Accuracy and sensitivity of the interrupter technique for measuring the response to bronchial challenge in normal subjects


ABSTRACT: The interrupter technique is a non-invasive method for measuring airway calibre. Since the calculation of interrupter resistance (Rint) is critically dependent upon the analysis of the mouth pressure/time (Pmo(t)) curve obtained after flow interruption, we wanted to assess the relative merits of four different analyses of Pmo(t) curves, obtained under basal conditions and following methacholine-induced airway narrowing, in 10 healthy adults.

Four methods of analysing the Pmo(t) curves were used to calculate Rint values: Rintc, - a smooth curve fit with back-extrapolation; Rint₁₀, - two-point linear fit with back-extrapolation; Rintₚ, - calculated from the pressure change after the post-interruption oscillations had decayed (end-oscillation); and Rintₚₑ, - calculated from the pressure change at the end of the period of interruption. The airway response measured with the four Rint methods was compared with plethysmographic airway resistance (Raw). The sensitivity of the methods was determined by calculating a sensitivity index (SI), the change in resistance after challenge expressed in multiples of baseline standard deviation.

Values of Rintc were similar to Raw values under all conditions. Resistance values from the remaining Rint methods significantly exceeded Raw (mean basal difference: 0.13-0.34 kPa·l·s⁻¹; mean difference after challenge: 0.12-0.42 kPa·l·s⁻¹). Raw was the most sensitive method for detecting bronchoconstriction (doubling of Raw was equivalent to SI of 10.5). Of the Rint methods, Rint₁₀ gave the highest sensitivity index (SI=3.1), with a 42% mean change; Rintₑ, produced the greatest proportional change after challenge (55%), but with a lower SI (2.2).

We conclude that the method chosen to analyse mouth pressure/time curves obtained after airflow interruption determines the accuracy and sensitivity of the technique. Rint may provide a useful alternative for estimating airway resistance and for bronchial responsiveness testing where more conventional methods are not suitable.

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The interrupter technique for measuring respiratory airway resistance during spontaneous breathing was devised by Von Neergaard and Wiirz, in 1927 [1]. The method requires minimal subject co-operation, and can be carried out during spontaneous breathing. It therefore has enormous potential for measuring airway calibre in very young children and those unable to co-operate with conventional lung function techniques.

Two measurements are required to calculate the resistance of the airways: flow rate and the corresponding alveolar pressure (Palv). Whilst flow rate is relatively simple to measure, there is no direct non-invasive method for determining Palv. Estimates of Palv with the interrupter technique rely upon the assumption that following a brief interruption of airflow at the airway opening, Palv equilibrates rapidly with pressure measured at the mouth (Pmo). Palv may then be estimated from the post-occlusion pressure measured proximally to the site of occlusion at the mouth. Mouth pressure/time (Pmo(t)) curves following airflow interruption are composed of an initial rapidly changing phase, often accompanied by high frequency oscillations, followed by a secondary slowly changing phase [2]. Palv at the moment of occlusion can then be derived from the Pmo(t) curve by some form of back-extrapolation [3, 4]. The interruption resistance (Rint) is the ratio of the estimated Palv at the moment of interruption to the flow that existed just prior to interruption.

Several methods have been proposed for analysing the Pmo(t) curves to estimate Palv or an interrupter resistance in spontaneously breathing subjects. The level of the oscillating break ("break point") in the curve separating the initial from the secondary pressure change was assumed by early investigators to be an estimate of Palv [2, 3]. Others chose Palv as the point at which a line drawn through the centre of the oscillations intersected the upward stroke of the initial pressure change [5]. Values of interrupter resistance
have also been calculated from a pressure change taken midway between the initial and secondary pressure phase, resistance estimates significantly overestimating airway resistance (Raw) measured by plethysmography by approximately 20% in normal subjects [6, 7]. A revised technique, using a curvilinear back-extrapolation method for determining Palv, improved the absolute relationship between Rint and Raw [4]. Another empirical approach consists of a linear back-extrapolation to an arbitrary time point after occlusion [8]. More sophisticated methods have been designed, which fit a smooth curve to Pmo(t) data, and then back-extrapolate the curve a short distance through the oscillations [9, 10]. This technique has, so far, only been applied to anaesthetized and paralysed animals.

