Obstructive Sleep Apnea (OSA) in Children with Down Syndrome

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OSA – Obstructive Sleep Apnea

- What is it?
- What are signs and symptoms?
- Why do children/adults with Down syndrome have OSA?
- Why is it important to treat?
- Why do we have to get a sleep study?

Obstructive Sleep Apnea Syndrome (OSAS)

- Episodes of partial or complete airway obstruction during sleep
- Usually associated with:
  - Decrease in oxygen level - **hypoxemia**
  - and/or **hypercarbia** (high CO^2)

OSAS

- Prevalence: 2% or 500,000 children with OSAS in the USA
- Peak age is 2 to 5 years (developmental peak of T&A hypertrophy)
- Second peak in middle to late adolescence (more ‘adult’ symptoms)
- Children male = female
- Adolescent male > female

OSA

- More difficult to diagnosis in children than adults
- Signs and symptoms may not accurately reflect severity of disease

OSA – Presenting symptoms will determine who treats first

- Snoring - seen by ENT
- Failure to thrive - seen by pediatrician
- Sleepy children - seen by neurologist
- Behavior problem - seen by psych, treated for ADHD
- Difficulty breathing - seen by pulmonary

Diagnosis of OSAS
Snoring

- Not diagnostic of OSA
- Not always indicative of pathologic breathing patterns
- Sleep architecture can be normal
- Occurs in 7 - 10% of children on a regular basis
- Occurs in 20% on an intermittent basis

Diagnosis of OSAS
-Increased respiratory effort-

- Correlates with OSA
- Retractions, intercostal, sternal, suprasternal, supraclavicular, flaring of the nares, use of accessory muscles, paradoxical inward motion of the rib cage during inspiration
- Parents often describe the breathing as "frightening"

Diagnosis of OSA

Sleep patterns

- Restless sleep or recurrent body movements, recurrent awakenings are seen in OSA

Sleep Positions

- Bent forward at waist with chin extended
- Sleeping on back with back arched and neck hyperextended
- Sleeping sitting up

Diagnosis of OSAS
Excessive Daytime Sleepiness

- Not common in children with OSAS
- Children under 5 usually need a nap
- Adolescents are usually sleep deprived
- More common to see hyperactive behavior

Higher incidence of OSAS in:

- Obese children
- Children with asthma
- Older children who snore
- Children with craniofacial anomalies
  - Down syndrome

Down Syndrome

- Higher probability of developing OSA
- Higher risk due to:
  - Midface hypoplasia
  - Narrow nasopharynx
  - Large tongue
  - Muscular hypotonia
  - Small larynx and trachea
  - Increased upper respiratory infections
    - Delay in development of immune system
    - Small airway so secretions more easily obstruct airway
  - Higher incidence of gastroesophageal reflux

Down Syndrome

- 50% also have an underlying cardiac anomaly
  - So complications of more likely
    - Cor pulmonale (heart failure)
    - Pulmonary hypertension

Down Syndrome – OSA
History of OSA

- Why was it overlooked?
- Many complications of sleep apnea are disorders associated with DS:
  - Failure to thrive
  - Pulmonary hypertension
  - Behavioral problems

Before 1980's

- Despite 50% of children with DS born with cardiac anomalies, life saving surgery was not done
- Average life span 9 years
- Most children died from pulmonary hypertension, caused by the heart abnormalities

Down Syndrome - Legal Aspects

- Baby Doe 1981 Bloomington, Indiana
- Child with DS + tracheal-esophageal fistula
  - Any food eaten would go into the airway, causing pneumonia and death
- Hospital initially denied treatment
- Parents sued to obtain full care for their child

Child Abuse Amendments 1984

- All disabled infants must receive full care
  - Exceptions
    - Irreversible coma
    - Treatment would prolong dying
    - Treatment is futile or inhumane

After 1984

- Cardiac surgery done on all children with DS
- Still higher than expected incidence of pulmonary hypertension
- WHY??
- OSA!!

Parents Of Children With DS Underestimate Severity Of Their Child's Sleep Abnormalities

Marcus et al. (1991) In parents of children with Down syndrome:

- 68% of parents reported no symptoms of obstruction
- 100% had abnormal studies

Brouillette et al. (1984) In parents of children without Down syndrome:

In proven OSA, parents reported sleep difficulties correctly 96% and correctly reported apnea 78%

What's the big deal?
Why do we care about OSA?

Behavior Changes with OSAS

- Daytime sleepiness, hyperactivity, aggressive behavior in children with excessive snoring (n=781)
- Improvement seen after T&A
  - (Ali N et al Arch Dis Child 1991 and Guilleminault C et al Lung 1981)

- 25% of children with OSAS have bedtime sleep resistance: fighting sleep, refusing to go to bed each night.
- Night terrors, sleep walking
- Resolved after T&A
  - (Miyazaki S Am J Otolaryngol 1989)

OSAS and Cognitive Function

- Sleep-disordered breathing negatively effects school performance in children
- Impairs attention span, concentration, memory, motor skills, esp. fine motor

(Gozal D: Pediatrics 102:616-620, 1998)

- Effects on neuro-cognition were not related to <u>degree</u> of OSA
- Even seen in mild sleep abnormalities

(Bourke R et al. Sleep Medicine 12: 489-496, 2011)

Children who <u>snore</u> vs those who do <u>not snore</u>

In those who snore,

- **Increased hyperactivity**
- **Increased inattentive behavior**
- **Poor school performance in mathematics, science, spelling**

(Brockman PE et al Sleep Breath 2012)

OSAS and Cognitive Function

- **Hypoxemia assoc. with OSA is correlated with lower IQ performance testing**

(Kaemingk et. Learning in children and sleep disordered breathing: Findings of the Tuscon Children's Assessment of Sleep Apnea (TuCASA) Prospective Cohort Study. J of Internat Neuropsychol Soc 2003)

OSAS and Growth

- T&A hypertrophy can cause poor appetite, difficulty swallowing and decreased caloric intake
- Increased respiratory effort during sleep drains caloric resources
- CO_2 retention and acidosis may impair the physiologic release or end organ response of growth hormone

(Bates T et al Arch Dis Child, 1994)

Hypoventilation syndrome and hypercarbia

Associated with:

- Increased risk of systemic hypertension
- Abnormal cardiac rate variability
- Increased sleep fragmentation

- **What is the incidence of OSA in children with DS?**

Marcus et al (1991)

- Retrospective study
  - 53 “children”
  - Ages 4 weeks to 51 years (Mean age 7 years)
  - 100% abnormal sleep studies

  * Parents were poor predictors of OSA

Dyken et al (2003)

- Prospective study
  - 19 patients - Ages 3 to 18
  - Mean 9 years
  - OSA in 79%

* Parents were poor predictors of OSA

Obstructive Sleep Apnea Syndrome
Should all children with Down syndrome be tested?

