

Patient size	PIP / PEEP (init)	Set NO flow (ball)	Set FiO2	Meas NO flow	Ball	NO flow	Press comp	PIP / PEEP (with NO)	V _T	Bias Flow	Respiratory Care					Delivered NO	Delivered NO ₂	NO Calc 1	NO Calc 2	NO Calc 3
											Delivered FiO2	offset	FiO2 Calc 1	FiO2 Calc 2	FiO2 Calc 3					
											FiO ₂ d	FiO ₂ d - FiO ₂ SET								
4 kg	25 / 5	2	0.60	2.8	2.0	3.0	Y	25 / 5	23.6	11.4	0.67	0.07	0.66 (0.01)	0.65 (0.02)	0.65 (0.02)	12	0.2	17 (-5)	13 (-1)	15 (-3)
4 kg	25 / 5	2	0.80			3.0	Y	25 / 5	23.6	11.4	0.82	0.02	0.82 (0.00)	0.82 (0.00)	0.82 (0.00)	12	0.2	17 (-5)	13 (-1)	15 (-3)
4 kg	25 / 5	2	1.00			3.0	Y	25 / 5	23.6	11.1	0.97	-0.03	0.98 (-0.01)	0.98 (-0.01)	0.98 (-0.01)	13	0.2	17 (-4)	13 (0)	15 (-2)
4 kg	25 / 5	4	0.60	5.2	3.8	5.2	N	26 / 6	24.5	11.4	0.71	0.11	0.69 (0.02)	0.68 (0.03)	0.69 (0.02)	22	0.3	25 (-3)	22 (0)	25 (-3)
4 kg	25 / 5	4	0.80			5.2	N	26 / 6	24.5	11.4	0.84	0.04	0.83 (0.01)	0.83 (0.01)	0.83 (0.01)	22	0.3	25 (-3)	22 (0)	25 (-3)
4 kg	25 / 5	4	1.00			5.2	N	26 / 6	24.5	11.1	0.96	-0.04	0.97 (-0.01)	0.97 (-0.01)	0.97 (-0.01)	22	0.3	26 (-4)	23 (-1)	25 (-3)
4 kg	25 / 5	6	0.60	8.1	5.8	8.2	N	27 / 6	24.4	11.4	0.74	0.14	0.73 (0.01)	0.71 (0.03)	0.72 (0.02)	30	0.3	33 (-3)	30 (0)	32 (-2)
4 kg	25 / 5	6	0.80			8.2	N	27 / 6	24.4	11.4	0.85	0.05	0.84 (0.01)	0.84 (0.01)	0.84 (0.01)	30	0.4	33 (-3)	30 (0)	32 (-2)
4 kg	25 / 5	6	1.00			8.2	N	27 / 6	24.4	11.1	0.96	-0.04	0.96 (0.00)	0.96 (0.00)	0.96 (0.00)	31	0.4	34 (-3)	30 (1)	32 (-1)
4 kg	25 / 5	8	0.60	10.6	7.4	11.1	N	28 / 8	24.7	11.3	0.76	0.16	0.75 (0.01)	0.73 (0.03)	0.74 (0.02)	35	0.4	40 (-5)	35 (0)	38 (-3)
4 kg	25 / 5	8	0.80			11.1	N	28 / 8	24.7	11.3	0.86	0.06	0.85 (0.01)	0.84 (0.02)	0.85 (0.01)	36	0.5	40 (-4)	35 (1)	38 (-2)
4 kg	25 / 5	8	1.00			11.1	N	28 / 8	24.7	11.1	0.95	-0.05	0.95 (0.00)	0.96 (-0.01)	0.95 (0.00)	36	0.5	40 (-4)	36 (0)	38 (-2)
4 kg	25 / 5	10	0.60	13.7	9.1	14.2	N	29 / 10	24.8	11.5	0.78	0.18	0.77 (0.01)	0.75 (0.03)	0.76 (0.02)	40	0.5	44 (-4)	39 (1)	42 (-2)
4 kg	25 / 5	10	0.80			14.2	N	29 / 10	24.8	11.2	0.86	0.06	0.86 (0.00)	0.85 (0.01)	0.85 (0.01)	41	0.6	45 (-4)	40 (1)	42 (-1)
4 kg	25 / 5	10	1.00			14.2	N	29 / 10	24.8	10.9	0.94	-0.06	0.94 (0.00)	0.95 (-0.01)	0.95 (-0.01)	41	0.6	45 (-4)	40 (1)	42 (-1)
10 kg	18 / 5	2	0.60	2.7	1.9	2.7	N	19 / 6	60.5	11.3	0.68	0.08	0.66 (0.02)	0.65 (0.03)	0.65 (0.03)	11	0.3	15 (-4)	13 (-2)	15 (-4)
10 kg	18 / 5	2	0.80			2.7	N	19 / 6	60.5	11.3	0.81	0.01	0.82 (-0.01)	0.82 (-0.01)	0.82 (-0.01)	12	0.3	15 (-3)	13 (-1)	15 (-3)
10 kg	18 / 5	2	1.00			2.7	N	19 / 6	60.5	11.2	0.97	-0.03	0.98 (-0.01)	0.98 (-0.01)	0.98 (-0.01)	12	0.2	16 (-4)	13 (-1)	15 (-3)
10 kg	18 / 5	4	0.60	5.1	3.7	5.1	N	20 / 6	60.3	11.4	0.71	0.11	0.69 (0.02)	0.68 (0.03)	0.69 (0.02)	21	0.3	25 (-4)	22 (-1)	25 (-4)
10 kg	18 / 5	4	0.80			5.1	N	20 / 6	60.3	11.3	0.83	0.03	0.83 (0.00)	0.83 (0.00)	0.83 (0.00)	21	0.3	25 (-4)	23 (-2)	25 (-4)
