ANESTHESIOLOGY GRAND ROUNDS PRESENTATION
VICTOR TRAN (PGY3) - NOVEMBER 1ST , 2013

CLOSED LOOP ANESTHESIA SYSTEMS

THE FUTURE OF ANESTHESIOLOGY?

DISCLOSURES

- None!

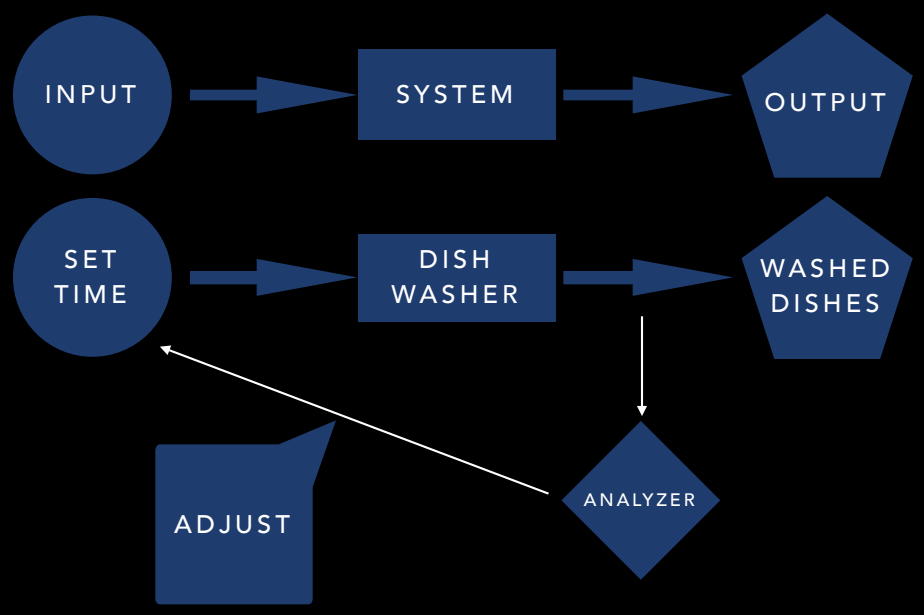
OBJECTIVES:

- Overview of closed loop anesthesia delivery systems (CLADS)
- Update on current closed loop delivery system applications / research

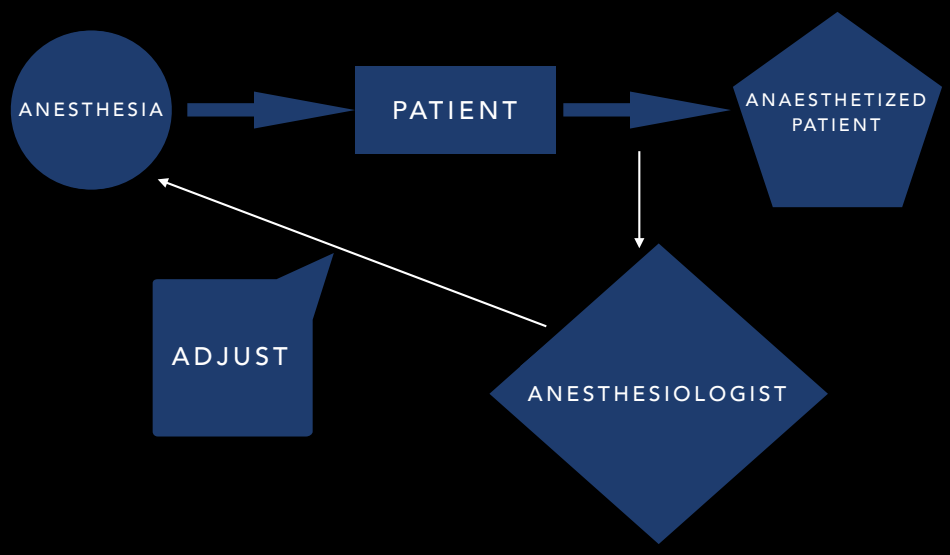
OPEN LOOP VS CLOSED LOOP

- open loop control
  - user applies an input to the system
  - the system performs
  - output is generated

