Establishing Australian Impulse Oscillometry System predictive equations from a community sample of non-smokers

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Treatise submitted in partial fulfilment of the requirements for the degree of Master of Public Health

Charles Darwin University

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NOTE

This treatise is presented in the form of a paper written for publication in Respirology with additional appendices.
ABSTRACT

**Background and Objectives:** Impulse Oscillometry (IOS) measures respiratory function during normal breathing by transmitting mixed frequency rectangular pressure impulses down the airways and measuring the resultant pressure and flow relationships which describe the mechanical parameters of the lungs. Computer analysis calculates respiratory impedance and its components, airways resistance and reactance, at a range of frequencies from 0.1Hz to 150Hz. The IOS software generates predictive normal values for each of the parameters measured including total airway resistance (R5), the proximal airway resistance (R20) as well as peripheral capacitive reactance (X5) however these are based on German data. No previous Australian normative data exists.

**Methods:** Cross-sectional study of 100 community dwelling adults, with 10 males and females per 10-year cohort. Inclusion criteria: age range 25-74 years, apparently good respiratory health. Exclusion criteria: smokers, asthmatics and others with acute or chronic respiratory disease. Both IOS and spirometry were conducted on all participants.

**Results:** Australian predictive normal equations have been generated and compared to the current published equations. The IOS parameters have been correlated with the spirometric data. Results have been analysed by gender, age, height and weight and compared with the predicted normal values for each parameter provided by the German manufacturer of the IOS instrument. Results given include calculation of mean, range, and SD.

**Conclusions:** A preliminary set of Australian predictive equations have now been produced for the IOS. These have been compared with international equations. IOS has potential application in a range of respiratory disease states and in population screening for occupational health (e.g. mining, & high dust load environments).
ACKNOWLEDGMENTS

I would like to thank my two wonderful daughters and my husband for their support and encouragement. I would also like to thank my supervisors for their advice and guidance. I would particularly like to mention Nancy Briggs, and thank her for statistical help when needed.

Financial support for this study was obtained from a grant from PHC RED and the Spencer Gulf Rural Health School.

Except where noted, all the work was done by the candidate.
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# Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATS</td>
<td>American Thoracic Society</td>
</tr>
<tr>
<td>ATSI</td>
<td>Aboriginal and Torres Strait Islanders</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>ERS</td>
<td>European Respiratory Society</td>
</tr>
<tr>
<td>FEF</td>
<td>Forced expiratory flow</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Forced expiratory volume in 1 second.</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;%FVC</td>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; as a percentage of forced vital capacity.</td>
</tr>
<tr>
<td>FOT</td>
<td>Forced Oscillation Technique</td>
</tr>
<tr>
<td>FVC</td>
<td>Forced vital capacity</td>
</tr>
<tr>
<td>GOLD</td>
<td>Global Initiative for Obstructive Lung Disease</td>
</tr>
<tr>
<td>H&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Height cubed</td>
</tr>
<tr>
<td>Hz</td>
<td>Hertz</td>
</tr>
<tr>
<td>IOS</td>
<td>Impulse Oscillometry System</td>
</tr>
<tr>
<td>kg</td>
<td>kilogram</td>
</tr>
<tr>
<td>kPa</td>
<td>kilopascals</td>
</tr>
<tr>
<td>L</td>
<td>Litre</td>
</tr>
<tr>
<td>PEF</td>
<td>Peak expiratory flow.</td>
</tr>
<tr>
<td>PL</td>
<td>Port Lincoln</td>
</tr>
<tr>
<td>R</td>
<td>Resistance</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>X</td>
<td>Reactance</td>
</tr>
<tr>
<td>Z</td>
<td>Impedance</td>
</tr>
</tbody>
</table>
Establishing Australian Impulse Oscillometry System predictive equations from a community sample of non-smokers

Introduction

The Impulse Oscillometry System (IOS) is a form of Forced Oscillation Technique (FOT) that measures respiratory function by applying mixed frequency rectangular pressure impulses to the airways.\(^1,2\) These impulses are superimposed on the normal breathing of the subject, requiring no specific respiratory manoeuvres. Computer analysis of the resultant pressure and flow relationships describes the mechanical parameters of the lungs – respiratory impedance (Z) and its components, airways resistance (R) and reactance (X), at a range of frequencies from 0.1Hz to 150Hz.

Resistance (R) describes the frictional or the resistive components of the respiratory tract and is predominantly influenced by the calibre of the airways, with the central airways contributing most.\(^1,3\) Reactance (X) reflects capacitance (or elastic properties) of the lung periphery and the inert properties (Inertance) of the column of air in the airways.\(^1,3\) Capacitance is the lungs’ ability to store the energy required for passive expiration and is displayed as the negative part of reactance and dominates at low frequencies. The measure of Inertance is always a positive value, and dominates at higher frequencies.\(^1,4\) As high frequency oscillations (>15-20Hz) are not transmitted to peripheral airways, higher frequencies reflect only large airways effects; low frequency oscillations (5-15Hz) are transmitted to the peripheral airways and therefore reflect both large airways and small airways effects.\(^1,4\) IOS is able to provide more information about the peripheral airways
than commonly used pulmonary function tests and is more sensitive and more responsive to small airway function than maximal effort forced spirometric measurements.\textsuperscript{1, 5}

The IOS software generates predicted normal values based on gender, age, height and weight. Each subject’s results are compared to the predicted values, for each of the parameters measured including total airway resistance (R5 – Resistance at 5Hz), the proximal airway resistance (R20 – Resistance at 20Hz) as well as peripheral capacitive reactance (X5 – Reactance at 5Hz).

