

**AP 01 FLOW-DEPENDENCE OF ANATOMICAL DEAD SPACE AND RELATIONSHIP TO SPIROMETRY IN HEALTHY SUBJECTS**

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**Introduction:** We have previously shown that in healthy subjects anatomical dead space (VD) measured by gas washout increases linearly with expired flow. We hypothesised that this relationship is due to flow-dependent non-uniform airway emptying. In this study we further investigate the flow-dependence of VD by partitioning VD into its volume compartments (VD<sub>p1</sub> and VD<sub>p2</sub>) and test the hypothesis that the flow-dependence of VD is associated with ventilatory capacity.

**Materials and Methods:** VD, VD<sub>p1</sub> and VD<sub>p2</sub> of 13 healthy subjects (age 19-35 years, 5 male) were measured using gas washout over a range of expiratory flows (0.2-4.5 L/s). Expired volume and molar mass were measured simultaneously using an ultrasonic sensor eliminating temporal misalignment errors. The flow-dependence of VD, VD<sub>p1</sub> and VD<sub>p2</sub> was determined by linear regression.

**Results:** All subjects had normal spirometry (mean, range): FEV<sub>1</sub>% (103.4%, 82-126%), FVC (107.3%, 90-126%). A positive linear relationship was found between VD and its volume compartments (VD<sub>p1</sub> and VD<sub>p2</sub>) and expired flow (see Table, mean, SD). The increase in VD with flow was almost entirely due to the increase in VD<sub>p1</sub>. Significant correlations (p<0.05) were found between the slope and intercept for VD, and VD<sub>p1</sub> and FEV<sub>1</sub> %pred and FVC %pred, but not for FEV<sub>1</sub>/FVC.

VD		VD <sub>p1</sub>		VD <sub>p2</sub>	
Slope (mL/L/s)	Intercept (mL)	Slope (mL/L/s)	Intercept (mL)	Slope (mL/L/s)	Intercept (mL)
55.1, 13.9	121.7, 36.4	55.9, 15.7	68.4, 26.4	-0.7, 10.2	53.1, 14.7

**Conclusions:** The flow-dependence of VD is almost entirely due to VD<sub>p1</sub> and is associated with indices of ventilatory capacity. We speculate that the flow dependence of VD is a consequence of non-uniform airway emptying, particularly at low flows. The flow-dependence of VD may offer a novel, simple and sensitive non-effort dependent tool to detect and quantify non-uniform airway function.

**Key Words:** Flow dependence, anatomical dead space, spirometry, inhomogeneity

**AP 02 ACINAR HETEROGENEITY IS DETECTED IN PATIENTS WITH CHRONIC BRONCHITIS**

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The relative contribution of the small airways has increasingly been documented as being important in a number of respiratory conditions. The COPD classification includes chronic bronchitis and emphysema and the T<sub>L</sub>CO has been used to help differentiate the two. The aim of this study was to document differences in acinar heterogeneity as measured by the Multiple Breath Nitrogen Washout (MBNW) in this mixed patient group.

**Methods:** Patients were recruited with an FER of <70%. Each subject had measurements of spirometry, gas transfer factor and acinar (Sacin) and conductive (Scond) heterogeneity as measured by the MBNW. Subjects were then divided into two groups using the T<sub>L</sub>CO lower limit of normal as a delineator for chronic bronchitis and emphysema.

**Results:** 64 patients were recruited. In the group with normal T<sub>L</sub>CO (n=49) the mean T<sub>L</sub>CO was 89% predicted, however Sacin was elevated at 0.199 L<sup>-1</sup> (upper limit of normal 0.137 L<sup>-1</sup>) and Scond was within normal limits. In the group with T<sub>L</sub>CO below the lower limit of normal (n=15, TLCO = 64% predicted) the Sacin was further increased to 0.295L<sup>-1</sup> (p=0.02) and Scond remained in normal limits.

**Conclusion:** We conclude that acinar heterogeneity is present in patients with chronic bronchitis, however Sacin heterogeneity is further increased in the presence of emphysema. There was no heterogeneity measured in the small conducting airways. This suggests in patients with chronic bronchitis that the site of inflammation is in the acinar region of the lung.

