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The Effect of an Oral Care Intervention in Decreasing the Expression of Proinflammatory Cytokines in Patients Receiving Chemoradiation for Oral Cancer: A Randomized Clinical Trial

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Purpose/Objective(s): Oral mucositis (OM) is one of the most debilitating adverse effects in patients undergoing radiation therapy (RT), chemoradiation therapy, or both. Currently, there are no effective therapies or preventive treatments for OM; rather, most suggested treatments are palliative in nature. Physiologically, chemotherapy (CT) and RT evoke a profound inflammatory response, resulting in damage to the vascular endothelium. The release of proinflammatory mediators is responsible for mucosal injury and compromises the integrity of the protective epithelial barrier, which can result in an increased susceptibility to infection. The objective of this pilot study was to associate the effects of a novel oral care protocol on OM severity and to evaluate salivary proinflammatory cytokines in cancer patients undergoing RT or CT/RT.

Materials/Methods: A total of 16 subjects undergoing RT or CT/RT were enrolled prior to starting treatment. All subjects received a baseline standard of care oral/dental prophylaxis plus fluoride application prior to the start of RT or CT/RT. Patients were assigned to an oral health interventional group (IG) or control group (CG). Subjects assigned to the CG followed a biweekly treatment schedule in which they had their teeth brushed by a dental professional and were asked to follow standard of care (SOC) oral hygiene instructions at home. Subjects randomized to the IG received the Oral Mucosal Deterging and Periodontal Debridement (OMDP) protocol and attended weekly treatment visits at which they had their teeth brushed by a dental professional, periodontal debridement, tooth polishing, and flossing. Subsequently, the cleansing and deterging of the oral mucosal surfaces was performed using a soft-bristled toothbrush and an antibacterial agent (alcohol-free chlorhexidine mouth rinse). Subjects in the IG were instructed to continue to follow the OMDP protocol at home. Stimulated whole saliva samples were collected at baseline (prior to OM development), on the onset of OM, during cancer treatment, and 2 months after the end of RT or CT/RT. Changes in the levels of proinflammatory cytokines were measured.

Results: Salivary inflammatory biomarkers, noted in levels of IL-10, IL-13, IL-4, and TNF-α had a significant increase in the CG and reduced or stayed the same under IG.

Conclusion: These results suggest that overall inflammation was consistently higher as compared to baseline with control treatment and lower than or similar to baseline with the OMDP treatment, providing encouragement for the effectiveness of the oral care protocol as a coadjuvant treatment for this population.

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Three-Dimensionally Printed Bolus in Head and Neck Electron Radiation therapy

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Purpose/Objective(s): When treating head and neck cutaneous or other superficial cancers with electron radiation therapy, custom bolus is often used to optimize dose distribution to improve treatment volume coverage and minimize dose to normal tissues. We aim to improve on this custom bolus technique with patient-specific 3-dimensionally printed bolus.

Materials/Methods: Following computed tomographic simulation, the patient DICOM imaging data is transferred to the radiation treatment planning system. Target volumes and organs at risk are contoured and a plan is created using a standard, noncustom bolus technique. Following completion of the standard plan, a custom bolus is then created as a DICOM-RT structure with forward planning in an attempt to decrease unnecessary dose to organs at risk and increase treatment volume coverage and dose homogeneity. Custom bolus is tagged with a marker to assist in orientation and alignment during patient setup. An in-house algorithm is then used to translate the custom bolus from DICOM-RT to stereolithography file format to transfer to a 3-dimensional printer.

Results: Our institution has successfully modeled custom bolus and converted the bolus to appropriate format for 3-dimensional printing; creating personalized bolus for individual patients that can be used in electron radiation therapy to the head and neck. Our preclinical model supports improved treatment volume coverage and decreased dose to normal tissues with the printed custom bolus. Images of the comparative dosimetric evaluation of the printed custom bolus to standard bolus electron radiation therapy will be presented.