10 kg	18 / 5	4	1.00			5.1	N	20 / 6	60.3	10.9	0.96	-0.04	0.97 (-0.01)	0.97 (-0.01)	0.97 (-0.01)	22	0.3	26 (-4)	23 (-1)	25 (-3)
10 kg	18 / 5	6	0.60	7.9	5.7	8.1	N	20 / 7	60.9	11.3	0.74	0.14	0.73 (0.01)	0.71 (0.03)	0.72 (0.02)	29	0.3	33 (-4)	30 (-1)	32 (-3)
10 kg	18 / 5	6	0.80			8.1	N	20 / 7	60.9	11.2	0.84	0.04	0.84 (0.00)	0.84 (0.00)	0.84 (0.00)	30	0.4	34 (-4)	30 (0)	32 (-2)
10 kg	18 / 5	6	1.00			8.1	N	20 / 7	60.9	11.1	0.96	-0.04	0.96 (0.00)	0.96 (0.00)	0.96 (0.00)	30	0.4	34 (-4)	30 (0)	32 (-2)
10 kg	18 / 5	8	0.60	10.6	7.4	11.0	N	21 / 8	60.7	11.4	0.76	0.16	0.75 (0.01)	0.73 (0.03)	0.74 (0.02)	36	0.4	39 (-3)	35 (1)	38 (-2)
10 kg	18 / 5	8	0.80			11.0	N	21 / 8	60.7	11.2	0.84	0.04	0.85 (-0.01)	0.84 (0.00)	0.85 (-0.01)	36	0.5	40 (-4)	35 (1)	38 (-2)
10 kg	18 / 5	8	1.00			11.0	N	21 / 8	60.7	10.9	0.95	-0.05	0.95 (0.00)	0.96 (-0.01)	0.95 (0.00)	36	0.5	40 (-4)	36 (0)	38 (-2)
10 kg	18 / 5	10	0.60	13.0	9.1	14.1	N	22 / 10	61.8	11.3	0.77	0.17	0.77 (0.00)	0.75 (0.02)	0.76 (0.01)	40	0.5	44 (-4)	40 (0)	42 (-2)
10 kg	18 / 5	10	0.80			14.1	N	22 / 10	61.8	11.1	0.86	0.06	0.86 (0.00)	0.85 (0.01)	0.85 (0.01)	40	0.5	45 (-5)	40 (0)	42 (-2)
10 kg	18 / 5	10	1.00			14.1	N	22 / 10	61.8	10.9	0.94	-0.06	0.94 (0.00)	0.95 (-0.01)	0.95 (-0.01)	41	0.6	45 (-4)	40 (1)	42 (-1)
20 kg	18 / 5	2	0.60	2.8	2.0	2.8	N	18 / 6	122	11.4	0.67	0.07	0.66 (0.01)	0.65 (0.02)	0.65 (0.02)	12	0.2	16 (-4)	13 (-1)	15 (-3)
20 kg	18 / 5	2	0.80			2.8	N	18 / 6	122	11.2	0.81	0.01	0.82 (-0.01)	0.82 (-0.01)	0.82 (-0.01)	12	0.2	16 (-4)	13 (-1)	15 (-3)
20 kg	18 / 5	2	1.00			2.8	N	18 / 6	122	11.0	0.97	-0.03	0.98 (-0.01)	0.98 (-0.01)	0.98 (-0.01)	13	0.2	16 (-3)	13 (0)	15 (-2)
20 kg	18 / 5	4	0.60	5.2	3.8	5.3	N	19 / 6	120	11.3	0.71	0.11	0.70 (0.01)	0.68 (0.03)	0.69 (0.02)	22	0.3	26 (-4)	23 (-1)	25 (-3)
20 kg	18 / 5	4	0.80			5.3	N	19 / 6	120	11.1	0.83	0.03	0.83 (0.00)	0.83 (0.00)	0.83 (0.00)	22	0.3	26 (-4)	23 (-1)	25 (-3)
20 kg	18 / 5	4	1.00			5.3	N	19 / 6	120	10.9	0.96	-0.04	0.97 (-0.01)	0.97 (-0.01)	0.97 (-0.01)	22	0.3	26 (-4)	23 (-1)	25 (-3)
20 kg	18 / 5	6	0.60	7.8	5.6	8.1	N	20 / 7	121	11.2	0.74	0.14	0.73 (0.01)	0.71 (0.03)	0.72 (0.02)	29	0.3	34 (-5)	30 (-1)	32 (-3)
20 kg	18 / 5	6	0.80			8.1	N	20 / 7	121	11.2	0.84	0.04	0.84 (0.00)	0.84 (0.00)	0.84 (0.00)	30	0.4	34 (-4)	30 (0)	32 (-2)
20 kg	18 / 5	6	1.00			8.1	N	20 / 7	121	10.9	0.96	-0.04	0.96 (0.00)	0.96 (0.00)	0.96 (0.00)	30	0.4	34 (-4)	30 (0)	32 (-2)
20 kg	18 / 5	8	0.60	10.4	7.4	10.7	N	20 / 8	120	11.2	0.76	0.16	0.75 (0.01)	0.73 (0.03)	0.74 (0.02)	35	0.4	39 (-4)	35 (0)	38 (-3)
20 kg	18 / 5	8	0.80			10.7	N	20 / 8	120	11.1	0.85	0.05	0.85 (0.00)	0.84 (0.01)	0.85 (0.00)	35	0.5	39 (-4)	36 (-1)	38 (-3)
20 kg	18 / 5	8	1.00			10.7	N	20 / 8	120	10.8	0.95	-0.05	0.95 (0.00)	0.95 (0.00)	0.95 (0.00)	36	0.5	40 (-4)	36 (0)	38 (-2)

