Short and long term variability of the interrupter technique under field and standardised conditions in 3–6 year old children

R M j Beelen, H A Smit, R T van Strien, L P Koopman, J E Brussee, B Brunekreef, J Gerritsen, P J F M Merkus

Methods: The interrupter technique was studied under field and standardised conditions in children aged 3–6 years. Under field conditions, five investigators performed the measurements using two different measurement devices in random sequence. Both short term (20–30 minutes) and long term variability (median 38 days) were assessed in 32 children. Under standardised conditions, a single investigator conducted all measurements using a single device; the repeated measurements were conducted at the same time of day in a familiar quiet classroom. Long term variability (median 11 days) was estimated in 15 children. Within-subject standard deviations were estimated by analysis of variance with adjustment for the effects of different investigators and measurement devices on within-subject variability under field conditions.

Results: Under field conditions within-subject standard deviations for short and long term variability were 0.10 kPa/l/s (adjusted 0.10 kPa/l/s) and 0.13 kPa/l/s (adjusted 0.14 kPa/l/s), respectively. Under standardised conditions the within-subject standard deviation for long term variability was 0.10 kPa/l/s.

Conclusions: Measurement of interrupter resistance under field conditions only slightly increased the within-subject variability compared with standardised conditions. The results indicate that interrupter resistance is a stable individual characteristic over a period of some weeks.

Background: The short and long term variability of the interrupter technique was assessed to determine whether interrupter resistance is a stable individual characteristic over time. The effect of field and standardised measurement conditions on the within-subject variability of the interrupter technique was also examined.

Methods: The interrupter technique was studied under field and standardised conditions in children aged 3–6 years. Under field conditions, five investigators performed the measurements using two different measurement devices in random sequence. Both short term (20–30 minutes) and long term variability (median 38 days) were assessed in 32 children. Under standardised conditions, a single investigator conducted all measurements using a single device; the repeated measurements were conducted at the same time of day in a familiar quiet classroom. Long term variability (median 11 days) was estimated in 15 children. Within-subject standard deviations were estimated by analysis of variance with adjustment for the effects of different investigators and measurement devices on within-subject variability under field conditions.

Results: Under field conditions within-subject standard deviations for short and long term variability were 0.10 kPa/l/s (adjusted 0.10 kPa/l/s) and 0.13 kPa/l/s (adjusted 0.14 kPa/l/s), respectively. Under standardised conditions the within-subject standard deviation for long term variability was 0.10 kPa/l/s.

Conclusions: Measurement of interrupter resistance under field conditions only slightly increased the within-subject variability compared with standardised conditions. The results indicate that interrupter resistance is a stable individual characteristic over a period of some weeks.

Background: The short and long term variability of the interrupter technique was assessed to determine whether interrupter resistance is a stable individual characteristic over time. The effect of field and standardised measurement conditions on the within-subject variability of the interrupter technique was also examined.

Methods: The interrupter technique was studied under field and standardised conditions in children aged 3–6 years. Under field conditions, five investigators performed the measurements using two different measurement devices in random sequence. Both short term (20–30 minutes) and long term variability (median 38 days) were assessed in 32 children. Under standardised conditions, a single investigator conducted all measurements using a single device; the repeated measurements were conducted at the same time of day in a familiar quiet classroom. Long term variability (median 11 days) was estimated in 15 children. Within-subject standard deviations were estimated by analysis of variance with adjustment for the effects of different investigators and measurement devices on within-subject variability under field conditions.

Results: Under field conditions within-subject standard deviations for short and long term variability were 0.10 kPa/l/s (adjusted 0.10 kPa/l/s) and 0.13 kPa/l/s (adjusted 0.14 kPa/l/s), respectively. Under standardised conditions the within-subject standard deviation for long term variability was 0.10 kPa/l/s.

Conclusions: Measurement of interrupter resistance under field conditions only slightly increased the within-subject variability compared with standardised conditions. The results indicate that interrupter resistance is a stable individual characteristic over a period of some weeks.

Background: The short and long term variability of the interrupter technique was assessed to determine whether interrupter resistance is a stable individual characteristic over time. The effect of field and standardised measurement conditions on the within-subject variability of the interrupter technique was also examined.

