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Lights! Oxygen! Action! Hollywood anaesthesia is coming to a theatre near you

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By the time you are reading this editorial, '*La La Land*', an Academy Awards contender movie about love, passion, and professional challenges of two Hollywood dreamers, will have nearly swept the Oscars. In the dream world of general anaesthesia, the top la la land award should undoubtedly be bestowed on Gustafsson and colleagues[1] for their publication in the April issue of *British Journal of Anaesthesia*.

Straight out of the Hollywood movies, this blockbuster report demonstrates the feasibility of using high-flow nasal oxygen as the only means for providing oxygenation and gas exchange during simple laryngologic surgery. Neither mechanical nor jet ventilation was necessary, and only basic airway management manoeuvres were required on the part of the anaesthetist. All 30 patients studied sustained adequate oxygenation for up to 30 min and maintained stable vital signs. Immediate postoperative recovery was uneventful. Is this a fantasy world, science fiction, or a not-so-distant future?

I bet on the last option. It has been only a couple of years since Patel and Nouraei's[2] 'Aha!' moment of bringing high-flow nasal oxygen from the trenches of neonatal and adult intensive care units to the operating theatre and using it to prolong apnoea during tracheal intubation in 25 patients with difficult airways. Today, one can find at least 160 US and internationally registered clinical trials on diverse application of high-flow nasal oxygen and more than 15 investigations specifically related to its use in surgical patients (https://clinicaltrials.gov, http://apps.who.int/trialsearch/default.aspx, last accessed February 13, 2017).

An elegant term, THRIVE (Transnasal Humidified Rapid Insufflation Ventilatory Exchange), coined by Patel and Nouraei,[2] reiterates the difference between classic apnoeic oxygenation and active gas exchange afforded by humidified oxygen delivered through a specialized high-flow nasal cannula (HFNC) at rates of up to 70 litres min^{-1}. Fully conditioned gas reduces airway resistance, and high oxygen flow assures relatively constant fractional inspired O_2 and CO_2 elimination as a result of flushing of anatomical dead space.[3–6]

It is likely that in anaesthetized and paralysed patients, both apnoeic oxygenation and a flow-dependent, mild increase in upper airway pressure ($\leq$7 cm H_2O) are responsible for sustained oxygenation.[27–11] Increased airway pressure also results in alveolar recruitment, improved ventilation–perfusion matching, and reduced shunting.[2 4 11–13] It is important to note that oesophageal pressure remains low, at ~3 cm H_2O,[14] thereby not increasing the risk of gastric insufflation during THRIVE. Middle ear pressure also does not increase appreciably.[15]

Oxygenation via HFNC has been used successfully outside the operating room for treatment of acute respiratory distress syndrome and respiratory failure in neonates and paediatric patients,[16] for critically ill adults with both hypoxaemic and hypercapnic respiratory failure in the intensive care unit and emergency room,[3 17–20] for providing post-extubation respiratory support in the intensive care unit and improving oxygenation during reintubation attempts,[21–26] for patients with acute heart failure, central obstructive sleep apnoea, and for procedural sedation (e.g. interventional bronchoscopy).[16 27 28]

The results of the study by Gustafsson and colleagues[1] further reassure us that THRIVing in the operating room as part of general anaesthesia is possible. Airway patency afforded by suspension laryngoscopy allows unimpeded THRIVE delivery and maintenance of superior patient oxygenation. THRIVE does not require airway management beyond basic airway manoeuvres (e.g. oral airway insertion, jaw thrust), provides the surgeon with an enlarged, completely unobstructed laryngeal view, improves operating conditions, probably speeds up surgery, and may positively affect patient outcomes.

