PRODUCT OVERVIEW & CLINICAL BENEFITS

LÖWENSTEIN SLEEP THERAPY PRODUCTS

Putting the control of sleep treatment back into your hands.

A proud member of the Sleep Health Foundation Business Council

santé NEXT-GENERATION SOURCING

LÖWENSTEIN medical

PRODUCT OVERVIEW

Masks & APAP/CPAP Device Options

CARA Nasal & Full Face masks are a universal option suiting almost all faces & covering sizes from extra small nasal through to large full face masks. The CARA range of masks are premium quality with many exceptional features:

- **Award winning mask**
  CARA Nasal was awarded the international design prize Focus Open in 2018.
- **Sensational Silence**
  The exhalation system located near the ball-&-socket joint has slotted openings yielding a subtle diffuse air flow to the sides. The diffuse system has been perfected in the CARA family of masks.
- **Mask Cushion**
  The soft & supple cushion fits snugly & hugs the contours of the face.
- **Lightweight**
  CARA Nasal weighs less than an egg, CARA Full Face weighs less than a small bunch of grapes.
- **Ball-&-socket joint**
  360° with 3D rotation (via rotating sleeve) for freedom of movement.
- **Rotating sleeve**
  Small component that is removed to easily connect to breathing tube, it then clicks back onto the ball-&-socket joint where it can freely rotate.
- **Headgear**
  CARA headgear has been given the internationally recognized OEKO-TEX STANDARD 100 seal by the independent Hohenstein Institute. Upper portion of headgear can be adjusted for a perfect fit on any head size.
- **Forehead Support**
  Dual option for headgear straps to either manually thread onto traditional variants or thread through the middle permanent variant.
- **Material**
  Remarkable quality, durability, strength & flexibility!

	Features / Benefits	Platinum Range		Gold Range		Silver Range	
		Prisma 20A	Prisma 20C	Prisma SMART	Prisma SOFT	SOMNO balance e	SOMNO soft
Modes	CPAP	✓	✓	✓	✓	✓	✓
	APAP (autoCPAP)	✓		✓		✓	
	'Standard' or 'Dynamic' APAP Options	✓		✓			
Stabilisation	Obstruction detection FOT/FBT	✓	✓	✓	✓		
	Obstruction detection OPP					✓	✓
	Adaptive pressure regulation to eliminate obstructions (APAP)	✓		✓		✓	
	Adjust rate of pressure change per second (APAP)					✓	
Compliance & Comfort	softSTART	✓	✓	✓	✓	✓	✓
	Mask test	✓	✓	✓	✓	✓	✓
	Leak display during operation	✓	✓	✓	✓	✓	✓
	Pressure relief softPAP 1 & 2	✓	✓	✓	✓	✓	✓
	autoSTART-STOP	✓	✓	✓	✓	✓	✓
	Pressure relief softPAP 3 (with inspiration support)	✓	✓				
	Alarm Clock	✓	✓				
	Large intuitive colour touch screen	✓	✓				
	Large LED Display			✓	✓		
	LCD Display					✓	✓
	PrismaAQUA Humidifier (400ml)	✓	✓	✓	✓		
	SOMNOaqua Humidifier (300ml)					✓	✓
	Smart Aqua Control (Warm-up Boost + Flow Compensation)	✓	✓				
Data Review	Prisma RECOVER Deep Sleep Indicator	✓	✓	✓	✓		
	Patient review usage, AHI & leakage (if enabled by clinician)	✓	✓	✓	✓	✓	✓
	PrismaTS detailed clinical software	✓	✓	✓	✓	✓	✓
	Prisma Journal for patient (statistics & reports)	✓	✓	✓	✓		
	Remote connectivity (PrismaCLOUD)	✓*	✓*	✓**	✓**		
	SD Card	✓	✓	✓	✓	✓	✓
	Micro-USB cable	✓	✓				

*with external modem attachment
**Feature present in Prisma SMART max / Prisma SOFT max models only

FOT/FBT to distinguish central from obstructive apnoea

TRILevel Pressure Automatic adjustment of three pressure levels (PAP, EPAP & EEPAP

SCOPES LAB / ST / CR

Indications	Type of Therapy	Therapy Devices	
Central sleep apnea of Cheyne-Stokes variety associated with heart failure & with central, mixed or complex sleep apnea.	**AcSV Therapy** Ventilation by means of AcSV combined with automatic pressure adjustment to the patient's needs during current breath; automatic or pre-set backup frequency.	prismaCR The sleep medicine therapy solution for complex SDB (Sleep-Disordered Breathing)	
Obstructive mixed or complex sleep apnea & high/changing pressure needs, poor CPAP compliance, central apnea, nocturnal hypoventilation, respiratory insufficiency and/ or COPD.	**BILevel ST Therapy** Ventilation with varied pressure levels during inhalation & during early & late expiration phases (optional TriLevel). Backup frequency for additional safety. Optional automatic adjustment of EPAP and PDIFF based on airway obstructions. Prisma30ST offers optional adaptive pressure support to target volume with adjustable dynamics of pressure modification.	prisma25ST & 30ST BiLevel ST device optionally combined with the advantages of APAP & optionally with adaptive target volume (Prisma30ST only)	
Obstructive mixed or complex sleep apnea &; high/changing pressure needs, poor CPAP compliance.	**BILevel S Therapy** Ventilation with varied pressure levels during inhalation & during early & late expiration phases (optional TriLevel). Optional automatic adjustment of EPAP and PDIFF based on airway obstructions.	prisma25S BiLevel S device optionally combined with the advantages of APAP	
Obstruction of the upper airways. Fixed or variable pressure needs depending on position or sleep stage. Poor CPAP compliance. OSA & UARS with varying pressure needs.	**APAP Therapy** Ventilation with positive airway pressure which automatically adjusts to the needs of the patient to provide greater therapy flexibility. As an option, CPAP & APAP can be combined with the intelligent pressure relief softPAP. With adaptive APAP algorithm and two different APAP dynamics, the right treatment for every patient is guaranteed.	prisma20A APAP/CPAP Therapy flexibility with softPAP pressure relief (incl. breathing support option) & FOT	
		prisma SMART plus & max APAP/CPAP Therapy flexibility with softPAP & FOT plus = inbuilt bluetooth max = inbuilt bluetooth and cellular connectivity	
Obstruction of the upper airways. Fixed pressure needs.	**CPAP Therapy** Ventilation with constant pressure airway pressure to create pneumatic splint. CPAP can be combined with the intelligent pressure relief softPAP.	Prisma20c CPAP Therapy with softPAP pressure relief (incl. option for breathing support) & FOT	
		Prisma SOFT plus & max CPAP Therapy with softPAP & FOT plus = inbuilt bluetooth max = inbuilt bluetooth and cellular connectivity	
Dry mouth or nasopharyngeal systems during PAP therapy.	**Comfort purposes** Imparts humidity to airflow via water tub with heated rod element which integrates onto the side of the device.	PrismaAQUA Typically Included Humidifier compatible with all above devices. Comes in white and black to suit device.	
Excessive condensation in tube during PAP therapy.	**BILevel S Therapy** Provides warmth to humidified air via heated coils along the length of the tube.	PrismaHYBERNITE Optionally Included Heated tube compatible with following devices, only when used with humidifier: Prisma20C, 20A, 25S, 25ST, 30ST, CR.	
Excessive condensation in tube during PAP therapy.	**BILevel S Therapy** Provides warmth to humidified air via heated coils along the length of the tube.	HYBERNITE Superday Optionally Included Heated tube system compatible with devices used with humidifier. Recommended for Prisma SMART & SOFT plus & max.	

PRODUCT OVERVIEW

Specialist Products

	Features / Benefits	Specialist Products			
		Prisma LAB	Prisma CR	Prisma 25ST	Prisma 25S
Modes	CPAP	✓	✓	✓	✓
	APAP (autoCPAP)	✓		✓	✓
	BILevel S, auto S	✓		✓	✓
	BILevel S/T, auto S/T	✓		✓	
	BILevel T	✓		✓	
	AcSV**	✓	✓		
Stabilisation	Obstruction detection FOT/FBT/ OPP	✓	✓	✓	✓
	Adaptive pressure regulation to eliminate obstructions (autoEEPAP, APAP)	✓	✓	✓	✓
	Optional autoF	✓	✓	✓	
Synchron-isation	Automatic trigger technology	✓	✓	✓	✓
	rampIN	✓	auto	✓	✓
Compliance & Comfort	softSTART	✓	✓	✓	✓
	Mask test	✓	✓	✓	✓
	Leak display during operation	✓	✓	✓	✓
	TRILevel option	✓	✓	✓	✓
	Pressure relief softPAP	✓*	✓*	✓*	✓*
	autoSTART-STOP	✓	✓	✓	✓

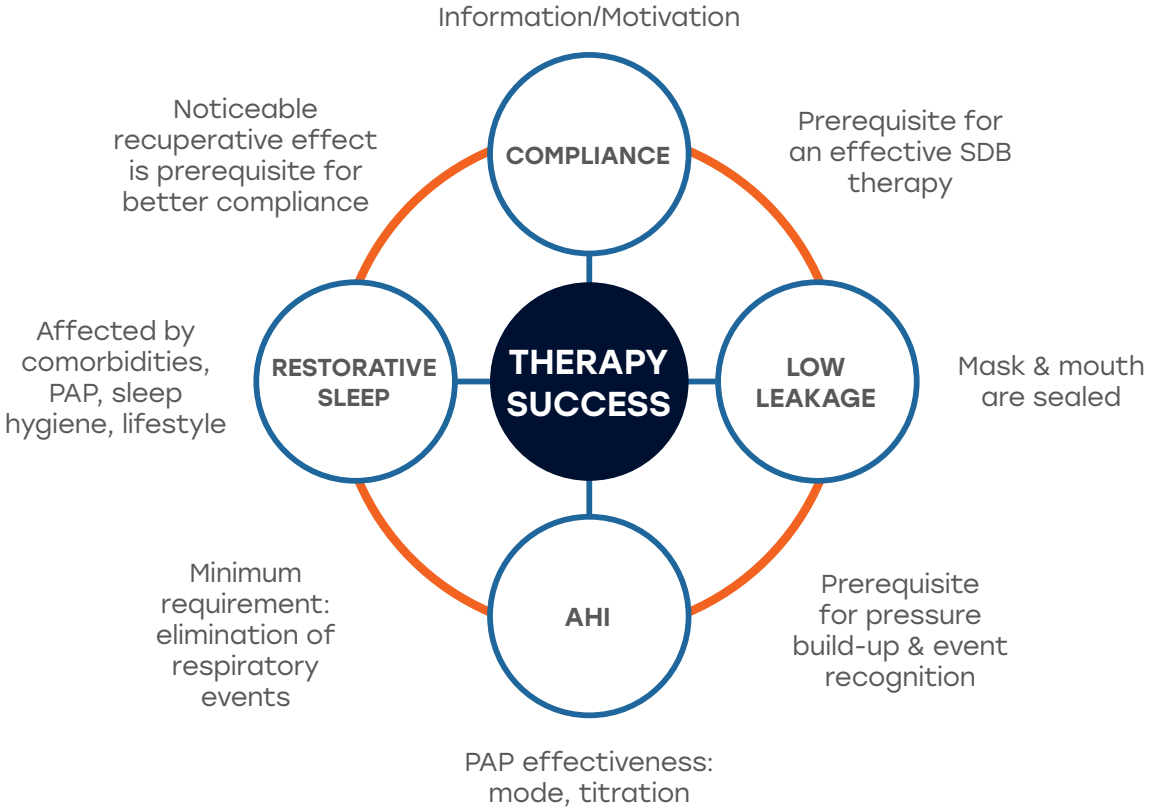
*in CPAP/APAP modes
**AcSV = Anticyclic Servoventilation

CLINICAL BENEFITS

What does successful sleep therapy treatment look like?

There is no set formula for the successful treatment of respiratory conditions (i.e. obstructive, central, mixed or complex sleep apnoea and/or respiratory insufficiency). The treatment process is a complex matter which unfolds over time & is intensely individual, as such patient-professional interaction is paramount. Hence, when it comes to PAP therapy (widely regarded as the gold standard of treatment of conditions such as OSA), we believe long-term success and optimum treatment outcome is consistently achieved through a practical test & trial process fine-tuned & tailored to an individual's experience & needs by a trained professional.

When asked what defines successful treatment specifically with sleep apnoea, the usual metric clinicians & specialists refer to is AHI (Apnoea Hypopnea Index) per hour. A score of less than 5 AHI/hr is the typical theoretical definition of clinical effectiveness in PAP therapy. In reality, therapy outcome revolves around more than AHI/hr. The following chart offers insight into how Santé & Löwenstein view therapy success as an interconnected series of key factors, centering around a comfortable & recuperative treatment (i.e. restorative sleep), whereby patients are motivated & happy to comply so that the loop of therapy success remains unbroken.



The Löwenstein Difference

The Löwenstein devices consistently demonstrate clinical efficacy (AHI<5/hour), with further key clinical features as follows:

- **Prisma RECOVER**
  Innovative feature that estimates deep sleep.
- **High accuracy of AHI detection**
  96% + accuracy level.
- **Proactive algorithm regulation**
  Epoch-based response with structured treatment pattern.
- **Dynamic & Standard Algorithm**
  2 settings to suit different patients & stage of treatment.
- **Stability of pressure adjustment**
  therapeutically effective with no unnecessary fluctuation.
- **Efficiency of pressure**
  Consistently low Pmax & Pmean.
- **Pressure relief SoftPAP**
  No compromise on clinical outcome.

Features are explored in detail below & in subsequent appendices.

PRISMA RECOVER

Applicable Products:
Prisma SMART & SOFT, Prisma20A & 20C.

The Löwenstein white paper edition “Sleep Quality in CPAP/APAP Therapy”* challenges the traditional perception of AHI as the only metric in APAP/CPAP Therapy. The paper outlines the importance of restorative or deep sleep (slow-wave-sleep) which shows a greater correlation to an improvement in daytime sleepiness compared to AHI. The innovative Prisma RECOVER algorithm (inbuilt within Prisma devices) analyses respiratory minute volume to provide an estimation of deep sleep. Deep sleep could be considered an important new metric of sleep quality in PAP therapy.

*Refer to Appendix 1

ACCURACY OF AHI DETECTION

Applicable Products:
SOMNObalance e / soft 2e (OPP technique), Prisma SMART & SOFT, Prisma20A & 20C, Prisma25S (FOT technology), Prisma25ST, Prisma30ST, PrismaCR & PrismaLAB (FOT technology, and FBT technology when backup frequency is applied).

Modern algorithms must be able to reliably distinguish between obstructive & central sleep events as a prerequisite to treating sleep disordered breathing efficiently. The Prisma devices use analysis of tidal volume and flow signal (relative minute volume) to identify events, along with forced oscillation technique to differentiate apnoea/hypopnea type, with an amplitude of approx. 0.4 hpa (or cmH20) which is superimposed by the device blower.* This minimalist amplitude would suggest little chance of disruption to the patient’s sleep, with a precise event recognition achieved. “Study Hunter: Benchtest of AHI agreement in APAP (20A)”** was carried out with 4 devices: AirSense 10 (Resmed), Dreamstation

Auto (Philips), S. Box (Sefam), Prisma20A (Löwenstein). It was concluded that Prisma20A together with Dreamstation Auto showed the highest accuracy.

SOMNO devices are also highly accurate, using flow-derived signals along with patented OPP technique to distinguish obstructive apnoea. SOMNObalance e received a scoring accuracy of 97% when subjected to a bench-test sequence of apnoea and snoring (this document is available at request).

*Refer to Appendix 2 pages 1-8
**Refer to Appendix 3

PROACTIVE ALGORITHM

Applicable products:
SOMNObalance e, Prisma SMART, Prisma20A, Prisma25S, 25ST, 30ST & LAB (when APAP, autoS, or autoS/T mode is used).

Löwenstein devices measure each breath of the patient & extract this into a suite of useful measures to characterise treatment and even sleep quality. Graphs available in the detailed signal data include respiratory flow & relative minute volume (all devices), obstruction & respiratory instability graphs (PrismaLINE devices). All devices categorise the presence of sleep disordered breathing within the detailed data into 'epochs' of 2-minute duration. There are 3 types of epochs according to degree of severity of obstruction: eFL (epoch flow limitation), eMO (epoch moderate obstruction) & eSO (epoch severe obstruction). In response to 2-minute epoch's, pressure adjustment is provided through a balanced, logical & consistent structure* which deviates the extent of pressure adjustment provided depending on where the current pressure is at on the Pmin to Pmax scale & severity of the obstruction. Since Pmin to Pmax is tailored to an individual's needs, the pressure is regulated in a way which avoids applying uncomfortable or sub-optimum pressure levels. The option of 'Standard' & 'Dynamic' algorithm in PrismaLINE devices provides a whole further dimension to how proactive the treatment is (refer to the following sub-heading).

*Refer to Appendix 2 page 9 onwards

STABILITY OF PRESSURE ADJUSTMENT

Applicable Products:
SOMNObalance e, Prisma SMART, Prisma20A, Prisma25S, 25ST, 30ST & LAB (when APAP, autoS, or autoS/T mode is used).

The challenge of the APAP algorithm is to provide stable, therapeutically effective & lowest possible pressures.

- Fast pressure decreases cause anew serious obstructions & arousals.
- Fast or extreme pressure increase in response to obstructions can cause arousal, lead to high mean pressures or high-pressure variability (more fast decreases).
- Inadequate increase to severe obstructions results in lengthy periods of subtherapeutic pressures.

The pressure regulation in Prisma20A (Auto) is therapeutically effective without unnecessary fluctuation*, whereby treatment is likely to be comfortable & well-balanced. The same algorithm response applies to the Prisma SMART in APAP as well as all other devices in PrismaLINE in APAP, autoS and autoS/T mode. The SOMNObalance e pressure regulation demonstrates a similar trend**.
Given the pleasant nature of the pressure regulation, it could be expected that the treatment dynamic offers the combined benefits of both CPAP & APAP. Overall pressure graph appears gradual, gentle & consistent, even with default pressure settings of 4 to 20.**

*Refer to Appendix 7, and Appendix 4 & 5 (Prisma20A)
**Refer to Appendix 7, page 5, graph F (SOMNObalance e) & graph G (Prisma20A)

EFFICIENCY OF PRESSURE

Applicable Products:
SOMNObalance e, Prisma SMART, Prisma20A, Prisma25S, 25ST, 30ST & LAB (when APAP, autoS, or autoS/T mode is used).

The Löwenstein philosophy is to provide a pressure regulation that strives for the most efficient pressures possible. Results show low AHI/events (less than 5 AHI/hr) with little difference between the Pmean & Pmax pressure, with both figures relatively low.*
*Refer to Appendix 6, page 6, Device F (SOMNObalance e) & Device G (Prisma20A), & Appendix 8, page 3, APAP Device E (Somnobalance).

PRESSURE RELIEF SOFTPAP

Applicable Products:
SOMNObalance e / soft 2e, Prisma SMART & SOFT, Prisma20A & 20C, Prisma25S, 25ST, 30ST, CR & LAB (also with optional TriLevel principle, further information available at request).

Löwenstein devices all come with options for SoftPAP expiration relief 1 (mild to moderate relief) & 2 (moderate to high relief). Both functions increase the amount of relief as the pressure level gets higher. Additionally, Prisma20A/C has a softPAP 3 option which provides moderate relief as well as pressure support slightly above set pressure at the beginning of the inspiration phase, this provides effective comfort to the overall breathing process & feelings of shortness of breath. BiLevel & AcSV devices feature Bisoft 1 & 2 that provide softEPAP using the same principles of regular softPAP, and the unique TriLevel principle which provides 3 units of relief on EPAP and then returns to an EEPAP (End Expiration Positive Airway Pressure) phase prior to IPAP, this has been clinically proven to offer the same tidal volume during treatment compared to conventional BiLevel whilst offering significantly lower average & IPAP pressure – supporting information is available at request.

SoftPAP demonstrates minimal clinical impact to AHI index according to a respiratory bench model evaluation of pressure-relief features*. By manually titrating devices to the exact point of fixed pressure at which the respiratory model simulated AHI of 60/h was normalised to residual AHI of 0/h (no events), & then applying pressure relief features, the clinical impact of adding these features could be assessed. Out of 6 different pressure relief features tested, 3 were able to maintain no events, whereas the other 3 resulted in residual AHI returning to 60/h. Löwenstein SoftPAP 2 & 3 were tested in the Prisma20A, both of which maintained no events, with measured mean pressures respectively 1.1 cmH2O & 0.8 cmH20 lower than the conventional required CPAP pressure. The only other pressure-relief feature tested which maintained no events measured mean pressure at just 0.2 cmH2O less than the conventional required CPAP pressure. By leaving no events & lowering mean pressure, it can be deduced that both the spontaneity and timing of Löwenstein SoftPAP settings provide considerable pressure relief on exhalation without clinical impairment.

