Nasal Breathing Quality and Health

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Rhinoforum 2019

Warsaw, Poland

Conflict of interest statement

The author is shareholder and CEO of Alaxo GmbH

which develops, manufactures and sells

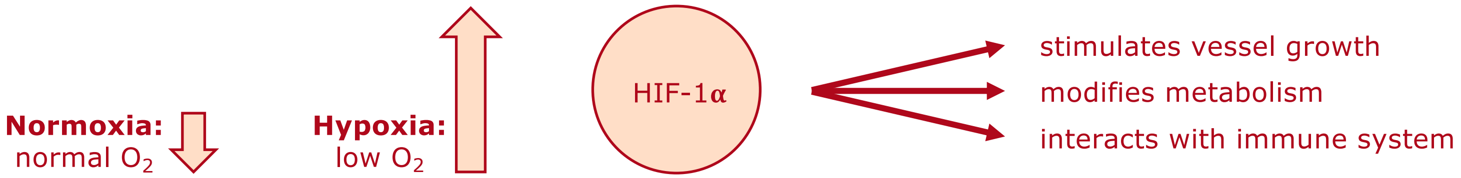
nasal and velopharyngeal nitinol stents

for mechanical splinting of the upper airway

Nobel Prize for Medicine 2019

„Mechanism of adaptation of cells to available oxygen"

- **Hypoxia-induced factor (HIF-1α)**: binds to DNA in an oxygen-dependent manner → controls expression of many genes *(Semenza und Wang 1992, Semenza 2005)*

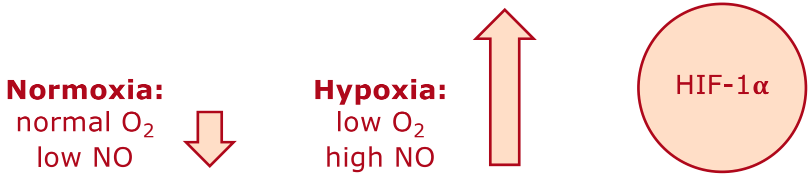


- Many cancer types create hypoxia → increase HIF-1α concentration → angiogenesis
- Nobel committee values importance of results for treatment of anemia, cancer, stroke, infections, wound healing, heart attack with new HIF-1α inhibitor drugs

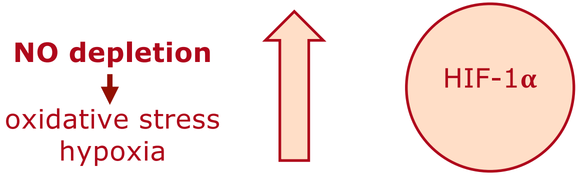
Nobel Prize for Medicine 2019

What has not been considered?

- **HIF-1α regulation is dependent on O_2, <u>nitric oxide (NO) and Reactive Oxygen Species (ROS)</u>**
- Low and medium NO levels physiologically normal; NO deprivation and high NO level critical



- NO deprivation → increased O_2 consumption → hypoxia → oxidative stress → HIF-1α activation by ROS: **<u>sensing system for oxidative stress</u>** *(Olson und van der Vliet 2011, Wagener et al. 2013, Movafagh et al. 2015)*



→ activation of inflammatory and cancer pathways

Nitric Oxide – Functions and Implications

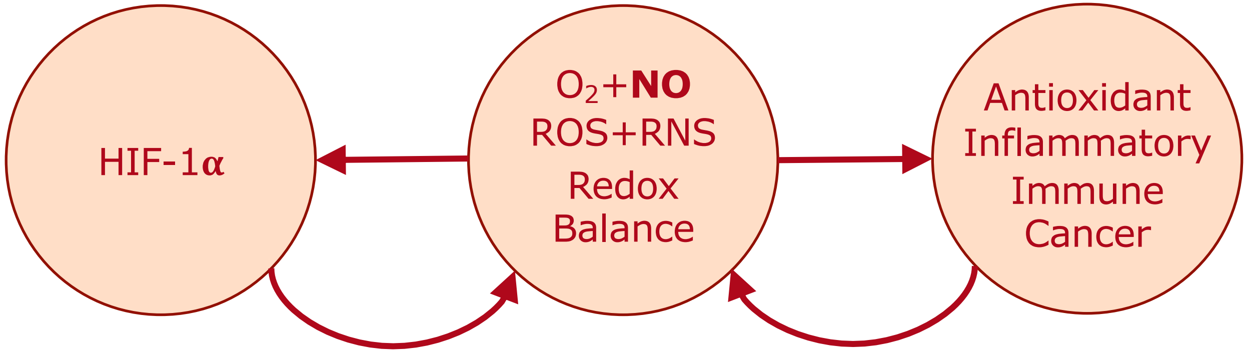
Essential multi-functional molecule in the body:

