



ReOxy[®]

New Medical Device

Non-invasive treatment of
cardiovascular &
metabolic diseases



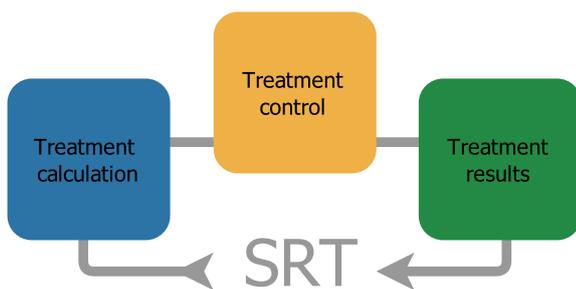
ReOxy is a new breathing therapy medical device, that treats a patient with individually dosed levels of reduced-oxygen (hypoxic) gas mixtures throughout the procedure.

The main objective to be achieved with use of the ReOxy device is short and long-term adaptive response at systemic, organic, tissue and cellular levels. These compensatory mechanisms of adaptation 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 patient bodily reaction define therapeutic parameters and controls 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 and timing for each patient individually in response to changes in vital indicators, i.e. blood oxygen saturation (SpO₂) 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.

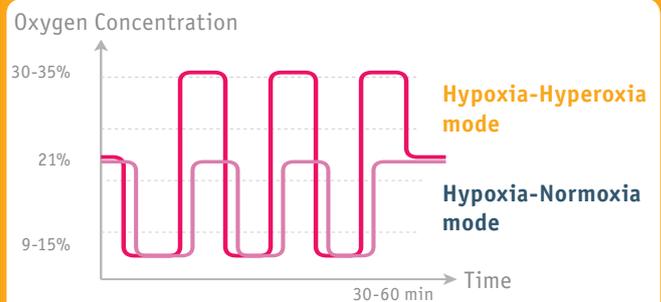
ReOxy purpose

- Interval Hypoxic Treatment in the “Hypoxia - Hyperoxia” mode (IHHT) based on SRT technology
- Hypoxic Preconditioning

Interval Hypoxic Treatment

Interval Hypoxic Treatment (IHT) consists of repeated short-term hypoxia (9-15% O₂), interrupted by brief periods of recovery. These periods of recovery could be either normoxic (21% O₂, Hypoxia-Normoxia mode), or hyperoxic (30-35% O₂, Hypoxia-Hyperoxia mode). Typical treatment course comprises 10-15 sessions.

The advantages of IHHT



- 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 (HP) refers to the exposure of organism, it's systems, organs, tissues or cells to moderate hypoxia that results in increased resistance to a subsequent episode of severe hypoxia. It mobilizes evolutionary acquired genome determined defense mechanisms of an organism.

This process involves an activation of multiple intracellular components including receptors, mitochondrial respiratory chain, key intracellular regulatory systems, early genes, superfamilies of the inducible and activation transcription factors (T. Serebrovskaya 2014).

The following types of protective effects of HP are distinguished: a rapid protective effect (early HP), when hypoxia and reoxygenation are followed immediately by increased tolerance to hypoxia and a delayed (late) HP effect, when increases in the resistance of organs and tissues to hypoxia are seen 16-24 h after hypoxia/reoxygenation [17, 18, 22, 26].

Clinical Effects of IHT

- Long-lasting antihypertensive effects [1, 2, 9, 19, 23, 24, 29]
IHT reduced BP, improved the patients' health status and physical performance, and normalized O₂ consumption and transport. The antihypertensive effect persisted for 6 months in 80% and for 1 year in 43% of the patients. Seventy-nine percent of these patients were able to discontinue medications after IHT. No unfavorable effects were observed [19].
- Increases exercise workload tolerance [1, 7, 8, 9, 11, 15, 16, 17, 21, 29]
Low exercise tolerance contributes to mortality in patients with coronary artery disease (CAD) and chronic obstructive pulmonary disease (COPD). Interval hypoxia might be a valuable preventive and therapeutic tool for these patients [4].
- Increase of myocardial tolerance to hypoxia/ischaemia (cardioprotective and antianginal effects)
IHT produced robust antianginal effects in patients with ischemic heart disease. These effects persisted for 3 months after IHT therapy in 88% of patients and for 6 months in 80% of patients [6,9, 19].
- Increase of myocardial vascularity, coronary blood flow (neangiogenesis – collateral capillaries outgrowth, endothelium-dependent vasodilatation) [3, 33, 35]
- Metabolic effect
Moderate IH protocols are reported to have beneficial effects on metabolism, including reduced body weight, cholesterol and blood sugar levels, and insulin sensitivity [25].
 - Normalises cholesterol levels, decreases LDL and triglycerides, increases HDL [5, 7, 9, 13, 14, 20, 27, 31]
 - Hypoglycaemic effect [5, 7, 31]
 - Increases body weight loss [11, 12, 32]
 - Suppresses the appetite [32, 34]
- Other effects
 - Significant improvement in quality of life [30]
 - Short-term memory and cognitive performance improvement [30]
 - Reduction of endothelial injury and dysfunction [10]

