

# Feasibility of high-frequency percussions in people with severe acquired brain injury and tracheostomy: an observational study

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## Abstract

People with severe acquired brain injury (pwSABI) frequently experience pulmonary complications. Among these, atelectasis can occur as a result of pneumonia, thus increasing the chance of developing acute respiratory failure. Respiratory physiotherapy's contribution to the management of atelectasis in pwSABI is yet poorly understood. We conducted a retrospective analysis on 15 non-cooperative pwSABI with tracheostomy and spontaneous breathing, hospitalized and treated with high-frequency percussion physiotherapy between September 2018 and February 2021 at the Neurological Rehabilitation Unit of the IRCCS "S. Maria Nascente - Fondazione Don Gnocchi", Milan. Our primary aim was to investigate the feasibility of such a physiotherapy intervention method. Then, we assessed changes in respiratory measures (arterial blood gas analysis and peripheral nighttime oxygen saturation) and high-resolution computed tomography lung images, evaluated before and after the physiotherapy treatment. The radiological measures were a modified radiological atelectasis score assigned by two radiologists, and an opacity score automatically provided by the software CT Pneumonia Analysis<sup>®</sup> that identifies the regions of abnormal lung patterns.

Treatment diaries showed that all treatments were completed, and no adverse events during treatment were registered. Among the 15 pwSABI analyzed, 8 were treated with Intrapulmonary Percussive Ventilation<sup>®</sup> and 7 with MetaNeb<sup>®</sup>. After a median of 14 (I-III quartile=12.5-14.5) days of treatment, we observed a statistical improvement in various arterial blood gas measures and peripheral nighttime oxygen saturation measures. We also found radiological improvement or stability in more than 80% of pwSABI.

In conclusion, our physiotherapy approach was feasible, and we observed respiratory parameters and radiological improvements. Using technology to assess abnormal tomographic patterns could be of interest to disentangle the short-term effects of respiratory physiotherapy on non-collaborating people.

## Introduction

Severe acquired brain injury (SABI) is the main cause of death and disability worldwide [1]. SABI generally arises as the neurolog-

ical consequence of a brain injury, which may also be associated with non-neurological complications, such as cardiovascular and respiratory impairments [1-3]. Focusing on respiratory complications, they have been proven to be significantly associated with an increased intensive care unit (ICU) stay, and their presence likely anticipates a worsening of neurological conditions [4]. People with SABI (pwSABI) report a high prevalence of respiratory complications (up to 80% of cases) [2], with pneumonia being the most common non-neurological complication, occurring in a range between 40 and 65% of people [5], and often preceded by atelectasis [2]. Chest physiotherapy can prevent respiratory complications and has therapeutic benefits in reducing atelectasis [4-6]. This result may be obtained through the adoption of interventions of secretion mobilization techniques and lung expansion therapies [7]. Mechanical devices to support lung expansion are generally combined with oscillating airflow and positive expiratory pressure therapy [8]. Nowadays, clinical practice is based on two main alternative devices for the treatment of atelectasis that seem promising: MetaNeb® System and Intrapulmonary Percussive Ventilation (IPV®) [7-8]. However, the literature underlines the scarce evidence regarding the clinical effectiveness of such devices and suggests deeper analysis to assess the precise physiological effects [9-12]. Particularly, none of the studies investigated the use of the two devices in the specific population of non-cooperative and tracheostomized pwSABI who spontaneously breathe with no mechanical ventilation support. Our study hypothesized that respiratory physiotherapy delivered to pwSABI using percussive devices could be feasible and safe. Therefore, the main objective of this study was to assess the feasibility of our physiotherapy approach; as a secondary aim, we assessed changes of various respiratory parameters and high-resolution computed tomography (HRCT); eventually, we compared the two devices (MetaNeb® and IPV®) used to treat patients in terms of radiologic scores.

## Materials and Methods

### Study design and participants

A single-center observational study was conducted at the Neurological Rehabilitation Unit of IRCCS “S. Maria Nascente - Fondazione Don Gnocchi”. All procedures are in accordance with the recommendations contained in STROBE. The protocol was approved by the local Ethics Committees and registered in ClinicalTrials.gov (NCT05630079). Medical records of people consecutively admitted for SABI from September 2018 to February 2021 were retrospectively investigated, and those treated with MetaNeb® or IPV® systems were included. Other inclusion criteria were: i) age over 18 years old; ii) spontaneous breathing 24h/24h; iii) presence of tracheostomy cannula; iv) presence of atelectasis diagnosed through HRCT; v) levels of cognitive functioning (LCF)  $\leq 5$ .