- Vasodilator → regulation of blood pressure (1998 Nobel Prize)
- Endocrine messenger (hormonal balance)
- Neurotransmitter (regulation of neuronal function)
- Growth hormone (regulation of cell division and tissue regeneration)
- Redox balance; strong antioxidant
- Regulation of diverse critical metabolic pathways
- Respiratory cycle (precondition of O_2 release from hemoglobin)
- O_2 sensor protein in the cell (2019 Nobel Prize) is controlled by NO
- Control of circulatory system and muscle functionality
- Antimicrobial agent: first defense line during inhalation

Body Functionality

„It´s all about balance“

Body health is dependent on maintenance of diverse homeostases



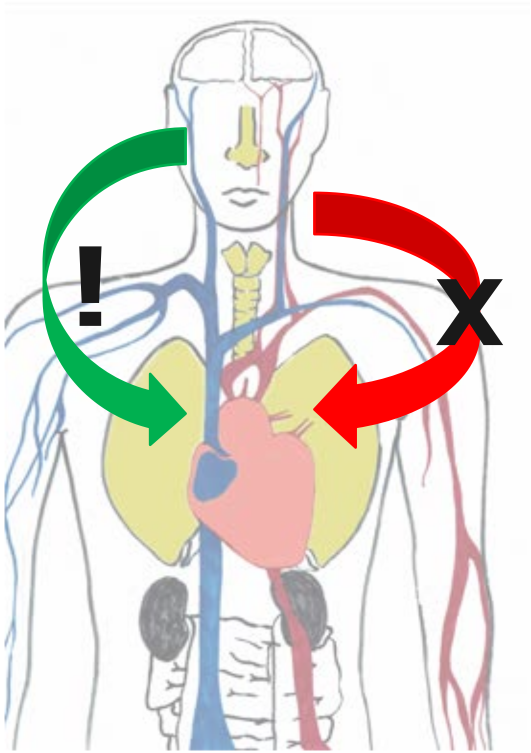
„How to achieve this balance?“

NO and Nasal Breathing

- **Up to 1,000fold higher NO production in sinuses than in vessel endothelium** *(Serrano et al. 2004)*

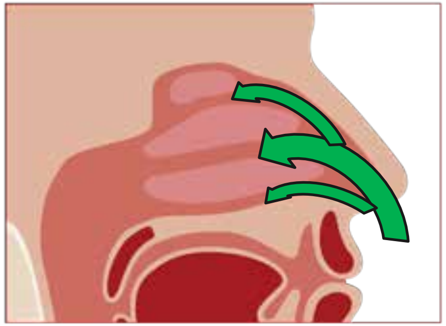
- **Nasal breathing transports NO from sinuses to the lung**

- With oral breathing only 10% NO transported compared to nasal breathing → NO deprivation



Nasal Fluid Mechanics

What is „normal“ nasal breathing?



Fluid mechanical studies:

- Mechanical flow model *(Simmen et al. 1999)*
- Computational Fluid Dynamics („CFD“) studies
  (e.g. Mösges 2013; Mlynski 2013; Zhao et al. 2014; Casey et al. 2017)

➢ Main airstream through middle nasal passage (not inferior!) plus flow through entire nasal cavity

➢ Statistically significant correlation with good patency of nasal cavity and subjective feeling of good nasal breathing

➢ Important: slow laminar flow; turbulent flow only in nasal vestibule and nasopharynx; turbulent share increases with flow velocity

