

# **Spectral Analysis of Respiratory Activity Provides a Second Autonomic Measure Associated With Spectral Analysis of Heart Rate Variability**

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## **INTRODUCTION**

Spectral analysis (SA) of heart rate variability (HRV) is known to enable non-invasive, quantitative measures of autonomic function. There are two methods of SA of HRV, one without SA of respiratory activity (RA) and one with SA of RA. SA of HRV *without* SA of RA was standardized in the 1996 Circulation Special Report by a panel from the European College of Cardiology and the North American Society for Pacing and Electrophysiology. The other method is based on SA of respiratory activity (RA) in conjunction with SA HRV (autonomic function computation or AFC method), according to the MIT approach. The AFC method provides subtle, but significant differing correlates.

The premise for the difference is that the AFC method starts with two independent, but concurrent signals, RA and EKG. Mathematically, two independent signals are required to fully describe (mathematically) a system with two independent parts. The SA package selected as a continuous wavelet transform (CWT) and is used to analyze both signals independently. Peer-reviewed published reports indicate that RA analysis is necessary to isolate parasympathetic from sympathetic activity. Our recent studies have borne this out and have shown that the MIT-based technique, (including RA spectral analysis) provides more specific and sensitive autonomic indices.

Further the CWT analysis improves the mathematical accuracy of the AFC parameters over the fast Fourier transform (FFT) method discussed in the Special Report in two ways. First, the FFT as a result of windowing requires a compromise between time and frequency fidelity. More accurate temporal resolution is achieved at the expense of frequency resolution, and vice versa. Second, the FFT requires stationary signals, biological (including autonomic) signals are inherently non-stationary. Clinically, this issue forces longer recording times and causes the FFT approach to miss rapid changes in autonomic responses. The CWT method resolves these mathematical issues.

An example of the difficulty with the spectral domain (SD) HRV (*without* SA of respiratory activity) method is that during paced, deep breathing when the breathing frequency is in the LF region, the HRV spectrum show little or no activity in the HF region and most of the activity in the LF region. Based on the definitions from the Special Report, this would suggest little or no PSNS (HF) activity during the pace breathing challenge and a significant amount of SNS (LF) activity. This is counter-intuitive. Paced, deep breathing should increase the PSNS output and possibly decrease the SNS.

In this study we compare and contrast the differences between the two approaches and present the results of the two approaches for the same clinical data set.

## **METHODS**

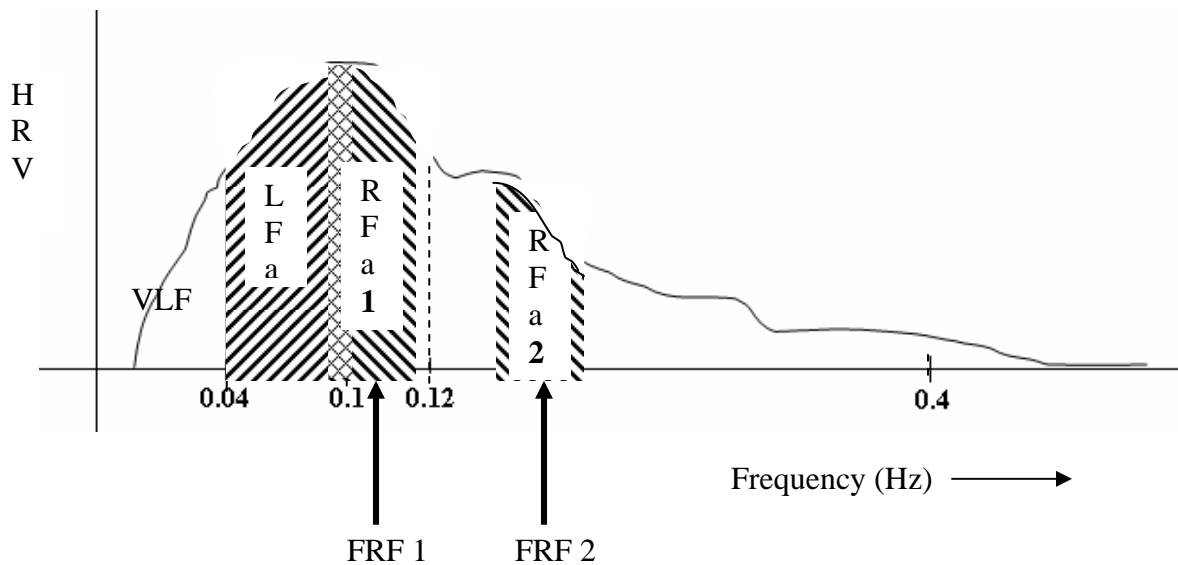
ANS function testing using the ANX-3.0 system (Ansar, Medical Device Technologies, Inc., Philadelphia, PA) was performed on 5752 patients (Table 1) in 38 ambulatory clinics nationwide. The 15.5' test clinical exam included a 5' resting baseline. The ANX-3.0 utilizes SA of RA and SA of HRV to compute SNS and PSNS output at rest and during various




