aimediq
Intelligent Medical Systems

ReOxy®

Innovative Solution for Sports Medicine

www.reoxy.co.uk

ReOxy®

ReOxy® is...

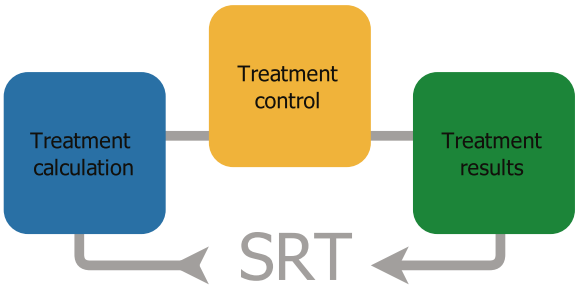
innovative breathing therapy medical device which treats a patient with individually selected reduced-oxygen (hypoxic) gas mixtures adjusted in real time during the procedure.

The main objectives to be achieved using the ReOxy® device are short and long-term adaptive responses at the whole body, system, tissue and cellular levels. These compensatory adaptive mechanisms have been scientifically proven to effectively treat cardiovascular and metabolic diseases. ReOxy® uses Self Regulated Treatment (SRT®) technology.

SRT®-technology relies upon the principle of biological feedback, where patients bodily reactions define therapeutic parameters and control them throughout the whole treatment session.

SRT® Technology

SRT® uses advanced software that reads and analyses information from a built-in pulse oximeter to adjust the supplied air mixture composition and session timing individually for each patient individually in response to changes in vital indicators, i.e. blood oxygen saturation (SpO_2) and heart rate.



Usage of innovative SRT®-Technology allows:

- Pre-treatment test – to evaluate zone of maximal therapeutic efficacy and to calculate individual treatment parameters;
- Treatment – to "keep" the patient in zone of maximal therapeutic efficacy by adjusting the treatment parameters in response to changes in patients state
- After the treatment – to calculate and store treatment parameters for the next treatment session.

ReOxy is CE-marked, approved and intended for improvement of physical exercise capacity in coronary artery disease patients.

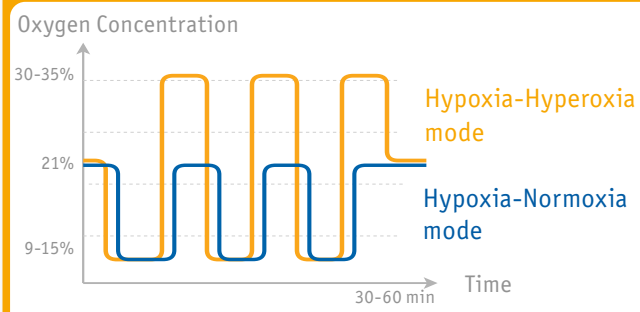
ReOxy® purpose

- Interval Hypoxic Treatment in the "Hypoxia - Hyperoxia" mode (IHHT®) based on SRT® technology
- Hypoxic Preconditioning
- Hypoxic Functional Test

Interval Hypoxic Treatment

Interval Hypoxic Treatment (IHT) consists of repeated short-term hypoxia (9-15% O_2), interrupted by brief periods of recovery. These periods of recovery could be either normoxic (21% O_2, Hypoxia-Normoxia mode), or hyperoxic (30-35% O_2, Hypoxia-Hyperoxia mode). Typical treatment course comprises 10-15 sessions.

The Advantages of Unique IHHT® Modality



- increase in the amplitude of the treatment factor, without more intense hypoxia (higher efficacy)
- shortening recovery periods and the procedure and total course duration

Hypoxic preconditioning

Hypoxic preconditioning refers to exposure of the body, it's systems, organs, tissues and cells to moderate hypoxia resulting in increased resistance to disease-related episodes of severe hypoxia. It mobilizes evolutionary acquired, genetically determined stress defense mechanisms.

