SUPPLEMENTAL MATERIAL

Predicting Adult Pulmonary Ventilation Volume and Wearing Compliance by On-Board Accelerometry During Personal Level Exposure Assessments

Rodes, C. E., Chillrud, S. N., Haskell, W. L., Intille, S. S., Albinali, F., Rosenberger, M.

PREFACE

The data and analyses presented in the main paper represent an initial reporting of a subset of a much larger integrated effort intended to examine innovative sensing of exposures, activity patterns, and energy expenditures at the personal level. The relatively narrow focus of the current analyses is describing initial approaches that facilitate more robust assessments of exposure by using triaxial accelerometers incorporated into personal exposure assessment devices. The focus in the main paper is reporting is the estimation of pulmonary ventilation in adults and children while performing a variety of physical activities. The breadth and complexity of this topic has resulted in significantly more material than is likely to be acceptable for publication. The importance of the topic, however, suggested submittal of additional supplemental material for the main paper Background, Materials and Methods, and Results sections.

1. Supplemental Background Material

The linking of accelerometry to ventilation volume to ultimately allow potential dose estimates is only useful when it is clear that the exposure monitor is truly being worn. Additional background material is provided here to supplement the limited information provided in the main paper on the importance of quantifying personal exposure monitor wearing compliance as a precursor step. Additional background is also provided on the potential importance of computing potential dose as an adjunct variable to less robust exposure measures.

1.1 Motion Sensing to Characterize Wearing Compliance Levels

The National Research Council (NRC, 2004) observed that the epidemiologic studies most-robustly linking airborne particulate matter (PM) with adverse health outcomes were those applying metrics with minimal exposure misclassification biases. Personal level exposure characterization devices have been applied in occupational settings for decades, albeit in rather cumbersome and expensive packages that have limited adoption in larger cohort studies in non-occupational settings. Recently, Rodes et al. (2010) showed that personal-level PM2.5 exposure measurements for the most-exposed (> 90th percentile) were substantially higher -- factors of two or more -- in a 3-year cohort study in Detroit, Michigan than those measured at either ambient or indoor measurements would have suggested. They also showed that accounting for confounding by adjusting for monitor wearing compliance was important to minimize misclassification bias. Rabinovitch et al. (2005) applied a wearing compliance threshold to identify statistically significant links between endotoxin exposures and changes in severity levels for asthmatic children carrying a burdensome 900g backpack-located system. Brook et al. (2010) used a 60% wearing compliance level to optimally-link cardiovascular changes to personal level exposures for participants in the Detroit cohort wearing a vest weighing a 2.3 kg

vest containing personal monitors. In both cases, a motion sensor was used to identify when a threshold level had been exceeded defining periods of protocol (wearing) compliance. Smaller, lighter, and more versatile sampling/sensing systems are definitely suggested as a developmental research goal to facilitate future cohort studies.

The application of motion sensing to estimate when a personal sensing system is actually moving, and hence likely to be worn, has been applied for at least the past decade in personal exposure studies conducted by RTI International and Columbia University. A capacitance-based motion sensor was developed over 10 years ago for inclusion with the pumping system, which resulted in a patented approach to characterizing wearing compliance (Lawless, 2003). Recent data (Rodes et al., 2010) applying the capacitance based approach confirmed that a substantial fraction of a general population cohort in Detroit, MI, were often wearing the personal monitors less than 50% of the time. Understanding the levels of wearing compliance allowed subsequent panel study analysts to adjust for the potential confounding and strengthened the linkages between exposure and vascular flow parameters (Brook et al., 2009).

While less-sensitive capacitance detection could readily identify ambulatory events as "worn," that approach was not sufficiently sensitive to correctly identify worn from unworn for low-energy events that can often comprise a large fraction of the daily activity patterns for adults. The application of more sensitive MEMS triaxial accelerometers offered the potential to improve the identification of wearing compliance, especially for low energy activities such as working at a computer. Another goal of the current work was to collect accelerometer data across a range of recumbent, sedentary, and ambulatory activities to determine if sufficient signals were produced that could identify worn versus unworn periods by simple threshold detection. Simple algorithms useable in either on-board or post-processing modes would support a binary (worn/not worn) wearing compliance variable that would be stored in real-time along with the exposure metric under study.

The Columbia group has extended the compliance approach by adding an activity monitor to the subject's wrist with a hospital band that cannot be taken off without cutting the hospital band so that the study team can identify when the subject is awake with time periods when the monitor is worn.

