ERJ Express. Published on January 31, 2019 as doi: 10.1183/13993003.02339-2018

EUROPEAN RESPIRATORY *journal*

FLAGSHIP SCIENTIFIC JOURNAL OF ERS

Early View

Original article

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Please cite this article as: Hui DS, Chow BK, Lo T, *et al*. Exhaled air dispersion during high flow nasal cannula therapy *versus* CPAP *via* different masks. *Eur Respir J* 2019; in press (https://doi.org/10.1183/13993003.02339-2018).

Exhaled air dispersion during high flow nasal cannula therapy versus CPAP via different masks

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Running title: Exhaled air dispersion from HFNC vs CPAP

Contributor: DH, BC and MC collaborated on study design, data acquisition and interpretation and writing up of the manuscript; BC performed data analysis. TL, OT, FK, DN and TC provided technical support to this study. DH is the guarantor of the content of the manuscript. All authors have read and approved the manuscript for submission.

Funding source: HMRF#15140282, Food & Health Bureau, HKSAR. The sponsor approved the study design but played no role in development of the research and manuscript

This article has an online data supplement.

Question: High flow nasal cannula (HFNC) is an emerging therapy for respiratory failure but the extent of exhaled air dispersion during treatment is unknown. We examined exhaled air dispersion during HFNC therapy versus CPAP on a human patient simulator (HPS) in an isolation room with 16 air changes/hr.

Methods: HPS was programmed to represent different severity of lung injury. CPAP was delivered at 5-20 cmH_2O via nasal pillows (Respironics Gel or ResMed Swift FX) or oronasal mask (Quattro, ResMed). HFNC, humidified to 37℃, was delivered at 10-60 L/min to the HPS. Exhaled airflow was marked with intrapulmonary smoke for visualization and revealed by laser light-sheet. Normalized exhaled air concentration was estimated from the light scattered by the smoke particles. Significant exposure was defined when there was ≥20% normalized smoke concentration.

Results [mean(SD)]: In normal lung condition, exhaled air dispersion, along the sagittal plane, increased from 186 (34) to 264 (27) mm and from 207(11) to 332 (34) mm when CPAP was increased from 5 to 20 cmH_2O via Respironics and ResMed nasal pillows, respectively. Leakage from the oronasal mask was negligible. Exhaled air distances increased from 65 (15) to 172 (33) mm when HFNC was increased from 10 to 60 L/min. Air leakage to 620 mm occurred laterally when HFNC and the interface tube became loose.

Conclusion: Exhaled air dispersion during HFNC therapy and CPAP via different interfaces is limited provided there is good mask interface fitting.

Key words: exhaled air, HFNC, CPAP, infection control

Take home message:

Exhaled air dispersion from high flow nasal cannula (HFNC) and CPAP is limited provided there is good mask interface fitting. However, exhaled air leakage to 620 mm laterally occurs when the connection between HFNC and the interface tube becomes loose.

Introduction

Severe acute respiratory tract infections (SARI) such as severe acute respiratory syndrome corononavirus (SARS-CoV) infection,[1] Middle East respiratory syndrome CoV (MERS-CoV) infection,[2] and avian influenza A(H7N9) and A(H5N1) may lead to respiratory failure with high case fatality rates.[3-5] Oxygen therapy via conventional nasal cannula or facemasks is important for managing respiratory failure during the early phase while non-invasive ventilation (NIV) or invasive mechancal ventilation (IMV) is required for the more severe cases.[1-6] However, these procedures may generate respiratory droplets,[7-9] and have led to nosocomial outbreaks of SARS.[10,11] A systematic review has identified tracheotomy, tracheal intubation, maunal ventilation, and NIV as risk factors for nosocomial transmission of SARS-CoV to HCWs.[10] Another study has shown that performance of resuscitation, bed separation distance < 1 m, staff members working despite having symptoms, NIV, and oxygen therapy ≥6 L/min were independent risk factors associated with super-spreading events of SARS-CoV infection.[11] Some of these risk factors were implicated in the nosocomial outbreaks of MERS-CoV infection.[12]

In recent years, high-flow nasal cannula (HFNC) therapy has emerged as a therapeutic modality for acute hypoxemic respiratory failure.[13] HFNC delivers heated humidified oxygen through short nasal prongs and supplies much higher flow rates than traditional nasal cannula systems.[13,14] The higher flow rate matches the patient's demand, reduces anatomic dead space by decreasing the extent of rebreathing, and provides a positive pressure in the upper airway.[15] In patients with acute hypoxemic respiratory failure, HFNC reduced inspiratory effort, and improved oxygenation and dynamic compliance.[16] HFNC reduced carbon dioxide tension in patients with stable hypercapnic chronic obstructive pulmonary disease (COPD) and the effect was flow

and leakage dependent through airway washout and reduction of functional dead space.[17] In patients with COPD recovering from an episode of acute hypercapnic respiratory failure of various etiologies, HFNC significantly decreased the neuro-ventilatory drive and work of breathing in comparisons to conventional oxygen therapy after tracheal extubation.[18] Likewise, CPAP has been widely applied for treating hypoxemia due to acute pulmonary oedema and prevention of atelectasis following abdominal surgery.[19]

Although patients with SARI requiring respiratory support should preferably be managed in negative pressure isolation rooms for infection control purpose, patients with early respiratory distress are increasingly being treated with HFNC or CPAP in the intensive care unit, general ward, and emergency room.[20] From the infection control point of view, it is important to understand the exhaled air dispersion distance and direction during application of HFNC and CPAP at different air flow rates, as operation of these respiratory therapies at high flow rates may potentially generate a large amount of aerosols. Unusual presentations of MERS-CoV infection in patients with renal or cardiac failure have been missed leading to a major nosocomial outbreak,[21] and the use of respiratory therapy may increase the risk of nosocomial transmission.[12] Such information would provide useful guidance for preventing nosocomial outbreaks when applying these treatment modalities in patients with respiratory failure due to SARI.