Shott SR, Amin R, Chini B, et al.

<u>Archives of Otolaryngology-Head and Neck Surgery</u>
2006;132: 432-436.

Shott et al 2006

- Prospective study
  - 56 patients
  - Ages 3-4 years
  - Mean age 42 months
  - 57% abnormal sleep studies

* Parents were poor predictors of sleep problems

OSA in Adults with DS

Trois MS et al J of Clinical Sleep Med 2009

- 16 adults
- 94% had OSA (69% had AHI>30)
- 88% had AHI >15, compared to 9% of general population
- 75% had oxygen levels less than 85%, compared to 8% in general population

Objective diagnosis of OSAS

- Sleep tape or sleep video
- Overnight oxygen oximetry
  - Evaluates oxygen level and heart rate only
  - No information regarding obstructive vs central apnea vs non-obstructive hypoxemia
- Polysomnogram (PSG) or sleep study
  - Provides the best, most complete data

Indications For Sleep Study In Children With DS

- Parental concerns of obstruction
- Poor sleep habits, frequent waking or unusual sleeping positions
- NEW 2011 American Academy of Pediatrics Guidelines:

Baseline sleep study obtained by age

<u>4 years old,</u> even if no obvious symptoms

Sleep studies in children with developmental delays

- Do we really need to go to Pediatric Sleep Lab?
- YES!!
- Success rate much higher
- At Cincinnati Children's Hospital, extra sleep tech present
- Parents need to be prepared
  - Your child <u>will</u> take off the monitors
  - If parents get frustrated, child gets frustrated

Polysomnogram – Sleep study

- EKG
- HR
- Oxygen saturation-pulse oximetry
- Thoracic and abdominal Piezo crystal belts (resp. effort)
- Nasal/oral thermistor (airflow)
- End tidal CO_2 by infrared absorption
- Pulse amplitude waves
- Snoring microphone
- Actigraph
- Body positioning and video monitoring
- EEG

Definitions of Sleep Abnormalities

- Need 'pediatric' definitions
- Important to assess definitions when evaluating sleep study reports
  - Obstructive apnea
  - Mixed apnea
  - Central apnea
  - Obstructive hypopnea
  - Respiratory disturbance index (RDI)
  - Hypoventialtion syndrome
  - Arousals
  - Arousal index

Obstructive Apnea

- Absence of airflow for at least 2 respiratory cycles, but abdominal and chest movement continue

Obstructive Index
Apnea-Hypopnea index (AHI):

Number of obstructive apneas and hypopneas per hour of sleep

- Normal <1-1.5
- Mild abnormal (mild OSA) 1-5
- Moderate abnormal (mod OSA) 5-15
- Severe abnormal (severe OSA) >15

Hypoxemia:
how low does the oxygen level fall during sleep?

- **Oxygen saturation should be above 92%**
- **Can have occasional drop to 90%**

Hypoventilation Syndrome

- You breathe in oxygen, but you also have to breathe out CO_2
- Abnormal if CO_2>50 mm Hg more than 10% of study time
- Seen with partial obstruction, hypoventilation, hypotonia of airway muscles

Arousals

- A protective mechanism
- Obstructive breathing causes protective reflex which curtails obstruction
- Occurs secondary to hypoxemia, hypercarbia, increased upper airway resistance
- Normal Arousal Index = 10

Repetitive Arousals and Sleep Fragmentation Can Cause:

- Blunted arousal response
- Delay in apnea termination
- More severe oxygen desats and CO_2 retention
- Symptoms of sleep deprivation
  - Daytime sleepiness
  - Lack of energy
  - Lack of initiative
  - May exacerbate behavior and learning disabilities

OSA and heart failure

Seen in those with

- Increased arousal index
- Lower minimal and mean oxygen saturation
- More frequent bradycardias during sleep

(Lee PC et al. Scientific World J 2012)

Treatment of OSA

- Removal of tonsils and adenoids (T&A) is the 1st line treatment
- Improves OSA in most, but doesn't always cure the OSA
- Post-operative sleep study <u>is important</u>
  - Only 30% have normal AHI after T&A
- Because of high incidence of residual obstruction after T&A, children should be observed overnight in hospital after T&A

What if there is still OSA after T&A?

- YES, there are treatments available
- Both medical and surgical

Persistent OSA after T&A Current treatments and new research: DYMOSA study

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Treatment of OSA

- Removal of tonsils and adenoids (T&A) is the 1st line treatment
- Improves OSA in most, but doesn't always cure the OSA
- So, post-operative sleep study is VERY important

T&A less successful for children with Down syndrome

- Merrell J and Shott S: Int J Pediatr. 2007
  - 37 patients with DS
  - Ages 3-4 years
  - After T&A, only 43% with DS had normal AHI
  - If AHI, hypoxemia and hypercarbia are all evaluated: Only 29% had normal sleep study after T&A
- Shete et al. 2010:
  - 11 patients with DS
  - Mean age 8.4 years
  - Only 18% had normal post-op AHI

Treatment is dependent upon appropriate diagnosis of source and level of the obstruction

