Zen and art of vocal mechanics: Unilateral Vocal Fold Paralysis

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- Non-Financial
  - Research focus relevant to the presentation topic

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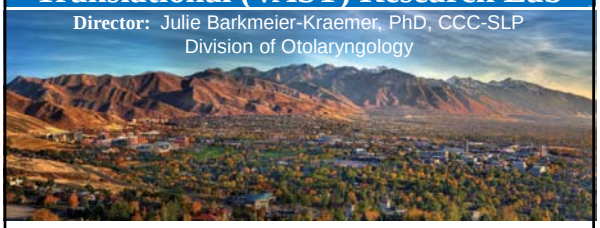

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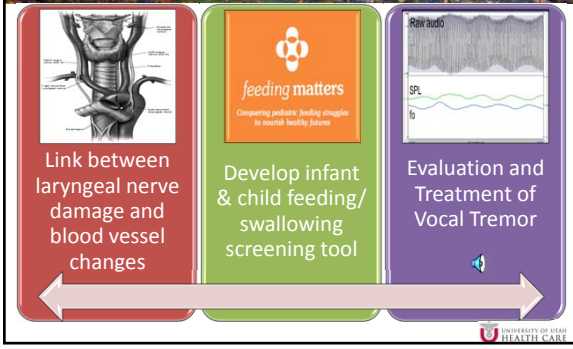

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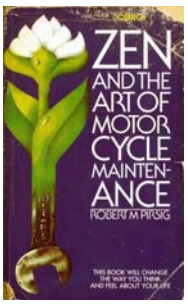
Background on the title of the talk

"You look at where you're going and where you are and it never makes much sense, but then you look back at where you've been and a pattern seems to emerge. And if you project forward from that pattern, then sometimes you can come up with something."

-Robert M Pirsig



Roadmap of Talk

- Review of laryngeal anatomy/physiology
- Vocal Fold Paralysis/Paresis: Background
  - Epidemiology
  - Etiologies
  - Clinical Characteristics
- Recurrent laryngeal nerve (RLN) research
  - What is so interesting about the nerve packaging?
  - The relationship between the RLN and aorta

Review of Laryngeal Anatomy/Physiology

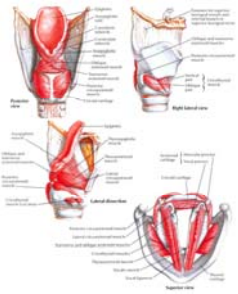


Image taken from:
http://ranzcrpart1.wikia.com/wiki/Larynx:Intrinsic_muscles

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Ianessa Humbert and Emily Plowman authored a book named Critical Thinking and the Art of Motorcycle Maintenance:

TEST POLL

TRUE

FALSE

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All of the following laryngeal muscles adduct the vocal folds EXCEPT:

Posterior cricoarytenoid

Thyroarytenoid

Interarytenoid

Lateral cricoarytenoid

Cricothyroid

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When this laryngeal muscle contracts, the vocal folds shorten:

Posterior cricoarytenoid muscle

Thyroarytenoid muscle

Interarytenoid muscle

Lateral cricothyroid muscle

Cricothyroid muscle

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This laryngeal muscle elongates the vocal folds when it contracts and is innervated by the Superior Laryngeal Nerve branch of the vagus nerve (CN X):

- Posterior cricoarytenoid muscle
- Thyroarytenoid muscle
- Interarytenoid musculature
- Lateral cricoarytenoid muscle
- Cricothyroid muscle

All of the following describe physiologic functions of the larynx EXCEPT:

- Regulates respiratory pressures and airflow during breathing and voice production.
- Protects the lower airway from food entry during swallowing through a sphincteric constriction produced by its three levels of folds.
- Is a frequent source of hypernasality due to poor adduction of the vocal folds.
- Serves as one of the articulators during speech production.