The interrupter method is influenced by the compliance of the upper airways [11–14], and by retarded equilibration between mouth and alveolar pressure in the presence of airway disease [6, 15, 16]. Its validity in airflow obstruction is controversial [17], because mechanical non-homogeneity of the lungs increases with airway disease. Theoretical studies have suggested that Raw may be estimated to a useful degree of accuracy with the interrupter technique, even in the presence of mild to moderate bronchocstriction, if the upper airways are well-supported [18]. However, with severe bronchocstriction, it may be difficult to reduce upper airway compliance sufficiently to identify Rint. The majority of experimental studies using this technique have been performed on paralysed tracheotomized animals or intubated patients in whom the compliant upper airways have been bypassed, and additional pressure changes due to muscular activity are avoided.

There have been relatively few reports of the usefulness of the interrupter technique in spontaneously breathing, non-intubated humans; also, few studies have attempted to compare the merits of the different types of analysis of post-occlusion Pmo(t) curves for detecting a response to nonspecific bronchial challenge.

The purpose of this study was to assess four methods [5, 8, 10, 19] of determining Palv by analysis of the interruption data obtained from spontaneously breathing healthy subjects. Their relative merits based on accuracy, repeatability and sensitivity, were compared with plethysmographically determined Raw. We wished to identify the most appropriate Rint technique for measuring baseline airway calibre and the change in calibre after inducing airway narrowing.

Methods

Subjects

Ten subjects (mean age (so) 31 (7) yrs: 3 females) were chosen from laboratory staff. They were healthy, free from respiratory disease, and had normal spirometry (forced expiratory volume (FEV) % pred [20], mean (so) 104(13)%; vital capacity (VC) % pred 97(16)%). Informed consent was obtained from all participants, and the study was approved by the Research Ethics Committee of the Royal Postgraduate Medical School.

Measurements

Body plethysmography. Airway resistance (Raw) was computed using an automated method [21], from pressure and flow measurements made whilst the subject panted at 2 Hz in a constant volume, whole-body plethysmograph [22]. A sine wave was fitted to each cycle of the pressure and flow waveforms, and the amplitudes and phase relationships of these sine waves was used to deduce a value for Raw. Information over the whole cycle was used to calculate a mean Raw for the whole breath.

Airflow interrupter method. Subjects breathed through a mouthpiece, the interrupter valve (Micro-medical Ltd, Rochester, UK) and a pneumotachograph, all of identical internal diameter (18 mm), placed in series. Rapid airflow interruption was achieved by an elliptical metal plate driven to occlude the lumen of a tube by a high-speed servomotor (Interelectric AG, Sarchstein, Switzerland). The time taken for the valve to close was 5–6 ms, allowing an accuracy in Rint determination of ±1% [23]. The valve was controlled by signals from a computer via a digital to analogue converter (Model AOB2, Industrial Computer Source, Chichester, UK). Airflow was measured with a heated Pneumotachograph (Fleisch No. 1), connected to a differential pressure transducer (Validyne MP-45, Northridge, Cal, USA), with a range of ±2 cmH₂O. Muth pressure was measured at the airway opening using a piezoresistive sensor (SCX01DN, Sensor Techniques, Rugby, UK) with a response time of 0.1 ms. Pressure and flow signals were sampled at 1,000 Hz using a 12-bit analogue to digital converter (DT2801-A, Data Translation, Marlboro, MA, USA). Control of analogue-to-digital and digital-to-analogue converters, and subsequent data acquisition, was made via a 286 personal computer using Anadat/Labdat data analysis software (Info-Dat, Montreal, Canada).

Subjects breathed quietly through the apparatus via a flanged mouthpiece with nose clipped, whilst flow was monitored on Labdat and on an oscilloscope screen. The flow rate, measured at or near mid-tidal expiration (0.2–0.4 l s⁻¹), was then used to program the valve to automatically trigger. A mid-expiratory occlusion lasting 100 ms was made during a period of regular breathing; subjects were unable to anticipate the trigger event, but could hear the valve closing.

