High-Frequency Ultrasound:

A Novel Diagnostic Tool to Measure Pediatric Tonsils in Three Dimensions

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Abstract

Objective

Various pathologies can affect the palatine tonsils. Ultrasound is a commonly used modality for assessing head and neck masses in children, however its use in tonsillar evaluation has not been widely explored. The objective of this thesis was to measure three-dimensional tonsillar size with ultrasound, in centimeters, and correlate these measurements with actual ex-vivo dimensions on pathology specimens.

Study Design

A prospective cohort study was done.

Setting

The study was set in a tertiary care children's hospital.

Subjects and Methods

Children undergoing tonsillectomy were included in the study. Transcervical high-frequency ultrasound (HFU) was performed prior to surgery to obtain three-dimensional measurements of the right and left palatine tonsils. Mean sizes were compared to ex-vivo tonsil measurements and correlations were obtained.

Results

Seventy-five consecutive children underwent a transcervical HFU, yielding a total of 150 tonsils analyzed. The mean differences between HFU and pathology measurements were -0.08 cm and -0.24 cm for the right and left cranio-caudal axes, -0.19 cm and -0.18 cm for the right and left medio-lateral axes, and 0.05 cm and 0.03 cm for the right and left antero-posterior axes. Correlation coefficients between ultrasound and pathology measurements were all above 0.5.

Conclusion

HFU can accurately measure the size of pediatric tonsils in three dimensions.

Résumé

Objectif

Une grande variété de pathologies peut affecter les amygdales palatines. L'échographie est une modalité couramment utilisée pour évaluer les masses cervico-faciales chez les enfants. Cependant, son utilisation dans l'évaluation des amygdales n'a pas été largement explorée. L'objectif de cette étude était de mesurer la taille des amygdales en trois dimensions avec l'échographie, en centimètres, et de corréler ces mesures avec les dimensions réelles ex-vivo sur des spécimens pathologiques.

Type d'étude

Nous avons réalisé une étude de cohorte prospective.

Réglage

L'étude a été réalisée dans un hôpital pour enfants en soins tertiaires.

Sujets et méthodes

Les enfants ayant subi une amygdalectomie ont été inclus dans l'étude. Une échographie transcervicale à haute fréquence (EHF) a été réalisée avant l'opération afin d'obtenir des mesures en trois dimensions des amygdales palatines. Les tailles moyennes ont été comparées aux mesures ex-vivo des amygdales et des corrélations ont été obtenues.

Résultats

75 enfants consécutifs ont subi une EHF transcervicale, avec un total de 150 amygdales analysées. Les différences moyennes entre les mesures de EHF et de pathologie étaient de -0,08 cm et -0,24 cm pour les axes cranio-caudaux droit et gauche, de -0,19 cm et -0,18 cm pour les axes médio-latéraux droit et gauche, et de 0,05 cm et 0,03 cm pour les axes antéro-postérieurs droit et gauche. Les coefficients de corrélation entre les mesures obtenues en échographie et en pathologie étaient tous supérieurs à 0,5.

Conclusion

L'EHF peut mesurer avec précision la taille des amygdales pédiatriques en trois dimensions.

Preface

Contribution of authors

Idea for project: Emily Kay-Rivest (EKR). Project supervisors: Dr. Sam J. Daniel (SJD) and Dr. Christine Saint-Martin (CSM). EKR, SJD and CSM participated in the conception and design of study. EKR performed the acquisition of data and patient recruitment. CSM helped in the ultrasound training process, along with the group of ultrasound technologists at the Montreal Children's Hospital. CSM also revised all ultrasound measurements. EKR drafted both manuscripts under supervision. Figures, tables and photos were created by EKR and CSM. Statistical analysis was done by ZhuoYu Wang. Dr. Maida Sewitch and Dr. Bernard Segal helped with the study design and review of the manuscripts.

Disclosures

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CHAPTER 1: Introduction

1.1 Rationale

A wide variety of pathologies can affect the palatine tonsils in children including tonsillar infections, hypertrophy and rarely neoplasms. In most children, tonsillar hypertrophy is thought to be associated with the spectrum of sleep-disordered breathing[1,2]. In rare cases, tonsillar asymmetry can be the presenting sign of a tonsillar lymphoma[3-7].

Ultrasound is a commonly used modality to assess head and neck masses[8]. However, for the examination of palatine tonsils, ultrasound is rarely used. Its use has been reported in the adult otolaryngology and emergency medicine literature, to differentiate a peritonsillar phlegmon from an abscess[9-23]. In the differentiation between tonsillar infections, ultrasound has shown excellent sensitivity and specificity[10,16,17,19-23]. Although these studies were among small cohorts of patients, it seems that ultrasound may be an acceptable imaging modality to assess tonsillar size and pathology.

In the pediatric realm, the first report of tonsillar ultrasound use was an article by Bandarkar et al., where the authors described the ultrasound findings of tonsillar infections in children, with detailed photographic descriptions[13]. They used transcervical ultrasound to differentiate tonsillitis, peritonsillar cellulitis, intratonsillar abscess and peritonsillar abscess. They concluded that transcervical ultrasound can easily and accurately assess the palatine tonsils and is a feasible and non-invasive option in children.

Despite showing great promise for identifying tonsillar pathologies, there are no previous studies that have confirmed the accuracy of tonsillar ultrasound in measuring tonsillar size in three dimensions. As a result, this thesis set out to explore these issues, leading to the thesis objectives highlighted in the following section.

1.2 Objectives

The main objective of this thesis was to measure three-dimensional tonsillar size with ultrasound, and to correlate the measurements with actual ex-vivo dimensions, as measured by pathology. The second objective was to perform comprehensive literature reviews of tonsillar pathologies, as well as of the tonsillar ultrasound literature. The third objective was to provide a comprehensive, user-friendly guide to performing tonsillar ultrasound.

1.3 Thesis outline

Chapter 2 presents a review of tonsillar pathologies. Chapter 3 presents a scoping review of previous usage of ultrasound for tonsillar imaging (manuscript 1). Chapter 4 describes the use of high-frequency ultrasound to measure pediatric tonsils three-dimensionally (manuscript 2). Chapter 5 contains an overall discussion with future directions. Chapter 6 presents overall conclusions and lists claims of originality. Chapter 7 contains the bibliography. Chapter 8 lists abbreviations. Various appendices are at the end of the thesis.

CHAPTER 2 – Tonsillar Pathologies: A Comprehensive Review of the Literature

This chapter gives a basic description of tonsillar anatomy and physiology as well as a review of diseases that affect the tonsils.

2.1 Anatomy and Physiology of the Tonsils

The palatine tonsils are made up of lymphoid tissue and located on the lateral pharyngeal wall in the oropharynx[24]. They are bound anteriorly by the palatoglossus muscle, and posteriorly by the palatopharyngeus muscle. The tonsil extends superiorly to the soft palate, and inferiorly to the lateral aspect of the tongue. The palatine tonsils are part of a circumferential ring of lymphoid tissue, called Waldeyer's ring[24]. Waldeyer's ring consists of the adenoids (or pharyngeal tonsil), palatine tonsils, lingual tonsils and tubal tonsils (or Gerlach's tonsils). The palatine tonsils are what we consider in lay terms as "tonsils".

The tonsil is covered by a capsule, which is formed by pharyngobasilar fascia. The medial surface of the tonsil is covered by a stratified squamous epithelium, which extends from the deep tonsillar surface, where it forms crypts.

Numerous vessels feed the tonsils, including the following: the tonsillar artery, ascending pharyngeal artery, tonsillar branch of the facial artery, dorsal lingual branch of the lingual artery and ascending palatine branches of the facial artery. The venous drainage occurs through the peritonsillar plexus, which drains into the lingual and pharyngeal veins, and eventually into the jugular vein[25]. There are no afferent lymphatic within the tonsils. Efferent lymphatics go to the jugulodigastric nodes and upper cervical nodes.

The tonsils arise from both endodermal and mesodermal layers of the embryo, developing in the third month of fetal life. The size of the tonsil is believed to grow with age, with a rapid phase of growth at five or six years of life.

The tonsils are considered secondary lymphoid organs. They contain B-cells predominantly. There is evidence that although the tonsils are not essential immunological organs, they do play a role in supplying immunoglobulin A precursor cells[26,27]. Despite this, it remains unclear whether removing the tonsils lead to a negative outcome on immunological status. Byars et al. studied 1.2 million children and found a possible association between increased respiratory infection and adenotonsillectomy[28]. These findings have not been replicated.

2.2 Tonsillar hypertrophy and Sleep-Disordered Breathing

Sleep-disordered breathing (SDB) contains a spectrum of diseases, varying in severity. It can range from simple snoring, all the way to obstructive sleep apnea syndrome (OSAS)[29]. It is defined as any abnormal respiratory pattern during sleep. Snoring is believed to occur in about 10-12% of children, whereas the estimated prevalence of OSAS is thought to be 1-3%[30-32]. Overall, SDB is believed to lead to changes in daytime behaviours, performance in school and overall quality of life of children[33-39].

The pathophysiology of SDB includes: adenotonsillar hyperplasia most commonly, followed by obesity, craniofacial anomalies, various congenital syndromes, prematurity, daycare exposure and frequent upper respiratory tract infections, and smoking exposure[40].

Tonsil and adenoid hyperplasia, the most common cause of SDB, may be a normal phenomenon in growing children. Usually, the hypertrophic tissue tends to dissipate in early adulthood. The most commonly used grading system used to define tonsillar size is the Brodsky scale[41]. 0 are tonsils within the tonsillar fossa, 1+ are tonsils just outside the fossa and occupying less than 25% of the width between the two anterior pillars, 2+ are tonsils which take up 26-50% of the pharynx, 3+ 51-75% of the pharynx, and finally 4+ which take up over 75% of the pharynx[42].

Usually, tonsillar hypertrophy is observed, if it does not cause any symptoms. However, in a child with SDB, depending on the severity of the disease, adenotonsillectomy (removal of the tonsils and adenoids under general anesthesia) may be considered.

Practice guidelines exist to outline indications for adenotonsillectomy[43]. The guidelines are clear for doing a tonsillectomy in the context of chronic infection. On the other hand, the guidelines are less clear in the context of SDB.

2.3 <u>Tonsillar and peritonsillar infections</u>

Many diseases affect the tonsils. The most common of which are infectious processes. To begin, tonsillar and peritonsillar infections include tonsillitis, peritonsillar cellulitis and peritonsillar abscess[44].

