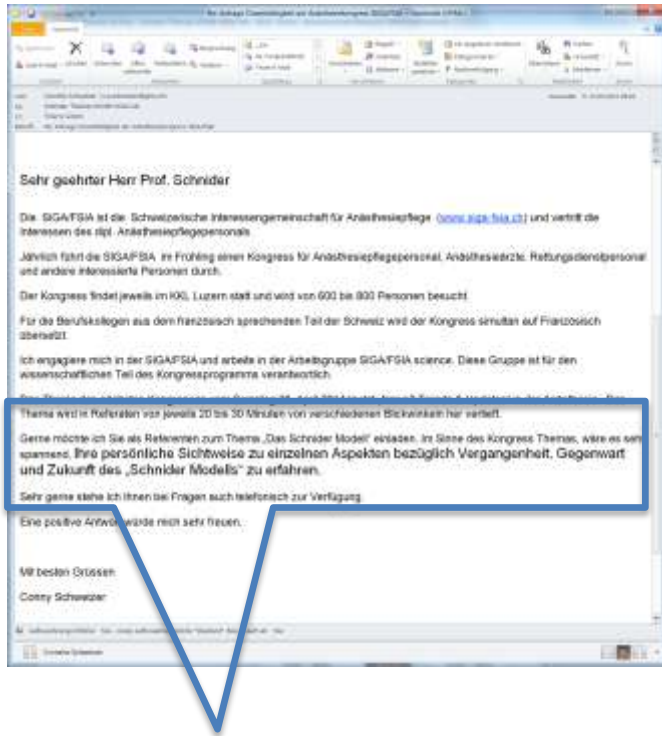


Das Schnider Modell

Thomas Schnider

*Klinik für Anästhesiologie, Intensiv-, Rettungs- und
Schmerzmedizin*

*Kantonsspital
St.Gallen*



«Im Sinne des Kongress Themas, wäre es sehr spannend, Ihre persönliche Sichtweise zu einzelnen Aspekten bezüglich **Vergangenheit, Gegenwart und Zukunft des „Schnider Modells“** zu erfahren.»

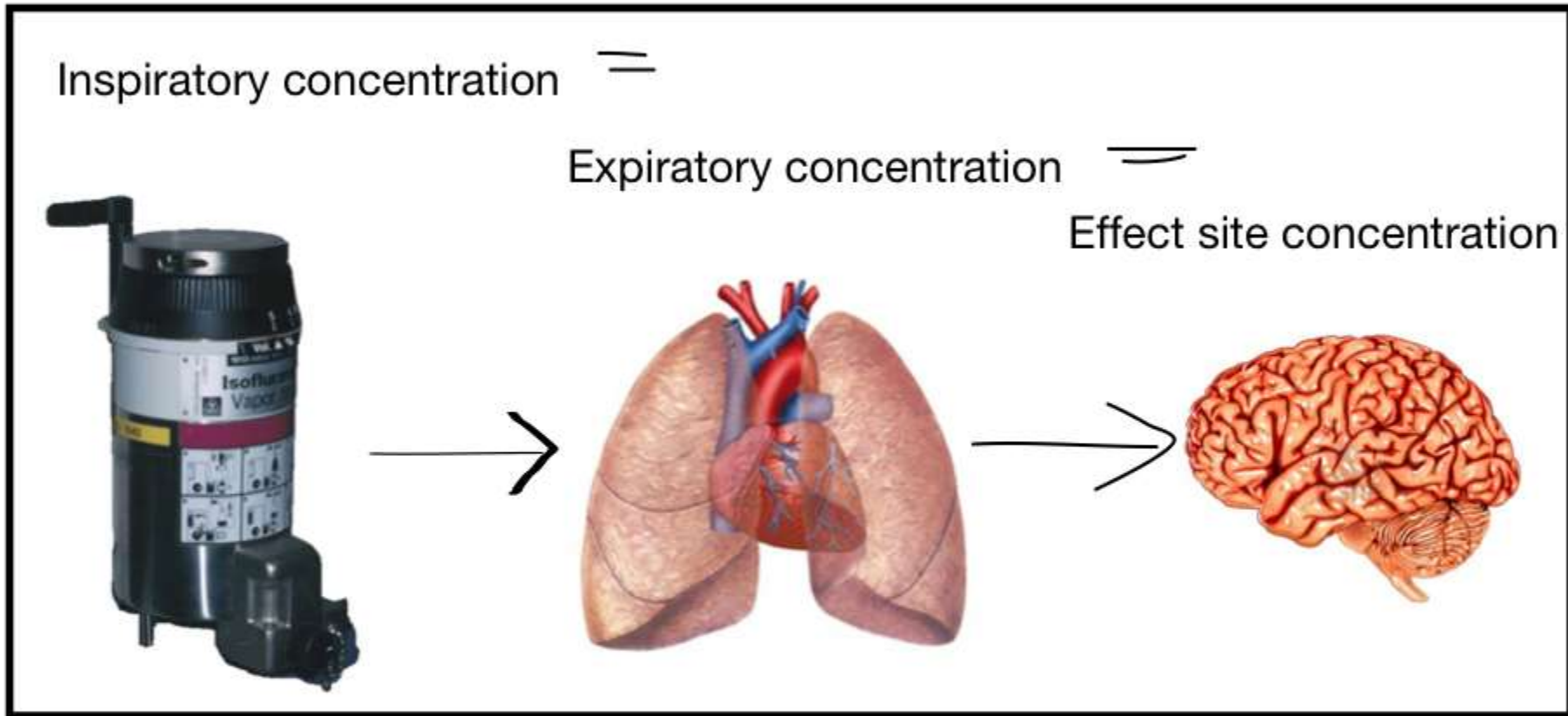
Das Schnider Modell

MODELL – WAS IST DAS?

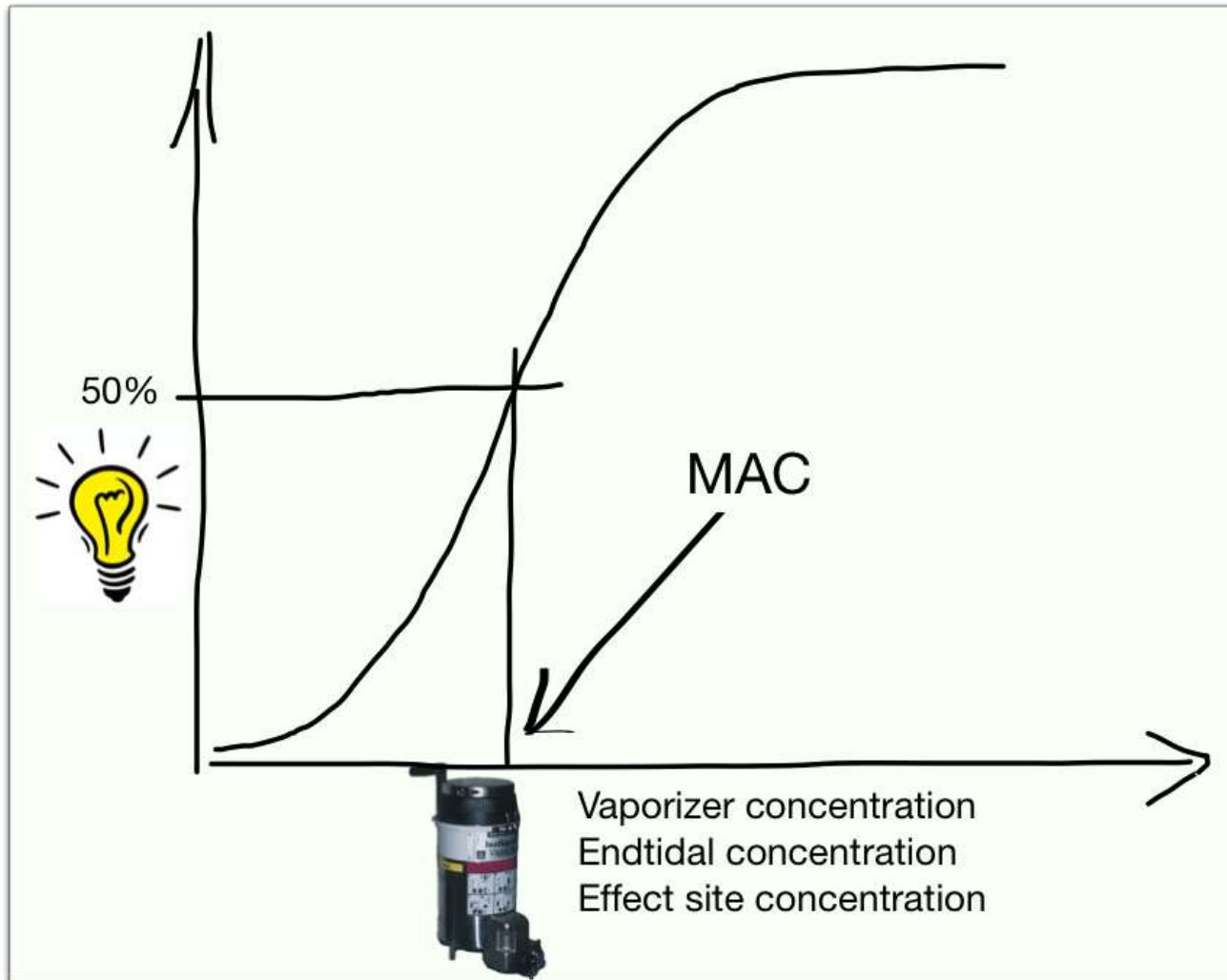
Konzentration wird gewählt!