Analysis of Pmo(t) curves following interruption

Following expiratory flow interruption, three distinct phases in the pressure signal were seen: 1) a rapid initial rise in pressure 2) pressure oscillations and 3) a secondary slower rise in pressure (fig. 1). Four different analyses were subsequently performed on the stored data for each Pmo(t) curve, in order to estimate Palv.
Fig. 1. - Representative recordings of mouth pressure (Pmo), obtained after flow interruption during mid-expiration, before (bottom curve) and after maximal bronchoconstriction (top curve). Each trace consists of a fast initial increase in Pmo, followed by a secondary slower increase, the two phases separated by high frequency oscillations.

For all analyses the pre-occlusion mouth pressure (Ppre), due to apparatus resistance, was taken just prior to valve movement (defined by the sudden rise in Pmo during interruption) (fig 1). Flow rate was also taken at this time point.

In each case, Pint, the effective pressure for calculating Rint, was taken as the difference between the estimate of Palv at interruption and Ppre. The interruption resistance was then calculated as the ratio of this pressure difference and the flow rate measured just prior to occlusion.

The four methods for estimating Palv are as follows:

1. Back-extrapolating a fitted curve (Pintc; Rintc). A polynomial curve fitting technique [10] was used to fit a smoothly increasing curve to the post-occlusion pressure signal, from the end of the oscillations obtained following interruption (usually lasting 15–25 ms from Ppre) (fig. 2a), to 100 ms after the onset of valve closure. This curve was then monotonically back-extrapolated through the oscillations to the time of half valve closure (3 ms after the onset of valve closure), in order to determine the post-occlusion pressure (Pintc).

2. End-oscillation pressure (Pintoc; Rintoc). The pressure value after the oscillations observed following interruption had ceased (Pintoc; fig. 2a), generally 15–25 ms after onset of valve closure, is approximately equivalent to a horizontal line drawn through the centre of the oscillations, a technique used by early investigators [5].

3. End-interruption pressure (Pintes; Rintes). The post-occlusion pressure (Pintes) occurring 100 ms after the onset of valve closure was chosen (fig. 2a). This pressure change, therefore, includes both the initial and secondary pressure changes. Similar methods to this have previously been used to provide an extended equilibration of mouth and alveolar pressure [15, 19].

4. Linear back-extrapolation (PintL; RintL). This method involves a simple, two-point, linear regression of the post-occlusion signal, back-extrapolated to an arbitrary time after airway occlusion [8] (fig. 2b). The moment of valve closure (t) was taken as the point at which 25% of the first pressure upstroke had been reached (fig. 1b). The mean pressure values for two 10 ms portions of the data centred on times t+30 ms and t+70 ms were then linearly back-extrapolated to 15 ms after the valve closure time (i.e. t+15 ms), to provide a value of pressure, PintL.

Experimental procedure

Following baseline plethysmography and baseline interruption measurements (mean of six technically satisfactory values of each), methacholine (Sigma Chemicals Ltd, Poole, UK) was inhaled in doubling concentrations from 4 mg·ml⁻¹ up to 256 mg·ml⁻¹, using a Wright nebulizer, driven by an airflow of 7 l·min⁻¹ and delivering 0.14±0.01
ml·min⁻¹. The aerosols were inhaled through a mouth-piece, during quiet tidal breathing with the nose clipped.Doubling concentrations of methacholine were inhaled for 2 min, at 5 min intervals. Ninety seconds after the end of each nebulization, the bronchial response was determined in the order: plethysmography (three measurements), Rint (six measurements), plethysmography (three measurements). All measurements were completed within 2.5 min. In our analysis, the average value of all six plethysmographic measurements was compared with the mean interrupter value. This is because we found that after the maximal methacholine concentration Raw fell slightly in all subjects from the first to the second set of measurements. The mean (sd) change was -15(20)% (p<0.05). Therefore, the most accurate estimate of airway calibre was considered to be the mean of both sets of plethysmographic recordings between which the single set of interrupter measurements was sandwiched. The challenge test continued until the subject showed a ≥100% increase in Raw from mean baseline, or the highest concentration of methacholine had been reached, or the subject was too dyspnoeic to continue. Airway obstruction was relieved at the end of the study by nebulized salbutamol (2.5 mg), and ipratropium bromide (250 μg).