Predicted normal values for pulmonary function tests are important to assist in diagnosis and estimation of prognosis, and also for research and epidemiology.\textsuperscript{6} IOS uses normal values for adults which are those provided by the manufacturer (Viasys Healthcare).\textsuperscript{7} The German sample population came entirely from Erfurt, an industrial city previously part of the German Democratic Republic which had suffered significant air pollution prior to the reunification of Germany in 1990.\textsuperscript{8} Sampling to establish these normal data was carried out in 1991-2.\textsuperscript{7} The German sample consisted of 506 subjects, ages were unevenly spread between 18 and 69; there were also unequal numbers of males and females. Current smokers were included in the sample analysis, but although the authors do not indicate numbers of smokers/non-smokers, they report a “high proportion of smokers”\textsuperscript{7}, similar to their normal population.

Predictive equations for IOS have recently been established for Japanese adults\textsuperscript{9} but there are differences in lung volumes between ethnic groups.\textsuperscript{6, 10} Internationally, predictive equations have been produced for FOT\textsuperscript{11}, but although FOT and IOS are similar, results
from each should not be regarded as interchangeable. There were no existing normal values for Australian adults at the outset of this study.

The aim of this study was to establish preliminary predictive equations for the IOS in an adult Australian Caucasian population. Our main hypothesis was that our IOS data would not be significantly different to the German data. A secondary hypothesis was that the spirometry results for our sample would not be significantly different to previously established Australian data.

Methods

A convenience age-stratified sample of at least 100 healthy adults, evenly spread between 25 and 74 years, was drawn from in and around Port Lincoln (PL) on the southern Eyre Peninsula, South Australia. A broad recruitment strategy included advertisements in newspapers and on local radio, and visits to local community service groups. Participants were initially screened for age, smoking history and asthma history when they rang to enquire about the study and an appointment was given to those who fitted the inclusion and exclusion criteria. At the appointment, informed written consent was obtained after a full explanation of the study. Height and weight were measured, and a brief questionnaire was completed including racial origin, history of smoking, and acute or chronic lung disease. We were targeting only people of Caucasian race as there are known to be differences in lung measurements between races. People of Aboriginal or Torres Strait Islander (ATSI), Asian or African races were therefore excluded. Participants younger than 25 years of age were also excluded as others have shown that lungs continue to mature up to the age of 20-25 years. Current smokers were excluded, as were past smokers if
they had smoked more than 10 cigarettes per day for more than 5 years. People with a history of asthma, other chronic lung disease, or current acute respiratory infection were also excluded.

A MasterScreen IOS (Viasys Healthcare, Wurzburg, Germany) with a Lily-type heated screen pneumotachograph, was used for both IOS and spirometry. Volume, pressure and ambient conditions were calibrated on each test day as per the manufacturer’s instructions. IOS was performed prior to spirometry, to ensure there was no effect of forced expiration on the smooth muscles of the respiratory tract.\(^{15-17}\)

A minimum of three IOS tests were performed for each participant, each for the duration of 30 seconds.\(^1\) Participants were seated comfortably throughout, with their head in a neutral position and they wore a nose clip. The investigator placed her hands firmly on the participants’ cheeks to minimise the shunt effect of the upper airways.\(^{15,17}\) It was emphasised that participants should keep their mouth tightly sealed around the mouthpiece and they should keep their tongue low in their mouth by tucking it under the mouthpiece. They were also asked to avoid swallowing or talking. Participants were quietly encouraged throughout each test to reassure them and to ensure as much freedom from artefacts as possible.\(^5\)

IOS was followed by a minimum of 3 spirometry tests which were performed according to American Thoracic Society (ATS) & European Respiratory Society (ERS) guidelines\(^{18}\), thus ensuring reproducibility. A full explanation of the requirements was given to the participant who was coached throughout using vigorous operator instructions.\(^1\) Participants
remained seated, and wore a nose-clip. They were reminded about keeping the seal around the mouthpiece tight.

One spirometry and one IOS result was selected per participant for analysis. Selection criterion for spirometry was by $\text{FEV}_1 + \text{FVC}$, with the highest result retained. IOS selection criteria were tidal volume between 0.5-1L, Coherence was $>0.9$ at 20Hz and the test was free of artefact.

Data were analysed in Statistical Package for Social Sciences (SPSS) Version 13.0 for Windows. Data were analysed separately for males and females using multiple linear regression. Dependent variables were entered separately for both spirometry and IOS parameters, along with independent variables of Age, Height and Weight. Regression analysis was repeated for each dependant variable using Height cubed ($H^3$) instead of Height; a third regression analysis was performed as weight was not significant for many parameters in the initial analyses. Hierarchical multiple regressions were then performed which enabled the selection of the most applicable equation for each parameter. Lower and Upper Limits of Normal were determined based on the sample size, the t-value and the obtained standard error of the predictor.19

Predictive equations were generated for spirometry, $\text{FEV}_1$, $\text{FVC}$, $\text{PEF}$, $\text{FEF}$ 25, $\text{FEF}$ 50, $\text{FEF}$ 75, (Forced Expiratory Flow at 25%, 50% and 75% of expiration) and $\text{FEV}_1 \% \text{FVC}$. For IOS, predictive equations were generated for Impedance at 5Hz ($Z_5$), Resistance at 5-35Hz ($R_5-35$), and Reactance at 5-35Hz ($X_5-35$).
Spirometry results were compared with existing Australian spirometry equations\textsuperscript{20} for FEV\textsubscript{1}, FVC, PEF, and FEV\textsubscript{1}%FVC. Using 4 phantom subjects of both male and female sex, of 45 and 65 years of age, values for each parameter were generated for comparison using each set of equations. Values rather than actual equations were compared because differences in the equations precluded direct comparison – PL’s were linear while the Gore et al equations\textsuperscript{20} contained quadratic and cubic elements.