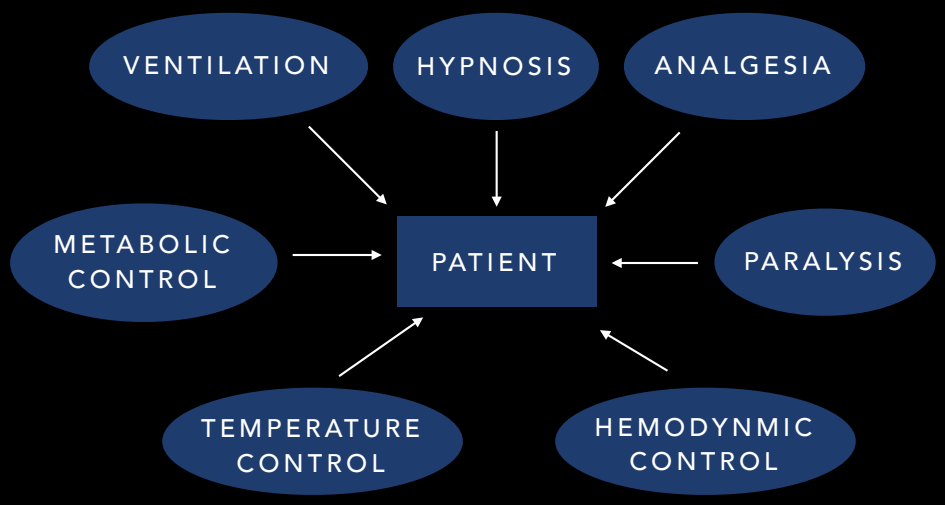
EXAMPLE: OPEN LOOP CONTROL



ANESTHESIA CLOSED LOOP



COMPLETE CLOSED LOOP DELIVERY



WHY CLOSED LOOP DELIVERY?

- Ideally…
  - consistent
  - monitor and analyze more frequently
  - act based on live analyzed data +/- models

WHY CLOSED LOOP DELIVERY?

- Most ideally…
  - allow anesthesiologist to focus on higher-clinical tasks and decisions



http://www.anaesthesiacases.com.au/freestyler/files/generated/Intubation_1_4837e4a032d16_w235.jpg
http://www.anesthesiology.uci.edu/UI/images/cline_02.jpg
http://2.bp.blogspot.com/_LPQZ94yv0kU/Rs-1Cx25hOI/AAAAAAAAAHc/G8bFOedS6aU/s400/Picture14.jpg
http://media.npr.org/assets/img/2013/02/26/nurse-phone-8013a6949bf2d335c91042a719ca128851dc356d-s6-c30.jpg
http://media.commercialappeal.com/media/img/photos/2008/05/16/a17eye2_t607.jpeg

RECAP:

- Anesthesiologists perform closed loop control on a day to day basis
- Closed loop anesthesia delivery systems (CLADS) goal:
  - decrease variation in anesthesia practice
  - constantly titrate anesthetics
  - allow the anesthesiologist to focus on higher clinical tasks

RECAP

- Closed Loop Systems employ a variety of control methods, allowing them to be:
  - reactive
  - predictive
  - adaptive
  - safe

TRANSITION INTO APPLICATIONS

- Timeline:
  - 1950's (Mayo and Bickford)
    - EEG based automatic delivery of volatile anesthetics
  - 1980's
    - end-tidal control of volatiles
    - closed loop control of neuromuscular blockers
    - MAP control

TRANSITION INTO APPLICATIONS

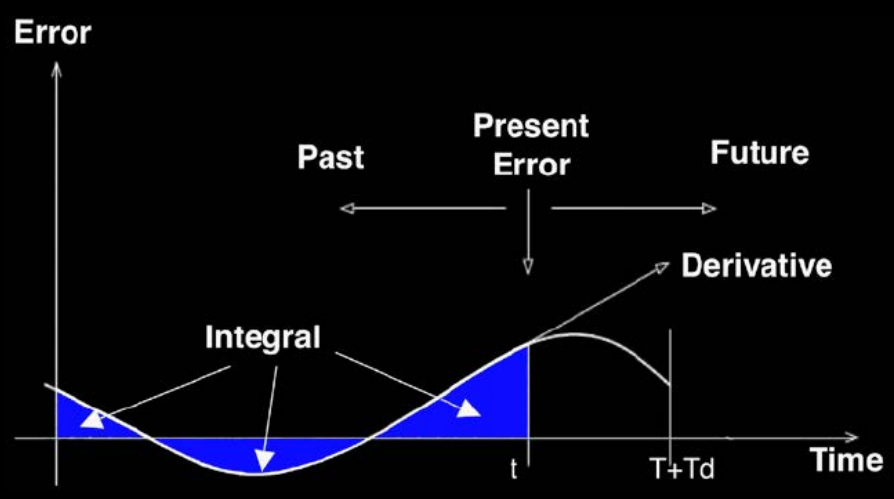
- Timeline:
  - 1989
    - Schwilden et al. published closed loop delivery of propofol guided by EEG - 11 healthy volunteers
  - mid 1990's
    - BIS monitor introduced
    - several guided controlled maintenance of volatile anesthetics
    - one group applied closed loop control for maintenance of isoflurance titrated to BIS & delivered alfentanyl to control mean arterial pressure (MAP)

