Deep Extubation Protocol for Total Intravenous Anesthesia following Ambulatory Elective Dental Surgery in Pediatric Patients: A Pilot Study

by

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Abstract

Background: There are currently no detailed protocols in the literature to guide deep extubation following total intravenous anesthesia (TIVA), particularly for dental procedures.

Objective: To adapt and modify a pre-existing deep extubation protocol and to determine the success rate and incidence of complications using the described protocol in children undergoing dental surgery using TIVA.

Method: Fifty healthy children 4-12yr of age who required general anesthesia for dental surgery were recruited. Deep extubation was performed using the adapted standardized deep extubation criteria and step-wise protocol checklist. Success rate of deep extubation and incidence of complications were assessed.

Results: The deep extubation success rate was 95.5%. The two most common respiratory complications were upper airway obstruction (32.5%) and mild oxygen desaturation ($SpO_2 < 95\%$ but $>90\%$) (47.5%). There were no laryngospasms, bronchospasms, aspiration or cardiac complications.

Conclusion: The deep extubation criteria and step-wise protocol checklist can be used to guide deep extubation following TIVA in children undergoing dental surgery.

Acknowledgements

Table of Contents

List of Tables

List of Figures

List of Appendices

Chapter 1

Introduction

1.1. Statement of the problem

Endotracheal extubation is a critical recovery step during emergence from general anesthesia (GA) as a patient's airway transitions from being maintained and protected by the anesthesiologist to being supported by his or her own protective airway reflexes. Thus, a carefully planned extubation strategy is paramount. Unfortunately, in contrast to intubation, limited research has focused on optimizing the process of tracheal extubation. In terms of timing of tracheal extubation, it can be performed when patients are awake with return of consciousness and protective airway reflexes. Alternatively, it can also be carried out when patients are still deeply anesthetized while maintaining spontaneous breathing. Awake extubation is commonly considered the standard technique as the recovery of protective reflexes means that the patient is able to maintain his/her own airway (Popat *et al.*, 2012). However, due to the absence of involuntary airway reflexes, deep extubation is generally associated with a smoother emergence and less trauma to the airway (Valley *et al.,* 1999; Fagan *et al.,* 2000; Valley *et al.*, 2003). Both awake and deep extubation have their own advantages and disadvantages and the choice of technique should be based on clinical judgment with both patient and surgical factors in mind. However, many anesthesiologists were reluctant to perform deep extubation in suitable clinical situations as they felt the lack of necessity or perceived increased risk of aspiration and laryngospasm (Daley, Norman and Coveler, 1999). Unfortunately, such reasoning is not evidence-based. Few randomized controlled trials compared the incidence of perioperative respiratory complications between awake and deep extubation and no significant differences were found (Patel *et al.,* 1991; Pounder, Blackstock and Steward, 1991; Koga, Vaughan and Latto, 1998; von Ungern-Sternberg *et al.,* 2013). However, all of the above studies utilized inhalational anesthetics as the main agent for maintaining GA. This technique is rarely practiced in ambulatory general anesthesia for dental surgery where total intravenous anesthesia (TIVA) is often used instead (Perrott *et al.*, 2003). Furthermore, the deep extubation protocols documented in

these studies were not clinically validated. This suggests potential inaccurate results when comparing awake and deep extubation.

In summary, deep extubation has known benefits. However the lack of standardized criteria and insufficiently documented and tested protocols may be reasons why a large proportion (30% to 55%) of anesthesiologists never practised deep extubation (Daley, Norman and Coveler, 1999; Rassam, 2005). The aim of this prospective non-randomized study was to develop a detailed decision-making step-wise protocol for deep extubation to ensure appropriate depth of anesthesia for deep extubation using TIVA technique. This pilot study will provide the foundation for further studies that compare awake and deep extubation approaches in ambulatory elective pediatric anesthesia for dental surgery.

Chapter 2

Literature review

2.1. Challenges in tracheal extubation

Tracheal extubation is associated with a considerable risk of complications and failure that can be more problematic than tracheal intubation. The potential risk of respiratory complications is particularly important in children, who are more prone to rapid oxygen desaturation due to increased oxygen demand coupled with decreased functional residual capacity. Asai *et al.* (1998) demonstrated a respiratory complication rate of 12.6% following tracheal extubation in elective surgery that was approximately three times more common than the complication rate of intubation (4.6%). Extubation failure (defined as the need for reintubation within 48 to 72 hours after a planned extubation) as a result of major airway complications is relatively rare with a reported rate between 0.1% to 0.45% for elective surgery (Cavallone and Vannucci, 2013). On the other hand, in the Fourth National Audit Project (NAP4) of the Royal College of Anaesthetists (2011) in the UK, it was reported that nearly one third (28%) of the major airway complications occurred during extubation or recovery with an extubation failure rate of 13% and a mortality rate of 5%. The may be explained by the fact that patients with severe comorbidities were included in the NAP4 thus increasing the rates of morbidity and mortality. The challenges in tracheal extubation lie in the combination of physiological and anatomical changes following surgery and general anesthesia (Artime and Hagberg, 2014). Efforts to improve the safety of intubation led to significant reduction in airway complications in the past two decades as revealed by the American Society of Anesthesiologists closed claims analysis for malpractices in 2005 (Crosby *et al.,*1998; Heidegger, Gerig and Henderson, 2005; American Society of Anesthesiologists Task Force on Management of the Difficult Airway, 2013; Piepho *et al.,* 2015). Unfortunately, the same improvement in outcome does not hold true for extubation due to lack of comprehensive guidelines in the literature until the 2012 publication of the Difficult Airway Society (DAS) Guidelines for the management of tracheal extubation.

Ambulatory sedation and GA for elective dental anesthesia were associated with a mortality rate that ranged from 1.2 to 1.4 per 1,000,000 cases (Nkansah, Haas and Saso, 1997; D'Eramo, Bookless and Howard, 2003). This low mortality rate was attributed to rigorous patient selection that excluded patients unsuitable for ambulatory GA, limited use of muscle relaxants and long-acting opioids and the minimally invasive nature of dental surgery (Nkansah, Haas and Saso, 1997; D'Eramo, Bookless and Howard, 2003). Unfortunately, as dental anesthesiologists or oral and maxillofacial surgeons rarely performed intubations for ambulatory GA for elective dental procedures, there was no data available regarding the rates of complication in tracheal extubation for comparison against hospital-based GA where intubations were commonly practiced (Nkansah, Haas and Saso, 1997; D'Eramo, Bookless and Howard, 2003, Perrott *et al.*, 2003).

2.2. Respiratory complications of tracheal extubation

Although tracheal extubation is associated with respiratory complications, it is rarely the cause. These complications are actually the result of intubation, surgery or anesthetic medications, and are simply masked by the presence of the endotracheal tube (ETT) and mechanical ventilation until after extubation. Respiratory complications following tracheal extubation can be divided into: 1) the "can't ventilate" category which consists of upper and lower airway obstruction and vocal cord dysfunction or, 2) the "won't ventilate" category which is mainly due to residual GA.

2.2.1. Decreased pharyngeal tone

The most common upper airway obstruction is due to soft tissue collapse following tracheal extubation as a result of decreased pharyngeal muscle tone. This is particularly problematic in obese patients, patients with obstructive sleep apnea (OSA) or those with neuromuscular diseases such as myasthenia gravis and certain types of muscular dystrophy (*e.g.* Duchenne and Becker). Studies have demonstrated that these patients have an increased sensitivity to opioids and residual anesthesia or

neuromuscular blockade with significant delay in recovery (Driessen, 2008; Adesanya *et al.,* 2010).

2.2.2. Laryngospasm

Laryngospasm is the second most common cause of upper airway obstruction following extubation with reported incidence ranging from 1.6% to 5% depending on the type of surgery, anesthetic technique and pre-existing patient risk factors (*e.g.* recent upper respiratory tract infection) (Visvanathan *et al.,* 2005; von Ungern-Sternberg *et al.,* 2010; Orestes *et al.,* 2012). Laryngospasm can lead to partial obstruction that presents as post-extubation stridor or complete airway obstruction. It is an exaggerated form of normal protective glottis closure reflex that is triggered by airways instrumentation (*e.g.* tracheal extubation) or irritation of the vocal cords during the light plane of anesthesia. Laryngospasm was more common following upper airway surgeries where residual surgical debris or blood may irritate the vocal cords (von Ungern-Sternberg *et al.,* 2010). Patients with upper respiratory tract infection (URTI) less than two weeks prior to undergoing GA were also at risk due to sensitized laryngeal reflexes and increased secretions (von Ungern-Sternberg *et al.,* 2010). Although laryngospasm is a clinical emergency and warrants immediate response, re-intubation is generally not required unless severe negative-pressure pulmonary edema develops as a result (Artime and Hagberg, 2014).

2.2.3. Laryngeal Edema

Despite laryngeal edema being another important cause of upper airway obstruction, the process of tracheal exbubation is unlikely to be the cause. Laryngeal edema typically occurs thirty to sixty minutes following tracheal extubation but its occurrence can be delayed for up to six hours after extubation (Miller, Harkin and Bailey, 1995). Laryngeal edema can be classified based on anatomical location: supraglottic, retroarytenoid or subglottic. Subglottic edema is more common in pediatric patients due to their narrow airway where increase in airflow resistance is inversely proportional to the decrease of radius to the fourth power (Karmarkar and Varshney, 2008; Artime and Hagberg, 2014). Associated risk factors include a tight-fitting ETT,

traumatic intubation, intubation duration more than one hour, persistent coughing and bucking on ETT and changes in head and neck position during surgery. The etiology of supraglottic edema was mainly related to surgery that includes post-surgical anatomical distortion, hematoma, hemorrhage, Trendelenburg position as well as aggressive fluid administration, multiple intubation attempts and multiple airway suctionings (Popat *et al.*, 2012). Laryngeal edema presents as inspiratory stridor similar to laryngospasm. The treatment of laryngeal edema depends on the severity and reintubation with a smaller size ETT may be required for severe cases.

2.2.4. Bronchospasm

Bronchospasm is one of the main causes of lower airway obstruction following tracheal extubation. Bronchospasm is relatively uncommon with a reported incidence of approximately 0.2% during GA (Olsson, 1987). However, it was demonstrated to be more common following airway surgery with an incidence of approximately 2% (von Ungern-Sternberg *et al.,* 2010; Orestes *et al.,* 2012). Bronchospasm can lead to partial obstruction that manifests as expiratory wheezing or complete obstruction. Similar to laryngospasm, bronchospasm is triggered by irritation of the lower airway by ETT or noxious stimuli such as foreign bodies, excessive secretions or blood in the lower airway during the light plane of anesthesia. Patients undergoing airway surgery, patient with reactive airway disease (asthma, recent URTI of less than two weeks duration, allergic rhinitis and/or chronic obstructive pulmonary disease), patients with smoke exposure and patients who were intubated (especially endobronchial intubation) were demonstrated to have an increased risk of bronchospasm (von Ungern-Sternberg *et al.,* 2010). Westhorp, Ludbrook and Helps (2005) reported that 20% of perioperative bronchospasm occurred during or following tracheal extubation. Bronchospasm may be caused by coughing and bucking on ETT, the act of extubation or excessive patient stimulation as the patient's air reflexes gradually return or more rarely, due to pulmonary edema or an anaphylactic reaction (Westhorpe, Ludbrook and Helps, 2005; Wood and Sladen, 2009). While mild bronchospasm can be treated with salbutamol, severe cases may necessitate administration of epinephrine and potentially reintubation (Orestes *et al.,* 2012).

2.2.5. Negative pressure pulmonary edema

Negative pressure pulmonary edema (NPPE) mainly develops as a secondary complication following an upper airway obstruction. Forceful inspiratory effort against an obstruction can generate a negative intrapleural pressure sufficient enough to disrupt the alveolar-capillary membrane leading to pulmonary transudation and mild hemorrhage (Karmarkar and Varshney, 2008; Artime and Hagberg, 2014). The incidence of NPPE is approximately 1 in 1000 following extubation and it occurs more commonly in healthy children and young adults (Udeshi, Cantie and Pierre, 2010). Although this condition is primarily associated with laryngospasm, it can also be caused by other forms of airway obstruction such as airway foreign body aspiration, laryngeal hematoma, bilateral vocal cord paralysis, kinked ETT as well as the patient biting on an oral ETT during emergence from GA (Udeshi, Cantie and Pierre, 2010). Respiratory distress often occurs within minutes after airway obstruction followed by coughing with "pink frothy sputum" and bilateral pulmonary crackles on auscultation (Artime and Hagberg, 2014). NPPE typically resolves within 24 hours with supportive care but severe cases may require reintubation (Udeshi, Cantie and Pierre, 2010).

2.2.6. Pulmonary aspiration

Pulmonary aspiration is a rare event in elective surgery when proper fasting guidelines are followed. Experts believed the implementation of strict fasting guidelines likely contributed to the reduction of the incidence of aspiration (American Society of Anesthesiologists (ASA), 2011). The fasting protocol in the 2012 Royal College of Dental Surgeons of Ontario (RCDSO) Standards of Practice was consistent with that documented in the 2011 ASA guideline. Both the ASA guidelines and the RCDSO Standards of Practice stated that no solid food or nonhuman milk should be ingested six hours before GA with breast milk and clear fluids allowed only up to four hours and two hours prior, respectively. The incidence of intraoperative vomiting during elective surgery was reported to be between 0.3% and 1.4% (Cohen, Cameron and Duncan, 1990). Intraoperative vomiting does not always lead to pulmonary aspiration. The diagnosis of true pulmonary aspiration events cannot be made unless the inhalation of a foreign object, gastric content or blood is visualized directly or interpreted on chest

imaging. Due to the challenges in diagnosing aspiration, especially in retrospective studies, it was difficult for researchers to accurately assess its incidence. The reported incidence of intraoperative aspiration ranged from 0.01% to 0.1% in elective surgeries and less than 10% of these events occurred during or after extubation (Tiret *et al*., 1988; Warner *et al.*, 1999; Murat, Constant and Maud'huy, 2004; Walker, 2013). Interestingly, a recent Swedish study demonstrated similar incidence of aspiration (0.03%) in children despite following an altered fasting guideline that allowed clear fluid intake until being called to the operatory room (Andersson, Zarén and Frykholm, 2015). Although dental procedures are considered as airway surgery, the risk of intraoperative aspiration is remarkably low. A large study from the United States involving 1,706,100 cases, reported an aspiration rate of 0.0035% during procedural sedations but no incidence of aspiration was reported during non-intubated GAs (D'Eramo, Bookless and Howard, 2003). Unfortunately, no data regarding the incidence of aspiration during intubated GA for dental procedures are available in the literature. Other types of airway surgeries such as otolaryngology (ENT) surgeries that were commonly performed while patients were intubated, were reported to have an aspiration incidence of approximately 0.015% (Tiret *et al.*, 1988; Sakai *et al.*, 2006).

