Assessment of Respiratory Mechanics With Forced Oscillations in Healthy Newborns

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SUMMARY. Background: Lung function data in healthy newborn infants are scarce largely due to lack of suitable techniques, although data for developmental and prenatal exposure studies are much needed. We have modified the forced oscillation technique (FOT) for the measurement of respiratory mechanical impedance (Zrs) in unsedated sleeping infants in the first 3 days of life. Methods: Zrs was measured during 30-s epochs of quiet sleep in term neonates born via spontaneous vaginal delivery with a non-invasive FOT between 8 and 48 Hz. Total respiratory resistance (R), compliance (C) and inertance (I) were obtained by fitting Zrs spectra. Cluster analysis was used to determine a set of minimal Zrs spectra representing optimal respiratory mechanics for each infant. Results: Successful measurements were obtained in each of the first 3 days in 30/38 (78.9%) neonates. Group mean (± SD) values of R, C, I, and resonant frequency pooled for the 3 days were 45.9 ± 16.6 hPa s L^{-1}, 0.97 ± 0.21 ml hPa^{-1}, 0.082 ± 0.031 hPa s^2 L^{-1} and 19.2 ± 3.2 Hz, respectively. Within-session variability represented by coefficient of variation was 5.34 ± 3.18% for R and 13.80 ± 8.57% for C. Greater between-session variability was observed for the individual infants; however, the only statistically significant change over time was a 13% increase in R from day 1 to day 2. Parameter interdependence was significant ($r^2 = 0.63$) between R and I reflecting the large contribution of the upper airways to the total Zrs. Conclusions: Noninvasive measurement of Zrs can be made in neonates during natural sleep with a high success rate, even in the first hours of life. **Pediatr Pulmonol.**

Key words: infant pulmonary function; neonatal pulmonary medicine; pulmonary function testing (PFT); pulmonary physiology.

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INTRODUCTION

Factors limiting lung function at birth are likely to have lifelong consequences,[1] however, the causes are largely unknown as relatively few studies have collected lung function data at birth and in early life.[2,3] The major reason for this lack of information is the difficulty in measuring lung function non-invasively in infants and young children, especially with techniques that do not require sedation.

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Measurement methods for respiratory function in early life vary extensively in sophistication, non-invasiveness and ease in implementation and interpretation.[4] Early studies of infant lung function investigated pulmonary mechanics via the measurement of oesophageal pressure[5–11]; pulmonary resistance (RL) and dynamic compliance (CL) are solid measures, although their assessment would be difficult in large cohorts and in follow-up studies. More current work on the mechanics of the total respiratory system employed the single-breath occlusion method,[12–17] which is based on simple time constant (resistance-compliance) modeling. Analysis of the spontaneous breathing waveform[18–20] is easy to implement (and hence popular), but its inferential nature imposes serious limits on its applications in lung mechanics as control of breathing also impacts on the outcome variables. In addition, most investigations on lung function have focused on neonates or infants with respiratory symptoms or those born preterm, and data on healthy term newborns are scarce.

The forced oscillation technique (FOT) has the potential to provide non-invasive assessments of lung function by direct measurement of respiratory system impedance (Zrs), describing the resistive (dissipative) and reactive (energy storage) properties of the respiratory system as functions of oscillation frequency.[4,21] The FOT is simply applied during (and without interruption of) spontaneous tidal breathing and is suitable for the non-invasive assessment of lung function in infants and young children.[4] While the majority of the lung function tests in infants are performed under sedation, this is not a requirement for the FOT. The present study was undertaken to demonstrate the feasibility of measuring lung function in the first few days of life in healthy newborn infants using FOT. The successful introduction of the FOT for the measurement of neonatal lung function will facilitate studies addressing the effects of prenatal exposures on lung function at birth, and for studies assessing the impact of low lung function at birth on the risk of subsequent respiratory disease.

MATERIALS AND METHODS

Healthy neonates born at term following spontaneous vaginal delivery at the Department of Obstetrics and Gynaecology, University of Szeged, Szeged, Hungary were included in the study. The neonates did not have any congenital deformation, and they were free of any sign of disease including respiratory symptoms at the time of the recruitment. Lung function was measured using a modified FOT on each of the first 3 days of life during natural sleep. The study was approved by the Clinical Ethics Committee of the University of Szeged (No. 91/2011) and mothers gave consent for their infants to participate.

