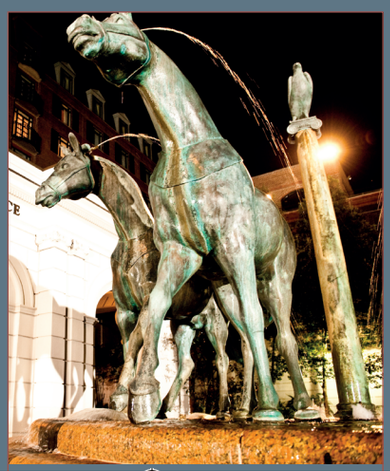
NORTH CAROLINA/SOUTH CAROLINA OTOLARYNGOLOGY AND HEAD & NECK SURGERY

2016 ASSEMBLY

FRIDAY PRESENTATIONS

JULY 29-31, 2016 BELMOND CHARLESTON PLACE - CHARLESTON, SC

This continuing medical education activity is jointly provided by the North Carolina Society of Otolaryngology and Head & Neck Surgery and Southern Regional Area Health Education Center.



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The Compound Action Potential in Subjects Receiving a Cochlear Implant

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The University of North Carolina, Chapel Hill

Disclosures

Co-authors of this study have received research contracts and/or consultant agreements with:

- MED EL Corporation
- Cochlear Corporation
- Advanced Bionics

The work itself was supported by a research contract with MED EL Corporation.

The Team

Surgeons

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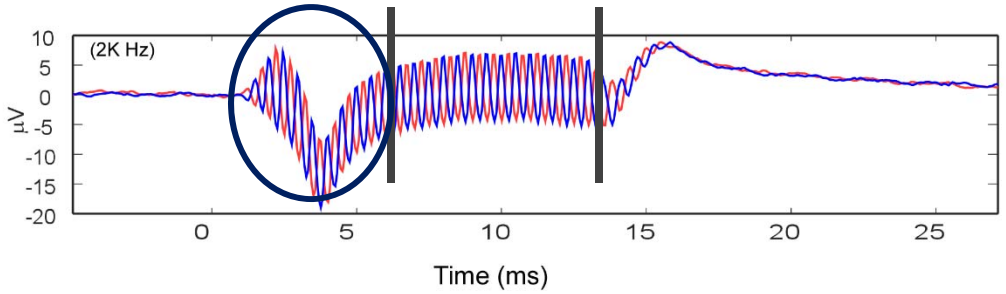
Background

Electrocochleography (ECochG): recording of electrical potentials from the cochlea

Our lab records **ECochG intraoperatively during cochlear implantation** with the goal of **understanding variability in speech perception outcomes**

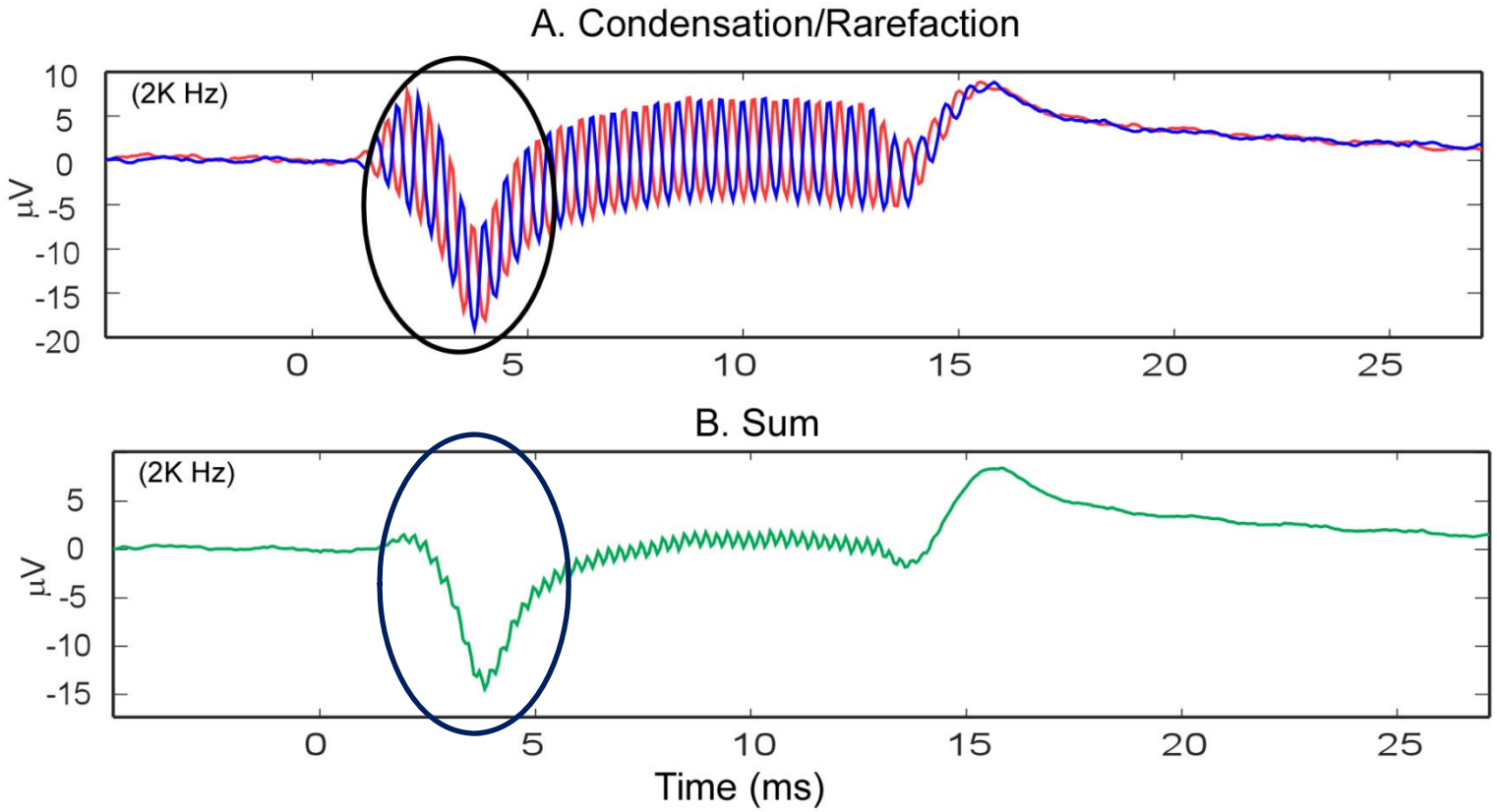
Total Response (TR)

- Can account for **40-50%** of variance in speech perception outcomes[1,2]
- Measurement of ongoing response summed across frequencies, which includes hair cell and neural components



This study investigated a purely neural portion of the ECochG response, the **compound action potential (CAP)**

The Compound Action Potential (CAP)



Hypothesis: Larger CAP = more functional nerve fibers = better speech perception

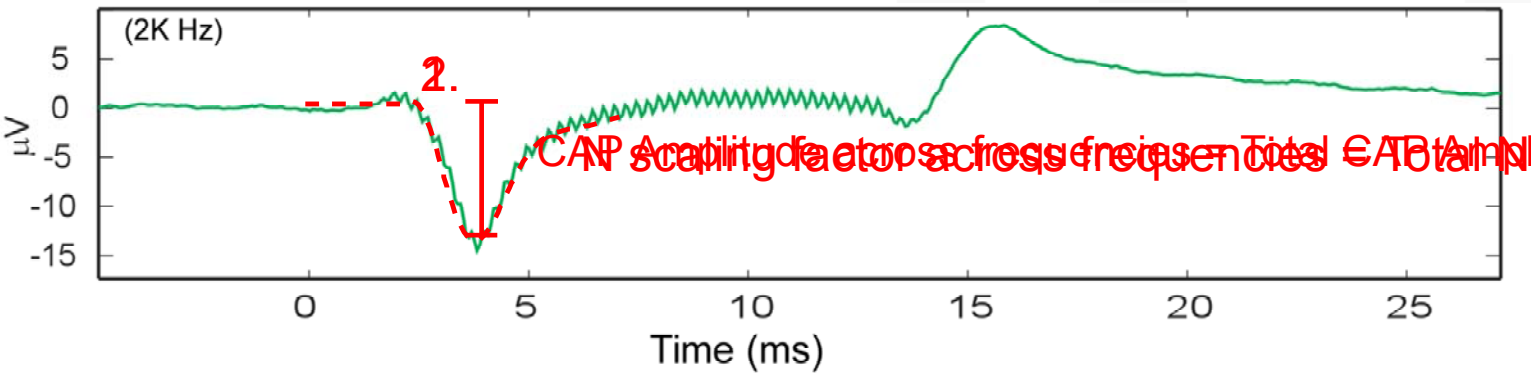
Methods

- Performed ECochG intraoperatively on 238 adult and pediatric cochlear implant recipients
- Measured the CAP in 2 ways:

1. Amplitude of the first negative deflection from baseline
2. Created an analytic model of the CAP using this equation developed by Chertoff[3]

$$\mathrm{CAP}(t) = N \int_{-\infty}^{t} P(\tau)U(t-\tau)d\tau \quad \text{where} \quad U(t) = e^{-kt}\sin(\omega t) \quad \text{and} \quad P(t) = \left(\frac{t-\alpha}{\beta}\right)^{\gamma-1} e^{-\left(\frac{t-\alpha}{\beta}\right)}$$

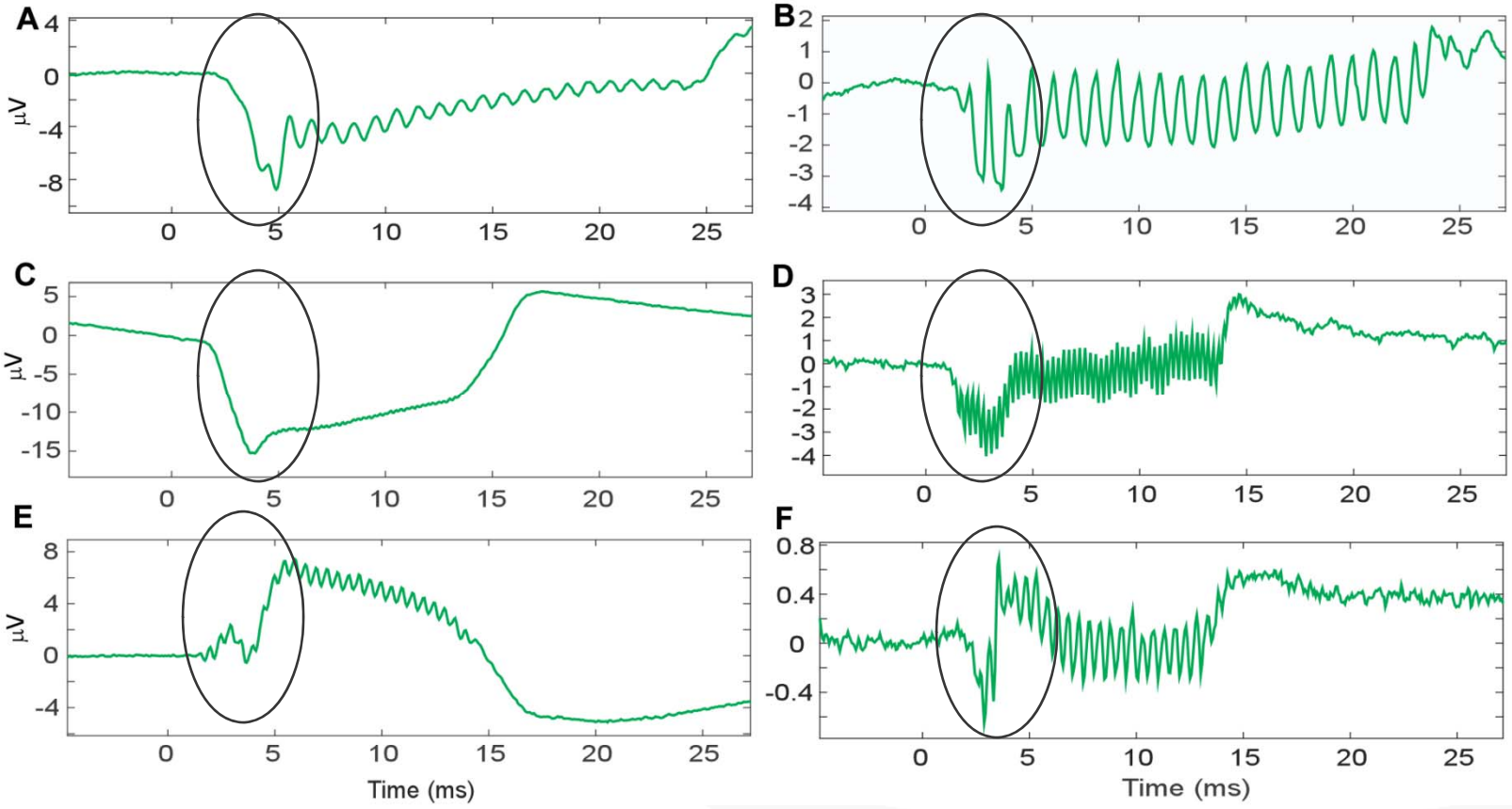
The "N" component is a scalar representing number of nerve fibers



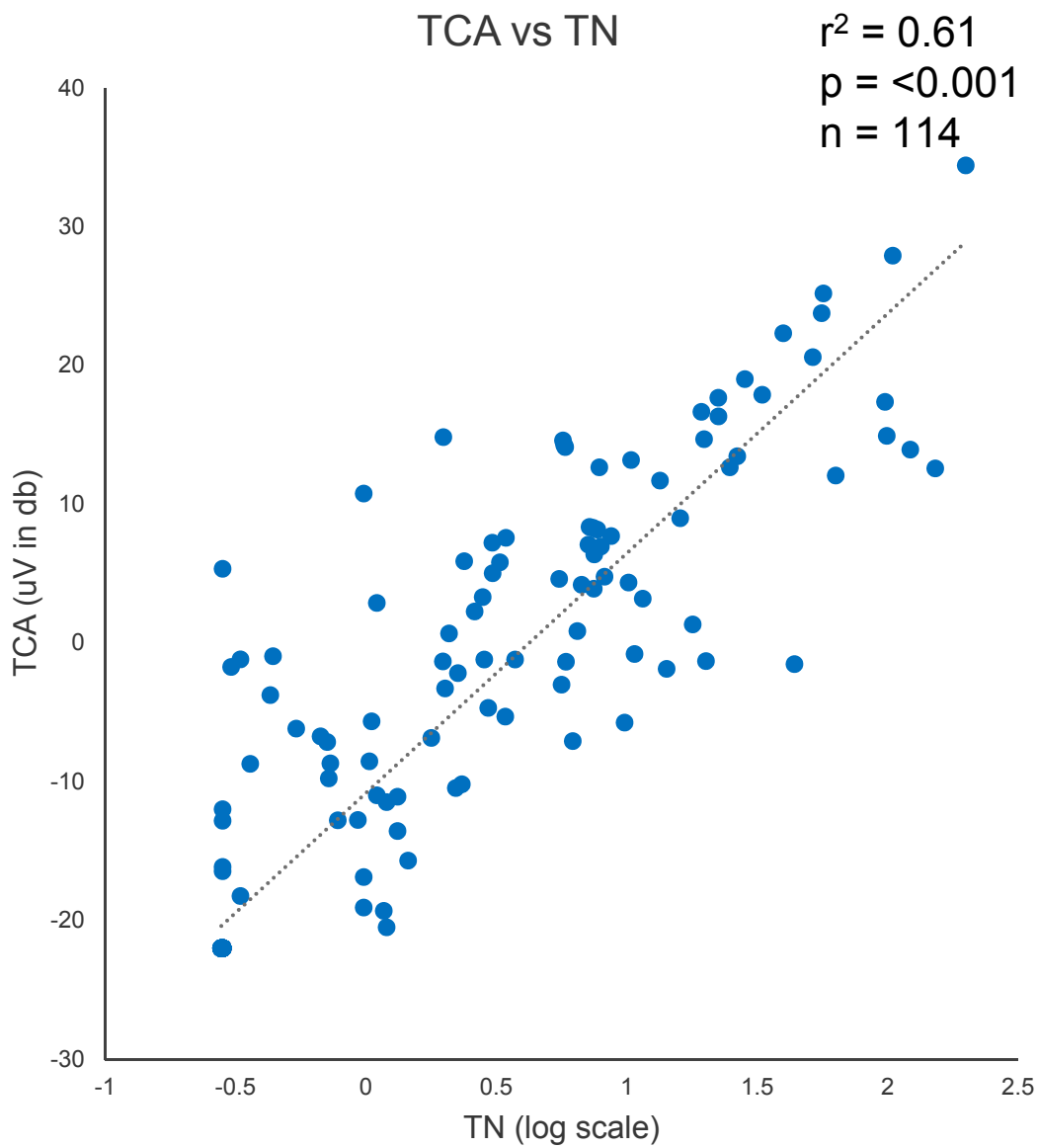
- Outcome measure for 51 adult subjects: CNC word test at 6 months

Results

-114 out of 238 subjects had evidence of CAP
-Among subjects that had a CAP, there was very diverse morphology

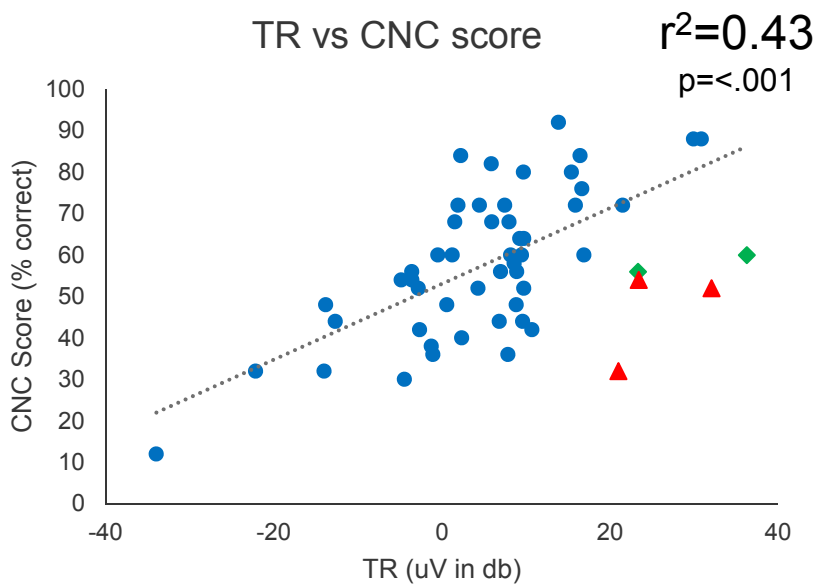


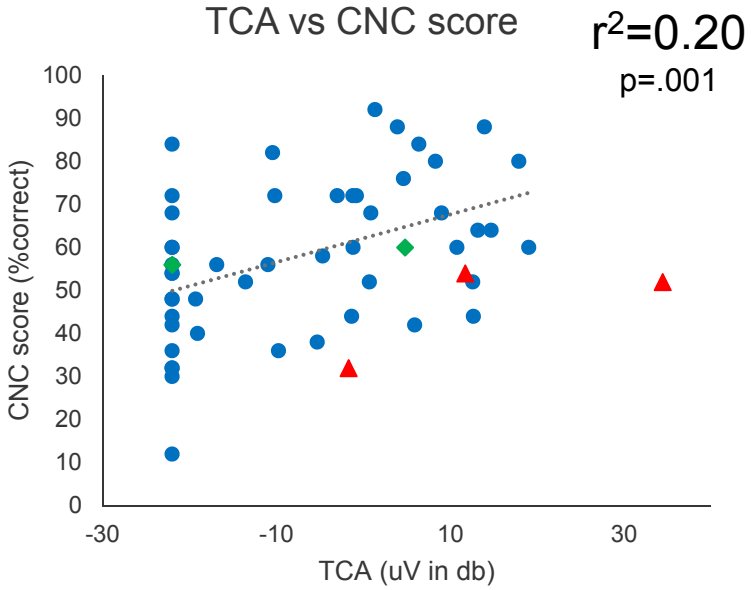
The Relationship Between Measurements of the CAP

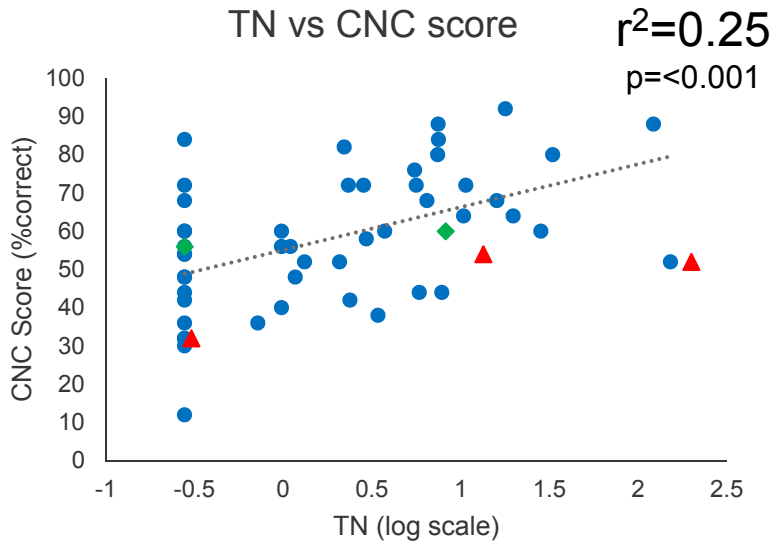


Speech Perception Outcomes

Outcomes group n=51
CNC scores obtained at 6 months







Regression analysis

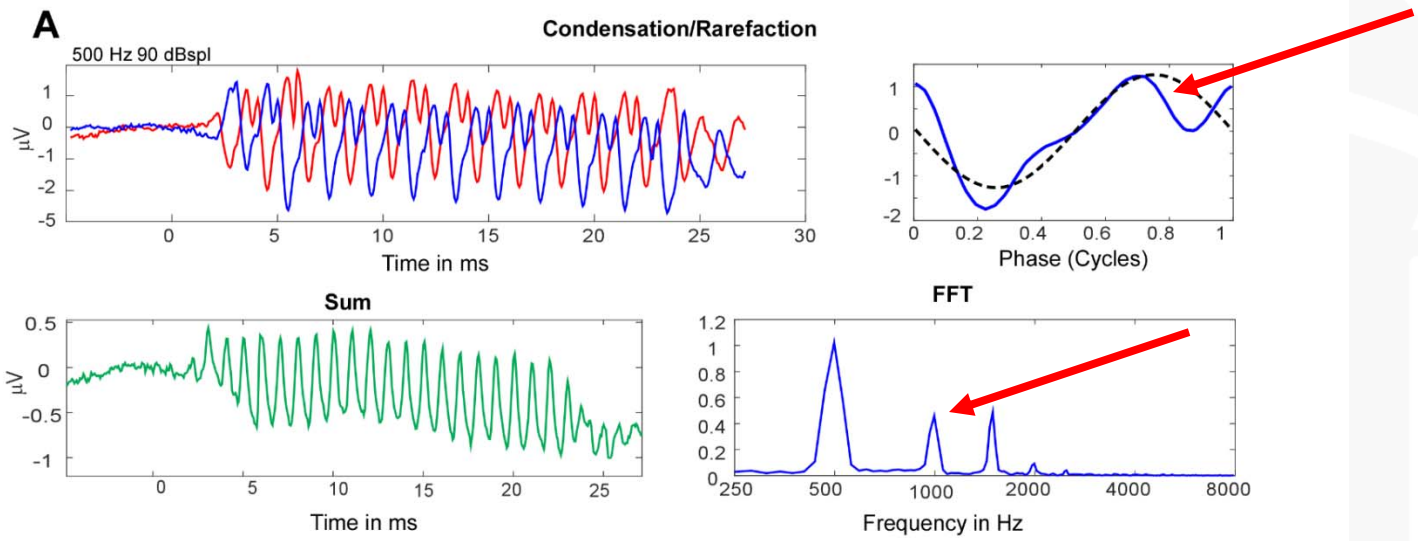
Regression variables	r^2	Adjusted r^2	Significance
TR alone	0.43	0.42	<0.001
TCA alone	0.20	0.18	0.001
TN alone	0.25	0.24	<0.001
TR +TCA	0.44	0.41	<0.001
TR+TN	0.45	0.42	<0.001

The ANN

The auditory nerve neurophonic was sometimes present in the absence of a CAP (n=15)

CAP –

ANN +



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Conclusions

- **The morphology of the CAP is significantly altered in CI subjects**

  1. loss of synchrony due to slow rise times to low frequency stimuli and large phase shifts at the CF
  2. complex interactions with components of the ongoing response like the SP and the CM

- **The size of the CAP does correlate with speech perception outcomes, but not as well as total response.**

- **Subjects without any observable CAP often still have functional nerve**

  Many subjects without CAP had good outcomes, and some had an ANN, another marker of neural activity

Bottom Line:

The CAP is extremely variable in CI subjects, and this limits its utility in outcome prediction

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- 4. Earl B. R., Chertoff M. E*.. Predicting auditory nerve survival using the compound action potential.* Ear Hear. (2010);31:7-21

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School of Medicine

Pericranial Flaps: A Viable Option for Large Septal Perforations

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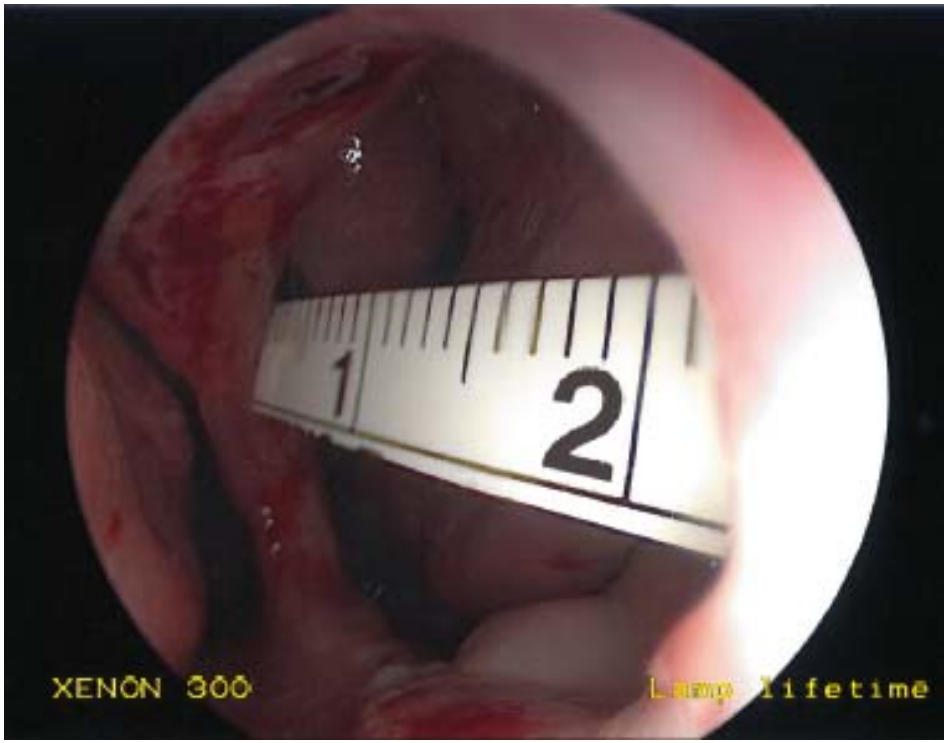
Department of Otolaryngology, Head & Neck Surgery
NC/SC Otolaryngology Assembly 7/2016

Case Report

- 30 yr old woman with large nasal septal perforation.
- Distant history of trauma to nose, otherwise considered idiopathic
- Ssx: nasal congestion, painful crusting
- Prior conservative management had failed, surgical options were limited given size of perforation.

Physical Exam

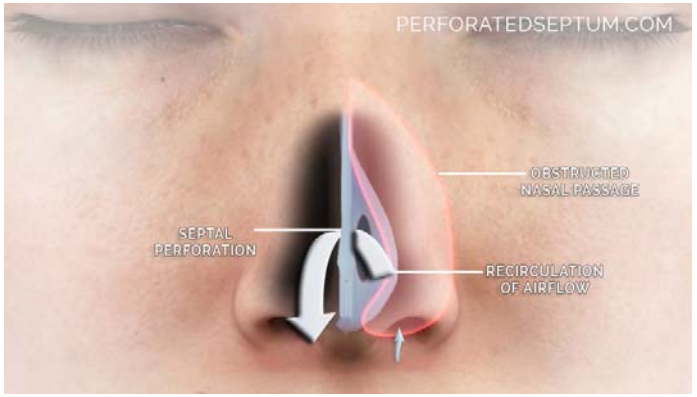
- Perforation involving almost entirety of the anterior cartilaginous nasal septum measuring 2.5cm x 2 cm
- Nasal dorsum and tip support still intact
- No bony septum involvement



.....WHAT NEXT???

Nasal Septal Perforations

- Incidence: ~1%
- Etiology:
  - Most common: iatrogenic (>50%)
  - Other entities: idiopathic, cocaine use, nasal trauma, nasal intubation, cautery, OTC decongestants, nasal steroids , inflammatory diseases, neoplasms, syphilis, tuberculosis, digital manipulation
- Most common symptoms:
  - Subjective nasal obstruction (72%)
  - Painful crusting (50%)
  - Recurrent epistaxis (31%)
  - Whistling
  - Malodorous discharge



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http://www.perforatedseptum.com/perforated-septum-treatment/

Management Options:

Asymptomatic/poor operative candidate/ active systemic disease

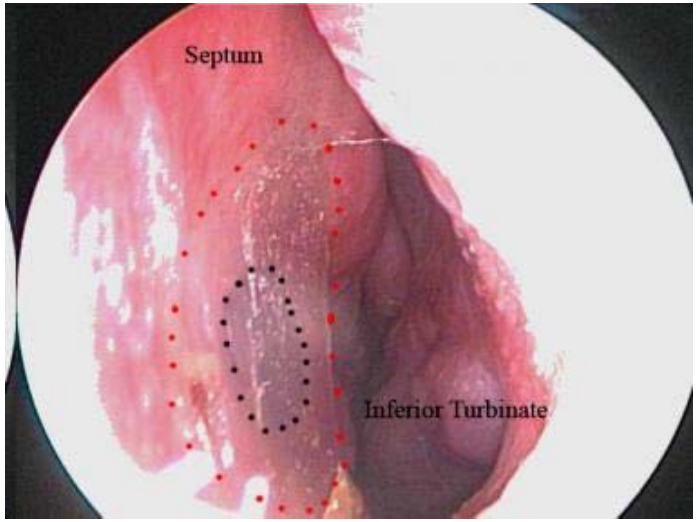
Small perforations

CONSERVATIVE MANAGEMENT

- <u>OPTIONS</u>

- Saline sprays, irrigations, ointments

- Nasoseptal prosthetics



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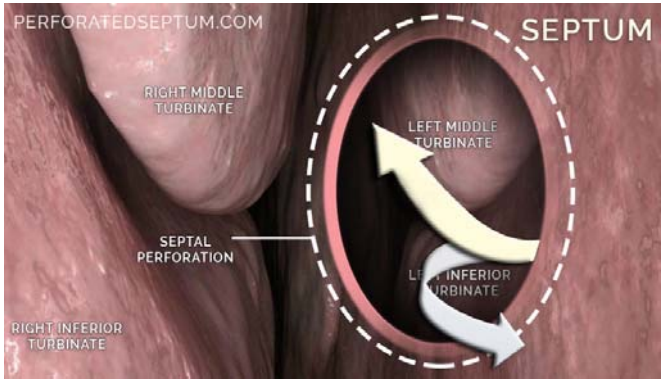
Management Options



- Surgical Repair Options:
  - Intranasal mucosal flaps:
    - Inferior turbinate, quadrangular cartilage flap, a variety of mucoperiosteal flaps
  - Combinations of intranasal mucosal flaps and interposition grafts
    - Temporalis fascia, mastoid periosteum, nasal septal tissues, acellular human dermal grafts, conchal cartilage, etc
  - Superiorly based buccinator myomucosal flap, etc etc

- Difficulty with large septal perforations… Which brings us to…

PERICRANIAL FLAPS

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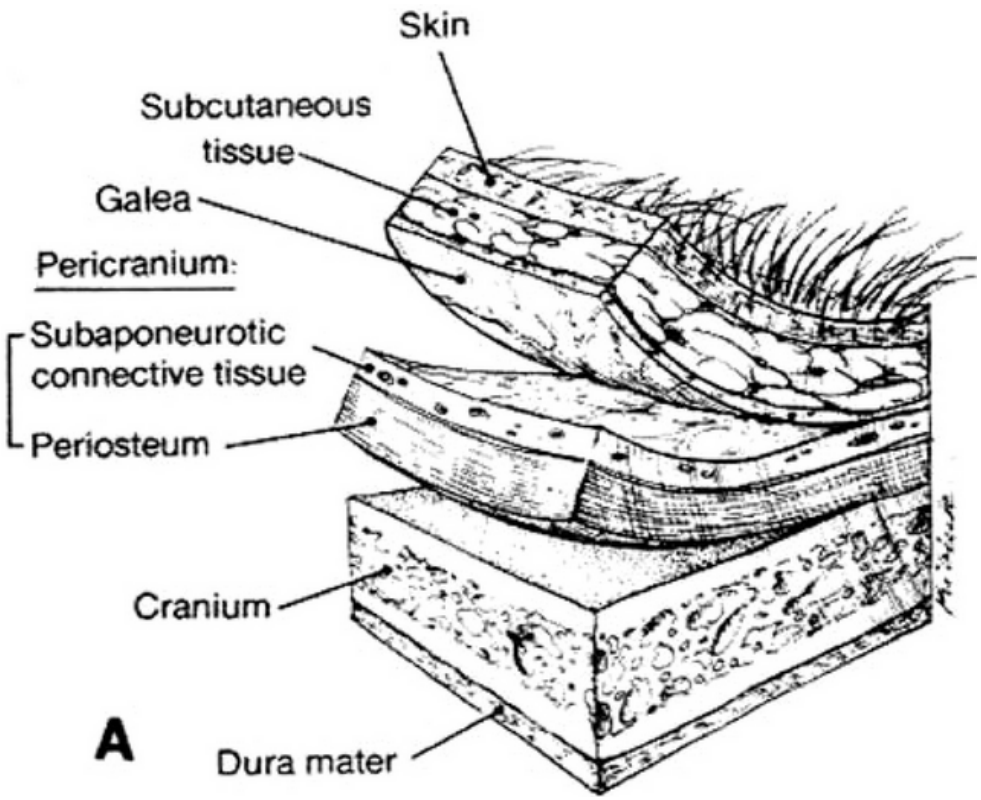
http://www.perforatedseptum.com/perforated-septum-treatment/

The Pericranial Flap



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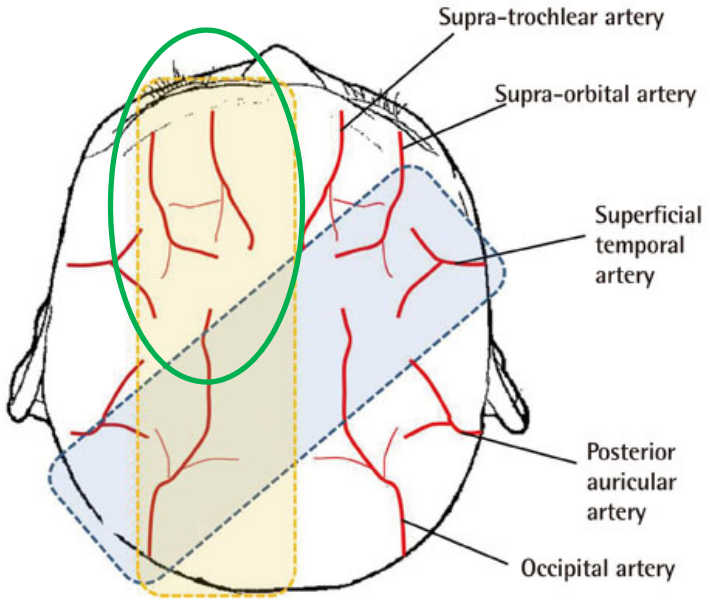
S C A L P

- Well known use in anterior cranial base, craniofacial reconstruction
- Based off of supraorbital & supratrochlear arteries

Sertel S et al. Pericranial Flap for Inner Lining in Nasal Reconstruction. *Annals of Plastic Surgery*. 2015 Sep 28



http://www.e-aps.org/search.php?where=aview&id=10.5999/aps.2013.40.4.341&code=2023APS&vmode=PUBREADER#!po=68.7500

Use in Nasal Septal Perforations

- First paper describing the surgical procedure, published in 2000

SURGICAL TECHNIQUE FOR RECONSTRUCTION OF THE NASAL SEPTUM: THE PERICRANIAL FLAP

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Accepted 11 May 1999

Abstract: *Background.* We describe a new technique for the surgical reconstruction of large-sized anterior septal perforations based on the pericranial flap.

Methods. The technique requires a standard open rhinoplasty combined with a pericranial flap harvested after a bicoronal approach and tunnelled to the nasal cavity. We present the case of a man with complete destruction of the nasal septum as a result of chronic cocaine abuse.

Results. Surgery resulted in a permanent and complete closure of the perforation.

Conclusions. The main advantage of this technique is the use of well-vascularized autogenous tissue and the minimal donor site morbidity. This technique provides a new method to close large nasal perforations. © 2000 John Wiley & Sons, Inc. *Head Neck* 22: 90–94, 2000.

Keywords: septum; reconstruction; cocaine; pericranial; flap; perforation

The incidence of septal perforation has increased in the last decade in direct relation to cocaine abuse.

Correspondence to: A. Samper

CCC 1043-3074/00/010090-05

When nasal perforations are small, the treatment should be conservative, with saline, serum, and mineral oils to decrease crust formation and the sensation of nasal obstruction. Surgical treatments for small to medium sized perforations include local mucosal flaps, prosthetic polymers of silicone, or compound flaps. Any of these options are acceptable, but the repair of symptomatic large perforations may be more difficult to manage.

In this article we report a new surgical technique suitable for cases of complete destruction of the nasal cartilaginous septum.