Values for IOS using the same 4 phantom subjects were calculated using the PL IOS predictive equations for Z5, R5-R35, and X5-X35. These values were compared with the predicted values generated for the same phantom subjects using the IOS manufacturer’s software as the predictive equations from the original German research were complex and were not amenable to direct comparison.

Ethics approval for this research was given by the University of Adelaide Human Research Ethics Committee, and the Human Research Ethics Committee of the Northern Territory Department of Health & Community Services and Menzies School of Health Research.

Results

Of 141 participants originally recruited, 9 were not tested because their smoking history was greater than that permitted by the study guidelines, or because of acute respiratory infection. Of the 132 participants who were tested, one person’s results were lost due to computer failure and six were excluded because of lack of any suitable IOS test result according to the selection criteria described earlier (see Table 1). Four of these participants were also unable to satisfactorily perform spirometry according to ATS/ERS guidelines.
Of the remaining 125 participants, 87.9% (n=58) of females and 89.8% (n=53) of males said they were never-smokers. Participant characteristics, spirometry results and IOS results are detailed in Table 2.

Table 1: Numbers recruited and number of valid tests

<table>
<thead>
<tr>
<th>Age cohorts</th>
<th>Number recruited (Male/female)</th>
<th>Valid tests Male/Female</th>
<th>Number excluded Male/Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-34</td>
<td>26 (12/14)</td>
<td>12/14</td>
<td>0/0</td>
</tr>
<tr>
<td>35-44</td>
<td>25 (12/13)</td>
<td>11/13</td>
<td>1/0</td>
</tr>
<tr>
<td>45-54</td>
<td>25 (11/14)</td>
<td>11/14</td>
<td>0/0</td>
</tr>
<tr>
<td>55-64</td>
<td>35 (15/20)</td>
<td>15/16</td>
<td>0/4</td>
</tr>
<tr>
<td>65-74</td>
<td>21 (10/11)</td>
<td>10/9</td>
<td>0/2</td>
</tr>
<tr>
<td>Total</td>
<td>132 (60/72)</td>
<td>59/66</td>
<td>1/6</td>
</tr>
</tbody>
</table>

Table 2: Subject characteristics, spirometry values and IOS results. (Mean and SD)

<table>
<thead>
<tr>
<th></th>
<th>Female N=66</th>
<th>Male N=59</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (range)</td>
<td>48.8 (25-72)</td>
<td>49.5 (25-74)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.6 ± 6.564</td>
<td>175.9 ± 8.77</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.3 ± 12.41</td>
<td>87.3 ± 11.494</td>
</tr>
<tr>
<td>FEV₁ (Litres)</td>
<td>2.982 ± 0.648</td>
<td>4.109 ± 0.735</td>
</tr>
<tr>
<td>FVC (Litres)</td>
<td>3.829 ± 0.710</td>
<td>5.308 ± 0.979</td>
</tr>
<tr>
<td>FEV₁ %FVC</td>
<td>77.597 ± 5.928</td>
<td>77.592 ± 4.841</td>
</tr>
<tr>
<td>R5 (kPa/l/s)</td>
<td>0.345 ± 0.096</td>
<td>0.284 ± 0.086</td>
</tr>
<tr>
<td>R20 (kPa/l/s)</td>
<td>0.292 ± 0.066</td>
<td>0.237 ± 0.067</td>
</tr>
<tr>
<td>X5 (kPa.l.s⁻¹)</td>
<td>-0.110 ± 0.046</td>
<td>-0.078 ± 0.027</td>
</tr>
</tbody>
</table>

Following multiple regression analyses, and hierarchical multiple regressions, the most parsimonious equation for each spirometry and IOS parameter was selected. This resulted in separate equations for males, and females, using age and height as independent variables, and using weight only where applicable. H³ was considered as a possible variable as it has been previously shown to bear a strong relationship to FEV₁ slope.²¹
When coefficients were calculated using $H^3$ instead of height as a variable, the results showed no difference when compared with those for Height alone; these have not been considered further (data available from author on request).

**Spirometry**

Analysis of the PL spirometry results showed that this was a normal sample, with normal distribution curves for most spirometry parameters. Spirometry comparisons using the phantom subjects described earlier are shown in Figure 1. The PL predictive equations for spirometry for males and females are given in Table 3.

Figure 1: Comparisons of PL spirometry with Gore et al using calculated spirometry values for phantom subjects, aged 45 years and 65 years.
Table 3: PL spirometry predictive equations

<table>
<thead>
<tr>
<th>Females</th>
<th>Constant to predict Lower Limit of Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁</td>
<td>-2.33418 - 0.03127xA + 0.0415639xHt†</td>
</tr>
<tr>
<td>FVC</td>
<td>-2.6983 - 0.0302xA + 0.0486057xHt</td>
</tr>
<tr>
<td>PEF</td>
<td>2.295973 - 0.04146xA + 0.041891xHt</td>
</tr>
<tr>
<td>FEV₁%FVC</td>
<td>[0.779214 - 0.00207xA + 0.000594xHt]x100</td>
</tr>
<tr>
<td>FEF25</td>
<td>-2.11995 - 0.03283xA + 0.0598105xHt</td>
</tr>
<tr>
<td>FEF50</td>
<td>-4.43898 - 0.03438xA + 0.0587381xHt</td>
</tr>
<tr>
<td>FEF75</td>
<td>-1.10288 - 0.03175xA + 0.0225357xHt</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Males</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁</td>
<td>-2.5412880 - 0.02968xA + 0.04617xHt</td>
</tr>
<tr>
<td>FVC</td>
<td>-4.056696 - 0.03503xA + 0.063107xHt</td>
</tr>
<tr>
<td>PEF</td>
<td>-2.777926 - 0.04350xA + 0.083903xHt</td>
</tr>
<tr>
<td>FEV₁%FVC</td>
<td>[0.838631 - 0.00048xA - 0.00022xHt]x100</td>
</tr>
<tr>
<td>FEF25</td>
<td>-2.443894 - 0.02235xA + 0.067707xHt</td>
</tr>
<tr>
<td>FEF50</td>
<td>-2.01844 - 0.02821xA + 0.04611xHt</td>
</tr>
<tr>
<td>FEF75</td>
<td>-0.370354 - 0.02219xA + 0.016329xHt</td>
</tr>
</tbody>
</table>