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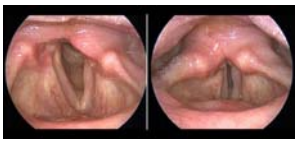
Vocal fold Paralysis/Paresis

- Voice Disorders affect 30% of U.S. adults (Roy, Merrill, Gray, Smith, 2005)
- **1%** of those seen for laryngeal problems have **laryngeal paralysis**
  - Similar to proportion of those diagnosed with laryngeal cancer (1.2% of laryngeal disorders)

(Cohen, Kim, Roy, Asche, & Courey, 2012)



https://www.bcm.edu/healthcare/care-centers/otolaryngology/conditions/vocal-fold-paralysis

Vocal Fold Paralysis/Paresis (VFP)

Example of Unilateral Vocal Fold Paralysis/Paresis

- Occurs when some or all of the intrinsic laryngeal muscles cannot contract resulting in impaired vocal fold movement

What is the difference between paralysis and paresis?

PARALYSIS

- Impaired neuromotor function of the larynx resulting in:
  - **Absent or severely reduced** laryngeal muscle fiber innervation/ activation indicated by
    - **Absent movement** of the arytenoid cartilage(s)
    - **Flaccidity** in tone

PARESIS

- Impaired neuromotor function of the larynx resulting in:
  - **Reduced** laryngeal muscle fiber innervation/activation indicated by
  - **Reduced mobility** of the arytenoid cartilages
    - Observe LEFT-RIGHT Vocal Fold Asymmetry, and
    - Incomplete Glottic Closure

Laryngeal EMG required for conclusive diagnosis

Etiologies

- **Surgical (iatrogenic)**
  - Cut nerve
  - Retraction of nerve (stretch & reduced tissue diameter)
  - Post-surgical edema -> ischemia\compression
- **Neoplasm**
  - Tumor(s) that compress against or invade the laryngeal nerve(s)
- **Idiopathic**
  - Depending upon clinical cohort, attributed to up to 42% of the vocal fold paralysis population
  - More frequently associated with those beyond age 45 years

Merati et al, 2006; Rosenthal et al, 2007; Sulica, 2008; Spataro et al, 2014

Vocal Fold Paralysis in Pediatric Populations

- Comprises 10% of all congenital laryngeal lesions
- Idiopathic = 36-47% (one of the top "causes")
- CNS etiology = 25-35% (typically brainstem level)
- Cardiothoracic surgery
  - Patent Ductus Arteriosis (PDA) Ligation Surgery
    - 8.8% incidence overall (Zbar et al, 1996)
    - 25% incidence in infants < 2kg (Smith et al, 2009)
- Cardiothoracic anomalies

Endoscopic Imaging Clinical Characteristics

1. **Impaired mobility of one or both vocal folds**
   - ➢ Immobile vocal fold may appear shortened compared to the other fold.
2. **Incomplete glottal closure**
   - – Longer open phase during vocal fold vibration (stroboscopy)
   - – Incomplete closure of the vocal folds
     - Mobile vocal fold may cross midline of the larynx to contact the immobile fold
3. **Presence of supraglottic activity**
   - ➢ Increased voicing effort
   - ➢ Increased engagement of extra- and supplemental laryngeal musculature

Adapted from presentation by Sheila Stager, PhD, *Current Assessment of Vocal Fold Paresis Patients,* presented at the 2014 Annual American Speech-Language-Hearing Association, Orlando, FL.

Auditory-Perceptual and Case Report Clinical Characteristics

Signs of Vocal Fold Paralysis

- Stridor
- Breathy-rough voice quality
- Run out of air quickly while talking
  - Inappropriate phrase breaks
  - Report breathing problems associated with talking
- Difficulty projecting voice
- Weak cough
- Coughing/choking
  - During the swallow with liquids
  - After the swallow with solids
- Recurrent pneumonia or upper respiratory infections since onset
- **Impaired laryngeal articulation clarity**

Clarity of Laryngeal Articulation

The ability to clearly articulate between:

- a word ending with a vowel (or sometimes ending with /t/ or /n/) and
- the following word that begins with a vowel – also known as inserting glottal stops

"**We eat eggs every Easter**" vs "**We were away a year ago**"

Courtesy of Sheila Stager, PhD, *Current Assessment of Vocal Fold Paresis Patients,* presented at the 2014 Annual American Speech-Language-Hearing Association, Orlando, FL.

