Exploring The Predictability Of The Decrement Time When Accounting For Interpatient Variability.

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Introduction: Context-Sensitive Half-time (CSHT), the time required to achieve half the blood concentration after a target-controlled infusion (TCI), has become a well-established term in anesthesia education since its introduction in 1992[1].

CSHT has also been used to predict emergence from anesthesia, specifically when to turn off a propofol infusion. The predication occurs despite generally being unable to accurately ascertain the current drug concentration or the drug concentration required for emergence. This abstract seeks to validate the predictability of CSHT, and its more general term, decrement time, with regard to inter-patient variability[2].

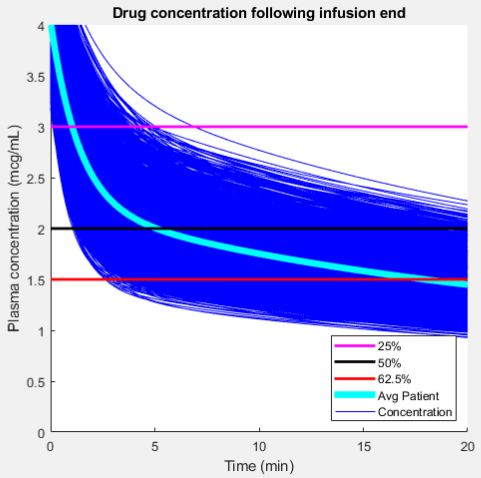
Methods: Using MATLAB (R2023a), 2000 patients set to be 50 years of age, 70 kg, 170 cm, and male were simulated using the Eleveld propofol model[3]. The model error from inter-individual variability was created by randomly setting the "η" values to be within [-0.75 to 0.75] of the standard deviation of each parameter (ω). The method described is similar in form to the methods described by Hu et al[4].

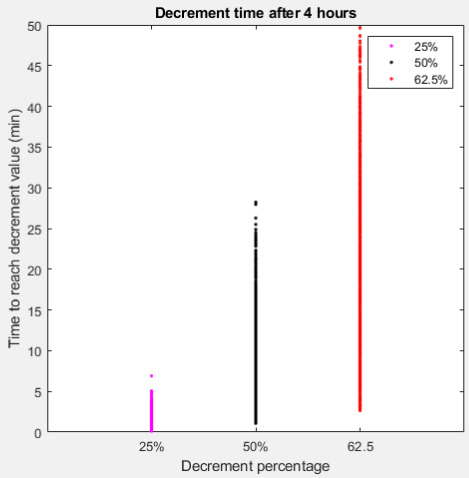
A TCI was simulated for an ideal patient to run for 4 hours at a set concentration of 4 mcg/mL. After 4 hours, the infusion was paused, and the decrement time was measured by identifying the time when the blood concentration would be 3, 2, and 1.5 mcg/mL (25%, 50%, and 62.5% decrement time, respectively).

Results: The simulation and corresponding decrement time are plotted in the attached Figure. The decrement times were calculated to have a median value of 1.05, 5.40, and 18.32 minutes for the 25%, 50%, and 62.5% decrement values, respectively. The lower and upper calculated ranges for these values in this patient population were 0.12-6.9, 1.07-28.23, and 2.63-59.2 minutes, respectively.

Conclusions: This simulation study shows that the Decrement time and CSHT cannot accurately reflect patient variability. Rather, the principal conclusion one can leverage is that as one increases the set concentration relative to the patient's emergence concentration, the lengthier and more unpredictable the patient's emergence will become after stopping the TCI pump. The study is limited by the fidelity of early phase pharmacokinetics of the model used, and further empirical studies will need to be performed.

1. Hughes, Michael A., Peter S.A. Glass, and James R. Jacobs, *Context-sensitive Half-time in Multicompartment: Pharmacokinetic Models for Intravenous Anesthetic Drugs.* Anesthesiology, 1992. **76**(3): p. 334-341.
2. Bailey, J.M., *Context-Sensitive Half-Times.* Clinical Pharmacokinetics, 2002. **41**(11): p. 793-799.
3. Eleveld, D.J., et al., *Pharmacokinetic-pharmacodynamic model for propofol for broad application in anaesthesia and sedation.* Br J Anaesth, 2018. **120**(5): p. 942-959.
4. Hu, C., J. Horstman, Damian, and L. Shafer, Steven, *Variability of Target-controlled Infusion Is Less Than the Variability after Bolus Injection.* Anesthesiology, 2005. **102**(3): p. 639-645.


Drug concentration following infusion end
Plasma concentration (mcg/mL)
Time (min)
25%
50%
62.5%
Avg Patient
Concentration


Decrement time after 4 hours
Time to reach decrement value (min)
Decrement percentage
25%
50%
62.5%