➢ Optimal diameter of middle nasal passage: 5.5 to 6.5 mm *(Mlynski 2013)*

Nasal Fluid Mechanics

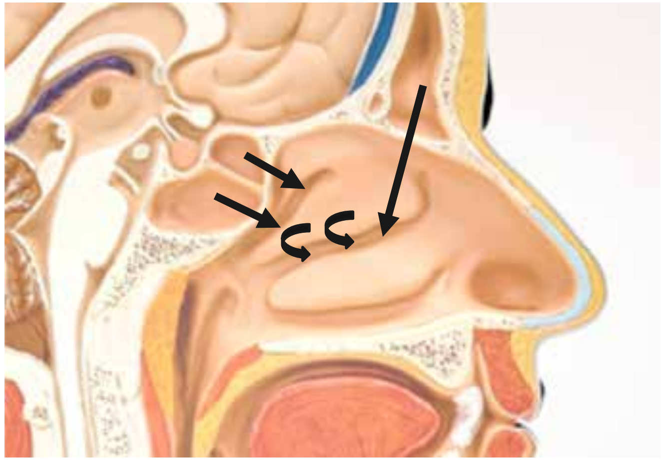
- Constricted nasal passages → increased flow velocity
  - ➢ concentration of airstream to lower area (pathological)
  - ➢ reduced contact time, inhaled air less well prepared for lung
  - ➢ relaxation in nasopharynx → negative pressure, turbulent flow, increased breathing resistance, suction phenomena → obstructions

- Strong nasal obstruction → nasal valve dysfunction due to altered flow pattern *(Lee et al. 2009)*

- Sinus ostia → here the NO must be "sucked off"
  → good nasal fluid mechanics required

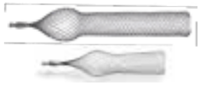
- Olfactory epithelium: upper nasal passage

- Breathing control and pharyngeal muscle tone receptors located in nose



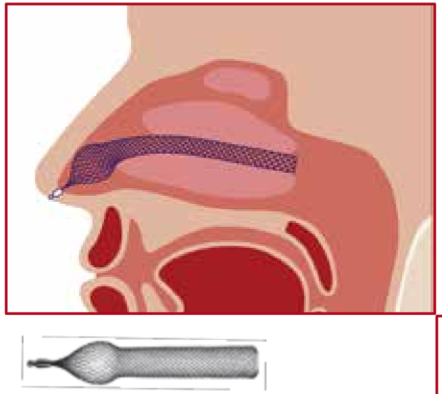
Sinus ostia in
middle and upper nasal passage

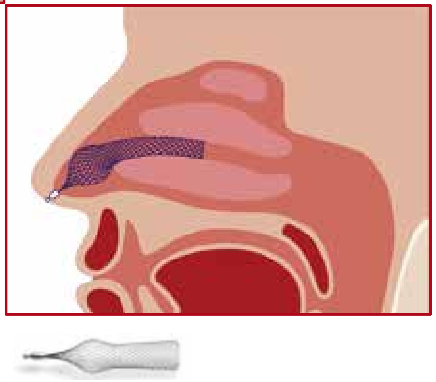
Mechanical Splinting Therapy

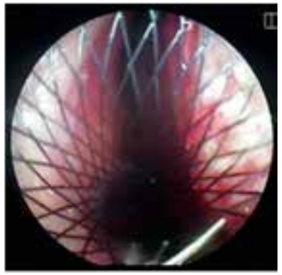


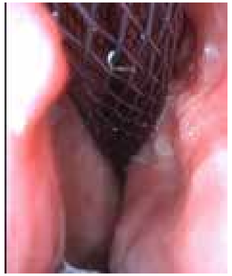
I. Nasal splinting with nitinol stents:

Mechanical splinting of middle nasal passage optimizes nasal airway → high nasal breathing efficiency

