customised offline analysis software (SimpleWashout, Igor Pro) by a single operator at each site. To test inter-operator agreement, every seventh MBW from each timepoint was randomly selected, without subject duplication, and used to calculate LCI values by both operators separately.

Results A total of 854 LCIs were performed during the trial, and technically acceptable measurements were achieved in 95.9% and 94.2% of tests at the two sites (mean 94.8%). 118 (13.8%) of LCIs were analysed independently by two operators, with a full range LCI values represented (range 7.24–19.21). The 95% limits of agreement (LoA) for LCI values were -0.04 to 0.04 (mean difference 0.00) and for FRC values were -0.01 to 0.01 (mean difference 0.00).

Conclusions Our results demonstrate that LCI is an achievable outcome measure in a multicentre trial in 94.8% of attempts. Separate offline analysis completed by two operators, with appropriate training and knowledge of the test, produces mean LCI and FRC inter-site differences of 0.00. LCI is feasible and appropriate for use as a surrogate endpoint in multicentre clinical trials using stringent methodology.

P210   **AIRWAYS RESISTANCE IN BRONCHIAL CHALLENGE TESTING**

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Introduction Measurement of airways resistance is an alternative to spirometry to assess airflow obstruction. This can be measured by the interrupter technique (RInt) using a hand held device. We wished to know how RInt compared to forced expiratory volume in 1 second (FEV1) during a histamine challenge test.

Methods Twenty-nine (13 male) patients, aged 48.9 (SD 15.3) years, referred for a histamine challenge test were enrolled. Patients had measurement of RInt then FEV1 after administration of saline and following doubling concentrations of histamine from 0.06 mg/ml to 8 mg/ml. Extrapolation of the log dose-response curve was undertaken to calculate the concentration (Provocation Concentration – PC) causing an increase airways resistance of 20, 40, 60, 80, 100, 120, 140 and 160% (RInt PC1.2 to RInt PC2.6) and a reduction in FEV1 by 20% (FEV1 PC20). The number of patients with a negative challenge (i.e. PC > 8 mg/ml histamine) was calculated for FEV1 and each change in airway resistance. Patients assessed their procedure provoked symptoms of breathlessness, dizziness and tiredness on a 100 mm visual analogue scale.

Results Geometric (SD) PC20 for FEV1 was 1.87 (0.5) mg/ml with 11 patients having a negative challenge. A RInt PC2.0 had the best agreement with FEV1 PC20 (Kappa 0.39 (p = 0.024)). There is a significant negative correlation between RInt and FEV1 (r = -0.94). The respective mean (SD) breathlessness, dizziness and tiredness scores for RInt were 26(4) mm, 18(3) mm, 22(4) mm and for spirometry were 40(4) mm, 27(5) mm, 31(5) mm. There was a significant (p < 0.05) difference for breathlessness.

Conclusion RInt was tolerated better than spirometry. A doubling of airways resistance had the best agreement with PC20 FEV1.

P211   **FEV1/FIV1 INDEX IN AMYOTROPHIC LATERAL SCLEROSIS PATIENTS**

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Amyotrophic lateral sclerosis (ALS) is a relentlessly progressive, presently incurable, neurodegenerative disorder that causes muscle weakness, disability, and eventually death. The ALS Functional Rating Scale (ALSFRS-R) is a validated rating instrument for monitoring the progression of disability in patients with ALS. The ALSFRS-R incorporates questions for the assessment of dyspnoea, orthopnea, and the need for ventilatory support. However, studies on the relationship of ALSFRS-R with objective measurements of respiratory function are scanty. Therefore, we set out to investigate the relationship of ALSFRS-R with respiratory function indices in ALS patients.

We studied 33 consecutive, ambulatory, Caucasian patients (21 men) with ALS. Seventeen patients had bulbar involvement. Two patients did not satisfactorily perform the lung function testing and they were excluded. ALSFRS-R was assessed. Routine lung function tests, maximum static expiratory (Pemax) and inspiratory (Pimax) mouth pressures were measured. Respiratory muscle strength (RMS) was also calculated.