Methods

This study examined the exhaled air dispersion and directions in a hospital isolation room with a dimension of 4.1×5.1×2.6m, negative pressure of -7.4 Pa and 16 air changes/hour (ACH) during (a) application of HFNC (Airvo 2, Fisher & Paykel,

Auckland, New Zealand) on a high-fidelity human patient simulator (HPS 6.1, Medical Education Technologies Inc, Sarasota, FL) at different oxygen flow rates (10-60 L/min) and (b) application of CPAP (5-20 cmH_2O) via two nasal pillows (Nuance Pro Gel, Respironics and Swift FX, ResMed) or an orofacial mask (Quattro Air, ResMed) on the HPS (Figure 1).

Our research group has published a series of field infection control experiments using the HPS to quantitatively display exhaled air dispersion (with smoke particles as marker) using a well-established laser smoke visualization technique during application of common respiratory therapies on the medical ward and in the hospital isolation rooms with negative pressure created by downward ventilation and floor-level exhausts.[22-30]

The HPS contains a realistic airway and a lung model that has been applied in our previous studies to simulate human respiration.[22-30] The HPS represents a 70-kg adult male sitting on a 45^{o}-inclined hospital bed. It can be programmed to breathe spontaneously to mimic different severity of lung injury by adjusting the oxygen consumption and lung compliance (Table 1).

Table 1. Three different lung settings of the human patient simulator (HPS) applied in this study.[22-30]

Settings	Normal lung condition	Mild lung injury	Severe lung injury
Oxygen consumption (ml/min)	200	300	500
Lung compliance (ml/cmH_2O)	70	35	10
*Respiratory rate (breaths/min)	12	25	40
*Tidal volume (ml)	700	300	150

*The respiratory rate and tidal volume were adjusted by the HPS to achieve primarily the target oxygen consumption and lung compliance.

Exhaled air dispersion distances from the HPS during application of HFNC at 10, 30 and 60 L/min of oxygen humidified to 37°C were captured using the established laser smoke visualization method.[22-30] Exhaled air dispersion during application of CPAP at 5, 10, 15 and 20 cmH_2O on the HPS via Quattro Air oronasal mask and nasal pillows was captured using the same method.

Flow visualization

Visualization of airflow around the HPS was facilitated by marking air with smoke particles produced by a M-6000 smoke generator (N19, DS Electronics, Sydney, Australia) as previously described.[22-30] The oil-based smoke particles, measuring < 1μm in diameter, are known to follow the airflow pattern with negligible slip.[31] The smoke was introduced to the right main bronchus of the HPS. It mixed with alveolar gas, and then exhaled through the airway. Sections through the leakage jet plume are then revealed by a thin laser light-sheet (Green, 532 nm wavelength,

Continuous-Wave mode) generated by a diode-pumped solid state laser (OEM UGH-800mW, Lambdapro Technologies, China), with custom cylindrical optics.[22-30]

Image analysis

As the smoke particles marked exhaled air that came out from the lower airways of the HPS before leaking from the mask, the concentration contours effectively represented the probability of encountering air around the patient that had come from within the mask and/or the patient's respiratory system. A contour value of 1 indicated a region that consisted entirely of air exhaled by the patient, where there was a very high chance of exposure to the exhaled air. A value near 0 indicated no measurable and a small chance of exposure to the exhaled air in the region. Significant exposure was arbitrarily defined as where there was ≥20% of normalized smoke concentration.[22-30] More technical details of image analysis and extraction are provided in the online supplemental file.

Statistical analysis: The dispersion distances were expressed as mean (±standard deviation). A generalized linear model was used to estimate the difference in exhaled air dispersion after application of HFNC adjusting for airflow rates and extent of lung injury (normal vs mild or severe). A similar model was created for studying exhaled air dispersion with CPAP therapy, adjusted for CPAP applied, severity of lung injury and type of mask. A p value < 0.05 would be considered as statistically significant. The study received non-ionizing radiation safety approval (N/DSCH/HMRF2015) by the Chinese University of Hong Kong.

Results:

Results are presented with reference to the median sagittal plane as mean (SD).

A) HFNC

When the HPS was programmed in normal lung condition and humidified air was delivered to the HPS, the exhaled air dispersion distances from HFNC along the sagittal plane above the nostrils increased significantly with increasing flow rate to a maximum of 172 (33) mm, $p<0.001$ (Figure 2a; table 2). With worsening severity of lung injury, the exhaled air distances from the HPS decreased significantly, $p<0.001$. An interaction term of severity of lung injury × flow rates affected exhaled air dispersion significantly, $p<0.001$.

Table 2. Exhaled air dispersion with normalized smoke concentration of 20% [mean (SD), in mm] during application of HFNC at 37°C under different severity of lung injury

Scenario	Lung Condition/Injury	Setting	Exhaled Air Dispersion Distance
1	Normal	60 L/min	172 (33)
2	Moderate	60 L/min	72 (18)
3	Severe	60 L/min	48 (16)
4	Normal	30 L/min	130 (11)
5	Moderate	30 L/min	61 (17)
6	Severe	30 L/min	37 (12)
7	Normal	10 L/min	65 (15)
8	Moderate	10 L/min	43 (10)
9	Severe	10 L/min	30 (8)

There was negligible lateral dispersion of exhaled air when the nasal cannula was tightly connected to the tubing. However, exhaled air dispersion extended to 620 mm laterally with a loose connection between the cannula and the interface tube when HFNC at 60 L/min was delivered to the HPS programmed in normal lung function (Figure 2b).

B) **CPAP**

a) Quattro Air Mask

There was no significant leakage from the Quattro Air mask when CPAP was applied at 5, 10, 15 or 20 cmH_2O. Exhaled air dispersed evenly via the vent holes located circularly around the elbow connection point in all directions in very low normalized concentration of smokes <20%. Thus there was no distinct exhaled air dispersion that could be measured (see supplemental figures 2a and 2b in the online supplement).

b) Nasal pillows

Figures 3a-c show the exhaled air dispersion from the Respironics Nuance Pro Gel and ResMed Swift FX nasal pillows at varying severity of lung injury. There was significant increase in exhaled air dispersion distance in both nasal pillows with increasing CPAP, $p<0.001$. Worsening severity of lung injury also reduced dispersion, $p<0.001$, There was however no difference in exhaled air dispersion between the two types of nasal pillows ($p=0.095$). An interaction term of severity of lung injury ×

CPAP affected exhaled air dispersion significantly, $p<0.001$ (Table 3, supplementary figures 3a and 3b in the online supplement).