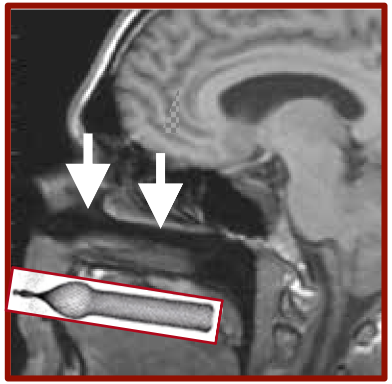


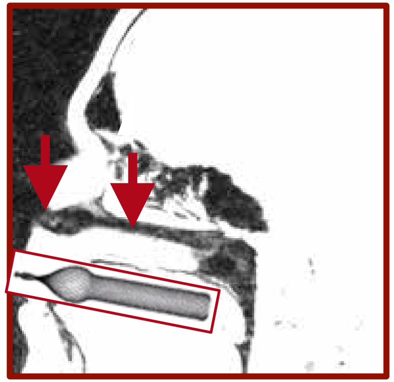






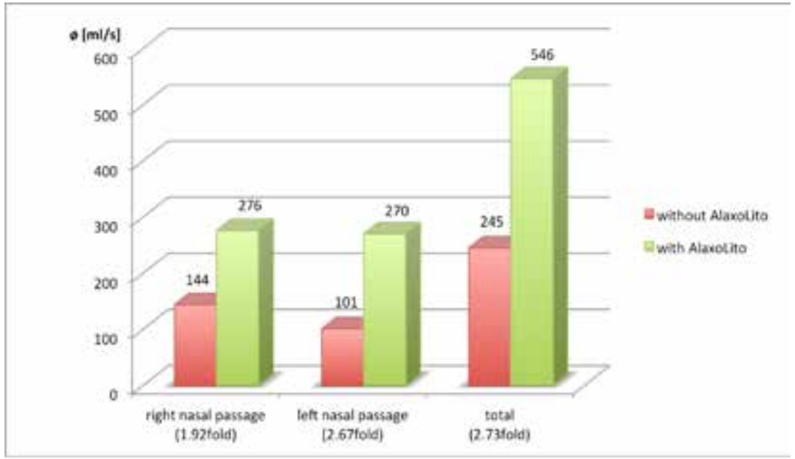
Stent in middle nasal passage



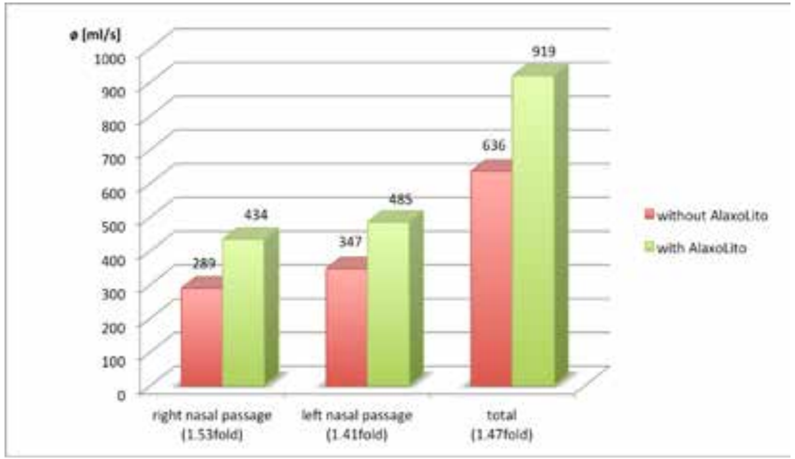


Mechanical Splinting Therapy

Nasal flow with AlaxoLito Nasal Stent



11 **patients** with decreased nasal breathing
plus >100%



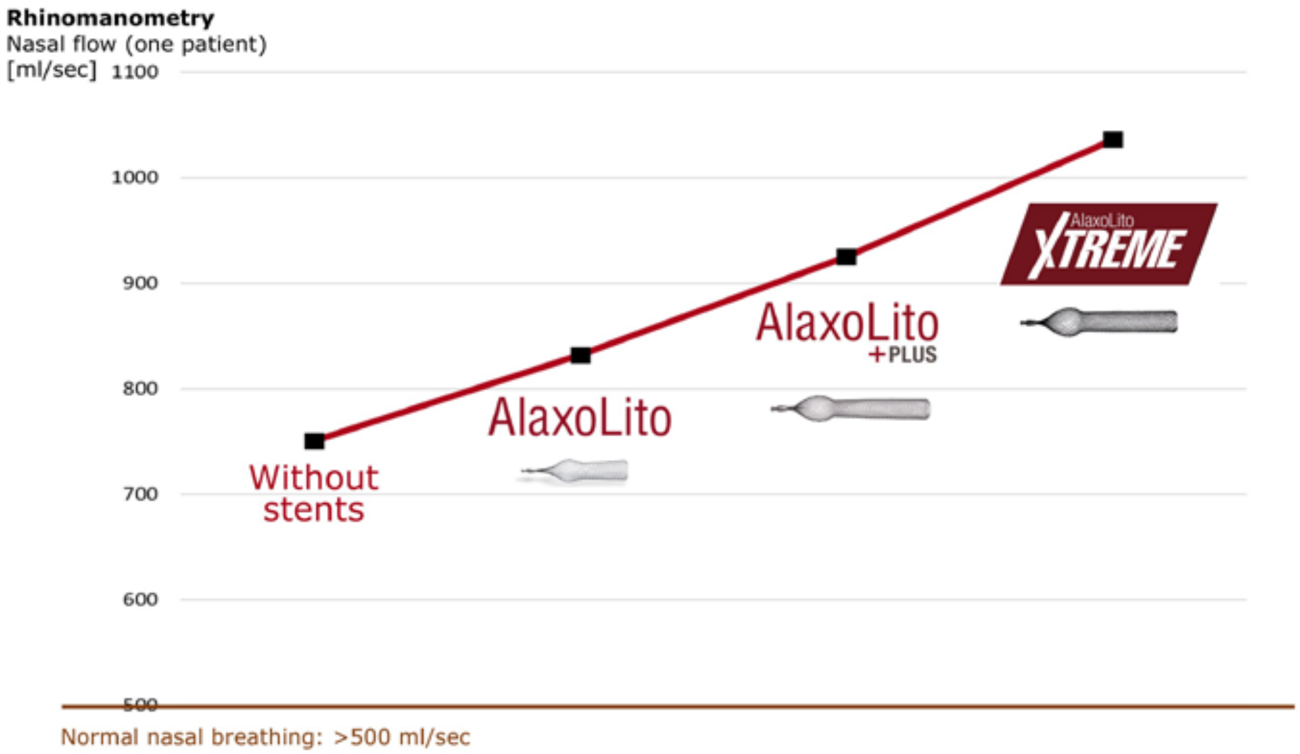
10 **healthy volunteers**
plus 50%