This process involves activation of multiple intracellular components including receptors, mitochondrial respiratory chain, key intracellular regulatory systems, early genes, superfamilies of the inducible and constitutively active transcription factors.

IHHT application for Sports Medicine and Rehabilitation

- Shortening of recovery period after sports injury [1, 8, 15]
- Rehabilitation of athletes/players with overtraining syndrome [5]
- Cardioprotection from physical overloads, acute ischemia [2, 5, 6]
- Increase in professional longevity (prevention of stress-associated diseases such as arterial hypertension, ischaemic heart disease, myocardial infarction, stroke)[2, 6, 7, 11, 13, 18]
- Adaptation to altitude training due to shortened acclimatisation period [19]
- Adaptation to intensive physical loads [5, 16]
- Improved resistance to different stress types including emotional loads and competitive stress [5, 16, 17, 20]

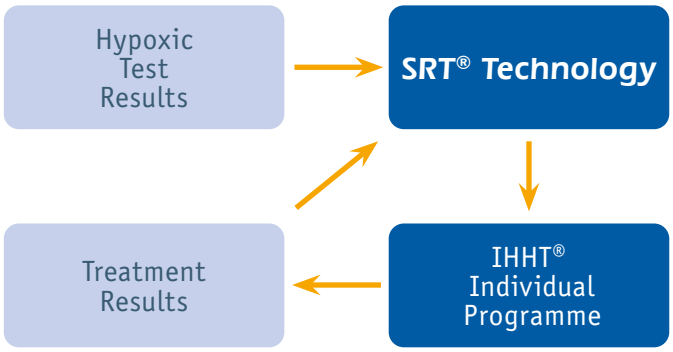
IHHT mechanisms:

- Direct influence of Hypoxia Inducible Factors (HIFs) on O_2 transportation and utilization mechanisms (hypoxic component)
- Indirect influence of Reactive Oxygen Species produced in reoxygenation phase (stress component)
- Phenomennon of hypoxic preconditioning (adaptation component)

Physiological effects:

- Improves physical exercise capacity [2, 3, 4, 6, 10, 22]
- Improves microcirculation [6, 9, 16, 17, 18, 19]
- Reduces endothelial dysfunction [16, 17, 19]
- Decreases blood pressure [6, 18]
- Increases myocardium and brain resistance to acute ischaemia [16, 17, 19]
- Reduces negative consequences of systemic oxidative stress [5, 11, 16, 17, 19, 20]
- Improves respiratory function, increases ventilatory response [1, 8, 13, 19, 20]
- Reduces metabolic markers, such as cholesterol and low density lipids [7, 11, 13]
- Modulates somatic motor function [1, 8, 15]

ReOxy® Treatment



- Interval Hypoxic Hyperoxic Treatment parameters are determined after a preliminary assessment of patient's ability to adapt to hypoxic gas mixtures, by doing the hypoxic test.
- Built-in intelligent software automatically identifies and suggests key treatment parameters for individual treatment programme, initially based on the results of the hypoxic test. Intensity of treatment parameters varies within the pre-set saftey limits throughout every procedure.
- At the end of each test, procedure and treatment course ReOxy generates a summary report in pdf.

IHHT® benefits

- a method based on more then 10 years of research and clinical trials
- a non-pharmaceutical treatment with minimal side-effects
- a unique solution for elderly/senior patients and patients with reduced physical abilities

Built-in Pre-Treatment Test

- hypoxic test
  Evaluates individual tolerance to hypoxia and determines individual parameters for further treatment procedures
- automatic analysis of test results
- automatic calculation of individual feedback parameters

Intelligent Control System

- individually-programmed operating modes
- monitoring of heart rate and blood oxygen saturation
- maintenance of patient database for data export and further statistical analysis
- possibilities for updating built-in software

Colour Control Display

- wide viewing angle and high contrast
- mode indication (hyperoxic / hypoxic)

