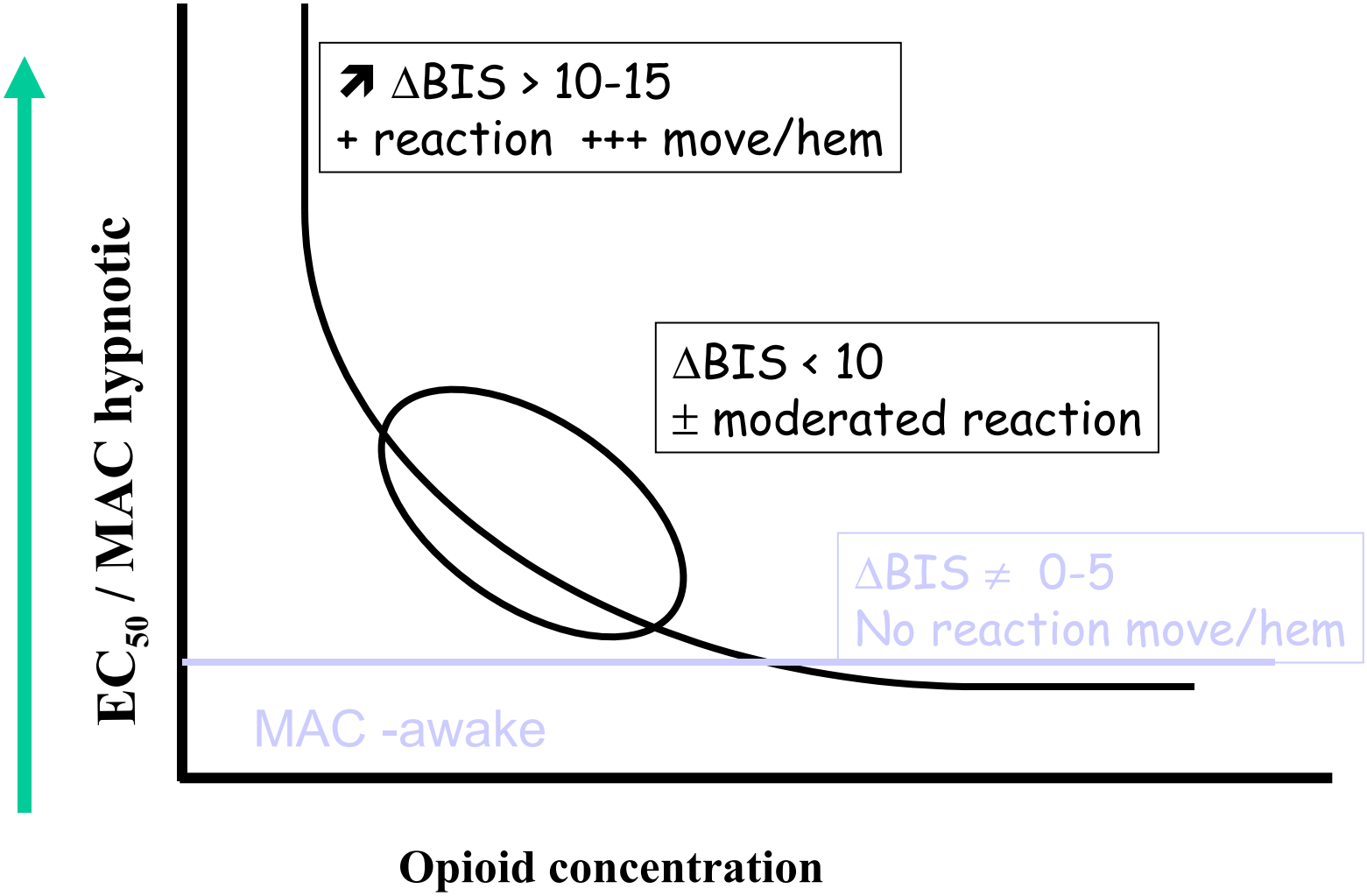
Requirements of propofol decreases with opioid more after stimuli than during the LVC

	Cp_{50} propofol (µg/ml)	+ fentanyl 1 ng/ml	+ fentanyl 3 ng/ml
Loss Verbal command	4,4	- 11%	- 17%
Incision	10	- 30%	- 50%
Intubation	17,4	- 30%	- 50%

Kazama, Anesthesiology 1997

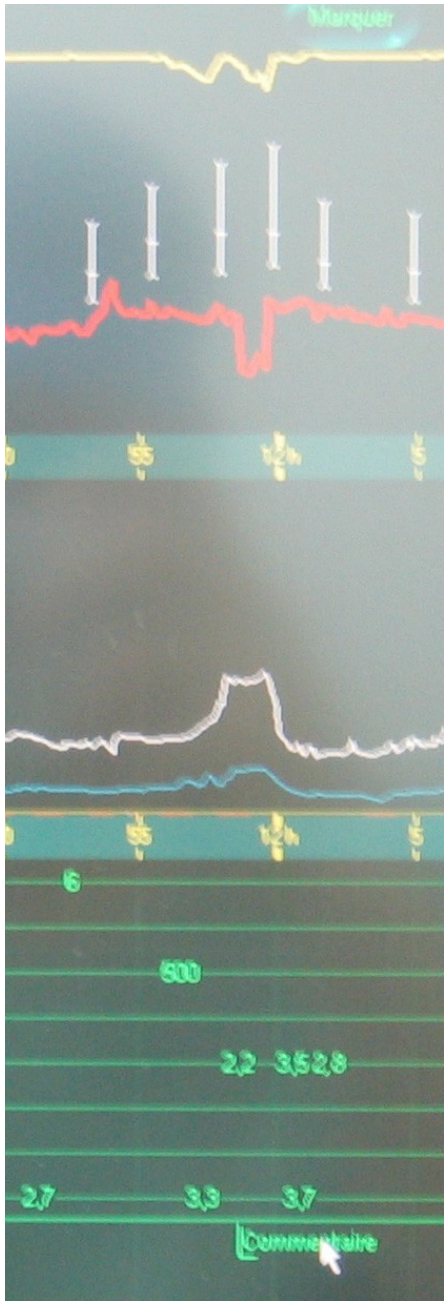
interaction opioid – hypnotic
opiod and hypnotic are synergic