ALSFRS-R (mean±SD) was 35 ± 9. Patients had: age, y=60 ± 10, FEV_1,%pred=83 ± 18, FVC,% pred=86 ± 20, TLC,% pred=94 ± 11, and DL_{CO},% pred=92 ± 18. Pemax,% pred was 80 ± 28, Pimax,% pred was 73 ± 31, and RMS,% pred was 77 ± 27. These pressures were below the normal limits in 15, 20, and 17 patients, respectively. ALSFRS-R was significantly correlated with Pemax%pred, RMS%pred, and FEV_1/FIV_1 (r = 0.46, p < 0.01; r = 0.38, p = 0.035; n = 20, r=-0.71, p < 0.001, respectively).

Abstract P210 Table 1

Measure	Fall in FEV$_1$ of 20% (FEV$_1$ 0.8)	RINT increase 20% (1.2)	RINT increase 40% (1.4)	RINT increase 60% (1.6)	RINT increase 80% (1.8)	RINT increase 100% (2.0)	RINT increase 120% (2.2)	RINT increase 140% (2.4)	RINT increase 160% (2.6)
Geom mg/ml	1.88	0.90	1.05	1.47	2.10	3.18	4.29	2.00	1.46
(SEM)	0.51	0.37	0.39	0.48	0.63	0.80	0.87	0.82	0.72
	11								
PC20 >8mg/ml (number of patients)*		13	12	13	14	16	19	21	23
						0.39	0.24	0.24	0.24
Kappa (p)		0.15 (0.41)	0.21 (0.26)	0.29 (0.11)	0.37 (0.039)	(0.024)	(0.149)	(0.149)	(0.149)

FEV1: Forced expiratory volume in 1 second, RInt airways resistance using the interrupter technique, Geom: geometric mean, mg; milligram, ml: millilitre, PC: provocation concentration (the concentration of histamine required to produce the desired effect), * The number of patients with a PC more than 8mg/ml i.e. deemed not to have asthma.

In conclusion, FEV_1/FIV_1 index has a good correlation with ALSFRS-R (n = 20, r=-0.71, p < 0.001, FEV_1/FIV_1 = 1.630 - [0.018 * ALSFRS-R] ± 0.165).

P212 PARASTERNAL INTERCOSTAL ELECTROMYOGRAPHY TO ASSESS NEURAL RESPIRATORY DRIVE IN HEALTHY ADULT SUBJECTS

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Neural respiratory drive (NRD), measured using the parasternal intercostal muscle electromyogram (EMGpara), relates to lung disease severity as quantified by conventional methods in a range of diseases. Reference data from healthy populations are required for the technique to be used as an independent measure of lung disease severity. EMGpara has previously been expressed as a percentage of that obtained during a maximal inspiratory effort (EMGpara%max), restricting the use of the technique to subjects able to reliably perform such manoeuvres. The aim of this study was to investigate variability of both raw EMGpara (rEMGpara) and EMGpara%max in healthy adults.

EMGpara was measured during tidal breathing in 43 healthy adult non-smokers (25 females, median (range) age 32 (19–79) years, mean (SD) BMI 23.4 (3.5) kg/m^2), using surface electrodes positioned bilaterally over the second interchondral space. Measurements were made with and without a mouthpiece/pneumotachograph *in situ* in 20 participants. Repeated measures were obtained within the same testing session in 27 subjects, and at least seven days later in 13 individuals. Spirometry, height, weight, BMI, fat free mass (FFM) via bioelectrical impedance and measures of regional fat distribution (waist/hip ratio and neck circumference) were also recorded.

Mean (SD) EMGpara%max and rEMGpara were 5.88 (3.63)% and 5.06 (2.26)μV respectively. Significant relationships were observed between anthropometric measures and rEMGpara and EMGpara%max (Table 1). rEMGpara and EMGpara%max were unrelated to spirometry variables. Median (range) rEMGpara and EMGpara%max increased significantly with the pneumotachograph in place (4.86 (2.11–8.19)μV *versus* 5.62 (2.47–10.98) μV and 4.77(1.68–17.00)% *versus* 6.78 (2.35–20.94)%, both p < 0.0001).

