



ReOxy[®]

Medical Device

**New generation of
therapeutic intervention**



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.

ReOxy therapeutic solutions are based on cell protection molecular mechanisms that regulate genes activity in response to varying levels of oxygen – NOBEL PRIZE in Medicine, 2019

ReOxy is the world's first medical device that provides a novel non-pharmacological intervention aimed at "activation of genes in response to varying levels of oxygen" by triggering physiological response to acute short-term hypoxia interrupted with hyperoxia.

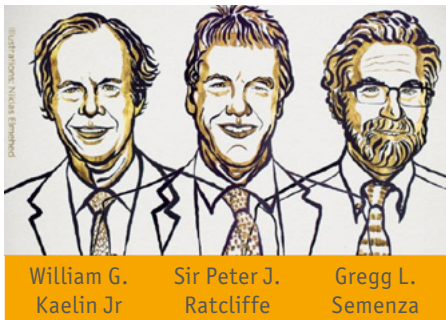
HIF Management

Hypoxia signaling pathway management is a new generation of therapeutic intervention leveraging the potential of hypoxia-inducible factor (HIF), first discovered and characterized in Dr. Semenza's laboratory. While having great potential as the regulator of oxygen homeostasis (including control of oxygen delivery, by regulating angiogenesis and vascular remodeling, and oxygen utilisation, by regulating glucose metabolism and redox homeostasis), HIF activation should be approached with caution.

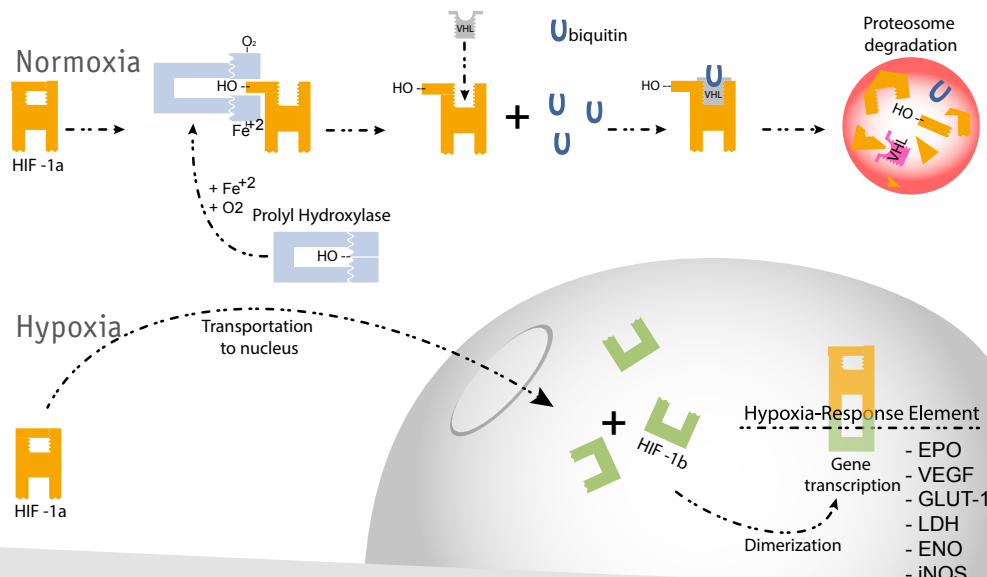
For the first time, the ReOxy device also implements a unique algorithm for calculating the safe and effective individual therapeutic hypoxic dose, which allows it's clinical use.