Measurement of Lung Function

The FOT measurements were made with purpose-built equipment (Fig. 1). A multi-component (8–48 Hz, peak-to-peak pressure of 2 hPa) forcing function was generated by a loud-speaker and delivered to the infant via a wave-tube (length 20 cm, internal diameter, 1 cm) through a face mask (Hudson RCI No. 41277, Teleflex Medical, Athlone, Ireland) and anti-bacterial filter (Humid-Vent,

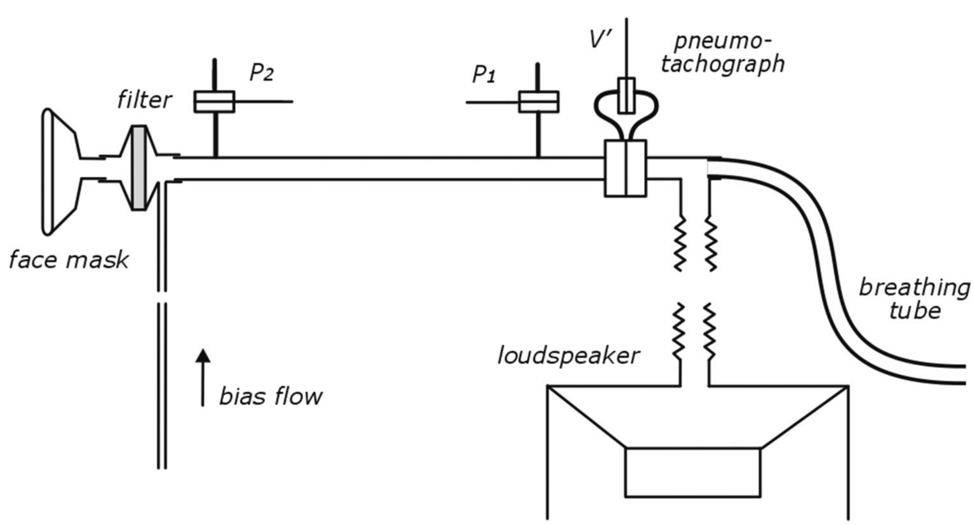

Fig. 1. Schematic representation of the equipment for the measurement of lung function with the forced oscillation technique (FOT). A loudspeaker is used to generate a multi-component forcing function. Pressure is measured at each end of a wave-tube (P1 and P2) for the estimation of respiratory impedance, and a pneumotachograph is used to monitor tidal breathing. A bias flow is employed to reduce the influence of equipment dead-space of the infant's breathing pattern.

No. 19502, Teleflex Medical). Inlet and outlet pressures of the wave-tube were sensed by identical transducers (ICS Model 33NA002D; ICSensors, Miltipas, CA). The mechanical impedance of the respiratory system (Zrs) was calculated as the load impedance on the tube,[22] following corrections for the parallel and in-series impedances of the filter and mask assembly. The deadspace of the equipment was continuously flushed by a bias flow of medical grade air at $2\,L\,min^{-1}$.

Zrs was measured during quiet sleep in the post-feeding period (5–60 min), with the head supported in a neutral position. On each measurement occasion, collection of a minimum of five technically-acceptable 30-s data epochs was targeted. However, if the measurements were interrupted by breathholds, cries or irregular breathing, and repeated placement of the mask was required to resume quiet sleep, further data epochs were collected to characterize the respiratory mechanics in the new conditions.

Model-Based Evaluation of Zrs

Each technically acceptable Zrs spectrum, i.e., those computed from regular breathing and not including a closure of the upper airways, cries, body movements and leaks around the face mask, was evaluated by fitting a resistance (R) - compliance (C) - inertance (I) model to the measured data: $Zrs = R + j\omega I + \left(\frac{1}{j\omega C}\right)$, where j is the imaginary unit and ω is angular frequency. Zrs values at 8 Hz were omitted from the estimation of R because of systematically higher values reflecting the contribution of tissue resistance (Fig. 2). In order to obtain a balanced contribution from the negative (elastance dominated) and positive (inertance dominated) data of Xrs in the model fitting, C and I were estimated from the Xrs data between 8 and 32 Hz. The Zrs spectra often exhibited large variability within a measurement occasion (Fig. 3). Therefore, in an attempt to represent "optimum" respiratory mechanics of the neonate on a measurement occasion, a subset of Zrs spectra belonging to the lowest values of R within a ±10% range and containing a minimum of three measurements was identified by cluster analysis, and the corresponding R, C, and I parameters were kept for further evaluation. Resonance frequency (*f*res) was calculated as $f\text{res} = \frac{1}{\left(2\pi\sqrt{CI}\right)}$.

