Title:  Raised volume forced expirations in infants: guidelines for current practice

Author:  ATS/ERS Consensus statement

On-line data supplement
1. **DETAILED MEASUREMENT PROTOCOL**

1) The infant should be loosely wrapped in a suitably sized jacket, ensuring that 3-4 adult fingers (rather than 2 adult fingers as originally recommended for the tidal RTC technique) can still be inserted between the inner inflatable part of the jacket and the infant’s sternum so that there is no restriction in inflation volume. A recent study has shown that jacket pressure transmission may be improved when a slightly looser jacket is applied. Thus, for centers using both the partial and full forced expiratory maneuvers, a looser jacket fit is recommended so that this jacket fit can be maintained for both techniques, thereby lessening the chance of arousing the child during any readjustments.

2) A leak free seal at the mask is essential. The mask seal can be checked during tidal breathing by performing a brief airway occlusion at end-inspiration. Nevertheless, leaks could still occur at the higher inflation pressures of RVRTC. An upward inspiratory volume drift during lung inflations or failure to reach pre-set inflation pressure may be indicative of air leak.

3) Commence data collection when mask seal is achieved and infant is in quiet sleep. Care should be taken to support the facemask and the assembled unit (breathing apparatus) during the procedure to ensure the weight of equipment is not placed on the infant’s face.

4) Depending on the precise design of the circuitry, e.g. unless the bias flow is close to the child’s nose, augmented tidal breaths should commence as soon as possible after the breathing apparatus is attached to avoid exposing the child to excessive dead space and/or resistance.

5) Set inspiratory flow to 1.5 times the peak tidal inspiratory flow.

6) Lung volume is raised to a standardized positive airway pressure of 30 cm H$_2$O unless specific contra-indications, (i.e. for small, immature infants, lower inflation pressure ($P_{inf}$) (e.g. 20 cm H$_2$O) may be more appropriate).

7) The precise $P_{inf}$ delivered at the airway opening (rather than “set” pressure) should be measured and reported for comparison.

8) The computer screen should display both time based traces and flow-volume curves to enable the operators to see when to start and stop the inflations, how well inflations are synchronized with the infant’s pattern of breathing, when relaxation occurs and when adequate pressure and volume plateaux are achieved.
9) Once passive expiration is observed (Fig 2, main document) the jacket is inflated to a predetermined/optimal jacket pressure at the end of the next inflation to force expiration from raised lung volume (4).

2. CURRENT METHODOLOGICAL DIFFERENCES AND AREAS FOR FUTURE RESEARCH

2.1 Data acquisition and signal processing

2.1.1 BTPS and drift correction

BTPS and drift corrections of signals collected using the RVRTC technique may have a significant effect not only on measured volumes, but also on flow obtained, especially at low lung volume. This is an area of practice where there is still considerable uncertainty (5). This will need further investigation, which is beyond the remit of this paper. For RVRTC data published to date (6-11), it has been assumed that expiratory flows from raised volume are at BTPS and no further corrections have been implemented. Some systems do however apply at least a partial BTPS correction to inspiratory flow during tidal breathing, and most apply a standard time-based ‘drift correction’ to volume (but not flow) during tidal breathing. The latter should theoretically adjust for any discrepancies in inspired and expired volumes due to changes in gas composition throughout the breath. However the magnitude of volume drift may be influenced by many other factors, including any offset on the flow transducer, whether or not PEEP is applied during the RVRTC, presence of leak, pressurization of inspired gas and so forth (5), and the extent to which such factors should be adjusted for simply on the volume signal rather than on the primary flow signal has rarely been considered, particularly with respect to the potential distortion of flow-volume relationships derived from forced expiratory maneuvers. The most common (though non-validated) current practice is to assess magnitude of any volume drift during tidal breathing prior to any lung inflations and then to implement the derived ‘drift
correction’ to the entire recording including the RVRTC maneuver and any tidal breaths collected after the RVRTC maneuver. While we are currently not able to make any recommendations, the potential effects of such “corrections” on parameters derived from both partial and ‘full’ forced expiratory maneuvers is such that some consensus with respect to ‘best future practice’ should be reached as soon as possible to avoid any systematic bias between recording systems.

Factors affecting drift during the RVRTC technique include the following:

- Differences in gas composition during inspiration / expiration, which will be more marked during RVRTC maneuvers.
- Increased magnitude of volume changes, and alterations in the relative duration of inspiration and expiration when compared with tidal breathing.
- Pressurization of the inspired gas to 30 cm H$_2$O with subsequent decompression during expiration. The potential magnitude of this effect depending somewhat on configuration of the system used.

