

TNI

Medical leaflet

Therapy with Nasal Insufflation

The unique nasal high flow therapy.



TNI *softFlow* 50



Your partner for respiratory support

Welcome

Dear TNI audience,

For ten years, TNI® medical AG has had one goal: to develop nasal high flow therapy in order to provide highly efficient and comfortable respiratory support to patients suffering from respiratory insufficiency.

We are committed to keeping you up to date with any information on Therapy with Nasal Insufflation (TNI) – the evolution of nasal high flow therapy – and the company behind this therapy: TNI® medical AG. In the following pages, we would like to give you an overview of TNI and the current technological and clinical knowledge. We would also like to invite you to regularly check our website www.tni-medical.com for current information on new TNI products, application recommendations as well as scientific publications and events.

Convince yourself of the efficiency, safety and comfort of TNI and get a genuine alternative to NIV for hospital and outpatient treatment of patients suffering from respiratory insufficiency. Set new standards – we will support you as a steadfast partner. Your patients will be grateful.

Best wishes,

A handwritten signature in black ink, appearing to read 'E. Anger', with a stylized, looping flourish at the end.

Ewald Anger, CEO



Contents

An overview	04
The Flow makes the difference	05
The outcomes	
Improved respiratory efficiency	06
Relief of the respiratory muscles	07
Lung protection	08
Better quality of life	09
Application: easy, secure, effective	10
Therapy air: humidification, application, monitoring	11
Study results on TNI	12
References	14

TNI

Therapy with Nasal Insufflation

An overview



A huge step in nasal high flow therapy.

TNI *softFlow 50* is the flagship of the TNI product family. It has been developed through intensive research and focussed development in Therapy with Nasal Insufflation (TNI).

The three pillars of TNI.

Due to the unique technology of the internal high flow generator, TNI *softFlow 50* generates a precisely regulated, stable high flow (TNI Flow) from room air or a mix of room air and oxygen. Controlled oxygen supply ensures oxygenation while, at the same time, the respiratory airways are humidified.

Convincing. The quality of life.

In practice, this therapy is more effective than conventional oxygen therapy and just as successful but much more comfortable than NIV (non-invasive ventilation). The use of a soft, comfortable and noise-optimized patient interface ensures recovering patients' quality of life. Being able to eat, drink and talk during therapy contributes significantly to higher patient compliance.

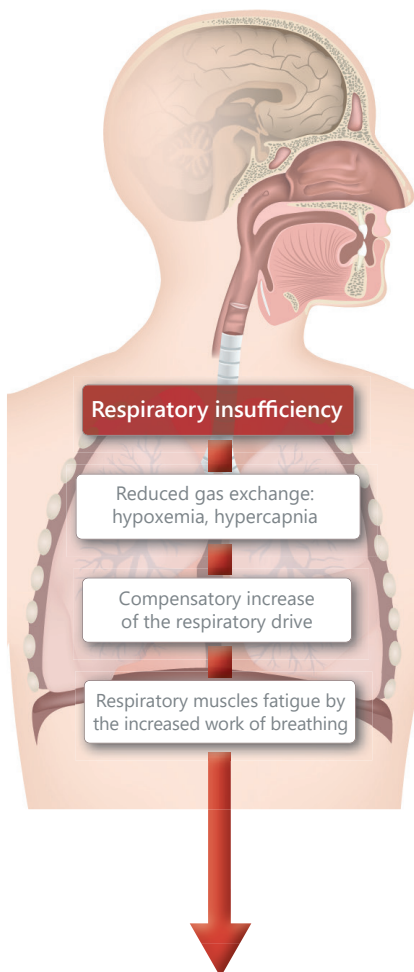
We can Flow.

A stable air flow is essential for treating hypoxemic and hypercapnic respiratory failure. Together with the TNI applicator (comprising respiratory circuit and patient interface), the TNI Flow generator guarantees a constant TNI Flow and in doing so, it is completely independent of external pneumatic systems. Due to this, the TNI *softFlow 50* is able to treat respiratory insufficiency and allows therapy at home as reliable and efficient as in the hospital.