TRANSITION INTO APPLICATIONS

- late 90's and early 2000's
  - PID control (proportional-integral-derivative)

$$u(t) = K\left(e(t) + \frac{1}{T_i}\int^{t} e(s)ds + T_d\frac{de(t)}{dt}\right)$$

PID



TRANSITION INTO APPLICATIONS

- late 90's early 2000's
  - Model predictive control
  - control tailored to a specific application, more complex than PID
  - allows for predictive future behaviour of the system

TRANSITION INTO APPLICATIONS

- 2000's and Present
  - adaptive control
  - intelligent control (Artificial intelligence, fuzzy logic, expert systems, neutral networks, genetic algorithms, reinforcement learning)
  - defy accurate mathematical description

APPLICATIONS

http://www.pushing-pixels.org/wp-content/uploads/2013/04/prometheus-medipod.jpg
http://cdn.bleedingcool.net/wp-content/uploads/2012/04/medpod.jpg?f6a06b

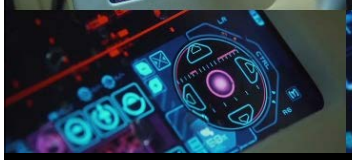
APPLICATIONS

- Present:
  - Pharmacological Anesthesia Robot (Mcgill University)
    - nicknamed “McSleepy”
  - Closed Loop Fluid Administration in Resuscitation
    - In Vivo - application

PHARMACOLOGICAL ANESTHESIA ROBOT - AKA MCSLEEPY

- McSleepy:
  - able to deliver hypnotic (propofol), paralytic (rocuronium), analgesic (remifentanyl)
  - all three phases of anesthesia (induction, maintenance, emergence)
  - first used in 2008 for partial nephrectomy
  - June 2013 presented an journal submission where they described preliminary results with 15 patients

APPLICATIONS



http://www.pushing-pixels.org/wp-content/uploads/2013/04/prometheus-medipod.jpg
http://cdn.bleedingcool.net/wp-content/uploads/2012/04/medpod.jpg?f6a06b

APPLICATIONS

2010: First robotic surgery via robotic delivered anesthetic
http://assets.muhc.ca/images/news/McSleepy-DaVinci_prostatectomy.jpg

MCSLEEPY

- Why was McSleepy different?
  - Developed a new pain score (Analgoscore based on HR and BP)
  - Able to provide anesthesia for all three phases
  - Electronically charts (anesthesia and surgical)
  - GUI & Voice Prompts
  - Telemedical applications

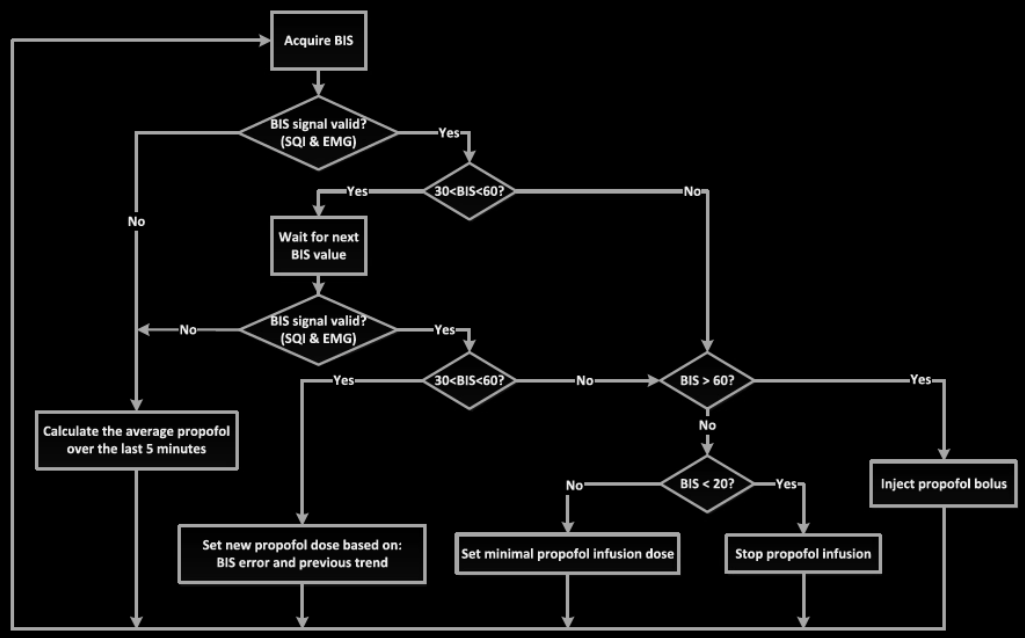
MCSLEEPY - HYPNOSIS

- BIS monitor to titrate hypnosis
- BIS averages used
  - average of 45 = target
  - average of 20 - 30 = minimal infusion
  - < 20 = stop
  - >60 = automatic bolus