Table 3. Exhaled air dispersion (20% normalized concentration of smokes in mm) during application of CPAP via Respironics and ResMed nasal pillows in different severity of lung injury

CPAP	Lung condition/injury	Respironics Nuance Pro Gel	ResMed Swift FX
20 cmH_2O	Normal	264 (27)	332 (34)
	Mild	245 (26)	300 (31)
	Severe	217 (21)	225 (22)
15 cmH_2O	Normal	253 (30)	230 (35)
	Mild	233 (29)	208 (24)
	Severe	193 (21)	195 (26)
10 cmH_2O	Normal	241 (30)	214 (32)
	Mild	211 (32)	181 (20)
	Severe	164 (26)	161 (24)
5 cmH_2O	Normal	186 (34)	207 (40)
	Mild	170 (30)	156 (16)
	Severe	148 (14)	149 (14)

Discussion:

This infection control study has demonstrated that exhaled air dispersion up to 172 (33) mm along the sagittal plane via HFNC at 60 L/min. When CPAP was increased from 5 to 20 cmH_2O via the Respironics gel nasal pillows or ResMed Swift FX nasal pillows, similar leakage distances can be detected up to 264 and 332 mm, respectively. As the severity of lung injury worsened, the exhaled air dispersion distances became

shorter for both HFNC and CPAP via nasal cannula. In contrast, when CPAP was increased up to 20 cmH_2O via the Quattro Air mask, there was no significant leakage, irrespective of the severity of lung injury.

Our findings are consistent with a study recently reported by our intensivists assessing the extent of environmental contamination in critically ill patients receiving HFNC or oxygen via a simple oxygen mask for gram-negative bacterial (GNB) pneumonia. Regardless of treatment modalities, GNB could hardly be detected in the air samples or settle plates located at 0.4 and 1.5 m from the patients managed in single isolation rooms with 6 or 12 ACH. These results suggested that HFNC did not enhance airborne and surface contamination.[32]

Our data show that HFNC did not increase spread of exhaled air despite operating at higher flow rates, likely due to the fact that positive end expiratory pressure (PEEP) remained small at 60 L/min. Interestingly, there was comparable spread (186-207 mm) when CPAP was applied at 5 cmH_2O to the HPS via the Respironics and ResMed nasal pillows respectively. CPAP via nasal pillows produced larger PEEP and hence exhaled air was dispersed further away. In the same isolation room setting, we have previously demonstrated that an exhalation jet spread almost horizontally outward from the nostrils of the HPS to 0.66 m and 1m towards the end of bed along the sagittal plane when oxygen flow via the conventional nasal cannula was increased

from 1 to 5 L/min respectively.[24] The longer exhaled air dispersion distance from the conventional low flow nasal cannula versus that from HFNC is likely due to the fact that the former was loosely applied on the nostrils, while HFNC and CPAP delivered via nasal route were tightly "fitted and strapped" to the face. In addition, air humidification at 37°C for HFNC therapy would generate larger droplets on exhalation with a shorter trajectory path due to gravity effect. These results are reassuring for the use of HFNC in the high dependency unit or medical ward despite much higher flow rates. Nevertheless, it is important to ensure a tight and proper connection at the nasal cannula and tubing interface as otherwise sideway dispersion to 620 mm may occur, although this is well within the respiratory droplet distance of up to 1.8 m.[33]

The WHO guideline for infection prevention and control of epidemic and pandemic prone acute respiratory infections in the healthcare setting has recommended droplet precautions (keeping a patient spatial separation distance of at least 1 m in an adequately ventilated ward if a single room is not available and HCW should wear a surgical mask with eye protection within 2 m from the patient) and contact precautions (HCWs should maintain good hand hygiene and wear gloves and gowns, in addition to cleaning and disinfection of surfaces and equipment in patient care environment). However, if the disease is caused by airborne pathogens such as

tuberculosis or a novel pathogen with unknown route of transmission, then airborne precautions such as wearing N95 masks and a negative pressure isolation room should be implemented.[34] These principles are applicable to the use of HFNC for patients with respiratory failure due to infective aetiology.

The Quattro Air full face mask is different from other NIV face masks with respect to the design of exhaust ventilation.[26,28] There are circular vent holes, evenly distributed circularly around the elbow connection point of the air tubing, which allow continuous flow of air out of the mask (supplemental figure 2b). Thus there was no distinct exhaled air jet of significant normalized concentration that could be measured during application of CPAP at different pressures via a single circuit on the HPS. In contrast, application of NIV via a single circuit and other face masks with an exhalation port such as Mirage (ResMed),[26] Comfortfull 2 and Image 3 (Respironics) could lead to more widespread exhaled air leakage to 500, 800 and 950 mm, respectively,[28] especially at higher inspiratory pressures and in connection with the whisper swivel device.[28] From the infection control and prevention point of view, another safe way of applying NIV is through a helmet with a good seal at the neck interface via a double circuit.[29] Among patients with ARDS, a single center randomized trial has shown that treatment with helmet NIV resulted in a significant reduction of intubation rates with reduction in 90-day mortality versus NIV via face

mask.[35] Although there is lack of data to recommend the use of NIV for pandemic viral illness, it is reasonable to provide a cautious trial in carefully selected patients with acute hypoxemic respiratory failure in experienced centers equipped with negative pressure isolation rooms.[36]

Early CPAP has been reported as a simple way to prevent deterioration of respiratory function and complications in patients with haematologic malignancy.[37] However, a multi-centre randomized trial of 374 immunocompromised subjects showed that early NIV was not associated with clinical benefits in terms of mortality, nosocomial infections, duration of IMV or length of ICU stay versus standard oxygen therapy,[38] while another more recent randomized trial has shown that HFNC did not significantly reduce 28-day mortality versus standard oxygen therapy in immunocompromised patients (n=776) with acute hypoxemic respiratory failure.[39] In contrast, another randomized open-label study of 310 patients with acute hypoxemic respiratory failure has shown that HFNC led to lower risk of tracheal intubations and 90-day mortality in comparisons with NIV or standard oxygen therapy.[40] A post-hoc analysis of 82 immunocompromised patients enrolled in a larger trial of patients with acute respiratory failure suggested no benefit of NIV, either for tracheal intubation or survival.[41] Currently, there is recommendation for the use of bilevel NIV or early CPAP for immuno-compromised patients with acute respiratory failure,[36] but the role

of HFNC in such patients deserves further evaluation given the limited dispersion of exhaled air as shown by this study and lack of airborne and surface contamination in the GNB environmental contamination study.[32]

Recently an experimental study on healthy subjects has shown that a combination of HFNC delivering nasal high flow within a sealed helmet connected to a PEEP valve, can provide a stable PEEP and effective washout of carbon dioxide from the upper airway with negligible carbon dioxide rebreathing.[42] More studies are needed to determine whether HFNC has advantages over NIV in managing different types of respiratory failure. Development of more securely fitted mask interface connection and less turbulent exhaust ventilation is needed to minimize the risk of nosocomial transmission during application of HFNC and NIV in patients with respiratory failure due to SARI.