CASE REPORT

We present the case of a 55-year-old male, who had been a chronic cocaine abuser for 20 years and who had a massive perforation of nasal septum (Figure 1). The perforation involved the whole cartilaginous portion of the nasal septum except for the portion at the dorsum and apex (Figure 2). The patient's main complaint was chronic and continuous nasal crust formation. He

Anatomic Properties of Flap

293

Kulak Burun Bogaz Ihtis Derg 2010;20(6):293-298

Experimental Study / Deneysel Çalışma

Reconstruction of large nasal septal perforations with a three layer galeal pericranial flap: an anatomical and technical study

Geniş nazal septal perforasyonların üç katmanlı galeal perikranyal flep ile onarımı: Anatomik ve teknik çalışma

Bahar Keleş, M.D.,[1] Kayhan Öztürk, M.D.,[1] Aynur Emine Çiçekçibaşı, M.D.,[2] Mustafa Büyükmumcu, M.D.[2]

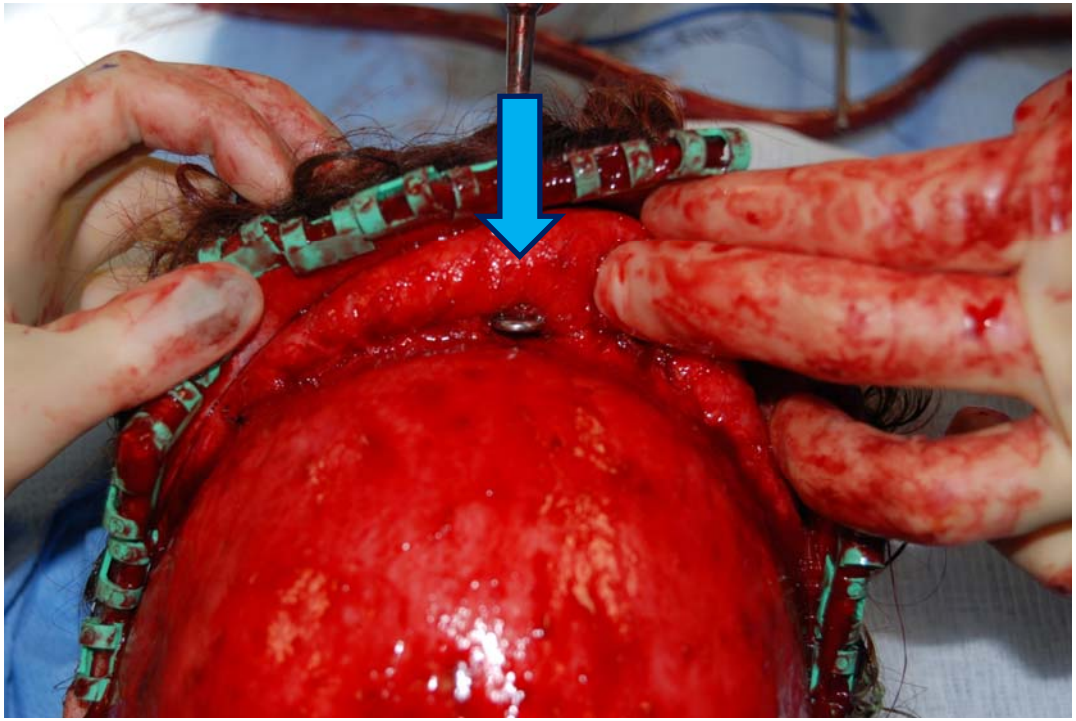
Departments of [1]Otolaryngology, [2]Anatomy, Medicine Faculty of Selçuk University, Konya, Turkey

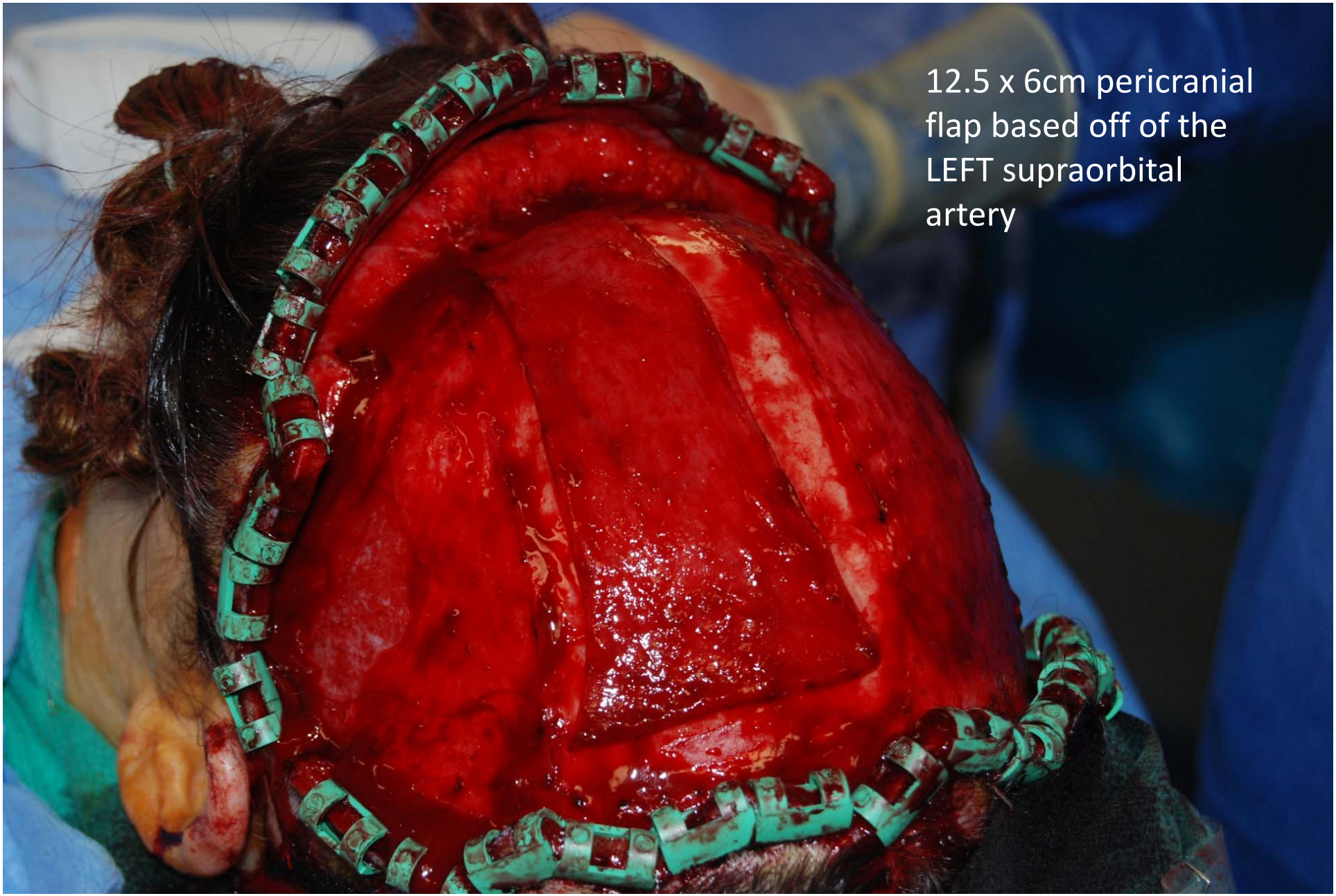
- Paper out of Turkey describing 6 cadaveric dissections to determine reliability and size of pericranial flap, in its use in nasal septal perforation repair
- Average length: 54.1mm +/- 4.9mm
- Average width: 51.6mm +/- 7.8mm
- Results: More than adequate available tissue, reliable vascular supply. All nasal septal perforations were repaired.

Surgical Procedure

- Open rhinoplasty for ideal access to septum
- Exposure of nasal dorsum to nasion, elevating soft tissue envelope.
- Bilateral mucoperichondrial flaps were elevated
- Bicoronal incision
- Tunnel was constructed to pass flap through to the nasal septum.

CONSTRUCTED TUNNEL





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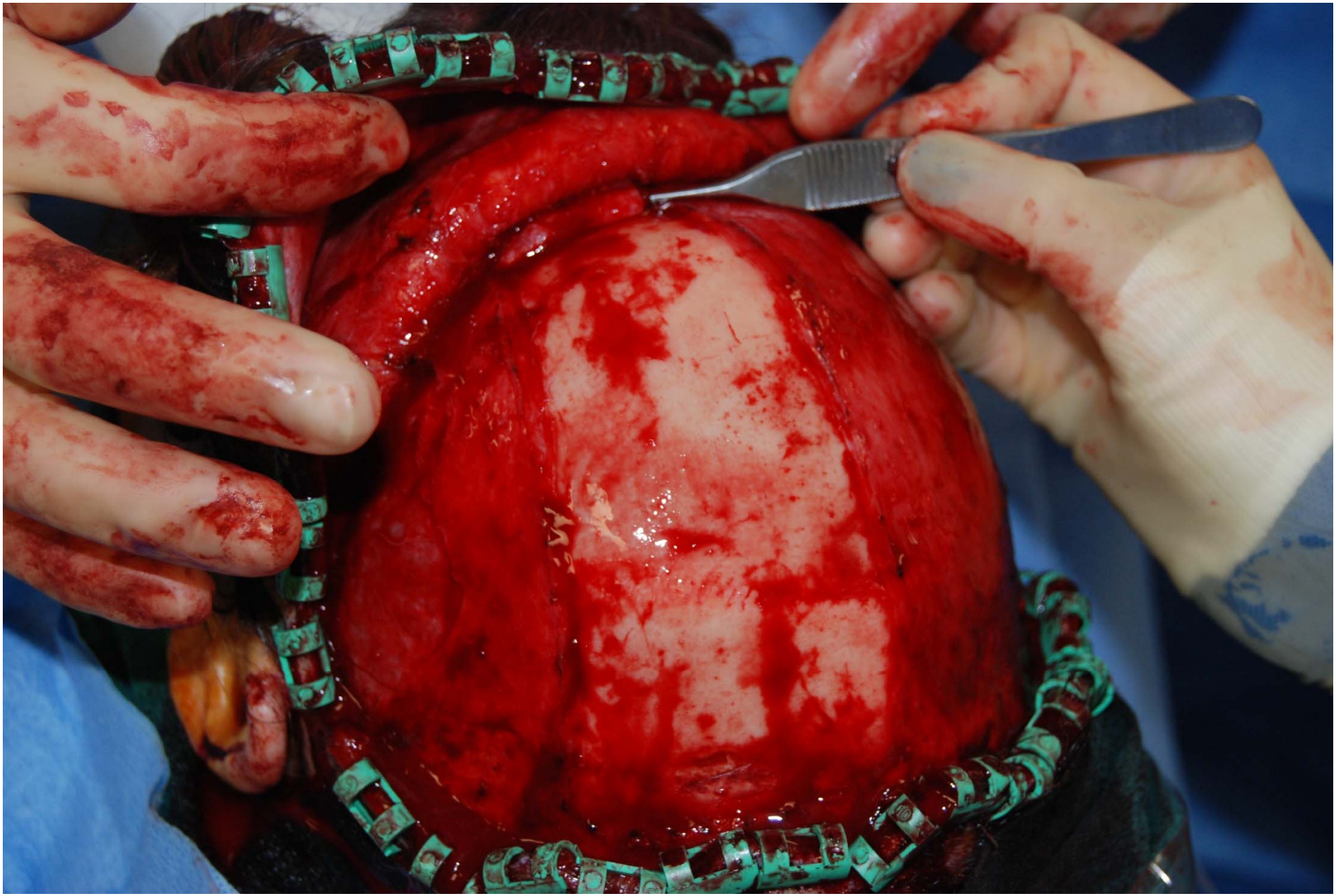

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Intranasal insertion

- Flap passed into perforation
- Paloma described dividing both ULCs and creating 2 layers of the flap.

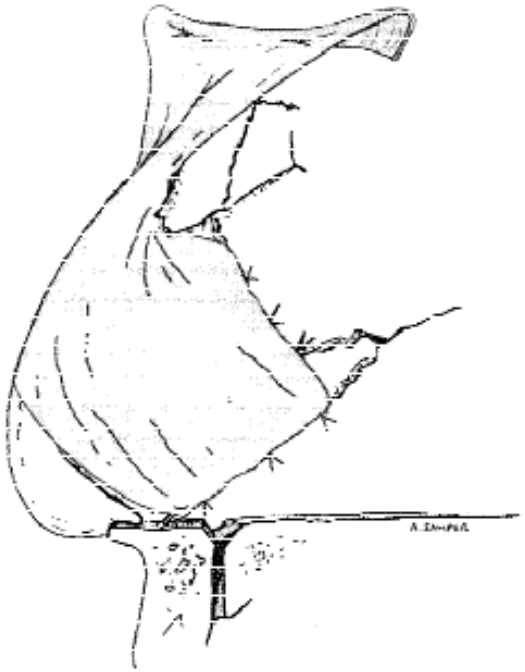
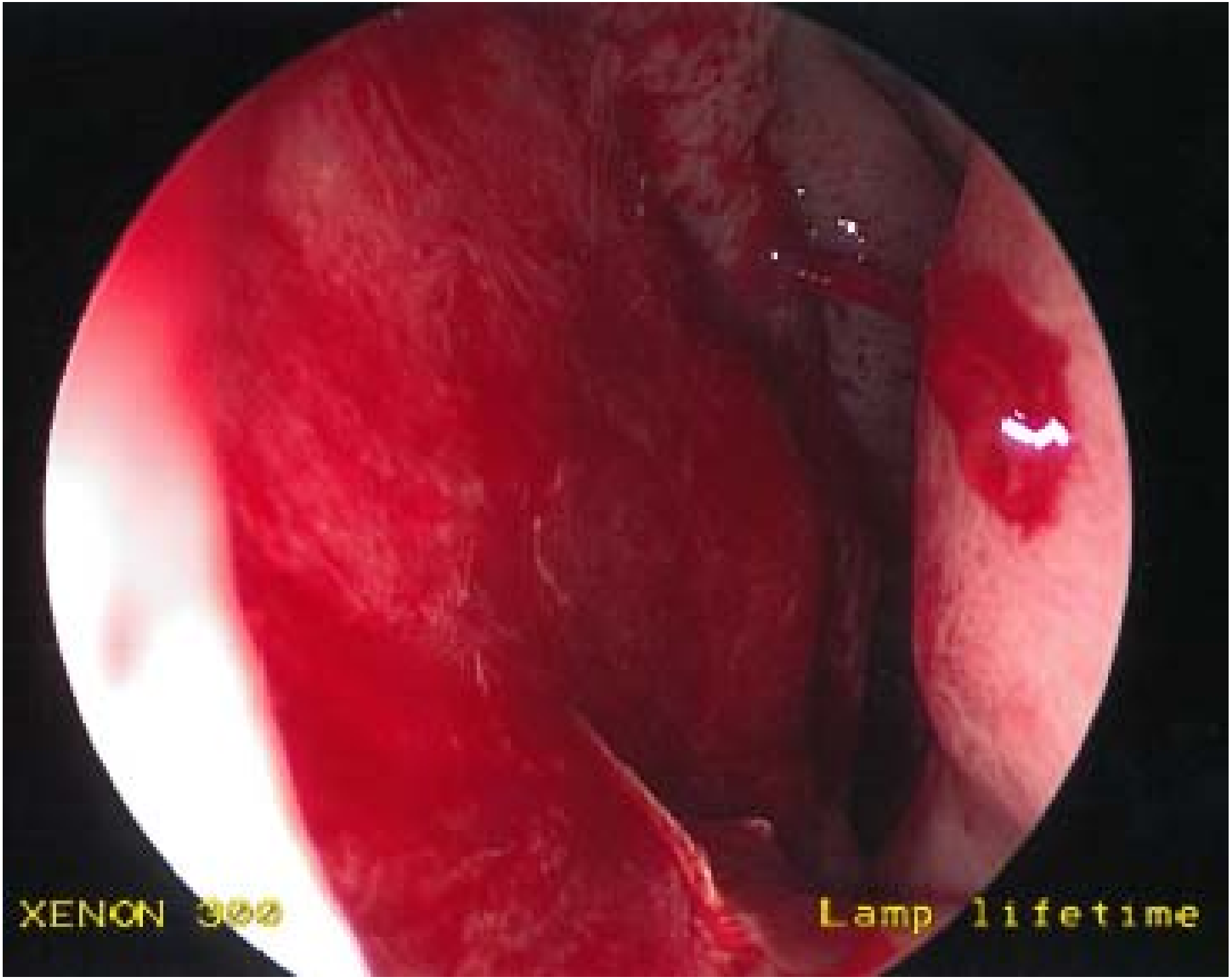


FIGURE 5. New septum made of 2 layers of well-vascularized tissue.

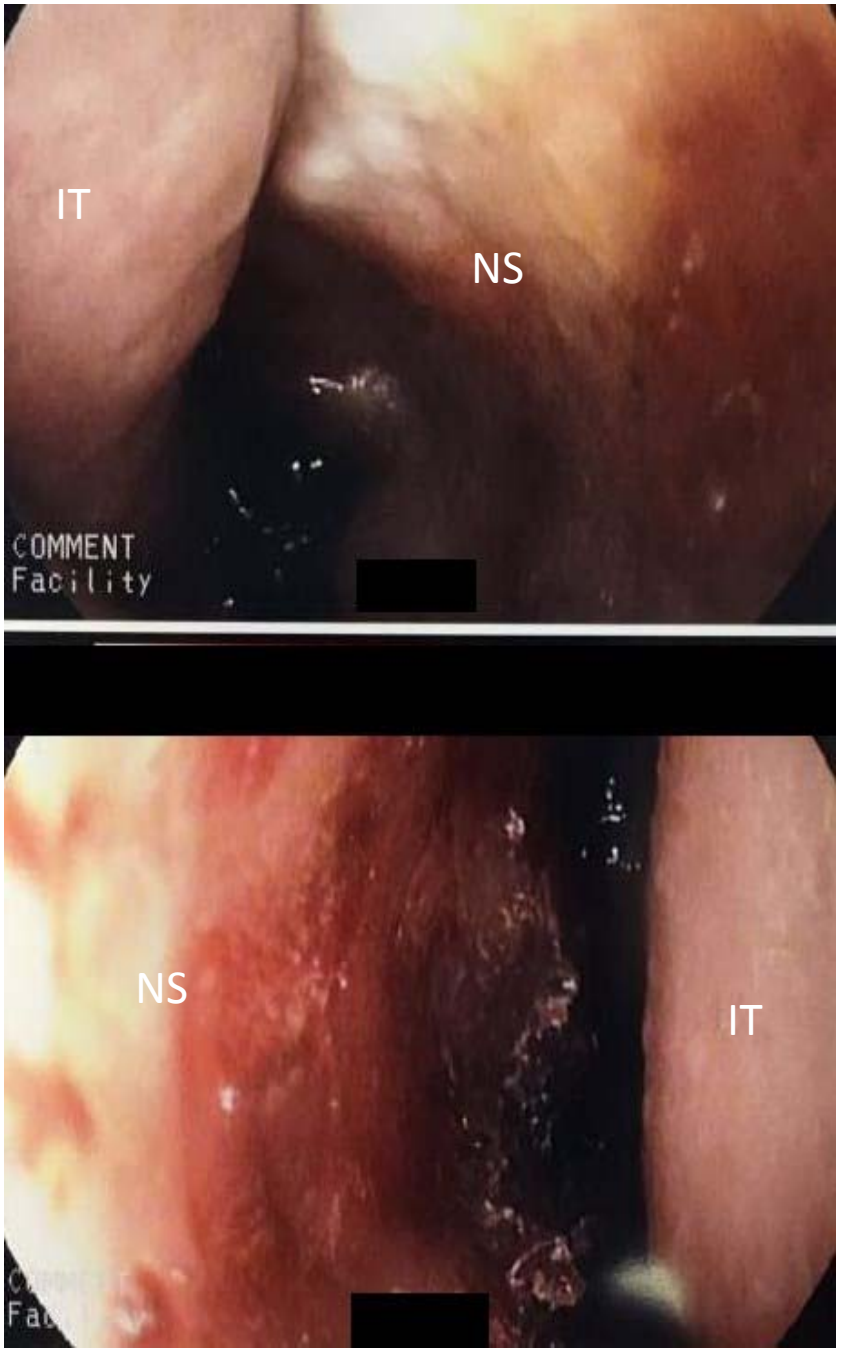
Paloma et al

- Our method differed slightly as more width was necessary.
- R ULC only was separated from dorsal septum
- Flap was draped with superficial perichondrial surface draped over right and deep raw surface visible on left.

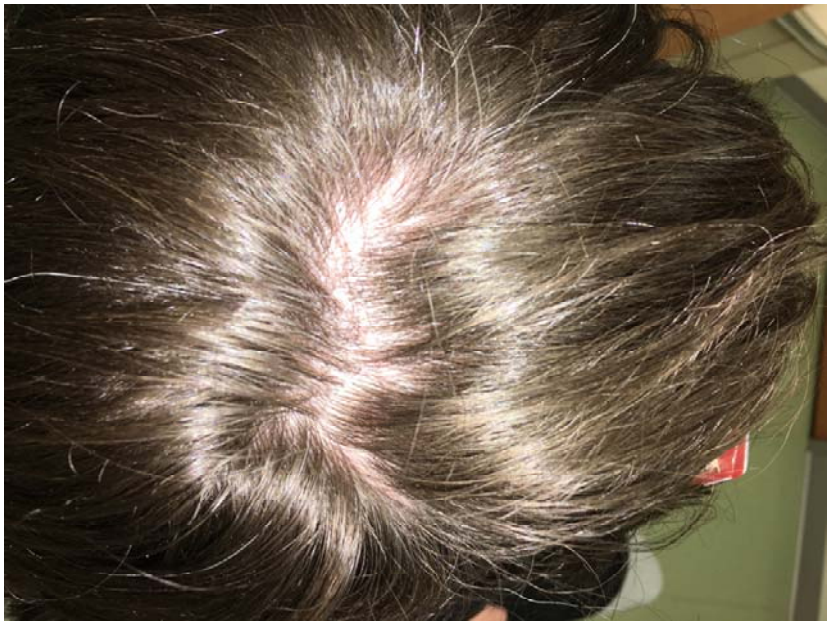

XENON 300
Lamp lifetime

Post-operative course

- Uncomplicated immediate post-op
- 6 month follow up, flap intact and viable. No remaining perforation.
- Satisfied with cosmetic and functional result



9 month follow up



- Unfortunately, posterior flap has pulled away by 2-3mm.
  - Patient remains asymptomatic, as perforation is much smaller and more posteriorly based.
- Donor site has healed remarkably well.
  - Patient is satisfied with scar and lack of visibility.

CONCLUSION

- Large septal perforations remain very difficult to close
- The pericranial flap is a viable option to gain closure of large septal perforations.
- Special thank you to Dr. Brian Downs

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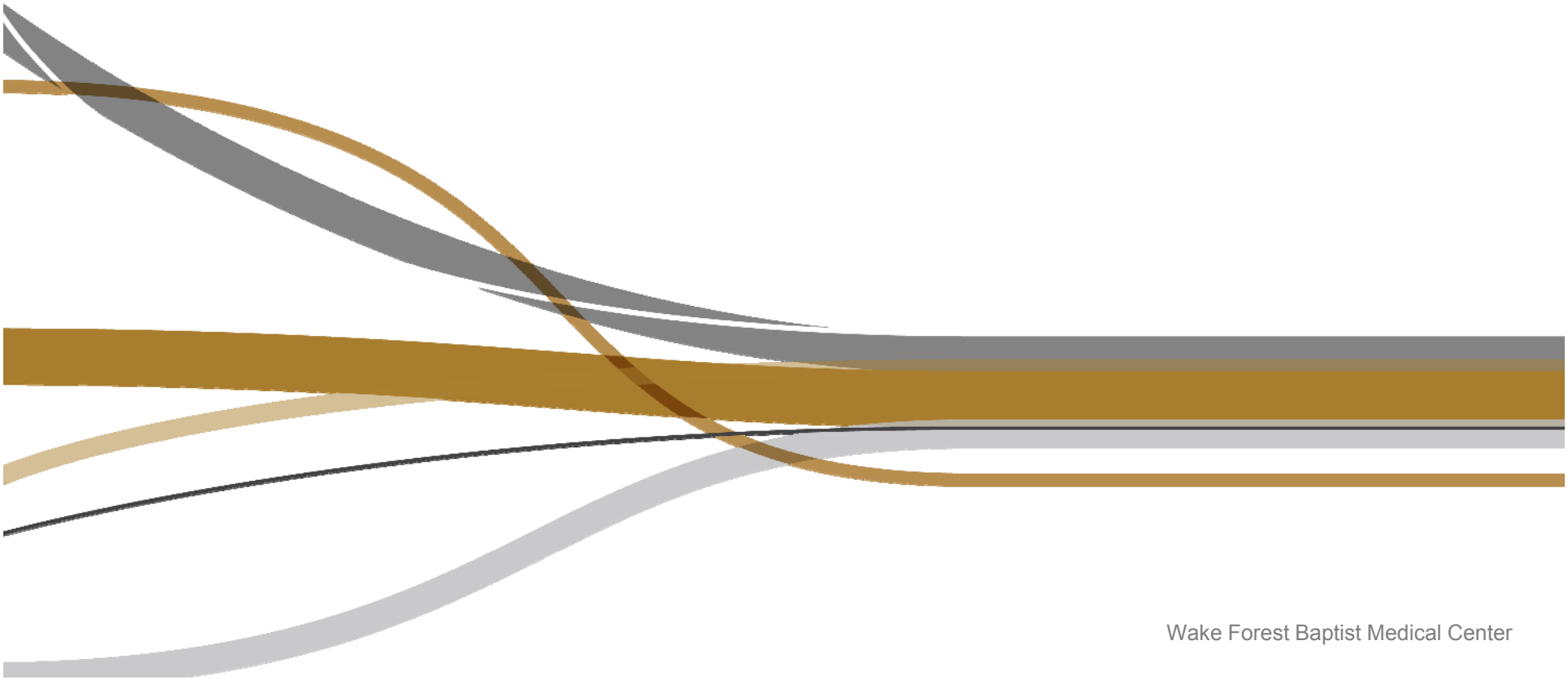
THANK YOU!



TICK BITE-RED MEAT ANAPHLAXIS THE ALPHA-GAL STORY

Robert E. Taylor, MD
Triangle ENT and Allergy
Durham, NC

Goals

- Identify patients at risk.
- Understand biological factors involved.
- Recognize how tick-bite red meat anaphylaxis is different from other causes of anaphylaxis

Definition

- Delayed anaphylactic IgE response to Galactose-alpha-1,3 Galactose (alpha-Gal)
- Reaction to ingestion of all mammalian meat except primates
- Reaction occurs 4-8 hours after ingestion
- Syndrome initiated by tick bite from Lone Star tick
- Reaction does not occur after eating poultry or seafood

Background

- Alpha-gal is an oligosaccharide found on certain receptor sites of all mammals except primates and humans.
- Because of its absence, humans develop IgG antibodies which are the cause of xenobiotic transplant rejections.
- IgE response appears to be initiated by reaction to the alpha-gal injected from the saliva in the bite of a Lone Star tick.
- The appearance and distribution of humans with this syndrome are found in a pattern that overlaps the distribution of the Lone Star tick species in the Atlantic Coast and Mid Eastern US states.

Identifying Underlying Causes

- Summation of 2 unusual clusters of cases:
  - Immediate reaction to chemotherapy agent – cetuximab (Erbitrix-R), chimeric monoclonal antibody used to treat colorectal and head and neck cancers.
  - Occurred with initial infusion indication prior sensitization.
  - Reactions were regional-most common in Tennessee, Arkansas, Alabama, Missouri, North Carolina and Virginia.
  - Patients who reacted had immediate response to skin testing with cetuximab and had antibodies to cetuximab.
  - Sensitization eventually tracked to post-translational modification with glycosylation of the Fab fragment of IgG with alpha-gal.

Identifying Underlying Cause

- Summation of 2 unusual clusters of cases:
  - Clusters of patients demonstrating delayed anaphylactic reaction consisting of severe local or severe whole body itching, hives, angioedema, GI upset and possibly anaphylaxis.
  - 70% of cases had accompanying airway distress.
  - Reactions were delayed from 4-8 hours after eating.

What Tick Bite-Red Meat Anaphylaxis Is Not

- Protein peptide based IgE anaphylaxis
  - Immediate severe reaction occurring within 30-60 minutes of ingestion
  - Most commonly nuts, shellfish, milk
- Pork-Cat Anaphylaxis
  - Cross reaction between cat albumin and pork albumin
  - Prick test positive for Cat and Pork antigens
  - Immediate severe reaction
  - Does not cross react with other mammalian antigens

What Tick Bite-Red Meat Anaphylaxis Is Not

- Milk Protein Anaphylaxis
  - More common in children
  - Immediate response
- Cross Reactive Carbohydrate Determinants (CCD)
  - Antibody binding glycoproteins
  - Widespread in pollens, foods, insect venoms
  - Not clinically important – “blocking antibodies”
  - Incidental “immune therapy”

What Is Tick Bite-Red Meat Anaphylaxis?

- An IgE reaction to Galactose-alpha-1,3 galactose (alpha-gal)
- Onset of anaphylaxis occurs 4-8 hours after ingestion on red mammalian meat
- No reaction to seafood or poultry
- Most likely initiated by tick bite from Lone Star tick in US
- Most common in Atlantic Coast and Mid Atlantic states
- Also found in Australia (Paralytic tick) and Europe (Castor Bean tick)
- Symptoms include urticaria, angioedema, GI distress, asthma exacerbation and hypotension

What Is Tick Bite-Red Meat Anaphylaxis?

- Reactions decrease in 18-24 months if no further tick bites
- Cross reactivity has been reported with dairy products and animal derived gelatin
- Possible reactions to heparin and cardiac valve replacement
- Basis for immediate anaphylaxis with IV cetuximab
- No reported deaths but incidence is unknown
- Diagnosis:
  - Prick test negative but ID test positive
  - Prick-Prick test positive
  - Serum IgE panel

My Patient Experience 2012-2016

Total Patients – 31

M-16

F-15

Caucasian-28

African- American -3

Age

10-20 yo – 4

20-40 yo – 3

40-60 yo -7

Over 60 yo - 17

Alpha-gal levels

< 2 – 7

2-10 – 8

11-30 – 4

> 30 - 5

Did not test - 7

Case Examples

Case Examples

- RD
  - Self diagnosed 20+ years ago
  - Avoids red meat
  - Continues to get tick bites
  - Alpha-gal – 14.10
  - RAST - negative
- DW
  - Nurse practitioner – La Crosse Allergy Clinic
  - Treated with SLIT beef
  - Alpha-gal 37 -9
  - Tolerates red meat

Case Examples

- WL
  - Tick bite 2 months prior
  - Severe anaphylaxis after driving from the Coast
  - Awoke to EMR resuscitation
  - Alpha-gal – 52.30
- HH
  - Facial rash and swelling - +/- dairy reaction
  - RAST + beef, lamb, dairy
  - Probable reaction to gelatin
- SR
  - Urticaria
  - RAST + beef, pork, lamb, dairy
  - Alpha-gal 1.49
  - LDA x 8
  - Eats red meat without reactions

Take Aways From Patient Experiences

- No alpha-gal test
  - Secondary to cost
  - Prior IgE RAST – all significantly + for beef, pork, dairy
- 50% of patients did not remember a tick bite
- 50% had severe enough reactions to seek immediate medical care
- Almost all had RAST IgE panels with positive responses to milk, beef and pork

Summary

- Alpha-gal allergy seems to be a newly described type of allergic reaction.
- The triggering event appears to be initiated by the bite of the Lone Star tick.
- The antigen involved is a carbohydrate moiety instead of a protein/peptide antigen.
- Onset of the allergic reaction occurs 4-8 hours after ingestion of mammalian meat.
- This reaction is a spectrum of responses ranging from diffuse pruritus or diarrhea up to severe anaphylaxis.

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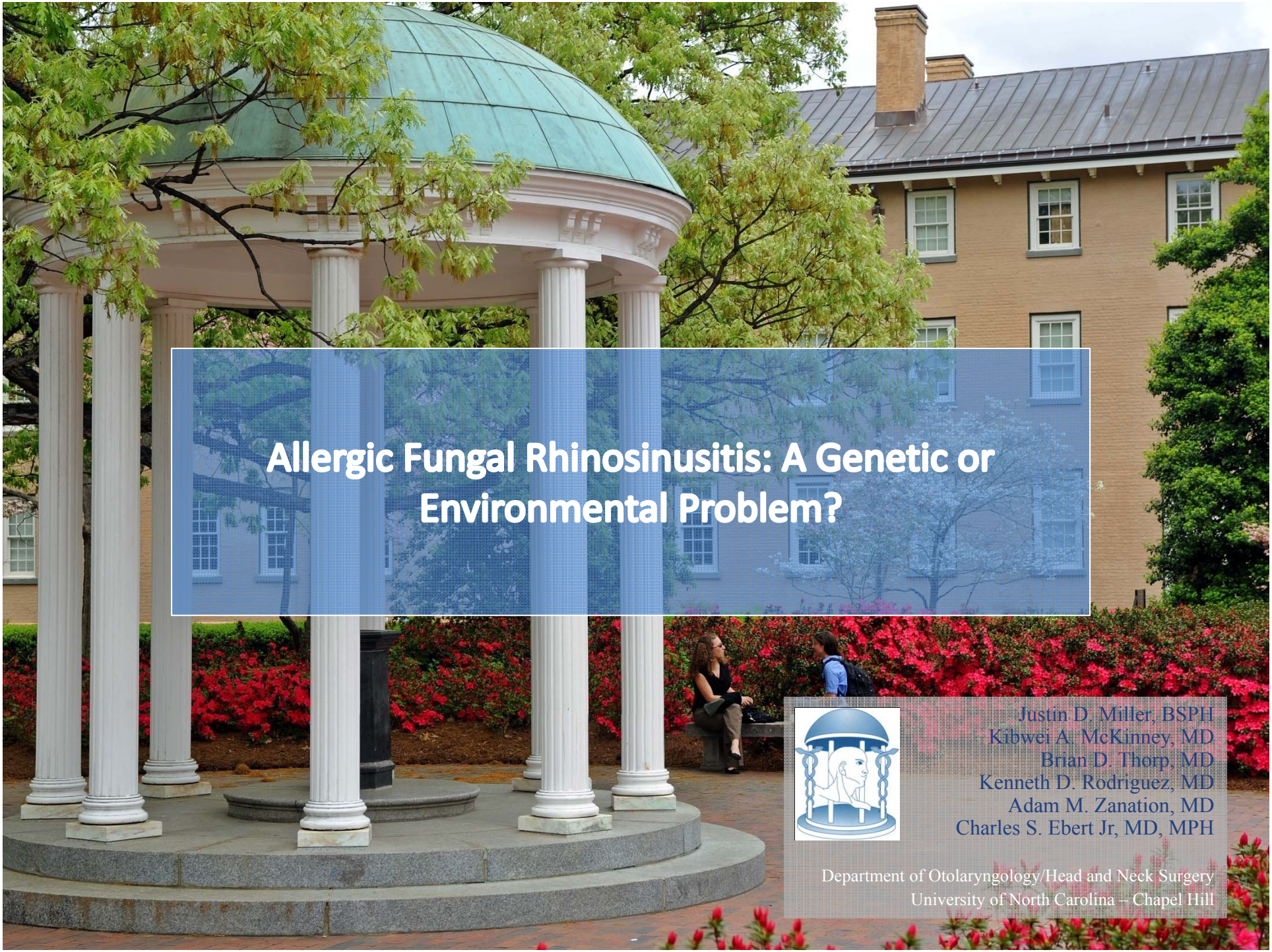

Allergic Fungal Rhinosinusitis: A Genetic or Environmental Problem?

Justin D. Miller, BSPH
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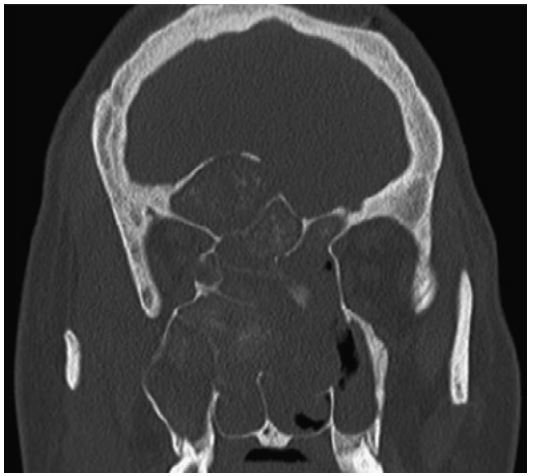
Allergic Fungal Rhinosinusitis

- Recalcitrant subtype of Chronic Rhinosinusitis (CRS)
  - Pathophysiology is multifactorial and diagnosis controversial
- Bent and Kuhn Diagnostic Criteria[2]
  - Type 1 Hypersensitivity
  - Sinonasal Polyps
  - Characteristic CT Findings
  - Eosinophilic (Allergic) Mucin
  - Fungal Elements



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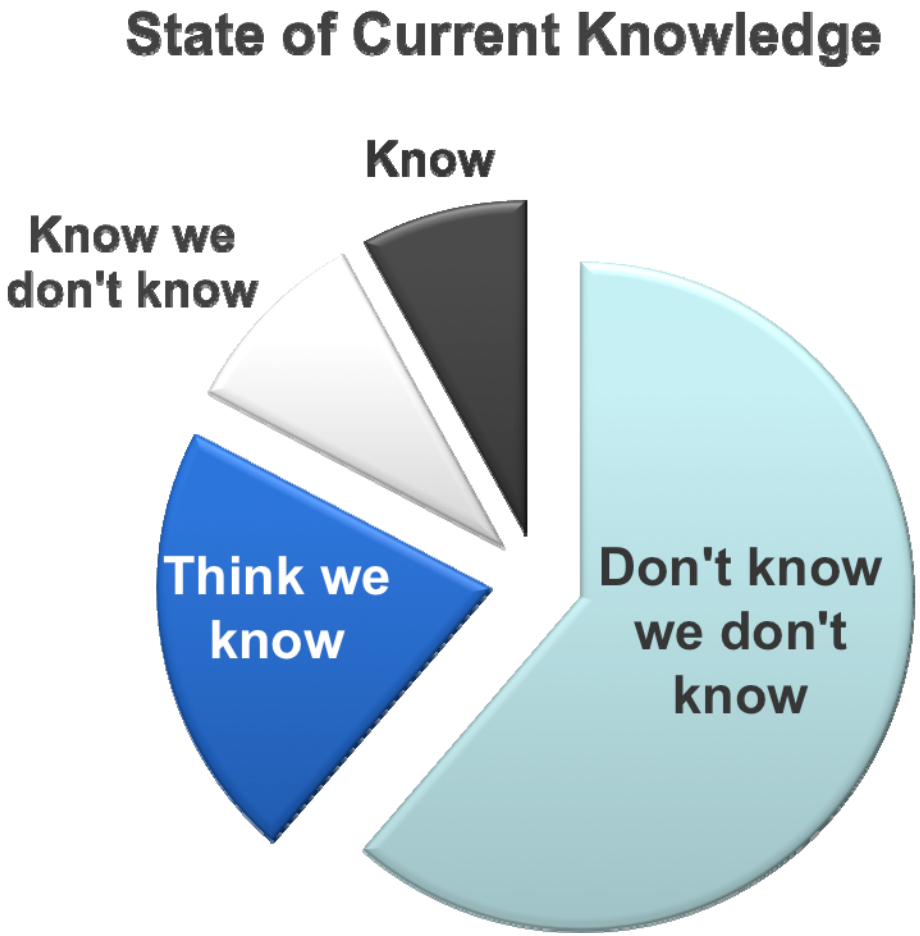
Etiology of Chronic Rhinosinusitis



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What we think we know: AFRS

- Characterized by intense eosinophilic inflammatory response
  - Etiology remains a mystery
- Most common etiologic factors discussed
  - Immune responses to microorganisms:
    - Planktonic forms of bacteria and fungi
  - IgE-mediated allergy

- Fails to describe why only some patients develop intense eosinophilic inflammatory response although bacterial and fungal antigen exposure is nearly universal.