MCSLEEPY - HYPNOSIS

- Safety protocols:
  - artifacts (electrocautery or muscle activity)
  - signal quality index (SQI)
  - BIS measurements valid only if:
    - SQI > 40%, EMG <40 dB
  - If BIS measurement was lost or contaminated
    - administers propofol based on the mean value over the last 5 minutes

MCSLEEPY - HYPNOSIS



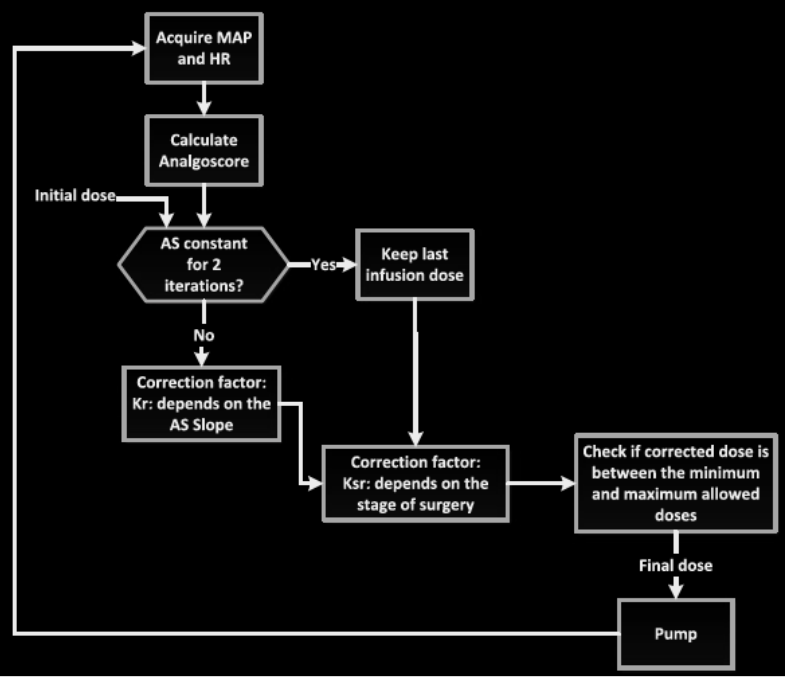
MCSLEEPY - ANALGESIA

- Analgoscore (AS) - was the variable titrated
  - ranges from -9 (very profound) to +9 (very superficial) analgesia
  - calculated every 2 seconds (HR was measured every 2s and the BP every 2 minutes)
  - $Dose_{remi} = previousDose_{remi} \times K_r \times K_{sr}$
  - Kr = coefficient proportional to last and present AS score
  - Ksr = coeffient based on the stage of surgery

MCSLEEPY - ANALGESIA

- Safety protocols:
  - MAP and HR can be affected by other factors
  - hypovolemia defined as: increase HR with no increase in MAP
  - vagal reactions defined as: decrease in HR with no decrease in MAP
  - when encountered: delivered preset minimal remi

MCSLEEPY - ANALGESIA



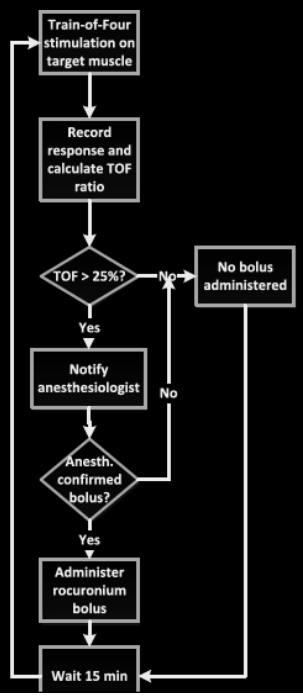
MCSLEEPY - PARALYSIS

- Based on phonomyography
  - peripheral nerve stimulator, TOF adductor pollicis and corrugator supercilii muscles
  - TOF measurement every 15 minutes
  - If TOF > 25 system would give the anesthesiologist the option of no bolus, bolus moderate, bolus profound
  - moderate = 0.15mg/kg, profound = 0.2mg/kg