This study is limited by the use of smoke particles as markers of exhaled air because there is no safe and reliable marker that can be introduced into human lungs for study. As the smoke particles in this study mark the continuous air phase, our data contours are referring to exhaled air and represent the "upper bound" estimates for the dispersion of droplets, which would be expected to follow a shorter trajectory than the exhaled air jet because of gravitational effects, but not fully reflect the risk of droplet transmission.[22-30]

In summary, exhaled air dispersion distance during application of HFNC at 60 L/min is shorter than those from application of CPAP via commonly used nasal pillows. However, sideway leakage to 620 mm may occur in the presence of a loose connection between HFNC and the interface tubing. Exhaled air dispersion during application of CPAP via the Quattro Air face mask and a single circuit is a safe option for patients with respiratory infections complicated by respiratory failure due to its negligible leakage through the circular vent holes if NIV via helmet through a double circuit is not available.

Acknowledgment:

DS Hui is the guarantor of the content of the manuscript, including the data and analysis. DS Hui, BK Chow and MTV Chan were responsible for the study design, data interpretation, and writing up of manuscript. O Tsang, S Ng, F Ko, T Lo, and T Gin provided technical support for the study.

Financial support: We thank the Food & Health Bureau, HKSAR, for funding this study (HMRF#15140282). The sponsor approved the study design but played no role in development of the research and manuscript

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Figure Legend

Figure 1: Setting of the isolation room in relation to the laser device and the video camera. The light-sheet was initially positioned in the median sagittal plane of the HPS and subsequently shifted to the paramedian planes. This would allow investigation of exhaled air in the regions directly above and lateral to the mask of the HPS.[22-30] All leakage jet plume images revealed by the laser light-sheet were captured by a high definition video camera (Sony High-Definition digital video camcorder, HDR-SR8E ClearVid complementary metal oxide semiconductor Sensor, Carl Zeiss® Vario-Sonnar T* Lens, Jena, Germany), with optical resolution of 1,440 × 1,080 pixels per video frame.

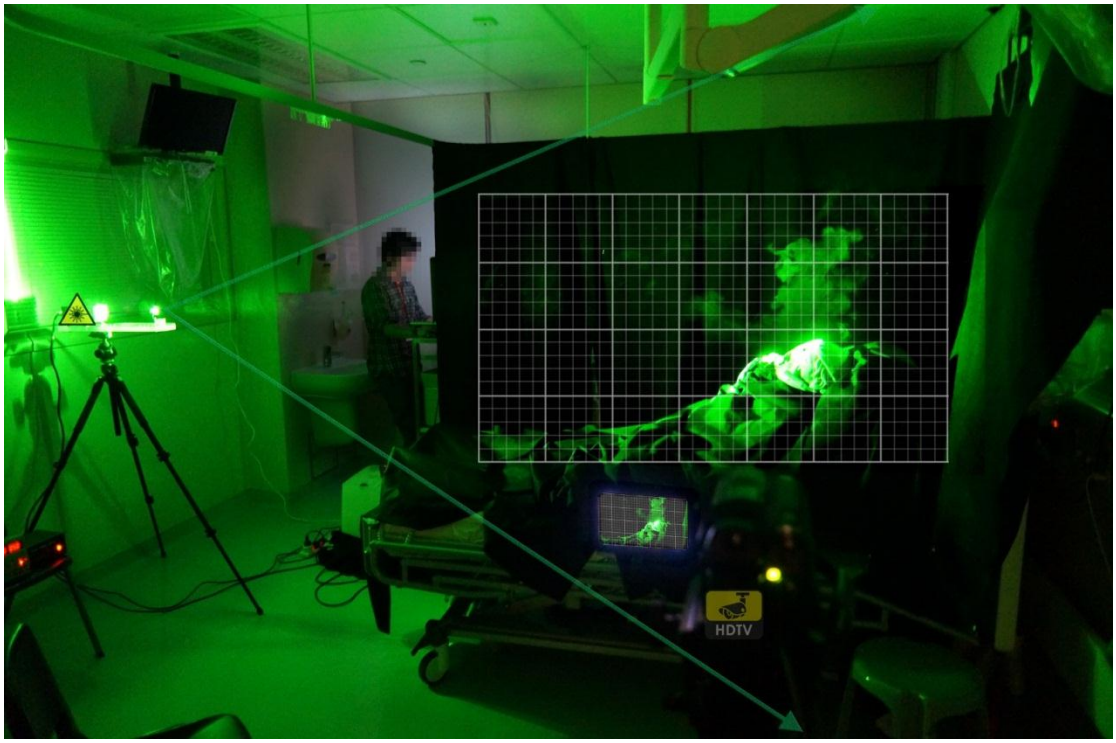
Figure 2a. Graphic coloured images of exhaled air leakage during application of HFNC on the HPS lying at 45° on the bed in different severity of lung injury. The top, middle and bottom rows represent the HPS being programmed in normal lung condition, mild and severe lung injury, respectively.