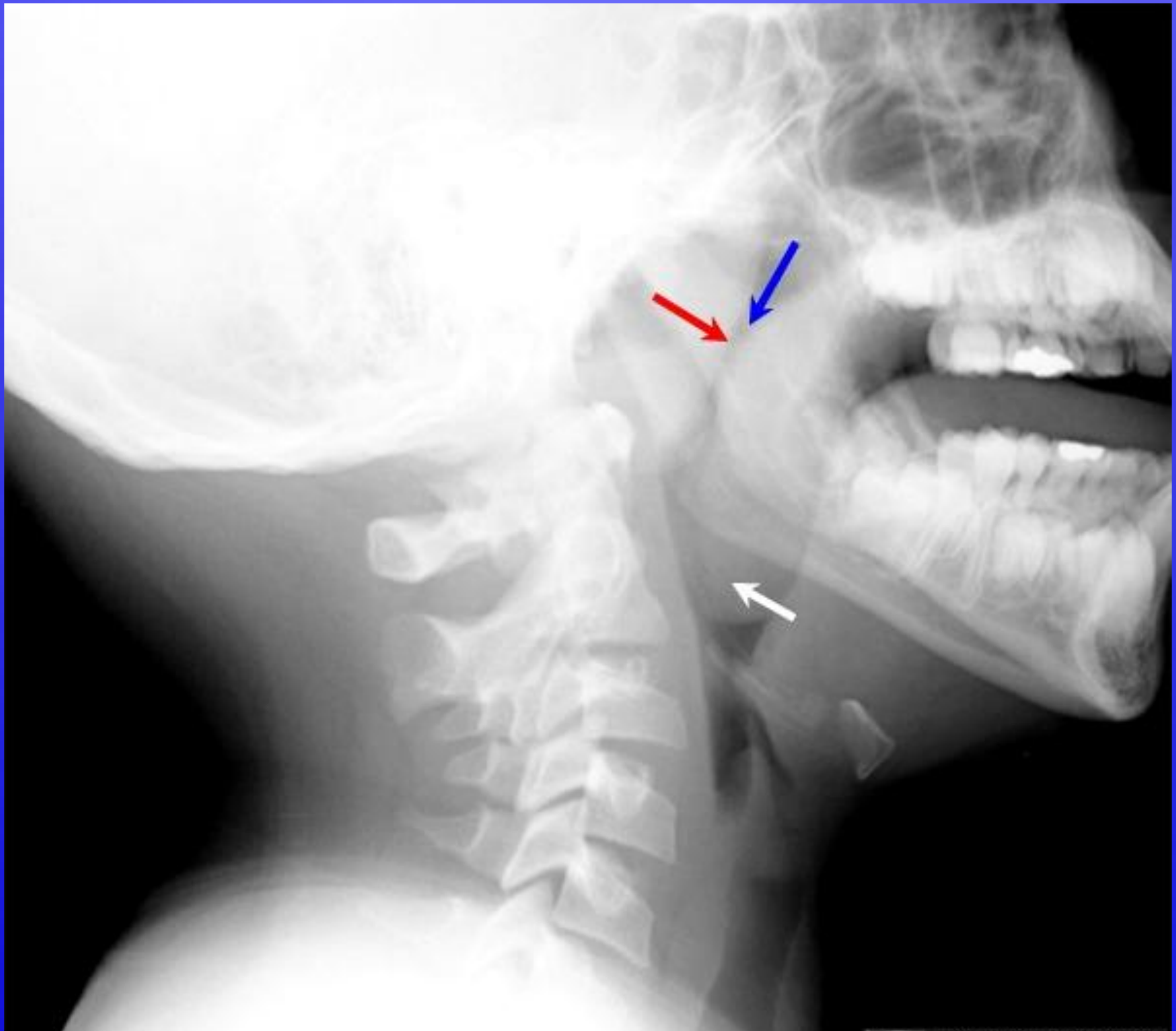
What if T&A fails?
Define the level of obstruction

- Lateral neck xray
  - Regrowth of adenoids: Seen in 63%
  - Enlarged lingual tonsils : Seen in 30-40%
- Flexible endoscopy
  - In the office setting or operating room
- Fluroscopy of airway
- Cine CT
- Cine MRI

Lateral neck xray

White arrow = lingual tonsils **Red Arrow = adenoids**

Blue arrow = nasopharyngeal airway



What if T&A fails?
Define the level of obstruction

- Flexible endoscopy
  - In the office setting or operating room
- Fluroscopy of airway
- Cine CT
- Cine MRI

Cine MRI

- High resolution, dynamic examination of the airway
- Defines multiple levels of obstruction
- Useful especially in complex airways, eg. children with DS, craniofacial anomalies
- Done while child is asleep or mildly sedated

Cine MRI

- Fast gradient echo sequence
- 128 consecutive images over 2 minutes
- Displayed in cine format – creating a “movie” of airway motion
- Obtained when there is snoring or oxygen desaturations
- Allows you to assess multiple levels of airway at the same time
  - Can see cause and effect levels of obstruction

Results of cine MRI used to:

- Plan further treatment of airway obstruction
- Assess success of subsequent intervention

Causes of persistent obstructive sleep apnea despite previous T&A in children with Down syndrome as depicted on static and dynamic cine MRI

(Donnelly LF, Shott SR, LaRose CR, Chini BA, Amin RS
Am J Roentgenol July, 2004)