*A = Age (years), †Ht = Height (cm)

**IOS**

IOS comparisons of PL IOS and Viasys results using the same phantom subjects are shown in Figure 2a and 2b.
Figure 2a. Comparisons of Resistance for phantom subjects aged 45 and 65 years: PL IOS and Viasys Healthcare

Figure 2b: Comparisons of Reactance: PL IOS and Viasys Healthcare

Legend for Figure 2a and 2b:

- PL IOS
- Viasys Healthcare
Impedance (Z5) scores were found to be very similar to the Vogel and Smidt results.

Resistance (R5-35) in the PL examples were higher than the values predicted by the Vogel and Smidt equations at the higher end of the frequency scale, and show a different pattern across the frequencies. Reactance (X5-35) scores in the PL sample were greater at each end of the spectrum than those predicted by the Viasys equations.

The resulting predictive equations for the IOS parameters for males and females are shown in Table 4.

Table 4: PL IOS predictive equations for females and males.

<table>
<thead>
<tr>
<th>Females</th>
<th>Constant to predict Upper Limit of Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z5</td>
<td>=0.87961 + 0.00091xA* - 0.003403xHt†</td>
</tr>
<tr>
<td>Z5</td>
<td>=0.768067 + 0.00064xA - 0.002759xHt</td>
</tr>
<tr>
<td>Z5</td>
<td>=0.559851 + 0.00075xA - 0.001813xHt</td>
</tr>
<tr>
<td>Z5</td>
<td>=0.52147 + 0.0006xA - 0.001601xHt</td>
</tr>
<tr>
<td>Z5</td>
<td>=0.482071 + 0.000338xA - 0.001254xHt</td>
</tr>
<tr>
<td>Z5</td>
<td>=0.503739 + 3.33E-05xA - 0.001226xHt</td>
</tr>
<tr>
<td>Z5</td>
<td>=0.466316 - 9.5E-05xA - 0.000768xHt</td>
</tr>
<tr>
<td>Z5</td>
<td>=-0.46885 + 0.00092xA + 0.002451xHt</td>
</tr>
<tr>
<td>Z5</td>
<td>=-0.21099 - 0.00044xA + 0.001314xHt</td>
</tr>
<tr>
<td>Z5</td>
<td>=-0.13365 + 0.00026xA + 0.000799xHt</td>
</tr>
<tr>
<td>Z5</td>
<td>=0.00572 - 0.00074xA + 0.00063xHt</td>
</tr>
<tr>
<td>Z5</td>
<td>=0.081076 - 0.0007xA + 0.000413xHt</td>
</tr>
<tr>
<td>Z5</td>
<td>=0.237074 - 0.00018xA - 0.000354xHt</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Males</th>
<th>Constant to predict Upper Limit of Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z5</td>
<td>= 1.23361 - 0.00169xA + 0.00429xWt† - 0.00698xHt +0.158</td>
</tr>
<tr>
<td>Z5</td>
<td>= 1.16723 - 0.00171xA + 0.00432xWt - 0.00668xHt +0.161</td>
</tr>
<tr>
<td>Z5</td>
<td>= 1.14788 - 0.00153xA + 0.00402xWt - 0.00663xHt +0.152</td>
</tr>
<tr>
<td>Z5</td>
<td>= 0.99137 - 0.00133xA + 0.00329xWt - 0.005549xHt +0.136</td>
</tr>
<tr>
<td>Z5</td>
<td>= 0.921629 - 0.00132xA + 0.00274xWt - 0.00488xHt +0.131</td>
</tr>
<tr>
<td>Z5</td>
<td>= 0.90598 - 0.00141xA + 0.00246xWt - 0.00460xHt +0.136</td>
</tr>
<tr>
<td>Z5</td>
<td>= 0.93259 - 0.00137xA + 0.00252xWt - 0.00463xHt +0.15</td>
</tr>
<tr>
<td>X5</td>
<td>=-0.35932 + 0.00013xA + 0.00156xHt +0.055</td>
</tr>
<tr>
<td>X5</td>
<td>=-0.18314 + 0.00038xA - 0.00095xWt + 0.00135xHt +0.053</td>
</tr>
<tr>
<td>X5</td>
<td>=-0.19214 + 0.00034xA - 0.00117xWt + 0.00169xHt +0.062</td>
</tr>
<tr>
<td>X5</td>
<td>=-0.09332 + 0.00032xA - 0.00099xWt + 0.00127xHt +0.069</td>
</tr>
<tr>
<td>X5</td>
<td>= 0.045 + 0.00027xA + 0.00022xWt +0.075</td>
</tr>
<tr>
<td>X5</td>
<td>= 0.12837 + 0.00048xA + 2.4E-05xHt +0.069</td>
</tr>
</tbody>
</table>

*A = Age (years), †H = Height (cm), ‡W = Weight (kg).