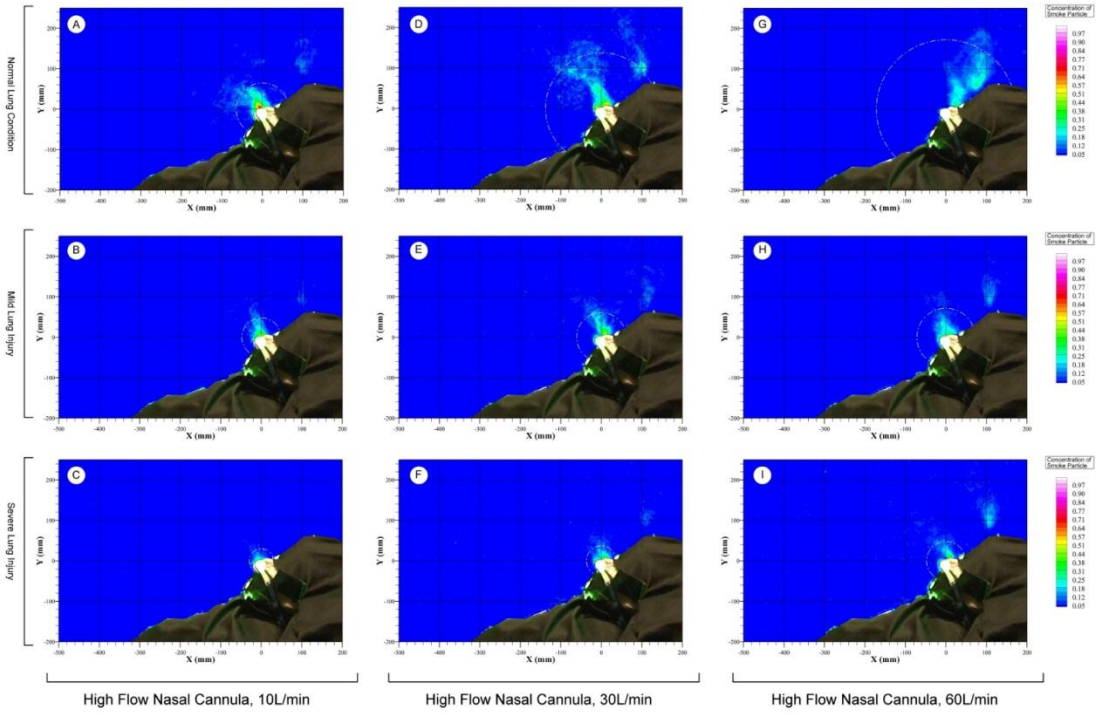
Figure 2b. A photograph with an arrow showing a loose connection between the HFNC and the interface tube resulting in exhaled air leakage laterally to 62cm.

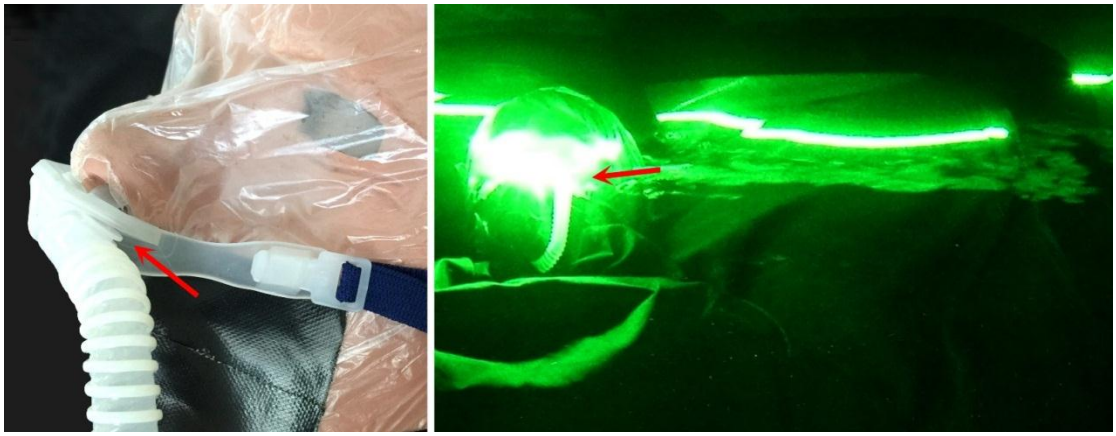
Figure 3a. Changes of exhaled air dispersion with increasing CPAP and worsening degree of lung injury in Respironics Nuance Pro Gel and Resmed Swift FX nasal pillows. There was significant increase in exhaled air dispersion distance in both nasal pillows with increasing CPAP, $p<0.001$. Worsening severity of lung injury also reduced dispersion, $p<0.001$, There was however no difference in exhaled air dispersion between the two types of nasal pillows ($p=0.095$).

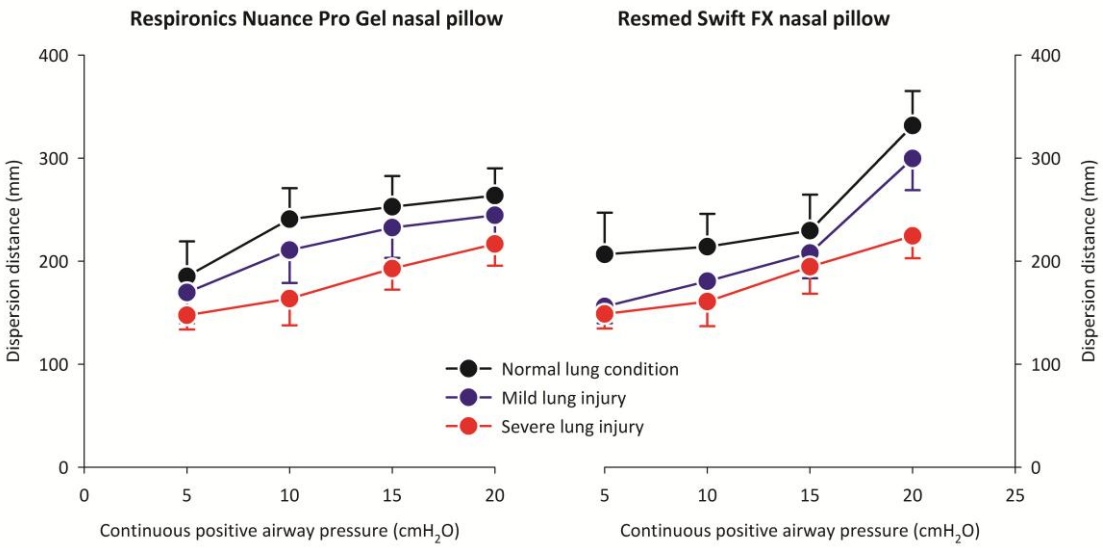
Figure 3b. Graphic coloured images of exhaled air during application of CPAP via ResMed Swift FX nasal pillows. The top, middle and bottom rows represent the HPS being programmed in normal lung condition, mild and severe lung injury, respectively.