Exclusion criteria were: age <18, cardiac events, pneumothorax, pneumonectomy, hemoptysis, systolic blood pressure >180 or <80 mm Hg, heart rate >130 beats/min, and no consensus by the legal tutor.

### Respiratory physiotherapy practice

The standard internal procedure for people with a tracheostomy tube consists of the following: at hospital admission, the presence of atelectasis is evaluated through a chest X-ray, followed (if necessary) by HRCT. Respiratory parameters such as arterial blood gas analysis (BGA) and the monitoring of nighttime peripheral oxygen

saturation (SpO<sub>2</sub>) are recorded. Various clinical parameters are assessed and recorded, such as LCF (a scale between 1: no response and 8: normal response), body mass index (BMI), SABI etiology, and pharmacological therapy. Then, a respiratory physiotherapy treatment with the MetaNeb® system or IPV® is used for atelectasis treatment. The use of one device rather than the other depends on its availability in the department. After approximately 2 weeks, people are reassessed. The clinical protocol for atelectasis resolution through two devices involves 3 daily treatments of 20 minutes each, performed at approximately 4-hour intervals. Each treatment with the MetaNeb® system consists of four cycles: 5 minutes of continuous positive expiratory pressure (CPEP) for lung re-expansion (cycle I), 5 minutes of chest high-frequency oscillation for secretion clearance (cycle II), 5 minutes of CPEP (cycle III), 5 minutes of chest high-frequency oscillation (cycle IV). Each treatment with IPV®2-C consists of 3 daily treatments of 20 minutes with the higher mean airway pressure (MAP) and percussion frequency tolerated by the people and percussion inspiratory/expiratory time ratio: 1/1.2. Both treatments (MetaNeb® and IPV®) are performed by respiratory physiotherapists, and the pressure set is the highest tolerated by the people. The two treatments were associated with the administration of aerosols with 10 mL of saline solution 0.9% and carried out by connecting the tracheostomy cannula cuffed to the catheter mount. All people are treated in lateral decubitus with lung compromise in an antigravity position. When it is not possible, they are placed in a supine anti-trendelenburg position. During the treatment, each person is monitored, and each respiratory physiotherapist compiles a diary (e.g., heart rate, SpO<sub>2</sub>, date of beginning of the treatment, and pressure set). Treatment is interrupted only if, during the procedure, there are episodes of vomiting or desaturation (drop SpO<sub>2</sub>  $\geq 3\%$  not resolved with bronchoaspiration performed by a respiratory physiotherapist). To avoid adverse events due to the adoption of such postures, enteral nutrition is usually interrupted at least 1 hour before treatment.

### Aims and outcome variables

As our primary aim, feasibility was assessed by reviewing treatment diaries, reporting MAP administered, the posture assumed, the number of severe adverse events (e.g., episodes of desaturation, defined as a drop in SpO<sub>2</sub>  $\geq 3\%$  not fixable after bronchoaspiration and vomiting), and the number of treatments completed.

As our secondary aim, we assessed eventual changes of the respiratory (BGA and the monitoring of SpO<sub>2</sub> during the night) and radiological parameters. We compared respiratory parameters evaluated before and after physiotherapy intervention. To assess changes in HRCT acquired before and after physiotherapy intervention, we used two approaches. First, a modified radiological atelectasis score (mRAS) was assigned by two radiologists, then an opacity score (OS) was obtained with a software that uses an artificial intelligence algorithm to automatically detect and quantify abnormal computed tomography (CT) patterns commonly found in lung infections. Eventually, radiologic scores (mRAS and OS) were also compared between pwSABI using IPV® and MetaNeb®.

The atelectasis was evaluated by two independent radiologists (they provided blind scores to each other and blindly in terms of devices). A mRAS [13] (8-point scale from 0 to 4), ideated in accordance with two radiologists working at *Fondazione Don Gnocchi ONLUS*, was assigned to each HRCT, with the following criteria: 0 - no atelectasis; 1 - linear atelectasis; 1.25 - linear atelectasis, 1/3 of hemidiaphragm; 1.50 - linear atelectasis, 2/3 of hemidiaphragm; 1.75 - complete hemidiaphragm; 2 - lobar consolidation; 3 - lobar collapse; 4 - bronchial consolidation. Then, the HRCTs were semi-

automatically processed using the Software Siemens Syngo.via CT Pneumonia Analysis (Siemens Healthineers, Erlangen, Germany), which allows the quantification of lung CT hyperdense areas for research purposes. The software is based on an artificial intelligence algorithm, and it automatically segments lungs, lobes, and detects abnormal CT patterns usually present in lung infections (opacity regions). The quality of the automatic segmentation was checked by an expert radiologist, who modified the contours using the editing tool, if necessary. The volume of the opacity regions was extracted for each lobe and expressed as absolute volumes (in mL) and as a percentage over the lobe volume. Based on the percentage of opacity of a specific lobe, an OS was provided by the software. OS has a range of 0-4 with an incremental step of 1. The values are given with the following criteria: 0 - no opacity; 1 - percentage of opacity  $\leq 25$ ; 2 - percentage of opacity between 25 and 50; 3 - percentage of opacity between 50 and 75; 4 - percentage of opacity above 75. The left and right lungs were separately evaluated, and the respective OS was obtained, summing up the OS of each lobe.