Nobel Prize 2019

Oxygen sensing decoded



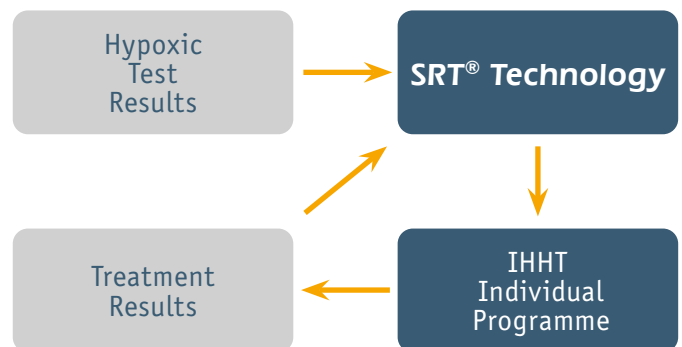
For their discoveries of how cells sense and adapt to oxygen availability



SRT Technology

ReOxy uses Self Regulated Treatment (SRT®) technology. SRT-technology relies upon the principle of biological feedback, where patient bodily reaction defines therapeutic parameters and controls them throughout the whole treatment session.

SRT-technology uses advanced software that 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 the 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.



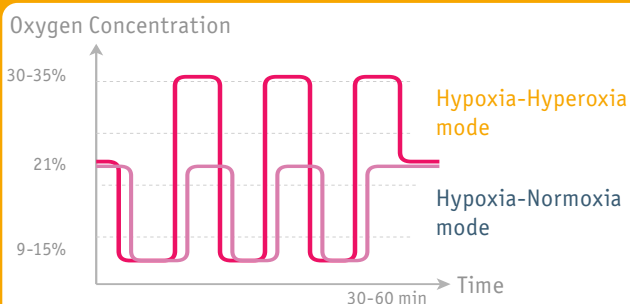
ReOxy provides

- Personalised Interval Hypoxic Treatment in the “Hypoxia - Hyperoxia” mode – IHHT
- 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).

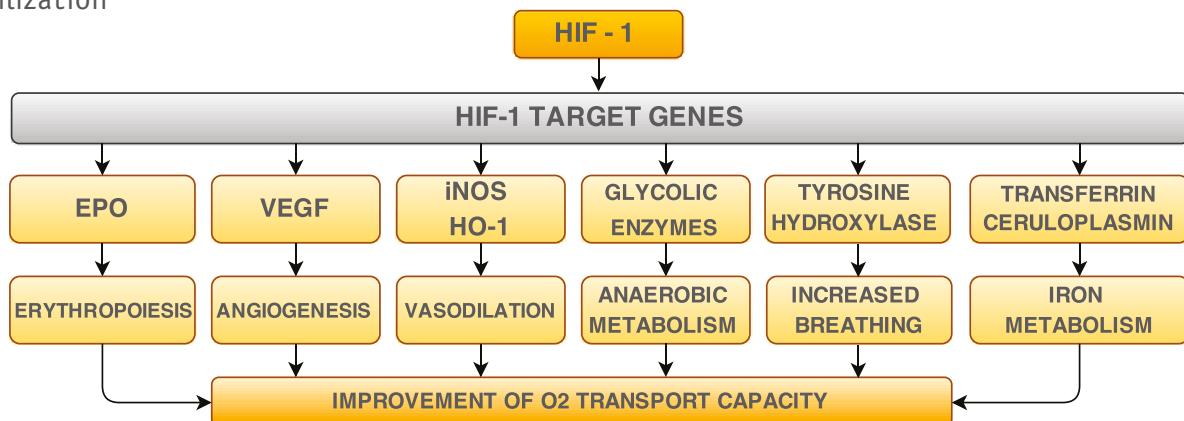
The advantages of IHHT



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



HIF-1 as a key regulator of O₂ delivery and utilization



The normal physiological response to reduced tissue perfusion is that the resulting tissue hypoxia induces HIF-1 activity, which activates the transcription of genes that participate in angiogenesis and iron metabolism. These factors stimulate the remodeling of collateral blood vessels, leading to increased blood flow.

