Presenter's Name: Han, Ji Hyun

Additional Author(s): McCord C, Darling MR, Armstrong J

Abstract Title: Osteomyelitis of the jaw: An investigational study of the frequency of Streptococcus anginosus infection

Abstract:

Introducton: The term Osteomyelitis (OM) means inflammation/infection of the bone marrow. The initial source of infection can be caused by a multitude of different factors; however, this process continues to propagate until the source of infection has been removed. In recent years, a subset of patients, who present with clinically aggressive disease have been found to demonstrate S. anginosus organisms on culture. We hypothesize that S. anginosus is associated with a distinct subset of jaw OM that are clinically aggressive, associated with poor clinical outcomes, and demonstrate distinguishing clinicopathologic features. The objectives are to examine the clinical and histological characteristics of OM to determine if differences exist between S. anginosus and non-S. anginosus OM, and use broad range 16sRNA gene PCR and sequencing to characterize the microbial groups responsible for the difference seen in patients that respond well to treatment versus the ones that do not.

Methods: A retrospective chart review of the records of patients diagnosed with OM in the OMFS/dental departments of LHSC from January 1, 2002 until January 31, 2021 will be completed. Cases will be grouped according to their outcome; poorly responding and responding well. Following this, a broad range 16sRNA gene PCR and sequencing will be performed on formalin-fixed paraffin embedded tissues (FFPE) obtained from the patients found during the retrospective chart review to determine the microbial groups present in tissue and bone samples. Future investigating into inflammatory markers, cytokines or signalling genes may be completed following the outcome of the initial 16sRNA microbial group identification. The data will be statistically analyzed.

Results: The retrospective chart review included a total of 87 patients, 45 females and 42 males. Out of the 87 patients, 56 samples were determined to be OM. 14 samples have confirmed S. anginosus in the microbiology obtained at the time of the biopsy. Further results are to be determined.

Discussion: Very few studies exist which have examined the relationship between S. anginosus and OM of the jaw. It is expected that S. anginosus organisms cause a more severe aggressive OM, which may also be associated with other environmental or personal risk factors of the individuals. The data from this study will help guide future clinical decision making in the treatment of OM of the jaw to help improve patient outcomes and reduce patient morbidity.

POSTER PRESENTATIONS 2
2C: ORAL BIOLOGY & MEDICINE

Presenter's Name: Holder, Natasha

Additional Author(s): Sadikovic B, Shimizu M, Howlett C, McCord C

Abstract Title: Epigenetic Analysis of Glandular Odontogenic Cyst

Abstract:

Glandular odontogenic cyst (GOC) is an uncommon benign cystic lesion that occurs in the jaws. GOC is unique to most cysts found in the jaws in that it can have variation in clinical presentation and may behave aggressively. Aggressive lesions can lead to an increased risk of recurrence and extensive bony destruction. Based on the criteria we have available to diagnose GOC, it can be difficult to predict how individual lesions will behave. This study aims to use a molecular technique called DNA methylation analysis to examine epigenetic features of glandular odontogenic cyst, both in indolent and aggressive cases, and to compare these features to other lesions which show microscopic overlap with GOC (dentigerous cyst and intraosseous mucoepidermoid carcinoma). It is expected that the molecular profiles of GOC will be distinct from dentigerous cysts and intraosseous mucoepidermoid carcinomas, but any overlap may suggest a common link in the development and behaviour of these lesions. The results of this study have the potential to guide future clinical decision making.

Presenter's Name: Hung, Anton

Additional Author(s): Schruder C, Kaiyum R, McCord C, Mermut O

Abstract Title: Optical Coherence Tomography for Evaluating Oral Cancer

Abstract:

Introduction: Optical imaging within tissues is promising for the medical screening and diagnosis of various diseases, such as oral cancer and pre-cancer. Clinically identifying oral cancers during routine screening is challenging and there is disagreement regarding its effectiveness at reducing mortality. Optical Coherence Tomography (OCT) is a non-invasive interferometry technique that allows micron-scale resolution images of complex structures in oral tissue. From the images generated by OCT, we hope to quantitatively map the attenuation of the light signal throughout the tissue. The computed maps might then be used for differentiating between cancerous and non-cancerous oral tissues, enhancing clinicians' capacity to screen for oral cancer.

Methods: We acquired 248 tissue samples from prospective oral patient biopsies of a variety of pathological diagnoses and used OCT to capture 3 images per tissue. Using MATLAB, we developed computational models to create optical attenuation maps from our OCT data. Our calculations are built upon the principles of the Beer-Lambert Law. One variation of the Beer-Lambert model incorporates an additional parameter, the confocal point spread function, to account for the confocal properties of the OCT apparatus. We compared the accuracy of our computational models by testing with intralipid phantom samples.