BIS detects indirectly the underdose of Opioid after the stimuli

Limit of hypnotic titration with BIS: Awakening



- If Ec P is too low to obtain 40<BIS<60
  - risk unexpected awakening
  - Because Ec P = EcP awakening value
- The relation between BIS and EcP is not linear
  - a small decreased EcP :
    - increases very much BIS value
    - awakening appears with risk of awareness

« BIS does not avoid awakening
- But in increasing rapidly the level of hypnosis avoid the awareness
- For that, It is necessary to use the BIS alarm
- Risk of awareness is rare if BIS is near 50

- BUT IT INCREASES WHEN BIS is over 65 » D. Longrois

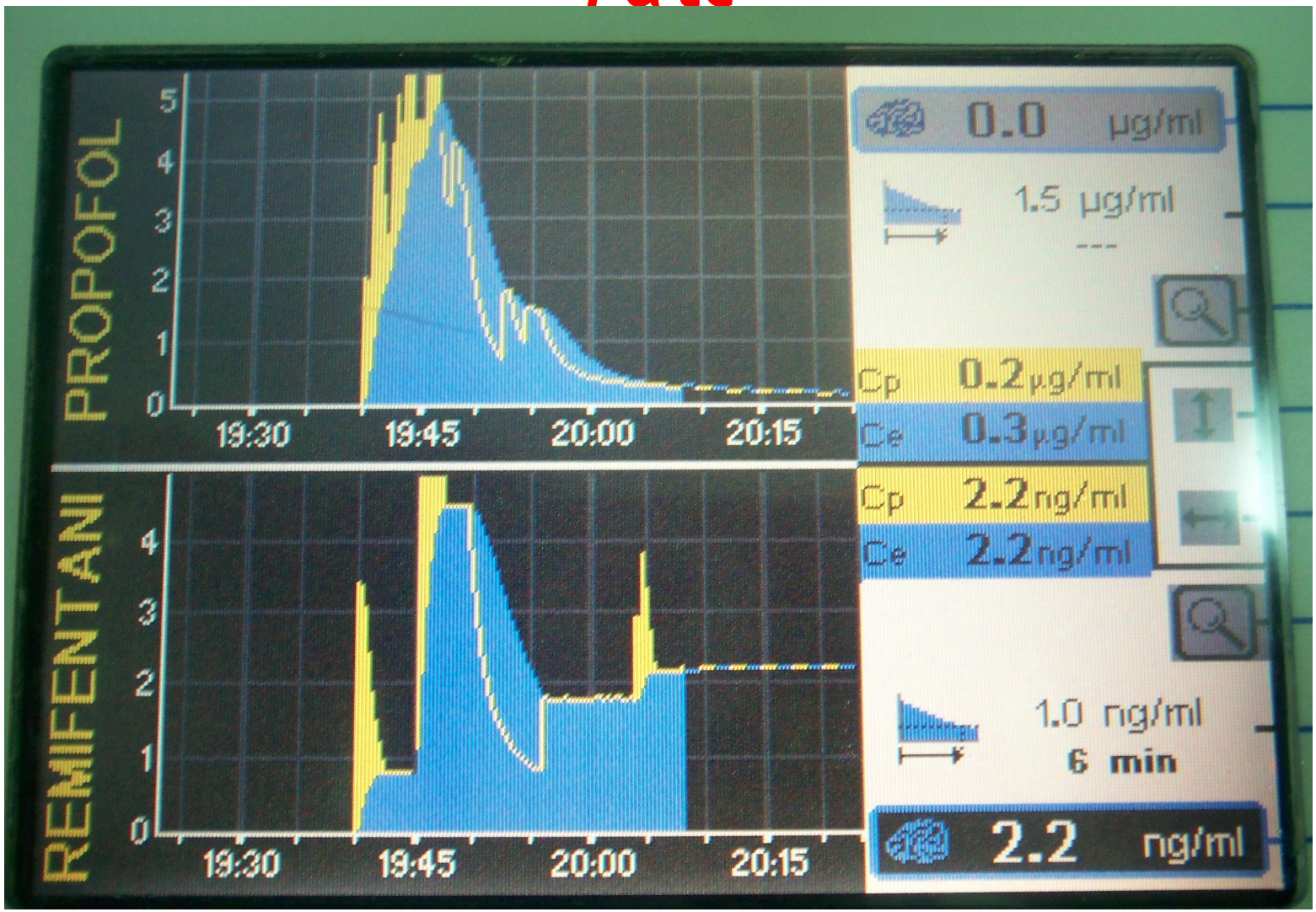
Effect Site and Pharmacodynamics

- **In clinical practice**
  - Knowledge of the keo of the drug and of the PHK set used
  - Independent titration of opioid and hypnotic
  - Smooth and progressive effect-site TCI based on the individual response

