American Thoracic Society Documents

ATS/ERS Statement: Raised Volume Forced Expirations in Infants
Guidelines for Current Practice

Over the past few years, a series of documents (1–8) have been produced by the American Thoracic Society/European Respiratory Society Task Force on Standards for Infant Respiratory Function Tests, and this document represents part of this series. The aim of this task force is to summarize what is currently seen to be good laboratory practice, and to provide recommendations for users and manufacturers of infant lung function equipment and software. Recently, infant lung function equipment has been developed and marketed that uses the raised volume technique. Because this equipment is now also available to clinicians as well as researchers, standardization of the technique is critical (9, 10). Although consensus has been reached on many aspects of the raised volume technique, there are still several issues that require further investigation. Therefore, the format for this article is to summarize what is current practice and the rationale for these practices and, where it has been possible to reach a general consensus after widespread communication on an international level, to provide recommendations. Areas that require further study to facilitate future developments in this field have also been highlighted.

It is important to emphasize that the recommendations presented here apply only to spontaneously breathing infants and do not invalidate previously published data collected with less automated systems or without all the quality control suggested within. It is recognized that this document will need regular updating in response to advances in both technology and our knowledge regarding the application and interpretation of these tests. In the meantime, every attempt has been made to avoid being too prescriptive to allow for future developments, while at the same time offering guidance as to minimum standards for those developing equipment and performing tests.

Standards for measuring forced expiratory maneuvers in infants using the tidal rapid thoracoabdominal compression (RTC) technique have been described previously (6). Much of the equipment required for the measurement of forced expiration at raised lung volume is identical to that used for the tidal RTC, but additional equipment is required to raise lung volume toward total lung capacity. The theoretic background and practical details of how to apply the raised volume technique have been described previously (11), and details regarding general equipment and software specifications are described elsewhere (3, 4). The current document will focus on the methodologic and analytic issues that relate specifically to the raised volume technique. It is anticipated that acceptance and application of these recommendations will be of value when attempting to compare data between centers, develop or use reference data, or participate in multicenter trials that use parameters derived from raised volume forced expirations as outcome measures.

DATA ACQUISITION AND SIGNAL PROCESSING

Data acquisition requirements have been described previously (2). Points of particular relevance to raised volume RTC (RVRTC) measurements are as follows:

1. Minimum sampling rate should be at least 100 Hz.
2. Raw data should be saved for quality control and, if necessary, reanalysis (e.g., if improved algorithms and/or additional parameters are introduced in future).

There are currently major differences between centers or systems used with respect to the way in which data are corrected to body temperature, pressure, and saturation and/or "drift" corrected. This may have a significant effect not only on measured volumes but also on flows obtained, especially at low lung volume. This will need further investigation, because the potential effects on parameters are currently unknown (Section E2.1 in the online supplement).

METHODS

Two methods have been described for determining "full" maximal expiratory flow–volume curves in infants, namely the RVRTC technique (12–16) and the negative-pressure forced deflation method (17, 18). Due to the more invasive nature of the latter, which is limited to use in intubated subjects, the RVRTC has been more widely used in both healthy infants (19–22) and in those with respiratory disease (23–28). This
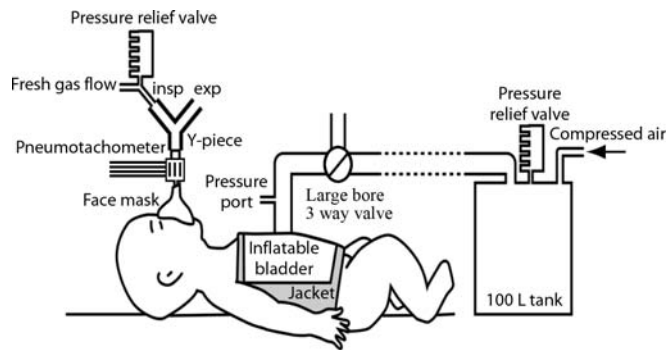

Figure 1. Schematic illustration of equipment used for the raised volume rapid thoracoabdominal compression (RVRTC) maneuver. exp = expiratory; insp = inspiratory.

document will therefore focus on recommendations for the RVRTC technique.

During the RVRTC technique, the infant's lungs are passively inflated toward total lung capacity before applying thoracoabdominal compression pressure to force expiration.

In brief, to obtain forced expiratory maneuvers from raised lung volume, an inflatable jacket, which extends from the infant's axillae to the iliac crest, is loosely wrapped around the infant's torso (Figure 1). A respiratory pause is produced by administering several rapid lung inflations to an elevated lung volume before inflating the jacket to forced expiration from raised lung volume toward residual volume (RV). Jacket inflation must be maintained until forced expiration is complete.

Additional information regarding methodology and data analysis, including illustrations of technically unacceptable data, is provided on the online supplement.

Equipment

Further details and justification of the recommendations presented have been published previously (1–4). General recommendations regarding choice of facemasks, pressure transducers, jacket, pressure source, and valves, together with guidelines for optimizing data acquisition, are as presented for tidal forced expirations (6).