## Data collection

Patients' data were extracted from the clinical and rehabilitation records. Data were recorded anonymously and were identifiable by an alphanumeric code. The researchers in charge of the statistical analysis had access to an anonymized database whose data did not allow tracing the identity of the interested parties.

## Statistical analysis

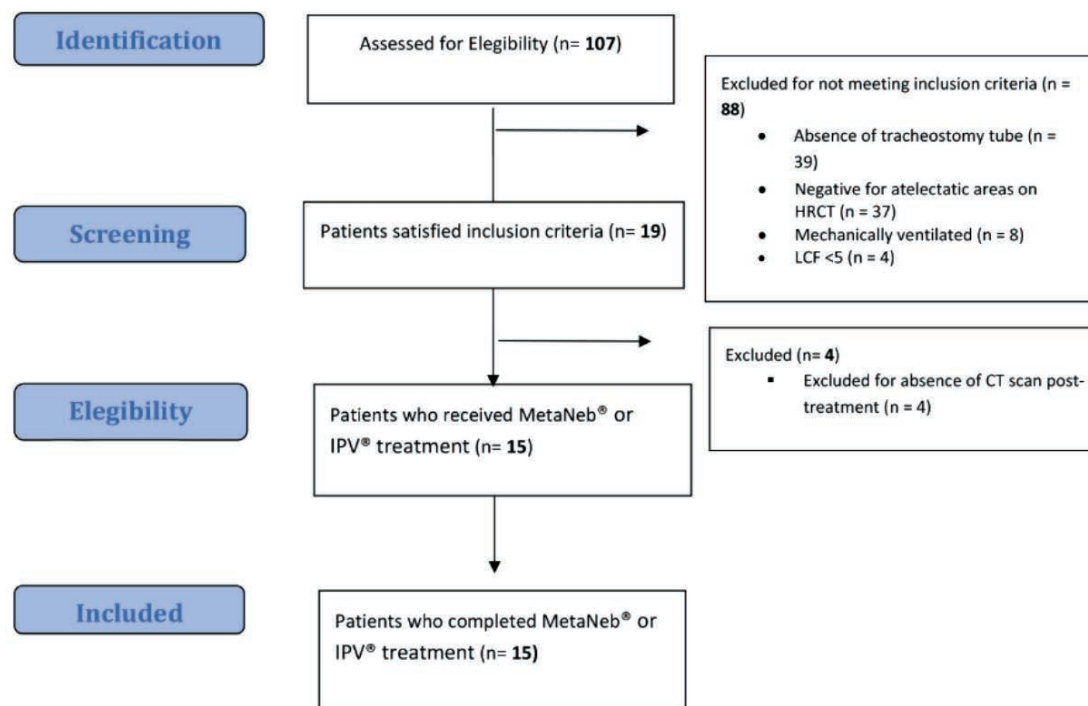
Descriptive characteristics are reported as mean (standard deviation), median (I-III quartile), and frequencies (percentages), where appropriate. Differences of mRAS across time points in the right

and left lungs were calculated for each subject and each radiologist's evaluation. Due to the nature of mRAS and OS (ordinal variables), the level of agreement between the two radiologists was assessed using Kendall's coefficient of concordance ( $K_w$ ), ranging from 0 (no agreement) to 1 (complete agreement). In particular, levels of concordance are classified as:  $<0.20$  poor, 0.2-0.4 fair, 0.42-0.60 moderate, 0.61-0.80 good, and 0.81-1 very good agreement. The concordance between the two radiologists was evaluated, considering left and right sites independently. To summarize the mRAS for each patient, the mean of the two evaluations was chosen as a final delta score. This score was compared with the OS obtained by the software Syngo.via CT Pneumonia Analysis. In particular, due to different evaluation scales (mRAS by radiologists and OS by software), the variation of each score ( $\Delta$ =follow-up-admission) was classified and labeled as improvement ( $\Delta < 0$ ), stability ( $\Delta = 0$ ) or worsening ( $\Delta > 0$ ), and a concordance was estimated through  $K_w$ . The change in respiratory parameters pre- and post-physiotherapy was evaluated by a paired  $t$ -test. For all estimates, a 95% confidence interval (CI) was determined, and a  $p$ -value less than 0.05 was considered statistically significant. All analyses were performed using the R software version 4.0.3 [14].