ULB ERASMUS

Induction by steps with low P infusion rate

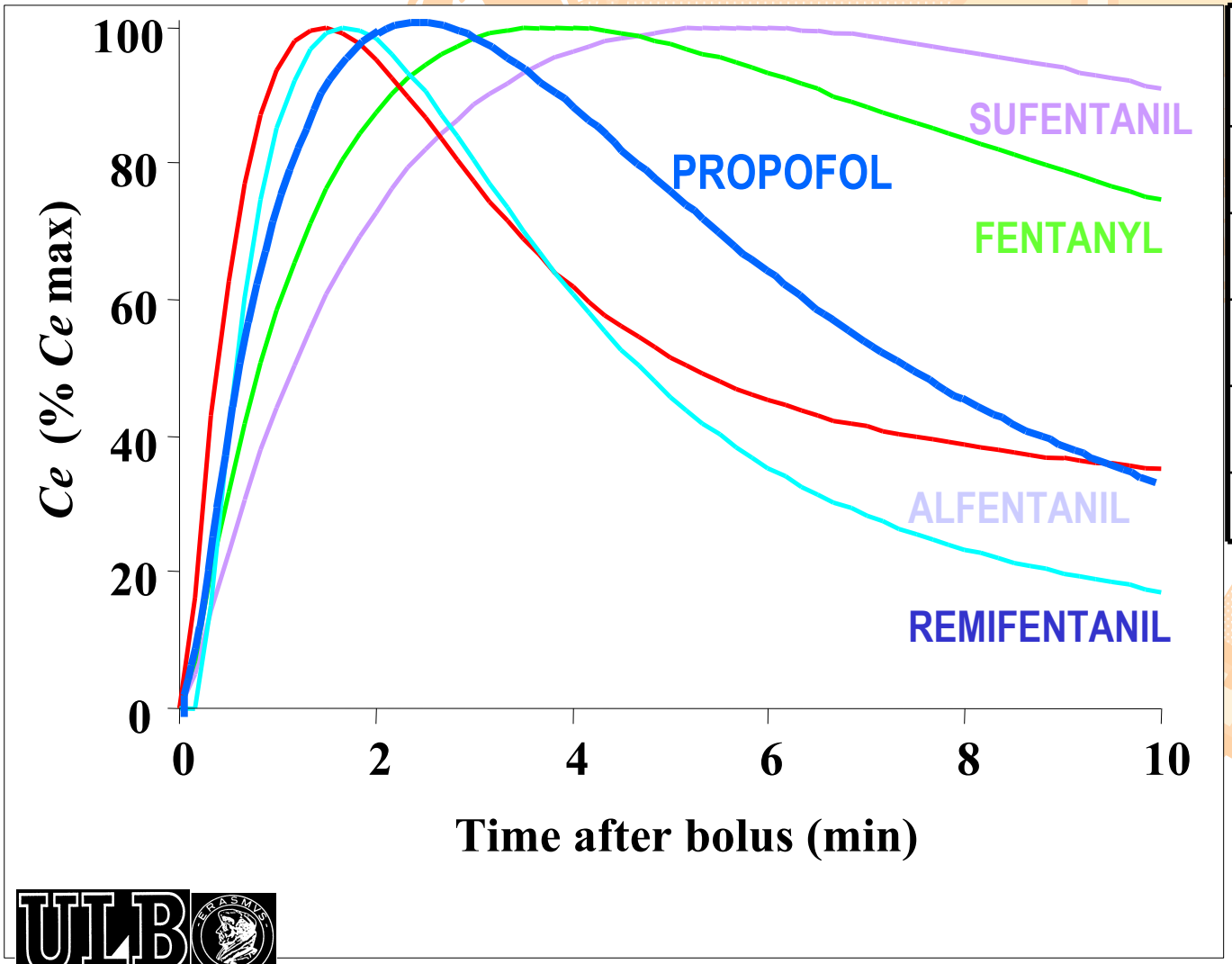
Low Infusion rate (200ml/h) limits P plasma C Peak



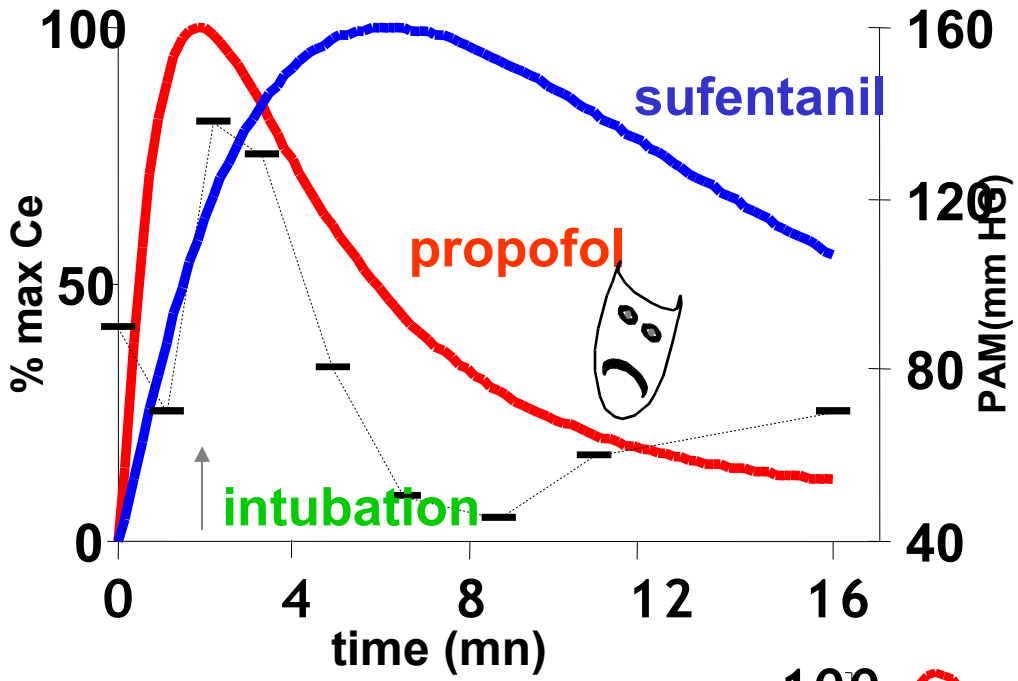
Sometimes we set up the rate (Max 1200ml/h)