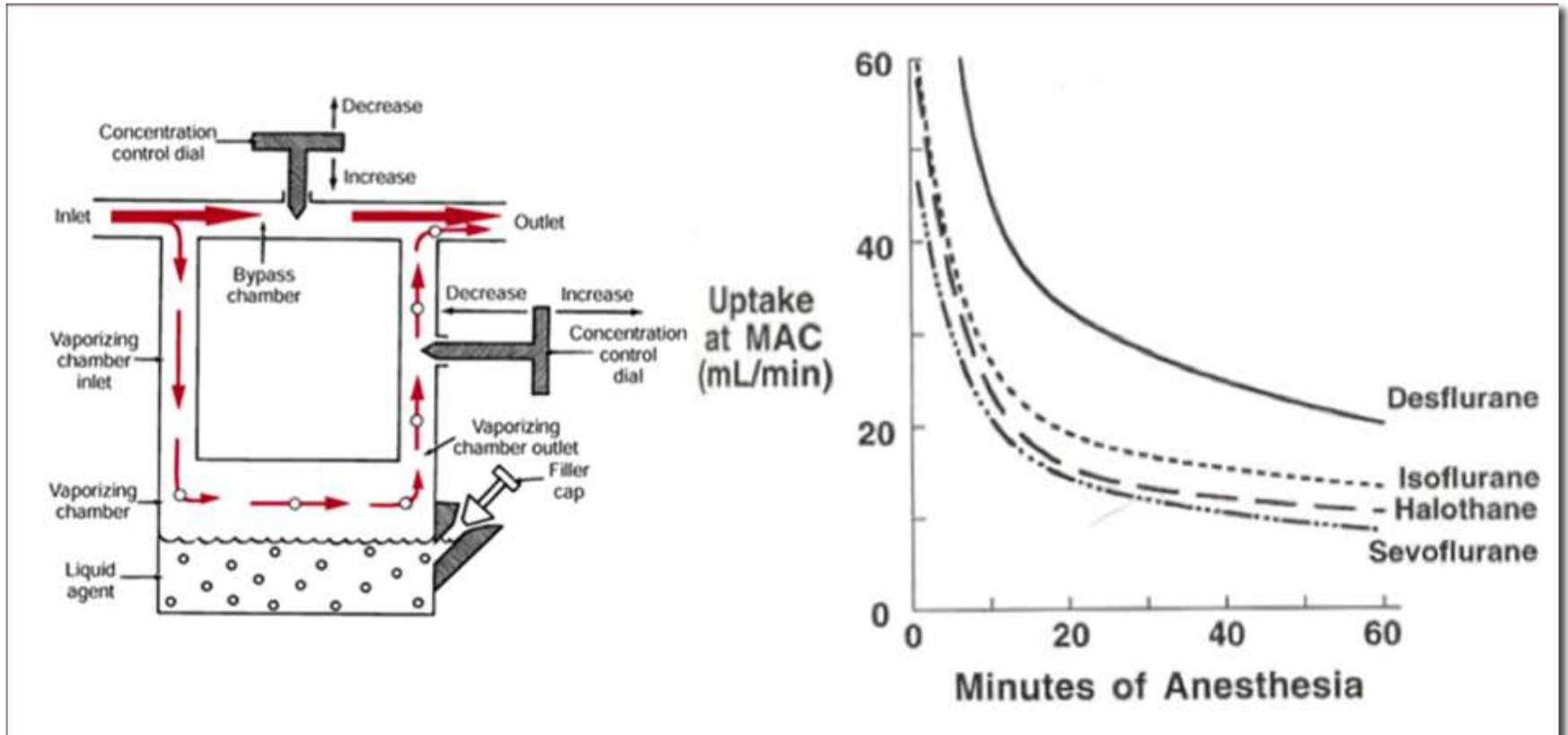
Die Annahme:



MAC - Wirkung

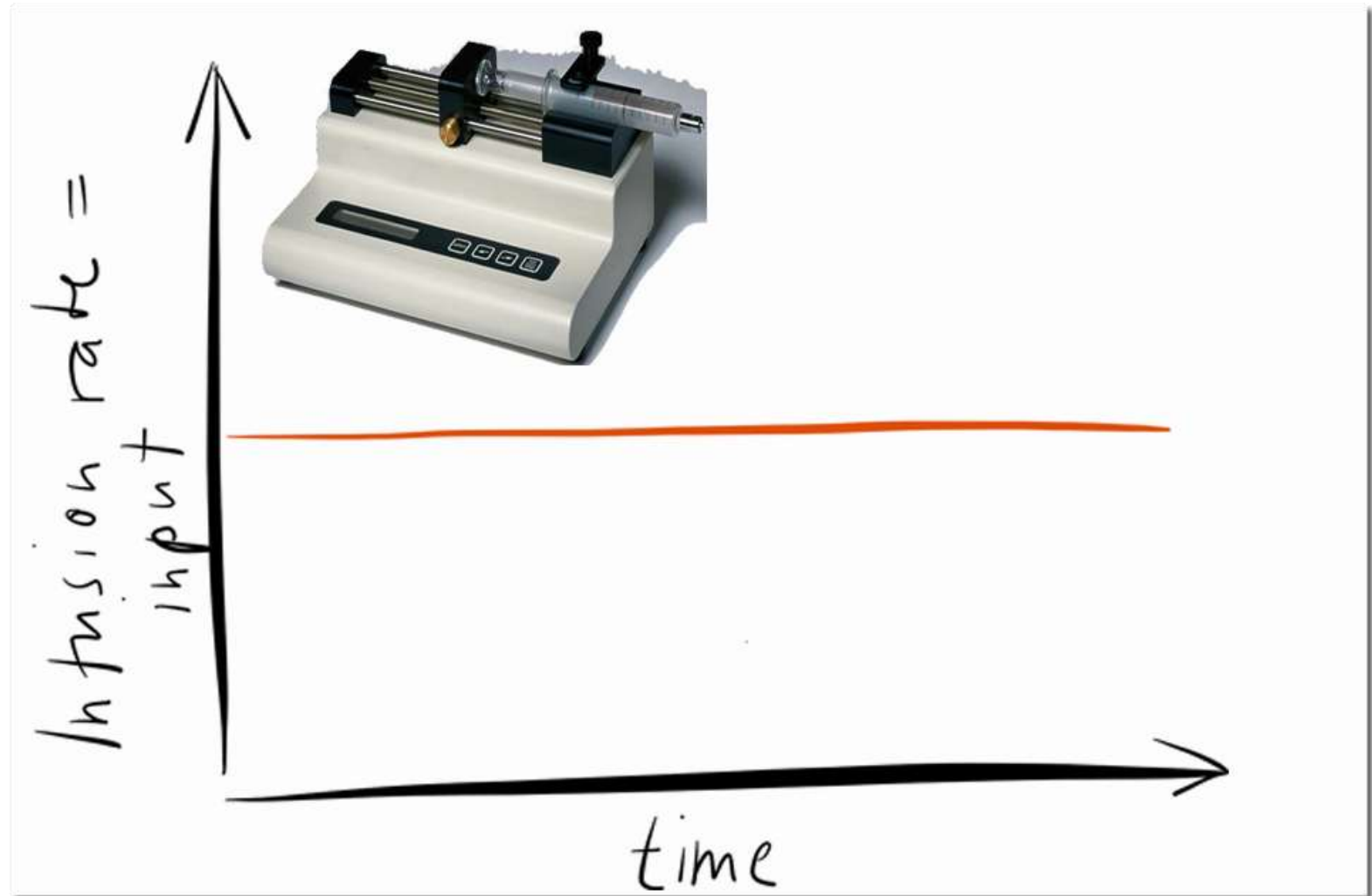


Verdampfer Einstellung konstant Abgabe von Volatilem ändert!