## Results

### Study population

A total of 107 pwSABI were screened for inclusion in our study, and 15 patients were included in the final sample (Figure 1). Table 1 reports patients' characteristics at admission. Patients were mainly classified as level 2 (generalized response, 40%) or level 3 (localized response, 33%) on the LCF scale (Table 1).



**Figure 1.** Flow chart of the study. CT, computed tomography; HRCT, high-resolution computed tomography; LCF, levels of cognitive functioning.



**Table 1.** Baseline characteristics of the study population.

Study population	
N	15
Males, n (%)	11 (73.3)
Age [median (I-III quartile)]	57 (45.50, 70)
BMI [median (I-III quartile)]	20.10 (17, 22.90)
LCF scale, n (%)	
1: no response	1 (6.7)
2: generalized response	6 (40)
3: localized response	5 (33.3)
4: confused-agitated response	1 (6.7)
5: confused- inappropriate response	2 (13.3)
Cuffed tracheostomy tube=yes, n (%)	12 (80)
Open tracheostomy tube=yes, n (%)	12 (80)
PEG=exclusively, n (%)	13 (86.7)
MBDT=positive, n (%)	6 (40)
PCF Reflex=yes, n (%)	15 (100)
Antibiotics=yes, n (%)	11 (73.33)
Antiepileptics=yes, n (%)	7 (46.67)
Inhalation therapy=yes, n (%)	8 (53.33)
ABI etiology=Traumatic, n (%)	8 (53.3)

BMI, body mass index; LCF, levels of cognitive functioning; PEG, percutaneous endoscopic gastrostomy; MBDT, modified evans blue dye test; PCF reflex, peak cough flow reflex.

## Feasibility

Diary treatment inspection showed that 588 (100%) treatment sessions were completed. Technical difficulties in device setup or treatment delivery were not mentioned in the records, and MAP between 10 and 25 cmH<sub>2</sub>O was used for both devices. There were no reports of discomfort or poor treatment tolerance by the subjects with pressure set below 25 cmH<sub>2</sub>O and percussion frequencies (IPV® group) below 400 cycles/min. The average number of completed sessions by each subject was 42. Each session lasted 40 minutes during which patients were treated, postured, and received bronchoaspiration performed by respiratory physiothera-

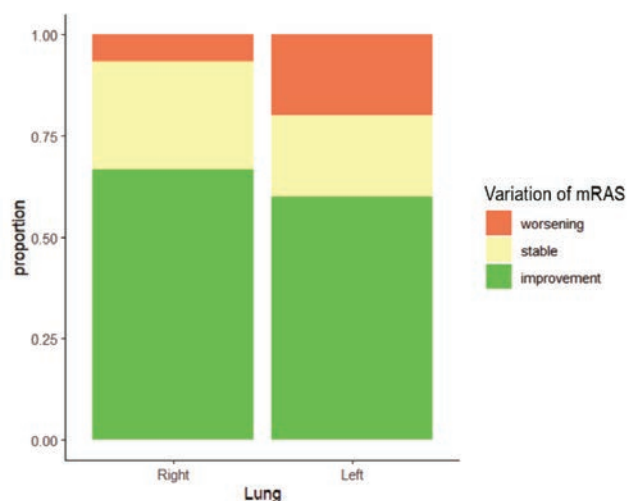
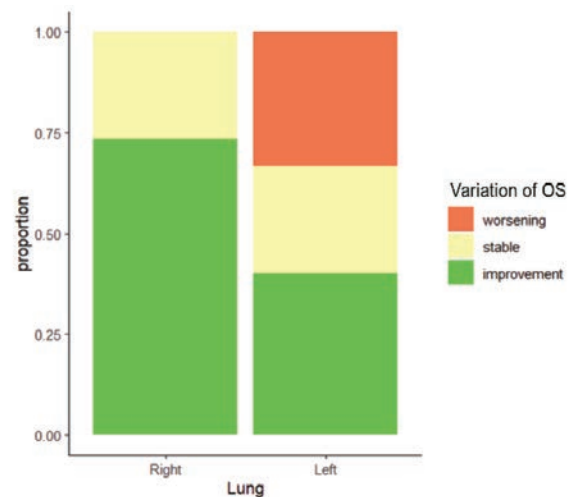
pists. The occurrence of any minor adverse events during or immediately after the IPV® or MetaNeb® session was a requirement for bronchoaspiration, associated with the 3% drop in desaturation, resolved immediately after broncho-aspiration through the tracheostomy tube. There were no major adverse events reported. The treatment diary for 4 patients (2 using IPV® and 2 using MetaNeb®) with strong rigidity, dystonia, and consolidating fracture showed that it was impossible to alternate the two decubitus positions or to use the prone position, forcing them to adopt specific positions.