Tonsillitis is an infection of the palatine tonsils. Viruses are the main culprits of tonsillitis[45]. In cases when the cause is bacterial, the most common species is *Streptococcus pyogenes* (group A beta-hemolytic streptococcus or GAS)[45]. This pathogen causes 10% of pharyngitis/tonsillitis in adults, and 15-

30% of infections in children aged 3-15 years old (Inesss Guidelines). The diagnosis of GAS infection is made clinically, based on the McIsaac score. Elements within this grading system include history of fever over 38 degrees Celsius, presence of tonsillar exudates, tender anterior cervical adenopathy, absence of cough, and age. Most cases are believed to recover within 3-5 days without any therapy. If treatment is required, then penicillin is the antimicrobial of choice[45].

Peritonsillar cellulitis is an inflammatory reaction of the tissue between the capsule of the tonsil and the pharyngeal muscle, caused by infection, without associated pus collection. Usually, this type of infection is treated with oral antibiotics.

Peritonsillar abscesses consists of a collection of purulent fluid that accumulates between the palatine tonsil capsule and the fascia of the superior constrictor muscle on the lateral aspect[13]. It affects adolescents most frequently. It has an estimated incidence between 14 and 40 per 100,000 in patients below the age of 18[13]. Although common, peritonsillar abscesses have a risk of serious morbidity, including rupture of the abscess, or tracking of the infection down to the mediastinum. There is also a small reported risk of sepsis from this infection. Peritonsillar abscesses tend to be polymicrobial, but the predominant bacterial species involved are *Streptococcus* pyogenes and *Staphylococcus* aureus. The gold standard for diagnosis of a peritonsillar abscess is needle aspiration, which allows for immediate confirmation of this pathology[18]. However, needle aspiration in a child can be extremely challenging. The most commonly used modality at this point in time, when the diagnosis of a peritonsillar abscess is uncertain, is a contrast-enhanced computed tomography (CT) scan[18]. In adults, this modality is utilized frequently. Currently, using ultrasound to diagnose peritonsillar abscess is not considered a standard of care. This will be discussed more in detail in the sections below.

2.4 Tonsillar malignancies

The tonsils can also harbour malignancies, including lymphoma and squamous cell carcinoma. Lymphoma is the third most frequent malignancy of childhood, as it accounts for 12% of cancers in children below the age of 15[5]. In the head and neck area, non-Hodgkin's lymphoma is the most commonly encountered. The WHO lymphoma classification characterizes Waldeyer ring lymphomas based on morphology, immunoarchitecture and phenotype, as well as on clinical behaviour[6]. There have been reports of several types of tonsillar lymphomas in the literature, including Burkitt's lymphoma, diffuse large B-cell lymphoma, extranodal marginal zone lymphoma, extraosseous plasmacytom, low-grade follicular lymphoma, mucosa-associated lymphoid tissue, mantle cell lymphoma, and peripheral T/natural killer-cell lymphoma[6].

It is sometimes difficult to diagnose a tonsillar lymphoma, because tonsillar asymmetry is a frequent physical examination finding. The literature suggests that certain elements on history should alert a physician to an increased risk of tonsil malignancy. Features on history include: persistent cervical lymphadenopathy (over 2 weeks), any history of malignancy, any constitutional symptoms (unintended weight loss, night sweats, persistent fever). On physical exam, alarming features include: asymmetric consistency of tonsils on palpation, changes in appearance or ulceration of tonsil mucosa and lymphadenopathy[46].

Currently, the algorithm for dealing with an enlarged or abnormal-appearing tonsil is as follows. For a child or an adult, if there is high clinical suspicion (more than one of the above outlined elements), it is recommended that a tissue sample for histology be obtained. If there is low clinical suspicion, but one of the above-mentioned findings, recommendations differ between adults and children. For an adult, it is recommended to undergo CT or PET scan. In children, it is suggested to check tonsils every 4 weeks for 3 months total, looking for changes in symptoms or physical exam. It is important to educate patients regarding the development of concerning symptoms, such as weight loss and night sweats[46].

Many studies have demonstrated that tonsillectomy for unilateral tonsil enlargement (UTE) is overly aggressive, given that isolated tonsil lymphoma is extremely rare. Furthermore, numerous studies have shown that visual examination through the mouth does not accurately measure tonsillar size[4]. Harley et al. looked at a cohort of children, 47 of whom were determined on physical examination to have asymmetric tonsils. Three-dimensional measurement of these tonsils following tonsillectomy revealed poor correlation with intraoral observations, which may be due to deeper tonsillar fossae that make one tonsil seem larger than the other[4].

Given these findings, Hwang et al. released a Best Practice algorithm, encouraging observation in asymptomatic UTE[46]. Despite this recommendation, many clinicians continue to intervene surgically, as lymphoma cannot be ruled out without pathologic confirmation. In our experience, these children undergo multiple investigations including antibiotic trials, blood tests, oncology consultation and sometimes, tonsillectomy. Currently, tonsillectomy is the only method to confirm with certainty that a child with an asymmetric tonsil does not harbour a malignancy. Although tonsillectomy is a commonly performed surgery, it is not without complications. It leads to severe post-operative pain, as well as a 4% risk of post-tonsillectomy haemorrhage. The significant patient morbidity and anxiety-provoking nature of these investigations is what prompted us to seek a better alternative for these children.

Squamous cell carcinoma (SCC) is the most common malignancy affecting the tonsils of adult patients. The topic of tonsillar SCC has gained popularity in the literature, since the discovery of its association with the human papilloma virus (HPV)[47]. As SCC of the tonsil was once believed to be a disease of tobacco and alcohol users, there has been a rise in incidence of SCC in young white men under the age of 50[48]. These tumors tend to have an excellent prognosis.

2.5 Tonsillar Asymmetry

Several studies have examined the relationship between unilateral tonsillar enlargement and lymphoma of the tonsil in children[4,7,46]. In general, examination of the palatine tonsils is done via transoral visualization. A 2012 report suggested that tonsillar asymmetry in children may be an illusion due to difference in the depth of the tonsillar fossa[4]. They performed a prospective cohort study in children with asymmetric tonsils that underwent tonsillectomy. Among 258 children, 47 (18.2%) were found to have asymmetric tonsils on physical exam. This was compared with a group of 43 children who appeared to have symmetric tonsils. Three-dimensional examination of the resected tonsils revealed very poor correlation between intraoral examination and actual size. They attributed this inaccuracy to differences in the depth of the tonsillar fossa.

Three main grading scales exist for tonsillar size, including: the Brodsky Grading Scale, the Friedman Grading Scale, and finally the Three-Grade Scale. A recent report recruited 116 children aged 3 to 14 to measure the interobserver and intraobserver reliabilities of each scale. They found that the Brodsky grading scaled offered the highest interobserver and intraobserver reliability (intraclass correlation coefficients 0.721 and Pearson correlation coefficient 0.911) [41].

The most up to date review of the literature regarding the significance of tonsillar asymmetry in children was published in 2015 by Guimaraes et al[5]. Investigators performed a systematic review and meta-analysis of the association between unilateral tonsillar enlargement and lymphoma in children.

In total, they identified 71 children with tonsillar lymphoma, 52 of whom had tonsillar asymmetry, and 46 had other suspicious factors for malignancy. Only 6 of the children in the cohort had tonsillar asymmetry alone as the presenting complaint. The group also identified 27 articles describing children with tonsillar asymmetry, encompassing a total of 284 children. Among these children, 94 had benign lymphoid hyperplasia, 52 had lymphoma, 51 had chronic tonsillitis, and the remainders had unspecified benign findings. Investigators concluded that tonsillar asymmetry has a sensitivity of 73% for detecting lymphoma and a likelihood ratio for tonsillar asymmetry harbouring a malignancy of 1.44 (CI: 1.22-1.70). Further analysis revealed that if there was presence of tonsillar asymmetry with the occurrence of another sign of malignancy, the likelihood ratio of lymphoma jumped to 8938.43 (CI: 860.98-92 750.66).

In summary, a majority of children with tonsillar asymmetry do not have lymphoma. However, if a child is noted to have this asymmetry, it is necessary to rule out malignancy. The main challenge lies in the fact that oftentimes, the tonsils seem asymmetric, but ex-vivo it is noted that they were, in reality, the same size. Physical examination correlates poorly with true size. Being able to know the size of both tonsils before doing further investigations would be of great use.

The following chapter, Chapter 3, will present a scoping review of the use of ultrasound for tonsillar imaging in order to determine whether ultrasound has been used previously, as well as the context of its use.

CHAPTER 3: **The Use of Ultrasound for Tonsillar Imaging: A Scoping Review of the Literature (Manuscript 1)**

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3.1 Abstract

Background

The palatine tonsils can be affected by various pathologies, including infection, hypertrophy and malignancy. The use of ultrasound to image the tonsils is not routinely practiced at this time. The objective of this study was to capture the scope of literature exploring tonsillar ultrasound in children and adults.

Methods

A scoping review was conducted. Studies included were those addressing one of four main themes: (1) indications for tonsillar ultrasound in adults, (2) indications for tonsillar ultrasound in children, (3) technique for tonsillar ultrasound and (4) cost-effectiveness of tonsillar ultrasound. Twenty-four eligibile studies were identified from a systematic literature search and relevant information was summarized.

Results

The majority of tonsillar ultrasound has been used to differentiate between various tonsillar and peritonsillar infections. Most studies were conducted in adults. A small number of publications suggest that ultrasound usage may help to understand other tonsillar pathologies, such as malignancy. Ultrasound is also believed to be a cost-effective alternative to computed tomography (CT).

Conclusions

Currently, tonsillar ultrasound is not the primary modality for imaging adult and pediatric tonsils. This review suggests that it may be as accurate as CT, as well as more cost-effective.

3.2 Introduction

Ultrasound is commonly used for assessment of head and neck masses. For example, it is the primary modality for thyroid imaging[49]. The improving quality of ultrasound images has led to an increase in its use. Ultrasound has been described recently as an adjunct for monitoring recurrent disease within the cervical lymph nodes in cases of head and neck squamous cell carcinoma (SCC)[49]. Indeed, several surgeons are beginning to incorporate sonography into their clinical practice.

Despite these advances, the use of ultrasound for imaging palatine tonsils is not considered a first line tool. Among adults, pathologies involving the tonsils are mostly infections, such as peritonsillar abscesses, and malignancies. The incidence of human-papilloma virus (HPV)-related tonsil cancers has risen drastically over the past 20 years[21,50]. The focus of malignancy can often be small and difficult to identify on physical examination. At this time, computed tomography (CT) is primarily used for their detection, as well as for subsequent monitoring for recurrence post-treatement.

Among children, the main tonsillar pathologies include infection, hypertrophy, and rarely malignancy. In this group, once again, the diagnosis remains a challenge. Differentiating between tonsillar infections can be difficult in children, as physical examination is not always reliable. In the case of tonsillar hypertrophy, there is frequently a discrepancy between physical exam and severity of sleep-disordered breathing. As in adults, the most commonly used modality for imaging the tonsils in children is CT.