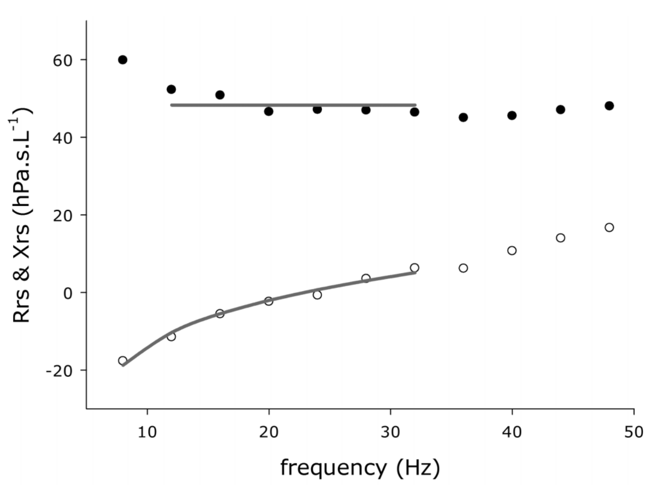

Fig. 2. Schematics of the fitting a resistance (R) – compliance (C) – inertance (I) model to the measured total respiratory resistance (Rrs, closed circles) and reactance (Xrs, open circles) data. Thick lines represent the average values for Rrs and the best-fitting C–I curves to the Xrs data in the 12–32 Hz range. See text for explanation.

Statistical Analysis

Repeated measures analysis of variance with the mixed linear model and Bonferroni–Holms correction (SAS® *Proc Mixed*, SAS Institute Inc., Cary, NC, USA) was used to determine differences in R, C, I, and *f*res among individual measurements from every infant over the first 3 days of life. The relationships between anthropometric and spontaneous breathing variables and respiratory mechanics were examined by using Pearson's correlation analysis, and the *t*-test was used in the comparison between sexes. Differences at a P value of < 0.05 were considered statistically significant.

RESULTS

Thirty-eight healthy neonates were enrolled in the study. Measurements of lung function on each of the first 3 days of life were obtained from 34 infants; measurements were unsuccessful in 2 due to nasal congestion and 2 who did not tolerate the face mask. In 4 further infants, leaks around the face mask were identified during the data analysis, reducing the study population to 30 infants who were born at a mean gestational age of 38.7 ± 1.2(SD) weeks, with a mean birth weight (BW) of 3249 ± 368 g and body length (BL) of 49 ± 2 cm, with no sex-related differences observed. Full details of each infant are listed in Table 1.

During a study session, the time between the first and last Zrs technically acceptable recording ranged from 3 to 20 min (average 9 min). Tidal volume (V_T), breathing frequency (*f*br), and minute ventilation (MV) were on average 24.3 ± 5.9 ml, 60.7 ± 14.1 min^{-1} and 1407 ± 382 ml, respectively. Small differences were seen between *day 1* and *day 3* in the average *f*br (from 61.5 to 58.8 min^{-1}, $P = 0.057$) and in V_T (from 23.6 to 25.2 ml, $P = 0.07$), with no changes in MV. The coefficients of variation of *f*br and V_T in each neonate were on the average 10.6 and 11.2%, respectively, with no difference between study days.

The group mean values of R, C, I, and *f*res data pooled for the 3 days were $45.9 \pm 16.6\,hPa\,s\,L^{-1}$, 0.97 ± 0.21 ml hPa^{-1}, $0.082 \pm 0.031\,hPa\,s^2\,L^{-1}$ and 19.2 ± 3.2 Hz, respectively. R varied significantly ($P < 0.0001$) over the