IOS parameters of Impedance at 5Hz (Z5), Resistance at 5-35Hz (R5-35) and Reactance at 5-35Hz (X5-35)
Discussion

The PL IOS study recruited a convenience sample of healthy Australian adults of Caucasian origin, and tested their respiratory function using both IOS and spirometry. The sample was evenly age-stratified, with equal numbers of males and females. The IOS and spirometry data have been compared and the IOS data used to produce predictive equations.

Analysis of the PL spirometry predictive equations showed that these were similar to the existing Australian predictive equations published in 1995 by Gore et al. The spirometry values generated by the PL study were generally slightly higher than those of Gore et al which may indicate a generational difference resulting from increased growth and better nutrition. FEV$_1$, FVC, and PEF were all considered to be essentially the same. FEV$_1$ in the PL phantom 65yo female subject was lower than the Gore et al values, and PEF for males was only slightly lower. When FEV$_1$%FVC results from both equations for the phantom 65 year old female were compared, the PL predicted value was noticeably lower than that produced by Gore et al’s predictive equation, while for a male of the same age the results were closer but still lower. One possible explanation for these differences is that Gore et al had a lower proportion of older people in their sample than this study. The PL spirometry results support the Global Initiative for Obstructive Lung Disease (GOLD) guidelines which suggest that there should not be a fixed FEV$_1$/FVC ratio, as age-related decline in FEV$_1$ may result in over-diagnosis of COPD in the elderly. Despite all other parameters being normally distributed, FEF 75 did not show a normal distribution, being skewed to the right. We attempted to use standard parameters of age, height, and weight, but this
skewed distribution of FEF 75 may be indicating early lower airways changes in those who claim to be normal.

We have compared the preliminary PL IOS predictive equations with the only other IOS predictive equations produced for Caucasian adults. Our results show some differences to the German predicted values, in both Resistance and Reactance. This could be because the PL sample excluded current smokers as well as having a low percentage of past smokers compared with the original study which included a high proportion of smokers. Possibly 50% of smokers will have small airways disease, which would result in the mean Resistance in the 5-20Hz range being higher in the German sample. This would have the effect of increasing the Upper Limit of Normal in the German predictive equations. This study purposely selected an area of rural South Australia with no known air pollution which enabled recruitment of healthy participants with healthy lungs to determine the normal range, screened out the current smokers and only allowed past-smokers with previously low smoking rates to participate.

Limitations of the PL IOS study include a small sample size of 125, although the sample was evenly spread between gender and age 25 to 74 years. Purposive sampling of volunteers may have introduced a volunteer bias. Other selection limitations include the possibility of undiagnosed asthma not excluded by bronchodilator testing, and possible participant use of over-the-counter medications such as salbutamol. The PL IOS predictive equations are only applicable to adult Australians of Caucasian race. They should not be used on people of ATSI race, Asian race or African race, nor should they be used for Australians under the age of 25, or over the age of 75 years. In this study, less than 5% of
participants were not able to provide an acceptable IOS result which may be relevant to population studies.

The PL IOS study attempted to validate preliminary predictive IOS equations by measuring IOS and spirometry concurrently. Despite some difference in the spirometry comparisons, for which we have offered possible explanations, we believe that the PL IOS predictive equations are valid for a Caucasian adult Australian non-smoking population and that they should be used in preference to the German predictive equations.

It is recommended that further research using a larger random population sample should now occur. This should result in predictive equations that increase the reliability of the Australian IOS predictive equations. Methodology of a larger population study is being planned. This will enable comparison of a larger data set with the PL IOS equations and will result in more representative equations being produced. It will also include a comparison of current smokers, ex-smokers and non-smokers and a more rigorous questionnaire of respiratory symptoms in apparently healthy participants.
APPENDIX 1 - LITERATURE REVIEW

The lungs are the site of the gaseous exchange of respiration. To facilitate this exchange, the mechanics of breathing enable air to be inhaled and exhaled. Air movement is driven by the contraction and relaxation of the diaphragm and the intercostal muscles. The airways are classified as extra-thoracic or intra-thoracic, and are also described as being proximal (or central), and distal (or peripheral). The central airways are large-calibre, and are stiff and hence resistive to airflow. The peripheral airways are elastic – stretching on inspiration, and collapsing on expiration. This paper is concerned with the mechanics of the respiratory system, i.e. the forces involved in respiration, and will not be dealing with the gaseous exchange of respiration.

Commonly, airway function is measured by spirometry. Spirometry measures timed forced inspiration and expiration of lung volume by the subject and is used for screening patients who are at risk of developing lung diseases, as well as monitoring progression of disease in those who are already affected. Spirometry can be performed in primary care settings, as well as specialised lung function laboratories. Other lung function tests performed in specialised laboratories include whole body plethysmography and the oesophagus technique. Plethysmography requires equipment that is both expensive and bulky, and relies on the subject’s cooperation. The oesophagus technique to determine pulmonary resistance by simultaneous recording of airflow and oesophageal pressure is invasive. Spirometers are becoming increasingly smaller and more portable; they assess limitation of airflow but still require the subject’s full cooperation in performing specific respiratory manoeuvres that are not part of normal breathing. These manoeuvres have been described by Enright et al as “an almost athletic breathing...
manoeuvre\textsuperscript{30} and are time-consuming to perform correctly.\textsuperscript{31} This deep inspiration and forced expiration can affect airway tone.\textsuperscript{16}

Forced Oscillation Technique (FOT) has developed over the last 50 years, and is increasingly being used as a further technique in the diagnosis and management of obstructive and restrictive airways disease. In FOT the mechanical properties of the respiratory system are described by the response to small forced pressure pulses (i.e. sound waves) which are applied externally.\textsuperscript{26} FOT was first described in the 1950s\textsuperscript{32}, with further early studies being done by Mead\textsuperscript{33} and Fisher et al.\textsuperscript{25} These works involved using manual systems of measurement.\textsuperscript{5} The introduction of computer-driven equipment and analysis occurred in the 1970s.\textsuperscript{34} Computer analysis by Fast Fourier Transform (FFT) enabled easier use of the FOT application, as well as providing further information from the tests.\textsuperscript{5} Some FOTs use sinusoidal signals at single frequencies.