Yasuda et al. Anesthesiology 1991

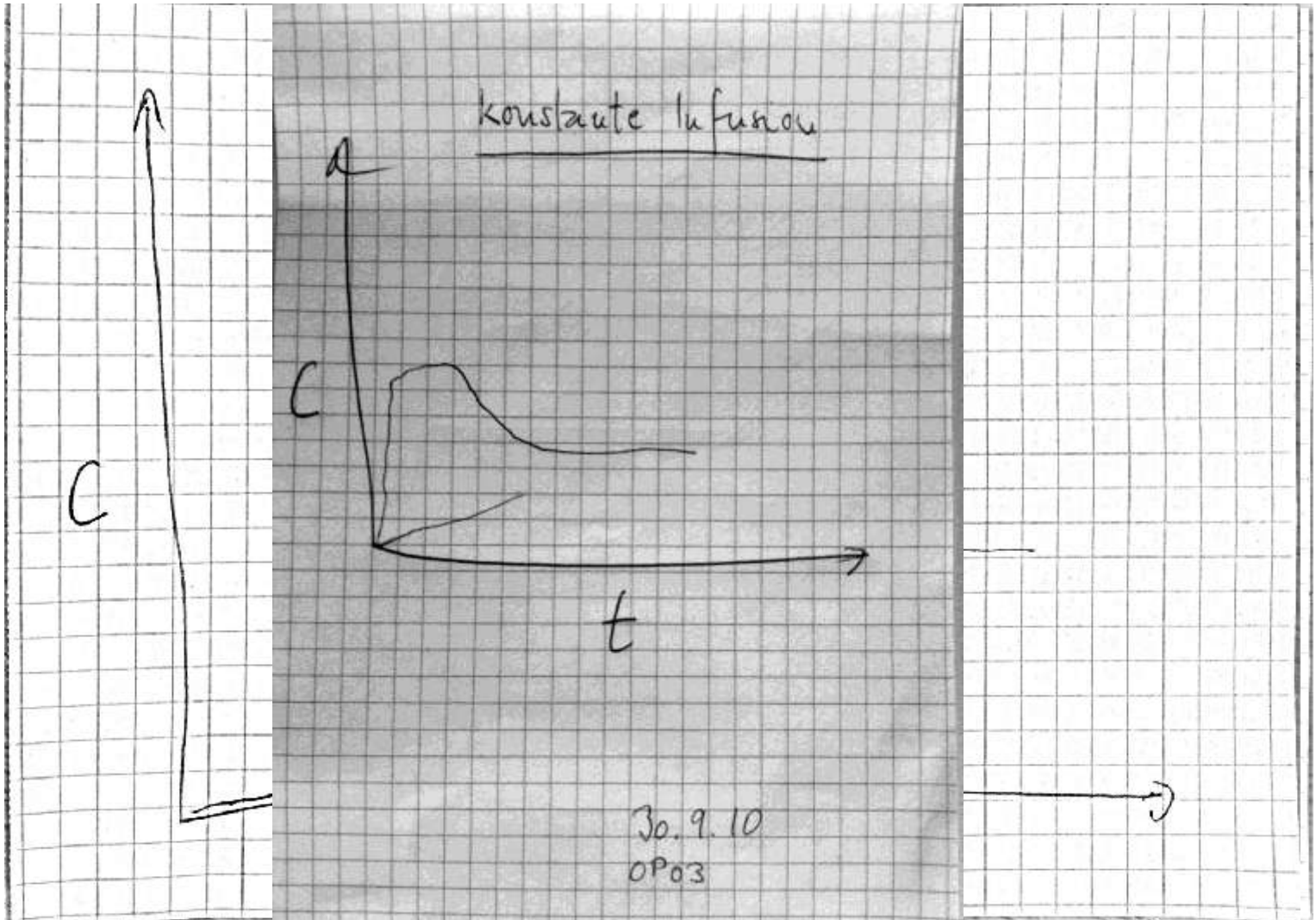
TIVA: Zufuhr konstant



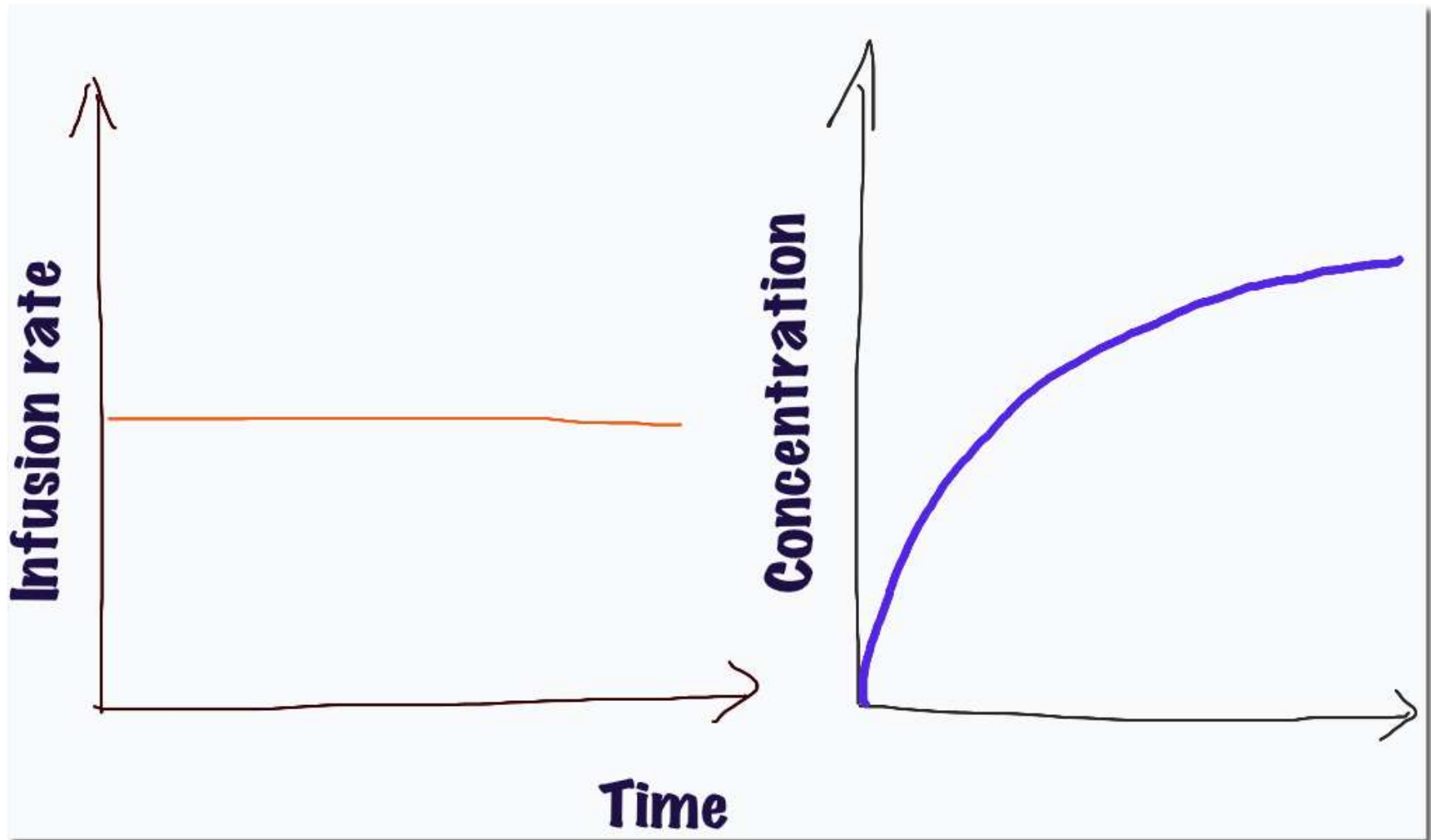
Konstante Infusion:

Wie sieht der Verlauf
der Konzentration aus?

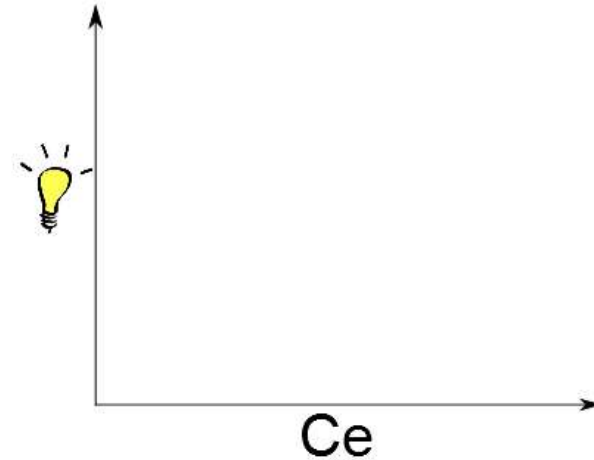
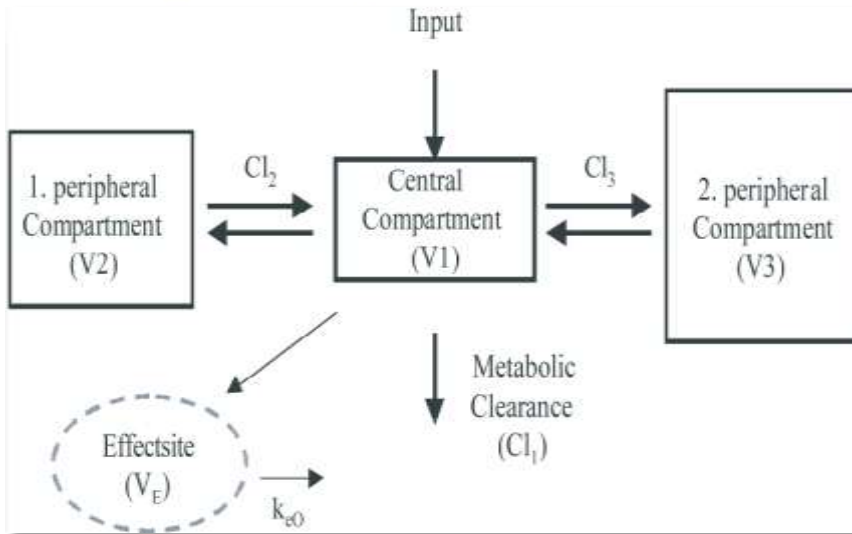
Antworten:



TIVA/konstante Infusion:



Input - Konzentration - Wirkung



Das Schnider Modell

VERGANGENHEIT

POSTOPERATIVE INFECTIONS TRACED TO CONTAMINATION OF AN INTRAVENOUS ANESTHETIC, PROPOFOL

SIIRI N. BENNETT, M.D., MICHAEL M. McNEIL, M.B., B.S., M.P.H., LEE A. BLAND, M.A., M.P.H., MATTHEW J. ARDUINO, M.S., DR.P.H., M. ELSA VILLARINO, M.D., M.P.H., DENNIS M. PERROTTA, PH.D., DALE R. BURWEN, M.D., SHARON F. WELBEL, M.D., DAVID A. PEGUES, M.D., LEONARDO STROUD, M.D., M.P.H., PAUL S. ZEITZ, D.O., M.P.H., AND WILLIAM R. JARVIS, M.D.