ReOxy® Button

- manual gas flow switch

ReOxy 60-2001

Blending and supply of gas mixtures

- gas mixtures supplied:
  - hypoxic (10-14% O_2)
  - hyperoxic (30-40% O_2)
- automatic switching of gas flows (SRT-Technology)
- automatic flow volume regulation

Multi-level safety system

- automatic identification of the maximal treatment efficiency zone
- automatic switch between gas flows when reaching maximal and minimal threshold values
- manual gas flows switch
- integrated safety valve (automatic supply of ambient air)
- alarm signals (acoustic and visual warnings)

ReOxy benefits

- More than 10 years of research in IHT clinical applications
- SRT-technology: Individual Treatment Programme and Control
- Unique patented built-in software algorithms
- Hypoxia-Hyperoxia mode: improved treatment factor amplitude with reduced possible side effects
- Fully automated procedure, easy to operate
- Built-in pulse oximeter for real-time treatment parameters control
- Patient safety (multi-level controls, physiological and technical alarms)
- Compact, mobile, autonomous (no need for a specially equipped room)

ReOxy®

- Sensory Multifunctional Display
  - simple, user-friendly interface

On-screen Multi-language Keyboard

USB Port
  - data export: medical and technical reports

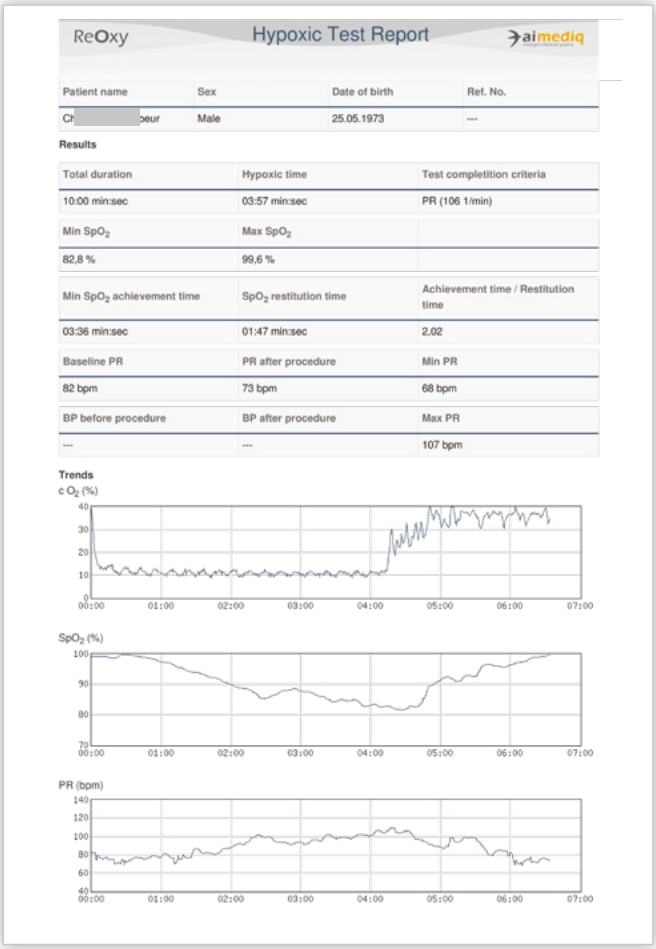
- Hinge Joint
  - reliable fixation in the most convenient position

- Pulse Oximetry Sensor
  - reliable reading and fast signal processing

- Antibacterial Filter

- Breathing Circuit

Procedure Report PDF


ReOxy Hypoxic Test Report aimediq

Patient name	Sex	Date of birth	Ref. No.
Ch[redacted]beur	Male	25.05.1973	---

Results

Total duration	Hypoxic time	Test completition criteria
10:00 min:sec	03:57 min:sec	PR (106 1/min)
Min SpO_2	Max SpO_2	
82,8 %	99,6 %	
Min SpO_2 achievement time	SpO_2 restitution time	Achievement time / Restitution time
03:36 min:sec	01:47 min:sec	2,02
Baseline PR	PR after procedure	Min PR
82 bpm	73 bpm	68 bpm
BP before procedure	BP after procedure	Max PR
---	---	107 bpm