MCSLEEPY - PARALYSIS

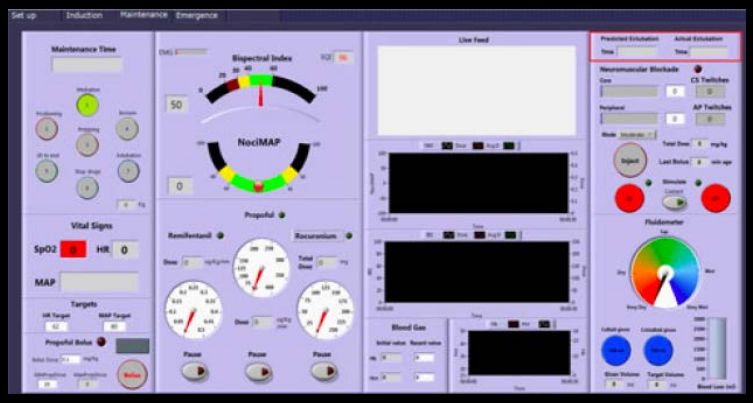
- Safety Protocols:
  - not able to deliver paralysis if BIS > 60
  - not able to bolus within 5 minutes of previous bolus
  - lock out period 20 minutes prior to the end of surgery (this can be manually overridden)

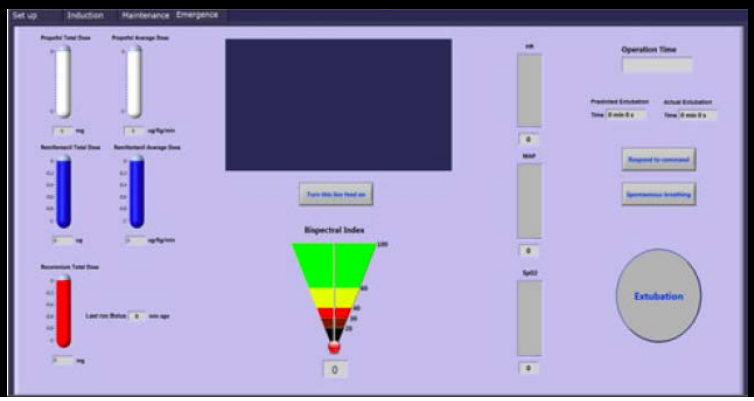
MCSLEEPY - PARALYSIS




Set up
Induction
Maintenance
Emergence
PATIENT'S DATA
ANESTHESIA
Remifentanil
Propofol
Rocuronium
Surgery
Drugs
START


Set up
Induction
Maintenance
Emergence
Elapsed Time
Bispectral Index
Remifentanil Induction
Propofol Induction
Rocuronium Induction


Set up
Induction
Maintenance
Emergence
Maintenance Time
Bispectral Index
NociMAP
Live Feed
Vital Signs
SpO2
HR
MAP
Targets
Propofol Bolus
Remifentanil
Propofol
Rocuronium
Neuromuscular Blockade
Fluidometer
Blood Gas