maneuvers known to evoke autonomic perturbations [Akselrod, 1981; 1985; 1987; 1988]. SA of both RA and HRV is performed using CWT. The method is referred to as Autonomic Function Computations (AFC). The autonomic indices computed are: 1) the low frequency area (LFa) as a measure of isolated sympathetic output, 2) the respiratory frequency area (RFa) as a measure of isolated parasympathetic output, and the sympathovagal balance (SB) which is the ration of LFa to RFa. The ANX-3.0 is also programmed to compute the parameters from the method in the standards article [Malek, *et al.*, 1996]: 1) low frequency (LF), 2) high frequency HF, and the ratio LF/HF which is an empirical measure of sympathetic output.

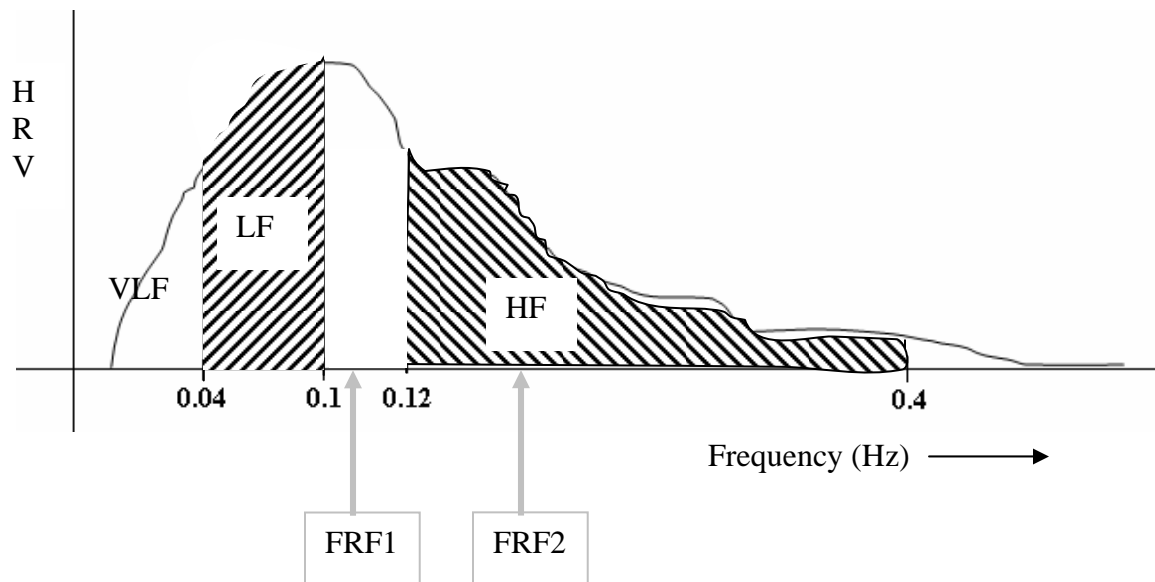
The method of computing autonomic function (AF) from AFC is presented in Figure 1 [Vinik 2004; Aysin, 2006]. Figure 2 describes the spectral domain HRV *without* respiratory activity analysis (SD HRV) method as published in the standards article [Malek, *et al.*, 1996]. Figure 1 is then compared with Figure 2. The graph in Figure 1 can be considered to be a hypothetical slice in time in the time-frequency analysis of the CWT. This example of a computational step in the AFC is provided to allow for a comparison between the FFT approach of SD HRV and the CWT approach of AFC.



For the SD HRV method (Fig. 2), the low frequency (LF) region was defined as being from 0.04 Hz to 0.12 Hz. The area under the HRV spectrum within the LF band is widely accepted to be a measure of SNS output as modulated by PSNS output. (The area under a spectral curve within the frequencies of operation of a particular system is mathematically defined as the power, activity, or tone of that system for the time period of observation.) The high frequency (HF) region was defined as being from 0.15 Hz to 0.40 Hz, a fixed, wide-band frequency region, and marginally accepted to be a measure of PSNS output. The ratio of the two (LF/HF) was accepted on an empirical basis as a better measure of SNS change. Theoretically, by dividing the two terms the PSNS modulation from the LF term would be divided out.