when agitation appears with young people, drugs or alcohol consumers

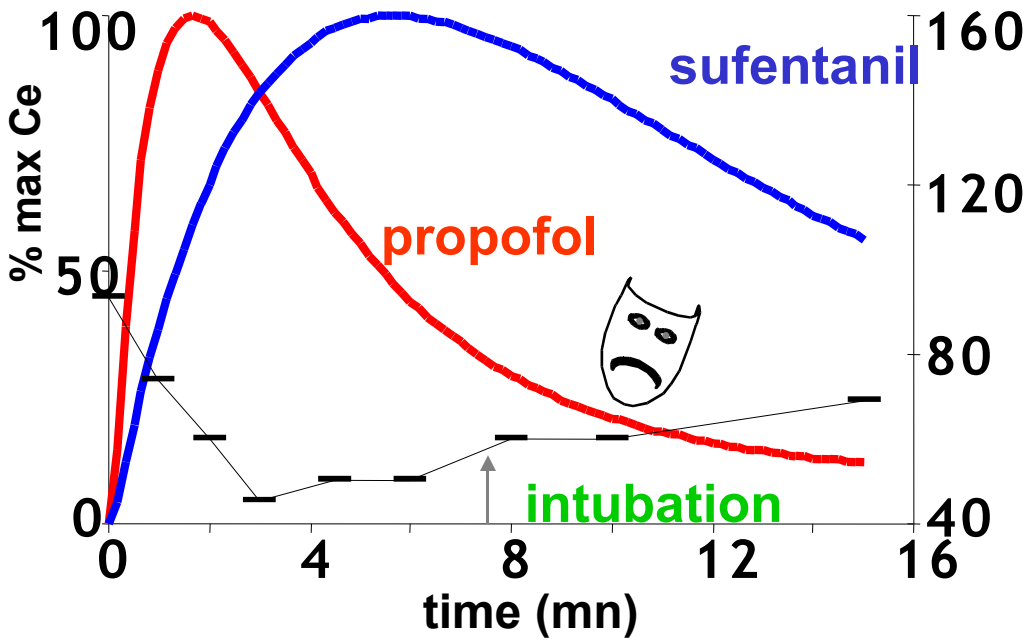
Induction et time to peak



Drogue	K_{eo} min-1
Propofol	**0.27**
Alfentanil	0.63
Remifentanil	0.58
Fentanyl	0.12
Sufentanil	0.11

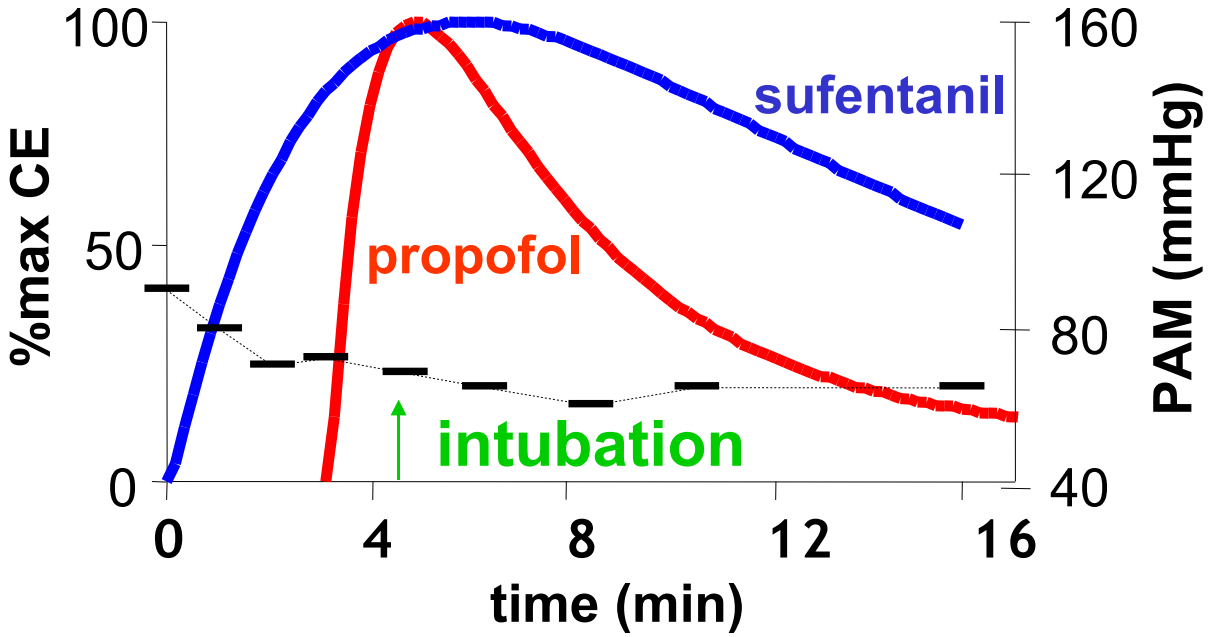


Early Intubation



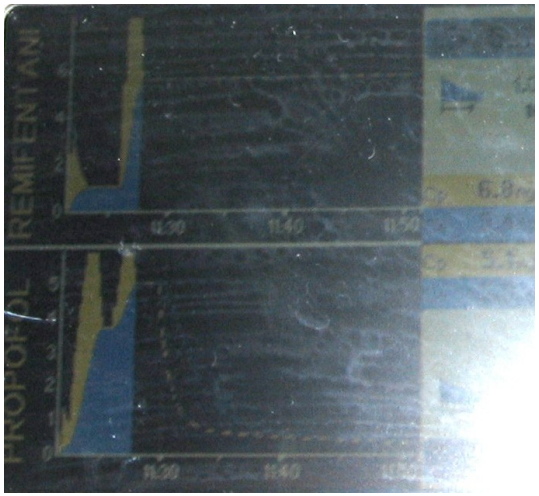
Delayed Intubation

Optimised Interaction for Intubation



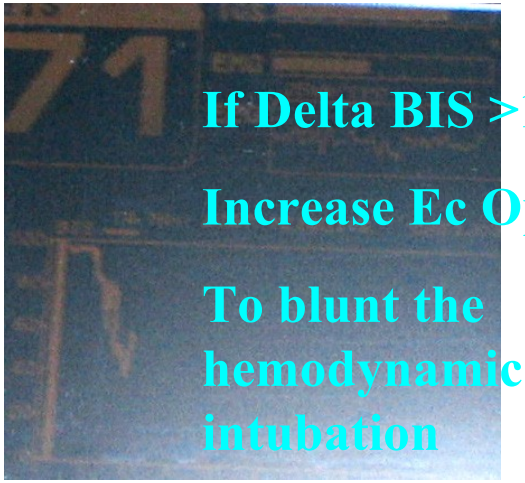
With Remifentanil, propofol should be started first because by beginning remifentanil infusion prior to propofol, the patient is likely to stop breathing before loosing consciousness.