**Key Words:** ventilation heterogeneity, COPD

## ANZSRS ASM 2008 – Posters

### AP 03 PERIPHERAL AIRWAY FUNCTION DECLINES FOLLOWING ALLOGENEIC BONE MARROW TRANSPLANTATION

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**Introduction:** Bronchiolitis obliterans affects approximately 25% of allogeneic stem cell transplant recipients (HSCT). Spirometry is an insensitive indicator of peripheral airway function.

**Aim:** To determine if parameters derived from the multiple breath nitrogen washout (MBNW), or other complex measures of respiratory function are more sensitive markers of disease.

**Methods:** A cross sectional study of 18 clinically stable HSCT recipients. Subjects had measurements of spirometry, lung volumes, diffusion, Sacin and Scond by MBNW (measures of acinar and conductive airway function respectively), fractional exhaled nitric oxide (FeNO) at 200ml/sec, and resistance (Rrs) and reactance (Xrs) by forced oscillation technique (FOT).

**Results:** Mean  $\pm$ SD age was  $48 \pm 14$  yrs, FEF25-75 was  $83 \pm 28$  % predicted, Sacin was  $0.341 \pm 0.220L^{-1}$  (normal  $<0.13$ ) and Scond was  $0.073 \pm 0.031L^{-1}$ , (normal  $<0.04$ ). Rrs was  $137 \pm 27\%$  predicted. Median FeNO was 7.4ppb (range 6-36). Median time since HSCT was 166 days (range 92-874). Sacin, adjusted for age and smoking, was related to the time from HSCT ( $r=0.62$ ,  $p=0.006$ ); as was FEV1 % predicted ( $r=0.21$ ,  $p=0.03$ ). However, Scond, Rrs, Xrs, RV/TLC, FEV1/FVC and FEF25-75 were all unrelated after adjusting for known predictors. FeNO was unrelated to all parameters of airway function.

**Conclusion:** Function of the acinar airways as measured by Sacin worsens with increasing time from HSCT. However, FOT measurements and, in the most part spirometry, are dissociated from such time related changes. This suggests that Sacin is sensitive to changes in very peripheral airways in HSCT recipients and that further work is needed to determine its potential clinical utility.

**Key Words:** Peripheral airway function, nitrogen washout, forced oscillation technique.

**Support:** University of Sydney Bridging Grant U1089 and Cooperative Research Centre for Asthma.

## ANZSRS ASM 2008 – Posters

### AP 04 HOME-BASED SPIROMETRIC AND INSPIRATORY CAPACITY MEASUREMENTS IN SEVERE COPD ARE REPRODUCIBLE

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Remote in-home measurement of a variety of physiological variables (telemonitoring) provides an alternative management approach for patients with chronic disease. There are few data demonstrating the intra-patient reproducibility of such measurements in COPD.

**Aim:** To determine reproducibility of unsupervised spirometry, including measurement of inspiratory capacity (IC) in the home in severe COPD.

**Methods:** Observational study of patients with severe COPD performing daily spirometry via a telemonitoring system (Medcare Systems, Australia). Measurements were performed, over a 4-week exacerbation-free period. Patient characteristics (mean±SD): n=14, M/F: 6/8, age 69±11yrs, FEV1 0.82±0.33L, previous personal computer (PC) familiarity 64%. Initial supervised training was provided to all patients. Spirometer calibration was checked at the beginning and end of the study.

**Results:** Results are presented as coefficients of variation (CoV).

CoV (%) (n=14 subjects)							
	FEV1	FEV6	FVC	IC	PEF	RR	SpO2
<b>Mean (SD)</b>	7.0 (2.4)	6.6 (2.3)	7.5 (3.0)	7.6 (2.7)	12.4 (6.2)	10.1 (3.4)	1.7 (1.0)
<b>Range</b>	3.9 - 12.7	3.8 - 12.0	1.8 - 14.0	4.3 - 12.0	6.6 - 31.1	6.5 - 19.8	0.7 - 4.0

No calibration errors were detected.

**Discussion:** The reproducibility of these data compares favourably with published data for laboratory-based measurements and provides a reference for future studies involving serial monitoring in patients with COPD.