Trends

Trends

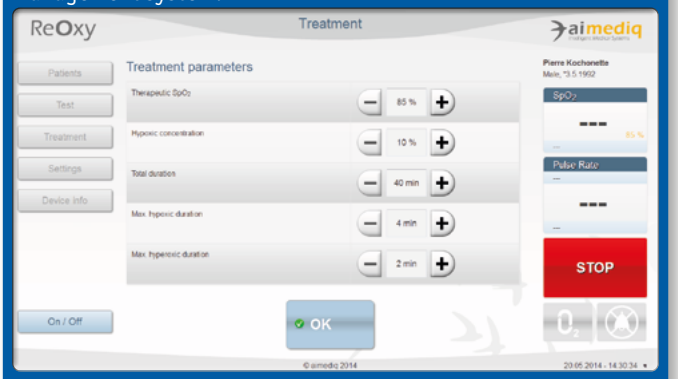
c02 - Oxygen concentration supplied to a patient via mask

Sp02 - Individual Sp02 reaction to 02 concentration changes

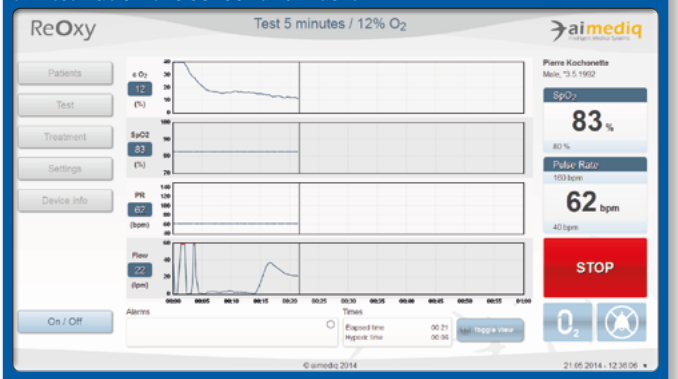
PR - Individual pulse rate reaction to 02 concentration changes

Easy to operate

Select or add a patient to the patient & procedure database management system.



Confirm the calculated procedure parameters and alarm limits. Put on the sensor and mask.



During the procedure, ReOxy® monitors Sp02, PR and 02. The procedure lasts for 30-60 min.

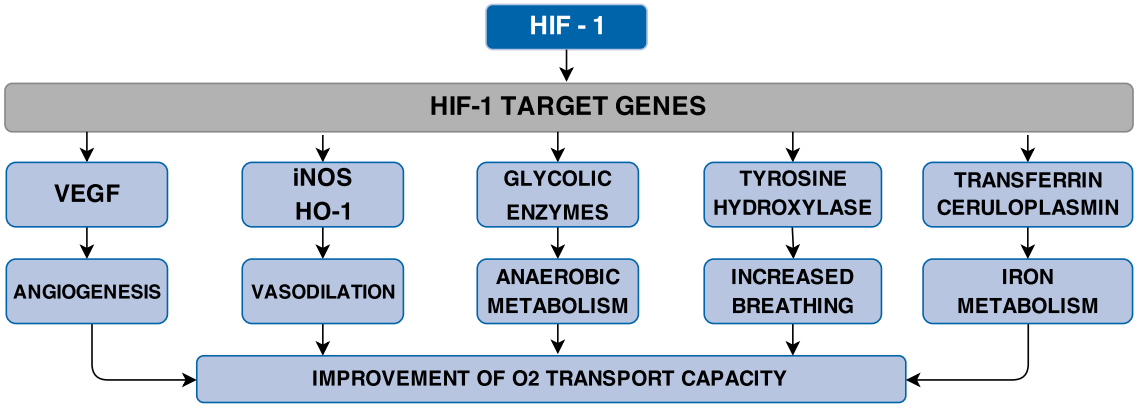
Remove the mask and sensor. Evaluate the automatically generated procedure report.

