What’s Next for Drug Infusion Devices:

1 - Journey from “Smart Pumps” to Physiological Closed Loop Control
2 - Integration of Pumps with Electronic Health Records, in the OR
3 - Infusion Pump Performance Testing & “Standard Concentrations”

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Biosketch and Disclosures

• Physician and Biomedical Engineer at MGH since 1979
  – Aircraft Pilot (50 years; ATP): transition to full digital AI-enabled safety & excellence
  – Cardiac Anesthesiologist: high consequence care with multiple vasoactive drug infusions
  – MGH multidisciplinary innovation teams to address issues of safety, excellence, and workforce support

• Disclosures
  – ~15 Patents in the public domain
  – Codonics Safe Label System under license
  – Wearable EEG, Flow-Rate Measuring Pump: Pump Control patents unlicensed

Objectives/Outline

• Computerized Control of Drug Infusion Pumps
  1. Optimize Drug Delivery Onset in Pediatrics and with Highly Concentrated Vasoactives
  2. PCLC – Physiological Closed Loop Control
     1. Blood Pressure
     2. Brain State
     3. A system of care involving triage, brain state monitoring, and multimodal IV analgesia

• Infusion Pump Auto-Programming and Auto-Documentation in the Operating Room
  – Is the solution “hiding in plain sight”?

• Assessing Infusion Pump Performance
  – Old: Trumpet Curves and Startup Graphs
  – New IEC and AAMI standards - PK-CV &
  – Precise DIY testing with a micro-needle and drip-counting
  – Why this matters under S4S and Shift to LVP’s
Computerized Control of Infusion Pumps for Physiological Closed-Loop Control

Once a dose has been entered, the pump automatically calculates the effective rate in ml/h and displays it as well.

Implement Goal-Directed Therapy Across MGH: A Single Platform For Pediatrics and Adults

Drug Error in a 24-hour old CHD patient...
CONCENTRATED High Alert Medications have been pre-mixed in 50 ml syringes and floor stocked by MGH Pharmacy for all OR and critical care environments for ~30 years; now a shift to pre-mixed standard concentration bags and delivery from LVPs.
Physiological Closed Loop Control of Brain State (PCLC)

- **Need/Vision**: personalized physiological control based on signal processing (e.g., EEG), control algorithms that can auto-adjust drug delivery devices. (Autopilot)
- **Problem**: data shows that current brain state management in ICU and Operating Rooms may fail to protect patients from over medication (especially the elderly and children), resulting in avoidable burst suppression and potential suboptimal outcomes.
- **Solution**: education; scalable miniaturized technology for brain state signal acquisition, processing, display, guidance, and control of infused drugs and inhalation agents; integration into anesthesia machines, multi-modal anesthesia, controllable infusion pumps; strategic partnerships.
- **Model**: Research and Development supported by NIH funding.
- **Patrick Purdon / Emery Brown / Brandon Westover @ MGH**
  - [The Art of Talking Science](https://youtu.be/SKtwXgOrk5A)
  - [“The Art of Talking Science” videocast](https://purdonlab.mgh.harvard.edu)
  - [https://eegforanesthesia.iars.org/](https://eegforanesthesia.iars.org/)
MGH Wireless EEG Sensor

Component of 2 main parts:
- Electrode Head
- Electrode Holder

Usage:
- Used for neurological monitoring and therapy
- Portable and wireless

HST "Closed Loop Control of Physiological Systems (Jan, 2019)

HST
Harvard-MIT Health Sciences and Technology

Special Topic: Introduction to Closed-Loop Control of Physiological Systems

Instructor: YAP

Course Description:
- Course Title: Introduction to Closed-Loop Control of Physiological Systems
- Instructor: YAP
- Location: MIT, MA

Course Website: https://stellar.mit.edu/s/42/182/HST.050

Pre-requisites:
- Permission of instructor
- Restrictions: Enroll students prior to the credit year

MIT Institute: L.E.L (BiGEE)

The primary goals of this course are to highlight the basic techniques employed in control theory and systems analysis, and to give students an appreciation of how these principles can be applied to manipulate physiological systems to achieve a desired response. Topics covered include:
- Feedback control in physiological systems
- Modeling and control of biological systems
- Control strategies for drug delivery

Course Instructors: Jagadeesh An, Giorgio Chaharmatz, John Abel, Shiao Helen, Jason Wiste

MIT PhD Thesis and Usage and Flow Properties of Clinical-Grade Infusion Pumps for Physiological Closed-Loop Controlled Drug Delivery (submitted 12/18/19 to TBME)
We propose a rational strategy for multimodal general anesthesia where one chooses a combination of agents that act at different targets in the nociceptive system to control nociception intraoperatively and pain postoperatively. Because these agents also decrease arousal, the doses of hypnotics and/or inhaled ethers needed to control unconsciousness are reduced.