Methods: The interrupter technique was studied under field and standardised conditions in children aged 3–6 years. Under field conditions, five investigators performed the measurements using two different measurement devices in random sequence. Both short term (20–30 minutes) and long term variability (median 38 days) were assessed in 32 children. Under standardised conditions, a single investigator conducted all measurements using a single device; the repeated measurements were conducted at the same time of day in a familiar quiet classroom. Long term variability (median 11 days) was estimated in 15 children. Within-subject standard deviations were estimated by analysis of variance with adjustment for the effects of different investigators and measurement devices on within-subject variability under field conditions.

Results: Under field conditions within-subject standard deviations for short and long term variability were 0.10 kPa/l/s (adjusted 0.10 kPa/l/s) and 0.13 kPa/l/s (adjusted 0.14 kPa/l/s), respectively. Under standardised conditions the within-subject standard deviation for long term variability was 0.10 kPa/l/s.

Conclusions: Measurement of interrupter resistance under field conditions only slightly increased the within-subject variability compared with standardised conditions. The results indicate that interrupter resistance is a stable individual characteristic over a period of some weeks.
Study B: Variability under standardised conditions

The study population measured under standardised conditions consisted of 15 healthy children randomly selected from a daycare centre and a kindergarten. These children had no history of any cardiorespiratory disease and had no respiratory symptoms at the time of the study.

Measurement of interrupter resistance

Expiratory interrupter resistance was measured by the interrupter technique using a commercial device (MicroRint, Micromedical Ltd, UK) because expiratory interrupter resistance seems slightly more sensitive in detecting subclinical differences in airway calibre within and between subjects than inspiratory interrupter resistance. The children were carefully instructed how to perform the test. During the test the children were sitting and were quietly breathing through the device via a mouthpiece with a nose clip, the lips firmly sealed around the mouthpiece, and the neck slightly extended. The cheeks and throat were supported by the hands of the investigator standing behind the child in order to decrease upper airway compliance. Optimal passive cooperation by the children was enhanced by showing a video movie. After a period of quiet breathing, a single expiratory interruption was triggered at the peak of tidal flow during 100 ms. The children were unable to anticipate the trigger event but were able to hear the valve closing.

In each subject 10 occlusions were performed and the median of five or more technically satisfactory readings was taken as a valid measurement. If necessary, the procedure was repeated until at least five acceptable readings were obtained. Attempts were not accepted if the mouth pressure-time curve and/or flow-time curve did not fulfill criteria as described in the literature. If the child did not breathe quietly. The median resistance value, number of completed interruptions, reasons for failure, and a subjective judgement of the measurement quality by the investigator were recorded. This protocol was used in both study groups.

Variability was assessed in children with no respiratory symptoms and no use of respiratory drugs during the 12 hours before the test on both measurement days. There was no difference in respiratory symptoms on the different measurement days in the children in either study group.

Study A: Variability under field conditions

Intermittent resistance was measured at the homes of the 32 children. Two measurements, 20–30 minutes apart, were performed to assess short term variability. To evaluate long term variability a third measurement was conducted a few weeks after the first measurement (median 38 days, range 22–77). It was possible to conduct a third measurement in 25 of the 32 children. Because the interrupter technique was studied under field conditions, five different investigators performed the measurements using two different measurement devices (both MicroRint) in random sequence. A short questionnaire was administered on the child’s health status during the previous 2 weeks and on medication use 12 hours before the measurement.

Study B: Variability under standardised conditions

Measurement of interrupter resistance in study B was conducted according to the same protocol as in study A. However, in this study the interrupter resistance was measured under standardised conditions—that is, all measurements were conducted by a single investigator using a single device for all measurements. Repeated measurements were also conducted at the same time of the day and were carried out in a familiar and quiet classroom. Two measurements were made in 15 healthy children to evaluate long term variability. The median interval between the two measurements was 11 days (range 7–13).

Data analysis

Analysis of variance was conducted to estimate within-subject standard deviations (SDw) for short and long term variability of the interrupter technique. SDw is the usual measure of variability when within-day or between-day variability is studied. It was calculated from the analysis of variance results as the square root of the pooled within-subject sum of squares divided by its degrees of freedom. In the study under field conditions, adjustment was made for the effects of different investigators and measurement devices on within-subject variability by including these factors as independent variables in the model.

