

THE UNIVERSITY OF VIRGINIA  
DEPARTMENT OF OTOLARYNGOLOGY – HEAD & NECK SURGERY  
PRESENTS

THE 42ND ANNUAL FITZ-HUGH SYMPOSIUM

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RESIDENT RESEARCH PRESENTATIONS

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Thursday June 21, 2018 at 2:30 pm

*Riggs Auditorium*

Practice patterns in botulinum toxin injection for the treatment of voice disorders ..... McGarey (Daniero)

Physics-based analysis of pulse-synchronous tinnitus.....Hyde (Kesser/Dong)

Micro-filtration as a means to purify water for sinus rinses: a functional and financial analysis..... Peters (Payne)

Prevalence and inflammatory features associated with incidental laryngeal clefts  
in children presenting severe, treatment-refractory wheeze and asthma..... Gilbow (Early/Teague)

Activation of hedgehog (Hh) signaling pathway enhances craniofacial bone  
regeneration in a critical-sized rat mandibular defect.....Miller (Christophel)

Head and neck squamous cell carcinoma in a young patient cohort ..... Dougherty (Jameson)

*[break]*

Efficacy of empiric antimicrobial prophylaxis after FESS .....Bartels (Payne)

A novel injectable for glottal insufficiency, a rabbit model .....Koehn (Daniero)

Predicting uncontrolled post-operative pain after neck dissection..... Corby (Fedder/Jameson)

Evaluating correlation between hearing loss and middle ear volume in patients  
with a tympanic membrane perforation.....Casale (Kesser)

Efficacy of different modalities of concordant imaging in the management of  
primary hyperparathyroidism .....Reed (Shonka)

Cervical inlet patch as an etiology of symptomatic upper cervical  
esophageal dysfunction.....Schoeff (Daniero)

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## RESIDENT RESEARCH ABSTRACTS

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### Practice patterns in botulinum toxin injection for the treatment of voice disorders

*Patrick McGarey MD; Seth Martin MS3; James Daniero MD*

**Background:** Laryngeal injection of botulinum toxin (Botox) is the primary treatment modality for spasmodic dysphonia and is used to treat other voice disorders including essential voice tremor and muscle tension dysphonia.

**Objective:** To compare patterns of use of laryngeal Botox injections for voice disorders and to identify inefficiencies and barriers in providing this service that result from regulatory, insurance, and industry control.

**Methods:** A 26 item survey was written and approved for distribution by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) and the National Spasmodic Dysphonia Association (NSDA). It was distributed to Otolaryngologists who perform laryngeal Botox injections via the E-mail lists of the AAO-HNS Voice Committee, the Fall Voice Conference, and the American Laryngological Association Neurolaryngology Study Group.

**Results:** There were 81 survey participants who collectively reported performing >1700 laryngeal Botox injections for voice disorders monthly (M=21.7 pts/month). Regarding Botox vial use, 53% of participants reported using multiple doses per vial for different patients during a single clinic day, while 14% reported using pharmacy pre-drawn aliquots. 26% of participants reported using an individual vial per patient and discarding the unused remainder, with an associated annual cost in wasted Botox of \$68,500 per physician.

**Conclusions:** Laryngeal injection of Botox is an important treatment modality for spasmodic dysphonia and other voice disorders. There is wide variation in injection practices regarding management of Botox vials. Adherence to an individual vial per patient policy is associated with significant waste of health care resources and may impact patient access to care.