Apparatus for Raising Lung Volume

The apparatuses for the raised volume technique includes a mask, a flow meter, an external air supply, valves for occluding the airway for an automated system or a T-piece connector for a manual inflation system, and a safety pressure relief valve for the control of inflation pressure. Although new types of flow meters (e.g., ultrasonic) are currently being developed and validated for use, the pneumotachometer (PNT) remains the most commonly used device at present and therefore will generally be referred to in this document.

The PNT should be a low-resistance, low-dead-space device with a linear range appropriate for the high flows encountered during this technique (Table 1) (2, 11) and must remain linear when heated (3). If the PNT is pressurized, the system should be evaluated to ensure that artifactual transients are not introduced into the flow signal.

In some centers, the use of air-filled cushioned masks is preferred, to facilitate removal of the apparatus between maneuvers. Others strongly recommend the use of therapeutic putty to achieve an airtight seal during lung inflations. The rationale for the latter is that mask air leaks are more likely to occur

during RVRTC than tidal RTC because of the higher airway opening pressures attained (20, 28) and pressing too hard on the mask and face to achieve such a seal could result in depression of the jaw and compression of the nasal airway, leading to underestimation of measured flows. However, minimal differences in results were observed when data using both methods were collated (19), suggesting that, with care and experience, either approach is acceptable. However, it is recommended that new investigators in infant lung function testing should at least initially use masks, with and without putty, to assess whether comparable data are obtained with both methods in the same subject.

Recommendations:

- The PNT should be a low-resistance, low-dead-space device with a linear range appropriate for the high flows observed during this technique and age/weight of the infant.
- It is essential to maintain an airtight seal between the mask and the face during the procedure, and to prevent any upper airway compression during application of high inflation pressures.

Areas for further research:

- If the PNT is pressurized during the maneuvers (up to 30 cm H_2O), then its performance should be ascertained under such conditions.
- Investigations should be made into the potential effects on measured parameters of differences in type of mask used, with or without putty, to achieve a leak-free seal.

Size of Reservoir and Pressure Source

A drum of 50- to 100-L capacity has been used to inflate the jacket. Further details are as described previously (6, 29). The jacket must be inflated through wide-bore tubing to ensure rapid inflation. To ensure that jacket pressure is sustained during jacket inflation, the recommended minimum size for the reservoir chamber should be at least 50 L, because very small reservoirs would require higher reservoir pressures to deliver 100 to 120 cm H_2O to the jacket.

Recommendations:

- Minimum bore of connecting tube: 25 mm
- Minimum size of the reservoir chamber for jacket inflation: 50 L

Valves

For automated systems, valve-opening speeds of less than 20 ms are easily achieved electronically. In addition to the multiple valves that are used for the tidal RTC technique (6), the following are required for the RVRTC system:

TABLE 1. RANGE OF FLOWS LIKELY TO BE ENCOUNTERED DURING TIDAL BREATHING AND FORCED EXPIRATORY MANEUVERS IN INFANTS

Infant Weight (*kg*)	Flow Range (ml · s⁻¹)		
	Tidal Breathing	Tidal RTC	Raised Volume RTC
< 2	0–100	0–200	0–500
2–4	0–200	0–500	0–1,000
4–10	0–300	0–1,000	0–3,000
10–15	0–500	0–1,500	0–3,000

Definition of abbreviation: RTC = rapid thoracoabdominal compression.
Ranges refer to the highest peak flows likely to be encountered during testing in healthy infants. Note: As a result of further experience with these techniques, these ranges differ slightly from those previously quoted by Frey and colleagues (3).

1. Valve on the inspiratory side of the circuit to control the pressure applied to the airway opening by a pressure relief valve in the apparatus for raising lung volume
2. Valve to close the downstream end of the bias flow to inflate the lungs to a preset pressure
3. Valve to allow passive expiration to atmosphere once airway pressure has reached the preset pressure (e.g., 30 cm H_2O [2.94 kPa]) and plateau on the inspiratory volume signal is achieved

Depending on the equipment used, the rise time of jacket inflation (i.e., from 10–90% of jacket inflation) may take 70 to 100 ms to achieve (14). Thus, simultaneous activation of jacket inflation and the release of the valve for raising lung volume will result in a somewhat delayed forced expiration (i.e., full jacket inflation achieved after passive expiration has commenced; Figure E1 in the online supplement). Furthermore, flows at high lung volume (e.g., forced expiratory flow [FEF]$_{25/50}$) may be overestimated. To ensure that forced expiration is timely (i.e., initiated at the end of the augmented breath), a common approach is to activate jacket inflation just before (10–100 ms) release of airway occlusion (13, 15, 23, 28). Precise timing will depend on whether this is performed manually or using automated valves and on the rise time for jacket inflation. Whichever approach is used, care must be taken to minimize the period when the airway is exposed to high pressures (most centers aiming for < 50 ms, but *see also* Section E2.3.1 on assessment of transmission pressures at raised lung volume).