27 patients – Mean age 9.9 years

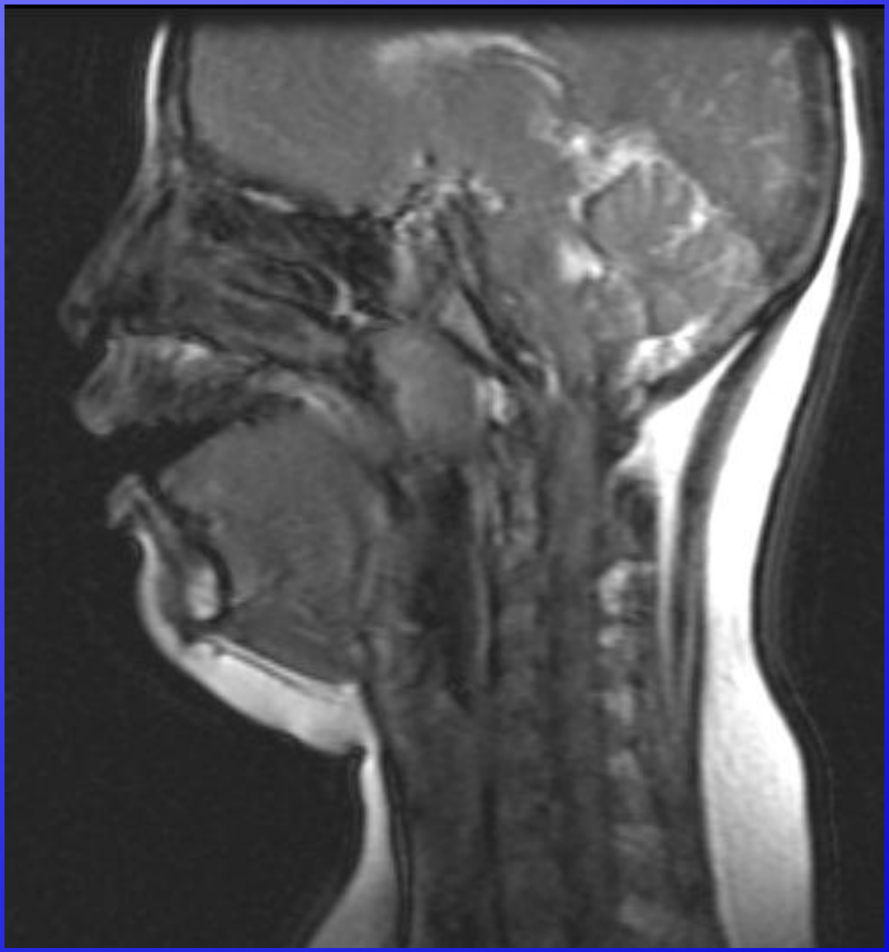
Macroglossia	74%
Glossoptosis	63%
Recurrent adenoids	63%
Enlarged lingual tonsils	30%
Hypopharyngeal collapse	22%

Case 1

- 12 yr old F with DS
- T&A at age 4
- Parents reported no sleep problems, but patient fell asleep in my office
- Obstructive AHI= 4.1
- Desats to upper 80's
- Arousal index = 20.6

Case 1 – Cine MRI

- Adenoid regrowth
- Hypopharyngeal collapse due to nasopharyngeal obstruction
- Glossoptosis



Case 1 – Treatment and results

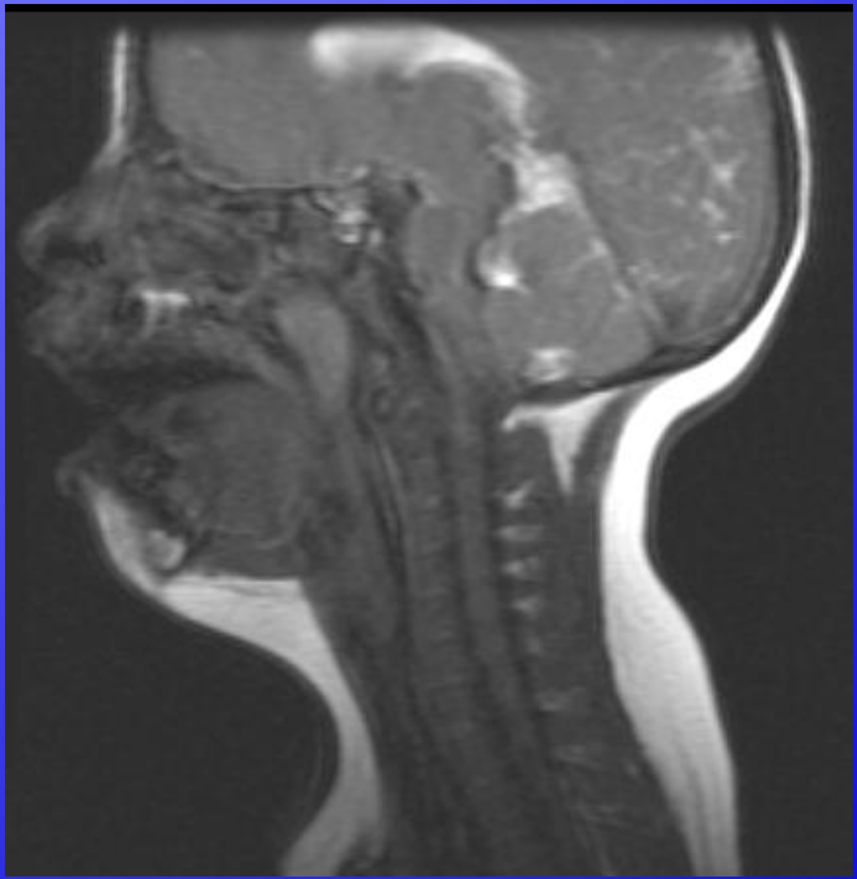
- Revision adenoidectomy done
- Post-op sleep study
  - Obstructive AHI = 0.4
  - Oxygen desaturations resolved
  - Arousal index = 10

Case 2:

- 7 year old F with DS
- T&A at age 3
- Sleep study at age 7 (parents denied sleep problems)
- Obstructive AHI = 17.9
- Oxygen desats to 79%
- Arousal index = 39
- End tidal CO_2 > 50 for 40% of TST

Case 2 – Cine MRI

- Adenoid regrowth
- Nasopharyngeal collapse
- Glossoptosis
- Hypopharyngeal collapse