Nevertheless, CO_2 build-up and ensuing acute respiratory acidosis are expected to be the main factors limiting use of THRIVE in otherwise healthy patients. Gustafsson and colleagues[1] quantified the rate of increase of the arterial partial pressure of CO_2 (Pa_{CO_2}) at ~0.24 kPa min^{-1} (1.8 mm Hg min^{-1}) and the decrease in pH to $\geq$7.13, which gives us appreciation for the safety and limitations of THRIVE in general anaesthesia. These results suggest that routine use of transcutaneous CO_2 monitoring may be advisable for procedures lasting longer than 30 min. Randomized trials investigating the most effective intraoperative ventilation strategies that counteract hypercapnia with minimal or no disturbance to the surgical field, such as high-frequency infraglottic jet ventilation and high- or low-frequency supraglottic jet ventilation, are warranted. Apnoeic intermittent ventilation using a small (e.g. 5.0 mm internal diameter) microlaryngeal tube placed through the suspension laryngoscope may be most effective in that regard, but repeated tracheal intubations carry a risk for vocal cord and laryngeal injury. The feasibility of adding advanced non-invasive ventilation capabilities to the HFNC–patient interface may need to be explored by manufacturers.

Despite the demonstrated intraoperative haemodynamic stability during THRIVE,[1] summative cardiovascular effects of hyperoxia, moderate permissive hypercapnia, and total i.v. anaesthesia demand further investigation. Hyperoxia may provoke coronary vasoconstriction, reduce circulation in peripheral

vascular beds, and decrease cerebral O_2 consumption as a result of neurotoxic effects of reactive oxygen species (see Nimmagadda and colleagues).[29] Many of these effects should be mitigated by concomitant increase in Pa_{CO_2} and associated improvement in coronary blood flow[30] and systemic oxygen delivery, which are promoted by increased cardiac output and decreased peripheral vascular resistance.[31–35] Acute hypercapnic acidosis may be protective for the heart and other organs,[36 37] but caution is required if severe hypercapnia (Pa_{CO_2} >10 kPa, or 75 mm Hg) is reached, because of associated myocardial depression.[38] Propofol–remifentanil anaesthesia can be expected to reduce cardiac output further, and therefore careful patient selection for THRIVE administration is warranted. On the upside, propofol is a powerful antioxidant, which scavenges free radicals and protects against peroxidative injury in the presence of hyperoxia.[39–45] The safety of the intriguing interplay between THRIVE-induced pathophysiology and anaesthetic pharmacology needs to be elucidated carefully.

Capitalizing on Oscar Wilde's famous quote, 'I can resist anything except temptation', it is enticing to try to take a peek into the future of advanced oxygenation techniques in general anaesthesia. Without the need for traditional airway management, one can easily map out a diverse range of common short surgical and diagnostic procedures that might be suitable for HFNC application. THRIVE also has an enormous potential to reduce the risk of complex airway management, and early reports of its use in these settings are encouraging.[2 21 46 47 48] Some stiff competition awaits in attempted development of i.v. oxygen delivery systems that use miniature (4 μm diameter) lipid oxygen-containing microparticles.[49] When administered i.v. to asphyxiated rabbits, lipid oxygen-containing microparticles maintained full-body oxygenation and normal vital signs, preventing organ injury and death from systemic hypoxaemia.[49] It may not be long until this product becomes commercially available,[50] potentially forcing us to readdress the whole concept of difficult airway management. Novel efficient extracorporeal CO_2-removal devices requiring simple percutaneous venous access, no systemic anticoagulation, and minimal blood flow rates of <0.5 litres min^{-1} have been developed.[51] Using such a decapneization device, Rispoli and colleagues[52] efficiently removed CO_2 during 40 min of apnoea, while providing apnoeic oxygenation to the patient during tracheal resection. Could this technique provide a boon for future use of THRIVE in prolonged and complex upper airway surgery?

We are living in the exciting times of rapidly proliferating major technological advancements. What was thought impossible only a few years ago will soon become a mundane reality in the operating theatre. As if playing a perfect movie trailer, Gustaffson and colleagues[1] send us on a fascinating journey that holds promise for a thorough redefinition of many aspects of routine anaesthesia care.

La la land? No more.

