Closed-Loop Control of General Anesthesia: “My Clinical Experience”

Ngai LIU, M.D.
50 patients, ETHER
“Major Surgical procedures
varying age, both sexes
Without untoward effect “
Feasibility of Feedback control of Propofol During GA Maintenance Using the BIS monitor
Proportional-Differential + TCI propofol (Schnider) + Feed-forward
Feasibility of closed-loop titration of propofol guided by the Bispectral Index for general anaesthesia induction: a prospective randomized study

European Journal of Anaesthesiology


June 2006, pp 470-475

Prospective randomized study
20 patients/group

Manual vs Automated induction
We wanted to compare our closed-loop controller to the manual TCI Titration in varying conditions of routine clinical anesthesia. Including minor and major surgery.

The titration of remifentanil TCI during the surgical procedure was decided by the physician in charge of the patient in both groups.

End point: $40 < \text{BIS} < 60$ during maintenance.
Adequate anesthesia was more frequent in the Closed-loop group

70 ± 21 vs 89 ± 9,
p = 0.0001

Adequate anesthesia was more frequent in the Closed-loop group

Anesthesiology 2006; 104:686–95
Assessment of surgical stress during general anaesthesia
M. Huiku\textsuperscript{1,2}, K. Uutela\textsuperscript{1,3}, M. van Gils\textsuperscript{2}, I. Korhonen\textsuperscript{2}, M. Kymiäläinen\textsuperscript{1,4}, P. Meriläinen\textsuperscript{1,4}, M. Paloheimo\textsuperscript{1,3}, M. Rantanen\textsuperscript{4,5}, P. Takala\textsuperscript{1,6}, H. Viertio-Oja\textsuperscript{1,7} and A. Yli-Hankala\textsuperscript{1,8}
Case report

Male 72 years
History of coronary disease (CABG and Angioplasty)
Beta-blocker

Tympanoplasty

General Anesthesia
Closed-loop
    Propofol
Manual TCI of Remifentanil
Bolus of Atracurium
Instability!  
Oscillation!
Your hypothesis?
Anesthesia depth

Dynamic Balance between

Hypnosis and Analgesia

Poor Analgesia

BIS Instability (oscillation)!
With a Closed-loop BIS-Propofol system, we obtain a stable level of hypnosis and the BIS can also reflect the degree of inhibition of response to noxious stimuli.

If BIS suddenly increases in response to noxious stimuli, this could be a deficit in the analgesic component of anesthesia, and this requires an increase of analgesia.

We have implemented a second closed-loop controller between Remifentanil and BIS using a Proportional-differential algorithm.

\[
GA = LOC + \text{Inhibition of noxious stimuli}
\]

P. Glass Anesthesiology 1998, 88; 5-6
T. Bouillon et al Anesthesiology 2004
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We learn from failure Not from success.
Male 27 years, Kidney Transplantation, HTA
Male 27 years, Kidney Transplantation, HTA
Male 27 years, Kidney Transplantation, HTA

Incision  Retractor

Temps (en secondes)
Male, Kidney Transplantation, HTA

Graph Title

Temps (en secondes)

0
20
40
60
80
100
120

1
301
601
901
1201
1501
1801
2101
2401

Bis

Incision
Retractor

grefferénale
remifentanil
propofol

Male, Kidney Transplantation, HTA
Propofol and Remifentanil guided solely by the BIS: Manual vs Closed-loop

- Prospective Randomized, Multicenter
  After informed consent
  Ethical Committee and AFSSAPS approval
- Foch, Argenteuil, Angers, Besançon.
- Manuel vs Dual-loop
- 100 patients per group
- End points
  - Percentage 40-60
  - Movement, HD
  - Behavior of the controller during all types of surgery
  - ASA IV

A854 ASA Meeting Chicago 2006
Percentage of Time 40-60

71 % ± 19 vs 82 % ± 12 (p < 0.0001)
Feedback control of Propofol-SE

Response Entropy Increases During Painful Stimulation

Peggy Wheeler, MD, William E. Hoffman, PhD, Verna L. Baughman, MD, and Heidi Koenig, MD

(J Neurosurg Anesthesiol 2005;17:86–90)
Dual-loop in ICU,
Prospective randomized study (E. Bourgeois SFAR 2007)
Manual (n=14) vs Dual-loop sedation (n=15)

50 % → Propofol
What did the Closed-loop controller teach me?
Female 20 years, 1.70 m, 50 kg, PK Schnider
Closed-loop propofol, Remi fixed (4 ng/ml)
Female 20 years, 1.70 m, 50 kg, PK Schnider
Closed-loop propofol (1%), Remi fixed (4 ng/ml)
Piglet 22 Kg
3 month!
Propofol 2 %
Closed-loop administration of propofol and remifentanil guided by the Bispectral Index in patient requiring an emergency lung volume reduction

Paediatr Anaesth. 2007 Sep;17(9):909-10.