Certain reports have indicated that ultrasound may be an excellent tool for tonsil imaging. It is non-invasive and avoids radiation exposure. The objective of the current study is to explore the literature surrounding tonsillar ultrasound in adults and children, a topic has not been comprehensively reviewed.

3.3 Methods

A scoping review of the literature was performed based on the framework proposed by Arksey and O'Malley[51]. We followed the five-stage process proposed by their group: (1) identifying a research question, (2) identifying relevant studies, (3) study selection, (4) charting data, (5) collating, sumamrizing and reporting results[51].

Medline and EMBASE databases were used for the search. Keywords were combined within the search and included "tonsil ultrasound", "tonsillar ultrasound", "oropharynx ultrasound", as well as associated terms, in children and adults. Our search was limited to studies in English only, and animal studies were excluded. A single reviewer screened titles and abstracts to verify that the the study was within the scope of the research question. Included studies were those addressing one of four main themes: (1) indications for tonsillar ultrasound in adults, (2) indications for tonsillar ultrasound in children, (3) technique for tonsillar ultrasound and (4) cost-effectiveness of tonsillar ultrasound. Eligible studies were randomized controlled trials, non-randomized controlled trials, observational studies, cross-section studies, cohort studies, case series and case reports. The majority of studies were case series. Articles were reviewed and divided based on the themes outlined above. Findings were subsequently summarized.

3. 4 Results

3.4.1 Indications for tonsillar ultrasound in adults

The literature describing tonsillar ultrasound in adults dates back to the early 1990s. Until recently, the focus was entirely on tonsillar infection differentiation, in particular differentiating between peritonsillar abscess, peritonsillar phlegmon and peritonsillar cellulitis. Indeed, the first traceable report of ultrasound use was by Mosges et al., in 1990, where intraoral ultrasound was suggested as a means of differentiating between peritonsillar abscess and cellulitis[52]. This report was followed by a series of publications throughout the 1990s aimed at using ultrasound to avoid invasive management of individuals with peritonsillar infections. Buckley et al. reported on the value of both intraoral and transcutaneous sonography by performing these tests on 16 patient volunteers[19]. They found intraoral sonography to be superior to transcervical imaging for the diagnosis of peritonsillar abscess. Boesen and Jensen reported that transcervical ultrasound could correctly diagnosis peritonsillar abscess in 92% of cases[53]. Ahmed et al. used a 7.5 MHz transducer to once again to differentiate tonsillar infections[20]. They found false negative rate of 9% and false positive of 20%. Finally, in 1993, Haeggstrom et al. re-demonstrated this high accuracy, with a 91% correct detection rate of peritonsillar abscess[21].

In 1999, Scott et al. pursued the study of peritonsillar infections and ultrasound diagnosis[18]. They performed a prospective study of 14 patients and found that clinical impression alone was unreliable (sensitivity 78%, specificity 50%). They compared this to computed tomography (CT) scan, which had a sensitivity of 100% and specificity of 75% and to intraoral ultrasound, which had a sensitivity of 89% and a specificity of 100%. They concluded once again that transoral ultrasound was a useful way to distinguish abscess from cellulitis.

Other reports have emerged on this topic, all drawing the same conclusions[10,16,17,22,54,55]. Most publications are in the otolaryngology and emergency medicine literature. A recent publication was released in the *American Journal of Emergency Medicine*, entitled “Think ultrasound first for peritonsillar swelling”, where they summarize their experience with both intraoral and transcervical ultrasound for peritonsillar abscess diagnosis[23]. The authors indicate that especially in cases with severe trismus, transcutaneous ultrasound can be an excellent adjunct. Another study out of Brazil compared transcutaneous to intraoral ultrasound in peritonsillar infections, and found 95% sensitivity and 95.2% specificity for intraoral examination, compared to 80% sensitivity and 92.8% specificity for transcervical ultrasound[56]. For over 30 years now, it has been reported that both intraoral and transcervical ultrasound are accurate and useful in the diagnosis peritonsillar infections in the adult population.

New to the literature is the use of ultrasound for the diagnosis of adult oropharyngeal cancer. The first paper was published in *Neuroradiology/Head and Neck imaging* in 2015[57]. In their report, Coquia et al. begin by describing the shortcomings of conventional imaging modalities for examination of the oropharynx and the potential uses of ultrasound. They make direct comparisons of CT and MRI to equivalent ultrasound images and conclude that ultrasound is quite accurate for the visualization of the tonsils and base of tongue, a well as being cost-effective and portable. They believe that oropharyngeal ultrasound is a promising modality.

In 2018, Faraji et al. assessed performance and accuracy of physicians reading oropharyngeal ultrasound[58]. Their main objective was to evaluate the reader performance of oropharyngeal anatomy with ultrasound. They showed slideshows of static ultrasound images (both normal and malignant anatomic variations) of the oropharynx to 6 blinded readers. They found that 87% of base of tongue tumors were identified correctly on ultrasound. Median accuracy, sensitivity and specificity were 79%, 73% and 85% respectively. For palatine tonsils, 84% of images were identified correctly. Median accuracy, sensitivity and specificity were 77%, 74%, and 78%. They also studied measurement errors in tonsil tumor images. Median measurement error in the long and short axes were 3.8% and 6.5% respectively. Overall, two main types of errors were identified. The first was agreement on central focus of the tumor and the second was failure of readers to agree on border extent. They concluded that there is good sensitivity, specificity and accuracy of reads on oropharyngeal ultrasound. Indeed, this modality shows great promise, at has comparable rates of sensitivity and specificity as CT scan[59].

3.4.2 Indications for tonsillar ultrasound in children

Literature in pediatric tonsillar ultrasound has emerged only in the past four years. The first study was published in *The Laryngoscope*, in 2015, where Fordham et al. present a prospective, single-arm cohort study of 43 children aged of 2 and 20[15]. They performed transcervical ultrasound to determine if the children had a peritonsillar abscess. As in the adult population, they found tonsillar ultrasound to have a sensitivity of 100% and specificity of 76.5% in the diagnosis of peritonsillar abscess. Positive and negative predictive values were 52.9% and 100% respectively. It was concluded to be a useful modality in the diagnosis of pediatric PTA.

Around the same time of the above-mentioned publication, an article entitled “Tonsil ultrasound: technical approach and spectrum of pediatric peritonsillar disease” was published[13]. It was the first article to describe the spectrum of tonsillar infections in children, with detailed photographic descriptions. Transcutaneous ultrasound was used to demonstrate the appearance of uncomplicated tonsillitis, peritonsillar cellulitis, intratonsillar abscess and frank peritonsillar abscess. A description of a parapharyngeal abscess was also documented. They were the first group to describe the technique for imaging the tonsil. Furthermore, they went into detail about the normal appearance of the tonsil on ultrasound, describing it as a “well-defined, ovoid soft-tissue structure with subtly lobulated margins.” They note that a normal tonsil is hypoechoic to the adjacent submandibular gland and that its parenchyma is striated in appearance with alternating linear hyperechoic and hypoechoic band (due to tonsillar crypts).

Following Bandarkar et al.'s description of tonsillar ultrasound technique, four more publications appeared in the pediatric field, all released in 2017. The first was by Ozturk, who set out to assess the palatine tonsils of children with transcervical ultrasound and understand if their size was correlated with age, gender and body mass index[11]. They studied 680 healthy children who underwent voluntary transcervical ultrasound. They gathered the following patient information including age, gender, body weight, height, body mass index and tonsil volume on ultrasound and then searched for associations between these parameters. They found statistically significant positive correlations between age, BMI and tonsil volume. In essence, as children grow, their tonsils grow as well.

Asimakopoulos et al. presented a single-instituion prospective study of 26 children aged 2-6 years old, who were underoing tonsillectomy [12]. Prior to tonsillectomy, they performed a transcervical ultrasound with the child under general anesthesia. They measured ultrasound dimensions and then compared them to actual ex-vivo tonsil volumes. They found that the measurements were well correlated. Estimated volume as per ultrasound was calculated with the formula height x length x width x 0.523, a formula that is also used for testicular volume measurement. They found a correlation coefficient of 0,89 between ultrasound measurement and ex-vivo measurements and concluded that ultrasound can accurately assess tonsillar volumes in children. They did not document each individual measurement however, and it is unclear what axis led to volumetric discrepancies. This is the main weakness of their study.

Hosokawa et al. examined the tonsils of a cohort of Japanese children with ultrasound[60]. Their goal was to determine how well the tonsils could be viewed, by reviewing retrospectively the neck ultrasounds of 99 children in both the transverse and longitudinal planes bilaterally. They found that bilateral tonsils were evaluable in 96% of patients. Furthermore, they noted the various echogenicity of the tonsils, which were designated as either "imperceptible, low echoic, or striated in appearance". Nearly the entire cohort (97% on the right and 90% on the left) of tonsils evaluated had a striated appearance. They continued by dividing the ultrasonographic images based on four grades, depending on how well the tonsil borders could be distinguished, with 0 being the worst, and 3 being the best. The mean grades were 2.44/2.03 for the right transverse/longitudinal images, and 2.4/2.12 for the left transverse/longitudinal images. They found that the grades in children over the age of 3 were significantly higher than those of younger patients.

Finally, Hong et al. set out to answer a question that had not yet been documented in the literature: what is the normal size of pediatric tonsils based on age[44]? The goal of their study was to establish normal tonsillar measurements and volumes according to age in pediatric populations. They performed a retrospective study on 161 patients who had documented neck ultrasounds for other indications and measured tonsillar sizes in the transverse and anteroposterior dimensions. Most exams had been performed with 5-12 MHz linear array transducer. Length, height and width were calculated and volume was measured by multiplying these measurements x 0.523. Mean tonsillar volume were 1.58 cm3 +/- 1.26 : 0.3+/- 0.14 for less than 1 year old, 1.27 cm3+/- 0.57 for 1 to 5 year-olds, 2.06 cm3 +/- 1.09 for 5 to 10 year-olds, and 2.19 cm3 +/- 1.48 for over 10 year-olds. No volumetric differences were found between sexes. Tonsillar volumes increased with age. There were positive correlations between height, weight and tonsillar volume, but this did not show statistical significance.

Overall, as in adults, ultrasound is shown to be accurate and useful in detecting tonsillar and peritonsillar pathologies. Unlike adults however, there are no reports in children of transoral tonsillar ultrasound. There are no reports documenting associations between findings on tonsillar ultrasound and children with sleep-disorder breathing. There is no literature on using tonsillar ultrasound to assess children with tonsillar asymmetry and suspected lymphoma. A summary of all studies reviewed can be found in the following Table.