Declaration of interest

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References

1. Gustafsson IM, Lodenius Å, Tunelli J, Ullman J, Jonsson Fagerlund M. Apnoeic oxygenation in adults under general anaesthesia using Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE)—a physiological study. *Br J Anaesth* 2017; **118**: 610–7
2. Patel A, Nouraei SA. Transnasal Humidified Rapid-Insufflation Ventilatory Exchange (THRIVE): a physiological method of increasing apnoea time in patients with difficult airways. *Anaesthesia* 2015; **70**: 323–9
3. Jeong JH, Kim DH, Kim SC, *et al*. Changes in arterial blood gases after use of high-flow nasal cannula therapy in the ED. *Am J Emerg Med* 2015; **33**: 1344–9
4. Vargas F, Saint-Leger M, Boyer A, Bui NH, Hilbert G. Physiologic effects of high-flow nasal cannula oxygen in critical care subjects. *Respir Care* 2015; **60**: 1369–76
5. Frizzola M, Miller TL, Rodriguez ME, *et al*. High-flow nasal cannula: impact on oxygenation and ventilation in an acute lung model. *Pediatr Pulmonol* 2011; **46**: 67–74
6. Van Hove SC, Storey J, Adams C, *et al*. An experimental and numerical investigation of CO_2 distribution in the upper airways during nasal high flow therapy. *Ann Biomed Eng* 2016; **44**: 3007–19
7. Parke R, McGuinness S, Eccleston M. Nasal high-flow therapy delivers low level positive airway pressure. *Br J Anaesth* 2009; **103**: 886–90
8. Parke RL, Eccleston ML, McGuinness SP. The effects of flow on airway pressure during nasal high-flow oxygen therapy. *Respir Care* 2011; **56**: 1151–5
9. Parke RL, McGuinness SP. Pressures delivered by nasal high flow oxygen during all phases of the respiratory cycle. *Respir Care* 2013; **58**: 1621–4
10. Ritchie JE, Williams AB, Gerard C, Hockey H. Evaluation of a humidified nasal high-flow oxygen system, using oxygraphy, capnography and measurement of upper airway pressures. *Anaesth Intensive Care* 2011; **39**: 1103–10
11. Chanques G, Riboulet F, Molinari N, *et al*. Comparison of three high flow oxygen therapy delivery devices: a clinical physiological cross-over study. *Minerva Anestesiol* 2013; **79**: 1344–55
12. Corley A, Caruana LR, Barnett AG, Tronstad O, Fraser JF. Oxygen delivery through high-flow nasal cannula increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. *Br J Anaesth* 2011; **107**: 998–1004
13. Parke RL, Bloch A, McGuinness SP. Effect of very-high-flow nasal therapy on airway pressure and end-expiratory lung impedance in healthy volunteers. *Respir Care* 2015; **60**: 1397–403
14. Lampland AL, Plumm B, Meyers PA, *et al*. Observational study of humidified high-flow nasal cannula compared with nasal continuous positive airway pressure. *J Pediatr* 2009; **154**: 177–82
15. Piastro K, Chaskes M, Agarwal J, Parnes S. The effect of high flow nasal cannula oxygen therapy on middle ear pressure. *Am J Otolaryngol* 2016; **37**: 221–4
16. Nishimura M. High-flow nasal cannula oxygen therapy in adults: physiological benefits, indication, clinical benefits, and adverse effects. *Respir Care* 2016; **61**: 529–41
17. Frat JP, Thille AW, Mercat A, *et al*. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med* 2015; **372**: 2185–96
18. Rittayamai N, Tscheikuna J, Praphruetkit N, Kijpinyochai S. Use of high-flow nasal cannula for acute dyspnea and hypoxemia in the emergency department. *Respir Care* 2015; **60**: 1377–82
19. Roca O, Hernández G, Díaz-Lobato S, *et al*. Current evidence for the effectiveness of heated and humidified high flow nasal cannula supportive therapy in adult patients with respiratory failure. *Crit Care* 2016; **20**: 109