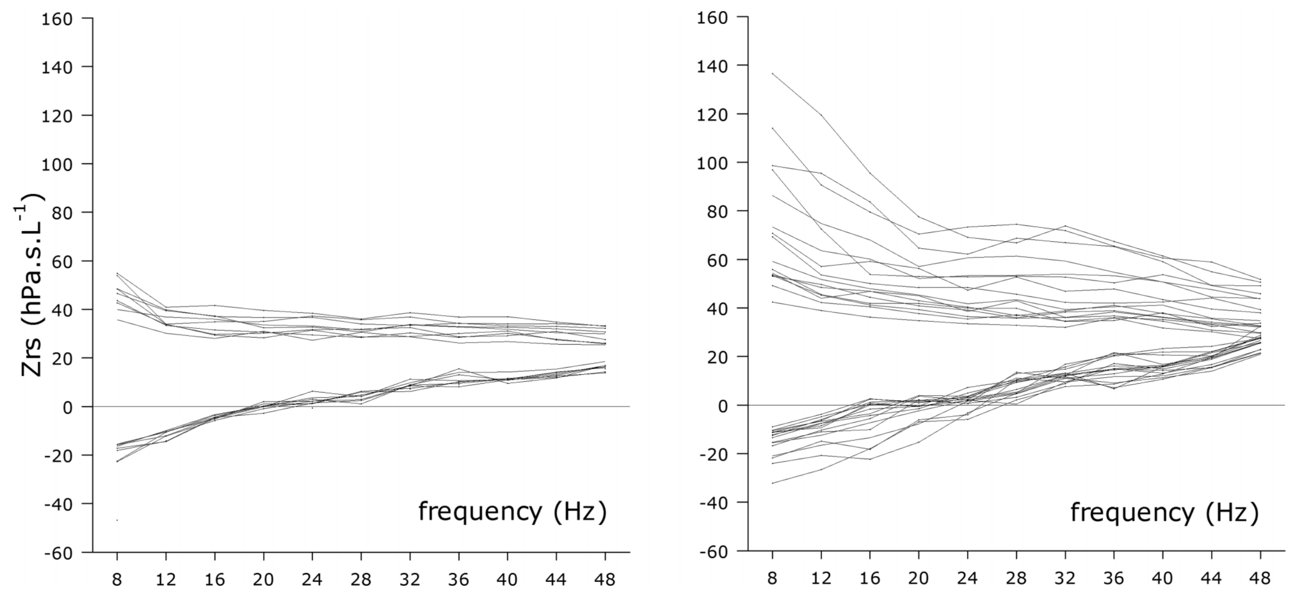

Fig. 3. Impedance (Zrs) spectra in terms of resistance (top) and reactance (bottom) versus frequency from two neonates, obtained in the same measurement sessions on the first day of life. Note the large variability in Zrs spectra in one case (right) and the subset of spectra belonging to low Rrs values.

TABLE 1— Demographic Data of the Neonates

Neonate	GA (wk)	BW (g)	BL (cm)	TC (cm)	Sex	APGAR
#1	38	3580	50	33	M	9,10,10
#2	40	3200	51	32	M	10,10,10
#3	38	2820	45	31	M	9,10,10
#4	40	3730	52	34	F	9,10,10
#5	37	2660	47	31	M	9,10,10
#6	39	2870	47	32	F	9,10,10
#7	40	3330	48	32	F	6,7,9
#8	37	2660	49	29	M	9,10,10
#9	37	2450	47	29	F	9,10,10
#10	37	3160	50	32	M	9,10,10
#11	38	3430	49	34	F	9,10,10
#12	40	3180	47	33	F	9,10,10
#13	39	3480	49	34	M	10,10,10
#14	39	3700	50	33	F	8,10,10
#15	37	2920	49	31	M	9,10,10
#16	39	3440	51	33	F	10,10,10
#17	40	3940	53	33	M	9,10,10
#18	38	3100	49	32	M	10,10,10
#19	40	3650	51	34	F	9,10,10
#20	37	3280	47	32	M	10,10,10
#21	38	2830	47	30	F	10,10,10
#22	41	3280	51	32	F	8,9,10
#23	39	3260	50	31	M	9,10,10
#24	40	3800	53	33	M	9,10,10
#25	39	3240	50	31	F	9,10,10
#26	37	3260	50	32	M	9,10,10
#27	39	3410	48	34	F	10,10,10
#28	39	3020	48	31	F	9,10,10
#29	38	3060	46	31	F	10,10,10
#30	40	3720	49	35	F	10,10,10

GA, gestational age; BW, body weight; BL, body length; TC, thoracic circumference; APGAR scores at 1, 5 and 10 min.

study period, primarily due to an increase between *day 1* and *day 2* (13%, $P < 0.001$), whereas C and I did not change (Fig. 4).

The within-session variability of parameters as characterized by the group mean coefficients of variation (CoV = 100 SD/mean) was ~3 times higher in C and I than that in R (13.80 ± 8.57 and 13.97 ± 6.59 *vs* 5.34 ± 3.18%), for all days. The individual CoV data are shown in Table 2.

Analysis of possible anthropometric and breathing pattern determinants (Table 3) of the Zrs did not show any dependence of the parameters on BW, BL, thoracic circumference or sex, except the weak correlations found between C and BW, and between C and BL. R and I were significantly correlated with *f*br and MV, whereas the significant determinants of C were V_T and MV (all $P < 0.01$). Statistically significant interrelationships were observed between R, C and I.