*Refer to Appendix 9, Page 3, Table 2

CONCLUSION

Evidence suggests Löwenstein devices exhibit proactive, efficient & stable pressure adjustments when treating sleep disordered breathing & other respiratory conditions. This gives insight into why many Löwenstein users experience benefits to their breathing & sleep which could be expected to carry over to health, including: more natural breathing, less arousals from pressure & leakage independent of AHI events, greater sleep quality (i.e. more sleep), lower blood pressure, less side effects in the thoracic region which likely carry through to the brain organs and all bodily tissues & greater PAP compliance (prerequisite to improving outcome of therapy). These results reportedly carry over to quality of life, i.e. feeling fresh, energetic & motivated.

From a clinical standpoint, the accuracy of AHI, understanding of the structured algorithm response, option for 2 algorithm settings, extensive clinical data with epoch-based categorisation, & deep sleep indicator via respiratory minute volume provide extensive & varied information for professionals to optimise the treatment outcome for their patients. Lastly, the option of adding suitably timed pressure relief 'SoftPaP' settings during treatment, including TriLevel in the devices traditionally known as BiLevel, adds another dimension to patient comfort & overall pressure reduction without any evidence of negative clinical impact.


CARA
Full Face
CARA

APPENDIX CONTENTS

APPENDIX 1

Sleep Quality in CPAP/APAP Therapy

links compliance, leakage, AHI and therapeutic success

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Sleep Quality in CPAP/APAP Therapy

links compliance, leakage, AHI and therapeutic success

Despite good compliance and unremarkable AHI in PAP therapy, patients may still suffer from non-restorative sleep with related symptoms. Therefore in the future, devices in the prisma series will offer another criterion for the assessment of therapy success: a deep sleep indicator.

The key to success with PAP therapy

Compliance: With good compliance, CPAP therapy can reduce symptoms, prevent secondary cardiovascular disease and prolong life. Diverse studies have proven the effectiveness of CPAP therapy in connection with compliance or with compliance of more than four hours (Palm, Midgren, Theorell-Haglöw, Janson, & Lindberg, 2017), (Antic et al., 2011), (Billings M.E. et al., 2014), (Bouloukaki I. et al., 2017), (Kasai T., Narui K. et al., 2008), (Kingshott R.N. et al., 2000), (Peker Y. et al., 2016), (Abuzaid A.S. et al., 2017), (Weaver et al., 2007).

AHI/Leakage: A second decisive factor is effectiveness. Only therapeutically effective CPAP – and not sub-therapeutic treatment – improves symptoms and secondary diseases (Siccoli M.M. et al., 2008), (Mulgrew et al., 2010), (Habukawa M. et al., 2005), (Bakker et al., 2014). Leaks at mask and mouth, which are unpleasant for the patient, impair pressure stability, event recognition and APAP regulation of the PAP devices.

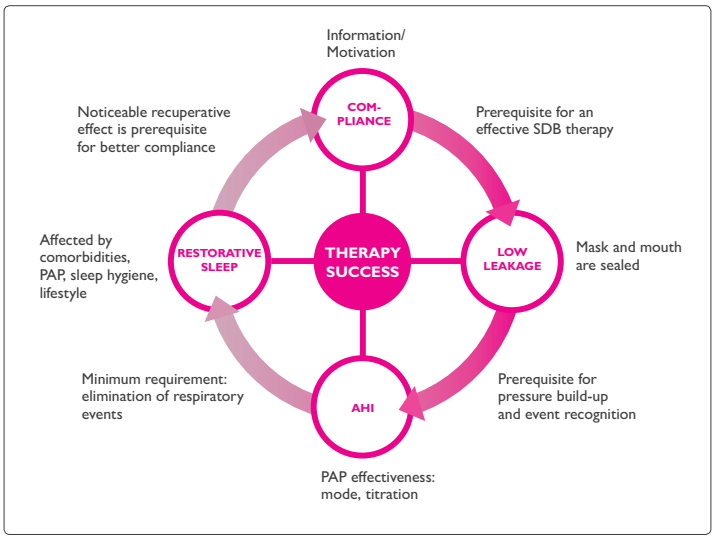

Figure 1: The PAP therapy chain of effects with patient's therapy success at the center.

APPENDIX 1
Pgs. 3-4

Restorative Sleep: Even with good compliance and effectively reduced AHI, increased daytime sleepiness remains a problem for up to 40 percent of patients (Antic et al., 2011). AHI is a poor predictor of improvement in daytime function (Kingshott R.N. et al., 2000), (Weaver, Woodson, & Steward, 2005), (Kirkham, Heckbert, & Weaver, 2015). Causes other than a persistent respiratory disorder may be responsible for continued poor sleep.

An increased risk of reduced compliance exists for patients with insomnia because the patients consider the respiratory mask and the therapy device to be particularly bothersome. Insomnia persists in up to 30 percent of patients treated with PAP (Björnsdóttir E. et al., 2013), (Philip et al., 2017).

Compared to AHI, hypnogram-based parameters with and without PAP therapy show that the amount of deep sleep has a higher correlation with an improvement in symptoms (McArdle N. & Douglas N.J., 2001), (Walsh et al., 2008), (Kasai T. et al., 2008).

Even the extent of a fall in blood pressure in CPAP treatment correlates more strongly with improvements in the sleepiness scale than with improvements in AHI/ODI resulting from therapy (Robinson G.V., Langford B.A., Smith D.M., & Stradling J.R., 2008).

When symptoms improve, the patient is motivated to adhere to therapy. When compliance improves, therapy succeeds and thus the chain of events continues in a self-reinforcing feedback loop. Restorative Sleep is the true goal of PAP therapy.

prisma RECOVER: Estimation of deep sleep from breathing pattern

The innovative prisma RECOVER algorithm continuously analyzes the patient's breathing pattern during PAP therapy. Respiration during deep sleep is more stable than in all other sleep or wake stages (see Figure 2).

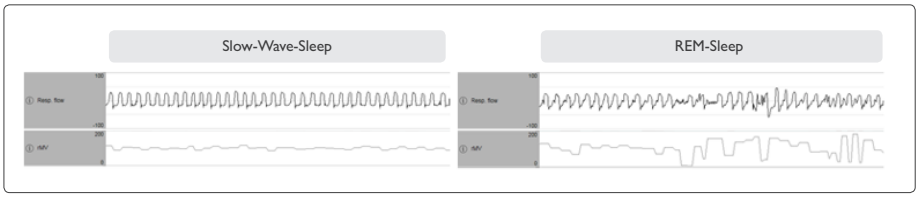

Figure 2: Stable breathing in deep sleep stage as compared to variable breathing in REM sleep; above: airflow [l/min]; below: relative minute volume [%]

prisma RECOVER determines the current breathing variability from the fluctuations in respiratory minute volume, which are based on the deviation of rMV from 100 percent. When the variability is lower than the threshold optimized across several patients, stable breathing indicates deep sleep; the respective time period is then added to the estimated length of the deep sleep stage.

It can thus be assessed whether the patient has slept soundly and long enough. This means of assessment requires no additional sensors or extra effort. Stable NREM sleep combined with a low AHI throughout the night can indicate sufficient undisturbed REM sleep.

In summary, in devices of the prisma series for the first time therapy success can be evaluated with regard to sleep quality in prisma JOURNAL, prismaTS or in telemonitoring with prisma CLOUD.

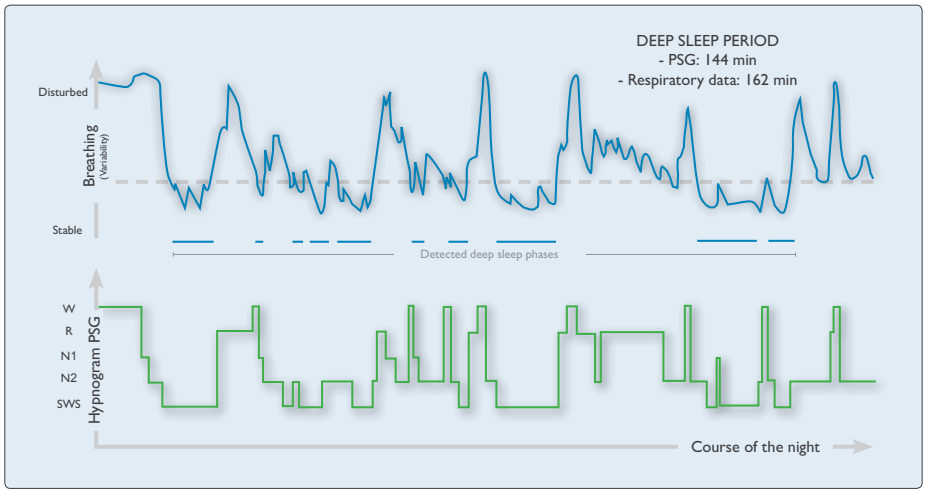

Figure 3: Example of deep sleep recognition in a patient during the first night of APAP therapy

APPENDIX 1
Pgs. 5-6

Internal validation data compared to PSG recording

A retrospective comparison (re-simulation of respiratory signals with prisma RECOVER) with n=41 patients in APAP therapy yielded a correlation of $r = 0.649$, $p < 0.0001$.

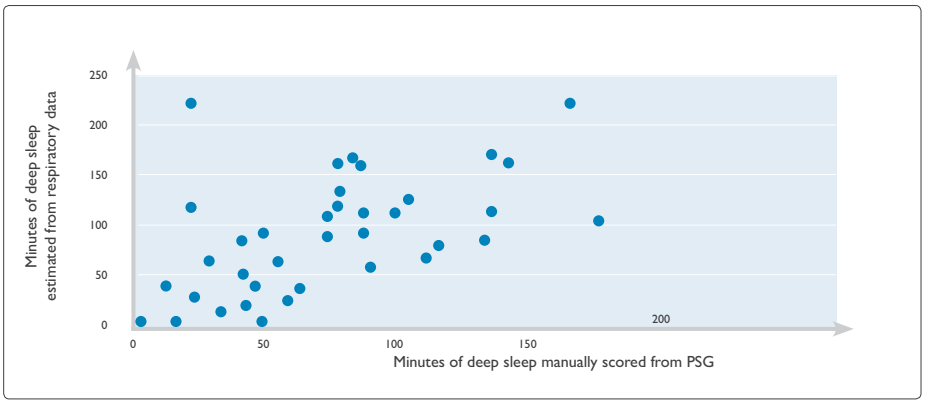

Figure 4: Comparison of length of deep sleep, determined from PSG and respiratory data

In an assessment of agreement among human scorers using the EEG, the intraclass correlation for time spent in deep sleep was 0.628 (R&K) and 0.698 (AASM) (Danker-Hopfe et al., 2009). The results underscore the performance of prisma RECOVER. Because different measurement methods and even different scorers using identical measurement methods can deviate in the assessment of deep sleep duration, patients should always be asked about their subjectively perceived symptoms in a suspected case and as part of routine monitoring.

Limitations:

- Periods of sleep without PAP use cannot be taken into account for deep sleep duration. They do not correspond per se to the therapy goal, and it must be assumed that such periods have a limited restorative effect for patients affected by Sleep-Disordered Breathing (SDB).
- In the presence of increased undesired leaks, the airflow signals measured by the PAP device are likely to be faulty. Consequently, the time spent in deep sleep is underestimated. Before AHI and deep sleep are evaluated, problems with mask and mouth leaks should be resolved.

Mean values for length of deep sleep periods

The literature (Dorffner, Vitr, & Anderer, 2015) provides the following age-dependent mean values for deep sleep periods of healthy subjects with application of AASM 2012 rules.

Age	Women	Men
40 years	99 minutes	84 minutes
60 years	94 minutes	69 minutes
80 years	90 minutes	55 minutes

Possible causes of non-restorative sleep in PAP therapy

Sub-optimum PAP therapy: In isolated cases moderately high AHIs or leakage values can disturb sleep; in such cases other events such as snoring, RERAs (Respiratory Effort-Related Arousals) and flow limitations should be investigated. In the case of increased central AHI (e.g., TECSA or treatment-emergent Central Sleep Apnea), the AcSV mode (prismaCR) should be used.

Impairment caused by PAP therapy itself: Patients may be bothered by dry mouth, mask problems or the therapy pressure (Kasai T. et al., 2008). That applies especially to patients with anatomic narrowing of the upper airways (Park P. et al., 2017). If necessary, a change of mask should be made or a humidifier – additionally with heated tube system – should be used (Palm et al., 2017).

The devices in the prisma series are distinguished by their very low operating sound and proven comfort functions. Furthermore, the pressure reaction in APAP mode is therapeutically effective without unnecessarily high pressure increases, according to an independent bench test (Isetta et al., 2016).

Comorbidities: Diverse disorders such as insomnia (Björnsdóttir E. et al., 2013), (Philip et al., 2017), PLM (Mwenge G.B., Rougui I., & Rodenstein D., 2017), diabetes, allergies, anemia, depression (Fernandez-Mendoza et al., 2015) can impair restorative sleep. They must be treated separately from respiratory disorders in order to improve sleep.

External factors: Sleep hygiene, stress, noise, diet, alcohol consumption, not enough sleeping time can likewise impair sleep's restorative power. These factors can be identified in a conversation with the patient and action taken to improve them.

APPENDIX 1
Pgs. 7-8

Conclusion

Assessing and optimizing the time spent in deep sleep in combination with compliance, AHI and leakage can significantly improve therapeutic success under PAP therapy. Such results conform to the objective of sleep medicine, which is not only the elimination of respiratory events, but the improvement in the restorative effect of sleep.

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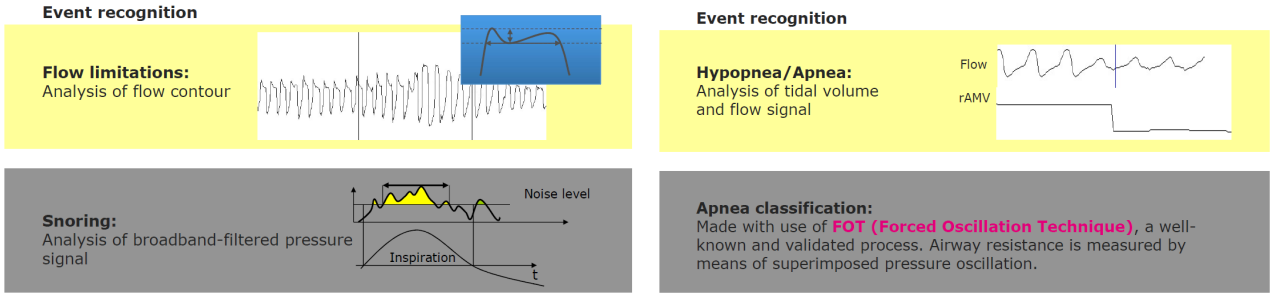
APPENDIX 2

01 Apnea Differentiation

APAP Function



Proactive Regulation of the Algorithm

The best way to distinguish different types of apnea:

- The automatic regulation of APAP / (E)EPAP requires reliable apnea information. In cases of obstructive apnea, therapy pressure is raised in order to prevent further obstructions.

- In fixed modes such as CPAP, S, ST, apnea information is important in determining whether the therapy is going smoothly or if setting or even the mode have to be changed

- Two measuring processes are available:

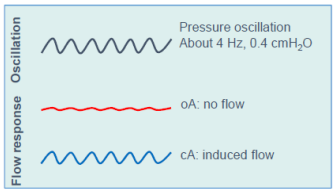
FOT: Forced Oscillation Technique (in all modes WITHOUT backup frequency)
FBT: Forced Breath Technology (in all modes WITH backup frequency)

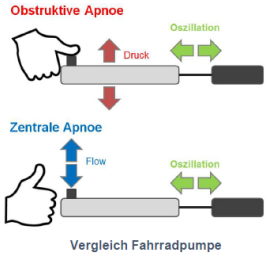
APPENDIX 2
Pgs. 5-8

FOT - Functionality

- With the help of Forced Oscillation Technique (FOT), our CPAP & APAP therapy devices reliably distinguish between obstructive & central apnea.

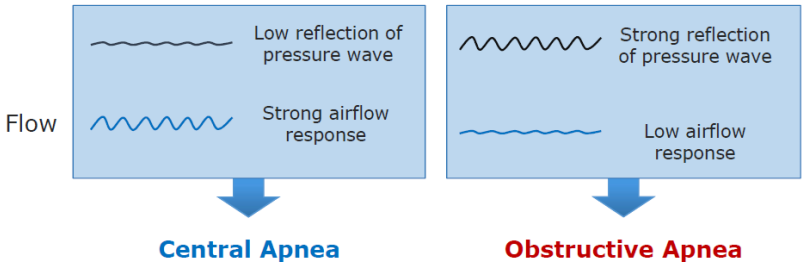
- The sensitive FOT process uses airflow & pressure to measure resistance & obstruction in the upper airways to which the device then reacts.





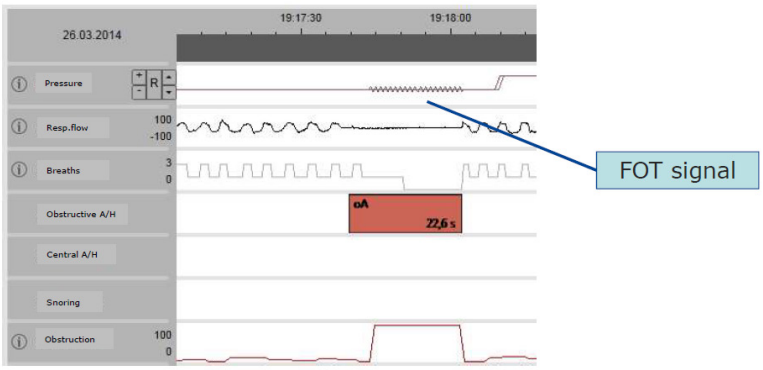
APAP Functionality

In the event of apnea, an oscillation signal is applied which has a frequency of about 4 Hz & an amplitude of 0.4 mbar.
The flow response is the critical criterion in determining whether the apnea is central or obstructive.



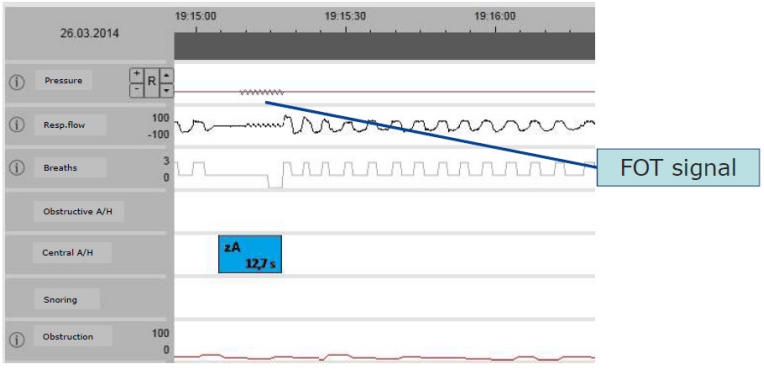
Example of oA with FOT

Oscillation frequency: 4 Hz (4 oscillations /s)
Oscillation Amplitude: 0.4 hPa



Example of cA with FOT

Oscillation frequency: 4 Hz (4 oscillations /s)
Oscillation Amplitude: 0.4 hPa



APPENDIX 2
Pgs. 9-12

02 | Two APAP Settings

Proactive Regulation of the APAP

- Challenge: To combine stable, therapeutically effectiveness & lowest possible pressure.
- A pressure decrease that is too fast or too extreme causes anew serious obstructions & arousals.
- A pressure increase that is too fast or too extreme in response to mild obstructions leads to high mean pressures or high pressure variability (another fast decrease)
- An inadequate increase in the event of severe obstructions results in long periods with subtherapeutic pressures.

NEW with two APAP settings: The right therapy for every patient

Two APAP Settings - Standard vs. Dynamic

Choose your preferred setting:

- No acceptance of high pressures
  ! Activate softPAP too
- Side effects / Leaks
  at high pressures
- Arousals caused by pressure
  increases

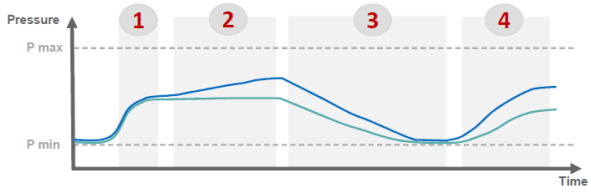
-> OSA, mixed sleep apnea

APAP DYNAMIC **APAP STANDARD**

- Partial obstructions cause persistent sleepiness
- High pressure variability based on sleep stage, positions, etc.

-> OSA, UARS

Two APAP Settings - Standard vs. Dynamic



1 Phase with oA, oH, (RERA)
2 Phase with flow limitations
3 Phase without event
4 Phase with snoring

APAP dynamic:
- Dynamic increase to prevent events with risk of desaturation / arousals
- Further mild increase to normalize flow curve
- Pressure decrease from elevated level
- Rapid pressure response and high sensitivity to snoring

Maximum normalization of inspiratory flow curve and prevention of snoring and flattening

APAP standard:
- Dynamic increase to prevent events with risk of desaturation / arousals
- Pressure is maintained to prevent reoccurrence of severe events (increase in lowest quartile)
- Pressure decrease, starting from standard level
- Epoch-based response (every two minutes) to snoring with conventional sensitivity

The same reliable response to severe events; additional, cautious pressure increase in response to mild events with goal of promoting maximum patient acceptance

APPENDIX 2
Pgs. 13-16

Two APAP Settings

You have a choice between two different settings for APAP management.