Only TNI can be as effective as NIV in hospital and homecare treatment!

Nasal High Flow

The FLOW makes the difference



TNI Flow:

Stable high flow
Air / Mixture of air and O₂,
humidified and warmed

Consistent CO₂ washout:

- > from the anatomical dead space
- > from the small respiratory tracts

Steady O₂ supply:

- > stable FiO₂

PEEP*

Preventing end-expiratory collapse of alveoli

Recruiting further areas in the lungs

*positive end-expiratory pressure

Higher breathing efficiency:

- > pO₂ increases and pCO₂ decreases

Increase of tidal volume

Decrease of respiratory rate

Facilitated work of breathing

Relief of breathing muscles



Comfortable patient interface

TNI softFlow 50

Unique technology:
the internal high flow generator



Reduction of risk

Hypercapnic
respiratory failure

Mechanical ventilation

TNI

Therapy with Nasal Insufflation

Improved respiratory efficiency

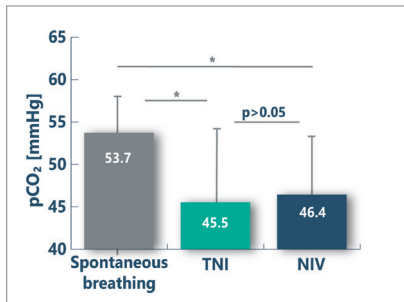


Fig. 1 pCO₂ levels of hypercapnic COPD patients during spontaneous breathing following TNI and NIV. * Significant p value. Source: Bräunlich et al., 2015a

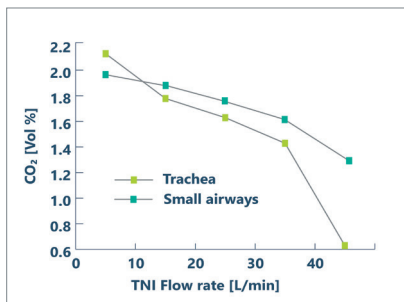


Fig. 2 CO₂ changes in the respiratory tract of a lung model proportionally to the TNI Flow rates. Source: Bräunlich et al., 2017

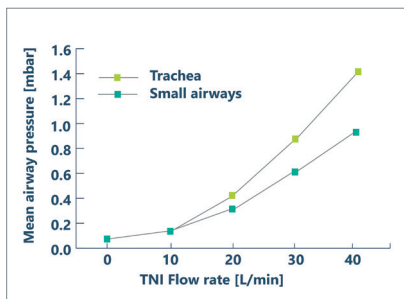


Fig. 3 Increase of mean airway pressure in the trachea and small airways proportionally to the TNI Flow rates. Source: Bräunlich et al., 2017

Reduction of hypercapnia

Studies with chronic hypercapnic COPD and IPF patients show that applying TNI for a short time reduces arterial pCO₂. At higher flow rates, pCO₂ decreases even further. A significant decrease in pCO₂ was noticed in stable hypercapnic COPD patients who were treated with TNI at home for several weeks. The normocapnic value remained stable during the following NIV treatment (Bräunlich et al., 2013a, 2015a, 2016; Fig.1).

➔ Mechanism: Washout effect

The washout effect is viewed as the central mechanism of pCO₂ reduction. Supplying a flow rate exceeding the inspiratory demand results in a constant washout of breathed air (rich in CO₂) out of the nasopharynx and the small airways. Of essential value is a stable air flow during inspiration and expiration. This is guaranteed by the technology of the TNI Flow generator in combination with the TNI applicator. CO₂ elimination increases with higher flow rates (Bräunlich et al., 2017, Fig. 2).

Efficient oxygenation

TNI efficiently treats chronic hypoxemic respiratory insufficiency without causing any side effects. This was confirmed during a clinical comparison with conventional O₂ therapy in stable O₂-dependent COPD patients. The application of TNI Flow alone (without adding O₂) already resulted in an improved oxygenation. A comparatively lower volume of O₂ had to be added to the therapy air to reach the same level of oxygenation as with pure O₂ therapy (Vogelsinger et al., 2013).

