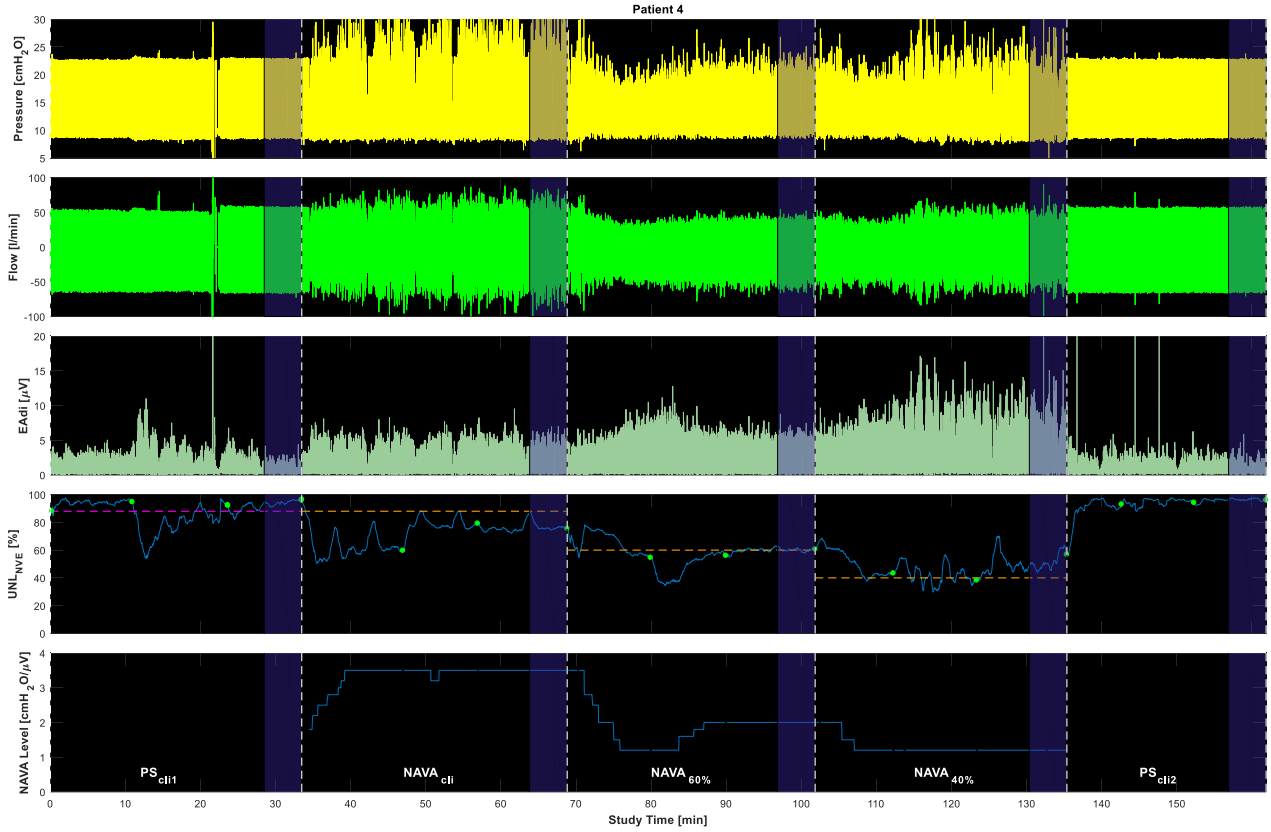
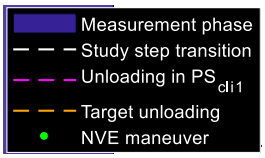
Screening test

The screening test was performed in neurally adjusted ventilatory assist (NAVA) starting with a low assist (NAVA level 0.5cmH_2O/µV) and increased in steps of 0.1 to observe if the peak EAdi was decreasing.

SDC-Fig. 1A. Study overview – Patient example



SDC-Fig. 1A. Example of patient 4 over the full study period. The randomization order was: $NAVA_{cli}$-$NAVA_{60\%}$-$NAVA_{40\%}$.



Legend to Fig. 1A.