Abstract *Background.* Between June 1990 and February 1993, the Centers for Disease Control and Prevention conducted investigations at seven hospitals because of unusual outbreaks of bloodstream infections, surgical-site infections, and acute febrile episodes after surgical procedures.

Methods. We conducted case-control or cohort studies, or both, to identify risk factors. A case patient was defined as any patient who had an organism-specific infection or acute febrile episode after a surgical procedure during the study period in that hospital. The investigations also included reviews of procedures, cultures, and microbiologic studies of infecting, contaminating, and colonizing strains.

Results. Sixty-two case patients were identified, 49 (79 percent) of whom underwent surgery during an epidemic period. Postoperative complications were more frequent during the epidemic period than before it. Only exposure to propofol, a lipid-based anesthetic agent, was

significantly associated with the postoperative complications at all seven hospitals. In six of the outbreaks, an etiologic agent (*Staphylococcus aureus*, *Candida albicans*, *Moraxella osloensis*, *Enterobacter agglomerans*, or *Serratia marcescens*) was identified, and the same strains were isolated from the case patients. Although cultures of unopened containers of propofol were negative, at two hospitals cultures of propofol from syringes currently in use were positive. At one hospital, the recovered organism was identical to the organism isolated from the case patients. Interviews with and observation of anesthesiology personnel documented a wide variety of lapses in aseptic techniques.

Conclusions. With the increasing use of lipid-based medications, which support rapid bacterial growth at room temperature, strict aseptic techniques are essential during the handling of these agents to prevent extrinsic contamination and dangerous infectious complications. (*N Engl J Med* 1995;333:147-54.)

A Randomized, Double-blind, Age-stratified, Two-period, Cross-over, Comparison
of the Safety, Efficacy, and Pharmacokinetics of ZENECA ZD0859#1 with Diprivan™
(propofol) in Healthy Subjects

Trial 0859IL/0051

FINAL

Date: 26 August 1994
Amended: 03 November 1994

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Diprivan is a trademark, the property of ZENECA Limited

Population; Schnider et al. 1997

Table 1. Study population

inf	age	weight	height	gender
25	34	46.3	158	f
25	31	123	196	m
25	62	79.4	170	m
25	65	79.4	182	m
25	77	74.8	183	m
25	70	62.6	175	m
50	30	64.4	170	m
50	27	74.8	188	m
50	46	93.4	182	m
50	41	90.7	178	f
50	72	88.4	183	m
50	75	64.4	168	f
100	29	95.2	188	m
100	26	88.4	178	m
100	55	44.7	168	f
100	51	79.8	175	f
100	81	74.8	178	m
100	72	70.3	170	f
200	31	91.2	180	f
200	25	63.5	158	f
200	62	86.2	180	m
200	38	88.4	173	f
200	74	70.3	160	f
200	75	44.4	155	f

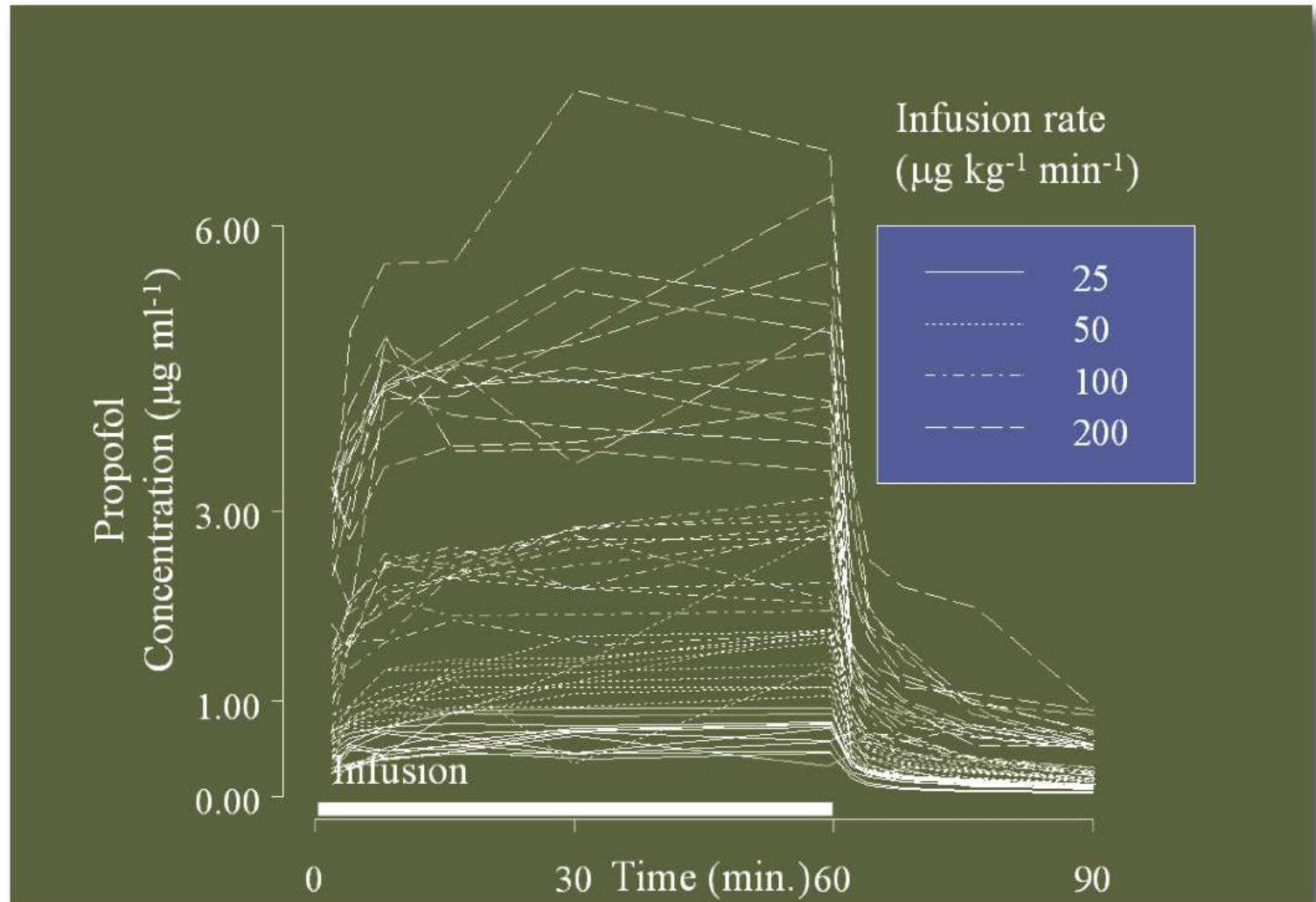


Nur mit gleichzeitiger
Messung der Wirkung
kann die Blut – Hirn
Transferkonstante
berechnet werden!





Schnider et al. 1997



Eckdaten der Studie:

- Freiwillige (bis 81 Jahre)
- Normalgewicht

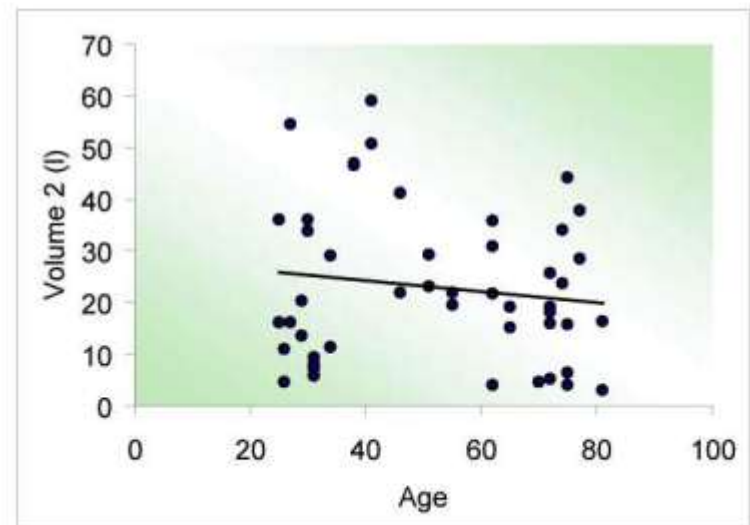
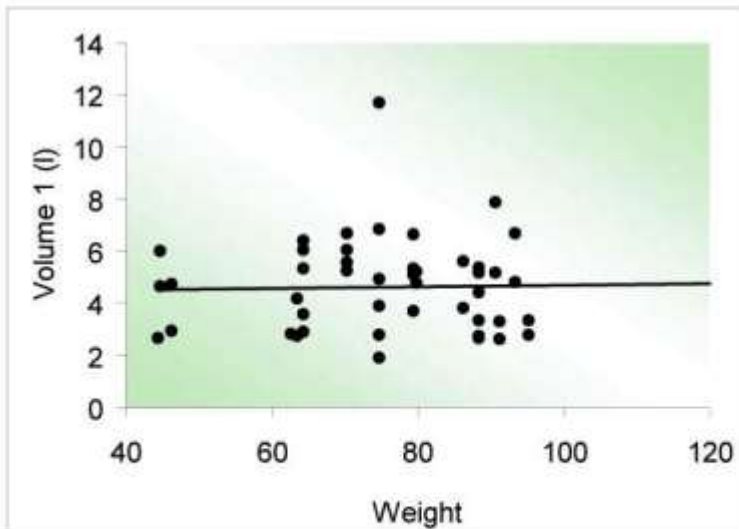
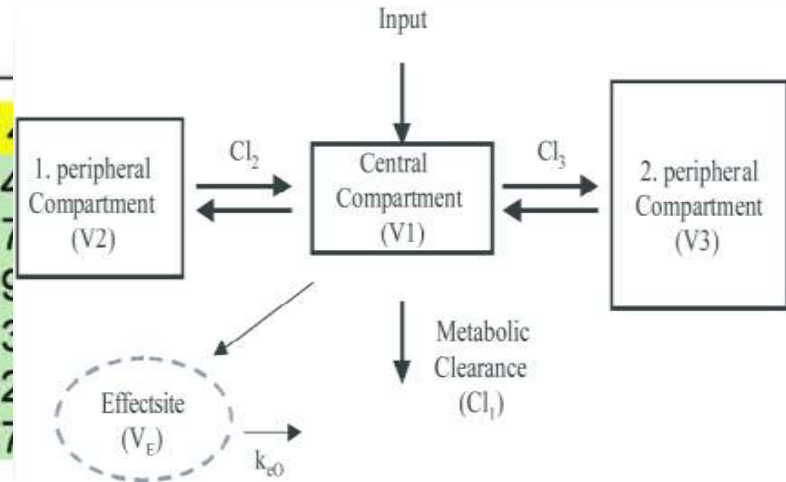
- Bolus: 2/1 mg/kg
- Nach 60 min.: Infusion (60 min.): 25, 50, 100, 200 $\mu\text{g kg}^{-1} \text{ min}^{-1}$ (Grosser Infusionsbereich!)
- **Gleichzeitige Messung der Wirkung (EEG)**

Das Schnider Modell kann und soll deshalb für **Wirkort TCI** verwendet werden

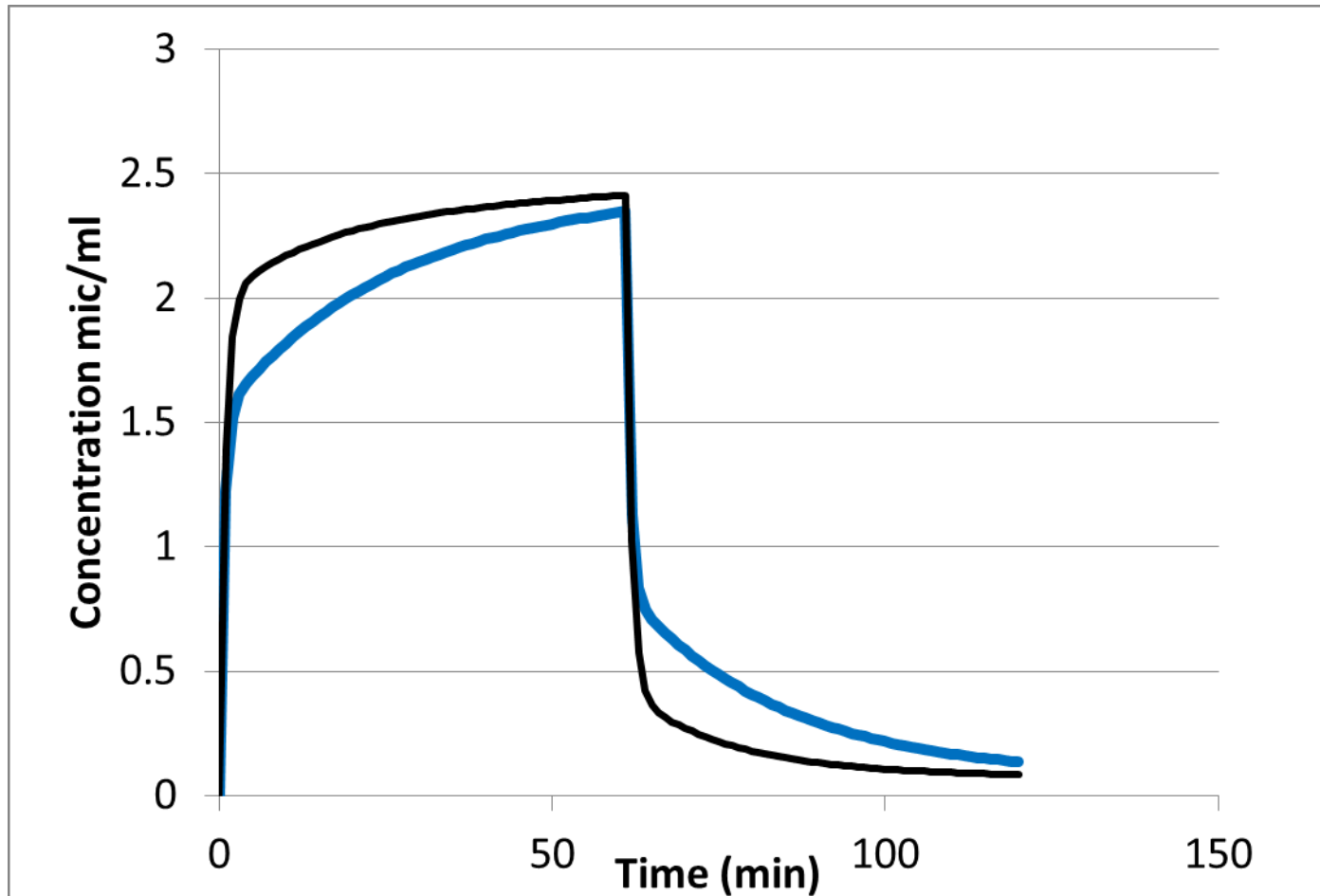
Beziehung zw. Parameter und Kovariaten

Schnider et al. Anesthesiology 1997

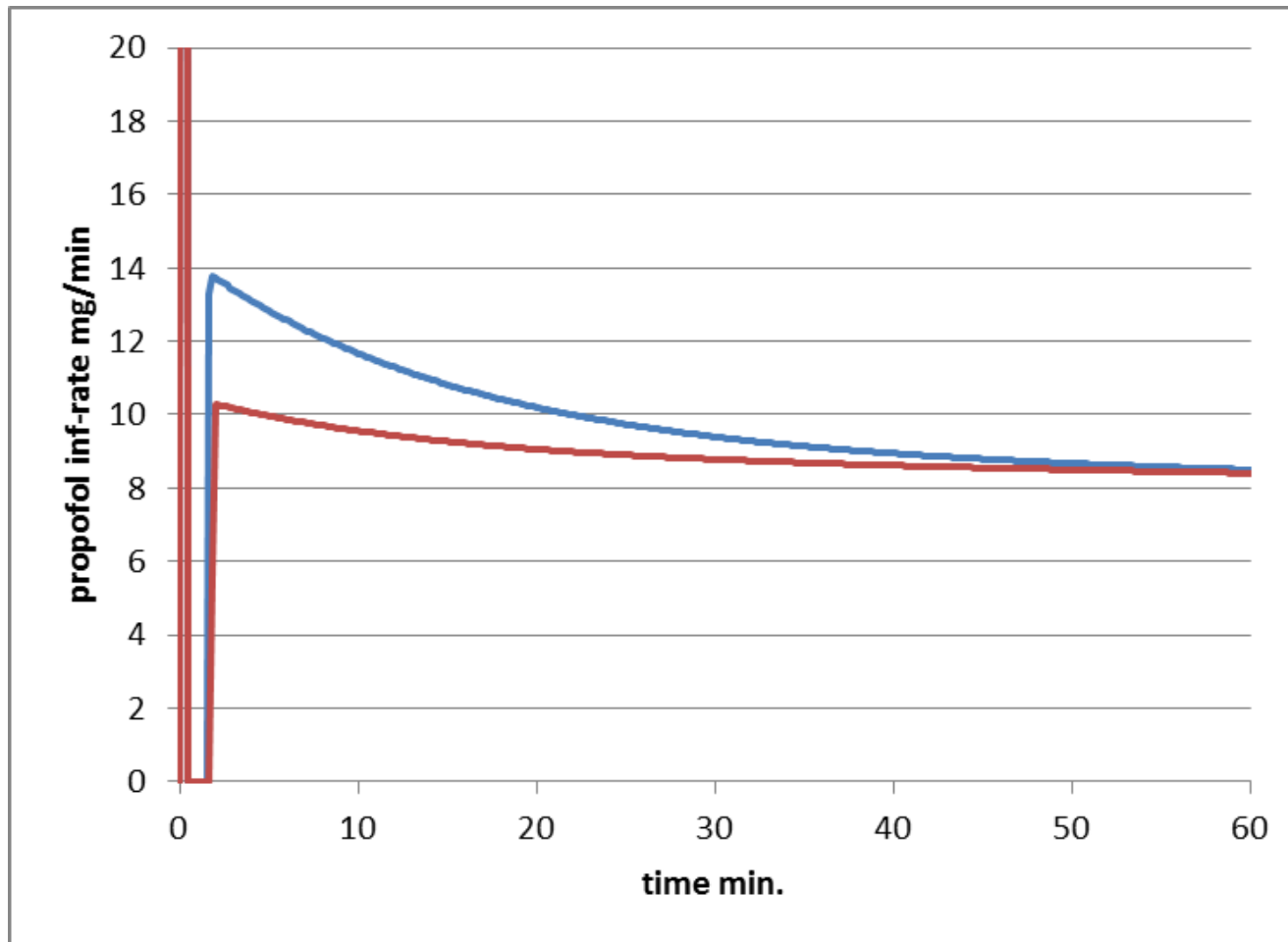
	Patient 1	Patient 2	Patient 3	Patient 4
V1	2.93	4.75	5.33	6.4
V2	11.29	29.03	36.02	33.7
V3	145.00	302.30	677.81	211.9
Cl1	1.40	1.69	2.65	3.3
Cl2	0.90	1.54	1.68	2.2
Cl3	0.71	0.84	0.89	0.7