During the augmented breaths prior to forced expiration in the RVRTC, calculation of true drift is extremely difficult as the EEL may be influenced by a) presence of any positive end expiratory pressure (PEEP), and b) child expiring further towards relaxation volume (EEV) than during tidal volume.

As mentioned above, correction of volume drift without corresponding correction to the flow signal can distort the shape of the flow-volume curve and lead to bias between systems used. As this issue will need further investigation and is currently under debate, further guidance will be published once more information is available.

Area for future research:

- To ascertain ‘best practice’ for BTPS and drift correction of signals from RVRTC.
2.2 *Duration of inflations/augmented breaths prior to jacket inflation*

In some centers, to aid relaxation and standardize applied pressure at the airway opening, particularly on the breath prior to jacket inflation, lung inflation has been held until both a pressure and volume plateaux was observed (Fig 3). The mean duration of plateaux on the pressure and volume signals has been reported to be 150-250 millisecond and 50-100 millisecond respectively (1;12). Failure to reach a plateau on both the pressure and volume signals on the breath prior to forced expiration will give rise to more variability in the measured parameters (13). However, care should be taken to ensure that the inflation pressure is released as soon as the volume plateau is reached to avoid increased risk of gastric distension. A sustained drop in airway opening pressure or failure to reach a pre-determined value can usually be attributed to leaks around the mask.

Some centers deliberately (14) or inadvertently use a relatively short expiratory time to create positive end expiratory pressure (PEEP) during the inflations. This may help to stabilize upper airways that have a tendency to collapse, such as during snoring. In addition, the application of PEEP of 3 to 5 cm H_2O may assist in the generation of improved quality of forced expiratory flow-volume curves especially in those with symptoms of upper airway obstruction. While the application of PEEP does not seem to affect flows at low lung volume, flows at high lung volume including peak expiratory flow (PEF) and FEF_{25} may be reduced due to increased expiratory resistance of the circuitry.

In addition, some centers attempt to calculate expiratory reserve volume in relation to the end expiratory level that is re-established during tidal breathing following release of jacket inflation (15). While providing potentially valuable information, accuracy of this approach is dependent
on the absence of drift on the volume signal, the consistency of BTPS conditions and the absence of any effect of the RVRTC maneuver on lung mechanics or FRC.

Areas for future research:

? To ascertain the influence of volume history on RVRTC parameters.
? To ascertain most accurate method of assessing expiratory reserve volume.

2.3 Achievement of flow limitation
The ‘optimal’ jacket pressure during which flow limitation is achieved can be assessed during either the tidal RTC (if partial forced expiratory flow volume maneuvers are also performed) (1;16) or during the RVRTC itself (8). Assessment of ‘optimal’ jacket pressure during the tidal RTC technique appears to be valid for subsequent application during RVRTC provided the jacket fit is not adjusted between tests, since further increases in flow and volume were not achieved when higher jacket pressure was used (1). In addition, the jacket fit applied should be slightly looser than that recommended for tidal RTC in order to minimize restriction of inflation volume and improve jacket pressure transmission while maintaining the same jacket fit for both techniques (1). However, achievement of flow limitation is dependent on the precise equipment and techniques used. It is therefore advisable for new users to assess flow limitation from full flow volume curves. This is achieved by repeating maneuvers with increasing jacket compression pressures until the highest volumes and flows are obtained (8;15;17). While the former method has the advantage that both the time required for data collection and the number of lung inflations to which the infant is exposed is minimized, the latter method of estimating ‘optimal’ jacket pressure appears equally valid, but requires more lung inflations, which could potentially increase the risk of gastric distension and the possibility of influencing airway-parenchymal mechanics (18).
2.3.1 Jacket pressure transmission

Jacket pressure transmission is not routinely assessed in all centers but, in those that do, it is most commonly assessed at end tidal inspiration (9;19;20). While it has been suggested that assessment of pressure transmission at raised lung volume (i.e. end inflation) may be more informative (4), it cannot be generally recommended due to high transient intrathoracic pressures generated and increased risk of leaks (12). In an attempt to standardize the technique, it has been suggested that a constant transmission pressure of 20-25 cm H\(_2\)O (2-2.5 kPa) would be suitable for all infants during the RVRTC maneuvers (19). Since this level of transmission pressure will fail to achieve flow limitation in some healthy infants while causing negative flow dependence and glottic closure in others (1), most centers still prefer to adjust jacket pressure to obtain maximal flows within each individual. The latter approach has been shown to be discriminative a) between healthy infants and those with airway disease, b) in response to treatment and c) in detecting adverse pre and postnatal influences on early lung development (8-10;21). It also has the added advantage of simulating procedures used during spirometry in older subjects, which will potentially facilitate longitudinal follow up through the preschool and school aged years. Nevertheless, the potential advantages of standardizing both inflation and transmission pressures (7;19) and the fact that this approach, if applied carefully, could increase the discriminative power of this technique even further, should not be overlooked and deserves further investigation.