Std (Standard): 	Strong response to apnea and hypopnea, but not as strong a response to flattening and snoring	**Goal:** Mean pressure and leakage kept as low as possible
dYn (Dynamic): 	Intense response to normalize breathing; likewise intense response to mild obstructions and occurrences of snoring and phases with flattening.	**Recommendation:** Use for patients who benefit from higher pressures.

Standard-APAP: Algorithm Details

- **An epoch = 2 minutes**
- Goal: Acclimation phase to a new pressure, no provocation of events or arousals
- In general: pressure change at the end of the epoch
- In event of obstructive hypopnea (oH) & obstructive apnea (oA), up to two times in the epoch
- **eSO** events: oA, oH
  Snoring > eight breaths in the epoch
- **eMO** events: RERA,
  Snoring > four breaths in the epoch

Dynamic-APAP: Algorithm Details

- **An epoch = 2 minutes**
- Goal: Acclimation phase to a new pressure, no provocation of events or arousals
- In general: pressure change at the end of the epoch
- Response to snoring (after six breaths), immediate response to obstructive hypopnea (oH) & obstructive apnea (oA), up to two times in the epoch
- **eSO** events: oA, oH
Snoring > six breaths in the epoch
- **eMO** events: RERA,
Snoring > three breaths in the epoch

APAP: Algorithm Details

- Pressure range (Pmax-Pmin) is divided into four quartiles
- Dynamic depending on pressure range
- **Example**
Pmax 18 hPa, Pmin 10 hPa

Q1: 10-12 hPa
Q2: 12-14 hPa
Q3: 14-16 hPa
Q4: 16-18 hPa

	eSO	eMO*	eFL*	
			Std	*dYn*
Quartile 1	1.5 hPa	1.0 hPa	0.5 hPa	0.5 hPa
Quartile 2	1.0 hPa	1.0 hPa	--hPa	0.5 hPa
Quartile 3	1.0 hPa	0.5 hPa	--hPa	0.2 hPa
Quartile 4	0.5 hPa	0.5 hPa	--hPa	--hPa

Pressure increase dependent on events

**** Increase max. 4 hPa above eSO pressure***

APPENDIX 2
Pgs. 17-20

APAP: Waiting Time to Pressure Decrease

- An event-free waiting time must occur before the first pressure decrease takes place.
- The decrease also depends on the quartile & severity of the previous obstruction.
- If several epochs with obstructions occur, the one that counts is the longest within the related waiting time, not the sum of all or something similar.

	eSO	eMO	eFL
Quartil 1	10 min	6 min	4 min
Quartil 2	8 min	6 min	4 min
Quartil 3	8 min	4 min	2 min
Quartil 4	6 min	2 min	--

Waiting time after epoch with obstruction, depending on type of epoch

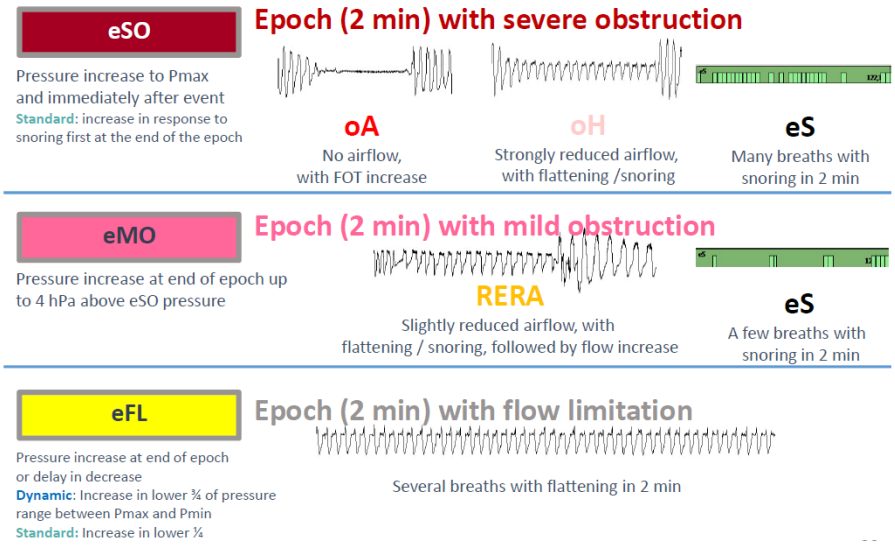
APAP: Pressure Decrease

- If no events occur, the pressure is decreased again.
- Example:

Pmin 8 hPa, Pmax 16 hPa
Q1: 8h Pa - 10h Pa
Q2: 10h Pa - 12h Pa
Q3: 12h Pa - 14h Pa
Q4 14h Pa - 16h Pa

	Decrease in hPa
Quartile 1	0.25 hPa every 4 min
Quartile 2	0.25 hPa every 4 min
Quartile 3	0.5 hPa every 2 min
Quartile 4	1.0 hPa every 2 min

prisma - Algorithm in Detail



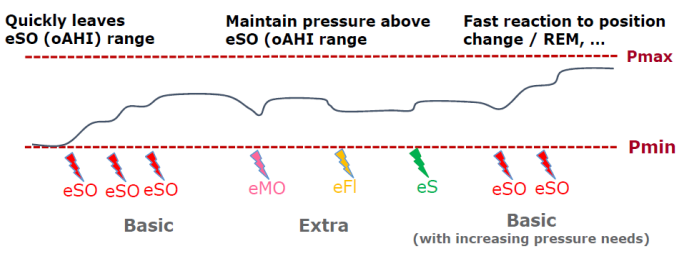
prisma - Algorithm in Detail

- **Basic protection:** Pressure reaction to severe obstructions (AHI-relevant!) strong & long enough to guarantee a low Rest Index.

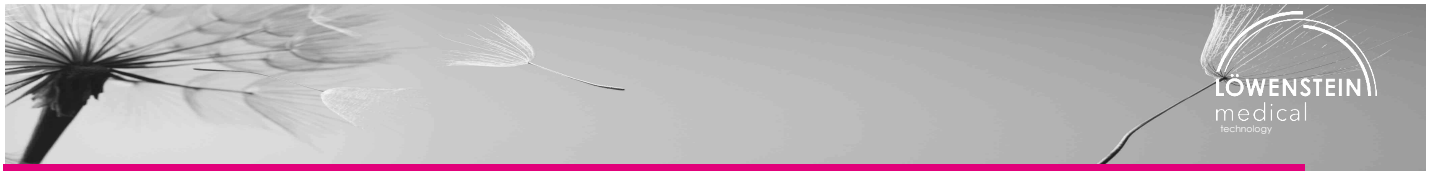
Identical in APAP **Standard** & **Dynamic**

- **Extra Protection:** Milder obstructions delay the decrease or lead to further increases, depending on the quartile: Normalization of respiratory curve, "safe distance" to pressure ranges with severe obstructions

In APAP **Dynamic** stronger, additional increase in **Standard**



APPENDIX 3



Study Hunter: Benchtest of AHI agreement in APAP (20A)

Benchtest Evaluation of AHI agreement between PAP algorithm and polygraph in predominant CSA patients

Y. Rétory; S. Liu; S. Hardy; F. Cottin; G. Roisman, M. Petitjean; Poster presentation ERS 2019.

Background:

A reliable event detection is the prerequisite to treat sleep disordered breathing efficiently, the major parameter being the apnea-hypopnea-index (AHI). A correctly detected AHI is as well essential for an effective intervention based on the device software and especially based on telemonitoring. It is known that there are differences in detecting and scoring methods between the devices of different manufacturers that might significantly influence the patients' therapy. In this benchtest by ALEHOS the AHI detected by different devices have been compared to the data measured by a polygraph and scored according to AASM to evaluate the reliability of apnea-hypopnea detection as well as to visualize the differences.

Overall Message:

Switching from one APAP-device to another without further PG control might have significant consequences on the patients' therapy due to very different accuracy levels of AHI scoring.

Main Results:

Even though there was a high correlation between AHI detected by the different devices and detected by the PG overall, there are differences in AHI scoring between the tested devices.
AHI generated by the device may not be an absolute indicator of treatment efficiency in patients with suspicious CSA, but prisma20A shows the highest accuracy level (together with Philips dreamstation) of 96% with PG as reference.
Resmed and Sefam reached an accuracy level of 84% and 88% respectively.
Overall apnea detection of PAP devices correlated better to the results by PG than hypopnea detection of PAP devices.

Method:

- 25 breathing sequences measured on 4 central sleep apnoea (CSA)patients
- Simulated on an artificial lung
- on 4 devices that have been compared: AirSense 10 (Resmed), Dreamstation Auto (Philips), S.Box (Sefam), prisma20A (Löwenstein)

APPENDIX 4

Study Hunter: APAP Effectiveness in prisma

Examination of the Effectiveness of FOT-based auto-CPAP Therapy Device in the Treatment of Patients with Obstructive Sleep Apnea

S.D. Herkenrath, M. Treml, N. Anduleit, K. Pietruska, M. Schwaibold, W.J. Randerath, Scientific Institute for Pneumology at University of Cologne.
Poster (German, English, French), ERS 2018

Background:
The Forced Oscillation Technique (FOT) is proven to be a sound method for apnea classification in APAP devices. This clinical study examines

- The effectiveness of pressure regulation and
- analyses associations between applied therapy pressure and mask leakage.

Overall Message:
The algorithm in prisma20A does not need to fear the comparison with competition!
The algorithm is effective. The results apply to all APAP modes in prisma devices as well.

Main results:

- Obstructions were treated effectively.
- Even at higher pressures there was no risk that APAP pressure is “overshooting”.
- Even though most patients wore a nasal mask there was hardly any mouth leakage measured.

Further Conclusion:

- Our devices do not provoke or induce central events.
- It was proven that APAP pressure was only moderately increased to treat events effectively (Löwenstein philosophy).

Method:

- 34 OSAS patients, baseline diagnosis of AHI >15
- Open pressure thresholds from 4hPa – 20hPa
- 1 diagnosis night, 1 therapy night
- Standard APAP regulation

Further Comment:
Further publications are in progress. You will be informed.

APPENDIX 5

Study Hunter: APAP effectiveness in prisma

Extended evaluation of the efficacy of a proactive forced oscillation technique-based auto-CPAP algorithm

S. D. Herkenrath, M. Treml, N. Anduleit, K. Richter, A. Pietzke-Calcagnile, M. Schwaibold, R. Schäfer, R. Alshut, A. Grimm, L. Hagmeyer, W. J. Randerath, Sleep and Breathing, https://doi.org/10.1007/s11325-019-01901-8

Background:

As published by Zhu et. al there are significant differences in the efficacy of APAP devices.[1] There are also limitations to APAP in favor of CPAP (e.g. blood pressure reduction), that is why a reliable pressure regulation is even more important. The Forced Oscillation Technique (FOT) is a proven method for reliable apnea classification to ensure adequate pressure regulation in APAP devices. In a prospective, interventional trial the APAP mode in prisma was examined regarding:

- The effectiveness of pressure regulation in terms of evaluating upper airway obstructions,
- Flow contour analyses during hypopneas.

Overall Message:

The APAP algorithm in prisma-devices show optimal suppression of respiratory events with adequate pressure regulation (therapy P50=7hPa). The majority of rare residual respiratory events was detected by prisma. Sleep quality increased independently from pressure level.

Main Results:

(1) Apneas were differentiated reliably, obstructions were treated effectively, the arousal index significantly decreased.
(2) The APAP mode significantly increased REM and slow wave sleep; independently from therapy pressure level, thus improving sleep quality overall.

Further Conclusion:

- Five patients presented TECSA (treatment emergent central sleep apnoea) and were supposedly mainly suffering from central apneas coinciding with upper airway obstructions, they also showed significantly higher (mouth) leakage (associated with higher CO_2 washout) and pressure levels. These events were correctly detected by FOT, but pose challenges to adequate therapy.[2]

3) It was proven that APAP pressure was only moderately increased to treat events effectively (Löwenstein philosophy in standard regulation).

Method:

- Inclusion: 46 patients with severe OSAS (AHI 36), mostly obese with routine PSG for suspected OSA
- 43 patients with nasal mask.
- prisma LAB in APAP standard mode, open pressure threshold from 5-20hPa, 15min softSTART.
- 1 diagnosis night, 1 therapy night

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[1] Zhu K, Roisman G, Aouf S, Escourrou P (2015) All APAPs are not equivalent for the treatment of sleep disordered breathing: a bench evaluation of eleven commercially available devices. J Clin Sleep Med 11:725–734. https://doi.org/10.5664/jcsm.4844

[2] Please refer to the therapy option of adjustable pressure limits (Pmax oA) in prisma- devices, also in detail described in the **White Paper Edition by LMT "Central Respiratory Events during CPAP / EPAP Therapy**"

APPENDIX 6

PLOS | ONE

RESEARCH ARTICLE

Novel Approach to Simulate Sleep Apnea Patients for Evaluating Positive Pressure Therapy Devices

Valentina Isetta[1,2], Josep M. Montserrat[2,3,4], Raquel Santano[1], Alison J. Wimms[5], Dinesh Ramanan[5], Holger Woehrle[5], Daniel Navajas[1,2,6], Ramon Farré[1,2,4]*

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OPEN ACCESS

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Abstract

Bench testing is a useful method to characterize the response of different automatic positive airway pressure (APAP) devices under well-controlled conditions. However, previous models did not consider the diversity of obstructive sleep apnea (OSA) patients' characteristics and phenotypes. The objective of this proof-of-concept study was to design a new bench test for realistically simulating an OSA patient's night, and to implement a one-night example of a typical female phenotype for comparing responses to several currently-available APAP devices. We developed a novel approach aimed at replicating a typical night of sleep which includes different disturbed breathing events, disease severities, sleep/wake phases, body postures and respiratory artefacts. The simulated female OSA patient example that we implemented included periods of wake, light sleep and deep sleep with positional changes and was connected to ten different APAP devices. Flow and pressure readings were recorded; each device was tested twice. The new approach for simulating female OSA patients effectively combined a wide variety of disturbed breathing patterns to mimic the response of a predefined patient type. There were marked differences in response between devices; only three were able to overcome flow limitation to normalize breathing, and only five devices were associated with a residual apnea-hypopnea index of <5/h. In conclusion, bench tests can be designed to simulate specific patient characteristics, and typical stages of sleep, body position, and wake. Each APAP device behaved differently when exposed to this controlled model of a female OSA patient, and should lead to further understanding of OSA treatment.

Introduction

Obstructive sleep apnea (OSA) is a prevalent breathing disorder and is considered a major public health issue, affecting 5–15% of the general population and increasing with both body mass index and age (up to at least 60–65 years) [1,2]. OSA is characterized by repetitive narrowing

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collection and analysis, decision to publish, or preparation of the manuscript. The specific roles of these authors are articulated in the 'author contributions' section.

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and closure of the upper airway during sleep [3] that results in brain arousal, intermittent hypoxia, negative intrathoracic pressure swings, and increased sympathetic activity. OSA is associated with a reduction in quality of life, daytime sleepiness, traffic accidents, neurocognitive impairment, metabolic, cardiovascular disease [4] and malignancies [5].

The treatment of choice for OSA is the application of continuous positive airway pressure (CPAP) to the patient's nose or mouth through a mask during sleep at home. This pressure in the mask is transmitted to the pharyngeal area, splinting the collapsible upper airway walls thereby avoiding obstruction. Auto-adjusting positive airway pressure (APAP) devices, which are increasingly being used, are driven by algorithms that measure abnormal sleep breathing events, analyze the patient's breathing pattern and eventually increase the delivered pressure in response to airway obstruction, or decrease pressure when breathing is stable to increase patient comfort [6–11]. In theory, APAP devices should be ideal for treating a range of patients with different characteristics, and for effectively treating OSA despite within-night and night-to-night variations in the upper airway collapsibility experienced by each individual patient [12–16]. However, commercially available APAP devices contain undisclosed proprietary algorithms, and therefore the way that they measure and respond to specific breathing patterns varies [17]. In addition, some APAP manufacturers are introducing new algorithms based on specific patient characteristics. This move towards personalized medicine in the treatment of OSA means greater choice for patients and more variability in APAP algorithms. Therefore, understanding how each device responds to different OSA patterns requires comparative studies using well defined references.

Bench testing is a useful method to characterize the response of different APAP algorithms under well-controlled conditions, thus avoiding the biological variability inherent in clinical trials. However, previously used bench test models have been based on subjecting the APAP device under test to a repetitive string of disturbed breathing patterns, without providing a sufficiently wide spectrum of events. These limitations mean that variety in patient characteristics and phenotypes, or the changes that occur during different sleep stages and body positions over the course of a night's sleep, cannot be taken into consideration. This is particularly relevant given that different subpopulations of OSA patients (e.g. children, men, women, the elderly) exhibit specific traits in their sleep-related breathing disorders [18].

Therefore, the aims of this proof-of-concept study were: 1) to design a new complex and versatile bench test approach for realistically simulating respiratory events throughout the course of the night in an OSA patient, mimicking breathing disturbances across different phenotypes, and 2) to implement a full night example of a female OSA phenotype and use this to compare the responses of several currently-available APAP devices.

Materials and Methods

The hardware of our new model was based on a previously described bench test [19]. This fully computer-driven model comprises a servo-controlled pump able to deliver a flow that replicates any breathing waveform stored in the computer. An obstruction valve allows the simulation of controlled obstructive events by imposing mechanical impedances previously recorded in patients with OSA. Two other valves can mimic leaks and mouth breathing, and a loud-speaker-in-box system can superimpose simulated snoring onto the breathing flow. The test bench is equipped with two sensors, one to measure pressure at the simulated patient entrance and one to measure the actual flow generated by the patient simulator. A calibrated leak based on a 4-mm internal diameter (ID) orifice [20] mimics the mask leak (exhalation port) in nasal masks. In previous studies, this system was fed by a collection of disturbed breathing events, such as obstructive and central apneas, hypopneas, flow limitation, mask leaks and mouth expiration [19,21].

To design the new OSA simulator model we developed a novel approach aimed at realistically replicating a typical night of sleep for a female patient. With this aim, we considerably expanded our library of disturbed breathing patterns anonymously extracted from polysomnography recordings obtained from real OSA patients and we incorporated several new adjustable features into the simulator. Specifically, the new patient model can be set to react to the pressure delivered by the APAP device (PAP-responsive mode) or to reproduce a fixed scenario of disturbed breathing events (Steady mode), depending on the device characteristics being tested. Moreover, the severity of the simulated OSA profile is now fully modifiable by changing the frequency and duration of each breathing event. Various artefacts were introduced into the event spectrum, such as changes in tidal volume and breath rate, to replicate typical events during wake such as irregular breathing, swallowing, moving and talking. By combining these new features, we aimed to create a new OSA model concept model that can realistically replicate a whole night of sleep, including phases of wake, rapid eye movement (REM) and non-REM sleep, and change in body position, each one designed to mimic different characteristics in terms of upper airway collapsibility.

For this study specifically, as an example of an entire night of sleep-disordered breathing (SDB), the bench test model was set to simulate the disturbed patterns of a female OSA patient with the following characteristics: long sleep latency (45 min), low positive airway pressures (PAPs) required to overcome obstructive events, high proportion of flow limitation events versus apneas, higher apnea-hypopnea index (AHI) during REM sleep, and only minor positional effects on upper airway collapsibility. The features and structure of this female-specific OSA patient simulation are detailed in Table 1. The breathing pattern of the simulated patient depended on the PAP applied by the device under test, with a total duration of 4 hours and 15 minutes. APAP pressure values required to normalize breathing during each stage of the simulation are shown in Fig 1. The simulated night consisted of programming the different stages described in Table 1, starting with 45 minutes of simulated awake stage (sleep onset) followed by a succession of different sleep stages with the features detailed in Table 1 (e.g. breathing frequency, number and types of respiratory events) and a final awake short period. In this way we were able to model a patient exhibiting different sleep breathing characteristics throughout consecutive sleep stages.

Ten different commercially available APAP devices were tested using the new bench test model and the female-specific simulation described above: AirSense 10 (A) and AirSense 10 AutoSet for Her (B) by ResMed; Dreamstar by Sefam (C); Icon by Fisher & Paykel (D); Resmart by BMC (E); Somnobalance (F) and Prisma 20A (G) by Weinmann; System One by Respironics (H); iCH (I) and XT-Auto by Apex (J). Each APAP device was connected with its own tube to the bench model. Default APAP settings were used (minimum pressure 4 cmH_2O, maximum pressure 20 cmH_2O). Each device was tested twice and the results averaged to obtain the final values.

Results

The new OSA patient simulator could effectively combine a great variety of SDB elements to mimic the response of the predefined patient type. The responses of the assessed APAP devices to the new female-specific bench test model are summarized in Table 2. There was considerable variation among devices, particularly with respect to the mean and maximum nasal pressures applied, and the ability to overcome obstructive events and flow limitation, The residual AHI was calculated as the number of residual obstructive events per hour and the residual flow limitation was measured as the portion of the test in minutes (excluding the initial 45-minute wake period) that the simulated patient remained on flow limitation.