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### Physics-based analysis of pulse-synchronous tinnitus

*Justin Hyde MD; Xuanming Zhao BS; Junshi Wang MS; Pan Han MS; Haibo Dong PhD; Bradley Kesser MD*

Pulse-synchronous tinnitus (PST) has been linked to multiple anatomical variants of the central nervous system venous outflow tract (CVOT) including transverse sinus (TS) stenosis and sigmoid sinus (SS) dehiscence. It is unknown if mechanical turbulence, specific flow velocities and their resultant forces along the VOT, and the inherent anatomy are the mechanisms of bone erosion and SS dehiscence, resulting in PST. In this work, a combined experimental and computational approach is conducted to study the fluid dynamics of the blood flow in CVOT. Highly accurate CVOT models are reconstructed from human computed tomography (CT) scans of a patient. Two CVOT models of the patient are obtained on the symptomatic side with PST and the contralateral, asymptomatic side, respectively. A turbulent model enabled commercial Reynolds averaged Navier-Stokes (RANS) flow solver is used to simulate the corresponding pulsatile blood flow through the vessels. Results have shown distinct differences in the flow characteristics between the two models, including total pressure (TP) and dynamic pressure (DP) on the vessel walls, velocity magnitude (VM), and turbulent kinetic energy (TKE). Significant fluctuations in TKE are observed on the symptomatic side with PST. The findings lend evidence to the hypothesis that there are specific anatomic variables that play a role in turbulent flow, asymmetric force points, and show strong evidence as the etiology for bone erosion regarding a dehiscent SS and resultant PST. The methods and resulted findings from this work are expected to bring novel understanding on PST and provide guidance for surgical interventions

## Micro-filtration as a means to purify water for sinus rinses: a functional and financial analysis

*R. Daniel Peters MD, John Steinke PhD, Larry Borish MD, Spencer Payne MD*

**Objectives:** To determine the capacity of a commercially available sinus rinse micro-filtration system to purify contaminated water. To evaluate the relative cost burden of using such a system.

**Study Design:** Bench translational research and cost analysis.

**Methods:** Distilled water, tap water, and stream water were evaluated for bacterial content, before and after micro-filtration. Samples were plated on blood agar and chocolate agar and assessed at 24, 48, and 72 hours. Presence or absence of bacterial growth was noted. Cost of using the micro-filtration system for a one year period was determined. This was compared to the cost of using a standard rinse system and distilled water.

**Results:** At 72 hours, Distilled water and tap water did not produce any visible colonies on either the blood agar or chocolate agar plates. This applied to both pre- and post-filtered samples. Prior to filtration, stream water produced visible colony growth at 24 hours. No colony growth was observed at 72 hours after micro-filtration of stream water. The results were duplicated. The cost of using each system, per manufacturer recommendations, for a period of one year was determined. The cost of the NeilMed system was \$138.94 while the cost of the SinuCleanse system was \$93.92.

**Conclusions:** Micro-filtration is an effective means of removing bacteria from water to be used for sinus rinses. The capacity for the micro-filtration system to remove all bacteria is not known. Use of the micro-filtration system allows patients to save \$45.02 per year.

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## Prevalence and inflammatory features associated with incidental laryngeal clefts in children presenting with symptoms of severe, treatment-refractory wheeze and asthma

*Reed Gilbow MD; W. Gerald Teague MD; Stephen Early MD*

**Objectives:** To characterize epidemiologic, symptomatic, and phenotypic markers for laryngeal cleft in children with treatment-refractory asthma or laryngeal wheeze.

**Design and Methods:** Pediatric-age patients with severe, therapy-resistant, poorly controlled asthma or wheeze were recruited from either the pediatric otolaryngology or pulmonology clinics. Each child had direct laryngoscopy and bronchoscopy with collection of bronchoalveolar lavage fluid (BALF) and blood samples shared between the clinical and research laboratories through protocols approved by the University of Virginia Institutional Review Board (UVA HSR # 17555, UVA HSR# 10905, and UVA HSR# 10634). The examination results, demographic, anthropometric, treatment, blood and lung fluid inflammatory markers, aspiration markers, lung function, tests for BALF pathogens, and gross ciliary motion were recorded in a pass-word protected data set. Laryngeal cleft status was determined during direct laryngoscopy with probing of the cleft with a right-angle probe. Statistical analysis was performed in SPSS v25 and included between group comparisons using non-parametric analysis.

**Outcomes and Measures:** Post-assessment prevalence of asthma and inflammatory markers in cleft + and cleft - children.