20 kg	18 / 5	10	0.60	13.5	9.1	14.1	N	22 / 10	118	11.1	0.78	0.18	0.77 (0.01)	0.75 (0.03)	0.76 (0.02)	40	0.5	45 (-5)	40 (0)	42 (-2)
20 kg	18 / 5	10	0.80			14.1	N	22 / 10	118	11.1	0.86	0.06	0.86 (0.00)	0.85 (0.01)	0.85 (0.01)	40	0.5	45 (-5)	40 (0)	42 (-2)
20 kg	18 / 5	10	1.00			14.1	N	22 / 10	118	10.8	0.94	-0.06	0.94 (0.00)	0.95 (-0.01)	0.95 (-0.01)	41	0.6	45 (-4)	41 (0)	42 (-1)

Supplementary Table 1. Full bench test results using a volume targeted (6 mL/kg) ventilation strategy. See text for full list of abbreviations and details of calculations.

The 4 kg simulation was performed at 30 bpm while the 10 kg and 20 kg simulations were performed at 20 bpm. Units in table: NO and NO₂ - ppm, flow - L/min, V_T - mL.

Principle settings and results are in bold and calculated values are shaded. Labels are provided in the second row where appropriate. Patient size = simulated patient size.

PIP/PEEP (init) = Initial PIP and PEEP pressures required without NO flow present to achieve the targeted 6 mL/kg tidal volumes. Meas. = measured. Delivered NO flows

(F_{NOpre}) only measured once for each INOblender flow setting. Ball = INOblender flow as read from the top of the flowmeter ball after connecting tubing. Press comp =

indicates if pressures delivered by babyPAC could be compensated for, Y = Yes, N = No. PIP/PEEP (with NO) = PIP and PEEP pressures required with NO flow present

when unable to compensate to original pressure with PEEP set to the lowest achievable PEEP and PIP set to that required to achieve the targeted 6 mL/kg tidal volumes.