PS_{cli1}: UNL_{NVE} was based on three repeated NVE-measurements during PS. The resulting median level of 88% is indicated with a dashed magenta line. This became the target level for $NAVA_{cli}$. The EAdi is heavily suppressed during PS_{cli1} due to the high unloading. The disturbance seen at around 22 minutes is due to airway suctioning.

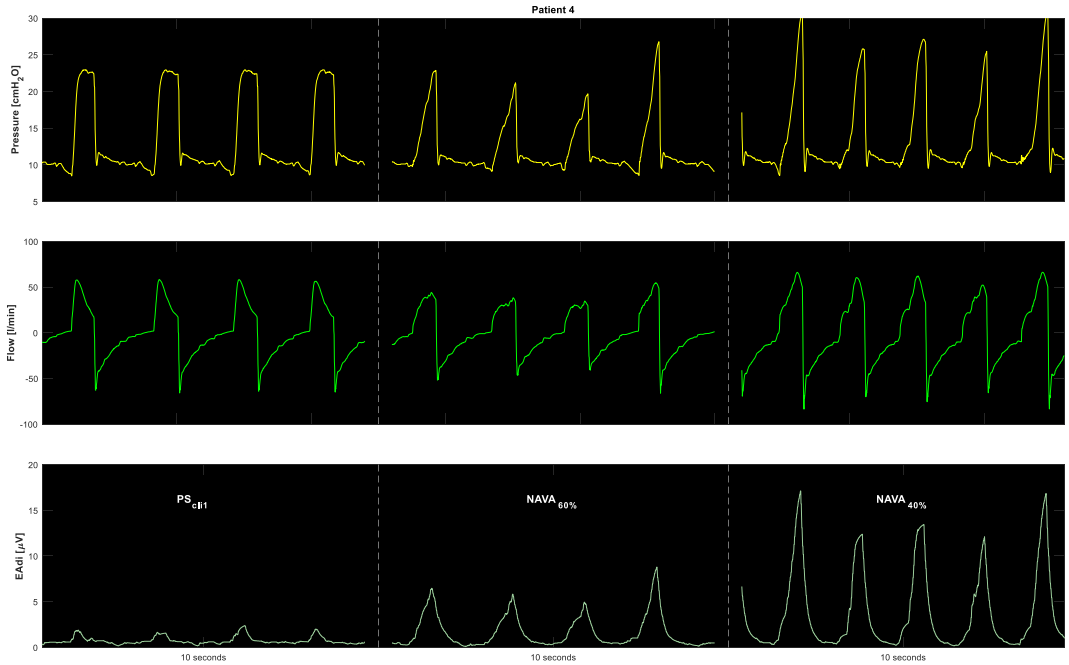
$NAVA_{cli}$: NAVA level was initially set to 1.8 $cmH_2O/\mu V$ based on the overlay window in SERVO-i to get started in NAVA. However, since the UNL_{NVE} displayed on the Servo Trend Tool indicated a too low unloading, the NAVA-level was then increased up to 3.5 $cmH_2O/\mu V$. In this patient however the $NAVA_{cli}$ target could not be reached.

$NAVA_{60\%}$: The NAVA level was adjusted, based on the UNL_{NVE} displayed on the Servo Trend Tool, in order to maintain the target of 60% unloading.

$NAVA_{40\%}$: The NAVA level was reduced to 1.2 $cmH_2O/\mu V$ to reach the target of 40% unloading. The EAdi increased with the reduction of unloading.