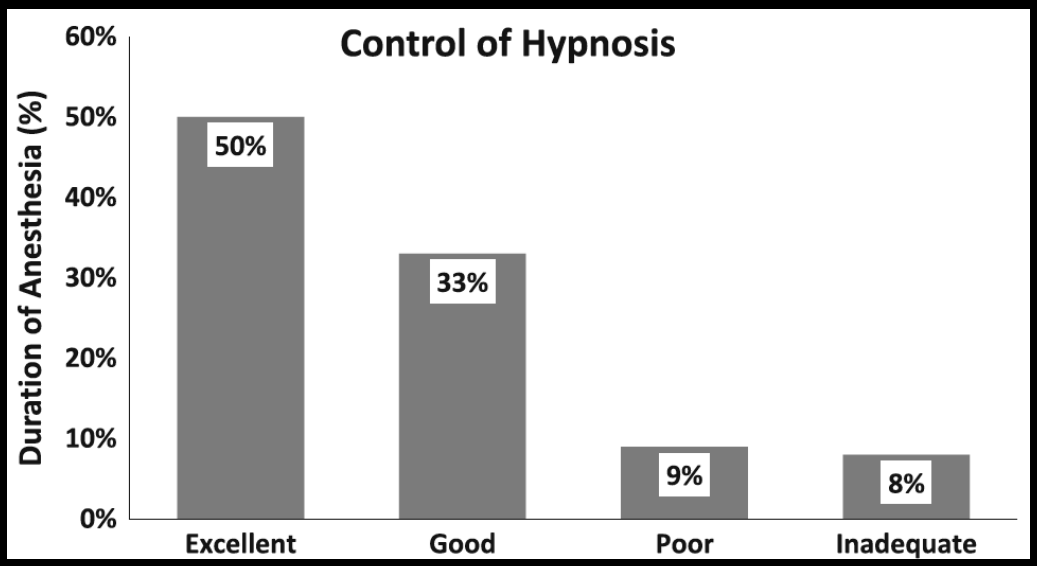

Set up
Induction
Maintenance
Emergence
Operation Time
Bispectral Index
Extubation

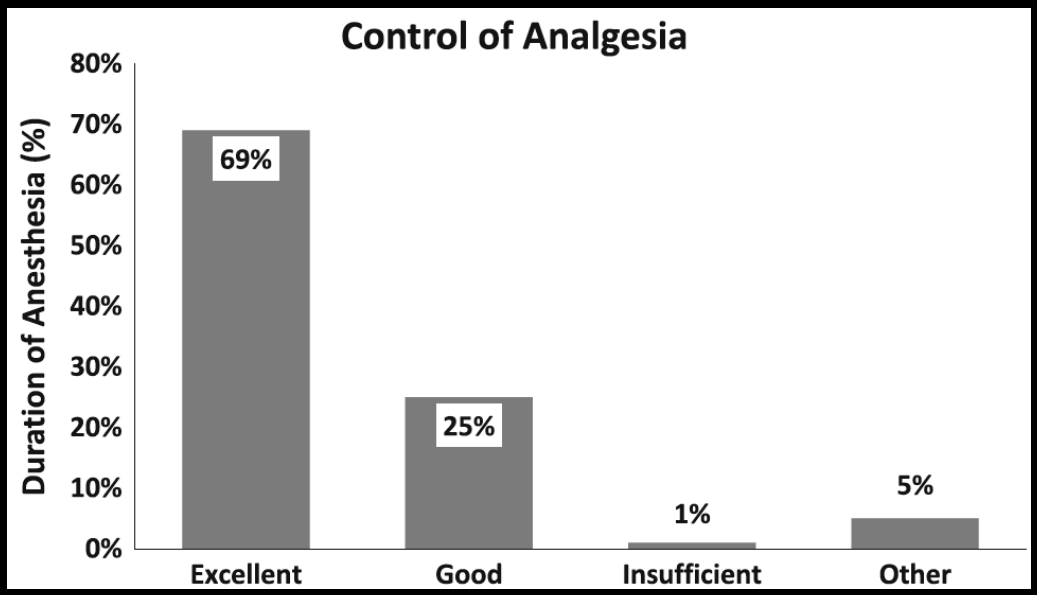
MCSLEEPY RESULTS:

- 15 patients: 3 F and 12 M
- Age: 57 +/- 13 years
- Weight: 79 +/- 16 kg
- Duration of anesthesia: 191 +/- 61 minutes
- Mean doses of drugs:
    - propofol: 129 +/- 23 ug/kg/min
    - remifentanyl: 0.16 +/- 0.06 ug/kg/min
    - rocuronium: 1.5 +/- 0.48 mg/kg

MCSLEEPY RESULTS:

- Precision of the system assessed by Varvel's performance indicies
- widely used to assess performance of closed loop systems
    - ***Performance error*** (difference between real vs target values)
    - ***Median performance error*** (bias to describe direction of error)
    - ***Median absolute performance error*** (size of the error)
    - ***Wobble*** (intra individual variability of PE)
    - ***Divergence*** (evolution of the controllers performance through time)


Control of Hypnosis
Duration of Anesthesia (%)
60%
50%
40%
30%
20%
10%
0%
50%
33%
9%
8%
Excellent
Good
Poor
Inadequate


Control of Analgesia
Duration of Anesthesia (%)
80%
70%
60%
50%
40%
30%
20%
10%
0%
69%
25%
1%
5%
Excellent
Good
Insufficient
Other

LIMITATIONS:

- did not discuss time to set up or issues with the system
- did not address the application of long acting narcotics
- new pain score although validated in its application via Varvel's performance indices; has never been used before

MCSLEEPY

- Why was McSleepy different?
    - Developed a new pain score (Analgoscore based on HR and BP)
    - Able to provide anesthesia for all three phases
    - Electronically charts (anesthesia and surgical)
    - GUI & Voice Prompts
    - Telemedical applications