Safety Issues

The monitoring of heart rate and oxygen saturation with pulse oximetry should be maintained during all measurements until the infant is fully awake, because even healthy infants may respond adversely to trigeminal stimulation or airway occlusion (30). Inclusion of a capnograph (for monitoring end-tidal CO_2 [ET$_{CO_2}$]) within the circuitry was recommended initially because of theoretic concerns regarding the potential for significant falls in Pa$_{CO_2}$ associated with the rapid delivery of repeated lung inflations to 30 cm H_2O. Monitoring revealed, however, that delivery of two to five inflations produced only modest declines in ET$_{CO_2}$ (2–6 mm Hg), which were not likely to result in significant reductions in cerebral blood flow and potential seizures. Some monitoring devices may also increase system resistance and could potentially influence results (3). Although some centers continue to monitor ET$_{CO_2}$ during all studies for medicolegal reasons, it was agreed after a raised volume workshop in 1999 that, for spontaneously breathing infants, use of a capnograph was not routinely necessary unless the infant was oxygen-dependent or had a history of apnea or seizures in whom ET$_{CO_2}$ monitoring would be required at all times. The precise configuration and safety measures required will also depend on local regulations and protocols.

The risk of gastric distension, or aerophagia, which may occur secondary to repeated lung inflations, should also be minimized by the careful positioning of the infant and by minimizing the number of maneuvers performed.

Areas for future research:

- To investigate impact of dead space on RVRTC parameters
- To investigate the effect of increased apparatus resistance at high flows

Calibration

To ensure accurate recordings, the following should be done:

1. All channels should be calibrated, or a calibration check performed before every infant study according to manufacturer's recommendations.
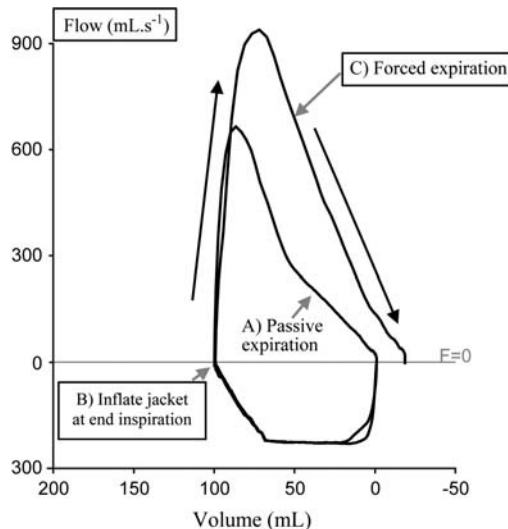

Figure 2. RVRTC flow–volume loop.

2. Calibration tools should be checked at least every 2 yr (preferably annually).
3. Calibration should be performed under identical conditions (including F$_{I_{O_2}}$) as during measurements.

To validate the flow–volume calibration factors, a series of volume or flow signals are delivered at different rates to simulate the full flow range likely to be encountered (Table 1), and checked to ensure that the signals are within ± 2.5% of the delivered values. Details of flow calibration are as described previously (3). Calibration factors/checks should be displayed, recorded, and saved with test results for subsequent quality control checks.

Measurement Protocol

Posture. Measurements should be made with infants and young children lying supine, with the neck and/or shoulders supported in the midline in slight extension. Optimization of head position to achieve maximum patency of the upper airway in each infant is essential when using this technique to obtain smooth, reproducible flow–volume curves. Repositioning is necessary if noisy breathing occurs, but care should be taken to avoid overextension. The position is stabilized using a neck roll or head ring.