F_iO₂ offset (measured - set) = F_iO_{2d} - F_iO_{2SET}. F_iO₂ error (measured - calculated) = F_iO_{2d} - F_iO_{2th}. NO error (measured - theoretical) = NO_d - NO_{th}.

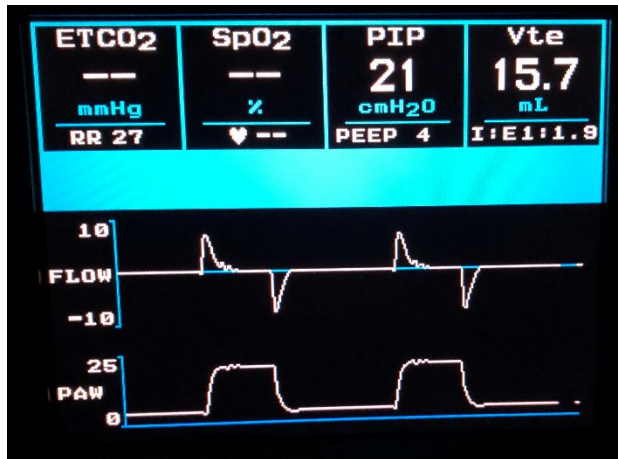
Set NO flow (ball)	Set FiO2	Meas NO flow	Ball	NO flow	Press comp	V _T	Bias Flow	Delivered FiO2	Respiratory Care			Delivered NO	Delivered NO ₂	NO Calc 1	NO Calc 2	NO Calc 3	
									FiO2 offset	FiO2 Calc 1	FiO2 Calc 2						FiO2 Calc 3
									FiO2d- FiO2SET								
F _{NOset}	FiO2 _{SET}	F _{NOpre}		F _{NO}		Fb	FiO _{2d}				NO _d	NO _{2d}					
2	0.21	2.9	2	2.9	Y*	14.9	12.5	0.35	0.14	0.34 (0.01)	0.31 (0.04)	0.34 (0.01)	12	0.2	15 (-3)	12 (0)	15 (-3)
2	0.40			2.9	Y*	14.9	12.8	0.54	0.14	0.49 (0.05)	0.47 (0.07)	0.49 (0.05)	12	0.2	15 (-3)	12 (0)	15 (-3)
2	0.60			2.9	Y*	14.9	12.7	0.69	0.09	0.66 (0.03)	0.64 (0.05)	0.65 (0.04)	13	0.2	15 (-2)	12 (1)	15 (-2)
2	0.80			2.9	Y*	14.9	12.4	0.82	0.02	0.82 (0.00)	0.82 (0.00)	0.82 (0.00)	13	0.2	15 (-2)	12 (1)	15 (-2)
2	1.00			2.9	Y*	14.9	12.5	0.94	-0.06	0.98 (-0.04)	0.98 (-0.04)	0.98 (-0.04)	13	0.2	15 (-2)	12 (1)	15 (-2)
4	0.21			5.1	Y†	13.8	12.5	0.43	0.22	0.41 (0.02)	0.39 (0.04)	0.42 (0.01)	20	0.2	23 (-3)	21 (-1)	25 (-5)
4	0.40			5.1	Y†	13.8	12.6	0.59	0.19	0.54 (0.05)	0.53 (0.06)	0.55 (0.04)	21	0.2	23 (-2)	21 (0)	25 (-4)
4	0.60			5.1	Y†	13.8	12.4	0.71	0.11	0.69 (0.02)	0.68 (0.03)	0.69 (0.02)	21	0.2	23 (-2)	21 (0)	25 (-4)
4	0.80			5.1	Y†	13.8	12.6	0.83	0.03	0.83 (0.00)	0.83 (0.00)	0.83 (0.00)	21	0.2	23 (-2)	21 (0)	25 (-4)
4	1.00	5.1	3.9	5.1	Y†	13.8	12.4	0.93	-0.07	0.97 (-0.04)	0.97 (-0.04)	0.97 (-0.04)	21	0.3	23 (-2)	21 (0)	25 (-4)
6	0.21	7.8	5.5	7.8	Y‡	13.3	12.4	0.48	0.27	0.48 (0.00)	0.45 (0.03)	0.49 (-0.01)	27	0.2	31 (-4)	28 (-1)	32 (-5)
6	0.40			7.8	Y‡	13.3	12.5	0.62	0.22	0.59 (0.03)	0.57 (0.05)	0.60 (0.02)	28	0.3	31 (-3)	28 (0)	32 (-4)
6	0.60			7.8	Y‡	13.3	12.5	0.72	0.12	0.72 (0.00)	0.70 (0.02)	0.72 (0.00)	28	0.3	31 (-3)	28 (0)	32 (-4)
6	0.80			7.8	Y‡	13.3	12.6	0.83	0.03	0.84 (-0.01)	0.83 (0.00)	0.84 (-0.01)	28	0.3	31 (-3)	28 (0)	32 (-4)
6	1.00			7.8	Y‡	13.3	12.5	0.92	-0.08	0.96 (-0.04)	0.97 (-0.05)	0.96 (-0.04)	28	0.4	31 (-3)	28 (0)	32 (-4)
8	0.21			10.6	Y§	12.5	12.4	0.53	0.32	0.53 (0.00)	0.50 (0.03)	0.53 (0.00)	33	0.3	37 (-4)	33 (0)	38 (-5)
8	0.40			10.6	Y§	12.5	12.5	0.65	0.25	0.63 (0.02)	0.61 (0.04)	0.64 (0.01)	33	0.3	37 (-4)	33 (0)	38 (-5)
8	0.60			10.6	Y§	12.5	12.5	0.75	0.15	0.74 (0.01)	0.72 (0.03)	0.74 (0.01)	33	0.4	37 (-4)	33 (0)	38 (-5)
8	0.80			10.6	Y§	12.5	12.5	0.84	0.04	0.85 (-0.01)	0.84 (0.00)	0.85 (-0.01)	34	0.4	37 (-3)	33 (1)	38 (-4)
8	1.00	10.4	7.3	10.6	Y§	12.5	12.3	0.91	-0.09	0.95 (-0.04)	0.96 (-0.05)	0.95 (-0.04)	34	0.4	37 (-3)	34 (0)	38 (-4)
10	0.21	13.2	9.2	13.8	Y	11.8	12.4	0.57	0.36	0.57 (0.00)	0.54 (0.03)	0.57 (0.00)	38	0.4	42 (-4)	38 (0)	42 (-4)
10	0.40			13.8	Y	11.8	12.4	0.67	0.27	0.66 (0.01)	0.64 (0.03)	0.66 (0.01)	38	0.4	42 (-4)	38 (0)	42 (-4)
10	0.60			13.8	Y	11.8	12.4	0.76	0.16	0.76 (0.00)	0.74 (0.02)	0.76 (0.00)	38	0.4	42 (-4)	38 (0)	42 (-4)
10	0.80			13.8	Y	11.8	12.4	0.84	0.04	0.85 (-0.01)	0.85 (-0.01)	0.85 (-0.01)	39	0.5	42 (-3)	38 (1)	42 (-3)
10	1.00			13.8	Y	11.8	12.3	0.91	-0.09	0.95 (-0.04)	0.95 (-0.04)	0.95 (-0.04)	39	0.5	42 (-3)	38 (1)	42 (-3)