The AFC approach (Fig. 1) [Vinik 2004; Aysin, 2006], based on Akselrod *et al.* [1981, 1985, 1987, 1988], uses SA of RA to compute the term “Fundamental Respiratory Frequency” (FRF). The FRF is the peak mode of the RA spectrum and is a measure of Vagal outflow, or the mean frequency of the RSA. The work of Akselrod *et al.* determined the appropriate, narrow-band, frequency region bounding the FRF to capture the PSNS (Vagal) influence on the heart for the time period of observation. This frequency region can shift as the subject’s breathing rate changes. The area under the HRV spectrum within this frequency region is the respiratory frequency area (RFa) and is a measure of PSNS output. The low frequency band as defined in the standards article [Malek, *et al.*, 1996] is the same for the AFC approach. The only but significant difference is that, if the breathing rate is slow and is within the LF band, the RFa computation will remove this portion of the spectral area from the low frequency band. That is to say, the PSNS modulation is removed from the SNS measure. As a result, the LFa term does not contain any PSNS influence. The ratio of the two (LFa/RFa, or L/R ratio) therefore is now a measure of “Sympathovagal Balance” [Low, 1997].



**Figure 1:** ANS monitoring based on spectral domain HRV and spectral domain respiratory activity (RA). FRF1 and FRF2 would have been determined in the RA spectrum and indicate average Vagal activity over the sampling period. These would represent two different time samples: FRF1 could be during deep breathing when the respirations were slowed. FRF2 could be during normal breathing when the respirations are faster. Granted the HRV spectrum would also be different at these different time, but for ease of illustration, they are combined on one spectrum. As we see, FRF1 causes the respiratory frequency area (RFa, ) to overlap the low frequency area (LFa, ) (the cross-hatched area ). This overlap represents the “as modulated by the PSNSs” portion of the LF. In this case, it is included in the RFa (PSNS) computation and removed from the LFa (SNS) computation, leaving the LFa as a measure of the SNSs *without* the PSNS modulation. FRF2 does not “invade” the low frequency area, but it also does not require all of the HF to determine PSNS tone. This approach returns more specific measures of SNS and PSNS activity, and thereby enables the L/R ratio to be a true measure of sympathovagal balance.



**Figure 2:** ANS monitoring based on spectral domain HRV alone. The low frequency (LF, ) and high frequency (HF, ) regions are fixed and separated. FRF1 and FRF2 from Fig. 1 are also represented here for illustration. As we see, only FRF2 is in the HF range and therefore, only it is captured by the HF measure of PSNS output.

Patients with arrhythmia (more than 10 ectopic beats during the exam) were omitted, leaving 4204 patients (2530 females, 2310 hypertensives, 1613 diabetics, 953 patients with congestive heart failure, 331 Parkinson patients, see Table 1). There were 537 patients younger than 30, 1686 patients between 30 and 55, and 2691 patients over 55, including 776 patients over 75. Statistical Analyses included polynomial trend analysis of resting sympathetic and parasympathetic function, and sympathovagal balance.

## RESULTS & DISCUSSION

Resting (initial baseline) data for the total population are presented in Figure 3. The resting low frequency data (LFa and LF; Fig. 3, top row) are similar in that they both (generally) decrease with age to less than 25% of maximum values and both stop decreasing in the sixth decade. The spread of the patient points (the scatter plots) is greater for the SD HRV method (Fig. 3, top right) method than for the AFC method (Fig. 3, top left), and the trend for the SD HRV method is to increase in the geriatric years. The lack of increase for the LFa may be representative of the wide use of beta-1-adrenergic antagonists.

In a similar way the RFa (Fig. 3, middle left) and the HF (Fig. 3, middle right) are similar. They both (generally) decrease with age to less than 25% of maximum values and both stop decreasing in the sixth decade. The spread of the patient points (the scatter plots) is greater for the SD HRV method (Fig. 3, middle right) method than for the AFC method (Fig. 3, middle left). In this case, however, both have trends that increase during the geriatric years. This increase has been documented [Umetani, *et al.*, 1998]. The rate of decline in the RFa as compared to the HF is steeper prior to both curves becoming flatter. The HF trend looks very similar to the LF trend.

Whereas the RFa trend is steeper than the LFa trend. The more rapid decrease in PSNS (RFa) output over time is also documented [Vinik, *et al.*, 2004].

The ratio data (Fig. 3, bottom row) are similar in terms of the spread of the scatter points. The SD HRV averages are more variable and the trend line is steeper than for the AFC data.