Laryngeal Clarity

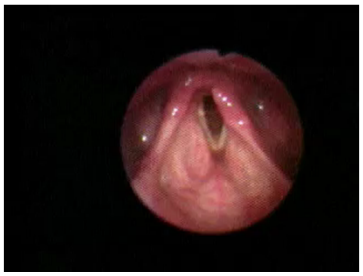
- Only voice disorders with RLN injury demonstrate poor laryngeal clarity
- Approximately 65% of those with RLN exhibit poor clarity
- Poor laryngeal clarity is also associated with poor quality cough production
- In patients more than a year post onset, laryngeal clarity is often good; if not, it is evidence of continued nerve injury

Adapted from a presentation by Sheila Stager, PhD, *Current Assessment of Vocal Fold Paresis Patients,* presented at the 2014 Annual American Speech-Language-Hearing Association, Orlando, FL.

Good Laryngeal Clarity

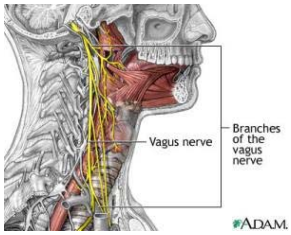
Courtesy of Sheila Stager, PhD, *Current Assessment of Vocal Fold Paresis Patients,* presented at the 2014 Annual American Speech-Language-Hearing Association, Orlando, FL.

Poor Laryngeal Clarity



Courtesy of Sheila Stager, PhD, *Current Assessment of Vocal Fold Paresis Patients,* presented at the 2014 Annual American Speech-Language-Hearing Association, Orlando, FL.

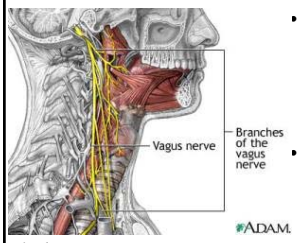
Determining the Site of Lesion



- Lesions can occur at any point along the vagus nerve from the brainstem to the musculature.
- Symptoms/signs help determine location

Taken from: https://12cranialnerves.wordpress.com/cranial-nerve-10-vagus-nerve/

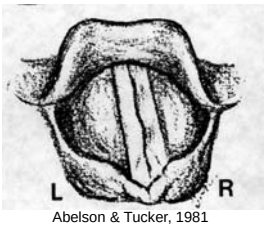
Site of Lesion and Clinical Signs



Taken from: https://12cranialnerves.wordpress.com/cranial-nerve-10-vagus-nerve/

- **Pharyngeal plexus**
  - Hypernasal resonance, nasal emission during speech
- **Superior laryngeal nerve (SLN)**
  - Impaired pitch range
  - Diagonal glottal angle with upward pitch glide
  - Laryngeal penetration without protective airway response
- **Recurrent laryngeal nerve (RLN)**
  - Excessive breathiness, reduced ability to project the voice, irregular vocal fold vibration, silent aspiration

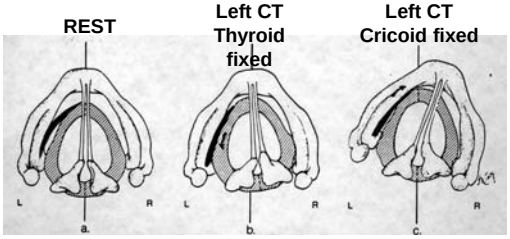
Clinical Presentation of impaired SLN



Abelson & Tucker, 1981

- Bilateral vocal fold mobility
- Diagonal glottal angle during approximation ("twisting of larynx")
- Reduced pitch range
- Reduced laryngeal sensitivity to secretions and other food boluses
- Represent a small proportion (~5%) (Stager, 2014)

Glottal angle as indication of SLN damage



Cricoid rotates to paralyzed side

Thyroid rotates To paralyzed side

Abelson & Tucker, 1981

Case Examples

Normal Laryngeal Function

Vocal Fold Paresis

Case History:
- 57 yo female
- Gradual 6-8 month onset of a rough, hoarse voice quality.
- No report of swallowing or breathing problems.
- Voice is 35% of normal.

Surgical History:
- Anterior Cervical Disc Fusion (ACDF) 22 years ago
- Thyroidectomy 2 years prior
- No reported voice changes after either.

Occupation: Supervisory role for a commercial corporation requiring personnel and phone voice use.