In addition to promoting O₂ delivery, HIF-1 also activates the transcription of genes encoding enzymes, transporters, and mitochondrial proteins that decrease O₂ utilization, again functioning as a master regulator to switch cells from oxidative metabolism to glycolytic metabolism

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

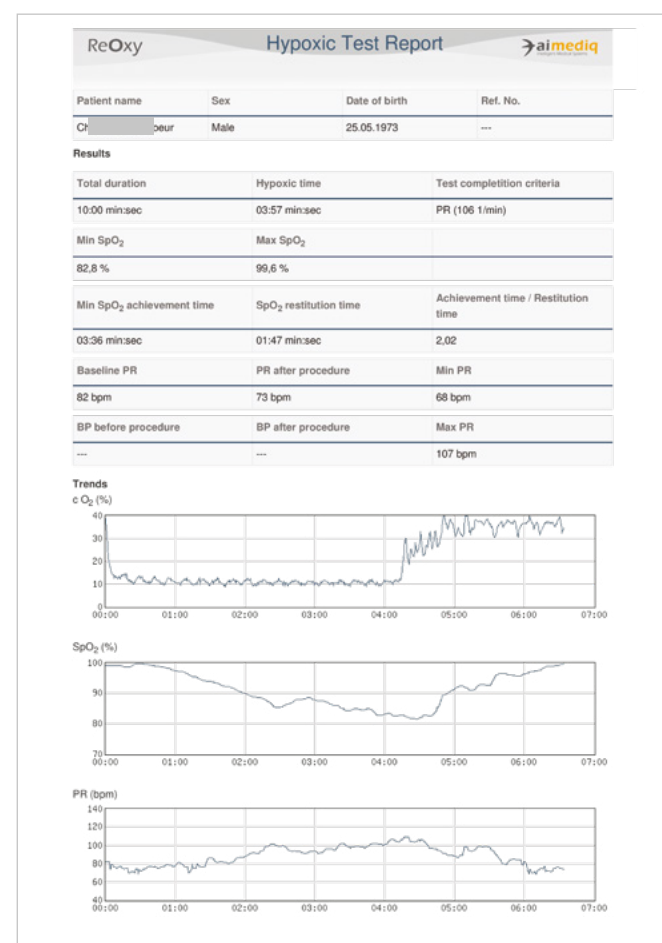
Pulse Oximetry Sensor

- 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

ReOxy Patients

Patient Details

First name: Pierp, Last name: F, Date of birth: 22.11.1983, Sex: Male, Ref. No: ---

Diagnosis: Additional info: ---

Buttons: Back, Roll, Pause, Create Report, Show all procedures (3)

Date/Time	Procedure	Duration	O ₂ Concentration	Min. SpO ₂
11.12.2014 - 11:29:33	Treatment	30:00	12 %	---
08.12.2014 - 13:05:04	Treatment	20:00	10 %	---

Buttons: On / Off

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

ReOxy Treatment

Treatment parameters

Therapeutic SpO₂: 85 %

Hypoxic concentration: 10 %

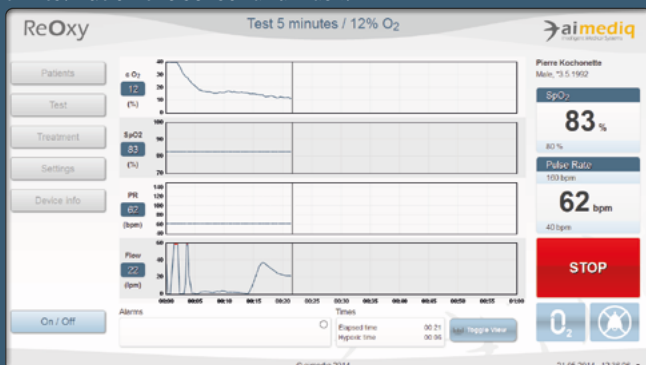
Total duration: 40 min

Max hypoxic duration: 4 min

Max hypoxic duration: 2 min

Buttons: On / Off, OK

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.