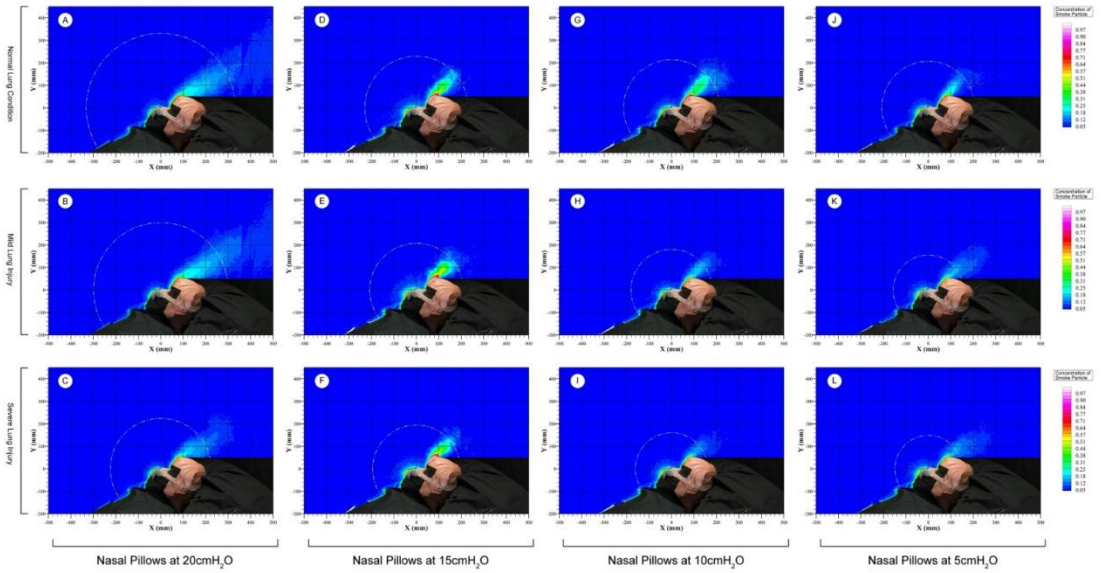
Figure 3c. Graphic coloured images of exhaled air during application of CPAP via Respironics Nuance Pro Gel nasal pillows. The top, middle and bottom rows represent the HPS being programmed in normal lung condition, mild and severe lung injury, respectively.

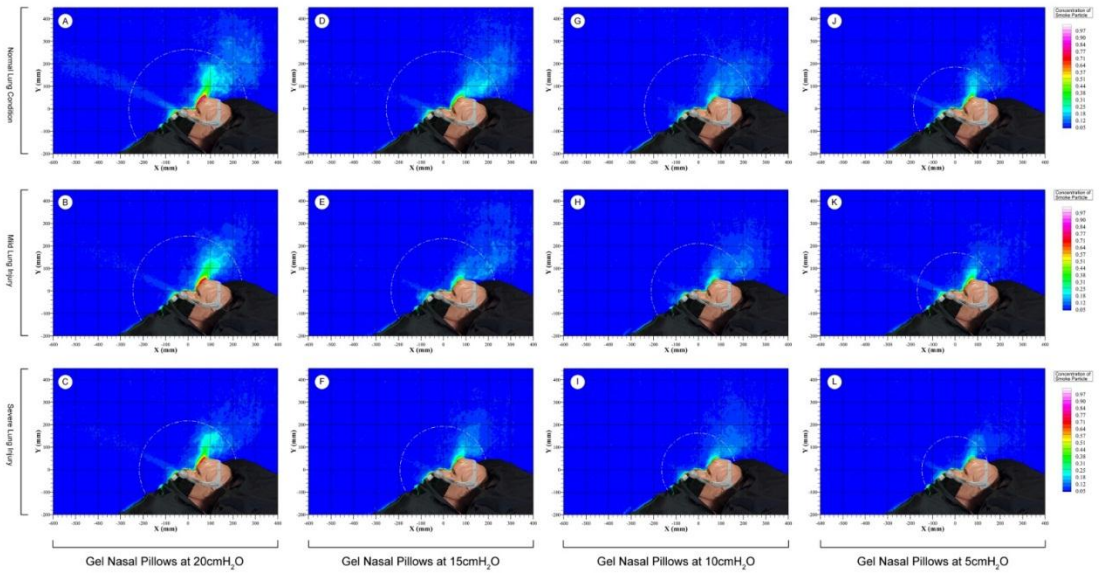

HDTV


Normal Lung Condition
Mild Lung Injury
Severe Lung Injury
A
B
C
D
E
F
G
H
I
Y (mm)
X (mm)
Concentration of Smoke Particle
0.97
0.90
0.84
0.77
0.71
0.64
0.57
0.51
0.44
0.38
0.31
0.25
0.18
0.12
0.05
High Flow Nasal Cannula, 10L/min
High Flow Nasal Cannula, 30L/min
High Flow Nasal Cannula, 60L/min




Respironics Nuance Pro Gel nasal pillow
Resmed Swift FX nasal pillow
Dispersion distance (mm)
Continuous positive airway pressure (cmH2O)
Normal lung condition
Mild lung injury
Severe lung injury


Nasal Pillows at 20cmH2O
Nasal Pillows at 15cmH2O
Nasal Pillows at 10cmH2O
Nasal Pillows at 5cmH2O


Gel Nasal Pillows at 20cmH2O
Gel Nasal Pillows at 15cmH2O
Gel Nasal Pillows at 10cmH2O
Gel Nasal Pillows at 5cmH2O

Online data supplement

Image analysis

We estimated normalized smoke concentration in the exhaled air from the light scattered by the particles. The analysis was based on principle that the intensity of scattered light was proportional to particle concentration under the conditions that the intensity of laser illumination and the size and shape of the smoke particles were constant (monodisperse).[1]

Image capture and frame extraction

Motion video of at least 20 breathing cycles at specified air flow rate was captured and individual frames extracted as gray scale bitmaps for intensity analysis. Frames are extracted from the beginning of each inspiration, to generate an ensemble average for the corresponding instant of the respiratory cycle.[2-10] The time at which the normalized concentration contours spread over the widest region, from the nostrils of the HPS, was chosen for the ensemble average to estimate the greatest dispersion distance. This was found to be approximately at the mid-respiratory cycle.[2-10]