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Table 1. Description of the patient simulation implemented in the bench test model.

Stage	Duration	AHI	Features
Sleep onset	45 min	-	
			16 breaths/min
			V_T 500 mL
			Random insertion of changes in breathing rate and V_T, and swallowing
Non-REM cycle 1	60 min	15/h	
			Body position: side
			Apneas (0–5 cmH_2O): event length 12 sec
			Hypopneas (5–7 cmH_2O): event length 16 sec
			Flow limitation (7–9 cmH_2O)
			Normal breathing (>9 cmH_2O)
REM cycle 1	15 min	30/h	
			Apneas (0–8 cmH_2O): event length 18 sec
			Hypopneas (8–10 cmH_2O): event length 16 sec
			Flow limitation (10–12 cmH_2O)
			Normal breathing (>12 cmH_2O)
Non-REM cycle 2	45 min	15/h	
			Body position: side
			Apneas (0–5 cmH_2O): event length 12 sec
			Hypopneas (5–7 cmH_2O): event length 16 sec
			Flow limitation (7–10 cmH_2O)
			Normal breathing (>10 cmH_2O)
REM cycle 2	25 min	30/h	
			Apneas (0–7 cmH_2O): event length 18 sec
			Hypopneas (7–9 cmH_2O): event length 16 sec
			Flow limitation (9–11 cmH_2O)
			Normal breathing (>11 cmH_2O)
Non-REM cycle 3	30 min	15/h	
			Apneas (0–5 cmH_2O): event length 18 sec
			Hypopneas (5–7 cmH_2O): event length 16 sec
			Flow limitation (7–10 cmH_2O)
			Normal breathing (>10 cmH_2O)
REM cycle 3	30 min	30/h	
			Body position: supine
			Apneas (0–9 cmH_2O): event length 18 sec
			Hypopneas (9–11 cmH_2O): event length 16 sec
			Flow limitation (11–13 cmH_2O)
			Normal breathing (>13 cmH_2O)
Awake	5 min	-	Normal breathing

AHI: apnea-hypopnea index; REM: rapid eye movement; V_T: tidal volume.

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Breathing normalization with a residual AHI <5/h was only achieved with devices A, B and D; devices E, H, I and J were associated with more than five residual events per hour. Pressure changes of each device throughout the whole test are displayed in Fig 1.

Considering the 45-minute wake period, there was significant variation in the behaviour of the different devices. Table 3 shows the pressure values reached by each tested device at the end of the simulated wake period. Device C did not increase the pressure during wake periods.

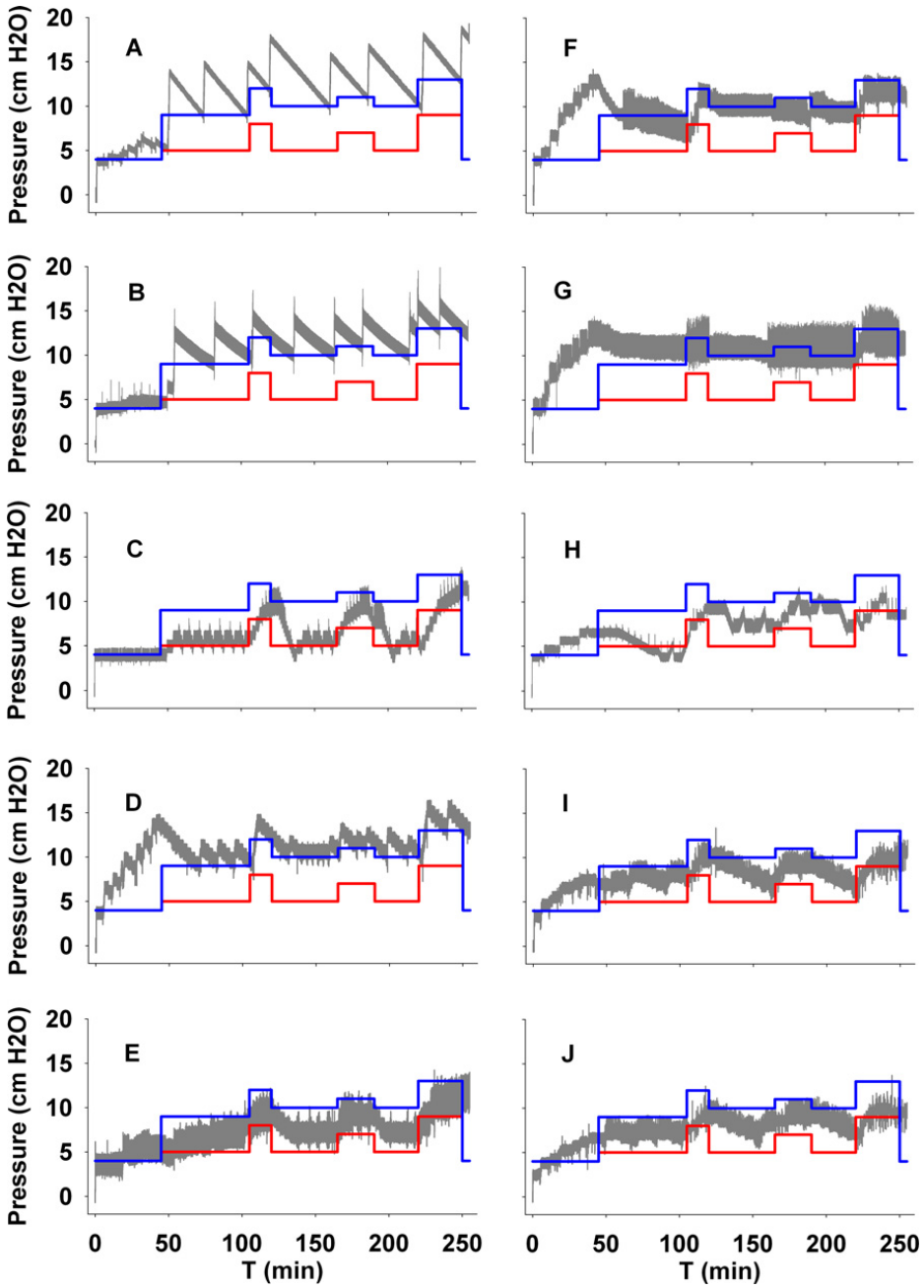

Fig 1. Pressure trends over a full simulated night (grey line) for all APAP devices tested. A device that delivered pressures above the blue line achieves full breathing normalization, while if it delivered pressures just above the red line only obstructive apneas were overcome.

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Table 2. Reponses of automatic CPAP devices to a specific simulated OSA patient.

Device	P_{max}, cmH_2O	P_{mean}, cmH_2O	Residual AHI, /h	Overcome obstructive events?	Overcome flow limitation?	Residual flow limitation, min (% sleep time)
A	18.65	13.25	0.7	Yes	Yes	4 (2%)
B	15.4	11.8	0.7	Yes	Yes	4 (2%)
C	11.4	6.75	16.5	No	No	24 (12%)
D	15.3	11.3	0.6	Yes	Yes	24.5 (12%)
E	11.35	7.7	11.9	No	No	81 (40%)
F	12.6	9.5	2.4	Yes	No	167 (81%)
G	12.1	10.05	1.6	Yes	No	122 (60%)
H	12.45	7.75	10	No	No	76 (37%)
I	10.6	8.3	6.5	Yes	No	142 (69%)
J	10.1	8.2	8.5	No	No	132.5 (65%)

AHI: apnea-hypopnea index; P_{max}: maximum positive airway pressure applied; P_{mean}: mean positive airway pressure; A: AirSense 10 by ResMed; B: AirSense 10 AutoSet for Her by ResMed; C: Dreamstar by Sefam; D: Icon by Fisher & Paykel; E: Resmart by BMC; F: Somnobalance by Weinmann; G: Prisma 20A by Weinmann; H: System One by Respironics; I: iCH by Apex; J: XT-Auto by Apex.

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Three devices (A, B and E) displayed only mild pressure increases (<2 cmH_2O). Moderate pressure increases (2.5–3 cmH_2O) were displayed by three devices (H, I and J), and significant pressure increases (>7 cmH_2O) were seen from three devices (D, F and G). Three examples of different responses during the simulated wake period are presented in Fig 2, together with the flow signal generated by the simulator during the initial awake phase, which consisted of normal breathing with some events inserted simulating flow alterations due to irregular breathing (E) and swallowing (S). Devices A, B and D contain algorithms aimed at automatically detecting sleep onset (for A, B AutoRamp mode and for D SenseAwake mode). Devices A and B showed similar pressure increases with AutoRamp mode turned off, while device D responded with higher pressure increases when the SenseAwake mode turned off.

To assess whether the observed variations in pressure during wake had an influence on the results of testing, a subset of devices that showed a moderate to significant pressure increase during sleep onset (D, G, H and I) were retested without the wake phase of the test. In this

Table 3. Pressure values reached by each device after 45 minutes of simulated wake.

Device	APAP pressure after 45 min of simulated wake (cmH_2O)
A	5.4 (5.8 with AutoRamp OFF)
B	4.8 (5.2 with AutoRamp OFF)
C	4.0
D	11.2 (14.5 with SenseAwake OFF)
E	4.6
F	11.8
G	11.7
H	6.5
I	6.8
J	6.9

A: AirSense 10 by ResMed; B: AirSense 10 AutoSet for Her by ResMed; C: Dreamstar by Sefam; D: Icon by Fisher & Paykel; E: Resmart by BMC; F: Somnobalance by Weinmann; G: Prisma 20A by Weinmann; H: System One by Respironics; I: iCH by Apex; J: XT-Auto by Apex.

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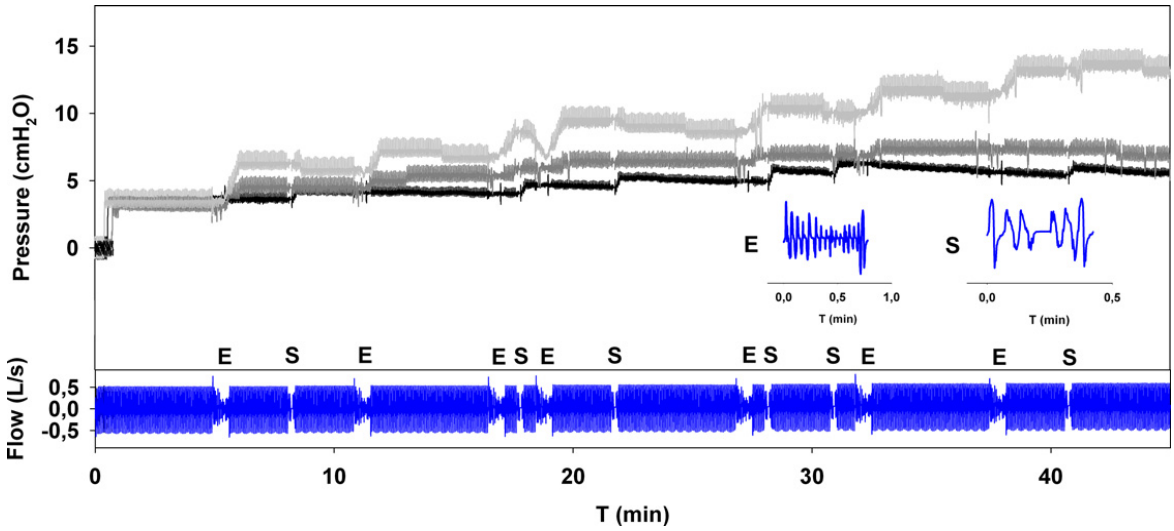

Fig 2. Pressure trends for three different APAP devices tested during the initial 45-minute simulated wake period. Device A (black line) showed a mild pressure increase (< 2 cmH_2O), device I (dark grey line) showed a moderate pressure increase (2.5–3 cmH_2O), while device D (light grey line) showed a high pressure increase (>7 cmH_2O) in response to the breathing pattern simulating 45 minutes of wake period (blue line). E: erratic breathing; S: swallowing.

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additional analysis (Table 4), the responses of the tested devices were relatively similar to the ones in the previous tests that included the 45-minute sleep onset phase. The largest change was seen in device D, where the residual AHI increased from 0.6 to 6 events per hour.

Discussion

We successfully developed and carried out a proof-of-concept test of a novel optimized bench model easily adaptable to simulate different SDB patterns found in OSA, including periods of wake, periods representing different sleep stages and phases of more or less severe SDB events. This tool can be useful to objectively evaluate bench test performance of different APAP devices with realistic breathing patterns covering a wide range of patient phenotypes. In its "Steady mode", the simulator could also assess the capacity of APAP, as well as CPAP, devices to estimate treatment duration and detect residual respiratory events of a fixed predefined disturbed breathing scenario.

The presentation and severity of OSA varies greatly depending on patient characteristics such as gender, age, body mass index, and craniofacial structure [18,22]. Specific patient

Table 4. Results of device re-testing without the sleep onset period.

Device	P_{max}, cmH_2O	P_{mean}, cmH_2O	Residual AHI, /h	Overcome events	Overcome flow limitation	Residual flow limitation, min (% sleep time)
D	14.6	8.95	6	Yes	Yes	9 (4%)
G	11.65	9.25	2.6	Yes	No	164 (80%)
H	11.45	7.35	6.6	No	No	70 (34%)
I	11.3	7.9	9.6	Yes	No	107.5 (52%)

AHI: apnea-hypopnea index; NA: not available; P_{max}: maximum positive airway pressure applied; P_{mean}: mean positive airway pressure; D: Icon by Fisher & Paykel; G: Prisma 20A by Weinmann; H: System One by Respironics; I: iCH by Apex.

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subgroups have been gaining a lot of attention recently because of their clinical relevance. At one end of the age spectrum, elderly patients tend to present with severe OSA and snoring becomes less common. In addition, the frequency of central events increases, although obstructive events still predominate [23]. In contrast, children with OSA have frequent snoring, restless sleep, mouth breathing, apneas, gasping, and laboured or paradoxical breathing [24]. With the growing trend towards personalized therapy, specific patient breathing patterns will be increasingly studied as manufacturers work to design the most optimal treatment for each phenotype.

One good example of this is OSA in females versus males. It is well-known that the polysomnographic features of female OSA are different from those of male OSA. Overall, women have less severe OSA with, on average, a lower AHI [25] and shorter apneas [26]. Women also have more episodes of upper airway events during REM sleep [25]. Body position is far less important for the severity of OSA in women, while OSA severity in men is based more on position than sleep state [25]. Furthermore, women may take longer to fall asleep, but have fewer awakenings during sleep [27]. Regardless of the patient's gender, there is also significant night-to-night variation in OSA, based on factors such as body posture, sleep stages, and previous drug or alcohol intake [28]. Besides OSA pathophysiology, gender influences also patients' PAP requirements [29], as generally female patients require lower pressures. Such considerable variability between phenotypes highlights the relevance of the simulation approach taken in this study. In our optimized bench test we implemented a dynamic pattern ("PAP-responsive") simulating a female patient phenotype (although an individual male patient may also present with this OSA pattern), which included long periods of flow limitation, low AHI, and short, low-severity obstructive events. Only three of the APAP devices tested were able to achieve full breathing normalization by overcoming all types of disturbed events including flow limitation. Considering the potential for increased flow limitation in female patients, which may lead to breathing disturbances, the effectiveness of treatment in patients presenting with a high component of flow limitation should be carefully examined.

Published data comparing different APAP algorithms is scarce, particularly for devices recently launched into the market. Pevernagie *et al* examined two APAP devices and found that the residual apnea-hypopnea index (AHI) was lower during use of one device compared with the other (3.5±5.6/h vs 9.9±31.0/h), and that the amount of snoring during the night was significantly higher with one device [30]. A similar study by Nolan *et al* compared three commercially available devices. The authors found that mean pressure and patient compliance were significantly lower on one of the APAP devices [17]. Differences between algorithms combined with a lack of information regarding how different auto-adjusting devices work has led to the perception that auto-adjusting devices are a 'black box' which should be used with caution [31]. In this study, we also found considerable variation among devices in both the magnitude of response to obstructive events, the time taken to increase pressure during disrupted breathing, and device behaviour during the simulated wake period. With the exception of one device, which did not increase the pressure at all, most devices at least slightly increased pressure during simulated wakefulness. Some devices showed quite an intense pressure response during the wake period of the test, with one reaching almost 14 cmH_2O and two reaching 12 cmH_2O. Due to the potential impact this could have on patient comfort, pressure changes during wake periods should be assessed in clinical practice, particularly in patients who report difficulties falling asleep while using PAP therapy or issues with comfort at higher PAP pressures.

As stated above, our finding of considerable variability in the response of APAP devices when subjected to the same breathing pattern under well-controlled conditions is in agreement with previous reports [19,21,32]. These variations can be attributed to the individual algorithms within each APAP device. Each algorithm analyses flow and pressure to determine whether there is a breathing disturbance, and then initiates the most appropriate response to

correct such a disturbance. For instance, it is interesting to note that, as we explained previously [21], the simulated hypopneas in our model were defined according to specific values of a flow-limitation pattern index initially introduced by Teschler et al [33]. Therefore, it could be possible that automatic CPAP devices set to detect hypopneas using this index, or something similar, could be more suitable for detecting our simulated events than other devices that use other metrics to define and detect hypopneas. Another reason for the observed different response in the automatic CPAP devices tested is that the optimal rate of pressure increase after detection of obstructive events has not been clinically defined. In fact, APAP devices are designed to normalize breathing at a rate which treats actual SDB, avoiding any response to false events, thereby unnecessarily modifying pressure. The results of this bench test have shown that, under well-controlled conditions, there are marked variations in response by different APAP devices, and that there may be high residual AHI or uncontrolled flow limitation in some female patients on some APAP devices. Therefore, all APAP devices should not be considered equal, and efficacy and patient comfort should be carefully examined following APAP initiation.

It must be noted that our results are restricted to the specific patterns of disturbed breathing used in this bench test to simulate a specific OSA patient. It is possible that the response of the tested devices would have been different from the ones reported here if SBD was simulated using different patterns or patient phenotypes. In addition, a limitation of this study is that one device of each type was used. Hence, a more complete assessment would require testing of a larger number of each type of device randomly obtained from those available in the market. Finally, it should be stressed that although bench testing is a useful way to investigate the behaviour of different devices, testing outcomes may vary in clinical practice due to the almost unlimited spectrum of events and phenotypes found in real life. Indeed, crucial factors such as changes in loop gain, and upper airway compliance and pharyngeal critical pressure are not considered in our model. Accordingly, bench testing should be considered as a preliminary assessment before clinical evaluation in patients.

In conclusion, this study showed that a dynamic bench model tailored to represent specific OSA patient phenotypes, incorporating a variety of disturbed breathing events within the same simulated night, including different degrees of severity along sleep stages, and a period of wakefulness, can be useful to characterize treatment responses of commercially-available APAP devices. This demonstrates that bench testing can be modified to better represent a "real" patient, and that APAP devices can show markedly different responses to the same simulated breathing patterns. Realistically mimicking OSA patients during bench testing is useful as a first step to aid in the understanding of actual APAP device responses observed in the clinical setting, and can be helpful in selecting the device that best meets the individual needs of each patient, thereby improving comfort and increasing adherence to therapy, which is essential for effective treatment and reducing the consequences of OSA [34].

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Author Contributions

Conceived and designed the experiments: VI JMM RS AJW DR HW DN RF. Performed the experiments: VI RS RF. Analyzed the data: VI RS RF. Contributed reagents/materials/analysis tools: JMM AJW HW DN RF. Wrote the paper: VI JMM AJW HW DN RF.

APPENDIX 6
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APPENDIX 7

Efficacy of a FOT-based auto-CPAP device for the treatmer

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Background / Aims

- The forced oscillation technique (FOT) uses pressure oscillations to asses the airway resistance. It is an established technology to regulate automatic CPAP devices.
- Former generations of APAP devices used an oscillatory pump to generate the superimposed pressure. The generated volume movements were rather small so that leakage and certain mask types negatively affected the accuracy of the FOT.
- The new APAP devices of the Löwenstein Medical Technology prismaLINE generate a superimposed pressure by the blower itself, allowing a markedly higher volume movement. This enables a more reliable assessment of the obstruction even in technically challenging situations (e.g. higher leakage).
- The device's APAP algorithm regulates the pressure dynamically depending on the set pressure range, which is divided in quartiles. The severity of detected obstructions and the current pressure quartile define the extent of pressure regulation.
- This clinical study aimed to investigate therapeutic efficacy and pressure regulation of the APAP device in OSA patients, especially in challenging situations such as treatment emergent central sleep apnea (TE-CSA) and higher leakage.

Methods

- In this prospective cohort study, newly diagnosed OSA patients (AHI>15/h, <20% central respiratory events) were treated with the prismaLAB/prisma20A in APAP mode during an in-lab polysomnography (PSG).
- The pressure range was set to 5-20 hPa.
- Distribution of therapy pressures and resulting leak rates were analyzed by dividing each PSG in 5min-sections.