What we think we know: AFRS

- Epidemiology of AFRS[1]:
  - **Individual Characteristics:**
    - » Southern/Southeastern US
      - Warm, humid, higher mold counts
    - » African American
    - » Male
    - » Young Age at Presentation
  - **Population Characteristics:**
    - » High percentage of patients below poverty level
    - » Low county median household income
- However, there is a paucity of data investigating the association of epidemiologic markers with disease severity

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Fungal Proteases

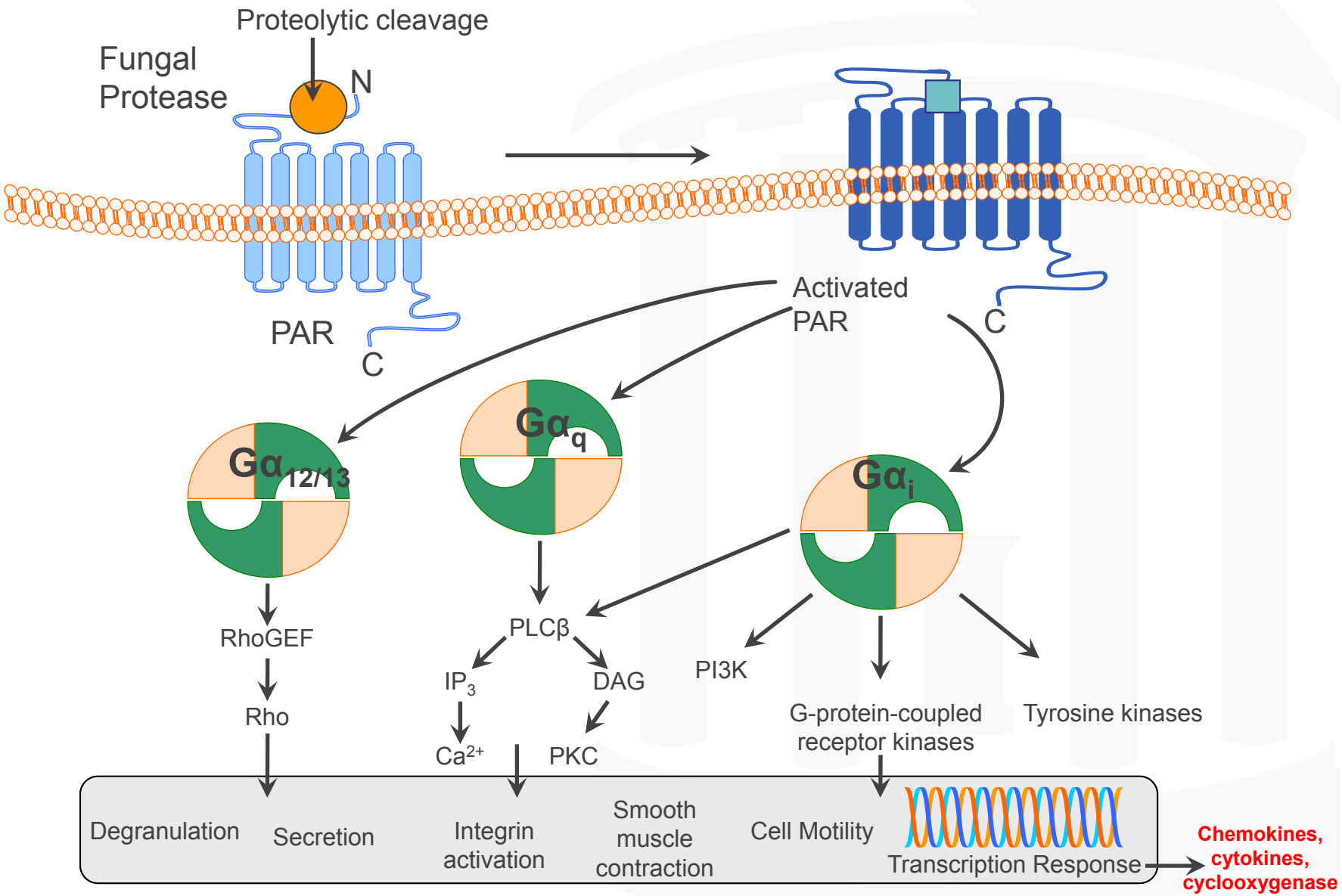
Potential contributor to exaggerated inflammatory process

- Essential part of fungal physiology and development
- Present on most airborne particles
  - Including dust[1]
- Activate/enhance the innate & adaptive immune response
  - Direct activation of epithelial cells → morphologic changes, cell desquamation, and production of pro-inflammatory cytokines (IL-6 and IL-8)[2]
  - Synergize dendritic cell signaling and T-cell stimulation
  - IgE-induced inflammation

1. Goplen N, Karim MZ, Liang Q, Gorska MM, Rozario S, Guo L, Alam R. Combined sensitization of mice to extracts of dust mite, ragweed, and Aspergillus species breaks through tolerance and establishes chronic features of asthma. J Allergy Clin Immunol. 2009;123:925–32.
2. Kauffman HK, Tomee JFC, Marjolein A, van de Riet A, Timmerman JB, Borger P. Protease-dependent activation of epithelial cells by fungal allergens leads to morphologic changes and cytokine production. J Allergy Clin Immunol. 2000;105:1185–93.

Protease-activated Receptors

- Play integral role in immune system interface with environmental fungi
- Family of proteolytically activated 7-transmembrane G protein-coupled receptors
  - Widely expressed in airway epithelium, mast cells, eosinophils, neutrophils, monocytes-macrophages, lymphocytes, smooth muscle, endothelium, fibroblasts and neurons
- Four types of PARs
    - PAR-1, PAR-2, PAR-3, PAR-4


Proteolytic cleavage
Fungal Protease
N
PAR
C
Activated PAR
C
$G\alpha_{12/13}$
$G\alpha_q$
$G\alpha_i$
RhoGEF
Rho
PLCβ
IP_3
DAG
Ca^{2+}
PKC
PI3K
G-protein-coupled receptor kinases
Tyrosine kinases
Degranulation
Secretion
Integrin activation
Smooth muscle contraction
Cell Motility
Transcription Response
Chemokines, cytokines, cyclooxygenase

Study Design

Hypothesis

- There is differential expression of PARs in patients with AFRS compared to normal controls and patients with CRSwNP

Study Design

- Prospective comparison of PAR gene expression in patients with AFRS to patients with and without sinus inflammatory disease

Methods

- Exclusion criteria
  - Diagnosis of organic disease process that may confound interpretation of genomic data
- Specimen Collection
  - Ethmoid mucosa (not fungal material or allergic mucin)
    - Placed in RNAlater stored at 4ºC for 24 hrs then snap frozen
  - mRNA extracted, quantified and integrity confirmed
    - Background data correction was performed

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Patient Demographic Characteristics

Number of Patients			25
	AFRS		15
	CRSwNP		5
	Controls (MIPS)		5
Gender Ratio (M:F)			1.3:1
	AFRS (M)		10 (67%)
	CRSwNP (M)		3 (60%)
	Controls (M)		3 (60%)
Race	AFRS	AA	13 (86%)
		C	1 (7%)
		H	1 (7%)
	CRSwNP	AA	3 (60%)
		C	2 (40%)
		H	0
	Controls	AA	1 (20%)
		C	4 (80%)
		H	0
Mean age	AFRS		20.2 ± 6.7
	CRSwNP		42.6 ± 16.8
	Controls		57.8 ± 15.2
Mean Total IgE	AFRS		1276

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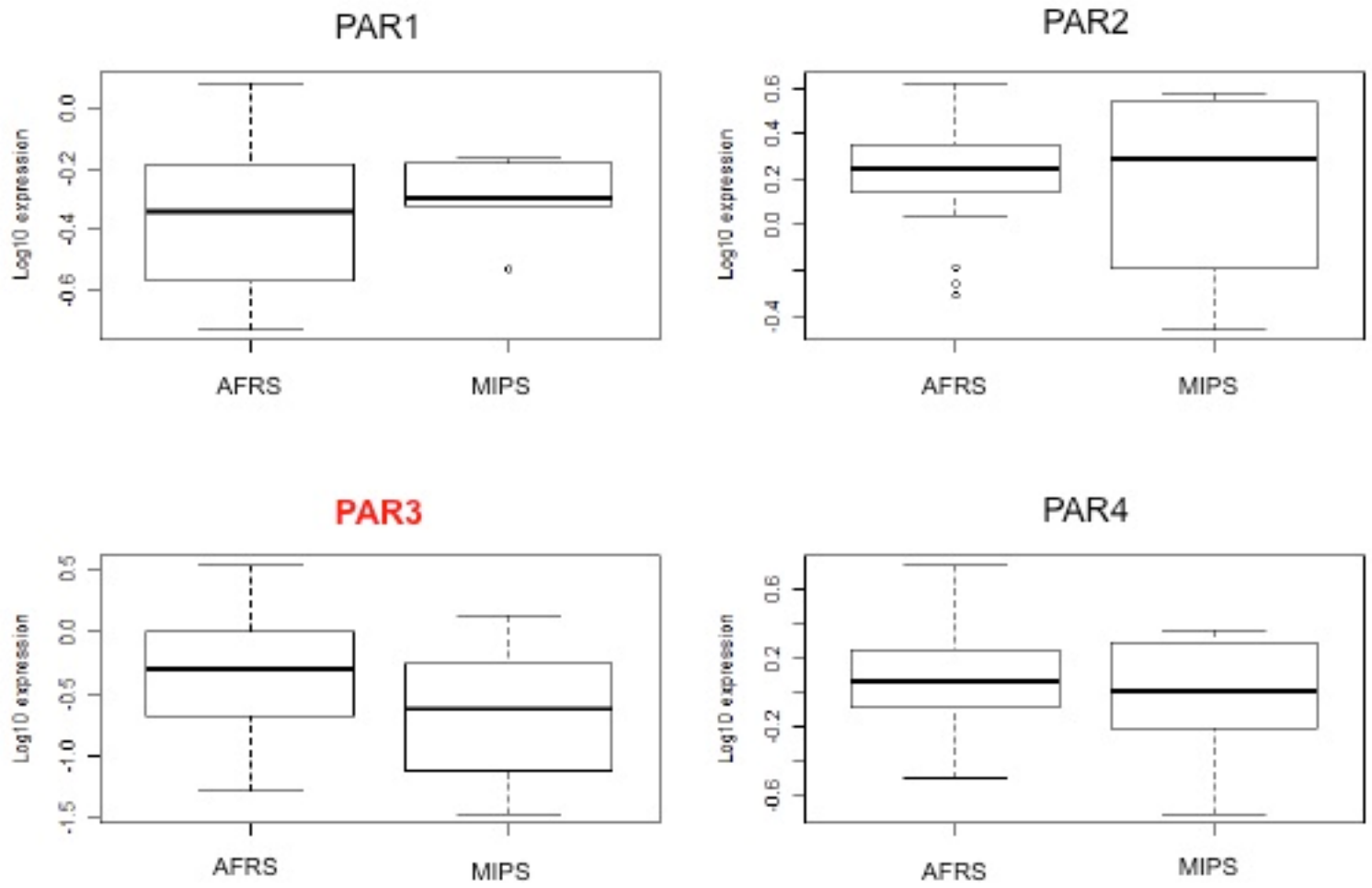
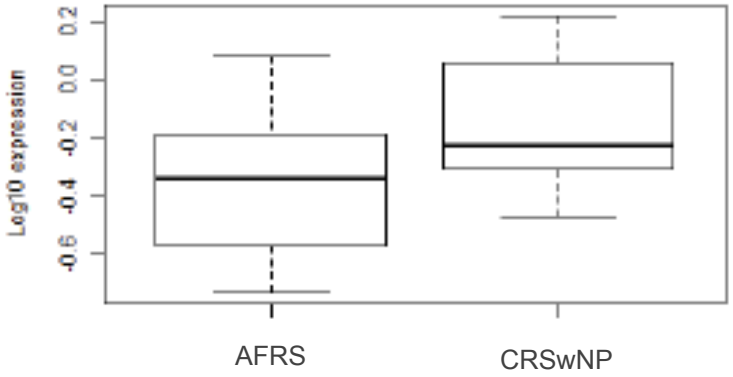
Results

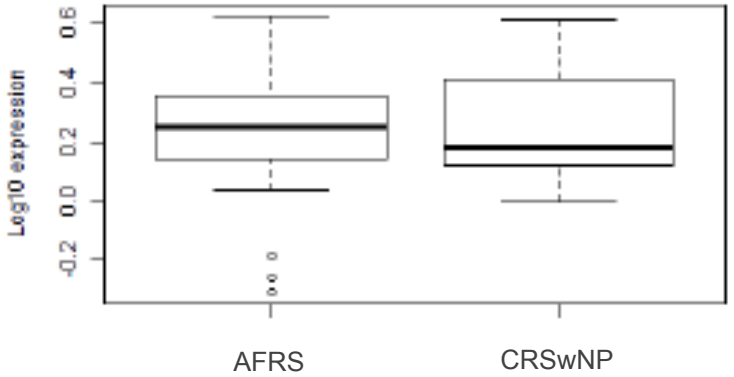
Comparisons	AFRS vs. MIPS		AFRS vs. CRSwNP		CRSwNP vs. MIPS	
	P value	Fold Change	P value	Fold Change	P value	Fold Change
PAR1	0.81	0.86	0.26	0.62	0.67	1.39
PAR2	0.81	1.09	0.82	0.91	0.72	1.18
PAR3	0.03	2.21	0.59	1.32	0.67	1.66
PAR4	0.58	1.26	0.84	0.96	0.67	1.30


PAR1
Log10 expression
0.0
-0.2
-0.4
-0.6
AFRS
MIPS
PAR2
Log10 expression
0.6
0.4
0.2
0.0
-0.4
AFRS
MIPS
PAR3
Log10 expression
0.5
0.0
-0.5
-1.0
-1.5
AFRS
MIPS
PAR4
Log10 expression
0.6
0.2
-0.2
-0.6
AFRS
MIPS

PAR1



PAR2



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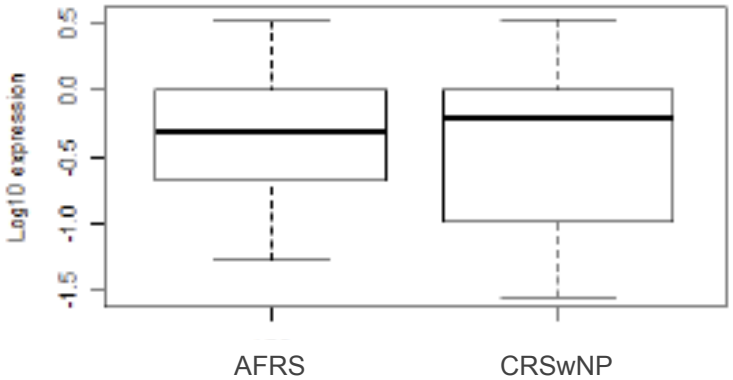
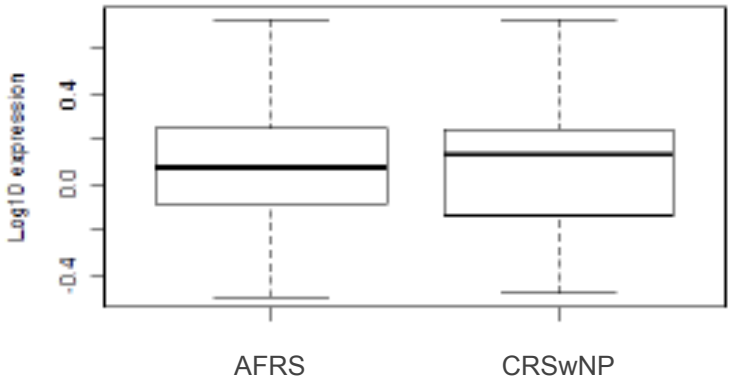
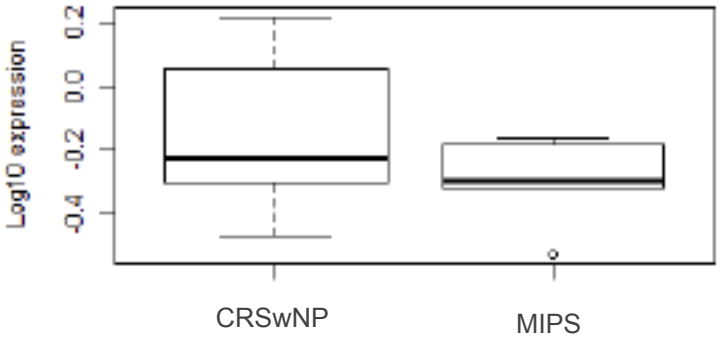


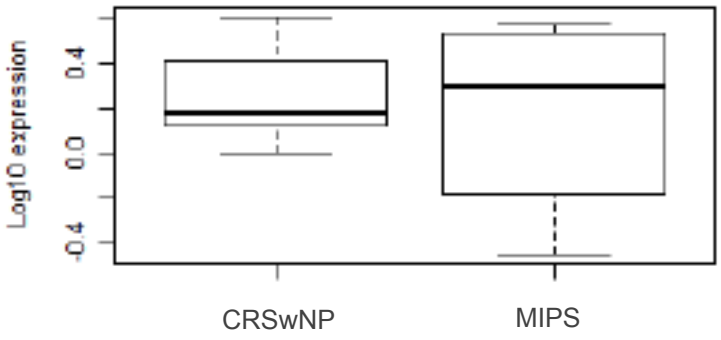
PAR4



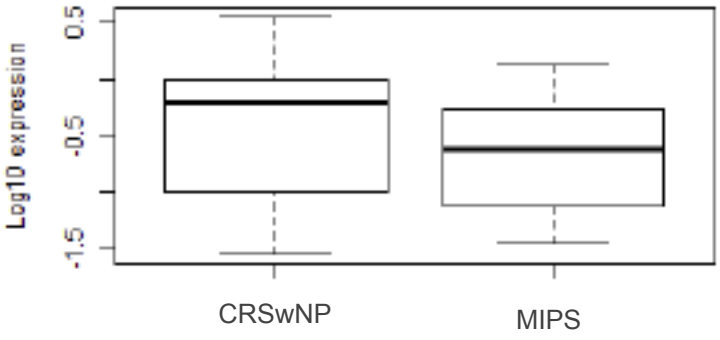
PAR1



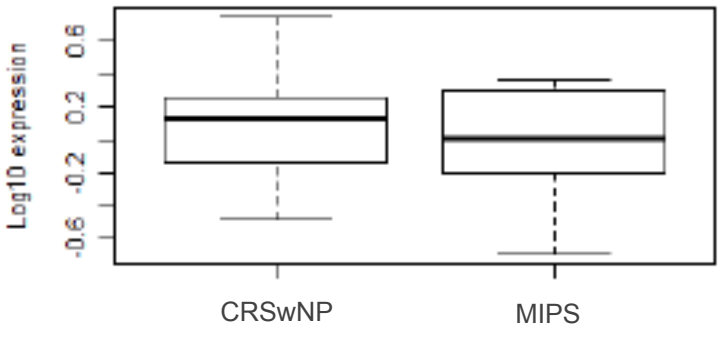
PAR2



PAR3



PAR4



Relationship of PARS Expression/Demographics to Disease Severity

- Identifying predictors of disease severity could lead to earlier diagnosis and more aggressive treatment in select groups
  - » Avoiding serious and morbid complications of severe AFRS

Relationship of Disease Severity to Demographics

- Identifying predictors of disease severity could lead to earlier diagnosis and more aggressive treatment in select groups
  - » Avoiding serious and morbid complications of severe AFRS

Study Objective:

Evaluate components of disease severity with patient age, sex, race, socioeconomic status and health care access.

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Relationship of Disease Severity to Demographics

- Methods:
  - Retrospective Analysis
    - 93 patients (2000-2013)
    - Diagnosed by Bent and Kuhn criteria
  - Explored associations between variables of disease severity and patient demographics
    - Fisher's Exact, Wilcoxon Rank-Sum, Pearson correlations, multivariable linear regression models

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Relationship of Disease Severity to Demographics

Demographics

Individual

- Race
- Age at Diagnosis
- Gender
- Insurance Status

County Data

- Income per Capita
- PCP per Capita
- Old/Overcrowded Housing per Capita
- Rural Population per Capita

Disease Severity

Radiographic

- Orbito-cranial Involvement
- Bone Erosion
- Lund-Mackay Score

Innate

- Total IgE
- ≥Class IV Mold Allergy

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RESULTS:
COHORT PROFILE

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Cohort Profile

Gender		
Gender	**Frequency**	**Percent**
Male	53	57.6%
Female	39	42.4%

Race		
Race	**Frequency**	**Percent**
African American	54	59.3%
White	33	36.3%

Insurance		
Insurance	**Frequency**	**Percent**
Private	51	55.4%
Uninsured/ Medicaid	29	31.5%
Military	10	10.9%
Medicare	2	2.2%

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AFRS Geographic Variance

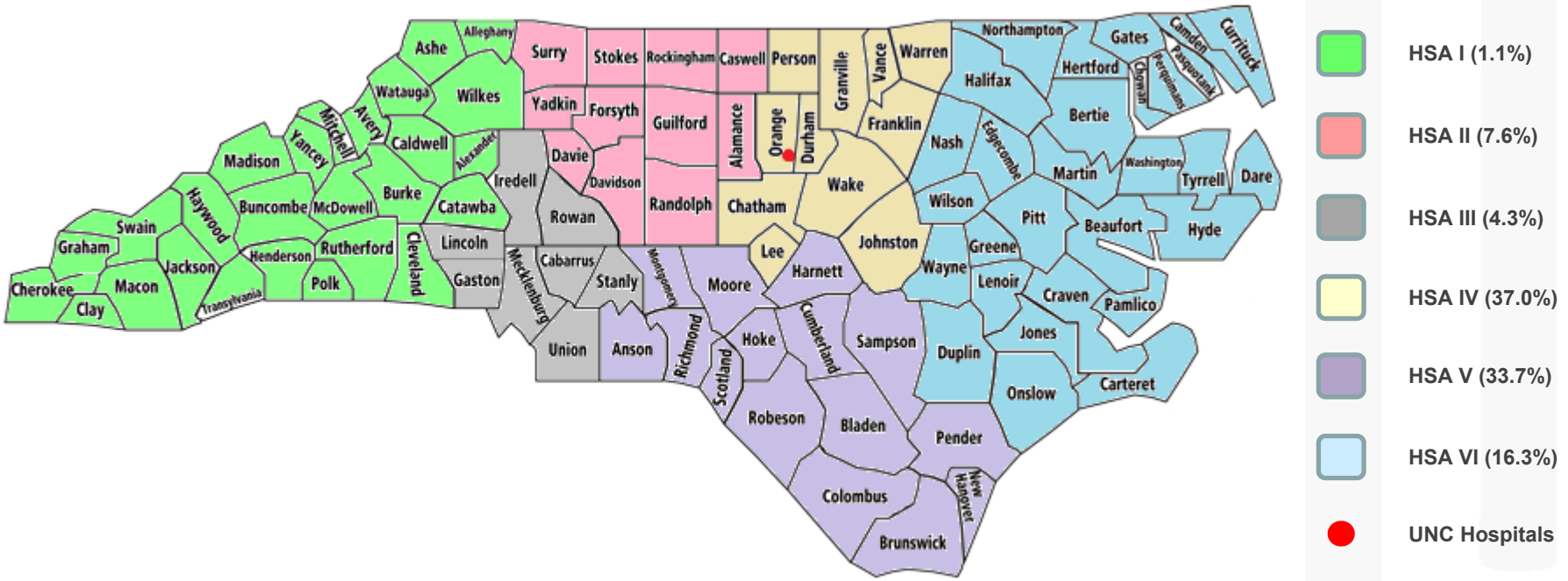

Figure 1. Percentage of Patients in North Carolina Health Service Areas

RESULTS:
DISEASE SEVERITY

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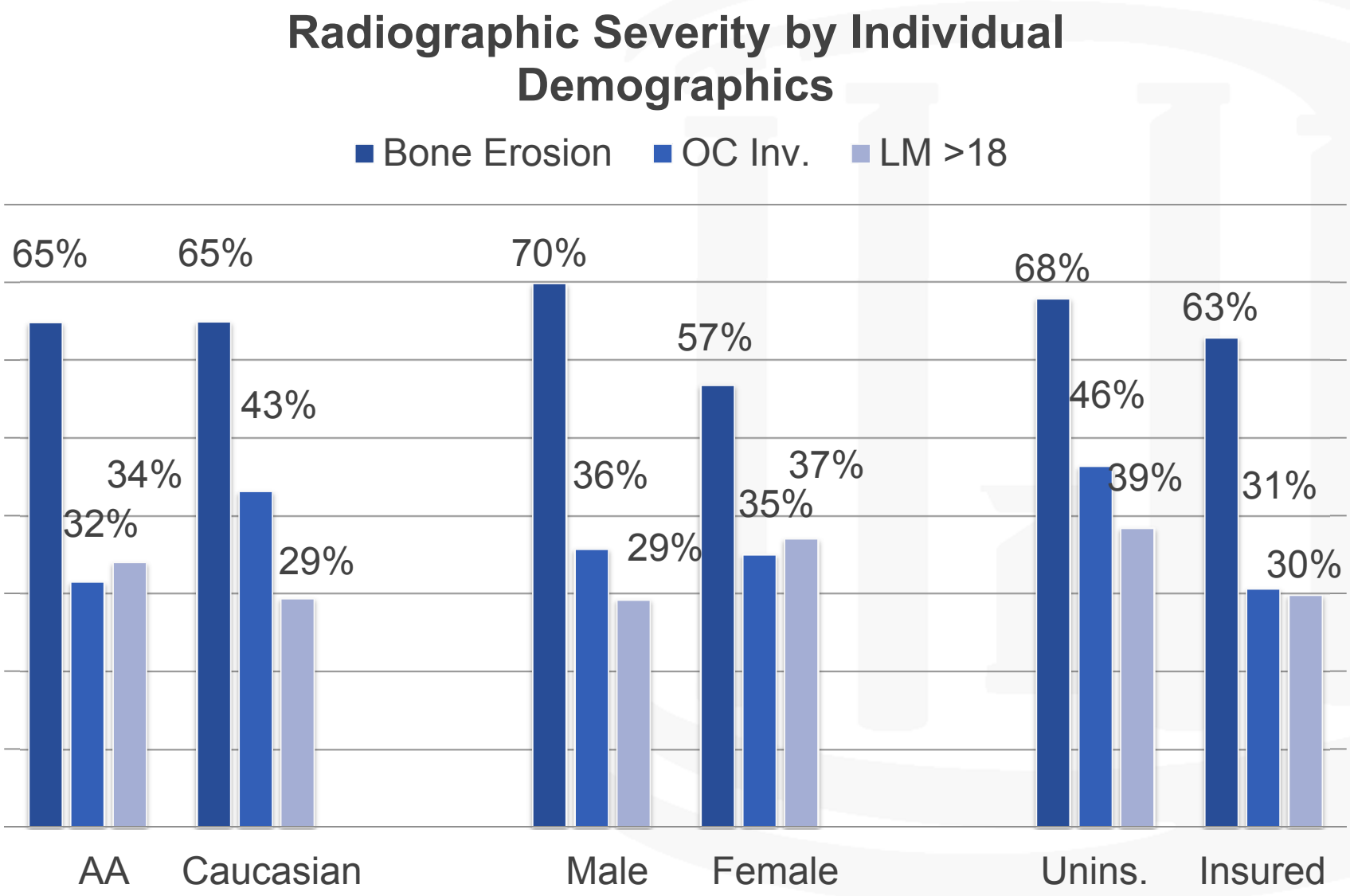
Radiographic Associations



Radiographic Associations

County-Specific Associations with Disease Severity							
	Radiographic						
	Bone Erosion		OC Inv.		Lund-Mackay		
	No	Yes	No	Yes	≤6	6-17	>18
Income/Capita ($)	26909	22285	26000	22371	26267	22285	24591
	p=0.01*		p=0.06¶		r(81)=0.05;p=0.68		
PCP/100 Residents	0.09	0.07	0.09	0.07	0.1	0.08	0.09
	p=0.37		p=0.02*		r(81)=0.19;p=0.09		
Rural Population/Cap.	0.13	0.29	0.13	0.32	0.16	0.13	0.31
	p=0.30		p=0.01*		r(81)=-0.01;p=0.93		
Overcrowded/Cap.	0.01	0.02	0.02	0.02	0.01	0.02	0.01
	p=0.24		p=0.07¶		r(81)=0.15;p=0.19		
Older Housing/Cap.	0.1	0.11	0.11	0.11	0.11	0.11	0.11
	p=0.02*		p=0.10		r(81)=0.01;p=0.96		

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Radiographic Associations

County-Specific Associations with Disease Severity							
	Radiographic						
	Bone Erosion		OC Inv.		Lund-Mackay		
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	p=0.30		p=0.01*		r(81)=-0.01;p=0.93		
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Older Housing/Cap.	0.1	0.11	0.11	0.11	0.11	0.11	0.11
	p=0.02*		p=0.10		r(81)=0.01;p=0.96		

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Radiographic Associations

County-Specific Associations with Disease Severity							
	Radiographic						
	Bone Erosion		OC Inv.		Lund-Mackay		
	No	Yes	No	Yes	≤6	6-17	>18
Income/Capita ($)	**26909**	**22285**	26000	22371	26267	22285	24591
	p=0.01*		p=0.06¶		r(81)=0.05;p=0.68		
PCP/100 Residents	0.09	0.07	0.09	0.07	0.1	0.08	0.09
	p=0.37		p=0.02*		r(81)=0.19;p=0.09		
Rural Population/Cap.	0.13	0.29	0.13	0.32	0.16	0.13	0.31
	p=0.30		p=0.01*		r(81)=-0.01;p=0.93		
Overcrowded/Cap.	0.01	0.02	0.02	0.02	0.01	0.02	0.01
	p=0.24		p=0.07¶		r(81)=0.15;p=0.19		
Older Housing/Cap.	**0.1**	**0.11**	0.11	0.11	0.11	0.11	0.11
	p=0.02*		p=0.10		r(81)=0.01;p=0.96		

UNC SCHOOL OF MEDICINE

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PCP/100 Residents	0.09	0.07	0.09	0.07	0.1	0.08	0.09
	p=0.37		p=0.02*		r(81)=0.19;p=0.09		
Rural Population/Cap.	0.13	0.29	0.13	0.32	0.16	0.13	0.31
	p=0.30		p=0.01*		r(81)=-0.01;p=0.93		
Overcrowded/Cap.	0.01	0.02	0.02	0.02	0.01	0.02	0.01
	p=0.24		p=0.07¶		r(81)=0.15;p=0.19		
Older Housing/Cap.	0.1	0.11	0.11	0.11	0.11	0.11	0.11
	p=0.02*		p=0.10		r(81)=0.01;p=0.96		

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Radiographic Associations

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PCP/100 Residents	0.09	0.07	**0.09**	**0.07**	0.1	0.08	0.09
	p=0.37		**p=0.02***		r(81)=0.19;p=0.09		
Rural Population/Cap.	0.13	0.29	**0.13**	**0.32**	0.16	0.13	0.31
	p=0.30		**p=0.01***		r(81)=-0.01;p=0.93		
Overcrowded/Cap.	0.01	0.02	**0.02**	**0.02**	0.01	0.02	0.01
	p=0.24		**p=0.07¶**		r(81)=0.15;p=0.19		
Older Housing/Cap.	0.1	0.11	0.11	0.11	0.11	0.11	0.11
	p=0.02*		p=0.10		r(81)=0.01;p=0.96		

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Conclusion

- Markers of disease severity (bone erosion and orbito-cranial involvement) in AFRS are associated with:
  - Lower Income
  - Rural Counties
  - Poor Housing Quality
  - Decreased Health Care Access
- PAR3 gene expression increased in AFRS patients compared to non-diseased controls
  - Small sample size
  - Lack of validation data
- However, disease severity only associated with socioeconomic status by county level
  - Disease's predilection for a certain population may be secondary to healthcare accessibility or living conditions rather than race or genetics.

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at CHAPEL HILL

Thank you for your attention.

Role of neural activity in predicting speech perception outcomes in pediatric cochlear implant subjects.

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Andrew K. Pappa BS,
William C. Scott BA,
Kevin D. Brown MD/PhD,
Douglas C. Fitzpatrick PhD

University of North Carolina at Chapel Hill,
Department of Otolaryngology

Conflict of Interest Disclosure

Co-authors of this study have received research contracts and/or consult agreements with:

- MED EL Corporation
- Cochlear Corporation
- Advanced Bionics

The work itself was supported by a research contract with MED EL Corporation.

Our Research Team

Principal Investigator

- Douglas C. Fitzpatrick PhD

Surgeons

- Harold Pillsbury MD
- Kevin D. Brown MD/PhD
- Craig A. Buchman MD, Washington University in St. Louis
- Oliver F. Adunka MD, The Ohio State University

Audiologists

- Lisa R. Park AuD
- Holly F. Teagle AuD

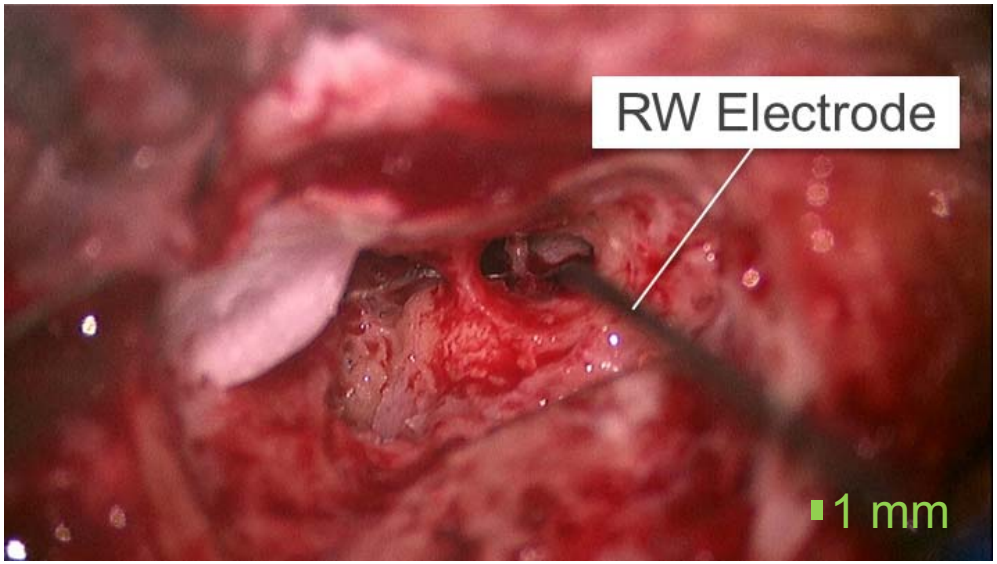
Residents and Students

- Tatyana E. Fontenot MD
- Andrew K. Pappa BS
- Christopher K. Giardina BS
- William C. Scott BA

There is wide variability in speech perception outcomes in CI recipients.