20. Gaunt KA, Spilman SK, Halub ME, Jackson JA, Lamb KD, Sahr SM. High-flow nasal cannula in a mixed adult ICU. *Respir Care* 2015; **60**: 1383–9
21. Hernández G, Vaquero C, Colinas L, *et al*. Effect of postextubation high-flow nasal cannula vs noninvasive ventilation on reintubation and postextubation respiratory failure in high-risk patients: a randomized clinical trial. *JAMA* 2016; **316**: 1565–74
22. Rittayamai N, Tscheikuna J, Rujiwit P. High-flow nasal cannula versus conventional oxygen therapy after endotracheal extubation: a randomized crossover physiologic study. *Respir Care* 2014; **59**: 485–90
23. Hernández G, Vaquero C, González P, *et al*. Effect of postextubation high-flow nasal cannula vs conventional oxygen therapy on reintubation in low-risk patients: a randomized clinical trial. *JAMA* 2016; **315**: 1354–61
24. Miguel-Montanes R, Hajage D, Messika J, *et al*. Use of high-flow nasal cannula oxygen therapy to prevent desaturation during tracheal intubation of intensive care patients with mild-to-moderate hypoxemia. *Crit Care Med* 2015; **43**: 574–83
25. Besnier E, Guernon K, Bubenheim M, *et al*. Pre-oxygenation with high-flow nasal cannula oxygen therapy and noninvasive ventilation for intubation in the intensive care unit. *Intensive Care Med* 2016; **42**: 1291–2
26. Stéphan F, Barrucand B, Petit P, *et al*. High-flow nasal oxygen vs noninvasive positive airway pressure in hypoxemic patients after cardiothoracic surgery: a randomized clinical trial. *JAMA* 2015; **313**: 2331–9
27. La Combe B, Messika J, Labbé V, *et al*. High-flow nasal oxygen for bronchoalveolar lavage in acute respiratory failure patients. *Eur Respir J* 2016; **47**: 1283–6
28. Simon M, Braune S, Frings D, Wiontzek AK, Klose H, Kluge S. High-flow nasal cannula oxygen versus non-invasive ventilation in patients with acute hypoxaemic respiratory failure undergoing flexible bronchoscopy—a prospective randomised trial. *Crit Care* 2014; **18**: 712
29. Nimmagadda U, Salem MR, Crystal GJ. Preoxygenation: physiologic basis, benefits, and potential risks. *Anesth Analg* 2017; **124**: 507–17
30. Nomura F, Aoki M, Forbess J, Mayer J Jr. Effects of hypercarbic acidotic reperfusion on recovery of myocardial function after cardioplegic ischemia in neonatal lambs. *Circulation* 1994; **90**: 321–7
31. Mas A, Saura P, Joseph D, *et al*. Effects of acute moderate changes in PaCO2 on global hemodynamics and gastric perfusion. *Crit Care Med* 2000; **28**: 360–5
32. Walley KR, Lewis TH, Wood LD. Acute respiratory acidosis decreases left ventricular contractility but increases cardiac output in dogs. *Circ Res* 1990; **67**: 628–35
33. Akça O, Doufas A, Morioka N, Iscoe S, Fisher J, Sessler D. Hypercapnia improves tissue oxygenation. *Anesthesiology* 2002; **97**: 801–6
34. Akça O, Liem E, Suleman MI, Doufas A, Galandiuk S, Sessler D. Effect of intra-operative end-tidal carbon dioxide partial pressure on tissue oxygenation. *Anaesthesia* 2003; **58**: 536–42
35. Blackburn JP, Conway CM, Leigh JM, Lindop MJ, Reitan JA, Weaver PC. Myocardial carbon dioxide response curves. *Br J Anaesth* 1970; **42**: 559
36. Crystal GJ. Carbon dioxide and the heart: physiology and clinical implications. *Anesth Analg* 2015; **121**: 610–23