SHIFT TO FUTURE RESEARCH

Closed-Loop Fluid Administration Compared to Anesthesiologist Management for Hemodynamic Optimization and Resuscitation During Surgery: An In Vivo Study

- by Rinehart et al. published in November 2013 issue of Anesthesia and Analgesia

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- Methods: 16 Yorkshire Pigs underwent 2 phase hemorrhage protocol and were resuscitated by either:
- 1) Anesthesiologist
- 2) Learning Intravenous Resuscitator (LIR)
- Compared median hemodynamic values and variation of hemodynamics between the two groups

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- LIR goal: optimize hemodynamics based on goal direct fluid management
- application settings: to be used in the OR or in the ICU
- goal application: to support practitioners

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- Methods:
    - Pigs were premeditated with ketamine and xylazine (anti-sialagogue)
    - induced with pentobarbital and fentanyl then intubated
    - maintained with isoflurane, fentanyl, rocuronium
    - mechanically ventilated

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- Methods:
  - Monitored by:
    - HR, BP, SaO2, CVP, CO, SV, PPV, MVSaO2, UO, ABG
    - Right and Left femoral artery catheter (right used to induce hemorrhage)
    - Right IJ central line w/ Swan-Ganz pulmonary artery catheter w/ mixed venous sat
    - Suprapubic urinary catheter, real time UO

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- How does the LIR algorithm work? 3 components
  - 1) Model Layer: PPV, CO, HR, MAP
  - 2) Model built from previous clinical trials
  - Predicts the increase in SV expected from a fluid bolus
  - 3) Adaptive layer tracks boluses given and patient responses to correct the model layer and any potential errors

- Strengths:
  - no presuppositions about the patient undergoing management, no absolute targets for management (Can be applied to any system with a Frank Starling curve human or pig)
  - Fluid agnostic (doesn't matter what fluid you deliver)

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- LIR Fluid protocol:
  - would initial deliver colloid solution until a total of 33ml/kg achieved
  - then alternated successive liters of crystalloid and colloid
  - i-STAT (ABG) performed every 45 minutes
  - whole blood administered for HGB < 70
  - fluid administration facilitated by technician (no anesthesia training)
  - no access to pressors

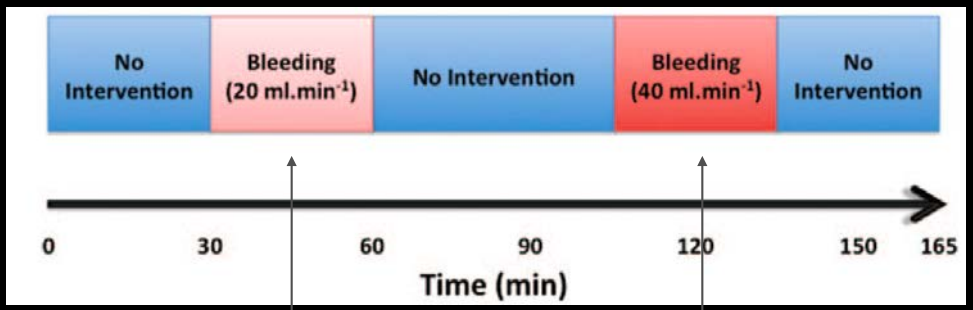
LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- Anesthesia providers:
  - told the patient was a healthy 18 year having open abdominal surgery
  - had access to crystalloid, colloid, whole blood
  - also had access to phenylephrine and ephedrine
  - if enquired, they were told whether or not the animal was bleeding
  - had access to i-STAT (ABG) at their discretion

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- Constants:
  - Fluid administered via pumps (max flow of 2.4L/h)
  - monitors
  - maintenance fluid administration of 3ml/kg/hour of Ringers after induction

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM



600CC OVER 30 MIN

1200CC OVER 30 MIN

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

Table 2. Summary of Baseline Values for Anesthesiologist Practitioner and Closed-Loop Fluid Management Groups

	Baseline hemodynamic variables		
	Anesthesiology practitioner	Closed-loop	*P* value
BSA (m^2)	1.60 [1.59–1.65]	1.61 [1.59–1.64]	0.94
HR (bpm)	94 [90–104]	86 [83–91]	0.10
CI_{SG} (L/min)	3.1 [2.6–3.7]	3.3 [3.0–3.5]	0.98
SVI_{SG} (mL)	33 [31–36]	36 [32–39]	0.34
MAP (mm Hg)	78 [76–100]	84 [78–96]	0.52
CVP (mm Hg)	15 [14–16]	13 [12–15]	0.12

Data are reported as median [25%–75%].
BSA = body surface area; HR = heart rate; CI_{SG} = Swan-Ganz cardiac index; SVI_{SG} = Swan-Ganz stroke volume index; MAP = mean arterial pressure; CVP = central venous pressure.