The MasterScreen Impulse Oscillometry System (IOS) (Viasys; Wurzburg, Germany), is a commercial version of FOT that uses multi-frequency pressure signals produced by an external loudspeaker.\textsuperscript{7} These signals last 120msec each and alternate between positive pressure and negative pressure (pushing and pulling back), 5 times each second.\textsuperscript{5} The signals are superimposed on tidal breathing, and the resultant pressure and flow relationships (processed by FFT) describe the mechanical parameters of the lungs.\textsuperscript{1, 26, 35} Because IOS requires only passive cooperation it is much simpler to perform than those tests that require full and active cooperation such as spirometry and whole body plethysmography. This means it can be used for those unable to perform the difficult manoeuvres necessary for spirometry such as the very young, the old and infirm, those with cognitive difficulties and can also be adapted for use with patients being mechanically
Further applications include monitoring of lung transplant patients who are not allowed to perform forced respiratory manoeuvres post-operatively.¹

IOS measures the pressure and flow produced at the airway opening (the mouth) in response to brief pressure impulses. The instantaneous pressure-flow relationship reflects the overall characteristics, or impedance, of the respiratory system and displays this in the form of an impedance spectrum (Z).²⁷ Impedance is described as “…an objective and differentiated image of lung mechanics”²⁷ and can be further split into its two components - Resistance (R) and Reactance (X). These 2 components reflect specific but different properties of the lungs.

Resistance (R) describes the frictional or the resistive components of the respiratory tract. It is influenced by the calibre of the airways, both extrathoracic and intrathoracic, and the structure of the surface of the airway wall, lung tissue and chest wall.¹, ³, ²⁶, ²⁷ The main component of R is influenced by the central or proximal airways but peripheral or distal airways also contribute.¹, ³ Resistance is computed as the ratio between pressure and flow signals which are in-phase.¹, ³, ²⁶ Measurements of R at different Hz reflect different characteristics of proximal or distal airways.

Reactance (X) is computed as the out of phase pressure and flow signals. X reflects the imaginary part of impedance, comprising both the elastic properties (or Capacitance) of the lung periphery and the inert properties (Inertance) of the column of air in the airways.¹, ³ Capacitance is the lungs’ ability to store the energy required for passive expiration and is displayed as the negative part of reactance and dominates at low frequencies. The measure of Inertance is always a positive value, and dominates at higher frequencies.¹, ⁴ The
resonant frequency (F_{res}) of the respiratory system occurs when the pressure and the flow responses are equal, when reactance equals zero.$^{4, 26}$

High frequency oscillations (>15-20Hz) are not transmitted to peripheral airways, therefore higher frequencies reflect only large airways effects; low frequency oscillations (5-15Hz) are transmitted to the peripheral airways and therefore reflect both large airways and small airways effects.$^{1, 4}$ FOT provides more information about small peripheral airways than is available from commonly used pulmonary function tests and is more sensitive and more responsive to small airway function than maximal effort forced spirometric measurements.$^{1, 5}$ This information is deduced from X as well as R.

FOT has shown its usefulness in early diagnosis and management of peripheral airways disease over several decades, with several advantages over other diagnostic tests. Body plethysmography resistance (R_{aw}) includes only extrathoracic and intrathoracic resistance, while R includes chest wall and lung tissue as well.$^{1}$ R_{aw} is more greatly influenced by large airways than by small airways resistance whereas R is influenced by small airway resistance. FOT shows greater sensitivity to peripheral airway disease than the forced spirometry measurements.$^{5, 36}$

The use of FOT and IOS in diagnosis and monitoring of respiratory conditions, and in epidemiology have been demonstrated.$^{37-40}$ FOT shows greater sensitivity than spirometry in measuring response to treatment; small airways function in particular is more accurately assessed using FOT than spirometry.$^{16, 17, 36, 41}$ The portability of the IOS unit enables ease of use in the primary care clinic, at the bedside, or at the place of work for occupational studies.$^{1}$
Predicted normal values for pulmonary function tests are important to assist in diagnosis and estimation of prognosis, and also for research and epidemiology. These should be derived from the same population for which they are to be used. Predictive equations for spirometry in Australian adults exist. IOS currently uses normal values for adults which are those provided by the manufacturer (Viasys), although it is possible to enter local predictive equations that are more applicable to the population. The German sample population came entirely from Erfurt, an industrial city previously part of the German Democratic Republic which had suffered significant air pollution prior to the reunification of Germany in 1990. Sampling to establish these normal data was carried out in 1991-2. The German sample consisted of 506 subjects, ages were unevenly spread between 18 and 69; there were also unequal numbers of males and females. Current smokers were included in the sample analysis, but although the authors do not indicate numbers of smokers/non-smokers, they report a “high proportion of smokers”, so their sample was representative of their population.

With regard to IOS, the only normal values for adults other than those provided by the manufacturer (Viasys), are those for Japanese subjects. It is noted that there are differences in lung volumes between races. There are no existing normal values for Australian adults. Internationally, there have been predictive equations produced for FOT, but it has been shown that although results are similar, they should not be regarded as interchangeable.