DISCUSSION

The FOT offers a non-invasive assessment of the resistive and elastic properties of the respiratory system, and its sophistication, sensitivity and the minimum cooperation required from the subject have led to increasing use in the lung function laboratories.[4,21] The data from the present study are the first to report measurements with the FOT in healthy term newborn infants. As the commercially available FOT devices are not suited for the infants, only a few investigations have addressed oscillation mechanics in this age group. The

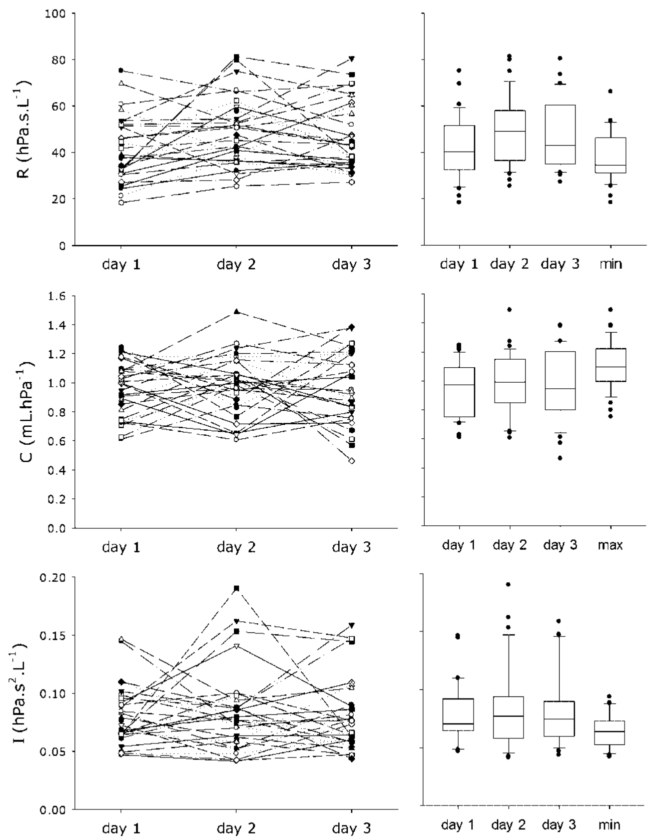

Fig. 4. Respiratory mechanical parameters on each of the first 3 days of life. Left: Estimates of resistance (R), compliance (C) and inertance (I) calculated for each neonate, plotted with different symbols and connecting lines. Right: box and whisker plots of R, C and I displaying the median and inter-quartile range for each parameter (dashed lines correspond to the mean values); right-hand boxes indicate the minimum values of R and I and the maximum value of C reached in the 3 days in each neonate.

subjects in those reports were older infants[23–33] who were sedated except in one study[32] or paralyzed, and most studies included subjects with respiratory complications.[23–26,28,31] Therefore, the results of the present study must be discussed in the context of the few observations made in the first days of life using other techniques.

The following specific issues arise in the discussion of the present results: the feasibility and potential of the non-invasive forced oscillatory measurements as performed during natural sleep in unsedated neonates; the physiological interpretation of the impedance data; and the variability of impedance parameters in the first days of life with the elucidation of the underlying mechanisms and its impact on the prediction power relating to the potential changes in lung function in later life.

Feasibility

The success rate in the present study that reflects successful measurements on each day was 79%. The major source of error was leak around the face mask, which was discovered only during post-hoc evaluation of the recordings. Leak detection can be improved with practice, indicating a likely higher success rate in experienced hands. Nevertheless, a success rate of 79% is similar[13] or higher than that of other follow-up studies[6,7,9] with different techniques and similar subject numbers. Simple tidal breathing methods, such as inductance plethysmography[17] can reach higher ($>90\%$) success rates. Only a few studies based on the single-breath occlusion technique[15,34] report success rates, which were as low as 50–55% due to the absence of relaxation, instability of end-expiratory volume (EELV) or expiratory flow braking. With the oscillations superimposed on uninterrupted tidal breathing as in the present study, obvious artefacts, such as glottic closure, apnoeic intervals, noisy breathing and long expirations suggesting a marked flow breaking can be identified in and omitted from the recordings. However, the changes in EELV and associated laryngeal or respiratory muscle flow braking will influence FOT measurements and contribute to within-session variability of respiratory resistance and compliance.