ReOxy Patients

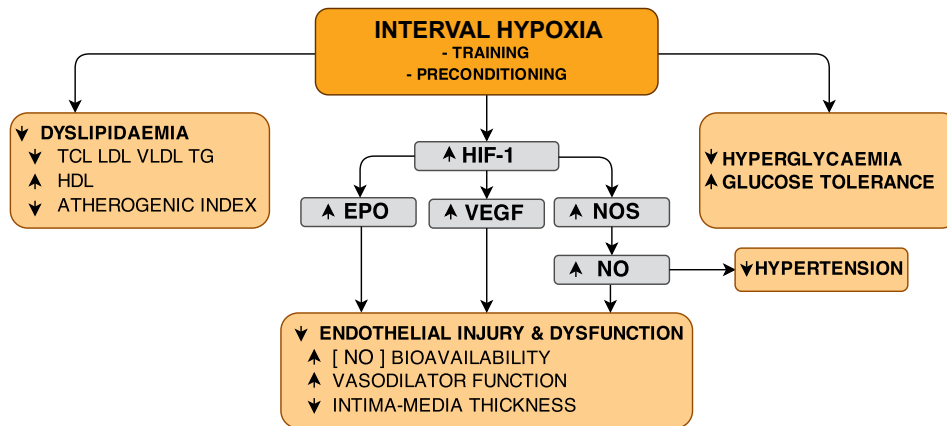
Treatment result

Patient	Therap F	Age	21
Date	11.12.2014 - 11:29:33	Duration of whole test	21:12
Hypoxic concentration	12 %	Therapeutic SpO ₂	85 %
Max. hypoxic duration	04:00	Max. hypoxic duration	04:00
N hypoxic	4	N hypoxic	4
Total hypoxic time	10:05	Eff. hypoxic time	06:30
Au. hypoxic duration	02:31	Au. hypoxic duration	01:51
Au. min/max SpO ₂	81 / 98	Au. min/max PR	83 / 109
Blood Pressure (Start)	---	Blood Pressure (End)	---