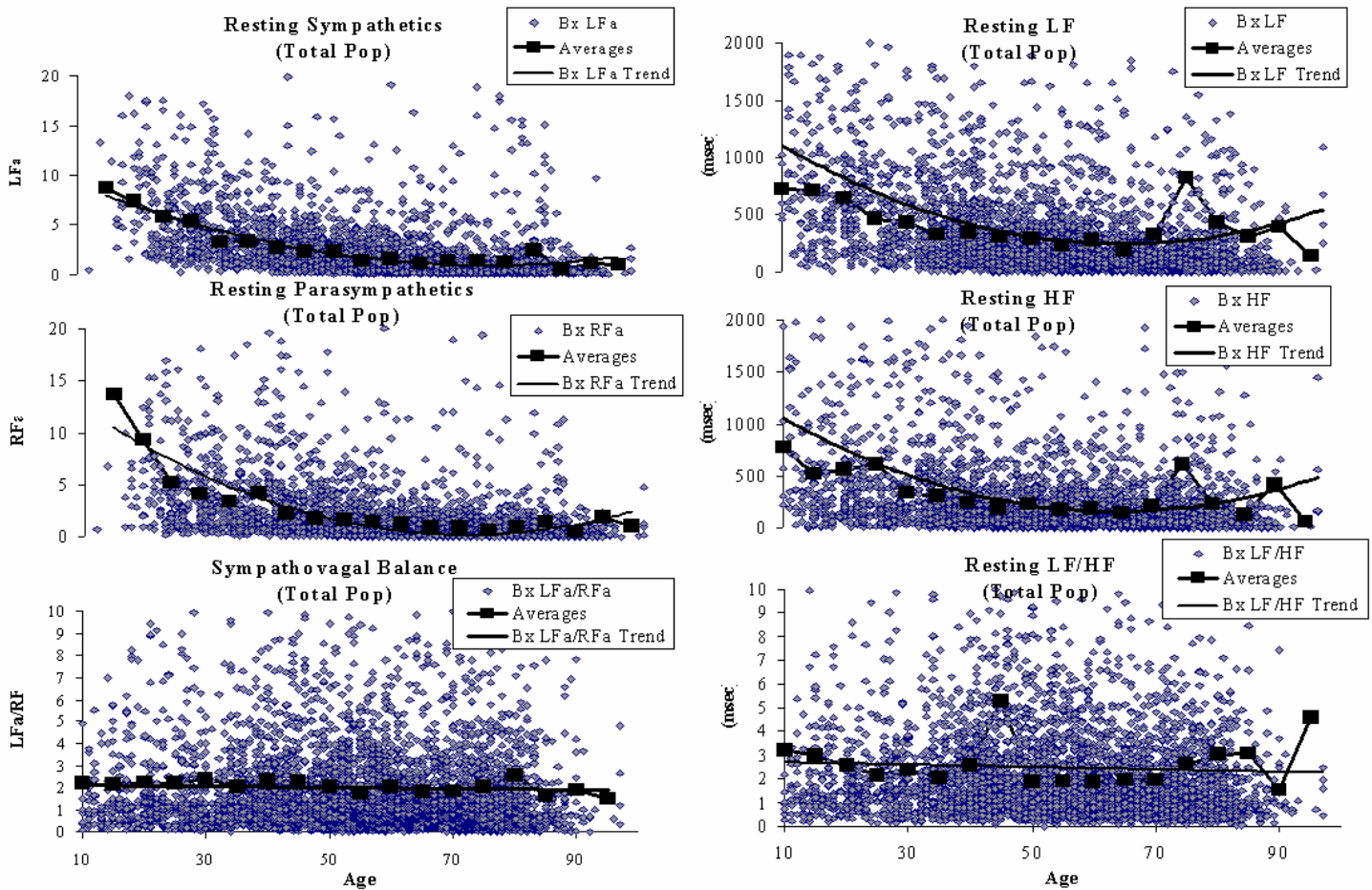


Figure 3: Resting ANS data for the entire population as computed by the AFC method (left column) and the SD HRV method (right column). The top row presents low frequency indices: LFa (left) and LF (right). The middle row presents the respiratory and high frequency indices: RFa (left) and HF (right). The bottom row presents the ratio indices: LFa/RFa or Sympathovagal Balance (left) and LF/HF (right). The scatter points are individual patient data. Plotted against the scatter points are the patient averages by age group. Patient averages (Averages) are represented by squares, and the associated trend line are also include on each graph. See text for details.

Table 1: Patient cohort population statistics by age.

Age	<9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85-89	90-94	95-99
Female	9	45	73	108	119	111	192	248	247	281	272	268	275	267	285	137	54	9	7
Male	14	33	48	41	47	63	83	140	132	189	225	199	195	214	140	120	17	6	1
Total	23	78	121	149	166	174	275	388	379	470	497	467	470	481	425	257	71	15	8

## CONCLUSIONS

Given the mathematical similarities and differences between the two computational methods, the resulting clinical data seem to follow. The differences seem to suggest that the increased mathematical accuracy of the AFC approach enables more of the documented clinical features to be represented.

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