Conclusion: We have developed a model to attempt to personalize head and neck electron radiation therapy with a 3-dimensionally printed custom bolus. This model is currently under preclinical testing for head and neck cancer.

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Induction Chemotherapy Followed by Concurrent Chemoradiation Therapy Versus Concurrent Chemoradiation Therapy Upfront in Locally Advanced Oral Cavity Cancer: Systematic Review and Meta-Analysis of Individual Data

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Purpose/Objective(s): The initial treatment for locally advanced oral cavity squamous cell carcinoma (SCC) comprises surgery followed by radiation therapy with or without chemotherapy. However, nonsurgical treatment could be an option. This study was performed to evaluate the effectiveness of induction chemotherapy in nonsurgical protocols for oral cavity SCC patients.

Materials/Methods: Randomized controlled trials evaluating sequential therapy (induction chemotherapy followed by chemoradiation therapy [Chemo group]) versus chemoradiation therapy alone (Control group) in head and neck cancer were analyzed. Two of the authors independently evaluated the studies regarding eligibility criteria and risk of bias.

Results: Three studies fulfilled the eligibility criteria. All of them included different sites of locally advanced head and neck SCC. The individual data of oral cavity cancer patients were retrieved from 2 studies (Paradigm and Decide trials). Data from the third study were not retrieved, and this trial was not considered for analysis. A total of 65 patients were randomly assigned to the Chemo group (n = 34) and the Control group (n = 31). Both trials were classified as having low risk of bias. No significant overall benefit in favor of induction chemotherapy was found regarding mortality rate (Chemo group, 9/34; Control group, 8/31 [3-year mortality:

heterogeneity: $X^2=0.00$, df=1 ($P=.97$); $I^2=0\%$; test for overall effect: $Z=0.04$, $P=.97$) and progression-free survival (Chemo group 9/34; Control group 12/31 [3-year progression-free rate: heterogeneity: $X^2=0.07$, df=1 ($P=.79$); $I^2=0\%$; test for overall effect: $Z=1.05$, $P=.29$]).

Conclusion: Induction chemotherapy when administered before chemoradiation therapy did not improve clinical outcomes in comparison to upfront chemoradiation therapy in patients with locally advanced oral cavity cancer.

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Risk Factors for Local, Regional, or Distant Recurrence in Human Papillomavirus–Positive Oropharyngeal Cancer

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Purpose/Objective(s): Human papillomavirus (HPV)-associated squamous cell carcinomas of the oropharynx are increasingly seen as a separate disease entity from smoking-associated oropharyngeal cancers, with a much higher likelihood of cure. The current American Joint Commission on Cancer (AJCC) staging system for HPV-positive oropharyngeal cancer is not prognostic for outcome. We evaluated a variety of potential prognostic factors in order to propose potential new components for a staging system.

Materials/Methods: After gaining institutional review board approval, we queried an institutional database for patients with HPV or p16-positive nonmetastatic oropharyngeal cancers treated with definitive radiation therapy (RT), and 245 cases were identified. Patient, tumor, and treatment factors were abstracted from the charts. In addition, pretreatment imaging was reviewed, including computed tomography (CT) in 99.6%, positron emission tomography/CT in 94.3%, and magnetic resonance imaging in 7.3% to obtain precise size, location, number, and extent of primary and nodes. Outcomes, including local control (LC), regional control (RC), locoregional control (LRC), and freedom from distant metastases (FFDM) were calculated from the end of RT and estimated via Kaplan-Meier method. Comparisons were made via log-rank test.