Supplementary Table 2. Test results for 4 kg patient simulation using pressure controlled ventilation. Ventilation settings: PIP 20 cmH₂O, PEEP 5 cmH₂O and rate 30 bpm (inspiratory time 1 sec and expiratory time 1 sec). See text for full list of abbreviations and details of calculations. Units in table: NO and NO₂ - ppm, flow - L/min, V_T - mL. Principle settings and results are in bold and calculated values are shaded. Labels are provided in the second row where appropriate. Meas. = measured. Delivered NO flows (F_{NOpre}) only measured once for each INOBlender flow setting. Ball = INOBlender flow as read from the top of the flowmeter ball after connecting tubing. Press comp = indicates if pressures delivered by babyPAC could be compensated for, Y = Yes, N = No. * PIP reset to 20 cmH₂O but PEEP could not be reduced below 6 cmH₂O. † PIP reset to 20 cmH₂O but PEEP could not be reduced below 7 cmH₂O. ‡ PIP reset to 20 cmH₂O but PEEP could not be reduced below 8 cmH₂O. § PIP reset to 20 cmH₂O but PEEP could not be reduced below 9 cmH₂O. || PIP reset to 20 cmH₂O but PEEP could not be reduced below 10 cmH₂O. F_{iO₂} offset (measured - set) = F_{iO_{2d}} - F_{iO_{2SET}}. F_{iO₂} error (measured - calculated) = F_{iO_{2d}} - F_{iO_{2th}}. NO error (measured - theoretical) = NO_d - NO_{th}.

