Title: Real-Time Monitoring of Exhaled Propofol Reflects Changes in Propofol Effect Without Hysteresis (ASA 2012 abstract A052)

Background: Propofol is exhaled during anesthesia and can be measured in breath in real time.1 After i.v. administration propofol equilibrates between blood and lung and between blood and brain as its effect-site. If these equilibration coefficients are similar, changes in exhaled propofol might closely match effect site changes in the brain. As a result, a graph plotting brain effects against exhaled propofol concentrations would show no hysteresis, and exhaled propofol concentrations (Cexp) could be used as a clinical surrogate for propofol effect and propofol concentrations in the brain. Therefore, we examined human volunteers to determine the hysteresis between Cexp and propofol effect during propofol anesthesia.

Methods: Following IRB approval 20 volunteers (ASA I, age 29.3±8.0 yrs, BMI 25.4±4.3) underwent propofol anesthesia. The study protocol consisted of 4 consecutive phases with increasing and decreasing propofol blood concentrations. Phase I: Rapid propofol infusion of 0.4 mg/kg/min (0-10 min); phase II (10 - 30 min): no infusion; phase III (30 - 90 min): four escalating infusion rates (for 15 min each) to achieve targeted plasma concentrations of 2, 3, 4 and 5 mg/ml; phase IV (90 min until wake-up): no infusion, recovery. Cexp was determined continuously by ion molecule reaction mass spectrometry (V&F, Absam, Austria). The Bispectral Index (BIS, Covidien, Boulder, CO) was measured as a surrogate for the cerebral propofol effect. Twenty-one arterial blood samples per volunteer were collected and propofol plasma concentrations modelled using NONMEM® (ICON, Ellicot City, MD). Individually predicted plasma concentrations and measured Cexp were plotted vs. BIS and evaluated graphically.

Figure 1: Dose-response curve for propofol of one sample study person

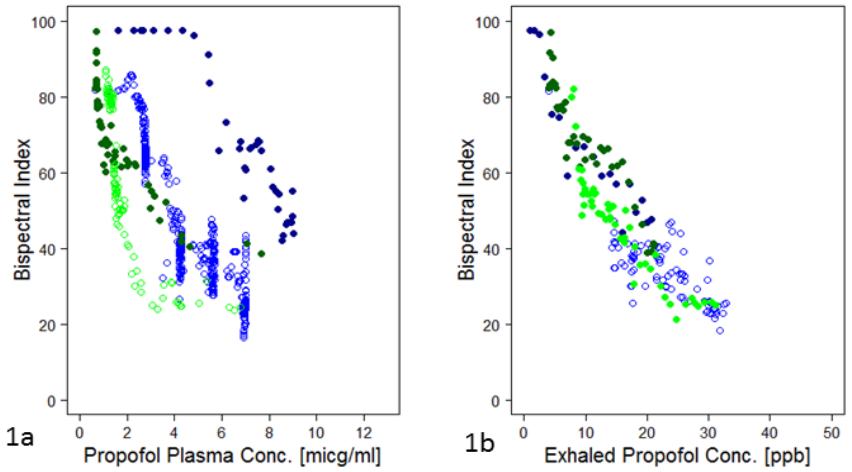
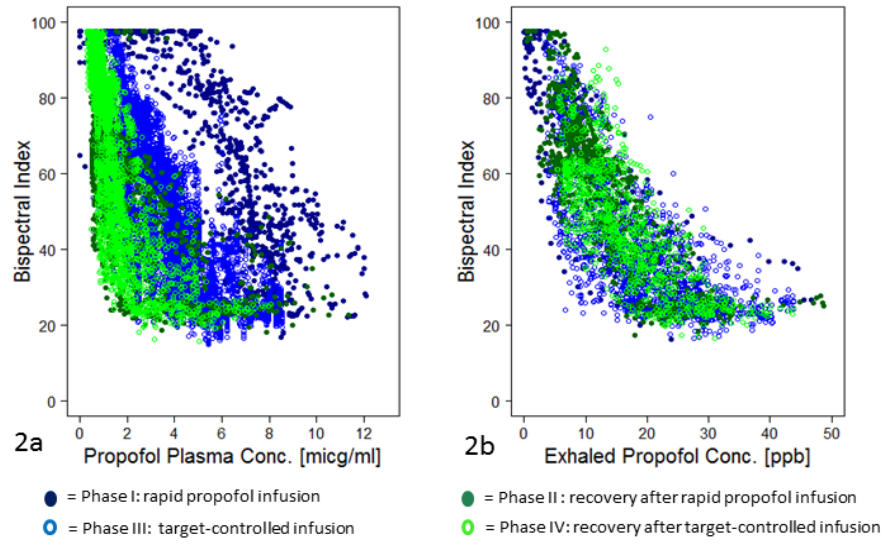


Figure 2: Dose-response curve for propofol of all 20 study persons



Results: When individually predicted propofol plasma concentrations were plotted against BIS a hysteresis loop for plasma propofol and BIS could be observed. However, this hysteresis was not present for Cexp. During increasing and decreasing plasma propofol concentrations similar breath concentration were associated with the very same effect. Figures 1a and 1b show data from one sample individual, figures 2a and 2b show data from all study persons. Dark blue (phase I) and light blue circles (phase III) reflect measurements during propofol infusion, dark green (phase II) and light green circles (phase IV) measurements during the recovery periods without propofol infusion.

Conclusion: The lack of hysteresis between exhaled propofol concentrations and propofol effect suggests that exhaled propofol concentrations and propofol effect follow changes in propofol plasma concentrations within a similar time frame. This supports the clinical utility of propofol breath monitoring. Ongoing work will compare propofol effect site concentrations and breath concentrations by means of population PKPD modeling.

Reference: 1) Anesthesiology 2007; 106:665-74.