Electrocochleography (ECochG)

The measurement of stimulus-evoked cochlear potentials, with isolation of the potentials to the cochlea achieved by proximity through electrode placement in the ear canal, promontory, round window, or within the cochlea



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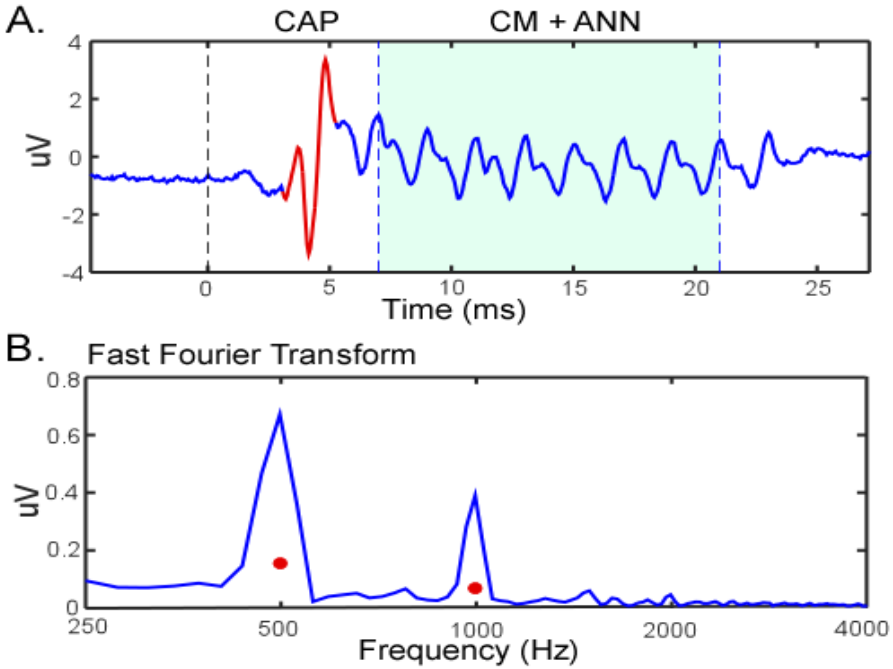
Electrocochleography and ECochG-TR

Response to 500 Hz stimulus:



250 Hz 500 Hz 750 Hz 1 kHz 2 kHz 4 kHz → **ECochG-TR**

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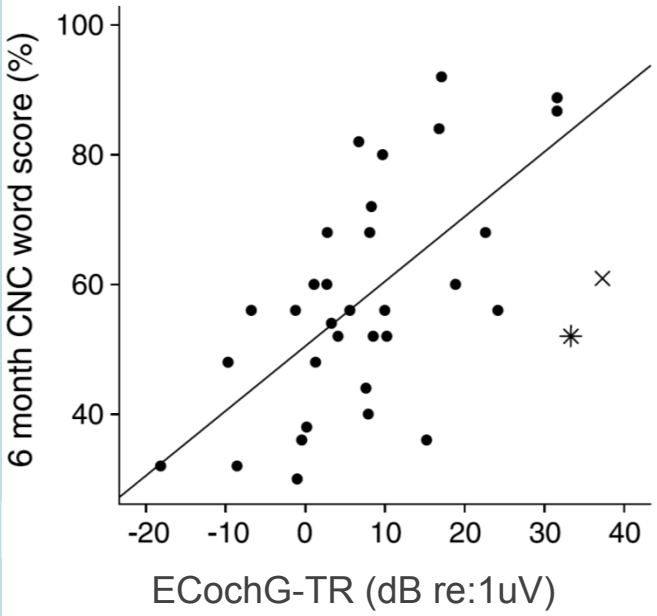
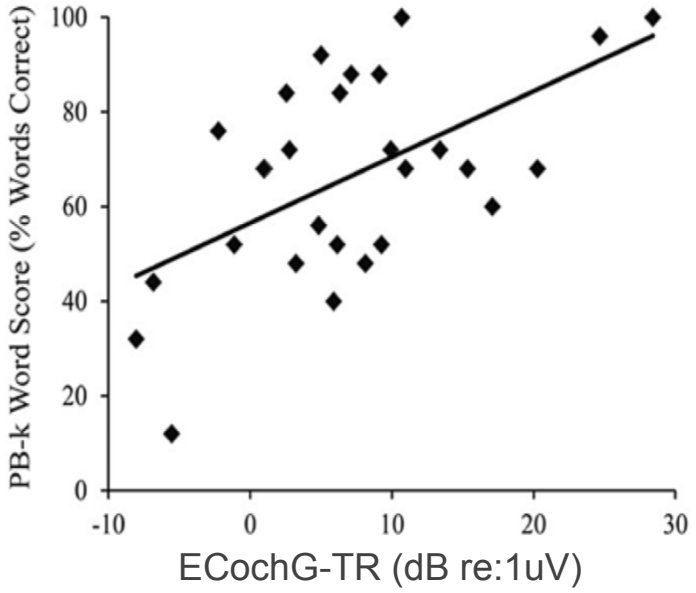
McClellan et al. 2014:



Adults: 40% of variability
R^2=0.4, n=32, *p<0.001*

Formeister et al. 2015:



Children: 32% of variability
R^2=0.32, n=28, *p=0.002*

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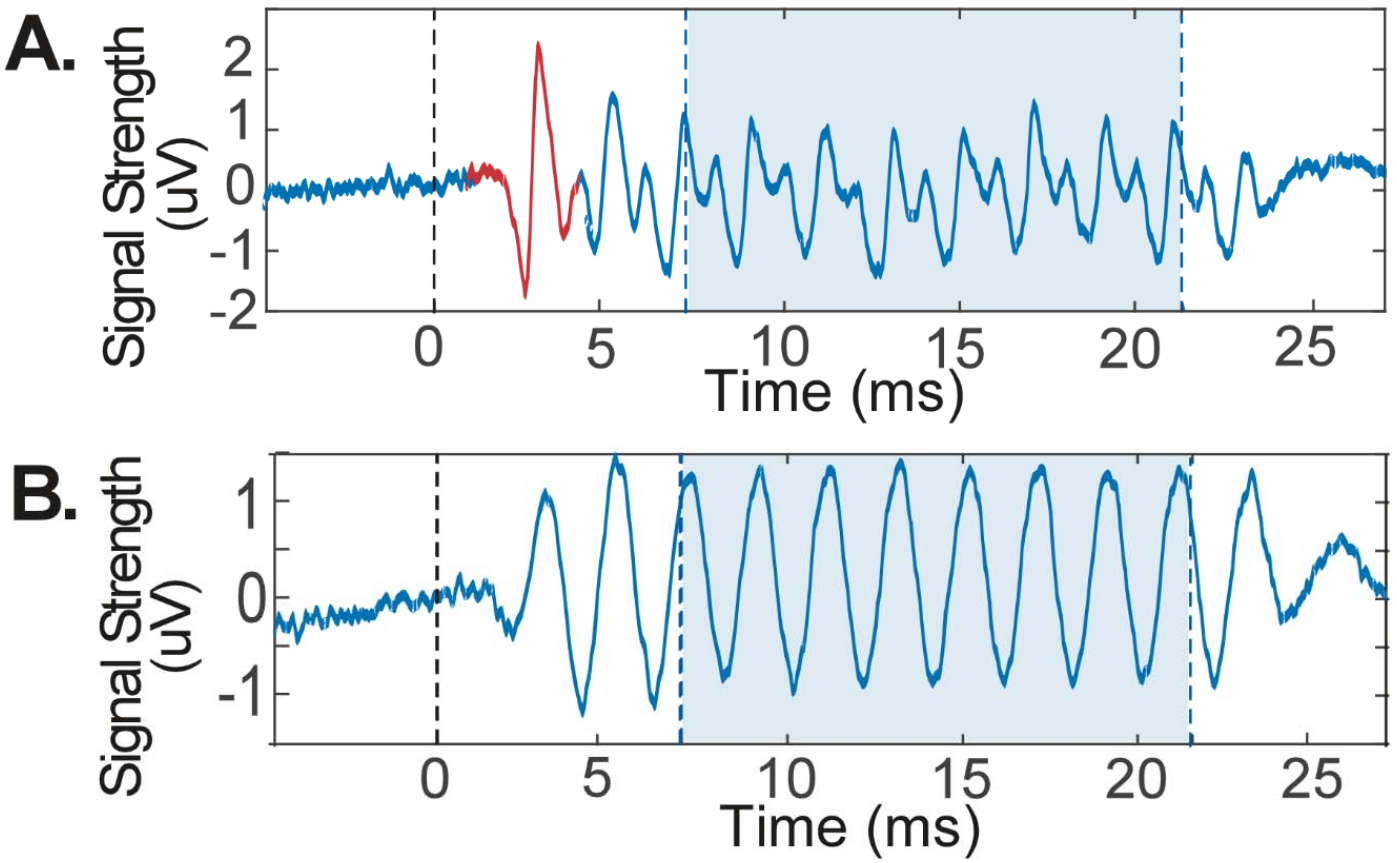
Neural Activity: The CAP



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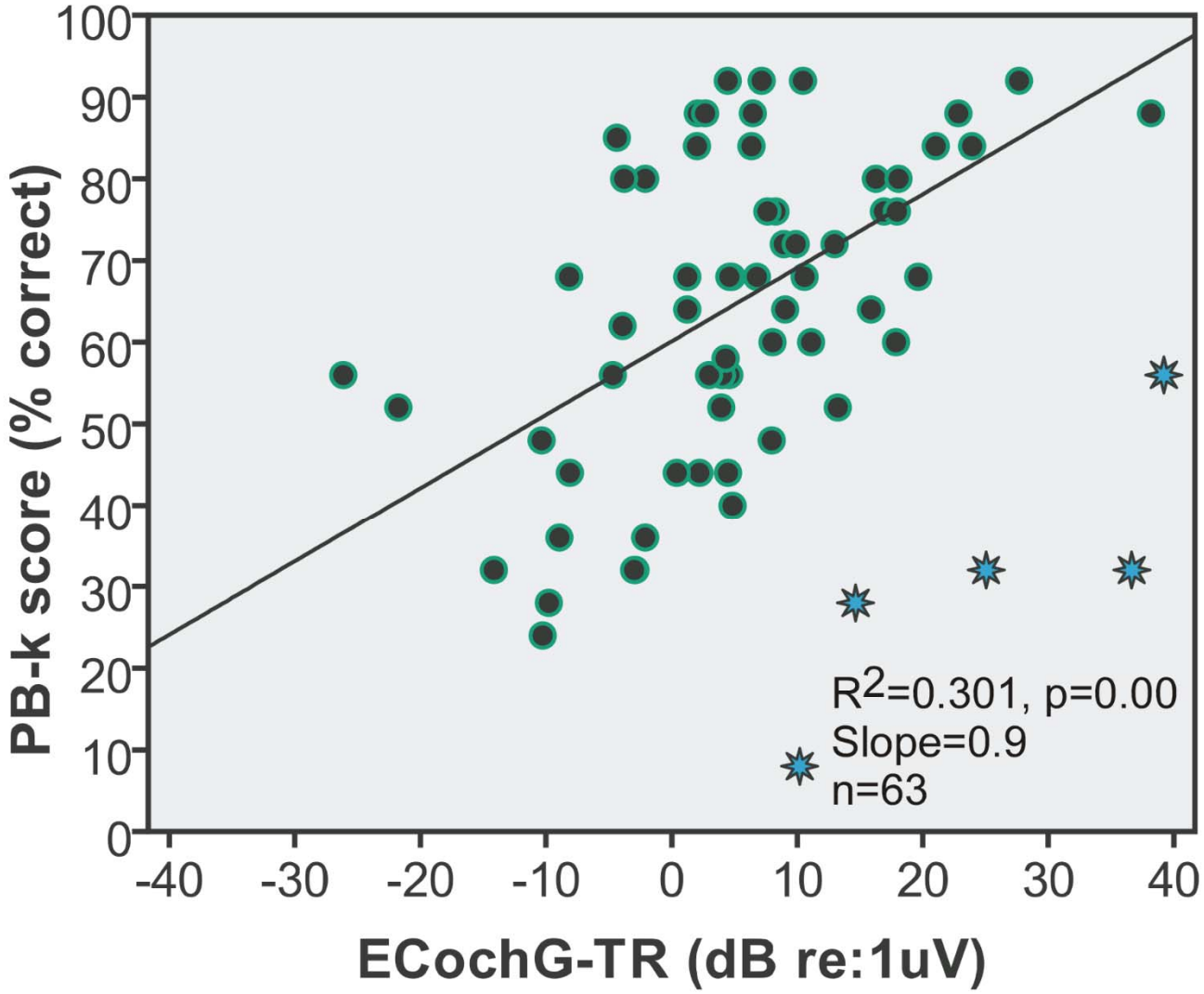
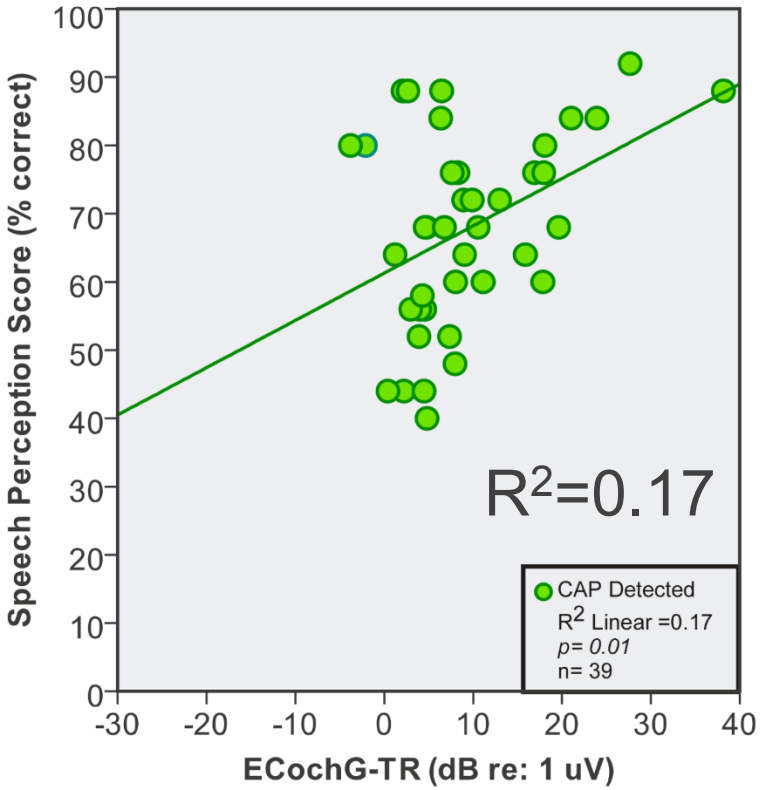
Objective:

Examine the utility of CAP measurements as an adjunct to ECochG-TR in predicting pediatric speech perception outcomes.

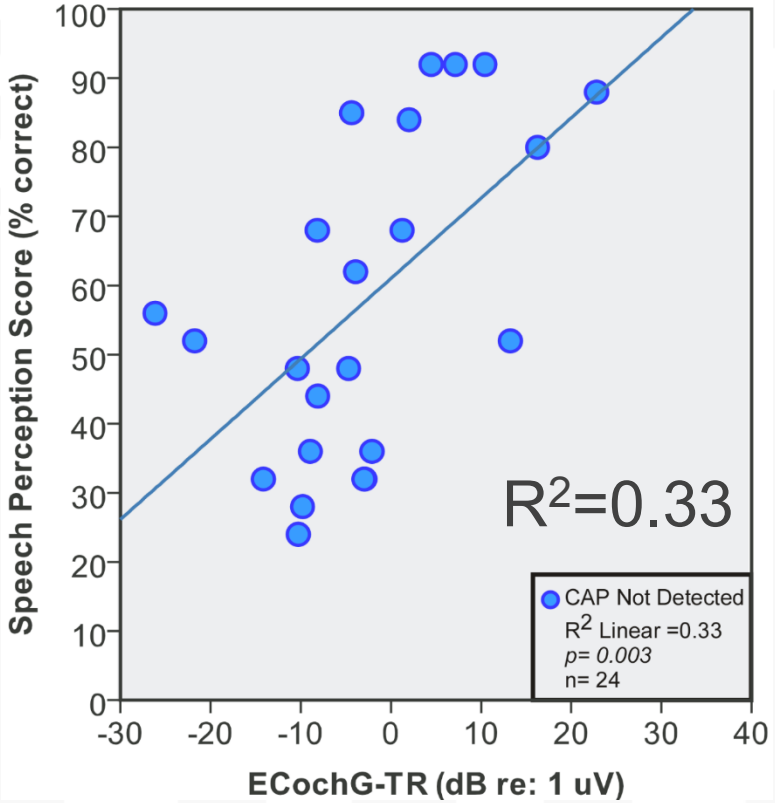
ECochG-TR


PB-k score (% correct)
100
90
80
70
60
50
40
30
20
10
0
-40
-30
-20
-10
0
10
20
30
40
ECochG-TR (dB re:1uV)
R2=0.301, p=0.00
Slope=0.9
n=63

CAP detected



CAP not detected



9.49 dB re:1uV	**Mean ECochG-TR**	-0.4 dB re:1uV	*p<0.001*
68.6%	**Mean PB-k score**	58.3%	*p>0.05*

Non-ANSD

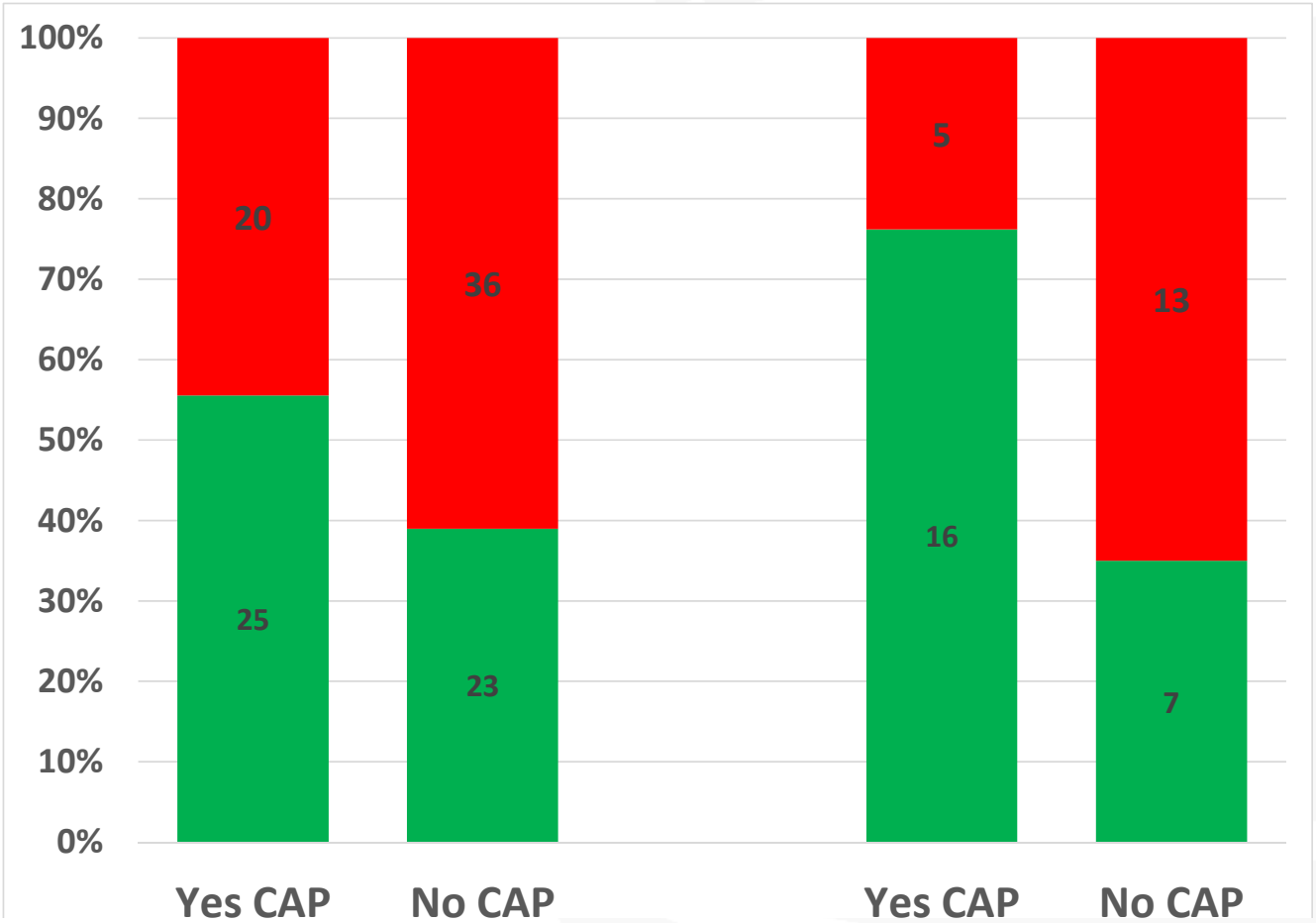
55.5% vs 39.0%

p=0.09

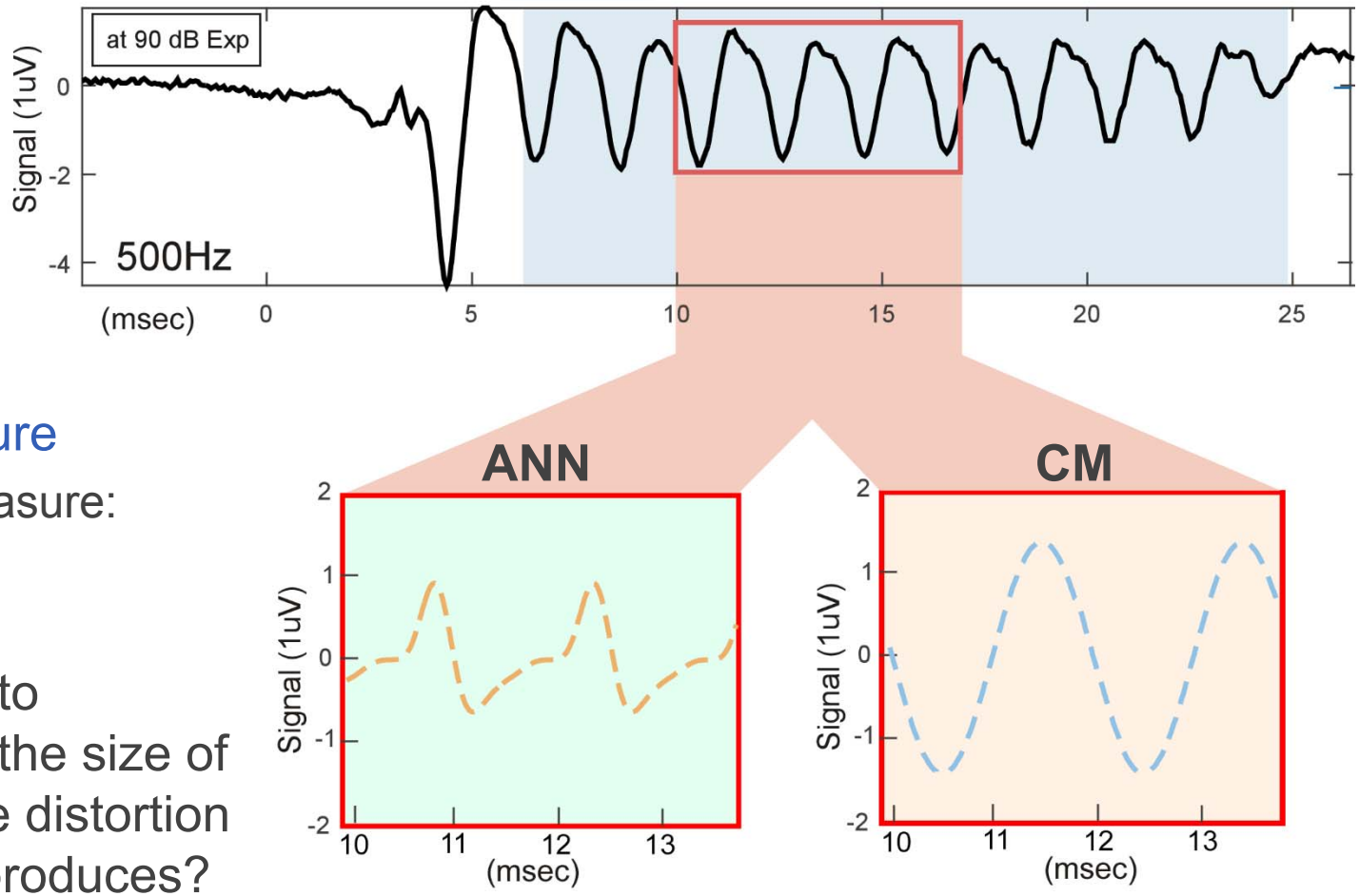
ANSD

76.2% vs 35.0%

p=0.008

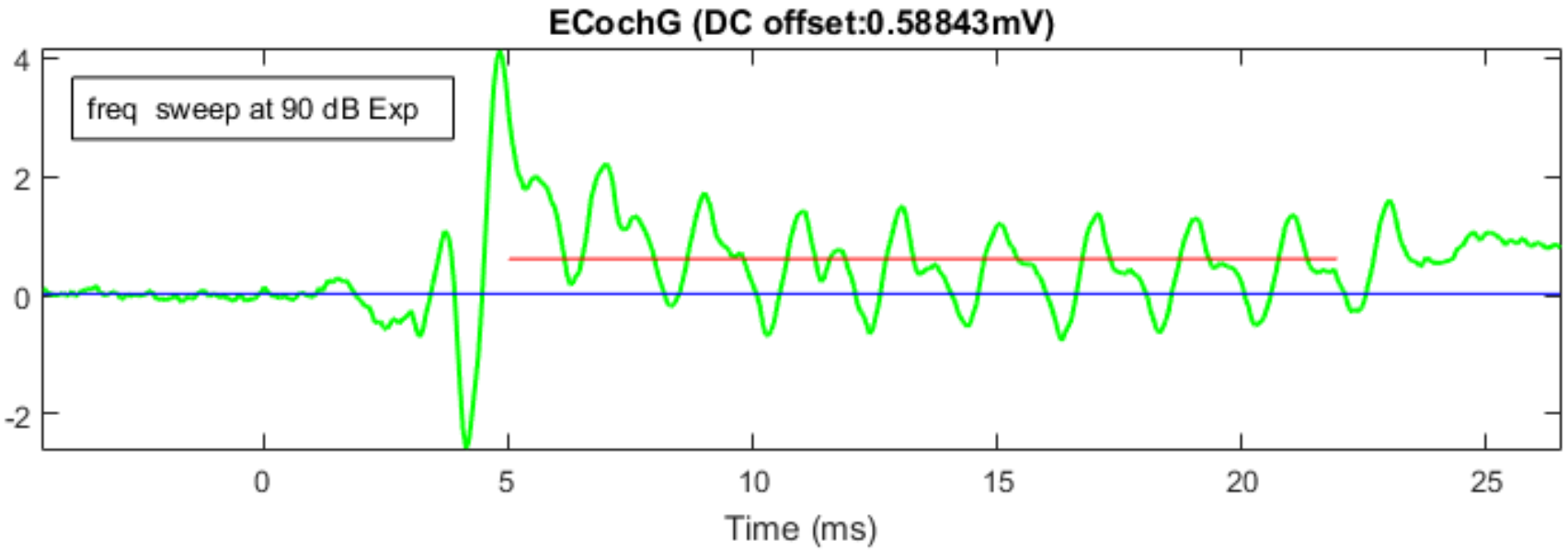


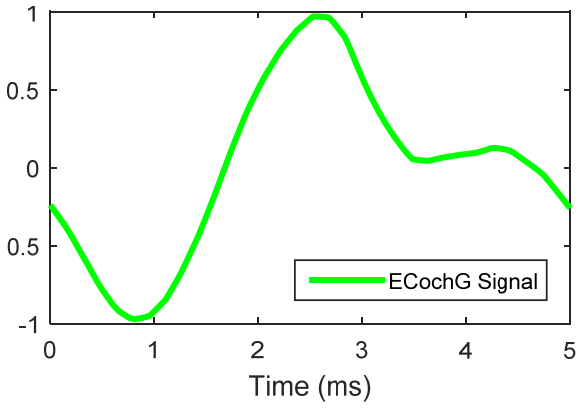
Do ECochG features have prognostic significance: The ANN

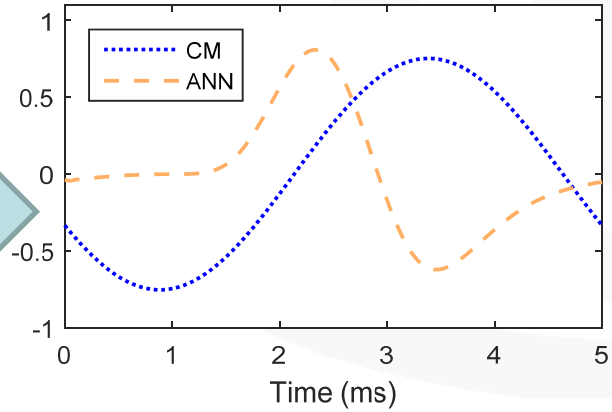


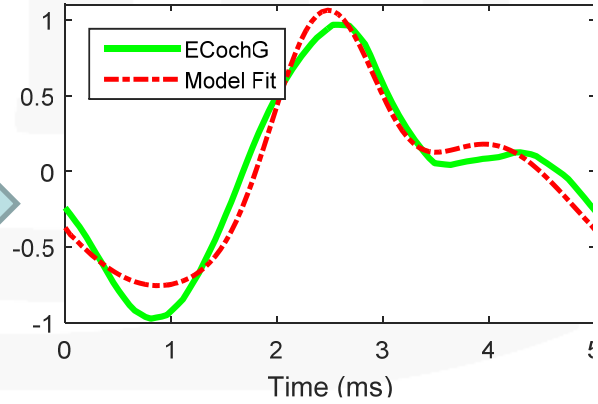
- Difficult to measure
  - » Subjective measure: nerve score
  - » Is it possible to approximate the size of ANN from the distortion in the CM it produces?

Do ECochG features have prognostic significance : The ANN









Conclusions

The CAP did not improve upon ECochG-TR's ability to predict specific speech perception scores in the general pediatric population.

- ***Why?***

The CAP could help identify the specific patients who may have difficulty achieving speech perception, especially in children with ANSD.

- Marker of severity of the neural/synaptic lesions in the peripheral auditory system.

Main References

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Thank you!

Outcomes and Predictors of Mortality in Invasive Fungal Sinusitis:

A 10 Year Retrospective Review of Invasive Fungal Sinusitis at a Major Medical Center

Helen Moses, PGY 4

Duke Otolaryngology - Head and Neck Surgery
A Division of the Department of Surgery

OVERVIEW

- **Invasive Fungal Sinusitis:**
  - **The problem**
  - **Diagnosis & treatment**
  - **Management strategy**
- **Research Study:**
  - **Methods**
  - **Results**
  - **Conclusions**

INVASIVE FUNGAL SINUSITIS

- First described in 1885 – Mucormycosis
- First IV antifungal in 1958 – Amphotericin
- Estimated 50-80% mortality
  - **Dependent on underlying abnormality**
- Associated morbidity is extensive
- Culprits
  - **Aspergillosis**
  - **Zygomycetes including**

  Rhizopus, mucormycosis

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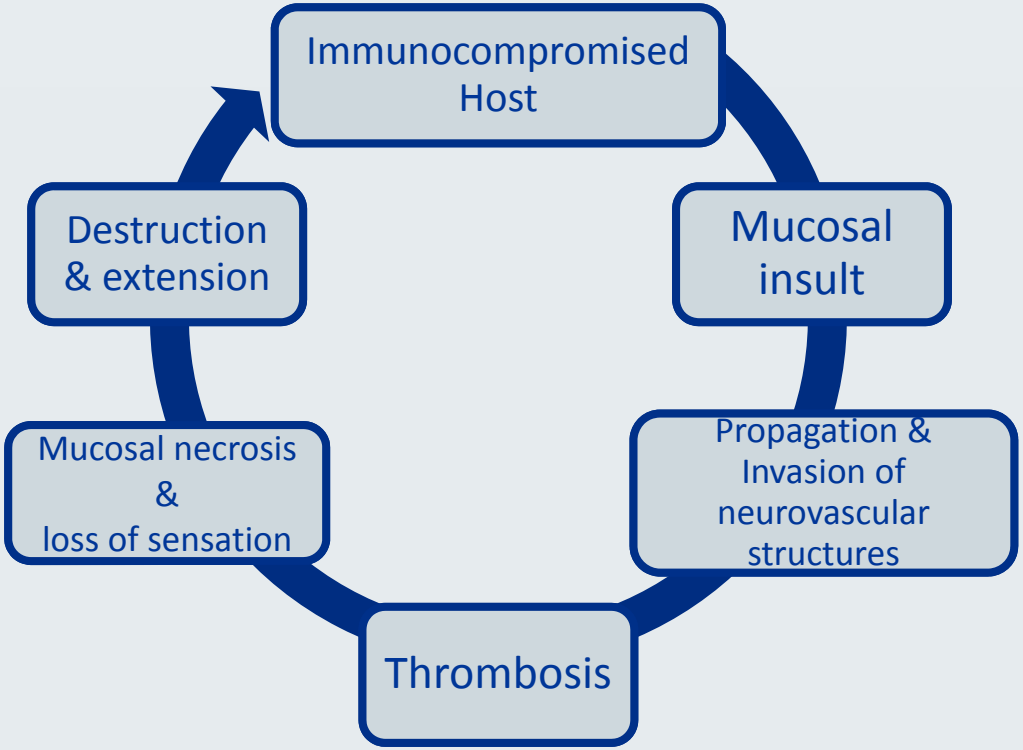
INVASIVE FUNGAL SINUSITIS

- Host factors
  - Diabetic patients
  - Hematologic malignancies
  - Bone marrow transplant & solid organ transplant
- Symptoms
- Prognostic factors
  - Extent of involvement
  - ANC < 1,000/mm^3
    - (duration of ANC < 600)
  - Recovery from neutropenia
  - Mucormycosis



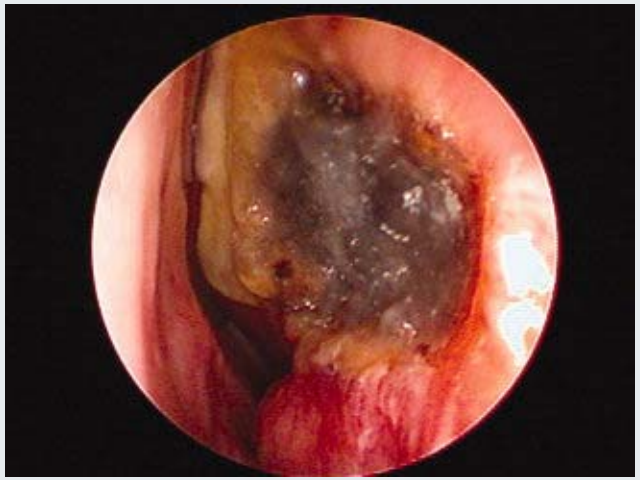
DIAGNOSIS

- High suspicion
- Endoscopic examination to assess:
  - Appearance/integrity of mucosa
  - Sensation
  - Role of endoscopic-guided biopsies
- Pathological Diagnosis including morphological identification
  - Staining
  - Limitations of cultures

DIAGNOSIS

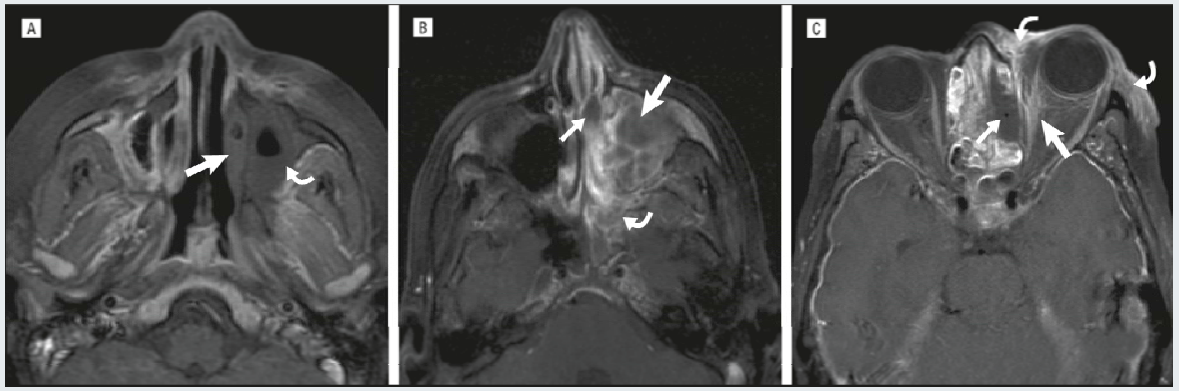
- *An Early Detection Protocol for Invasive Fungal Sinusitis in Neutropenic Patients Successfully Reduces Extent of Disease at Presentation and Long term Morbidity*
- Author: DelGaudio and Clemson, 2010
- Population: 2 Groups of 14 patients each corresponding to prior to and after institution of early detection protocol
- Results of early detection:
  1. Fewer sites involved at diagnosis
  2. Fewer surgeries
  3. Less long-term morbidity

  BUT NO DIFFERENCE IN MORTALITY



IMAGING: Multi-modality

- **Advantages of CT**
  - Soft tissue involvement
  - Mucosal thickening
  - Bone erosion
- **Advantages of MRI**
  - Better delineation of blood vessel involvement
  - Intracranial extension
  - Loss of contrast enhancement
  - Infiltration of orbital fat & areas of cellulitis



Groppo ER, El-Sayed IH, Aiken AH, Glastonbury CM. Computed Tomography and Magnetic Resonance Imaging Characteristics of Acute Invasive Fungal Sinusitis. *Arch Otolaryngol Head Neck Surg*. 2011;137(10):1005-1010.

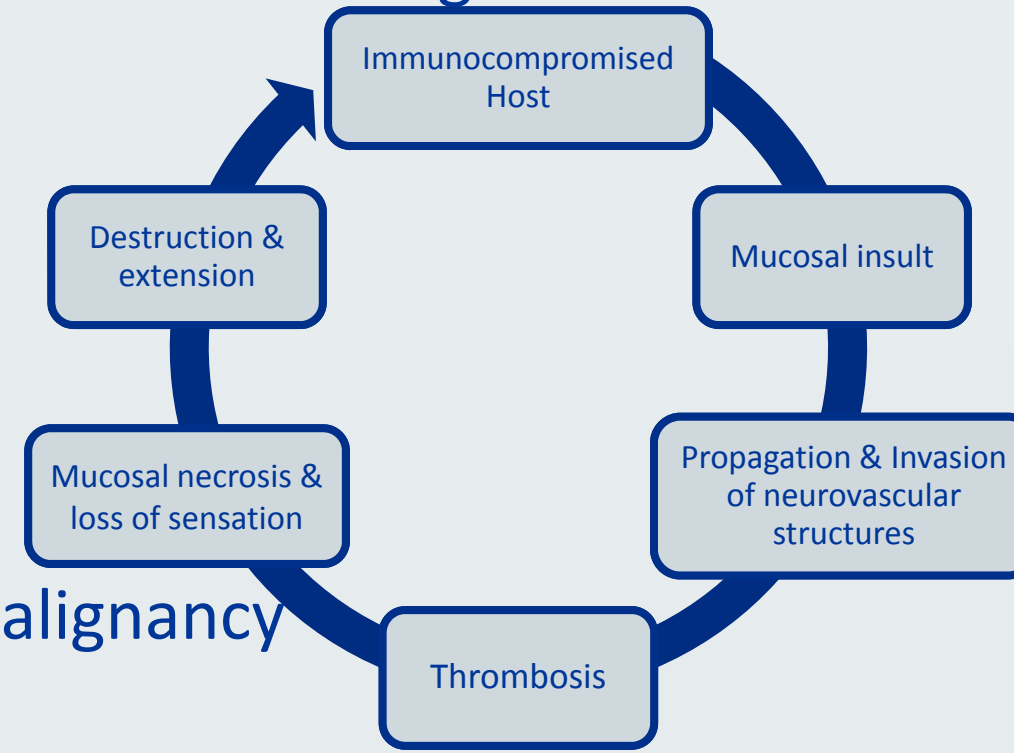
PRINCIPLES OF TREATMENT

- Rapidity of Diagnosis
- Medical Management
  - Correct underlying metabolic derangements
  - Address neutropenia & host factors
  - Targeted therapy
- Surgical Management
  - Extent of surgery
  - Operative details
- Adjunctive Management
  - HBO
  - Iron metabolism

U Wali[a,], Abdullah Balkhair[b], Abdullah Al-Mujaini[a] **Cerebro-rhino orbital mucormycosis: An update. Journal of infection and public health.** Volume 5, Issue 2, April 2012, 116–126

MEDICAL MANAGEMENT

- Correction of underlying metabolic derangements
  - Diabetic ketoacidosis
  - Renal disease
- Correction of underlying neutropenia
  - Transplant patients or those with hematologic malignancy
  - WBC transfusions
  - Granulocyte colony-stimulating factor (Parikh et al 2004)



Parikh, S. L., Venkatraman, G., & Delgaudio, J. M. (2004). Invasive fungal sinusitis: A 15-year review from a single institution. *American Journal of Rhinology, 18*(2), 75-81. Retrieved from http://search.proquest.com/docview/230842756?accountid=10598

SURGERY

- Mainstay of treatment
  - Surgery is independent predictor for improved survival
- Mortality
  - antifungals alone 70% and greater
  - antifungal + surgery as low as 14%
- Endoscopic vs Open Surgical Approach
  - Endoscopic surgery = improved survival (63% vs 54%)

J Turner et al. (2013), Survival outcomes in acute invasive fungal sinusitis: A systematic review and quantitative synthesis of published evidence. The Laryngoscope, 123: 1112–1118
Roden et al 929 cases in 2005 Epidemiology & outcome of zygomycosis: a review of 929 reported cases. Clin Infect Dis 2005;41:634-653

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STUDY OBJECTIVES:

1) Assess IFS patient demographics, and mortality from disease as primary outcome
2) Evaluate common underlying causes of immunosuppression, such as chemotherapy, bone marrow transplant, and low absolute neutrophil count (ANC)
3) Test for potential risk factors associated with mortality

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METHODS

- **Inclusion criteria**: histopathologic confirmation of IFS verified at this institution, 2004-2015
- **Primary outcome variable:** mortality.
- **Demographic variables:** age, sex, ethnicity
- **Risk factor variables:** absolute neutrophil count (ANC), immunosuppression, malignancy, bone marrow transplantation.