Pulmonary aspiration although rare is a serious event as it can lead to upper or lower airway obstruction and damage to the pulmonary tissue. The severity of the sequelae is dependent on the type, size and volume of matter aspirated, age and existing comorbidities of the patient and the management of the aspiration event (Kelly and Walker, 2015). The AIMS study in 1999 reported an overall mortality of approximately 4% following intraoperative aspiration in adults while the NAP4 report in 2011 cited aspiration to account for 50% of all deaths associated with GA during their study period. The inclusion of emergency surgeries and unhealthy patients (ASA ≥ III) likely played an important role in the high mortality rate recorded in these studies. In contrast, a retrospective study involving 118, 371 pediatric patients by Walker (2013) showed that healthy patients undergoing elective surgeries were less likely to experience severe deterioration that required overnight stay in hospital or admission to intensive care unit (ICU) with reintubation following aspiration comparing to unhealthy patients or those undergoing emergency surgeries (10% vs. 28.6%). Walker (2013) reported no incidence

of mortality in his study. Other large pediatric studies in the past two decades showed similar results (Warner *et al.*, 1999; Andersson, Zarén and Frykholm, 2015).

There are multiple risk factors for intraoperative pulmonary aspiration. The primary patient related risk factor is a full stomach as well as conditions that: 1) decreased gastric sphincter tone (*e.g.* severe gastroesophageal reflux disease (GERD)), 2) increased abdominal pressure (*e.g.* pregnancy and obesity) or, 3) delayed gastric emptying (*e.g.* gastrointestinal pathology, bowel obstruction, diabetes and chronic opioid use). Anesthesia related risk factors included opioid use, inadequate fasting time, Trendelenburg position, use of a supraglottic device for airway management, epistaxis from nasal intubation and abdominal strain due to coughing and bucking on ETT as a patient emerged from GA (Kelly and Walker, 2015).

2.2.7. Vocal cord dysfunction

There are two main types of vocal cord dysfunction following tracheal extubation. The more common type is due to injuries to the recurrent laryngeal nerve causing vocal cord paralysis. It is often caused by trauma from head and neck surgery but can also be a result of traumatic intubation or pressure trauma from a tight fitting ETT near the anterior branch of the recurrent laryngeal nerve (Ellis and Pallister, 1975). The ASA closed claims analysis (2005) showed that 33% of airway injuries resulting in claims occurred at the larynx with 34% of such causing vocal cord paralysis. Unilateral paralysis typically presents as hoarseness in a patient's voice following extubation with no other complications. However, bilateral paralysis is more serious as it can result in upper airway obstructions requiring reintubation (Artime and Hagberg, 2014). A large retrospective study in 2007 reported that intubation accounted for approximately 7% of all vocal paralysis with two-thirds of the paralysis being unilateral (Rosenthal, Benninger and Deeb, 2007). The second type of vocal cord dysfunction is caused by paradoxical vocal cord motion during which the vocal cords adduct during inspiration. This is a rare condition and females and/or those with recent URTI or emotional stress are at risk. It can present as inspiratory stridor after extubation or total airway obstruction requiring reintubation in severe cases (Arndt and Voth, 1996).

2.2.8. Hypoventilation

Residual GA can depress a patient's respiratory drive following extubation even in an apparently alert patient. This problem is more common with heavy use or overdose of opioids during GA, prolonged anesthesia and prolonged intubation with mechanical ventilator support (*e.g.* ICU patients). Elderly patients or those with comorbidities such as advanced kidney and liver disease, metabolic derangements (*e.g.* hypoglycemia, metabolic alkalosis), OSA and/or chronic obstructive pulmonary disease (COPD) were also demonstrated to be at risk (West, 2012). This problem can be minimized by careful weaning from mechanical ventilation and achieving spontaneous ventilation with appropriate breathing frequency (between 8 to 45 breaths per minute) and tidal volume (more than 6 mL/kg) prior to completion of surgery (Baumeister *et al.*, 1997; Thiagarajan *et al.*, 1999). Reintubation is rare and is reserved for patients who are not amendable to supportive therapy and reversal agents.

2.3. Other complications of tracheal extubation

The most important non-respiratory complications relate to increases in intracranial pressure and systemic arterial pressure during extubation. The underlying mechanism is postulated to be related to catecholamine release as a result of coughing and bucking on ETT during emergence from GA (Hartley and Vaughn, 1993, Kothari *et al.*, 2014). The use of opioid reversal agents to facilitate extubation was also associated with hypertension and tachycardia (Blaise *et al.*, 1990). Studies showed that tracheal extubation was associated with a 10% to 30% increase in systemic arterial pressure and heart rate that could last for five to fifteen minutes (Lowrie *et al.*, 1992; Miller, Harkin and Biley,1995). Furthermore, Leech, Barker and Fitch (1974) and Hartley and Vaughan (1993) reported significant elevations in intracranial pressure during extubation. These hemodynamic changes are typically well tolerated in children or healthy adults. However, they are of major concerns in patients with cardiovascular pathoses who are at risk for myocardial infarctions or cerebrovascular pathoses such as intracranial lesions or arteriovenous malformations who are at risk for intracranial hemorrhage (Wellwood *et al.*, 1984; Hartley and Vaughan, 1993). Another complication of concern is bleeding

or wound dehiscence (*e.g.* extraction socket) that was associated with coughing and bucking and elevation in systemic blood pressure (Sheta *et al.*, 2011).

2.4. Difficult airway and its impact on extubation

A difficult airway was defined by the ASA as a clinical situation in which an experienced anesthesiologist encounters difficulty with face mask ventilation and/or tracheal intubation (ASA, 2013). Difficult airways accounted for up to 25% of anesthesia-related deaths (Nagaro *et al.,* 2003; Frerk and Cook, 2011). The cause of difficult airway is multifactorial and many investigations were conducted to assess various contributing patient and anesthesia factors to aid anesthesiologists in anticipating this problem (ASA, 2013). Established independent risk factors for difficult mask ventilation for elective surgery included age greater than 55 years, presence of a beard, edentulism, male sex, Mallampati class 4 airway, history of OSA, overweight (with a Body:Mass index (BMI) > 26 kg/m^2). On the other hand, validated risk factors associated with difficult intubation were long central incisors, large overbite, inability to bite upper lip with lower incisors, narrow palatal arch, short thyrohyoid and thyromental distance, macroglossia, Mallampati class 3 or 4 airway and limitation in neck movement (Faris, Zayaruzny and Spanakis, 2011; Shah, Dubey and Yadav, 2013).   For simplification, Langeron *et al.* (2000) classified mask ventilation into five grades (grade 0-4) with grade 2 as difficult mask ventilation requiring oral airway or other adjuvant and grade 3 as inadequate or unstable mask ventilation requiring two practitioners. The reported incidence of grade 2 mask ventilation in adult elective surgery was approximately 20% while it ranged from 0.8% to 7.8% for grade 3. Grade 4 was described as impossible mask ventilation with rare incidence of 0.01% to 0.15% in adults (Langeron *et al.* 2000; Law *et al.* 2013). In children older than one year, Valois-Gomex *et al.* (2013) reported an incidence of 6.6% for difficult mask ventilation (Grade 2 or above). Traditionally, the difficulty of intubation was determined by the laryngeal view, which was how well the vocal cords could be visualized under direct laryngoscopy. Full laryngeal view often translated into easy intubation with the exceptions of structural airway malformation or subglottic stenosis associated with various congenital conditions (*eg.* Down's syndrome) or prolonged intubation (Choi and

Zalzal, 2000; Schweiger *et al.,* 2013). Cormack and Lehane (1984) classified the laryngeal view under direct laryngoscopy into 4 grades. Difficult laryngoscopy was associated with grade 3 (only epiglottis visible) and grade 4 (no laryngeal structure visible) and their combined incidence ranged from 0.8% to 7% in adults. The proportion of children with difficult laryngoscopy (Grade 3 or above) is smaller than the proportion of adults with reported incidence ranging from 0.07% to 0.7% (Law *et al.* 2013). Despite this seemingly high incidence of difficult airway, the incidence of the "can't intubate and can't ventilate" situation (approximately 0.02%) and intubation failure (failure to intubate within three attempts) (0.9-1.9%) drastically decreased during induction due to advances in anesthesia equipment and technologies with the implementation of well-established guidelines (Cook and MacDougail-Davis, 2012; Law *et al.* 2013).

Besides during induction and intubation, a difficult airway also has a significant impact on tracheal extubation due to the possibility of requiring mask ventilation and reintubation for management of complications. Reintubation was often regarded by anesthesiologist as more challenging than the initial intubation especially in the presence of difficult airway due to potential airway edema from prior intubation attempts during induction (Artime and Hagberg, 2014). Moreover, physiological changes, contamination from head and neck surgeries and prolonged intubation create additional obstacles and may convert a simple airway into a difficult one (Artime and Hagberg, 2014). In 2012, the DAS Guidelines for managing tracheal extubation suggested assessment for potential difficult airway during extubation based on three categories: 1) pre-existing airway difficulties, 2) perioperative airway deterioration and, 3) restricted airway access. Patients with pre-existing airway difficulties were difficult to mask ventilate and/or tracheal intubate at induction of GA or were indicated to have such difficulties by past anesthetic records. Patients with pre-existing airway difficulties also included those who were obese and those with OSA or risk factors for aspiration of gastric content. Airways with perioperative airway deterioration were described as those who were normal at induction but became difficult due to edema, hemorrhage, hematoma or distorted anatomy. These changes might be the result of surgical or non-surgical factors such as trauma from intubation or unfavorable patient positioning (*e.g.* Trendelenburg). Lastly, restricted airway access was defined by limitation in jaw, head and neck movements due

to surgery (*e.g.* mandibulomaxillary fixation) or conditions such as cervical spine instability and rheumatoid arthritis affecting the TMJ and/or cervical spine. Patients who belonged to the any of the three categories had an elevated risk of potential complications and thus, these patients should be extubated awake and a carefully planned sequence of action must be established prior to extubation in order to regain control of the airway in the event that the extubation fails.

2.5. Timing of extubation

2.5.1. Awake extubation

Traditionally, the method of awake extubation is taught and practised by anesthesiologists (Karmarkar and Varshney 2008; Popat *et al.*, 2012). It was defined (Miller 2010) as "tracheal extubation after the return of appropriate response to verbal stimuli with recovery of protective respiratory reflexes". However, beside the return of protective airway reflexes, wakefulness in anesthesia is also determined by the presence of eye opening and facial grimacing, purposeful movement and the ability to maintain adequate ventilation with full control of airway reflexes (Sheta *et al.,* 2011). Awake extubation was considered a standard technique since the recovery of protective reflexes means that the patient is able to maintain his/her own airway (Artime and Hagberg, 2014). According to the DAS Guidelines (2012), this method was most ideal for patients with difficult airways. Furthermore, with return of airway tone, the risks of respiratory complications in the post-anesthesia care unit are less dependent on the skill level of the nurses in charge of recovery (Daley, Norman and Coveler, 1999).

Awake intubation has three major disadvantages. Firstly, when the patient's protective airway reflexes return, tracheal irritation may cause the patient to cough or buck against the ETT. Coughing was the most common problem encountered during awake extubation with a wide range of reported incidence (6-96%) depending upon various patient (*e.g.* recent URTI), surgical (*e.g.* airway surgery) and anesthetic factors (*e.g.* use of opioids) (Hans, Marechal and Bonhomme, 2008; Nho *et al.* 2009; von Ungern-Sternberg *et al.*, 2010; Sheta *et al.,* 2011; Hamilton *et al.,* 2012; Shen, Hu and Li, 2012; Jun, Park and Kim, 2014). Although coughing is not a complication but rather a normal physiological airway protective response, it was shown to be associated with a

number of respiratory complications. These included oxygen desaturation (Sheta *et al.,* 2011), laryngeal edema (Koka *et al.,* 1977), risk of regurgitation of gastric contents due to increased abdominal pressure (Irwin, 2006) and potential bronchospasm (Westhorpe, Ludbrook and Helps, 2005). Persistent coughing was also shown to cause hypertension, tachycardia, arrhythmias, increased intracranial pressure (Leech, Barker and Fitch, 1974; Blaise *et al.,* 1990) as well as increased risk of surgical site bleeding and wound dehiscence (Sheta *et al.,* 2011). Multiple techniques were demonstrated to significantly minimize the coughing reflex during emergence such as the use of topical or intravenous lidocaine spray, use of TIVA, remifentanil infusion or subhypnotic dose of propofol as well as the "no touch" technique (Hans, Marechal and Bonhomme, 2008; Nho *et al.* 2009; von Ungern-Sternberg *et al.,* 2010; Sheta *et al.,* 2011; Hamilton *et al.,* 2012; Shen, Hu and Li, 2012; Jun, Park and Kim, 2014). The "no touch" technique was particularly effective by reducing the incidence of multiple coughs from 90% to 13% (Sheta *et al.,* 2011). Unfortunately, despite the implementation of these techniques, the incidence of persistent cough still remained relatively high (more than 10%) (Hamilton *et al.,* 2012).

The second disadvantage of awake extubation was the risk of laryngospasm. Due to time pressure, some anesthesiologists may rely on clinical sign of the swallowing reflex as the surrogate end point for wakefulness. Although this may indicate return of laryngeal reflexes, it does not always correspond to return of consciousness; the patient may be in a plane of anesthesia between the awake and the deep states (Miller, Harkin and Bailey, 1995). Airway instrumentation during this state may lead to laryngospasm as the level of anesthesia is not sufficient to prevent laryngeal reflexes but is too deep for the patient to have full control (Hartley and Vaughan, 1993).

Thirdly, patients have a tendency of clenching their jaws together during emergence that can occlude an oral ETT (Negus, 1997; Liu and Yih, 1999). This can potentially lead to avulsion of teeth thus increasing the risk of aspiration and development of negative pulmonary pressure edema following extubation (Liu and Yih, 1999). Simple management such as placing a bite block prior to emergence from GA can prevent this issue (Negus, 1997).

2.5.2. Deep extubation

A number of anesthesiologists advocated for the use of an alternative extubation method known as deep extubation, particularly in children (Aouad *et al.*, 2009; Ansermino *et al.*, 2005; Shen *et al.,* 2012; Hu *et al.,* 2014). Miller (2010) defined deep extubation as "tracheal extubation in spontaneously breathing patients under the absence of any protective respiratory reflexes". The ability to maintain adequate spontaneous ventilation without mechanical support is crucial in deep extubation (Popat *et al.*, 2012). Some benefits of deep extubation are known. It was demonstrated to result in a smoother emergence with decreased likelihood of breath-holding, and bucking and coughing on ETT that were common with awake extubation (Valley *et al.,* 1999; Valley *et al.*, 2003). Thus, this technique can potentially minimize oxygen desaturation due to prolonged straining, airway trauma, cardiovascular complications (*e.g.* hypertension, tachycardia, dysrhythmias), increased intracranial pressure as well as wound dehiscence at surgical sites (*e.g.* extraction sockets) (Leech, Barker and Fitch, 1974; Lowrie *et al.,* 1992; Sheta *et al.*, 2011). As well, deep extubation may be beneficial particularly in pediatric patients with reactive airway disease (*e.g.* asthma) and URTI, both of which were known to be at risk for developing perioperative respiratory complications (von Ungern-Sternberg *et al.*, 2010). Asthma affected approximately 13% of children in Canada (Garner and Kohen, 2008) while 20-30% of children were reported to have rhinitis of various causes during a significant part of the year (Nathan *et al*., 1997). Minimizing airway stimulation in these children may consequently reduce respiratory complications such as laryngospasms and bronchospasms (Fagan *et al.*, 2000; Sheta *et al.,* 2011).

