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Visualization of the Oropharynx during Head and Neck Cancer Examinations

by

Courtney Perrachione

A thesis

submitted in partial fulfillment

of the requirements for the degree of

Master of Science in the Department of Dental Hygiene

Idaho State University

Spring 2015

To the Graduate Faculty:

The members of the committee appointed to examine the thesis of Courtney Perrachione find it satisfactory and recommend that it be accepted.

_____

Tara Johnson, RDH, PhD,
Major Advisor

_____

JoAnn Gurenlian, RDH, MS, PhD,
Committee Member

_____

Paula Phelps, MHE, PA-C
Graduate Faculty Representative

Idaho State
UNIVERSITY

Office for Research Integrity
921 South 8th Avenue, Stop 8046 • Pocatello, Idaho 83209-8046

November 13, 2014

Courtney Perrachione, RDH, BS, CHES
Stop 8048
Dental Hygiene
Pocatello, ID 83209

RE: Your application dated 11/5/2014 regarding study number 4189: Visualization of the Oropharnyx during Head and Neck Cancer Examinations

Dear Ms. Perrachione:

I have reviewed your request for expedited approval of the new study listed above. This is to confirm that I have approved your application.

Notify the HSC of any adverse events. Serious, unexpected adverse events must be reported in writing within 10 business days.

Submit progress reports on your project in six months. You should report how many subjects have participated in the project and verify that you are following the methods and procedures outlined in your approved protocol. Then, report to the Human Subjects Committee when your project has been completed. Reporting forms are available on-line.

You may conduct your study as described in your application effective immediately. The study is subject to renewal on or before 11/13/2015, unless closed before that date.

Please note that any changes to the study as approved must be promptly reported and approved. Some changes may be approved by expedited review; others require full board review. Contact Tom Bailey (208-282-2179; fax 208-282-4723; email: humsubj@isu.edu) if you have any questions or require further information.

Sincerely,

Ralph Baergen, PhD, MPH, CIP
Human Subjects Chair

Phone: (208) 282-2179 • Fax: (208) 282-4723 • www.isu.edu/research

Acknowledgements

Tara Johnson, RDH, PhD., without whom none of this would have been possible. Thank you for your dedication, availability, and insight.

JoAnn Gurenlian, RDH, MS, PhD., who spent innumerable hours revising and giving amazing feedback and support. Thank you for all of your guidance

Paula Phelps, MHE PA-C, graduate faculty representative extraordinaire. Thank you for your perspective and continued support.

James Guffey, PhD., for his statistical acumen and phenomenal commitment to education and dedication to students everywhere.

Meg Long-Woodhouse, RDH, BS, for her countless hours evaluating intraoral photographs.

The Idaho State University Dental Hygiene Class of 2015 for their willingness to participate in this study.

My friends and family who were a constant source of support and encouragement.

Thank you, everyone.

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List of Abbreviations

OC – Oral cancer

HPV – Human papillomavirus

OPC – Oral and pharyngeal cancer

OCS – Oral and pharyngeal cancer screenings

COE – Comprehensive oral examinations

ANOVA – Analysis of variance

PI – Principle investigator

NIDCR – National Institute of Dental and Craniofacial Research

PGA – Palatoglossal arch

PPA – Palatopharygeal arch

U –Uvula

TO – Palatine Tonsils

TR – Tonsillar Recess

IF – Isthmus of Fauces

PPW – Posterior Pharyngeal Wall

CP – Circumvallate Papillae

SP – Soft Palate

List of Appendices

Visualization of the Oropharynx during Head and Neck Cancer Examinations

Thesis Abstract—Idaho State University (2015)

The purposes of this study were to determine differences in visibility of the oropharynx using five methods of tissue retraction and to identify clinician perceptions/preferences of those techniques.

A nonprobability convenience sample of student clinicians visualized the oropharynx of two patients using each method. Participants completed a survey of their perceptions of the best visibility and their preferred method. Two hundred ten intraoral photographs were evaluated using an anatomical checklist. Data were analyzed using descriptive statistics, Chi-square goodness of fit and Analysis of Variance.

The combination of mirror/"ahh" followed by tongue depressor/"ahh" were perceived as providing the best visibility and were the most preferred. Mean visibility scores from photograph evaluation were best for the combined methods with significantly lower visibility for single-step methods.

Dental hygienists should request their patients say "Ahh" in conjunction with either a dental mirror or tongue depressor for adequate tongue retraction and visualization.

Chapter 1

Introduction

Cancer is the second leading cause of death in the United States (after heart disease) for both men and women of all ages (Siegel, Ma, Zou, & Jemal, 2014). In 2014, it is anticipated there will be 42,500 new cases of oral cancers diagnosed in the United States (Siegel, Ma, Zou, & Jemal, 2014). This number is an increase from the 41,400 new cases documented in 2013 (Seigel, Naishadham, & Jemal, 2013). There is an 85% five year survival rate for oral cancers diagnosed in Stage 1, which drops to less than 40% for oral cancers diagnosed as Stage 4 (Siegel, Ma, Zou, & Jemal, 2014). The most common sites for oral cancer (OC) are the tongue, floor of mouth, soft palate, and oropharynx. Tobacco, alcohol, poor oral hygiene and genetics continue to be important risk factors for head and neck cancer overall; however, the human papilloma virus (HPV) is now recognized as one of the primary causes of oropharyngeal squamous cell cancers. The incidence of head and neck cancers in the U.S. has fallen in recent years, consistent with the decrease in tobacco use. By contrast, the incidence of HPV-related oral and pharyngeal cancer (OPC) is on the rise (Tachezy et al., 2009; Marur et al., 2010).

An increase in incidence of OPC, specifically in the tonsils and at the base of the tongue, has been seen in the US, most notably in individuals aged 40–55 years. Moyer (2014) reported that 80-95% of OPCs are associated with HPV. Similarly, Colevas (2014) noted a 225% increase in incidence of HPV-related tumors between 1984 and 2004. Unlike most tobacco-related head and neck tumors, patients with OPC usually do not have a history of tobacco or alcohol use. However, oral HPV infection is common in smokers as well as non-smokers and is an important cause of OPC in both groups (Moyer, 2014).

Head and neck comprehensive examinations involve a visual inspection of the face, neck, lips, labial mucosa, buccal mucosa, floor of the mouth, tongue, and palate; as well as the palpation of head and neck, tongue and the floor of the mouth (Moyer, 2014). The oropharynx involves the posterior one-third of the tongue, the soft palate, the side and back walls of the throat, and the tonsils should be inspected as a continuation of the oral cavity evaluation (Rethman, et al., 2010). Recommended armamentarium for a conventional OC screening includes sterile gauze, mouth mirror, tongue depressor and adequate overhead lighting. An active gag reflex and inadequate retraction of the tongue often hinder examination of this general area, consequently, due to the location, premalignant lesions and OPCs can be difficult to visualize (Brocklehurst et al., 2013). There are several adjunct technologies available to aid health professionals in screening for oral cancer. Adjunct technologies include: brush biopsies, toluidine blue, ViziLite Plus, MicroLux DL, and Velscope (Lingen, Kalmar, Karrison, & Speight, 2007). Even though these technologies have not yet been shown to be more effective than conventional oral examinations alone, it is important to note that all of the methods available still require adequate visibility of the oral cavity (Lingen et al., 2007).

According to Walsh, Rankin, and Silverman (2013), 80% of dental hygienists reported screening for OC and pre-malignant lesions, yet only 20% of patients indicated ever having a head and neck cancer examination. Moyer (2014) described a slightly higher average (30%) of individuals over 18 having had an oral cancer exam in their life. These inconsistencies could be due to patients not understanding what the hygienist was doing as they performed the exam, or a limited access to dental care within the populations surveyed. The three most commonly reported barriers to performing an OC screenings (OCS) include: no time during an appointment, the dentist performing an OCS prior to dental hygiene exam and the dental hygienist not feeling

comfortable with their ability to perform the exam sufficiently (Cotter et al., 2011). Dental hygienists reported they were more likely to perform an OCS on all patients if they had previously found a cancerous lesion during an exam (Cotter et al., 2011). Lack of time has been reported as the number one barrier to performing a thorough OCS, even though a complete screening can be completed in as little as 90 seconds (Vijay, Kumar & Suresan, 2012).

Statement of the Problem

Despite significant research showing that OC examinations by visual means can increase the number of oral malignancies detected in early stages, in turn reducing morbidity and mortality rates, professionals are still not routinely screening for this disease. Reasons for the reported low occurrence of visual OC screenings include lack of time and lack of training (Vijay, Kumar & Suresan, 2012). Additionally, the oropharyngeal region of the oral cavity is difficult to see using any visual screening technique. Consequently, there is a need for a method of visualizing and identifying premalignant lesions and OPC that is accurate and practical for all clinical settings.

Purpose of the Study

The purposes of this study were to determine differences in visibility of the oropharynx during oral cancer screenings using five methods of tissue retraction; and to identify clinician perceptions of visualization techniques.

Professional Significance of Study

Many OPCs are linked to HPV infections and manifest in the oropharynx; often these cancers are not detected until later stages of development (Baumeister et al., 2014). Dental hygienists are trained and educated in oral lesion detection and screening methods. Still, the occurrence of *full* intra/extra-oral exams for head and neck cancer screenings at dental hygiene

appointments is infrequent (Laronde, 2014). One deterrent to comprehensive and accurate screenings by dental hygiene clinicians could be limited visibility of the oropharynx during exams. By determining effective methods to better visualize potential premalignant or malignant lesions, OPCs may be detected at an earlier stage and clinicians may become more comfortable with visualization procedures.

This study meets the following Healthy People 2020 Oral Health Objectives: OH-6: Increase the proportion of oral and pharyngeal cancers detected at the earliest stage; OH-14.2: Increase the proportion of adults who received an oral and pharyngeal cancer screening from a dentist or dental hygienist in the past year (U.S. Department of Health and Human Services, 2014).

This study also meets the following National Dental Hygiene Research Agenda (NDHRA) items: D4. Clinical Dental Hygiene Care: Investigate how dental hygienists identify patients who are at-risk for oral/systemic diseases and A1. Health Promotion/Disease Prevention: Assess strategies for effective communication between the dental hygienist and client (American Dental Hygienists' Association, 2007).