Application of cricoid pressure. During the application of positive pressure at the airway opening, it is possible that entry of air into the stomach will produce gastric distension and potentially decrease FRC and FVC as well as flow parameters. The risk of gastric distension during lung inflations increases with the magnitude of applied pressure, number of maneuvers performed, and duration of lung inflation after a plateau on the volume signal has been achieved. In an attempt to minimize aerophagia, some centers (20, 31) routinely use the "Sellick maneuver" (32), whereby cricoid pressure is applied during lung inflations with release just before activating thoracoabdominal compression. However, this practice remains controversial (33, 34) and deserves additional investigation. Because RVRTC data collected at 30 cm H_2O from two centers who did (United States and Brazil) and one who did not (London) apply cricoid pressure were comparable (Figures 4 and 5; Figures E4 and E5), this issue may not be as critical as originally believed. Nevertheless, great care must be taken to avoid gastric distension by careful positioning of the infant and minimizing the number of maneuvers performed. Furthermore, attempts to collect data from the RVRTC technique should be
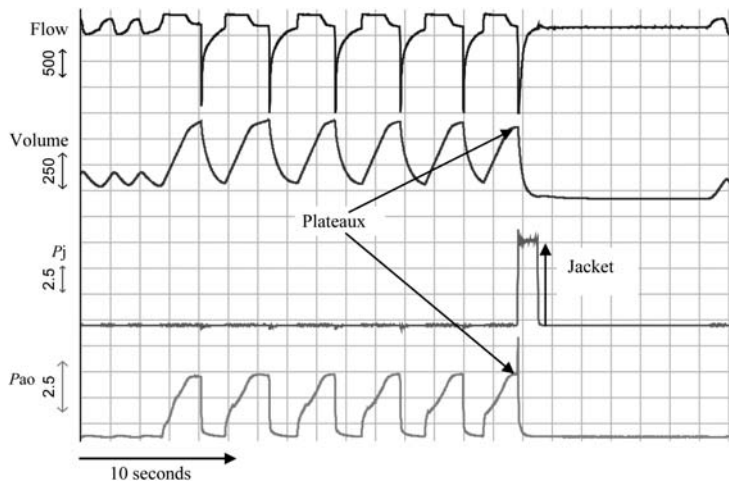
Figure 3. Time-based trace of an RVRTC maneuver. The upward slope of the volume signal denotes inspiration and the downward slope denotes expiration. In instances where the initiation of jacket inflation is timed to occur simultaneously as the release of inflation pressure, due to the rise time required for jacket inflation, no spike on airway opening pressure (Pao) will be observed. Pj = jacket pressure.

terminated if there is evidence of sequential reduction in FVC or inflation volume from run to run, or any clinical signs of regurgitation or vomiting.

Area for future research:

- Evidence that application of cricoid pressure prevents gastric distension needs to be established, together with optimal methods for early detection of aerophagia.

Inflation pressure. One of the major methodologic differences among laboratories has been the different inflation pressure (Pinf) used to raise lung volume (19, 23, 24, 35), which will affect the expired volumes and flows (13). Most currently available reference data derived from the RVRTC technique have been obtained using an inflation pressure of 30 cm H_2O (19), although others have used 20 cm H_2O in some very small or young infants (35) or in an attempt to minimize problems due to leak or gastric distension. To facilitate collaboration and comparison of results between centers, it is suggested to standardize RVRTC measurements to 30 cm H_2O, unless there are specific contraindications. To deliver a pressure of 30 cm H_2O, the inspiratory flow is set to 1.5 times the peak tidal inspiratory flow (Table 1), although this rate may be increased or decreased depending on the child's responses to get a smooth, gentle inflation. The airway opening pressure attained should always be checked, as the pressure delivered by the equipment (e.g., Neopuff) may be flow-dependent if very low flows are used. Furthermore, the rise time may be very slow in an infant with large or compliant lungs, with danger of not reaching volume and pressure plateaus in a timely fashion. Ideally, the actual pressure at airway opening during data collection should be displayed and reported so that the operator can adjust the flow, if necessary, to optimize the pressure delivered. The operator must take full responsibility for
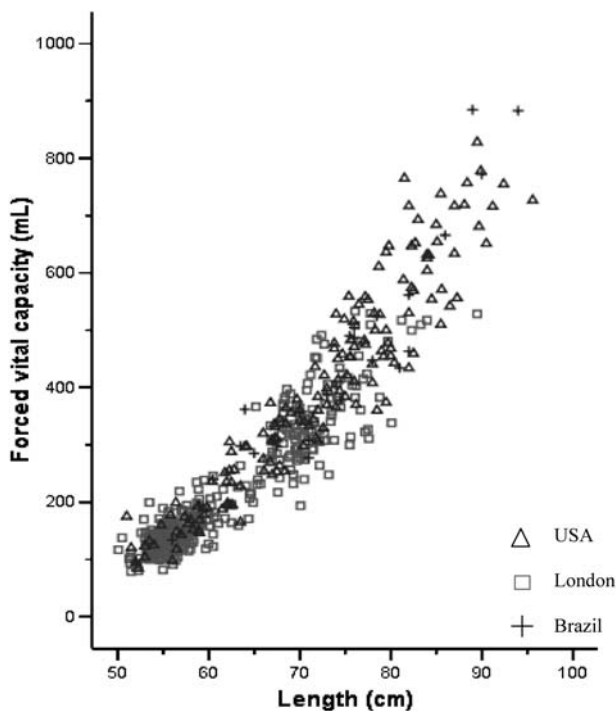