Adaptation to low oxygen tension (hypoxia) in cells and tissues leads to the transcriptional induction of a series of genes that participate in angiogenesis, iron metabolism, glucose metabolism, and cell proliferation/survival. The primary factor mediating this response is the hypoxia-inducible factor-1 (HIF-1), an oxygen-sensitive transcriptional activator [17].

Ischemic diseases such as stroke and heart attack are caused by localized hypoxia manifested as cerebral and myocardial ischemia, respectively. Increase of the VEGF expression by HIF-1 or HIF-2 could induce formation of new blood vessels of the target area in the brain and heart, thereby providing increased blood flow and oxygen supply, and reducing harmful effects of ischemia [20].

Restoration of endothelial function and increase in nitric oxide synthesis [18], as well as development of HIF-1 mediated hypoxia tolerance of myocardium are the most likely mechanisms behind beneficial IHHT effects in CAD. Together with the heart rate decrease reported in both patient and healthy elderly populations, and the relevant metabolic effects (such as lowering LDL, triglycerides and cholesterol) [2, 22], these changes are likely to contribute to lowering frequency of angina attacks.

Anti-hypertensive IHT mechanisms include hypoxic stimulation of endothelial NO production, which causes vasodilation and opening of reserve capillaries [19].



Repeated intermittent systemic exposure to hypoxia, a treatment known as intermittent hypoxic training (IHT), has been shown to enhance exercise capacity and performance in endurance athletes [4], by trigerring hematological and non-hematological adaptations [9], and to improve cardiopulmonary efficiency and running economy in athletes [10, 3]. Also, exposure to hypoxia alternated with periods of exposure to normoxia (IHT) has been found to be efficacious in coronary artery disease and chronic obstructive pulmonary disease in patients by increasing their tolerance to physical exertion without exercising [2] and improvg autonomic cardiovascular control [14]. Based on this findings, a new form of hypoxia exposure (Intermittent Hypoxia-Hyperoxia Training, IHHT), featuring recovery periods consisting of breathing a hyperoxic gas mixture, has been recently introduced and tested in a study aimed at enhancing exercise tolerance and re-balancing ANS in patients with coronary artery disease [6]. This new approach has been designed taking into consideration that breathing a hyperoxic gas mixture allows quicker oxygen saturation after being exposed to hypoxia, potentially reducing the time of the hypoxic–hyperoxic exposure cycle. At the same time, animal model studies demonstrated that replacing normoxia by hyperoxia within a cycle of hypoxia exposure creates a stronger stimulus to enhance reactive oxygen species signalling, so this form of exposure results in higher resistance of membrane structures and improved antioxidant capacity [20]; this aspect could be relevant in OTS athletes in the light of a recently published study showing that oxidative stress resistance and antioxidant capacity are critical for these athletes.

Safety

To our knowledge, there weren't a single case of a patient abandoning IHHT trials due to side effects development. Minor side effects observed during IHHT studies, such as dizziness, mild sedation, shortness of breath, or brief limited blood pressure rise, were noted in a few patients only. These negative sensations and adverse effects quickly disappeared after a small increase in the supplied O_2 concentration.

Short-term hypoxic exposures did not provoke angina attacks in CAD patients with myocardial infarction in the past, and were well tolerated even by senior (65 to 75-year-old) individuals [22].

No significant side effects specific to hypoxia-hyperoxia combination have been reported so far [5, 6].

It should be noted that all hypoxia-hyperoxia mode studies reviewed have been done employing ReOxy.

Risk analysis performed for patients with CVD has not revealed any reported serious ReOxy device-related adverse effects. The following non-serious ReOxy-related side effects have been reported:

- 6 cases of chest discomfort during the procedure which have resolved on their own and with no ECG deviations observed out of 584 procedures performed [5],
- 4 cases of mild headache and 2 of mild dizziness which have resolved on their own out of 584 procedures [5],
- transient mild blood pressure elevation above patient's normal levels have been reported in 1 out of 35 patients in a single published studyy [22],

Transient moderate heart rate elevation from the initial baseline level during the IHT procedure as a common adaptational reaction to hypoxia.