Table. Summary of articles describing indications for tonsillar ultrasound in children and adults

Author/Year	Study type	Number of patients	Population	Indication	Modality	Main Findings
Boesen & Jensen 1991[53]	Case series	27	Children and adults	Differentiating peritonsillar infections	Transcervical ultrasound	Sensitivity 92%
Haeggstrom et al. 1993[21]	Case series	12	Children and adults	Detected presence of PTA	Intraoral ultrasound	Useful tool for detecting PTAs
Buckley et al. 1994[19]	Case series	21	Children and adults	Differentiating peritonsillar infections	Transcervical and intraoral ultrasound	Intraoral more accurate than transcervical
Ahmed et al. 1994[20]	Prospective cohort study	27	Adults	Differentiating peritonsillar infections	Transcervical ultrasound	Sensitivity 91%, specificity 80%
Strong et al. 1995[54]	Case series	16	Adults	Differentiating peritonsillar infections	Intraoral ultrasound	Sensitivity 90%, specificity 83%
Scott et al. 1999[18]	Case series	14	Adults	Differentiating peritonsillar infections	Intraoral ultrasound	Sensitivity 89%, specificity 100%
Blavais et al. 2003[61]	Case series	6	Children and adults	Differentiating peritonsillar infections	Intraoral ultrasound	Sensitivity 100%, specificity 100%
Lyon and Blaivas 2005[62]	Case series	43	Adults	Differentiating peritonsillar infections	Intraoral ultrasound	Ultrasound is reliable, accurate and safe
Araujo Filho et al. 2006[56]	Prospective cohort study	39	Adults	Differentiating peritonsillar infections	Transcervical and intraoral ultrasound	Intraoral sensitivity 95.2%, specificity 86.9% Transcervical sensitivity 80%, specificity 92.8%

Costantino et al. 2012[63]	Randomized-controlled clinical trial	28	Adults	Differentiating peritonsillar infections	Intraoral ultrasound	100% diagnostic accuracy
Salihoglu et al. 2012[55]	Case series	26	Adults	Differentiating peritonsillar infections	Intraoral ultrasound	Considered a good modality for differentiation
Rehrer et al. 2013[10]	Case report	1	Adults	Differentiating peritonsillar infections	Transcervical ultrasound	Detected presence of PTA
Fordham et al. 2015[15]	Prospective cohort study	43	Children	Differentiating peritonsillar infections	Transcervical ultrasound	Sensitivity 100%, specificity 70%
Nogan et al. 2015[17]	Prospective cohort study	24	Adults	Differentiating peritonsillar infections	Intraoral ultrasound	Sensitivity 100%, Specificity 70%
Coquia et al. 2015[57]	Observational study	NA	Adults	Detection of oropharyngeal lesions	Transcervical ultrasound	Ultrasound may be an important adjunct to MRI and CT
Halm et al. 2016[16]	Case report	1	Children	Differentiating peritonsillar infections	Transcervical ultrasound	Detected presence of PTA
Bandarkar et al. 2016[13]	Pictorial essay	NA	Children	Technical approach to ultrasound of peritonsillar infections	Transcervical ultrasound	NA
Bacon et al. 2016[22]	Case report	1	Adult	Differentiating peritonsillar infections	Intraoral ultrasound	Useful tool for detecting PTAs
Asimakopoulos et al. 2017[12]	Prospective cohort study	26	Children	Assessing tonsil volume	Transcervical ultrasound	Ultrasound is a suitable method to objectively measure tonsil volume
Ozturk 2017[11]	Case series	680	Children	Assess palatine tonsil size in healthy children	Transcervical ultrasound	Normative values described, ultrasound is safe, non-invasive and easily accessible

Hong et al. 2017[44]	Prospective cohort study	161	Children	Assessing normative tonsil sizes	Transcervical ultrasound	Described normative tonsillar volumes based on age
Hosokawa et al. 2017[60]	Case series	99	Children	Understanding how well tonsils can be viewed with ultrasound	Transcervical ultrasound	Bilateral tonsils were successfully evaluated in 96% of patients
Froehlich et al. 2017[64]	Review article	NA	Children and adults	Differentiating peritonsillar infections	Transcervical and transoral ultrasound	Ultrasound is a safe and accurate alternative to CT for differentiating between tonsil infections
Faraji et al. 2018[58]	Case series	24	Adults	Detection of tonsillar and tongue base malignancy	Transcervical ultrasound	Median accuracy of 80% in distinguishing tumor and non-tumor tissue

3.4.3 Tonsillar ultrasound technique, including transducer type

There is one main publication outlining a precise sonography technique for tonsil examination, which was mentioned in the pediatric section above[13]. They begin by describing appropriate patient positioning for the ultrasound: supine with neck extended. They continue by explaining the proper technique: by placing the transducer under mandible and visualizing the submandibular gland first, with the transducer parallel to the mandible. The tonsil is immediately deep to submandibular gland. They also describe that the floor of mouth and tongue base can be seen, as well as facial vessels. They suggest using a linear, high-frequency transducer (between 9 and 15 MHz). Many of the other studies report using a high-frequency linear probe as well[3,11,13,15,16,22,23]. There are no publications reporting the use of curved probes. There is no report describing specific ultrasound machines that are better or worse at visualizing the tonsils.

3.4.4 Cost-savings associated with tonsillar ultrasound

Only one study has been identified that describes the cost-savings associated with the use of tonsillar ultrasound. The paper was published in 2017 by Huang et al., in the *Laryngoscope*[9]. Their objective was to analyze children with three diagnoses: acute tonsillitis, peritonsillar phlegmon and peritonsillar abscess, and compare the clinical outcomes and cost-savings between children who underwent tonsillar ultrasound versus those who did not.

They retrospectively analyzed two cohorts of children presenting with signs and symptoms of peritonsillar infection, with 78 children who had tonsillar ultrasound compared to 101 children who did not. The children who underwent ultrasound were a consecutive group, who were enrolled prospectively in the study. For the children who did not undergo ultrasound, they simply used retrospective data of children treated prior to initiation of the study. Mean age of these patients was 12.3 years and 13.6 years respectively. For the children who had an ultrasound, they used transcervical, high-frequency ultrasound with a linear probe. The examination was performed by a radiology technician and verified by an attending radiologist. The control group was comprised of children having been diagnosed with a PTA, who did not undergo ultrasound. They measured the following outcomes: length of stay, readmission, and/or medical treatment failure requiring surgical intervention. They also evaluated costs of CT scans and transcervical ultrasounds, as well as the charges associated with stays in hospitals, procedures performed and otolaryngology consultations based on billing codes. They finally looked at facility fees, medications used, and anesthesiology and radiology fees for sedation (if was necessary for CT scan).

The study showed that patients who underwent ultrasound in the context of tonsillar infection were significantly less likely to undergo CT scan, and also less likely to undergo a surgical procedure. They were also significantly less likely to have a length of stay longer than 23 hours.

In terms of costs, the children who underwent ultrasound incurred median costs of 296$ compared to 510$ in the patients who did not have an ultrasound, although this difference was not statistically significant. They concluded that ultrasound is safe and cost-effective in patients with peritonsillar infection. No other study of this type has been published since.

3.5 Discussion

The current scoping review assessed the literature surrounding tonsillar ultrasound. Four main themes were evaluated: (1) indications for tonsillar ultrasound in adults, (2) indications for tonsillar ultrasound in children, (3) technique for tonsillar ultrasound and (4) cost-effectiveness of tonsillar ultrasound.

This study highlighted that tonsillar ultrasound has been practiced in adult medicine for over 30 years. The main indication for its use is differentiating various peritonsillar infections. It carries excellent sensitivity, specificity and accuracy. Furthermore, the recent literature suggests that it may be an important adjunct in oropharyngeal cancers in the future.

In children, several studies have revealed that tonsillar ultrasound is also accurate and useful for differentiating tonsil infections. As expected, only transcervical ultrasound has been evaluated in this population. With the excellent results described in several studies, we questioned why this modality is not being used more frequently. One theory is that oftentimes, children are simply observed with a trial of intravenous antibiotics, and only undergo imaging if they subsequently worsen. Another reason may be that radiologists are not comfortable with the technique.

Important questions remain unanswered in the pediatric literature. The first is whether tonsillar ultrasound can help with predicting the severity of sleep-disordered breathing. As mentioned in Chapter 3, there can be important discrepancies between the physical examination and the SDB severity. Using ultrasound to measure tonsil size, as well as understanding its position within the pharynx, could be an interesting concept.

The second unanswered question is regarding the use of tonsillar ultrasound in the management of pediatric unilateral tonsillar enlargement (UTE). These patients are often managed aggressively, and may undergo tonsillectomy to achieve pathological confirmation to rule out an underlying malignancy. Many studies have demonstrated that tonsillectomy for UTE is overly invasive, given that isolated tonsil lymphoma is rare[46]. For this reason, we suspect that tonsillar ultrasound could be an important adjunct in managing patient with UTE, once the technique is mastered.

Finally, the literature provides one major description of how to perform tonsillar ultrasound through a pictoral essay and one description of cost-savings of this modality compared to CT.

3.6 Conclusions

Currently, the main indication for tonsillar ultrasound is to differentiate between tonsillar infections in adults and children. Tonsillar ultrasound is sensitive, specific and accurate at diagnosing tonsillar infections. It is easy to perform and appears to be cost-effective compared to other imaging modalities.

3.7 Linking statement

This study suggests that the main gaps in the literature are: (1) confirming the accuracy of ultrasound when measuring tonsils in three-dimensions, (2) assessing if three-dimensional tonsillar measurements correlate with severity of SDB, and (3) assessing if tonsillar ultrasound may be an adjunct in managing patients with UTE. The first gap is addressed in Chapter 4 (Manuscript 2).

CHAPTER 4: **High-Frequency Ultrasound: A Novel Diagnostic Tool to Measure Paediatric Tonsils in Three Dimensions (Manuscript 2)**

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4.1 Abstract

Objective

Various pathologies can affect the palatine tonsils. Ultrasound is a commonly used modality for assessing head and neck masses in children, however its use in tonsillar evaluation has not been widely explored. The objective of this study was to measure three-dimensional tonsillar size with ultrasound, in centimeters, and correlate the measurements with actual ex-vivo dimensions on pathology specimens.

Study Design

We performed a prospective cohort study.

Setting

The study was set in a tertiary care children's hospital**.**

Subjects and Methods

Children undergoing tonsillectomy were included in the study. Transcervical high-frequency ultrasound (HFU) was performed prior to surgery to obtain three- dimensional measurements of the right and left palatine tonsils and were compared to ex-vivo tonsil measurements. Mean sizes were compared and correlations were obtained.

Results

75 consecutive children underwent a transcervical HFU, with a total of 150 tonsils analyzed. The mean differences between HFU and pathology measurements were -0.08 cm and -0.24 cm for the right and left cranio-caudal axes, -0.19 cm and -0.18 cm for the right and left medio-lateral axes, and 0.05 cm and 0.03 cm for the right and left antero-posterior axes. Correlation coefficients between ultrasound and pathology measurements were all above 0.5.

Conclusion

HFU can accurately measure the size of pediatric tonsils in three-dimensions.