➔ Mechanism: constant FiO₂ + PEEP

The stable high TNI Flow guarantees continuous supply of therapy air with an FiO₂ value that is individually adjusted to the patient's deficit. It remains stable even during high breathing frequency. As the flow rate increases, a PEEP builds up: an expiratory alveolar collapse is avoided and otherwise insufficiently ventilated areas of the lung are recruited. As a consequence, the gas exchange improves (Bräunlich et al., 2016, 2017; Fig. 3; McGinley et al., 2007).

Relief of the respiratory muscles

Facilitated work of breathing

In patients suffering from chronic respiratory insufficiency, the respiratory muscles are constantly overloaded. During TNI, the desired effect of a respiratory therapy can be noticed: COPD patients were breathing slower and deeper; the respiratory minute ventilation decreased (Bräunlich et al., 2013a). The respiratory muscles were thus relieved, rested and were able to resume their ventilating function again.

In comparison to breathing room air or O₂, TNI facilitated work of breathing during sleep in COPD patients (Biselli et al., 2016; Fig. 4). Reaction due to an improved exchange of gas and a reduced sympathetic tone is discussed as mode of action. Sympathetic activity decreased in REM and Non-REM phases in COPD patients during TNI, but not during an O₂ therapy as shown in clinical studies (Schneider, DGP congress 2017, Symposium "Symposium „NHF: The better alternative?“).

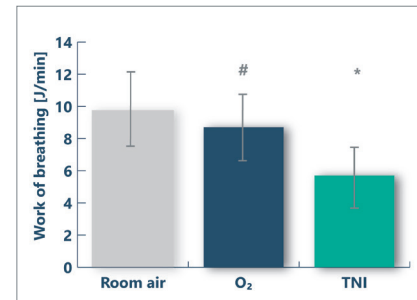


Fig. 4 Decrease of work of breathing in COPD patients during TNI, compared to room air and O₂ therapy during sleep. Significant p value # as compared to room air, * as compared to room air and oxygen. Source: Biselli et al., 2016

TNI ensures

- > pCO₂ ↓
- > pO₂ ↑
- > work of breathing ↓

Comments from the DGP congress 2017 // Symposium "NHF: The better alternative?"

Prof. H. Wirtz, Pneumology dept. , Uniklinikum Leipzig

"NIV is seen as standard therapy for hypercapnic respiratory insufficiency which, however, is not always tolerated by the patients. TNI is an alternative for these patients in particular: TNI supports ventilation - the task of the breathing pump - which counteracts parenchyma failure and improves the gas exchange. In addition, patients being treated with TNI save energy they would have to spend on conditioning the respiratory gas."

Prof. Kähler, Lungenzentr. Süd-West, Wangen im Allgäu

"NHF is not NHF - each system applies a different way of generating high flow. Thus, not all systems are equally suitable for hospital and homecare use.

Using NHF in weaning is promising with regard to the duration of stay in intensive care and the reintubation rate."

TNI

Therapy with Nasal Insufflation

Lung protection

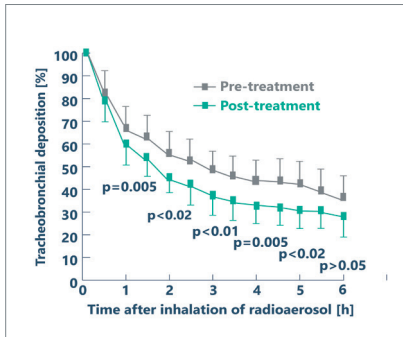


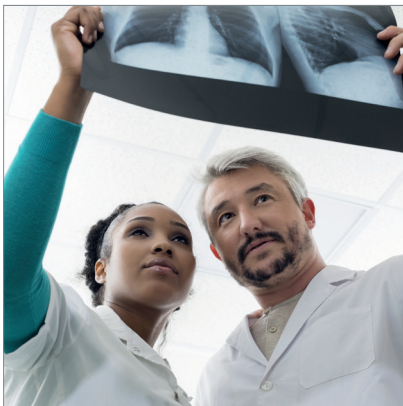
Fig. 5 Tracheobronchial deposition at baseline and following breathing gas humidification. Source: Hasani et al., 2008