References:

1. Astorino TA, Harness ET, White AC. Efficacy of Acute Intermittent Hypoxia on Physical Function and Health Status in Humans with Spinal Cord Injury: A Brief Review. Neural Plast. 2015;2015:409625. doi: 10.1155/2015/409625. Epub 2015 Jun 8.
2. Burtscher M, Gatterer H, Szubski C, et al. Effects of interval hypoxia on exercise tolerance: special focus on patients with CAD or COPD. Sleep Breath (2007); 14: 209–220.
3. Burtscher M, Gatterer H, Faulhaber M, et al. Effects of intermittent hypoxia on running economy. Int J Sports Med (2010); 31: 644–650.
4. Czuba M, Waskiewicz Z, Zajac A, et al. The effects of intermittent hypoxic training on aerobic capacity and endurance performance in cyclists. J Sports Sci Med (2011); 10: 175–183.
5. Glazachev OS, Susta D, Dudnik E. A programme based on repeated hypoxia-hyperoxia exposure and light exercise enhances performance in athletes with overtraining syndrome: a pilot study. Clin Physiol Funct Imaging. 2015 Oct 7. doi: 10.1111/cpf.12296.
6. Glazachev OS, Pozdnyakov Y, Urinskiy A, et al. Interval normobaric hypoxic-hyperoxic training increases exercise tolerance in patients with coronary artery disease. Eur J Prev Cardiol (2013); 20(Supplement 1): S 109.
7. Glazachev OS, Zvenigorodskaia LA, Dudnik EN, Iartseva LA, Mishchenkova TV, Platonenko AV, Spirina GK. [Interval hypoxic-hyperoxic training in the treatment of the metabolic syndrome]. Eksp Klin Gastroenterol. 2010;(7):51-6. Russian. PubMed PMID: 21033083.
8. Gonzalez-Rothi EJ, Lee KZ, Dale EA, Reier PJ, Mitchell GS, Fuller DD. Intermittent hypoxia and neurorehabilitation. J Appl Physiol (1985). 2015 Dec 15;119(12):1455-65. doi: 10.1152/japplphysiol.00235.2015. Epub 2015 May 21.
9. Hamlin M, Hellemans J. Effect of intermittent normobaric hypoxic exposure at rest on haematological, physiological, and performance parameters in multi-sport athletes. J Sports Sci (2007); 25: 431–441.
10. Katayama K, Sato K, Matsuo H, et al. Effect of intermittent hypoxia on oxygen uptake during submaximal exercise in endurance athletes. Eur J Appl Physiol (2004); 92: 75–83.
11. Kayser B, Verges S. Hypoxia, energy balance and obesity: from pathophysiological mechanisms to new treatment strategies. Obes Rev. 2013 Jul;14(7):579-92.
12. Kon M, Ohiwa N, Honda A, Matsubayashi T, Ikeda T, Akimoto T, Suzuki Y, Hirano Y, Russell AP. Effects of systemic hypoxia on human muscular adaptations to resistance exercise training. Physiol Rep. 2014 Jun 6;2(6). pii: e12033. doi: 10.14814/phy2.12033. Print 2014 Jun 1.
13. Krivoschekov SI, Tszo N, Neshumova TV, Kuzovleva TS, Kuznetsov OM. Influence of ten sessions of interval hypoxic training on effectiveness of respiratory metabolism and the lipid level in blood of patients with angina in health resort treatment. Hyp. Med. 1996. Vol. 4. No. 1:14-15.
14. Haider T, Casucci G, Linser T, et al. Interval hypoxic training improves autonomic cardiovascular and respiratory control in patients with mild chronic obstructive pulmonary disease. J Hypertens (2009); 27: 1648–1654.pulmonary disease. J Hypertens (2009); 27: 1648–1654.
15. Hayes HB, Jayaraman A, Herrmann M, Mitchell GS, Rymer WZ, Trumbower RD. Daily intermittent hypoxia enhances walking after chronic spinal cord injury: a randomized trial. Neurology. 2014 Jan 14;82(2):104-13. doi: 10.1212/01. WNL.0000437416.34298.43. Epub 2013 Nov 27.
16. Lei Xi, Serebrovskaya TV. Intermittent hypoxia: from molecular mechanisms to clinical applications. Nova science publishers. 2009.
17. Lei Xi, Serebrovskaya TV. Intermittent hypoxia and human diseases. Springer. 2012.
18. Lyamina NP, Lyamina SV, Senchiknin VN et al. Normobaric hypoxia conditioning reduces blood pressure and normalizes nitric oxide synthesis in patients with arterial hypertension. J Hypertens. 2011. Nov;29(11):2265-72.
19. Neubauer JA. Invited review: Physiological and pathophysiological responses to intermittent hypoxia. J Appl Physiol. 2001. Apr;90(4):1593-9.
20. Sazontova TG, Arkhipenko YUV. Intermittent hypoxia in resistance of cardiac membrane structures: role of reactive oxygen species and redox signaling. In: Intermittent Hypoxia: From Molecular Mechanisms to Clinical Applications (eds Xi, L, Serebrovskaya, TV) (2009), pp. 147–187. Nova Science Publishers Inc., New York, USA.
21. Semenza G. Signal transduction to hypoxia-inducible factor 1. Biochem Pharmacol. 2002. Sep;64(5-6):993-8.
22. Shatilo VB, Korkushko OV, Ischuk VA, Downey HF, Serebrovskaya TV. Effects of intermittent hypoxia training on exercise performance, hemodynamics, and ventilation in healthy adults. High Alt Med Biol. 2008. Spring;9(1):43-52.