Hypothesis and Research Questions

***Null hypothesis*.** There is no statistically significant difference in visibility of the oropharynx when retracting the tongue using a tongue depressor, dental mirror, having the patient say "ahh", a combination of tongue depressor and saying "ahh", or a combination of dental mirror and saying "ahh".

Research questions. Is there a difference in visibility of the oropharynx when retracting the tongue using a tongue depressor, dental mirror, having the patient say "ahh", a combination of tongue depressor and saying "ahh", or a combination of dental mirror and saying "ahh"?

What are dental hygiene clinicians' perceptions of oropharynx visualization using each of five conventional methods (tongue depressor, dental mirror, having the patient say "ahh", a combination of tongue depressor and saying "ahh", or a combination of dental mirror and saying "ahh") for tongue retraction?

Conceptual Definitions

- Oral Cancer Screening: "the process by which a practitioner evaluates an asymptomatic patient to determine if he or she is likely or unlikely to have a premalignant or malignant lesion" (Rethman et al., 2010).
- Gag Reflex: The physical response of a patient to begin choking when a stimulus is applied. Hypersensitive gag reflex is defined as a patient's gag reflex being initiated when the clinician touches the anterior two thirds of the patient's tongue or oral cavity structures.
- Visibility: The ability of the clinician to see the structures of the oropharynx unobstructed by other oral tissues such as the tongue or buccal mucosa.

Operational Definitions

- Oropharynx: area in the posterior of the oral cavity where the oral cavity meets the pharynx. Borders include anterior pillars of the pharyngeal fauces, circumvallate papillae, junction of the hard and soft palate, and the posterior pharyngeal wall. (University of Vermont, n.d.).
- Oropharyngeal cancer: malignant lesions involving structures of the oropharynx which include the structures where the oral cavity and pharynx merge, such as: palatine and lingual tonsils, posterior third of the tongue, soft palate, and the posterior pharyngeal wall (Steinau et al., 2014).

- Premalignant lesion: lesions that may convert to a malignancy if left untreated. Examples include erythroplakia and leukoplakia (Steinau et al., 2014).
- Tongue Depressor: instrument typically made out of wood used to depress the tongue in order to increase visualization of the posterior structures of the oral cavity. Sometimes referred to as a "tongue blade" (Thompson & Boyer, 2006).
- Visual Screening: method of disease detection wherein the clinician uses direct and indirect vision in order to see the structures of the oropharynx and oral cavity.
- Armamentarium: the instruments and tools required for a procedure.
- Dental Mouth Mirror: a small mirror with a handle used in dental procedures for indirect visualization, illumination, and retraction (Darby & Walsh, 2010)
- Say "ahh": technique for oropharynx visualization where the patient says the word "ahh" which naturally depresses their tongue and exposes more posterior structures in the oropharynx that might not be visible otherwise.
- Combined method with dental mirror: use of both a dental mirror for retraction and having the patient say "ahh" to increase visualization of the oropharynx.
- Combined method with tongue depressor: use of both a tongue depressor for retraction and having the patient say "ahh" to increase visualization of the oropharynx.

Summary

Oral and oropharyngeal cancers are associated with severe morbidity and high mortality. Dental hygienists are in a unique position to be able to screen a large number of people for pre-malignant and malignant lesions in order to detect cancer in the earliest stages of development. Oral cancers detected early have a much better prognosis. With the increase in OCs associated with HPV infections, and the posterior presentation of HPV+ lesions, it is important for

healthcare providers to be able to visualize the oropharynx, base of the tongue, and lingual/palatine tonsils. By determining the most effective way for professionals to visualize these areas, there is an increased likelihood of thorough OCSs, thus facilitating early detection and a potential reduction in morbidity and mortality from OPCs.

Chapter II

Literature Review

Oral cancers (OC) continue to be a devastating health problem. Health care professionals agree about the importance of opportunistic oral cancer screenings (OCS), yet nearly half of OC patients are diagnosed with advanced stage disease, for which prognosis is poor. All oral cancer examinations require adequate visualization of the oral cavity, oropharynx, and associated structures; however, no research has been conducted regarding the most effective method for visualization of these areas.

In order to understand the impact suitable visualization has on premalignant and malignant lesion detection, this literature review examines the incidence and etiology of OCS, rates of OCS, and barriers to screening by health professionals. Adjunct screening technologies are reviewed as well as information regarding professionals who should perform OCS and recommendations to improve screening implementation. Search engines used to collect information included: PubMed, EbscoHost, Cochrane Library, and Medline Plus. Key terms for this search included: oral cancer, oral cancer screening, oropharynx visibility, oropharynx visualization, adjunct technology in oral cancer screening, HPV, HPV and oral cancer, cancer statistics, barriers to oral cancer screening, dental hygiene and oral cancer, dentist and oral cancer, oral cancer screening rates, and patient reported cancer screening.

Oral Cancer Incidence, Morbidity, and Mortality

One in four deaths in 2013 was attributed to cancer, which is the second leading cause of death for all men and women after heart disease (Siegel, Ma, Zou, & Jemal, 2014). There were 42,440 newly diagnosed cases of OC (30,220 men 12,220 women) in the U.S. between 2013 and 2014 (Siegel, Ma, Zou, & Jemal, 2014). Of these aforementioned cases, 13,590 were cancer

located on the tongue, 11,920 in the oral cavity proper, 14,410 located in the pharynx, and 2,520 located in other oral sites (Siegel, Ma, Zou, & Jemal, 2014). Additionally, oral cancer diagnoses are predicted to rise 45% by 2027 (Laronde, 2014).

Seven thousand eight hundred ninety deaths related to OC were reported in 2013, and the five-year survival rate for all stages of diagnosis has not significantly improved from the five-year rate of 53% in 1975 (Siegel, Ma, Zou, & Jemal, 2014). Survival rates are better for lower stages (83% for localized cancers, 59% for regional spread, and 36% if there is distant metastasis); however, only 31% of cancers are diagnosed at the localized stage, compared to 64% diagnosed in advanced stages (Siegel, Ma, Zou, & Jemal, 2014).

While oral cancer may be treated by surgery, radiation and/or chemotherapy, the long-term morbidity can still be devastating. Oropharyngeal cancers and treatment lead to problems with xerostomia, eating and swallowing difficulties, trismus, nausea, vomiting, chronic pain, permanent disfigurement, dysarthria, dysphagia, and masticatory dysfunction (Stefanuto, Doucet, Robertson, 2014). Many patients also report problems with mood disorders, anxiety, and depression (Stefanuto, Doucet, Robertson, 2014).

Demographics, Signs, and Symptoms of Oral Cancers

The most common form of OC (90%) is squamous cell carcinoma of the soft tissues in the oral cavity and oropharynx (Moyer, 2014). Oropharyngeal cancers include the structures where the oral cavity and pharynx merge, these include: palatine and lingual tonsils, posterior third of the tongue, soft palate, and the posterior pharyngeal wall (Steinau et al., 2014). The most common sites for squamous cell carcinoma include: the tongue (posterior third and lateral borders), the floor of the mouth, and the oropharynx (Walsh, Rankin, & Silverman, 2013). Early signs of oral cancer can include erythroplakia, leukoplakia, and other lesions that persist for more

than two weeks (Walsh et al., 2013). Signs and symptoms also can include soft tissue masses, ulcers, and radiolucencies of unexplained origin (Cotter et al., 2014). Official diagnosis comes through biopsy and microscopic evaluation (Walsh et al., 2013). Lesions may be absent of pain which leads to the fact that two thirds of lesions diagnosed as oral cancers are diagnosed in advanced stages of development (Walsh et al., 2013).

Most oral cancers develop during the fifth to seventh decades of life; this is due in part to prolonged exposures to risk factors and interaction with other agents, which can trigger malignant transformations (Johnson et al., 2011). Malignant lesions typically take several years to progress from localized to advanced stages (Kumar & Suresan, 2012). Treatment at earlier stages is often less invasive, has a higher rate of success, and is up to three times less expensive than treatment methods for advanced stage oral cancers (Kumar & Suresan, 2012; Walsh et al., 2013). Prior to 1995 less than one third of patients diagnosed with oral cancer reported no behaviors that are considered major risk factors (i.e. smoking), in recent years almost two thirds of patients who develop oral cancers are individuals who have reported no major risk factor behaviors (Dahlstrom et al., 2013).

Risk Factors

Tobacco and heavy alcohol use remain the most influential risk factors for the development of oral and pharyngeal cancers (Walsh et al., 2013). Along with tobacco and alcohol, human papillomavirus has recently been recognized as an independent risk factor for OPC (Steinau et al., 2014). Other risk factors include age, sun exposure, previous cancer diagnosis, low consumption of fruits and vegetables, high consumption of meats, use of betel quid or areca nut, being edentulous (or partially edentulous), lack of knowledge about risk factors and symptoms, and lack of access to preventive therapies (Cotter et al., 2011; Moyer,

2014; Walsh et al., 2013). Many risk factors are synergistic and removing even one risk factor can reduce the probability of developing cancer significantly (Cotter et al., 2011).

The use of betel quid is a common practice in many Asian countries. The betel quid is often made up of betel leaves, areca nut, slaked lime, and possibly tobacco or other spices, and is chewed on by individuals during the day (Johnson et al., 2011). The betel quid contains very high quantities of nitrosamines, known carcinogens (Johnson et al., 2011).

Smoking rates have declined in recent decades in many economically developed countries (Simard, Torre, & Jemal, 2014). In the United States smoking rates peaked in the 1960's (approximately 40% of the population) and have declined since, with current smoking rates at approximately 20% (Pytynia, Dahlstrom, & Sturgis, 2014; Simard et al., 2014). This decline is due to the known health hazards of smoking tobacco and the implementation of smoking cessation programs that have become well established in the past few decades (Simard et al., 2014). The use of smokeless tobacco, also containing many known carcinogens, has increased due to public smoking restrictions and claims from manufacturers as to the increased safety of the product over smoking (Johnson et al., 2011).