The main hypothesis of this study is that we will be able to produce preliminary predictive equations for the IOS, for the Australian Caucasian adult population. Secondary hypotheses are that our data won’t be significantly different to the German data, and that
our spirometry results will not be different to a previously produced Australian population sample.
# Port Lincoln Lung Study Questionnaire

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family name</td>
<td></td>
</tr>
<tr>
<td>First name</td>
<td></td>
</tr>
<tr>
<td>Full Address</td>
<td></td>
</tr>
<tr>
<td>Postal address (if different)</td>
<td></td>
</tr>
<tr>
<td>Phone number</td>
<td></td>
</tr>
<tr>
<td>How would you best describe your ethnicity?*</td>
<td>Aboriginal or Torres Strait Islander? Caucasian? African? Asian?</td>
</tr>
<tr>
<td>Date of birth</td>
<td></td>
</tr>
<tr>
<td>Age (calculated)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Height (measured by researcher) cm</td>
<td></td>
</tr>
<tr>
<td>Weight (measured by researcher) Kg</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
</tr>
<tr>
<td>Place of work</td>
<td></td>
</tr>
<tr>
<td>GP’s name</td>
<td></td>
</tr>
<tr>
<td>GP’s phone number</td>
<td></td>
</tr>
</tbody>
</table>

* (Aboriginal, African & Asian to be excluded at this stage)
Do you think you have healthy lungs?
Yes  
No  

Are you a current smoker?
Yes  
No  

Have you ever been a regular smoker?
Yes  
No  

If yes how many cigarettes per day  
For how many years?
(If >10/day for >5 years, exclude from this study)  

Have you lived in the same house with a regular smoker?
Yes  
No  

Have you ever had asthma?
Yes  
No  
If yes:  
how bad?  
Admitted to hospital?  
On medication?  
(If any asthma exclude from this study)  

Have you ever had other lung disease? (e.g. tuberculosis, heart failure, dust disease, asbestosis)
Yes  
No  
Specify  
(If yes exclude)  

For YES answers to problems with breathing/asthma/other lung disease questions: I'm sorry, at this stage we need healthy people with healthy lungs. Maybe we can contact you again in the future if we change our parameters.
APPENDIX 3 – Participant Information

Participant information for the
Port Lincoln Lung Function Study

Lung function is usually measured by spirometry. Spirometry equipment has been readily available, is relatively cheap and has been the best method of testing people’s lungs. One disadvantage of spirometry is that you need to learn how to blow into it, to achieve good quality results. This limits its use in children and people with severe lung disease.

Impulse Oscillometry (IOS) is an alternate method of measuring lung function. IOS measures lung function by transmitting a sound wave down the airway and measuring reflected sound. You will need to hold a mouthpiece in your mouth and breathe normally for 30 seconds. You will hear a soft repeated pulse of sound and feel sound waves pulsating into your mouth while measurement takes place. This is not a loud sound and is not an unpleasant sensation. IOS measurement and analysis will occur instantaneously by computer. You will also be asked to do the usual spirometry technique; to take a big breath and blow as hard and long as possible into the IOS instrument. You will be asked to do this 3 times.

The tests will be undertaken in the Spencer Gulf Rural Health School campus at the Port Lincoln Hospital. You should allow half an hour for your appointment.

Neither of the breathing tests should cause you any discomfort nor upset your breathing in any way. If you do feel unwell we will arrange for you to be seen in Port Lincoln hospital Accident and Emergency (adjacent building) and contact your usual doctor. All IOS and spirometry results will be reviewed by Associate Professor Crockett, a member of the research team. Abnormal results which might represent undiagnosed respiratory disease will be explained to you and you will be encouraged to see your usual medical practitioner. If your test shows abnormal results, you and your medical practitioner will be given a copy of your IOS and spirometry measurements and interpretation.

We are collecting an initial sample from healthy, non-smoking people living in a town with no known occupational dust exposure (Port Lincoln) before expanding into Adelaide. Your personal information will be kept confidential by the research team. The results of the research may be presented at conferences and published in medical journals as well as in Wendy Newbury’s Masters thesis, but individuals will not be identified, nor will data be published in a form that could be linked to any individual.
Your participation is voluntary and you can withdraw at any time. Your participation/non-participation will not affect the medical services you receive. We have included for your information, The University of Adelaide’s independent complaints form.

**Investigators:**

Professor Jonathan Newbury  
Spencer Gulf Rural Health School  
University of Adelaide & University of South Australia.  
PO Box 3200, Port Lincoln SA  5606  
Phone:  0418 818 469

Associate Professor Alan Crockett  
Discipline of General Practice  
University of Adelaide. SA  5005  
Phone:  08 8303 3460

Mrs Wendy Newbury  
Masters of Public Health candidate  
Menzies School of Health Research, Charles Darwin University.  
PO Box 3200, Port Lincoln SA  5606  
Phone:  0439 849 768
APPENDIX 4 – Participant Consent Form

THE UNIVERSITY OF ADELAIDE HUMAN RESEARCH ETHICS COMMITTEE

STANDARD CONSENT FORM
FOR PEOPLE WHO ARE PARTICIPANTS IN A RESEARCH PROJECT

1. I, .....................................................(please print name)
   consent to take part in the research project entitled:
   Port Lincoln Impulse Oscillometry (IOS) Study

2. I acknowledge that I have read the attached Information Sheet entitled: Participant
   information for the Port Lincoln Impulse Oscillometry (IOS) Study

3. I have had the project, so far as it affects me, fully explained to my satisfaction by the
   research worker. My consent is given freely.