While deep extubation appears to have many benefits, many anesthesiologists believed that deep extubation may result in more frequent upper airway obstructions and may increase the risk of aspiration (Daley, Norman and Coveler, 1999). Intraoperative aspiration can be a significant cause of mortality and morbidity when the event is linked to solid matter or gastric contents ($\geq$ 0.4mlL/kg at pH < 2.5) during anesthesia (Engelhardt and Webster, 1999). However, in healthy children (ASA I and II) undergoing elective surgery where proper fasting guidelines were followed, the risk of aspiration was demonstrated to be extremely rare in the past two decades with an incidence of less than 0.1%. Furthermore, more than 90% of these patients showed

either no or transient postoperative respiratory symptoms that resolved with supplemental oxygen and/or antibiotics with no incidence of mortality (Warner *et al.,* 1999; Walker, 2013; Andersson, Zarén and Frykholm, 2015). No association between deep extubation and aspiration was established in any studies to date (Pounder *et al.,* 1991; Patel *et al.,* 1991; Koga *et al.,* 1998; Valley *et al.,* 1999; Valley *et al.*, 2003; Shen *et al.,* 2012; von Ungern-Sternberg *et al.,* 2013; Hu *et al., 2014*). Laryngospasm or bronchospasm (1.6-5% and 1.8-2% respectively) were shown to occur more commonly than aspiration. Since the risk of aspiration was small and its outcomes in healthy children undergoing elective surgery were rarely severe (*e.g.* requiring overnight stay or reintubation and admission to ICU), the use of deep extubation to avoid the more common complications of laryngospasm and bronchospasm may represent a favourable balance of risks and benefits for patients. Also, in studies that investigated deep extubation, it was found that upper airway obstructions were managed effectively with simple physical maneuvers and oral airways (Valley *et al.,* 1999; Valley *et al.*, 2003; Shen *et al.*, 2012; Hu *et al.*, 2014). The safety of this technique is enhanced by careful patient selection and monitoring; The DAS Guidelines (2012) indicated that this technique should be used in healthy, fasted patients with a low risk of difficult airway, who can be monitored until fully awake.

There are limited accounts in the literature on how to perform deep extubation. All available data on how to achieve the depth of anesthesia suitable for deep extubation are based on the use of inhalational agents (Valley *et al.,* 1999; Valley *et al.*, 2003; Shen *et al.*, 2012; Hu *et al.*, 2014). Valley *et al* (1999, 2003) demonstrated the use of minimum alveolar concentration (MAC) of 1.5 with sevoflurane, isoflurane and desflurane while Hu *et al* (2014) and Shen *et al* (2012) used a MAC of 1.3 with sevoflurane and a MAC of 1.0 with sevoflurane combined with remifentanil infusion. All of the above MAC values were not clinically validated. Coughing or laryngospasms during extubation were reported in three of these studies suggesting that the level of anesthesia was not adequate for deep extubation. In addition, inhalational anesthetic agents are not administered for maintenance of GA in total intravenous anesthesia (TIVA), a technique that is commonly used by dental anesthesiologists in ambulatory pediatric GA for elective dental surgery (Perrott *et al.*, 2003). Thus, it may be difficult to

generalize the technique described in the above studies in the dental anesthesia setting. No research to date has studied the use of TIVA to perform deep extubation.

2.6. Past studies comparing awake extubation with deep extubation

Four randomized controlled trials compared the incidence of perioperative respiratory complications between awake and deep extubation. Pounder *et al.* (1991) compared awake and deep extubation using halothane and isoflurane in healthy children undergoing various types of elective surgeries. A MAC value of 2.0 was chosen as the end point for anesthesia level for deep extubation. Deep extubation with isoflurane resulted in significantly fewer instances of coughing than awake extubation (4% vs. 72%, $P < 0.05$) with no difference in the incidence of laryngospasm, breath-holding and airway obstructions. Interestingly, there was significant difference in the lowest oxygen saturation value between the awake and the deep extubation group with isoflurane (87.4% ± 11.2% awake vs. 96.5% ± 2.1% deep, $P < 0.05$) or halothane (89.0% ± 11.2% awake vs. 97.1% ± 1.9% deep, $P < 0.05$). The study by Patel *et al.* (1991) involved a population base similar to that in Pounder's. A MAC value of 1.0 for halothane was chosen as the end point of anesthesia level for deep extubation. There were no statistically significant differences in the incidence of laryngospasm and excessive coughing between awake and deep extubation. Koga *et al.* (1998) studied the two techniques in healthy adults receiving elective non-oral surgery. There was no mention of the MAC value used for deep extubation and the level of anesthesia was not standardized. For the deep extubation group, GA was maintained with 1-2% of isoflurane with 66% nitrous oxide until patients were extubated. The author reported a higher incidence of straining on ETT with the awake extubation group and a higher incidence of airway obstruction in the deep extubation group. Unfortunately, the author did not mention if these differences were statically significant. Von Ungern-Sternberg *et al.* (2013) compared awake and deep extubation in children with increased airway reactivity undergoing adenotonsillectomy. In addition to a MAC value of 1.0 with sevoflurane, pupil size and respiration rate were used to assess depth of anesthesia. Patients who were extubated awake had a significantly higher incidence of coughing

(60% vs. 36%, *P* < 0.05) and those who were extubated deep had significantly higher incidence of airway obstruction (26% vs. 8%, *P* < 0.05). There were no differences in the incidence of bronchospasm, laryngospasm and postoperative stridor. Similar to the results in Patel's study, deep extubation was associated with consistently higher oxygen saturation trends (SpO$_2$) through emergence and recovery compared to awake extubation (*P* < 0.05). Although the difference in the total number of respiratory complications in the operatory room and the recovery unit was not statistically significant, the awake extubation group had a significantly higher incidence of developing hoarse voice one day following the operation (48% vs. 26%, *P* < 0.05).

2.6.1. Limitations of prior investigations

Critical review of the studies examining the deep extubation technique and perioperative complications demonstrated some common shortcomings. Most notably was the use of MAC of inhalational anesthetics for determining depth of anesthesia before extubation. MAC is the concentration of inhalational general anesthetic agent in the lungs that is required to prevent motor response to surgical stimulus in 50% of subjects. A MAC value 1.0 or higher was typically required for skin incision and surgery when intravenous drugs were not administered (Eger, 2001). Although using MAC as a surrogate end point is convenient, MAC for individual patients is dependent on multiple factors such as patient's age, surgical stimulus, use of other anesthetic agents and body temperature (Heier and Steen, 1996; Eger, 2001; Mapleson, 2003). Additionally, airway irritation and instrumentation such as laryngoscopy, tracheal intubations and extubations are noxious stimuli such that the depth of anesthesia required to eliminate any responses during these procedures is often deeper compared to that for skin incision (Nishino *et al*., 1990, Nishino *et al*., 1996; Kaul and Bharti, 2002; Ishikawa *et al*., 2005). The presence of coughing reflex during extubation in all of these studies suggested that not all patients were under adequately deep anesthesia during deep extubation. Thus, the use of MAC as a surrogate for the measurement of appropriate anesthetic depth for deep extubation might have resulted in inaccurate comparisons between awake and deep extubation (Patel *et al.,* 1991; Pounder *et al.,* 1991; Koga *et al.,* 1998). Compared to MAC, clinical signs were demonstrated to provide more accurate means to assess depth of anesthesia

(Heier and Steen, 1996). Von Ungern-Sternberg *et al.* (2013) incorporated Guedel's signs of pupil size changes and respiratory rate in addition to MAC to determine if patients were within the surgical plane of anesthesia prior to extubation. However, as Guedel's signs were developed based on ether-based anesthesia, intraoperative use of intravenous anesthetics agents such as opioids that were shown to alter pupil size and respiratory rate rendered such assessments inaccurate (Schuttler, 1989). Another major flaw common to these studies was the lack of protocol used to standardize the process of deep extubation besides implementing a MAC threshold value. The variability in the deep extubation technique among anesthesiologists such as prophylactic use of oral or nasal airway or positioning might potentially result in confounding factors. Finally, in some of these studies, there was no definition and standardization for individual respiratory complication. This could have led to discrepancies among evaluators and difficulties when comparing results.

2.7. The Difficult Airway Society Guidelines for deep extubation

Like the DAS difficult intubation guidelines published in 2004 and 2015 (Henderson *et al.*, 2004; Frerk *et al.,* 2015), the DAS Guidelines on management of tracheal extubation (Popat *et al.*, 2012) were created in an attempt to provide anesthesiologists with evidence-based guidance to reduce the risk of complications associated with extubation. The DAS extubation guidelines included systematic algorithms for patient assessment to identify those at risk for complications as well as a general step-wise protocol and selection criteria for various extubation techniques. The DAS followed the standards used by other internationally recognized scientific societies such as the Canadian Airway Focus Group (CAFG) and the ASA in formulating airway management guidelines (Crosby *et al*., 1998; ASA Task Force on Management of the Difficult Airway, 2003). A total of 6215 scientific publications from 1970 to 2008 were retrieved in a structured literature search, of which only 327 were considered relevant. However, as no large randomized controlled trials or meta-analyses related to extubation were available, expert opinion, book chapters and comments were taken into consideration in formulating the DAS Guidelines on management of tracheal extubation. The level of evidence of all publications was graded based on the Oxford Centre for

Evidence Based Medicine criteria (2011) and only the highest level of evidence available was used to support each recommendation. The draft version of the extubation guidelines was circulated and reviewed by interested members of the DAS and acknowledged international experts. Revised algorithms were then made available on the DAS website for all invited members to comment prior to publication.

The first and only step-wise deep extubation sequence in the literature was established by the DAS in 2012 as part of the guidelines for managing tracheal extubation. Although the DAS outlined a step-by-step sequence to guide anesthesiologists in performing deep extubation, they failed to provide adequate criteria for assessing depth of anesthesia as well as details on how to achieve a level of anesthesia appropriate for deep extubation. These shortcomings created challenges when utilizing the DAS deep extubation protocol such that additional specifications were required before it could be adapted for clinical use, particularly for provision of dental care for children using TIVA technique.

2.8. Summary

Tracheal extubation is a critical milestone in the patient's recovery process and it carries potential risk of developing complications especially in the presence of a difficult airway. Clinical judgment regarding the timing and method of extubation is dependent on patient and surgical factors as well as the anesthesiologist's preference. The clinician's decision to extubate is dependent upon the return of patient's airway protective reflexes such as coughing and gagging and the ability to breathe spontaneously without ventilatory support. The likelihood for a patient to maintain a patent upper airway without assistance is also influenced by surgical factors such as bleeding control. Deep extubation has known benefits and may offer advantages over awake extubation especially in patients with reactive airway diseases or cardiovascular pathoses. However the lack of standardized criteria and insufficiently documented protocols that can promote favourable outcomes may be reasons why deep extubation is regarded by some anesthesiologists as less advantageous compared to awake extubation, and therefore is not as commonly practised.

Chapter 3

Study purpose and research questions

3.1. Study purpose

The purpose of this prospective non-randomized pilot study was to assess the success rate of the adapted detailed deep extubation decision-making criteria and step-wise protocol for the dental setting using the TIVA technique. This pilot study will provide the foundation for further studies that compare the deep and awake extubation techniques in ambulatory elective pediatric general anesthesia for dental surgery.

3.2. Specific objectives of the study

To adapt and modify a pre-existing deep extubation decision-making criteria and step-wise protocol for children undergoing ambulatory elective general anesthesia for dental surgery using the TIVA technique and to determine the success rate of deep extubation and incidence of complications with the use of the adapted protocol.

Chapter 4

Methodology

4.1. Study participants

This study recruited children ages four to twelve years inclusively who required dental treatment under general anesthesia and were suitable to receive care at the Pediatric Surgicentre, Faculty of Dentistry, University of Toronto. Inclusion criteria were: 1) patients with an American Society of Anesthesiology (ASA) Class I or II physical status (see Appendix 4.1), and 2) English speaking parents. Exclusion criteria were: 1) patients with an ASA physical status higher than Class II, 2) known risk factors for malignant hyperthermia (see Appendix 4.2), 3) known risk factors for perioperative respiratory complications (see Appendix 4.3), 4) potential difficult airway (See Appendix 4.4) and 5) history of postoperative emergence agitation or delirium. The usual preclinical assessment was used to further identify exclusion criteria (see Appendix 5.1, 5.2, 5.3)

4.2. Study design

In this prospective study, children presenting for elective GA for dental surgery underwent planned deep extubation using the proposed standardized decision-making criteria for deep extubation and step-wise deep extubation clinical protocol. Facility and departmental permissions were obtained. Ethics approval was received from University of Toronto, Research Ethics Board (Protocol reference number: 32212; Appendix 11).

4.3. Recruitment

All pediatric patients at the University of Toronto, Faculty of Dentistry Surgicentre required a preoperative consultation appointment prior to GA. At the anesthesia consultation conducted by the anesthesia resident, the study was described and explained, and the Information Sheet (see Appendix 1) and Consent Form (see Appendix 2) were provided to the parents of the children who met the inclusion criteria. A standardized written assent form was also provided to children age seven or above to

obtain permission for their participation (see Appendix 3). On the days when the principal researcher was scheduled to perform the anesthesia consultation, a registered nurse carried out the recruitment process to minimize conflict of interest. However, the principal researcher was available to address any questions or concerns regarding the study without further persuasion.

On the day of surgery, the patients and the parents were reconfirmed with respect to their study participation consent, and any further questions were answered. Written informed consent and assent were sought prior to treatment. All participants had the option of withdrawing prior to induction of GA, or withdrawing participation (use of their information) any time after extubation. Participants could not withdraw during the procedure, as they were under GA and parents/guardians were not allowed in the operatory room.

4.4. Dentistry Protocol

All dental procedures were performed as per usual accepted standards with appropriate local anesthesia by pediatric dental residents, under supervision of a pediatric dentist staff. General dental procedures included (but were not limited to) restorations and/or extractions, and/or root canals, and /or pulpectomies and/or pulpotomies of the primary and/or permanent dentition.