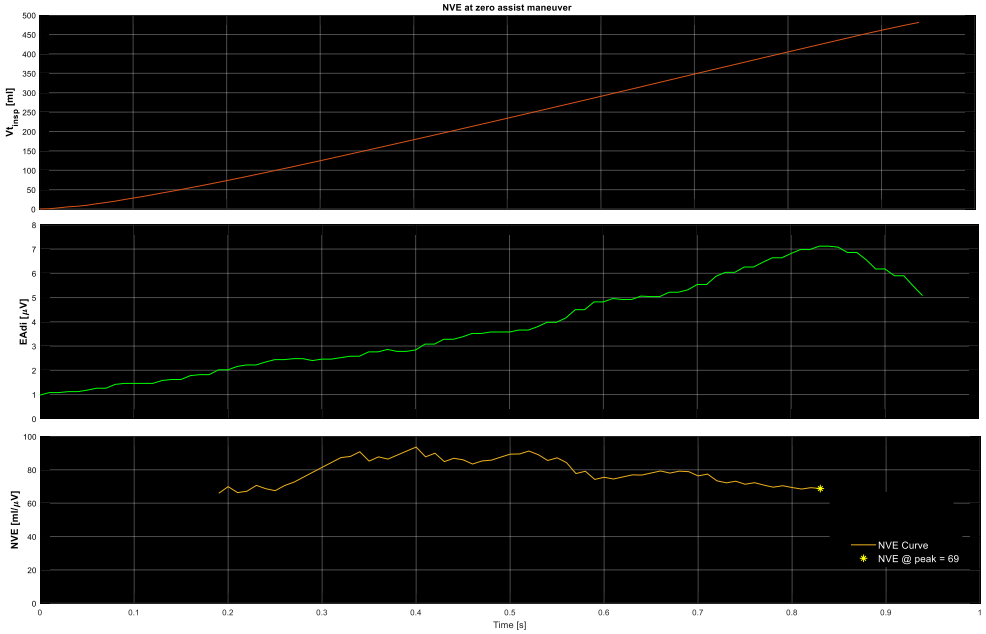
PS_{cli2}: The EAdi returned to similar levels as in PS_{cli1}.

SDC-Fig. 1B Ventilator curves in different study steps



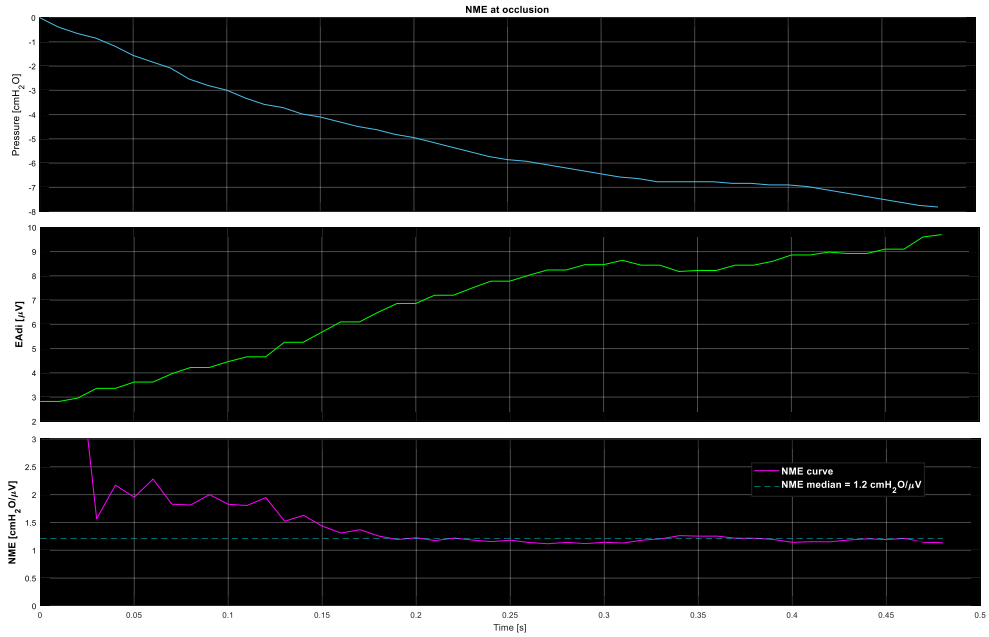
SDC-Fig. 1B shows one example of ventilation curves from patient 4 respectively in PS_{cli1}, $NAVA_{60\%}$ and $NAVA_{40\%}$. Observe the progressive increase in EAdi with reduced unloading.