Improved mucociliary clearance

It has been verified that an optimized breathing gas conditioning leads to an improved self-cleaning function of the ciliated epithelium, the mucociliary clearance. Mucus in the lung becomes more fluid facilitating removal and expectoration (Hasani et al., 2008, Fig. 5). The TNI humidification technology reliably provides warming and humidification of the therapy air, which is balanced with the physiological demand of the lungs. The TNI applicator is heated for its entire length to the nostrils, which guarantees that humidity remains stable without condensing in the patient circuit. Humidity reaches the patient's respiratory tract.

TNI ensures

- > no drying-out of the mucosa
- > improval of mucociliary clearance
 - mucus dissolution and removal
 - lower risk of respiratory infections



From practice

Prof. H. Schneider, Johns Hopkins University, Baltimore, USA
DGP congress 2017, Symposium "NHF: The better alternative?"

"Application fields of NHF include any conditions benefitting from an improved respiratory efficiency. This mainly relates to patients suffering from stable COPD, restrictive lung diseases such as ILD or pulmonary hypertension as well as neuromuscular disorders. Patients suffering from pneumonia, cystic fibrosis, bronchiectasis and asthma benefit from an improved mucociliary clearance and an increase in PEEP."

Better quality of life

Comfort

The TNI applicator's small, soft and noise-optimized nasal cannula was developed guaranteeing a comfortable feel without causing any pressure marks and skin irritation. It is suitable for use during sleep.

A key advantage of TNI is the fact that the patient can almost unrestrictedly eat, drink and talk during therapy.

Humidification of therapy air prevents side effects such as dry nasal and oral mucosa, which in turn significantly contributes to the therapy tolerance. The patient can regulate the therapy air temperature according to comfort.



In addition to the therapy efficiency, TNI's comfort further adds to the patients' compliance.

Efficiency of therapy + comfort = better quality of life

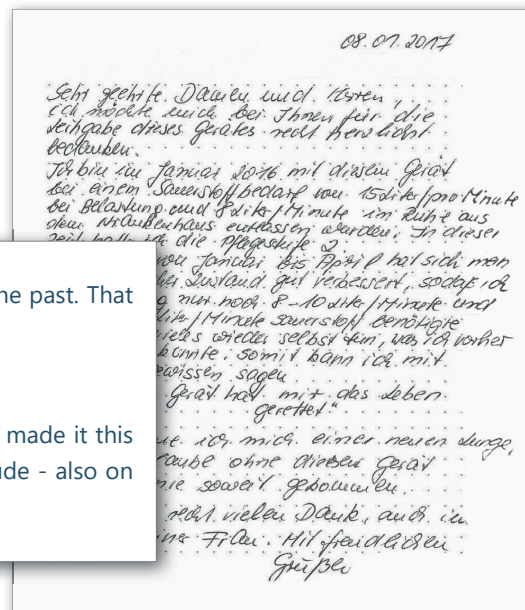
Patient letter

We are very grateful for receiving such a feedback from our patients.

"... I was able to do so many things I could not even think to do in the past. That is why I can say:

This device saved my life!

Now, I am very happy with my new lung and I think I wouldn't have made it this far without this device. I would like to once again express my gratitude - also on behalf of my wife ..."



TNI

Therapy with Nasal Insufflation

Application: easy, secure, effective

In which patients can TNI *softFlow 50* be used?

For treating respiratory insufficiency type I and II in patients suffering from

- > COPD (chronic obstructive pulmonary disease)
- > ILD (interstitial lung disease)



The three pillars of efficient TNI

TNI Flow

The flow rate can be accurately determined, according to the patient's individual ventilation demand.

In combination with the TNI applicator, the TNI Flow generator guarantees a stable air flow during inspiration and expiration independent of the environment and pneumatic systems.