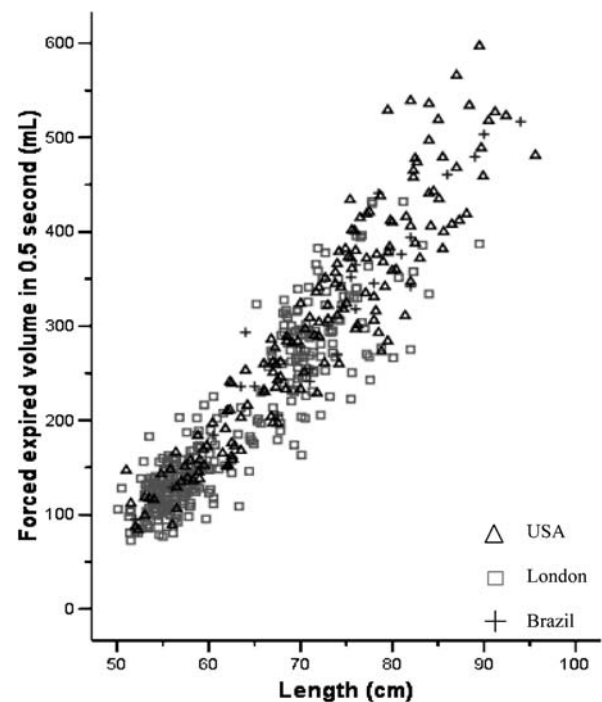*Figure 4.* Scatterplot of forced vital capacity versus length according to centers.

Figure 5. Scatterplot of forced expired volume in 0.5 s versus length according to centers.

checking Pinf before data collection, whether using an automated or manual system.

Recommendations:

- Inflation pressure of 30 cm H_2O
- Set inspiratory flow to 1.5 times the peak tidal inspiratory flow
- Record pressure achieved at airway opening, not simply the "set" inflation pressure

Number of inflations/augmented breaths. Currently, there is a wide variation in pattern of ventilation before the forced expiration. The rate of lung inflation will depend on the relative size of the lungs and magnitude of bias flow, whereas the volume achieved for any standardized pressure will be directly proportional to the infant's respiratory compliance. The rate of lung inflation may need to be adapted to the individual infant's breathing pattern, and to aid relaxation and standardize applied pressure at the airway opening, some centers tend to hold the inflation until both a pressure and volume plateau were observed (Figure 3). This inflated breath hold uses the stimulus of lung expansion to maintain vagally mediated pulmonary stretch receptor input and inhibit subsequent inspiratory effort via negative feedback to facilitate relaxation of the respiratory system. However, the longer the breath hold is maintained the greater the risk of gastric distension. Others have used a relatively short expiratory time to create positive end expiratory pressure during the inflations to stabilize airways that have a tendency to collapse (36). While there are advantages to adapting rate and pattern to entrain the child's breathing pattern, such differences may alter volume history and affect lung mechanics (37). As a compromise, a minimum of 2–5 inflations is recommended.

Area for future research:

- Further validation is required to ascertain the separate effects of the number and size of lung inflations on respiratory mechanics as well as on results obtained from RVRTC.

Duration of lung inflation immediately prior to jacket inflation. To ensure a standard pressure–volume history prior to jacket inflation, it is essential that the last lung inflation reach an inflation pressure of 30 cm H_2O and that a brief volume plateau is attained before forcing expiration. A plateau is defined when there is minimal change in the measured signal over a specified period of time. For the RVRTC this has been defined as < 2% change in volume (in relation to total inflation volume) over a 100-ms period, whereas for pressure, it can be defined as < 2% change in pressure over a 100-ms interval or an SD of ≤ 0.3 cm H_2O over the same period (Figure 3).

Area for future research:

- To ascertain the influence of volume history on RVRTC parameters

Achievement of flow limitation. While some have argued that it is better to apply standardized conditions of both inflation and transmission pressure rather than attempting to reach flow limitation (23), most centers (20, 22, 38, 39) are currently attempting to reach flow limitation, as defined by no further increase in flow despite increasing applied jacket pressure, and this approach is therefore described below (*see* Section E2.3).

The amount of pressure transmitted is dependent on the design of the jacket and how tightly it is placed. "Flow limitation" should be assessed individually for each infant under the precise measurement conditions being used during testing. The "optimal" jacket pressure is defined as that above which (5–10 cm H_2O) no further increase in flows (FEF_{75} or FEF_{25-75}) and volumes (FVC or FEV_t) can be obtained (i.e., flow limitation achieved

at least over the lower portion [50%] of the forced expiratory curve). Increasing the jacket pressure will help to achieve flow limitation at high lung volume. However, as this may be accompanied by glottic closure and reflex stiffening of the chest wall, together with negative flow dependence at low lung volumes, the use of excessive jacket pressure must be avoided (14). Nevertheless, in some healthy infants, irrespective of jacket pressure used, flow limitation may not be achieved at high lung volumes.

The optimal jacket pressure can be assessed during either the tidal RTC (if partial FEF- volume maneuvers are also performed) (14) or the RVRTC itself (Section E2.3) (19).

Recommendation:

- Increase jacket pressure until no further increase in flow and volume parameters are obtained.

Area for future research:

- To assess the effect of multiple RVRTC maneuvers on subsequent FEF variables.