SDC-Fig. 2 Neuro-ventilatory efficiency maneuver



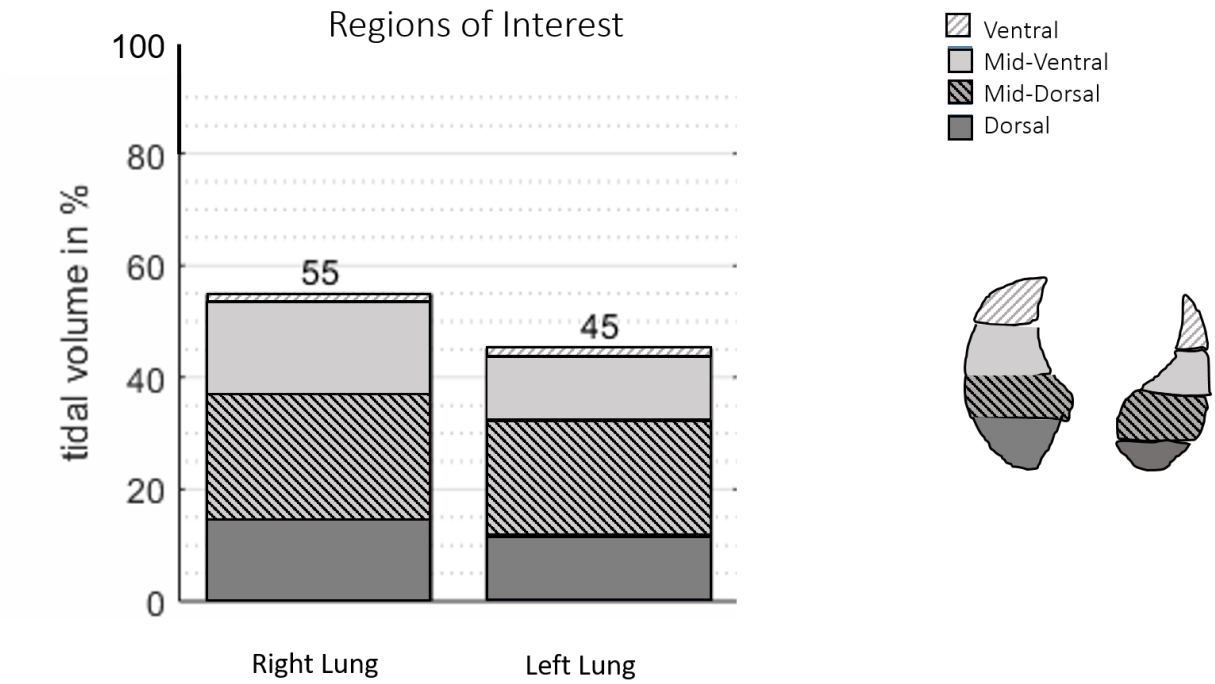
SDC-Fig. 2: Example of the ventilator curves during a zero-assist maneuver performed in order to obtain the neuro-ventilatory efficiency index. Vt_{insp}= inspiratory tidal volume, EAdi= electrical activity of the diaphragm, NVE= neuro-ventilatory efficiency.

SDC-Fig. 3 Neuro-mechanical efficiency maneuver



SDC-Fig. 3: Example of the ventilator curves during an occlusion maneuver performed in order to obtain the neuro-mechanical efficiency index. Paw= airway pressure, EAdi= electrical activity of the diaphragm, NME= neuro-mechanical efficiency.

SDC-Fig. 4 Regions of Interest of the right and left lung



SDC-Fig. 4: Example of the quantification of the different regions of interest in the lungs obtained from the output of the software for the analysis of the electrical impedance tomography images.

Global inhomogeneity index (GI)

According to the study by Zhao et al[1] to obtain the GI some calculation steps are required. First the difference between impedance at end inspiration and end expiration is determined for each breath, the so called tidal image. Then the median value between different tidal images is obtained, in our study 10 breaths were analyzed for each patient at each step. To determine the relative variation in each region of the lung occurring during tidal breathing, the difference in impedance from the median value is calculated. The sum of these differences from the median is then divided by the sum of all the impedance values in the lung (1). By this operation the GI becomes a value that can be compared between patients[1] or in the same patient in different ventilatory conditions.

$$GI = \frac{\sum_{x,y \in lung} |DI_{xy} - Median(DI_{lung})|}{\sum_{x,y \in lung} DI_{xy}} \qquad (1)$$