The underlying assumption of the model is that variability is independent of the level of interrupter resistance. To examine this assumption, the differences between paired measurements were plotted against their means (Bland-Altman plot).

RESULTS

The characteristics of the two study populations are shown in table 1. The children and their parents readily accepted the tests. Bland-Altman plots of individual differences between paired measurements against their mean interrupter resistance values are shown in fig 1 for measurements under field conditions using a short term interval (fig 1A) and a long term interval (fig 1B) between paired measurements. Variability was found to be independent of the level of interrupter resistance in both study populations (p>0.8 for regressions of differences against means).

Mean baseline values of interrupter resistance, mean baseline interrupter resistance Z scores, and SDw values are shown in table 2. Under field conditions the SDw for long term variability was slightly higher than for short term variability. The SDw for long term variability under field conditions was also only slightly higher than the SDw for long term variability under standardised conditions. Adjusting for the effects of different investigators and different measurement devices hardly changed the within-subject variability results in the study under field conditions.

Table 1 Baseline characteristics of the children in the study performed under field conditions (study A) and in the study performed under standardised conditions (study B)

<table>
<thead>
<tr>
<th></th>
<th>Population measured under field conditions</th>
<th>Population measured under standardised conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Short term variability</td>
<td>Long term variability</td>
</tr>
<tr>
<td>No of boys</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Age (years)</td>
<td>4.3 [0.2] (3.7–4.9)</td>
<td>4.3 [0.3] (3.7–4.9)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>106.3 [4.5] (98.0–119.0)</td>
<td>105.7 [3.6] (98.0–111.0)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>18.8 [2.5] (14.9–24.7)</td>
<td>18.5 [2.5] (14.9–24.7)</td>
</tr>
</tbody>
</table>

Values are mean (SD), range.
Short and long term variability of the interrupter technique

The SDₜ for short term variability was found to be comparable to the SDₜ reported by others. Previous studies considered short term variability satisfactory, where a low SDₜ indicates a small variability over time. Klug et al. found an SDₜ for short term variability of 0.08 kPa/l/s in healthy children 2–7 years of age. Furthermore, an SDₜ of 0.14 kPa/l/s was reported for short term variability in asthmatic children.¹

A recent study by Lombardi et al.¹¹ studied the long term repeatability of the interrupter technique in 26 children with a history of either cough or wheeze, with a mean interval of 2.5 months between the two measurements. Interrupter resistance repeatability was defined as two standard deviations of the paired differences between the two sets of measurements and was estimated as 0.21 kPa/l/s. The results of our study show that, although assessed in healthy children and with different statistical analysis methods, long term variability was comparable with that estimated by Lombardi et al. This may suggest that interrupter resistance is a stable individual characteristic, even over a longer period of time. This is important, for instance, in studying long term effects of an intervention on interrupter resistance.

For studying the effects of an intervention and a placebo on interrupter resistance in a clinical trial, the required number of subjects in both groups can be calculated.¹² With a common variance of 0.04 kPa/l/s in the two groups (calculated from the observed standard deviation of 0.2 kPa/l/s (table 2)), a significance level of 0.05, and a power of 80%, 28 subjects are required in each group to detect a difference of 0.15 kPa/l/s between the effects in both groups.

Because we investigated variability of the interrupter technique in study A under field conditions, several factors such as different investigators, different measurement devices, and measurement at different times of the day may have randomly influenced within-subject long term variability.¹³ In study B the conditions during which interrupter resistance was measured were standardised—that is, a single investigator conducted the measurements using a single device and the investigator and device were stable during the measurements. Furthermore, the repeated measurements were conducted at the same time of day in a familiar and quiet classroom. The within-subject variability results hardly changed after adjustment for the effects of different investigators and different measurement devices on within-subject variability in study A, and both unadjusted and adjusted long term within-subject variability in the study under field conditions was only slightly higher than under standardised conditions. This indicates that the measurement conditions had little influence on variability.

The clinical characteristics of the children might have differed between the two study groups. None of the children measured under standardised conditions in study B had a history of any cardiorespiratory disease or current respiratory symptoms. The 32 children in study A had no history of cough or wheeze, with a mean interval of 2.5 months between the two measurements. Interrupter resistance repeatability was defined as two standard deviations of the paired differences between the two sets of measurements and was estimated as 0.21 kPa/l/s. The results of our study show that, although assessed in healthy children and with different statistical analysis methods, long term variability was comparable with that estimated by Lombardi et al. This may suggest that interrupter resistance is a stable individual characteristic, even over a longer period of time. This is important, for instance, in studying long term effects of an intervention on interrupter resistance.