Rhinomanometry (Dr. Peter Renner, Cologne, Germany)

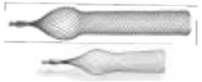
Normal nasal breathing: >500 ml/sec

Single Case Study Prof. Kotecha

Zhang and Kotecha (2019)



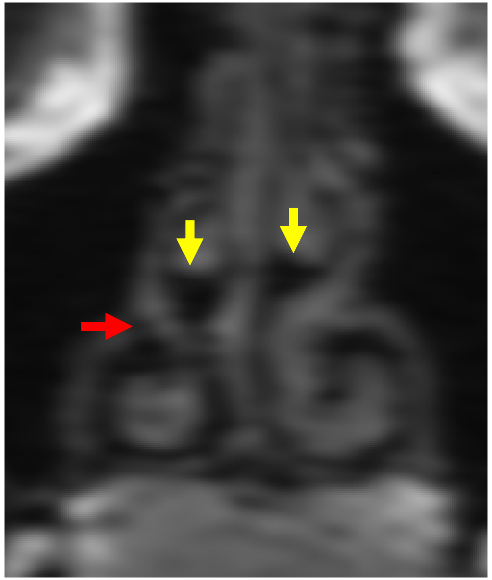
Single Case Study Prof. Kotecha



Zhang and Kotecha (2019)

Prior to use of
nasal stents

1 year use of
AlaxoLito Plus
Nasal Stent



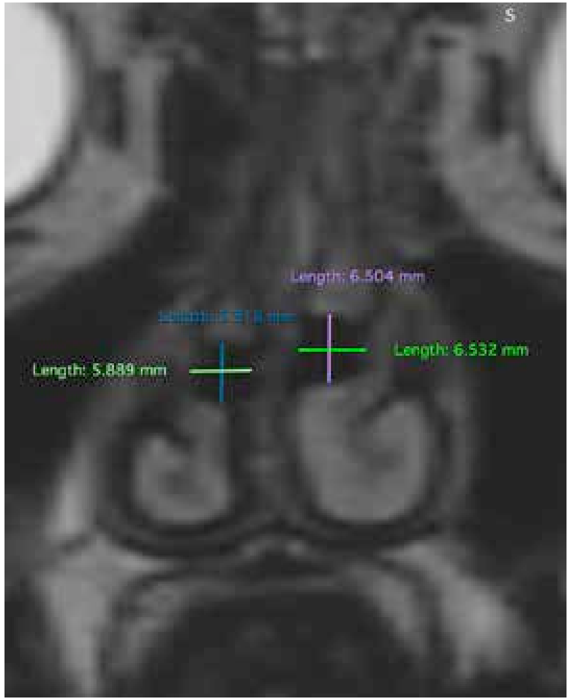
1 year use of
AlaxoLito Plus
Nasal Stent