Inflation of jacket. Jacket inflation is triggered to force expiration as passive inflation approaches zero flow on the flow–volume loop. The mean duration of the rise time of jacket inflation (i.e., from 10–90% of jacket inflation) should be less than 100 ms (14). Jacket inflation should be maintained until forced expiration is complete, as seen by zero flow crossing on the FEF-volume curve or as determined by an expiratory or inspiratory threshold indicative of end expiration in automated systems. The trigger to deflate the jacket should be activated as soon as this threshold is reached. It should be noted that time for lung emptying increases with age and in the presence of airway disease. Although forced expiratory time from raised volume is usually less than 1 s in healthy infants, it may exceed 4 s in those with lung disease. As a guide, the setting for jacket deflation should be defaulted to a maximum of 5 s for spontaneously breathing infants, with jacket deflation being triggered either by this default setting or by end expiration, whichever is the sooner (Section E2.4).

Recommendations:

- Duration of the jacket rise time should be less than 100 ms.
- Jacket inflation must be maintained until forced expiration is complete.

Area for future research:

- To establish suitable criteria for determining end of forced expiration and/or inspiratory threshold after forced expiration

Monitor display during data collection. The following onscreen displays are recommended:

1. A continuous display of tidal volume or flow whenever the mask and apparatus are connected, not just during data collection
2. Ability to re-zero flow reliably before commencement of data collection (2)
3. Time-based displays of flow, volume, airway opening pressure (Pao), jacket pressure (Pj), and flow–volume plot
4. Alignment of the flow–volume plot to display expiration above and inspiration below the *x* axis (Figure 2)
5. An overlay of the three "best" curves (Section E2.6) with operator interaction to disable/enable as necessary
6. Selected results from all valid trials, with those from the best trial highlighted

Other features such as trend plot of results to identify best trial and the ability to toggle or zoom in on specific window display (e.g., flow–volume loop or individual trials to facilitate quality control) would be desirable.

TABLE 2. RECOMMENDED PARAMETERS AND SUGGESTED ABBREVIATIONS

Long Form	Unit	Short Form	Definition
Forced vital capacity* at specified inflation pressure	ml	FVCp	Expired volume from specified inflation pressure (i.e. generally 3 kPa) during the forced expiration
Forced expired volume* in 1 s	ml	FEV_1	Expired volume during the first second after start of forced expiration
FEV in 0.75 s	ml	$FEV_{0.75}$	Expired volume during the first 0.75 second after start of forced expiration
FEV in 0.5 s	ml	$FEV_{0.5}$	Expired volume during the first 0.5 second after start of forced expiration
FEV in 0.4 s	ml	$FEV_{0.4}$	Expired volume during the first 0.4 second after start of forced expiration
Trial FVC		FVCtr	Trial FVC
Maximal expiratory flow at x% FVC	$ml \cdot s^{-1}$	$MEF_\%$	Expiratory flow during forced expiration when x% of FVCtr left to be exhaled
Forced expiratory flow* at 50% FVC	$ml \cdot s^{-1}$	FEF_{50} (MEF_{50})	Expiratory flow during forced expiration at 50% of the trial FVC exhaled
FEF at 75% FVC	$ml \cdot s^{-1}$	FEF_{75} (MEF_{25})	Expiratory flow during forced expiration at 75% of the trial FVC exhaled
FEF at 85% FVC	$ml \cdot s^{-1}$	FEF_{85} (MEF_{85})	Expiratory flow during forced expiration at 85% of the trial FVC exhaled
FEF at 90% FVC	$ml \cdot s^{-1}$	FEF_{90} (MEF_{10})	Expiratory flow during forced expiration at 90% of the trial FVC exhaled
FEF between 25–75% of FVC	$ml \cdot s^{-1}$	FEF_{25-75} (MEF_{75-25})	Mean expiratory flow during forced expiration between 25 and 75% of the trial FVC exhaled (i.e., $0.5 \times FVCtr/[t25-t75]$)
$FEV_{0.5}/FVC$		$FEV_{0.5}/FVC$	Ratio of $FEV_{0.5}$ to FVC
Peak expiratory flow	$ml \cdot s^{-1}$	PEF	Peak expiratory flow during forced expiration
Inflation volume* of the last breath	ml	VIj	Inflation volume before jacket inflation to the forced expiration
Inflation pressure* of the last breath	kPa	PIj	Inflation pressure before jacket inflation. Average of the last five data points before the peak mouth pressure.
Jacket pressure	kPa	Pj	Jacket pressure
$V_{PEF}/\%FVC$	%	VP%FVC	Ratio of the expired volume at peak expiratory flow and the total expiratory volume as %
Duration of forced expiration	s	tFE	Expiratory time of the forced expiration. Use the time axis after back extrapolation to determine start of expiration and zero flow crossing as end. If no zero crossing identified before jacket released do not report tFE.
Time to peak expiratory flow	s	tPEF	Expiratory time until peak expiratory flow of the forced expiration. Use the time axis after back extrapolation to determine start of expiration.
Inspiratory time of the squeezed breath	s	tIj	Inspiratory time of last inspiration before jacket inflation to force expiration
Jacket compression time	s	tj	Time during which jacket is inflated. Only reported if zero flow crossing is not identified.