Human Papillomavirus (HPV) as a Risk Factor

Over recent decades, there has been a shift in the prominent risk factors for oral cancer. While tobacco and alcohol use are still primary factors, human papillomavirus (HPV) has been detected in over 70% of diagnosed oropharyngeal cancers (OPC) including 80% of tonsillar cancers (Steinau et al., 2014). HPV-16 is the most common strain with regards to cancer development, both cervical and oropharyngeal (Steinau et al., 2014). HPV-16 is associated with 85-95% of HPV positive oropharyngeal cancers (Moyer, 2014). It is surmised that the microanatomy of the lymphoepithelial tissue of Waldeyer's ring (mostly that of the lingual and

palatine tonsils with deep invaginations and tonsillar crypts) may expose immature basal cells to HPV infection making that area especially prone to infection (Steinau et al., 2014). The ability of the virus to disrupt the cell cycle control causes increased proliferation and inhibits apoptosis which encourages malignant cell growth and multiplication (Baumeister, Reiter, Welz, Becker, & Harreus, 2014). Of patients with diagnosed OPC, 66% of men and 53% of women tested HPV-16 positive at the site (Steinau et al., 2014). From 1988 to 2004, HPV-associated OPC increased threefold from 0.8 to 2.6 cases per 100,000 (Moyer, 2014). In a different study, Colevas (2014) reported a 225% increase in HPV associated OPC between 1984 and 2004. The largest increase occurred within the last decade with a 5% annual increase since 1984 (Pytynia, et al., 2014).

The majority of HPV associated OPC patients are male (82%), white (77%), over 49 (77%), with private insurance (54%), or Medicare (18%). HPV associated OPC is diagnosed on average 5 years earlier than HPV negative oropharyngeal cancers (Chen, Zhu, & Fedewa, 2014; Moyer, 2014). In general, HPV positive OPC have a better prognosis than HPV negative oropharyngeal cancers due to a younger age at diagnosis and a lighter smoking/alcohol usage history (Habbous et al., 2013). HPV associated OPC typically present with small primary tumors and extensive nodal dispersal; patients seek treatment due to symptoms associated with the nodal dispersal rather than the cancerous lesion itself (Pytynia et al., 2014).

Conventional Oral Cancer Screening

Oral cancer screenings are considered a secondary prevention mechanism to detect cancerous or pre-malignant lesions early (Kumar & Suresan, 2012). An oral cancer screening must begin with a thorough review of a patient's health history (Rock, Takach, & Laronde, 2014). Clinicians need to evaluate for risk factors and behaviors that would impact a patient's

chances of developing oral cancer. Oral cancer screenings include visual inspection of the face, neck, lips, labial mucosa, buccal mucosa, gingiva, and floor of the mouth. Screenings should include palpation of lymph nodes, tongue, floor of mouth, and oral mucosa (Moyer, 2014). Oral cancer screenings typically begin with an extra-oral exam and are followed by an intra-oral exam.

During extra-oral exams a clinician should look for asymmetry and swelling (Rock et al., 2014). Clinicians palpate several lymph nodes in the head and neck region including occipital, submental, submandibular, cervical, supraclavicular nodes looking for tender, enlarged, firm, or fixed nodes (Rock et al., 2014). Intraoral exams include visual inspection and palpation of all tissues including the tongue, mucosa, and salivary glands. Clinicians visualize the oropharynx for lesions on the posterior wall of the pharynx, palatine tonsils, and base of the tongue. These areas are often only visible with the use of a depression device (dental mirror or tongue depressor) and full extension of the tongue (Rock et al., 2014). To view the posterior lateral borders of the tongue, a clinician should use gauze to stretch the tongue and roll it side to side for visual and tactile examination (Rock et al., 2014). The American Cancer Society recommends comprehensive oral cancer screenings every year for all individuals over the age of 40 (Walsh et al., 2013).

Adjunct Technologies Used for Screening

There are several adjunct technologies available to aid clinicians in early detection of cancerous lesions in the oral cavity; although, these technologies require supplemental knowledge and training on the use of each specific adjunctive screening instrument before professionals integrate these techniques into practice (Rock et al., 2014). Lingen, Kalmar, Karrison, and Speight (2007) advocate that effective screening tests should: be simple, detect the

disease early, at pre-malignant stages, while still treatable, and have high sensitivity and specificity (Lingen, Kalmar, Karrison, & Speight, 2007). Sensitivity is defined as the proportion of subjects with the disease that test positive while specificity is defined as the proportion of individuals without the disease that test negative (Lingen, et al., 2007).

Lingen et al. (2007) describe four methods used during oral cancer screenings. Methods include: standard screening, oral cytology (brush biopsy), toluidine blue (tolonium chloride), and light based detection systems (ViziLite Plus, MicroLux DL, and VELscope). Brush biopsies are used in-office for lesions that may otherwise go un-referred; however, brush biopsies yield a high percentage of false negatives (Lingen, et al., 2007). Toluidine blue is a dye used to stain nucleic acids in abnormal tissue and therefore detect mucosal abnormalities (Lingen, et al., 2007). Tissue reflectance systems include ViziLite and MicroLux. These methods require the patient to first rinse with a 1% acetic acid solution which removes surface debris and increases visibility of cell nuclei through slight cellular dehydration (Lingen, et al., 2007). The acetic acid rinse is followed by a visual examination of the oral cavity using a blue white light source; one recorded problem with these methods is the number of false positive results (Lingen, et al., 2007).

Narrow emission tissue fluorescence (VELscope) is another adjunctive procedure (Lingen, et al., 2007). An intense blue light (400-460nm) causes normal tissues to fluoresce a pale green color whereas abnormal tissue will fluoresce as a darker green (Lingen, et al., 2007). Problems with this method include the need for equipment to be frequently calibrated, and the most abnormal lesions detected by fluorescence were already visible clinically without the use of additional technology (Lingen, et al., 2007). There is currently no validation that these adjuncts can reliably detect lesions before standard visual examination (Lingen, et al., 2007). Monteiro et

al., (2014) also determined that sensitivity and specificity of oral cancer screenings were not increased when adjunct therapies were used. Regardless of detection method, suspicious lesions must be biopsied and evaluated at a cellular level to determine the cancerous nature of the lesion (Wu & Laronde, 2014). Although no screening technique has shown 100% accuracy, all methods require adequate visualization of the oral cavity and oropharyngeal tissues.

Who Should Perform Oral Cancer Screenings

Oral cancer screenings fall under the scope of practice of several health care providers. Dental professionals (dental hygienists, dentists, and oral surgeons), otolaryngologists, and primary care providers (doctors, physician assistants, and nurses) are all individuals trained to provide oral cancer screenings for patients (Moyer, 2014). The American Cancer Society recommends provision of oral cancer screenings during all periodic health examinations (Moyer, 2014). While many of these professionals cannot legally diagnose cancerous lesions, they are instrumental in the detection and referral of suspicious and possibly pre-malignant lesions (Cotter et al., 2011).

In a study by Anderson, Smith, and Brown (2013) generalist physician's assistants were more likely to perform oral cancer screenings and refer for dental care procedures than specialist physician's assistants. The study found that, with education and training, physician assistants were capable and willing to check for oral malignancies and dental needs and refer to the proper specialists (Anderson, Smith, & Brown, 2013). Macek and Yellowitz (2008) found that dentists were the most likely to provide oral cancer screenings (70%) with 23% of screenings being performed by doctors, 1% by nurses and 7% by dental hygienists. The authors of the study posit that the percentages for dentists/dental hygienists may be skewed due to patients being unaware of the specific roles of clinicians in a dental office (Macek & Yellowitz, 2008).

Oral Cancer Detection Rates Based on Oral Cancer Screenings

Routine oral cancer screenings are associated with detection of oral cancer lesions at earlier stages and a reduction in morbidity and mortality (Kumar & Suresan, 2012; Sankaranarayanan et al., 2013). Early detection is defined as a lesion that is four centimeters or less and which has not spread (Cotter et al., 2011). Sankaranarayanan et al., 2013 conducted a 15-year follow-up study on a cluster-randomized sample of 96,500 individuals in Kerala, India. The purpose of the study was to determine the long-term impact of routine screenings on oral cancer morbidity and mortality (Sankaranarayanan et al., 2013). Patients who had repeated screenings every three years had a 34% decrease in oral cancer mortality rates (Sankaranarayanan et al., 2013). Patients with oral cancer who had zero screenings were typically diagnosed when the cancer was at stage 3 (16%) or stage 4 (37%) 32% were diagnosed at an unknown stage (Sankaranarayanan et al., 2013). Individuals who had been screened four times were diagnosed at stage 1 (40%) or stage 2 (35%) with a much better prognosis; 9% were diagnosed at stage 3 and 16% at stage 4 a 79% reduction in mortality rates for those who had three to four screenings in 15 years (Sankaranarayanan et al., 2013). Of lesions detected during screenings 23% were found to be benign, 70.8% were pre-cancerous and 5.8% were cancerous (Sankaranarayanan et al., 2013). The authors concluded that routine oral cancer screenings using visualization of the oral cavity reduced the mortality rate of oral cancers through early detection (Sankaranarayanan et al., 2013). Of patients with oral cancer who had routine dental visits, 70% were diagnosed early compared to only 40% of patients with oral cancer without routine dental care (Moyer, 2014).

Moyer (2014) compiled data from seven studies and reported the sensitivity of Comprehensive Oral Examinations (COE) ranged between 18-94%, and the specificity between

54-99%. How et al. (2011) reported the sensitivity and specificity of visual and tactile procedures for OCS at 98.9% and 98.7% respectively. Oral cancer screenings cost less than $6 per person and the cost per life saved has been reported to be $835 dollars. (Sankaranarayanan et al., 2013).

Oral Cancer Screening Rates

Ideally, all oral health practitioners should provide risk factor assessments and OCS for all patients (Cotter et al., 2011). However, Macek and Yellowitz (2008) found that most OCS are performed only when there is a specific problem reported by patients. Between 2002 and 2008 oral cancer screenings were reported to have increased from 33% to 39% (Viswanath et al., 2013). The study also found that lesions discovered at a dental office typically presented at an earlier stage than lesions found during screenings at medical offices (Viswanath et al., 2013).