**Key Words:** Telemonitoring, spirometry, reproducibility

## ANZSRS ASM 2008 – Posters

### AP 05 COPD AND CHF IN AN ELDERLY RURAL POPULATION

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**Background:** Prevalence of Chronic Obstructive Pulmonary Disease (COPD) is reported to affect 12-18% of those over 55 years. COPD is a risk factor for Congestive Heart Failure (CHF) with 10-30% of people with COPD reported to have CHF. Prevalence of both diseases in a rural population has not been ascertained. This study estimates prevalence and management of COPD and CHF in an elderly central west population.

**Design:** Cross-sectional population study of randomly selected participants.

**Methods:** Spirometry and cardiorespiratory questionnaire were conducted in 195 55-75 year old central west NSW residents. Those with obstructive lung disease ( $FEV_1/FVC < 0.7$  and  $FEV_1 < 80\%$  Pred) had 4 puffs of salbutamol administered via a spacer and spirometry was repeated after 15 minutes. Participants with less than 12% and 200ml reversibility in  $FEV_1$  or FVC were considered to have COPD, and had echocardiography performed.

**Results:** 40.5% (79) reported having difficulty breathing. 7% (14), had obstructive 5% (10) mixed, and 20.5% (40) restrictive lung disease ( $FEV_1/FVC > 0.7$  and  $FVC < 80\%$  Pred). Of those with obstructive or mixed disease, 8.7% (17) demonstrated non-significant reversibility or COPD. 38.5% (5/13) of those with COPD demonstrated Pulmonary Artery Pressure (PAP) greater than 30mmHg indicating CHF.

**Conclusion:** Prevalence of COPD in this elderly rural population is lower than previously reported in urban populations. The prevalence of CHF in those with COPD was higher than previously reported.

**Grant support:** CSU competitive grant

**Key Words:** Chronic Obstructive Pulmonary Disease, Congestive Heart Failure, Epidemiology

**AP 05 CHANGES IN CROSS POWER SPECTRA OF INTER-LEAD ECG AT OBSTRUCTIVE SLEEP APNEA TERMINATION**

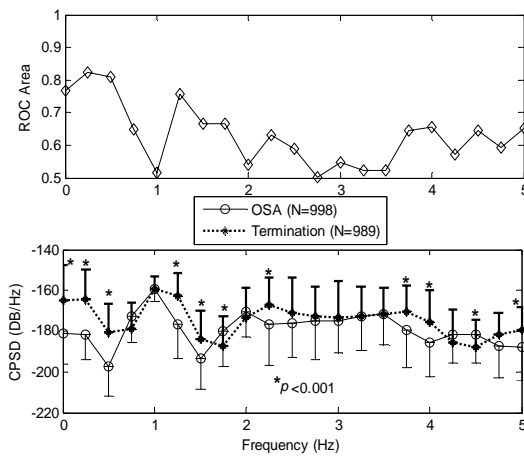
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The end of an obstructive sleep apnea (OSA) episode is identified as airflow increase/recovery accompanying increased inspiratory effort and sympathetic cardiovascular responses. To better relate those changes with cardiac performance, this study assesses the changes of cross power spectrum density (CPSD) of ECG signals between two leads induced during and at the termination of OSA episode.

**Methods:** ECGs (2 leads) from 4 patients overnight sleep studies were examined for location of the pre-scored apnea events. Total 998 clips (5-second window containing a cycle of inspiration and expiration) during OSA and 989 clips at termination of OSA events from each lead were extracted. CPSD analysis was performed between two leads ECG clips for OSA and its termination. CPSDs at all frequencies were compared by receiver operating characteristics (ROC) analysis.

**Results and conclusion:** The bottom panel of the figure shows the mean and SDs of CPSDs (1-5Hz) in which maximum areas (>0.8) under ROC curves (as shown in upper panel) were found to be at 0.4 and 0.6 Hz. On the other hand, ROC areas at all other frequencies were less than 0.8. In summary, the results show significant ( $p < 0.001$ ) increases in CPSDs at apnea termination. It could be used as marker for detecting the rhythmic respiratory related activity toward the end of obstructive apnea.