In the meantime, new users should be aware that most of the published reference data are derived from systems that have attempted to record maximal expiratory flows and volumes, assessed on an individual basis.

Recommendation:

? Increase jacket pressure until ‘flow limitation’ (as defined by no further increase in flow with increasing jacket pressure) is achieved.

RVRTC standardization repository

03 March 2004
2.4 Inflation of jacket

It is essential that jacket inflation is maintained throughout the entire expiration. However, the best approach to clarify inspiratory threshold following forced expiration is still to be determined. The use of zero flow crossing to determine the end of forced expiration or start of spontaneous inspiration is generally not appropriate as this criteria would include the expiratory pause. Some centers currently use $-5\text{mL.s}^{-1}$ to determine end expiration while others use up to $-20\text{mL.s}^{-1}$. The latter threshold may be preferable as a default value, provided it can be reduced when necessary for younger/smaller infants.

Areas for future research:

? To establish criteria for the determination of end of forced expiration and/or an inspiratory threshold following forced expiration.

? To reach agreement regarding duration of forced expiration. Currently this parameter is being reported both with and without inclusion of apneic pause.

2.5 Order of test

A recent study has reported that the raised volume technique can invoke measurable physiological changes in respiratory mechanics, as shown by a significant group mean reduction in maximum flow at functional residual capacity ($V'_{\text{maxFRC}}$) when measurements were repeated shortly after the raised volume technique (18). Consequently, the potential physiological effects of the raised volume technique on the underlying lung and airway mechanics need further investigation if we are to distinguish the effects of disease or therapeutic interventions from those of growth and development on the numerous parameters that can be derived from this increasingly popular technique. Meanwhile, the potential impact of the order of tests should be assessed in any given infant lung function protocol.

Area for future research:
To assess the effect of multiple RVRTC maneuvers on lung volumes and respiratory mechanics particularly in infants with reactive airway disease.

### 2.6 Quality control parameters

Parameters that can be displayed and recorded to provide quality assurance and facilitate comparison of data within and between centers include:

1) Number of acceptable maneuvers (n).
2) Total number of maneuvers performed (n_{tot}).
3) Inflation pressure of the ‘forced’ breath ($P_{ij}$); note that $P_{ij}$ should be calculated from the plateau attained and not from the maximum value recorded, which may represent a brief transient. For data to be comparable between infants whose lung volume has been raised to a pre-set inflation pressure (e.g. 30 cm H$_2$O [2.94 kPa]), those with fluctuations in $P_{ij} > 5\%$ (i.e. < 28.5 cm H$_2$O [2.8 kPa] or > 31.5 cm H$_2$O [3.1 kPa]) should be excluded as small differences in $P_{ij}$ will result in significant differences in FVC, FEV$_1$ and FEF$_{50}$ (13).
4) At the end of the RVRTC maneuver and before the onset of spontaneous inspiration, a period of apnea lasting at least 1-2 seconds should be recorded; otherwise FVC and FEF$_{50}$ data may not be acceptable due to failure to reach residual volume.
5) Jacket pressure ($P_j$) in kPa, calculated by excluding any overshoot and taking the mean $P_j$ over a plateau (minimum 100 milliseconds) towards the middle or end of jacket inflation, is calculated for each trial.
6) Rate of inflations.
7) Duration of inflation immediately prior to forced expiration ($t_{ij}$ in millisecond).
8) Inflation volume immediately prior to forced expiration ($V_{ij}$ in mL). If the infant takes a spontaneous breath/sigh in addition to the inflation, resulting in a higher inspiratory volume during the last lung inflation, or inspires early during forced expiration such that ‘FVC’ is less than inflation volume, data should be excluded.
9) Jacket compression time ($t_{comp}$ in seconds, i.e. duration of jacket inflation).
10) Jacket rise time ($t_{rise}$ in millisecond, i.e. time taken for jacket inflation (between 10-90% maximum $P_j$).
11) Jacket lead time ($t_{\text{lead}}$; in millisecond; i.e. the interval between end inspiration and onset of jacket inflation, which ideally should be zero).