Hypnotic Titration:
Ec P at LER: 3,7µg .ml^{-1}
BIS LER: 45



For intubation : Ec P LER+0-30%
Ec Remi to 6 ng.ml^{-1}(4-6) depends on

Opioid Titration :
Delta BIS during laryngoscopy



If Delta BIS >10

Increase Ec Opioid

To blunt the hemodynamic response to intubation

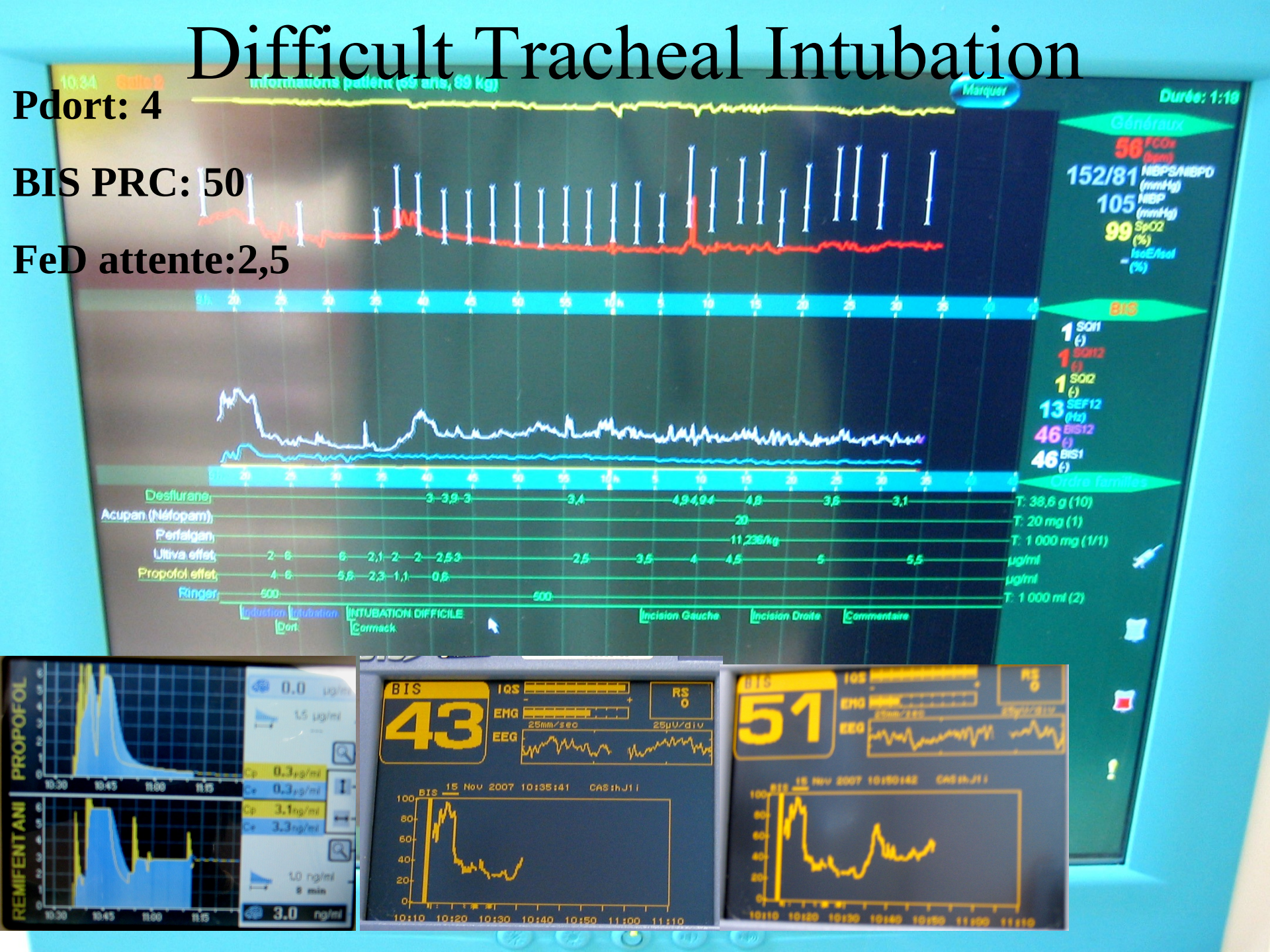
« Even curarised patient, high interest with patient received ß-bloquing agent » V. Billard