Indications for IHT

Cardiovascular diseases:

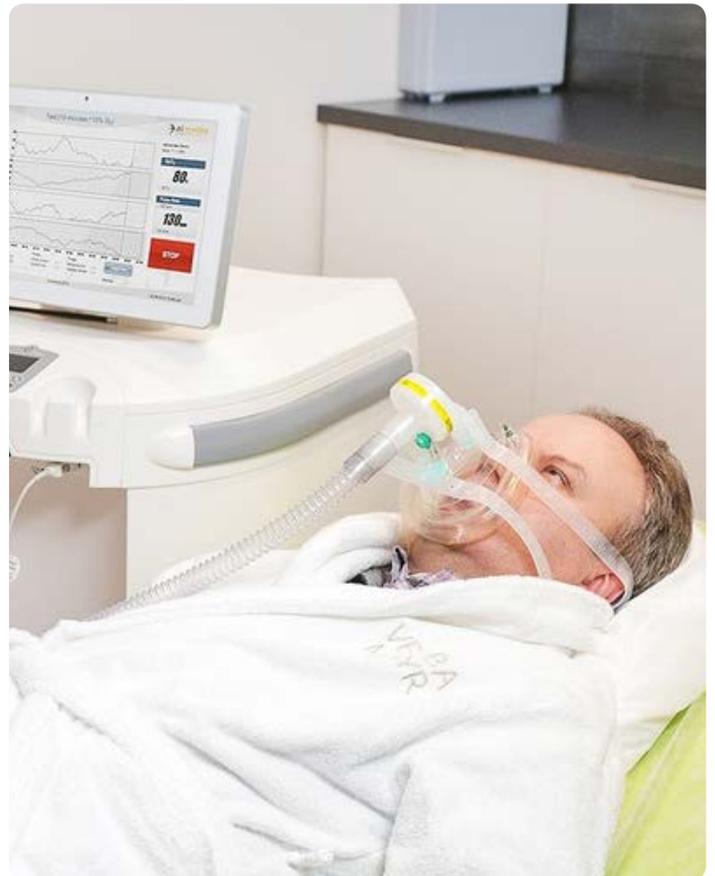
- Arterial Hypertension
- Ischaemic Heart Disease

Metabolic disorders:

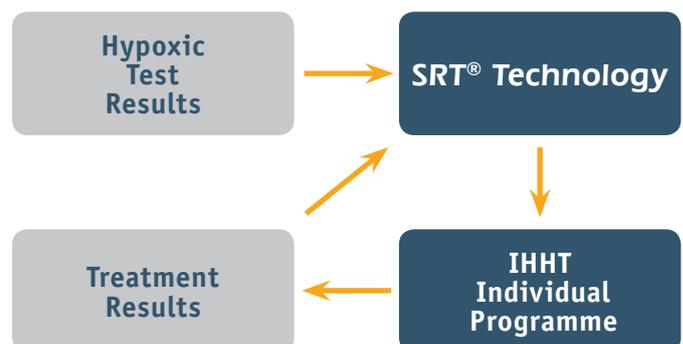
- Obesity
- Metabolic Syndrome

Further Applications:

- Rehabilitation after Myocardial Infarction and cardiac surgery
- Chronic Heart Failure (in research)
- Rehabilitation after Chronical Spinal Cord Injury



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. The intensity of the treatment parameters varies within the pre-set limits throughout every procedure.
- At the end of each test, procedure and treatment course ReOxy generates a summary report in pdf.