12) Percent difference between two highest values of FVC, FEV$_t$ and FEF$_{\%}$.

13) Coefficient of variation of $P_j$ ($P_j$-cv), This is based on the mean (SD) of all technically acceptable maneuvers and where $n \geq 2$.

13) Duration of forced expiration ($t_{\text{FE}}$ in seconds). This should only be reported if zero flow (or appropriate threshold) is attained before the maneuver is automatically terminated by exceeding the default setting for duration of jacket inflation. If not, simply report $t_{\text{comp}}$.

14) Peak expiratory flow (PEF in mL.s$^{-1}$).

15) Volume expired at PEF ($V_{\text{PEF}}$ in mL).

16) $V_{\text{PEF}}$ as percentage FVC ($V_{\text{PEF}}\%$ FVC), which should not exceed 10%.

17) Equipment and version of the software with which data were collected.

18) Apparatus deadspace ($V_D$, app; in mL).

19) Type of mask, e.g. Rendell Baker size 1 or 2.

20) Whether putty was used.

Note: FVC obtained from the RVRTC technique is only an estimate. Even when using $P_j$ of 30 cm H$_2$O (2.94 kPa), infants have been observed to sigh at end inflation, resulting in considerable further increases in lung volume. Similarly chest wall reflexes may limit the extent to which expiration to residual volume occurs.

2.7 Rejection criteria of RVRTC data

Technically acceptable maneuvers are those in which forced expiration proceeds smoothly without evidence of early inspiration, marked flow transients or glottic closure and that the infant has breathed out fully towards residual volume. A minimum of 2 technically acceptable maneuvers with FVC, FEV$_t$ and FEF$_{\%}$ within 10% of each other are required, before reporting a result. Examples of rejection criteria are shown in figures E1-3.
2.8 Further investigations

Technical and physiologic issues within the RVRTC which require further investigation are highlighted below:

- the best way to adjust for BTPS/drift correction in RVRTC data.
- the performance of the PNT if pressurized during the maneuvers.
- whether the use of different types of masks or method of sealing such masks influence parameters obtained.
- whether ETCO$_2$ monitoring should be recommended for RVRTC studies in all spontaneously breathing infants, or only in those with severe lung disease.
- the impact of dead space on RVRTC parameters.
- the effect of increased resistance at high flows.
- whether application of cricoid pressure prevents gastric distension.
- the optimal inspiratory threshold following forced expiration.
- the separate effects of the number, size and duration of lung inflations on results obtained from RVRTC.
- the influence of volume history on RVRTC parameters.
- the best methodological approach to achieve actual reproducible inflation pressure of 30.0 cm H$_2$O during the last inflation prior to jacket activation, as opposed to the pre-determined inflation pressure.
- the separate effects of lung inflation and repeated thoraco-abdominal compression on lung mechanics and measures of RVRTC in infants.
- the relative advantages/disadvantages of assessing optimal jacket pressure in each infant vs. the use of a standardized transmission pressure for all infants.
- the effect of multiple RVRTC maneuvers on subsequent measures of lung and airway mechanics especially in infants with reactive airway disease.
Figure legends

Figure E1  Full jacket inflation achieved after release of inflation pressure, hence late peak expiratory flow (PEF) is observed. This may result in overestimation of flows at high lung volume.

Figure E2  Marked flow transients due to nasal or upper airway flutter on forced expiration. These flow transients can often be eliminated by adjusting the mask so that it does not partially obstruct the nose or adjusting the position of the head and neck or jaw.

Figure E3  Early inspiration during forced expiration.

Figure E4  Scatter plot of forced expiratory flow at 75% vital capacity (FEF_{75}) vs. length according to centers.

Figure E5  Scatter plot of mean forced expiratory flow from 25-75% vital capacity (FEF_{25-75}) vs. length according to centers.
Figure E1

Inflated breath prior to forced expiration

Late PEF due to late activation of jacket inflation

Flow (mL·s⁻¹)

Volume (mL)
Figure E2

Flow (mL.s$^{-1}$) vs. Volume (mL)
Figure E3

[Graph showing flow (mL/s) versus volume (mL) with labels indicating early inspiration and F=0.]
Figure E4

Forced expiratory flow at 75% FVC (mLs⁻¹) vs. Length (cm)

- USA
- London
- Brazil
Figure E5

Mean expiratory flow between 25-75% FVC (mL·s⁻¹) vs. Length (cm)

- USA
- London
- Brazil
3. REFERENCES