Results: We were able to successfully write a program to generate attenuation maps from the OCT scans of our oral tissues. Both the regular Beer-Lambert model and our modified Beer-Lambert model can be used to visualize light attenuation in different areas of oral tissue. Our maps can be used to accurately calculate attenuation coefficients for our tissues.

Discussion: Using OCT to measure light attenuation helps dental clinicians to gain critical information about oral tissue lesions. The imaging power of OCT has potential benefits for improving oral cancer screening. OCT allows clinicians to obtain a quantitative characterization of tissue lesions that can inform clinical decision-making. Further investigation can be done to correlate the calculated attenuation coefficients with the patient diagnoses.

POSTER PRESENTATIONS 2
2C: ORAL BIOLOGY & MEDICINE

Presenter's Name: Jacques, Kathleen

Additional Author(s): Jackson-Boeters L, Darling MR

Abstract Title: S100A7 Expression and Straticyte as Predictors for Malignant Transformation In Actinic Cheilitis

Abstract:

Introduction: Actinic Cheilitis (AC) is a premalignant lesion of the lip, associated with UV radiation from sunlight. Progression to invasive squamous cell carcinoma is the most significant outcome of AC. Lip squamous cell carcinoma (LSCC) is estimated to constitute up to 24.7% of all oral cancer, and nodal metastasis rates have been reported between 10-19%. Currently, oral pathologists rely primarily on grading of oral epithelial dysplasia to predict the risk of transformation to cancer. This has not proven to be reliable, except for in cases of severe dysplasia, thus there is a need for a more reliable method for predicting transformation. S100A7 is the potential biomarker being investigated for early detection of potentially malignant lesions.

Methods: 19 confirmed consecutive cases of AC in 2014 were selected. 2 cases had subsequent biopsies resulting in 21 specimens. Also included were 5 cases of AC that progressed to LSCC, 7 cases of AC associated with a previous or current LSCC, and 10 cases of hyperkeratotic (HK)/ normal epithelium. Cases were reviewed by light microscopy to confirm original diagnosis. All specimens, and high and low risk control samples, were stained by immunohistochemical methods for S100A7, P38 and ERK proteins. Stains were evaluated using a semi-quantitative analysis assigning an immunoreactive score based on stain intensity and proportion of cells stained, and an image analysis software (QuPath) to measure area of epithelium stained.

Results: Highlighted regions of interest on the AC specimens show an increase in S100A7 expression compared to surrounding normal tissue. Initial QuPath analysis, comparing the stained epithelial area to the total epithelial area, shows highest levels of staining in AC to SCC specimens. Awaiting further data analysis and results.

Discussion: Preliminary results show S100A7 as a potential predictable biomarker for the transformation of AC to LSCC. Early detection is important to decrease morbidity and invasive surgery. A more reliable objective method to predict the transformation of AC, and other potentially malignant lesions, to cancer is needed.

Presenter's Name: Lovell, Jeff

Additional Author(s): Jackson-Boeters L, Armstrong J, Darling MR

Abstract Title: S100A7 as a biomarker for predicting transformation in a potentially malignant lesion: lichen planus.

Abstract:

Oral potentially malignant disorders (PMD) are changes in the oral mucosa that are clinically recognizable. One PMD of specific interest is oral lichen planus (OLP). OLP has a malignant transformation rate of approximately 1.09%. Current literature reports that incisional biopsy and grading of dysplasia are not reliable diagnostic or predictive tools for malignant transformation. As a result, novel and more accurate methods for predictive risk of malignant transformation in these lesions should be examined. Tissue biomarkers, such as S100A7, may provide a more accurate method of risk determination.

Hypothesis: We hypothesize that S100A7 is increased in the epithelium of Lichen Planus lesions and other potentially malignant lesions which transform into dysplasia and malignancy. The proposed mechanism is through phosphorylation of proteins such as P38, ERK1/2, and JNK of the MAPK signalling pathway.

Objectives:
1) To show that there is greater expression of S100A7 in Lichen Planus and other PMD's than in normal epithelial control tissues.
2) To show that there is a greater expression of S100A7 in Lichen Planus and other PMD's that progress to dysplastic lesions and frank OSCC than in lesions that do not progress.
3) To evaluate the expression of P38, ERK ½, and JNK in Lichen planus lesions that progress vs. lesions that do not progress.
4) To test the utility of an image-based algorithm (Straticyte) utilizing S100A7 in Lichen Planus and other PMD's in accurately predicting progression.