* Mean and coefficient of variation (CV) for FVC, FEV_t, $FEF_\%$, and other marked parameters are calculated from at least three technically acceptable maneuvers, where $CV = (100 \times SD/mean)\%$.

DATA ANALYSIS

Criteria for Acceptable Data

Technically acceptable maneuvers are those in which relaxation of the respiratory system is evident before the RTC maneuver (i.e., passive expiration, confirmed by visual inspection of the volume–time plot showing an exponential decay of flow) and where forced expiration proceeds smoothly without evidence of early inspiration, marked flow transients, or glottic closure (Figure 2). In addition, peak expiratory flow should be achieved before 10% volume is expired to avoid reporting of supramaximal flows at low lung volumes due to late or slow application of the forcing function. If errors are to be avoided in assessments of FVC and FEF at fixed proportions of FVC ($FEF_\%$), it is essential to ensure the infant has breathed out fully toward RV, ideally with a brief apneic pause after release of the jacket pressure. Examples of unacceptable data, such as early inspiration, late RTC, and so forth, are shown in Figures E1–E3.

Quality Control Parameters

Parameters that can be displayed and recorded to provide quality assurance and facilitate comparison of data within and between centers are documented in Section E2.6. Such quality control parameters should be reported when describing RVRTC measurements in infants. The use of the standard abbreviations, as indicated in Table 2, is recommended. Quality control during data analysis is facilitated by the ability to

1. Align FEF-volume loops (*1*) at start of forced expiration, (*2*) at RV to detect changes in FVC secondary to gastric distention, and (*3*) along the descending limb of the flow-volume curve.
2. Overlay all and/or selected technically acceptable loops.
3. Exclude (but not delete) selected (technically acceptable) trials during the analysis process.
4. Overlay successive flow–volume loops from the same test.
5. Overlay flow–volume loops from different tests (e.g., pre- and postintervention study).
6. Store and display selected flow–volume curves for subsequent reference.

Additional information regarding parameters that can be displayed and recorded to provide quality assurance and facilitate comparison of data within and between centers is on the web-based repository (online supplement Section E2.6).

REPORTING RESULTS

At least two technically acceptable maneuvers are required before reporting a result, provided that FVC, FEF_{25-75}, and $FEV_{0.4/0.5}$ are within 10% of each other. If there is only one good curve or variability is greater than 10% between the two maneuvers, then no result should be reported. The commonly reported parameters calculated from the RVRTC are as follows: FVC, $FEV_{0.5}$, FEF_{50}, FEF_{75}, FEF_{85}, and FEF_{25-75}. In infants younger than 3 mo, $FEV_{0.4}$ should also be reported because rapid lung emptying at this age often precludes measurements made beyond 0.5 s (15, 27). For clarity, $FEF_\%$ (U.S. convention) defines the forced expiratory flow when %FVC had been expired while $MEF_\%$ (European convention) relates to forced flows when %FVC remains in the lungs (i.e., FEF_{75} is equivalent to MEF_{25}). While maximal flow at FRC ($\dot{V}max_{FRC}$) is the parameter of primary interest obtained from partial forced expiratory maneuvers in infants, this parameter is not reported from RVRTC because the "end expiratory level" during the period of lung inflations may either be lower than that maintained dynamically during spontaneous breathing due to complete passive expiration, or relatively elevated due to presence of inadvertent or deliberate positive end-expiratory pressure. For this reason, reporting $\dot{V}max_{FRC}$ from RVRTC is likely to be highly variable and would

not correspond to that obtained from partial curves. Forced flows and volumes should be reported from the "best" trial. The best trial is generally defined as the one with either the highest sum of FVC and $FEV_{0.4/0.5}$ (15, 21) or the highest sum of FVC and FEF_{25-75} (19, 40). Differences between these two methods of selecting the "best" loop have been reported to be minimal (41). In contrast to partial forced expiratory maneuvers, these measurements are independent of changes in FRC, and it is therefore recommended that values from the "best" curve (not mean) are reported. The three best curves should be used for the calculation of mean (SD) and coefficient of variation, where "best" is based on technical criteria (*see* CRITERIA FOR ACCEPT-ABLE DATA).

Although values of $FEF_\%$ have a higher within-subject variability, these parameters have been reported to be more discriminative then FEV_t in some (20) but not all (15) studies. Of all the RVRTC FEF parameters, FEF_{75} and FEF_{25-75} have been found to be the least variable (15). FEF_{25-75} represents the average flow over an extensive volume range and is determined by dividing the volume expired between 25 and 75% of the FVC by time (in s) for this volume to be expired and is therefore less likely to be influenced by subtle flow transients (40). This is the standard method used in spirometry for older subjects (42). However, it is not certain whether flow will in fact always be limited at the higher lung volumes. On the other hand, as lung volume, and hence driving pressure and intraairway pressure, decreases, smaller airways are more likely to be flow limited (43), so that the integrated output of FEF at lower lung volumes (e.g., FEF_{75}), although not directly indicative of smaller airway function *per se*, may contain more clinically useful information regarding small airway function. Currently, the usefulness of flows measured at even lower lung volumes (e.g., FEF_{85} and FEF_{90}) is unknown.