4.5. Anesthetic protocol

4.5.1. Preoperative, induction and intubation protocol

All patients were required to follow the RCDSO preoperative fasting guidelines. All children received a single dose of midazolam premedication orally (0.75 mg/kg, 20 mg max) given 15 minutes prior to induction of GA or intramuscularly (0.1 mg/kg) given 5 minutes prior to induction of GA to provide anxiolysis and to facilitate induction of GA. Standard anesthesia monitoring parameters for assessing patient's vital signs included 3-lead ECG, automated non-invasive blood pressure, capnography and pulse oximetry. All children were preoxygenated with 100% oxygen at 5 L/min using a clear face mask. Induction of GA was achieved with sevoflurane and nitrous oxide (50:50

N$_2$O:O$_2$). Upon loss of consciousness and loss of eyelash reflex, intravenous access was attempted and the induction was then supplemented with propofol (2.0 mg/kg) and remifentanil (2.0 µg/kg) until apnea was achieved. All children were intubated with an uncuffed ETT of appropriate internal diameter using the formula [(Age/4) + 4] mm. ETT was upsized by 0.5 mm in internal diameter if there was significant air leak resulting in inadequate ventilation (*ie.* oxygen desaturation $\leq$ 95%). Lack of audible air leak at a maximum pressure of 20 cmH$_2$O warranted the ETT to be downsized by 0.5 mm smaller in internal diameter. A moistened gauze throat pack was placed around the ETT after the oropharynx had been suctioned to decrease risk of aspiration from water and foreign bodies.

4.5.2. Maintenance protocol

All GAs were maintained with an intravenous infusion of propofol and remifentanil mixed in a ratio of 10mg:5 µg (propofol:remifentanil). The rate of infusion was set based on the rate of propofol administration on the infusion pump, typically ranging from 150-250 µg/kg/min in order to achieve adequate depth of anesthesia. Spontaneous ventilation was achieved and maintained whenever possible but controlled ventilation was used when necessary. An end-tidal carbon dioxide (ETCO$_2$) value less than 55 mmHg was maintained. Anesthetic agents such as fentanyl, dexmedetomidine and midazolam were limited to the induction period or at least one hour prior to emergence due to their long sedative effects (45-60 mins). Ketamine was prohibited for intraoperative use and for premedication due to its potential bronchodilating effect as well as its association with increased risk of laryngospasm. All children received dexamethasone (0.1 mg/kg) and ketorolac (0.5 mg/kg, 15 mg max) shortly after induction. Use of lidocaine for non-dental related purpose was prohibited due to its possible inhibitory effect on airway reflexes.

4.5.3. Patient selection for deep extubation

The deep extubation contraindication checklist was used to identify patients who were unsuitable for deep extubation following the completion of dental treatment. The deep extubation contraindication checklist was adapted from the 2012 DAS Guidelines

of managing tracheal extubation. Modifications were made to better suit the described checklist to ambulatory GA for elective dental procedures provided with TIVA. A draft version of the deep extubation contraindication checklist was circulated among staff dental anesthesiologists at the Faculty of Dentistry, University of Toronto for comments and revisions were made prior to implementation in this study. Patients with residual neuromuscular blockade and potential difficult airway were contraindicated to deep extubation. Difficult airway risk factors included difficult ventilation, difficult intubation, presence of nasal polyps, adenoids and/or Brodsky scale 4 tonsils, obesity with BMI > 95th percentile, OSA, uncontrolled gastroesophageal reflux disease (GERD), excessive nasopharyngeal bleeding during intubation, uncontrolled bleeding from surgical site (see Appendix 4.4).

4.5.4. Extubation protocol

All deep extubations in this study were performed using the decision-making criteria and step-wise deep extubation protocol checklist (see Appendix 6). The decision-making criteria and step-wise protocol checklist were adapted from the deep extubation sequence detailed in the 2012 DAS Guidelines of managing tracheal extubation. Modifications were made based on data extracted from randomised controlled trials (Baumeister *et al.*, 1997; Thiagarajan *et al.,* 1999) and expert opinions from staff anesthesiologists at The Hospital for Sick Children and the Michael Garron Hospital in Toronto as well as staff dental anesthesiologists at the Faculty of Dentistry, University of Toronto. The draft version of the deep extubation decision-making criteria and step-wise protocol checklist was circulated among staff dental anesthesiologists at the Faculty of Dentistry, University of Toronto for comments and revisions were made prior to implementation in this study.

Before anesthesiology residents were eligible to participate in the study, they completed a clinical simulation prepared by the primary investigator. During the simulation, the anesthesiology residents were asked to perform deep extubation using the decision-making criteria and step-wise deep extubation protocol checklist provided. Questions regarding the protocol were addressed in the review session following the clinical simulation. A two-week familiarization period prior to the commencement of the
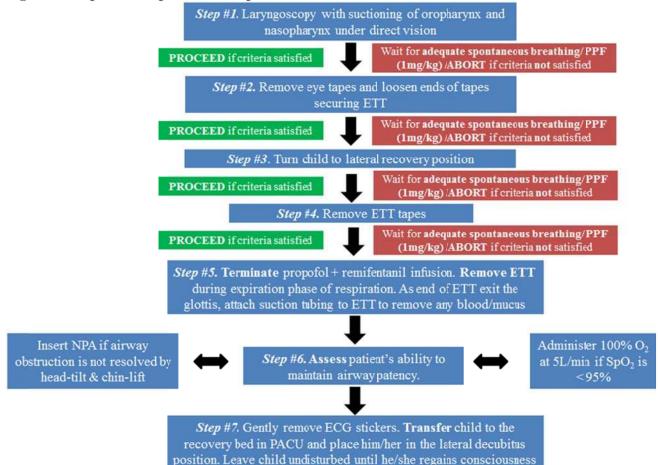
study was provided to ensure anesthesia residents had adequate time to become acquainted to deep extubation using the checklist. A written copy of the checklist was provided to the anesthesia resident prior to induction of GA in every case.

Prior to completion of dental procedures, all patients were reassessed by an anesthesia resident for contraindications to deep extubation. If there were no contraindications, an initial dose of propofol (1 mg/kg) was given. Patients were evaluated using the standardized decision-making criteria shown below (see Figure 1.) to ensure optimal conditions and appropriate depth of anesthesia for deep extubation (See Appendix 6 for complete intraoperative checklist). The anesthesia resident then performed deep extubation using the step-wise protocol shown below (see Figure 2.) (See Appendix 6 for complete intraoperative checklist). Between each of the steps, compliance with the decision-making criteria checklist was confirmed before proceeding. Hemodynamic stability and adequate spontaneous ventilation effort were required at each step of the protocol. Any patient response in the presence of adequate spontaneous ventilation indicated inadequate depth of anesthesia for deep extubation and was managed by the use of a single supplemental dose (1 mg/kg) of propofol. Deep extubation was aborted if the criteria for deep extubation were not satisfied after two cumulative doses (1 mg/kg) of propofol (1 initial and 1 supplemental dose). In such cases, patients were extubated awake and removed from the study.

Figure 1. Decision-making criteria

Patient stable with adequate spontaneous ventilation?
- ❑ Stable hemodynamics
- ❑ $SPO_2 \geq 95\%$
- ❑ Spontaneous breathing
- ❑ Adequate tidal volumes (>6mL/kg)
- ❑ Respiratory rate between 8-25bpm
- ❑ End-tidal CO2 <55mmHg
- ❑ Maximal inspiratory pressure > -15cm H2O

Presence of patient response?
- ❑ Regular respiratory rate & **no change** in pattern
- ❑ No coughing
- ❑ No breath holding
- ❑ No gagging/bucking on ETT
- ❑ Lack of facial grimacing
- ❑ Lack of spontaneous eyes opening
- ❑ Lack of purposeful body movements

Figure 2. Step-wise deep extubation protocol

Step #1. Laryngoscopy with suctioning of oropharynx and nasopharynx under direct vision

PROCEED if criteria satisfied / Wait for **adequate spontaneous breathing/PPF (1mg/kg)** /**ABORT** if criteria **not** satisfied

Step #2. Remove eye tapes and loosen ends of tapes securing ETT

PROCEED if criteria satisfied / Wait for **adequate spontaneous breathing/PPF (1mg/kg)** /**ABORT** if criteria **not** satisfied

Step #3. Turn child to lateral recovery position

PROCEED if criteria satisfied / Wait for **adequate spontaneous breathing/PPF (1mg/kg)** /**ABORT** if criteria **not** satisfied

Step #4. Remove ETT tapes

PROCEED if criteria satisfied / Wait for **adequate spontaneous breathing/PPF (1mg/kg)** /**ABORT** if criteria **not** satisfied

Step #5. Terminate propofol + remifentanil infusion. **Remove ETT** during expiration phase of respiration. As end of ETT exit the glottis, attach suction tubing to ETT to remove any blood/mucus

Insert NPA if airway obstruction is not resolved by head-tilt & chin-lift

Step #6. Assess patient's ability to maintain airway patency.

Administer 100% O_2 at 5L/min if SpO_2 is <95%

Step #7. Gently remove ECG stickers. **Transfer** child to the recovery bed in PACU and place him/her in the lateral decubitus position. Leave child undisturbed until he/she regains consciousness

4.5.5. Recovery Protocol

All patients were transported to a recovery bed and placed in the lateral decubitus position by the anesthesiology resident and the nurse after ensuring that they were able to maintain adequate airway patency. Digital video recording of the patient recovery began immediately following transfer. The recovery supervisor, either an anesthesiology staff member or a registered nurse, remained present throughout the recovery to monitor the patient until he/she was ready for discharge. If not previously placed, a nasopharyngeal airway (NPA) was inserted to maintain airway patency if airway obstruction was present and was not mitigated by the head-tilt-chin-lift maneuver. The nasopharyngeal airway was removed after the child regained consciousness (*e.g.* eye opening, purposeful movement, facial grimacing) as determined by the recovery supervisor. As per usual clinical protocol, in case of oxygen desaturation

to ≤ 94%, 100% oxygen at 5 L/min was administered passively with a clear face mask until oxygen saturation ≥ 95%. Flow rate of oxygen was increased by 1 L/min increment if oxygen saturation remained ≤ 94%. All patients were discharged to the care of their guardians after they satisfied discharge criteria (Aldrete score ≥ 9) (see Appendix 7)

4.6. Data collection

Perioperative data collection was completed by use of paper-based reporting forms, vital signs monitor printouts, and recovery room video recordings. All descriptive demographic data were captured using the faculty standard anesthetic record.

4.6.1. Primary outcome

The primary outcome of this study was the success rate of deep extubation that was defined by the percentage of patients in whom deep extubation was accomplished using the decision-making criteria and step-wise deep extubation protocol

Dental anesthesia residents were given the decision-making criteria checklist and the step-wise deep extubation protocol checklist (see Appendix 6) for each patient prior to induction of GA. As dental procedure was terminated, a stopwatch timer was started by the recovery supervisor. After the checklist was used to assess for contraindications to deep extubation by the dental anesthesia resident, it was handed to the recovery supervisor for data recording. Violations to any criterion for deep extubation, supplemental propofol bolus required to deepen the patient at any step of the protocol, failure to achieve deep extubation were marked in the checklist provided. The data were used to analyze the success rate of the decision-making criteria and step-wise clinical protocol for deep extubation.

4.6.2. Secondary outcomes

The secondary outcomes were: 1) the incidence of perioperative respiratory and cardiac complications, 2) the quality of emergence and recovery which was rated globally by two independent research assistants using a 10-point Likert scale, 3)

patient's oxygen saturation trends, and 4) time from end of procedure to extubation, to PACU and to discharge.

In the operatory room, all perioperative complications were recorded by the recovery supervisor using the standardized clinical data recording form (see Appendix 8) until the patient was discharged. The following perioperative complications were recorded: increase (>20%) in blood pressure and/or heart rate compared to preoperative baseline, arrhythmia, episodes of laryngospasm, bronchospasm, oxygen desaturation < 95% and < 90% longer than 5 seconds, airway obstruction, coughing/bucking prior to or during removal of ETT, persistent coughing after removal of ETT longer than 10 seconds, breath-holding or apnea longer than 5 seconds, cyanosis, postoperative stridor, vomiting/aspiration as well as all airway interventions (see Appendix 8 for definitions of complications). The patient's oxygen saturations were recorded by printout using a dedicated vital signs monitor every 5 minutes from the termination of the dental procedure until 45 minutes after extubation. In the events of oxygen desaturation < 95% and < 90%, breath-holding and coughing/bucking, a second timer was started to record the duration of such events. Registered nurses in charge of recovery were instructed to notify the anesthesiology staff/resident for verification and treatment in cases of suspected laryngospasm and bronchospasm.

A digital video camera was set up in the recovery room to capture the patient's emergence and recovery. The patient along with their vital signs (blood pressure, heart rate, oxygen saturation) and breathing patterns (through a precordial stethoscope connected to a speaker) were captured in the video. The recovery supervisor in the recovery room verbally announced the details of any airway interventions to notify the video viewer. This video was viewed postoperatively by two research assistants (two anesthesia resident volunteers) who independently assessed and recorded any respiratory and cardiac complications, incidence of postoperative nausea and vomiting (PONV), degree of postoperative emergence agitation and incidence of postoperative emergence delirium using a separate standardized video data assessment form (see Appendix 10). Postoperative emergence delirium was determined using a validated scale (Sikich and Lerman, 2004) (see Pediatric Anesthesia Emergence and Delirium Score under Appendix 10). The research assistants then rated the quality of the emergence and

recovery globally using a 10-point Likert scale provided in the data recording sheet (see Appendix 10) based on their record data. Until discharge, time, oxygen saturation readings and other outcome measures continued to be recorded by the attendant to prevent loss of data in the event of technical difficulties with digital video recording.

4.7. Sample size calculation

Fifty children were recruited to participate in the study. This sample size was estimated based on the assumptions used by von Ungern-Sternberg (2013), with consideration for the sample size required for one-arm in a hypothetical future two-armed randomized controlled trial of "deep" versus "awake" extubation. According to von Ungern-Stermberg's findings (2013), if one or more perioperative respiratory complications occurred in 35% of 'awake' group and 10% of 'deep' group (odds ratio of 0.206), a significance level of $\alpha = 0.05$ with 80% power would require a sample size of 43 patients in each group to detect a difference. There was an estimated 10% chance of appointment cancellation at the Surgicentre. Therefore, for the purpose of this pilot study, an a *priori* sample size of 50 patients (approximately equivalent to a single arm of a future randomized control study) was deemed appropriate to pilot the protocols.

4.8. Data analysis

The data analysis in this study was descriptive in nature. Data were initially entered into a Microsoft Excel spreadsheet. The database was then exported to SPSS version 20.0 for statistical analysis.

4.8.1. Primary outcomes

The success rate of deep extubation was shown in a table that included the number of patients who met the deep extubation criteria, the number of deep extubations aborted and the cumulative success rate at each step.

