

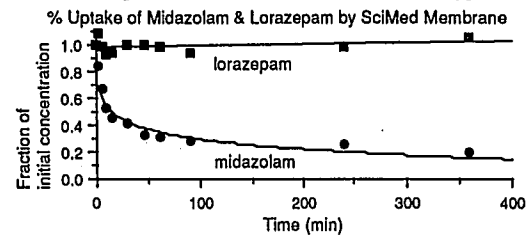
TITLE UPTAKE OF LORAZEPAM AND MIDAZOLAM BY THE SCIMED MEMBRANE OXYGENATOR**AUTHORS** D. ROSEN, M.D., K. ROSEN, M.D., P. LEONG, M.D.**AFFILIATION** Section of Pediatric Anesthesiology, C.S. Mott Children's Hospital, Department of Anesthesiology, University of Michigan Medical School, Ann Arbor, MI 48109-0800.

Introduction Case studies report patient awareness and recall during anesthesia and surgery occur in as many as 1.2% of all surgical patients. In order to provide amnesia, lorazepam and midazolam are routinely supplemented to high dose narcotic anesthesia during cardiac surgery and upon initiation of cardiopulmonary bypass (CPB). Several studies have recently documented the uptake of anesthetic drugs by the oxygenator in the CPB circuit. It has been determined that the primary site of uptake of these anesthetic agents is the oxygenator membrane. A study by Rosen, *et al.*, comparing five different oxygenators has shown that the SciMed brand has the greatest capacity for uptake of fentanyl. The SciMed oxygenator is made of a silicon rubber sheet impregnated with dextran fibers. The potential for subtherapeutic plasma levels of lorazepam and midazolam exist if the drugs are taken up by the oxygenator membrane. The purpose of this study is to compare the interaction of lorazepam and midazolam with the SciMed Oxygenator Membrane using a previously validated *in vitro* model.

Methods Serial dilutions of H3 midazolam at 30, 60, and 200 ng/ml, and C¹⁴ lorazepam, 200 ng/ml, were prepared with Normosol-R (Abbot labs), and adjusted to pH 7.4 at 37°C. All experiments were carried out at 25°C. Multiple 1 cm² pieces of membrane were cut, and their exact surface area was calculated using the known density provided by the membrane manufacturer. The membrane squares were placed in 2 ml of agitated lorazepam and midazolam solutions, which were then further agitated to minimize any boundary layer phenomenon. Solution samples were assayed for lorazepam or midazolam at 0, 1, 5, 15, 30, 45, 60, 90, 120, and 360 minutes. All analyses were performed using liquid scintillation techniques.

Results The lorazepam uptake by the SciMed membrane was negligible when compared with midazolam. The lorazepam solution concentration remained unchanged when exposed to isolated SciMed membrane squares. In contrast, the midazolam solution concentration decreased significantly from its initial concentration in all cases. The midazolam concentration decreased to 40% of its initial concentration during the first 60 min, then leveled off at 30%-20% of its initial concentration by 360 minutes.

Discussion This is the first study to compare the potential for uptake of lorazepam and midazolam by the SciMed Oxygenator Membrane during CPB. Although studies have demonstrated that serum midazolam levels do not correlate well with clinical sedation, there exists a potential for subtherapeutic plasma levels of midazolam if great amounts are taken up by the membrane oxygenator. Our experiments utilizing isolated membranes squares consistently demonstrate that only 30%-20% of the initial midazolam concentration is left by 360 minutes, compared to an unchanged lorazepam concentration. Due to its negligible uptake by the oxygenator membrane, lorazepam levels should be able to be easily maintained throughout the bypass period, and may be expected to produce reliable sedation and amnesia. The interaction of a patient with the CPB is a complex clinical phenomenon, and other factors such as reversibility of binding, effect of protein binding and effect of multiple compartments need to be determined in order to fully apply this data to the clinical setting. Additionally, these results apply only to the SciMed® brand of membrane oxygenators, and should not be generalized to other makes of membrane oxygenators.

**A475****TITLE:** NONINVASIVE CONTINUOUS ESTIMATE OF CARDIAC OUTPUT DERIVED FROM THE FINAPRES[®] WAVE FORM.**AUTHORS:** I Gratz, DO, J Kraidin, BA, NG deCastro, MD, A Jacobi, MD, P Spagna, MD**AFFILIATIONS:** Dept. of Anesthesia and Cardiothoracic Surgery, The Medical College of PA Philadelphia, PA 19129

There are patients whose condition may not justify invasive monitoring but in whom cardiac output (CO) determination is warranted. We have developed an algorithm for the Finapres[®] which can estimate CO noninvasively based on the pulse contour analysis of the waveform. This study compared the result obtained by this method with the conventional thermodilution technique. Twenty-six patients scheduled for elective CABG gave written informed consent to participate in this IRB approved study. Patients ranged in age from 44 to 80, weighed 55 to 118 kg and were ASA III. A history of aortic valve disease or significant preoperative dysrhythmias excluded them from the study. Premedication consisted of morphine and scopolamine 1-2 hrs prior to surgery. Specific monitoring consisted of an Edward 7F thermodilution PA and radial artery catheters. The Finapres[®] finger probe was applied to the middle finger on the opposite hand. Anesthesia was standardized and consisted of sufentanil, O₂, and vecuronium. The Finapres[®] was monitored continuously

and pressure output data was transmitted through a preamplifier with signals recorded on a standard audio cassette at 9.4 cm/sec. CO were performed in triplicate using the thermodilution technique at 4 predetermined times (pre- and postinduction, post bypass and before leaving the OR). The Finapres[®] waveforms were marked for these same time periods. The cassette was played back using a Vetter recording device through a preamplifier, amplifier and A/D converter. The data line was connected to Direct Memory Access (DMA) which served as the post for data entry into a Compaq 386 computer operating at 20 MHz. The program for analyzing the waveforms was written in Turbo C and monitors the data in real time, polling it for information at 100 Hz. As it receives information it passes it to the algorithm. The DMA board remembers the last 32761 data points so that the program need not store any of the information in computer RAM in the form of a huge data array. The algorithm analyzes the Finapres[®] waveform and determines the instantaneous cardiac output by using a modified pulse contour method without the need for a patient calibration factor. A total of 89 paired CO were made on the 27 patients. The average thermodilution CO (COT) was 4.56±.81 L/min and the Finapres[®] CO (COF) measurement was 4.56±.72 L/min (95% CI of the difference = 0 to 3.2%). The pooled data for the COT and COF showed a correlation coefficient of 0.79 (P<0.01). This method can, therefore, be used as a safe and comparable alternative to thermodilution technique for the measurement of CO.