Difficult Tracheal Intubation

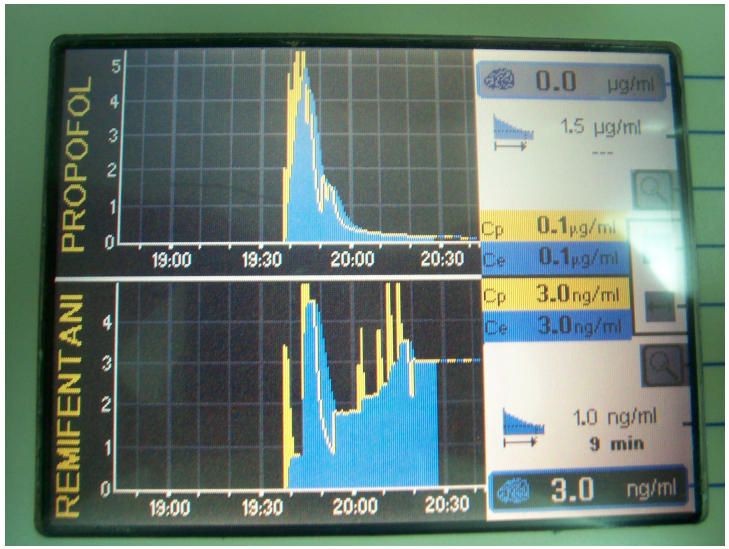
Pdort: 4

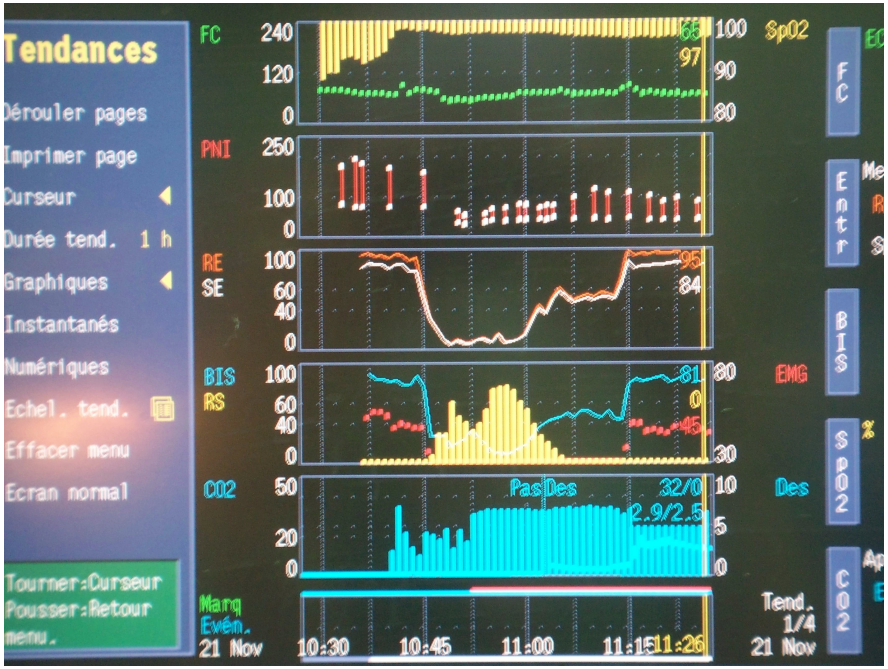
BIS PRC: 50

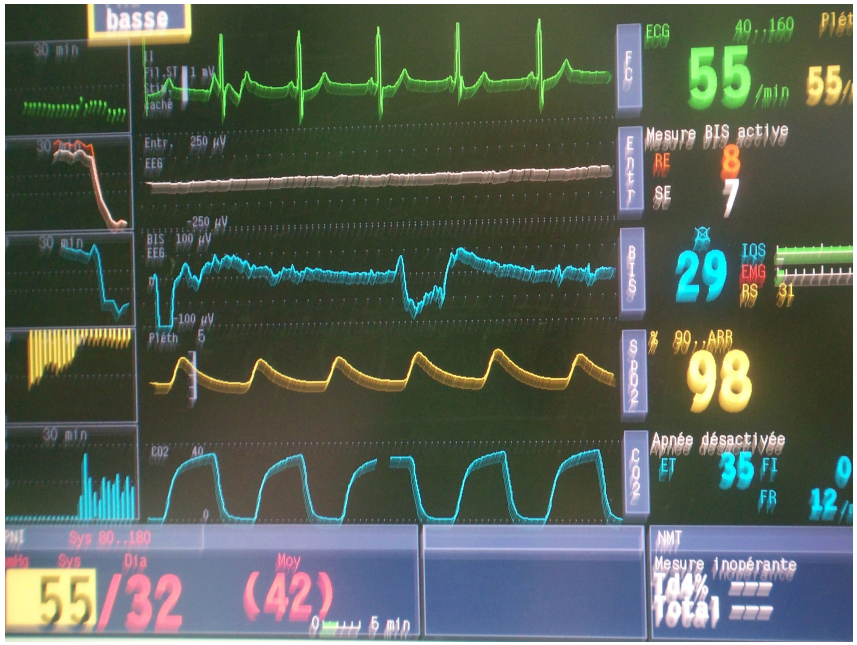
FeD attente:2,5



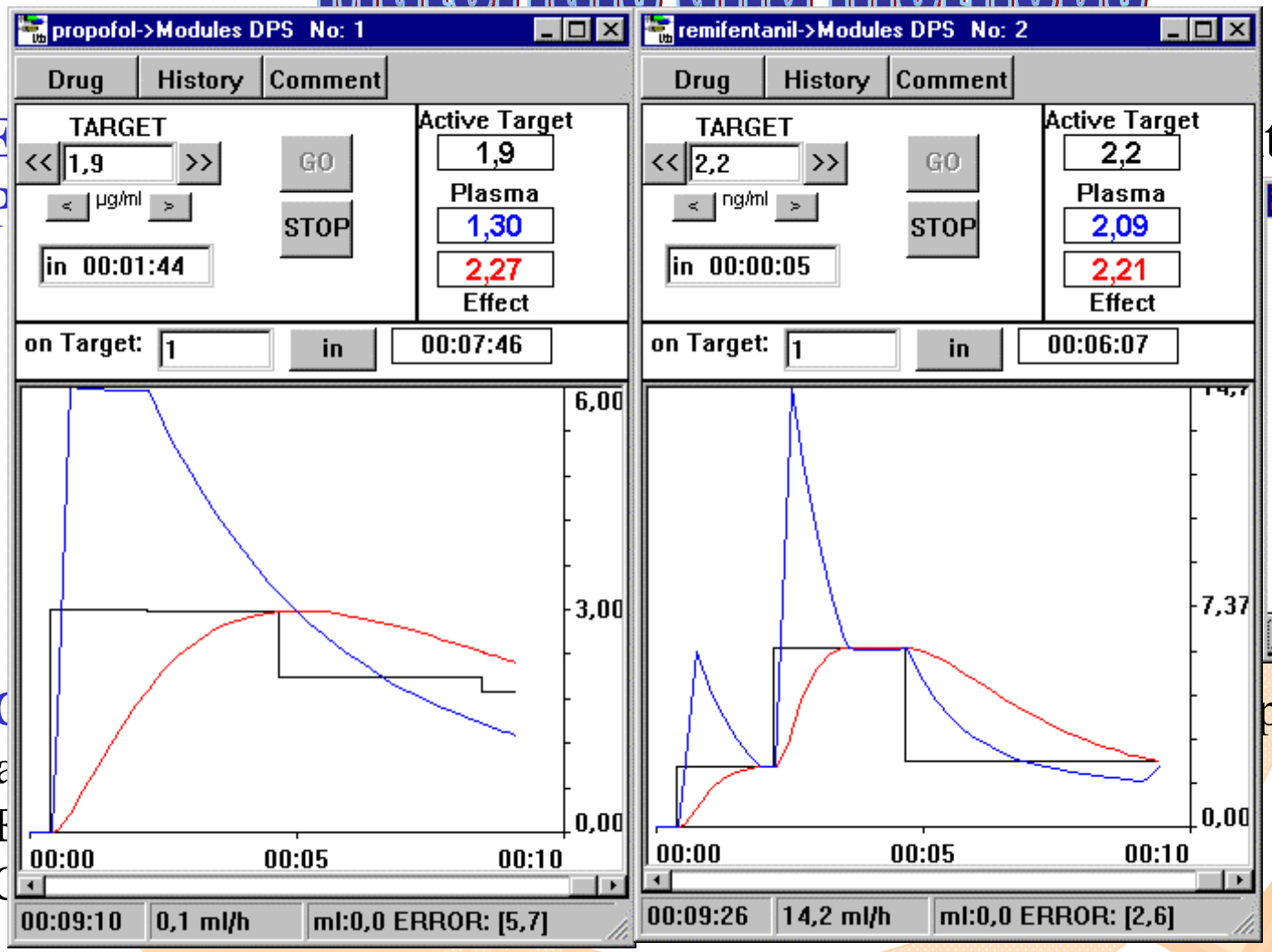
Elderly Patient

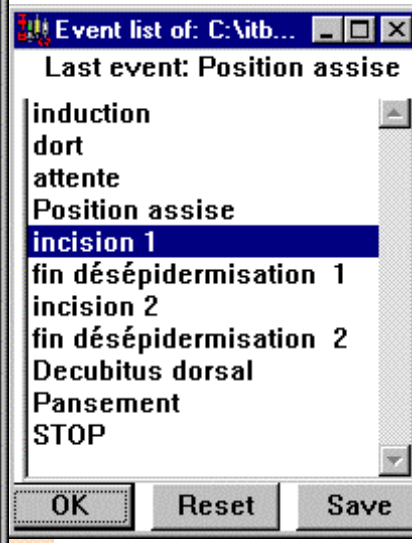






Materials and methods





- E
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t

pressure

- **Statistics**:
  - **Previous EsC and real EsC** are compared
  - **Correlation ratios** calculated with SPSS software (threshold: $p<0.01$)

Toolbox L. Barvais Bruxelles

Results

Induction | Intubation | Incision | End of Surgery | Extubation

TIME OF INDUCTION | WAITING | SURGERY | AWAKENING

GROUP 1

TIME OF INDUCTION			WAITING	SURGERY		AWAKENING		
5 min 38 (± 4 min 10)			46 min (± 20 min 20)	2h51 (± 0h49)		6 min (± 4 min 04)		
EsC P LER (µg/ml)	P (mg/kg)	R (µg/kg)	EsC P sitting position (µg/ml)	P (mg/kg/h)	R (µg/kg/min)	EsC PE (µg/ml)	EsC R (ng/ml)	EsC PE / EsC P ler
2,29 ± 0,61	2,37 ± 0,4	2,05 ± 0,51	2,24 ± 0,43	5 ± 1,16	0,11 ± 0,03	1,38 ± 0,26	0,75 ± 0,32	0,73 ± 0,23

GROUP 2

TIME OF INDUCTION			WAITING	SURGERY		AWAKENING		
5 min 00 (± 4 min 23)			47min37 (± 20 min 20)	3h15 (± 0h53)		5 min (± 4, min 46)		