4.8.2. Secondary outcomes

Respiratory and cardiac complications and airway interventions were expressed as incidences per individual patient who was extubated deep. The time from end of procedure to extubation, to PACU and to discharge were reported as mean ± one standard deviation. The median oxygen saturation along with its interquartile range was calculated in 5-minute intervals from the termination of the dental procedure until 45 minutes after the extubation.

Intra-class correlation (ICC) was used to assess inter-rater reliability of the two independent evaluators in scoring the quality of the emergence and recovery. A training session was provided by the primary researcher where the two evaluators scored five post-anesthetic recovery videos independently. The training was repeated until an ICC value > 0.75 was obtained; a threshold for inter-rater agreement that is consistent with thresholds employed in medical research (Liddy, Wiens and Hogg, 2011; Slagle *et al.,* 2002).

Chapter 5

Results

5.1. Participant demographics

Although fifty children were recruited for this study, only forty-four datasets were available. Four children with active URTI and two children who violated fasting guidelines were excluded. Demographic data were presented in Table 1. The mean age of this cohort of children was 5.4 ± 1.9 years and two-thirds of the subjects were male. Approximately 40% of the children were ASA II with mild asthma (84.1%) and history of URTI within two to four weeks (22.7%) being the main contributing factors.

Table 1. Patient demographics, n = 44

		Number (proportion)	Mean ± 1 SD
Sex	Male	28 (63.6%)	
	Female	16 (36.4%)	
Age (yr)			5.4 ± 1.9 yr
Weight (kg)			19.8 ± 4.4 kg
ASA physical status	I	26 (59.1%)	
	II	18 (40.9%)	
Asthma Severity	None	37 (84.1%)	
	Mild	7 (15.9%)	
History of URTI (2-4weeks)	2-4 weeks	10 (22.7%)	
	> 4 weeks	32 (79.3%)	
Midazolam premedication administered	PO (mg)	34 (71.3%)	0.74 ± 0.04 mg/kg
	IM (mg)	10 (22.7%)	0.10 ± 0.01 mg/kg
GA adjunct administered	Fentanyl (µg/kg)	8 (18.2%)	0.7 ± 0.32 µg/kg
	Dexmedetomidine (µg/kg)	4 (9.1%)	0.6 ± 0.19 µg/kg
	Dexamethasone (mg/kg)	44 (100%)	0.1 ± 0.02 mg/kg
	Ketorolac (mg/kg)	44 (100%)	0.5 ± 0.03 mg/kg
	Lidocaine (mg/kg)	18 (45%)	1.8 ± 1.3 mg/kg

The majority (71.3%) of the children received oral midazolam premedication but ten out of forty-four children refused to take the medication orally and were premedicated through the intramuscular route. The mean dose of midazolam administered was 0.74 ± 0.04 mg/kg orally and 0.10 ± 0.01 mg/kg intramuscularly. Both

doses were consistent with those stated in the protocol. Fentanyl was administered in eight cases with a mean dose of 0.7 ± 0.32 μg/kg whereas dexmedetomidine was administered in four cases with a mean dose of 0.6 ± 0.19 μg/kg. All patients received dexamethasone and ketorolac intraoperatively with an average dose of 0.1 ± 0.02 mg/kg and 0.5 ± 0.03 mg/kg respectively. These average doses were also consistent with those stated in the protocol. Lidocaine was given in eighteen cases only as local anesthetic through buccal infiltration and inferior alveolar nerve block with an average dose of 1.8 ± 1.3 mg/kg. No patient received midazolam, ketamine or succinylcholine intraoperatively. The majority of children received similar types of dental treatment. All forty-four children received restorative treatment on an average of 5 ± 2 teeth while forty-one children received pulpotomy treatment with stainless steel crown on an average of 3 ± 1 teeth. A mean number of 2 ± 1 dental extractions were performed in thirty-nine children. The types of dental treatment performed were summarized in Table 2.

Table 2. Types of dental treatment performed, n = 44. Mean number of treatment per patient rounded to the nearest whole number.

	Number of patient received treatment (proportion)	Mean number of treatment per patient ± 1 SD
Extraction	39 (88.6%)	2 ± 1 teeth
Pulpotomy with stainless steel crown	41 (93.2%)	3 ± 1 teeth
Restorative	44 (100%)	5 ± 2 teeth

5.2. Outcomes of deep extubation

Deep extubation was successfully carried out in forty-two of forty-four patients using the deep extubation decision-making criteria and step-wise protocol checklist demonstrating an overall success rate of 95.5%. The cumulative success rate at each step of the step-wise protocol was summarized in Table 2. One child failed to meet the deep extubation criteria at step #1 due to bucking against the ETT. The bucking stopped after a supplemental bolus of propofol was administered but resumed during step #2. Deep extubation was aborted and patient was extubated awake. Another child also showed signs of bucking against the ETT as he was turned into the lateral decubitus position

(step #3). Deep extubation was aborted and awake extubation was carried out due to persistent bucking against the ETT despite receiving a supplemental bolus of propofol.

Table 3. Cumulative success rate at each step of the deep extubation step-wise protocol, n = 44

Protocol Step	No. of patients proceeding to next step	No. of patients satisfying deep extubation criteria	Aborted	Cumulative Success Rate
Step #1	44	43	0	100%
Step #2	43	43	1	97.7%
Step #3	43	42	0	97.7%
Step #4	42	42	1	95.5%

5.3. Complications

Forty-two children were extubated deep but only forty of them were included when calculating the incidence of complications and the incidence of various airway interventions required (Table 3 and Table 4 respectively). Two children were excluded from the sample pool due significant epistaxis following the removal of nasal ETT. In both cases a nasopharyngeal airway was placed as a stent by the anesthesiologist in charge in attempt to stop the bleeding. There were no major complications such as laryngospasm, bronchospasm, vomiting, aspiration or arrhythmia. In the operatory room (OR), there were four cases of desaturation with SpO_2 less than 95% for longer than 5 seconds as a result of airway obstruction. Two of such cases were relieved with supplemental oxygen and head-tilt-chin-lift while two required additional use of a nasopharyngeal airway (NPA).

One child desaturated to a SpO_2 of 89% soon after he was transported to the post-anesthesia care unit (PACU) as a result of airway obstruction. A NPA and jaw thrust were required to relieve the obstruction and the child's oxygen saturation returned to above 95% with supplemental oxygen. Additionally, fifteen children experienced mild oxygen desaturation (SpO_2 less than 95%) lasting longer than 5 seconds in the PACU. Nine of such cases were due to airway obstruction relieved by head-tilt-chin-lift. However, three children required continuous head support to maintain airway patency and a NPA was placed in those three cases. After emergence from GA, one child had persistent cough with epistaxis. An oxygen saturation trend following extubation was

shown in Figure 3. The median oxygen saturation values remained higher than 95% from end of procedure to discharge with the lowest SpO_2 at 7 minutes post-extubation. No patients had blood pressure and heart rate that exceeded 20% of their preoperative baseline values.

Table 4. Incidence of complications in the operatory room, in PACU and combined. Data in number (proportion), n=40.

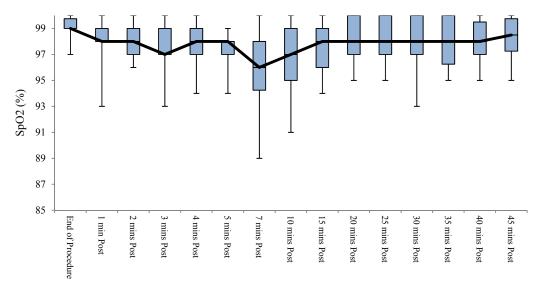|	OR	PACU	OR and PACU
Bronchospasm	0 (0%)	0 (0%)	0 (0%)
Laryngospasm	0 (0%)	0 (0%)	0 (0%)
Desaturation <95% > 5s	4 (10%)	15 (37.5%)	19 (47.5%)
Desaturation <90% > 5s	0 (0%)	1 (2.5%)	1 (2.5%)
Airway Obstructions	4 (10%)	9 (22.5%)	13 (32.5%)
Breath-holding	0 (0%)	0 (0%)	0 (0%)
Persistent Cough > 10s	0 (0%)	1 (2.5%)	1 (2.5%)
Postop Stridor	0 (0%)	0 (0%)	0 (0%)
Vomiting/aspiration	0 (0%)	0 (0%)	0 (0%)
BP>20% of baseline	0 (0%)	0 (0%)	0 (0%)
BP>30% of baseline	0 (0%)	0 (0%)	0 (0%)
BP>40% of baseline	0 (0%)	0 (0%)	0 (0%)
HR>20% of baseline	0 (0%)	0 (0%)	0 (0%)
HR>30% of baseline	0 (0%)	0 (0%)	0 (0%)
HR>40% of baseline	0 (0%)	0 (0%)	0 (0%)
Arrhythmia	0 (0%)	0 (0%)	0 (0%)

Table 5. Incidence of required airway intervention in OR, in PACU and combined. Data in number (proportion), n=40.

	OR	PACU	OR and PACU
NPA (for airway obstruction)	2 (5%)	3 (7.5%)	5 (12.5%)
Supplemental O_2	4 (10%)	16 (40%)	20 (50%)
Head-tilt-chin-lift	4 (10%)	9 (22.5%)	13 (32.5%)
Jaw Thrust	1 (2.5%)	1 (2.5%)	2 (5%)
Tongue Extension	0 (0%)	0 (0%)	0 (0%)
Positive Airway Pressure	0 (0%)	0 (0%)	0 (0%)
Suction	2 (5%)	2 (5%)	4 (10%)
Propofol	0 (0%)	0 (0%)	0 (0%)
Succinylcholine	0 (0%)	0 (0%)	0 (0%)
Salbutamol	0 (0%)	0 (0%)	0 (0%)

5.4. Other outcomes

The mean total procedural time was 121.6 ± 33.6 minutes. On average, it required 4.9 ± 1.5 minutes to extubate, 6.9 ± 1.7 minutes to transfer the patients to PACU and 65.3 ± 16.8 minutes to discharge once the dental procedures were completed (see Table 5). Two outliers were removed when calculating the mean time from end of procedures to PACU due to additional time required (16.5 mins and 18 mins) to manage patient's epistaxis prior to transfer. The mean score for the overall quality of the emergence and recovery between two evaluators was 8.7 out of 10. An intra-class correlation coefficient of 0.81 indicated an almost perfect agreement between the two evaluators based on the interpretations of Landis and Koch (1977). Two patients had postoperative emergence agitation; however, there were no incidents of postoperative emergence delirium.

Figure 3. Oxygen saturation at the end of dental procedure and post-extubation in children who were extubated deep. Data in median with interquartile range.

Table 6. Total procedural time and time required from end of procedure to extubation, to PACU and to discharge. Procedural time = start to completion of dental procedures.

	Mean time ± 1 SD (min)
Total procedural time	121.6 ± 33.6
End of procedure to extubation	4.9 ± 1.5
End of procedure to PACU	6.9 ± 1.7
End of procedure to discharge	65.3 ± 16.8

Chapter 6
Discussion

Appropriate anesthetic depth to carry out deep extubation was achieved in forty-two out of forty-four patients (95.5%) by using the described step-wise protocol. More importantly, the decision-making criteria functioned as a fail-safe screening tool to avoid extubating patients in a light plane of anesthesia where they were between fully awake and deeply anesthetized. This was demonstrated by the lack of passive and active airway reflexes such as breath-holding or coughing immediately following the removal of the ETT in all patients. Any airway instrumentation during light plane of anesthesia can result in undesirable airway responses, namely laryngospasm. Thus, the ability to accurately verify the depth of anesthesia and to recognize when deep extubation should be aborted is crucial to this technique. Although deep extubation was aborted in the two children who had persistent coughing/bucking against the ETT, they were both extubated awake without any major respiratory complications. This advantage differentiates the described technique from many of the suggested methods in the previous studies that did not adequately assess the depth of anesthesia prior to deep extubation.

6.1. Design of the deep extubation decision-making criteria and step-wise protocol checklist

The DAS Guidelines for Management of Tracheal Extubation in 2012 was the first publication to discuss in depth with regards to patient selection and to outline the steps involved in carrying out deep extubation. Although the DAS provided a universal step-by-step deep extubation sequence, the sequence did not contain any information on how to achieve adequate depth of anesthesia while maintaining the patient's spontaneous respiration effort, a step that is fundamental to deep extubation. Moreover, the DAS deep extubation sequence did not contain a tool to assess the patient's level of anesthesia through the whole procedure until the ETT was removed. The step-wise protocol in this study was built upon the one in the DAS while attempting to improve on these shortcomings. As such, the difficult airway risk factors list in the DAS was

modified to create the deep extubation contraindication checklist in this study to better suit the pediatric patient base in dental anesthesia. Due to the elective and ambulatory nature of dental anesthesia, pediatric patients who were unhealthy (ASA > II) were not commonly accepted for treatments, thus allowing our deep extubation contraindication list for dental anesthesia to be simplified. This was especially true with any patient who had known history, risk factors (*e.g.* obesity) or congenital conditions (*e.g.* cervical spine instability) associated with difficult airway.

To deepen the patient's anesthetic level, a total of two propofol boluses, 1 mg/kg each, were recommended. The initial bolus was mandatory and should be given only after ensuring that the patient had no contraindications for deep extubation. The dosage of this initial propofol bolus, unfortunately, was empirical. Although there were data on the effective site concentration of propofol (Eleveld *et al*, 2014) or the level of anesthesia (eg, bispectral index (BIS)) needed for intubation (Messieha, Guirguis and Hanna, 2011), it required the use of a target-fusion pump or a BIS monitor. Furthermore, the concentration of propofol required to eliminate airway reflexes while preserving spontaneous respiration had yet to be determined by research. Despite the empirical nature of the initial propofol bolus dose, it served the purpose of increasing depth of anesthesia beyond that required for the maintenance phase and also allowed the practitioner to gauge the patient's anesthetic depth. Apnea following this initial bolus indicated the absence of airway reflexes (Oberer *et al.*, 2005). Only one supplemental dose of propofol was allowed as a rescue dose if airway reflexes returned prior to completion of deep extubation. Further repeated doses might be unlikely to produce sufficient conditions for deep extubation, and it may be more beneficial to extubate the patient awake.

The first four steps in the step-wise protocol served the purpose of preparing the patient for deep extubation as well as to provide a source of stimuli allowing the anesthesiologist to assess the level of anesthesia using the decision-making criteria checklist. If the patient was not adequately anesthetized, direct laryngoscopy with airway suctioning (step 1) and movement of ETT while turning the patient into the lateral decubitus position (step 3) were both powerful stimuli that could precipitate airway reflexes (Hagberg, Georgi and Krier, 2005). It may be argued that the lateral

decubitus position can potentially create difficulty in mask ventilation and reintubation when complications arise. However, it was suggested that this position was beneficial in the absence of difficult airway as it could protect the airway from aspiration as well as decreasing airway obstruction by positioning the tongue away from the posterior pharyngeal wall (Karmarkar and Varshney, 2008).