Buttons: Back, Treatment Report, On / Off

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

Compensatory mechanisms of adaptive responses to interval hypoxia

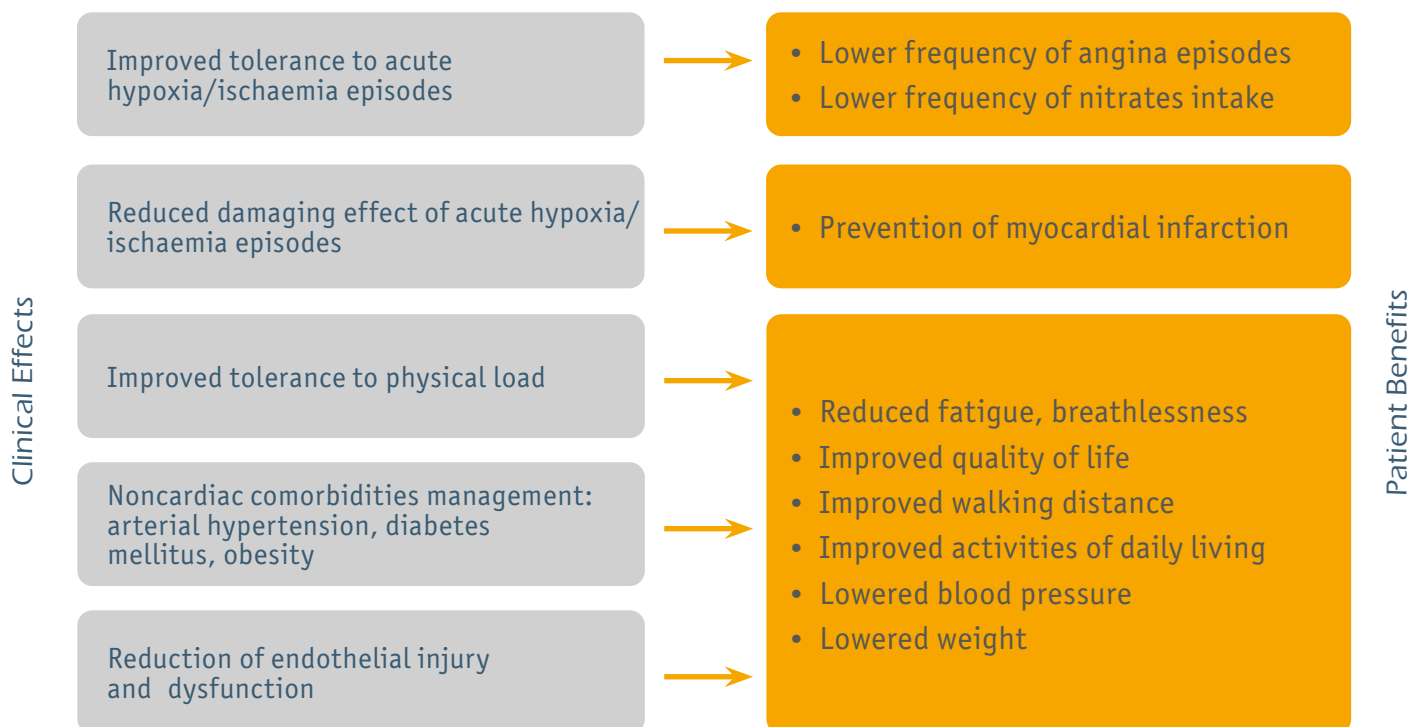


Ischemic diseases such as stroke and heart attack are caused by localized hypoxia manifested as cerebral and myocardial ischemia, respectively. The increase of the VEGF expression by HIF-1 or HIF-2 could induce the formation of new blood vessels of the target area in the brain and heart, thereby providing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

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

Restoration of endothelial function and increase in nitric oxide synthesis, 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), these changes are likely to contribute to lowering the frequency of angina attacks.

IHT Effects & Benefits



ReOxy Benefits

Challenges of cardiac rehabilitation



17.7 million

CVD related deaths
annually in the world



#1 killer

1/3 of all deaths
worldwide are caused by
CVD (mainly heart attack
and stroke)



€210 billion

is the estimated costs of
CVD to the European Union
economy annually

Cardiac Rehabilitation (CR) Programs – main tool to reduce CVD mortality, morbidity, hospital admissions, and improve quality of life.

Exercise training – a key CR component highly recommended by the European Society of Cardiology.

The pool of patients eligible for CR is thus steadily increasing.

Only about 10-30% percent of eligible patients participate in CR programs limiting

Clinical factors: contraindications, limitations (obesity, orthopedic problems, severe concomitant diseases, senior age) and comorbidities.

Non-clinical factors: geographical distance and transport issues, local shortages of resources, lack of qualified personnel

Today there is a strong unmet need in the development of a CVR treatment method that could be used for all categories of patients, including seniors, and patients with severely decreased functional and physical capabilities, which until now have been routinely excluded from CR programmes. The consequences of not having them include elevated disease management costs, reduced the quality of life and lead to avoidable deaths.

Our solution – the game-changer for CVD rehabilitation using innovative personalised therapeutic method IHHT based on SRT technology effective in patients with limited physical exercise ability.

ReOxy Safety

There has been not one single case of a patient who had to abandon trials due to the development of side effects in all studies known to the 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-old).

No significant side effects specific to hypoxia-hyperoxia combination have been reported so far.

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

Indications for IHT

Rehabilitation of cardiac patients

- Ischemic Heart Disease
- Rehabilitation after Myocardial Infarction
- Chronic Heart Failure

Further applications (in research)

- Rehabilitation after Stroke
- Rehabilitation after Chronic Spinal Cord Injury
- Rehabilitation after Trauma
- Dementia & Mild cognitive impairment
- Frailty in elderly patients
- Metabolic Disorders

Risk analysis performed for patients with CVD has not revealed any reported serious ReOxy 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,
- 4 cases of mild headache and 2 of mild dizziness which have resolved on their own in 584 procedures,
- transient mild blood pressure elevation above patient's levels have been revealed in 1 of 35 patients in one published study,

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

Technical data

Model	60-2001
O2 concentration, hypoxic gas mixture	10-14%
O2 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, SpO2, O2
SpO2 measurement range	1-100%
SpO2 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	SpO2, 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 L 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

ReOxy Distributors



ReOxy, SRT and IHHT are registered trademarks of Ai Mediq S.A., Luxembourg.
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