Signal Processing Methods to Improve Concordance of Bispectral Index with End-Tidal Anesthetic Concentration

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Introduction: The titration of inhaled anesthetics is often guided by either measuring end-tidal anesthetic concentrations (ETAC) or an EEG-based surrogate of anesthetic concentration at the effect-site, the bispectral index (BIS). The relative effectiveness is equivocal and debated [1][2]. Patients have widely variable relationships between ETAC and BIS response, which has been used in some studies as a surrogate for anesthetic susceptibility. The largest concordance analysis to date showed that the B-Unaware population had a median intraindividual ETAC – BIS correlation of -0.16 (interquartile range -0.031, -0.50)[3]. BIS has been shown to be susceptible to noise from various artifacts, including muscle activity and experimental sound[4]. Noise in the BIS signal, particularly around anesthesia induction and emergence, produces significant biases in the statistics relating these markers of sedation. Here, a low-pass butterworth filter was optimized to improve the signal-to-noise of the BIS signal and maximize concordance between BIS and ETAC.

Methods: We identified general anesthesia cases with at least 5 minutes of simultaneous BIS and ETAC measurements, excluding pediatric and cardiac cases, resulting in 21,766,061 BIS/ETAC measurement pairs across 32,667 cases. Sampling rate for BIS and ETAC was q15 seconds. ETAC was age and equivalence adjusted. Data analysis was performed in R, with the 'data.table' package leveraged for column-oriented data storage. The cross correlation of each individual's BIS and ETAC datastream was calculated to assess concordance. We evaluated cross correlations as a function of offsets between ETAC and BIS to assess for a lag between ETAC change and BIS response. A butterworth filter was used to design a low-pass filter to eliminate the high frequency noise from both datastreams. This filter was then used with original data and event information to create case visualizations and produce processed datastreams. Nonparametric distributions are reported as median value [interquartile range] and evaluated for differences with a Wilcoxon paired signed rank test.

Results: The optimized butterworth filter has an order of 1 and critical frequency of .22 min^{-1}. This suggests that signal components with frequencies on the order of seconds are largely noise, and robust changes in BIS occur on the order of minutes. As shown in Figure 1b, the intra-case BIS-ETAC cross correlations were significantly different when calculated on filtered versus raw datastreams with the median filtered datastreams more concordant than raw datastreams (correlation coeff -0.53 [-0.75 to -0.19] versus -0.43 [-0.64 to -0.17], respectively, $p<2.2 \times 10^{-16}$). Correlations for both raw and filtered datastreams are much higher than previously reported.[3]
Conclusions: Although BIS and ETAC are both surrogate measures for depth of anesthesia when titrating anesthetics, they have variable relationships to each other on a case-by-case

basis. Here we optimize butterworth filter parameters to remove the high frequency noise components of these datastreams and find improved concordance. Developing signal filters can increase sensitivity and enable analysis of induction and emergence trends to provide further insights into anesthetic sedation responses.

References:

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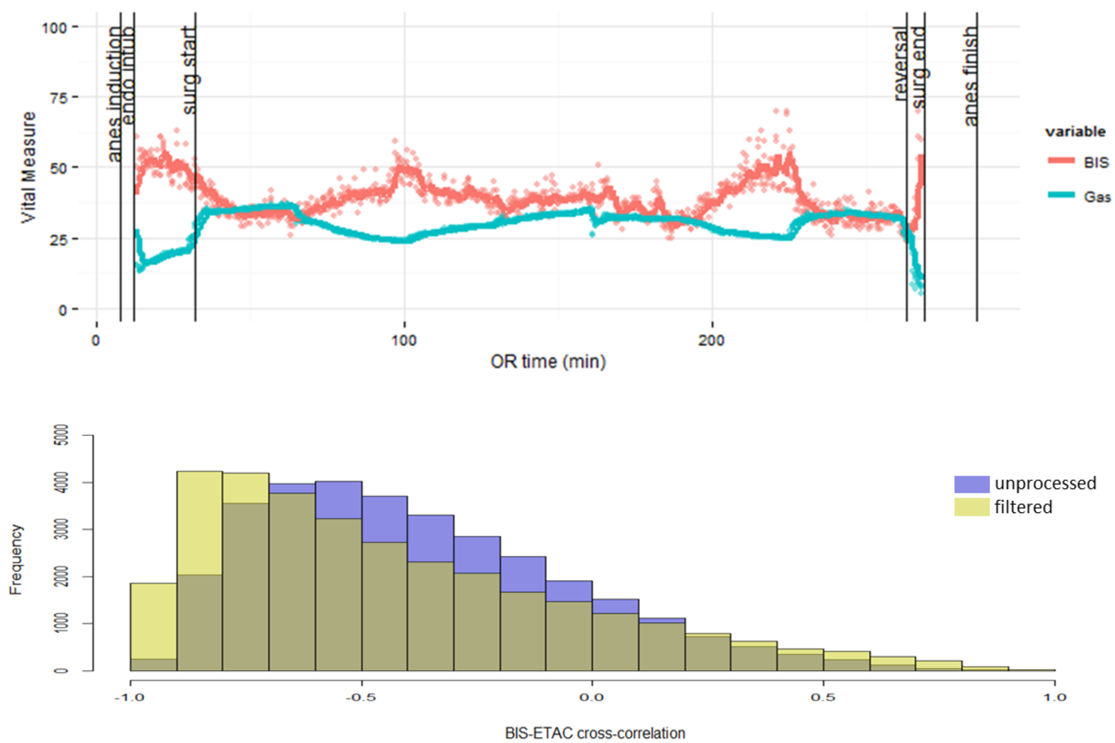

Figure 1: a) Representative case showing BIS (red) and ETAC (blue). Unprocessed measurements are plotted as points, and the filtered signal is plotted as a line. ETAC is scaled by 25. **b)** Distribution of case-by-case BIS-ETAC cross-correlations with unprocessed (purple) and filtered (yellow) datastreams. Filtering shifts the distribution to the left, indicating improved cross-correlation.