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IFS Cohort

Patient Parameter	No. of Patients (%)
Total	34
Age (mean)	49
Age < 18yo	4
Male	20 (59)
Caucasian	20 (59)

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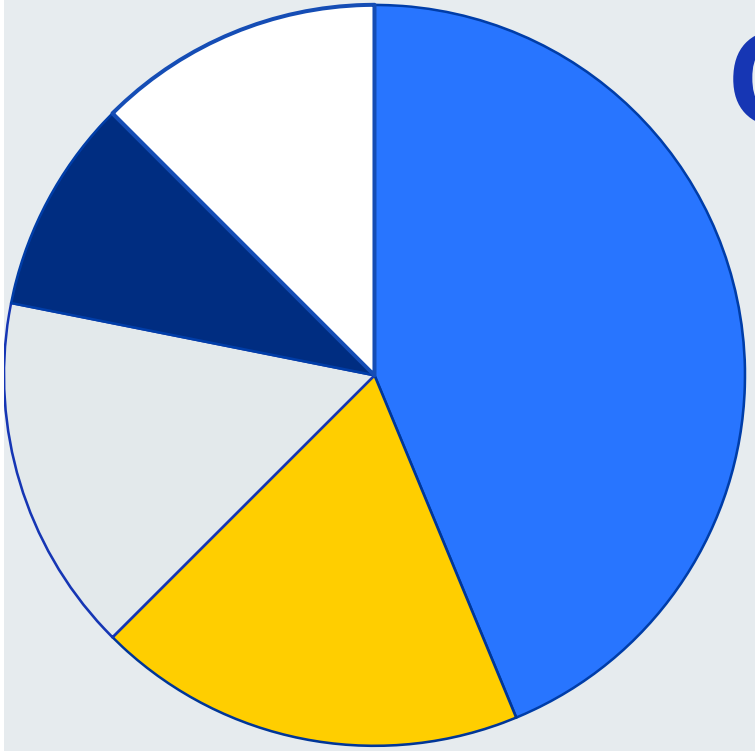
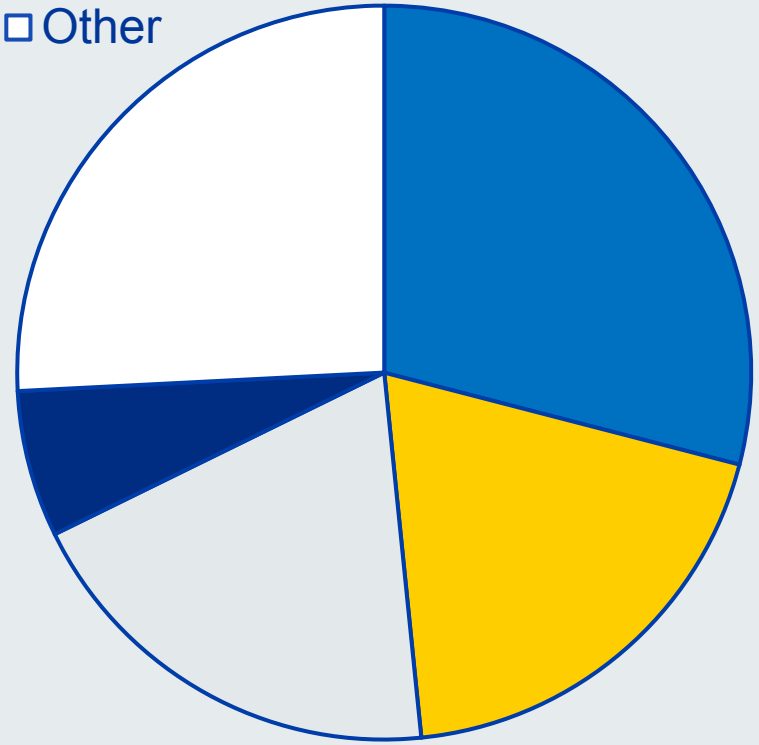
Cohort



- AML
- ALL
- Lymphoma
- Solid Organ
- Other

ANC



- Undetectable
- ≤ 100
- 101 -249
- 250 - 500
- > 500

RESULTS

Patient Parameter	No. of Patients (%)
Leukemia	20 (59)
Chemotherapy	26 (77)
Bone Marrow Tx	10 (29)
ANC = 0	9 (18)
Outcome:	
Mortality	**17 (50%)**

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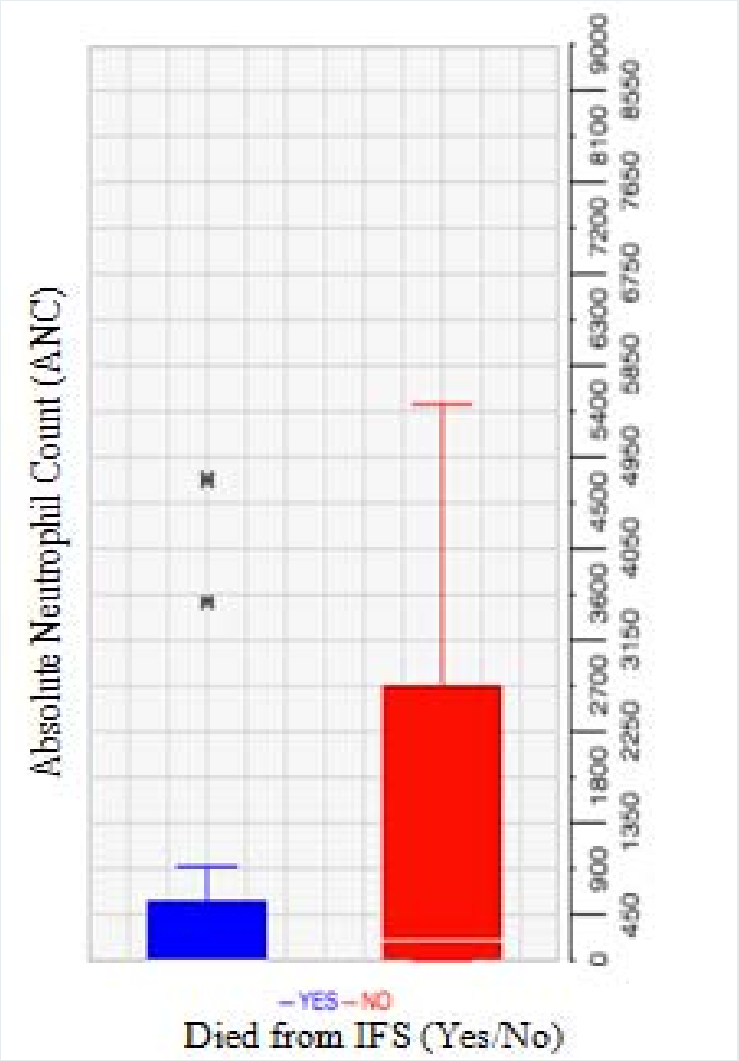
RESULTS

- Death attributable to IFS, 47.1% with ANC=0
- 17.7% survived IFS with an undetectable ANC at the time of diagnosis (p=0.0668)



OBSERVATIONS

- Backward selection model failed to identify risk factors for mortality
- *Degree* of neutropenia did not correlate with mortality
- Recovery of ANC (*duration)*
  - 5 patients from ANC = 0 → survival
  - 4/5 within a 10 day period

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CONCLUSIONS

1. IFS overall mortality remains high at 50% despite medical and surgical advances.
2. Non-detectable ANC at time of diagnosis may be linked to mortality, although it was not statistically significant (p=0.0668).
3. While this is one of the largest cohort to date in literature, this study also likely underpowered.
4. Diagnosis of IFS alone portends a poor prognosis and once diagnosed, individual patient factors do not appear to impact survival.

LIMITATIONS

1. No CPT code specifically for invasive fungal sinusitis.

2. Study is underpowered, but consistent with prior retrospective reviews.
   - Low threshold, high suspicion?

3. Microbiology data is incomplete regarding speciation.

Thank You:

1. Nikita Chapurin, MS, BA
2. Dr. Rose Eapen
3. Maragatha Kuchibhatla, PhD

References:

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The Evaluation and Management of Bilateral Vocal Fold Immobility

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Otolaryngology – Head and Neck Surgery
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Disclosures

- No relevant conflicts of interest.

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Definitions

- Bilateral vocal fold paralysis
- Bilateral vocal fold paresis
- Posterior glottic stenosis
- Glottic stenosis

What is the Problem?

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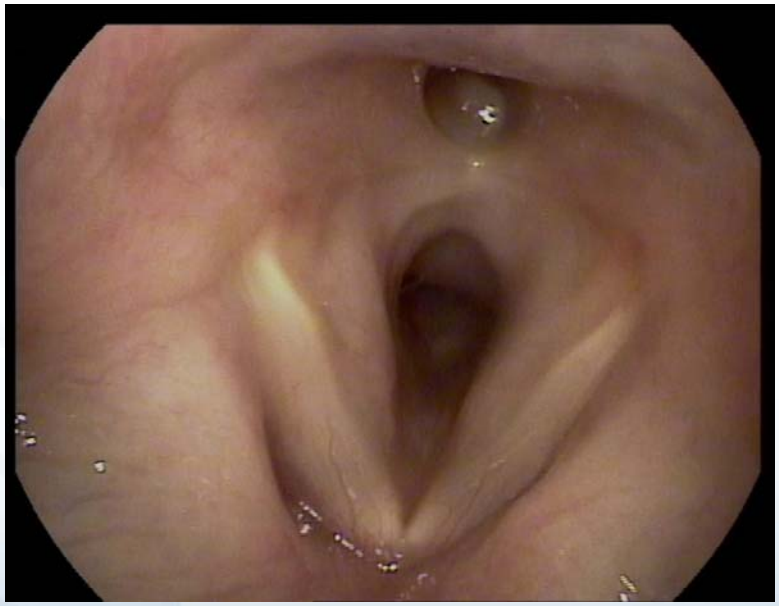
Posterior Glottic Stenosis (PGS)

- Decreased vocal fold immobility due to scarring in the posterior glottis
- Most common cause is endotracheal intubation
  - Other causes are RA, SLE, Granulomatous Disease, Radiation
- Incidence 12% in patients intubated > 10 days



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Whited RE Laryngoscope 1983

Predisposing factors

- Duration of intubation
- Repeat intubation
- ETT size (> 8-0)
- Comorbidities (e.g. DM)
- Ischemic conditions
- ? Presence of NGT
- ? Motion of ETT
- ? GERD

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Hillel et al Ann Otol Rhinol Laryngol 2016

Posterior Glottic Stenosis (PGS)

- Mechanism of Injury (evolves over time)
  - Inflammation and ulceration
  - Granulation tissue, chondritis
  - Scar formation versus re-epithelization

Ideal to intervene here

- Important to accurately discriminate between mechanical versus neurologic causes of vocal fold immobility
  - Different management
  - Different prognosis

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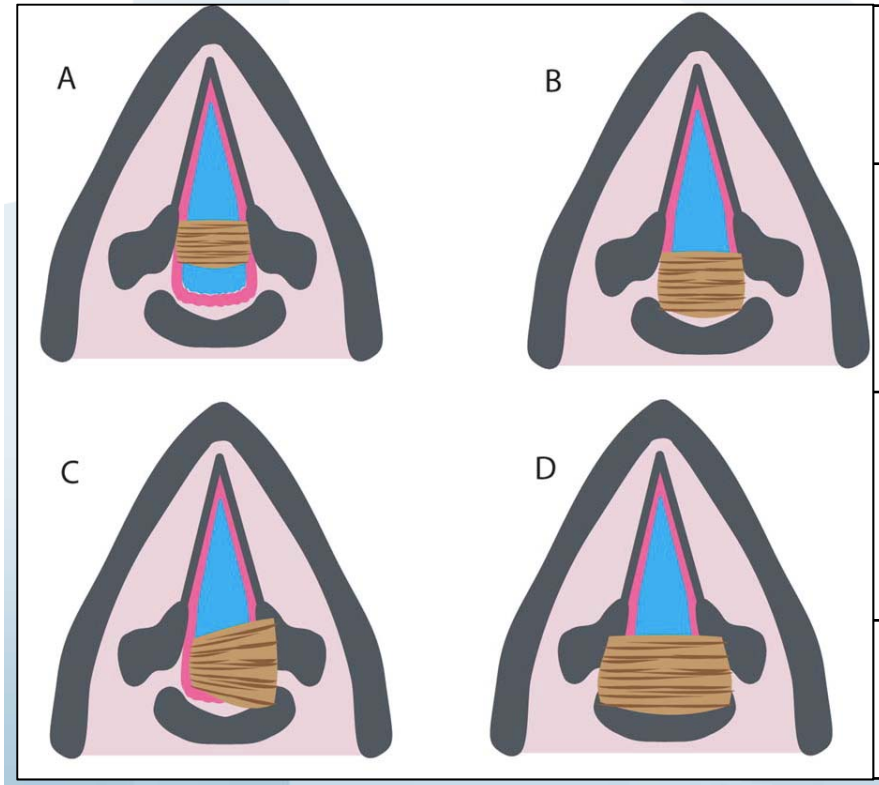
Bogdasarian “Types” of PGS



Type I	Interarytenoid synechia
Type II	Posterior commissure stenosis (mobile TVF)
Type III	Posterior commissure stenosis with unilateral CA joint ankylosis
Type IV	Posterior commissure stenosis with bilateral CA joint ankylosis

From: Meyer & Wolf 2011 Laryngoscope

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Bogdasarian & Olson Otolaryngol Head Neck Surg 1980

Management of PGS

- Medical
- Surgical
  - Office based procedures
  - Endoscopic procedures
  - Open surgical procedures

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Medical Management

- Manage contributing conditions (if present)
  - Antibiotics
  - Antacid medications
- Inhaled corticosteroids
  - Helpful for granulation tissue
  - Mainly prophylactic
- Systemic steroids
  - Controversial
  - Not widely used or recommended

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Endoscopic Surgical Management

- Initial Management
  - Scar lysis
    - Mitomycin C?
  - Intralesional steroid injections
    - Into scar
    - Into CA joints
  - Glottic balloon dilation
    - To aid in joint mobilization, posterior expansion

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Endoscopic Surgical Management

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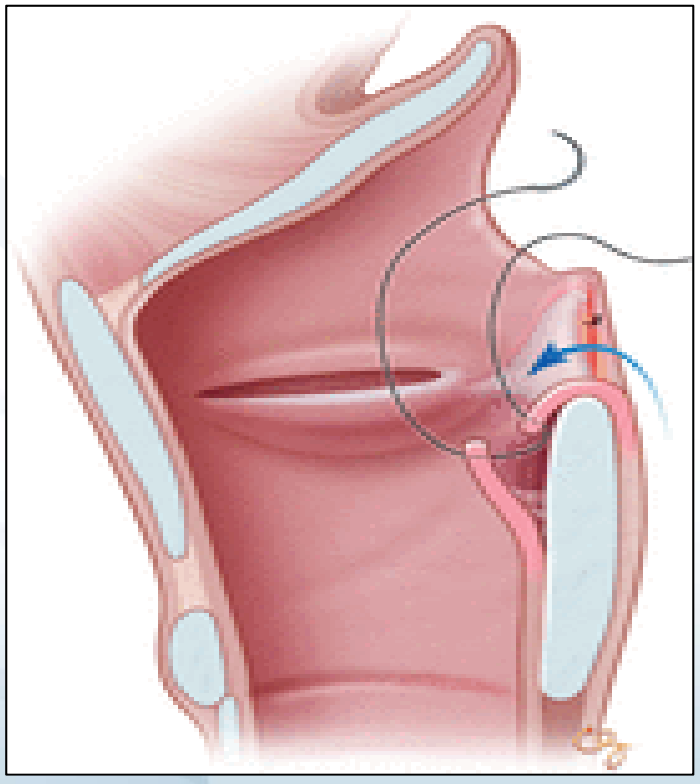
Endoscopic Surgical Management

- Other considerations
  - Suture lateralization
  - Posterior mucosal advancement flap
  - Partial Posterior Cordectomy
  - Arytenoidectomy
  - Posterior Cricoid Split with Cartilage Graft



Damrose & Beswick 2016

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Open Surgical Management

- Tracheostomy
  - Most present with stridor, airway compromise
  - Significant majority undergo tracheostomy
- Laryngofissure
  - Scar removal
  - Flap graft
  - Stent placement
- Posterior cricoid split with rib graft

Outcomes & Prognosis

- Types I & II better prognosis due to lack of CA joint ankylosis
- Meyer & Wolf 2011
  - 13 patients with Type I PGS
  - 12/13 presented with tracheostomy
  - Endoscopic management with lysis, steroid injection, balloon dilation
  - 7 (54%) regained normal TVF motion
  - 10 (83%) were successfully decannulated

Outcomes & Prognosis

- Damrose & Beswick 2016
  - 10 PGS patients
    - 7 with stage II stenosis
    - 3 with stage IV stenosis
  - Modified endoscopic postcricoid advancement flap
  - 7 (70%) regained normal TVF motion (all “stage II”)
  - 10 (100%) were successfully decannulated

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MUSC Data

- 59 patients evaluated with bilateral vocal fold immobility at MUSC in the last 5 years.
- Etiology
  - Intubation 20 (34%) - all PGS w/ scar
  - Radiation 12 (20%)
  - Thyroidectomy 12 (20%)
  - Other 15 (25%)

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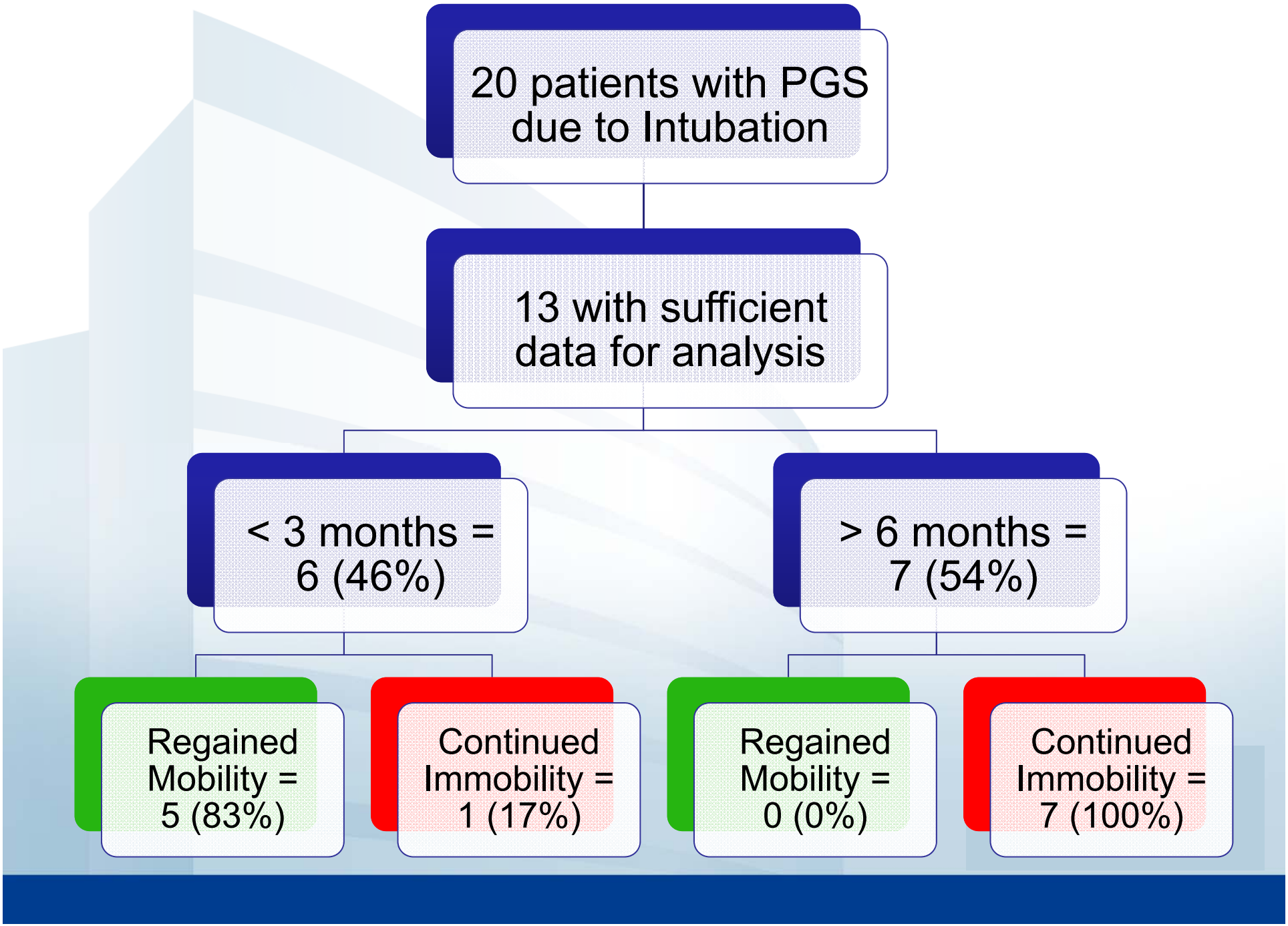
20 patients with PGS due to Intubation
13 with sufficient data for analysis
< 3 months = 6 (46%)
> 6 months = 7 (54%)
Regained Mobility = 5 (83%)
Continued Immobility = 1 (17%)
Regained Mobility = 0 (0%)
Continued Immobility = 7 (100%)

Pearls

- Suspect PGS in patient with history of intubation.
- Early intervention may result in better return of TVF mobility.
- Repeat scar lysis and steroid injections may be necessary.
  - Consider advanced procedures only after conservative fail.
- Avoid additional trauma to posterior commissure mucosa (e.g. from laser or laryngoscope).

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Perspectives in Facial Reanimation

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Disclosures

- None

Objectives:

- Explore the individual and societal impact of facial paralysis
- Review the treatment options available
- Discuss outcomes of various treatments with an emphasis on quality of life

Case

- 40yo history of left Bell's Palsy 6 years prior
- Treated with steroid and antivirals
- Presents with partial recovery but wants to know what else can be done?

Effects of facial paralysis

- Functional
- Psychological
- Social

- Mitigating these effects defines treatment goals

Functional deficits

- Upper face
  - Brow ptosis and visual field deficits
  - Ineffective blink leading to eye dryness, irritation, epiphora, exposure keratitis and blindness
- Mid face
  - External nasal valve collapse and nasal obstruction
- Lower face
  - Oral incompetence
  - Articulation difficulties

Goal #1

- Minimize functional deficits

Psychosocial implications

- Psychological distress contributes more to social disability than functional impairments
- Facial paralysis often leads to social isolation with depressive symptoms present in 65% of patients (3-5x general population)
- 20-30% of pts deemed "cured" by their physicians reported subjective problems with facial movement

VanSwearingen JM, et al. Psychological distress: Linking impairment with disability in facial neuromotor disorders. Otolaryngol Head Neck Surg.1998;118:790–796
Byrne PJ. Importance of facial expression in facial nerve rehabilitation. Curr Opin Otolaryngol Head Neck Surg. 2004;12:332-335
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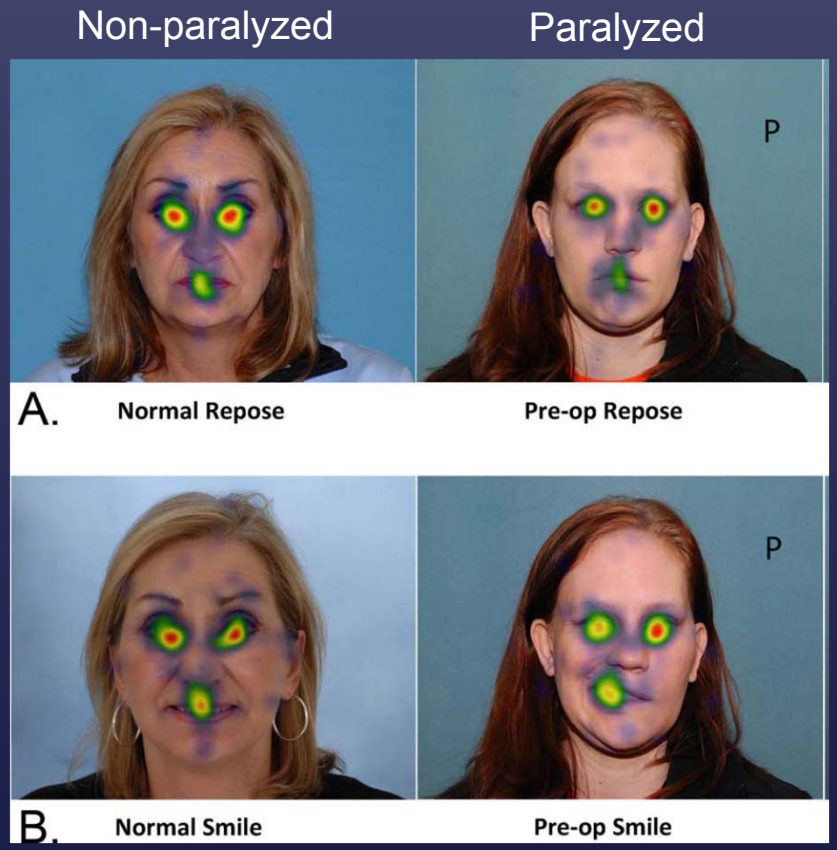
Importance of a face

- Defines individual identity
- Verbal and non-verbal communication
- Emotional expression

Observation in facial paralysis

- Paralyzed faces are viewed symmetrically in repose but attention shifts to the normal side when smiling
- Asymmetry when smiling draws attention away from the eyes.



Dey JK, Ishii L, Byrne PJ, Boahene K, Ishii M. Seeing is believing: objective evaluating the impact of facial reanimation surgery on social perception. Laryngoscope. 2014;124:2489-97

Goal #2

- Re-direct eye gaze to the central triangle
- Minimize distracting features

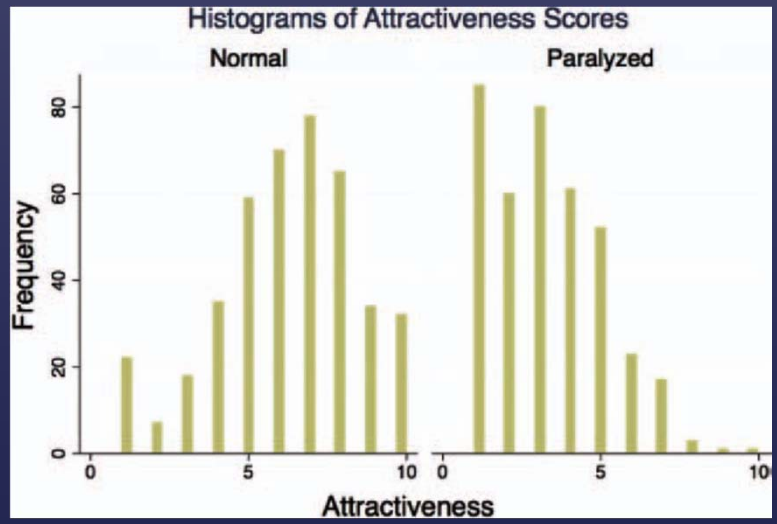
Attractiveness

- Elements of facial attractiveness are highly studied
- Includes: symmetry, averageness, youthfulness, sexual dimorphism
- Facial paralysis affects symmetry and averageness
- Attractive individuals demonstrated better self-esteem, more fulfilling relationships, academic & occupational success, and improved QOL
- Incorporating aesthetic surgical techniques can improve attractiveness of patients with facial paralysis

Dey JK, Ishii M, Boahene KDO, Byrne PJ, Ishii L. Changing perception: facial reanimation surgery improves attractiveness and decreases negative facial perception. Laryngoscope. 2013;124:84-90

Attractiveness

- Observers rate paralyzed faces as 1 SD less attractive than normal faces
- Perceived facial features affected:
  - Mouth (30%)
  - Eyes (21%)
  - Nose (21%)
  - Brow (15%)
  - Forehead (10%)

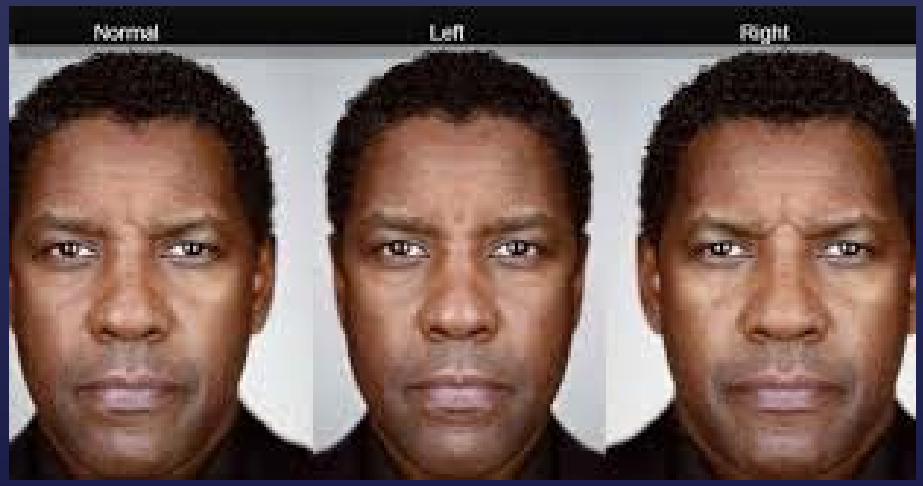


- Smiling improves attractiveness for normal faces, but does not change or even decreases attractiveness for paralyzed faces

Ishii L, Godoy A, Encarnacion CO, et al. Not just another face in the crowd: society's perception of facial paralysis. Laryngoscope. 2012;122:533-38

Symmetry

- Perfect symmetry is never present
- Subtle asymmetries are imperceptible and normal
- What amount of facial asymmetry reaches conscious awareness?



ORIGINAL ARTICLE

Threshold of Visual Perception of Facial Asymmetry in a Facial Paralysis Model

Eugene A. Chu, MD; Tarik Y. Farrag, MD, MSc; Lisa E. Ishii, MD; Patrick J. Byrne, MD

- >3mm asymmetry needed at OC and brow for conscious detection

C Chu EA, Farrag TY, Ishii LE, Byrne PJ. Threshold of visual perception of facial asymmetry in a facial paralysis model. Arch Facial Plast Surg 2011;13:14–19

Goal #3

- Improve overall facial attractiveness
- Improve symmetry to below detectable range

Emotional expression

- Facial expressions of emotion are universal and highly conserved
- 6 primary emotions recognized across cultures
  - Happiness
  - Disgust
  - Surprise
  - Sadness
  - Anger
  - Fear

Darwin C. The Expression of the Emotions in Man and Animals. London: John Murray; 1872
Elfenbein HA, Ambady N. On the universality and cultural specificity of emotion recognition: a meta-analysis. *Psychol Bull* 2002; 128:203–35

Social importance of emotion

- “Emotional contagion” describes the ability to recognize and empathize with emotions in others
- “Affect display” describes the ability of an individual to accurately display the desired emotion
- Accurate formation and interpretation of emotion is a complex cognitive function that develops at a young age

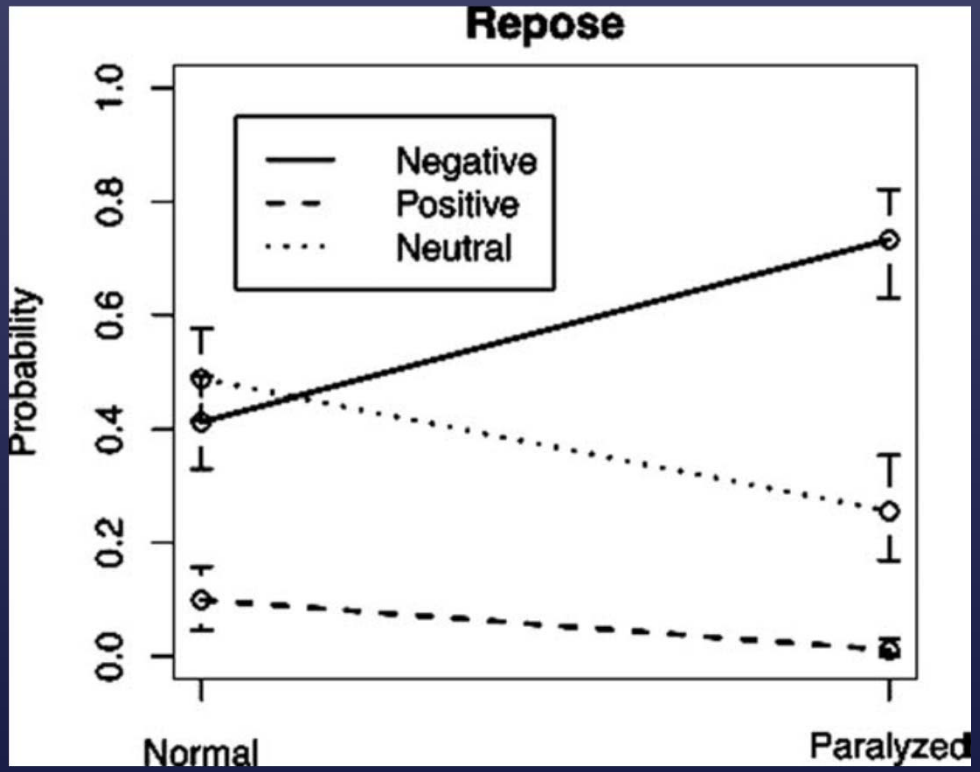
Ishii L, Godoy A, Encarnacion C, et al. What faces reveal: impaired affect display in facial paralysis. Laryngoscope. 2011;121:1138-43
Byrne PJ. Importance of facial expression in facial nerve rehabilitation. Curr Opin Otolaryngol Head Neck Surg. 2004;12:332-335

Define the emotion…

What Faces Reveal: Impaired Affect Display in Facial Paralysis

Lisa E. Ishii, MD, MHS; Andres Godoy, MD; Carlos O. Encarnacion, BS; Patrick J. Byrne, MD; Kofi D. O. Boahene, MD; Masaru Ishii, MD, PhD

- In repose, paralyzed faces were much more likely to be viewed negatively and less likely to be viewed positively
- 73% of paralyzed faces categorized as negative



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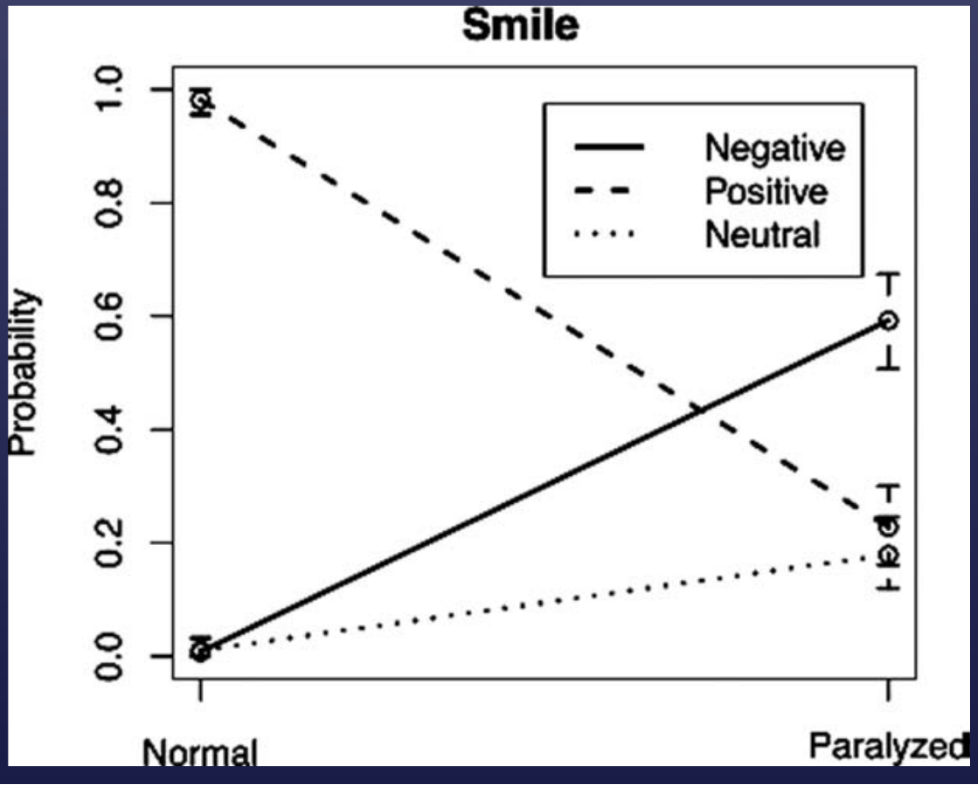
- When smiling 96% of normal faces were viewed positively vs. 23% for paralyzed faces
- 59% of paralyzed faces categorized as negative even when smiling



Goal #4

- Improve affect display

Quality of life

- Facial paralysis has a dramatic impact on patient-reported QOL
- Utilizing utility outcome scores, paralysis ranked below monocular blindness and on par with ESRD and HIV
- Participants willing to sacrifice 8yrs of life with paralysis for a normal face
- Would undergo a procedure with 21% chance of death to reverse paralysis

Coulson SE, O'dwyer NJ, Adams RD, et al. Expression of emotion and quality of life after facial nerve paralysis. Otol Neurotol. 2004;25:1014-1019.
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Sinno H, Thibaudeau S, Izadpanah A, et al. Utility Outcome scores for unilateral facial paralysis. Ann Plast Surg. 2012;69:435-38

Measuring QOL

- Systematic review of 28 questionnaires found 3 specific to facial paralysis
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Goal #5

- Improve quality of life

Goals of facial reanimation

- More than just treating the deformity…

- Minimize functional deficits
- Re-direct eye gaze to central triangle of face
- Improve facial symmetry
- Improve facial attractiveness
- Improve affect display
- Restore QOL

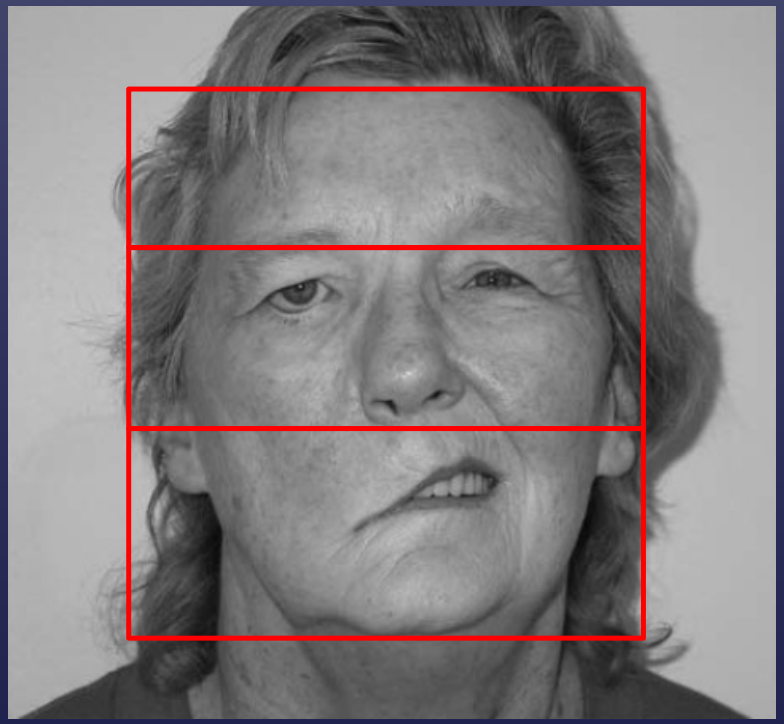
Treatment options

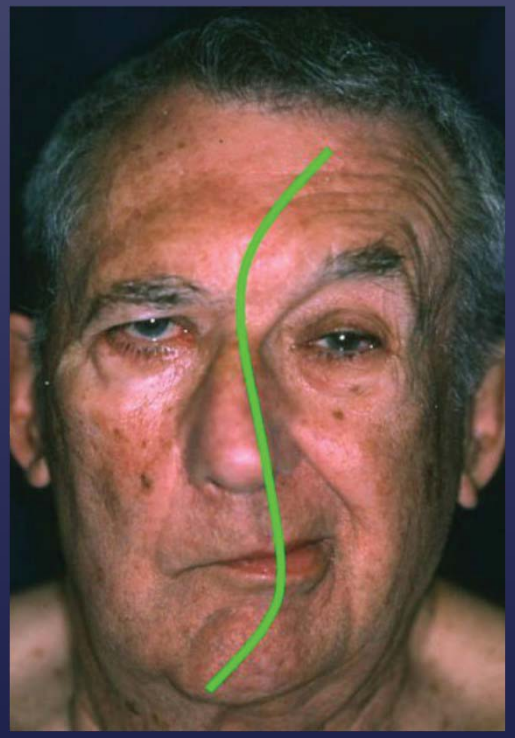
- Wide variety available
- Factors include duration of paralysis, extent of paralysis, facial thirds, patient comorbidities