## Modified atelectasis score by radiologists

At admission, none of the pwSABI showed a bronchial consolidation. The mRAS [13] variation in the right and left lungs is depicted in Figure 2. The mean differences of mRAS were equal to -0.48 (0.54) and -0.20 (0.48) for the right and left lung, respectively. Most of the variations of mRAS highlighted an improvement in the atelectasis area: 12/15 and 14/15 subjects in the left and right lung, respectively. While 3 of 15 (left lung) and 1 (right lung) of 15 of subjects showed worsening areas in the lung that were in the dependent position during the treatment. Significant differences were found between pre- and post-values for mRAS (right lung,  $p=0.0056$ ; left lung,  $p=0.0381$ ). The improvement and the stability were confirmed in most of the people (>80%) (Table 2). The agreement between the two radiologists was reported as good for the right lung (Kw=0.70; 95% CI 0.54-0.84) and moderate-good for the left lung (KW=0.56; 95% CI 0.38-0.75), and both were statistically significant ( $p<0.001$ ). The evaluation between the two radiologists was not concordant for 4 subjects, but the outcome of resolution or worsening was in accordance.

## Comparison using opacity score

The variation in the OS after 14 (2) days of treatment is described in Figure 3. Overall, the mean differences of OS were equal to -1.40 (1.12) and -0.53 (1.64) for right lung ( $p=0.0017$ ) and left lung ( $p=0.0553$ ), respectively. Using the Syngo.via software, the improvement and the stability were confirmed in 13/15 subjects (Table 2). The agreement between the mRAS variation

**Figure 2.** Variations of modified-radiological atelectasis score (mRAS) from admission to follow-up.**Figure 3.** Variations of opacity score (OS) from admission to follow-up for the right and left lung.

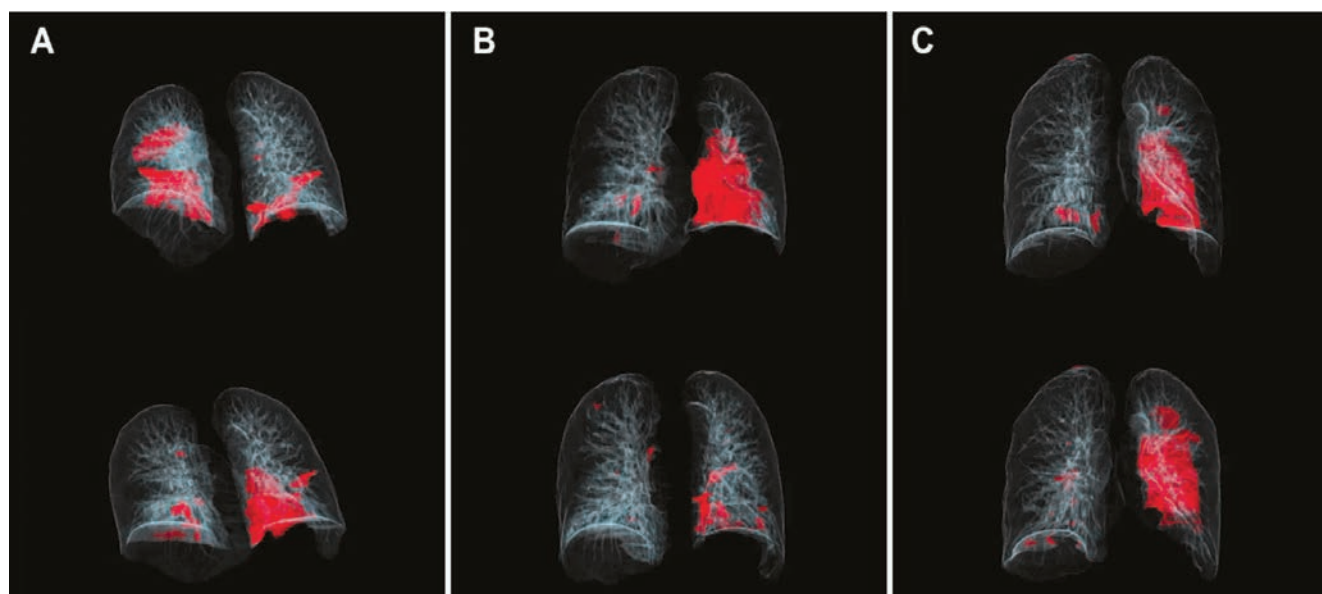
and OS variation was moderate and statistically significant for both the right (Kw=0.545; p=0.0218) and the left lung (Kw=0.596; p=0.0126). Figure 4 shows example cases that

remained stable, improved, or worsened after the treatment. As for stability example, subject A of Figure 4 was a female subject with traumatic brain injury (TBI), LCF 3, 43 years old, with a BMI of

**Table 2.** Variations of modified-radiological atelectasis score and opacity score expressed as mean difference with standard deviation (follow-up - baseline), for the whole group of patients and separately for those treated with MetaNeb and intrapulmonary percussive ventilation.