4.2 Background and Rationale

A wide variety of pathologies can affect the palatine tonsils in children including tonsillar infections, hypertrophy and rarely neoplasms. In most children, tonsillar hypertrophy is thought to be associated with the spectrum of sleep-disordered breathing[1,2]. In rare cases, tonsillar asymmetry can be the presenting sign of a tonsillar lymphoma[3-7].

Ultrasound is a commonly used modality to assess head and neck masses[8]. However, for the examination of palatine tonsils, ultrasound is rarely used. Its use has been reported in the adult otolaryngology and emergency medicine literature, to differentiate a peritonsillar phlegmon from an abscess[9-23]. In the differentiation between tonsillar infections, ultrasound has shown excellent sensitivity and specificity[10,16,17,19-23]. Although these studies were among small cohorts of patients, it seems that ultrasound may be an acceptable imaging modality to assess tonsillar size and pathology.

In the pediatric realm, the first report of tonsillar ultrasound use was an article by Bandarkar et al., where the authors described the ultrasound findings of tonsillar infections in children, with detailed photographic descriptions[13]. They used transcervical ultrasound to differentiate tonsillitis, peritonsillar cellulitis, intratonsillar abscess and peritonsillar abscess. They concluded that transcervical ultrasound can easily and accurately assess the palatine tonsils. Overall, it is a feasible and non-invasive option in children.

Despite showing great promise for identifying tonsillar pathologies, there are no studies in the literature that confirm the accuracy of tonsillar ultrasound in measuring tonsillar size in three dimensions. The objective of this study was to measure three-dimensional tonsillar size with ultrasound, in centimeters, and correlate the measurements with actual ex-vivo dimensions, as measured by pathology.

4.3 Methods

4.3.1 Study Design

We performed transcervical ultrasound of the palatine tonsils on 75 consecutive children scheduled to undergo tonsillectomy at a tertiary care pediatric hospital. The study period was from September 1st 2017 to December 21st 2017. Institutional Review Ethics Board approval was obtained (MUHC-2018-3757).

4.3.2 Participants

Children aged 18 years of age or less undergoing palatine tonsillectomy were eligible for inclusion. This encompassed children undergoing tonsillectomy for any indication, including sleep-disordered breathing, recurrent tonsillitis, and tonsillar asymmetry. Tonsillectomies were all performed in the same manner: in an extracapsular fashion, with monopolar cautery. Children were excluded if their parents did not agree to participation; there were no other exclusion criteria. Written informed consent was obtained from all parents.

4.3.3 Ultrasound Technique and Data Collection

The same sonographer performed all the ultrasounds, using a BK Ultrasound 800 (BK medical) machine, with a high-frequency linear probe (6-18 MHz, 38.4 x 3.5 mm). The sonographer was blinded to all patient information.

After induction of general anaesthesia, ultrasound was performed in a supine position, with a shoulder role in place. The ultrasound machine was usually set to a frequency of 12 MHz, which was adjusted if necessary. This frequency was appropriate for almost all children. The depth of the image was set at 4 cm. We adjusted gain, usually between 50 and 70%, depending on the soft tissues of the child.

The focus depth was also adjusted based on the location of the tonsil. These parameters were determined prior to beginning the study, while performing ultrasounds on children known to the authors. A protocol needed to be created, as the previous descriptions in the literature of tonsillar ultrasound either lack an ultrasound technique description, or the description is vague and difficult to replicate.

The right tonsil was evaluated first, in the sagittal plane followed by the transverse plane. See figures 1 and 2 for the exact technique utilized. The same images were repeated for the left neck.

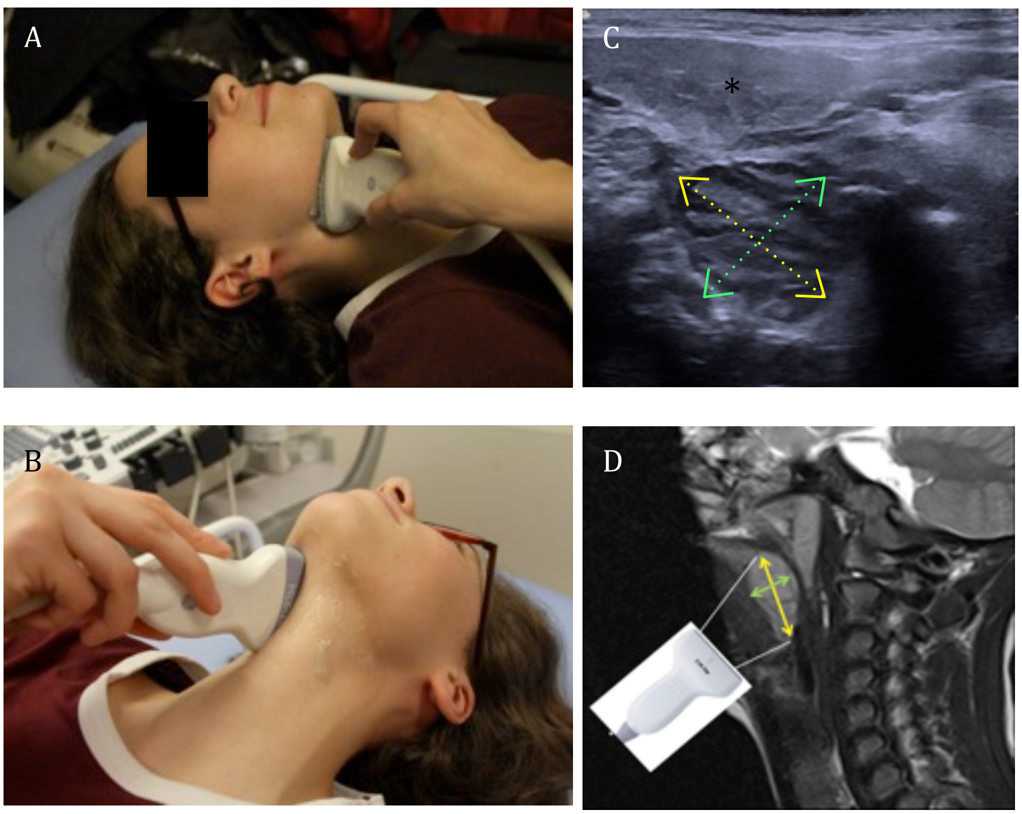
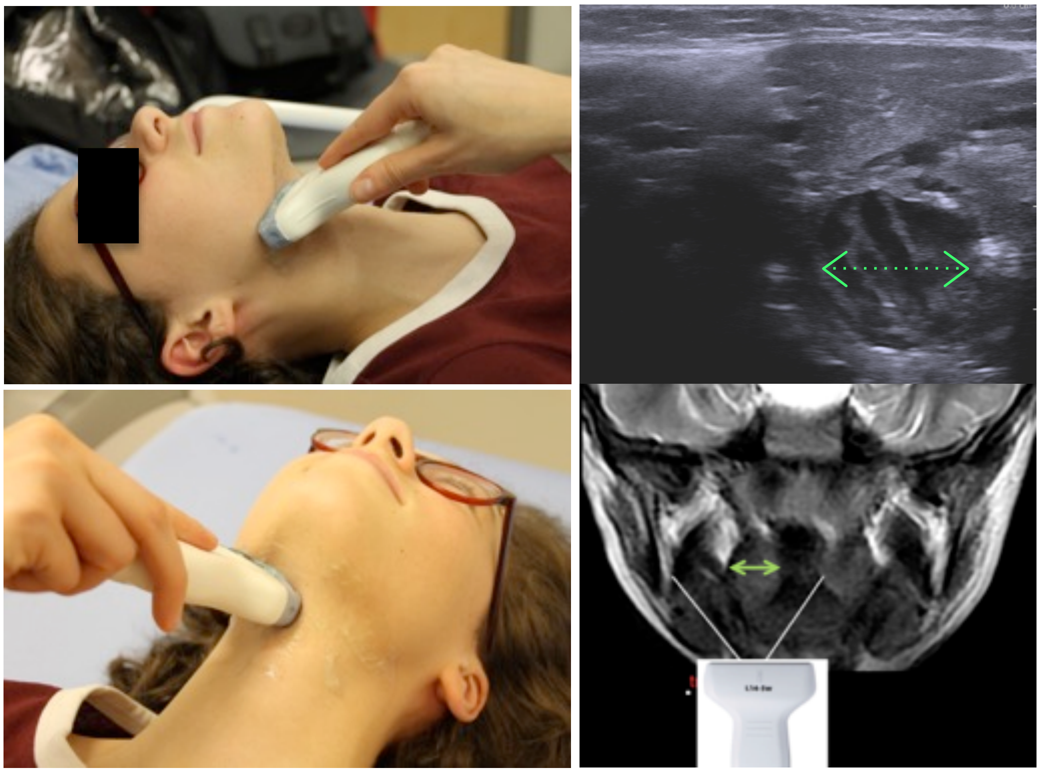


Figure 1. Sagittal acquisition of the tonsil, showing the cranio-caudal axis and the antero-posterior axis of the tonsil. A. Demonstration of the positioning of the probe in order to obtain the sagittal view on the tonsil. B. A second view of the probe positioning, still in the sagittal acquisition. C. Ultrasound image of the tonsil in the sagittal plane, yellow arrow is the cranio-caudal axis, green arrow is the antero-

posterior axis, and asterisk represents the submandibular gland. D. Equivalent MRI image of the tonsil, same color scheme as above.



B D

Figure 2. **Transverse acquisition of the tonsil, showing medio-lateral axis.** A. Demonstration of the positioning of the probe in order to obtain the transverse view on the tonsil. B. A second view of the probe positioning, still in the transverse acquisition. C. Ultrasound image of the tonsil in the transverse plane, green arrow is the medio-lateral axis. D. Equivalent MRI image of the tonsil, same color scheme as above.

Following this, the ultrasonographer left the room and did not attend the tonsillectomy. All images were reviewed by the same attending fellowship-trained pediatric head and neck radiologist, where the best images were selected for a single measurement of each dimension. Removed tonsils were sent to pathology as per routine proceedings in our hospital, prior to fixation, where they were weighed, measured, and analyzed by three pathologists. These pathologists were blinded to clinical information and ultrasound measurements. Patient information was collected at the end of the study period, once all ultrasound images had been confirmed.

The data collected included: age, sex, weight, height of each child and indications for tonsillectomy (recurrent tonsillitis, sleep-disordered breathing, tonsillar asymmetry). Pathology data included weight in grams, height (equivalent in vivo to cranio-caudal axis), width (equivalent in vivo to medio-lateral axis), length (in vivo equivalent to antero-posterior axis) of each tonsil, as well as final pathologic diagnosis. Volume of the tonsils was estimated with the formula length x width x height x 0.523 (used for volume estimation of elliptical shapes)[12,65]. Tonsillar volume was measured by water displacement.