**Key words:** Sleep apnea, ECG, Cross power spectrum analysis

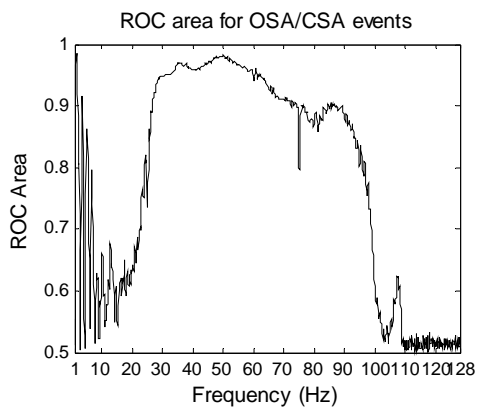
**AP 07 DIFFERENTIATING CENTRAL AND OBSTRUCTIVE SLEEP APNEA EVENTS IN ECG RECORDINGS**

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Changes in chest muscle signal reflect the changes in involuntary breathing effort as evident during obstructive sleep apnea (OSA) event. In contrast, central sleep apnea (CSA) event is not accompanied with breathing effort. The aim of this study is to differentiate CSA events from OSA ones using power spectral density (PSD) features of ECG signal over 5 second period.

**Methods:** Total 953 CSA and 7147 OSA events were selected from single lead ECGs (sampling rate=256 Hz) collected from 4 patients overnight sleep studies. Only 5-second ECG (which contains a cycle of inspiration and expiration) clips were extracted from pre-scored apnea events. PSD values of ECG clips at all frequencies (1-128 Hz) were calculated and compared. Receiver operating Characteristics (ROC) analysis was used to estimate the event recognition ability of PSDs at all frequencies.



**Results:** The areas under ROC curves between PSD values of ECG clips during OSA and CSA events are presented in the figure. The ROC areas ( $>0.95$ ) were found to be in the range of 1.5-2 Hz and 30-60 Hz, which reflects the influence of beat to beat heart rate and tonic chest muscle signals respectively during obstructed or unobstructed breathing disorders.

**Conclusions:** The PSDs within 30-60 Hz show the stable range for discrimination between CSA and OSA events. These results indicate that it may be possible to diagnose OSA and CSA noninvasively and breath by breath from shorter segments of ECG signals.

**Key words:** Sleep apnea, ECG, Power spectrum analysis

**AP 08 MENTHOL THROAT LOZENGE USE DOES NOT AFFECT THE DLCO MEASUREMENT**

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Ethanol has previously been shown to interfere with the infra-red (IR) multigas analyser commonly used in the measurement of the carbon monoxide transfer factor (DLCO) [1]. This is due to an overlap in the IR absorption spectra of ethanol and methane (CH<sub>4</sub>). Menthol, a common ingredient in throat lozenges, displays similar IR spectral properties as Ethanol, thus could be expected to interfere with the IR measurement of CH<sub>4</sub> in a similar fashion.

**Aim:** Determine the effect of Menthol containing throat lozenges on the measurement of DLCO.

**Methods:** Nine healthy subjects performed DLCO according to ATS/ERS guidelines (Sensormedics Encore 229D) on 2 separate days in a randomised cross-over trial. In the control arm, baseline measurements were obtained, and repeated after 25 minutes. In the active arm, subjects waited 15 minutes after the baseline study before sucking a throat lozenge (Vicks Vapour Drop – 7mg menthol). Repeat measurements were performed immediately upon completion of the lozenge, approximately 25 minutes post baseline. ANOVA and paired t-tests were used to assess differences in DLCO and KCO.

**Results:** 5 females and 4 males (Age 22 to 49 years) participated. Close inspection of the IR CH<sub>4</sub> and CO tracings during the DLCO manoeuvre post-menthol, failed to detect any unusual analyser response similar to that previously described with ethanol interference. DLCO (mean  $\pm$  sd) was  $23.5 \pm 6.0$  mL/min/mmHg pre-menthol and  $23.3 \pm 6.1$  mL/min/mmHg post-menthol (p=0.3). This change in DLCO post-menthol was not significantly different to that observed post-control (p = 0.34). There was no significant difference in KCO (p = 0.4). Menthol also had no significant effect on spirometry indices FEV1 and FVC.