There is a definitive discrepancy between OCS occurrence rates based on health care professional self-reported data and information from individual patients regarding their screening history. Walsh, Rankin, and Silverman (2013) conducted surveys of 1,500 dental hygienists to determine if continuing education courses presented to oral health professionals would impact the occurrence of comprehensive oral examinations and tobacco cessation counseling in dental offices. The authors report that almost all dental hygienists surveyed believe that oral cancer screenings are "very important;" but only half do a complete extra- and intra-oral exam (Walsh et al., 2013). Only 75% of those professionals doing thorough screenings tell the patient what they are doing and very few use any adjunct technology for screenings (Walsh et al., 2013). The study showed that almost 80% of dental hygienists did perform an intra-oral exam on patients who were over the age of 40 and reported a history of smoking (Walsh et al., 2013) The authors determined that continuing education courses did positively impact counseling and examination rates of occurrence (Walsh et al., 2013) .

A 2011 study by Cotter et al found that 45.8% of dental hygienists always performed an oral cancer screening. Of dental hygienists surveyed, 23.5% reported they performed an oral cancer screening at initial appointments and 47.4% reported they performed a screening at re-care appointments (Cotter et al., 2011). The study found a correlation between years in practice and performance of an oral cancer screening with 51.2% of dental hygienists who had been practicing for 16 or more years performing an oral cancer screening for all patients at every appointment (Cotter et al., 2011). 49% of dental hygienists surveyed reported they were "very comfortable" with intra-oral exam procedures, but only 26% reported being "very comfortable" with extra-oral procedures (Cotter et al., 2011).

Kumar and Suresan (2012) used questionnaires to conduct a descriptive cross-sectional survey of 250 private dental practitioners in Bangalore to assess oral cancer knowledge, attitude, and screening behaviors of dental professionals. The authors found that no more than 37% of dentists routinely performed an oral cancer screening for all patients. The same study found that 68% of dentists recorded the tobacco and alcohol behaviors of their patients, but only 31% offered any behavioral or cessation counseling after determining risky behaviors (Kumar & Suresan, 2012). The survey also found that only 12% refer suspicious lesions but 24% would perform a brush biopsy of the lesion in the office (Kumar & Suresan, 2012). The authors determined that dental professionals were in need of educational interventions in order to increase the professionals' knowledge of oral cancer and adequate screening procedures for early detection of oral and oropharyngeal cancers (Kumar & Suresan, 2012).

While typically around half of oral healthcare providers report completing routine oral cancer screenings, only 20% of American's over the age of 40 report having had an oral cancer screening performed on them (Walsh et al., 2013). When the process was described as an exam

where the clinician "pulled on the tongue" or palpated the neck the number rose to 29.4% of patients saying they had experienced that procedure (Moyer, 2014). The same study reported that individuals over the age of 40 who were smokers were the least likely group of responders to have received an oral cancer screening, despite being at the highest risk for developing oral cancer (Moyer, 2014; Viswanath et al., 2013).

The discrepancy in reported findings could be due to patient unawareness of the procedure that was being completed. This inconsistency could also point to a lack of access to care for those surveyed. If individuals are unable to go to a dental appointment they would not have the opportunity to have an oral cancer screening performed. More research on the percentage of patients receiving oral cancer screenings during dental or medical appointments needs to be conducted in order to determine if the lack of screenings is due to clinicians not performing exams, or lack of access to dental care for individuals.

Barriers to Screening

Even though the oral cavity (excluding the oropharynx) is readily visible and easily accessible, and the early detection of oral cancers leads to a much better prognosis, the rates of oral cancer screenings are still low (Sankaranarayanan et al., 2013). Common reasons listed for professionals not performing thorough screenings include: lack of time, insufficient knowledge, or the fact that a different professional in the same office performs the exam (Kumar & Suresan, 2012). In the survey of 250 dental practitioners conducted by Kumar and Suresan described earlier, 57% of dentists reported that their oral cancer knowledge was out of date and only 68% reported that they felt they were adequately trained for oral cancer screenings even though between 68-90% reported that an oral cancer screening should be performed for all patients over the age of 40 (Kumar & Suresan, 2012).

Another barrier to care is clinician discomfort in discussing more personal information with patients. Daley et al. (2011) found that only 9% of dentists discussed HPV with their patients. This was mostly reported as being caused by a worry of liability concerns and male clinician discomfort talking to female patients (Daley et al., 2011). There was also a concern for adequate privacy when discussing possibly sensitive matters due to the open-door layout typical to dental offices (Daley et al., 2011). Overall dentists reported a desire for more established research and professional guidelines and policies regarding the discussion of HPV and possible vaccine recommendation before they would feel comfortable discussing the virus routinely (Daley et al., 2011). The authors of the study posit that the public will recognize the role of oral healthcare providers in discussing HPV associated oral cancers before there is professional acceptance and readiness for the responsibility (Daley et al., 2011).

In a 2011 study by Cotter et al., it was determined that there was a lack of professional and public knowledge about the importance of early detection for increased survival of OPC and 22% reported a lack of time for screenings during appointments. Kumar and Suresan (2012) report that a thorough oral cancer screening with complete extra- and intra-oral exam could take as little as 90 seconds for trained professionals. Other reasons discovered by the Cotter et al. survey (2011) included the dentist preferring the dental hygienist to not perform an oral cancer screening, or the dentist performs the exam before the dental hygienist sees the patient (23%). Cotter et al. (2011) remind health professionals that clinicians can be held legally liable for not accurately documenting or detecting suspicious lesions.

Johnson et al., (2011) noted a failure of primary care professionals to recognize signs and symptoms indicative of cancer. This is especially significant when Macek and Yellowitz (2008) found that adults in the United States are more likely to have a yearly medical exam than an

exam from a dentist. In one study, 79% of doctors reported knowing the procedures for an oral cancer screening but less than 50% knew the early signs and symptoms of oropharyngeal cancers (Viswanath et al., 2013). Maybury, Horowitz, and Goodman (2012) recommend requiring all dental and dental hygiene students to perform a set number of supervised oral cancer screenings for accreditation, graduation, and licensure. The article also discussed the importance of training doctors, nurses, and physician's assistants to perform oral cancer screenings, as well as educating the public about oropharyngeal cancer risk factors and symptoms (Maybury, Horowitz, & Goodman, 2012).

Delays in Diagnosis

In a 2014 article, Stefanuto, Doucet, and Robertson explored delays in oral cancer diagnosis. The authors conducted a literature review, which included eighteen English-language, retrospective case-controlled studies from Medline, PubMed, and the Cochrane database (Stefanuto, Doucet, & Robertson, 2014). The purpose of the study was to update readers as to the current issues surrounding the delay of treatment for oral cancer (Stefanuto et al., 2014). The authors divided diagnostic delay into two categories: patient delay and professional delay. On average patient delay lasts between 3.5 and 5.4 months while professional delay is about 14-21 days; for comparison a squamous cell carcinoma tumor can double in size in three months (Stefanuto et al., 2014). Patient delays are typically due to the patient's use of home remedies and waiting for healing from those treatments, association of the lesion with other etiology, and a misinterpretation of symptoms (Stefanuto et al., 2014).. The study found no correlation between income, education level, and length of patient delay (Stefanuto et al., 2014).

Professional delay occurs between the time a professional notices a lesion, refers the lesion for diagnosis, and the official diagnosis is made (Stefanuto et al., 2014). The study found

that 78% of doctors refer the patient on the day of detection and a definitive diagnosis is made within 3-6 weeks (Stefanuto et al., 2014). The average clinical stage at referral from a dental office was 1.94, while the average stage at referral from a physician was 3.0 and only 18% of physicians provide oral exams to half or more of their patients (Stefanuto et al., 2014). On average referrals from dental offices were made during screenings of patients who reported no screenings while referrals from physician's offices came from appointments related to symptoms from the lesion or disease (Stefanuto et al., 2014). The authors concluded that patient delay still constitutes the greatest cause of delay in head and neck cancer treatment, which may be the reason most cancers are diagnosed at a late stage of development (Stefanuto et al., 2014).

Summary

Oral cancer is a major health problem with 42,440 new cases between 2013 and 2014 (Siegel, Ma, Zou, & Jemal, 2014). Of those new cases the majority were located on the posterior tongue or in the oropharynx area of the oral (Siegel, Ma, Zou, & Jemal, 2014). In 2013 oral cancer caused 8,390 deaths and is still the 8th most common new cancer in men (Siegel, Ma, Zou, & Jemal, 2014). Laronde (2014) predicts the number of new oral cancer cases will rise 45% by 2027. Even if the cancer can be treated, the long term effects can still be devastating; these effects can include problems with xerostomia, eating and swallowing difficulties, trismus, nausea, vomiting, chronic pain, permanent disfigurement, dysarthria, dysphagia, masticatory dysfunction, mood disorders, anxiety, and depression (Stefanuto, Doucet, Robertson, 2014).

Squamous cell carcinoma is the most common form of oral cancer and typically presents on the tongue (posterior third and lateral borders), the floor of the mouth, and the oropharynx (Walsh et al., 2013). Early signs of oral cancer can include erythroplakia, leukoplakia, and other lesions that persist for more than two weeks, soft tissue masses, ulcers, and radiolucencies of

unknown etiology (Cotter et al., 2014; Walsh et al., 2013). Lesions may not be associated with any pain or physical symptoms the patient is aware of which can impact length of time before diagnosis (Walsh et al., 2013).

Tobacco and heavy alcohol use remain the most influential risk factors for the development of oral and pharyngeal cancer, however, HPV, particularly HPV-16, has recently been recognized as an independent risk factor for the development of oropharyngeal cancers as well (Steinau et al., 2014; Walsh et al., 2013). Other risk factors may include age, sun exposure, previous cancer diagnosis, low consumption of fruits and vegetables with a high consumption of meats, use of betel quid or areca nut, lack of knowledge about risk factors and symptoms, and lack of access to preventive therapies (Cotter et al., 2011; Moyer, 2014; Walsh et al., 2013). These risk factors are synergistic in nature and the probability of developing cancer can be greatly reduced by removing even one risk factor (Cotter et al., 2011).

Oral cancer screenings are an effective method to reduce the morbidity and mortality of oral cancers through early detection (Kumar & Suresan, 2012). Screenings should begin with a thorough health history review and evaluation of risk factors (Rock et al., 2014). After health history evaluation clinicians should perform extra- and intra-oral examinations where lymph nodes and oral tissues are palpated and visually inspected for symmetry, firm or tender areas, color changes, and lesions. (Moyer, 2014). Proper visualization of these areas require the use of a tongue depressor or dental mirror, gauze, and full tongue extension (Rock et al., 2014). While there are several adjunct technologies on the market to aid oral cancer screenings (oral cytology (brush biopsy), toluidine blue (tolonium chloride), and light based detection systems such as ViziLite Plus, MicroLux DL, and VELscope), none of these have proven to be more effective

than standard screenings alone (Rock et al., 2014). However, all adjunct technology methods still require adequate visualization of the oral cavity and oropharynx.