SDC-Table 1. Criteria for Discontinuation

Criteria	Physiologic parameters
Respiratory signs	RR> 35/min or RR < 8/min or SpO_2 < 90% for ≥ 5min or Abdominal Paradox or diaphoresis, dyspnea
Cardiovascular signs	Acute arrhythmias
Neurologic signs	Changes in mental status or signs of distress
Metabolic signs	Fever > 0,5° C increase during the study

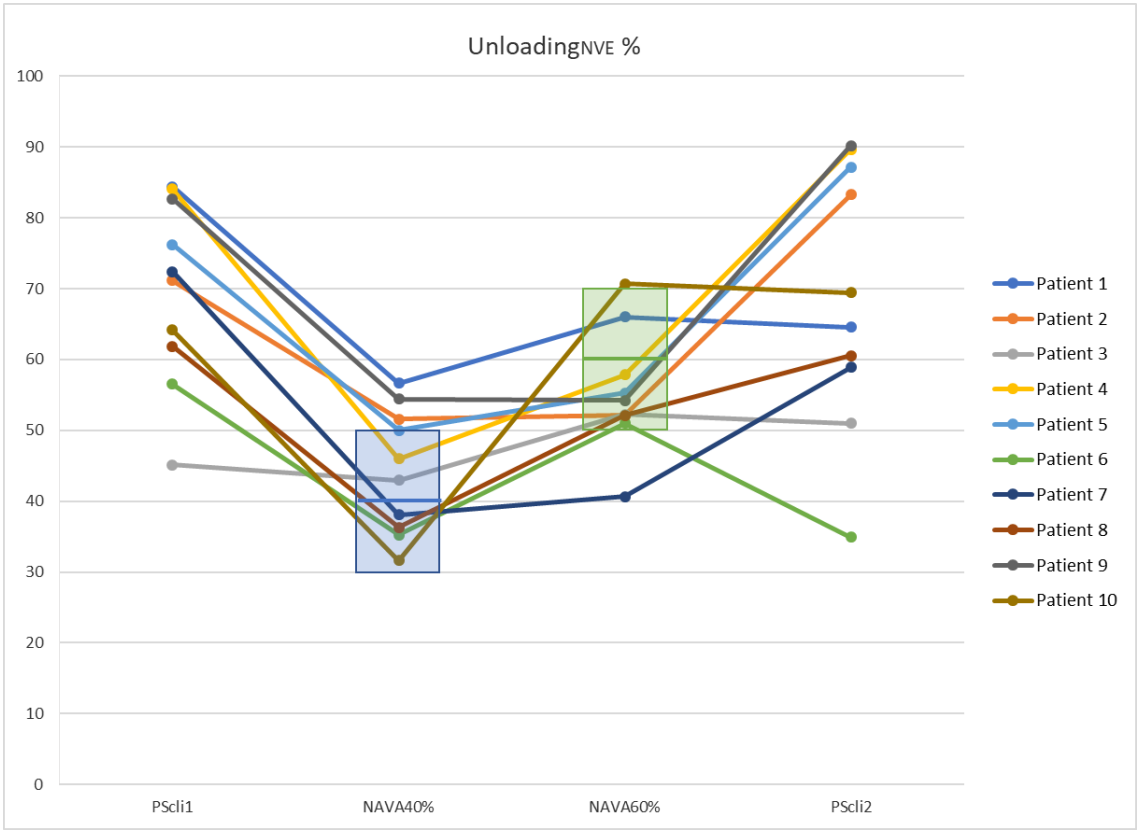
SDC-Table 1 reports the criteria that were used for discontinuation of the study and are based on changes in physiologic parameters. RR= Respiratory Rate, bpm= beats per min.