4. Although I understand that the purpose of this research project is to improve the quality
   of medical care, it has also been explained that my involvement may not be of any
   benefit to me.

5. I have been given the opportunity to have a member of my family or a friend present
   while the project was explained to me.

6. I have been informed that, while information gained during the study may be published,
   I will not be identified and my personal results will not be divulged.

7. I understand that I am free to withdraw from the project at any time and that this will
   not affect medical advice in the management of my health, now or in the future.

8. I am aware that I should retain a copy of this Consent Form, when completed, and
   the attached Information Sheet.

   ..................................................................................................................
   (signature) (date)

WITNESS

I have described to ..................................................(name of subject)

the nature of the research to be carried out. In my opinion she/he understood the

Explanation.

Status in Project: ….. Project Officer ............................................................

Name: ….. Wendy Newbury .................................................................

..................................................................................................................
   (signature) (date)
APPENDIX 5 – Sample IOS reports

**Primary Care Respiratory Unit**
** Discipline of General Practice**
** School of Population Health & Clinical Medicine**
** The University of Adelaide**
** ADELAIDE SA 5005**

<table>
<thead>
<tr>
<th>Last Name:</th>
<th>xxx</th>
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<tbody>
<tr>
<td>First Name:</td>
<td>xxx</td>
</tr>
<tr>
<td>Date of Birth:</td>
<td>20/05/1977</td>
</tr>
<tr>
<td>Sex:</td>
<td>Female</td>
</tr>
<tr>
<td>Profession:</td>
<td>Height: 161 cm</td>
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<table>
<thead>
<tr>
<th>Pred</th>
<th>Actl</th>
<th>% (A/F)</th>
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<tbody>
<tr>
<td>Date</td>
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<td></td>
</tr>
<tr>
<td>Time</td>
<td>10:11</td>
<td></td>
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</table>

- **FVC** [L]: 3.49, 4.14, 116.0
- **FEV1** [L]: 3.03, 3.45, 113.0
- **FEV1 & VC Max** [%]: 03.39, 03.30, 96.7
- **PEF** [L/s]: 6.00, 6.41, 122.4
- **PEF 75** [L/s]: 2.00, 1.71, 02.5
- **PEF 50** [L/s]: 4.38, 3.59, 01.7
- **PEF 25** [L/s]: 6.00, 7.61, 126.5

- **VT** [L]: 0.41
- **Z bei 5 Hz** [kPa/L/s]: 0.34
- **R at 5 Hz** [kPa/L/s]: 0.34
- **R at 10 Hz** [kPa/L/s]: 0.32
- **R at 15 Hz** [kPa/L/s]: 0.30
- **R at 20 Hz** [kPa/L/s]: 0.28
- **R at 35 Hz** [kPa/L/s]: 0.22
- **X at 5 Hz** [kPa/L/s]: -0.01
- **X at 10 Hz** [kPa/L/s]: 0.03
- **X at 15 Hz** [kPa/L/s]: 0.06
- **X at 20 Hz** [kPa/L/s]: 0.10
- **X at 35 Hz** [kPa/L/s]: 0.20
- **Resonant frequency** [L/s]:
- **Rcentral** [kPa/L/s]:
- **Rperipheral** [kPa/L/s]:
- **Cwall** [L/kPa]:

---

**Diagram:**

- Flow [L/min]
- FEV1
- [Flow vs. Volume]
- [Z vs. Frequency]
- [R vs. Frequency]
- [X vs. Frequency]
Primary Care Respiratory Unit  
Discipline of General Practice  
School of Population Heath & Clinical Medicine  
The University of Adelaide  
ADELAIDE SA 5005

Last Name: xxx  
First Name: xxx  
Date of Birth: 31/05/1962  
Sex: male  
Profession: 

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Pred</th>
<th>Actl</th>
<th>% (A/P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>02/03/</td>
<td>04:03</td>
<td></td>
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</tbody>
</table>

FVC [L] 4.08 5.74 140.9  
FEV 1 [L] 3.37 4.88 144.6  
FEV 1 % VC MAX [%] 79.29 84.67 107.0  
PEF [L/s] 8.45 10.96 125.7  
FEF 75 [L/s] 1.85 2.57 139.2  
FEF 50 [L/s] 4.58 7.50 163.9  
FEF 25 [L/s] 7.32 9.86 134.7  

VT [L] 0.56 0.44 78.9  
Z bei 5 Hz [kPa/l/s] 0.28 0.21 73.5  
R at 5 Hz [kPa/l/s] 0.28 0.18 64.1  
R at 10 Hz [kPa/l/s] 0.27 0.16 59.7  
R at 15 Hz [kPa/l/s] 0.25 0.15 57.6  
R at 20 Hz [kPa/l/s] 0.24 0.14 55.9  
R at 35 Hz [kPa/l/s] 0.20 0.18 86.0  
X at 5 Hz [kPa/l/s] 0.00 -0.10 -253  
X at 10 Hz [kPa/l/s] 0.02 -0.01 -30.4  
X at 15 Hz [kPa/l/s] 0.06 0.02 63.2  
X at 20 Hz [kPa/l/s] 0.07 0.07 98.9  
X at 35 Hz [kPa/l/s] 0.13 0.17 128.0  

Resonant frequency [Hz] 11.76  
Bcentral [kPa/l/s] 0.12  
Pperipheral [kPa/l/s] 0.10  
Cwall [kPa/l] 2.00

![Graph](image)
APPENDIX 6 – IOS

Cross-sectional diagram of IOS¹

IOS in use.
(Demonstration only: photo used with permission)
REFERENCES


