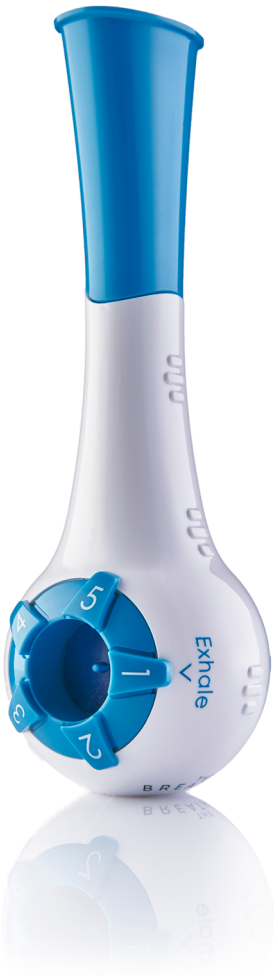
THE BREATHER™

ONE DEVICE – MANY THERAPIES

BENEFITS OF RMT

1. RMT rationale, functional benefits and physiological context



The rationale behind respiratory muscle training (RMT) is equivalent to strength training any other muscle of the body - training with resistance increases muscle strength, while training at low intensity for longer times increases endurance. These types of training lead to different structural adaptations of the muscle. In the case of RMT, breathing against a resistance will increase inspiratory and expiratory muscle strength, if the resistance is applied to both parts of the breath cycle. This will result in an increase in muscle fibres (hypertrophy), as well as in thickening of the diaphragm (McConnell book chapter 4).

These benefits of RMT are observed in healthy people, athletes and patients with underlying respiratory muscle weakness, making it a universally useful training method. Manifestation of increased respiratory muscle strength include improved exercise tolerance, capacity and performance, depending on the individual's baseline. That the increase in respiratory muscle strength leads directly to the observed benefits has been shown by (1), as maximal inspiratory pressure (the most important outcome measurement of RMT) directly correlates with ventilation, performance in the 6-minute walk test and health related quality of life (before and after RMT).

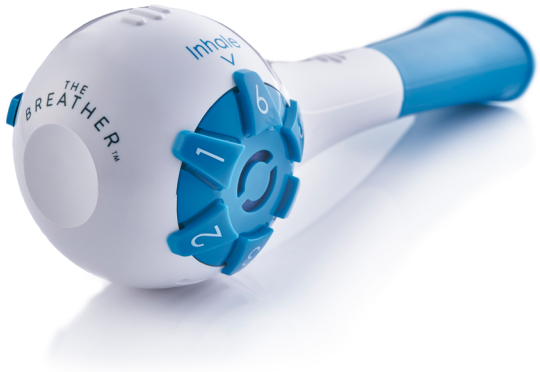
Patients with impaired respiratory muscle strength will start RMT from a lower baseline than athletes or healthy people. They will experience the same benefits, but usually show a steeper increase in respiratory muscle strength, as more improvement is possible if the baseline is lower. An important consequence of RMT in patients is the reduction of dyspnea, which is especially pronounced in patients with COPD, asthma and heart failure.

The respiratory, cardiovascular and peripheral muscle systems are linked due to oxygenation of the blood by breathing, which then gets circulated by the heart to the peripheral muscles.

to the peripheral muscles. RMT therefore affects the cardiovascular and muscle systems, and vice versa. As an example, general exercise increases respiratory muscle strength, though not to the same extent as RMT does. Important additional benefits of RMT include increased blood flow to the limbs and improvement of autonomic cardiac control (in patients with heart failure). It also decreases muscle sympathetic nerve activity, which is linked to the demonstrated ability of RMT to lower blood pressure (2).

A further crossover between respiratory system and musculature is the diaphragm, which is the main breathing muscle, but also plays an essential role in controlling the spine during postural control. Respiratory muscle weakness is therefore linked to poor posture control and back pain. The RMT-mediated improved diaphragm functionality is able to reduce back pain and reinstate posture control (3).

In summary, RMT strengthens the respiratory muscles, which affects blood oxygenation, cardiac function, peripheral muscle capacity, posture control and dyspnea. This gives RMT a central role in supporting and healing the respiratory, cardiovascular and skeletal system.



2. RMT METHODS

Two commonly used RMT methods exist, threshold and resistive RMT. Comparison of the two methods has demonstrated comparable efficacy.

Normocapnic hyperpnea is a third and more complex RMT method, which is not widespread at the moment, and relies on expensive equipment, training and supervision. It shows similar benefits to threshold and resistive RMT.