Intensity averaging and concentration normalization

All gray scale frames were read into a program specifically developed for this study (MathCad 8.0, Cambridge, MA, USA) along with background intensity images taken with the laser switched off.[2-10] The background intensity image was subtracted from each frame, pixel by pixel to remove any stray background light and the pixel intensity values were averaged over all frames to determine the ensemble averaged intensity. The resulting image was the total intensity of light scattered perpendicular to the light sheet by the smoke particles and was directly proportional to smoke

concentration under the conditions mentioned above. The image was normalized against the highest intensity found within the leakage jet plume to generate normalized particle concentration contours.[2-10]

Supplemental References

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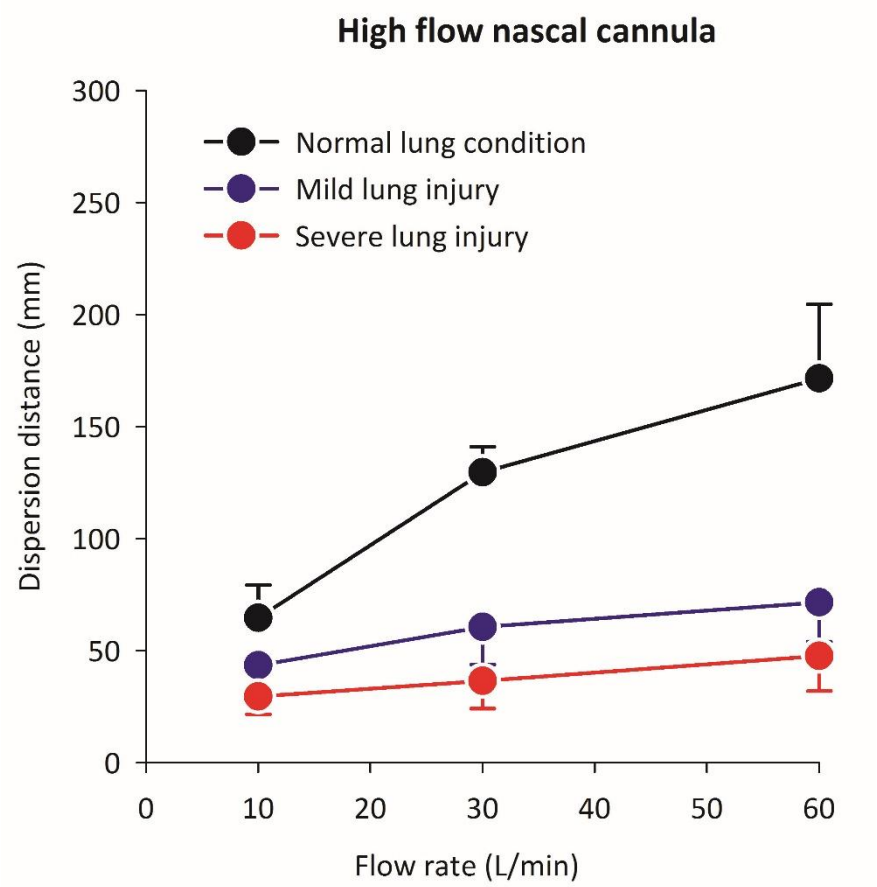
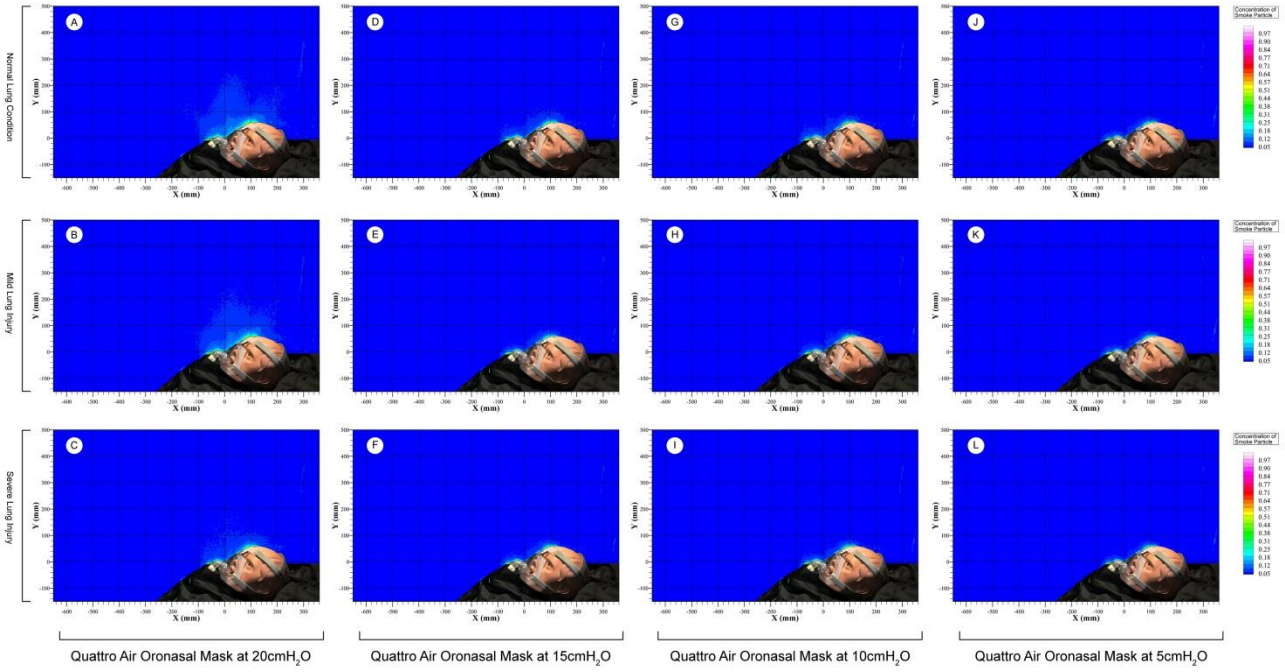
Supplemental figure 1. Changes of exhaled air dispersion with increasing flow rate and worsening degree of lung injury in high flow nasal cannula.