SDC-Table 2. Demographic data

Sex	Age (years)	Height (cm)	Weight (kg)	BMI	Diagnosis	Days from Intubation	PEEP (cmH_2O)	FIO_2	MAAS
M	64	175	75	24	ICH and TBI	3	5	0.30	1
M	23	174	57	19	TBI and cervical fracture (C6). Lung contusion	4	10	0.35	2
M	43	184	94	28	Cervical fracture (C7)	11	6	0.30	3
M	21	182	75	23	TBI	22	10	0.30	2
F	65	161	116	45	Cervical fracture (C6)	5	10	0.40	3
M	39	190	93	26	TBI	10	7	0.30	2
M	62	174	66	22	Status Epilepticus	5	10	0.40	2
M	64	180	95	29	ICH	4	10	0.30	0
M	33	183	76	23	TBI	11	10	0.25	2
M	55	175	101	33	ICH	13	10	0.35	2

SDC-Table 2 reports the demographic data of the patients included in the study. M = male, F = female; ICH = Intra-Cranial Hemorrhage; TBI = Traumatic Brain Injury; BMI = Body Mass Index; MAAS = Motor Activity Assessment Scale.

SDC-Fig. 5 Unloading$_{NVE}$ %



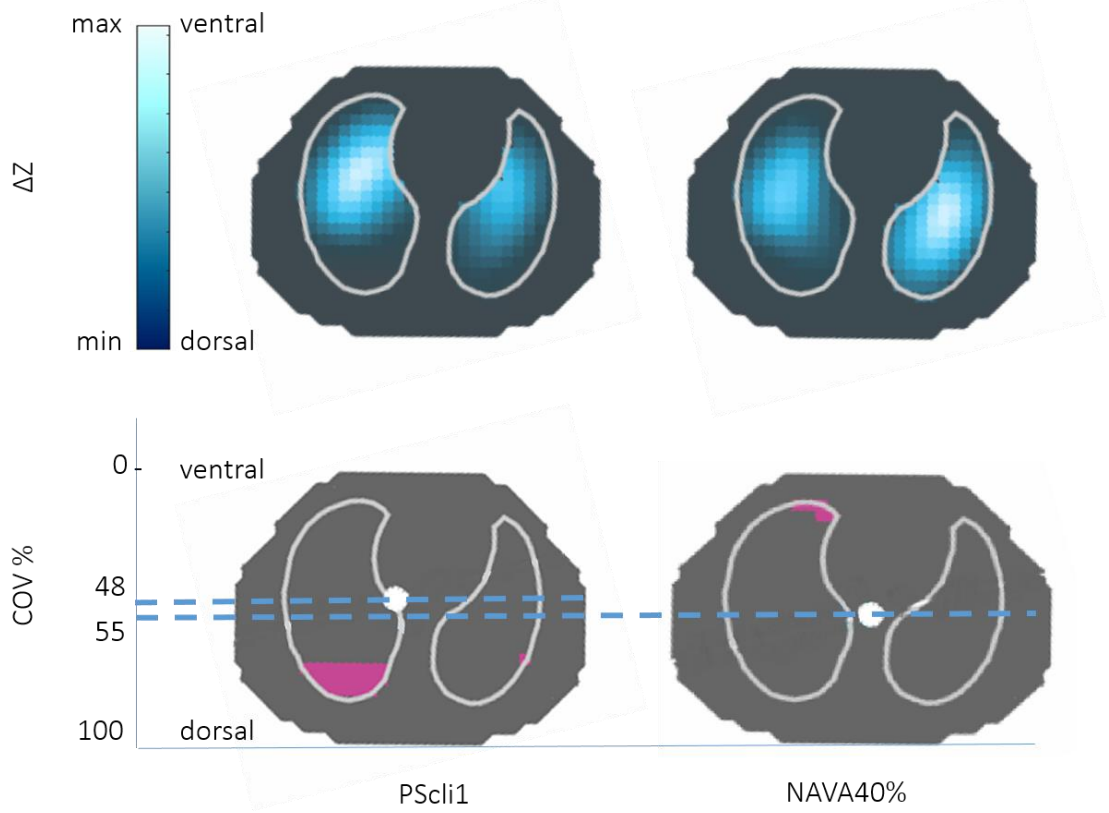
SDC-Fig. 5 illustrates the mean respiratory muscle unloading based on the neuro-ventilatory efficiency index reached in every patient during each 30 min study step. The blue rectangle indicates a range of ±10% from the 40% target unloading. The green rectangle indicates a range of ±10% from the 60% target unloading. PS$_{cli1}$: pressure support, Nava$_{40\%}$: Nava at 40% unloading; Nava$_{60\%}$: NAVA at 60% unloading; PS$_{cli2}$: same as PS$_{cli1}$.