9-years-old boy 25 kg
Giant lobar emphysema
SpO₂ = 85 % with 10 l/min O₂

Dual-loop Propofol-Remifentanil Induction and Maintenance
Intrathecal morphine
Right postero-lateral thoracotomy
Middle lobe resection
Lower lobe atypical resection
Closed-loop administration of propofol and remifentanil guided by the Bispectral Index for transsphenoidal surgery in a patient with extreme gigantism

Age: 24
Weight: 125 kg
Height: 2.48 m!
Induction  Maintenance
Propofol      0.9 mg/kg  5.2 mg/kg/h
Remifentanil  1.9 µg/kg  0.30 µg/kg/min

40-60 : 83 %
< 40 : 15 %
> 60 : 2 %
GS : 23
Extubation : 7 min
Female, 69 years, 1.60 m, 85 kg
Aortic Stenosis
Aortic valve repair
Female, 69 years, 1.60 m, 85 kg
Aortic Stenosis
Aortic valve repair
Female, 69 years, 1.60 m, 85 kg
Aortic Stenosis
Aortic valve repair

Propofol: 0.8 mg/kg
Remifentanil: 2.6 µg/kg
Feedback control
Continuous Titration to effect compensates for most of PK Errors!

Model
Concentration
Drug

Safety +++

The impact of the PK model in a controller is low
Safety

Closed-loop controller during cardiac arrest

![Graph showing BIS and Propofol Concentration over time](Image)
Safety

Closed-loop controller during cardiac arrest
Conclusion

• Feasibility of Dual-loop
• Reliable and safe
• Closed-loop controller could fundamentally change the practice of Anesthesia !!!

“The clinician will always hold the ultimate responsibility for patient safety”
O’Hara Anesthesiology 92

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Open loop TCI
Semi-closed loop TCI
Closed-loop
What is the best for the physician?
## Emergence

<table>
<thead>
<tr>
<th></th>
<th>Manual TCI (n = 81)</th>
<th>Closed-loop (n = 83)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extubation Time (min)</td>
<td>10 ± 7</td>
<td>7 ± 4</td>
<td>0.017</td>
</tr>
</tbody>
</table>

Greater predictability and better planning of the recovery phase
Conclusions

- Models are poor and will not get much better
- Quality achievable with open-loop techniques (e.g. TCI) is limited
- Closed loop control is needed

- Need to understand sensitivity and robustness
- Need sensors

Sensors could fundamentally change the practice of anesthesia

Prof. Manfred MORARI
Case male 59 y

Norepinephrine (mg/h)

Main events

- Fibero
- TEE
- nursing
- nursing
- Fibero
- TEE

| %<40 | 4 |
| %<45 | 23 |
| %>=60 | 2 |
| %>=70 | 0 |
| %30-50 | 59 |
| %45-60 | 75 |
| %40-60 | 94 |
Closed-loop Anesthesia decreases the incidence of Too Deep Anesthesia

Weldon Anesthesiology 2002 : A1097
Lennmarken ASA 2003 : A303
Monk, ASA 2004 : A1361

Prolonged deep anesthesia was associated with increased risk of one year mortality!

Anesthetic Management and One-Year Mortality After Noncardiac Surgery  
(Anesth Analg 2005;100:4–10)

Terri G. Monk, MD, MS*, Vikas Saini, MD, FACCI, B. Craig Weldon, MD*, and Jeffrey C. Sigl, MD†

Figure 3. Efficiency of the system during maintenance of anesthesia. 40 < BIS < 60 = percentage of time in which the BIS value was between 40 and 60 during the maintenance. BIS < 45 = percentage of time in which the Bispectral index (BIS) value was below 45. BIS < 40 = percentage of time in which the BIS value was below a value of 40. BIS > 60 = percentage of time in which the BIS value was greater a value of 60. Manual TCI: Manual TCI group guided by the BIS. Closed-loop: Closed-loop group. # p < 0.0001, ns: not significant.