Besides serving as a guide for systemic assessment of wakefulness through observing respiratory rate and pattern, airway reflexes and purposeful movements, the decision-making criteria checklist also incorporated evaluation of hemodynamic vitals and spontaneous respiration effort to ensure that the patient was optimized prior to extubation. A higher upper limit (55 mmHg) for end-tidal CO_2 was set in the criteria checklist compared to the normal physiological range (35-45 mmHg). Permissive hypercapnia was an acceptable practice in healthy spontaneous breathing children under GA (Akça, 2006). This was due the combination of hypoventilation induced by anesthetic agents (*e.g.* propofol and remifentnail) and increased airway resistance caused by the small internal diameter of the ETT. Mild to moderate hypercapnia were shown to be well tolerated in healthy children during elective surgeries in the absence of any cardiovascular, intracranial or acid-base abnormalities (Akça, 2006). In contrast, a lower limit for respiration rate was permitted in this protocol as long as the oxygen saturation was above 95%. Normally, children have a higher respiratory rate (15 to 30 breaths per minute) compared to adults to compensate for their high oxygen demand (Fleming *et al.,* 2011). However when under GA, their oxygen demand, particularly their cerebral metabolic rate for oxygen consumption, can drastically decrease (by up to 50%) (Szabo, Luginbuehl and Bissonnette, 2009). Thus anesthetic induced hypoventilation may be considered of limited consequence in healthy children. Unfortunately, the appropriate number for respiration, tidal volume and maximal inspiratory pressure required for successful extubation in pediatric patient following elective surgery have not been well established in the literature. The respiratory parameters in the decision-making criteria of this study were based on validated indices (*eg.* the rapid shallow breathing index and the CORP index) used for determining whether a pediatric patient could be wean from mechanical ventilation in the intensive care unit successfully (Baumeister *et al.*, 1997; Thiagarajan *et al.,* 1999).

6.2. Complications of deep extubation

The two major respiratory complications encountered following deep extubation using the described decision-making criteria and step-wise protocol were airway obstruction and mild oxygen desaturation (SpO_2 < 95% but > 90%). Airway obstruction is a common problem with deep extubation as the level of pharyngeal tone required to maintain airway patency is correlated with the depth of anesthesia (Artime and Hagberg, 2014). Although upper airway obstructions due to soft tissue collapse are often easily managed, it requires vigilant patient monitoring to recognize the problem early to prevent further complications such as oxygen desaturation and potential negative pressure pulmonary edema (Murphy *et al.*, 2008; Udeshi, Cantie and Pierre, 2010). This is particularly important in children, in whom high oxygen demand coupled with low functional residual capacity can rapidly lead to oxygen desaturation (Tourneux *et al.* 2008). The total incidence of airway obstruction was 32.5% in this study. Approximately one-third (incidence of 12.5%) of these obstructions required a nasopharyngeal airway and the remainder were resolved by a simple head-tilt-chin-lift maneuver. Although the incidence may appear to be very high, it was relatively infrequent in comparison to the results reported in other studies. In the literature, the incidence of airway obstruction following deep extubation ranged from 26% to 88% while the incidence of obstruction that required an airway adjunct (*e.g.* oral airway or nasopharyngeal airway) ranged from 8% to 65% (Valley *et al.,* 1999; Valley *et al.*, 2003; Sheta *et al.,* 2011, Shen *et al.*, 2012, von Ungern-Sternberg *et al.*, 2013; Hu *et al.*, 2014). The lower incidence of airway obstructions in this study might be attributable to the use of propofol and remifentanil for maintenance of GA. Studies have shown that both a sub-hypnotic dose (0.3-0.5 mg/kg) of propofol or a slow infusion (0.02-0.05 μg/kg/min) of reminfentanil prior to extubation could potentially blunt airway reflexes and thus lowering the incidence of unwanted airway responses (Batra *et al.*, 2005; Jun, Park and Kim, 2014; Hu *et al.*, 2014). This implied maintaining GA with propofol and remifentanil in this study, hence TIVA, potentially allowed deep extubation to be performed at a lighter depth of anesthesia that resulted in fewer airway obstructions compared to using inhalational anesthetic.

Another common complication following deep extubation that was encountered in this study was mild oxygen desaturation (SpO_2 < 95% but > 90%) in both OR and PACU with an incidence of 47.5%. Many factors can contribute to oxygen desaturation following deep extubation. It this study they were primarily caused by airway obstruction and hypoventilation which were both readily resolved with supplemental oxygen and a simple head-tilt-chin-lift maneuver. There was one patient who had severe desaturation (SpO_2 < 90%) as a result of airway obstruction who also required a NPA for airway support. Although, the incidence of mild oxygen desaturation in this study was within the higher range reported in the literature (16.7% to 55%), there was a much lower incidence of severe desaturation in comparison (12.5% to 25%) (Valley *et al.,* 1999; Valley *et al.*, 2003; von Ungern-Sternberg *et al.*, 2013). The reasons for the relatively high incidence of mild oxygen desaturation encountered in this study might be multifactorial. First, in contrast to most studies, supplemental oxygen was not mandatory following deep extubation in this study unless the patient's SpO_2 fell below 95% as stated in the step-wise protocol. Second, propofol and opioids such as remifentanil were shown to result in greater depression of ventilation in comparison to inhalational agents which were more likely to preserve spontaneous respiration (Haq *et al.,* 2008). Propofol has a context-sensitive half-life of distribution between ten to fifteen minutes following a two to three hours of continuous infusion while remifentanil has no context-sensitive half-life and 99.8% of which will be eliminated in less than seven minutes (Kapila *et al.*, 1995). Despite achieving spontaneous ventilation prior to extubation, the patient could revert to a deeper level of anesthesia following transfer to PACU due to the lack of stimulus to counteract the level of residual anesthesia. Third, although the mean transfer time following extubation to PACU was short (approximately two minutes), patients were susceptible to airway obstruction as positions optimal for sustaining airway patency were difficult to maintain during the transfer. This was illustrated by post-extubation oxygen trend graph (Figure 3.) that showed the lowest median oxygen saturation was at the seven minute interval which coincided with the mean time required to transfer patients to PACU following the completion of dental procedures. Finally, the criteria for oxygen desaturation varied between different studies. In contrast to the five seconds criteria in the current study, von Ungern-Sternberg (2013) quantified mild

oxygen desaturation as SpO_2 below 95% for longer than ten seconds. The stricter criteria in this study might potentially play a role in the higher incidence of oxygen desaturation compared to that reported by von Ungern-Sternberg (26%). If the criterion for mild desaturation was extended to ten seconds in this study, its incidence was lowered to 22.5%. Interestingly, awake extubation may not necessary lead to lower incidence of desaturation as one might believe. Both Patel *et al*. (1991) and von Ungern-Sternberg *et al*. (2013) showed that awake extubation was associated with a lower mean oxygen saturations compared to deep extubation particularly before extubation and for five minutes following extubation. Authors in both studies suspected the lower mean oxygen saturation trend in awake extubation was due to breath-holding and coughing/bucking against ETT followed by atelectasis.

The third most common complication encountered following extubation in this study was epistaxis. There was a large range of the incidence of epistaxis following nasal intubation in children cited in the literature. Elwood *et* al (2002) first reported an incidence of 29% with an untreated ETT whereas Watt *et* al (2007) reported an incidence of 56%. Although epistaxis is generally caused by nasal intubation rather than extubation, it has a major impact on patient management following deep extubation. Uncontrolled nose bleeding in combination with the lack of airway protective reflexes following extubation can create airway obstruction as well as increase the potential risk of aspiration. Two children had significant epistaxis immediately after deep extubation in this study and one occurred during recovery in PACU. The two cases that took place immediately after extubation were uncontrollable with suctioning, topical nasal vasoconstrictor spray (Otrivin) and nasal packing with cotton rolls. The dental anesthesia resident in charge elected to insert a nasopharyngeal airway as a stent to tamponade the bleeding that successfully stopped the bleeding in both cases until the patients regained consciousness. Insertion of NPA was also a potent airway stimulant, and the absence of airway reflexes (*e.g.* coughing, breath-holding, and laryngospasm) indicated that both patients were still under appropriate depth of anesthesia. Unfortunately, as placement of NPA may be a confounding factor that can lower the incidence of other complications namely airway obstruction and oxygen desaturation,

these two patients were excluded when calculating the incidence of complications and airway interventions.

Aspiration was rated as the number one contraindication for deep extubation and the third reason (besides lack of necessity and potential laryngospasm) why anesthesiologists avoid practising deep extubation (Daley, Norman and Coveler, 1999). None of the patients in this study had vomiting or aspiration following deep extubation. This was consistent with the low incidence of perioperative pulmonary aspiration in elective surgery reported in the past literatures (Kelly and Walker, 2015). Furthermore, in all previous studies that examined deep extubation, no aspiration following extubation was reported (Patel *et al.*, 1999; Pounder *et al.*, 1999; Valley *et al.,* 1999; Fagan *et al.,* 2000; Valley *et al.*, 2003; Shen *et al.*, 2012, von Ungern-Stermberg, 2013; Hu *et al.*, 2014). This evidence was in direct contrast to the common belief that aspiration was a significant risk with deep extubation (Daley, Norman and Coveler, 1999). Although one may argue that dental surgeries can potentially contaminate the airway and increase the risk of aspiration, this is not supported by the findings in the literature. Despite the lack of intubation and use of laryngeal mask airways, Nkansah *et al.* (1997) reported no incidence of aspiration in a survey of 2,830,000 cases of deep sedations and GAs within Ontario, Canada. D'Eramo *et al.* (2003) also reported no incidence of aspiration during 80,323 cases of GAs within Massachusetts, United States. Use of throat packs and high volume suction during dental surgeries as well as the lack abdominal straining due to coughing against ETT might play an important role. There was also no incidence of laryngospasm and bronchospasm during or after deep extubation in this study. Although this might be due to lack of airway irritation as the patient's airway protective reflexes returned, such a conclusive statement could not be made based on this study since no control (*e.g.* awake extubation) was used for comparison.

6.3. Future changes to the step-wise deep extubation protocol

The relatively higher incidence of airway obstruction and mild oxygen saturation compared to other complications warrant two changes to the current protocol. Firstly, to minimize the incidence of airway obstruction, a NPA should be placed immediately

after extubation. However, insertion of a NPA is a potent stimulus and may irritate the airway resulting in unwanted airway responses such as laryngospasm. Thus the depth of anesthesia must be assessed with the decision-making criteria prior to NPA insertion. On the other hand, once the NPAs are placed, they are generally well tolerated and cause minimal stimulation (Tong and Smith, 2004). In addition, prophylactic placement of a NPA may potentially help minimize the risk of epistaxis following extubation. Secondly, to minimize oxygen desaturation, the patient should be provided with supplemental O_2 prior to transfer to PACU and until he/she regains consciousness. By filling the patient's functioning residual capacity with 100% oxygen, this can counteract potential episodes of hypoventilation as well as airway obstructions that might occur during the transfer process.

6.4. Limitations

This study had several limitations. First, the anesthetic protocol was standardized in attempt to minimize confounding factors that might affect the outcome of deep extubation. For this reason, anesthetic agents besides propofol and remifentanil were limited. Premedication was restricted to midazolam only. Although oral midazolam has a longer half-life compared to the intramuscular route, both routes of administration were allowed. This was because the oral route was shown to have no impact on emergence and recovery when surgical time was longer than 60 minutes (Brosius and Bannister, 2002; Cote *et al.,* 2002). Ketamine was prohibited in this study due to its potential bronchodilating effects as well as possible association with increased risk of laryngospasm as a result of increased secretions (Hirota and Lambert, 1996; Green *et al.*, 2009). The pharmacokinetic profiles of these effects were not well established in the literature and might affect the incidence of complications following extubation. Fentanyl was restricted in use to within one hour prior to completion of dental procedures as it has a longer duration of action (30 to 45 minutes) compared to propofol and remifentanil and might increase the risk of hypoventilation and airway obstruction following extubation (McClain DA and Hug Jr, 1980). Although the propofol and remifentanil TIVA technique outlined in this study is commonly used in dental anesthesia, many dental anesthesiologists augment this technique with various sedatives. Unfortunately,

the restricted use of other anesthetic agents in this study might have led to an overestimation of the efficacy and safety profile of this protocol as well as limiting its generalizability in outside practice.

The second limitation was related to the patient inclusion and exclusion criteria of this study which was heavily influenced by the patient selection guideline implemented at the University of Toronto, Faculty of Dentistry Surgicenter. As an ambulatory clinic providing GAs for elective dental treatments, the Faculty of Dentistry Surgicenter had strict patient selection criteria in place in order to maximize patient safety and to minimize risk of complications. As a result, unhealthy children (ASA > II) and ones who were not optimized for GA were not commonly accepted for treatments. This included children with reactive airway diseases (*e.g.* URTI within four weeks of treatment and active asthma) and those with potential difficult airways. This limited our ability to assess the efficacy of the deep extubation contraindication checklist since majority of the children who were eligible to participate in this study had no contraindications to deep extubation.

The third limitation was due to the operatory room setup at the Faculty of Dentistry Surgicenter. Ideally prior to extubation, the patient should be transferred from the dental chair to a stretcher and be placed in a position that is optimized for maintaining airway patency during transfer. In addition, patient should be left untouched prior to emergence from anesthesia in order to minimize the amount of stimulations that can precipitate unwanted airway responses such as laryngospasm (Sheta *et al.*, 2011). In the current study, patients were manually carried to PACU by a dental anesthesiologist or a registered nurse following deep extubation due to lack of sufficient space within the operatory room to routinely accommodate a transfer with a stretcher. Although this had no apparent impact on the incidence of laryngospasm and bronchospasm, it might have increased our incidence of airway obstruction and oxygen desaturation as patient's airway patency was difficult to maintain during transfer.

Finally, postoperative stridor can happen immediately after extubation but it can also present hours afterward as a result of laryngeal edema (Miller, Harkin and Bailey, 1995). However, since postoperative follow-up was not included in this study, the incidence of postoperative stridor was potentially underestimated.

6.5. Clinical significance and implications

Deep extubation has long been a technique of controversy. Despite some anesthesiologists advocated the use of deep extubation under suitable clinical situations due to its potential benefits, many believed that extubation should always be performed in awake patients (Daley, Norman and Coveler, 1999, Rassam *et al.*, 2005). Aside from its application, the approach to deep exutbation was also a topic of heavy debate. This was evident by the large degree of variations in the technique amongst anesthesiologists demonstrated in a survey from the UK and Ireland (Rassam *et al.*, 2005). In the past decade a few researchers examined different methods for performing deep extubation using inhalational GA agents, yet no study to date has explored this technique with the use of TIVA (Valley *et al.,* 1999; Valley *et al.*, 2003; Shen *et al.*, 2012 and Hu *et al.*, 2014). Thus, this study is the first to formulate a step-wise protocol on how to achieve an anesthetic level that is suitable for deep extubation using TIVA. In addition, this is also the first study to provide a decision-making criteria checklist to help guide the assessment of anesthetic depth during deep extubation in a systematic manner. Although this protocol was associated with a number of minor respiratory complications, incidences of major respiratory complications were limited. High success rate coupled with minimal complications demonstrated the reliability of the described deep extubation protocol .