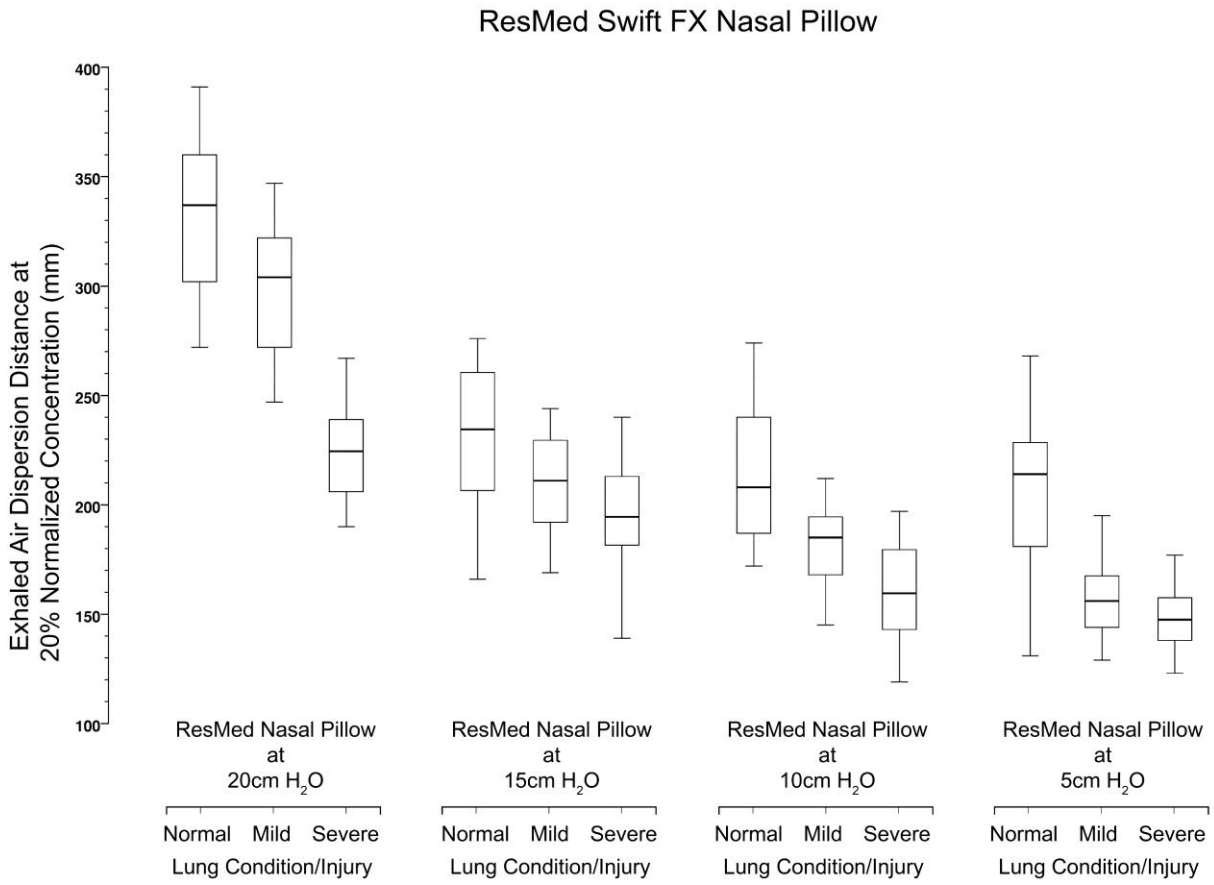


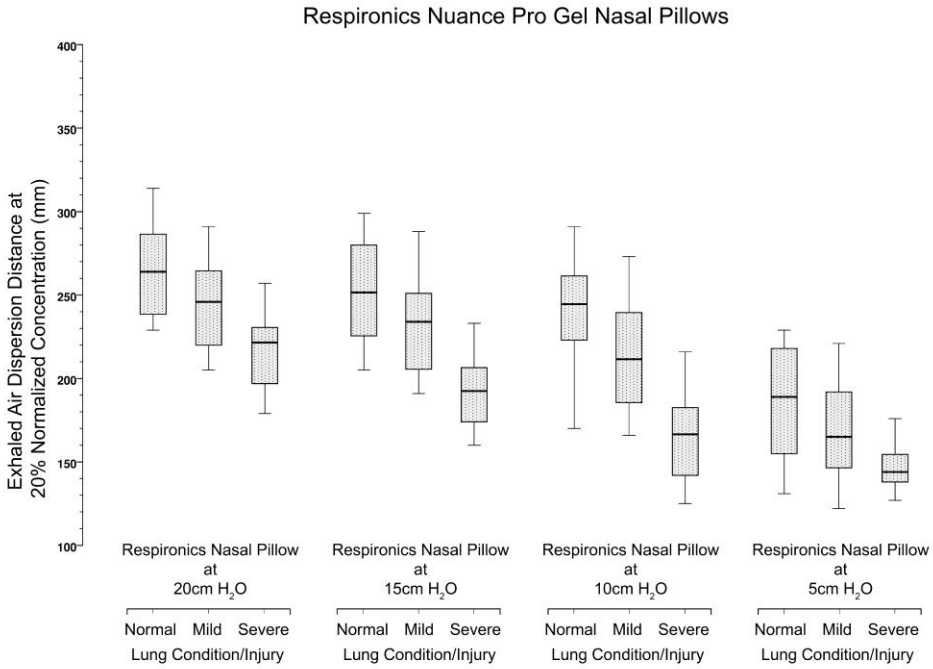
Supplementary figures 2a and 2b showing exhaled air dispersion from the

ResMed Quattro face mask and a close up view of the mask respectively



Supplementary Figure 3a and 3b showing box plots of exhaled air dispersion distances from the ResMed and Respironics nasal pillows respectively




Respironics Nuance Pro Gel Nasal Pillows
Exhaled Air Dispersion Distance at 20% Normalized Concentration (mm)
400
350
300
250
200
150
100
Respironics Nasal Pillow at 20cm H2O
Respironics Nasal Pillow at 15cm H2O
Respironics Nasal Pillow at 10cm H2O
Respironics Nasal Pillow at 5cm H2O
Normal Mild Severe
Lung Condition/Injury