For studying the effects of an intervention and a placebo on interrupter resistance in a clinical trial, the required number of subjects in both groups can be calculated.¹² With a common variance of 0.04 kPa/l/s in the two groups (calculated from the observed standard deviation of 0.2 kPa/l/s (table 2)), a significance level of 0.05, and a power of 80%, 28 subjects are required in each group to detect a difference of 0.15 kPa/l/s between the effects in both groups.

Because we investigated variability of the interrupter technique in study A under field conditions, several factors such as different investigators, different measurement devices, and measurement at different times of the day may have randomly influenced within-subject long term variability.¹³ In study B the conditions during which interrupter resistance was measured were standardised—that is, a single investigator conducted the measurements using a single device and the investigator and device were stable during the measurements. Furthermore, the repeated measurements were conducted at the same time of day in a familiar and quiet classroom. The within-subject variability results hardly changed after adjustment for the effects of different investigators and different measurement devices on within-subject variability in study A, and both unadjusted and adjusted long term within-subject variability in the study under field conditions was only slightly higher than under standardised conditions. This indicates that the measurement conditions had little influence on variability.

The clinical characteristics of the children might have differed between the two study groups. None of the children measured under standardised conditions in study B had a history of any cardiorespiratory disease or current respiratory symptoms. The 32 children in study A had no history of asthma, signs of eczema, or respiratory symptoms at the time the measurements were made, but 12 of them had a history of wheezing or whistling in the chest. The mean baseline

---

**DISCUSSION**

Our study has shown that within-subject variability of the interrupter technique over a period of some weeks was comparable to within-subject variability over a period of 20–30 minutes, indicating that interrupter resistance may be a stable individual characteristic over a period of some weeks. The repeatability of interrupter resistance measurements over both short and long term intervals was satisfactory. Furthermore, within-subject variability over a period of some weeks under field conditions was only slightly higher than under standardised conditions, in spite of the fact that five observers and two pieces of equipment were involved.

---

**Table 2** Within-subject variability of the interrupter technique

<table>
<thead>
<tr>
<th></th>
<th>Population measured under field conditions</th>
<th>Population measured under standardised conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Short term variability</td>
<td>Long term variability</td>
</tr>
<tr>
<td>Mean (SD), range baseline Rint (kPa/l/s)</td>
<td>0.99 (0.22) (0.60–1.41)</td>
<td>0.97 (0.20) (0.60–1.29)</td>
</tr>
<tr>
<td>Mean baseline Rint Z score*</td>
<td>0.59</td>
<td>0.41</td>
</tr>
<tr>
<td>SDₜ (kPa/l/s)</td>
<td>0.10</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Rint=interrupter resistance; SDₜ=within-subject standard deviation.

*Z scores calculated as (measured Rint – predicted Rint)/(RSD of the reference population). Predicted Rint values calculated based on regression equation by Merkus et al."
interrupter resistance Z scores were higher in the study performed under field conditions than in the study performed under standardised conditions. However, in all the children in both study groups there was no difference in respiratory symptoms between different measurement days.

Another difference between the two study groups was that different time intervals between the two measurements were used to evaluate variability (median 38 days in study A and 11 days in study B). A longer time interval between two measurements might increase variability.\(^\text{11}\)

In conclusion, our study suggests that interrupter resistance is a stable individual characteristic over time, given the satisfactory within-subject standard deviations for both variability over a period of 20–30 minutes and over a period of some weeks. Measurement under field conditions only slightly increased the within-subject variability compared with standardised conditions, indicating that the interrupter technique is suitable for use in clinical and epidemiological studies where observer, measurement device, and time of measurement cannot always be controlled.