- Static Procedures:
- Brow lift
- Lid loading/suspension
- Suture suspension
- Static sling

- Dynamic Procedures:
- Nerve graft
- Nerve transfer
- Regional muscle transfer
- Free muscle transfer

Facial thirds





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Bergeron CM, Moe KS. The evaluation and treatment of the upper eyelid paralysis. Facial Plastic Surg. 2008;24:220-230

Upper third

- The forehead and brow were only perceived by 10-15%
- Brows play an important role in facial expression & recognition
- Dynamic brow animation with nerve graft, nerve transfer, and cross-facial nerve grafting often yield disappointing results
- Goal is to restore symmetry, may need to treat both sides

Ishii L, Godoy A, Encarnacion CO, et al. Not just another face in the crowd: society's perception of facial paralysis. Laryngoscope. 2012;122:533-38
Byrne PJ. Importance of facial expression in facial nerve rehabilitation. Curr Opin Otolaryngol Head Neck Surg. 2004;12:332-335

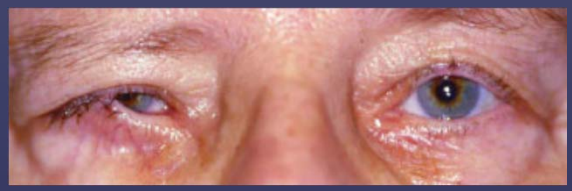
Brow Lift

- Elevate affected brow
  - Endoscopic, coronal, mid-forehead, temporal, direct brow lift
- Decrease dynamic activity of normal brow with chemodenervation
- Consider upper blepharoplasty

Meltzer NE, Byrne PJ. Management of the brow in facial paralysis. Facial Plastic Surg. 2008;24:216-219

Periocular management

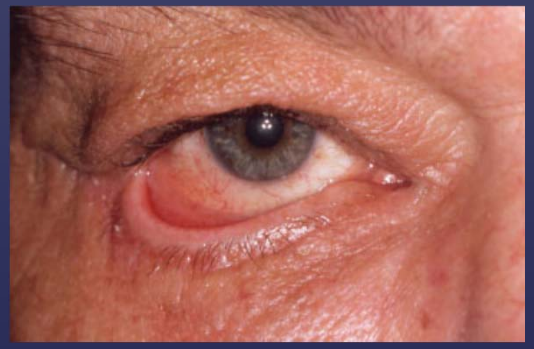
- Eye health is vitally important
- Evaluate for risk factors for exposure
  - Bell's phenomenon
  - Anesthesia of the cornea
  - Dry eye history
  - Negative vector
- Upper eyelid loading may benefit patients with lagophthalmos
  - Lower complication/extrusion rates with platinum chain

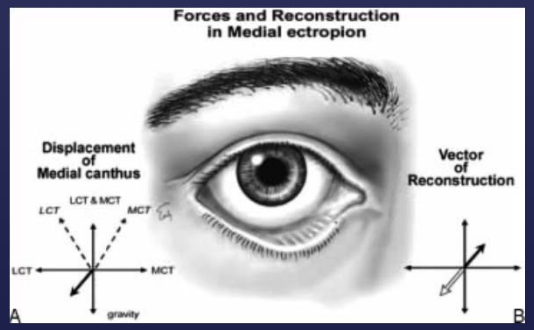


Bergeron CM, Moe KS. The evaluation and treatment of upper eyelid paralysis. Facial Plastic Surg. 2008;24:216-219

Lower lid treatment

- Careful analysis is required to provide the correct procedure on an individualized basis
  - Lateral canthopexy
  - Medial canthopexy
  - Tarsal strip lid shortening
  - Spacer grafting
  - Dynamic re-innervation procedures
  - Muscle transfer





Bergeron CM, Moe KS. The evaluation and treatment of lower eyelid paralysis. Facial Plastic Surg. 2008;24:216-219
Henstrom DK, Lindsay RW, Cheny ML, Hadlock TA. Surgical treatment of the periocular complex and improvement of quality of life in patients with facial paralysis. Arch Facial Plast Surg. 2011;13:125-128

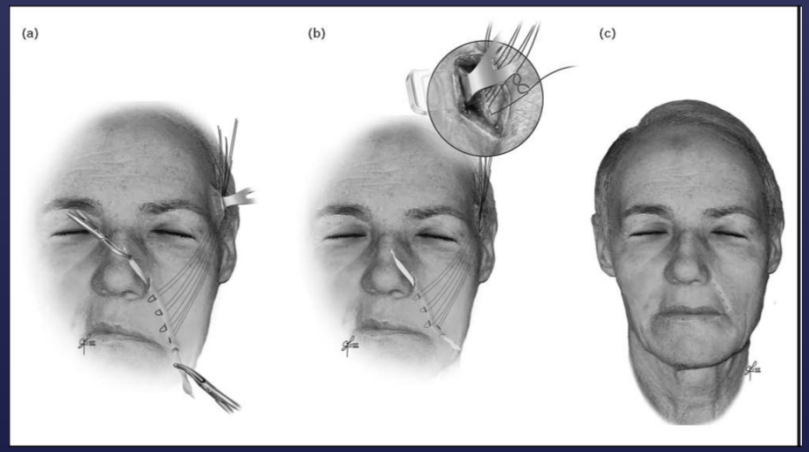
Middle third

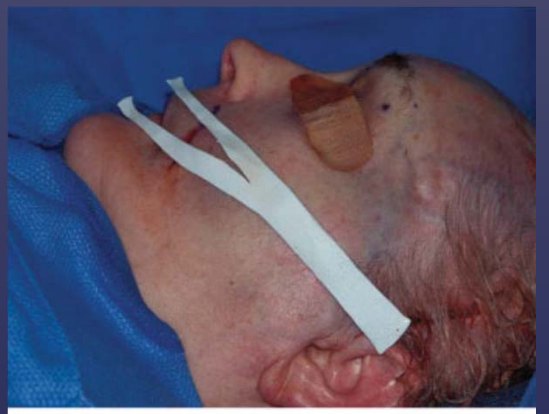
- Nasal valve collapse treated with standard rhinoplasty techniques
- Static slings and suture suspension are options for nasal valve and mid face in select patients to improve symmetry
- Dynamic re-innervation or directed muscle transfer
- Consider fillers and other aesthetic adjuncts to improve midfacial symmetry and enhance overall attractiveness

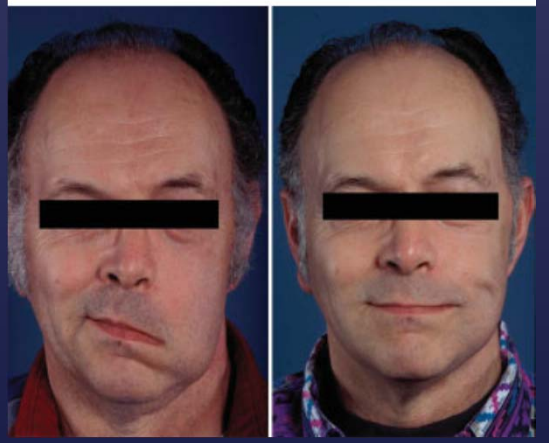
Liu YM, Sherris DA. Static procedures for the management of the midface and lower face. Facial Plastic Surg. 2008;24:211-215

Lower third-static procedures

- Provide symmetry at rest only. Play a role in select patients with multiple comorbidities or poor prognosis
- Various materials used
  - Suture
  - Fascia lata
  - Gore-tex
  - Alloderm





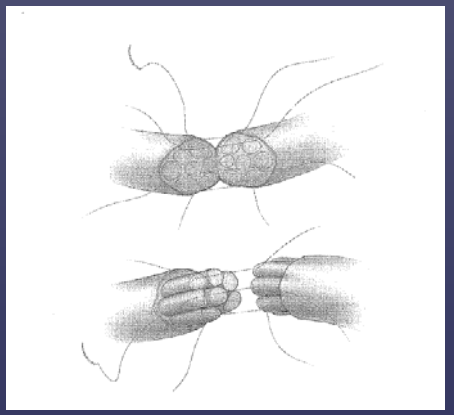


Liu YM, Sherris DA. Static procedures for the management of the midface and lower face. Facial Plastic Surg. 2008;24:211-215
Meltzer N, Alam D. Facial paralysis rehabilitation: state of the art. Curr Opinion in Otolaryngology & Head and Neck Surgery. 2010;18:232-237

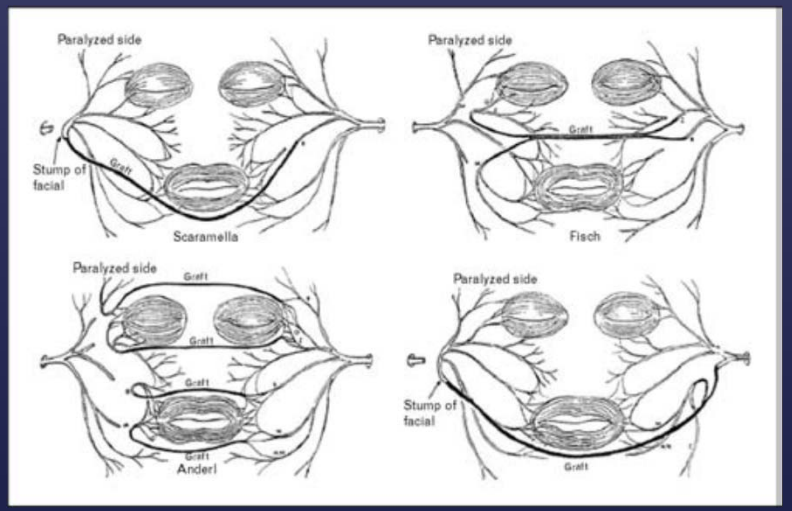
Lower third-neural procedures

- Suitable only for short duration of paralysis (<1.5-2 yrs)
- Requires intact motor endplate units
- Better results with earlier intervention
- Potential for spontaneous and mimetic movement

Mimetic nerve function



- Cable graft if proximal segment available
  - Great auricular, sural, medial cutaneous nerve of arm

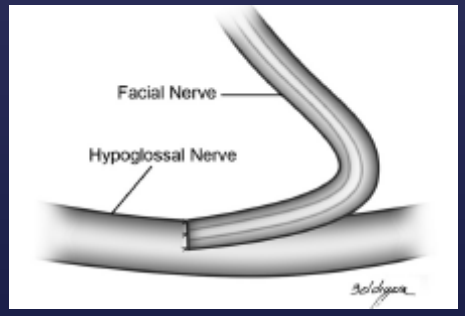


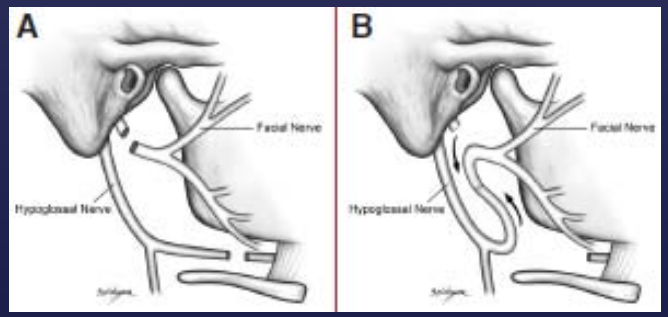
- Cross-facial nerve graft
  - Can target specific branches
  - Requires sacrifice of normal nerve
  - Best results if done early
  - Results can be unpredictable

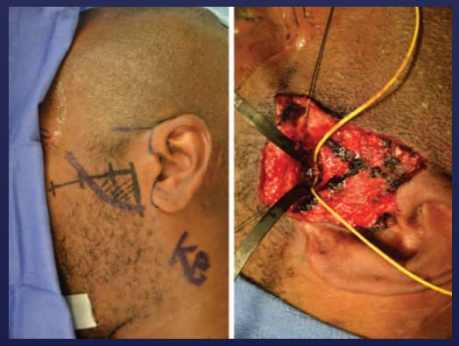
Meltzer N, Alam D. Facial paralysis rehabilitation: state of the art. Curr Opinion in Otolaryngology & Head and Neck Surgery. 2010;18:232-237

Nerve transfers

- Hypoglossal or masseteric transfer if proximal stump absent
- Lacks spontaneity and requires sacrifice of additional CN
- Synkinesis and mass movement a problem with transfers to main trunk
- Potential for more movement due to larger axon load (1500-2500 axons in masseteric vs 100-200 in CFNG)







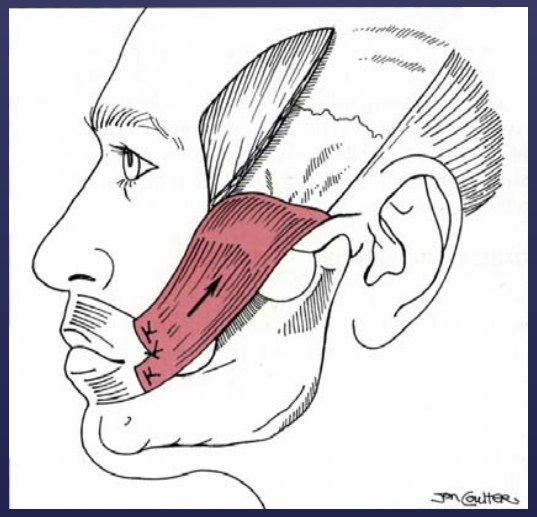
Collar RM, Byrne PJ, Boahene KDO. The subzygomatic triangle: rapid, minimally invasive identification of the masseteric nerve for facial reanimation. Plast Reconst Surg. 2013;132:183-188

Lower third-muscle transfer

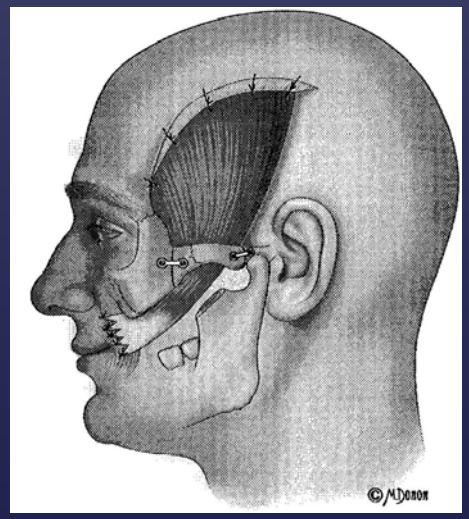
- Suitable for long-standing paralysis for dynamic oral commissure elevation
- Regional muscle transfer
  - Temporalis/masseter
  - Temporalis tendon
- Free muscle transfer
  - Gracilis
  - Pectoralis minor
  - Latissimus

Temporalis transfer

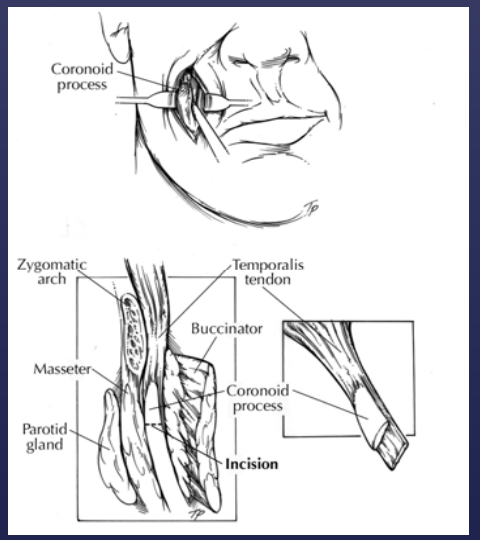
- Progressed to minimally invasive orthodromic tendon transfer



Temporalis transfer
Gillies



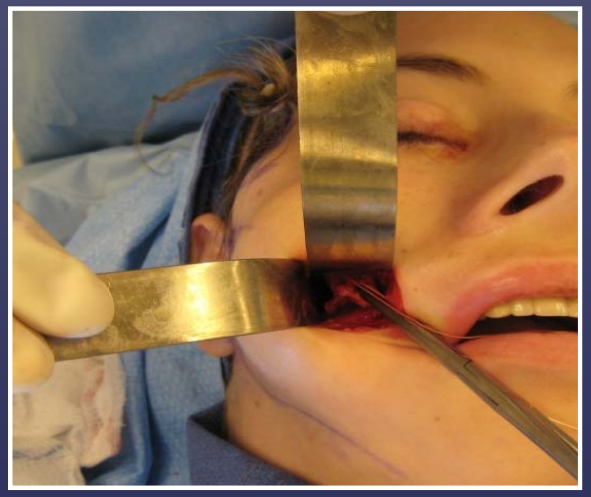
Lengthening myoplasty
Labbé



MIT3
Byrne/Boahene

MIT3

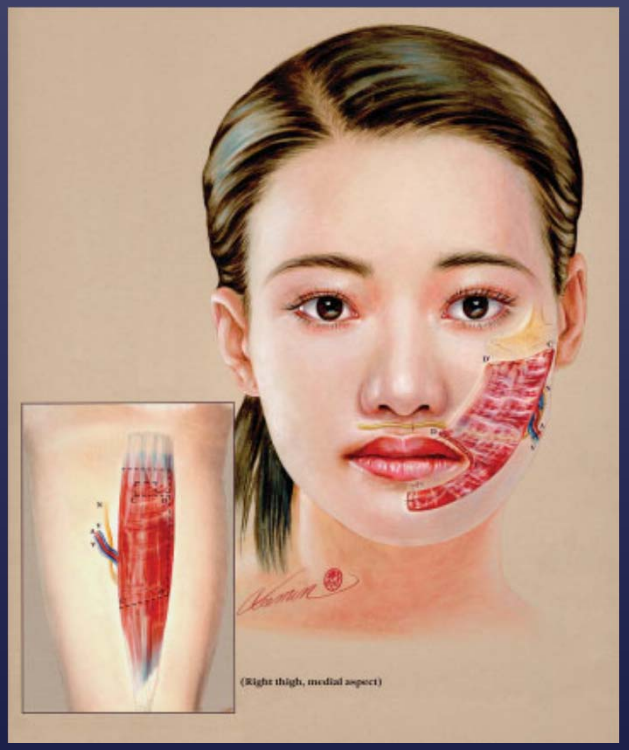
- Transfacial vs. transoral
- Use nerve stimulation to determine optimal muscle length for inset
- May require extension with fascia lata for optimal tension



Byrne PJ, et al. Temporalis tendon transfer as part of a comprehensive approach to facial reanimation. Arch Facial Plast Surg. 2007;9:234-41
Boahene KD, Farrag TY, Ishii L, Byrne, PJ. Minimally invasive temporalis tendon transposition. Arch Facial Plast Surg. 2011;13:8-13

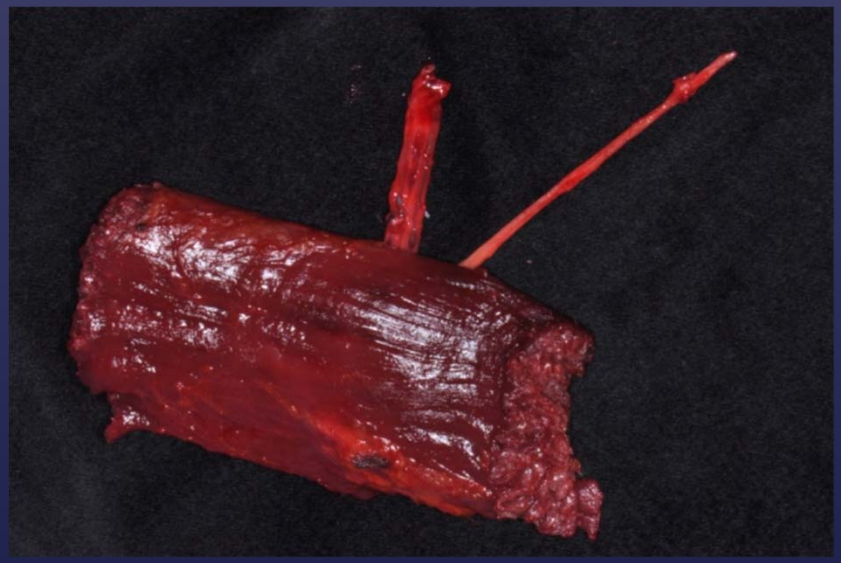
Free muscle transfer

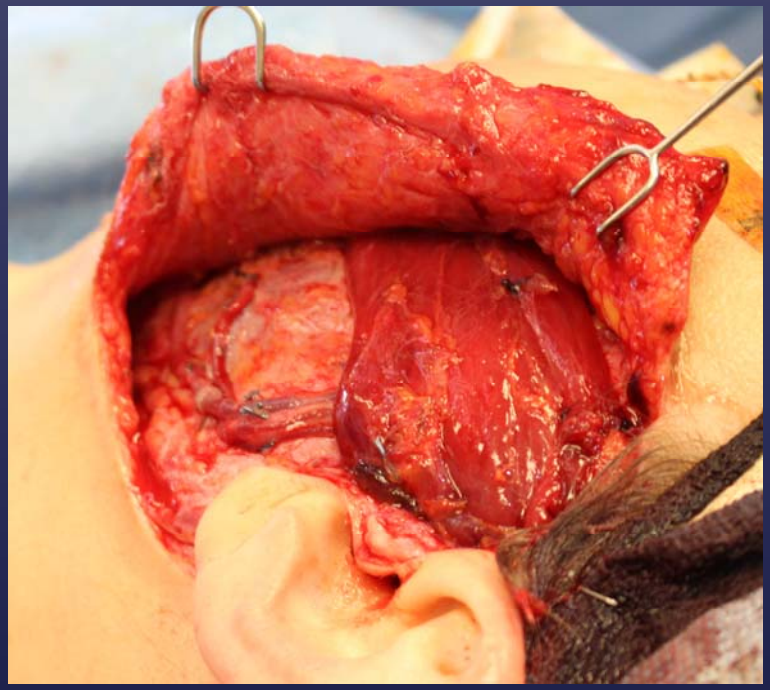
- Gracilis flap has become most popular donor site
- 2 stage technique with cross-facial sural nerve graft
  - Spontaneous smile
- Single stage technique with masseteric nerve
  - Increased excursion and reliability
- Double innervation with CFNG and masseteric nerve



Chuang DCC. Free tissue transfer for the treatment of facial paralysis. Facial Plast Surg. 2008;24:194-203

Gracilis free flap





Gracilis motion

Photos courtesy of Patrick Byrne, MD

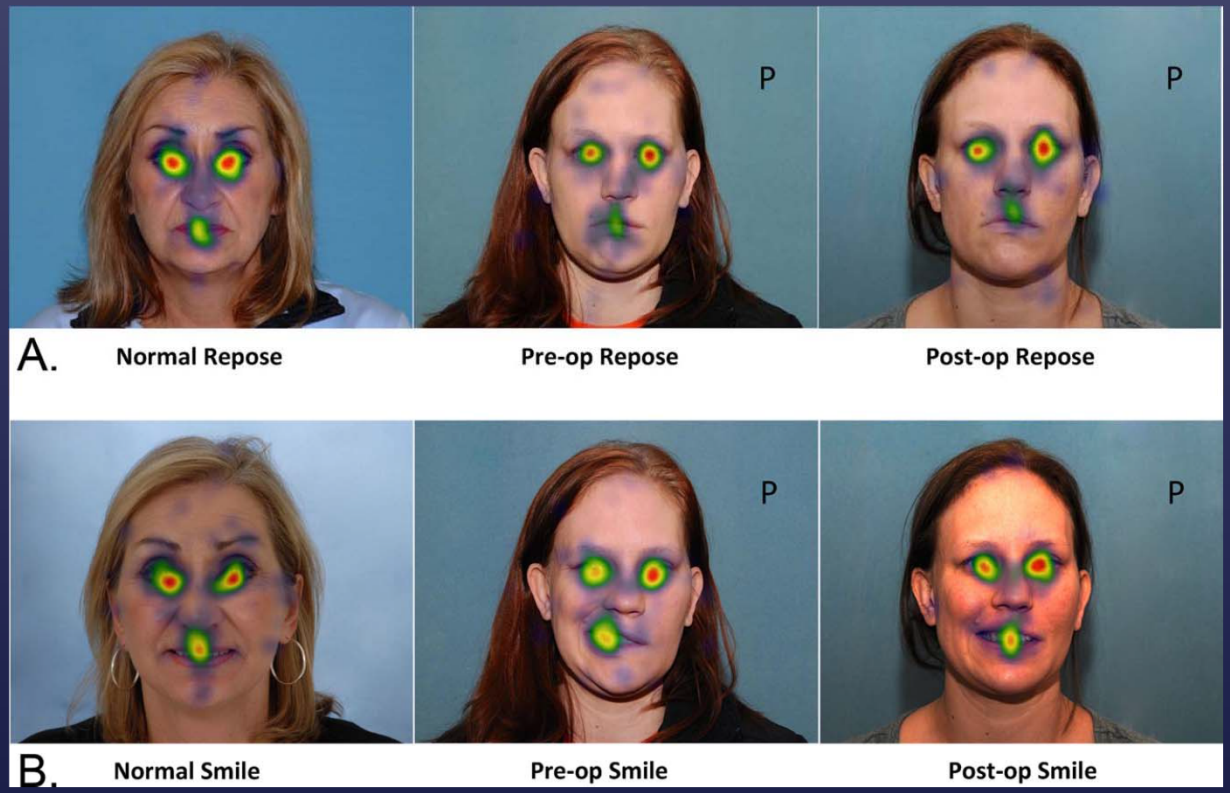
Outcomes

Treatment goals:

- Re-direct eye gaze to central triangle of face
- Improve facial symmetry
- Improve facial attractiveness
- Improve affect display
- Restore QOL

Eye-gaze

- Facial reanimation surgery restored eye gaze to the central triangle of the face even when smiling



Dey JK, Ishii L, Byrne PJ, Boahene K, Ishii M. Seeing is believing: objective evaluating the impact of facial reanimation surgery on social perception. Laryngoscope E-pub

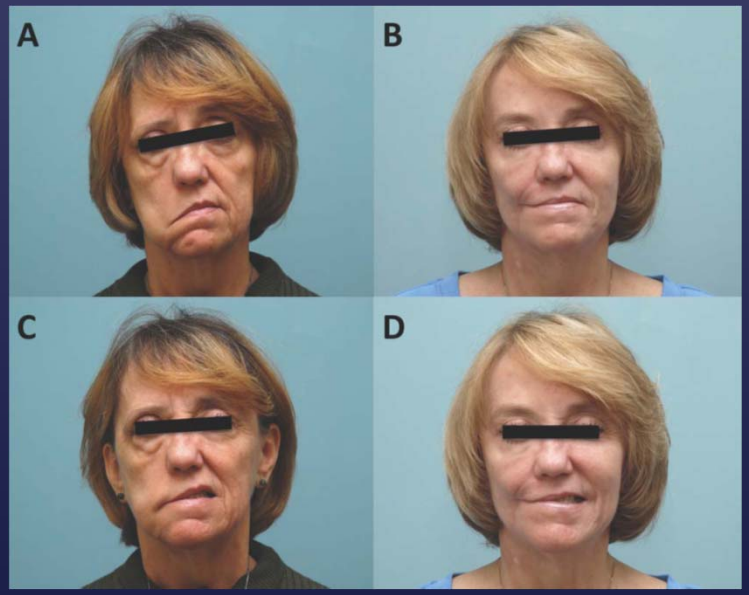
Facial symmetry

- Facial symmetry is improved with focused treatment of each of the facial thirds

Lindsay RW, Bhama P, Hadlock TA. Quality-of-Life Improvement After Free Gracilis Muscle Transfer for Smile Restoration in Patients With Facial Paralysis. JAMA Facial Plast Surg. doi:10.1001/jamafacial.2014.679

Attractiveness

- Facial re-animation procedures improves attractiveness but not to the level of non-paralyzed faces



Dey JK, Ishii M, Boahene KDO, Byrne PJ, Ishii L. Changing perception: facial reanimation surgery improves attractiveness and decreases negative facial perception. Laryngoscope. 2013;124:84-90

Quality of life

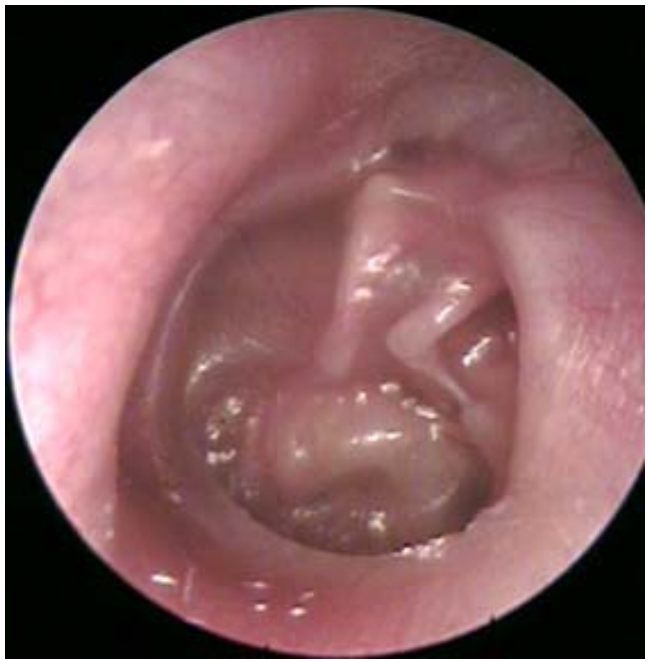
- Periocular treatment improves QOL
  - Henstrom DK, Lindsay RW, Cheny ML, Hadlock TA. Surgical treatment of the periocular complex and improvement of quality of life in patients with facial paralysis. Arch Facial Plast Surg. 2011;13:125-128
- Gracilis free flaps improve QOL in both adults and children (similar for CFNG and masseteric)
  - Lindsay RW, Bhama P, Hadlock TA. Quality-of-Life Improvement After Free Gracilis Muscle Transfer for Smile Restoration in Patients With Facial Paralysis. JAMA Facial Plast Surg. doi:10.1001/jamafacial.2014.679
  - Hadlock T, et al. Free Gracilis Transfer for Smile in Children The Massachusetts Eye and Ear Infirmary Experience in Excursion and Quality-of-Life Changes. Arch Facial Plast Surg. 2011;13(3):190-194
- Temporalis tendon transfer and 12-7 nerve transfer improve QOL
  - Kecskes G, et al. Lengthening Temporalis Myoplasty Versus Hypoglossal-Facial Nerve Coaptation in the Surgical Rehabilitation of Facial Palsy: Evaluation by Medical and Nonmedical Juries and Patient-Assessed Quality of Life. Otology& Neurotology 2009;30:217-222

Conclusions

- Treatment of facial paralysis should be individualized and address psychosocial & functional issues
- Surgical options are evolving and should be discussed with and applied to patient care in a thoughtful, organized fashion
- Continued improvement should focus on systematic data collection using validated outcomes instruments with collaboration among institutions

Thank You

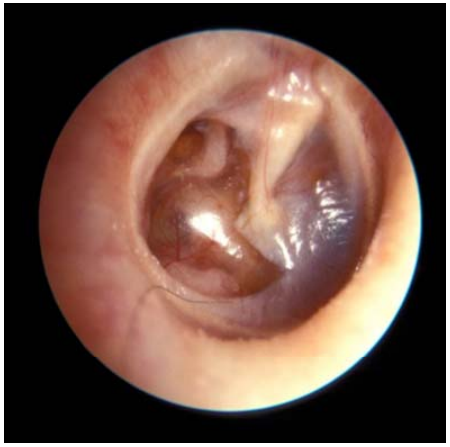
Management Options for the Atelectatic Ear

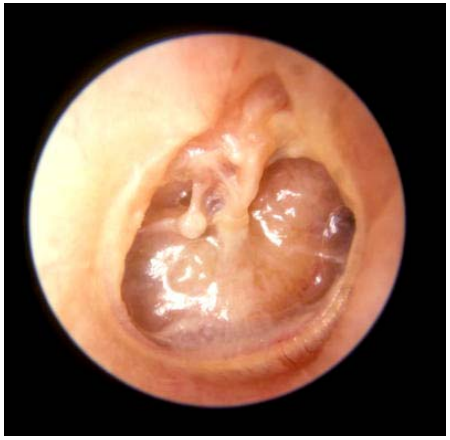


Calhoun D. Cunningham, M.D.
Assistant Professor
Duke Head and Neck Surgery &
Communication Sciences

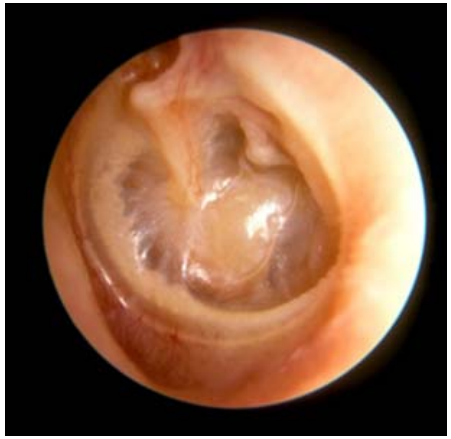
- *No Financial Disclosures*

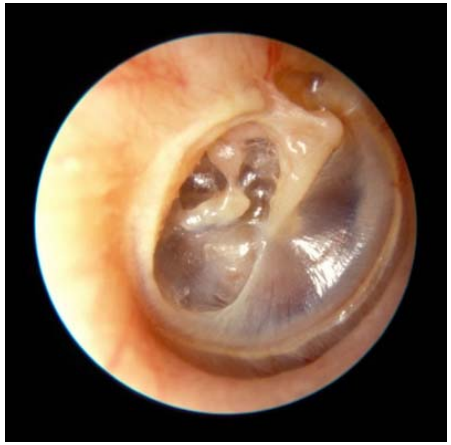
Tympanic Membrane Atelectasis



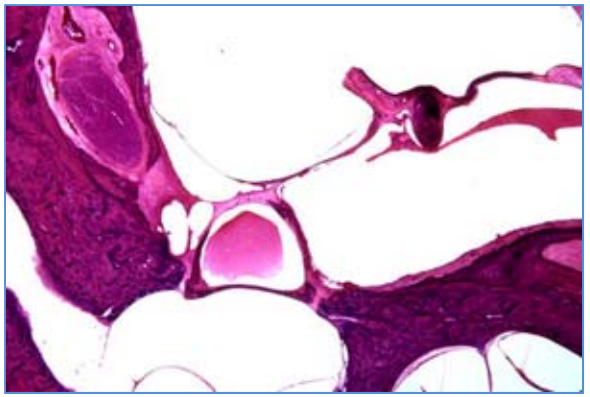


- Chronic adhesive otitis media
- Non-purulent form of OM
- Severely retracted TM
- Obliterated middle ear cleft
- With or without effusion
- Hearing Loss





Pathogenesis



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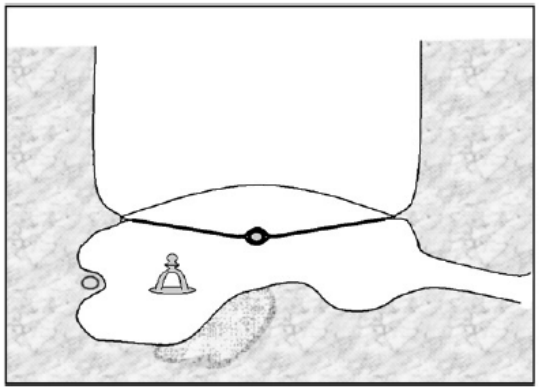
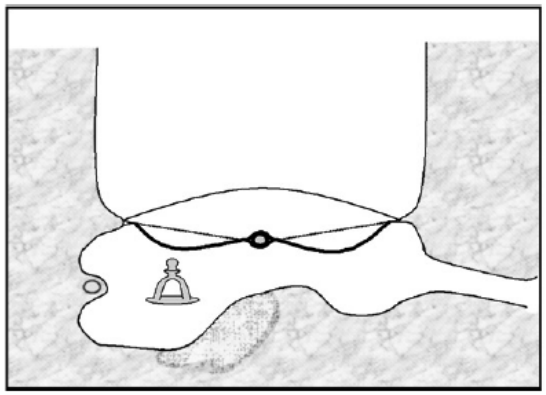
- Eustachian tube dysfunction
- Recurrent infections
  - Mucosal changes lead to increased resorption of middle ear gases
  - Attenuation of middle fibrous layer leading to atrophic/flaccid TM

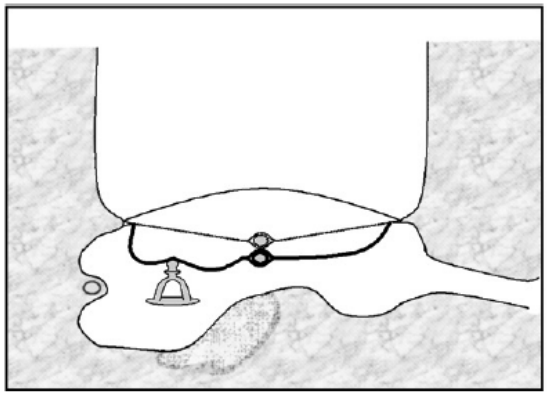
Dornhoffer Classification



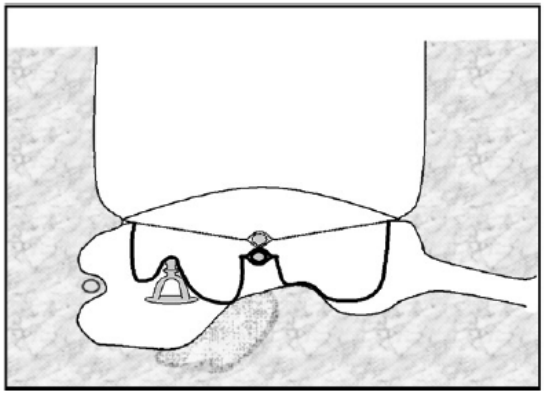
Normal Ear



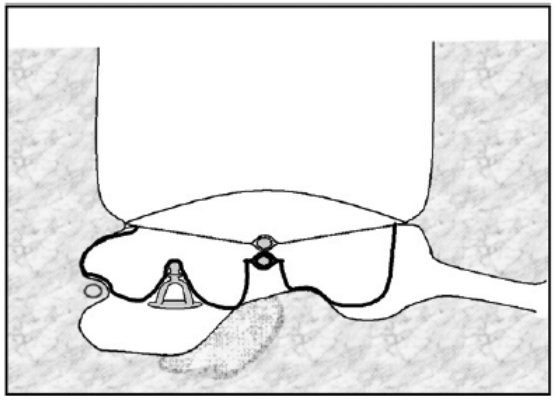
Grade I Atelectatic Ear



Grade II Atelectatic Ear



Grade III Atelectatic Ear



Grade IV Atelectatic Ear

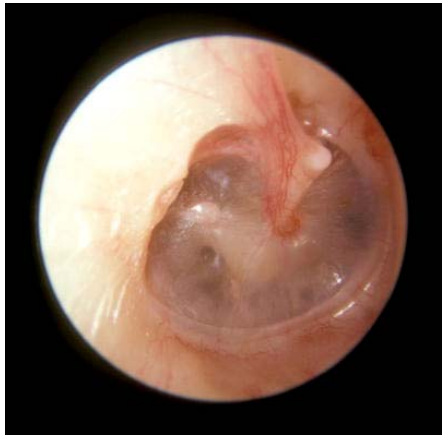
Otolaryngol Clin N Am 2006;39:1211-19

Clinical Evaluation

- Otomicroscopy
- Audiogram
- Sinus / allergy evaluation
- Adenoid hypertrophy

Otomicroscopy

- Degree of retraction / adhesion
  - Pneumatic otoscopy
  - Valsalva maneuver



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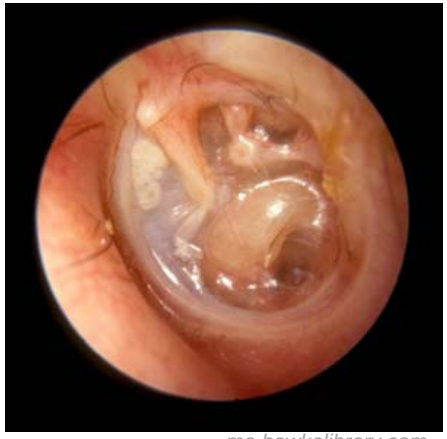

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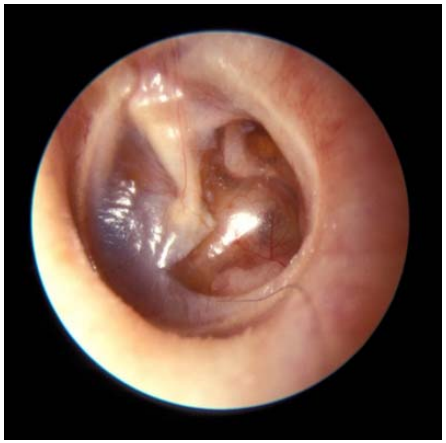
- Incus necrosis

Otomicroscopy

- Effusion present



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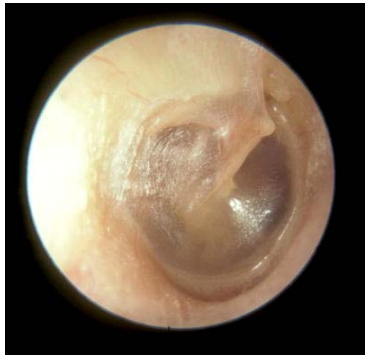
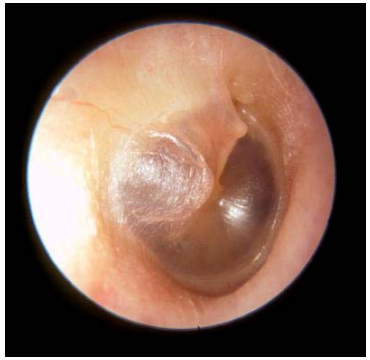
- Eustachian tube function
  - Valsalva maneuver
  - Politzerization





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Clinical Evaluation

- Otomicroscopy
- Audiogram
- Sinus / allergy evaluation
- Adenoid hypertrophy

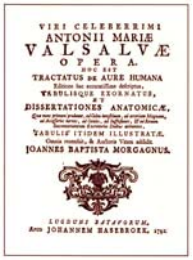
Medical Management

- No evidence of cholesteatoma
- Dry ear
- Good patient compliance
- First line of treatment for most children

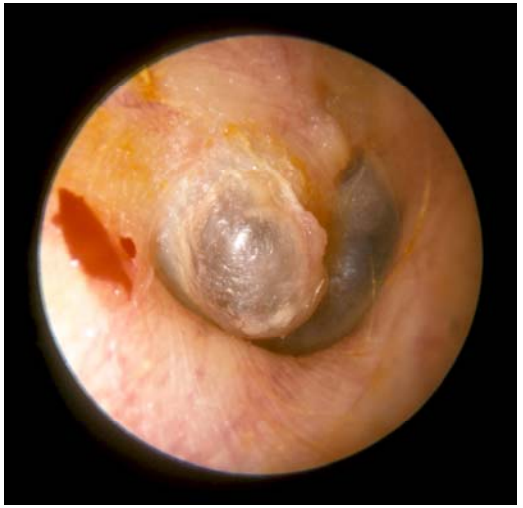
Medical Management

- Valsalva maneuvers
- Identify habitual “sniffers”
- Nasal steroids
- Treatment of sinus / allergy issues
- Treatment of adenoid/tonsil pathology
- Observation +/- hearing aid

Valsalva Maneuver


VIRI CELEBERRIMI
ANTONII MARIÆ
VALSALVÆ
OPERA.
HVC AVCTORIS
TRACTATUS DE AURE HUMANA
TABULIS ÆNEIS ORNATUS,
ET
DISSERTATIONES ANATOMICÆ,
TABULIS ITIDEM ILLUSTRATÆ.
Omnia recusa, & Auctore Vivo edita
IOANNES BAPTISTA MORGAGNUS.