Oral cancer screenings fall under the scope of practice of several health care providers including: dental professionals (dental hygienists, dentists, and oral surgeons), primary care providers (doctors, physician's assistants, and nurses), and otolaryngologists (Moyer, 2014). While most of these professionals cannot legally diagnose cancerous lesions, they can be instrumental in the early detection and referral of suspicious lesions (Cotter et al., 2011). The American Cancer Society recommends OCSs be provided during all periodic health examinations (Moyer, 2014).

Conventional OCSs have a reported sensitivity of 98.9% and 98.7% specificity (How et al., 2011). Routine screenings can reduce mortality by 79% and increase the rates of early detection by almost 50% (Sankaranarayanan et al., 2013). Despite the data that screenings are an effective method to reduce morbidity and mortality, less than half of dental hygienists surveyed reported always performing a screening for their patients, and less than 30% of adult Americans reported ever having an oral cancer screening performed on them (Cotter et al., 2011; Walsh et al., 2013). Common barriers to care include lack of time and insufficient knowledge (Kumar & Suresan, 2012).

With patients delaying, on average, three and a half to five and a half months between lesion detection and seeking professional care, it is vital that health care providers screen patients routinely to detect lesions early and improve patient prognosis (Stefanuto, Doucet, Robertson, 2014).

Despite the importance of visualization of the oropharynx in early detection of oral cancers; there is currently no research available regarding the visibility of the oropharynx and

structures of the oral cavity proper. There is also no literature comparing the use of a tongue depressor, dental mirrors, or having a patient say “ahh” to examine the oropharynx. By conducting research on the various methods of oropharynx visibility, information can be made available to practicing health care providers and students in health care programs to aid in more effective oral cancer screenings and promote early detection of cancerous or pre-malignant lesions.

In order to combat the rising incidence of oral cancers, it will be up to health professionals to perform routine cancer screenings and educate patients on risk factors and symptoms of oral cancer. While most professionals agree on the importance of oral cancer screenings, compliance is still low for performing screenings. Increased screenings will lead to increased rates of oral cancers detected in the early stages, and will reduce the morbidity and mortality of the disease.

Chapter III

Methodology

Design Overview

This study identified differences in visibility between five conventional oropharynx visualization methods: retraction of the tongue via the use of a tongue depressor, mouth mirror, having the patient say "ahh", a combination of tongue depressor and the patient saying "ahh", and a combination of mouth mirror and the patient saying "ahh". Using each of the five identified methods, participating student clinicians visualized the oropharynx during a regularly scheduled dental hygiene appointment and completed a survey regarding their perceptions of variation in visibility levels. Intra-oral photographs were taken of the oropharynx for each of the five methods tested by the clinicians and a nine-item anatomical structure checklist was used to score the photographs for visibility.

Hypothesis and Research Questions

***Null hypothesis*.** There is no statistically significant difference in visibility of the oropharynx when retracting the tongue using a tongue depressor, dental mirror, having the patient say "ahh", a combination of tongue depressor and saying "ahh", or a combination of dental mirror and saying "ahh".

***Research questions*.** Is there a difference in accuracy of visibility of the oropharynx when retracting the tongue using a tongue depressor, dental mirror, having the patient say "ahh", a combination of tongue depressor and saying "ahh", or a combination of dental mirror and saying "ahh"?

What are dental hygiene clinicians' perceptions of accuracy of oropharynx visualization using each of five conventional methods (tongue depressor, dental mirror, having the patient say

"ahh", a combination of tongue depressor and saying "ahh", or a combination of dental mirror and saying "ahh") for tongue retraction?

Variables

The independent variables in this study included five conventional methods used for tongue retraction to visualize the oropharynx. The dependent variable is visibility of oropharyngeal structures.

Research Method and Design

A quantitative, descriptive study design was used to identify the most accurate method of tongue retraction for visualization of the oropharynx. Participants used each of five conventional methods of tongue retraction during a regularly scheduled dental hygiene appointment. Intraoral photographs were taken of each method and scored by comparing the photograph to a nine-item checklist of oropharyngeal anatomical structures to determine how many of the structures were visible. Additionally, participants were surveyed to determine perceptions of visibility level and preference of each visualization method.

Description of Setting

This study took place at the ISU Dental Hygiene Clinic in Pocatello, Idaho during DENT 4403C Advanced Clinical Practice I clinical sessions. Participating student clinicians used five conventional tongue retraction methods for visualization of the oropharynx during a regularly scheduled clinic appointment with two separate patients. Appointments were scheduled on Tuesdays and Thursdays, 8 a.m.to 12 p.m. and 1 p.m. to 5 p.m. and data was collected over a two week period during November and December 2014.

Research Participants

Sample description. A convenience sample of 25 senior dental hygiene students at Idaho State University were asked to participate.

S*ample inclusion and exclusion criteria.* Participants did not demonstrate the visualization methods for data collection outside of a regularly scheduled dental hygiene appointment. Participants demonstrated the five visualization methods with a patient who: consented to intraoral photographs, could be in a supine or semi-supine position, was not anesthetized and did not have a moderate to severe gag reflex.

Human subjects' protection. All participating student clinicians provided written informed consent (Appendix A). This study qualified for an expedited review by the ISU Human Subjects Committee under Category 5: "Materials collected for non-research purposes. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis)". Patients involved signed a consent form for permission to take intra-oral photos during the study and for the use of those photographs in future publications (Appendix B).

Data Collection

***Procedure/protocol*.** During regularly scheduled clinic sessions, the principal investigator (PI) had each participant visualize the oropharynx by using a tongue depressor, mouth mirror, having the patient say "ahh", having the patient say "ahh" in combination with a tongue depressor and having the patient say "ahh" in combination with a mouth mirror. Student dental hygienists had an instructional session prior to data collection to familiarize techniques for all tested methods. Clinicians tested each method in a different sequence as instructed by the PI in order to counter-balance order bias. Clinicians allowed a 30 second to one minute rest between

methods to prevent patient fatigue. Each participant completed these five visualization methods with two separate patients. Following visualization methods on each of two separate patients, participants completed a survey related to their perceptions of the level of oropharynx visualization permitted by each method (Appendix C).Visibility of the oropharynx was documented for each method with an intraoral photograph; each photograph set was coded with the same identifier. Intraoral photograph sets were scored using the Anatomical Checklist for Intraoral Photograph Comparison (Appendix D).

Instruments. Data were collected through a seven question survey taken by participating clinicians (Appendix C), and intraoral photograph comparisons of visible anatomical structures (Appendix D). Both instruments for data collection were created by the PI for use during the proposed study and tested for reliability and validity prior to use.

Reliability and validity. The survey instrument was pilot tested with five clinical faculty members for clarity and content validity. A content validity index was completed for the oropharynx visualization survey. Test-retest reliability was determined by administering the survey at two different points in time to the same individuals. Intra-rater reliability was established by test-retest using the anatomical structure checklist to score the sets of photographs. Photographs were evaluated by a single rater who was not involved in data collection to prevent any unintentional inherent investigator bias. All intraoral photographs were taken by the PI, aligning the front of the intraoral camera with the incisal edge of the patient's maxillary anterior central incisors to ensure reliability between photographs.

Statistical analysis. Data were analyzed using descriptive statistics, χ^2 goodness of fit test, and Analysis of Variance (ANOVA).

Limitations. Due to subjectivity in clinician identification of severity of a gag reflex, variability exists with this particular exclusion criterion that may adversely affect the visualization method. Possible photographer fatigue could have been a limitation if not enough time was allotted between intraoral photographs of each retraction method. A limitation of this proposed study comes from the small sample size and narrow range of healthcare clinicians (dental hygiene students), which may impact the generalizability of this study to practicing dental hygienists.

Summary

This study provided the dental hygiene community with important information that can be applied to clinical practice in the implementation of head and neck cancer screenings, as well as dental hygiene education regarding OPC examinations. Results discussion and conclusions for this study will be reported in the form of a manuscript, in the subsequent section of this document, to be submitted for publication in the Journal of Dental Hygiene. The sections of the manuscript reflect the specifications as outlined in the author guidelines (Appendix E).

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Visualization of the Oropharynx during Head and Neck Cancer Examinations

Courtney Perrachione RDH, MS, CHES, Tara L. Johnson, RDH, PhD, Assistant Professor Idaho State University, JoAnn R. Gurenlian, RDH, MS, PhD, Professor Idaho State University

Contact Information: Courtney Perrachione
1316 E Whitman, Pocatello ID, 83201
P: (660) 216-8891
F: (208) 282-4071
perrcour@isu.edu

Courtney Perrachione, RDH, MS, CHES, is a clinical instructor in the Department of Dental Hygiene, Tara L Johnson, RDH, PhD, is an Assistant Professor in the Department of Dental Hygiene, and JoAnn Gurenlian, RDH, MS, PhD, is a Professor and Graduate Program Director, Department of Dental Hygiene, Division of Health Sciences, at Idaho State University.

Key words: oropharynx, visualization, oropharyngeal cancer, dental mouth mirror, tongue depressor, oral cancer screening.

This study meets the following National Dental Hygiene Research Agenda (NDHRA) items: D4. Clinical Dental Hygiene Care: Investigate how dental hygienists identify patients who are at-risk for oral/systemic diseases and A1. Health Promotion/Disease Prevention: Assess strategies for effective communication between the dental hygienist and client (American Dental Hygienists' Association, 2007).

ABSTRACT

Purpose

The purposes of this study were twofold: 1) to determine differences in visibility of the oropharynx during OPC screenings using five methods of tissue retraction; and 2) to identify clinician perceptions of visibility levels and preferences when using those visualization techniques.