	Overall	METANEB	IPV	p*
N	15	7	8	
<b>mRAS</b>				
mRAS left lung, mean (SD)	-0.20 (0.49)	-0.25 (0.35)	-0.16 (0.60)	0.725
mRAS right lung, mean (SD)	-0.48 (0.55)	-0.29 (0.53)	-0.64 (0.54)	0.224
mRAS left lung, n (%)				0.700
Improvement	9 (60.0)	4 (57.1)	5 (62.5)	
Stability	3 (20.0)	2 (28.6)	1 (12.5)	
Worsening	3 (20.0)	1 (14.3)	2 (25.0)	
mRAS right lung, n (%)				0.512
Improvement	10 (66.7)	4 (57.1)	6 (75.0)	
Stability	4 (26.7)	2 (28.6)	2 (25.0)	
Worsening	1 (6.7)	1 (14.3)	0 (0.0)	
<b>OS</b>				
Mean (SD) both lungs	-1.93 (2.25)	-2.00 (2.45)	-1.88 (2.23)	0.919
Right, mean (SD)	-1.40 (1.12)	-1.00 (1.00)	-1.75 (1.16)	0.207
Left, mean (SD)	-0.53 (1.64)	-1.00 (1.91)	-0.12 (1.36)	0.321
Right, n (%)				0.459
Stability	4 (26.7)	3 (42.9)	1 (12.5)	
Improvement	11 (73.3)	4 (57.1)	7 (87.5)	
Left, n (%)				0.736
Improvement	7 (46.7)	3 (42.9)	4 (50.0)	
Stability	3 (20.0)	2 (28.6)	1 (12.5)	
Worsening	5 (33.3)	2 (28.6)	3 (37.5)	

mRAS, modified radiological atelectasis score; OS, opacity score; SD, standard deviation; IPV, intrapulmonary percussive ventilation. \*Mann-Whitney U test and  $\chi^2$  test for the comparison of the two devices.



**Figure 4.** Volume rendering reproduced from Siemens Syngo.via software CT. Analysis of three subjects: A, B, C, before (top) and after (bottom) treatment. The segmented lung opacities are shown in red. Subject A: left lung opacity score (OS) before treatment=1; OS after treatment=2; right lung OS before treatment=2; OS after treatment=1; considering both lungs, OS variation=0 (Stability). Subject B: left lung OS before treatment=4; OS after treatment=1, right lung OS before treatment=0; OS after treatment 0; considering both lungs, OS variation=-3 (improvement). Subject C: left lung OS before treatment=3; OS after treatment= 4; right lung OS before treatment=1; OS after treatment=0. Considering both lungs, OS variation=+1 (worsening).

22.1 and without antibiotic therapy at admission. HRCT showed the presence of atelectasis in the lower and upper right lung lobes and the inferior left lung lobe. She was treated with the MetaNeb® system (CPEP 12-15 cmH<sub>2</sub>O) in supine and anti-trendelenburg positions. The prone position could not be achieved due to the presence of spinal fractures. OS did not change with treatment, due to a slight improvement on the right lung but a worsening in the left one. As an example of improvement, subject B of Figure 4 was a male with TBI, LCF 1, 51 years old, a BMI of 20.3, and without antibiotic therapy at admission. HRCT showed the presence of atelectasis in the lower left lung lobe. He was treated with the MetaNeb® system (CPEP 14-16 cmH<sub>2</sub>O) in right lateral decubitus (left lung in antigravity position). OS improved after treatment (from 4 to 1). As an example of worsening, subject C was a male with TBI, LCF 2, 73 years old, a BMI of 17.5, and without antibiotic therapy at admission. HRCT showed the presence of atelectasis in the lower left lung lobe. He was treated with IPV® (MAP 8-12 cmH<sub>2</sub>O, 240 percussions/minute) in supine and anti-trendelenburg position. The prone position could not be achieved due to the presence of muscular spasms and tightness. After the treatment, OS worsened (from 3 to 4) due to a deterioration of the previous atelectasis found in the lower left lung lobe.