SDC-Table 3. Clinically set PS (PS_{cli1})

Patient	PS_{cli1} (cmH_2O)	UNL_{NVE} in PS_{cli1} (%)	UNL_{NME} in PS_{cli1} (%)
1	10	87(79;93)	86(84;87)
2	10	77(62;87)	77(76;80)
3	7	46(35;55)	48(43;52)
4	12	88(78;95)	89(87;92)
5	12	79(67;85)	85(83;87)
6	4	60(45;71)	25(20;30)
7	10	77(66;85)	65(56;70)
8	8	64(54;72)	61(58;63)
9	9	86(76;94)	87(83;89)
10	8	63(54;76)	38(32;43)

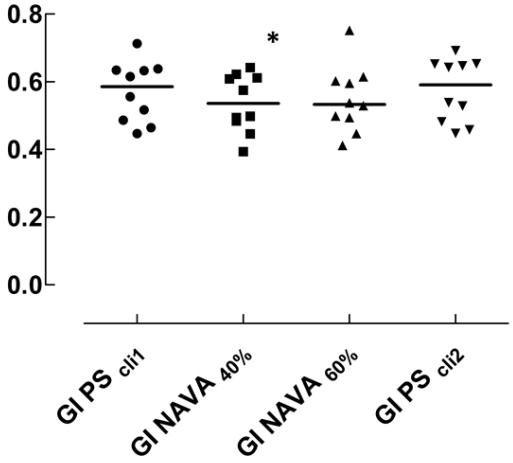
SDC-Table 3 illustrates the pressure support level clinically set (PS_{cli1}) in the patients and the percent respiratory muscle unloading measured with the neuro-ventilatory efficiency index and with the neuro-mechanical efficiency index during pressure support. UNL_{NVE}: $Unloading_{NVE}$; UNL_{NME}: $Unloading_{NME}$; The UNL_{NVE} reported is based on the entire PS_{cli1} period.

SDC-Fig. 6 Center of ventilation



SDC-Fig. 6 Example of electrical impedance tomography images of one patient while ventilated in pressure support (PS_{cli1}) on the left and in Nava with 40% muscle unloading ($Nava_{40\%}$) on the right. The upper picture shows the impedance variation, the picture at the bottom shows the change in position of the center of ventilation (CoV) from 48% in PS_{cli1} to 55% in $Nava_{40\%}$, more towards the dorsal regions of the lungs. ΔZ: impedance variation during tidal breathing. The dashed blue lines indicate the position of the CoV. The purple areas are regions of the lung not ventilated during tidal breathing.

SDC-Fig. 7 Global inhomogeneity index



SDC-Fig. 7 illustrates the global inhomogeneity index (GI) changes during the ventilation in the different study steps, obtained from the analysis of the electrical impedance tomography data. PS_{cli1}: pressure support, $Nava_{40\%}$: Nava at 40% unloading; $Nava_{60\%}$: NAVA at 60% unloading; PS_{cli2}: same as PS_{cli1}. Friedman RM anova GI p= 0.022; * p= 0.014 PS_{cli2} vs $Nava_{40\%}$