Methods

A nonprobability convenience sample of senior dental hygiene students (N=25) was asked to participate. Clinicians visualized the oropharynx of two patients using each of five conventional methods. Patients who were anesthetized or could not be supine/semi-supine were excluded. Following visualization, participants completed a survey related to their perceptions of the best visibility and preference of method. Visibility using each of the five methods was documented with an intraoral photograph and scored using an anatomical checklist. Data were analyzed using descriptive statistics, Chi-square goodness of fit test and Analysis of Variance (ANOVA).

Results

The combination of mirror/"ahh" was perceived as providing the best visibility (52.5%), followed by the combination of tongue depressor/"ahh" (37.5%). The combination of mirror/"ahh" was most preferred (55%) followed by the combination of tongue depressor/"ahh" (32.5%). Forty-two intraoral photographs for each of the five visualization methods were evaluated based on the visibility of nine anatomical structures. Mean visibility scores were best for the combined methods and had significantly lower visibility for single-step methods.

Conclusions

Dental hygienists should request their patients say “ahh” in conjunction with a dental mirror or tongue depressor for adequate tissue retraction and visualization. For high-risk individuals, mirror laryngoscopy should be considered. Consistent guidelines for OPC screenings should be developed and implemented across disciplines.

Introduction

Cancer is the second leading cause of death in the United States (after heart disease) for both men and women of all ages. In 2014, there were 42,500 new cases of oral and pharyngeal cancer (OPC) diagnosed in the United States and 8,390 deaths. This number represents a 10% increase from those new cases documented in 2013.[1, 2] Additionally, OPC diagnoses are predicted to rise significantly in the next 15 years.[3] Survival rates are dramatically higher when OPC is diagnosed early; however, less than a third of new cases are diagnosed at the localized stage, compared to over half which are diagnosed in advanced stages.[4,5] Of oral cancer lesions, 35% were located in the oropharynx.[1]

The Oropharynx consists of the structures where the oral cavity and pharynx merge, these include: palatine and lingual tonsils, posterior third of the tongue, soft palate, and the posterior pharyngeal wall.[6] While tobacco and heavy alcohol use remain the most influential risk factors for the development of all OPCs, recently, human papillomavirus (HPV) has been recognized as another independent risk factor.[7,8,9] The incidence of head and neck cancers in the U.S. has fallen in recent years, consistent with the decrease in tobacco use.[10,11] By contrast, the incidence of HPV-related OPC is on the rise specifically in the tonsils and at the base of the tongue and most notably in individuals 40–55 years old.[12,13,14,15] HPV has been detected in over 70% of diagnosed OPCs, including 80% of tonsillar cancers. HPV-16, the most common high-risk strain, is associated with 85-95% of HPV-positive OPCs.[8,16]

Intraoral exams include visual inspection and palpation of oral tissues including the tongue, mucosa, and salivary glands; a thorough exam can be completed in as little as 90 seconds.[17,18] Clinicians must visualize the oropharynx for detection of lesions on the posterior wall of the pharynx, palatine tonsils, and base of the tongue. These areas are often only visible

with the use of a depression device (dental mirror or tongue depressor) and/or full extension of the tongue.[18] Recommended armamentarium for a conventional OPC screening includes sterile gauze, mouth mirror, tongue depressor and adequate overhead lighting. An active gag reflex and inadequate retraction of the tongue often hinder examination of the posterior region of the oral cavity. Although there are several adjunct technologies on the market to aid OPC screenings: oral cytology (brush biopsy), toluidine blue (tolonium chloride), and light based detection systems (ViziLite Plus, MicroLux DL, and VELscope), it is important to note that all of the methods available still require adequate viualization of the oral cavity.[19] Consequently, premalignant lesions and OPCs can be difficult to visualize.[20] Currently, there is a lack of official, consistent, guidelines regarding visualization recommendations for the oropharynx.[21]

Although a majority of dental hygienists report performing routine OPC screenings, visibility of structures for the early identification of premalignant lesions or OPC has not been addressed.[7] Considering the increase in HPV-related OPCs afflicting a younger demographic in the absence of traditional risk factors, it is essential that dental hygienists recognize and use the most effective method for oropharyngeal visualization.[9] Additionally, understanding gaps in practices is central to planning educational programs in dental hygiene curricula, as well as for continuing education courses.[22] Therefore, the purposes of this study were twofold: 1) to determine differences in visibility of the oropharynx during OPC screenings using five methods of tissue retraction; and 2) to identify clinician perceptions of visibility levels and preferences when using those visualization techniques.

Methods and Materials

A nonprobability convenience sample of senior dental hygiene students (N=25) at Idaho State University were asked to participate in this visualization by tissue retraction methods study.

The study qualified for an expedited review by the ISU Human Subjects Committee (#4189). Participating student clinicians obtained consent from their patients to take intra-oral photos during the study, and for the use of those photographs in any future publications. Patients who were anesthetized or who could not be supine/semi-supine were excluded from having oropharyngeal visualization procedures photographed.

The independent variables in this study included five conventional methods for tongue retraction to visualize the oropharynx via the use of: 1) a tongue depressor only; 2) a mouth mirror only; 3) having the patient say "ahh"; 4) a combination of tongue depressor and the patient saying "ahh"; and 5) a combination of mouth mirror and the patient saying "ahh". The dependent variable was visibility of nine oropharyngeal structures. Visibility of each structure was scored as: 1 = good (greater than 75% was visible); 2 = fair (50% to 75% was visible); and 3 = poor (less than 50% was visible).

Participants were provided a 15-minute instructional session prior to data collection to familiarize themselves with visualization techniques for all tested methods. During regularly scheduled clinic sessions, participating senior clinicians visualized the oropharynx of two patients using each of the previously mentioned conventional methods. Each method was performed in a different sequence as instructed by the principle investigator (PI) to counter-balance order bias. Participants allowed a 30 second to one minute rest between methods to prevent patient fatigue. Each participant completed the same five visualization methods with two separate patients. Following visualization, participants completed a survey related to their perceptions of the level of visibility offered by each method and the clinician's preferred method.

Visibility using each of the five methods was documented with an intraoral photograph coded with the same identifier. Intraoral photograph sets were scored using an Anatomical Checklist for Intraoral Photograph Comparison.

Five clinical faculty members scored the oropharynx visualization survey instrument for clarity and content validity using the Content Validity Index (100% validity). A single rater, not involved in data collection, scored photographs to prevent unintentional inherent investigator bias. Intra-rater reliability was established by test-retest using the anatomical structure checklist to score each set of photographs. The individual evaluating photographs scored the initial checklist and re-test checklist exactly the same for 100% intra-rater reliability. All intraoral photographs were taken by the principle investigator (PI) and calibrated by aligning the front of the intraoral camera with the incisal edge of the patient's maxillary central incisors to ensure reliability between photographs.

Data were analyzed by Minitab® 17 using descriptive statistics, Chi-square goodness of fit test and Analysis of Variance (ANOVA).

Results

The results of this study are presented based on clinicians' perceived visibility, preferred method of visualization and intraoral photograph analysis compared to a checklist of visible anatomical structures.

Clinicians' Perceived Visibility

Twenty-one student clinicians participated in this clinical study with a total of 40 survey responses returned. A summary of perceived visibility as reported separately for two patients by each participant is shown in Table 1. The combination of mirror/"ahh" was perceived as providing the best visibility, followed by the combination of tongue depressor/"ahh".

Clinicians' Preferred Method of Visualization

The combination of mirror/"ahh" was most preferred followed by the combination of tongue depressor/"ahh" indicating a statistically significant difference in clinician preference of oropharynx visualization when comparing the combined methods to the single-step methods (Table 2).

Comparison of Intra-oral Photographs with Anatomical Structures Checklist

Forty-two intraoral photographs for each of the five visualization methods (n = 210) were evaluated based on the visibility of nine anatomical structures. Differences in mean scores for visibility of the nine anatomical structures related to each of the five visualization methods is summarized in Figure 1 and Figure 2. There was a significant difference in the mean visibility of circumvallate papillae, palatoglossal arch, uvula, and the soft palate; whereas, the palatine tonsils, palatopharyngeal arch, posterior pharyngeal wall, tonsillar recess, and isthmus of fauces all had statistically similar mean visibility scores. Figure 3 pictures the method showing the most (tongue depressor/"ahh") and the method showing the fewest ("ahh") visible structures based on the Anatomical Checklist.

Discussion

The primary screening test for OPC is a systematic clinical examination of the oral cavity. According to the World Health Organization and the National Institute of Dental and Craniofacial Research (NIDCR), an oral cancer screening examination should include a visual inspection of the face, neck, lips, labial mucosa, buccal mucosa, gingiva, floor-of-the-mouth, tongue, and palate.[23,24] Dental hygienists are in a prime position to enhance early detection of OPC because they see their patients regularly and have the opportunity to provide an OPC screening at each appointment. Standard of care practices include a complete head and neck

examination by palpation, visualization, or both. Yet, due to the limited access of the oropharynx, screening for OPC in this area allows for visualization only. This study was undertaken to identify differences in visualization of oropharyngeal structures using five distinct methods of tissue retraction, clinicians' perceived visibility using each of the five methods and their preference for one method over the others.

While participants preferred using either the combination of dental mirror/"ahh" or tongue depressor/"ahh" retraction method over a single-step method, preference was not always aligned with the literature regarding recommended procedures specific to visualization of the oropharynx. For example, in the document *Screening for Oral Cancer: U.S. Preventive Services Task Force Recommendation Statement*, the only adjunct to visual inspection listed was "Mouth mirrors can help visualize all surfaces."[16] As well, the NIDCR recommends visually inspecting the oropharynx using a small, long-handled mirror to check for abnormal areas.[25]

Perceived "higher" visibility (as determined by the number of structures participants felt they could see) was also significantly noted for the dental mirror/"ahh", followed closely by tongue depressor/"ahh" retraction methods. Clinicians perceived significantly lower levels of visibility using the single-step methods of tissue retraction with the dental mirror, tongue depressor or "ahh". These perceptions were supported by evaluation of intraoral photographs, which show the combined methods (e.g. dental mirror/"ahh", and tongue depressor/"ahh") having higher levels of visibility than single-step retraction methods. Moreover, results indicated that using a tongue depressor to lower the middle portion of the tongue and having the patient simultaneously say "ahh" was the best retraction method to provide a view of the Palatoglossal Arch (Figure 1).