Variability

The day-to-day fluctuations in R, C, and I warrant consideration. It appears that in some neonates the lowest Zrs levels, as assessed by the low mean R, may not be reached during each measurement session, thus single sessions may be insufficient to characterize the optimal respiratory mechanics in a given infant. The day-to-day variations may be connected to different sleep phases[35–37] encountered in the successive sessions. By pooling data from all measurement occasions and identifying the minimum-R set in each neonate the likelihood of finding the optimum mechanical parameters (Fig. 4) increases.

Drorbaugh et al.[8] observed fluctuations in CL during successive measurements between a few minutes and a few days after birth that are comparable with the day-to-day variations in R and C in the present study. Repeated measurements of RL and CL between 1 hr and 1 wk also revealed considerable fluctuations, which appeared to correlate with the quietness of the infant during the measurement.[7] Overall, the variability of the FOT parameters obtained in the present study does not exceed that observed in previous studies employing different techniques. The sample size calculations (Table 4) suggest that 30% differences in the parameters of primary physiological importance (R and C), i.e., differences that are likely to be of clinical significance, can be detected with 80% power with group sizes of ≤ 20.

TABLE 2— Intraindividual Coefficients of Variation (%) of Resistance (R), Compliance (C) and Inertance (I) Recorded on Each of the First 3 Days of Life

	R			C			I		
Neonate	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
#1	5.88	8.41	4.60	9.70	16.47	16.55	13.76	16.19	14.39
#2	6.10	6.14	1.44	9.79	9.49	3.33	19.80	8.02	8.50
#3	14.19	8.43	7.01	10.13	3.91	17.67	25.52	17.78	11.62
#4	1.90	4.10	10.78	9.31	1.57	20.42	5.13	3.35	5.92
#5	5.45	4.37	1.48	12.77	26.56	9.13	10.16	19.65	8.87
#6	5.69	6.85	5.34	10.60	14.59	6.51	11.43	14.86	6.40
#7	13.14	5.13	1.70	8.57	16.57	11.38	11.14	11.88	17.56
#8	2.80	2.56	5.08	18.87	2.99	16.88	5.98	1.69	18.25
#9	3.97	5.19	2.39	2.98	19.68	9.68	2.97	14.19	2.71
#10	2.19	4.03	0.86	16.51	15.10	15.18	25.59	13.81	17.95
#11	5.86	10.00	6.32	10.56	31.32	6.52	12.07	10.04	13.11
#12	7.42	2.77	3.28	8.03	8.28	18.02	15.38	8.90	10.95
#13	1.80	5.14	4.64	15.75	18.77	24.87	8.99	32.25	18.25
#14	12.28	11.46	4.69	21.94	14.63	9.32	24.63	29.69	23.13
#15	6.11	3.25	2.34	3.92	13.74	49.83	10.10	25.82	27.82
#16	1.37	5.19	11.50	18.16	7.96	0.62	22.02	8.26	14.90
#17	6.96	7.31	11.22	2.96	15.06	12.15	6.95	14.51	27.56
#18	7.91	1.76	5.19	10.67	18.69	9.45	10.51	13.47	12.84
#19	2.49	2.31	8.07	11.28	4.95	16.78	10.21	20.36	13.80
#20	6.83	5.56	3.93	7.42	9.91	8.02	13.03	7.23	6.75
#21	7.42	4.21	10.83	20.08	9.89	17.37	14.16	14.30	9.93
#22	7.81	1.05	2.74	9.44	21.01	30.36	7.86	16.47	24.06
#23	1.84	1.26	3.05	7.80	8.79	9.34	10.58	22.02	8.03
#24	1.23	5.00	10.18	7.27	19.19	22.96	9.41	17.17	18.05
#25	3.21	5.07	3.91	22.84	11.50	16.06	8.94	12.28	17.67
#26	3.03	3.18	4.95	14.09	13.29	15.54	10.70	16.62	25.02
#27	7.68	4.76	7.31	25.68	14.07	52.93	9.25	7.41	16.01
#28	4.13	8.19	13.37	11.27	6.33	10.82	8.22	12.99	25.38
#29	2.66	3.27	8.33	6.43	11.07	10.07	8.71	15.51	6.18
#30	5.88	1.12	6.48	4.58	22.46	17.34	14.58	16.02	14.87
mean	**5.36**	**4.90**	**5.77**	**11.65**	**13.59**	**16.17**	**12.26**	**14.76**	**14.88**
SD	**3.48**	**2.60**	**3.44**	**5.95**	**6.89**	**11.49**	**5.86**	**6.85**	**6.89**