**Results:** A total of 284 procedures were recorded over an 8 year period (63% male, 37% female). The overall prevalence of laryngeal cleft was 19%, with no difference in male sex proportion (61% male with cleft, 63% male without cleft,  $p = 0.7$ ). There was a statistically significant difference in age (cleft present + 4.5 years, cleft - 6.2 years,

p=.009). Asthma was less prevalent in the cleft positive group (64% vs 80%, p = 0.02). Amongst systemic inflammatory markers, children who were cleft + had relatively lower total IgE (p=.03) and blood eosinophilia (p=.04), p cleft + group (p=.04), but otherwise, no other BALF patterns were significant. PFT findings were also not statistically significant. Interestingly, though symptoms of aspiration were statistically significant (45% vs 6%, p < 0.001), cleft status did not correlate with BALF amylase (p=.163).

**Conclusion:** Incidental laryngeal clefts are commonly found (19%) in children who undergo diagnostic direct laryngoscopy and bronchoscopy for treatment-refractory asthma and wheezing. Children with clefts are more likely to be pre-school age and less likely to meet diagnostic criteria for asthma or have objective findings suggestive of evolving asthma. Although some difference in systemic inflammatory markers was noted, no specific markers were identified in either serum or BALF. We submit that pre-school-age children with treatment-refractory respiratory symptoms should undergo direct examination for laryngeal clefts as well as consideration for a swallow study pre-operatively if respiratory symptoms are accompanied by signs and symptoms of dysphagia.

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## **Activation of Hedgehog (Hh) signaling pathway enhances craniofacial bone regeneration in a critical-sized rat mandibular defect**

**Matthew Miller MD; Logan McColl; Michael Arul; Jonathan Nip; Vedavathi Madhu; Gina Beck; Kishan Mathur; Vashaana Sahadeo; Jason Kerrigan; Stephen Park MD; Jared Christopher MD MPH; Abhijit Dighe; Sangamesh Kumbar; Quanjun Chi**

**Objective:** Osseous craniofacial defects are currently reconstructed with bone grafting, rigid fixation, free tissue transfer, and/or recombinant human bone morphogenetic protein- 2 (rhBMP-2). While these treatment options often have good outcomes, they can be associated with significant morbidities and many patients are not candidates for free tissue transfer.

Our lab and others have had limited success in using growth factors and mesenchymal stem cells to induce craniofacial bone regeneration. In order to improve efficacy of this therapeutic approach we considered two recent findings: 1) Gli1+ stem cells give rise to all craniofacial bones in the adult and are activated during injury repair; and 2) a novel, mechanically-competent polysaccharide (PS) scaffold shows superior outcomes in supporting osteogenesis compared to PLGA. The glioma-associated oncogene protein 1 (Gli1) is the transcriptional activator of Hedgehog signaling and is turned on only upon activation of smoothened. We hypothesized that in a rat mandibular defect, PS constructs cross-linked with SAG, VEGF, and BMP-6 would significantly increase bone regeneration compared to FDA-approved rhBMP-2.

**Design and Participants:** Bilateral critical-sized defects were created in the angle of rat mandibles. The defects were either left untreated or one of the PS scaffolds was implanted: PS, PS<sup>VEGF</sup>, PS<sup>VEGF+SAG</sup>, PS<sup>BMP-6</sup>, PS<sup>BMP-6+SAG</sup>, PS<sup>VEGF+BMP-6</sup>, PS<sup>VEGF+BMP-6+SAG</sup>, PS<sup>BMP-2</sup>, PS<sup>BMP-2+SAG</sup>. The rats were sacrificed after 8 weeks and bone regeneration was evaluated using MicroCT.

**Results:** There was minimal healing observed in the untreated mandibles. Addition of SAG increased bone regeneration and bone density in all groups and maximum bone healing was seen in the PS<sup>VEGF+BMP-6+SAG</sup> group.