Methods: Tissue samples of cases of OLP, Lichenoid mucositis, oral epithelial dysplasia's and normal epithelial controls will be obtained from the department of Pathology and Laboratory Medicine at Western University and University Hospital.These will be stained via immunohistochemical methods. The staining will be quantified by semi-quantitative means using an immunoreactivity score and Qupath analysis based on the proportion of epithelial cells staining, and the intensity of staining. The area of staining will also be measured using Straticyte image analysis, and an algorithm applied to determine low and high risk levels in the non-cancerous tissues. Demographic information such as gender, age, smoking status, alcohol consumption, site of lesion, and histopathological diagnosis will be acquired. We will be descriptively assessing MAPK protein expression in these tissue samples.

Results and Discussion: Awaiting statistical analysis

POSTER PRESENTATIONS 2
2C: ORAL BIOLOGY & MEDICINE

Presenter's Name: Pokharel, Binit

Additional Author(s): Lin S, Samsoondar J, Tan D, Misra T, Lam V, Wu N, Keow S, Pham M, Martinez J, Cecchini MJ

Abstract Title: Relationship Between Cellularity and Driver Aberrations in Non-Small Cell Lung Cancer

Abstract:

Non-small cell lung cancer (NSCLC) staging foremost involves the size of the tumour and its involvement of other structures. Tumour size, however, may only be an estimate for the number of cells in tumour; thus, there may be more validity in assessing the cellular density (cellularity) per given area rather than overall size. Using analog methods, counting individual cells by pathologists is entirely unfeasible; however, our previous studies have shown that, by using the image analysis software QuPath, tumour cells can be counted automatically with minimal manual inputs. Identification of tumour driver mutations—changes in DNA sequences critical to the unrestrained proliferation of the cancer cells—is useful for developing therapies to target and block growth of tumour. There is evidence in literature that suggests there may be a difference in the number of cells and cellularity (tumour cells/area) between unique drivers. Our study aimed to explore this potential correlation in lung adenocarcinoma and lung squamous cell carcinoma cases. We hypothesized that there were significant differences in cellularity between unique driver mutations among the cases in both NSCLC subtypes. Digital slides of lung adenocarcinoma (LUAD; n = 102) and lung squamous cell carcinoma (LUSC; n=90) were obtained from The Cancer Genome Atlas (TCGA). Cellularity values from these cases were then derived using QuPath software's whole slide image analysis tools. A list of driver genes, obtained from a previous report, were used to determine driver mutations for the LUSC and LUAD cases. Cases were separated by driver gene and mutation groups; cellularity values were compared between groups. Preliminary results showed that LUAD cases with the KRAS driver gene were significantly more cellular compared to the rest of the LUAD driver gene cohorts. Conversely, no significant differences in cellularity were found between drivers in the preliminary LUSC dataset (n=20). Major implications of the study include strengthening the argument for developing genetic treatments to NSCLC without the need for genomic analyses in NSCLC. However, sufficient tissue and cell counts submitted for genomic analyses are required in future studies to eventually reach this outcome in clinical practice.

Presenter's Name: Rosic, Damir

Additional Author(s): McCord C, Darling MR, Lapointe H, Khan ZA

Abstract Title: Characterizing Human Papillomavirus Associated Oral Epithelial Dysplasia

Abstract:

Background: The role of high risk (HR) Human papillomavirus (HPV) has been well documented in the development and progression of oropharyngeal squamous cell carcinoma and cervical cancer. In fact, greater than 70% of oropharyngeal cancer cases are believed to be associated with HR HPV. Currently, literature projects the association of HPV with oral cancers as being approximately 6%, HR HPV infection has been identified in a subset of oral dysplastic lesions. Due to the rarity of this lesion, literature describing HPV associated OED is limited.

Objectives: To identify and characterize cases of HPV associated oral epithelial dysplasia that are p16 positive and show E6/E7 expression by RT-PCR. To determine the utility and accuracy of tissue-based HPV 16 E6 antibody for HR HPV in the diagnosis of HPV associated oral epithelial dysplasia.

Methods: This is a retrospective study of archived tissues submitted to the Oral Pathology Diagnostic Service in the Division of Oral Pathology, at Western University. Consecutive cases of carcinoma-in situ (CIS) and/or Bowenoid dysplasia have been identified from the Oral Pathology database for the years 2002-2019. 115 cases were identified which showed histopathologic features of HPV infection. Cases that met the acceptability criteria were stained for p16 (Roche) using standard immunohistochemical techniques. A subset of cases was assessed for E6 (Abcam) by immunohistochemistry. All cases deemed diffusely positive for p16 were subsequently investigated for HPV 16 E6 mRNA by RT-PCR.