Results

- 46 patients were examined (16 female, age 61 [52–72] years, BMI 32 [28–36] kg/m², median [interquartile range]).
- Median AHI was significantly reduced by APAP (36/h vs. 2/h, table 1, figure 1).
- Per patient median pressure values were mostly below 12 hPa and the extent of unintentional leak was rather low, although mostly nasal masks were used (n=43) (Table 1, figure 3).
- The amount of slow wave and REM sleep increased with APAP therapy and was comparable among the different pressure quartiles, as was the arousal index (Table 1, figure 4).
- Six patients (13%) showed treatment-emergent central sleep apnea (TE-CSA), defined as a central apnea index (cAI) under APAP treatment of >5/h and <5/h during diagnosis (figure 1).
- TE-CSA patients had a significantly higher central AHI and higher mixed apnea index during diagnosis, but comparable median therapy pressure (figure 2).

	Diagnosis	APAP
Time In Bed, TIB (min)	432 (412-456)	421 (396-456)
Total Sleep Time, TST (min)	335 (294-374)	308 (270-375)
Slow Wave Sleep (%TST)	20 (14-29)	*29 (19-34)***
REM Sleep (%TST)	16 (11-21)	*24 (14-30)***
Apnea-Hypopnea Index, AHI (/h)	36 (23-55)	*2 (1-6)****
Hypopnea Index, HI (/h)	14 (9-19)	*1 (1-3)****
Obstructive AHI (/h)	36 (22-54)	*1 (1-3)****
Central AHI (/h)	0 (0-2)	*1 (0-3)***
Obstructive AI (/h)	16 (6-34)	*0 (0-0)****
Central AI (/h)	0 (0-1)	*0 (0-2)**
Mixed AI (/h)	0 (0-5)	*0 (0-0)****
Oxygen Desaturation Index (/h)	28 (19-51)	*2 (1-4)****
SpO2<90% (%TIB)	4 (1-10)	*0 (0-0)****
Arousal Index (/h)	30 (22-45)	*15 (10-19)****
Respiratory Arousal Index (/h)	16 (9-28)	*1 (0-1)****

Individual median pressure	Number of patients
5-8 hPa	28
9-12 hPa	16
13-16hPa	2
17-20 hPa	0

Table 1: Results of diagnostic and APAP PSG. Data are median and interquartile range. */**/*** = p<0.05/0.01/0.001 APAP vs. diagnosis. Lower part shows number of patients with a median pressure within the corresponding therapy pressure quartiles based on setting of 5-20 hPa.

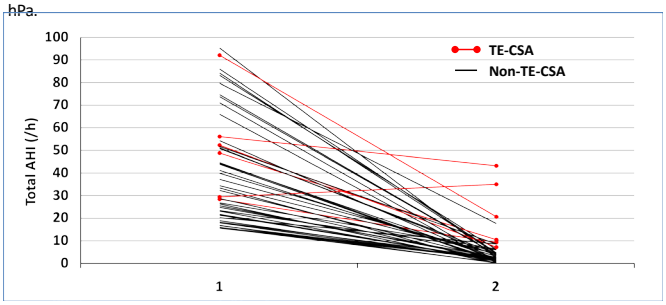

Figure 1: Individual changes of total AHI from diagnostic PSG to APAP PSG.

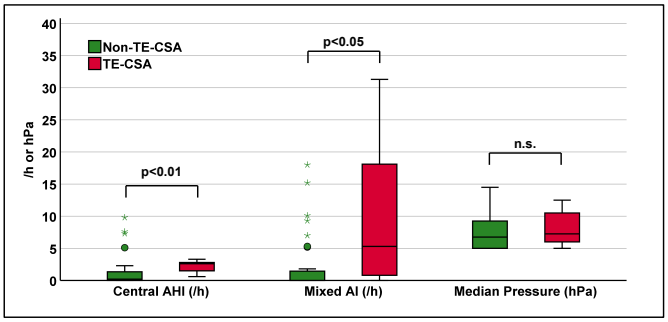

Figure 2: Central AHI and mixed AHI of diagnostic polysomnography and median pressure during therapy in comparison between patients with treatment-emergent central sleep apnea (TE-CSA) and without TE-CSA (Non-TE-CSA). n.s. = not significant.

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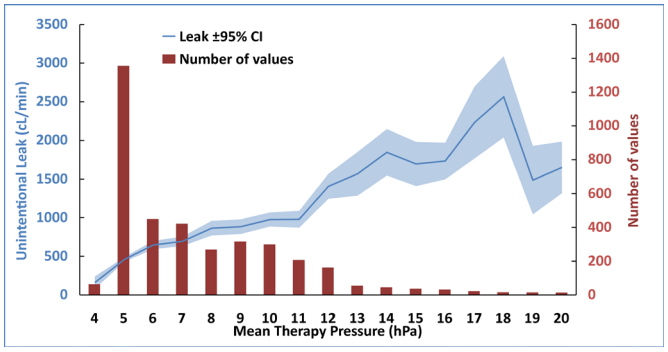

Figure 3: Mean values of unintentional leak and number of values within different mean pressure levels based on analysis of 5-min-sections of all APAP therapy nights.

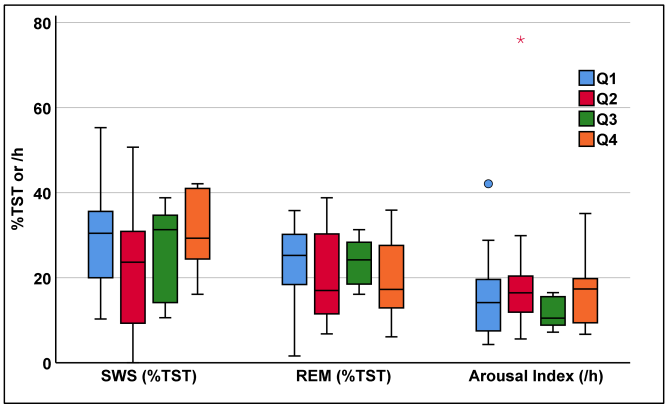

Figure 4: Relative amount of slow wave sleep (SWS), REM sleep and arousal index under APAP therapy for patients within different pressure quartiles (Q1-Q4). Pressure quartiles were chosen based on actual individual median pressures of all patients.

Conclusion

- **The prisma20A highly significantly reduces respiratory events in OSA without indication for inadequate pressure increases in spite of broad pressure limits up to 20 hPa. Due to the relatively low pressure levels the overall leakage also remained low and did not negatively affect APAP therapy.**
- **Higher pressures did not negatively impact sleep quality.**
- **The prevalence of TE-CSA in this study is in accordance with published literature. The device's pressure regulation in TE-CSA patients was not inadequately high, indicating that there was no relevant misclassification of central respiratory events.**
- **A relative high portion of mixed and central apneas in the diagnostic PSG, indicative of disturbed breathing regulation, could possibly be a predictor for TE-CSA.**

APPENDIX 8

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Comparative assessment of several automatic CPAP devices' responses: a bench test study

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ABSTRACT Automatic continuous positive airway pressure (APAP) devices adjust the delivered pressure based on the breathing patterns of the patient and, accordingly, they may be more suitable for patients who have a variety of pressure demands during sleep based on factors such as body posture, sleep stage or variability between nights. Devices from different manufacturers incorporate distinct algorithms and may therefore respond differently when subjected to the same disturbed breathing pattern. Our objective was to assess the response of several currently available APAP devices in a bench test.

A computer-controlled model mimicking the breathing pattern of a patient with obstructive sleep apnoea (OSA) was connected to different APAP devices for 2-h tests during which flow and pressure readings were recorded. Devices tested were AirSense 10 (ResMed), Dreamstar (Sefam), Icon (Fisher & Paykel), Resmart (BMC), Somnobalance (Weinmann), System One (Respironics) and XT-Auto (Apex). Each device was tested twice.

The response of each device was considerably different. Whereas some devices were able to normalise breathing, in some cases exceeding the required pressure, other devices did not eliminate disturbed breathing events (mainly prolonged flow limitation). Mean and maximum pressures ranged 7.3–14.6 cmH_2O and 10.4–17.9 cmH_2O, respectively, and the time to reach maximum pressure varied from 4.4 to 96.0 min.

Each APAP device uses a proprietary algorithm and, therefore, the response to a bench simulation of OSA varied significantly. This must be taken into account for nasal pressure treatment of OSA patients and when comparing results from clinical trials.

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There are considerable differences between APAP devices subjected to simulated OSA
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Conflict of interest: Disclosures can be found alongside this article at openres.ersjournals.com

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Introduction

Continuous positive airway pressure (CPAP) is the treatment of choice for patients with obstructive sleep apnoea (OSA), regardless of disease severity [1, 2]. CPAP has been shown to decrease elevated blood pressure, improve cardiovascular disease outcomes, and reduce the risk of fatal and nonfatal cardiovascular events [3–5]. It also improves excessive daytime sleepiness and restores impaired cognitive function [6].

Adherence to CPAP therapy is necessary for achieving satisfactory treatment outcomes [7]. However, CPAP compliance tends to be suboptimal, both in terms of treatment acceptance and hours of CPAP use per night, with compliance reported to be as low as 30–60% [8]. Although therapy acceptance depends on patient characteristics, equipment-related factors are crucial in determining CPAP adherence.

Automatic CPAP (APAP) is an alternative treatment for CPAP-intolerant OSA patients [1] and was developed to improve compliance. APAP devices reduce mean nocturnal pressure by automatically adjusting the delivered pressure based on the changing requirements of the patient [9–14]. Accordingly, APAP therapy might be more suitable for patients who have a variety of pressure demands during sleep based on factors such as body posture, sleep stage or variability between nights [15–19]. However, data on the advantage of APAP over CPAP for the general population of OSA patients remain controversial [20, 21]. APAP does seem to be better suited for specific OSA phenotypes, although defining the optimal target population for this therapy requires further research.

Given the technical complexity of APAP engineering, each manufacturer designs its own solution to detect disturbed breathing events and potential artefacts selectively, and to define a strategy for automatic adaptation of nasal pressure. Therefore, the use of different proprietary algorithms in APAP devices usually leads to distinct responses to the same sleep-related breathing conditions. As a result, devices from different manufacturers cannot be considered equal, particularly with respect to clinical performance. Despite existing studies comparing APAP technologies, the ongoing development of more technologically advanced devices and their availability on the market means that objective analyses are required to provide reliable data on which to base clinical decisions. Thus, the aim of this study was to compare the responses of several currently available APAP devices using a bench test simulation of OSA disturbed breathing patterns.

Methods

The bench test method used in this study was described in detail previously [22, 23]. Briefly, the bench test simulator comprised a flow generator controlled by a computer. The piston-based flow generator can reproduce mathematically designed breathing flows or replicate respiratory flows of patients recorded during polysomnography (PSG). A computer-controlled obstruction valve allows the simulation of central or obstructive events. The bench platform is equipped with two sensors (one for pressure and one for flow) and data are recorded on the computer for subsequent analysis. Conventional tubing connects the APAP device under test to the simulated OSA patient.

The disturbed breathing events employed in this study were extracted from real PSG recordings of OSA patients as previously described [22]. The simulator was set to reproduce the breathing events depending on the positive airway pressure (PAP) applied (figure 1): 1) apnoeas with obstruction for PAP <5 cmH_2O; 2) severe hypopnoeas for PAP between 5 and 7 cmH_2O; 3) mild hypopneas for PAP between 7 and 10 cmH_2O; 4) prolonged flow limitation for PAP between 10 and 12 cmH_2O; and 5) normal breathing for PAP >12 cmH_2O. Each test started with 15 min of normal breathing to simulate the time before sleep onset, followed by 2 h of simulated OSA.

The study was performed on seven APAP devices currently in clinical use: AirSense 10 (A) manufactured by ResMed (San Diego, CA, USA), Dreamstar (B) by SEFAM (Villers-lès-Nancy, France), Icon (C) by Fisher & Paykel (Auckland, New Zealand), Resmart (D) by BMC (Beijing, China), Somnobalance (E) by Weinmann (Hamburg, Germany), System One (F) by Respironics (Murrysville, PA, USA) and XT-Auto (G) by Apex (New Taipei City, Taiwan). For the AirSense 10 device, two different inbuilt algorithms were tested, standard (A1) and response (A2) settings, with the Expiratory Pressure Relief setting off. Each device was equipped with its corresponding tubing. The minimum and maximum pressures were set at 4 and 20 cmH_2O, respectively. Any other programmable settings were left at their default values. Ramp time was off for all devices and no humidification was used during any of the testing. Each test was repeated twice and the corresponding average result is reported.

Results

The responses of the assessed APAP devices are summarised in table 1. There was considerable variation among devices, particularly with respect to the mean and maximum nasal pressures applied, the time to reach maximum nasal pressure, and the residual apnoea–hypopnoea index (number of residual obstructive events per hour). More than five residual obstructive events per hour were observed with devices B, D, F

APPENDIX 8
Pgs. 3-4

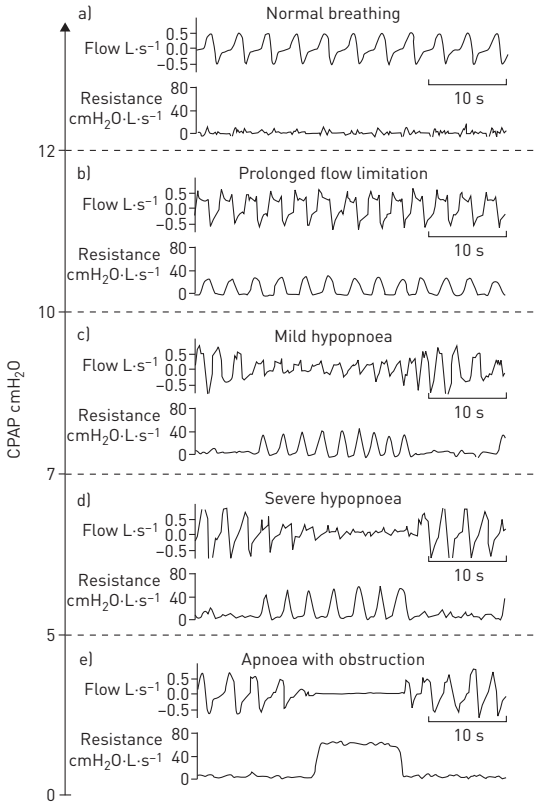

FIGURE 1 Breathing patterns reproduced by the simulated obstructive sleep apnoea patient depending on the continuous positive airway pressure (CPAP) applied by automatic CPAP devices: a) normal breathing; b) prolonged flow limitation; c) mild hypopnoea; d) severe hypopnoea; e) apnoea with obstruction. Reproduced from [23] with permission from the publisher.

and G. Breathing normalisation (defined as the avoidance of any obstructive event: apnoea, hypopnoea or flow limitation) was only achieved with the A1, A2 and C devices. Figure 2 shows examples of the first 30 min of device response for one device that achieved breathing normalisation (A2) and another that was unable to overcome obstructive events (B).

TABLE 1 Reponses of automatic continuous positive airway pressure (APAP) devices to obstructive sleep apnoea simulated by the bench test

APAP device	P_{max} cmH_2O	t_{max} min	P_{mean} cmH_2O	Residual AHI events per h	Breathing normalisation
A1	17.9, 17.8	22.4, 19.0	14.6, 14.6	2.0, 2.0	Yes , yes
A2	15.4, 15.6	40.3, 57.7	13.4, 13.5	2.0, 1.5	Yes, yes
B	10.5, 10.5	130.6, 121.3	6.7, 7.9	74.5, 71.0	No, no
C	13.4, 13.9	28.0, 44.1	12.4, 12.2	3.0, 3.0	Yes, yes
D	10.7, 10.7	75.1, 103.7	9.7, 9.7	26.5, 32.5	No, no
E	10.4, 10.4	20.7, 18.9	10.2, 10.2	3.5, 2.5	No, no
F	11.9, 12.1	34.4, 36.0	10.1, 10.1	11.5, 13	No, no
G	10.5, 11.0	32.2, 83.2	9.9, 9.9	33, 26.5	No, no

The two values for each variable correspond to the results obtained in the two test repetitions in each device. P_{max}: maximum positive airway pressure applied; t_{max}: time to reach P_{max}±0.3 cmH_2O; P_{mean}: mean positive airway pressure; AHI: apnoea–hypopnoea index; A1: AirSense 10, standard setting; A2: AirSense 10, response setting; B: Dreamstar; C: Icon; D: Resmart; E: Somnobalance; F: System One; G: XT-Auto.

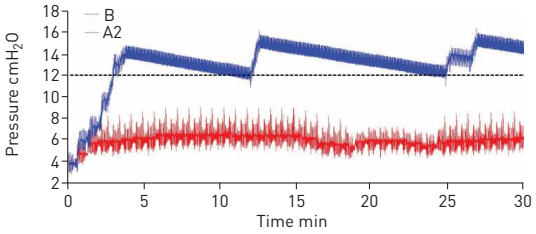

FIGURE 2 Example of the first 30-min response of two automatic continuous positive airway pressure devices: one achieving breathing normalisation (AirSense 10, response setting (A2)) and another unable to eliminate obstructive events (Dreamstar (B)). The dashed black line represents the pressure required to achieve breathing normalisation (12 cmH_2O).

The assessed devices also showed different performances in the rate of pressure increase after occurrence of the first obstructive event. Tracings of the initial 10 min of the test results are shown in figure 3. Device A1 responded to obstructive events with a step-wise increase in pressure sufficient to overcome obstruction (mean maximum pressure 17.9 cmH_2O). A2 increases in pressure were more gradual but the pressures reached (mean maximum 15.5 cmH_2O) were sufficient to normalise breathing. Devices C and E also showed a rapid and pronounced pressure increase after the first obstructive event, even if only device C reached a pressure sufficient to normalise breathing (mean maximum 13.6 cmH_2O). The other devices increased pressure more slowly and none of them was able to completely normalise breathing.

Discussion

This bench test investigated the response of seven currently used APAP devices and found marked differences in their responses to a simulated breathing pattern mimicking that of an OSA patient. Only two devices were able to achieve breathing normalisation and to reach a residual AHI <5, although the nasal pressures reached in some cases were higher than those required to normalise breathing in the simulated patient. Moreover, the rate of pressure increase in response to obstructive events was considerably different when comparing the tested APAP devices.

The findings obtained when testing currently available devices in this study are similar to those in previous reports, which showed variability in the response of APAP devices when subjected to the same breathing pattern under well-controlled conditions [22–24]. Thus, the fact that APAP devices behave differently should not be attributable to the lack of technical maturity originally found in new technologies but to the manufacturers strategy of offering devices with differentiated functioning features aimed at better treating patients. In fact, it is most likely that this inter-device response variation can be attributed to the different in-built algorithms operating in each device.

- The first step in the algorithms incorporated into APAP devices should analyse the pressure/flow data recorded by in-built transducers to identify different types of breathing events (*e.g.* apnoeas, hypopneas, snoring and flow limitation).

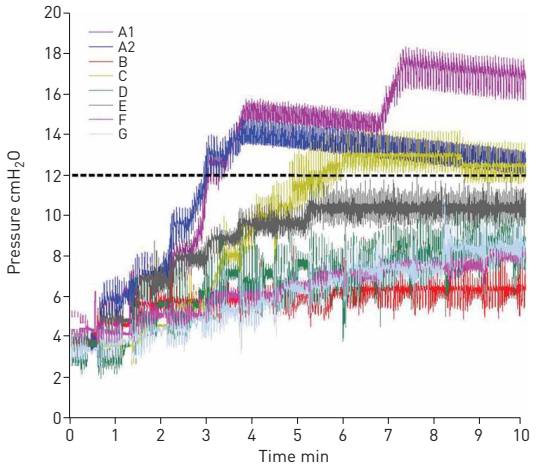

FIGURE 3 Pressure increase delivered by the tested automatic continuous positive airway pressure devices during the first 10 min of the bench test. The dashed black line represents the pressure required to achieve breathing normalisation (12 cmH_2O). A1: AirSense 10, standard setting; A2: AirSense 10, response setting; B: Dreamstar; C: Icon; D: Resmart; E: Somnobalance; F: System One; G: XT-Auto.

APPENDIX 8
Pgs. 5-6

- The algorithm must also distinguish breathing events from artefacts (*e.g.* swallowing, coughing and speaking). Indeed, variation among devices response will depend significantly on the detection of events with no well-established definition, such as flow limitation, the detection of which remains open to interpretation. Therefore, the ability of a device to recognise and classify this event depends on the potential agreement between the specific flow limitation pattern simulated in the bench study and the event definition implemented in the APAP device algorithm.
- Once breathing events have been detected, the algorithm should decide when and for how long to modify the applied nasal pressure. The differences observed in this study were, therefore, not unexpected and do not necessarily imply incorrect device performance. For instance, the optimal rate of pressure increase after detection of obstructive events, which varied considerably between the devices tested (figure 3), is not clear. Specifically, a difficult balance needs to be found between a response that is fast enough to ensure avoidance of disturbed breathing and soft enough to avoid patient awakening in response to a sudden nasal pressure increase.

In addition, it should be noted that default settings were used during testing of most of the devices in this study and that it is possible that selecting other response thresholds could have an impact on their performance. Whether or not such modifications would increase the number of devices able to normalise breathing under the test conditions used in this study or the values of nasal pressure applied to normalise breathing is unknown.