EsC P LER (µg/ml)	P (mg/kg)	R (µg/kg)	EsC P sitting position (µg/ml)	P (mg/kg/h)	R (µg/kg/min)	EsC PE (µg/ml)	EsC R (ng/ml)	EsC PE / EsC P ler
1,85 ± 0,37	2,08 ± 0,4	1,96 ± 0,59	1,76 ± 0,31	4,33 ± 0,86	0,11 ± 0,023	1,32 ± 0,26	0,82 ± 0,38	0,73 ± 0,23

GROUP 3

TIME OF INDUCTION			WAITING	SURGERY		AWAKENING		
6 min 00 (± 3 min)			45 min 27 (± 5 min 53)	3h19 (± 0h43)		6 min (± 3 min)		
EsC P LER (µg/ml)	P (mg/kg)	R (µg/kg)	EsC P sitting position (µg/ml)	P (mg/kg/h)	R (µg/kg/min)	EsC PE (µg/ml)	EsC R (ng/ml)	EsC PE / EsC P ler
1,88 ± 0,05	2,27 ± 0,56	2,05 ± 0,65	1,66 ± 0,29	3,64 ± 0,88	0,10 ± 0,02	1,22 ± 0,23	0,86 ± 0,35	0,61 ± 0,11

Decision matrix of Gurman modified by V Crinquette

(Assessment of depth of general anesthesia Int J Cln Monit Comput 1994:185-9)

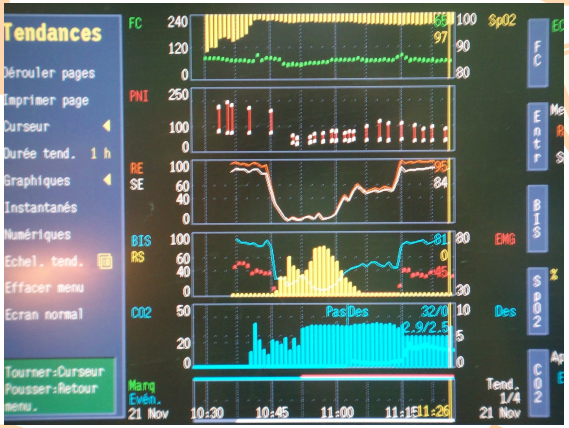
BIS	PAM>120%PAMpo or Tachycardia	PAM =PAMpo Preop value	PAM< 80%PAMpo
>60	↑ Propofol PFS+Opioid SD- Nicardipine	↑ Propofol	Volemic expansion and /or Vasopressor then ↑ Propofol
40<BIS<60	PFS+ ↑ Opioid PLS- Nicardipine		Volemic expansion +/-vasopressor Si bradycard: ↓ O.
<40	Propofol ↓ PFS+ Opioid SD- Nicardipine	Propofol ↓	Propofol ↓↓ ± volemic expansion ±vasopressor