Nasoendoscopic Exam

Left-sided Unilateral Vocal Fold Paralysis

Nasoendoscopic Exam

Speech Assessment

Paragraph sample

Sustained “ah”

Sustained “ee”

Throat clear

Case History: 42 yo male with onset of left UVP s/p dissection of aortic aneurysm 3 months earlier. Treated with Cymetra injection to medialize immobile vocal fold. No swallowing or breathing issues.

Left-sided Unilateral Vocal Fold Paralysis

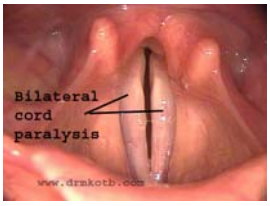
Flexible Endoscopic Evaluation of Swallowing

Case History

- 72 yo female with left CP angle tumor s/p excision
- CNs V, VI, VII, X, XI, and XII were reportedly intact at the time of surgery
- CN IX showed tumor invasion
- Breathy voice and dysphagia s/p surgery
- FEES Findings
  - Impaired pharyngeal clearance with left > right
  - Left Unilateral Vocal Fold Paralysis (UVP)

Bilateral Vocal Fold Paralysis

Case Example



Spontaneous Recovery

- **PEDIATRIC POPULATIONS**: 16-64% recover between 6 weeks – 5 years post onset (Strychowsky et al, 2014)
- **ADULT POPULATIONS**: Depending upon the etiology, 6% - 52% within 6-9 months post onset (Sulica, 2008; Mau et al, 2017)

Spontaneous Recovery Issues

"Recovery" is loosely defined across cohort studies:

Laryngeal muscle activity vs. Laryngeal function

– Laryngeal muscle activity often = SYNKINESIS (Blitzer et al, 1996; Sanuki et al, 2014)

– Laryngeal function in these individuals is abnormal
- In adults, UVP associated with 2nd highest VHI scores of all voice disorders (Avg = 68/120, ranging 65-71) (Bielamowicz & Stager, 2006)
- In adults, 38% exhibited aspiration & pharyngeal weakness (Domer et al, 2014)

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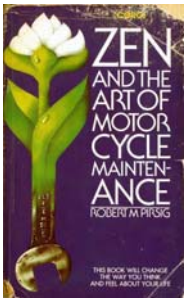
What is so interesting about the RLN packaging?

"Some things you miss because they're so tiny you overlook them. But some things you don't see because they're so huge."

-Robert M Pirsig



Unilateral Vocal Fold Paralysis Asymmetry

- ~2/3 of Unilateral vocal fold paralysis involves the left recurrent laryngeal nerve (RLN).

Spataro EA, Grindler DJ, Paniello RC. Etiology and time to presentation of unilateral vocal fold paralysis. *Otolaryngol Head Neck Surg*, 2014, 151(2): 286-293).

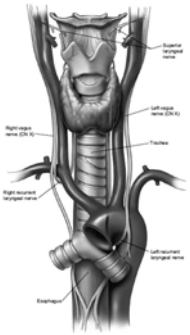
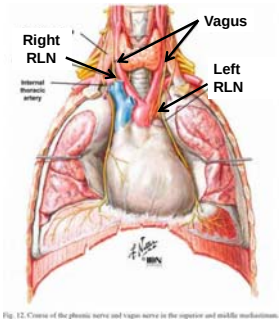


Figure taken from: Campbell EO, Samlan RA, McMullen NT, Cook S, Smiley-Jewell S, Barkmeier-Kraemer J. Developmental changes in the connective tissues of the porcine recurrent laryngeal nerve, J Anat, 2013, 222:625-633.

Etiologies of RLN Dysfunction

- **Trauma (e.g. post-surgery)**
  - Thyroid surgery
  - Cardiothoracic surgery
  - Anterior Cervical Neck Fusion
  - Esophagectomy
  - Lung surgery
- **Neoplasm**
- **Aortic Aneurysm**
- **"Idiopathic"**



Spataro EA, Grindler DJ, Paniello RC. Etiology and time to presentation of unilateral vocal fold paralysis. *Otolaryngol Head Neck Surg*, 2014, 151(2): 286-293).