Temporal Changes

Previous reports of changes in respiratory mechanics during a study period are not consistent. Chu et al.[6] observed a ~32% increase in CL (but none in FRC) in healthy term newborns between < 3 and > 24 hr of age. Cook et al. measured RL and CL in 23 normal newborns[7]; the repeated measurements at a few hours and few days of age in several newborns did not reveal any systematic time-dependence in either variable. Lodrup Carlsen et al.[13] measured healthy term newborns on 5 successive days; most of the changes in Crs and Rrs occurred between the measurements at ~1 hr after birth and 1 day later. Sandberg et al. [18] studied healthy term neonates born by Caesarean section (CS) or vaginal delivery (VD) at 2 and 26 hr of age; Rrs increased from 29 to 59 hPa s L^{-1} in the CS group and from 36 to 56 hPa s L^{-1} in the VD group, whereas there was no change in Crs. It is therefore not surprising that in the present study, where the time of the

TABLE 3— Pearson Correlation Coefficients Between Respiratory Mechanical Parameters (Resistance, R; Compliance, C; Inertance, I), Spontaneous Breathing Measures (Breathing Frequency, *f*br; Tidal Volume, VT; Minute Ventilation, MV) and Anthropometric Data (Body Length, BL; Thoracic Circumference, TC; Head Circumference, HC; Body Weight, BW)

	R	C	I	*f*br	VT	MV	BL	TC	HC	BW
R	1	−0.33*	0.80*	−0.25#	−0.13	−0.24#	−0.05	0.11	0.04	0.01
C	−0.33*	1	−0.29*	−0.05	0.32*	0.23#	0.21#	0.20	0.18	0.30*
I	0.80*	−0.29*	1	−0.34*	0.07	−0.27#	−0.10	−0.03	0.05	−0.08

*$P < 0.01$
#$P < 0.05$

TABLE 4— Sample Size Calculations

	R (hPa s L^{-1})		C (ml hPa^{-1})	
mean ± SD	45.9 ± 14.6		0.97 ± 0.21	
power	80%	90%	80%	90%
difference	numbers/group			
25%	27	36	14	18
30%	19	25	10	13
35%	15	19	8	10
40%	12	15	6	8
45%	9	12	5	7
50%	8	10	5	6

Sample size (numbers/group) required to detect a difference of 25%, 30%, …, 50% in mean R and C between groups using *t*-tests and $\alpha = 0.05$, with power of 80% and 90%. The calculations are based on the values of R and C from all individual Zrs data sets (n = 368 measurements).

day 1 measurements ranged between 1 and 24 hr, no initial increase in C was observed. Interestingly, although in accord with earlier observations,[13,16] significantly lower levels of R measurements were observed in the present study on *day 1* than later, a finding that may be explained by hormonal activity connected to the labor.[38]

Resistance and Compliance

The few studies that involved the FOT[23,24,27,28,30–33] or the high-speed interruption technique[25] included infants who had respiratory illnesses, were premature or beyond the neonatal period[32]; therefore the Zrs data cannot be compared with that in the present study. Nevertheless, C measured using small-amplitude oscillations at frequencies much higher than the spontaneous breathing rate gives an effective compliance of the respiratory system, which is about 1 ml hPa^{-1},[28,30,32] i.e., ~5 times lower than the CL or Crs values estimated from spontaneous breathing or end-inspiratory occlusions. Our average estimate of C (0.97 ± 0.21 ml hPa^{-1}) relates similarly to the values of Crs or (Crs/BW) obtained with the single-breath occlusion technique: 4.9 ± 0.6,[15] 0.88–1.35 ml kg^{-1} hPa^{-1},[13] and CL (or CL/BW) from transpulmonary measurements: 4.9,[11] 1.9–9.6 ml hPa^{-1} [8] and 1.29 ± 0.30 ml kg^{-1} hPa^{-1}.[9]

As the resistance data are less influenced by the measurement frequencies, our mean R data are close to the previously reported values of Rrs obtained from transfer impedance measurements,[39] with the occlusion technique,[13,15,16] and RL determined from tidal breathing.[5,7,11] No inertance data that could be compared with our results have been reported in the literature.