Furthermore, the results in the current study also suggested other potential benefits of deep extubation. The short period of time required from termination of the procedure to patient transfer to PACU translated to more efficient operatory room turnover and case flow. This might potentially result in fewer anesthesia or surgical mistakes due to time pressure. Moreover, the incidences of postoperative emergence agitation and delirium were low in this study. Lack of awareness and straining against the ETT might play an important role in providing the smoother emergence seen with deep extubation, that might in turn decrease the likelihood of postoperative emergence agitation and delirium.

Since deep extubation using the described decision-making criteria and the step-wise protocol for deep extubation were demonstrated to be reproducible, it can be implemented in future randomized controlled trial as a comparison against awake

extubation. This may further determine whether timing of extubation will have significant impact on the clinical outcomes such as incidence of respiratory complications and recovery profile in ambulatory pediatric GA for dental treatment.

Lastly, the described protocol in this study was an adaptation from the DAS deep extubation protocol combined with modifications based on limited expert opinions. Despite the demonstrated potential benefits, prior to being qualified as a guideline that can be published and be utilized in clinical practice, it must first meet the standards shared by other airway management guidelines published by internationally recognized scientific societies. A draft copy of this adapted deep extubation protocol should be circulated among members of nationally acknowledged anesthesiologist groups such as the Canadian Anesthesiologists' Society (CAS), Canadian Airway Focus Group (CAFG), Canadian Academy of Dental Anesthesia (CADA) and American Society of Dental Anesthesiologists (ASDA) for comments and revisions prior to submission for publication. Perhaps the availability of a detailed evidence-based protocol that can allow deep extubations to be performed efficiently, safely and reliably may encourage other anesthesiologists to utilize this technique.

Chapter 7
Conclusion

In conclusion, the results of this pilot study demonstrated that the use of the adapted detailed decision-making criteria and step-wise protocol could produce a high success rate of deep extubation in children undergoing ambulatory general anesthesia for elective dental procedures. Upper airway obstructions and mild oxygen desaturation were the two main complications associated with deep extubation in this study but their incidences compared favorably to those reported in the literature. Although these complications were relatively minor in nature, vigilant patient monitoring and early intervention were crucial to prevent further deterioration and potential development of major complications. Both the high success rate and the low incidence of complications suggested that this adapted decision-making criteria and step-wise protocol could provide the foundation for future studies that compare the deep and awake extubation techniques in ambulatory elective pediatric general anesthesia for dental surgery. Finally, it is important to note that deep extubation is not a technique that can be applied universally and requires careful patient selection with various patient, anesthesia and surgical factors in mind. Incorrect use of deep extubation may lead to hazardous complications that outweigh its benefits.

Appendix 1. Study information sheet

Faculty of Dentistry
University of Toronto

Discipline of Dental Anesthesia
416-979-4900 ext 4324

Information Sheet

Title of Study:
Deep Extubation Protocol for Total Intravenous Anesthesia following Ambulatory Elective Dental Surgery in Pediatric Patients: A Pilot Study

January, 2015

Whose study is this?
My name is Dr. Tsz Wai Gavin Ip, and I am a dentist studying to become a specialist in dental anesthesia, meaning I am being trained to put patients to sleep for their dental treatment. I am currently registered in the Dental Anesthesia Masters of Science program at the Faculty of Dentistry, University of Toronto. This is my Masters thesis research project.

What is the subject of the study?
When children receive general anesthesia, it is common practice to place a tube in their windpipe to assist their breathing while they sleep. The term **'intubation'** refers to placement of the breathing tube, while '**extubation'** refers to removal of the breathing tube. Extubation can be done as the children are waking up or while they are still deeply asleep which are referred as '**awake extubation**' and '**deep extubation**', respectively. Both techniques are currently practiced by anesthesiologists. I am doing a study that assesses the feasibility and complications of using our standardized method and protocol checklist for deep extubation in young children who will be asleep under anesthesia for their dental procedures.

How much time does this study take?
This study will be performed at the time of your child's treatment in the Pediatric Surgicentre. **No further appointments are necessary**.

Who can participate in the study?
We are looking for healthy children from ages 4 to 12 to participate in this study. The anesthesia resident will evaluate your child and let you know if he/she is eligible for the

study. If your child is eligible, we will ask if you would be willing to have your child participate in our study.

What will happen if we participate?

If you choose to participate, at the end of your child's dental surgery, the breathing tube will be removed from your child while he/she is deeply asleep by a resident anesthetist using the '**deep extubation'** technique. This technique will be carried out using a standardized method and protocol checklist we have developed for this study. This method is meant to help prevent airway complications during extubation and to improve the quality of post-operative recovery for your child. The quality of your child's recovery will be observed and video recorded following extubation until discharge. The video recordings are for study purposes and will be stored securely and only be viewed by the investigation team.

Will participation change the quality of care for my child?

No. Compared to a non-study participant, the quality of anesthesia and dentistry care will be same. Deep extubation may also be performed in non-study participants according to our standardized method and protocol checklist. The <u>only difference in treatment</u> is that the <u>timing </u>of extubation for your child is predetermined and the quality of recovery from anesthesia is judged and video recorded between the time of extubation and the time of discharge. Before you decide to participate, you will also have the opportunity to ask any questions and have them answered.

What happens if I don't want my child to participate in the study?

Your participation in this study and that of your child are **completely voluntary** and you have the option of **withdrawing prior to induction of general anesthesia or any time after extubation**. Your participation **cannot be withdrawn during the procedure** due to safety reasons. **Your participation status will not affect the care for your child** that includes the dental treatment, the delivery of a safe anesthetic, and the decision to use an alternate extubation technique (awake) if more appropriate. All treatments regardless of participation will be performed in accordance to the Guidelines set by the Royal College of Dental Surgeons of Ontario.

What are the risks and benefits of participation?

The potential risks and complications of this study are the routine and usual complications of <u>placement</u> of a breathing tube. The most common complications include prolonged coughing, change in voice and a squeaky or wheezing sound with breathing. These complications are mild and temporary and may last for 1 to 2 days following anesthesia. The resident anesthetist and the supervising staff anesthetist are well trained and will properly and safely manage your child in the event of any complications. **There is no direct benefit to you or your child for participation in this**

study. However, your participation can help us refine our deep extubation protocol and technique and may potentially benefit children undergoing anesthesia in the future.

What will be done with the information you collect?

Your privacy and confidentiality are always protected. You and your child's personal and health information will remain secure, private and confidential and will be used internally within the dental school in the context of this research project. The protection of your personal health information is governed by law under the Ontario *Personal Health Information Protection Act (PHIPA)*. This act sets out rules that must be followed when collecting, using or sharing personal health information for research purposes. Information such as anesthetic records and treatment will be placed in the chart as per good record keeping practice. All information including digital video recordings will be kept in a safe, locked drawer in the dental school until the conclusion of the study. The digital video recordings will only be viewed by the investigation team and will not be presented or published. A faculty identification chart number will be assigned to your child so that his or her information will remain anonymous in all communications, presentations and publications. All paper and electronic data related to this study will be stored for two years after publication of study findings. The results from this study will be presented in a thesis dissertation, at scientific meetings, and/or teaching in educational and academic settings. We plan to publish the results in a scientific journal at the conclusion of the study. Paper copies of all anesthetic records will be stored securely for 10 years after your child's last treatment as per usual protocol according to the Royal College of Dental Surgeon of Ontario guidelines. Electronic copies of all anesthetic records, however, will be stored in the password-protected faculty system indefinitely as per the faculty protocol and are accessible by your child health/dental care providers in the faculty of dentistry.

Contact Information

The following contacts may be kept for your reference:

- If you have any questions about your rights as participants, you may contact the Office of Research Ethics at ethics.review@utoronto.ca or 416-946-3273.
- If you have any questions about the study, you may directly email **Dr.Tsz Wai Gavin Ip** (dental anesthesia resident) gavin.ip@mail.utoronto.ca or call 416-979-4900 ext. 4324 OR **Dr.Carilynne Yarascavitch** (Head of the Discipline of Dental Anesthesia, University of Toronto Faculty of Dentistry) c.yarascavitch@dentistry.utoronto.ca or call 416-979-4900 ext. 4324 OR **Dr. Michael J. Casas,** (Thesis project supervisor) michael.casas@sickkids.ca or call 416-813-6018

If you are interested in the results of this study, you may also request a summary of the research findings via my email.

Appendix 2. Informed consent form

Faculty of Dentistry
University of Toronto

Discipline of Dental Anesthesia
416-979-4900 ext 4324

Consent Form

Principal Investigator: Dr. Tsz Wai Gavin Ip, D.D.S., M.Sc. Candidate, Dental Anesthesia, Faculty of Dentistry, University of Toronto

Research Supervisor: Dr. Michael J.Casas, D.D.S., M.Sc., FRCDC

Study title: Deep Extubation Protocol for Total Intravenous Anesthesia following Ambulatory Elective Dental Surgery in Pediatric Patients: A Pilot Study

Purpose of Research: This study investigates the perioperative complications of deep extubation using a standard protocol in the context of intubated pediatric ambulatory elective general anesthesia for dental surgery

I _____, the legal guardian and/or parent of _____ have listened to the explanations about the purpose of the study and what it entails. I have had an opportunity to discuss any concerns or questions that I may have. I am satisfied with the explanation that I have been given. I understand that the possible complications in participating in this study involving 'deep extubation' are similar to the routine practice of breathing tube removal. These include prolonged coughing, change in voice, post-anesthesia stridor and reflexive airway obstructions.

I understand and am willing to accept the risks to participate in this study. I understand that neither I nor my child is obligated to complete the study once it begins and that participation is voluntary and that we may withdraw at any time.

Any information that is acquired about my child during this study will be confidential and neither the name nor any other identifying information will be made available to anyone other than the investigators, nor will such information appear in any publications.

I have read and understood the attached information sheet. I have had an opportunity to ask any questions I may have had, and my questions have been answered to my satisfaction.

_____   _____
Date   Date

_____   _____
Signature of Witness   Signature of Parent/legal guardian

_____   _____
Print Name   Print Name

Appendix 3. Assent form

Faculty of Dentistry
University of Toronto

Discipline of Dental Anesthesia
416-979-4900 ext 4324

Assent Form

Principal Investigator: Dr. Tsz Wai Gavin Ip

Research Supervisor: Dr. Michael J.Casas

Study title: Deep Extubation Protocol for Total Intravenous Anesthesia following Ambulatory Elective Dental Surgery in Pediatric Patients: A Pilot Study

Why are we doing this study?
When children go to sleep to get their teeth fixed, we usually place a tube to help them breathe while they are sleeping. We are doing a study to improve the way we remove the breathing tube while you are still deeply asleep to see if we can make your wake up more comfortable.

What happen during the study?
When your teeth are fixed, we will remove the breathing tube while you are still deeply asleep. Then, you will be moved to the recovery room where you will wake up slowly. While you are waking up, our nurse will be there to take care of you. You may have coughing, hoarse voice and/or may hear a squeaky or strange sound while breathing after you wake up. When this happens, it usually lasts for a short period of time and you will feel normal soon. A video camera will be set up to record your stay in the recovery room to allow us to study your wake up.

Are there good things and bad things about the study?
The good thing about this study is that since the breathing tube will be removed while you are still deeply asleep, you will not remember the breathing tube. You will not feel the breathing tube tickling your throat so when you wake up it may be more comfortable. There are <u>no</u> bad things about this study.

Who will know about what I did in the study?
Only the sleep doctors and the nurse will be able to see your results in this study. The video recording of your wake up will only be viewed by the sleep doctors. After this study is completed, your results may be published in an article that scientists and other doctors will read. Your name or other information about you will not be in the article.

Can I decide if I want to be in the study?

Nobody will be angry or upset if you do not want to be in the study. We are talking to your parent/legal guardians about the study and you should talk to them about it too. Even if you decide to participate now, you will still have the choice to not be in the study before you go to sleep and after you wake up.

"I was present when _____ read this form and said that he or she agreed, or assented, to take part in this study".

_____   _____
Date   Date

_____   _____
Signature of Witness   Signature of Person who Obtained Assent

_____   _____
Print Name   Print Name

Appendix 4. Patient inclusion and exclusion criteria

Appendix 4.1. American Society of Anesthesiologists (ASA) physical status classification
> (ASA, 1963)

I. A normal healthy patient

II. A patient with mild system disease

III. A patient with a severe systemic disease that limits activity but is not incapacitating

IV. A patient with an incapacitating system disease that is a constant threat to life

V. A moribund patient not expected to survive 24 hours with or without an operation

E. Patient who require emergency operation

Appendix 4.2. Risk factors for malignant hyperthermia
> (Fischer, Bader and Sweitzer, 2010)

1. History of malignant hyperthermia or known positive susceptibility test results

2. Family history of malignant hyperthermia

3. Disorders associated with increased malignant hyperthermia risk including central core disease, King-Denborough syndrome and Multiminicore disease

4. Neuromuscular disorders such as Duchenne's, Becker's and myotonic muscular dystrophy, that can potentially precipitate malignant hyperthermia-like metabolic reactions upon use of inhalational anesthetics and succinylcholine

Appendix 4.3. Risk factors for perioperative respiratory complications
> (Ungern-Sternberg *et al*, 2010)

1. Moderate or severe asthma defined by the 2012 British Thoracic Society guidelines on the management of asthma (See Appendix 5.1)

2. Upper respiratory tract infection < 2 weeks

3. Active allergies which may lead to airway inflammation or increased nasal discharge (*e.g.* asthma, allergic rhinitis/conjunctivitis)

Appendix 4.4. Risk factors for potential difficult airway during extubation (DAS Guidelines for the management of tracheal extubation, 2012)

1. Difficult ventilation (*ie.* cannot achieve adequate bag-mask ventilation (BMV) without using 2 hands for masking holding or using adjunctive airway device such as oral-airways)

2. Difficult intubation (*ie.* indication based on past anesthetic record, airway malformations, head and neck pathologies, cervical spine damage/instability or syndromes associated with difficult airways)

3. Presence of nasal polyps, adenoids and/or Brodsky scale 4 tonsils (See Appendix 5.2)

4. History of excessive nasopharyngeal bleeding during intubation

5. Obese with BMI > 95th percentile

6. Obstructive sleep apnea syndrome (OSAS) (See Appendix 5.3)

7. Uncontrolled gastroesophageal refleux disease (GERD)

Appendix 5. Screening criteria and questionnaires

Appendix 5.1: Screening criteria and classification of asthma
(Adapted from British Thoracic Society Guidelines on the
Management of Asthma, 2012 and National Heart, Lung, and Blood
Institute, 2007)