Connective Tissues of Peripheral Nerves

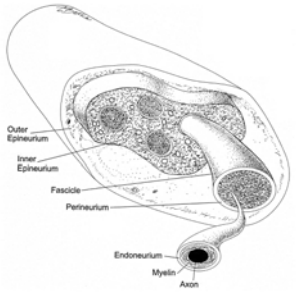


Figure Taken From: Barkmeier & Luschei, 2000

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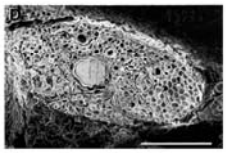


the subthalamic nucleus

the nucleus ambiguus

a cross-section of a blood vessel

the recurrent laryngeal nerve

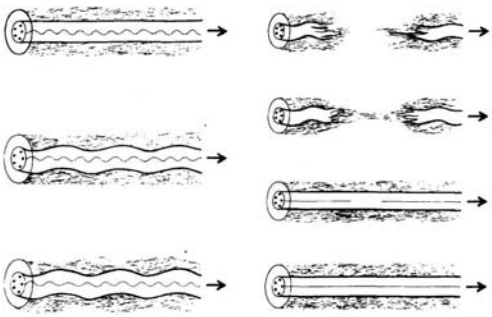


FIGURE 8. Changes occurring in the various components of a nerve trunk as it is stretched to structural failure. Only one fasciculus in the nerve is represented. (From Sunderland S: *Nerves and Nerve Injuries*. Edinburgh, Churchill Livingston, 1979. Used with permission.)

Nerve Connective Tissues

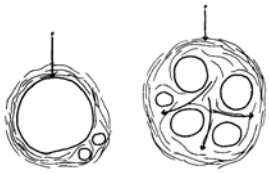
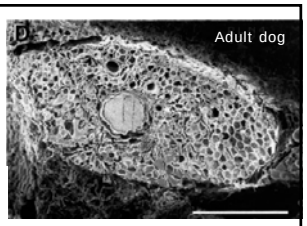
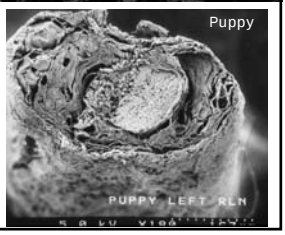


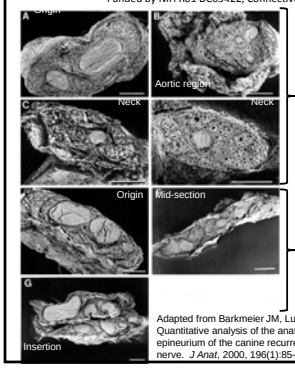
FIGURE 9. Dispersion of compression stresses by the epineurial tissue. (From Sunderland S: *Nerves and Nerve Injuries*. Edinburgh, Churchill Livingston, 1979. Used with permission.)





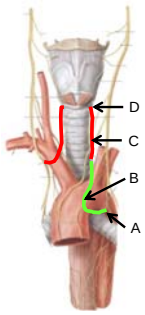
The RLN differs in connective tissue quantity and composition between the thorax and neck regions

Funded by NIH R01 DC05422, Connective Tissues as a Factor in Vocal Fold Paralysis



Left RLN

Left Flexor Hallicus Longus



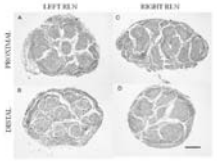
Adapted from Barkmeier JM, Luschei ES. Quantitative analysis of the anatomy of the epineurium of the canine recurrent laryngeal nerve. *J Anat*, 2000, 196(1):85-101.

Journal of Anatomy

J. Anat. (2013) 222, pp625–633 doi: 10.1111/joa.12048

Developmental changes in the connective tissues of the porcine recurrent laryngeal nerve

Ellen O. Campbell,[1] Robin A. Samlan,[1,5] Nathaniel T. McMullen,[2] Sarah Cook,[1,3] Suzette Smiley-Jewell[4] and Julie Barkmeier-Kraemer[1,4]



- Piglet nerves (N=8) were homogenous along their length
- No differences were found in Epineurium amount or composition