Technical data

Model	60-1001	60-2001
O_2 concentration, hypoxic gas mixture	10-14%	10-14%
O_2 concentration, hyperoxic gas mixture	30-40%	30-40%
Capacity	not less than 25 litres/minute	not less than 25 litres/minute
Gas flows switching	- automatic mode SRT - manual mode	- automatic mode SRT - manual mode
Length of treatment	30-60 minutes	30-60 minutes
Monitored parameters	Pulse, SpO_2, O_2	Pulse, SpO_2, O_2
SpO_2 measurement range	1-100%	1-100%
SpO_2 accuracy of measurement	70-100% +/-2%, 0-69% +/-3%	70-100% +/-2%, 0-69% +/-3%
HR measurement range and accuracy	25-240 +/-3%	25-240 +/-3%
EU pulse oximeter standards	EN 60601-1, EN 60601-1-4, EN 865, EN 475	EN 60601-1, EN 60601-1-4, EN 865, EN 475
Alarm signals	SpO_2, HR, sensor, power (acoustic and visual warnings)	SpO_2, HR, sensor, power (acoustic and visual warnings)
Data interface	- 6" built-in colour multifunctional display	- 6" built-in colour multifunctional display - 15'' touch-screen colour display
Saving and exporting data	n/a	- internal memory - USB port
Output pressure	< 2 kPa	< 2 kPa
Noise level	< 50 dB	< 50 dB
Dimensions (H x L x W)	90 x 70 x 50 cm	120 x 70 x 50 cm
Weight	38 kg	44 kg
Voltage	230 V / 50 Hz	230 V / 50 Hz
Power consumption	450 VA	540 VA
Manufacturer's warranty	2 years	2 years
Dedicated patient kits	Single-patient breathing circuit (2 sizes)	Single-patient breathing circuit (2 sizes)
Standard Delivery	ReOxy 60-1001, patient kits, pulse oximetry sensor	ReOxy 60-2001, patient kits, pulse oximetry sensor

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