The subjects were placed in an identical, comfortable, seated posture. A noseclip was worn, and the cheeks and floor of the mouth were supported with both hands, during interrupter and plethysmographic measurements.

Expression of results and statistical analysis

Dose response curves were constructed for each method by plotting the resistance value against log concentration of methacholine. The provocative concentration which caused an increase in Raw of 100% (PC₁₀₀Raw) from the mean baseline value was determined by linear interpolation between data points. Extrapolation of the dose response curve by up to one doubling concentration beyond the maximum administered was allowed, to permit some censored data to be included [24].

The accuracy of Rint values was assessed by comparing them with the values of Raw under baseline conditions, and at PC₁₀₀Raw according to BLAND and ALTMAN [25]. Baseline repeatability was assessed using the within-subject coefficient of variation (CV), the standard deviation of repeat measurements expressed as a percentage of the mean.

Sensitivity was expressed as a percentage change of the resistance value at PC₁₀₀Raw from baseline. It was also expressed using a sensitivity index (SI), [26, 27] calculated as:

\[
SI = \frac{\text{resistance at PC₁₀₀Raw} - \text{baseline resistance}}{\text{within-subject SD of baseline resistance}}
\]

The SI indicates the absolute increase in resistance after challenge, in multiples of the baseline standard deviation.

Baseline values and values calculated at PC₁₀₀Raw were compared using Wilcoxon's matched-pairs signed-ranks test. Log transformed SI values and percentage changes at PC₁₀₀Raw were analysed using analysis of variance (ANOVA) and paired t-test.

Results

Complete data were obtained for all participants. Dose response curves were extrapolated in two subjects.

Accuracy: comparison of Rint and Raw under basal conditions and after challenge

Comparisons between baseline resistance values measured using body plethysmography and the four interrupter techniques are represented as scatter plots of differences about the mean, shown in figure 3. Values of Rint and Raw were not significantly different. Rint, Rint₂, and Rint₄ values exceeded Raw (mean difference 0.12, 0.13 and 0.34 kPa·l⁻¹·s⁻¹, respectively, p<0.0001) (fig. 3). Median Rint, and Rint₄ values were not significantly different, whereas all other Rint comparisons were significantly different from each other (p<0.01) (table 1).

Comparison of resistance values measured using the plethysmographic method and the interrupter technique at PC₁₀₀Raw after bronchial challenge are listed in table 1. Differences between values of Rint and Raw at PC₁₀₀Raw plotted against the mean are shown in figure 3 for all interrupter methods. Rint and Rint₂, overestimated Raw by the same difference as in basal conditions (mean difference 0.12 kPa·l⁻¹·s⁻¹ for both, p<0.05) (fig. 3). For Rint₄ the mean difference was 24% higher than the baseline difference (0.42 kPa·l⁻¹·s⁻¹), whereas Rint₃ values were similar to Raw after challenge. All Rint methods showed a trend towards increasing disparity from Raw at higher mean resistance values.

Variability of resistance values under basal conditions

The mean within-subject coefficient of variation for six baseline measurements (table 1) was greater for the interrupter methods (range 14–28%), than for plethysmographic measurements (10%).

Sensitivity to detect change in resistance following bronchial challenge

The order of relative sensitivity based on the proportionate change in resistance, was calculated for an increase in Raw of 100% (table 2). Median values were used to allow for the non-parametric distribution of data. Raw was significantly more sensitive than any of the Rint methods (p<0.005). Among the Rint parameters, Rint₃ produced the greatest percentage change. Rank order of the geometric mean values of the sensitivity index are shown in table 2. Raw was again the most sensitive of all methods (p<0.005). Of the interrupter methods, the highest SI value was obtained for Rint₄.
Table 1. - Data at baseline and after bronchial challenge at provocative concentration of methacholine required to increase Raw by 100% (PC\textsubscript{100} Raw)