NIH R01 DC05422, Connective Tissues as a Factor in Vocal Fold Paralysis

Journal of Anatomy
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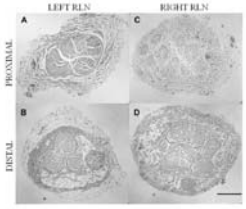
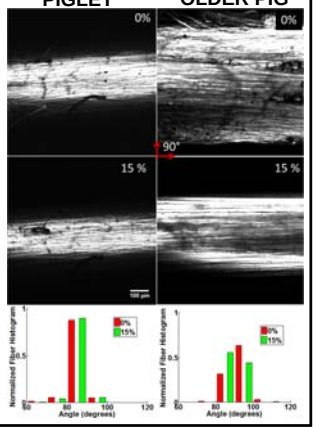


Juvenile pig (N = 10) left RLN showed significant differences:

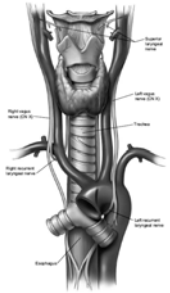
- Collagen: Thorax > Neck
- Adipose: Thorax < Neck
- Fascicles: Thorax > Neck (right and left RLN)

BIOMECHANICAL DIFFERENCES *(Williams et al, 2014)*

- **YOUNG vs OLD:**
  - Piglet RLNs > stiffness at lower strain levels than Older Pigs
- **LEFT RLN vs RIGHT RLN in OLDER PIGS**
  - Left RLN > stiffness than right RLN
- **LEFT RLN DIFFERS BETWEEN PROXIMAL AND DISTAL REGIONS:**
  - Thorax > Neck:
    - Stiffness
    - Fiber alignment suggests complex loading at aorta



The Relationship Between the RLN and Aorta



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Idiopathic Unilateral Vocal Fold Paralysis (UVP)

- 12-24% of UVP (Sulica, 2008; Spataro et al, 2014)
- 2/3 exhibit left vocal fold impairment (Chen et al, 2015)
- Age of onset averages 54 years (± 12 years) (Sulica, 2008; Chen et al, 2015)

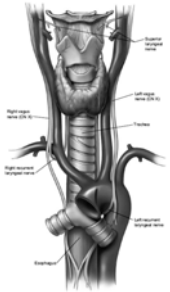


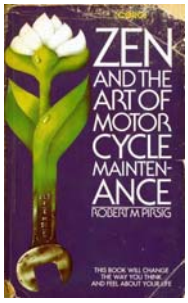
Figure taken from: Campbell EO, Samlan RA, McMullen NT, Cook S, Smiley-Jewell S, Barkmeier-Kraemer J. Developmental changes in the connective tissues of the porcine recurrent laryngeal nerve, J Anat, 2013, 222:625-633.

University of Utah Health Care

Background on the title of the talk

"The number of rational hypotheses that can explain any given phenomenon is infinite."

-Robert M Pirsig



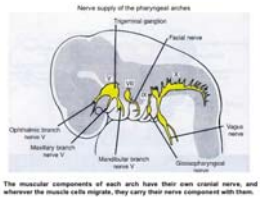
Idiopathic Etiology?

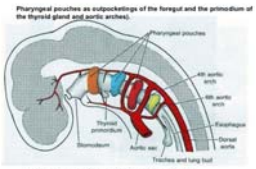
- Viral etiology 
- RLN cell body apoptosis 
- Age-related changes?
  - Connective Tissues
  - Vascular

Why does the left RLN have a longer route down to the level of the heart compared to the right RLN that remains in the neck region?

Start the presentation to see live content. Still no live content? Install the app or get help at PollEv.com/app

The nervous system develops alongside the vascular system





http://www.slideshare.net/615396/development-of-head-and-neck-final

Development of major blood vessels

Aortic Arch (Vascular) Age-Related Changes

- Compliance decreases with aging > 10 years of age (Lang et al, 1994; Länne et al, 1994)
- Ortner's Syndrome and onset of left-sided UVP associated with aneurysm (Subramaniam et al, 2011; Zangirolami et al, 2015)

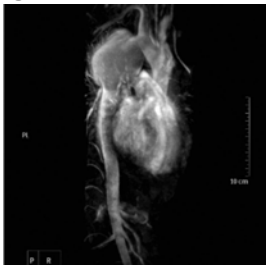


Figure 4 taken from: Zangirolami ACA, de Oliveira FV, Tepedino MS. (2015). Ortner's Syndrome: Secondary Laryngeal Paralysis Caused by a Great Thoracic Aorta Aneurysm. Int. Arch. Otorhinolaryngol. vol.19 no.2, http://dx.doi.org/10.1055/s-0034-1397331.