Although bench testing is useful to understand and characterise the response of APAP devices under well-controlled conditions, this evaluation method has some limitations. Defining a model of OSA patient does not allow reproduction of the almost infinite variation in breathing events observed in clinical practice, or uncontrolled mask leaks, snoring or mouth expiration. Accordingly, it is possible that the responses of the tested devices would have been different from those reported if OSA was simulated by another model. In fact, bench testing should be considered a preliminary evaluation before the device is fully assessed in the clinical setting. However, this testing has shown that the high residual AHI seen in some devices should be further investigated in clinical practice to ensure that patients using these devices do have their sleep apnoea effectively treated. Bench test results can thus be useful when selecting the most suitable device for each patient to improve comfort and treatment compliance, and when interpreting the results of clinical studies if different devices are involved.

In conclusion, this bench study showed considerable response differences between several currently used APAP devices when subjected to a specific simulated OSA breathing pattern. Although APAP is a useful therapy, these results underline the concept that the actual implementation of APAP depends on the product-specific engineering solutions and algorithms adopted by each manufacturing company, which has implications for clinical application.

Lessons for clinicians

- This bench test study assessed how currently available APAP devices respond to a simulated OSA patient. Regardless of the simplified experimental setting employed in this work, as compared with the complexity of events found in the clinical arena when treating OSA patients, the following practical lessons can be derived.
- The way that each commercial APAP device modifies nasal pressure when subjected to disturbed breathing patterns is different.
- These differences in response among APAP devices are not necessarily caused by incorrect performances. Instead, they are the result of the particular engineering solutions implemented in each device.
- Knowing the specific functioning features of each APAP device (*e.g.* sensitivity in detecting the different obstructive events, tolerance to events before increasing pressure and speed of pressure changes) may help to understand treatment compliance in specific patient phenotypes.
- Choosing the optimal APAP device for the needs/preferences of each individual patient may improve therapy compliance.

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APPENDIX 9

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SCIENTIFIC INVESTIGATIONS

Pressure-Relief Features of Fixed and Autotitrating Continuous Positive Airway Pressure May Impair Their Efficacy: Evaluation with a Respiratory Bench Model

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Study Objectives: Pressure-relief features are aimed at improving the patient's comfort during continuous positive airway pressure (CPAP) treatment for obstructive sleep apnea. The objective of this study was to determine the effect of these therapy features on fixed CPAP and autotitrating CPAP (APAP) treatment efficacy.

Methods: Seven pressure-relief features applied by three CPAP devices were included in our study (Remstar Auto: C-Flex 3, C-Flex+ 3, A-Flex 3, P-Flex; AirSense 10: EPR 3; Prisma 20A: SoftPAP 2 and 3). In fixed CPAP, the devices were subjected to a 10-min bench-simulated obstructive apnea sequence (initial apnea-hypopnea index, AHI = 60/h) with and without pressure-relief features. In APAP, the sequence was lengthened to 4.2 h (initial AHI = 58.6/h). The residual AHI and mean/median pressure were compared with and without pressure-relief features.

Results: Compared to conventional CPAP, where pressure was adjusted to be just sufficient to control the simulated obstructive events, C-Flex+ 3, P-Flex, and EPR 3 failed to normalize the breathing flow and did not reduce the AHI. The mean pressures with the three features, respectively, were 1.8, 2.6, and 2.6 cmH_2O lower than the conventional CPAP. Compared to conventional APAP, similar levels of control were observed with pressure-relief features, apart from P-Flex where the delivered mean pressure was lower and residual AHI greater. The device-reported mean/median pressures in APAP with A-Flex 3, P-Flex, EPR 3, and SoftPAP 3 were higher than that measured on the bench.

Conclusions: Pressure-relief features may attenuate CPAP efficacy if not adjusted for at the time of their introduction. In clinical practice, efficacy can be ensured by increasing the therapeutic pressure delivered by fixed CPAP or by enabling the pressure-relief features prior to initial pressure titration. Device-reported pressures in APAP devices with pressure relief activated may overstate delivered pressures.

Keywords: CPAP treatment, pressure-relief features, bench test

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INTRODUCTION

Continuous positive airway pressure (CPAP) is an effective treatment for obstructive sleep apnea (OSA). However, the effectiveness of treatment mainly depends on regular use of CPAP device and the patient's tolerance to the treatment. Many factors are involved in CPAP adherence: side effects related to the equipment such as nasal discomfort and difficulty adapting to the pressure, disease severity, patient characteristics and motivation, and other surrounding factors, such as family, physician, healthcare professionals, and their interventions.[1–3]

One side effect of CPAP treatment is the difficulty of exhaling against a positive pressure, which is considered as a cause of reduced adherence to CPAP. As a solution, various CPAP delivery modalities have been developed on the basis that a lower expiratory pressure would be better tolerated. Auto-titrating CPAP (APAP) adjusts the pressure and maintains the airway patency in real time during the therapy, and the adherence of APAP has been reported as same as that of conventional CPAP.[4] Bilevel PAP is designed to provide a lower expiratory pressure to reduce the average pressure level, although no improvement in adherence has been reported.[4–7] Pressure-relief CPAP is another modality of pressure delivery, which is proposed as an optional therapy feature for the patient's comfort during the treatment and has been implemented in most fixed CPAP or APAP devices. This CPAP modality is aimed at reducing pressure during expiration to facilitate patient exhalation.

Currently, almost all CPAP manufacturers provide their own proprietary versions of pressure-relief CPAP. However, there is no instruction or caution from the manufacturers regarding the use of these features, which are often added after the initial

BRIEF SUMMARY
Current Knowledge/Study Rationale: Pressure-relief features are aimed at improving the patient's comfort during CPAP treatment for OSA. However, the effect of these therapy features on CPAP treatment efficacy is not well determined.
Study Impact: Pressure-relief features may impair the efficacy of CPAP treatment. The treatment efficacy can be ensured by increasing the therapeutic pressure or by enabling the pressure-relief features prior to initial pressure titration.

Table 1—Pressure evolution of studied pressure-relief features during one breathing cycle (summarized from the provider manuals of the CPAP devices and reference 15).

	Pressure during inspiration	Pressure during the transition to expiration	Pressure during the beginning of expiration	Pressure at the end expiration
Remstar Auto				
C-Flex Level 1, 2 and 3	Set pressure.	Set pressure.	Pressure drops proportional to expiratory flow (3 levels of settings for C-Flex and C-Flex+/A-Flex).	Set pressure.
C-Flex+ (for fixed CPAP) and A-Flex (for APAP) Levels 1, 2, and 3		Pressure drops by 1 (if set pressure = 5) or 2 cmH_2O (if set pressure ≥ 6).		1 (if set pressure = 5) or 2 cmH_2O (if set pressure ≥ 6) below the set pressure.
P-Flex (only for APAP)[a]		Pressure drops by up to 4 cmH_2O depending on the set pressure.[b]		Up to 4 cmH_2O below the set pressure.
AirSense 10 AutoSet				
EPR Level 1, 2 and 3	Set pressure.	Pressure drops by 3 levels: 1, 2, or 3 cmH_2O (3 levels of settings), but remains ≥ 4 cmH_2O.		
Prisma 20A				
SoftPAP Level 1 and 2	Set pressure.	Pressure drops depending on the set pressure (2 levels of settings).[b]		Set pressure.
SoftPAP Level 3	Set pressure with supplementary pressure support.	Pressure drops as the same way as SoftPAP 2 does.		

Set pressure: user-set pressure for fixed continuous positive airway pressure (CPAP); device-ordered autotitration pressure for autotitration continuous positive airway pressure (APAP). [a]P-Flex is exclusive for the French market. [b]Values undisclosed by the manufacturers.

titration when the patient complains of excessive pressure. In addition, most studies on such therapy feature are restricted to C-Flex (Philips Respironics, Murrysville, PA, USA), and the literature does not consistently support its usefulness.[8–16] For other pressure-relief features available on the market, the additional benefits still remain unclear.[3,17]

Bench studies have been proposed to evaluate the responses of APAP devices in different conditions, such as the presence of predefined sleep disordered breathing (SDB) patterns and air leak,[18–25] whereas no such study to date has focused on pressure-relief CPAPs and APAPs. We investigated seven pressure-relief features developed by three CPAP device manufacturers with a previously reported bench model.[25]

METHODS

Bench Model and Simulation of Obstructive Apneas

Evaluations were carried out on a previously described bench model.[25] Consisting of an active lung model and a Starling resistor, the bench model is able to simulate different SDB patterns such as obstructive apneas, hypopneas, and flow limitations. The human upper airway is mimicked by the Starling resistor, and the control of airway patency can be achieved by adjusting the pressure inside the resistor. The CPAP device and the bench are connected by a standard tubing (1.8 m long and 22 mm in diameter), and a calibrated leak port (24 L/min at 10 cmH_2O) is presented in order to mimic the intentional leak in nasal masks. Mask pressure (P_m) and airflow (V') are recorded for further analyses.

During obstructive apnea simulation, the breathing effort is generated by the piston movement. The pressure inside the Starling resistor is set at 9 cmH_2O, and the critical closing and full opening pressures were measured at around 6 and 11 cmH_2O, respectively.

Studied Pressure-Relief Features

Three CPAP devices were included in the current study: Remstar Auto P-Flex (Philips Respironics), AirSense 10 AutoSet (Resmed, Sydney, Australia) and Prisma 20A (Weinmann, Hamburg, Germany). Studied pressure-relief features and their principles are shown in **Table 1**. During the test, each feature was set at the maximum level if adjustable, i.e., achieving the maximally reduced pressure during expiration.

Pressure-Relief CPAP/APAP Efficacy

Protocol

FIXED CPAP: With simulated apneas, a manual titration of pressure was first conducted to obtain the therapeutic pressure for each CPAP device with pressure-relief features disabled (conventional CPAP): the pressure was increased from 4 cmH_2O in a stepwise manner with a minimum increment (0.5 cmH_2O for Remstar Auto and Prisma 20A, 0.2 cmH_2O for AirSense 10 AutoSet) until the breathing flow was fully normalized. Afterward, the devices were set at obtained titration pressure, and subjected to a predefined short obstructive apnea sequence with pressure-relief features enabled. The short breathing sequence lasted 10 min, which was considered

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Table 2—Comparison of pressure-relief features in fixed continuous positive airway pressure mode: residual apnea-hypopnea index, apnea index, and measured pressures during a 10-min obstructive apnea sequence (initial apnea index = 60/h).

	Residual AHI (events/h)	Residual AI (events/h)	Measured mean pressure (cmH_2O)
Remstar Auto: Manual titration pressure = 11 cmH_2O			
Conv. CPAP	0	0	10.9
C-Flex 3	0	0	10.7
C-Flex+ 3	60	0	9.1
P-Flex	60	0	8.2
AirSense 10 Autoset: Manual titration pressure = 10.8 cmH_2O			
Conv. CPAP	0	0	10.8
EPR 3	60	0	8.2
Prisma 20A: Manual titration pressure = 10.5 cmH_2O			
Conv. CPAP	0	0	10.7
SoftPAP 2	0	0	9.6
SoftPAP 3	0	0	9.9

All results were identical for two independent repetitions. Titration pressure was noted as the device pressure and the pressure-relief feature was disabled during the continuous positive airway pressure (CPAP) titration. Conventional CPAP: fixed CPAP without pressure-relief feature. P-Flex is only available in autotitrating continuous positive airway pressure (APAP) mode; here the minimum pressure was set identical to the maximum to achieve a constant therapy pressure. AHI, apnea-hypopnea index; AI, apnea index.

sufficient because fixed CPAP efficacy is time-independent. A 30-sec obstructive apnea occurred every minute, i.e., total apnea-hypopnea index (AHI) = 60/h. A similar reference test was carried out without pressure-relief feature (conventional CPAP) for each device. Tests were repeated twice for reproducibility. A third test was executed if the coefficient of variance of the first two tests was higher than 10%.

APAP: The devices were set to APAP mode with open pressure range (4–20 cmH_2O), and subjected to a long obstructive apneas sequence with pressure-relief features enabled. The long breathing sequence lasted 4.2 h, including a 6-min normal breathing session at the beginning, which was considered as a baseline. A 20-sec obstructive apnea occurred every minute and thus the total AHI was 58.6/h. A similar reference test was carried out for each device without pressure-relief feature (conventional APAP). Tests were repeated twice for reproducibility. A third test was executed if the coefficient of variance of the first two tests was higher than 10%.

Data Analysis

For each test, mean or median pressure was calculated from the P_m. Also, residual AHI and apnea index (AI) were derived from the peak-to-peak flow amplitude (ΔV', derived by calculating the upper and lower envelops of the flow curve). Each residual event was scored by considering both the amplitude reduction and the corresponding duration, i.e., $\Delta V' \leq 10\%$ of baseline: apnea; $10\% < \Delta V' \leq 70\%$: hypopnea, with a duration ≥ 10 sec.[25–27] In addition, the AHI, AI, and pressure data on the device report were also noted for comparison. Results were averaged on two tests for fixed CPAP and on three tests for APAP. All the analyses were performed with MATLAB (MathWorks Inc., Natick, MA, USA).

Statistical Analysis

One-way analysis of variance, preceded by Levene's test for equality of variance, was applied to compare the AHI, AI, and pressure with and without pressure-relief feature. Kruskal-Wallis test was applied if Levene's test was positive (Medcalc Software, Mariakerke, Belgium).

Relationship between Conventional and Pressure-Relief CPAP

Different severities of upper airway obstruction were simulated by changing the pressure inside the Starling resistor from 3 to 16 cmH_2O with increment of 1 cmH_2O. At each obstruction level, the effective pressures (device pressure) obtained by the manual CPAP titration were compared between conventional and pressure-relief CPAP.

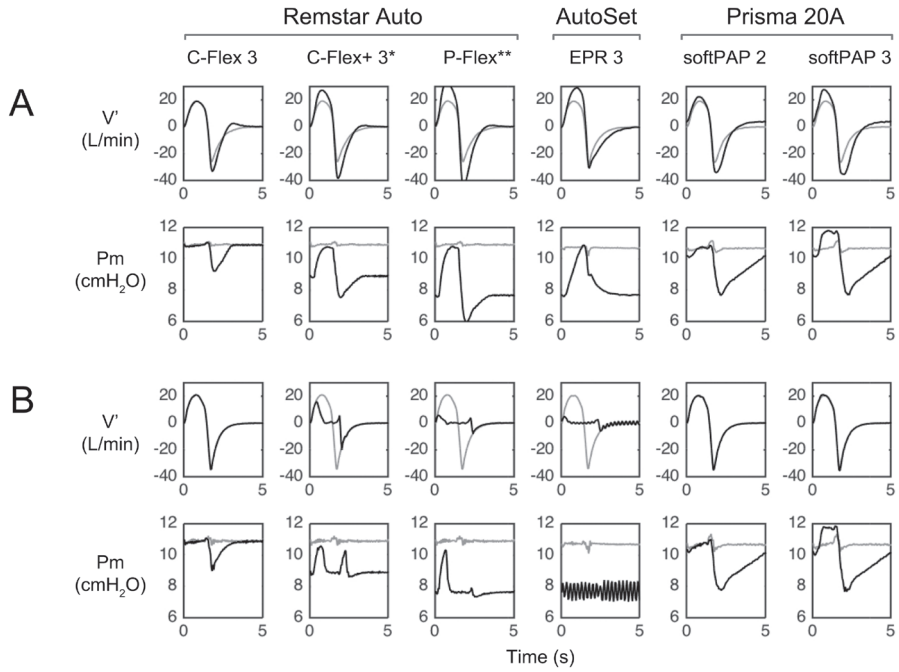
RESULTS

Pressure-Relief CPAP/APAP Efficacy

Fixed CPAP

Measured flow and pressure waveforms of each pressure-relief feature during normal breathing and obstructive apnea are shown in **Figure 1**. The residual AHI and measured pressure are shown in **Table 2**. Compared to conventional CPAP (without pressure relief), the C-Flex+ 3, P-Flex and EPR 3 pressure-relief features were ineffective to normalize the breathing flow and to reduce the AHI. The measured pressures with these features were 1.8, 2.6, and 2.6 cmH_2O respectively lower than that with the conventional CPAP. However, with C-Flex 3 and SoftPAP 2 and 3, the CPAP devices maintained the same treatment efficacy compared to the conventional CPAP and normalized the breathing flow (**Table 2**), despite the fact that their mean pressures

Figure 1—Measured mask airflow and pressure waveforms of fixed CPAP.



Measured mask airflow and pressure waveforms of fixed continuous positive airway pressure (CPAP) with (black curves) and without (gray curves) pressure-relief feature during normal breathing and obstructive apnea. For each device, the pressure was set as the same value as the manual titration pressure of conventional CPAP (without pressure-relief feature). Panel A: recordings during normal breathing. Of note, with C-Flex+ 3, P-Flex and EPR 3, the device-delivered pressure curve was shown as a pressure support accompanied by a positive expiratory pressure that was about 3 cmH_2O lower than the initial CPAP value. Panel B: recordings during obstructive apneas. The black and gray flow curves are superposed in C-Flex, and SoftPAP 2 and 3. With C-Flex+ 3, P-Flex, and EPR 3, the device-delivered pressure was around 3 cmH_2O lower than the initial setting. As a consequence, breathing could not be normalized. The pressure oscillations observed in EPR 3 was due to the upper airway patency detection with forced oscillation technique. *C-Flex+: identical to A-Flex in APAP mode. **P-Flex: only available in APAP mode. Here the minimum pressure was set identical to the maximum in order to make the device work as a fixed CPAP. Pm, mask pressure; V', airflow.

were 0.2, 1.1, and 0.8 cmH_2O lower than the conventional CPAP values.

APAP

The residual AHI, AI, and pressure are shown in **Table 3**. Regarding the bench-assessed residual AHI, no clinically significant increase was found with any pressure-relief features included in this study except P-Flex: the bench-assessed AHI increased from 9.1/h with the conventional APAP (APAP without pressure relief) to 20.6/h with P-Flex ($p < 0.05$) whereas the initial AHI was 58.6/h. Similarly, the bench-assessed AI with A-Flex 3 and P-Flex slightly increased from 0.5/h with the conventional APAP to 1.4 and 1.8/h respectively ($p < 0.05$ for both). The AI with EPR 3 slightly increased from 0.2/h with the conventional APAP to 0.7/h ($p < 0.05$).

In addition, the bench-measured mean pressure of P-Flex was 1.9 cmH_2O lower than the conventional APAP ($p < 0.05$), whereas this pressure drop was only 0.3 cmH_2O for EPR 3 ($p < 0.01$) and 0.4 cmH_2O for SoftPAP 3 ($p < 0.05$). In the device reports of A-Flex 3, P-Flex, EPR 3, and SoftPAP 3, respectively, the mean/median pressures were 1.9 ($p = 0.002$), 2.8 ($p < 0.001$), 2.5 ($p < 0.001$) and 0.9 cmH_2O ($p = 0.04$) higher than the mean/median pressures measured on the bench.

Relationship between Conventional and Pressure-Relief CPAP

Comparisons of effective treatment pressures (device pressure) between conventional and pressure-relief CPAP are shown in **Figure 2**. CPAP with C-Flex 3 (**Figure 2A**), and SoftPAP 2 and 3 (**Figure 2C**) were identical to the conventional CPAP in terms of efficacy. However, CPAP with C-Flex+ 3 (**Figure 2A**), P-Flex (**Figure 2A**), and EPR 3 (**Figure 2B**) should be set higher than conventional CPAP to achieve the same efficacy when CPAP > 4 cmH_2O.

DISCUSSION

This study demonstrates the effect of pressure-relief features on fixed CPAP and APAP treatment efficacy for OSA. Compared

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Table 3—Comparison of pressure-relief features in autotitrating continuous positive airway pressure mode: residual apnea-hypopnea index, apnea index, and pressures during a 4.2-h obstructive apnea sequence (initial apnea index = 58.6/h).