<table>
<thead>
<tr>
<th>Values</th>
<th>Plethysmograph</th>
<th>Interrupter methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline values</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>0.15</td>
<td>0.27</td>
</tr>
<tr>
<td>25th percentile</td>
<td>0.10</td>
<td>0.23</td>
</tr>
<tr>
<td>75th percentile</td>
<td>0.21</td>
<td>0.30</td>
</tr>
<tr>
<td>Mean intrasubject CV (%) (sd)</td>
<td>10 (2)</td>
<td>16 (10)</td>
</tr>
<tr>
<td>At PC\textsubscript{100} Raw</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>0.22</td>
<td>0.33</td>
</tr>
<tr>
<td>25th percentile</td>
<td>0.17</td>
<td>0.30</td>
</tr>
<tr>
<td>75th percentile</td>
<td>0.30</td>
<td>0.48</td>
</tr>
</tbody>
</table>

All resistance values are in kPa·s\(^{-1}\). CV: coefficient of variation; Raw: airway resistance; Rint: interrupter resistance. Four methods were used to analyse the mouth pressure/time curves, obtained after flow interruption, to calculate Rint values: Rint\textsubscript{c} - a smooth curve fit with back-extrapolation; Rint\textsubscript{L} - a two-point linear fit with back extrapolation; Rint\textsubscript{EO} - calculated from the pressure change after the post-interruption oscillations had decayed (end-oscillation); and Rint\textsubscript{EO} calculated from the pressure change at the end of the period of interruption.

Table 2. - Sensitivity of resistance techniques based on the percentage change from baseline and sensitivity indices at the concentration of methacholine required to increase Raw by 100%

<table>
<thead>
<tr>
<th>Rank order</th>
<th>Technique</th>
<th>Median</th>
<th>Change %</th>
<th>Sensitivity index</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rank</td>
<td></td>
<td>25th and</td>
<td>Mean Range</td>
</tr>
<tr>
<td>1</td>
<td>Raw</td>
<td>100</td>
<td>50</td>
<td>10.5 7.0-14.3</td>
</tr>
<tr>
<td>2</td>
<td>Rint\textsubscript{c}</td>
<td>55</td>
<td>85</td>
<td>3.1 0.8-25.0</td>
</tr>
<tr>
<td>3</td>
<td>Rint\textsubscript{EO}</td>
<td>47</td>
<td>64</td>
<td>2.6 0.4-26.3</td>
</tr>
<tr>
<td>4</td>
<td>Rint\textsubscript{Eo}</td>
<td>42</td>
<td>56</td>
<td>2.2 0.4-11.7</td>
</tr>
<tr>
<td>5</td>
<td>Rint\textsubscript{EO}</td>
<td>34</td>
<td>61</td>
<td>1.9 0.2-28.2</td>
</tr>
</tbody>
</table>

For abbreviations see legend to table 1.
ACCURACY AND SENSITIVITY OF INTERRUPTER TECHNIQUE

Discussion

The objectives of this study were to examine the accuracy, repeatability and sensitivity of the interrupter technique, using the plethysmographic method as our standard. Four different methods of analysing the Pmo(t) curve obtained after airway interruption were assessed. We found that the determination of Palv using a smooth curve fit, back-extrapolation technique produced resistance values which were similar to Raw; all other Rint methods gave values which significantly exceeded Raw. The most sensitive technique was to measure Pmo at end occlusion, although the relationship of this measurement to changes in airway calibre is less certain.

Experimental critique

The interrupter method is based on several theoretical assumptions: the respiratory system is considered as a single compartment model consisting of a rigid airway ending in an alveolus; the gas within the airway is incompressible; interruption of airflow occurs instantaneously; the pressure measured at the mouth immediately after interruption is equal to the alveolar pressure which was producing the airflow immediately before the interruption. The method further assumes that during the brief occlusion, alveolar pressure is rapidly equilibrated with airway opening pressure, and that there is no movement of the thoracic tissue [1, 4]. After an interruption of airflow, there is a rapid change in mouth pressure lasting about 10 ms, followed by a sharp break in the curve accompanied by oscillations, and the pressure proceeds to rise at a much slower rate (fig. 1). These two phases of the Pmo(t) curve are influenced by different factors. In tracheotomized, paralysed, closed-chest dogs, the initial pressure change has been found to equal the pressure drop across the conducting airways, with a very small contribution from the chest wall [28, 29]. Under normal conditions, the secondary phase of the curve reflects viscoelastic pressure dissipations in the tissues of the respiratory system in the normal lung (stress recovery), and, in addition, gas redistribution within compartments of different time constant (pendelluft) in a constricted lung [30].