Case 2 – Further treatment and results

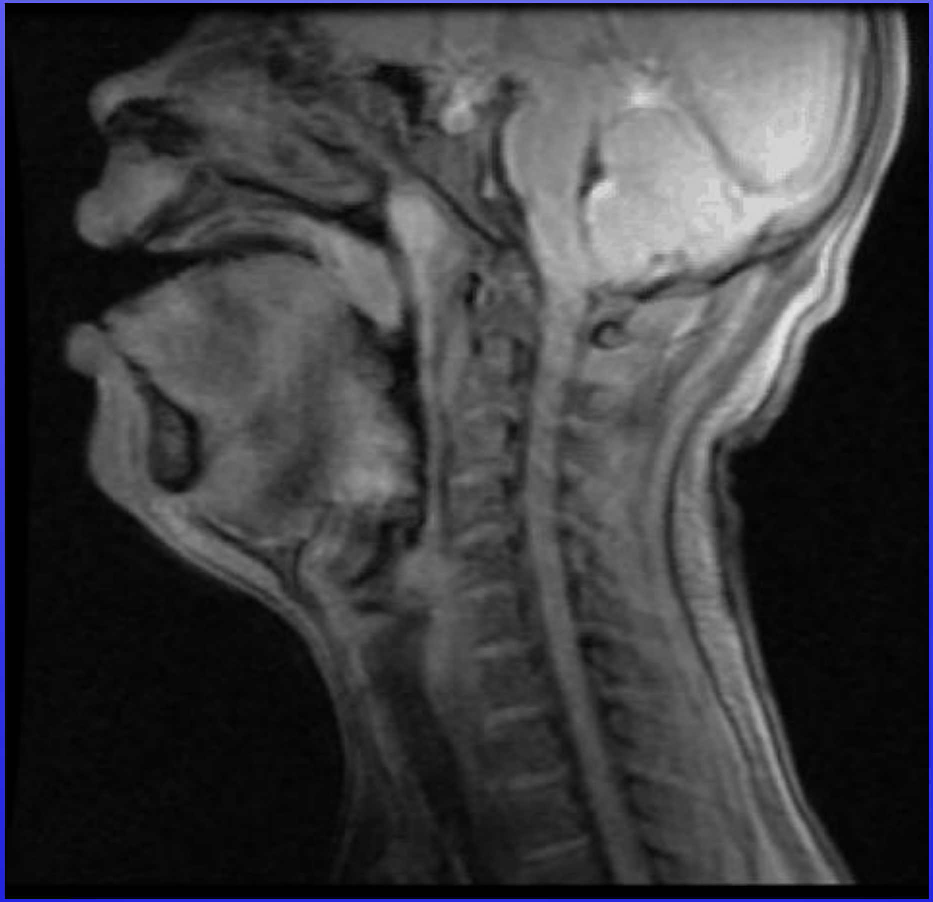
- Revision adenoidectomy, partial excision of soft palate, radiofrequency reduction to base of tongue, Repose genioglossus advancement

- Post-op repeat sleep study:
  - Obstructive index = 2.2
  - No oxygen desats below 93%
  - Arousal index 13
  - Hypercarbia resolved

Case 3

- 8 year old male with DS
- Mild retrognathia (small jaw)
- s/p T&A age 3
- Snores, apneic pauses, daytime sleepiness
- Sleep study:
  - AHI 12
  - desats to 87%
  - hypercarbia

Case 3 : Sleep cine MRI



Case 3

- Lingual tonsillectomy done
- Post –operative PSG
  - AHI 1.2
  - No desats below 92%
  - Still with mild hypercarbia

OSAS – Further surgical options:

- Depends on level(s) of residual obstruction
  - Base of tongue collapse
  - Oropharyngeal collapse
  - Nasopharyngeal collapse
  - Hypopharyngeal collapse

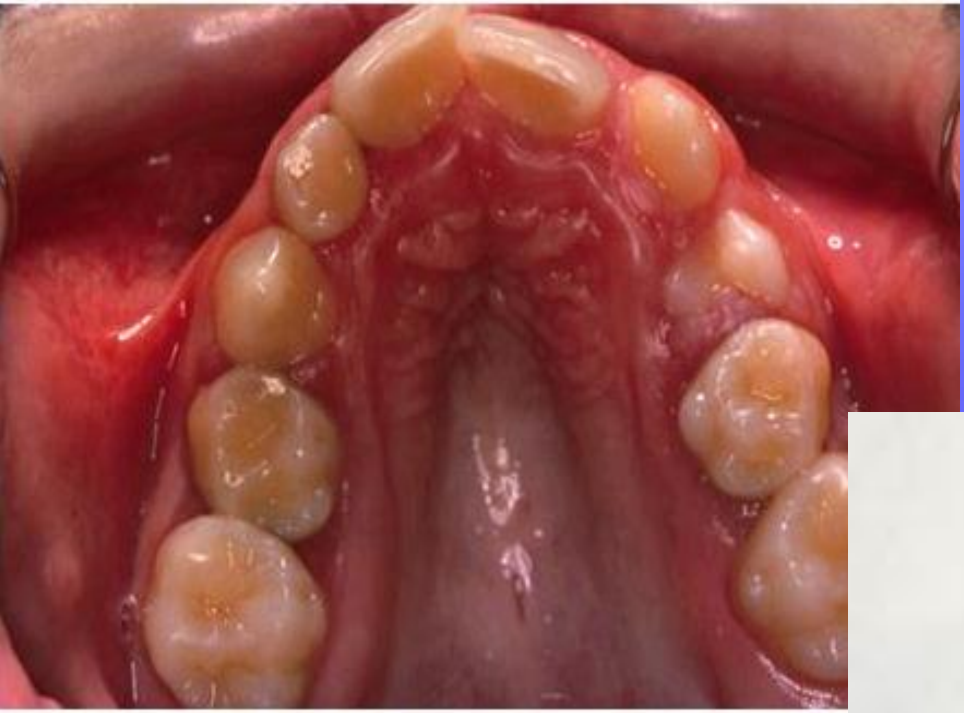
Medical options for persistent OSA

- Weight loss if needed
- Supplemental oxygen
- Intranasal steroids and anti-leukotrienes
- CPAP – Continuous positive airway pressure
  - Requires child's cooperation
  - Not tolerated well, but it <u>does</u> work
  - Nasal delivery may be more successful ("No mask" or nasal pillows)
  - Higher success if able to admit child for CPAP training
  - Need yearly repeat sleep study to confirm that settings are correct

CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)




Palate expansion



Oral splints and dental appliances

OSA – Surgical options for base of tongue obstruction

- Lingual tonsillectomy
- Radiofrequency reduction to base of tongue
- Genio-glossus advancement
  - Pull segment of jaw bone forward
  - "Repose" genioglossus advancement
- Midline partial glossectomy with coblation
- Resection of wedge of base of tongue

Medical and Surgical Treatment after T&A

- Continuous Positive Pressure Ventilation
  - CPAP
  - It works…. But only it you use it
- Surgical Treatment
  - May need to address multiple levels with multiple surgeries
  - Success rates around 60%

We need to do better

- There is a critical need for a better diagnostic modality
- Need to take into account:
  - Airway anatomy
  - Tissue compliance
  - Collapsibility
- All 3 are needed to predict surgical outcome and improve surgical planning