Classifications	Clinical Signs and Symptoms	Pharmacological Treatment
Mild Intermittent Step 1 Treatment	-Signs and symptoms ≤ 2 times / week -Generally asymptomatic with normal peak flows between exacerbations -Exacerbation brief, although intensity may vary -Nighttime symptoms occur ≤ 2 times / month -FEV_1 or PEFR ≥ 80% or more of predicted value	-Short-acting inhaled β_2 agonist (bronchodilator), as needed ->10-12 puffs / day indicates poorly controlled asthma
Mild Persistent Step 2 Treatment	-Signs and symptoms ≥ 2 times / week but < once / day -Exacerbations may affect activity -Nighttime symptoms occur ≥ 2 times / month -FEV_1 or PEFR ≥ 80% or more of predicted value	-Addition of inhaled steroids in addition to inhaled short acting β_2 agonist -Budesonide or beclomethasone 100mcg BID or fluticasone 50mcg BID or equivalent
Moderate Persistent Step 3 Treatment	-Daily symptoms -Daily use of short-acting β_2 agonist -Exacerbations that affect activity occur ≥ 2 times / week and may last for days -Nighttime symptoms occur ≥ once / week -FEV_1 or PEFR 60% to 80% or more of predicted value	-Addition of inhaled long acting β_2 agonist to inhaled steroids and short acting β_2 agonist -Increased inhaled steroids -Addition of leukotriene antagonists or theophylline
Severe Persistent Step 4 Treatment	-Continuous signs and symptoms, frequently exacerbated -Frequent nighttime symptoms -Limited physical activity -FEV_1 or PEFR ≤ 60% or more of predicted value	-Increased inhaled steroid up to 800mcg of budesonide equivalent / day -Continuous or frequent use of oral steroids

Appendix 5.2: Brodsky Grading Scale for Tonsillar Size
(Adapted from Ng *et al.*, 2010)

Grade 0: tonsils within the tonsillar fossa

Grade 1: tonsils just outside of the tonsillar fossa and occupy ≤25% of the oropharyngeal
width)

Grade 2: tonsils occupy 26%-50% of the oropharyngeal width

Grade 3: tonsils occupy 51%-75% of the oropharyngeal width

Grade 4: tonsils occupy >75% of the oropharyngeal width

Appendix 5.3: Screening Criteria for Obstructive Sleep Apnea
(Adapted from Schwengel *et al.,* 2009)

1. Does your child have difficulty breathing during sleep?
2. Have you observed symptoms of apnea? (no chest/abdominal movements or blue lips)
3. Have you observed sweating while your child sleeps?
4. Does your child have restless sleep?
5. Does your child breathe through his/her mouth when awake?
6. Does your child snore while he/she sleeps? Does he/she snore every night?
7. Does your child have behavioural problems?
8. Does your child have persistent daytime sleepiness?

Appendix 6. Deep extubation criteria and step-wise deep extubation protocol checklist

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ad

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☐ At completion of dental treatment 100% inspired O_2
☐ Verify location of emergency drugs for laryngospasm (propofol, succinylcholine, atropine)

Contraindications to deep extubation?

Contraindicated   Not Contraindicated

☐ Residual neuromuscular blockade
☐ Difficult ventilation
☐ Difficult intubation
☐ Nasal polyps, enlarged adenoids and/or tonsils   or tonsils
(Brodsky scale 4)
☐ Obese with BMI > 95th Percentile
☐ OSAS
☐ Uncontrolled GERD
☐ No hemostasis

Awake Extubation   Deep Extubation

☐ Give Propofol 1mg/kg bolus

"Deep Extubation **Criteria**"

"Step-wise Deep Extubation **Protocol**"

ent

d

Patient satisfies these "Deep Extubation **Criteria**"?

Patient stable with adequate spontaneous ventilation (ASV)?
- ☐ Stable hemodynamics
- ☐ $SPO_2 \geq 95\%$
- ☐ Spontaneous breathing
- ☐ Adequate tidal volumes (>6mL/kg)
- ☐ Respiratory rate between 8-25bpm
- ☐ End-tidal CO2 <55mmHg
- ☐ Maximal inspiratory pressure > -15cm H2O

ing

Presence of patient response?
- ☐ Regular respiratory rate & **no change** in pattern
- ☐ No coughing
- ☐ No breath-holding
- ☐ No gagging/bucking on ETT
- ☐ Lack of facial grimacing
- ☐ Lack of spontaneous eyes opening
- ☐ Lack of purposeful body movements

d

Yes | No

if

Patient stable with ASV?

d to

Yes | No

Wait for return of ASV

Supplemental propofol bolus given?

d to

Yes | No

Abort and extubate fully awake

Give supplemental propofol bolus **(1mg/kg)** according to instructions

awake

Appendix 7. Modified Aldrete Score
(Adapted from Aldrete and Kroulik,1970)

Parameters	Description of Patient	Score
Activity level	Moves all extremities voluntarily/on command	2
	Moves 2 extremities	1
	Cannot move extremities	0
Respirations	Breathes deeply and coughs freely	2
	Is dyspneic, with shallow, limited breathing	1
	Is apneic	0
Circulations (blood pressure)	Is 20mmHg > preanesthetic level	2
	Is 20 to 50mmHg > preanesthetic level	1
	Is 50mmHg > preanesthetic level	0
Consciousness	Is fully awake	2
	Is arousable on calling	1
	Is not responding	0
Oxygen saturation (pulse oxymetry)	Has level >90% when breathing room air	2
	Requires supplemental O_2 to maintain level >90%	1
	Has level <90% with O_2 supplementation	0

Appendix 8. Clinical outcome measures and definitions

Laryngospasm	Defined as partial or complete glottis closure reflex leading to upper airway obstruction not amendable to head-tilt-chin-lift, jaw thrust, use of airway adjuncts.
Bronchospasm	Defined as spasmodic contraction of bronchial smooth muscle leading to increased respiratory effort during expiration with wheezing on auscultation.
Airway Obstructions	Defined as partial or complete airway obstruction due to pharyngeal collapse with increased respiratory efforts and/or snoring that is amendable to chin-lift, jaw thrust and/or use of airway adjuncts.
Breath-holding/Apnea (>5sec)	Defined as breath-holding or lack of breathing effort for five seconds or more
Bucking	Defined as series of persistent, forceful gagging reflexes against an ETT that mimics a Valsalva maneuver.
Postoperative Stridor	Defined as a harsh respiratory sound during inspiration due to narrowing or partial obstruction of the upper airway

Appendix 9. Clinical data reporting form

Types of perioperative respiratory complications:

Laryngospasm **(L)**	Desaturation <95% > 5s **(D95>5)**	Cyanosis **(C)**
Bronchospasm **(B)**	Airway Obstruction **(AO)**	Persistent Coughing >10s **(PC)**
Desaturation <90% > 5s **(D90>5)**	Breath-holding > 5s **(BH)**	Postoperative Stridor **(S)**

Clinical Data Reporting Form   **Pg.1**

Patient no:_____   **Date:**_____

Sex: M / F   **Age:**___   **Weight:**_____Kg   **ASA:** I / II

Baseline Vitals:

BP:_____   **HR:**_____   **SPO$_2$:**_____

Time from end of procedure to: **Extubation:**_____:_____   **PACU:**_____:_____
                                                               Discharge:_____:_____

Please record any perioperative complications, necessary airway interventions (AI) and the time on timer in the operatory room and recovery room following anesthetic termination using the legend provided at the top and bottom of this form:

Events in operatory room:

Time on timer (hr:min)	Types of Complications	Types of AI

Other types of perioperative complications:

BP > 20% baseline **(BP>20)**	HR > 20% baseline **(HR >20)**	Arrhythmia **(A)**
BP > 30% baseline **(BP>30)**	HR > 30% baseline **(HR >30)**	Vomiting/Aspiration **(VP)**
BP > 40% baseline **(BP>40)**	HR > 40% baseline **(HR >40)**	

Types of airway interventions

Maneuvers: **Emergency Drugs: (Type/Route/Dosage)**

Chin Lifts **(CL)**	Tongue Extension **(TE)**	Propofol **(P)**
Head Tilt **(HT)**	Positive Pressure Ventilation **(PPV)**	Succinylcholine **(SCH)**
Jaw Thrust **(JT)**		Salbutamol **(S)**

Types of perioperative respiratory complicatons:		
Laryngospasm **(L)**	Desaturation <95% > 5s **(D95>5)**	Cyanosis **(C)**
Bronchospasm **(B)**	Airway Obstruction **(AO)**	Persistent Coughing >10s **(PC)**
Desaturation <90% > 5s **(D90>5)**	Breath-holding > 5s **(BH)**	Postoperative Stridor **(S)**

Clinical Data Reporting Form   Pg.2

Events in the recovery room:

Time on timer (hr:min)	Types of Complications	Types of AI

Other types of perioperative complications:		
BP > 20% baseline **(BP>20)**	HR > 20% baseline **(HR >20)**	Arrhythmia **(A)**
BP > 30% baseline **(BP>30)**	HR > 30% baseline **(HR >30)**	Vomiting/Aspiration **(VP)**
BP > 40% baseline **(BP>40)**	HR > 40% baseline **(HR >40)**	

Types of airway interventions

Maneuvers:		Emergency Drugs: (Type/Route/Dosage)
Chin Lifts **(CL)**	Tongue Extension **(TE)**	Propofol **(P)**
Head Tilt **(HT)**	Positive Pressure Ventilation **(PPV)**	Succinylcholine **(SCH)**
Jaw Thrust **(JT)**		Salbutamol **(S)**

Appendix 10. Video data assessment form

Types of perioperative respiratory complications:

Laryngospasm **(L)**	Desaturation <95% > 5s **(D95>5)**	Cyanosis **(C)**
Bronchospasm **(B)**	Airway Obstruction **(AO)**	Persistent Coughing/Bucking >10s **(PC)**
Desaturation <90% > 5s **(D90>5)**	Breath-holding > 5s **(BH)**	Postoperative Stridor **(S)**

<u>Video Data Assessment Form</u>   **Pg.1**

Patient no:_____   **Date:**_____

Sex: M / F   **Age:**____   **Weight:**_____Kg   **ASA:** I / II

Baseline Vitals:

BP:_____   **HR:**_____   **SPO₂:**_____

Please record any perioperative complications, necessary airway interventions (AI) and the time on timer in the operatory room and recovery room following anesthetic termination using the legend provided at the top and bottom of this form:

Events in operatory room:

Time on timer (hr:min)	Types of Complications	Types of AI

Other types of perioperative complications:

BP > 20% baseline **(BP>20)**	HR > 20% baseline **(HR >20)**	Arrhythmia **(A)**
BP > 30% baseline **(BP>30)**	HR > 30% baseline **(HR >30)**	PONV
BP > 40% baseline **(BP>40)**	HR > 40% baseline **(HR >40)**	Vomiting/Aspiration **(VP)**

Types of airway interventions

Maneuvers: **Emergency Drugs: (Type/Route/Dosage)**

Chin Lifts **(CL)**	Tongue Extension **(TE)**	Propofol **(P)**
Head Tilt **(HT)**	Positive Pressure Ventilation **(PPV)**	Succinylcholine **(SCH)**
Jaw Thrust **(JT)**		Salbutamol **(S)**

Types of perioperative respiratory complications:		
Laryngospasm **(L)**	Desaturation <95% > 5s **(D95>5)**	Cyanosis **(C)**
Bronchospasm **(B)**	Airway Obstruction **(AO)**	Persistent Coughing/Bucking >10s **(PC)**
Desaturation <90% > 5s **(D90>5)**	Breath-holding > 5s **(BH)**	Postoperative Stridor **(S)**

Video Data Assessment Form   **Pg.2**

Events in the recovery room:

Time on timer (hr:min)	Types of Complications	Types of AI

Pediatric Anesthesia Emergence Delirium (PAED) Score					
Behaviour	**Not at all**	**Just a little**	**Quite a bit**	**Very much**	**Extremely**
Makes eye contact with caregiver	4	3	2	1	0
Actions are purposeful	4	3	2	1	0
Aware of surroundings	4	3	2	1	0
Restless	0	1	2	3	4
Inconsolable	0	1	2	3	4

Emergence delirium is defined as a Pediatric Anaeshtesia Emergence Delirium (PAED) score of ≥ 12 for ≥ 5mins duration despite active calming efforts

PAED SCORE:_____

Please rate the overall quality of the emergence and recovery by circling the number using the 10 level Likert scale below where 1 indicates poor quality and 10 indicates excellent quality:

POOR   1   2   3   4   5   6   7   8   9   10   **EXCELLENT**

Other types of perioperative complications:		
BP > 20% baseline **(BP>20)**	HR > 20% baseline **(HR >20)**	Arryhthmia **(A)**
BP > 30% baseline **(BP>30)**	HR > 30% baseline **(HR >30)**	PONV
BP > 40% baseline **(BP>40)**	HR > 40% baseline **(HR >40)**	Vomiting/Aspiration **(VP)**

Types of airway interventions
Maneuvers: **Emergency Drugs: (Type/Route/Dosage)**

Chin Lifts **(CL)**	Tongue Extension **(TE)**	Propofol **(P)**
Head Tilt **(HT)**	Positive Pressure Ventilation **(PPV)**	Succinylcholine **(SCH)**
Jaw Thrust **(JT)**		Salbutamol **(S)**

Appendix 11: Ethics approval

UNIVERSITY OF TORONTO

OFFICE OF THE VICE-PRESIDENT,
RESEARCH AND INNOVATION

PROTOCOL REFERENCE # 32213

October 22, 2015

Dr. Michael Casas
FACULTY OF DENTISTRY

Dr. Tsz Wai Gavin Ip
FACULTY OF DENTISTRY

Dear Dr. Casas and Dr. Tsz Wai Gavin Ip,

Re: Your research protocol entitled, "Deep extubation protocol for total intravenous anesthesia following ambulatory elective dental surgery in pediatric patients: A pilot study"

ETHICS APPROVAL	Original Approval Date: October 22, 2015 Expiry Date: October 21, 2016 Continuing Review Level: 1

We are writing to advise you that the Health Sciences Research Ethics Board (REB) has granted approval to the above-named research protocol under the REB's delegated review process. Your protocol has been approved for a period of **one year** and ongoing research under this protocol must be renewed prior to the expiry date.

Any changes to the approved protocol or consent materials must be reviewed and approved through the amendment process prior to its implementation. Any adverse or unanticipated events in the research should be reported to the Office of Research Ethics as soon as possible.

Please ensure that you submit an Annual Renewal Form or a Study Completion Report 15 to 30 days prior to the expiry date of your current ethics approval. Note that annual renewals for studies cannot be accepted more than 30 days prior to the date of expiry.

If your research is funded by a third party, please contact the assigned Research Funding Officer in Research Services to ensure that your funds are released.

Best wishes for the successful completion of your research.

Yours sincerely,

Elizabeth Peter, Ph.D.
REB Chair

Daniel Gyewu
REB Manager

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