Recommendations:

- Results from the "best" curve, defined as the one with either the highest sum of FVC and $FEV_{0.4/0.5}$ or FEF_{25-75}, are reported, provided they are within 10% of the next best loop.
- Reported parameters should include the following: FVC, $FEV_{0.4}$, $FEV_{0.5}$, FEF_{50}, FEF_{75}, FEF_{85}, and FEF_{25-75}.

REFERENCE DATA

Reference equations based on 155 healthy infants from two centers, with ages between 3 and 149 wk, have been published (19). The extent to which these "normative data" are applicable to other populations or data collected using different equipment has yet to be established. Preliminary work collating these data with those from an additional 253 healthy full-term infants (353 test occasions) studied at the Institute of Child Health, London, 155 infants from the United States and 25 infants from Brazil (M. Jones, unpublished data) has shown that FVC and $FEV_{0.5}$ are highly correlated to body length but this relationship was markedly nonlinear (Figures 4 and 5). In this collated population, FEF_{85} and FEF_{90} but not FEF_{75} were significantly diminished in boys compared with girls. Further work is being undertaken to examine the determinants of the various parameters derived from the RVRTC before publishing updated prediction equations using the collated data.

FUTURE WORK

During the past 10 yr, considerable progress has been made in developing and validating the RVRTC technique. Use of the RVRTC technique has, however, generally been limited to a few specialized laboratories throughout the world. Although recent availability of this technique on commercially available devices will lead to an increased use of this measure in the clinical setting, there are still many unanswered questions both from a physiologic and a clinical standpoint. Technical and physiologic issues within this technique, which require further investigations, are highlighted in the online supplement (Section E2.8).

Issues relating to clinical application of this technique that require further work include the need to evaluate the following:

- Within- and between-occasion repeatability before establishing clinical usefulness in assessing baseline airway function and response to intervention
- Effect of ethnic group, sex, birth weight, gestational age, and environmental and social factors on RVRTC parameters
- Prognostic value of parameters derived from the RVRTC with respect to subsequent respiratory morbidity (e.g., in cystic fibrosis and wheezing illnesses)

Because of the complexity of the technique and difficulties in studying large numbers of infants, multicenter collaboration will be crucial if these questions are to be addressed in a timely fashion. To ensure advances in this area of infant lung function testing, continued collaboration among international laboratories should be maintained.

SUMMARY OF RECOMMENDATIONS

The RVRTC technique provides the means of assessing airway function over an extended volume range.

Equipment

General recommendations regarding choice of facemask, pressure transducers, inflatable jacket, pressure source, and valves and connecting tubing, together with guidelines for optimizing data acquisition, are as published previously for the tidal RTC technique.

The apparatuses for the raised volume technique include the following:

- Mask
- PNT: this should be a low-resistance, low-dead-space device with a linear range appropriate for the high flows encountered during this technique and age/weight of the infant (e.g., up to 3,000 ml · s^{-1} in infants up to 10 kg)
- External air supply
- Valves for control of lung and jacket inflations
- Safety pressure relief valve for the control of inflation pressure

Data Collection

- The infant's chest and abdomen should be loosely wrapped (3–4 adult fingers' breadth) in a suitably sized jacket.
- Measurements should be made with the infant in a supine position with optimization of head position to achieve maximum patency of the upper airway.
- A leak-free seal at the mask is essential.
- Set inspiratory flow during lung inflations to approximately 1.5 times the peak tidal inspiratory flow.
- Raise lung volume to a standardized positive airway pressure of 30 cm H_2O unless specific contraindications exist.
- Record pressure at airway opening.
- Jacket inflation must be maintained until forced expiration is complete.
- Increase jacket pressure until no further increase in FVC and $FEF_\%$ is obtained.

Data Analysis

Technical acceptable maneuvers are those where

- Relaxation of the respiratory system is evident.
- Forced expiration proceeds smoothly without evidence of early inspiration, marked flow transients, or glottic closure.
- Peak expiratory flow is achieved before 10% volume is expired.

Reporting Results

- A minimum of two technically acceptable maneuvers are required before reporting a result, provided that FVC, FEF_{25-75}, and $FEV_{0.4}$ or $FEV_{0.5}$ ($FEV_{0.4/0.5}$) are within 10% of each other.
- The "best" trial is defined as the one with the highest sum of FVC and $FEV_{0.4/0.5}$ or highest sum of FVC and FEF_{25-75}.
- Commonly reported parameters are as follows: FVC, $FEV_{0.5}$, FEF_{50}, FEF_{75}, FEF_{85}, and FEF_{25-75}. $FEV_{0.4}$ should also be reported in infants younger than 3 mo.

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