DYMOSA

Dynamic Computational Modeling of Obstructive Sleep Apnea in Down Syndrome

NIH RO1HL105206-01

The future: **DYMOSA**

Dynamic Computational Modeling of Obstructive Sleep Apnea in Down Syndrome

- **Cincinnati Children's Hospital: Otolaryngology, Pulmonary, Radiology**

- **University of Cincinnati: Aerospace Engineering**

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NIH 5 RO1HL105206-0

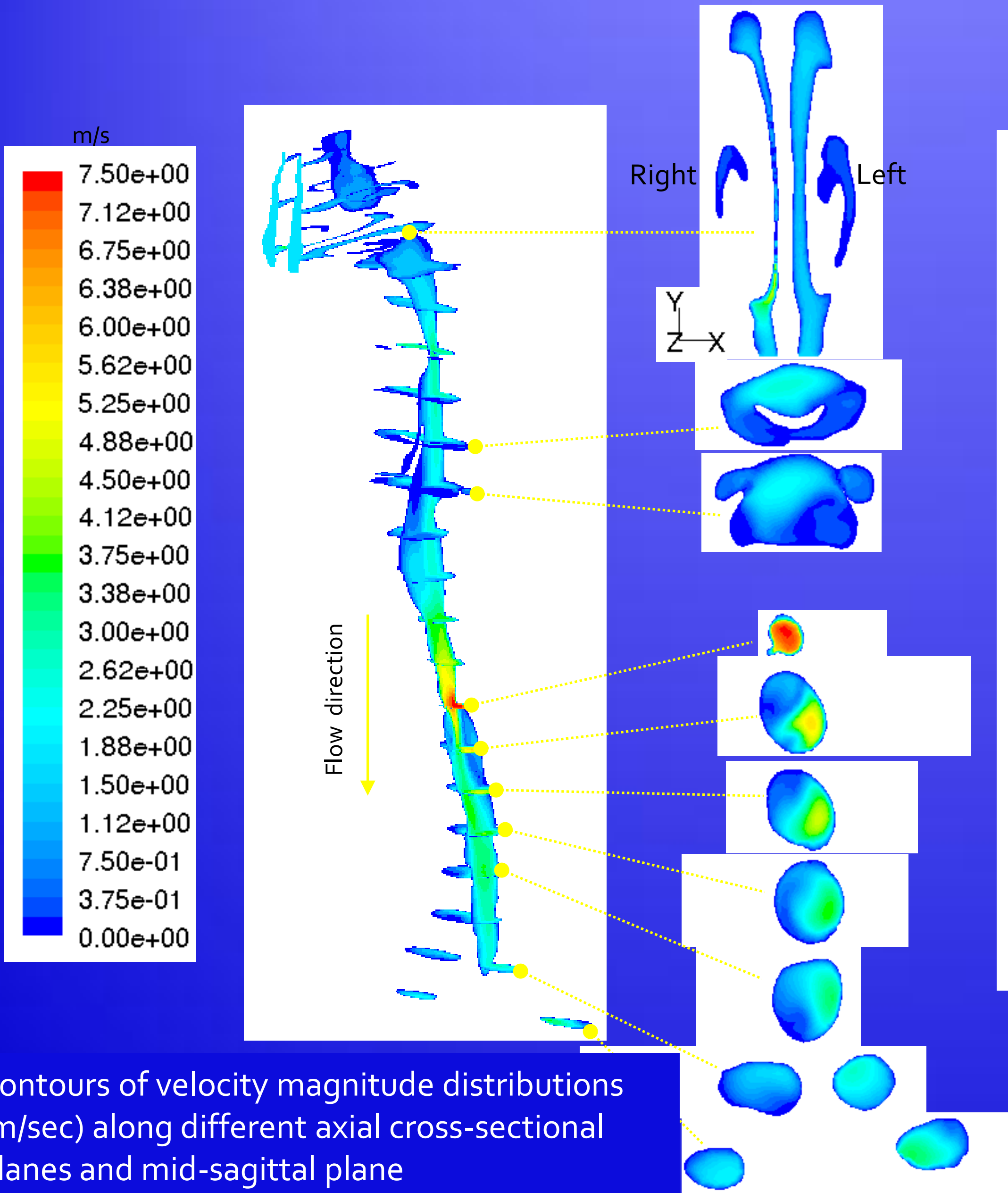
DYMOSA

- Using dynamic MRI imaging, create a 3D computational model of the airway
  - Apply Computational Fluid Dynamics modeling (CFD)
  - Apply Flow Structure Interaction modeling (FSI)
- Evaluate the flow of air through the model to determine major site of obstruction
- Perform virtual surgery on the model and evaluate how this changes air flow
- Use the model to plan and to predict surgical outcomes

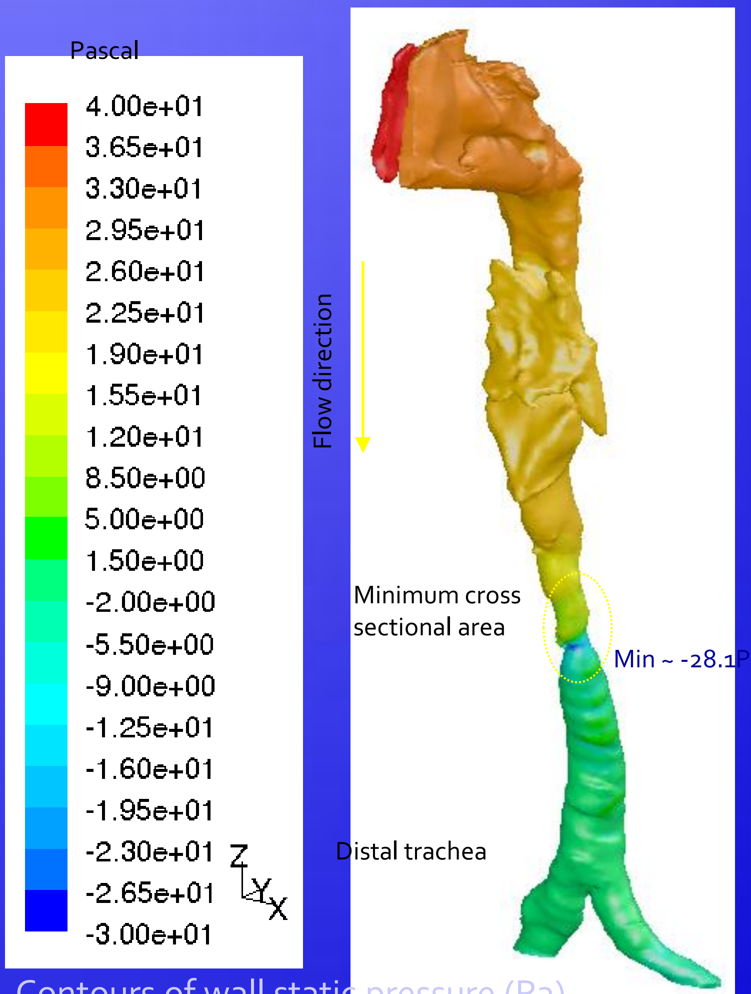
Computational Fluid Dynamics (CFD)