Oropharyngeal cancer is difficult to visualize and is usually located at the base of the tongue (the posterior third of the tongue), the soft palate (the posterior part of the roof of the mouth), the tonsils, or the lateral and posterior walls of the throat. This type of examination often requires mirror laryngoscopy using a curved mirror and direct light or flexible laryngoscopy using a speculum.[21] Although results from this study indicated the highest number of structures could be visualized by the mirror/"ahh" or tongue depressor/"ahh" retraction methods, patients who are at high risk for OPC may benefit from screening examinations with indirect mirror laryngoscopy. Through indirect mirror laryngoscopy clinicians can visualize the mucosal surfaces of the larynx and hypopharynx including the oropharyngeal vallecula and base of the tongue, as well as the pyriform sinuses and posterior pharyngeal wall.[26]

There were certain limitations to this study. A small sample of student clinicians was enrolled, and results should be interpreted within that context. The generalizability of this study is limited because it was not possible to include experienced medical and dental practitioners. However, there were ample trials of conventional tissue retraction methods and intraoral photographs to determine preference and visualization by student clinicians. This emphasizes the need to expand future studies to include practicing clinicians and other healthcare professionals who routinely examine the oral and pharyngeal structures.

Conclusion

Comprehensive head and neck examinations should be part of all medical and dental examinations. Given the high incidence of head and neck cancers, routine screenings are imperative in early diagnosis and impact the chance to decrease morbidity and mortality of the disease. HPV-associated OPC's present primarily in the oropharynx and at the base of the tongue necessitating accurate visualization of these areas during intraoral examinations. A dental mirror

or tongue depressor used alone for tongue retraction is not sufficient for adequate visualization. Dental hygienists should request that their patients say “ahh” in conjunction with either a dental mirror or tongue depressor for adequate tongue retraction and oropharyngeal visualization. Thus, examination armamentarium should include both a mirror and tongue depressor. Additionally, consistent guidelines for OPC screenings should be developed and implemented across disciplines. More research needs to be conducted with regard to possible adjunct technologies that would allow for better visualization of all areas of the oropharynx and base of the tongue. In the future, examination and screening for OPCs will likely include technologies aimed at detecting molecular markers of premalignant and malignant changes.

Acknowledgements

The authors would like to thank James Guffey Ph.D., Statistician Consultant and Meg Long, RDH, for their expert assistance.

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Table 1. Clinician Method with Best Perceived Visibility

Method	N	%	χ^2	p-value
Dental Mirror	1	2.5	6.125	0.0133
Tongue Depressor	1	2.5	6.125	0.0133
"Ahh"	2	5	4.5	0.0339
Mirror with "Ahh"	21	52.5	21.25	<0.0001
Tongue Depressor with "Ahh"	15	37.5	6.125	0.0133
Totals:	40*	100	--	--

Degrees of Freedom = 1
*of 42 possible returned surveys, 40 were completed

Table 2. Clinician Preferred Method of Oropharynx Visualization

Method	N	%	χ^2	p-value
Dental Mirror	2	5	4.5	0.0339
Tongue Depressor	2	5	4.5	0.0339
"Ahh"	1	2.5	6.125	0.0133
Mirror with "Ahh"	22	55	24.5	<0.0001
Tongue Depressor with "Ahh"	13	32.5	3.125	0.0771
Totals:	40*	100	--	--

Degrees of Freedom = 1

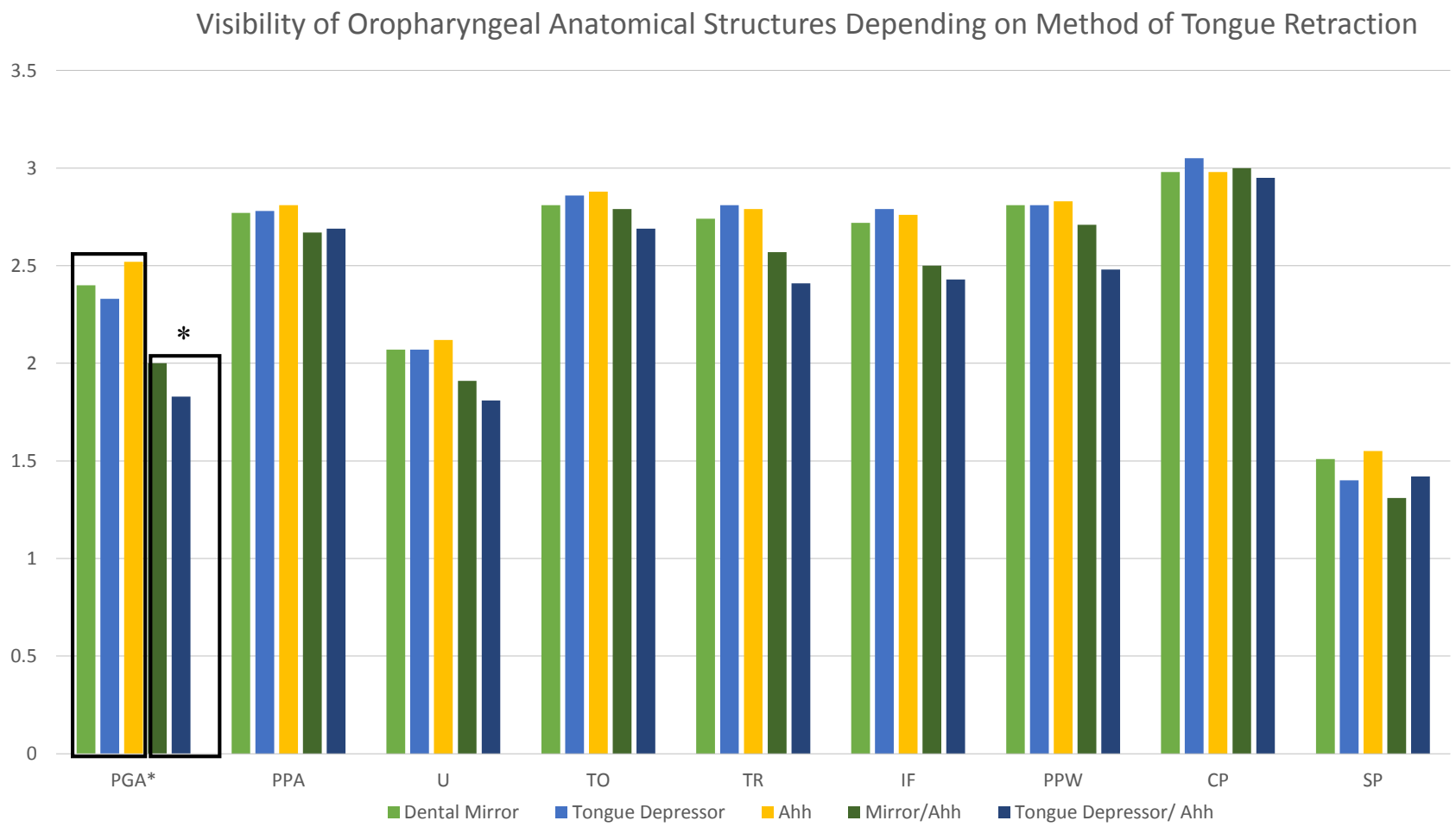
*of 42 possible returned surveys, 40 were completed

Figure 1. Mean Visibility Scores of Anatomical Structures Based on Method of Visualization

Structure	**Dental Mirror**	**Tongue Depressor**	**Ahh**	**Mirror/Ahh**	**Tongue Depressor/ Ahh**
Palatoglossal Arch	2.40	2.33	2.52	2.00	1.83
Palatopharyngeal arch	2.77	2.78	2.81	2.67	2.69
Uvula	2.07	2.07	2.12	1.91	1.81
Palatine Tonsils	2.81	2.86	2.88	2.79	2.69
Tonsillar Recess	2.74	2.81	2.79	2.57	2.41
Isthmus of Fauces	2.72	2.79	2.76	2.50	2.43
Posterior Pharyngeal Wall	2.81	2.81	2.83	2.71	2.48
Circumvallate Papillae	2.98	3.05	2.98	3.00	2.95
Soft Palate	1.51	1.40	1.55	1.31	1.42

1 = Clearly Visible, 2 = Partially Visible, 3 = Not Visible

Figure 2. Graph Representation of Mean Visibility Scores



1 = Clearly Visible, 2 = Partially Visible, 3 = Not Visible

*Statistically significant (p= 0.045) differences between visibility levels

Figure 3. Comparison of Best and Worst Visualization Methods

Best: Combination Method Mirror/“Ahh” Worst: Single-step Method “Ahh”

Appendix A

Consent Form

Visualization of the Oropharynx During Head and Neck Cancer Examinations

We are asking you to be in a research study. You do not have to be in this study. If you say yes, you may quit the study at any time. Please take as much time as you want to make your choice.

Why is this study being done?

We want to learn more about differences in visibility of the oropharynx among five conventional visualization methods.

We are asking senior student dental hygiene clinicians who are providing dental hygiene care for patients to help us.

What happens if I say yes, I want to be in the study?

If you say yes, we will:

- Have you visualize the oropharynx of a patient during a scheduled dental hygiene appointment by using a tongue depressor, mouth mirror, have the patient say "ahh", have the patient say "ahh" in combination with a tongue depressor and have the patient say "ahh" in combination with a mouth mirror.
- Each participant will complete these five visualization methods with two separate patients.
- Visibility of the oropharynx will be documented for each method with an intraoral photograph.
- Following visualization methods on two separate patients, you will complete a survey related to your perceptions of the effectiveness of each method.

How long will the study take?

This study will take about 10 minutes (per patient) of your regularly scheduled appointment time.

Where will the study take place?

This study will take place at the ISU Dental Hygiene Clinic during a regularly scheduled dental hygiene appointment.

What happens if I say no, I do not want to be in the study?

No one will treat you any differently. You will not be penalized in any way.

What happens if I say yes, but change my mind later?

You may stop being in the study at any time. You will not be penalized. Your relationship with the Department of Dental Hygiene will not change.

Who will see my visualization data and survey responses?

The only people who will see your personal study results will be the people who work on the study and those legally required to supervise our study.

Your survey answers and a copy of this document will be locked in our files.

When we share the results of our study in professional journals, at conferences, etc. we will not include your name. We will do our best to make sure no one outside the study will know that you are a part of the study.

Will it cost me anything to be in the study?

No.