4.3.4 Statistical Analysis

The statistical analysis began with a descriptive analysis, where a scatter plot was used to plot ultrasound measurements versus actual tonsil measurements. Paired T-test were used to compare the means of ultrasound measurements to pathology specimen measurements. Pearson correlation coefficients were obtained to assess correlation between ultrasound and pathology measurements. Mean differences in volumes of tonsils in vivo and ex vivo were determined.

4.4 Results

The study included 75 children undergoing transcervical, high-frequency tonsillar ultrasound (HFU), with a total of 150 tonsils measured and analyzed. Children were on average 4.9 years of age, with a majority undergoing tonsillectomy for sleep-disordered breathing. All patients had reactive hyperplasia as a final pathologic diagnosis. There were no cases of tonsil malignancy (Table 1).

Table 1. Characteristics of the children undergoing tonsillar ultrasound (n=75).

		n	%
Age (years)	Mean (SD)	4.9 (2.8)	
	Range	2-17	
Sex	Male	33	44
	Female	42	56
Weight (kg)	Mean (SD)	22.7 (11.8)	
Indication for tonsillectomy	Sleep-disorder breathing	69	92
	Recurrent tonsillitis	6	8
	Tonsillar asymmetry	0	
Final pathology	Reactive hyperplasia	75	100

SD: standard deviation, kg: kilograms

We subsequently compared ultrasound measurements to ex-vivo pathology measurements. Three dimensions were studied on both the right and left tonsils: cranio-caudal (CC), medio-lateral (ML), and antero-posterior [66] (Table 2).

Table 2. Ultrasound measures compared to pathology specimen measures in three axes.

Axis	Ultrasound measure (mean and SD in cm)	Pathology measure (mean and SD in cm)
CC axis	Right: 2.47 (0.36)	Right: 2.56 (0.38)
(mean and SD in cm)	Left: 2.34 (0.41)	Left: 2.58 (0.39)
ML axis	Right 1.69 (0.29)	Right 1.89 (0.28)
(mean and SD in cm)	Left: 1.58 (0.23)	Left: 1.77 (0.30)
AP axis	Right 1.44 (0.25)	Right 1.4 (0.27)
(mean and SD in cm)	Left 1.40 (0.23)	Left 1.76 (0.31)

SD: standard deviation

We analyzed accuracy of each measurement by determining the mean differences between ultrasound and pathology values with a paired T-test. The mean differences were measured for each individual axis, and are presented here in centimeters with 95% confidence intervals (Table 3). The largest mean differences are found in the left CC axis and right ML axis measurements, with a mean of 2.4 mm and 1.9 mm differences respectively. All mean differences except for left AP and Rt AP are presented as a negative value, showing that ultrasound generally underestimated the size of the tonsils.

Table 3. The results of the paired T-test comparing mean differences in measurements of HFU and pathology.

Axis	**Mean Difference (cm)**	**95% CI**
Rt CC	-0.082	(-0.166, 0.002)
Rt ML	-0.190	(-0.275, -0.105)
Rt AP	0.051	(-0.023, 0.125)
Lt CC	-0.240	(-0.331, -0.149)
Lt ML	-0.183	(-0.26, -0.107)
Lt AP	0.032	(-0.029, 0.093)

Pearson correlation coefficients were calculated between ultrasound and pathology measurements. All coefficients were above 0.5 for all axes, indicating a strong association, as shown in Table 4.

Table 4. Pearson correlation coefficient between HFU measurement and pathology.

Axis	Pearson correlation coefficient
Rt CC	0.69
Rt ML	0.50
Rt AP	0.51
Lt CC	0.66
Lt ML	0.51
Lt AP	0.60

Finally, differences in volumetric measurements were compared. The volumes were calculated in cm^3. The estimated volumes were calculated by multiplying height, length and width by the coefficient 0.523. This method is documented in the literature as a way to measure the volume of an elliptical shape[65]. The right and left tonsils showed differences between measured and actual volumes of -0.075 and -0.221 cm^3 respectively.

4.5 Discussion

Transcervical ultrasound has been used for over 30 years to detect peritonsillar infections in adults. Its use in children has only been reported in the past few years. Ultrasound is a non-invasive, radiation-free imaging modality that is useful in the evaluation of neck masses in children. Recently, ultrasound is gaining favour due to its capacity to visualize the oropharynx with precision[11-13,57,58,60]. One study in particular examined tonsil volumes of 26 children via ultrasound and reported good correlation of ultrasound and volumetric measurements. However, our study is the first to confirm that tonsil size in all three-dimensions are accurately measured with ultrasound and correlate with ex-vivo specimens. We are the first to identify challenges in measuring certain axes, and outline solutions to overcome them. Furthermore, we describe a complete technique for tonsillar ultrasound, with specific parameters, which can allow a head and neck radiologist, or an otolaryngologist with experience in ultrasound, to rapidly pick up this technique.

We performed a prospective analysis comparing tonsillar ultrasound measurements to actual pathology in 75 consecutive children undergoing tonsillectomy for any indication. Our results demonstrate that ultrasound can accurately measure tonsillar size, in all three axes (cranio-caudal, antero-posterior and medio-lateral). Overall, ultrasound mildly underestimated tonsillar size. It is hypothesized that since the majority of children underwent tonsillectomy for sleep-disordered breathing in our cohort, many of them had large tonsils that filled the entire ultrasound image field, sometimes slightly exceeding the field. This is believed to be the cause of the underestimation of size.

The medio-lateral axis of the tonsils was the least accurate measurement, with a mean difference between ultrasound and pathology of 2 mm (10% difference on average between measurements). Measuring the medio-lateral axis required holding the ultrasound probe in the transverse plane (Figure 2). In this axis, the mandible can prevent proper manoeuvring. This may be mediated by the use of a shorter probe. In our case, the only high-frequency probe to which we had access measured 38 mm. Furthermore, we noted a difference in accuracy between the right and left cranio-caudal axes. When evaluating the left side, the positioning of the probe requires the sonographer's right arm to reach over the patient's chest and be more extended. This may have led to a probe that was oriented in a slightly more oblique fashion, and thus not completely catching the longest cranio-caudal dimension. With this knowledge, the person performing the ultrasound can correct this orientation, by bring the table down to obtain a better reach, in order to give a more accurate measure.

In terms of volumetric measurements, we found that ultrasound was able to give an accurate volume, by using the traditional formula for ellipse volume. Once again, there was a mild underestimation of volume, likely related to the underestimation of each individual axis measurement.

Based on the results of the current study which showed that ultrasound can accurately measure tonsil size in three-dimensions, several future directions may be explored. For example, we have already started to use tonsillar ultrasound to objectively measure the tonsils of patients referred for a clinically perceived tonsil asymmetry, with the aim of creating a decision algorithm of whether to proceed with tonsillectomy or not.

Another important area of research would be to understand the association between tonsil size and the severity of sleep-disorder breathing. To this day, the literature is divided on whether tonsil size correlates with severity of sleep apnea in children and adults[67-69]. Two important questions remain unanswered: whether subjective tonsil size correlates with objective tonsil size, and whether subjective tonsil size correlates with the severity of sleep-disorder breathing. Jara et al. published a study reporting the subjective tonsillar size was more strongly associated with apnea-hypopnea index (AHI) than objective tonsillar volume[70]. They proposed the hypothesis that it is perhaps the space occupied by the tonsil within the airway, more than the size itself, which determines the AHI. Furthermore, Howard et al. showed subjective tonsil size did not correlate with preoperative AHI, and that only objective tonsillar size (ex-vivo) could truly predict the severity of OSA[71]. Overall, they advocate for a more accurate way to evaluate of tonsil size and comment on the value of having three-dimensional measurements. Tonsillar ultrasound shows great promise in answering this both questions, as we can not only measure tonsil size in three dimensions, but the surrounding pharyngeal structures can also be visualized.

Finally, our study has limitations. Although we evaluated a large number of patients with a consistent technique, these children were under general anaesthesia. We did not evaluate the margin of error in children who were awake. Furthermore, the same person performed all the ultrasounds, therefore inter-rater reliability was not assessed.

4.6 Conclusion

The above findings demonstrate that high-frequency ultrasound of the tonsils can accurately measure the palatine tonsils in three-dimensions. In addition to showing that ultrasound can differentiate between various tonsillar infections, it is helpful to know that measured dimensions are also correct. It may be a promising modality for evaluation of tonsillar pathology.

4.7 Linking statement

An important controversy in the literature is how to approach children with tonsil sizes that do not correlate with the severity of sleep-disordered breathing. With the knowledge that ultrasound is an accurate and non-invasive way to image the oropharynx, we suspect that it may be an important adjunct in SDB diagnosis and treatment. The next chapter (Chapter 5) reviews the literature surrounding this controversy.

CHAPTER 5: Overall Discussion

5.1 Relation to previous research

This thesis started by assessing previous research. In chapter 3, a scoping review assessed the literature surrounding tonsillar ultrasound. Four main themes were overviewed: (1) indications for tonsillar ultrasound in adults, (2) indications for tonsillar ultrasound in children, (3) technique for tonsillar ultrasound and (4) cost-effectiveness of tonsillar ultrasound. This review identified several questions and areas for potential clinical applications of ultrasound imaging. For example, ultrasound imaging may improve management of (a) in adults, oropharyngeal cancers, and (b) in children, sleep-disordered breathing, or unilateral-tonsillar enlargement.

Chapter 4 assessed high-frequency ultrasound imaging of paediatric tonsils. Findings showed that transcervical, HFU could accurately measure the size of palatine tonsils in three-dimensions. Also, this thesis is the first study to identify challenges in measuring different tonsillar axes, and to outline solutions to overcome these challenges.

5.2 Unanswered questions in sleep-disordered breathing: What you see is not necessarily what you get

5.2.1 Current diagnosis of obstructive sleep-apnea syndrome

Obstructive sleep-apnea syndrome (OSAS) is the leading indication for adenotonsillectomy. The gold standard for diagnosing OSAS is a polysomnogram, which generates an apnea-hypopnea index (AHI) score. A score between 0 and 1 is considered normal, mild OSAS is a score of 1-4, moderate OSAS is a score of 5-10, and severe OSAS is an AHI over 10. A survey in the United States demonstrated that

59% of adenotonsillectomies were performed for "obstructive breathing"[72]. However, it also showed than less than 10% of these children had undergone any form of objective testing prior to surgery. Therefore, their study suggests that most adenotonsillectomies are based solely on symptom history and physical examination, and a formal diagnosis of OSAS has never been made. Overall, it is generally understood that further testing prior to adenotonsillectomy is warranted, beyond clinical history and physical examination.