37. Contreras M, Masterson C, Laffey JG. Permissive hypercapnia: what to remember. *Curr Opin Anaesthesiol* 2015; **28**: 26–37
38. Akça O. Optimizing the intraoperative management of carbon dioxide concentration. *Curr Opin Anaesthesiol* 2006; **19**: 19–25
39. Kevin LG, Novalija E, Stowe DF. Reactive oxygen species as mediators of cardiac injury and protection: the relevance to anesthesia practice. *Anesth Analg* 2005; **101**: 1275–87
40. Zhang SH, Wang SY, Yao SL. Antioxidative effect of propofol during cardiopulmonary bypass in adults. *Acta Pharmacol Sin* 2004; **25**: 334–40
41. Halladin NL, Zahle FV, Rosenberg J, Gögenur I. Interventions to reduce tourniquet-related ischaemic damage in orthopaedic surgery: a qualitative systematic review of randomised trials. *Anaesthesia* 2014; **69** :1033–50
42. Bellanti F, Mirabella L, Mitarotonda D, *et al*. Propofol but not sevoflurane prevents mitochondrial dysfunction and oxidative stress by limiting HIF-1α activation in hepatic ischemia/reperfusion injury. *Free Radic Biol Med* 2016; **96**: 323–33
43. Gan X, Xing D, Su G, *et al*. Propofol attenuates small intestinal ischemia reperfusion injury through inhibiting NADPH oxidase mediated mast cell activation. *Oxid Med Cell Longev* 2015; **2015**: 167014
44. Ren X, Lv F, Fang B, *et al*. Anesthetic agent propofol inhibits myeloid differentiation factor 88-dependent and independent signaling and mitigates lipopolysaccharide-mediated reactive oxygen species production in human neutrophils in vitro. *Eur J Pharmacol* 2014; **744**: 164–72
45. Yang SC, Chung PJ, Ho CM, *et al*. Propofol inhibits superoxide production, elastase release, and chemotaxis in formyl peptide-activated human neutrophils by blocking formyl peptide receptor 1. *J Immunol* 2013; **190**: 6511–9
46. Badiger S, John M, Fearnley RA, Ahmad I. Optimizing oxygenation and intubation conditions during awake fibreoptic intubation using a high-flow nasal oxygen-delivery system. *Br J Anaesth* 2015; **115**: 629–32
47. Mir F, Patel A, Iqbal R, Cecconi M, Nouraei SA. A randomised controlled trial comparing transnasal humidified rapid insufflation ventilatory exchange (THRIVE) pre-oxygenation with facemask pre-oxygenation in patients undergoing rapid sequence induction of anaesthesia. *Anaesthesia* 2017; **72**: 439–43
48. Booth AW, Vidhani K, Lee PK, Thomsett CM. SponTaneous Respiration using IntraVEnous anaesthesia and Hi-flow nasal oxygen (STRIVE Hi) maintains oxygenation and airway patency during management of the obstructed airway: an observational study. *Br J Anaesth* 2017; **118**: 444–451
49. Kheir JN, Scharp LA, Borden MA, *et al*. Oxygen gas-filled microparticles provide intravenous oxygen delivery. *Sci Transl Med* 2012; **4**: 140ra88
50. Kheir JN, Polizzotti BD, Thomson LM, *et al*. Bulk manufacture of concentrated oxygen gas-filled microparticles for intravenous oxygen delivery. *Adv Healthc Mater* 2013; **2**: 1131–41
51. Ricci D, Boffini M, Del Sorbo L, *et al*. The use of CO_2 removal devices in patients awaiting lung transplantation: an initial experience. *Transplant Proc* 2010; **42**: 1255–8
52. Rispoli M, Nespoli MR, Mattiacci DM, Esposito M, Corcione A, Buono S. Intraoperative extracorporeal carbon dioxide removal during apneic oxygenation with an EZ-blocker in tracheal surgery. *A A Case Rep* 2016; **6**: 358–61