Without nasal stents

With nasal stents

Single Case Study Prof. Kotecha

Zhang and Kotecha (2019)



With AlaxoLito Xtreme Nasal Stent

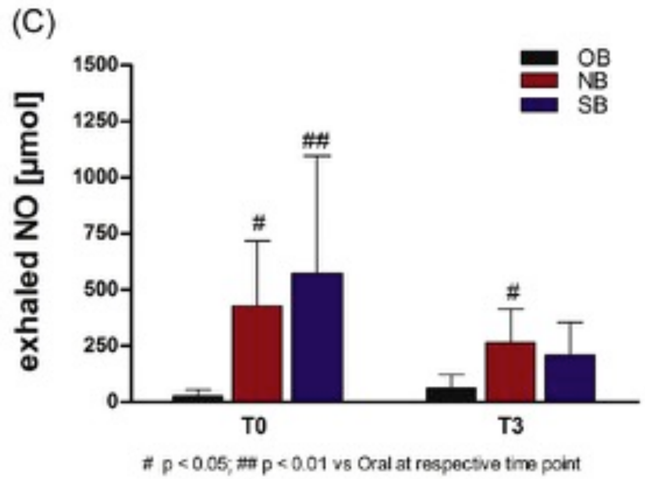
Clinical Study German Sport University Cologne

Clinical lead: Dr. Joachim Latsch

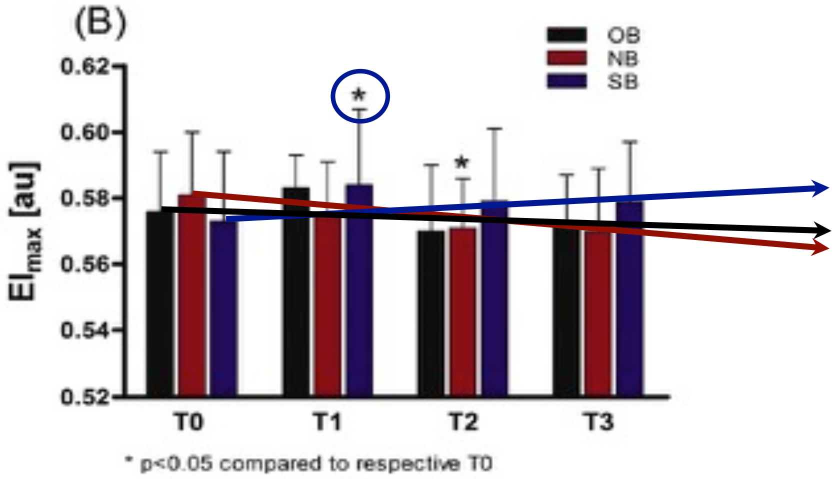
- With **AlaxoLito Plus Nasal Stent** in inferior nasal passage (2015)
- 13 volunteers, average trained sport students, selected for normal nasal anatomy
- **Comparison:**
  - oral breathing
  - nasal breathing
  - nasal breathing with stents
- **Prior to exercise → 3 steps of physical load → recovery phase**
- Randomised

Clinical Study German Sport University Cologne

Bizjak et al. (2019); AlaxoLito Plus Nasal Stent



Exhaled NO increasing with stents
T0: prior to exercise test
T3: after third level of physical load



RBC deformability increasing with stents
T0: prior to exercise test
T1: after first level of physical load
T2: after second level of physical load
T3: after third level of physical load

OB: oral breathing, NB: nasal breathing, SB: nasal breathing with stents

Clinical Study German Sport University Cologne

Schams (2016), Pyschny (2017), Lellau (2017), Bizjak et al. (2019)
AlaxoLito Plus Nasal Stent