Will being in this study help me in any way?

Being in this study will not help you, but may help people who are at risk for oropharyngeal cancer in the future.

Will I be paid for my time?

You will not be paid for your time.

Is there any way being in this study could be bad for me?

Yes, there is a chance that:

Your appointment time will increase by 10 to 15 minutes for each patient. However, you will be given management time and participation will not increase your overall treatment time goal.

We will do our best to protect your privacy.

What if I have questions?

Please call the head of the study Courtney Perrachione at (208) 282-3591 if you:

- Have questions about the study.
- Have questions about your rights.
- Feel you have been injured in any way by being in this study.

You can also call the Idaho State University Human Subjects Committee office at 208-282-2179 to ask questions about your rights as a research subject.

Do I have to sign this document?

No. You only sign this document if you want to be in the study.

What should I do if I want to be in the study?

You sign this document. We will give you a copy of this document to keep.

By signing this document you are saying:

- You agree to be in the study.
- We talked with you about the information in this document and answered all your questions.

_____

Your Name (please print)

_____ _____

Your Signature Date

Appendix B

Release of Photographs

Release of Photographs

I, _____, give my permission to use my intraoral photographs in the event of research publication. I understand that no personal information will be revealed and there will be no identifying data associated with the photographs.

Patient Signature: _____ Date: _____

Appendix C

Oropharynx Visualization Survey

Oropharynx Visualization Survey

Please choose the level of visibility for each tongue retraction/oropharynx visualization method according to the following scale:

Poor Visibility: inability to see isthmus of fauces/palatoglossal pillars or complete uvula
Fair Visibility: can see most of the isthmus of fauces/palatoglossal pillars and uvula
Good Visibility: can see full isthmus of fauces/palatoglossal pillars and complete uvula

Method	**Visibility**		
	Poor	**Fair**	**Good**
1.) Dental Mouth Mirror			
2.) Tongue Depressor			
3.) Say "Ahh"			
4.) Dental Mouth Mirror and Say "Ahh"			
5.) Tongue Depressor and Say "Ahh"			

6.) In your opinion, please select which method of visualization yielded the best visibility:

_____Mouth Mirror
_____Tongue Depressor
_____"Ahh"
_____Mouth Mirror and "Ahh"
_____Tongue Depressor and "Ahh"

7.) Please select which method of visualization you prefer and explain why:

_____Mouth Mirror
_____Tongue Depressor
_____"Ahh"
_____Mouth Mirror and "Ahh"
_____Tongue Depressor and "Ahh"

Reason:_____
_____
_____
_____
_____
_____

Appendix D

Anatomical Checklist for Intraoral Photograph Comparison

Anatomical Checklist for Intraoral Photograph Comparison

Please mark the technique used at the top of the page where indicated.
Check the box next to all oral anatomical structures which can be seen clearly, or partially, in the intraoral photographs. Mark N/A for any structures not present in the patient (i.e. palatine tonsils).

Method Used:

_____ Dental Mirror
_____ Tongue Depressor
_____ Saying “Ahh”
_____ Combination method with Dental Mirror and Saying “Ahh”
_____ Combination method with Tongue Depressor and Saying “Ahh”

Visible Anatomical Structures

	Clearly Visible (>75% of the structure is visible)	Partially Visible (50-75% of the structure is visible)	Not Visible (<50% of the structure is visible)	Not Applicable (N/A)
Palatoglossal Arch	☐	☐	☐	☐
Palatopharygeal arch	☐	☐	☐	☐
Uvula	☐	☐	☐	☐
Palatine Tonsils	☐	☐	☐	☐
Tonsillar Recess	☐	☐	☐	☐
Isthmus of Fauces	☐	☐	☐	☐
Posterior Pharyngeal Wall	☐	☐	☐	☐
Circumvallate Papillae	☐	☐	☐	☐
Soft Palate	☐	☐	☐	☐

Appendix E

Journal of Dental Hygiene

Author Guidelines

Journal of Dental Hygiene Author Guidelines

Author Guidelines
Starting with the Summer 2004 issue, the Journal of Dental Hygiene has been published online. The online format provides searching capabilities to Journal readers by establishing a link to dental hygiene research indexed through the National Library of Medicine and Medline. Click here to read the Journal of Dental Hygiene Author Guidelineson the ADHA site. Click here to learn more about NDHRA Statements.

Manuscripts are evaluated for quality, depth and significance of research, comprehensive evaluation of the available literature and the expertise of the author(s) in the given subject. Content must provide new information and be of general importance to dental hygiene. The Journal discourages submitting more than one article on related aspects of the same research. If multiple papers are submitted from the same project, significant differences in the papers must be evident.

Journal of Dental Hygiene - Author Guidelines

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Statement of Purpose

The Journal of Dental Hygiene (JDH) is the refereed, scientific publication of the American Dental Hygienists' Association (ADHA). It promotes the publication of original creative work related to dental hygiene research, education and evidence-based practice. The JDH supports the development and dissemination of a unique dental hygiene body of knowledge through scientific inquiry in basic, behavioral, clinical and translational research.

Author Guidelines

Starting with the Summer 2004 issue, the JDH has been published online. The online format provides searching capabilities to JDH readers by establishing a link to dental hygiene research indexed through the National Library of Medicine and PubMed.

Manuscript Requirements

Manuscripts are evaluated for quality, depth and significance of research, comprehensive evaluation of the available literature, and the expertise of the author(s) in the given subject.

Content must provide new information and be of general importance to dental hygiene. The JDH discourages submitting more than one article on related aspects of the same research. If multiple papers are submitted from the same project, significant differences in the papers must be evident.

Originality

Manuscripts must be original, unpublished, owned by the author and not submitted elsewhere. Authors are responsible for obtaining permission to use any materials (tables, charts, photographs, etc.) that are owned by others. Written permission to reprint material must be secured from the copyright owner and sent to ADHA when the manuscript is accepted for publication. The letter requesting permission must specifically state the original source, using wording stipulated by the grantor.

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Original Research Reports – Limited to 4,000 words (excluding cover page, abstract, references and tables/figures).

Include reports of basic, behavioral, clinical and translational studies that provide new information, applications or theoretical developments. Original Research Reports include an Abstract, Introduction (including the review of the literature and ending with a statement of the study purpose), Methods and Materials, Results, Discussion, and Conclusion.

Abstract: Approximately 250 words. Use the headings "Purpose" (purpose), "Methods" (design, subjects, procedures, measurements), "Results" (principal findings) and "Conclusion (i.e. Major conclusions)." The abstract must be able to stand alone. References should therefore be avoided.

Text: The body of the manuscript should be divided into sections preceded by the appropriate subheading. Major subheadings should be in capital letters at the left-hand margin. Secondary subheads should appear at the left-hand margin and be typed in upper and lower case and in bold face.

Introduction (including the literature review): Cite a variety of relevant studies that relate to the need for the current study and its significance. References should be as current as possible, unless a hallmark study is included. Compare findings of previous studies, clearly indicating all sources of concepts and data. When a source is directly quoted, use quotation marks. However, use of quotation marks should be limited. End this section with a clear statement of the purpose of the study, hypothesis or research objectives.

Methods and Materials: Describe the research design (e.g. randomized controlled trial) and procedures (e.g. IRB approval, target population, inclusion/exclusion criteria, recruitment, informed consent, variables to be tested, instruments, equipment, procedures and method of data analysis). Specify the measurements and statistical tests used as well as related levels of significance. Furthermore, assure an adherence to all pertinent federal and state regulations concerning the protection of the rights and welfare of all human and animal subjects.

Results: Summarize all relevant data and study findings. Do not repeat in the text the data reported in tables and figures verbatim, but do refer to the data and emphasize important findings (e.g. Table 1 shows that most of the subjects were African American and between the ages of 12 and 16).

Discussion: Evaluate and interpret the findings. Compare them with those of other related studies. Discuss how they relate to dental hygiene practice, profession, education or research. Include overall health promotion and disease prevention, clinical and primary care for individuals and groups and basic and applied science. Discuss study limitations; implications for dental hygiene practice, education, and research; and recommendations or plans for further study.

Conclusion: State the conclusions, theories, or implications that may be drawn from the study. This section should be one to two paragraphs or can be listed as bulleted points.

Literature Reviews – Limited to 3,000 words (excluding cover page, abstract, references and tables/figures).

A presentation of relevant and primary published material on a specific topic constitutes a comprehensive literature review. Such a review includes a summary and critique of the current status of the topic, and the aspects requiring further study.

Abstract: Literature reviews begin with a non-structured abstract — a brief statement of purpose, content summary, conclusions and recommendations.

Short Reports – Limited to no more than 2,000 words (excluding cover page, abstract, references and tables/figures). Illustrations should be limited to a total of no more than two (e.g. two figures, two tables, or one figure and one table).

The JDH publishes short reports related to dental hygiene. Short reports are limited in scope and should begin with a brief, non-structured abstract that describes the topic.

Text: A concise introduction (which includes a literature review), detailed description of the topic or activity, and discussion, conclusion and recommendations must also be included. References are necessary to support the rationale and methods presented.

A short report may describe a clinical case study, an educational innovation, a research method, a concept or theory, or other current topics.

Clinical Case Study: A report that describes a unique aspect of patient care not previously documented in the literature. Such reports usually focus on a single patient or groups of patients with similar conditions. Suitable topics include, but are not limited to, innovative preventive methods or programs, educational methods or approaches, health promotion interventions, unique clinical conditions, or pathologies and ethical issues.

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Text: Articles in this category should follow the basic structure for text outlined for Original Research Reports.

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Book citations: Spolarich AE, Gurenlian JR. Drug-induced adverse oral events. In: Daniel SJ, Harfst SA, Wilder RS, ed. Mosby's Dental Hygiene: Concepts, Cases and Competencies. 2nd ed. St. Louis, MO. Mosby/Elsevier Publishing. 2008. p. 259-276.

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Poole KE, Compston JE. Osteoporosis and its management. BMJ [Internet]. 2006 Dec 16 [cited 2007 Jan 4];333(7581):1251-6. Available from: http://www.bmj.com/cgi/reprint/333/7581/1251?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&andorexactfulltext=and&searchid=1&FIRSTINDEX=0&sortspec=relevance&volume=333&firstpage=1251&resourcetype=HWCIT

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