- > flow volume: 10–50 l/min
- > increments of 0.5 l/min



The flow rate should be significantly higher than the inspiratory demand. CO₂ elimination increases by raising the flow rate.



Applicator sizes cover different flow rates. The higher CO₂ washout required, the larger the applicator size needed.

Oxygen

O₂ addition can be titrated according to the patient's O₂ deficit.

- > supply from any external O₂ source
- > up to 20 l/min



Oxygenation remains efficient if the oxygen supply is simultaneously increased with the flow rates.

Humidification

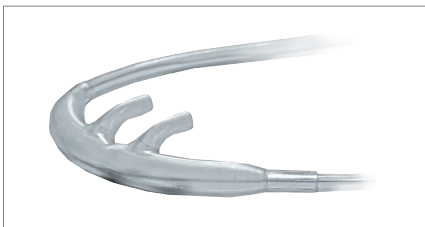
The level of humidification and the temperature of therapy air can be adjusted by the patient according to comfort.

- > dew point: 30–37°C DP
- > increments of 1°C DP



34–37°C DP is recommended for optimal humidification of the respiratory tract.

Therapy air: humidification, application, monitoring



Humidification of therapy air in hospital / homecare environment

Hospital humidifier

- > quick transfer between patients due to use of disposable components
- > respiratory infection control guaranteed by bacterial filter



Easy conversion from hospital to homecare mode:
immediate continuation of efficient TNI for the patient at home.

Homecare humidifier

- > easy handling when filling with drinking water
- > stable construction

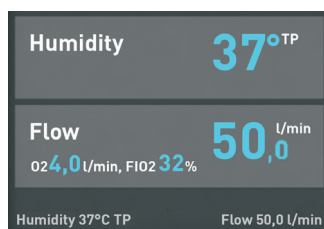
Therapy air supply

- > comfortable, soft silicone patient interface
- > noise-optimized
- > different sizes for customised therapy
- > heating up to the prongs prevents condensation
- > automatic applicator type recognition

Monitoring

The display provides information on

- > current humidification and nominal value
- > current flow rate and nominal value
- > O₂ flow rate
- > therapy air FiO₂





2017

"TNI causes an effective CO₂ washout in the small respiratory tracts."

Bräunlich, J., Goldner, F. & Wirtz, H. Nasal highflow eliminates CO₂ from lower airways. Respir. Physiol. Neurobiol. 242, 86–88

2016

"As compared to O₂ therapy, TNI results in a significant reduction of work of breathing and respiratory minute ventilation as well as in a reduction of CO₂ levels, if applied during sleep in patients suffering from chronic COPD."

Biselli, P.J.C. et al. Nasal High Flow therapy reduces work of breathing compared to oxygen during sleep in COPD and smoking controls – prospective observational study. J. Appl. Physiol. jap.00279

"TNI increases the breathing efficiency in COPD patients facilitating the work of breathing and decreases pCO₂ proportionally to the flow rate."

Bräunlich, J., Köhler, M. & Wirtz, H. Nasal highflow improves ventilation in patients with COPD. nt. J. Chron. Obstruct. Pulmon. Dis. 11

"Constant FiO₂ of TNI guarantees an effective oxygenation."

Bräunlich, J., and Wirtz, H. Nasaler Highflow: Oxygenierungsverhalten unter verschiedenen Flowstufen. Pneumologie 70, P13

2015

"In patients suffering from stable hypercapnic COPD, TNI reduces the pCO₂-value."

Bräunlich, J., Seyfarth, H.-J. & Wirtz, H. Nasal High-flow versus non-invasive ventilation in stable hypercapnic COPD: a preliminary report. Multidiscip. Respir. Med. 10

"The CO₂ washout effect increases proportionally to the increase of flow rate."

Bräunlich, J., Goldner, F. & Wirtz, H. Nasaler Highflow (NHF) – Quantifizierung des CO₂-Auswascheffektes in einem Lungenmodell. Pneumologie 69

"In combination of NHF and O₂ in TNI improves oxygenation (SpO₂), reduces the breathing rate and alleviates signs of dyspnoea in patients with chronic lung diseases."