\[\text{In conclusion, our study suggests that interrupter resistance is a}
\text{stable individual characteristic over time, given the satisfactory
within-subject standard deviations for both variability over a period of
20–30 minutes and over a period of some weeks. Measurement under
field conditions only slightly increased the within-subject variability
compared with standardised conditions, indicating that the interrupter
}\text{technique is suitable for use in clinical and epidemiological studies where
observer, measurement device, and time of measurement cannot
always be controlled.}\]

\[\text{ Authors' affiliations}\]
\[\text{R M J Beelen, R T van Strien, B Brunekreef, Department of}
\text{Environmental and Occupational Health, Institute for Risk Assessment}
\text{Sciences, Utrecht University, Utrecht, The Netherlands.}
\text{H A Smit, J E Brussee, Department of Chronic Disease Epidemiology,}
\text{National Institute of Public Health and the Environment, Bilthoven, The}
\text{Netherlands.}
\text{L P Koopman, P J F M Merkus, Department of Pediatrics, Division of}
\text{Respiratory Medicine, Sophia Children’s Hospital, Erasmus Medical}
\text{Centre, Rotterdam, The Netherlands.}
\text{J Gerritsen, Department of Pediatric Pulmonology, University Hospital}
\text{Groningen, Groningen, The Netherlands.}
\text{Funding: none.}\]

\[\text{REFERENCES}\]
\[\text{1 Merkus PJ, Mijnsbergen JY, Hop WC, et al. Interrupter resistance in
preschool children: measurement characteristics and reference values. Am}
\text{J Respir Crit Care Med 2001;163:1350–5.}\]
\[\text{2 Bridge PD, Ranganathan S, McKenzie SA. Measurement of airway}
\text{resistance using the interrupter technique in preschool children in the}
\text{ambulatory setting. Eur Respir J 1999;13:792–6.}\]
\[\text{3 Klug B, Bisgaard H. Measurement of lung function in awake}
\text{2–4-year-old asthmatic children during methacholine challenge and acute
asthma: a comparison of the impulse oscillation technique, the interrupter
technique, and transcutaneous measurement of oxygen versus
\[\text{4 Phagoo SB, Watson EA, Pride NB, et al. Accuracy and sensitivity of the
interrupter technique for measuring the response to bronchial challenge
\[\text{5 Bridge PD, Lee H, Silverman M. A portable device based on the
interrupter technique to measure bronchodilator response in
\[\text{6 Klug B, Bisgaard H. Specific airway resistance, interrupter resistance,
and respiratory impedance in healthy children aged 2–7 years. Pediatr}
\text{Pulmonol 1998;25:322–31.}\]
\[\text{7 Kannisto S, Vanninen E, Remes K, et al. Interrupter technique for
evaluation of exercise-induced bronchospasm in children. Pediatr}
\text{Pulmonol 1999;27:203–7.}\]
\[\text{8 Bisgaard H. Klug B. Lung function measurement in awake young
\[\text{9 Phagoo SB, Wilson NM, Silverman M. Evaluation of a new interrupter
device for measuring bronchial responsiveness and the response to
\[\text{10 Child F, Clayton S, Davies S, et al. How should airways resistance be
measured in young children: mask or mouthpiece? Eur Respir J
2001;17:1244–9.}\]
\[\text{11 Lombardi E, Sly PD, Concettuli G, et al. Reference values of interrupter
respiratory resistance in healthy preschool white children. Thorax
2001;56:691–5.}\]
of developing allergy born into a low risk environment? The PIAMA Birth}
\text{Cohort Study. Prevention and Incidence of Asthma and Mite Allergy. Clin
Exp Allergy 2001;31:576–81.}\]
\[\text{13 Bates JHT, Sly PD, Kochi T, et al. Effect of a proximal compliance on
interrupter measurements of resistance. Respir Physiol 1987;70:301–12.}\]
technique for the use of assessing airway obstruction in children. Pediatr}
\text{Pulmonol 1994;17:211–7.}\]
\[\text{16 Bland JM, Altman DG. Statistical methods for assessing agreement
\[\text{17 Fleiss JL. The design and analysis of clinical experiments. New York:}
\text{Wiley, 1986.}\]
\[\text{18 Klug B, Nielsen KG, Bisgaard H. Observer variability of lung function

\[\text{References}\]
Short and long term variability of the interrupter technique under field and standardised conditions in 3–6 year old children

Thorax 2003 58: 761-764
doi: 10.1136/thorax.58.9.761

Updated information and services can be found at:
http://thorax.bmj.com/content/58/9/761

These include:

References
This article cites 17 articles, 9 of which you can access for free at:
http://thorax.bmj.com/content/58/9/761#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/