1.2 Additional Rationale for Justifying Potential Dose Over Concentrations - Does estimating pulmonary ventilation and size of aerosol dose as a function of time advance the current art? Is the added complexity of including triaxial accelerometry in personal level exposure sensor packages justified? More strenuous activities often produce "personal aerosol clouds" from floor dust re-suspension and other processes, and those clouds have been surmised to enhance exposures for both adults and children (e.g. Rodes et al., 2001; Rabinovitch et al., 2005). Higher ventilation rates during these periods of elevated concentrations could indeed significantly increase both short term (e.g. hourly) and longer term (daily) dose levels in μg/min/kg. Is the frequency of occurrence for these periods high and/or the concentration excursions sufficiently high so that associative analyses linking exposures to adverse health outcomes would benefit from this additional stressor data manipulation?

Risk estimates for PM for a range of outcomes require either chronic and/or acute level exposure data that are the most appropriate for the underlying physiological response patterns. Clearly the values of predicting potential doses in real-time for personal exposure data are more valuable (appropriate) for the subset of health outcomes with response lag times in minutes and hours, rather that days or weeks. This subset includes a wide range of cardiopulmonary response

outcomes, including studies of environmental triggers for asthma (e.g. Delfino et al., 2002; Rabinovitch et al., 2005) and vascular flow (Brook et al., 2009; Brook et al., 2010), could significantly benefit from estimates of potential dose in real-time, rather that having to utilized less robust exposure data. The ability to predict minute ventilation rates (m^3/min) in real-time facilitates computation of potential doses as the simple cross-product with the concurrent exposure level (in $\mu g/m^3$), then divided by the body weight of particles in μg/min/kg.

The ability to robustly predict ***V*** data in real-time opens the door to predicting potential dose levels (μg/min/kg) instead of the more commonly collected exposures ($\mu g/m^3$). This could result is significant strengthening of associations between exposures to aerosol toxicants and adverse health effects in situations where the aerosol concentrations are elevated simultaneously with the ventilation volume. For example, walking events on residential carpeting can readily increase the vertical gradients within a room by factors of two to more between breathing zone levels and other room heights (Rosati et al., 2008). Re-suspended dusts in the breathing zone have been associated with increased exposures to endotoxin (Rabinovitch et al., 2005) during walking events. During these walking events, typical adult ventilation volumes increased from sedentary activities to walking at 4 mph (Activity 8 in Figure 5) by roughly a factor of three. Thus, modeling potential dose estimates with concentrations measured at a fixed location and using a constant ventilation rate rather than applying a measured and varying ***V***, would mis-characterize the peak respiratory burdens by a factors of 6 or more. While this single activity impact is substantial, it has to be placed in context with the amount of time each day that a participant actually is walking on an aerosol sink such as carpeting that would produce such extremes in peak concentrations and potential doses.

2. Supplemental Graphics and Tables

2.1 Figure 1S Rapid Data Viewer Example - An example of the viewer output for accelerometer data for an entire 2 hour scripted activity test is shown in Figure 1S, where the hip located Wocket is compared with the time series data, comparing the chest located Columbia, RTI, and Zephyr units, and the hip located Actigraph. Note the consistency of the time synching and the functionality for all units except the Columbia system was found to have been set up with a programming error and not responding properly. Modifying the on-board programming corrected the inconsistency. Importantly, the viewer data provided confidence that the accelerometer outputs across a very diverse range of brands and types, all provided nearly identical fine structure in the data.

2.2 Figure 2S Additional Photos of Testing During Indoor and Outdoor Cycling

2.3 Figure 3S Composite Linear Regression for All Participants for Activities 1 to 16.

2.4 Figure 4S Composite Regression Intercepts by Participant for RTI Monitors for All Participants for Activities 1 to 16.

2.5. Figure 5S Potential for Categorical Pattern Recognition from the Triaxial 20 Hz Data - As noted in the main paper (Section 4.5), an inability to identify when cycling was occurring would significantly bias the ventilation predictions. Review of the high frequency time series data for each scripted activity showed strong differences in the x, y, and z signals, strongly suggesting that focused efforts applying pattern recognition approaches could be very rewarding.