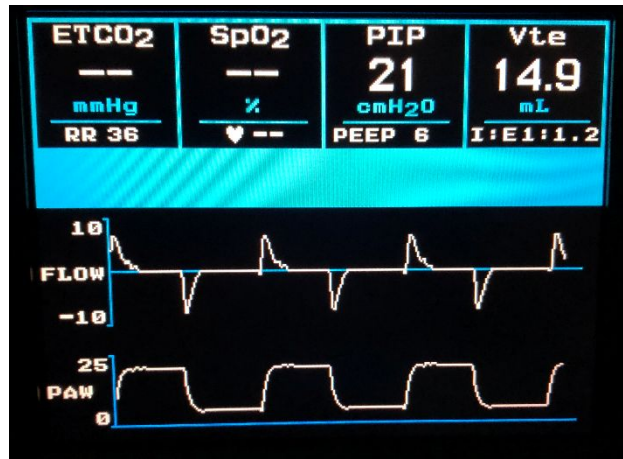


Supplementary Figure 1. Bias flow waveform examples. Photographs of sample bias flow waveforms at different rates (20 bpm and 40 bpm) and ventilation pressures (PIP 20 cmH₂O and 25 cmH₂O with PEEP 5 cmH₂O) at F_IO₂ of 0.60. Inspiration is indicated by the small decrease in flow with expiration marked by a small upwards deflection before stabilizing. A. 4 kg simulation with PIP 20 cmH₂O and PEEP 5 cmH₂O at 20 bpm. B. 4 kg simulation with PIP 20 cmH₂O and PEEP 5 cmH₂O at 40 bpm. C. 4 kg simulation with PIP 25 cmH₂O and PEEP 5 cmH₂O at 20 bpm. D. 10 kg simulation with PIP 20 cmH₂O and PEEP 5 cmH₂O at 40 bpm. E. 20 kg simulation with PIP 25 cmH₂O and PEEP 5 cmH₂O at 20 bpm.

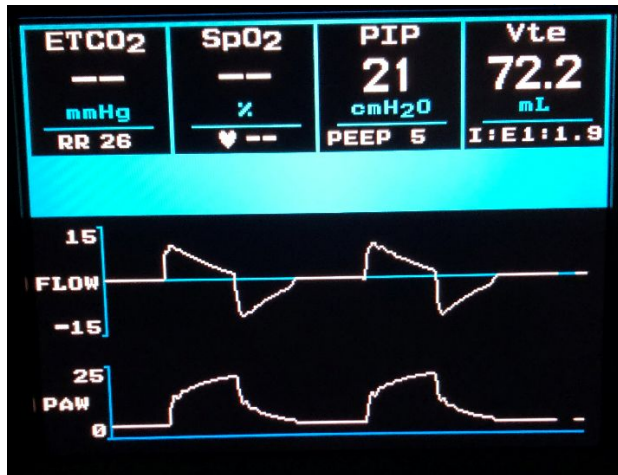
A



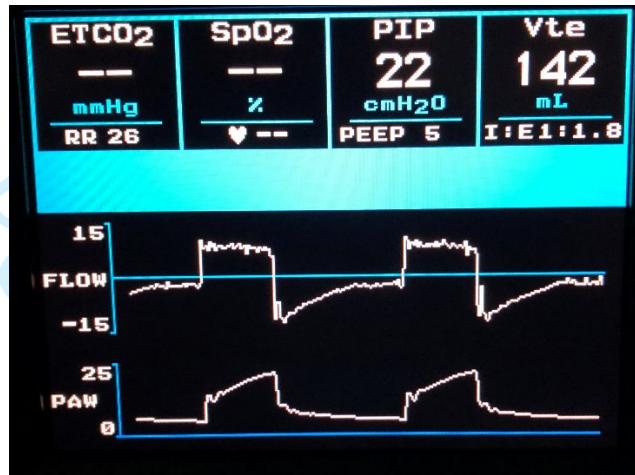
B



C



D



(see separate TIFF file for figure)

Supplementary Figure 2. Examples of flow and pressure waveforms. Photographs of sample flow and pressure waveforms measured between the circuit wye and test lung using a Respiratory Monitor (NM3 Respiratory Profile Monitor, Philips Respironics, Andover, MA, USA) for different size simulations and at different rates. Ventilator settings - PIP 20 cmH₂O, PEEP 5 cmH₂O. A. 4 kg simulation at 20 bpm. B. 4 kg simulation at 30 bpm. C. 10 kg simulation at 20 bpm. D. 20 kg simulation at 20 bpm (note the presence of some gas trapping).