A computational study of the role of the aortic arch in idiopathic unilateral vocal-fold paralysis

Megan J. Williams, Avinash Ayyalasomayajula, Reza Behkam, Andrew J. Bierhals, M. Eileen Jacobs, Julia D. Edgar, Randal C. Paniello, Julie M. Barkmeier-Kraemer and Jonathan P. Vande Geest

J Appl Physiol 118:465-474, 2015. First published 4 Decemb
doi:10.1152/japplphysiol.00638.2014

Modeling using human and pig data and one gated-MR of aortic arch in a human:

Model of mechanical strain levels imposed on the RLN by the aorta (6-16%) could potentially contribute to impaired function.

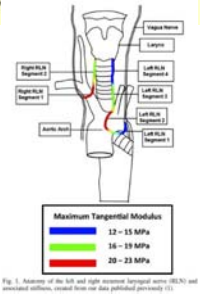


Fig. 1. Anatomy of the left and right recurrent laryngeal nerve (RLN) and associated stiffness, created from our data published previously (1).

Aortic arch compliance and idiopathic unilateral vocal fold paralysis

Reza Behkam, Kara E. Roberts, Andrew J. Bierhals, M. Eileen Jacobs, Julia D. Edgar, Randal C. Paniello, Gayle Woodson, Jonathan P. Vande Geest, Julie M. Barkmeier-Kraemer

Journal of Applied Physiology Published 18 May 2017 **Vol. no. , DOI:** 10.1152/japplphysiol.00239.2017

Groups

- Left-sided idiopathic UVP
- Age-Gender-matched Controls

Characteristics

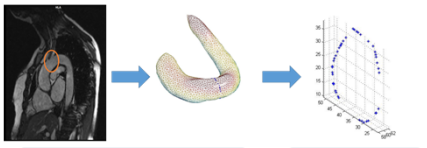
- N = 10 in each group (7 males, 13 females total)
  - 2 additional subjects excluded due to imaging noise
- Average age = 53 years (Ranged from 26-82 years)

Clinical Research Methodology

- Ungated and gated structural 1.5T MRI scans of the thoracic aortic arch
- Electrocardiogram (ECG)-gating
  - Diastole
  - Systole
- Blood pressure measures in supine

Age-related changes to blood vessels as possible idiopathic etiology

Compliance calculation



Locating Left RLN in MRI Images

Calculating Diameter Change

Aortic arch compliance and idiopathic unilateral vocal fold paralysis

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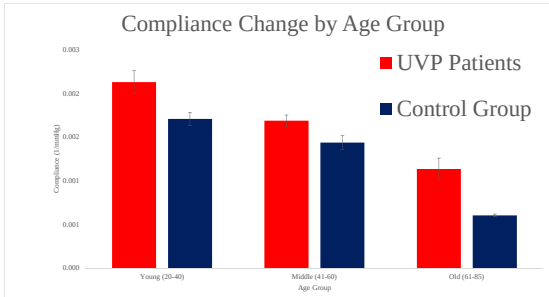

UVP compared to normal controls (p=0.0022) with power level of 99% (N = 20)

Future Directions: RLN and Vascular Interactions

- Investigate the causal association between idiopathic UVP and:
  - Aortic arch compliance
    - Biomechanical testing using pig model
      - Degree of compliance
      - Duration or cyclic rate factors
    - Simulate agents potentially causing changes in vessel wall (e.g. proteases)
    - Co-morbidities predictive of vascular compliance changes
  - Compression of the RLN between the aortic arch and pulmonary artery in individuals with hypertension

Research Findings Summary

1. RLN connective tissue quantity and composition differs with aging and between its locations in the neck and thorax regions.
2. The RLN shows biomechanical characteristics predicted by anatomical connective tissue composition and quantity differences.
3. Individuals diagnosed with left-sided idiopathic vocal fold paralysis demonstrated greater compliance than age- and gender-matched controls.

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  - Joshua Lopez

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