**Conclusion and Relevance:** Activating the hedgehog signaling pathway using smoothened agonist increases craniofacial bone regeneration compared to growth factors alone, including FDA-approved rhBMP-2. Pharmaceuticals targeting this pathway may offer a new reconstructive option for bony craniofacial defects as well as nonunion and delayed healing fractures. Further studies are needed investigating this therapeutic strategy in a more clinically-relevant segmental defect and to determine the safety of activating the hedgehog signaling pathway.

## Head and neck squamous cell carcinoma in a young patient cohort

*William Dougherty MD; Michael Dougherty BA; Joshua Kain MD; Brian Hughley MD; Mark Jameson MD PhD*

**Objective:** Head and neck squamous cell carcinoma (SCCA) is rare in patients under 40 years old. However, anecdotally, there is an apparent increase in the number of young patients with aggressive head and neck cancer, particularly of the oral tongue. Often these patients are non-smokers, and do not have the traditional risk factors or demographics of typical head and neck cancer patients (5<sup>th</sup> or 6<sup>th</sup> decade male smoker/drinker). We designed a multi-institutional collaboration between UVA and UAB to compare young patients treated for head and neck cancer to an older head and neck cancer population.

**Design:** A chart review was carried out on all patients under 40 years of age who were treated at UVA and UAB for p16- head and neck cancer (n=58). A randomized, stage and subsite matched, cohort of patients aged 55-65 was also analyzed for comparison (n=89).

**Patients:** Young (<40) and older (55-65) patients treated at UVA for p16- head and neck cancer

**Results:** A majority (73%) of the young patients with head and neck SCCA developed oral tongue primary tumors. Many of these patients were never smokers (55%) and/or female (40%). There is better overall survival in young patients with head and neck cancer (p=0.14), despite a similar disease free survival. Young patients with head and neck cancer had a longer conditional survival from time of recurrence (p=0.006)

**Conclusions:** This study is unique for the multi-institutional design to compare outcomes for young patients with head and neck cancer to an older cohort. While there are limitations of the data, the findings suggest that young patients with p16- oropharyngeal carcinoma have a better overall survival and conditional survival after first disease recurrence.

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## Efficacy of empiric antimicrobial prophylaxis after FESS

*Harrison Bartels MD; Ellen Shaffrey BS; Abel David BS; Spencer Payne MD*

**Background:** Functional endoscopic sinus surgery (FESS) is the current standard of care for treatment of chronic rhinosinusitis refractory to medical management. The use of empiric post-operative antibiotics is common practice among otolaryngologists but data supporting this use are mixed and limited. The objective of this study was to compare outcomes between patients who did and did not receive post-operative prophylactic antimicrobial therapy after undergoing endoscopic sinus surgery.

**Setting:** Tertiary Care University Hospital

**Methods:** A retrospective analysis was performed from 2012-2016 on patients who underwent endoscopic sinus surgery by a single provider during this time period. This time period represents two years before and after the practice of prescribing empiric antibiotic therapy post-operatively was discontinued. The primary outcomes include the number of antibiotic and systemic steroid prescriptions over a 6 month post-operative time period and number of days prior to the first prescription of antibiotics and systemic steroids.

**Results:** 450 patients who underwent endoscopic sinus surgery were identified over this period, of whom 301 met inclusion criteria. There was no significant difference between number of antibiotic or steroid courses between patients that did and did not receive post-operative antimicrobial prophylaxis. There was also no significant difference between time to first antibiotic or steroid prescription between the two groups.

**Conclusions:** There is no standard of care for post-operative antimicrobial therapy in patients undergoing functional endoscopic sinus surgery. Our data may support a more conservative approach that does not subject patients to the comorbidity and resistance concerns associated with empiric antimicrobial therapy.

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### **A novel injectable for glottal insufficiency, a rabbit model**

*Heather Koehn MD; Teresa Martz MS4; Sergio Ferrante MS4; Lauren Pruett BS; Junshi Wang BS; Donald Griffin PhD; James Daniero MD MS*

**Objective:** To demonstrate feasibility of injection laryngoplasty in a leporine model for the use of a treatment model for glottal insufficiency with a novel injectable biomaterial.