- Measures flow characteristics: velocity, turbulence, pressure, wall sheer stress
- RANS Formulation (Reynolds Averaged Navier-Strokes)
  - To date, most popular formulation to evaluate flow in the upper respiratory tract
  - Assumes rigid airway, not taking into account dynamic air flow and compliance of airway tissue

Results / CFD Data – Inspiration (RANS)



Contours of velocity magnitude distributions (m/sec) along different axial cross-sectional planes and mid-sagittal plane



Contours of wall static pressure (Pa)

The flow accelerates at the minimum cross-sectional area. The lowest static pressure values are found at the minimum cross-sectional area.

Flow Structure Interaction modeling (FSI)

- Takes into account collapsibility and compliance of the airway
- More applicable in flexible airway structures, especially when there is dynamic collapse

Flow Structure Interaction and Large Eddy Simulations

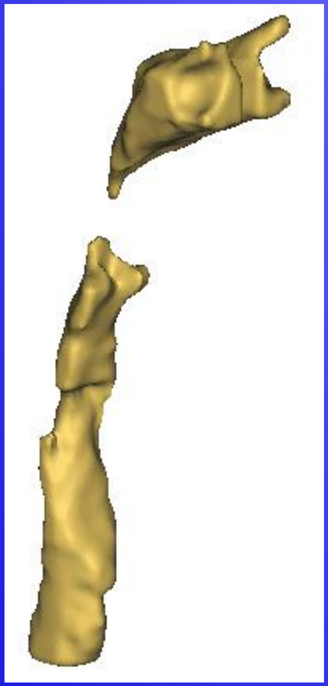
- LES or Large Eddy Simulations
  - New CFD technique
  - Used in Aerospace Engineering
- Better predicts airflow dynamics associated with pharyngeal turbulent flow
- Provides measurements of pressure, sheer stress and airflow velocity at <u>millions</u> of points within the upper airway

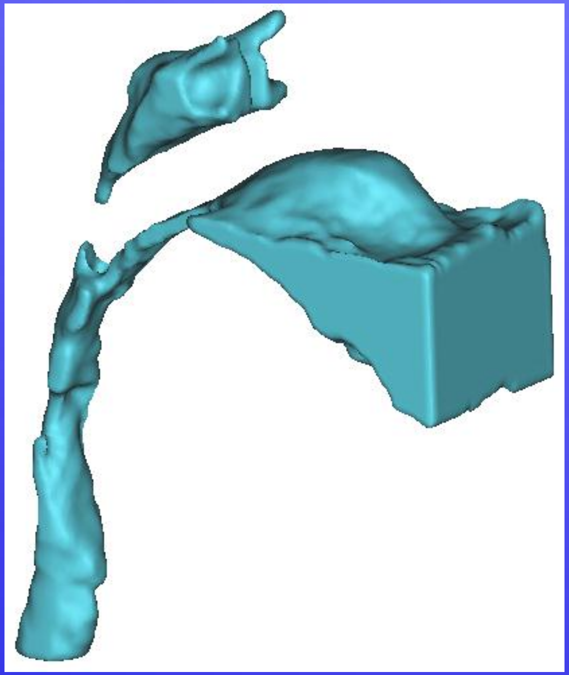
FSI and LES

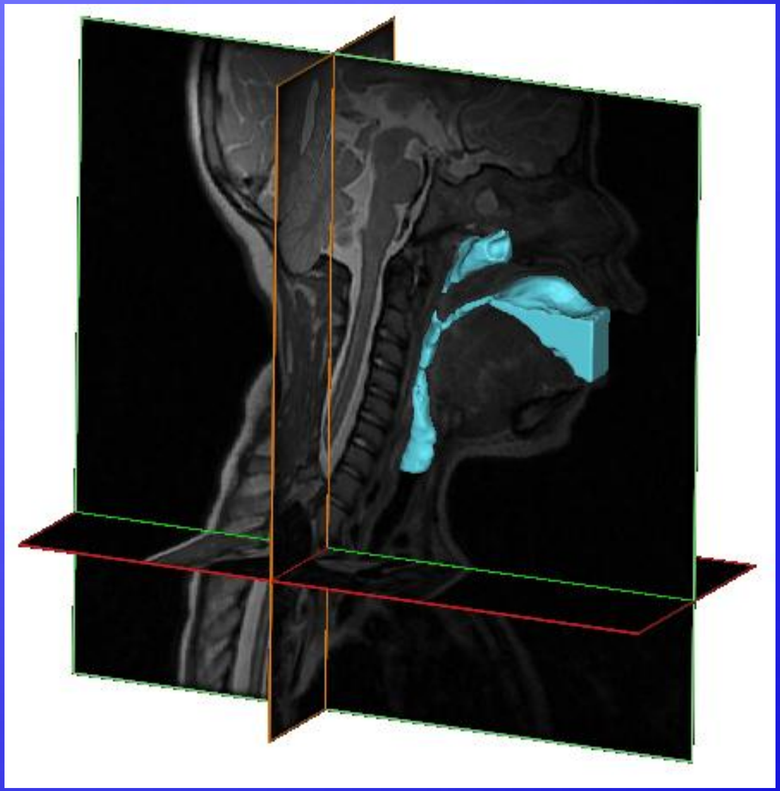
- LES can predict areas of vortices:
  - Concentrated rotational movement that form downstream to a constriction
  - Can form strong negative pressures that cause further collapse in a flexible airway
- RANS model does not capture vortices