Figure 4S shows an example comparison of each directional component for Sitting at a Computer, Walking at 2 mph on a Treadmill, and (Indoor) Cycling at 70 RPM for 5s periods (one hundred 0.05s time steps). Note that the resolution of the accelerometer signals (~0.02 G for each axis), combined with the obvious pattern differences by axis for the two more energetic activities should allow fairly specific activity determinations to be made on-board and storable along with the exposure data. That would be a huge advance in the technology, since this would be accomplished completely transparently to the participant - i.e. no time-activity diaries required! The analysis of the substantial data bases produced by the currently research to examine the possibilities is hoped to be the topic of dedicated paper in the near future. While rigorous pattern recognition software is certainly a possibility to distinguish between activity types, much simpler approaches may also be possible. Combinations of the magnitude, standard deviation, and simplistic presence/absence of a cyclical pattern across the x, y, and z directions appear to provide distinctive differences to at least identify cycling activities separately. Further investigation is definitely warranted.

2.6 Figure 6S On-Board Computation of Potential Dose from Exposure Data

The supporting Docking Station software for the RTI MicroPEM™ merges the real-time concentration data with real-time estimates of the ventilation volume to output potential dose levels in μg/min/kg. An example screenshot of this software showing the parallel outputs of exposure, estimated ventilation volume, and potential dose are provided in Figure 6S. This capability readily would allow parallel concentration and potential dose metrics against which biological or health outcomes could be linked to determine which variable provided the most robust statistics.

2.7 Table 1S Additional AUC Standard Deviations for Selected Activities Compared with an Unworn RTI MicroPEM Value

2.8 Table 2S Comparison of Linear Regression Data for Columbia Monitor - The linear regression data (***ACCEL*** versus ***V***) for the RTI monitor are provided in Table 4 of the main paper. The comparable regression data for the Columbia monitor are provided in Table 2S. Since the ACCEL variable is scaled differently for the Columbia monitor, the slopes cannot be compared directly (by participant) with the RTI data, but overall the regression data provided by the two different monitoring approaches are very similar. The only obvious differences for the Columbia data are slightly larger and more asymmetrical 95% confidence intervals about the slope (RTI -23.4%/+23.1%; Columbia -27.4%/+37.8%). These differences likely resulted from the slower 1 Hz data rate of the Columbia accelerometer compared with the much higher 20 Hz rate of the RTI unit.

3. Supplemental References

Brook, R., Bard, R., Burnett, R., Shin, H., Vette, A., Croghan, C., Phillips, M., Rodes, C. Thornburg, J. and R. Williams 2009. Differences in blood pressure and vascular response associated with ambient fine particulate matter exposures measured at the personal versus community levels. *Occupational and Environmental Medicine*, 2011;68:224e230. doi:10.1136/oem.

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Rabinovitch, N., Liu, A., Zhang, L., Rodes, C., Foarde, K., Dutton, S., Murphy, J., and E. Gelfand, 2005. Importance of the personal endotoxin cloud in school-age children with asthma", *Journal of Allergy and Clinical Immunology*, 116:1053-1057.

Rodes, C. and R. Wiener 2001. Indoor aerosols and exposure assessment, chapter 29 in Aerosol Measurement: Principles, Techniques, and Applications, P. Baron and K. Willeke eds., Wiley Interscience, New York, NY.

Rodes, C., Lawless, P. A., Thornburg, J. W., Williams, R. W, and C Croghan 2010. DEARS Particulate Matter Relationships for Personal, Indoor, Outdoor, and Central Site Settings for a General Population, *Atmos. Env.*, 44:11, 1386-1399.

Rosati, J., Thornburg, J. and C. Rodes, 2008. "Resuspension of Particulate Matter from Carpet Due to Human Activity", *Aerosol Science and Technology*, 42:472-482.

Figure 1S. Rapid review data screener allowed examining raw data for inconsistencies and potential validation issues; example shown highlighted logging issue with Columbia sensor