- Patient first assessed in clinic
- Instructed to perform maneuver 6-8 times per day
- Children instructed to blow nose if unable to perform
- Reassess after 4-6 week trial



Valsalva Maneuver

The Ear Popper

Valsalva Maneuver

Otovent Balloon

Medical Management

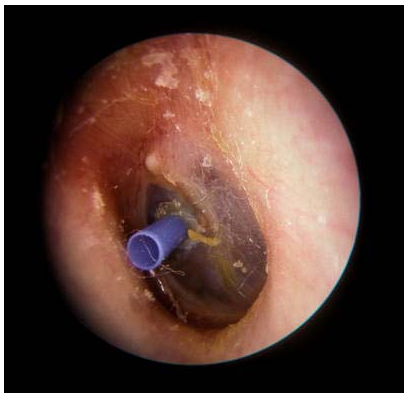
- Valsalva maneuvers
- Identify habitual “sniffers”
- Nasal steroids
- Decongestants
- Treatment of sinus / allergy issues
- Treatment of adenoid/tonsil pathology
- Hearing aid

Surgical Management

- Myringotomy and Tube
- PE tube with cartilage graft
- Cartilage tympanoplasty
- Balloon dilation eustachian tuboplasty

Myringotomy and Tube

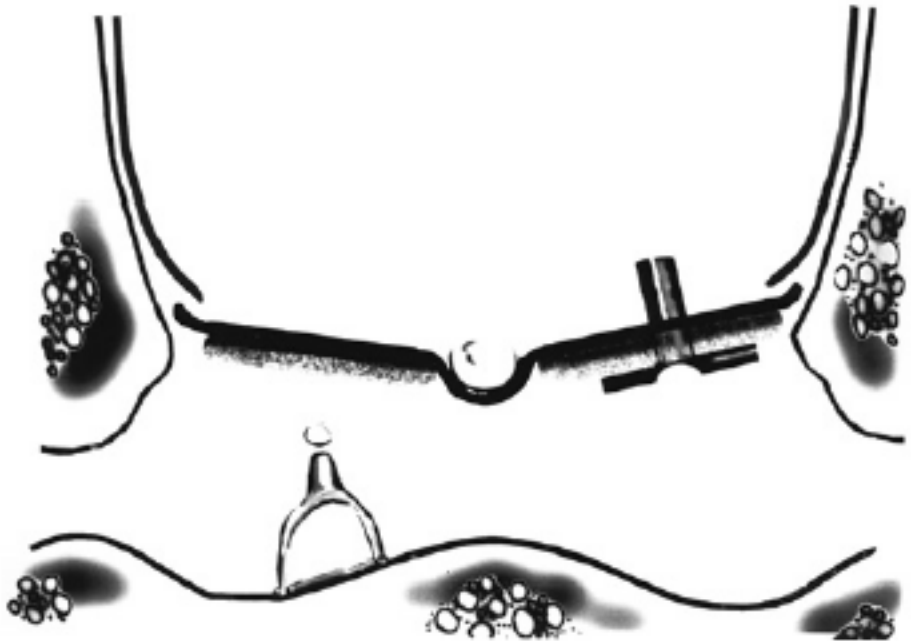
- Beneficial if some residual air remains in middle ear
- Adhesions not severe
- Long-term tube recommended
- Extrusion remains frequent due to weak/atrophic TM



Surgical Management

- Myringotomy and Tube
- PE tube with cartilage graft
- Cartilage tympanoplasty
- Balloon dilation eustachian tuboplasty

PE Tube with Cartilage Graft



Otolaryngol Clin N Am 2006;39(6):1161-76.

PE Tube with Cartilage Graft

- Recommended for permanent ventilation
- If poor chance of improving ET function
- If patient responds well to standard tube
- Requires anesthesia in OR
- Requires standard precautions with having a tube

Surgical Management

- Myringotomy and Tube
- PE tube with cartilage graft
- Cartilage tympanoplasty
- Balloon dilation eustachian tuboplasty

Cartilage Tympanoplasty

- Excellent option for reconstructing ear
- Provides rigid support preventing recurrent retraction
- Minimal to no effect on hearing
- Does not prevent effusion and tube may be required

Otolaryngology–Head and Neck Surgery (2008) 139, 747-758

INVITED ARTICLE

Cartilage tympanoplasty methods: Proposal of a classification

Mirko Tos, MD, MDSc, Copenhagen, Denmark; and Maribor, Slovenia

The 23 known cartilage tympanoplasty methods to reconstruct the eardrum are classified in six main groups. Each method is briefly defined, described, and illustrated:

Group A: Cartilage tympanoplasty with palisades, stripes, and slices. The eardrum is reconstructed by several, various, full-thickness pieces of cartilage with attached perichondrium on the ear canal side. In this group six different methods are described.

Group B: Cartilage tympanoplasty with foils, thin plates, and thick plates, not covered with the perichondrium. In this group four methods are included.

Group C: Tympanoplasty with cartilage-perichondrium composite inlaid grafts. The perichondrium flap suspends or fixates the cartilage. In this group four methods are included.

Group D: Tympanoplasty with special total pars tensa cartilage-perichondrium composite grafts. All three methods are used to close a total perforation, but differ from each. Three special methods are included in this group.

Group E: Cartilage-perichondrium composite inlaid grafts tympanoplasty for anterior, inferior, and subtotal perforations. Two on-lay and two underlay methods are included.

Group F: Special cartilage tympanoplasty methods: The cartilage disc is placed under the perforation, the perichondrium onto the denuded eardrum remnant.

The term cartilage tympanoplasty includes all methods of eardrum reconstruction with cartilage. The goal of this paper is to define, classify, briefly describe, and illustrate all known cartilage tympanoplasty methods. The 23 cartilage tympanoplasty methods will be classified into six main groups. In some methods, important modifications of the technique will be mentioned.

HISTORY OF CARTILAGE TYMPANOPLASTY

The cartilage was first used in ossiculoplasty by Ulsch in 1959, as an interposition graft, between the eardrum and the stapes,[1] and in 1961 as the columella between the footplate and the eardrum.[2] The first cartilage myringoplasty, using autologous septum cartilage, was performed by Salen[3] in 1963. Jansen[4] performed at the same time myringoplasty with homologous septum cartilage plates, without perichondrium. Since the early 1960s, Heermann[5,6] gradually developed the cartilage palisade method, starting with one small stapes-annulus plate,[7] placed onto the head of the stapes and onto the fibrous annulus at the six-o'clock position, continuing with a two-leg stapes-annulus cartilage plate.[8] The superior end of the plate was placed either onto the columella or onto the head of the stapes. The two very small ends are placed onto the fibrous annulus at the 5-o'clock and 7-o'clock positions. The next step was placement of one broad palisade onto the columella or the stapes and onto the fibrous annulus, covered with the fascia.[7] Since the 1980s the palisades were not covered with the fascia, and in 1992 Heermann[9] published the first illustration and description of the Heermann palisade method, as it is used today. The first composite cartilage-perichondrium graft, the annular graft, was introduced in 1967 by Goodhill,[10] the superior, or the attic composite inlaid graft in 1969 by McCleve;[10] the posterior pars tensa composite cartilage-perichondrium graft in 1973 by Linde;[11] and the total pars tensa composite cartilage-perichondrium graft in 1983 by Tobsdorff[12] and in 1985 by Nitsche.[13] The Tobsdorff graft was covered with the perichondrium on both sides, the Nitsche graft on the tympanic cavity side only. Nitsche was the first to use a graft with a wedge, to accommodate the malleus handle. Cartilage plates, without perichondrium, have been used already in the 1960s as reinforcement of the eardrum or the fascia. They were initially placed as the on-lay grafts,[4,14,15] later as underlay grafts.[16] The remaining, newer grafts and the corresponding methods will be mentioned, together with the classification.

THE NEED FOR A CLASSIFICATION OF CARTILAGE TYMPANOPLASTY METHODS

During the last 10 years, several new cartilage tympanoplasty methods have been published; some are similar to the palisades, the others are thin foils, thin plates, or thick

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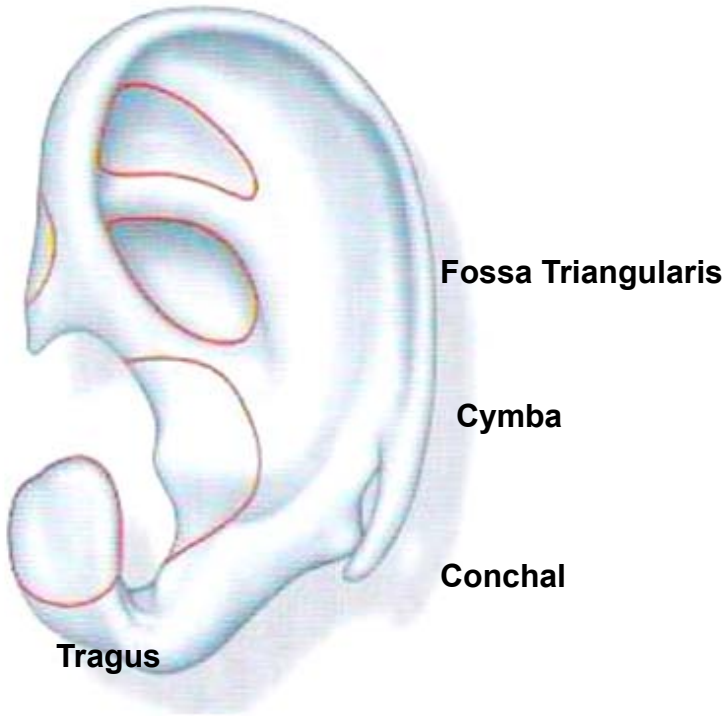
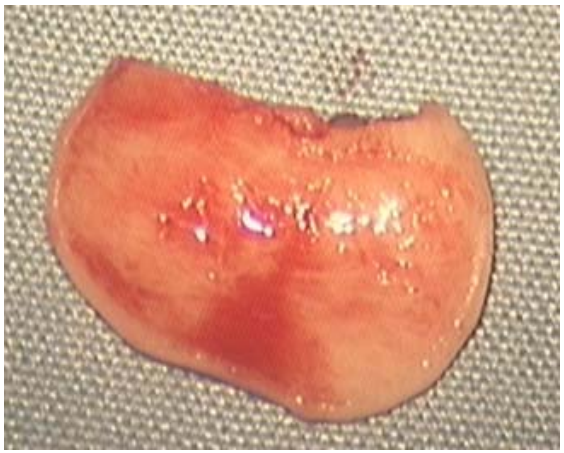
doi:10.1016/j.otohns.2008.09.021

Otolaryngol Head Neck Surg 2008;139:747-58

Harvest Sites





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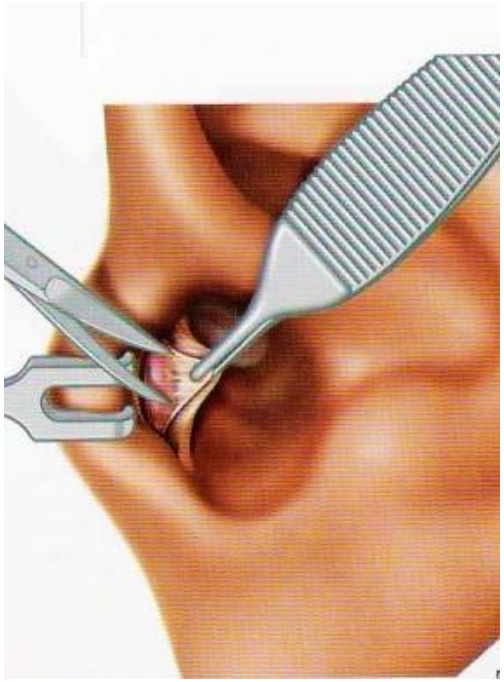
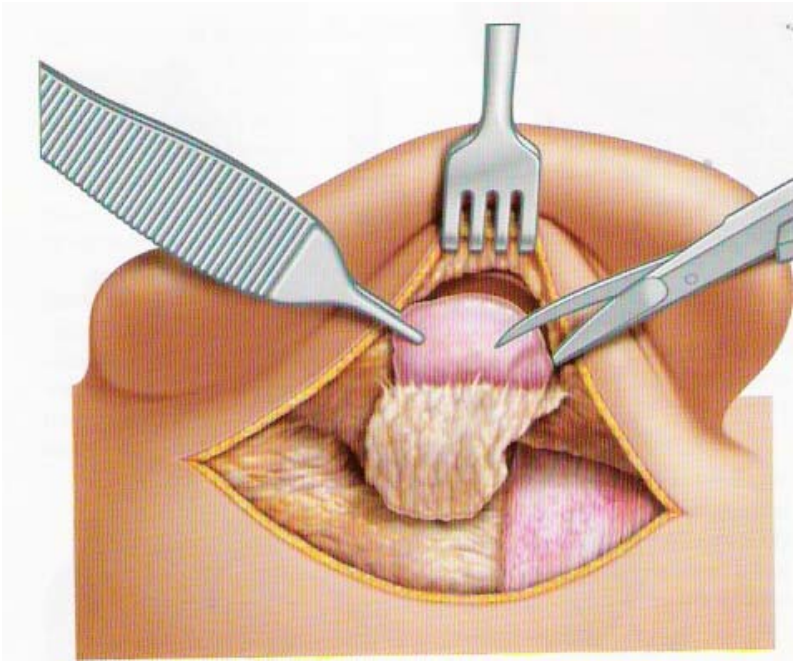


Transcanal

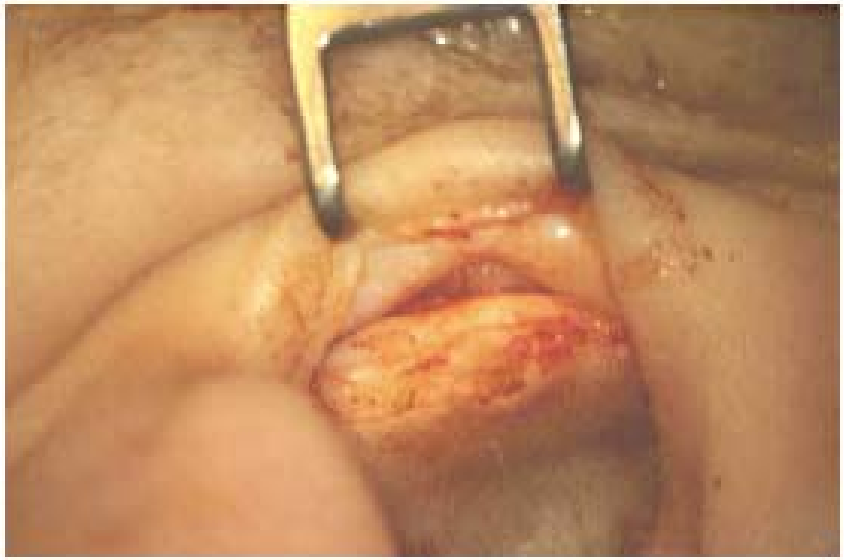


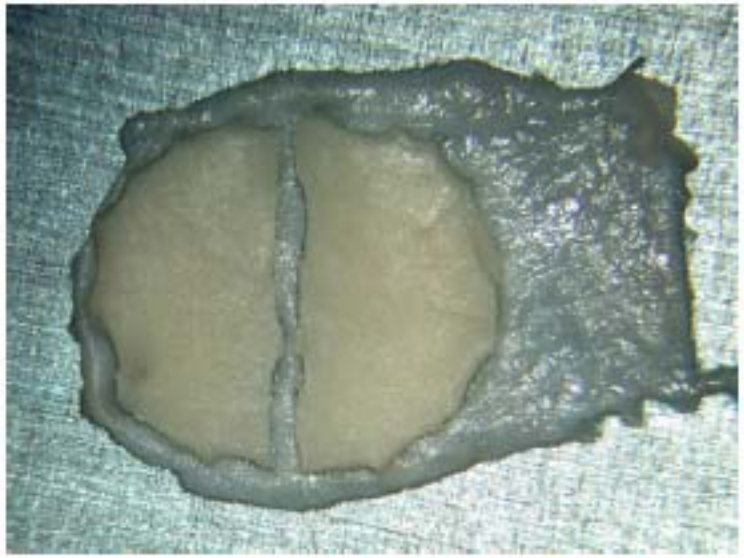
Post-auricular

Cartilage Tympanoplasty

- Perichondrium Cartilage Island Grafts
- Shield Grafts

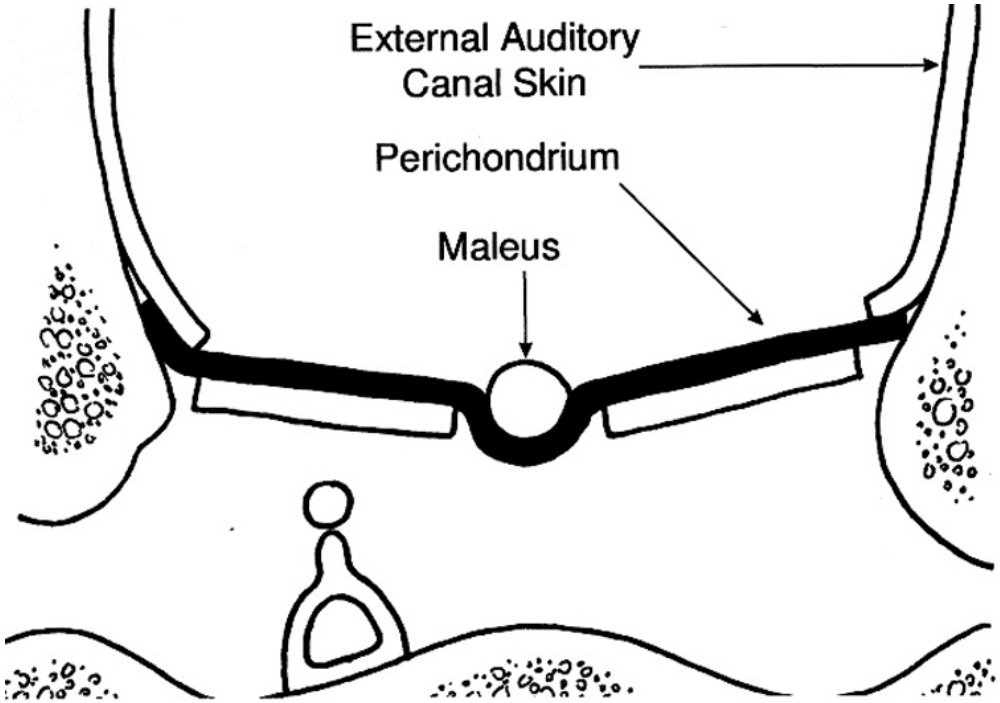
Perichondrium Cartilage Island Grafts





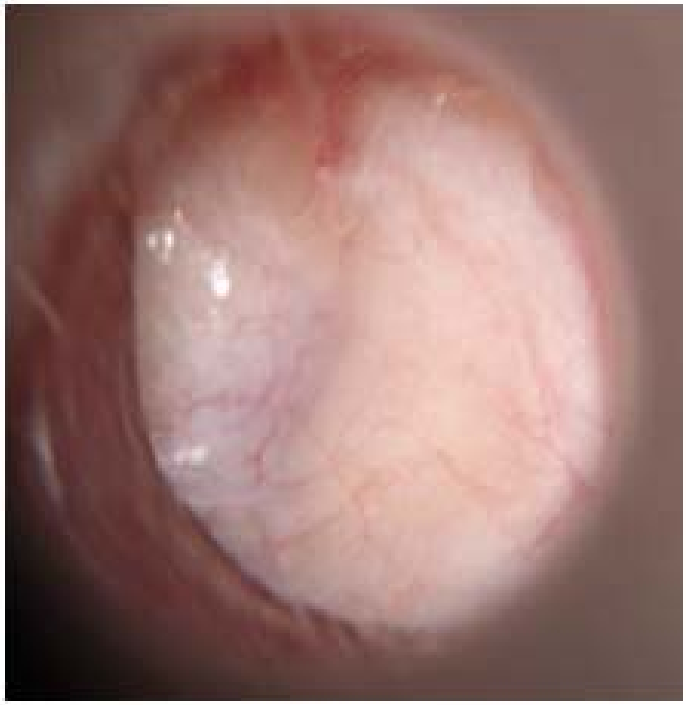
Otolaryngol Clin N Am 2006;39(6):1161-76.

Perichondrium Cartilage Island Grafts



Otolaryngol Clin N Am 2006;39(6):1161-76.

Perichondrium Cartilage Island Grafts



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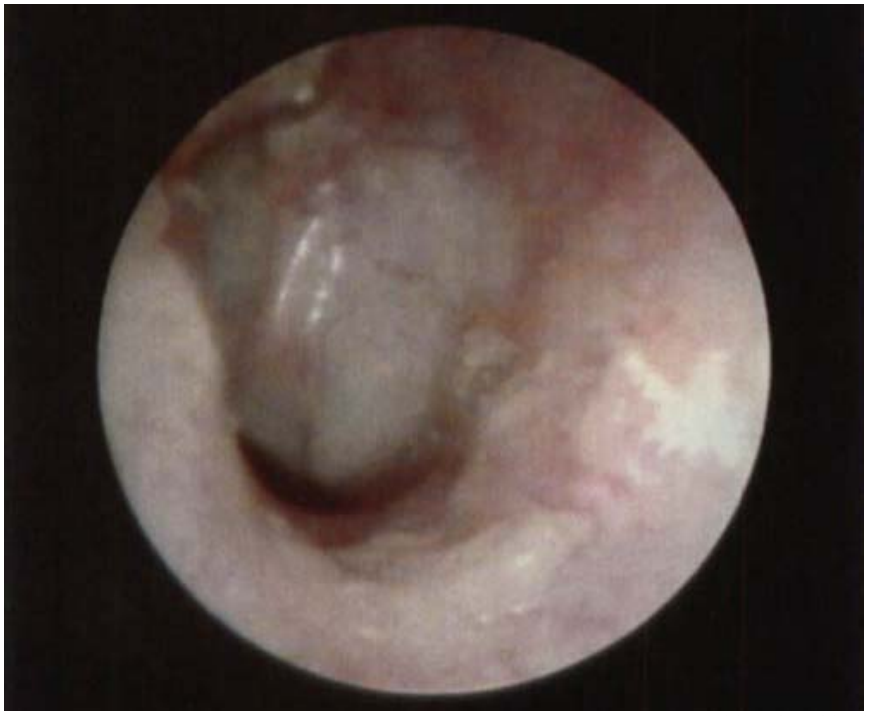
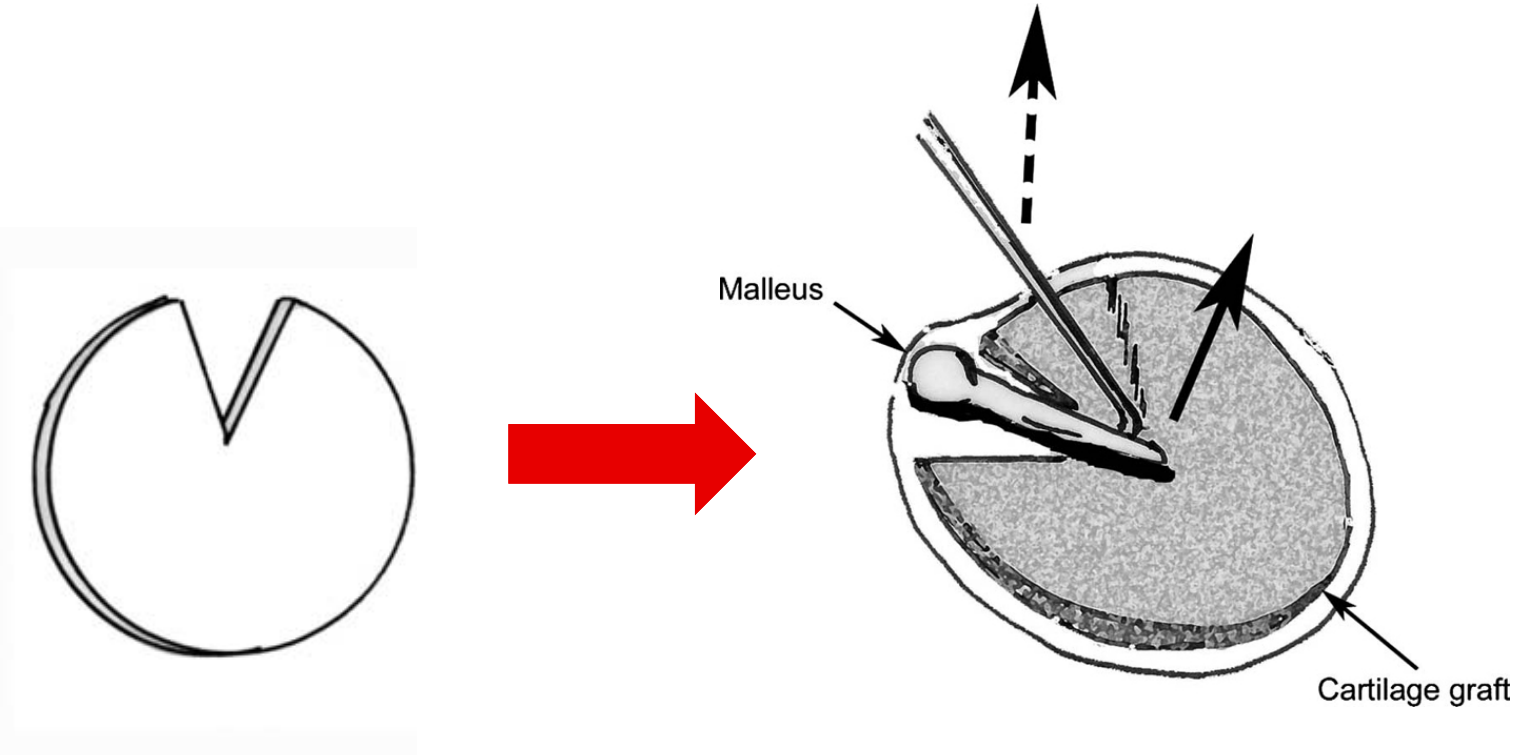


Laryngoscope 1997;107:1094-99.

Cartilage Tympanoplasty

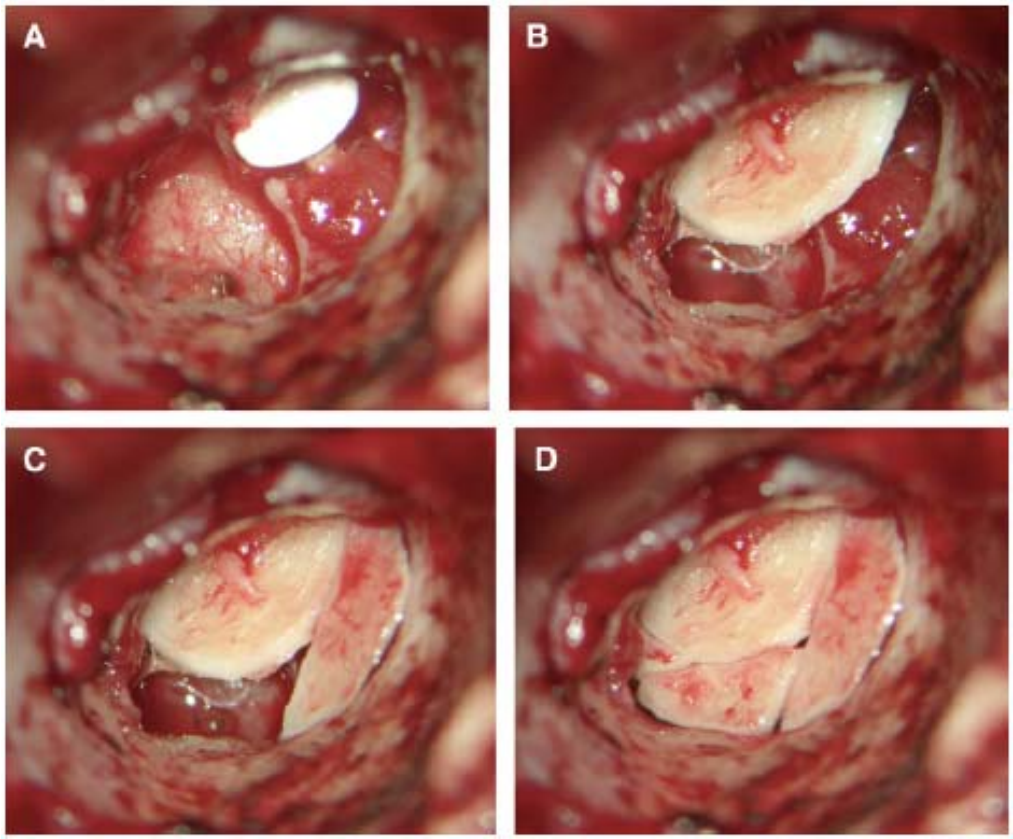
- Perichondrium Cartilage Island Grafts
- Shield Grafts

Shield Grafts



Otol Neurotol 2005; 26:838-41.

Shield Grafts



Otolaryngol Clin N Am 2006;39(6):1161-76.

Cartilage Typanoplasty - Disadvantages

- Creates opaque tympanic membrane
- Limits postoperative surveillance
- Difficult to place PE tube – Laser assisted
- CWD tympanomastoidectomy remains an option

Surgical Management

- Myringotomy and Tube
- PE tube with cartilage graft
- Cartilage tympanoplasty
- Balloon dilation eustachian tuboplasty

Balloon Dilation Eustachian Tuboplasty

Sivola and Poe (2014)

- 41 patients
- 80% able to valsalva post treatment
- None required replacement of tube

Otolaryngol Head Neck Surg 2014; 151(1) 125–130

Kivekas and Poe (2015)

- Histopathologic changes
- Thinning of mucosa, crush injury to submucosa and lymphocytic infiltrates
- Replaced with healthy epithelium and thinner layer of fibrous tissue

Laryngoscope 2015; 125(2):436-41

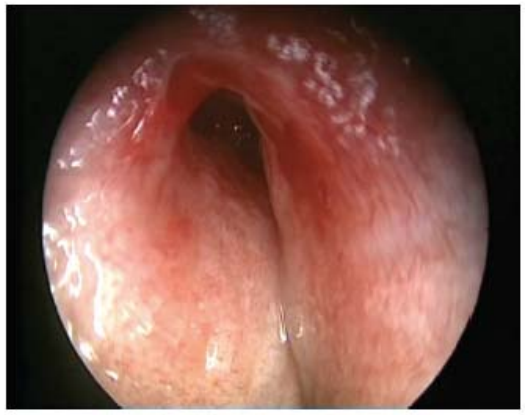
Balloon Dilation Eustachian Tuboplasty

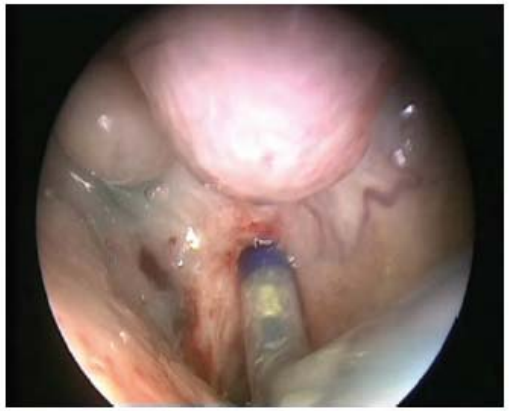
Poe (2011)

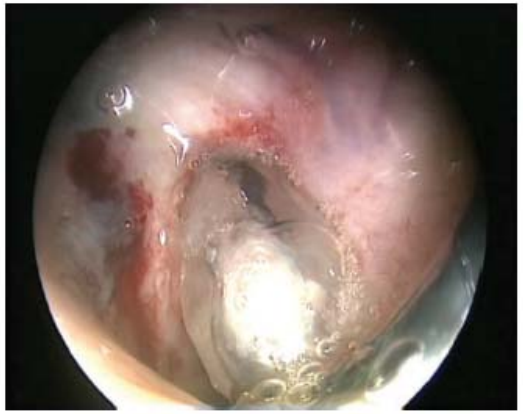
- Use of sinus balloon to dilate cartilagenous eustachian tube
- 11 Pts with longstanding COME and inability to valsalva
- Inflation to maximum of 12 atm for 1 min
- All Pts able to autoinsufflate following procedure

Balloon Dilation of the Cartilaginous Eustachian Tube

Dennis S. Poe, MD[1,2], Juha Silvola, MD, PhD[3], and Ilmari Pyykkö, MD, PhD[3]







Otolaryngol Head Neck Surg 2011;144(4):563-69.

Summary

- The atelectatic ear remains a difficult problem to treat
- Management depends on extent of disease
- Improving eustachian tube function should be initial focus
- OK to observe a stable ear
- Surgery recommended in presence of cholesteatoma or progressive changes
- Future treatments for ETD are underway

Relation of Laryngeal Botox Dosage to Patient Age, Vitality and Socioeconomic Issues

David Young, BA
Lucinda Halstead, MD
Medical University of South Carolina
Department of Otolaryngology, Head and Neck Surgery

Introduction

- Laryngeal dystonia
  - ADSD
  - ABSD
  - +/- tremor
- Prevalence of 3-6 per 100,000
- Women > Men

History of treatment

- Speech therapy/ psychotherapy
- 1976: Dedo *et al* and RLN resection
- 1984: Blitzer *et al* and botulinum toxin

Timeline:

- Time to diagnosis: 4.43 years
  - (Johns III, MM, *Unpublished data)*

- # of injections to find optimal dose: 1-5 injections
  - (Holden et al., 2007)

Botulinum Toxin, type A

- Considerable variability between practitioners
  - (Eskander et al., 2010)
  - Starting dose and titration vary considerably
  - 1-5 injections = 3 – 12+ months before consistent dose regimen achieved
- Presentation to treatment: 4.5 to 6 years

Current Literature

- Current literature has looked extensively at:
  - *Effectiveness* of BTX for SD
    - (Blitzer et al., 1998; Lundy et al., 1998; Tisch et al., 2003; Cannito et al., 2008; Helmstaedter et al., 2008; Vasconcelos et al., 2009; Blitzer, 2010; Braden et al., 2010; Tanner et al., 2011)
  - Longitudinal outcomes
    - (Blitzer et al., 1998; Blitzer, 2010; Novakovic et al., 2011)
  - Change in dose over time
    - (Holden et al., 2007; Birkent et al., 2009)
- Few have looked at factors that impact optimal dosage
    - (Vasconcelos et al., 2009; Tanner et al., 2011)

Our question

- How are patient age, BMI, and vitality related to the optimal effective dose of BTX?
- Does cost factor into the variability of BTX dosage?