Thus, under conditions of airway disease or obstruction, the pressure change is also influenced by slow equilibration of mouth with alveolar pressure. Because the point of interest between the two phases of the Pmo(t) curve is obscured by high frequency oscillations, Palv was determined at some point during the occlusion period. By estimating Palv in this way, values of interrupter resistance in early investigations were obtained, which were significantly greater than Raw [6, 7]. This is because the pressure change used in the calculation of Rint is composed not only of the initial pressure change, but also a component of the secondary change, which together would be expected to give a value of resistance exceeding Raw.

A curvilinear back-extrapolation proposed by Jackson et al. [4] produced a better agreement between interrupter resistance and plethysmographic resistance, despite overestimating Raw by at least 30% in healthy adults. This extrapolation technique was later implemented by Lustro et al. [12], who also found an overestimation of about 20%. In these studies, the differences from Raw were attributed to the different breathing patterns, and hence the glottic contribution to resistance, in the two methods. Because Rint is measured during quiet, tidal breathing, the upper airway adds an additional resistance in series with the airways. In practice, an estimate of Palv using this method in spontaneously breathing humans is hampered by a breakdown of the assumptions, especially in the presence of airflow obstruction [17]. It has been shown that in subjects with airway obstruction, but not in healthy subjects, the presence of a proximal compliant compartment, which includes the cheeks, trachea and pharynx, located between the resistive airway and the interrupter valve, will retard the equilibration of Palv and Pmo, thereby underestimating Raw [6, 14]. To allow for this, it has been suggested that the initial pressure change relating to Palv should be extended to include a portion of the secondary pressure phase [19]. Theoretical studies on the effect of a proximal compartment on the shape of the Pmo(t) curve in the presence of mild to moderate airway obstruction suggest that the interrupter method may still be valid, provided that the compliance of the upper airway is minimized by carefully supporting the cheeks [11].

Accuracy of Rint analysis

Using a smooth curve-fit, back-extrapolation to estimate Palv, Rint values were obtained which were not significantly different to Raw under basal conditions and following bronchoconstriction. In contrast, the curvilinear back extrapolation technique, proposed by Jackson et al. [4] for calculating interrupter resistance under normal conditions, yielded values which overestimated Raw. The technique of Jackson et al. [4] is somewhat similar in principle to the smooth curve fit used in the present study. However, in Jackson's method, only a portion of the post-occlusion data was used and judgement of the back-extrapolation was highly subjective. The smooth curve fit, back-extrapolation is totally dependent upon the overall shape of the second phase of the Pmo(t) profile (fig. 1). Hence, under normal conditions, changes in Pmo after the oscillations have ceased are small, and Palv is mainly due to the initial pressure change after interruption. With increasing airflow obstruction, the curve becomes progressively concave towards the X-axis (fig. 1). The determination of Palv then becomes dependent upon two factors: 1) the extent of the change in pressure over the smooth part of the Pmo(t) curve; and 2) the extent of back-extrapolation past the fitted data. Since the latter factor is the only one which is controllable, it is desirable to keep the back-extrapolation to a minimum, whilst still allowing a correction for the finite closure time of the valve [23].

We found that the remaining Rint methods produced values which were significantly greater than Raw. Both Rinf60
and \( R_{int} \), overestimated \( R_{aw} \) by a similar magnitude under basal conditions, these differences remaining unchanged after bronchoconstriction. \( R_{int} \) exceeded \( R_{aw} \) by the largest mean difference under basal conditions and represented the pressure after an extended equilibration period, at the expense of including the secondary pressure change. This difference increased after airway obstruction was induced (from 0.34 to 0.42 kPa·l⁻¹·s⁻¹), and implies an additional error using this interrupter method after bronchoconstriction. It has been suggested that the values of interrupter resistance using the pressure change after approximately 100 ms closure approximates to total respiratory resistance [15], the sum of airway resistance and the resistance of lung tissue, thoracic and abdominal wall. Abdominal muscles, which are considered to be inactive during tidal breathing may, however, be recruited at higher levels of ventilation [31, 32], and after induced bronchoconstriction. Thus, from the present study, it appears that subjects may not have been able to relax consistently during spontaneous expiration after inducing bronchoconstriction. In the present study, the similar values of \( R_{int} \) and \( R_{aw} \) under basal and obstructed conditions suggests that both methods are equally good for measuring airway resistance. The results also support the hypothesis, proposed by Bates et al. [11], that with sufficient upper airway support the interrupter technique may be useful for estimating airway resistance in bronchial obstruction. A doubling of airway resistance could be detected with the interrupter method using a smooth curve-fit, back-extrapolation to estimate \( P_{alv} \). This study was only an attempt to evaluate the interrupter method as a tool for assessing the response to bronchial challenge, and it was not intended to interpret changes on the basis of a lung model. The interpretation, especially under conditions of lung inhomogeneity due to bronchoconstriction, is still controversial, especially with respect to the influence of upper airways compliance [12].