Physiological Interpretation

The present study reveals a weak relationship between the values of the resistive and elastic parameters (R and 1/C, respectively), suggesting that the higher resistance of the total respiratory system is not strongly associated with a higher elastance (Fig. 5). This is not surprising in view of the relatively homogeneous population of our healthy term neonates, where other factors such as the dysanaptic lung growth[40] may weaken the relationship between the airway and tissue properties. However, the most likely explanation for this finding is that R contains a substantial contribution from extrathoracic airways (which may mask the interrelationship between the resistive and compliant properties of the respiratory tissues), and a similar contribution is expected to the inertance of the total respiratory system. Indeed, when I is plotted as a function of R a significantly stronger positive relationship is seen (Fig. 5). As the vast majority of total I (72%) originated from the nasal pathways in infants studied with the low-frequency FOT,[27] the close relationship observed in the present study suggests that the contribution of the nasal passages to R must be similarly large in neonates,

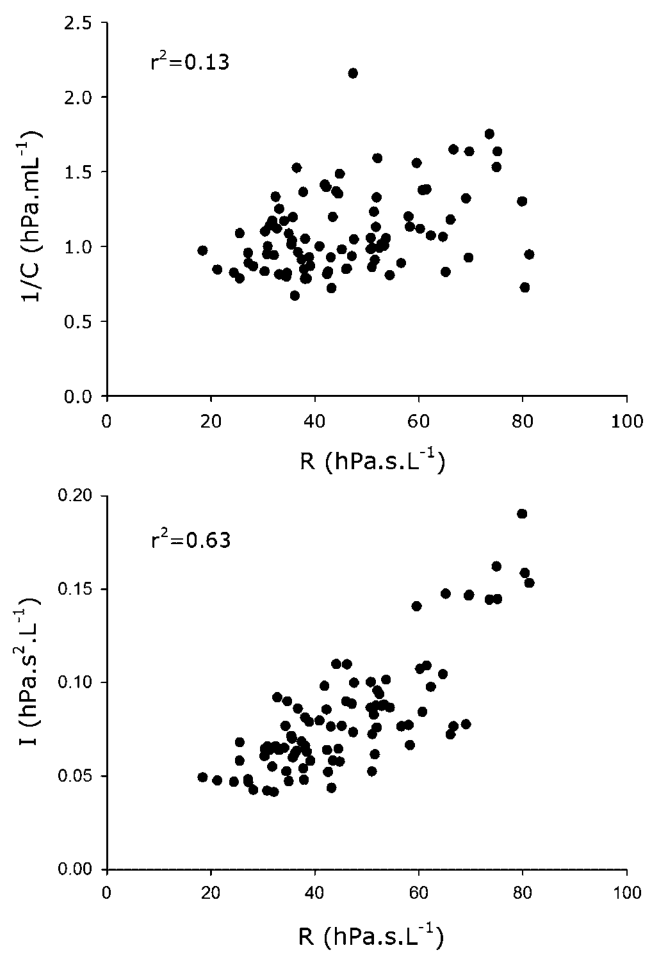

Fig. 5. Relationships between the reciprocal of compliance (1/C, top) and inertance (I, bottom) and the resistance (R) of the total respiratory system. Symbols correspond to the mean values from each neonate and measurement day.

i.e., around 50%. The masking effect of the nasal pathways on the resistive (and inertial) properties of the intrathoracic compartment is therefore an inevitable limitation of all measurements made noninvasively, i.e., through a face mask and the nasal passages. Nevertheless, the additional information on I offered by the FOT might help differentiate between groups where I and R are both elevated as a result of narrow upper airways, and where R is increased due to the restriction of the peripheral lung without a parallel rise in I.

Outcome Measures

The application of the FOT to newborn infants raises the question of the most appropriate outcome measures of neonatal lung mechanics. The specific airway and tissue parameters that can be obtained from low-frequency Zrs data collected during apnoea[33] are not available from medium-frequency measurements. *f*res and the area of reactance below zero (AX) are commonly derived from standard FOT and are reasonably informative measures of respiratory system compliance in children and adults breathing spontaneously through the mouth.[4] The utility of these variables is limited when Zrs is measured via the nasal pathways. Small nasal passages result in increased I (accompanying the elevation in resistance) and consequent decrease in *f*res and AX that are not related to lung mechanics. Therefore, the variables obtained from the classical R-I-C model fitting to the Zrs data appear to be the most appropriate measures for describing the mechanical status of the respiratory system in a newborn infant.

In conclusion, our data demonstrate that the measurement of lung function with forced oscillations superimposed on uninterrupted spontaneous breathing is feasible soon after birth. With all the limitations imposed by the variability of respiratory function in the neonatal period and the substantial contribution of the extrathoracic components to the total respiratory impedance, the FOT has the potential to produce outcome variables for studies assessing the effects of prenatal and perinatal factors on later respiratory health. This technique can also offer collection of baseline data for longitudinal studies measuring lung growth.

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