Underdose

Ideal

Overshoot

Open Loop TCI

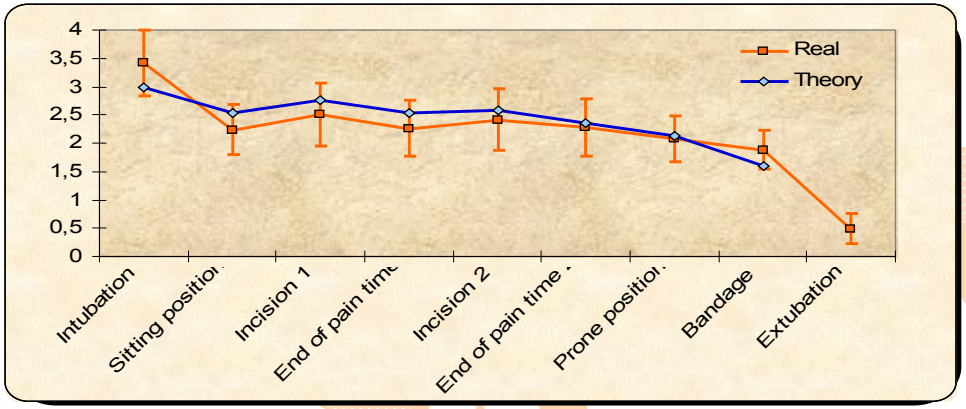


Half Closed Loop TCI

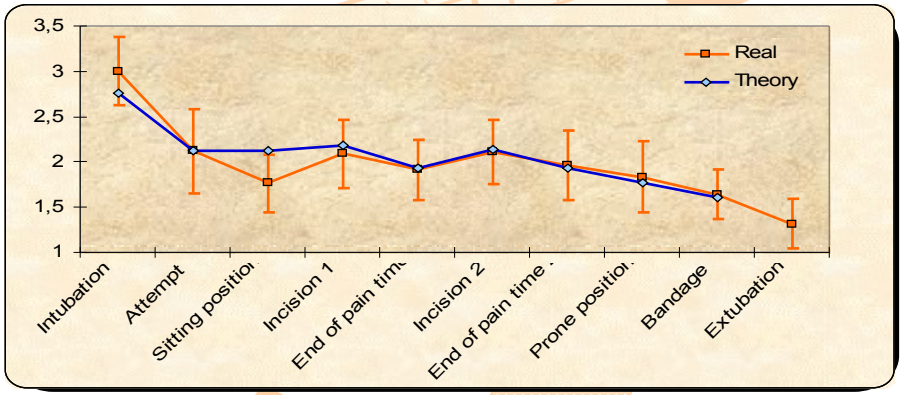
SCATA, ESTAIC London 21- 23 Nov. 2007

Comparaison between calculated EsC Propofol and real EsC P

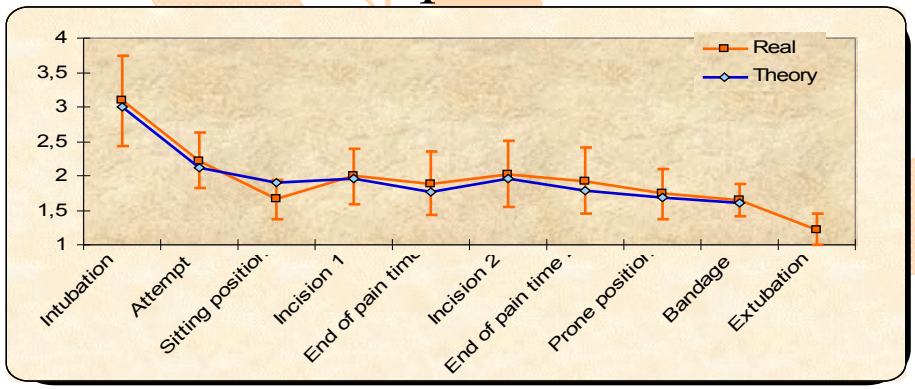
Groupe 1



Groupe 2



Groupe 3



Résultats

Groupe 1

	Remifent.	Propofol			R1	R2
Events	EsC (ng/ml)	Model CoeM	pEsC (µg/ml)	rEsC (mg/ml)	rEsC vs pEsC (01)	rEsC vs pEsC (02)
LER	2	-	-	**O1:2.29±0.63**	-	-
T2	6	1.30	2.99±0.8	3.41±0.58	**0.712****	-
T3	3	1.10	2.53±0.56	**O2:2.24±0.43**	**0.696****	-
T4(MP)	4	1.13	2.59±0.61	2.50±0.56	**0.751****	**0.811****
T5(LP)	3.6	1.04	2.39±0.57	2.26±0.49	**0.692****	**0.857****
T6(MP)	4	1.13	2.59±0.61	2.42±0.55	**0.711****	**0.757****
T7(LP)	3.6	1.04	2.39±0.55	2.28±0.51	**0.683****	**0.732****
T8	3	O.93	2.13±0.52	2.08±0.41	**0.683****	**0.747****
T9	1.5	-	1.60	1.87±0.34	-	-
Extub.	0.75	-	-	1.38	**$p<10^{-3}$**	

T2 : Intubation

T3: Waiting

T4 : Incision

Groupe 2

	Remifent.	Propofol	R2
Events	EsC (ng/ml)	Model CoeM	rEsC vs pEsC (02)
LER	2	-	-
T2	6	1.30	**O.909****
T3	2.7	1.00	**0.732****
T4(MP)	3.74	1.13	**0.890****
T5(LP)	3.02	1.02	**0.915****
T6(MP)	3.74	1.13	**0.918****
T7(LP)	3.02	1.02	**0.791****
T8	2.5	1	**0.694****
T9	1.5	-	-
Extub.	0.75	-	

Groupe 3

	Remifent.	Propofol	R2
Events	EsC (ng/ml)	Model CoeM	rEsC vs pEsC (02)
LER	2	-	-
T2	6	1.30	**O.984****
T3	2.7	1.00	**0.394**
T4(MP)	3.74	1.13	**0.934****
T5(LP)	3.02	1.02	**0.801****
T6(MP)	3.74	1.13	**0.859****
T7(LP)	3.02	1.02	**0.871****
T8	2.5	1	**0.913****
T9	1.5	-	-
Extub.	0.75	-	