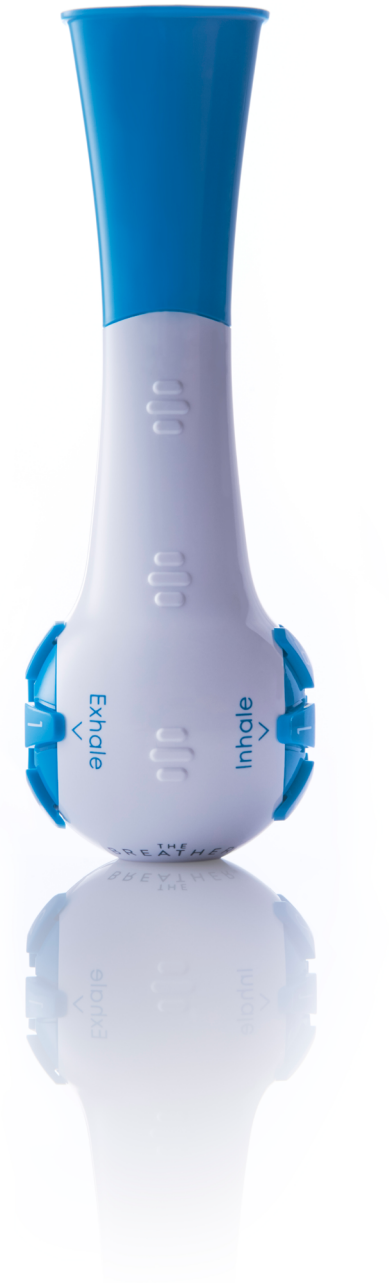
3. BENEFITS OF SPECIFIC IMT

IMT is the dominant methods used throughout the clinical studies and literature, with threshold IMT being most prominent. Therefore, all the above described benefits will be observed after IMT. IMT increases maximal inspiratory pressure (MIP or PImax) as primary outcome, but not MEP (with the exception of heart failure and asthma patients, in which the MEP improves as well in response to IMT!).

3.1. BENEFITS OF IMT ACROSS MAIN DISEASES

COPD

This is the main patient group in which RMT has been tested and approved. RMT improves inspiratory muscle strength and endurance, reduces dyspnea and increases exercise capacity in people with COPD, leading to an improved quality of life. Research shows that RMT is more effective in helping COPD patients than physical exercise alone. COPD patients usually use RMT at moderate to high intensity (60% to 80% of mouth pressure). RMT method: IMT.



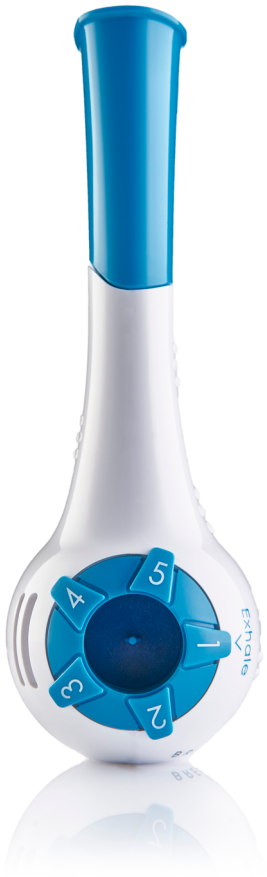
Specific outcomes improved in COPD patients:

- MIP/PImax
- MEP/PEmax
- 6MWT
- 12 minute walk test 12MWT
- POD
- QOL
- Peak minute ventilation VEpeak (during exercise)
- Peak oxygen uptake VO2peak (during exercise)
- Oxygen uptake efficiency slope OUES
- Uptake efficiency slope
- Maximal voluntary ventilation MVV
- Ventilatory efficiency
- Ventilatory oscillation
- MSVC
- Heart rate variability HRV
- Resting muscle sympathetic nerve activity MSNA
- Calf blood flow CBF
- Calf vascular resistance CVR
- Forearm blood flow FBF
- Forearm vascular resistance FVR
- DIaphragm movement

ASTHMA

Asthma often affects children, and is more severe in women than in men. RMT is effective in all asthma patients. RMT intensity is moderate, around 40% to 60% of PImax.
RMT can reduce the frequency of asthma attacks and improve the ability to perform daily tasks in adults and children with asthma. It can alleviate asthma symptoms and reduce the need for bronchodilators or inhalers. RMT method: IMT.

Specific outcomes improved in asthma patients:



- MIP
- MEP
- Peak expiratory flow (PEF)
- POD
- ß2 agonist consumption (bronchodilator use)

SLEEP APNEA

Obstructive sleep apnea can severely affect sleep quality and quantity, and quality of life. Sleep apnea is prevalent in the elderly. Applied RMT protocols for sleep apnea use either low or moderate intensity (40% to 75% of PImax).

RMT can severely reduce sleep apnea, especially in elderly people with sleep disorders. It improves sleep quality and quantity, and reduces the number of awakenings during the night and limb movements. RMT method: IMT.