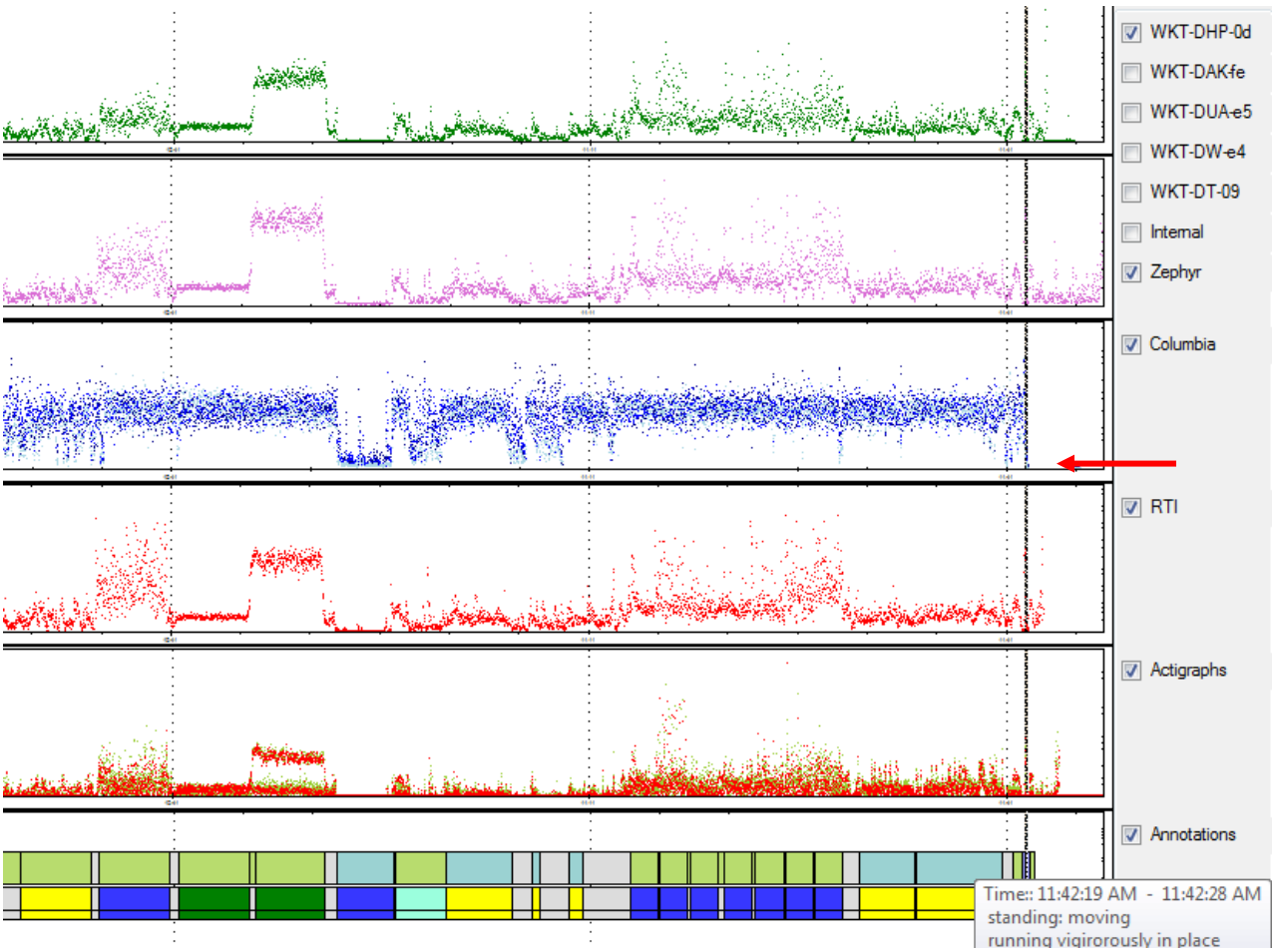

Figure 2S. Sensor array during stationary biking; outdoor bicycling

Figure 3S. RTI sensor relationship for ACCEL variable against ventilation volume (V) for all 22 participants, but activities 1 through 16 only. Note limited divergence of data points for the more strenuous treadmill 6 and 9% elevation at 4 mph.