Built-in Pre-Treatment Test

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

Intellectual Control System

- individually-programmed operating modes
- monitoring of heart rate and blood oxygen saturation
- maintenance of patient database, providing 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 flows switch



ReOxy 60-2001

Blending and supply of gas mixtures

- gas mixtures supplied:
 - hypoxic (10-14% O₂)
 - hyperoxic (30-40% O₂)
- 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)

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

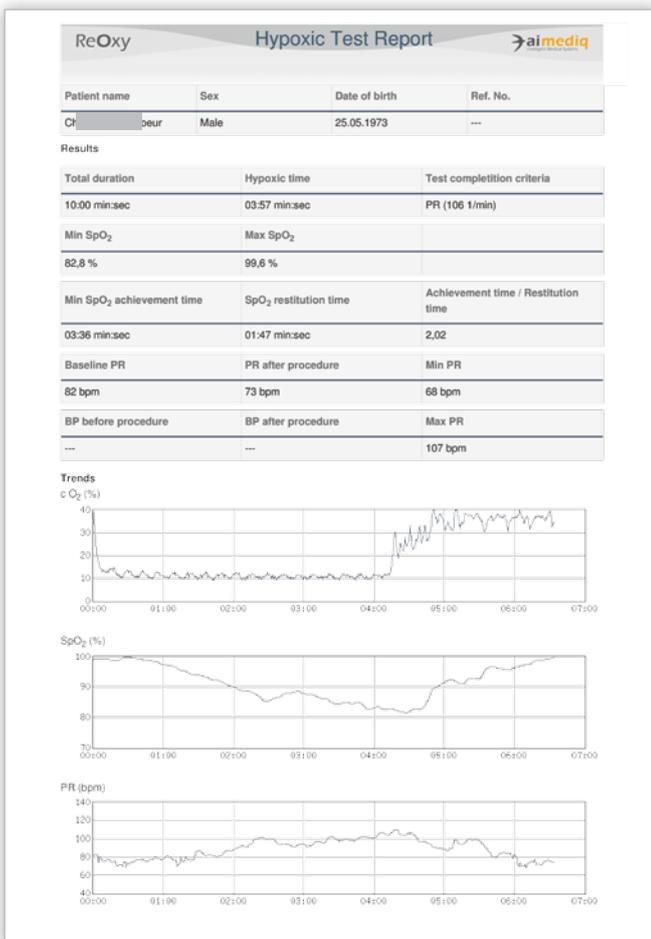
Pulse Oximetry Sensor

- reliable reading and fast signal processing

Antibacterial Filter

Breathing Circuit

Procedure Report PDF



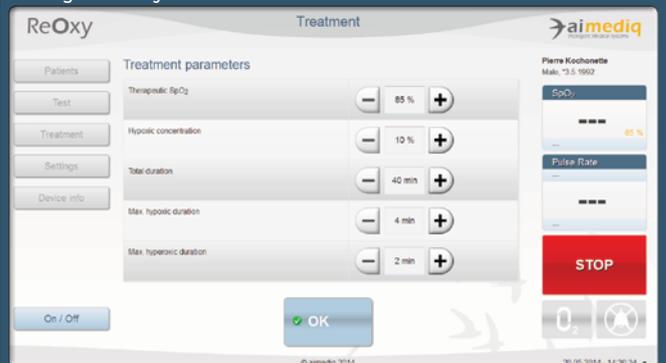
Trends

- cO₂ - Oxygen concentration supplied to patient via mask
- SpO₂ - Individual SpO₂ reaction to O₂ concentration changes
- PR - Individual pulse rate reaction to O₂ concentration changes