Study Design

- Retrospective chart review
  - Age, BMI
- All patients took SF-36 survey and answered questions about cost

Subject Selection

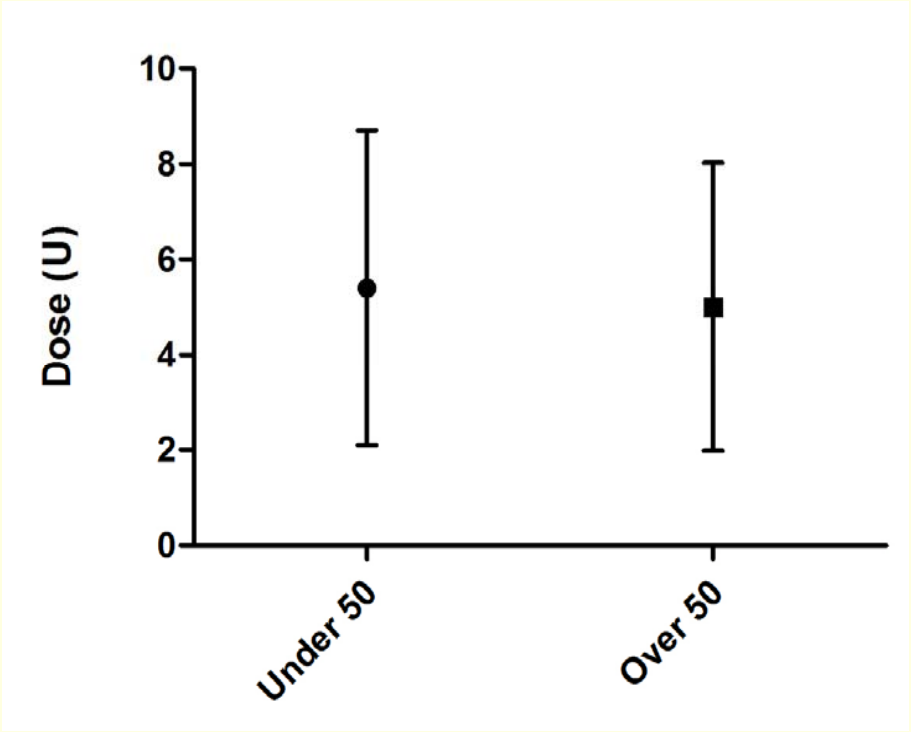
- 95 unique patients treated in our Botox clinic over 5 months
  - MUSC is the only laryngeal BTX clinic in SC
- Subjects selected based on:
  - 5+ injections of BTX with stable effective dose for at least 3 injections
  - ADSD and Tremor only
  - TA muscle only
    - Included unilateral and bilateral injections

Subject Demographics

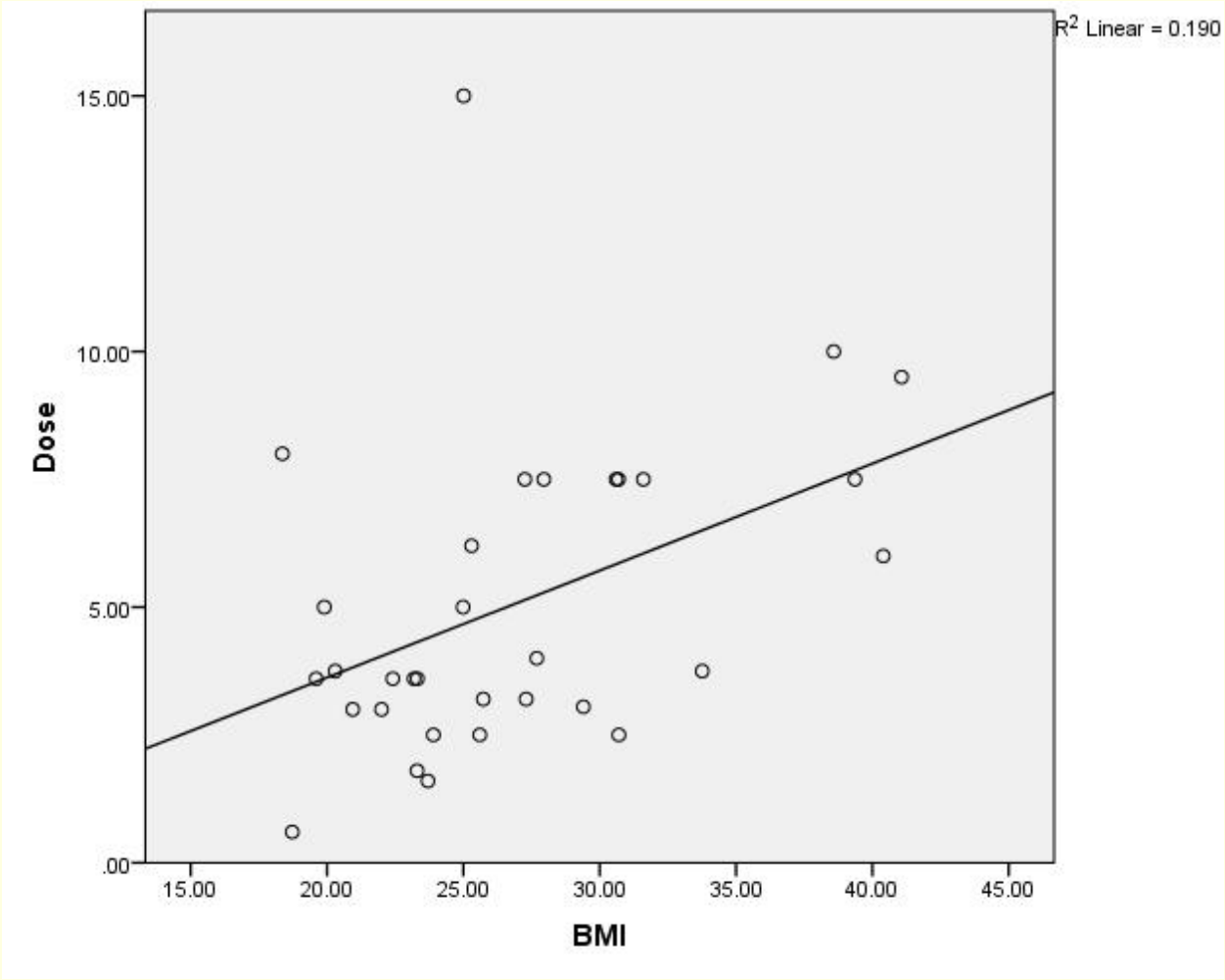
	ADSD	Tremor
# of subjects	n=18	n=14
Mean Age	58 ± 13	70 ± 10
Age Range	33-77	50-89
Gender	15 Female 3 Male	14 Female
Unilateral TA injections	5	8
Bilateral TA injections	13	6

Age and Effective Dose

- Grouped patients by age
- Compared with Mann-Whitney U test
  - *p= 0.54*
- Consistent with other published findings
  - (Vasconcelos et al., 2009)



Association of BMI and Effective Dose



Spearman's
r_s=0.42

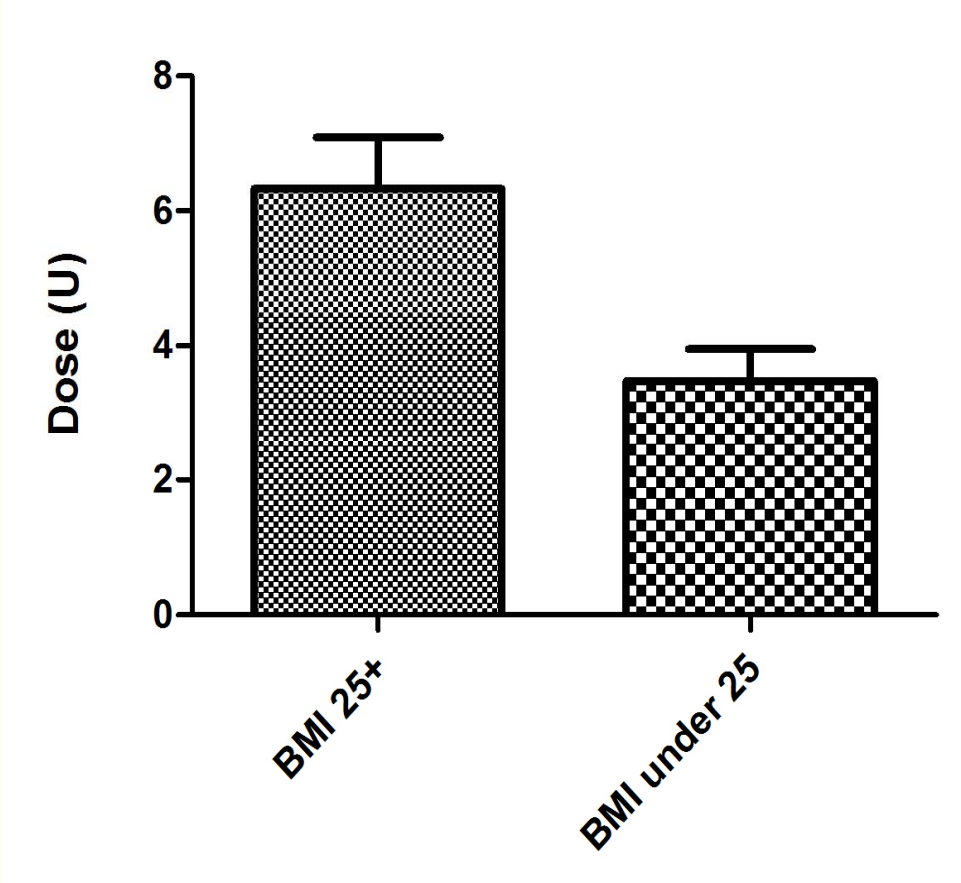
p=0.017

BMI and Effective Dose

- Divided patients into 2 groups:
  - BMI of less than 25
  - BMI of greater than 25
- Compared with Mann-Whitney U test

BMI and Effective Dose

- BMI over 25:
  - Median = **6.85 units**
- BMI under 25:
  - Median = **3.6 units**
    - *p=0.012*



BMI and Effective Dose

- Strong association between BMI and effective BTX dose
  - We believe this to be the first report in the literature

Influence of Vitality on Dose

- Used the SF-36 questionnaire to measure:
  - Overall health
  - Mental health
  - Physical health

Influence of Vitality on Dose for both ADSD and Tremor Combined

	Spearman's r	p value	Significant?
Overall Health	r = 0.22	p= 0.23	No
Physical Health	r = 0.20	p= 0.27	No
Mental Health	r = 0.14	p = 0.46	No

Vitality: Differences in ADSD and Tremor Groups

- Tremor group is older than ADSD group
  - Median age ADSD: 60.5 yrs
  - Median age Tremor: 72.0 yrs
    - p = 0.009
- Tremor group had a lower overall SF-36
  - Median SF-36 ADSD: 88.5
  - Median SF-36 Tremor: 71
    - p= 0.007

Influence of Vitality on BTX Dose: Differences in ADSD and Tremor

	ADSD (n=18)			Tremor (n=14)		
	r =	p =	Sig?	r =	p =	Sig?
Overall Health	0.50	0.04	Yes	-0.30	0.30	No
Physical Health	0.51	0.03	Yes	-0.34	0.24	No
Mental Health	0.43	0.07	No	-0.35	0.23	No

Summary of Vitality's Influence on BTX Dose

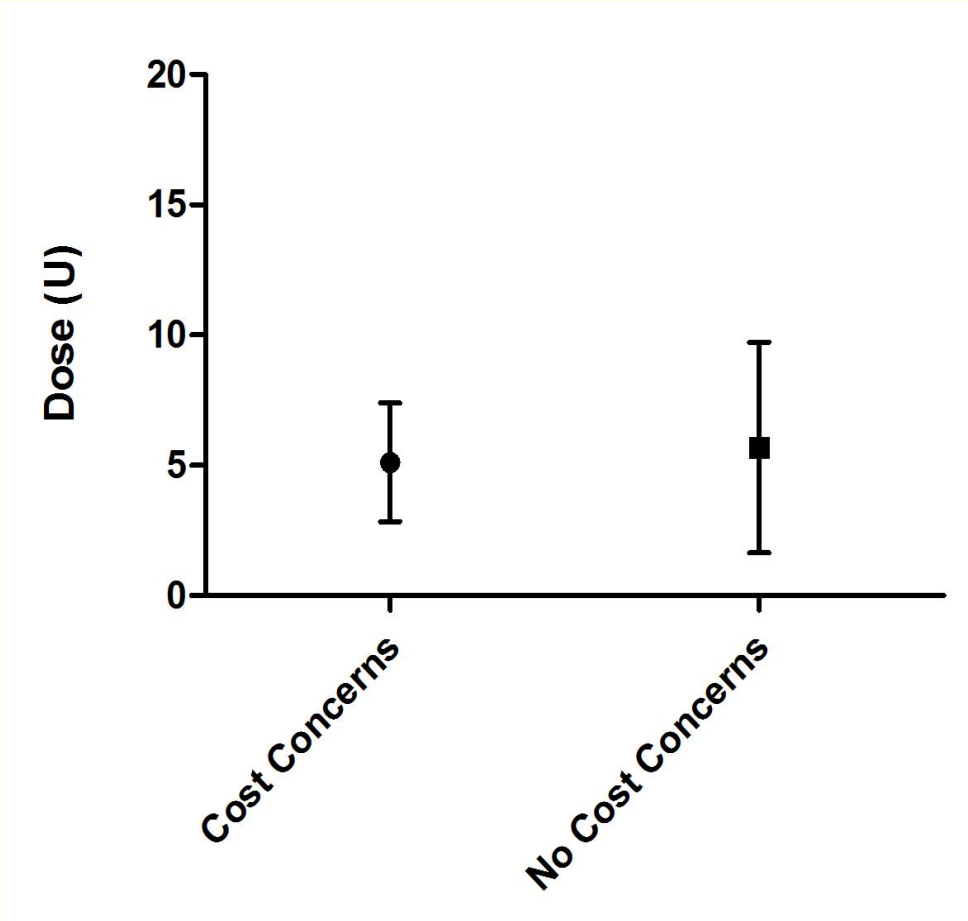
- Strong *positive* correlation between dose and overall health among the ADSD group
  - Increased activity = increased dose

Socioeconomic Factors

- Anecdotal evidence suggests that cost may factor into BTX dose
  - Some patients ask for higher doses to prolong treatment effect for financial reasons
  - 31% of our patients reported that cost had influenced their treatment in some way
    - 39% of ADSD group
    - 12% of Tremor group

Impact of Cost on BTX Dose in ADSD Patients

- No difference in median dose between cost-affected/non-affected groups
  - p=0. 89



Cost as a Confounding Variable

- Controlling for cost has minimal impact on correlations involving BMI and Overall health of ADSD patients
- Small sample size of subgroups

Discussion

- Our data indicate 2 factors, BMI and SF36, can be used to more effectively determine a patients optimal Botox dose.
  - First time these 2 factors have been examined in the literature
- It appears from our small sample that statistically, cost plays a minimal confounding role

Zinc as a Possible Mechanism

- Botulinum toxin is a zinc-dependent metalloproteinase (Simpson et al., 2001)
- Small RCT showed zinc increased BTX effectiveness (Koshy et al., 2012)

Zinc and BMI

- Inverse relationship between zinc levels and body fat
  - (Chen et al., 1996)
  - (Ortega et al., 2012)
- Larger patients may require higher doses

SF-36 Score and Zinc

- People with higher scores are more physically active

- Effect of increased activity on zinc levels:
  - Increase in serum zinc
  - Decrease in intracellular zinc
    - (Lukaski et al., 1984)
      (Lukaski, 2000)
      (McDonald and Keen, 1988)

Discussion

- Higher BMI/SF36
  - Higher starting dose
  - Faster titration up to optimal dose
- Low BMI/SF36
  - Decreased starting dose
  - Faster titration down to tolerable dose
- Could lead to fewer adverse events
  - Increased patient quality of life

Thank You

Opioid Prescribing for Acute and Chronic Pain

Christopher T. Grubb, M.D.

Anesthesiology and Pain Management

Greenville, North Carolina

East Carolina Anesthesia Associates, www.ecaa.com

East Carolina Pain Consultants, www.ecpc1.com

Prescription Medication Abuse: An Epidemic with Many Potential Causes

- Prescribing controlled medications without adequate screening or monitoring
- Dramatically increased rates of prescribing opioid analgesics
  - Expansion into chronic non-malignant pain
  - Past criticism of prescribers as "opioid-phobic"
  - Regulatory changes (e.g. Pain as the "5th vital sign")
- *Public expectations* regarding treatment
  - Preference for "pill to get rid of pain" vs pain management
  - Perception that pain treatment=opioid treatment
  - Preference for quick fix rather than comprehensive and multidisciplinary care
  - History of opioid effectiveness for acute pain syndromes

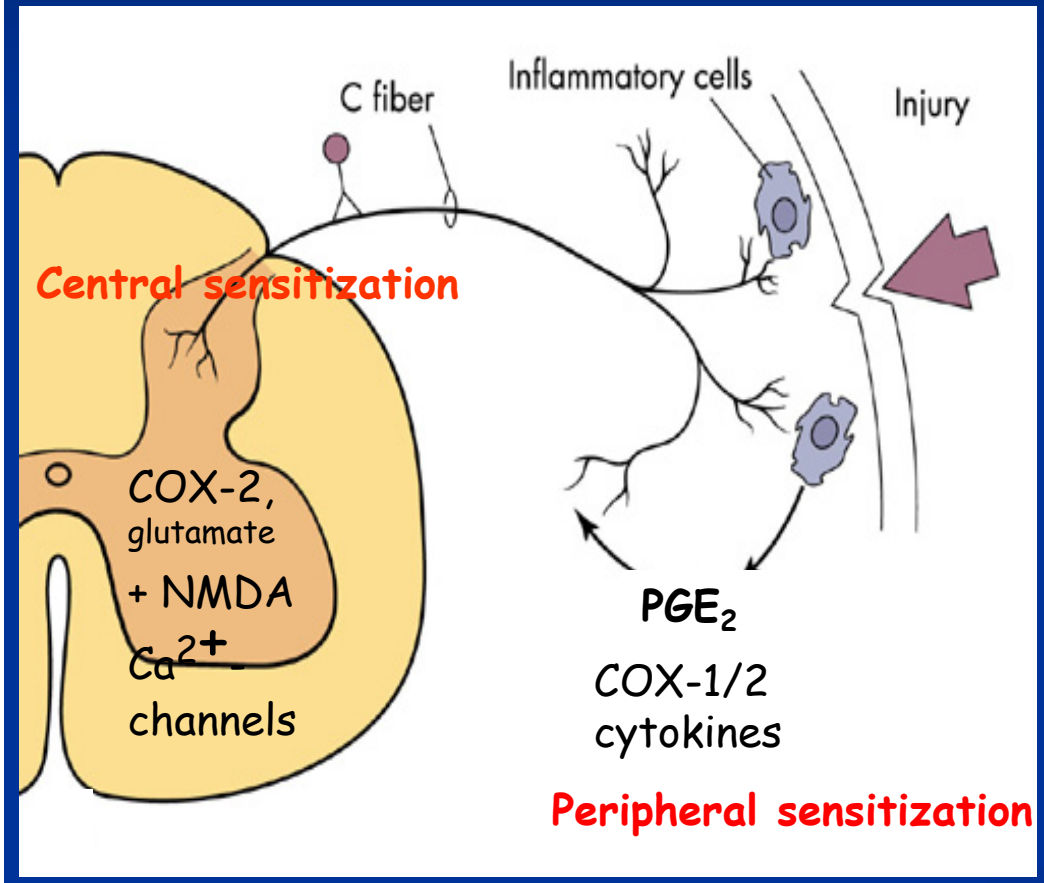
Classification of Pain

- *Acute Pain*: Pain persisting up to 3 months, usually associated with recent tissue injury (such as after surgery)
- *Chronic Pain*: Pain persisting for longer than 3-6 months; usually the result of a pathological neurologic cascade (likely during the acute pain phase)
- **Short-term treatment of acute pain can improve long-term outcomes**

Central Sensitization

- Also known as *CNS wind-up*
- C-fibers stimulate release of inflammatory mediators in dorsal root ganglion (DRG)
- Involves prostanoids, cytokines, Ca^{2+}-channels, TNF-α, NMDA, and others
- Prolonged central sensitization is theorized to be the root cause of most chronic pain conditions
- Goal: Prevent/Treat CNS sensitization

Target: Dorsal Root Ganglion and Spinal Cord



Injury (release of mediators)

↓

Peripheral sensitization

↓

Central sensitization

↓

Worsening Pain

Woolf CJ. Mechanism-based pain diagnosis: issues for analgesic drug development. Anesthesiology 2001; 95: 241-9

Alternatives for Acute Pain

- Tramadol equally effective as codeine/APAP for post-tonsillectomy pain in children[1]
- Selective NSAIDs
  - Diclofenac demonstrated no increased risk of secondary hemorrhage in retrospective study[2]
  - Celecoxib has no affect on platelets at supratherapeutic doses[3]
  - Equally effective as hydrocodone/APAP 7.5/750 after sinus surgery[4]

[1] Friedrichsdorf SJ, et al. J Opioid Manag. 2015 Jul-Aug;11(4):283-94.

[2] McKean SA. J Otolaryngol Head Neck Surg. 2008 Aug;37(4):577-81.

[3] Leese, PT, et al. J Clin Pharmacol. 2000. Feb;40(2):124-132.

[4] Church, CA, et al. Laryngoscope. 2006 Apr;116(4):602-6.

Classification of *Chronic* Pain

- *Nociceptive* –
  - Constant dull, aching, throbbing
  - Examples: bone/joint/muscle pain, cancer pain
- *Neuropathic* –
  - Burning, stinging/tingling/prickly, sharp, lancinating
  - Examples include radiculopathies, neuralgias
  - Due to central/peripheral nervous system pathology
    - Synaptic hyperactivity of nociceptors and interneurons
  - *Relatively resistant to opioids*

Nociceptive Pain Therapy

- NSAIDs – *Celecoxib* safe for chronic use, safe to take concomitantly with aspirin therapy
- Tramadol 100mg q6h
- Tylenol 1000mg q6h
- Physical therapy – maximize range of motion
- +/- opioids if patient proves efficacy by *increasing functioning*

Neuropathic Pain Therapy

- NSAIDs – scheduled dosing
- Antiepileptics – pregabalin (Lyrica) 150-600mg, gabapentin 1800-3600mg (*1800 mg/d minimum*)
- SNRI's – amitriptyline 25-200mg, duloxetine (Cymbalta) 60mg,
- Lidoderm patches (up to three at a time)
- Neuromodulation – Spinal Cord Stim., TENS
- **NO OPIOIDS** (except tramadol 100mg q6h prn)

Symptom-Control versus Mechanism-Based Pain Therapy

- Symptom-control paradigm is obsolete
- Newly-discovered pain mechanisms are emerging in medical literature
- Most mechanisms involve inflammatory response to injury, or neuro-inflammation
- Pain mechanisms are mediated neurologically, primarily at the *dorsal root ganglion* (DRG) and spinal cord

Clinical Interview: Pain Characteristics & Treatment History

Description of pain

Location | Intensity | Quality | Onset/ Duration | Variations / Patterns / Rhythms

What relieves the pain?

What causes or increases pain?

Effects of pain on physical, emotional, psychosocial function

Patient's pain & functional goals

Heapy A, Kerns RD. Psychological and Behavioral Assessment. In: Raj's Practical Management of Pain. 4th ed. 2008;279-95. Zacharoff KL, et al. Managing Chronic Pain with Opioids in Primary Care. 2nd ed. Newton, MA: Inflexion, Inc., 2010.

Limitations of Opioids

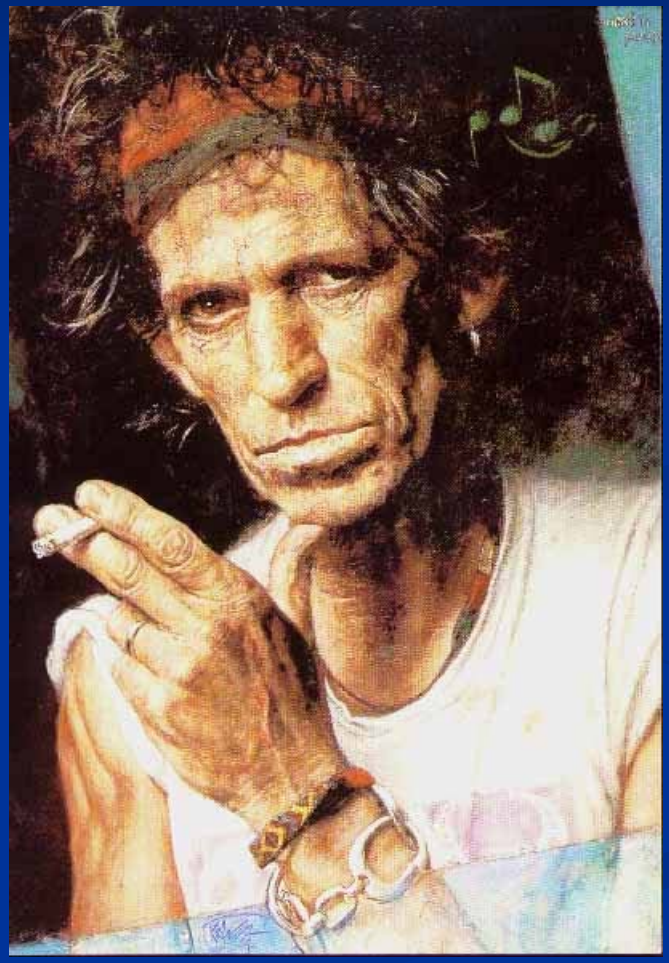
- SIDE EFFECTS – nausea, itching, sedation, constipation, respiratory depression (especially in sleep apnea patients)
- Risk of addiction, diversion, and overdose
- Risk of *pseudo*-addiction . . .
- Minimal effect on movement-evoked pain
- May *worsen* neuropathic pain – spinal morphine increased hyperalgesia in burn-injured rats*

* Van Elstraete AC et al. *Anesth Analg* 2005; 101: 1750-6.

Primary Goal of Opioid Pain Therapy: Functional Improvement

- Returning to work
- Ability to perform ADL's
- Improved relationships, especially with family
- Participating in recreational activities
- Goal should NOT be to eliminate pain
- Alleviating pain is LESS important than increasing physical functioning!

Consequence of Chronic Opioid Use



Initiating Treatment

Prescribers should regard initial treatment as a therapeutic trial

May last from several weeks to several months

Decision to proceed with long-term treatment should be intentional & based on careful consideration of outcomes during the trial

- Progress toward meeting therapeutic goals
- Presence of opioid-related AEs
- Changes in underlying pain condition
- Changes in psychiatric or medical comorbidities
- Identification of aberrant drug-related behavior, addiction, or diversion

Chou R, et al. *J Pain.* 2009;10:113-30

Clinical Interview: Patient Medical History

Illnesses relevant to the effects or metabolism of opioids:
Pulmonary disease, cognitive impairment
Opioid metabolism – Hepatic disease, renal disease

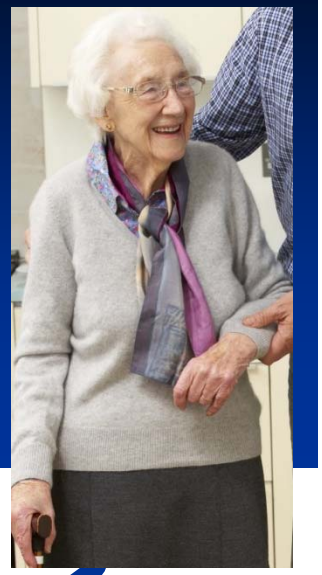
Illnesses possibly linked to substance abuse:

- Hepatitis
- HIV
- Tuberculosis
- Cellulitis
- STIs
- Trauma, burns
- Cardiac disease
- Pulmonary disease

Chou R, et al. *J Pain*. 2009;10:113-30. Zacharoff KL, et al. *Managing Chronic Pain with Opioids in Primary Care*. 2nd ed. Newton, MA: Inflexion, Inc., 2010. Department of Veterans Affairs, Department of Defense. *VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain*. 2010.

Special Considerations: Elderly Patients

Does patient have medical problems that increase risk of opioid-related AEs?



Respiratory depression more likely in elderly, cachectic, or debilitated patients

- Altered kinetics due to poor fat stores or altered clearance
- Monitor closely, particularly when initiating & titrating ER/LA opioids, as well as when other CNS depressants are given concomitantly
- Reduce starting dose to 1/3 to 1/2 the usual dosage in debilitated and opioid-naive patients
- Titrate dose cautiously

Older adults are more likely to develop constipation

- Routinely initiate a bowel regimen before it develops

American Geriatrics Society Panel on the Pharmacological Management of Persistent Pain in Older Persons. *J Am Geriatr Soc.* 2009;57:1331-46. Chou R, et al. *J Pain.* 2009;10:113-30.

Challenge: The Friday Afternoon Patient

Red Flag:

Patient requests new opioid or a dosage increase at an inopportune moment for the provider

It's 4 pm on Friday and you are four patients behind schedule. Mr. Kingston arrives without an appointment and asks you to increase his current dosage of hydrocodone because it's not relieving his pain. It would take you two minutes to say yes.

Action:

Check CSRS database.

Employ opioid-risk screening tools

Utilize urine drug testing

Be willing to say no

Challenge: The Delayed Surgery

Red Flag:

Patient may be stalling to continue an opioid regimen

Ms. Jones says she needs opioids to manage her pain until she can have surgery. She reports continued delays in getting to surgery. You phone the surgeon and discover that no date has been set and that she has cancelled several appointments.

Action:

Set expectations for time limitations.
Offer non-opioid therapies.
Consider referral to addiction specialist.

Pearls for Practice

- Document EVERYTHING
- Conduct a Comprehensive H&P

(General and pain-specific)

- Assess Risk of Abuse
- Weigh Risks with Expected Benefits
- Determine Whether a Therapeutic Trial is Appropriate

North Carolina Medical Board Policy for Use of Opiates in Pain (updated June 2014)

NCMB statement:

Patient evaluation and risk stratification

- NC CSRS should be part of every new evaluation and monitoring

Development of treatment plan and goals

- Avoid excessive or unnecessary use of medications

Informed consent and treatment agreement

Consider alternatives before initiating opioid trial

Periodic drug testing

Recognize risk of diversion, misuse and abuse

Consultation and referral

Documentation

Ensure Patients Understand Limitations of Opioid Therapy

Emphasize BEFORE beginning *trial* of opioid therapy:

-Pain treatment does not *equal* opioids.

-Opioids are not equally effective for all types of pain.

-Opioids are rarely sufficient as stand-alone therapy.

-Primary goal is functional improvement *(not eliminating pain*)

-Opioids have significant risk: impairment/dependence/overdose.

Therefore: Continuing opioid treatment depends on:

-Demonstrated *efficacy* (improved function and pain management)

-Demonstrated *safety* (no aberrant medication behaviors)

Primum Non Nocere
"First, Do No Harm"

High risk of drug abuse	Concomitant CNS depressants (especially benzo's)	Obstructive Sleep Apnea or significant pulmonary disease
Long-acting opioids for acute or short-term pain	Opioid dose based on severity or character of pain	Opioid dosing without consideration of opioid tolerance

Assess Risk of Abuse, Including Substance Use & Psychiatric Hx

Obtain complete history of current or past substance use

- Prescription drugs
- Illegal substances
- Alcohol & tobacco
  - Substance abuse history does not prohibit treatment with opioids, but may require additional monitoring & expert consultation/referral
- Family Hx of substance abuse & psychiatric disorders
- Hx of sexual abuse

Social history is also relevant…

Employment, cultural background, social network, marital history, legal history, & other behavioral patterns

NC Controlled Substances Reporting System (CSRS)

- Clinically-oriented monitoring program
- Provides state-wide data on dispensed controlled meds
- May be accessed by prescriber or other designated professional (PA or NP)
- Useful tool for initial risk assessment and for ongoing monitoring
- Information and registration available online: https://nccsrsph.hidinc.com

Risk Stratification for Opioid Therapy

	Low Risk	Medium Risk	High Risk
Etiology of Pain	Clear/Identified		Vague/Non-specific
Substance Abuse	Negative family or personal history	Past history but stable recovery	Active abuse or addiction
Psychiatric History	None	Few/stable	Multiple/unstable
Environment	Stable/Supportive Resources		Unstable/ Few resources
Activity Engagement	Employed, active, engaged in other therapies		Unemployed, Inactive, takes only opioids for pain
CSRS	One prescriber/Opioids low dose/	One prescriber/Moderate dose/Benzos	Multiple prescribers/High dose/Benzos/

Abuse and Dependence: "Addiction"

Use of a medication outside the normally accepted standard for that drug.

Recurrent problems in multiple life areas.

Continued use in spite of negative consequences.

Preoccupation with the drug, drug seeking behavior.

Loss of control of use.

Tolerance or physical dependence may or may not be present.

Physical dependence is not the same as abuse or addiction!

Adapted from DSM IV, APA,1994.

Aberrant Medication Taking Behaviors: Differential Diagnosis

- Misuse (confusion, poor understanding of regimen or rules)
- Pseudoaddiction[1] (seeking ongoing or better pain relief from a particular drug or class of drugs)
- Opioid-resistant pain (or pseudo-resistance)[2]
- Opioid-induced hyperalgesia[3] (unrelieved or worsening pain with escalating opioid doses)
- Abuse/Addiction
- Chemical coping (self-medication of psychological stress)
- Diversion

Weissman DE, Haddox JD. 1989; 2 Evers GC. 1997; 3 Chang C et al 2007

Challenge: The Broken Stereotype

Red Flag:

Making assumptions about a patient's risk without objective evidence

Ms. Yeun seems like a "good" patient. She has never abused opioids previously. She has been in the practice a long time, has never been a problem, and in fact, is rather enjoyable. She always brings Christmas cookies for the staff around the holidays.

Action: Require all patients receiving opioids to follow a treatment plan and adhere to defined expectations. Evaluate risk in all patients. Use patient-provider agreements, contracts, or other tools.

Reasons for Discontinuing Opioids

No progress toward therapeutic goals

Intolerable & Unmanageable AEs

Pain level decreases in stable patients

Nonadherence or unsafe behavior

- 1 or 2 episodes of increasing dose without prescriber knowledge
- Sharing medications
- Unapproved opioid use to treat another symptom (e.g., insomnia)

Aberrant behaviors suggestive of addiction and/or diversion

- Use of illicit drugs or unprescribed opioids
- Repeatedly obtaining opioids from multiple outside sources
- Prescription forgery
- Multiple episodes of prescription loss

Informed Consent

Before initiating a trial of opioid analgesic therapy, confirm patient understanding of informed consent to establish:

- **Analgesic & functional goals**
- **Expectations**
- **Potential risks**
- **Alternatives to opioids**

The potential for:

- Common opioid-related AEs (e.g., constipation, nausea, sedation)
- Other serious risks (e.g., abuse, addiction, respiratory depression, overdose)
- AEs after long-term or high-dose opioid therapy (e.g., hyperalgesia, endocrine or sexual dysfunction)

Consider Implementing a Patient-Prescriber Agreement (PPA)

- Obtain opioids from a single prescriber
- Fill opioid prescriptions at a designated pharmacy
- Safeguard opioids
    - Do not store in medicine cabinet
    - Keep locked (e.g., use a medication safe)
    - Do not share or sell medication
- Commitments to return for follow-up visits
- Comply with appropriate monitoring
    - e.g., random UDT & pill counts
- Frequency of prescriptions
- Enumerate behaviors that may lead to opioid discontinuation
- An exit strategy

Monitor Adherence and Aberrant Behavior

- Recognize & document aberrant drug-related behavior
- State PDMPs, where available
- Urine drug testing (UDT)
    - Positive for non-prescribed controlled substances
    - Positive for illicit substance
    - Negative for prescribed opioid

Family member or caregiver interviews

Opioid monitoring questionnaires

- Medication reconciliation (e.g., pill counts)

Address Aberrant Drug-Related Behavior

Behaviors that are **less** indicative of aberrancy

- **Unsanctioned dose escalations or other noncompliance with therapy on 1 or 2 occasions**
- **Unapproved use of the drug to treat another symptom**
- **Openly acquiring similar drugs from other medical sources**

Behaviors that are **more** indicative of aberrancy

- **Multiple dose escalations or other noncompliance with therapy despite warnings**
- **Prescription forgery**
- **Obtaining prescription drugs from non-medical sources**

Interpretation of UDT Results

Positive Result

Demonstrates recent use

- Most drugs in urine have detection times of 1-3 d
- Chronic use of lipid-soluble drugs: test positive for ≥1 wk

Does not diagnose…

- Drug addiction, physical dependence, or impairment

Does not provide enough information to determine

- Dose taken, frequency of use, or degree of opioid tolerance

Negative Result

Does not definitively indicate diversion

- Can be more complex than presence/absence of drug in urine

May be due to maladaptive drug-taking behavior

- Bingeing, running out early
- Other factors: e.g., cessation of insurance, financial difficulties

Educate Parents: Not in My House

- Note how many pills in each prescription bottle or pill packet
- Keep track of refills for all household members
- If your teen has been prescribed a drug, coordinate & monitor dosages & refills
- Make sure friends & relatives—especially grandparents—are aware of the risks
- If your teen visits other households, talk to the families about safeguarding their medications

Methods of Opioid Disp

If collection receptacle, mail-back program, or take-back event unavailable, throw out in household trash

- Take drugs out of original containers
- Mix w/ undesirable substance, e.g., used coffee grounds or kitty litter
- Less appealing to children/pets, & unrecognizable to people who intentionally go through your trash
- Place in sealable bag, can, or other container
- Prevent leaking or breaking out of garbage bag
- Before throwing out a medicine container
- Scratch out identifying info on label

Pearls for Practice

- Anticipate and Treat Common Adverse Effects
- Use Informed Consent and Patient Provider Agreements
- Use UDT and CSRS as Valuable Sources of Patient Data
- Monitor Patient Adherence, Side Effects, Aberrant Behaviors, and Clinical Outcomes
- Refer Appropriately if Necessary

Summary

Prescription opioid abuse & overdose is a national epidemic. Clinicians must play a role in prevention

- Understand how to assess patients for treatment with opioids
- Be familiar w/ how to initiate therapy, modify dose, & discontinue use of opioids
- Know how to manage ongoing therapy with opioids
- Know how to counsel patients & caregivers about the safe use of opioids, including proper storage & disposal
- Be familiar with general & product-specific drug information concerning opioids