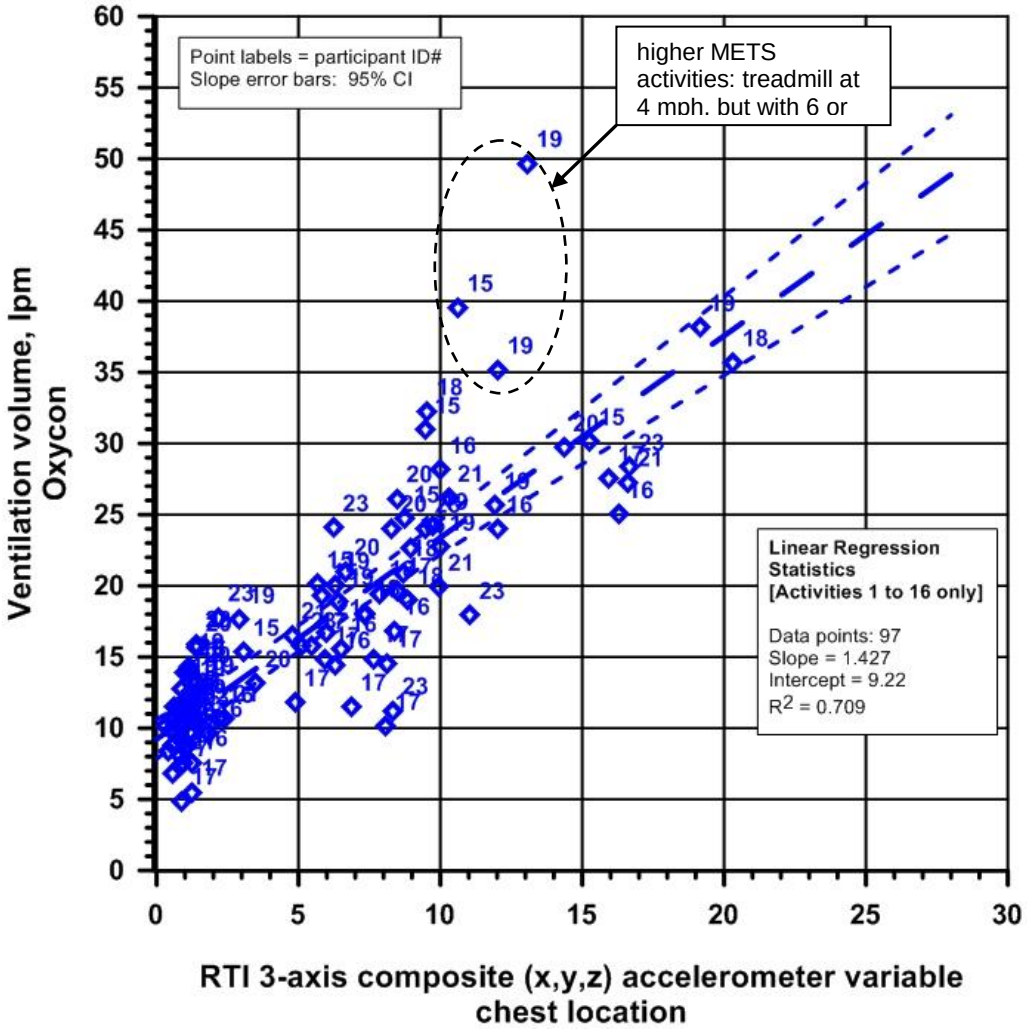

Figure 4S. RTI Composite Regression Intercepts (ACCEL versus V by Oxycon); activities 1 through 16, by participant for all tests. The median value of 10.7 lpm represents the composite ventilation volume at rest across all adults tested