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

Table 3. Summary of Overall Results for Anesthesiologist Practitioner and Closed-Loop Fluid Management Groups

	Overall hemodynamic results			
	Anesthesiology practitioner	Closed-loop	GEE *P* value for group effect	95% Wald confidence interval
HR (bpm)	95 [91–97]	92 [89–93]	**0.001**	**1.4–5.9**
CI_L (L/min)	3.5 [3.2–3.9]	3.7 [3.4–4.1]	**<0.0005**	**−0.5 to −0.2**
CI_{SG} (L/min)	3.3 [3.2–3.9]	3.8 [3.2–4.7]	**<0.0005**	**−0.4 to −0.2**
SVI_L (mL)	36 [31–38]	40 [34–45]	**<0.0005**	**−5.9 to −3.1**
SVI_{SG} (mL)	37 [34–41]	39 [37–52]	**<0.0005**	**−7.0 to −4.1**
MAP (mm Hg)	83 [81–85]	84 [80–90]	0.58	−3.0 to 1.7
CVP (mm Hg)	16 [16–17]	16 [15–17]	0.15	−0.3 to 2.0
PPV (%)	24 [18–29]	20 [18–22]	**0.001**	**1.5–6.3**
UF (mL/min)	6.0 [2.0–11.1]	10.0 [5.6–14.7]	**0.04**	**−2.5 to 0.2**
	Overall fluid administration			
	Anesthesiology practitioner	Closed-loop	Mann-Whitney *P* value	95% Hodges-Lehmann confidence interval
Total fluid given (mL)	3253 [2735–3926]	3685 [3230–4418]	0.28	−1650 to 430
Crystalloid given (mL)	954 [747–1913]	500 [500–1319]	0.23	−740 to 1600
Colloid given (mL)	966 [546–1426]	1661 [747–2869]	0.19	−2840 to 140
Blood given (mL)	741 [600–895]	728 [571–1105]	1.00	−450 to 340

Data are reported as median [25%–75%]. Boldface values are statistically significant.
HR = heart rate; CI_L = LiDCO cardiac index; CI_{SG} = Swan-Ganz cardiac index; SVI_L = LiDCO stroke volume index; SVI_{SG} = Swan-Ganz stroke volume index; MAP = mean arterial pressure; CVP = central venous pressure; PPV = pulse pressure variation; UF = urine flow rate; GEE = generalized estimating equation.

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- Results:
  - lower HR, better CI, SV, more optimal PPV values, and UO in the closed loop group
  - no statistical difference between MAP and CVP
  - no statistical difference in fluid administered
  - anesthesia delivered a median of 2 boluses of phenylephrine and 0 boluses of ephedrine

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- Conclusion:
  - under their conditions, the LIR could perform in-vivo resuscitation during mild and severe hemorrhage with reduced hemodynamic variability
  - GDFT has been shown to improve outcomes patients with shock

LEARNING INTRAVENOUS RESUSCITATOR (LIR) CLOSED LOOP SYSTEM

- Limitations:
  - LIR delivered more colloid which may have affected the results
  - there was no follow up of the pigs (ie. one group may have been more fluid overloaded at the end)
  - Anesthesiologist working in artificial environment

RECAP:

- McSleepy is a system that can provide anesthesia for induction, maintenance, emergence
- There exists a "smart" fluid administration closed loop system that bases its fluid on GDFT and real patient vitals

CLOSING STATEMENTS

- These systems are being pursued to act as "anesthesia co-pilots"
- Can have very useful applications in critical care and the OR
- Although we are far from having clinical applications in the next 5 years, the future is indeed exciting (or… extremely frightening if you hate computers)

QUESTIONS?

- Batman & Wonder Woman

REFERENCES:

- Rinehart et al. ***Closed loop fluid administration compared to anesthesiologist management for hemodynamic optimization and resuscitation during surgery: an in vivo study.*** Anesthesia and Analgesia. Nov 2013. 115-5.
- Dumont et al. ***Closed loop control of anesthesia: A primor for anesthesiologists.*** Anesthesia and Analgesia. Nov 2013. 115-5.
- Hemmerling et al. ***A technical description of a novel pharmacological anesthesia robot.*** Journal of Clinical Monitors and Computers. Jun 2013.
- Various google images as referenced in order in the presentation

END