Nocturnal pulse oximetry and polysomnography (PSG) are the most commonly performed tests to confirm the presence of OSAS in a child[73,74]. Polysomnography remains the gold standard for diagnosing OSAS, however it is expensive and not readily available. It uses multiple physiological parameters including: video recording, electroencephalogram, electrooculogram, submental and leg electromyogram, oronasal airflow, abdominal and chest wall movements, pulse oximetry, and end-tidal or transcutaneous partial pressure of carbon dioxide. Its complexity may explain why it is rarely ordered. In fact, an American survey reported that only 4% of respondents (otolaryngologists) were likely to order a polysomnogram prior to performing a tonsillectomy[72]. On the other hand, oximetry is an abbreviated and lower cost modality used to diagnose OSAS. It monitors the oxygen saturation and heart rate during sleep, and is usually done at home. The results of nocturnal oximetry recordings are relatively easy to interpret, and certain patterns are suggestive of OSAS. It is believed to have a high positive predictive value for OSAS diagnosis[74].

5.2.2 Discrepancies between physical examination and OSAS diagnosis

History and physical examination are not sufficient to make a diagnosis of OSAS. One systematic review of the literature by Brietzke et al. sought to answer the question: *can history and physical examination reliably diagnose pediatric obstructive sleep apnea/hypopnea syndrome?*[75]. Their group identified 12 articles that addressed this topic directly. They reported that 11 of the 12 articles concluded that history and/or physical examination could not reliably diagnose OSAS in the pediatric patient.

A few published studies have suggested that although subjective tonsil size is not reliable, perhaps tonsillar volumes (measured once the tonsils had been excised) are more predictive of the severity of OSA. Indeed, Lai et al. found a significant correlation between tonsil volume and AHI, but poor correlations between subjective grading and AHI[76]. Howard et al. also reported similar findings: objective tonsil measurements were significantly predictive of objective PSG-measured OSAS severity[71].

In 2017, Jara and Weaver sought once again to analyze the relationship between palatine tonsil size and severity of OSAS[70]. They performed a retrospective cohort study in adults. Their results were drastically different than previous results: they found that palatine tonsil grade was strongly associated with AHI, and that tonsil volume was not. In summary, there remains very different opinions in the literature regarding the relationship between physical examination and severity of OSAS.

It is clear that for the time being, “objectively measuring the tonsils” still involves removing them. At present there is no set modality to objectively measure tonsil sizes in vivo. In this context, tonsillar ultrasound may be an interesting adjunct to decision-making in children with suspected OSAS. It offers a simple and easy alternative to nocturnal oximetry and more importantly, to PSG. However, before answering this question, it must be confirmed that tonsil ultrasound can accurately measure tonsils in three dimensions. This question has led to a primary objective of this thesis: to report the accuracy of tonsillar ultrasound at measuring tonsils in three dimensions. Results from Chapter 4 suggest that this should be possible.

5.3 Future Directions

Based on the results of Chapter 4, several future directions may be explored. The group of Otolaryngologists at the Montreal Children's Hospital have already begun to use tonsillar ultrasound to objectively measure the tonsils of patients referred for a clinically perceived tonsil asymmetry, with the hope of creating a decision algorithm of whether to proceed with tonsillectomy or not. Furthermore, tonsillar ultrasound shows great promise in improving understanding of children with sleep-disordered breathing, as outlined above. Not only can it determine tonsil size, but it can also assess the surrounding pharyngeal structures as well. It is hoped that information from this thesis will improve the diagnosis and management of both tonsillar asymmetry and sleep-disordered breathing.

CHAPTER 6: Overall Conclusions and Claim of Originality

6.1 Overall Conclusions

This thesis set out (1) to review tonsillar pathologies, as well as the tonsillar ultrasound literature, so that gaps in knowledge could be identified, (2) to measure three-dimensional tonsillar size with ultrasound, and to correlate such measurements with actual ex-vivo dimensions, as measured by pathology, and (3) to provide a comprehensive, user-friendly guide to performing tonsillar ultrasound.

Chapter 2 reviewed tonsillar pathologies, overviewing tonsillar hypertrophy and its relationship with sleep-disorder breathing, as well as tonsillar infections, malignancies, and asymmetries.

Chapter 3 is a scoping review of the literature (manuscript 1) that overviewed indications for use of ultrasound for tonsillar imaging in adults and children; tonsillar techniques; and cost effectiveness. The review emphasized (a) the likely benefits of using ultrasound in children, (b) reasons why it has been underutilized, (c) its clinical potential benefits in diagnosis and management of sleep-disordered breathing, and unilateral tonsillar enlargement, and (d) its likely cost effectiveness.

Chapter 4 reports the accuracy of high-frequency ultrasound imaging to measure paediatric tonsils (manuscript 2). It showed that this technique could accurately measure both three-dimensional (CC, ML, AP) lengths, as well as estimated-elliptical volumes of pediatric tonsils – all confirmed by comparison to post-excision-pathological data. Reasons for slight underestimations were proposed.

6.2 Claim of originality

To my knowledge, this is the first study to confirm accuracy of ultrasound in measuring the tonsils in all three dimensions. Other studies have measured overall volumes, but the three-dimensional measurements were not reported.

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CHAPTE 8. LIST OF ABBREVIATIONS

CT	Computed tomography
GAS	Group A beta-hemolytic streptococcus
HFU	High-frequency ultrasound
HPV	Human papilloma virus
OSAS	Obstructive sleep apnea syndrome
PTA	Peritonsillar abscess
SCC	Squamous cell carcinoma
SDB	Sleep-disordered breathing
UTE	Unilateral tonsillar enlargement

Appendix 1: Ethics approval

Ultrasound 2

Protocol title
High-Frequency Ultrasound: A Novel Diagnostic Tool to Assess Tonsillar Size and Pathology in Children

Project type
Clinical Trial, Clinical Research

Research field
Otolaryngology, Head & Neck Surgery

REB
MUHC Research Ethics Board

Ethical evaluation site
Local evaluation

Project status
Authorized for research

Evaluations status

DPS_ped_ress	Approved
MUHC REB	Approved

Renewal date
2019-09-28

Primary user
Kay-Rivest, Emily

Local investigator
Daniel, Sam

Co-investigator
Saint-Martin, Christine

Numbers

2018-3757

Users

Daniel, Sam
Kay-Rivest, Emily

Status of project evaluations

Project	Authorized for research Next renewal 2019-09-28	2017-09-29	Levy, Sheldon
REB office	Approved 3 meetings	2017-09-29	Craven, Elizabeth
SEC	Not required		
DPS_ped_ress Feasibility	Approved 1 decision	2017-09-22	MARTELL, CATHERINE

project status

status	creation date	user
Authorized for research	2017-09-29 15:02	Levy, Sheldon
Under review	2017-07-12 17:29	Craven, Elizabeth
Submitted	2017-07-12 12:43	Kay-Rivest, Emily
Created	2017-07-12 12:17	Kay-Rivest, Emily

reb office

sec

feasibility - dps pediatrics ressources

Appendix 2: French informed consent form

INFORMATION SUR LA RECHERCHE ET FORMULAIRE DE CONSENTEMENT

Titre : Échographie haute fréquence: une nouvelle modalité pour évaluer la taille et les diverses pathologies amygdaliennes

Personnes responsables : Dr. Sam Daniel and Dr. Christine Saint-Martin

- Hôpital de Montréal pour enfants-CUSM

Source de financement : non-applicable

POURQUOI ÊTES-VOUS INVITÉ À PARTICIPER À CE PROJET DE RECHERCHE ?

Le département/service d'otorhinolaryngologie participe à des projets de recherche dans le but d'améliorer les traitements chez les enfants souffrant de problèmes avec les amygdales. Nous aimerions aujourd'hui votre participation. Nous vous invitons à lire ce formulaire d'information afin de décider si vous êtes intéressé à participer à ce projet de recherche. Il est important de bien comprendre ce formulaire. N'hésitez pas à poser des questions. Prenez tout le temps nécessaire pour décider.
Nous encourageons les parents à inclure leur enfant dans la discussion et la prise de décision dans la mesure où l'enfant peut comprendre.

Dans ce formulaire de consentement, « vous » signifie vous ou votre enfant.

POURQUOI MÈNE-T-ON CE PROJET DE RECHERCHE?

Plusieurs problèmes peuvent être causés par les amygdales. Ceux-ci incluent des infections telles que l'amygdalite. Ils englobent également les amygdales agrandies, ce qui peut entraîner divers problèmes de sommeil. Enfin, l'asymétrie d'une amygdale peut être la présentation unique d'un lymphome, bien que ce soit extrêmement rare.

L'échographie est largement utilisée dans l'évaluation de la plupart des masses de tête et de cou chez les enfants. C'est le même test qu'on fait chez les femmes enceintes afin de visualiser leur fœtus. Nous utilisons cette technique d'imagerie chez les enfants en raison de sa disponibilité et de l'évitement de radiation. L'échographie est non-invasive et rapide, et peut bien voir les amygdales en plaçant la sonde sur le cou de votre enfant. Nous croyons que l'échographie a le potentiel de devenir une modalité d'imagerie importante et utile pour les problèmes d'amygdale chez les enfants.

Notre objectif est de prouver que l'échographie est rapide et facile à utiliser, et décrit avec précision les caractéristiques et la taille des amygdales. Vous êtes invité à participer à l'étude parce que votre enfant va subir une amygdalectomie.

COMBIEN DE PERSONNES PARTICIPERONT AU PROJET DE RECHERCHE ?

Environ 200 participants prendront part à ce projet de recherche. Tous les participants proviendrons de notre établissement.

COMMENT SE DÉROULERA LE PROJET DE RECHERCHE?

Nous allons effectuer une échographie sur tous les enfants qui subissent une amygdalectomie. Chez votre enfant, nous aimerions effectuer deux échographies, une avant que votre enfant s'endorme, et l'autre une fois que votre enfant sera endormi. La durée de chaque échographie est de moins de 5 minutes. Nous comparerons ensuite les images d'échographie à la pathologie finale.

Nous allons collecter certaines informations du dossier de votre enfant, y compris son âge, sexe, la raison de l'amygdalectomie, d'autres problèmes de santé et les résultats de l'étude du sommeil s'ils en ont eu une avant.

Cette petite intervention avant leur amygdalectomie n'aura aucun impact sur la chirurgie elle-même. Toutes les amygdales, après leur enlèvement sont envoyées au service de pathologie pour analyse. Cela restera exactement le même.

COMBIEN DE TEMPS DURERA LA PARTICIPATION À CE PROJET DE RECHERCHE?

Les participants dans cette étude ne nécessiteront aucun suivi. Vous aurez simplement le suivi régulier post-amygdalectomie, tel que conseillé par votre chirurgien (habituellement 6 mois après la chirurgie).

QUELS SONT LES RISQUES?

Il n'y a aucun inconvénient ou risque dans cette étude. Votre enfant sera sous anesthésie pour environ 3 à 5 minutes de plus, le temps pour faire le test. Votre enfant sera endormi.