	Residual AHI (events/h)		Residual AI (events/h)		Median Pressure (cmH_2O)[a]		
	Bench	Device	Bench	Device	Bench	Device	p[b]
Remstar Auto							
Conv. APAP	9.1 ± 5.7	5.0 ± 3.0	0.5	3.7 ± 2.1	10.4 ± 0.9	10.3 ± 0.8	NS
C-Flex 3	13.4 ± 4.8	5.4 ± 1.7	0.5	5.2 ± 1.7	9.7 ± 0.6	9.7 ± 0.6	NS
A-Flex 3	7.5 ± 3.7	4.6 ± 1.8	1.4*	4.6 ± 1.8	9.3 ± 0.3	11.2 ± 0.4	0.002
P-Flex	20.6 ± 0.3*	13.8 ± 2.6*	1.8 ± 0.1*	13.8 ± 2.6**	8.5*	11.3 ± 0.1*	< 0.001
AirSense 10 AutoSet							
Conv. APAP	1.3 ± 0.5	0.8 ± 0.1	0.2	0.7	10.5 ± 0.1	10.5 ± 0.1	NS
EPR 3	1.4	10.2 ± 0.6**[c]	0.7*	1.4*	10.2 ± 0.1**	12.7 ± 0.1**	< 0.001
Prisma 20A							
Conv. APAP	2.4 ± 1.3	1.0	0.5	1.0	10.0 ± 0.1	10.0	NS
SoftPAP 2	2.1 ± 1.3	2.3 ± 1.2	0.6 ± 0.1	1.0	9.9 ± 0.2	10.5 ± 0.5	NS
SoftPAP 3	4.0 ± 1.2	3.7 ± 0.6*	0.5	1.0	9.6 ± 0.2*	10.5**	0.04

Results are given as mean ± standard deviation (n = 3). [a]For Remstar Auto, mean pressure was noted instead of median pressure. Conventional APAP: APAP without pressure-relief feature. [b]For the comparison of median/mean pressures between bench and device report. Statistical analysis: one-way analysis of variance preceded by Levene's test for equality of variance; Kruskal-Wallis test was applied if Levene's test was positive. [c]Large difference in residual AHI between the bench and the device, such as observed in EPR 3, was due to the difference in the definition of baseline that applied for sleep disordered breathing event scoring: for the bench, the baseline was considered as the 6-min normal breathing session at the beginning during which the pressure-relief feature was not activated; whereas for the device such as AirSense 10 AutoSet, a real-time baseline was utilized. Of note, this baseline could later be increased by "pressure supports" that were generated by the pressure-relief features such as EPR 3. *p < 0.05; **p < 0.01: comparison between pressure-relief and conventional APAP. APAP, autotitrating continuous positive airway pressure; NS, nonsignificant.

to conventional CPAP, the residual AHI significantly increased when the following pressure-relief features were turned on: C-Flex+ 3, P-Flex, and EPR 3. Compared to conventional APAP, the residual AHI only increased with P-Flex by 11.5/h in a 4.2-h breathing sequence with successive obstructive apneas.

Pressure-relief therapy features are developed to overcome patient difficulty of exhaling against a fixed pressure during CPAP treatment and improve the treatment adherence. However, for C-Flex, better adherence has not been proved consistently in clinical studies,[4,8,9,11–14,16,17] and the majority reported similar adherence[4,9,14,17] and treatment efficacy[9] between CPAP with and without C-Flex. Adherence and treatment efficacy are not reported in the literature for the other pressure-relief features.

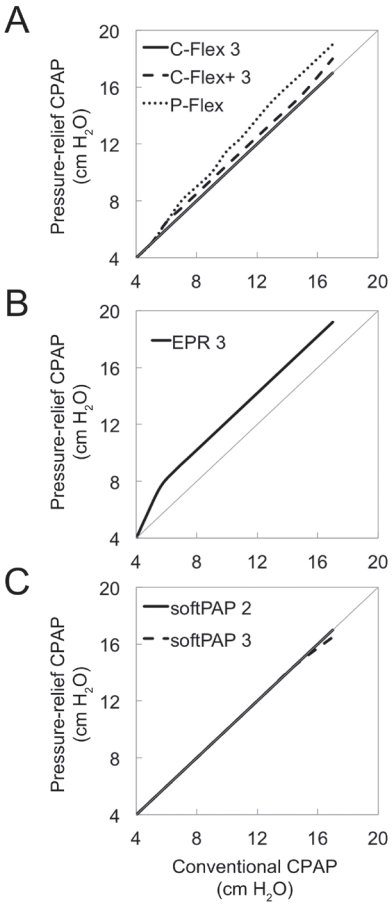
According to our results, we confirm the efficacy of C-Flex in fixed CPAP treatment.[9] However, obstructive SDB events remained untreated with C-Flex+ 3, P-Flex, and EPR 3, as a consequence of actual therapeutic pressure being lower than the titration pressure (**Table 2**). In short, these three modalities converted the pressure profiles into a "bilevel PAP" for the purpose of relieving the patient exhalation. C-Flex+ and P-Flex consist of an inspiratory positive airway pressure (IPAP) identical to the titration pressure of CPAP but an expiratory positive airway pressure (EPAP) at least 2 cmH_2O lower, with a further pressure decrease at the beginning of exhalation (**Figure 1A**). This modality of pressure delivery was not efficient to maintain the airway patency when apnea occurred (**Figure 1B**, column 2 and 3). For EPR 3, the therapeutic pressure decreased by 3 cmH_2O and apneas thus persisted (**Figure 1B**, column 4).

Because it has been demonstrated that apneas begin with upper airway narrowing at end-expiration and followed by collapse during ensuing inspiratory effort,[28] an airway pressure equal or higher than the full opening pressure, i.e., the conventionally titrated CPAP, should be applied to keep the airway patency during the end-expiration and the inspiration, as in the curves of C-Flex 3 and SoftPAP 2 and 3 shown in **Figure 1B** (Columns 1, 5, and 6). Alternatively, the airway patency can be achieved with a "bilevel PAP" pattern, with an EPAP that at least can alleviate the airway obstruction at end-expiration and allow sufficient patient-generated inspiratory airflow to trigger IPAP.[29] In this case, the EPAP must be higher than the critical closing pressure, and most importantly, the IPAP must be able to overcome the negative intraluminal pressure caused by the inspiratory effort and keep the upper airway patency during the remainder of inspiration.

In CPAP mode, C-Flex+ 3 and EPR 3 might lower the treatment efficacy on apneas if the device pressure is kept as same as that just sufficient to abolish flow limitations in conventional CPAP. As shown in **Figures 2A** and **2B**, the device pressure should be set higher to reach the same treatment efficacy as conventional CPAP. Accordingly, in the case of APAP with A-Flex 3 (A-Flex shares the same principle as C-Flex+) and EPR 3, the device autotitration pressure reported as the mean/median value was higher than that of the conventional APAP (**Table 3**) in order to compensate for the pressure reduction caused by the pressure relief. Consequently, similar bench-measured mean/median pressures and residual AHI were obtained between APAPs with and without A-Flex 3 and EPR 3 (**Table 3**). It should be highlighted that the device-reported pressures in conventional and pressure-relief APAPs are not comparable.

On the contrary, P-Flex APAP appeared to underperform in terms of residual AHI as well as in its response to apneas.

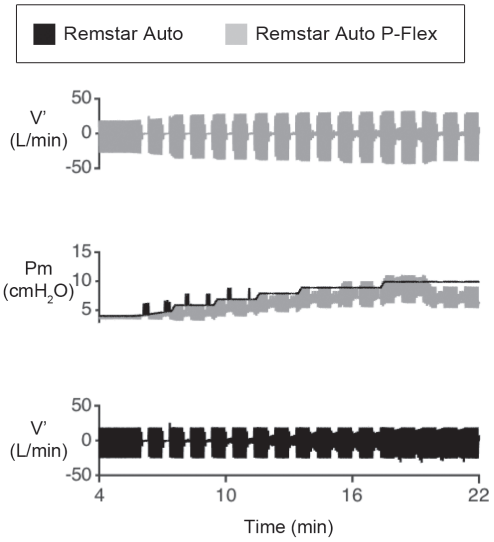
Figure 2—Comparisons between effective treatment pressures of the same efficacy (device set pressure) with and without pressure relief feature.



(A) Remstar Auto. **(B)** AirSense 10 AutoSet. **(C)** Prisma 20A. Conventional CPAP is continuous positive airway pressure without pressure-relief feature.

Figure 3 shows that despite the persistent apneas the autotitration pressure of P-Flex decreased around the 19th min after a foregoing pressure increase. This is a specificity of the algorithm of Remstar Auto (P-Flex) that intends to prevent inappropriate pressure increase to central apneas and non-responding events.[30] With this specific algorithm, such improper pressure decrease may also occur during autotitration in the case of successive obstructive apneas with severe upper airway obstruction. Compared to the conventional Remstar Auto APAP, the insufficient treatment pressure with P-Flex worsened such successive apneas and led to further decrease in autotitration pressure (**Figure 3**). Thus, this inappropriate response of P-Flex

Figure 3—Mask airflow and pressure profiles of Remstar Auto with and without P-Flex at the beginning of the 4.2-h obstructive apnea sequence.



Pm, mask pressure; V', airflow.

APAP resulted from both the specific autotitration algorithm and the reduced CPAP efficacy with pressure-relief feature.

Regarding APAP treatment with pressure-relief features, Mulgrew et al.[10] found a nonsignificant trend of greater subjective comfort with C-Flex. Kushida et al.[31] reported an equivalency in treatment adherence and efficacy between A-Flex and conventional CPAP after either 3 or 6 mo, but a higher AHI at the initiation phase. In a recent study, Chihara et al.[15] compared the adherence between conventional APAP, APAP with C-Flex and APAP with A-Flex, and found greater adherence in APAP with C-Flex. Of note, at the initiation of the studies of Kushida et al.[31] and Chihara et al.,[15] the APAP autotitration was carried out with the allocated pressure-relief feature.

Our results have an important clinical consequence for sleep apnea treatment. In clinical practice, the problem may arise when a pressure relief feature is later added to a conventionally titrated patient without increasing the titration pressure of the device. However, the negative effects that we document in the current study may be mitigated in the case of fixed CPAP initially titrated to a pressure level that is high enough to cope with sleep in unfavorable circumstances such as supine postures and rapid eye movement sleep stage because most SDB events will be abolished; or during "CPAP exploration", when the pressure can be up to 5 cmH_2O higher than that is just sufficient to abolish SDB events.[32] Similarly, in the case of APAP our findings could be relevant if the pressure range over which autotitration was allowed to occur had an upper limit that was set close to the effective (95th or 90th centile) pressure prior to

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activation of pressure relief. Thus, the treatment efficacy can be ensured by increasing the device pressure in fixed CPAP or by enhancing the full range of pressure in APAP. In the latter case, a well-functioning autotitration algorithm is indispensable. In addition, the pressure-relief features allocated for therapy should be enabled prior to the titration process. It should also be noted that the device-reported pressure in pressure-relief APAP is not comparable to that without pressure relief.

CONCLUSIONS

Pressure-relief features may lead to attenuated CPAP treatment efficacy depending on the applied settings and the device. In clinical practice, the therapy efficacy can be ensured by increasing the therapeutic pressure or by enabling the pressure-relief features prior to the manual or auto titration process. The pressures in the pressure-relief APAP device reports are not comparable to that of conventional APAPs.

ABBREVIATIONS

AHI, apnea-hypopnea index
AI, apnea index
ANOVA, analysis of variance
APAP, autotitrating continuous positive airway pressure
CPAP, continuous positive airway pressure
EPAP, expiratory positive airway pressure
IPAP, inspiratory positive airway pressure
OSA, obstructive sleep apnea
Pm , mask pressure
SDB, sleep disordered breathing
V', mask airflow
ΔV', peak-to-peak flow amplitude

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CARA MASKS

Sleep Soundly

The thoroughly modern nasal & full face masks in the CARA family satisfy patient requirements for a perfect fit, great wearing comfort, gentle, quiet exhalation & good skin compatibility.

The successful CARA masks wins over fans with it's lightness, the soft supple mask cushion, adjustable headgear, excellent fit and other clever details.

CARA offers the right solution to nearly every mask wearer, with many exceptional features:

- Soft, supple mask cushion in 3 sizes.
- Small diffuse exhalation system (1a, 1b).
- Lightweight (2).
- Colour-coded headgear - coloured (teal or syrah) part on tope.
- Upper portion of headgear can be adjusted for a perfect fit on any head size (3).
- Choice of manual threading assembly (4a, 4b).
- Quick-release cord for rapid removal (5).
- Ball-&-socket joint with 360° & 3D rotation for free movement (6).
- Extremely durable material.

USER GUIDE

Loosen both clips from the mask

Pull the headgear over your head.

Fasten the lower clips on the mask.

Adjust the upper portion of the headgear so that it is as loose as possible & as tight as necessary.

Adjust the lower portion of the headgear so that it is as loose as possible & as tight as necessary.

Position the headgear on the head so that the lower portion does not hit the ear lobes.

Adjust the forehead as loosely as possible; it does not have to lie on the forehead.

	CARA	CARA Full Face
Product Class as per Directive 93/42/EEC	IIa	IIa
Dimensions (W x H x D)	72 x 112 x 70 mm (Size XS) 72 x 117 x 70 mm (Size S/M) 72 x 118 x 70 mm (Size M/L)	93 x 145 x 89 mm (Size S) 95 x 160 x 90 mm (Size M) 95 x 174 x 91 mm (Size L)
Weight	58 g (Size XS) 59 g (Size S/M) 60 g (Size M/L)	93 g (Size S) 97 g (Size M) 102 g (Size L)
Therapy Pressure	4 hPa - 30 hPa	4 hPa - 25 hPa
Tube connector cone complies with EN ISO 5356-1	Ø 22mm (male)	Ø 22mm (male)
Temperature range • Operation • Storage	 +5°C to +40°C -20°C to +70°C	 +5°C to +40°C -20°C to +70°C
Flow resistance • at 50 l/min • at 100 l/min	 0.2 hPa 0.9 hPa	 0.15 hPa 0.5 hPa
Flow resistance, anti-asphyxia valve • Inspiration at 50 l/min • Expiration at 50 l/min	 - -	 0.6 hPa 0.8 hPa
Sound pressure level, anti-asphyxia valve • Open: • Close:	 - -	 0.5 hPa 2.2 hPa
Declared dual number noise emission values as specified in ISO 4871: • Acoustic pressure level: • Acoustic power level: • Uncertainty factor:	 18 dB(A) 26 dB(A) 3 dB(A)	 19 dBa(A) 27 dB(A) 3 dB(A)
Service life	up to 12 months*	up to 12 months*
Standards used	EN ISO 17510-2:2009	EN ISO 17510-2:2009

*Materials used in the manufacture of masks can age prematurely when they are exposed to aggressive cleaning products. It may therefore be necessary to replace mask parts earlier.

CE 0197

PRISMA20A

APAP Therapy Device

Therapy Flexibility for Obstructive Sleep Apnoea (OSA)

With the help of Forced Oscillation Technique (FOT), prisma20A reliably distinguishes between obstructive & central events.
In response to events, the prisma20A automatically provides continuous pressure adjustments tailored exactly to the patient‘s needs & thus delivers highly effective treatment.

Equipped with the option of combining both CPAP & APAP modes with the comfortable pressure relief softPAP, prisma20A offers a high degree of therapy flexibility.

Major features include:

- Ventilation modes CPAP, APAP.
- Identification of periodic breathing, RERA, snoring, hypopnea, apnoea & flow limitations.
- Two APAP settings - the right therapy for every patient (standard, dynamic).
- More comfortable breathing: CPAP with pressure relief softPAP, now also for inspiration support at low pressures (softPAP 3).
- Continuous check of mask, automatic mask recognition & mask test.
- High resolution therapy data for up to 14 days & detailed statistics for 366 days.
- Therapy software prismaTS for data analysis & remote control.
- With SD card & USB port
- Telemedicine connection via modem for prisma CLOUD.
- Eight clearly identified analogue signals for PSG feed.

Product Class as per Directive 93/42/EEC	IIa
Dimensions (W x H x D)	170 x 135 x 180 mm
Weight	about 1.4 kg
Temperature range • Operation • Storage	 +5°C to +40°C -25°C to +70°C
Permitted humidity, operation & storage	rel humidity 10% to 95%, no condensation
Air pressure range	700-1,060 hPa corresponds to altitude fo 3,000 metres
Diameter of breathing tube	22mm or 15mm
Electric rating	max. 40VA
System interface	12 V DC max. 10VA
Power consumption in: • Operation (therapy): • Standby:	230V 115V 0.11 A 0.22A 0.036A 0.019A

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Classification as per EN 60601-1-11 • Type of protection from electric shock: • Level of protection from electric shock: • Protection from damaging ingress of water & solids:	 Protection class II Type BF IP21
Alarms	leak & disconnection
Mean sound pressure/ Operation as per ISO 80601-2-70	about 26.5 dB(A) at 10 hPa (corresponds to sound pressure of 34.5 dB(A)
CPAP/APAP operating pressure range	4 to 20 hPa
Pressure Accuracy	< 20 hPa ± 0.6 hPa

Peak flow as per ISO 80601-2-70, modes APAP & CPAP, without humidifier	
4.0 hPa	235 l/min
8.0 hPa	230 l/min
12.0 hPa	220 l/min
16.0 hPa	215 l/min
20.0 hPa	210 l/min

Stability of the dynamic pressure (short-term accuracy) for 10 breaths/min as per ISO 175-1:2007 with the use of the 22-mm tube	
7.0 hPa	Δ p ≤0.24 hPa
10.0 hPa	Δ p ≤0.28 hPa
13.5 hPa	Δ p ≤0.3 hPa
20.0 hPa	Δ p ≤0.4 hPa

PRISMA20C

CPAP Therapy Device

CPAP Therapy with softPAP & FOT

Features intuitive navigation & setting of therapy parameters.
As with all device variants in the prismaLine, the prisma20C offers quick operation, thanks to the perfectly coordinated interaction between the state-of-the-art touch screen & smart Graphical User Interface.

With the help of Forced Oscillation Technique (FOT), the prisma20C distinguishes between obstructive & central events & gives the doctor a solid foundation for diagnostic & treatment decisions.

Major features include:

- Identification of periodic breathing, RERA, snoring, hypopnea & flow limitations.
- Pressure relief softPAP, additionally for inspiration.
- Support at low pressures (softPAP 3).
- Continuous mask fit check & automatic mask recognition, mask test.
- High resolution therapy data for up to 14 days & detailed statistics for 366 days.
- Therapy software prismaTS for data analysis & remote control.
- With SD card & USB port.
- Telemedicine connection via modem for prisma CLOUD.
- Eight clearly identified analogue signals for PSG feed
- Comfort functions such as autoSTART-STOP & softSTART
- Heated breathing tube prismaHYBERNITE
- Easy-to-use accessories

Product Class as per Directive 93/42/EEC	IIa
Dimensions (W x H x D)	170 x 135 x 180 mm
Weight	about 1.4 kg
Temperature range • Operation • Storage	 +5°C to +40°C -25°C to +70°C
Permitted humidity, operation & storage	rel humidity 10% to 95%, no condensation
Air pressure range	700-1,060 hPa corresponds to altitude fo 3,000 metres
Diameter of breathing tube	22mm or 15mm
Electric rating	max. 40VA
System interface	12 V DC max. 10VA
Power consumption in: • Operation (therapy): • Standby:	230V 115V 0.11 A 0.22A 0.036A 0.019A

CE 0197

Classification as per EN 60601-1-11 • Type of protection from electric shock: • Level of protection from electric shock: • Protection from damaging ingress of water & solids:	 Protection class II Type BF IP21
Alarms	leak & disconnection
Mean sound pressure/ Operation as per ISO 80601-2-70	about 26.5 dB(A) at 10 hPa (corresponds to sound pressure of 34.5 dB(A)
CPAP/APAP operating pressure range	4 to 20 hPa
Pressure Accuracy	< 20 hPa ± 0.6 hPa

Peak flow as per ISO 80601-2-70, modes CPAP, without humidifier	
4.0 hPa	235 l/min
8.0 hPa	230 l/min
12.0 hPa	220 l/min
16.0 hPa	215 l/min
20.0 hPa	210 l/min

Stability of the dynamic pressure (short-term accuracy) for 10 breaths/min as per ISO 175-1:2007 with the use of the 22-mm tube	
7.0 hPa	Δ p ≤0.24 hPa
10.0 hPa	Δ p ≤0.28 hPa
13.5 hPa	Δ p ≤0.3 hPa
20.0 hPa	Δ p ≤0.4 hPa

PRISMA SMART & PRISMA SOFT

Flexible Therapy for OSA

With the prisma SOFT & prisma SMART, discover the new generation of our CPAP/APAP devices.

The two innovative, simple-to-use prisma SOFT & prisma SMART devices complete the prismaLINE spectrum.

Benefit from our two all-rounders, pragmatically designed for practical use. We always develop with our partners' requirements in mind to create intuitive devices that are reliable, economical & state-of-the-art.

Major features include:

- Standard operating concept & clearly structured, target group-oriented menus (for patients & experts).
- Segment display - highly visible presentation of required information.
- prismaLINE range of accessories.
- Two different APAP dynamics in prisma SMART - the right therapy for every patient.
- Familiar features such as recognition of Cheyne-Stokes respiration & Forced Oscillation Technology (FOT) in the entire prismaLINE.

Product Class as per Directive 93/42/EEC	IIa	
Dimensions (W x H x D)	170 x 135 x 180 mm	
Weight	about 1.34 kg	
Temperature range • Operation • Storage	 +5°C to +40°C -25°C to +70°C	
Air pressure range	700-1,060 hPa corresponds to altitude fo 3,000 metres.	
Electric rating	max. 40VA	
System interface	24V DC max. 5 VA	
Power consumption in: • Operation (therapy): • Standby:	230V 0.13A 0.036A	115V 0.22A 0.053A

Classification as per EN 60601-1-11 • Type of protection from electric shock: • Level of protection from electric shock: • Protection from damaging ingress of water & solids:	 Protection class II Type BF IP1I
Mean sound pressure/ Operation as per ISO 80601-2-70	about 26.5 dB(A) at 10 hPa (corresponds to sound pressure of 34.5 dB(A).
Recommended maximum oxygen flow	15L / minute.

CE 0197

prismaLINE is the intelligent system solution for treatment of respiratory disorders.