Specific outcomes increased in people affected by sleep apnea:

- PImax
- Frequency of awakening during the night
- Apnea and hypopnea (improvement breathing pattern during the night)
- Desaturation in REM sleep (improvement of sleep quality)
- Periodic limb movements (more restful sleep)

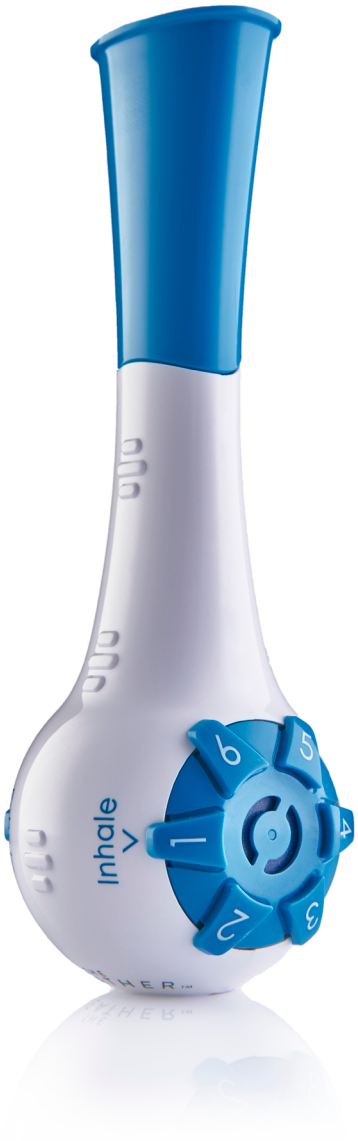
HYPERTENSION (HIGH BLOOD PRESSURE)

RMT can lower blood pressure. This effect is especially important for people with hypertension or high blood pressure, for examples as a result of autonomic imbalance. However, RMT also lowers the blood pressure in healthy people, which might prevent hypertension. RMT protocols use moderate to high intensity in healthy people (75% of PImax) and low intensity in people with hypertension (30% of PImax). RMT method: IMT.

Specific outcomes improved in people affected by hypertension or in healthy people:

- PImax
- PIF
- FVC
- Blood pressure
- Pulse pressure
- Heart rate variant
- Heart rate

LOW BACK PAIN



RMT strengthens the diaphragm, which is essential for breathing as well as for spinal postural control. Due to this double role, RMT can severely reduce low back pain while strengthening respiratory muscles, improve posture control and re-establish proprioceptive balance. RMT protocols use moderate intensity (60% of PImax). RMT method: IMT.

Specific outcomes improved in people affected by low back pain:

- PImax
- Relative proprioceptive weighting (improved posture)
- Low back pain severity

4. BENEFITS OF SPECIFIC EMT

EMT has been studied to a much lesser degree, only a few studies investigated this method. Interestingly, EMT seems to increase inspiratory as well as expiratory muscle strength, and peak expiratory flow (PEF). Improvements in PEF are associated with improved airway clearance and cough. EMT further improves swallowing and cough function and and penetration/aspiration in patients with swallowing dysfunction.

4.1. BENEFITS OF EMT ACROSS MAIN DISEASES

COPD

Adding EMT to IMT in COPD patients increases PEmax and PEpeak, but does not add further improvements to exercise capacity, dyspnea or QOL than IMT alone. Important: improvements of airway clearance or cough or any other parameters that might be improved by EMT were not tested in COPD patients!

PATIENTS WITH NEUROMUSCULAR DISEASES (NMD)

EMT has been tested in patients with disorders which affect the respiratory system and are associated with respiratory muscle weakness, such as Huntington's disease, Parkinson's disease and Duchenne Muscular Dystrophy. EMT improves maximal expiratory pressure MEP (expiratory muscle strength) and peak expiratory flow (maximum speed of expiration), and can improve cough function, respiratory load perception (perceived breathing effort), swallowing function, penetration-aspiration (efficacy of correct swallowing), and phonation (quality of speech). The evidence for EMT or combined IMT/EMT on patients with NMD is poor.

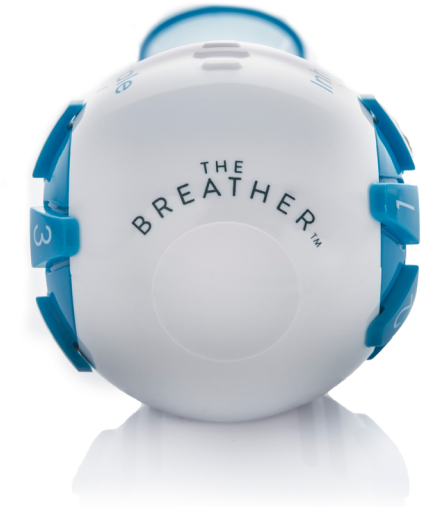
5. Patients of these diseases also benefit from improved respiratory strength

SPINAL CORD INJURY

RMT can help patients with spinal cord injury (SCI) in the acute phase by improving cough function, reducing dyspnea and increasing quality of life. RMT can also support people and athletes with chronic SCI by increasing exercise performance and lung capacity. RMT method: IMT or IMT+EMT

STROKE

Stroke patients usually have asymmetrical muscle and motor impairments. RMT can reverse asymmetry of diaphragm thickness. RMT method: IMT.



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3. Janssens L, McConnell AK, Pijnenburg M, et al. Inspiratory muscle training affects proprioceptive use and low back pain. Med Sci Sports Exerc. 2015 Jan;47(1):12-9