Y-A-T-IL DES AVANTAGES À PARTICIPER À CE PROJET DE RECHERCHE?

Vous ne retirerez aucun avantage direct en participant à cette recherche. Nous espérons que les connaissances acquises grâce à ce projet de recherche seront utiles à d'autres patients qui ont des problèmes d'amygdales.

QUELLES SONT LES AUTRES OPTIONS?

Vous pouvez choisir de ne pas participer à l'étude. Dans ce cas, votre enfant subit une amygdalectomie comme prévu et n'aura pas d'échographie avant la chirurgie.

QUELS SONT LES COÛTS?

Il n'y a aucun coût associé avec la participation dans cette étude.

QUELS SONT LES AUTRES ASPECTS FINANCIERS?

Il n'y a aucun autre aspect financier.

COMMENT LA CONFIDENTIALITÉ EST-ELLE ASSURÉE?

Tous les renseignements recueillis demeureront confidentiels dans les limites prévues par la loi. Votre identité sera protégée en remplaçant votre nom par un code de recherche. Seule l'équipe de recherche de votre hôpital aura accès au lien entre le code et votre nom.
Si les résultats généraux de ce projet de recherche sont publiés ou présentés lors de conférences scientifiques, votre nom et vos autres renseignements personnels ne seront pas utilisés.
Les données de recherche seront conservées pendant 7 ans de façon sécuritaire sous la responsabilité du chercheur principal de votre hôpital.

Des données codées seront conservées dans un ordinateur avec mot de passe, qui appartient à l'investigateur principal.
Pour votre sécurité, une copie du formulaire de consentement sera conservée dans votre dossier médical.

ETES-VOUS LIBRE DE PARTICIPER?

Oui. La participation à ce projet de recherche est volontaire. Vous êtes libre de refuser de participer à ce projet de recherche. Vous pouvez décider de cesser de participer au projet de recherche à n'importe quel moment. Si vous ne participez pas au projet de recherche ou vous vous retirez cela n'affectera pas la qualité des soins qui vous seront offerts.

Nous vous communiquerons toute nouvelle information qui pourrait avoir des conséquences pour votre santé, votre bien-être ou votre volonté de prendre part à ce projet de recherche.

PERSONNES-RESSOURCES

Si vous avez des questions concernant le projet de recherche ou si vous éprouvez un problème que vous croyez relié à votre participation au projet, vous pouvez communiquer avec le chercheur responsable du projet de votre hôpital :
-Hôpital de Montréal pour enfants-CUSM : Dr. Emily Kay-Rivest 514-867-9645
En cas d'urgence, veuillez vous rendre aux urgences de l'hôpital le plus près.

Pour tout renseignement sur vos droits, vous pouvez vous adresser au Commissaire local aux plaintes et à la qualité des services :
-Hôpital de Montréal pour enfants - CUSM : 514-412-4400, poste 22223

OU PUIS-JE OBTENIR PLUS D'INFORMATIONS?

Vous pourrez demander un résumé des résultats du projet de recherche; ceux-ci ne seront disponibles que lorsque le projet sera entièrement terminé.

Vous recevrez une copie signée de ce formulaire. En tout temps vous pouvez poser des questions à l'équipe de recherche.

COMITÉ D'ÉTHIQUE DE LA RECHERCHE

Le comité d'éthique de la recherche du CUSM a approuvé ce projet de recherche et en assure le suivi.

ASSENTIMENT ET CONSENTEMENT

Titre du projet de recherche : Échographie haute fréquence: une nouvelle modalité pour évaluer la taille et les diverses pathologies amygdaliennes

On m'a expliqué la nature et le déroulement du projet de recherche. J'ai pris connaissance du formulaire de consentement et on m'en a remis un exemplaire. J'ai eu l'occasion de poser des questions auxquelles on a répondu. Après réflexion, j'accepte de participer ou que mon enfant participe à ce projet de recherche.

J'autorise l'équipe de recherche à consulter mon dossier médical, ou le dossier médical de mon enfant, pour obtenir les informations pertinentes à ce projet.

En signant ce formulaire de consentement, vous ne renoncez à aucun de vos droits prévus par la loi. De plus, vous ne libérez pas les investigateurs et le promoteur de leur responsabilité légale et professionnelle advenant une situation qui vous causerait préjudice.

______________________________	______________________________	____________
Nom de l'enfant (Lettres moulées)	Assentiment de l'enfant capable de comprendre la nature du projet (signature ou Assentiment verbal obtenu par : __________________________________	Date

______________________________	______________________________	____________
Nom du parent, tuteur (Lettres moulées)	Consentement (signature)	Date

J'ai expliqué au participant et/ou à son parent/tuteur tous les aspects pertinents de la recherche et j'ai répondu aux questions qu'ils m'ont posées. Je leur ai indiqué que la participation au projet de recherche est libre et volontaire et que la participation peut être cessée en tout temps.

______________________________	______________________________	____________
Nom de la personne qui obtient le consentement	(signature)	Daet

Appendix 3: English informed consnt form

PEDIATRIC RESEARCH INFORMATION AND CONSENT FORM

Title : High Frequency Ultrasound: A Novel Diagnostic Tool to Assess Tonsillar Size and Pathology in Children

Persons responsible : Dr. Sam Daniel and Dr. Christine Saint-Martin

- Montreal Children's Hospital- McGill University Health Center

Funding Source: Not applicable

WHY ARE YOU BEING INVITED TO TAKE PART IN THIS STUDY?

The Otolaryngology – Head and neck surgery department/service participates in research studies to try to improve treatments for children with various tonsil issues. Today, we are inviting you to take part in a research study. Please read this information to help you decide if you want to participate in this research project. It is important that you understand this information. We encourage you to ask questions. Please take all the time you need to make your decision.
We encourage parents to include their child in the discussion and decision-making to the extent that the child is able to understand.
In this research information and consent form, "you" means you or your child.

WHY IS THIS STUDY BEING DONE?

A wide variety of problems can affect or be caused by tonsils. These can include infections, and enlarged tonsils, which can lead to various forms of breathing problems during sleep. Finally, when one tonsil is significantly bigger than the other, it can be a sign of a lymphoma, an extremely rare but serious condition.

Ultrasound is widely used as the initial imaging technique in the assessment of most head and neck masses in children. It is the same test done for pregnant women to visualize their fetus. We use this imaging technique in children due to its availability and avoidance of radiation. The techniques have evolved significantly since its early applications. It is non-invasive and quick, and we can see the tonsils by placing the probe on your child's neck. We believe that ultrasound has the potential to become an important and useful imaging tool for tonsil problems in children.
Our goal is to prove that ultrasound is quick and easy to use, and accurately describes tonsil features and size. You are invited to participate in the study because your child is undergoing a tonsillectomy.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

About 200 patients will take part in this study, all participants will be recruited from this hospital.

WHAT WILL HAPPEN ON THIS RESEARCH STUDY?

We will perform an ultrasound of the tonsils on children who are undergoing tonsillectomy. For your child in particular, we would like to perform two ultrasounds, one right before you child goes to sleep,

and the other one once your child is asleep on the operating table. The duration of each ultrasound is less than 5 minutes.
We will also collect information from your child's chart, including their age, sex, reason for tonsillectomy, other health problems they may have, and results of sleep study if they've had one before.
This small intervention before their tonsillectomy will have no impact on the surgery itself. All tonsils, after their removal, are sent to the pathology department for analysis. This will remain exactly the same. The removed tonsils will also be measured to compare the actual tonsil size to the measurements taken by ultrasound.

FOR HOW LONG WILL YOU PARTICIPATE IN THIS STUDY?

Participation in this study will not require any special follow up. You will simply have the regular follow up post-tonsillectomy, as advised by your surgeon (usually 6 months after surgery).

WHAT ARE THE RISKS?

There are no foreseeable risks or inconveniences to this study. There will be approximately 3 to 5 extra minutes of time spent under anesthesia in the operating room.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There is no direct benefit to you for participating in this research. We hope that what we learn from doing this study will help us find better ways to care for patients with tonsil problems in the future.

WHAT OTHER OPTIONS ARE THERE?

You can chose to not participate in the study. In this case, your child will undergo tonsillectomy as scheduled, and will not have an ultrasound before surgery.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?
There is no cost associated with participation in this study.
ARE THERE OTHER FINANCIAL ASPECTS?
There are no other financial aspects in this study.
HOW IS PRIVACY ENSURED?

All information obtained during the study will be kept confidential as required or permitted by law. Your identity will be protected by replacing your name with a research number. Only the research team will have access to the code linking your name to this number.
If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

The principal investigator at your hospital will be responsible for securely storing all the research data for 7 years. This includes the tonsil ultrasound photos. The data will be conserved in a password protected computer owned by the principal investigator.
For your safety, a copy of this signed consent form and some information about the research will be filed in your medical record.

IS YOUR PARTICIPATION VOLUNTARY?

Yes. Taking part in this study is voluntary. You may choose not to be in this study. You can decide to stop being in the study at any time. If you decide not to be in this study, or to stop participating in the study later on, this will not affect the quality of care you receive from your doctor.

We will tell you about any new information that may affect your health, well-being, or your willingness to stay in this study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions about this research project or if you suffer any problems you believe are related to your participation in this research, you can call the researcher responsible for the project in your hospital:
Montreal Children's Hospital: Dr. Emily Kay-Rivest (514) 867-9645.

WHERE CAN I GET MORE INFORMATION?

You may ask to receive a copy of the results of this research project; these will only be available after the entire project has been completed.
You will receive a signed copy of this form. You may ask the research team questions at any time.

RESEARCH ETHICS COMMITTEE

The research ethics committee of the MUHC approved this project and will monitor the project.

CONSENT AND ASSENT FORM

High Frequency Ultrasound: A Novel Diagnostic Tool to Assess Tonsillar Size and Pathology in Children

I have been explained what will happen on this study. I read the information and consent form including the annexes and was given a copy to keep. I was able to ask my questions and they were answered to my satisfaction. After thinking about it, I agree to, or I agree that my child will, participate in this research project.

I authorize the research team to consult my medical records or the medical records of my child to collect the information relevant to this project.
In no way does consenting to participate in this research study waive your legal rights nor release the sponsor or the institution from their legal or professional responsibilities if you are harmed in any way.

____

Name of participant (Print) | Asent of minor, capable of understanding | Date

____

Name of parent(s) or legal guardian (Print) | Signature | Date

____

Name of participant (18 years +) (Print) | Signature | Date

I have explained to the participant and/or his parent/legal guardian all the relevant aspects of this study. I answered any questions they asked. I explained that participation in a research project is free and voluntary and that they are free to stop participating at any time they choose.

________________________ ________________________ ____________

Name of Person obtaining consent (Print) | (signature) | Date