# Solubility of I-653, Sevoflurane, Isoflurane, and Halothane in Human Tissues

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*Tissue/blood partition coefficients of anesthetics are important indicators of the rate of tissue wash-in and wash-out, and wash-in and wash-out are determinants of the rates of induction of and recovery from anesthesia. In the present study of human tissues, we found that the tissue/blood partition coefficients (for brain, heart, liver, kidney, muscle, and fat) for the new anesthetic I-653 were smaller than those for isoflurane, sevoflurane, and halothane (anesthetics listed in order of increasing tissue/blood partition coefficients). For example, the respective brain/blood partition coefficients were 1.29 ± 0.05 (mean ± SD); 1.57 ± 0.10; 1.70 ± 0.09; and 1.94 ± 0.17. This indicates that induction of and recovery from anesthesia with I-653 should be more rapid than with the other agents. The finding of a lower tissue/blood partition coefficient for I-653 parallels the previous finding of a lower blood/gas partition coefficient.*

**Key Words:** ANESTHETICS VOLATILE—halothane, I-653, isoflurane, sevoflurane. PHYSICS, SOLUBILITY—volatile anesthetics.

Recovery from anesthesia with the new inhaled anesthetic, I-653, is more rapid than recovery from other potent inhaled agents (1). Although a major part of the rapidity of recovery is due to the low blood/gas partition coefficient (0.42) (2), low tissue/blood partition coefficients (especially a low brain/blood partition coefficient) may also be factors. A knowledge of tissue solubility also is required for simulation of anesthetic pharmacokinetics. Accordingly, we have simultaneously determined the tissue/gas partition coefficients of I-653, sevoflurane, isoflurane, and halothane in human brain, heart, liver, kidney, muscle, and fat, and calculated the respective tissue/blood partition coefficients.

## Materials and Methods

We determined tissue/gas partition coefficients with a modification of a method used previously (3). Specimens of adult human brain, heart, liver, kidney, muscle, and fat were obtained at autopsy within 48 hr of death. Specimens were obtained from 14 patients, but not all tissues were obtained from all patients (e.g., permission might not have been given to examine the brain, tumor may have invaded the liver). We excluded from our study, specimens collected from patients dying from infectious diseases or from diseases that might alter tissue components (e.g., congestive heart failure). Immediately after collection, tissues were prepared as follows. Arachnoid and pial membranes and vascular structures were stripped from brain (frontal lobe; roughly equal proportions of grey and white matter). We discarded pericardial membrane and endocardial lining from heart. For liver and kidney we removed the capsule, vessels, and ducts. We eliminated fascial structures and all visible fat from (psoas) muscle. We removed the vascular structures from (perirenal) fat. Each tissue was sliced into small cubes. An aliquot of tissues thus prepared was added to a precisely known volume of saline, and the total volume of tissue was measured by volume displacement. The tissue:saline volume ratio was in the range of 1:1–2, depending on the tissue. This mixture was homogenized using a Kinematica CH-6010 Kriens-Lu homogenizer at room temperature (about 22–24°C) after addition of a trace of antifoaming agent. The homogenate was frozen at −70°C until determination of the partition coefficient.

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