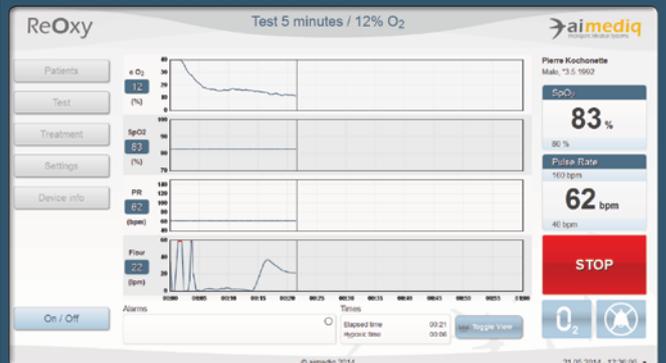
Easy to operate



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



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

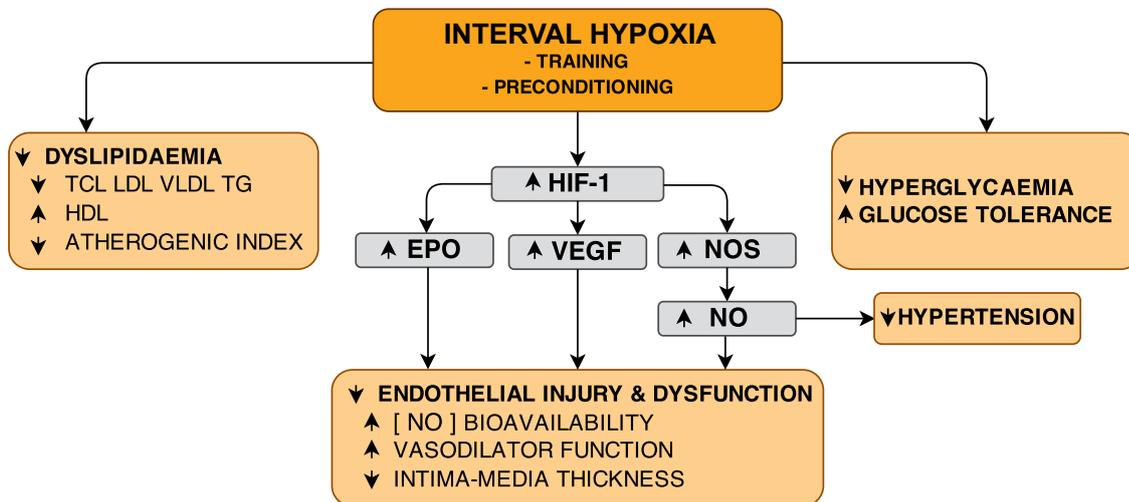


During the procedure, ReOxy monitors SpO₂, PR and O₂. The procedure lasts for 30-60 min.



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

Compensatory mechanisms of adaptive responses to interval hypoxia



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 [18].

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 the formation of new blood vessels of the target area in the brain and heart, thereby providing an increased blood flow and oxygen supply and reduce harmful response to ischemia [28].

Safety

There has been not one single case of a patient who had to abandon trials due to development of side effects in all studies known to manufacturer. Minor side effects observed during these studies are such as dizziness, sedation, shortness of breath, or brief blood pressure rise and were noted in a few patients only. These negative sensations and adverse effects disappeared after a small increase in the supplied O₂ concentration.

Short-term hypoxic exposures do not provoke angina attacks in IHD patients with MI in the past history and are generally well tolerated even by senior individuals (65 to 75-year-olds) [29].

No significant side effects specific to hypoxia-hyperoxia combination have been reported so far [8, 9].

It should be noted that the both hypoxia-hyperoxia mode studies reviewed have been done employing ReO₂.

Restoration of endothelial function and increase in nitric oxide synthesis [19], as well as development of HIF-1 mediated hypoxia tolerance of the myocardium are the most likely mechanisms involved. 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) [4, 29], these changes are likely to contribute to lowering frequency of angina attacks.

Anti-hypertensive IHT mechanisms include hypoxic stimulation of endothelial NO production, which provokes vasodilation and opening of reserve capillaries [26].

Risk analysis performed for patients with CVD has not revealed any reported serious ReO₂ device-related adverse events during the procedure. The following non-serious device-related adverse events have been noted:

- 6 cases of chest discomfort during the procedure without ECG deviations during 584 procedures which have resolved on their own [8],
- 4 cases of mild headache and 2 of mild dizziness which have resolved on their own in 584 procedures [8],
- transient mild blood pressure elevation above patient's levels have been revealed in 1 of 35 patients in one published study [29],

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

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Technical data

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

Presented by Ai Mediq S.A.



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