### Variation of respiratory parameters and differences between devices

The variation in respiratory outcomes is reported in Table 3: statistically significant improvements were found both in BGA and in night-time SpO<sub>2</sub> monitoring [fraction of inspired oxygen (FiO<sub>2</sub>), pH, partial pressure of CO<sub>2</sub> (PCO<sub>2</sub>), PO<sub>2</sub>/FiO<sub>2</sub> (P/F), arterial alveolar gradient (PAaO<sub>2</sub>), Arterial oxygen saturation (SO<sub>2</sub>), baseline SpO<sub>2</sub>, time with SpO<sub>2</sub><88%, mean SpO<sub>2</sub>, lower SpO<sub>2</sub> and mean of minima]. We did not find evidence of the difference between selected devices in terms of radiologic scores (Table 2).

## Discussion

In this study, 15 pwSABI have completed the intervention protocol either with the MetaNeb® System or IPV® without adverse events. To our knowledge, studies of the feasibility of IPV® and MetaNeb® System in non-cooperating pwSABI are not available. Nowadays, different techniques are used to expand atelectasis areas in respiratory physiotherapy [15]. PwSABI are very fragile, with different types of complications [16-18]. Respiratory complications show a high prevalence (up to 80%) [6,19]: Atelectasis is very common after a brain injury and is associated with the risk of pneumonia and acute respiratory failure, with the consequent negative effect on gas exchange. Since its inception, IPV® has been used either as a stand-alone modality or in conjunction with other chest physiotherapy techniques (CPT) for hypoxemia, pulmonary atelectasis, airway clearance, and respiratory acidosis in various clinical settings. Similar findings of improved oxygenation and reduced incidence of pneumonia were reported by Clini *et al.* [9] in 46 tracheostomized patients when IPV® intervention was added to CPT compared to CPT alone. Toussaint *et al.* suggest that IPV® increases the effectiveness of assisted mucus clearance techniques in tracheostomized Duchenne muscular dystrophy patients and children with atelectasis [7,20,21]. Huynh *et al.* suggested the efficacy of oscillation with the MetaNeb® system in reducing postoperative pulmonary complications [12]; moreover, Ferguson and Wright found an improvement of airway clearance and atelectasis area after treatment with MetaNeb® in an intubated child with extensive burns [11]. For the time being, different randomized controlled trial studies and systematic reviews [4,22-24] demonstrated how IPV is effective, feasible, and safe in a heterogeneous population of patients on various outcomes. Hassan *et al.* showed how IPV allowed a reduction in ICU length of stay, improved gas exchange, and reduced respiratory rate. However, none of these studies looked at the application of

**Table 3.** Variation of secondary outcomes across timepoints.

	Baseline	Follow-up	Mean difference (95% CI)	p
<b>Arterial blood gas analysis</b>				
FiO <sub>2</sub>	25.73 (6.49)	22.33 (2.55)	3.4 (0.60 to 6.19)	0.021*
PH <sub>i</sub>	7.48 (0.03)	7.45 (0.04)	0.02 (0.003 to 0.04)	0.029*
PCO <sub>2</sub> (mmHg)	37.53 (4.31)	39.67 (3.48)	-2.13 (-3.92 to -0.35)	0.023*
PO <sub>2</sub> (mmHg)	70.27 (14.44)	78.67 (7.80)	-8.40 (-17.41 to 0.61)	0.065
HCO <sub>3</sub> (mmol/L)	27.19 (3.79)	27.65 (2.98)	-0.46 (-2.07 to 1.15)	0.551
P/F	283.25 (69.88)	349.60 (51.68)	-66.35 (-99.75 to -32.94)	0.001*
PAaO <sub>2</sub>	67.56 (46.70)	29.63 (20.77)	37.93 (19.03 to 56.84)	0.001*
Lactates	1.23 (0.39)	1.29 (0.37)	-0.07 (-0.35 to 0.22)	0.619
SO <sub>2</sub> (%)	95.37 (3.90)	97.68 (1.25)	-2.31 (-4.39 to -0.22)	0.033*
<b>SpO<sub>2</sub> at night</b>				
FiO <sub>2</sub> (%)	27.93 (6.97)	22.27 (2.69)	5.67 (2.56 to 8.77)	0.002*
Baseline SpO <sub>2</sub> (%)	93.72 (1.90)	95.12 (1.35)	-1.40 (-2.35 to -0.45)	0.007*
T88 (%)	4.63 (5.66)	0.94 (1.56)	3.69 (0.87 to 6.51)	0.014*
Mean SpO <sub>2</sub> (%)	92.45 (2.12)	94.29 (1.87)	-1.84 (-2.77 to -0.91)	0.001*
Lower SpO <sub>2</sub> (%)	85.00 (4.26)	88.07 (2.52)	-3.07 (-5.17 to -0.97)	0.007*
Mean of minima (%)	90.85 (2.39)	93.03 (2.04)	-2.18 (-3.08 to -1.28)	<0.001*
Saturation index	14.91 (4.55)	16.47 (6.56)	-1.56 (-5.16 to -2.04)	0.368