**Study Design:** IACUC approval was obtained for the use of a leporine model. 32 rabbits were stratified into three treatment arms including MAP gel, Hyaluronic Acid, Saline. Injection laryngoplasty of the left vocal fold was performed. At intervals of 0,6,12, and 24 weeks the rabbits were phonated and sacrificed. Rabbits were phonated using a tracheotomy with high flow humidified oxygen delivered in a retrograde fashion with stimulation of cricothyroid muscle with 4mAmp. High-speed video was recorded at 4000fps and voice recording were collected and analyzed using KayPentax MDVP. Laryngeal specimens subsequently underwent pathologic analysis.

**Results:** 31 injections were performed, 4 served as test of the experimental design, of the 8 rabbits analyzed in the six week cohort, one was unable to be phonated due to a complication unrelated to procedure. The remainder showed feasibility of phonation, with acquisition of high speed video capture of mucosal wave and voice sample analysis with a Multi-Dimensional Voice Program. Gross histologic tissue integration demonstrated permanence of MAP gel injectable in the glottis at this time point.

**Conclusions:** This is a reproducible model of glottal insufficiency and injection laryngoplasty in the leporine model which demonstrates the feasibility of use of the MAP gel injectable as well as its tissue integration in the glottis.

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### **Predicting uncontrolled post-operative pain after neck dissection**

*Margeaux Corby MD; Bethany Horton PhD; Mark Jameson MD PhD; Katherine Fedder MD*

**Objectives:** The objective of this retrospective review is to identify demographic and surgical risk factors for uncontrolled post-operative pain and increased narcotic use in patients undergoing unilateral neck dissection.

**Study Design:** Retrospective cohort study

**Methods:** A chart review was performed of adult patients who underwent isolated unilateral neck dissection for HNSCC over a 5-year period at a single institution. Included patients had inpatient post-operative pain scores and narcotic use available in the electronic medical record.

**Results:** Retrospective data from 68 patient records show that in-hospital narcotic use and average and maximal pain decrease over time. There is a positive correlation between average pain and narcotic use as well as a positive correlation between the amount of narcotics given on different days in-hospital. Patient characteristics were considered in modeling average and maximal pain for post-op day 0 through post-op day 3. There were no statistically significant factors predicting post-operative average pain. When considering maximal pain in a covariate model, age remained significant (p-value 0.0495) for predicting maximum post-operative pain. A patient who is 10 years older than another is predicted to have approximately 0.1 points less pain.

**Conclusions:** Several recent national initiatives to reduce narcotic prescription have led to institutional changes, which affect every day clinical practice. Even maximal users of narcotic medication have decreased need for narcotics over the length of hospital stay and this should be reflected in the orders for these patients and when considering amount of narcotics given at discharge. Factors that intuitively may appear to increase a patient's post-operative pain such as prior chemotherapy, radiation or surgery, surgical duration or sacrifice of major neurovascular structures do not actually affect average pain. Greater maximum pain experienced by patients is predicted to occur in those patients who are younger.

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## **Evaluating correlation between hearing loss and middle ear volume in patients with a tympanic membrane perforation**

*Garrett Casale MD; Ellen Shaffrey BS; Bradley Kesser MD*

**Objective:** To investigate a possible correlation between the degree of conductive hearing loss (CHL) caused by an isolated tympanic membrane (TM) perforation and middle ear volume measured anatomically.

**Study Design:** Retrospective chart, audiometry, and computed tomography (CT) imaging review.

**Methods:** Adult patients with a diagnosis of isolated TM perforation between 2010 and 2018 were identified and their audiometric data collected. Middle ear volume was then calculated based on segmentation analysis from the patient's head or temporal bone CT scan. Univariate analysis was performed to determine a correlation between the calculated middle ear volume on CT imaging and the degree of conductive hearing loss as measured by the air bone gap on standard audiometry. Calculated middle ear volume was also compared to middle volume reported on tympanometry.