Bräunlich, J., Goldner, F. & Wirtz, H. Nasaler Highflow (NHF) – Konkurrenz für die Sauerstofftherapie? Pneumologie 69

! Please find more information on the studies
● at www.tni-medical.com





2013

"In COPD patients, tidal volumes increase due to TNI. Work of breathing is facilitated in patients suffering from obstructive or restrictive lung diseases."

Bräunlich, J. et al. Effects of nasal high flow on ventilation in volunteers, COPD and idiopathic pulmonary fibrosis patients. Respiration 85

"TNI lowers minute ventilation and breathing frequency while simultaneously increasing the tidal volume. The washout effect seems to be the key mechanism for the decrease in $p\text{CO}_2$."

Bräunlich, J., Köhler, M. & Wirtz, H. Nasaler High-Flow: Ist es ein wash-out-Effekt? Pneumologie 67

"TNI is a secure and efficient therapy procedure allowing oxygenation and reducing hypercapnia in COPD patients. TNI is superior to the classic O_2 therapy and improves oxygenation merely through nasal high flow."

Vogelsinger, H. et al. Highflow-Sauerstofftherapie bei hyperkapnischen COPD-Patienten: optimiertes Sauerstoffangebot – Daten aus der STIT-2-Studie. Pneumologie 67

"As compared to O_2 therapy, TNI alleviates nocturnal hypoventilation in COPD patients suffering from severe hypercapnic respiratory insufficiency."

Nilius, G. Nasal High Flow Oxygen Therapy Attenuates Nocturnal Hypoventilation In COPD Patients With Hypercapnic Respiratory Failure: B55. NON-INVASIVE VENTILATION. ATS 2013

2012

"Indices of sleep-related respiratory disorders improve during TNI."

Haba-Rubio, J. et al. Effect of transnasal insufflation on sleep disordered breathing in acute stroke: a preliminary study. Sleep Breath. Schlaf Atm. 16

"TNI does not negatively effect the cardiac performance and frequency, the stroke volume neither the mean arterial pressure and is thus a suitable alternative to CPAP for patients suffering from heart diseases."

Tiffin and Connelly. Differences in Hemodynamic Effects between CPAP and High Flow Therapy. RTSO Airwaves Fall

"Compared to CPAP, TNI does not raise the sympathetic tone."

Tiffin and Connelly. Differences in Neurophysiologic Effects between CPAP and High Flow Therapy. RTSO Airwaves Fall

2011

"In hypoxic patients, TNI is as effective as O_2 therapy during physical exertion. With regard to performance, energy and ventilation efficiency, TNI is superior."

Juhász. Comparison of two different O_2 -delivery systems during exercise in patients with chronic hypoxia. The European respiratory journal

2010

"Obstructive hypopnea can efficiently be treated with TNI."

Nilius, G. et al. Predictors for Treating Obstructive Sleep Apnea With an Open Nasal Cannula System (Transnasal Insufflation). Chest 137

2009

"Moderate to serious sleep apnea in children can efficiently be treated with TNI."

McGinley, B. et al. Effect of a high-flow open nasal cannula system on obstructive sleep apnea in children. Pediatrics 124