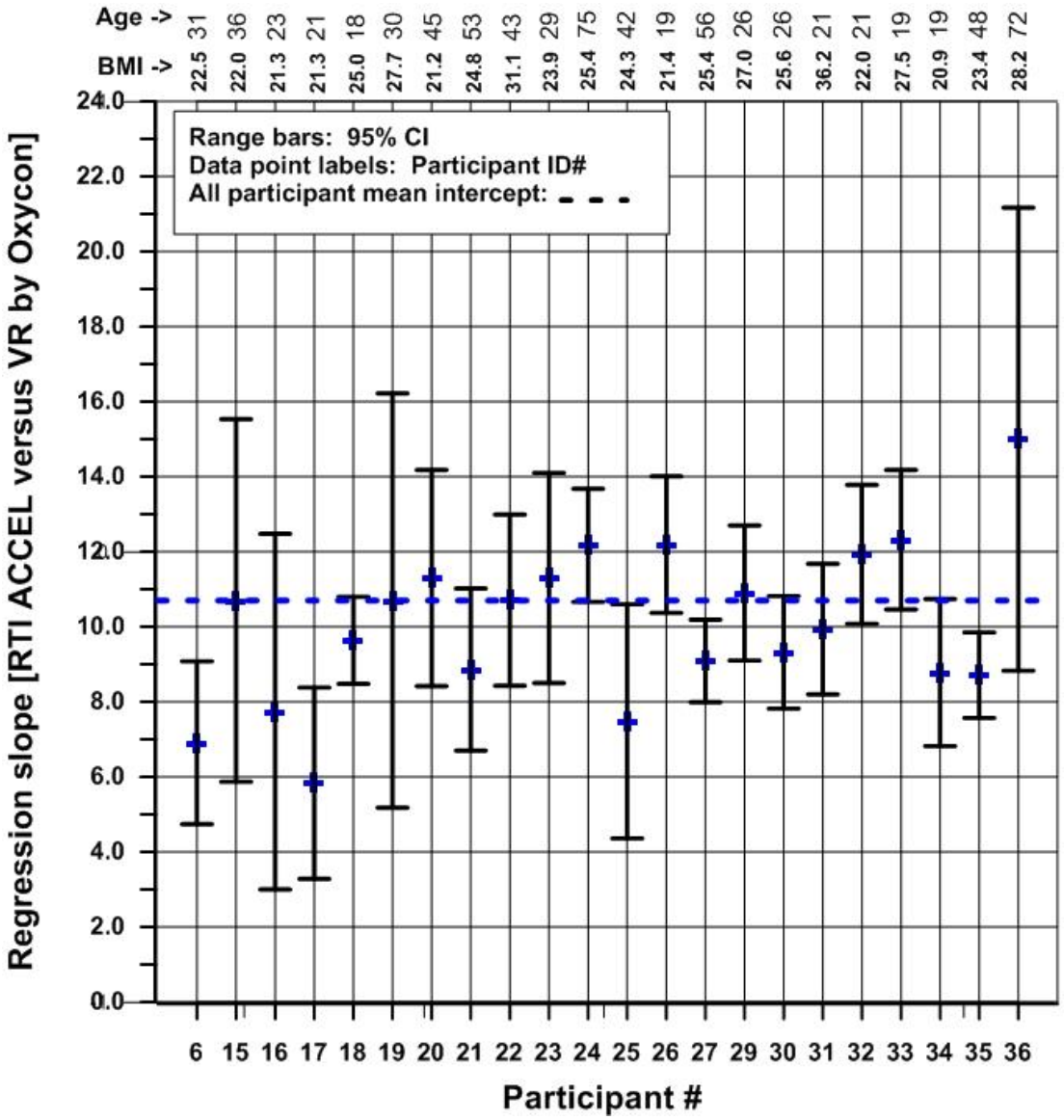

Figure 5S. RTI Accelerometric raw data example signatures by axis at an elevated 20 Hz collection rate, illustrating distinctive patterns that could leave to transparent activity type identification