Analysis of variance by subject was used to assess within-subject variability. Measurement error was higher for EMGpara%max than rEMGpara (upper 95% confidence limit of difference between repeat measures of EMGpara%max 3.14%, *versus* 2.35 μV for rEMGpara; within-subject coefficient of variation EMGpara%max 30.8% *versus* rEMGpara 24.5%).

rEMGpara appears to be a reproducible marker of NRD. Both rEMGpara and EMGpara%max are influenced by subjects' anthropometry. Further investigation is required to determine whether these influences are technical or physiological and must be considered when the technique is applied clinically or for research, or when developing reference values.

P213 THE IMPACT OF SLEEP DISORDERED BREATHING ON PERIPHERAL MUSCLE

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Introduction Chronic obstructive pulmonary disease is characterised by peripheral muscle wasting with consequent reduction in muscle strength and function. In this cohort of patients a reduction in muscle strength correlates with morbidity and mortality. Less well known are the characteristics of muscle in patients with sleep disordered breathing (SDB), a disease state that can also be dominated by inflammation, breathlessness and hypoxia. We sought to examine the impact of sleep disordered breathing on peripheral muscle size and strength.

Method 51 subjects were recruited: 15 healthy controls (HC) with a normal body mass index (BMI, <25 kg/m^2), 16 overweight and obese individuals with no SDB controls (SO), and 20 obese subjects with obstructive sleep apnoea (OSA). Subjects underwent measurements of Rectus Femoris Cross Sectional Area (RF_{CSA}) and quadriceps maximal voluntary contraction

Abstract P212 Table 1 Relationship of rEMGpara and EMGpara %max to anthropometric characteristics in 43 healthy adult subjects

	Correlation with raw EMGpara (r (p))	Correlation with EMGpara%max (r (p))
Height	-0.38 (0.01)	-0.60 (<0.0001)
Weight	-0.47 (0.001)	-0.57 (<0.0001)
BMI	-0.46 (0.002)	-0.35 (0.02)
FFM	-0.12 (ns)	-0.28 (ns)
Neck circumference	-0.43 (0.004)	-0.68 (<0.0001)
Waist/hip ratio	-0.23 (ns)	-0.48 (0.001)

Abstract P213 Table 1 Differences between groups in demographics, muscle size and strength

	HC n = 15	SO n = 16	OSA n = 2
Age (years)	21 (20–33)	32# (23–40)	58* (48–67)
M:F	16:4	6:10	9:11*
BMI (kg/m^2)	22.4 (19.0–23.6)	28.2*# (25.5–32.7)	38.5* (35.8–42.6)
FEV_1(L)	3.19 (2.44–3.74)	3.28 (2.84–4.72)	2.87 (2.31–3.31)
FVC(L)	4.04 (3.17–4.27)	4.20 (3.66–5.56)	3.68 (2.79–4.12)
RF_{CSA}/weight (AU)	7.6 (6.7–8.7)	8.59# (6.1–10.3)	5.6* (4.1–7.3)
QMVC/weight (AU)	0.49 (0.45–0.60)	0.56# (0.44–0.71)	0.34* (0.20–0.43)
Handgrip strength/weight (kg)	0.43 (0.36–0.48)	0.48# (0.37–0.57)	0.32* (0.21–0.40)
SMWD (metres)	560 (520–640)	565# (513–607)	420* (278–515)

*significantly different from HC (p < 0.05); #significantly different from OSA (p < 0.05)
Abbreviations: HC=Healthy Controls, SO=Simple Obesity/Overweight, OSA=Obstructive Sleep Apnoea, BMI-Body Mass Index, RF_{CSA}=Rectus Femoris Cross Sectiona Area, QMVC=Quadriceps Maximal Voluntary Contraction, SMWD=Six Minute Walking Distance