Nicht skalierender Einfluss von Alter:



TCl: 3 mic/ml



Das Schnider Modell

GEGENWART

Schnider Modell vor Gericht! (M. Jackson † /Murray Trial)



British Journal of Anaesthesia 104 (4): 452–8 (2010)
doi:10.1093/bja/aeq028 Advance Access publication February 26, 2010

BJA

Study of the time course of the clinical effect of propofol compared with the time course of the predicted effect-site concentration: performance of three pharmacokinetic–dynamic models

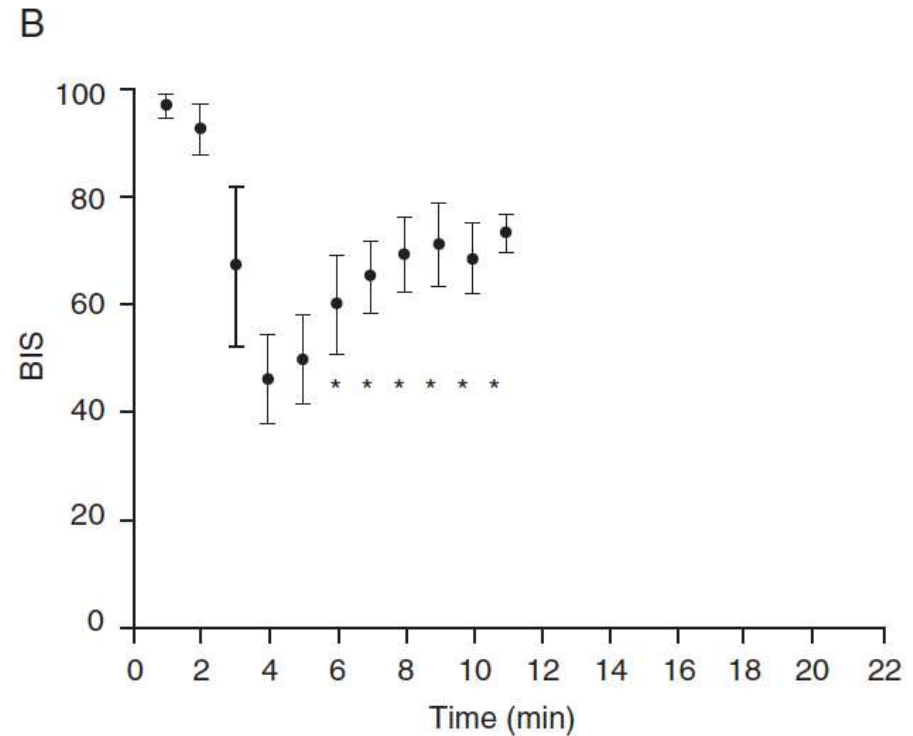
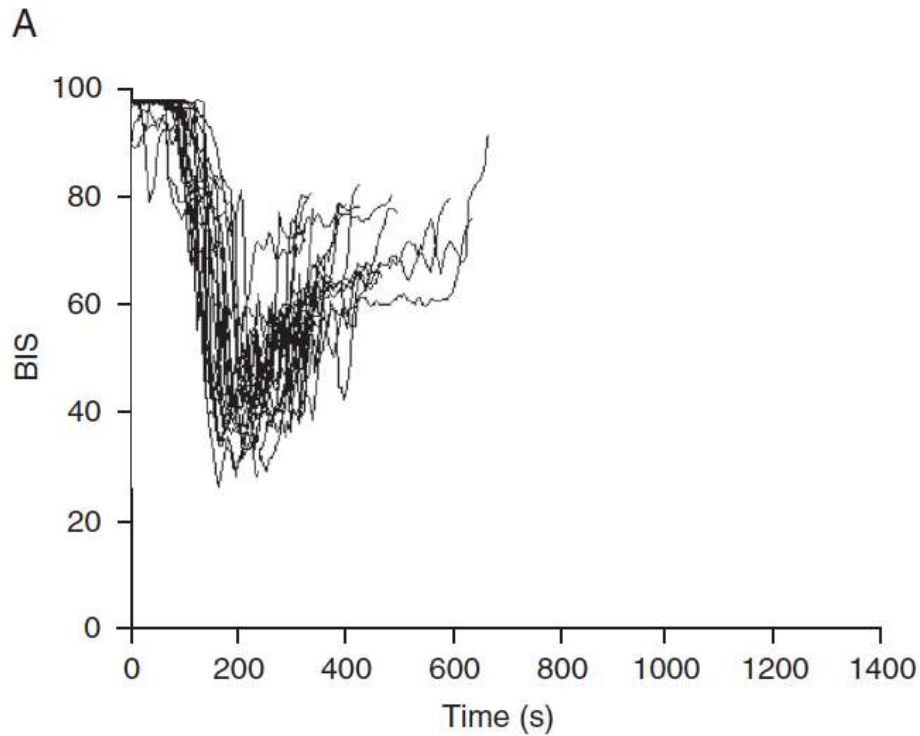
M. Coppens¹, J. G. M. Van Limmen¹, T. Schnider³, B. Wyler⁴, S. Bonte¹, F. Dewaele²,
M. M. R. F. Struys^{5 6} and H. E. M. Vereecke^{1*}

Study of the time course of the clinical effect of propofol compared with the time course of the predicted effect-site concentration: performance of three pharmacokinetic–dynamic models

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M. M. R. F. Struys^{5,6} and H. E. M. Vereecke^{1*}

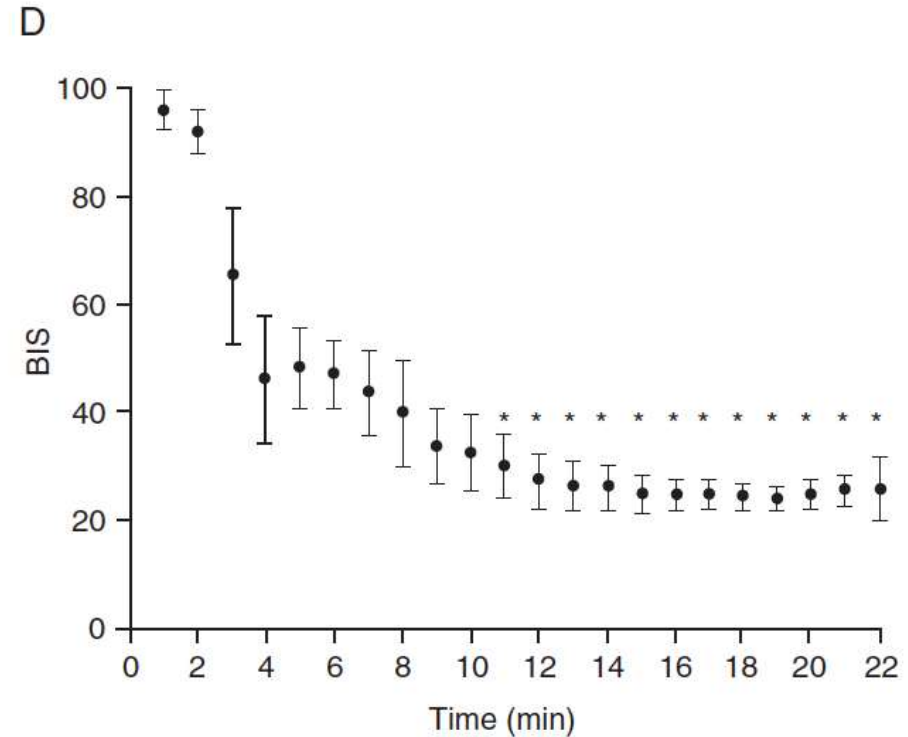
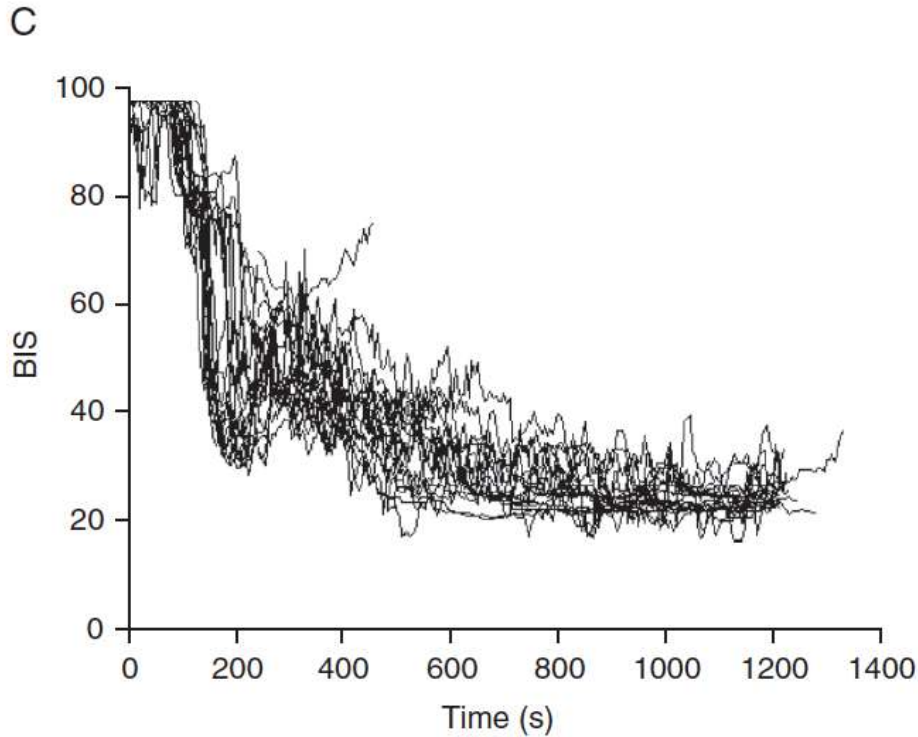
- Propofol 1%: Start 300 ml/h
- Berechnete Konzentration von “Loss of response to name calling” (LORNC)
-> Zielkonzentration (S,M)
- Wirkort TCI mit (dieser) Konzentration
- Mass für die Wirkung: BIS