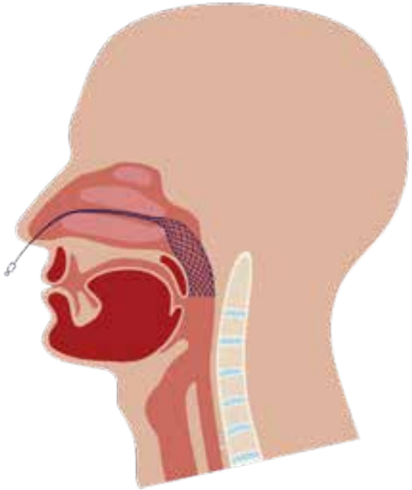
Selected results for stent-supported nasal breathing:

- Statistically significant **higher NO transport** from nose to lung, even at rest
- **Increased tidal volume**
- **Reduced breathing frequency**
- **Improved alveolar ventilation and lung perfusion** → optimized supply of O_2 + NO to the circulatory system and organs
- **Improved microcirculation** due to increased deformability of red blood cells
- **Increased parasympathetic activity**

Suggested for lung-compromised patients and to prevent exercise-induced asthma

Mechanical Splinting Therapy

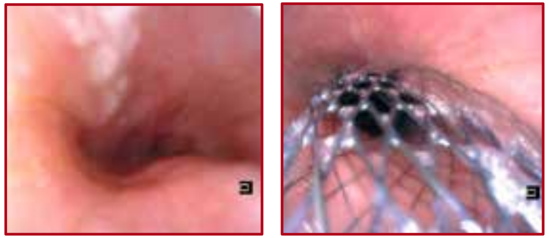
II. Velopharyngeal splinting with nitinol stents:



- Velopharyngeal obstructions in 3/4 of OSA patients *(Schellenberg et al. 2000; Hortscht 2009)*
- Prevention of suction phenomena (concentric collapse, antero-posterior collapse, etc.)
- Patency and constant cross section of velopharyngeal airway with stent (demonstrated by drug-induced sleep endoscopy) (*Powell et al. 2014*)
- Elimination of apneas with stent as efficient as with CPAP (*Traxdorf et al. 2016*)

Dr. János Juhász, Mainburg, Germany

Prof. Bhik Kotecha, RNTNE London, UK

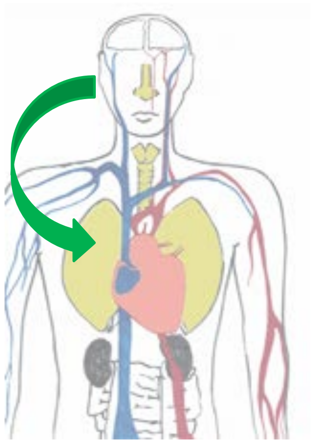


Mechanical Splinting Sleep Apnea Therapy

- **Nasal passage, nasal alar, nasal valve as root causes**
  - Relevance historically underestimated
  - In recent time increasingly recognized in scientific publications *(e.g. Poirrier 2013 , Passali et al. 2016)*
  - Pathological situations in the nose → unstable mouth breathing, reduced nasal-ventilatory reflexes, reduced NO concentration in the lung *(Poirrier 2013)*, oxidative stress *(Passali et al. 2016)*
- **Mechanical splinting of upper airway to restore natural nasal breathing**
  - Nasal passage (single case data AHI 37/h to 7/h)
  - Velopharynx (clinical studies plus several single case data AHI ~75/h to 5-10/h; strongest OSA patient AHI 101/h to 35/h)
  - Combination with mandibular advancement device possible
- **Combination of nasal stents with CPAP**
  - Prevents turbinate swelling → reduction of pressure [single case data -25%]
  - Prevention of nasal alar collapse caused by CPAP mask

Summary

- **Nasal breathing essential for physiology:**
  - NO transport from sinuses to lung
  - Supports maintenance of redox balance



- **Nasal fluid mechanics must be good to enable natural function of the nose:**
  - Frequently impaired → numerous diseases
  - Restoration of decreased and optimization of normal nasal breathing important
  - Laminar airflow in middle nasal passage and flow through entire cavity decisive
- Mechanical splinting of nasal passages and velopharynx with nitinol stents successful
- **Optimized NO flux from sinus to lung, circulatory system and organs essential to secure body health (to counteract numerous diseases)**

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