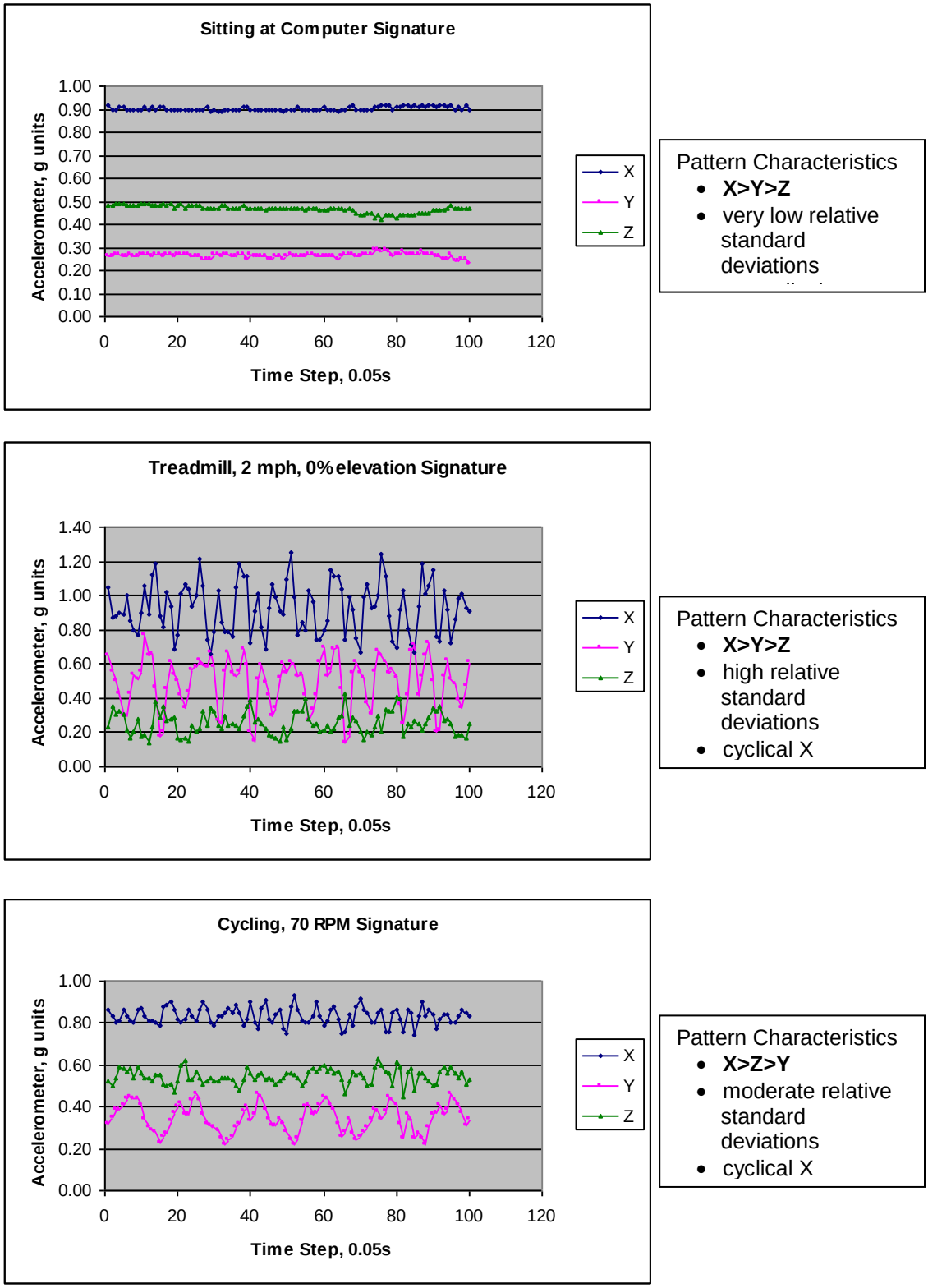

Figure 6S. Example screenshot of RTI MicroPEM™ output showing real-time traces for both aerosol concentration (µg/m^3) and potential dose (µg/min/kg). Included on this screen is the estimated ventilation volume (lpm), concurrent temperature and relative humidity, compliance level indication (worn/not worn), and a running estimate of the mass collected on the parallel filter, based on the nephelometer calibration. The ACCEL vs V regression slope and intercept is entered here as well (either an all cohort composite) or values specific for the participant), plus the participants body weight (kg).