**Conclusion:** The Sensormedics IR analyser was not susceptible to a single Menthol lozenge. There was no significant effect of the Menthol lozenge on CO diffusion measurements.

1 Punjabi et al Chest 2003;123:1082-89.

**Key Words:** DLCO, Menthol

**AP 09 CARDIOPULMONARY EXERCISE TEST QUALITY CONTROL PROGRAMS. DO WE NEED INTER-LABORATORY BIOLOGICAL CONTROL COMPARISONS? – A PILOT STUDY**

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Previous studies have shown large (up to 25%) inter-laboratory variability in cardiopulmonary exercise test (CPET) results. This is despite adherence to quality control guidelines and manufacturers instructions. For this reason inter-laboratory comparisons are recommended in multicentre studies. Our aim was to investigate if inter-laboratory biological control comparisons benefit our CPET-QC programs. Submaximal CPET tests were performed on two subjects tested between two participating centres (Centres A, and B). One of the subjects performed tests at a third Centre C. SensorMedics Vmax Legacy systems, with electromagnetically-braked cycle-ergometers, were used by each centre. CPET systems were maintained to manufacturers instructions, with conformance to current published CPET-QC recommendations. Within-subject exercise protocols were the same between centres, either 25W/min or 30W/min ramped. Iso-work (at 150 Watts) measures of  $\dot{V}'O_2$ ,  $\dot{V}'CO_2$ , heart rate (HR), and  $\dot{V}'E$  were compared.

**Results:**  $\dot{V}'O_2$  for Centre B, (2.03L/min (0.10(SD);N=10) was significantly higher in comparison to Centres A, (1.63(0.10(SD):N=6,  $p<0.05$ ) and C, (1.79(0.09(SD):N=5,  $p<0.05$ ). Centres A and C did not differ significantly.  $\dot{V}'CO_2$ , HR and  $\dot{V}'E$  were not significantly different between all centres.

Attention was directed at resolving the discrepancy in the measurement of  $\dot{V}'O_2$  at Centre B.

**Conclusions:** Inter-laboratory biological control comparisons alerted us to one centre's problem with their CPET measurements. This was despite apparent satisfactory CPET-QC. Further investigation is warranted to propose inter-laboratory biological control comparisons as an additional recommendation for CPET-QC.

**Key Words:** Exercise test, Quality control, Biological control.

## ANZSRS ASM 2008 – Posters

### AP 10 REVISED HISTORICAL SPIROMETRY REFERENCE RANGES UNDERESTIMATE CONTEMPORARY HEALTHY SPIROMETRY VALUES

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Recent modelling advances have allowed the collation of multiple spirometry reference datasets to create unified spirometry reference data for 4 to 80 year olds<sup>1</sup>. We compared the revised reference data with contemporary data to verify the appropriateness of the reference data for clinical use.

**Methods:** Spirometry collected by respiratory laboratories in Australia and New Zealand were collated and included if data was collected after 1999 and subjects were Caucasians with no history of smoking or respiratory disease. Z scores were calculated for FEV1, FVC, FEV1/FVC and FEF25-75.

**Results:** Spirometry from 886 subjects aged 4-80 years (46% male) from 10 centres were included. Mean (SEM) Z scores were significantly different from historical data ( $p < 0.05$ ) and were 0.152 (0.033) for FEV1, 0.194 (0.036) for FVC, -0.066 (0.032) for FEV1/FVC and 0.184 (0.036) for FEF25-75. Gender did not influence Z scores, while older subjects tended to have higher Z scores for FEF25-75 and FEV1/FVC ( $p < 0.01$ ) but not FEV1 or FVC.

**Conclusion:** The revised collated reference ranges offer significant advantages over the original reference datasets. This preliminary analysis suggests the use of this revised reference set may underestimate the presence of respiratory disease by a small but statistically significant degree.

<sup>1</sup>Stanojevic et al, Am J Resp Crit Care Med 2007

**Key words:** Spirometry, reference ranges.

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