Data are reported as mean (standard deviation). The statistical difference in the variation of characteristics across time points was evaluated by applying the t-test method for paired data. Statistically significant difference highlighted by\*. CI, confidence interval; FiO<sub>2</sub>, fraction of inspired oxygen; PCO<sub>2</sub>, partial pressure of carbon dioxide; PO<sub>2</sub>, partial pressure of oxygen; HCO<sub>3</sub>, bicarbonate levels; P/F, PO<sub>2</sub>/FiO<sub>2</sub>; PAaO<sub>2</sub>, arterial alveolar gradient; PaaO<sub>2</sub>, arterial alveolar gradient; SpO<sub>2</sub>, peripheral oxygen saturation; T88%, time with SpO<sub>2</sub><88%.

such intervention in non-cooperating pwSABI. In particular, using a specific software for atelectasis analysis, our study found variations in radiological scores, allowing the possibility of further investigation into the effect of IPV® and MetaNeb® [25-28]. We found that the variation of mRAS was improved after treatments; also, mRAS showed evidence of variation in the left and right lungs. Both radiologists found a worsening in 3 of 15 (left lung) and 1 of 15 (right lung) of subjects: the worsening was always located in the lung in decline position during the entire treatment, since the decline position is not facilitating the resolution of the atelectasis area [29]. However, also in this case, the software (OS) detected 5 of 15 subjects worsening in the left lung and no worsening in the right lung. The concordance of variations between the two scores was shown in 3/15 left lungs; the other 3 different lung evaluations had a minimal variation  $\leq 1$  point in both scores (OS and mRAS). The results of the OS were identified through the analysis of the Syngo.via software agree with the variations of the mRAS and show an improvement of at least one lung in 13/15 (86%) subjects [13]. Also, we noticed an improvement in BGA and nighttime SpO<sub>2</sub>. We registered an improvement even of pH: at baseline, pwSABI were in a condition of hyperventilation with an average pH of 7.48, which showed a reduction with physiological parameters at follow-up (average of 7.45). After treatment, FiO<sub>2</sub> set with Airvo2 (Fisher & Paykel Healthcare LTD, Rome, Italy) during day and night was reduced (FiO<sub>2</sub><40% required in both groups). Reduction of oxygen need could be related to an improvement of mucociliary clearance, but mainly for alveolar recruitment. Other studies have already reported an improvement in oxygenation in people with tracheostomy after IPV treatment [22,30]. PAaO<sub>2</sub> at baseline was severely altered [31,32]; after treatment, we reported an improvement of this index, likely due to parenchyma expansion and normalization of PaCO<sub>2</sub> [33,34]. These results suggest that antigravity position for compromised lung, in addition to high frequency percussion, could contribute greatly to the resolution of atelectatic area; sometimes, in pwSABI, the presence of stiffness, dystonia, and fractures does not allow proper lung location.

### Strengths and limitations of the study

This study explored feasibility, which we consider useful for the assessment of any physiotherapy intervention. Based on the data from 588 diary treatment sessions, treatment with IPV® and MetaNeb® seems to be feasible, without adverse events. Assessing the reproducibility of these results in a bigger sample is crucial for the implementation of these physiotherapy techniques in clinical practice and to unveil the short-term effects of respiratory physiotherapy in non-collaborating people. Also, this is one of the first studies in which a specific software has been used to detect uniquely radiological variations of atelectasis between baseline and follow-up, ensuring treatment with IPV® or MetaNeb®. Thirdly, we used a modified atelectasis score and an OS to evaluate changes in CT radiological images. On this topic, further studies are required for the recognition of a radiological score specific for non-collaborating people with atelectasis. We also acknowledge some limitations. Monitoring nighttime SpO<sub>2</sub> was performed in different conditions due to the fact that, at follow-up, patients had the cannula capped, and we cannot be sure that the patient actually slept. The small number of participants and the single-center design do not allow definitive conclusions about the feasibility of treatment with IPV® and MetaNeb® on pwSABI. Finally, the improvements that have been highlighted by the results of the study itself may be due both to the natural history of atelectasis and the effects deriving from antibiotic therapy.

## Conclusions

Respiratory physiotherapy provided through high-frequency percussion devices such as IPV® and MetaNeb® is generally safe and well tolerated in pwSABI; investigating the effects of these two devices on gas exchange and radiological variations seems an area worth further exploration. Using technology to assess abnormal tomographic patterns could also be of interest to disentangle the short-term effects of respiratory physiotherapy in non-collaborating people.

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