Verlauf BIS: Marsh



British Journal of Anaesthesia **104 (4):** 452–8 (2010)

Verlauf BIS: Schnider, k_{e0} 0.456



British Journal of Anaesthesia **104** (4): 452–8 (2010)

Wenn *Einschlaf* - Wirkort

Konzentration konstant gehalten:

- Marsh Parameter (k_{e0} von Diprifusor): Die **Patienten wachen auf!**
- Schnider Parameter: **BIS sinkt**

British Journal of Anaesthesia **104 (4):** 452–8 (2010)

Einfluss auf Einschlaf - Wirkort Konzentration?



ANESTHESIA & ANALGESIA

The Performance of Compartmental and Physiologically Based Recirculatory Pharmacokinetic Models for Propofol: A Comparison Using Bolus, Continuous, and Target-Controlled Infusion Data

Kenichi Masui, MD, PhD,*† Richard N. Upton, BSc, PhD,‡ Anthony G. Doufas, MD, PhD,§
Johan F. Coetzee, BSc, MB, ChB, MMed(Anes.), FCA(SA), Dip.Dat., PhD,|| Tomiei Kazama, MD, PhD,*
Eric P. Mortier, MD, DSc,† and Michel M. R. F. Struys, MD, PhD¶†

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August 2010 • Volume 111 • Number 2

when combining all this information, it seems that the Schnider model, although still not perfect, has the fewest shortcomings compared with the other models and could become the recommended model to be used for TCI and advisory displays. ■■

Das Schnider Modell

ZUKUNFT

CL wird u.a. durch LBM beeinflusst

$$Cl_1 = 1.89 + ((weight - 77) * ((LBM - 59) * (-0.0681))) + ((height - 177) * 0.0264)$$

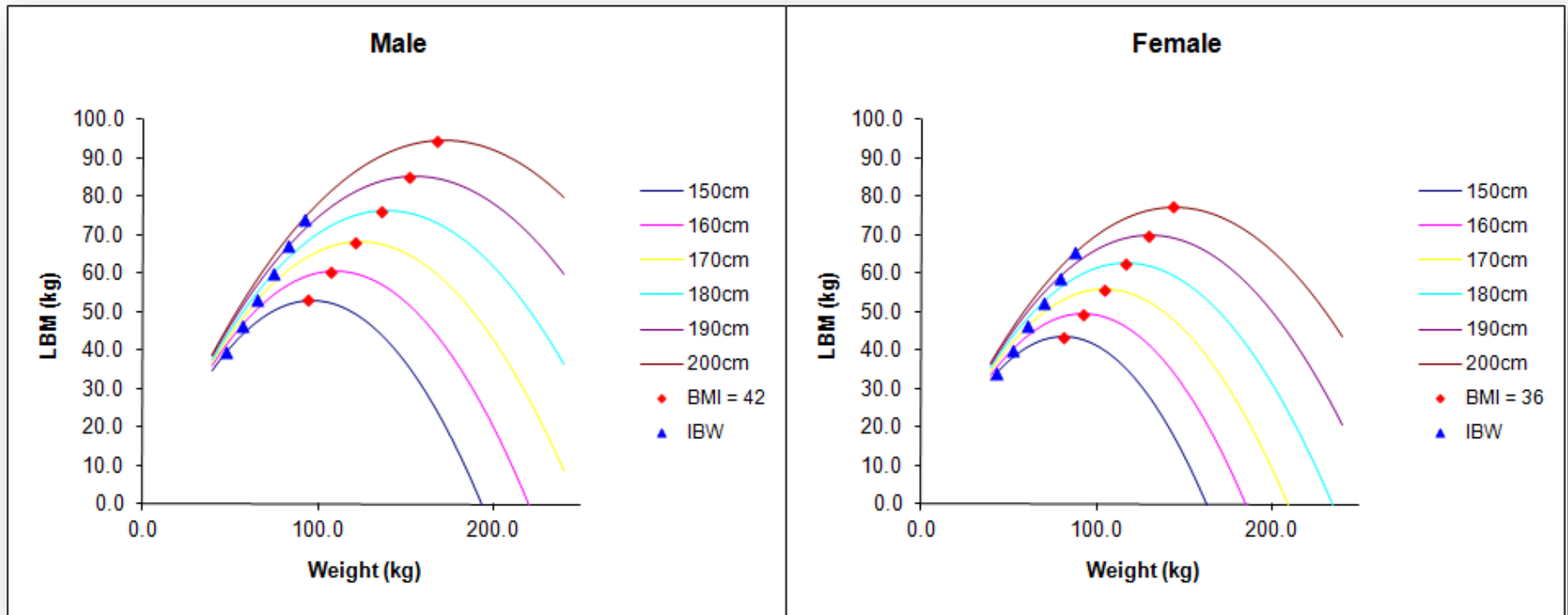
Problem LBM Berechnung!

$$LBM_M = 1.1 * weight - 128 \left(\frac{weight}{height} \right)^2$$

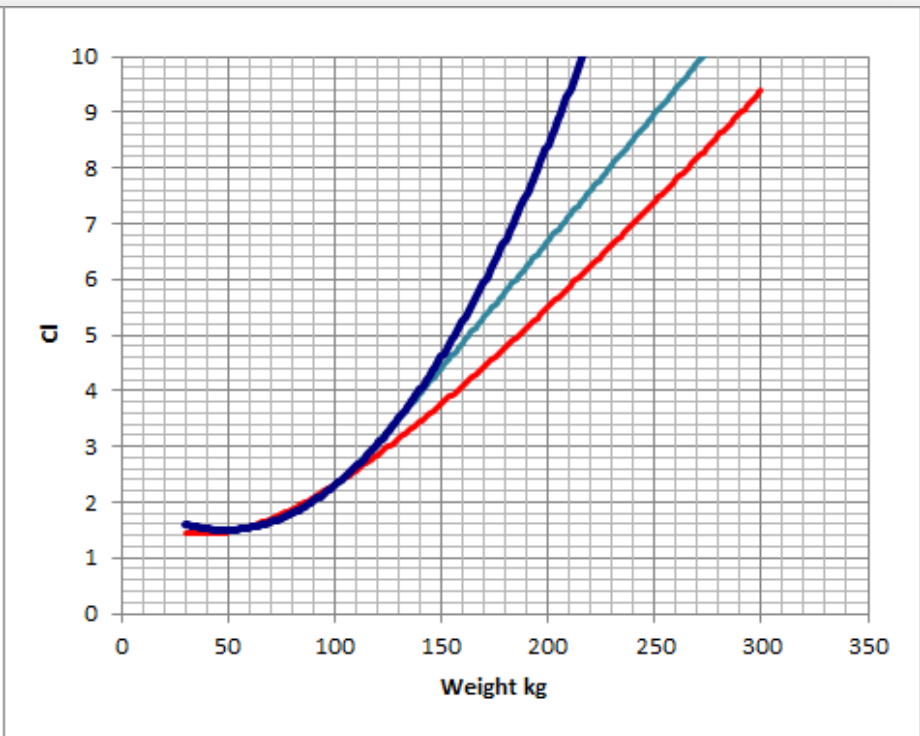
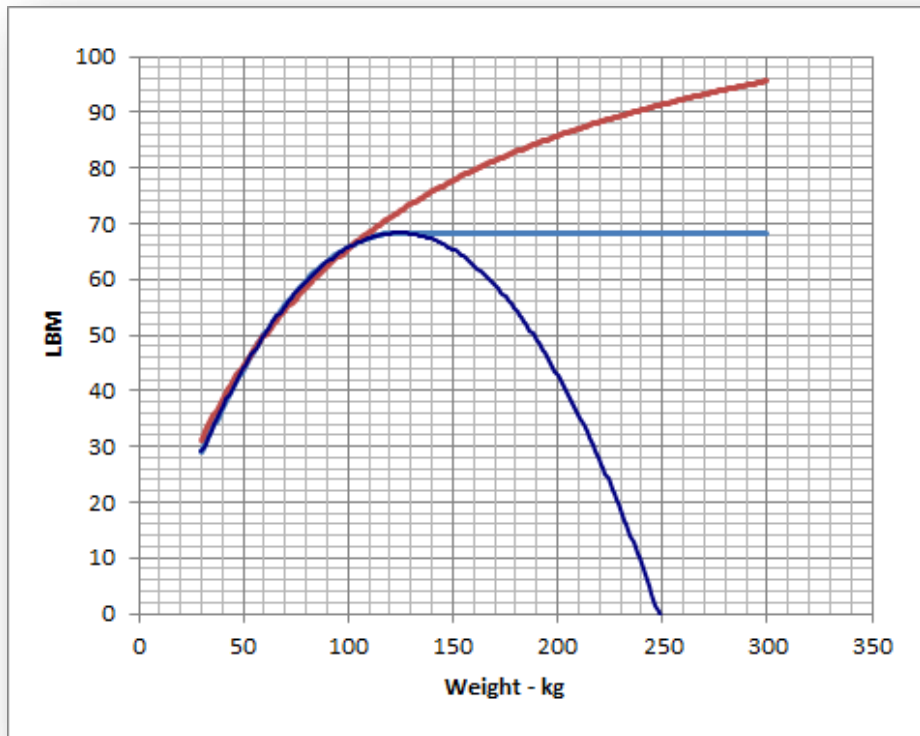
$$LBM_F = 1.07 * weight - 148 \left(\frac{weight}{height} \right)^2$$