**Repeatability and sensitivity of \( R_{int} \)**

The relative sensitivity and reliability of the interrupter technique for the assessment of the response to bronchial challenge was quantified by: 1) the within-subject CV, which indicates baseline repeatability of the measurement and is, therefore, intimately related to the relative sensitivity, which was quantified using a sensitivity index; and 2) the proportionate change of each parameter after challenge.

In this study, the measurement of \( R_{aw} \) was used as our reference resistance. It is, however, subject to errors in the presence of considerable airflow obstruction. After airflow obstruction is induced, the extrathoracic airways can act as a shunt impedance [33, 34], resulting in a loss of pressure across the obstruction. In this way, airway resistance is underestimated. This loss of pressure is dependent on the frequency of panting against the closed shutter in the measurement procedure, a frequency of less than 1 Hz avoiding this error [34]. The underestimate can be reduced by support of the extrathoracic airway [12]. In the technique we use, panting was performed at 2 Hz. However, there was a tendency for panting to become slower with valve occlusion; the obstruction induced was relatively moderate, and all subjects supported the upper airway during measurements. Overall, however, even with these precautions, there might be some tendency to underestimate \( R_{aw} \) after airway obstruction, thereby attenuating the apparent increment. Hence, the discrepancy in SI between plethysmography and the interrupter methods might be underestimated.

Our criterion for a moderate level of induced bronchoconstriction was an increase in \( R_{aw} \) of 100%. The measurement of specific airway conductance is considered to be more sensitive than \( R_{aw} \), because it corrects for variations in lung volume which may occur as a result of bronchial obstruction [17]. However, \( PC_{aw} \) was used, since it makes no such correction and is, therefore, directly comparable to interrupter measurements.

The measurement of \( R_{aw} \) was generally considerably more repeatable than interrupter measurements indicated by the lowest mean intrasubject CV, although \( R_{int} \) was comparable in repeatability, and also had the smallest CV of the interrupter methods investigated. This compares favourably with the repeatability of other variants of the interrupter method mentioned in the literature [7, 8, 35, 36]. The highest SI of the Rint methods was also obtained for \( R_{int} \). The fact that \( R_{int} \), despite having the largest proportionate change of the interrupter methods, turns out to have relatively low sensitivity, is due to it also having the largest intrasubject CV. Thus, the sensitivity of the method is essentially dependent on the degree of change and baseline variability.

In relation to individual data, rather than mean values, the sensitivity of all the Rint methods was relatively poor. In order to detect a significant bronchial response within subjects, it was necessary for the change in resistance to exceed a threshold of 2 x baseline so (or 2 x CV [17] (table 1). Whereas, doubling of \( R_{aw} \) was equivalent to a change of 7 to 10 so in airway resistance (table 2), for many individuals the commensurate overall change in \( R_{int} \) was less than 2 so.

In conclusion, the interrupter technique is simple to use, and requires minimal patient co-operation. Rint, determined using a smooth fit back-extrapolation technique (\( R_{int} \)), yielded resistance estimates which were similar to \( R_{aw} \) under basal conditions and induced bronchoconstriction. Rint, calculated from the pressure change at end occlusion (\( R_{int} \)), was the most sensitive interrupter method, although the relationship between this measurement and changes in airway calibre is less certain. The interrupter method may be useful for estimating airway calibre and for assessing the response to nonspecific challenge, where conventional lung function techniques are not suitable.

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