

## **The Influence of Covariates on Effect-Site Age-Adjusted MAC Fraction Estimated by GE-Navigator at the Point of First Response After Inhalational Anesthesia**

**Background:** We are interested in using effect-site levels to guide delivery of a wide range of drugs used in anesthesia. Based on this interest we have installed Navigator™ systems from GE in a number of our operating rooms. Navigator takes inputs from gas analyzers, syringe drivers and direct user input. The “outputs” are displays of the probability of recall and response to noxious stimulation along with calculated effect-site concentrations of a range of drugs. A number of drugs are not modeled in Navigator including morphine, clonidine and ketamine.

The primary aim of this ongoing study is to relate the point of first response to command to the predicted likelihood of response in a wide range of patients undergoing a variety of surgery. In this analysis we explore the effect of various covariates on the point of first response. Our hypothesis is that if the effect site modeling is valid then patient demographics and duration of surgery will have minimal effect on awakening volatile concentration.

**Methods:** This study was approved by the Regional Ethics Committee. Written consent was not required. The patients are an opportunistic sample of those having anaesthesia in an OR with Navigator at a time the investigator (MM) was available. All drugs were recorded by the investigator and modeled drugs entered into Navigator. The time at which subjects first responded to command was noted. The calculated Ce-sevo at this time was retrieved and adjusted for age and converted to a MAC-fraction. The effect of covariates including age, gender, BMI, ASA-PS, invasiveness of surgery, duration of surgery, Ce-fentanyl and use of non-modeled drugs was explored in univariate and multivariate models.

**Results:** Data from 146 patients was available. These are summarized in the Table. Patients woke at a mean age-adjusted effect-site MAC fraction of 0.26 (sd 0.14) vol%. There was no difference between sevoflurane and desflurane (95%CI diff - 0.116 to 0.007,  $p=0.0807$ ). The median (IQR) Ce-fentanyl was 0.84 (0.60, 1.12) ng/ml.

There was weak evidence that a one unit increase in ASA-PS, use of non-modeled drugs and being male decreased the MAC fraction at first response. There was also a suggestion of an effect of the degree of surgical insult. None of these effects reached statistical significance.

There was no evidence of an effect of fentanyl levels, age, duration of surgery or BMI.

**Comments:** The lack of effect of patient age, BMI or duration of surgery supports the use of calculated effect-site concentration as a measure of volatile dosing. Although opioids are included in interaction models underlying technologies such as Navigator we did not see an effect on awakening. This is consistent with older studies suggesting fentanyl levels greater than 2-4ng/ml are needed to alter MAC-

awake. The suggestion of an influence of ASA-PS and invasiveness of surgery is an area for further investigation.

**Table:** Summary of patient demographics and observed variables

<b>Variable</b>	<b>Number of obs.</b>	<b>Median (IQR)</b>
Age, years	146	54.5 (36.5, 71.8)
Sex	144	
<i>Female</i>		53% (76)
<i>Male</i>		47% (68)
BMI	146	26.7 (24.1, 30.1)
ASA	144	
1		24% (35)
2		42% (60)
3		31% (45)
4		3% ( 4)
Type of surgery	145	
<i>Minor</i>		17% (24)
<i>Intermediate</i>		57% (83)
<i>Major</i>		26% (38)
Duration, mins	143	88 ( 66, 128)
Other Drugs ( <i>ketamine, morphine</i> )	139	
<i>No</i>		48% (67)
<i>Yes</i>		52% (72)
Effect-site concentration at response		
<i>Sevoflurane, age adjusted (vol%)</i>	109	0.475 (0.362, 0.641)
<i>Desflurane, age adjusted (vol%)</i>	25	1.178 (0.865, 1.754)
<i>MAC-fraction, age adjusted</i>	133	0.226 (0.170, 0.321)
<i>Fentanyl</i>	143	0.840 (0.600, 1.120)