Effective use of this strategy requires simultaneous monitoring of antinociception and level of unconsciousness (INS comment: and multiple IV agents delivered by infusion pumps ...). (Anesth Analg 2018;127:1246–58)
**Infusion Pump O.R. “Integration”**

PROBLEM: Infusion Pump 'integration' in the OR can't work because no properly labeled IV drug bag or syringe is dispensed responsive to an order in CPOE, and because there is no EMAR or BCMA (bar code readers) in Operating Rooms.

**Scanned into Anesthesia Recordkeeping System**

Triggers "One Step Med" [protocols] [5/2019 release]

Pump is auto programmed via wireless network, and auto documentation commences.

**Non Patient Specific, Bar-Coded Source Drug Vial or Bag** ‘surrogate for pharmacy services’

**Safety: National Movement to Standardize Drug Infusion Concentrations**

- A national medication safety summit identified that a leading root cause of significant infusion errors is the lack of standardization
- The first national, inter-professional effort to standardize medication concentrations in order to reduce errors and improve transitions of care

https://www.ashp.org/Pharmacy-Practice/Standardize-Safety-Initiative

ASA Drug Concentrations will be posted at: https://www.asahq.org/standards-and-guidelines/resources-from-asa-committees#Quality

ASA Statement on Drug Concentrations: https://www.asahq.org/standards-and-guidelines/statement-on-drug-concentration-standardization

**S4S: FDA-funded Initiative**

ASHP IV Adult continuous infusion guidelines available at: https://www.ashp.org/Pharmacy-Practice/Standardize-Safety-Initiative/Initiative-Overview
Partners 2.0 – 2020
Standardizing Pump Platform

- Partners 2.0 initiative to standardize large volume pump platform across the system
- National initiative to standardize continuous infusion concentrations within the US
- Re-think SP vs LVP ratios

Vital Signs Instability (MDR to FDA)

- **Event Description**  A patient on dopamine ... frequent vital sign changes, and attributes .... issues related to changing out the syringe.
- **Manufacturer Narrative**  
  - The syringe module event log ..... a 35ml mononject syringe containing 29.5 ml was in ...  
  - The syringe module ... infuse at rates of 0.1519 ml/hr and 0.1012 ml/hr.  
  - ... no anomalies noted, and passed both the plunger force accuracy and plunger position accuracy tests.  
  - The root cause of the reported vital signs instability could not be identified.  
  - 2016/03-2015-0521

PK-CV² – Infusion Pump Performance

Intravenous delivery of many rapid acting drugs at flow rates under 10 ml/h requires IV pump flow that is sufficiently continuous and uniform to avoid inducing clinically significant fluctuations in the effect or site concentration.

The flow from most IV pumps cannot be evidently too smooth at low flow rates. Data provided by present day standards – the so-called “Trumpet Curve” – developed in the early 1990’s measures only peak flow errors and only at one relevant flow rate (1 ml/h) making it ineffective for practical evaluation of pump performance.

A new approach, being planned for adoption by AAMI and IEC, will measure measured flow (in and out) and the resulting pharmacokinetic response of a single compartment PK model using pump tubing sets at flow rates both below and above the pumps nominal rate. This approach will be a comprehensive measure of the performance of an IV pump and allow more accurate determination of the flow rate at which a pump is suitable for delivery of rapid acting drugs.

Some pump manufacturers are already applying this method to improve the design of their products. (courtesy of Robert Dwayne Butterfield; personal communication)

MS Note: Performance can be tested using formal gravimetric means - OR using a simple method of drop analysis with a micro needle at the outflow end of an infusion pump tubing set. (sims.nat@gmail.com)
Quantify LVP *No-Flow* Duration

**Will These Concentrations Work?**

Summary

- **Computerized Control of Drug Infusion Pumps**
  - Multiple use cases
  - Reason to advocate & implement
- **Integration of Pumps in OR setting**
  - Auto programming and auto-documentation may soon be possible; easy to implement
- **Standardized Concentrations**
  - National and Local initiatives
  - Examine proposed [] lists with care
  - Test pumps to quantify no-flow duration at low rates
Thank You!

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