Results: Preliminary results demonstrate that 74% (85/115) of cases investigated were positive for p16. E6 assessment by immunohistochemistry showed diffuse non-specific staining and was therefore not pursued further. Our p16 positive cases have been subjected to RT-PCR to detect and quantify HPV 16 E6 mRNA. The majority of cases occurred in men (89%) with a median age of 56.1 (range of 32-89). The most common anatomical site affected is the floor of mouth/ventral tongue (59%).
Presenter's Name: Jacques, Kathleen

POSTER PRESENTATIONS 2
2C: ORAL BIOLOGY & MEDICINE

Presenter's Name: Soparlo, Jeff

Additional Author(s): Jackson-Boeters L, Khan ZA, Darling MR

Abstract Title: Evaluating the utility of S100A7 in identifying oral dysplastic lesions that will progress to oral squamous cell carcinoma

Abstract:

Introduction: Recently, S100A7 has been shown to be a potential useful marker for identifying oral lesions at risk of transformation from dysplasia to squamous cell carcinoma. Our hypothesis is that potentially malignant oral epithelial lesions have increased expression of S100A7. The objective of our study is to semi-quantitatively evaluate the level of S100A7 expression in dysplastic lesions which have transformed into oral squamous cell carcinoma using immunohistochemistry, and correlate these results with other methods of analysis including 3-tier and, the 2-tier grading schemes, and Straticyte™. In addition, a pilot study evaluating the utility of QuPath™ will be caried out.

Methods: Formalin fixed paraffin embedded specimens from 48 patients with oral squamous cell carcinoma, whom had previous non-malignant biopsies from the same site, were included in the study. For comparison, 35 patients with multiple biopsies identifying dysplasia without malignant transformation, and 25 patients with hyperkeratosis were included for comparison. In addition to the 3-tier grade, the 2-tier grade was also completed for each specimen. Specimens were stained for S100A7 protein using a standard immunohistochemistry protocol. Expression of S100A7 was assessed semi-quantitatively, using an intensity and proportion scale, as well as by image analysis by Straticyte™ and QuPath™.

Results: S100A7 manual scoring of epithelium in the three study populations was caried out and compared to the 3-tier and 2-tier grading schemes, Straticyte™, and QuPath. Manual staining had strong correlational relationships with QuPath and Straticyte based on Pearson correlation coefficients, and was able to differentiate with statistical significance the dysplastic from the Control groups. Straticyte™, which utilizes a proprietary algorithm as part of the epithelial S100A7 stain assessment, was able to differentiate with statistical significance, the population of dysplastic tissue samples that progressed to OSCC, from those that did not.

Conclusion: S100A7 appears to hold potential for assisting in the identification of patients with OPMLs with dysplasia, that have an increased risk of malignant transformation as compared to those which do not.

POSTER PRESENTATIONS 2
2C: ORAL BIOLOGY & MEDICINE

Presenter's Name: Tang, Celina

Additional Author(s): Jackson-Boeters L, Darling MR

Abstract Title: One Health Evaluation of Oral Cancer and S100A7 as a Predictor of Malignant Transformation from Oral Potentially Malignant Lesions (OPMLs)

Abstract:

With oral cancers, driven by various environmental and socio-economic risk factors, impacting the quality of life of humans and animals alike, prevention and early diagnosis is crucial for effective treatment. Histopathological examination and dysplasia grading has historically been the standard for predicting the risk of oral potentially malignant lesions (OPMLs) undergoing malignant transformation in humans, but it is vital to seek more diagnostic and prognostic tools. Straticyte is one such tool that produces a percent probability risk for malignant transformation of OPMLs and classifies them as high, medium, or low risk by measuring expression of the protein, S100A7. Overexpression of S100A7, in addition to Mcm2, and Ki67, have been found in many cancers and premalignant tumours. It is hypothesized that Straticyte is a more accurate and reliable predictor of malignant transformation of OPMLs than the two- and three-tier dysplasia grading systems. To test this, tissue specimens of OPMLs and healthy controls was stained for the aforementioned proteins. The image analysis program, QuPath, was used to measure and compare the area and stain percentage between malignant and healthy tissues. The percent probability risk and risk classifications that Straticyte produced will be compared to QuPath's outputs and the two- and three-tier dysplasia grades. S100A7 is expected to be overexpressed in OPMLs, and Straticyte is expected to be a more accurate and reliable predicator of malignant transformation of OPMLs than the two- and three-tier dysplasia grading systems. Subsequently, a literature review investigating the role of environmental health and socio-economic risk factors for oral cancer in humans and dogs will be conducted. Key stakeholders involved in oral cancer will be identified, including, but not limited to, tobacco companies and the government. The literature review, protein biomarker research, and mapping of key stakeholders will enable a comprehensive investigation of oral cancer to improve prevention, diagnosis, and treatment of oral cancers in humans and dogs.