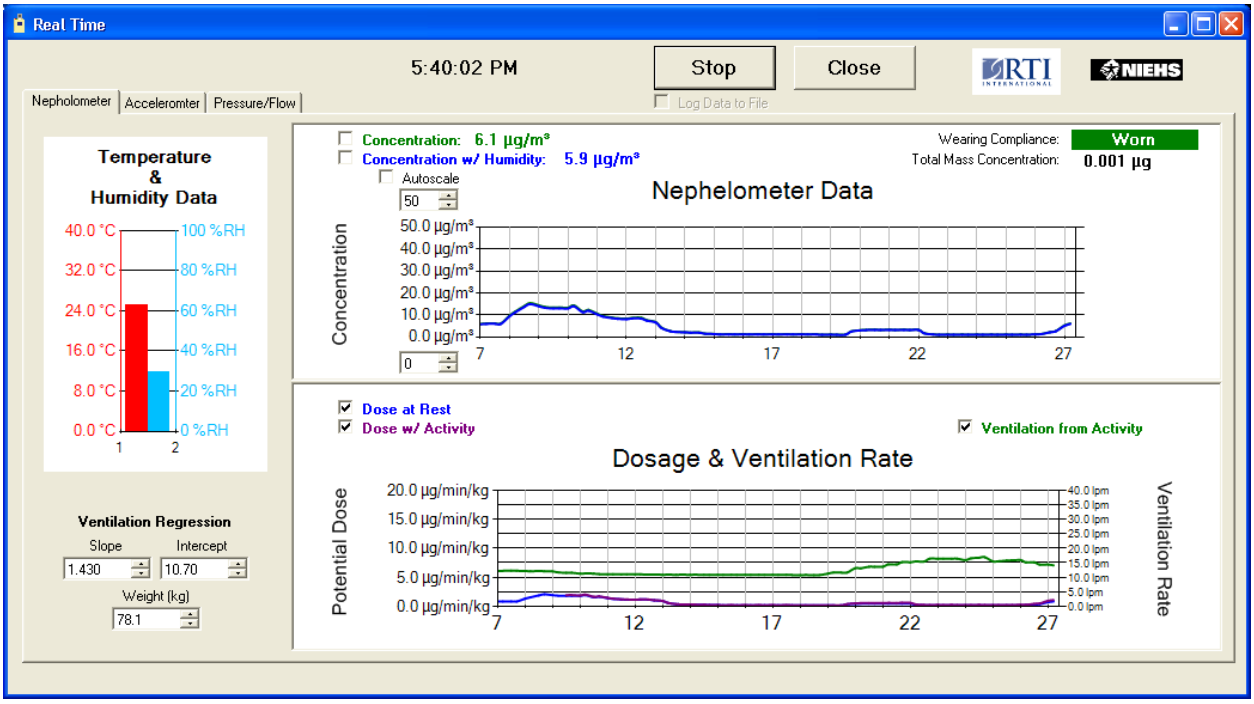

Table 1S. Computed triaxial standard deviations of the AUC variable (see text) for Participant #30, comparing that for an unworn unit with recumbent, sedentary, ambulatory, and bicycling activities.

Activity #	**Description**	**Category**	**$S_{x,y,z}$**
0	Unworn	na	0.0078
1	Lying down (but awake)	recumbent	0.016
3	Sitting at computer	sedentary	0.013
6	Sitting reading	sedentary	0.014
7	Walking on treadmill, 4 mph	ambulatory	0.22
19	Stationary indoor bicycling	higher energy, cycling	0.12
20	Outdoor bicycling	higher energy, cycling	0.21

Table 2S. Linear Regression Statistics for Columbia Exposure Monitor

					95% Confidence Intervals			95% Confidence Intervals	
Test #	Part. #	Columbia side	activities n	Columbia Slope	Slope -	Slope +	Columbia Intercept	Intercept -	Intercept +
1	6	na	12	36.80	22.9	48.7	7.26	5.15	9.37
2	15	R	11	32.60	11.50	53.70	13.00	6.32	19.70
3	16	R	8	38.90	24.90	51.30	7.16	3.52	10.80
4	17	R	11	30.00	2.30	57.80	7.31	2.07	12.50
5	18	R	8	31.10	25.00	37.20	9.30	2.25	11.40
6	19	R	13	39.70	23.30	56.10	11.70	5.64	17.70
7	20	R	9	34.70	26.90	42.40	11.80	9.74	13.86
8	21	L	12	36.20	26.30	46.10	8.63	6.29	10.95
9	22	L	14	52.90	41.10	64.70	11.20	8.10	14.29
10	23	L	11	18.90	7.73	30.10	12.80	9.31	16.40
11	24	L	12	45.80	31.10	60.60	12.80	8.76	16.80
12	25	L	12	36.00	25.60	46.40	7.40	5.00	9.80
13	26	L	13	20.30	16.20	24.30	12.60	10.60	14.60
14	27	L	13	41.40	34.60	48.20	9.31	7.56	11.10
15	29	L	15	19.10	7.37	30.90	14.90	10.10	19.80
16	30	L	13	33.90	26.10	41.80	9.64	7.39	11.90
17	31	L	13	50.50	36.90	64.10	11.70	7.71	15.70
18	32	L	13	35.20	27.60	42.80	12.10	10.00	14.20
19	33	L	11	40.30	26.80	53.80	12.60	9.12	16.00
20	34	L	na	na	na	na	na	na	na
21	35	L	12	44.00	34.70	53.40	9.04	6.62	11.50
22	36	L	14	81.50	54.80	108.30	15.30	8.90	21.60
		n	21	21	21	21	21	21	21
ALL DATA		median	12.0	36.10	26.20	49.75	11.70	7.64	14.25
		average	11.9	38.15	25.54	50.70	11.01	7.25	14.53
		std dev		13.4	12.1	17.1	2.5	2.5	3.5
		RSD %		35.2	47.3	33.7	22.6	34.7	24.0
		min	8	18.90	2.30	24.30	7.16	2.07	9.80
		max	15	81.50	54.80	108.30	15.30	10.60	21.60