Results: Median follow-up of patients alive at last contact was 36 months. All patients were treated with definitive RT alone (n=38, 15.4%) or concurrent systemic therapy and RT (n=209, 84.6%). LC was seen in 239 of 245 patients, for a 3-year LC rate of 97.8%. There were no statistically significant prognostic factors for local control, including tumor size or invasion of adjacent structures. RC was achieved in 235 of 245 patients (95.3% at 3 years). RC was less likely if there were 5 or more nodes (1-4 vs $\geq$5, $P=.05$), or if a lymph node was present in level 4 (level 3 or above vs level 4, $P=.005$). Distant metastases occurred in 21 patients, for a 3-year FFDM rate of 91.4%. Lower rates of FFDM were associated with a lymph node greater than 6 cm ($P=.02$), bilateral lymphadenopathy (unilateral vs bilateral, $P=.034$), 5 or more nodes (1-4 vs $\geq$5, $P<.001$), or if a lymph node was present in level 4 (level 3 or above vs level 4, $P<.001$).

Conclusion: Outcomes for patients with HPV-associated oropharyngeal cancer treated with definitive RT are excellent. The increasing burden of adenopathy, either by size, number, or bilateral involvement, or location in level 4 portended a higher risk of regional failure or metastasis. These factors may provide a basis for altering staging.

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Low-Level Laser Therapy and Laser Debridement for Management of Oral Mucositis in Patients With Head and Neck Cancer Receiving Chemotherapy and Radiation

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Purpose/Objective(s): Oral mucositis (OM) is a very common side effect of head and neck radiation therapy (RT) and concurrent chemotherapy and radiation (CRT) leading to severe pain, infection, weight loss, higher rates of hospitalization, higher financial cost of treatment, and breaks in therapy resulting in increased morbidity and reduced treatment efficacy. The 2014 guidelines from The Mucositis Study Group of the Multinational Association of Supportive Care in Cancer included a suggestion that low-level laser therapy (LLLT) was useful for the prevention of high-grade OM in patients receiving head and neck RT alone, but no comment could be made regarding its efficacy in the therapeutic setting for severe OM during RT or CRT. Our objective is to describe the technical aspects of the laser regimen we use in this setting and relate the qualitative experience we have had thus far.

Materials/Methods: Since 2013, 53 patients were referred to dentistry for laser therapy for significant and bothersome Radiation Therapy Oncology Group grade 2-3 OM, either during or after RT/CRT. Our regimen uses 2 lasers; a class IV Er, Cr: YSGG laser (λ =2.780 μm), as well as a class IV diode laser (λ =940 nm). The first laser is used to debride the entire surface of the ulcerated areas. Settings are 0.25 to 0.75 watts, 15 to 20 pps, 0 water, and 90 air flow rate. The next laser is then used as biostimulation for pain relief during CRT and for wound healing after CRT is completed. Instrument settings are 0.6 watts, 12 joules, continuous wave pulse (CW) for 20 seconds per site and 0.2 watts, (CW), 4 joules, 20 seconds per site for each situation, respectively. Treatments were administered once or twice weekly depending on severity and continued until complete resolution of ulcerations.

Results: Forty-one patients started laser treatments either during or within 1 month of RT/CRT completion. Twelve patients initiated treatments over 1 month after RT/CRT completion. All patients experienced full clinical resolution of oral ulcerations. The number of treatments patients received ranged from 2 to 15 with a median number of 7. Qualitatively, patients tended to report significant early pain relief, especially during the first 48 hours following laser treatments. Providers also felt that patients tended to heal more quickly once treatment was initiated, though, without a comparison group at this point, no definitive conclusion can be reached.

Conclusion: This report highlights the technical aspects of LLLT and our regimen for managing severe mucositis. Our qualitative experience thus far suggests benefits in pain relief and quicker recovery from severe mucositis. Additional studies are underway evaluating the feasibility, efficacy, and quality of life metrics.

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A Comparative Study of Patient-Reported Quality of Life, Xerostomia, and Dysgeusia in Oropharyngeal Squamous Cell Carcinoma (OPSCC) Treated With Volumetric Modulated Arc Therapy (VMAT) or Proton Pencil Beam Scanning (PBS)

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Purpose/Objective(s): Treatment for OPSCC can affect a number of outcomes related to quality of life (QOL). We explore differences in measures such as xerostomia, dysgeusia, weight loss, pain, and overall