James W. Research on Obesity. London: Her Majesty's Stationery Office; 1976

James eq.:



LBM beeinflusst Clearance



Das “LBM Problem” des Schnider Modells könnte einfach “geflickt” werden:

Aber:

Es bleibt Extrapolation!

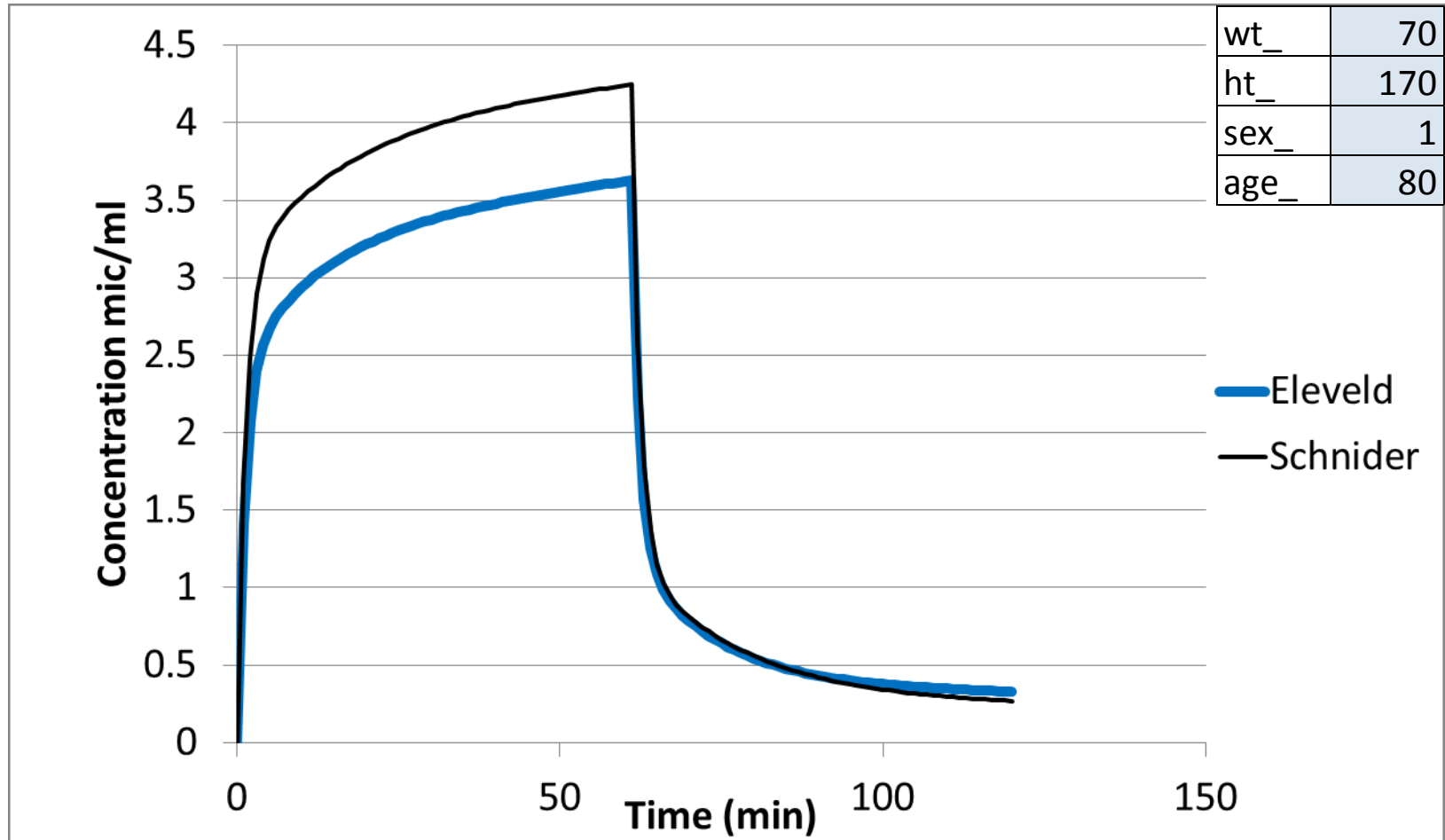
Mögliches zukünftiges Modell für Propofol:

Dataset	N		Sampling	Age (yr)	Weight (kg)	Reference	Source
Bailey et al, Learning set	30	patients	arterial	44-79	50-122	38	http://opentci.org/
Billard 1998 Propofol	51	patients	venous	29-69	40-89		http://opentci.org/
Coetzee Validation Study	30	patients	arterial	21-58	42-83		http://opentci.org/

21 Studien: 10927 Konzentrationen, 660 Pat/Freiw. 0.25 – 88 yr; 5.2 – 160 kg

Doufas Fixed Reduction Study	10	volunteers	arterial	21-44	57-82	40	http://opentci.org/
Doufas Redhead Study	29	volunteers	arterial	19-39	50-99		http://opentci.org/
Dyck et al.	59	volunteers	arterial	23-82	57-114	41	http://opentci.org/
Gepts et al.	16	patients	arterial	25-85	48-84	42	http://opentci.org/
Kataria et al.	53	patients	venous	3-11	15-60	43	http://opentci.org/
Schnider et al.	24	volunteers	arterial	25-81	44-123	44	http://opentci.org/
Servin et al, Propofol in obese patients	8	patients	arterial	25-66	97-160	45	http://opentci.org/
Servin et al, Propofol in alcoholic patients	30	patients	venous	19-72	51-97	46	http://opentci.org/
Struys et al, Propofol bolus study	10	volunteers	arterial	22-48	51-86	47	http://opentci.org/
Coppens et al, Propofol PK/PD in children	28	patients	venous	3-11	15-54	2	Personal communication (MMRF Struys)
Marsh et al, Propofol PK in children	37	patients	venous	2-17	12-54	3	Personal communication (M White)
Cortinez et al, Propofol PK in children	41	patients	arterial	0-2	5-11	14	Personal communication (I Cortinez)
Cortinez et al, Propofol PK in obese patients	19	patients	arterial	28-56	82-134	9	Personal communication (I Cortinez)
Servin et al, Propofol in cirrhosis	9	patients	arterial	24-56	50-96	48	Personal communication (I Glen)
Swinhoe et al, Diprifusor evaluation	41	patients	arterial	21-79	36-104	49	Personal communication (I Glen)
White et al, Age and gender covariates	107	patients	venous	17-88	42-100	50	Personal communication (M White)

Vergleich von Plasmakonzentrationen



Zusammenfassung

Das Schnider Modell (für TCI)...

- ... wurde vor 20 Jahren basierend auf Konzentrations- und Wirkungsmessungen entwickelt!
 - ➔ Bluthirn – Transfer konnte direkt ermittelt werden
- ... verschiedene Altersgruppen bis > 80 Jahre!
 - ➔ Einfluss von Alter!
- Nicht für (sehr) Adipöse entwickelt

A photograph of a house with a large tree in the foreground, with text overlaid. The house is on the left, and the tree is in the center. The text is in red with a black outline.

**In St.Gallen verwenden wir das
Schnider Modell!**

UND

**Die Zielkonzentration wird
entsprechend der beobachteten
Wirkung angepasst!**

Vielen Dank für die Aufmerksamkeit!