The prismaLINE represents a new dimension in operating convenience. The combination of a large monitor (touch screen or LED) & smart Graphical User Interface allows more intuitive & faster use than ever before.

This exceptional operating concept is found throughout the prismaLINE portfolio. Every prismaLINE device provides the user with ideal support for all kinds of work processes & for connectivity & accessories too.

SOMNOBALANCE E

autoCPAP device

The quietest autoCPAP therapy - balanced & flexible

The autoCPAP therapy device SOMNObalance e is equipped with Obstructive Pressure Peak (OPP) technology which reliably distinguishes obstructive from central events. With automatic & continuous pressure adjustments in response to patient needs, the device offers great flexibility in therapy options. A selection of modes, which can be combined with intelligent softPAP pressure relief, makes SOMNObalance e even more flexible. The SD card helps to significantly optimize work processes.

Comfortable Therapy

» Extremely quiet.
» Automatic needs-oriented pressure adjustment in phases of high pressure variability.
» softSTART.

Convenient Operation

» SD card to optimize work processes.
» Easy data transfer for therapy & compliance monitoring.
» Simple first-time device configuration.
» Uncomplicated exchange of devices.
» Practical device setting with the help of the master card.
» User-friendly patient information menu
» Extensive statistical data clearly presented.
» Convenient data and device management with PC-software prismaTS.
» Additional analogue signals for PSG feed: pressure, flow, leakage, OPP, relative respiratory minute volume.

Comfortable Therapy

» OPP technology (Obstructive Pressure Peak) distinguishes central & obstructive apnoea.
» In combination with further signals minor obstructive events are already treated to avoid severe obstructive events.
» Mask test ensures a comfortable & secure fit of the mask even at rising pressure levels during the night.
» Qualitative leakage display during therapy – to ensure effectiveness.

Product Class as per Directive 93/42/EEC	IIa
Dimensions (W x H x D)	210 x 90 x 270 mm
Weight	about 1.7 kg
Temperature range • Operation • Storage	 +5°C to +35°C -40°C to +70°C If device is operated at +40°C, the air supplied may have a temperature of up to 42°C
Permitted humidity, operation & storage	95% rel. humidity (no condensation)
Air pressure range	700-1,100 hPa (automatic altitude adjustment makes operations up to 2,500 meters possible)
Connection diameter air hose (mask side)	19.5 mm (suitable for 22 mm norm conus)
Electrical connection	115 - 230 V AC +10/-15%, 50-60 Hz with power unit or 12-24V DC +25/-15% with DC adapter
Fine filter separation level up to 1 µm: up to 0.3 µm:	 ≥ 99.5% ≥ 85%
Fine filter service life	about 250 hours in normal ambient air

Current Operation at: • Operation: • Standby:	230V 0.1A 0.02A	115V 0.2A 0.04A
	24V 0.9A 0.2A	12V 1.8A 0.4A

CE 0197

Classification as per EN 60601-1-11 • Type of protection from electric shock: • Level of protection from electric shock: • Protection from harmful penetration of water: • Operational type:	 Protection class II Type BF IPX1 continuous
Electromagnetic compatibility as per EN 6061-1-2 • Radio interference suppression • Radio interference resistance	Test parameters & limits may be requested from manufacturer. EN 55011 B EN 61000-4 parts 2 to 6, part 11
Mean sound level/ measured in patient position once meter from operating device as per EN ISO 17510:2009	about 25.8 dB(A) at 10hPa
Operational pressure range, pressure precision: (1 mbar 1hPa ≈ 1 cm H_2O)	4 to 20 hPa ± 0.6 hPa
Max. pressure in event of failure	< 40 hPa
Flow at max. rotation: 20 hPa 1151 l/min 10 hPa 145 l/min	 0 hPa 175 l/min tolerance ± 15 l/min
Heating of respiratory air	2.5°C

Short-term pressure constancy with 10 breaths/min as per EN ISO 17510-1:2009 at:	
20 hPa	Δ p = 0.2 hPa
16 hPa	Δ p = 0.2 hPa
12 hPa	Δ p = 0.2 hPa
8 hPa	Δ p = 0.2 hPa
4 hPa	Δ p = 0.2 hPa

SOMNOSOFT 2E

CPAP device

The quietest CPAP therapy - balanced & flexible

The CPAP therapy device SOMNOsoft 2e effectively treats Obstructive Sleep Apnoea. The intelligent pressure relief soft-PAP assists sensitive patients who have trouble exhaling
against high CPAP pressure.

The graphic presentation of obstructive & central events are reliably distinguished by OPP technology, gives the treating physician ideal
input for diagnoses & therapy decisions. Work processes are significantly optimized with use of the SD card.

Comfortable Therapy

- Extremely quiet.
- softSTART.

Convenient Operation

- SD card to optimize work processes.
- Easy data transfer for therapy & compliance monitoring.
- Simple first-time device configuration
- Uncomplicated exchange of devices
- Practical device setting with the help of the master card.
- User-friendly patient information menu
- Extensive statistical data clearly presented.
- Convenient data & device management with PC-software prismaTS.
- Additional analogue signals for PSG feed: pressure, flow, leakage, OPP, relative respiratory minute volume.

Safety

- OPP technology (Obstructive Pressure Peak) distinguishes central & obstructive apnoea for greatest therapy effectiveness & provides solid basis for decisions by doctor.
- Mask test ensures a comfortable & secure fit of the mask.
- Qualitative leakage display during therapy – to ensure effectiveness.

Product Class as per Directive 93/42/EEC	IIa
Dimensions (W x H x D)	210 x 90 x 270 mm
Weight	about 1.7 kg
Temperature range • Operation • Storage	 +5°C to +35°C -40°C to +70°C If device is operated at +40°C, the air supplied may have a temperature of up to 42°C
Permitted humidity, operation & storage	95% rel. humidity (no condensation)
Air pressure range	700-1,100 hPa (automatic altitude adjustment makes operations up to 2,500 meters possible)
Connection diameter air hose (mask side)	19.5 mm (suitable for 22 mm norm conus)
Electrical connection	115 - 230 V AC +10/-15%, 50-60 Hz with power unit or 12-24V DC +25/-15% with DC adapter
Fine filter separation level up to 1 µm: up to 0.3 µm:	 ≥ 99.5% ≥ 85%
Fine filter service life	about 250 hours in normal ambient air

Current Operation at: • Operation: • Standby:	230V 0.1A 0.02A	115V 0.2A 0.04A
	24V 0.9A 0.2A	12V 1.8A 0.4A

CE 0197

Classification as per EN 60601-1-11 • Type of protection from electric shock: • Level of protection from electric shock: • Protection from harmful penetration of water: • Operational type:	 Protection class II Type BF IPX1 continuous
Electromagnetic compatibility as per EN 6061-1-2 • Radio interference suppression • Radio interference resistance	Test parameters & limits may be requested from manufacturer. EN 55011 B EN 61000-4 parts 2 to 6, part 11
Mean sound level/ measured in patient position once meter from operating device as per EN ISO 17510:2009	about 25.8 dB(A) at 10hPa
Operational pressure range, pressure precision: (1 mbar 1hPa ≈ 1 cm H_2O)	4 to 20 hPa ± 0.6 hPa
Max. pressure in event of failure	< 40 hPa
Flow at max. rotation: 20 hPa 1151 l/min 10 hPa 145 l/min	 0 hPa 175 l/min tolerance ± 15 l/min
Heating of respiratory air	2.5°C

Short-term pressure constancy with 10 breaths/min as per EN ISO 17510-1:2009 at:	
20 hPa	Δ p = 0.2 hPa
16 hPa	Δ p = 0.2 hPa
12 hPa	Δ p = 0.2 hPa
8 hPa	Δ p = 0.2 hPa
4 hPa	Δ p = 0.2 hPa

PRISMA25S

BILevel-S therapy device

BI Level-S therapy for high/fluctuating pressure needs & CPAP intolerance

The prisma 25S offers intuitive navigation & parameter settings to simplify & accelerate user operation. Patients with obstructive, mixed or complex sleep apnoea who have high & /or fluctuating pressure needs & poor CPAP compliance will find the perfect therapy partner in prisma25S. In addition to a broad pressure range & apnoea differentiation by means of FOT, the device has process & comfort supporting features to deliver effective, safe & comfortable BiLevel-S therapy.

Key Features:

- Ventilation modes: CPAP, APAP, BILevel S, autoS.
- Broad pressure range (4 – 25 hPa) & several adjustable parameters for greater flexibility in therapy settings.
- Identification of periodic breathing, RERA, snoring, hypopnea, apnoea & flow limitations.
- Optionally with autoTRILevel principle.
- Optionally with auto Trigger (Trigger IN)
- High-resolution therapy data for 14 days & detailed statistics for 366 days.
- Therapy software prismaTS for data analysis & remote control.
- SD card & USB port.
- Telemedicine connection via modem for prisma CLOUD.
- Eight clearly distinguished analogue signals for PSG feed.
- Comfort functions such as autoSTART-STOP & softSTART.
- Heated breathing tube prismaHYBERNITE.
- Easy-to-use accessories.

Product Class as per Directive 93/42/EEC	IIa
Dimensions (W x H x D)	170 x 135 x 180 mm
Weight	about 1.4 kg
Temperature range • Operation • Storage	 +5°C to +35°C -40°C to +70°C
Permitted humidity, operation & storage	Rel. humidity 10% to 95%, no condensation
Air pressure range	700-1,060 hPa Corresponds to altitude of 3,000 metres.
Diameter of breathing tube	22 mm or 15 mm
Electric rating	Max. 40VA
System Interface	12V DC max. 10VA
Power consumption in: • Operation (therapy) • Storage	230V / 115V 0.11 A / 0.22 A 0.036 A / 0.019 A
Classification as per EN 60601-1-11 • Type of protection from electric shock: • Level of protection from electric shock: • Protection from harmful penetration of water:	 Protection class II Type BF IPX1
Alarms	Leak & disconnection

CE 0197

Modes	CPAP, APAP, BILevel S & autoS
Mean sound pressure/ Operation as per ISO80601-2-70	about 26.5 dB(A) at 10 hPa (corresponds to sound pressure of 34.5 dB(A))
CPAP operating pressure range	4 to 20 hPa
BILevel operating pressure range	4 to 25 hPa
Relative inspiration time: Ti/Tset	25% to 67%
Trigger	auto or can be set at three levels
Pressure increase speed	can be set at three levels
Back up frequency	0 bpm, 5 to 35 bpm, auto
Pressure accuracy	<20 hPa ± 0.6 hPa, ≥20 hPa ± 0.8 hPa

Peak flow as per ISO 80601-2-70, mode BIlevel, without humidifier	
4.0 hPa	235 l/min
10.5 hPa	225 l/min
17.0 hPa	215 l/min
23.5 hPa	200 l/min
25.0 hPa	195 l/min

Stability of the dynamic pressure (short-term accuracy) for 10 breaths/min as per ISO 17510-1:2007 with use of the 22-mm tube	
7.0 hPa	Δ p ≤ 0.24 hPa
10.0 hPa	Δ p ≤ 0.28 hPa
13.5 hPa	Δ p ≤ 0.3 hPa
20.0 hPa	Δ p ≤ 0.4 hPa

PRISMA25ST

BILevel-ST therapy device

BI Level-ST therapy with innovative setting concept (SCOPES)

Maximum flexibility for indication-specific pre-settings (SCOPES): the prisma25ST provides for individually tailored solutions.

The device is ideal for patients with obstructive, mixed or complex sleep apnoea with comorbidities. Equipped with automatic backup frequency, apnoea differentiation by FOT & many process & comfort supporting features, prisma25ST provides reliable, effective & whisper-quiet BILevel-ST therapy.

Key Features:

- Ventilation modes: CPAP, APAP, BILevel S, autoS, BILevel S/T, autoS/T, BILevel T.
- High level of safety due to auto back up frequency or high fixed back up frequency.
- Optionally with autoTRILevel principle.
- SCOPES for indication-specific pre-settings.
- Optional auto Trigger (Trigger IN).
- High resolution therapy data for up to 14 days & detailed statistics for 366 days.
- Therapy software prismaTS for data analysis & remote control.
- With SD card & USB port.
- Telemedicine connection via modem for prisma CLOUD.
- Eight clearly identified analogue signals for PSG feed.
- Comfort functions such as autoSTART-STOP & softSTART.
- Heated breathing tube prismaHYBERNITE.
- Easy-to-use accessories.

Product Class as per Directive 93/42/EEC	IIa
Dimensions (W x H x D)	170 x 135 x 180 mm
Weight	about 1.4 kg
Temperature range • Operation • Storage	 +5°C to +35°C -40°C to +70°C
Permitted humidity, operation & storage	Rel. humidity 10% to 95%, no condensation
Air pressure range	700-1,100 hPa Corresponds to altitude of 3,000 metres.
Diameter of breathing tube	22 mm or 15 mm
Electric rating	Max. 40VA
System Interface	12V DC max. 10VA
Power consumption in: • Operation (therapy) • Storage	230V / 115V 0.11 A / 0.22 A 0.036 A / 0.019 A
Classification as per EN 60601-1-11 • Type of protection from electric shock: • Level of protection from electric shock: • Protection from harmful penetration of water:	 Protection class II Type BF IPX1
Alarms	Leak & disconnection

Modes	CPAP, APAP, BILevel S, auto A, BILevel S/T, autoS/T, BILevel T
Mean sound pressure/ Operation as per ISO80601-2-70	about 26.5 dB(A) at 10 hPa (corresponds to sound pressure of 34.5 dB(A))
CPAP operating pressure range	4 to 20 hPa
BILevel operating pressure range	4 to 25 hPa
Relative inspiration time: Ti/Tset	25% to 67%
Trigger	auto or can be set at three levels
Pressure increase speed	can be set at three levels
Back up frequency	0 bpm, 5 to 35 bpm, auto
Pressure accuracy	<20 hPa ± 0.6 hPa, ≥20 hPa ± 0.8 hPa

Peak flow as per ISO 80601-2-70, mode BIlevel, without humidifier

4.0 hPa	235 l/min
10.5 hPa	225 l/min
17.0 hPa	215 l/min
23.5 hPa	200 l/min
25.0 hPa	195 l/min

Stability of the dymanic pressure (short-term accuracy) for 10 breaths/min as per ISO 17510-1:2007 with use of the 22-mm tube

7.0 hPa	Δ p ≤ 0.24 hPa
10.0 hPa	Δ p ≤ 0.28 hPa
13.5 hPa	Δ p ≤ 0.3 hPa
20.0 hPa	Δ p ≤ 0.4 hPa

CE 0197

PRISMACR

AcSV therapy device

The sleep machine therapy solution for complex SDB

Patients with periodic breathing or central, mixed or complex sleep-disordered breathing, are treated quickly & reliably by the innovative algorithm in prismaCR.

At the heart of the algorithm is a backup frequency combined with intra-breath regulation. It provides need-oriented pressure support during the current breath, a technology called Anticyclic Servoventilation (AcSV).

Key Features:

- Ventilation modes: CPAP, AcSV.
- Validated Anticyclic Servoventilation (AcSV) reacts quickly with smart adaptation of pressure support within one breath.
- Broad pressure range (4 – 30 hPa) & several adjustable parameters for greater flexibility in therapy settings.
- Identification of periodic breathing, RERA, snoring, hypopnea, apnoea & flow limitations.
- Optionally with autoTRILevel principle
- SCOPES for indication-related pre-settings.
- High-resolution therapy data for 14 days & detailed statistics for 366 days.
- Therapy software prismaTS for data analysis & remote control.
- SD card & USB port.
- Telemedicine connection via modem for prisma CLOUD.
- Eight clearly distinguished analogue signals for PSG feed.
- Comfort functions such as autoSTART-STOP & softSTART.
- Heated breathing tube.

Product Class as per Directive 93/42/EEC	IIa
Dimensions (W x H x D)	170 x 135 x 180 mm
Weight	about 1.4 kg
Temperature range • Operation • Storage	 +5°C to +35°C -40°C to +70°C
Permitted humidity, operation & storage	Rel. humidity 10% to 95%, no condensation
Air pressure range	700-1,060 hPa Corresponds to altitude of 3,000 metres.
Diameter of breathing tube	22 mm or 15 mm
Electric rating	Max. 40VA
System Interface	12V DC max. 10VA
Power consumption in: • Operation (therapy) • Storage	230V 115V 0.11 A 0.22 A 0.036 A 0.019 A
Classification as per EN 60601-1-11 • Type of protection from electric shock: • Level of protection from electric shock: • Protection from harmful penetration of water:	 Protection class II Type BF IPX1
Alarms	Leak & disconnection

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Modes	AcSV, CPAP
Mean sound pressure/ Operation as per ISO80601-2-70	about 26.5 dB(A) at 10 hPa (corresponds to sound pressure of 34.5 dB(A))
CPAP operating pressure range	4 to 20 hPa
AcSV operating pressure range	4 to 30 hPa
Relative inspiration time: Ti/Tset	25% to 67%
Back up frequency	5 bpm - 35 bpm, auto
Pressure accuracy	<20 hPa ± 0.6 hPa, ≥20 hPa ± 0.8 hPa

Peak flow as per ISO 80601-2-70, mode AcSV, without humidifier

4.0 hPa	235 l/min
10.5 hPa	225 l/min
17.0 hPa	215 l/min
23.5 hPa	200 l/min
25.0 hPa	195 l/min
30.0 hPa	190 l/min

Stability of the dynamic pressure (short-term accuracy) for 10 breaths/min as per ISO 17510-1:2007 with use of the 22-mm tube

7.0 hPa	Δ p ≤ 0.24 hPa
10.0 hPa	Δ p ≤ 0.28 hPa
13.5 hPa	Δ p ≤ 0.3 hPa
20.0 hPa	Δ p ≤ 0.4 hPa

PRISMALAB

Tritation device

The precise tritation device for every need.

The prismaLAB titration device features intuitive navigation & simple setting of therapy parameters. Like all prismaLINE devices, prismaLAB offers quick operation with perfectly coordinated state-of-the-art touch screen & smart Graphical User Interface. All modes & features of the prismaLINE are available in a single device for titration. All changes to modes & pressure levels can be conveniently made via the PC software prismaTS to ensure especially gentle care of the patient.

Key Features:

- Equipped with all modes & functions of prismaLINE therapy devices – from CPAP to innovative AcSV (Anticyclic Servoventilation).
- Continued therapy & soft pressure transitions at change of mode during the night.
- Continuous check of mask fit, automatic mask recognition & mask test.
- High resolution therapy data for up to 14 days & detailed statistics for 366 days.
- Therapy software prismaTS for data analysis & remote control.
- SD card & USB port.
- Telemedicine connection via modem for prisma CLOUD.
- Eight clearly identified analogue signals for PSG feed.
- Comfort functions such as autoSTART-STOP & softSTART.
- Heated breathing tube prismaHYBERNITE.
- Easy-to-use accessories.

Product Class as per Directive 93/42/EEC	IIa
Dimensions (W x H x D)	170 x 135 x 180 mm
Weight	about 1.4 kg
Temperature range • Operation • Storage	 +5°C to +35°C -40°C to +70°C
Permitted humidity, operation & storage	Rel. humidity 10% to 95%, no condensation
Air pressure range	700-1,060 hPa Corresponds to altitude of 3,000 metres.
Diameter of breathing tube	22 mm or 15 mm
Electric rating	Max. 40VA
System Interface	12V DC max. 10VA
Power consumption in: • Operation (therapy) • Storage	230V 115V 0.11 A 0.22 A 0.036 A 0.019 A
Classification as per EN 60601-1-11 • Type of protection from electric shock: • Level of protection from electric shock: • Protection from harmful penetration of water:	 Protection class II Type BF IPX1
Alarms	Leaks, disconnection (tube), apnoea, low minute volume, low tidal volume.

CE 0197

Modes	CPAP, APAP, AcSV, BILevel S, autoS, S/T, autoS/T, T, aPCV.
Mean sound pressure/ Operation as per ISO80601-2-70	about 26.5 dB(A) at 10 hPa (corresponds to sound pressure of 34.5 dB(A))
CPAP operating pressure range	4 to 20 hPa
BILevel operating pressure range	4 to 30 hPa
AcSV operating pressure range	4 to 30 hPa
Relative inspiration time: Ti/Tset	25% to 67%
Trigger	auto or can be set at 3 levels
Back up frequency	0 bpm, 5 bpm - 35 bpm, auto
Pressure accuracy	<20 hPa ± 0.6 hPa, ≥20 hPa ± 0.8 hPa

Peak flow as per ISO 80601-2-70, mode AcSV, without humidifier

4.0 hPa	235 l/min
10.5 hPa	225 l/min
17.0 hPa	215 l/min
23.5 hPa	200 l/min
25.0 hPa	195 l/min
30.0 hPa	190 l/min

Stability of the dynamic pressure (short-term accuracy) for 10 breaths/min as per ISO 17510-1:2007 with use of the 22-mm tube

7.0 hPa	Δ p ≤ 0.24 hPa
10.0 hPa	Δ p ≤ 0.28 hPa
13.5 hPa	Δ p ≤ 0.3 hPa
20.0 hPa	Δ p ≤ 0.4 hPa

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