**Results:** Greater middle ear volume correlated with smaller air bone gap; this trend approached but did not reach statistical significance ( $p=0.09$ ). There was a statistically significant difference between middle ear volume as determined by segmentation analysis compared to that determined by tympanometry (absolute average percent difference=33.8%; range -49.5% to +155.2%;  $p=0.026$ ).

**Conclusions:** As previously reported, middle ear volume may be correlated to degree of conductive hearing loss in the setting of isolated TM perforation, but our analysis did not reach statistical significance. Calculated middle ear volume by segmentation analysis on CT imaging may be a more accurate estimate of middle ear volume than tympanometry.

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## **Efficacy of different modalities of concordant imaging in the management of primary hyperparathyroidism**

*Robert Reed MD; Ellen Shaffrey MS4; David Shonka MD*

**Background:** Assess the predictive value of concordant imaging in management of primary hyperparathyroidism using different imaging modalities to evaluate the marginal value of intra-operative PTH monitoring.

**Methods:** Retrospective chart review of 112 patients operated on at a single institution for primary hyperparathyroidism. Imaging modality, intra-operative findings, pathologic analysis, and laboratory data was collected to assess value of concordant imaging.

**Results:** 89% of patients (100) were imaged with more than one imaging modality; 53% with US/4D-CT, 22% with US/SPECT, and 16% with 3+ imaging studies. Concordant imaging was achieved in 63% of patients. Concordant imaging correlated precisely with surgical findings in 82% of all patients, 85% with 4D/CT/US, and 82% with US/SPECT. When liberalized to assess correlation for just laterality of the adenoma, concordant imaging predicted operative findings 95% of the time in all patients, 94% with US/4D/CT, and 95% in US/SPECT/CT. Additionally, concordant imaging correlated with 50% reduction in PTH in measurements after adenoma excision in 94% all patients, 90% US/4D/CT and 100% US/SPECT/CT. Concordant imaging did not predict statistically significant differences in pre-operative PTH, serum calcium, or intra-operative gland weight compared to non-concordant adenoma.

**Conclusion:** Concordant imaging with ultrasound combined with 4D/CT or SPECT/CT is strongly predictive (94 and 95% respectively) of operative findings in identifying offending parathyroid adenomas causing hyperparathyroidism. In these patients, the marginal value of intra-operative PTH monitoring likely hinges on the added cost of OR time vs. surgeon tolerance of a small but potential increased risk of reoperation.

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## **Cervical inlet patch as an etiology of symptomatic upper cervical esophageal dysfunction**

*Stephen Schoeff MD; Patrick McGarey MD; James Daniero MD*

**Objective:** Review a unique exam finding that appears to be a poorly defined cause of atypical LPRD and cricopharyngeal dysfunction and discuss the impact on surgical decision-making of this finding

**Study design:** A case series of 5 patients seen over a 1 year period at a tertiary care center presenting for treatment of recalcitrant LPRD and/or cricopharyngeal dysfunction found to have a cervical inlet pouch on endoscopy.

**Results:** Four of five patients were confirmed pathologically to have heterotopic gastric mucosa. The patch was directly treated in three patients. Two were performed with excisional biopsy and cautery technique, while one patient had a prior history of recurrent inlet patch treated with multiple radiofrequency ablations. Each ablation led to a symptom free interval. Four patients also had severe CP dysfunction requiring surgical intervention with dilation or myotomy. The resolution of symptoms with directed treatment suggests a potential relationship to the development of recalcitrant LPRD and cricopharyngeal dysfunction, either as a causative factor or concomitant finding. PPIs were able to be weaned.

**Conclusion:** Whether as the root cause or as a reactive finding, gastric inlet patch appears to have a relationship with atypical LPRD symptoms and CP dysfunction as shown in our series. We consider it a relevant finding in the evaluation of these patients that can benefit from direct treatment. Further studies are warranted to determine the role of this finding in cervical dysphagia and implications of the finding in patient treatment and stratification.