References

- Biselli, P.J.C., Kirkness, J.P., Grote, L., Fricke, K., Schwartz, A.R., Smith, P.L., and Schneider, H. (2016). Nasal High Flow therapy reduces work of breathing compared to oxygen during sleep in COPD and smoking controls - prospective observational study. *J. Appl. Physiol.* 120, 00279.2016.
- Bräunlich, J., and Wirtz, H. (2016). Nasaler Highflow: Oxygenierungsverhalten unter verschiedenen Flowstufen. *Pneumologie* 70, P13.
- Bräunlich, J., Beyer, D., Mai, D., Hammerschmidt, S., Seyfarth, H.J., and Wirtz, H. (2013a). Effects of nasal high flow on ventilation in volunteers, COPD and idiopathic pulmonary fibrosis patients. *Respiration* 85.
- Bräunlich, J., Köhler, M., and Wirtz, H. (2013b). Nasaler High-Flow: Ist es ein wash-out-Effekt? *Pneumologie* 67, P21.
- Bräunlich, J., Seyfarth, H.-J., and Wirtz, H. (2015a). Nasal High-flow versus non-invasive ventilation in stable hypercapnic COPD: a preliminary report. *Multidiscip. Respir. Med.* 10, 27.
- Bräunlich, J., Goldner, F., and Wirtz, H. (2015b). Nasaler Highflow (NHF) – Quantifizierung des CO₂ – Auswascheffektes in einem Lungenmodell. *Pneumologie* 69, V427.
- Bräunlich, J., Goldner, F., and Wirtz, H. (2015c). Nasaler Highflow (NHF) – Konkurrenz für die Sauerstofftherapie? *Pneumologie* 69, P432.
- Bräunlich, J., Köhler, M., and Wirtz, H. (2016). Nasal highflow improves ventilation in patients with COPD. *Int. J. Chron. Obstruct. Pulmon. Dis.* 11, 1077–1085.
- Bräunlich, J., Goldner, F., and Wirtz, H. (2017). Nasal highflow eliminates CO₂ from lower airways. *Respir. Physiol. Neurobiol.* 242, 86–88.
- Haba-Rubio, J., Andries, D., Rey, V., Michel, P., Tafti, M., and Heinzer, R. (2012). Effect of transnasal insufflation on sleep disordered breathing in acute stroke: a preliminary study. *Sleep Breath. Schlaf Atm.* 16, 759–764.
- Hasani, A., Chapman, T., McCool, D., Smith, R., Dilworth, J., and Agnew, J. (2008). Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. *Chron. Respir. Dis.* 5, 81–86.
- Juhász (2011). Comparison of two different O₂ -delivery systems during exercise in patients with chronic hypoxia. (*The European respiratory journal*), p. 387.
- McGinley, B., Halbower, A., Schwartz, A.R., Smith, P.L., Patil, S.P., and Schneider, H. (2009). Effect of a high-flow open nasal cannula system on obstructive sleep apnea in children. *Pediatrics* 124, 179–188.
- McGinley, B.M., Patil, S.P., Kirkness, J.P., Smith, P.L., Schwartz, A.R., and Schneider, H. (2007). A Nasal Cannula Can Be Used to Treat Obstructive Sleep Apnea. *Am. J. Respir. Crit. Care Med.* 176, 194–200.
- Nilius, G. Nasal High Flow Oxygen Therapy Attenuates Nocturnal Hypoventilation In COPD Patients With Hypercapnic Respiratory Failure : B55. NON-INVASIVE VENTILATION.
- Nilius, G., Wessendorf, T., Maurer, J., Stoohs, R., Patil, S.P., Schubert, N., and Schneider, H. (2010). Predictors for treating obstructive sleep apnea with an open nasal cannula system (transnasal insufflation). *Chest* 137, 521–528.
- Tiffin, N.H., and Connelly, S.F. Tiffin and Connelly, RTSO Airwaves 2012_ Hemodynamics
- Tiffin, N.H., and Connelly, S.F. Tiffin and Connelly, RTSO Airwaves 2012_ Neurophysiology
- Vogelsinger, H., Halank, M., Wilkens, H., Geiser, T., Braun, S., Plattner, L., Janschek, E., Ott, S., Stucki, A., and Kaehler, C.M. (2013). Highflow-Sauerstofftherapie bei hyperkapnischen COPD-Patienten: optimiertes Sauerstoffangebot – Daten aus der STIT-2-Studie. *Pneumologie* 67, P40.

TNIFlow Makes The Difference





Your partner for respiratory support

TNI medical AG • Hofmannstraße 8 • 97084 Würzburg
Phone +49 931 20 79 29 02 • Fax +49 931 20 79 29 18
info@tni-medical.de • www.tni-medical.com

Medical leaflet art. no. 30220081 V2.0