SDC-Table 4. Individual ventilatory parameters

Patient	Airway pressure (cmH_2O)				Respiratory rate (bpm)				Tidal volume (ml)				EAdi (µV)			
	PS_{cli1}	$Nava_{40\%}$	$Nava_{60\%}$	PS_{cli2}	PS_{cli1}	$Nava_{40\%}$	$Nava_{60\%}$	PS_{cli2}	PS_{cli1}	$Nava_{40\%}$	$Nava_{60\%}$	PS_{cli2}	PS_{cli1}	$Nava_{40\%}$	$NAVA_{60\%}$	PS_{cli2}
1	6.7 (6.5;6.8)	6.2 (6;6.4)	9.2 (9.2;12.2)	7.8 (7.5;8.2)	9	10	9	10	625 (619;635)	557 (480;582)	597 (368;822)	549 (376;706)	1.2 (1;1.4)	3.8 (3.4;4.3)	10.1 (5.1;13)	8.4 (3.2;19.8)
2	12.3 (12;12.4)	11.5 (11.3;11.6)	11.5 (11.3;11.8)	11.8 (11.7;11.9)	17	14	12	12	348 (336;358)	380 (357;403)	435 (407;461)	424 (415;431)	4,1 (3.4;5.7)	6.8 (6.1;7.6)	5.2 (4.4;5.7)	1.5 (1.2;1.8)
3	8.1 (8;8.2)	8.2 (7.8;8.6)	8.6 (8;9)	8.3 (8.2;8.4)	14	14	18	15	526 (508;549)	527 (479;600)	499 (406;574)	538 (520;555)	6.9 (5.9;8.2)	11.3 (9.6;13.3)	4.7 (4;5.6)	10.9 (9.4;12.7)
4	13.4 (13.3;13.5)	12.3 (12;12.5)	12.3 (12;12.7)	13.5 (13.1;13.6)	17	22	20	15	493 (488;497)	418 (485;446)	409 (381;444)	517 (508;534)	1.7 (1.2;2)	7.4 (6;8.5)	5 (4.6;5.5)	1.8 (1.5;2.4)
5	12.9 (12.7;13.1)	11.5 (11.2;11.6)	11.7 (11.2;12.5)	12.5 (11.9;12.7)	12	18	16	10	471 (465;484)	331 (331;356)	308 (249;371)	478 (471;495)	2.9 (2.4;3.4)	3.9 (3.6;4.2)	2.9 (2.4;3.3)	2.6 (2.1;2.9)
6	8.3 (8.2;8.4)	8.6 (8.4;9)	10.5 (9.9;11.1)	8.3 (8.2;8.4)	19	17	16	19	509 (495;525)	535 (510;564)	591 (493;653)	488 (472;499)	6.5 (4.9;8)	4.7 (3.9;5.5)	4.5 (3.7;5.3)	5.4 (4.3;6.2)
7	13.6 (13.3;13.8)	11.3 (11.2;11.5)	13.8 (13.2;14.5)	13.8 (13.7;13.9)	14	17	19	20	693 (634;721)	532 (493;580)	566 (502;612)	532 (509;560)	2.6 (2;3.8)	5.6 (4.7;6.4)	5.4 (4.7;6.2)	6.9 (5.7;8.4)
8	12.1 (12;12.2)	11.5 (11.3;11.6)	12.2 (11.9;12.6)	12.5 (12.3;12.6)	15	16	16	18	604 (591;618)	551 (511;587)	583 (542;638)	589 (561;614)	3.9 (3.6;4.4)	6 (5.5;6.6)	4.6 (4.1;5.1)	5.1 (4.6;6.4)
9	13 (12.8;13.1)	11.5 (11.2;11.9)	11.7 (11.4;12.1)	13.2 (12.9;13.4)	16	18	20	15	524 (505;545)	451 (346;513)	434 (387;481)	542 (523;648)	0.8 (0.7;1.1)	5.1 (3.7;6.8)	2.4 (2;3)	0.8 (0.6;1.3)
10	11.7 (11.5;11.9)	10.8 (10.7;10.9)	10.9 (10.7;11.1)	11.7 (11.5;11.8)	9	11	11	9	926 (869;961)	817 (738;876)	704 (631;847)	945 (899;1004)	2.4 (1.8;2.7)	4.3 (3.9;4.9)	2.5 (2.1;3.3)	2.6 (1.9;2.9)

SDC-Table 4 reports the individual ventilatory parameters in the different study conditions. PS_{cli1}: pressure support, $Nava_{40\%}$: Nava at 40% unloading; $Nava_{60\%}$: NAVA at 60% unloading; PS_{cli2}: same as PS_{cli1}.

Reference list

1. Zhao Z, Moller K, Steinmann D, Frerichs I, Guttmann J, (2009) Evaluation of an electrical impedance tomography-based Global Inhomogeneity Index for pulmonary ventilation distribution. Intensive Care Med 35: 1900-1906