Vortices

Structure and Compliance



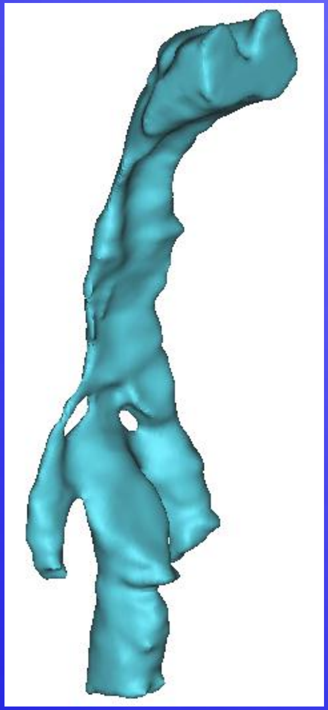


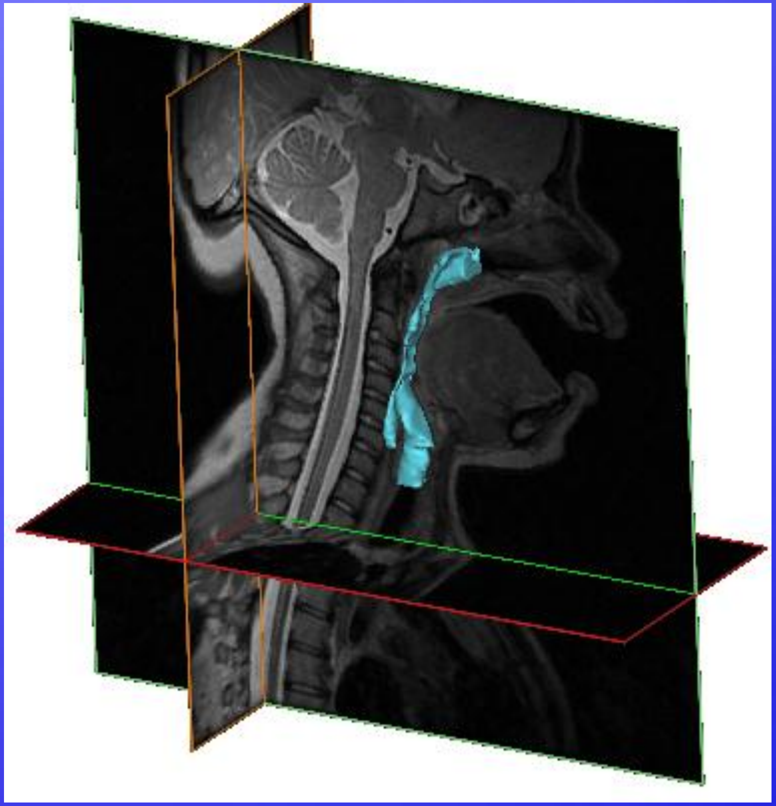


Volume with out Oral Airway: **5.34 cc**

Baseline Model

Structure and Compliance

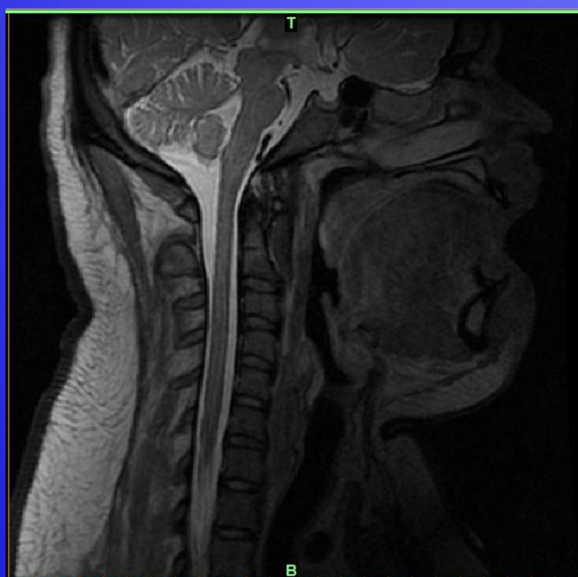


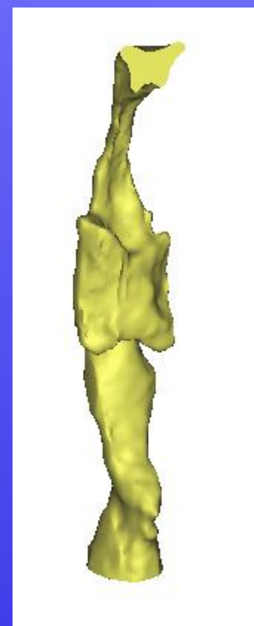


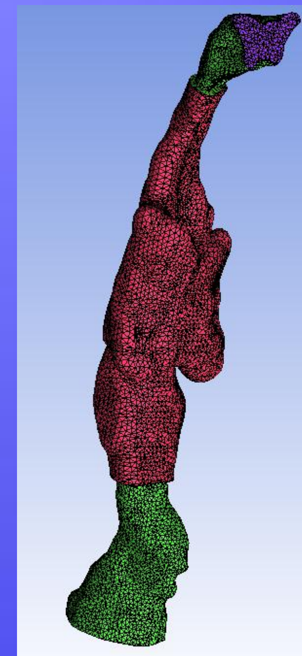
Volume of Pharyngeal Airway: **6.80 cc**

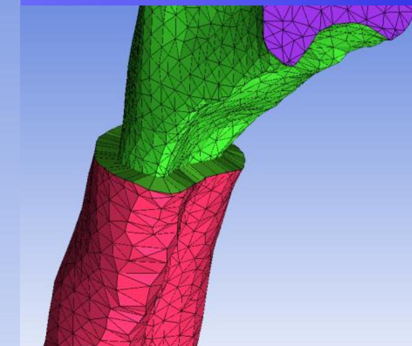
15 cm of H_2O Pressure Model

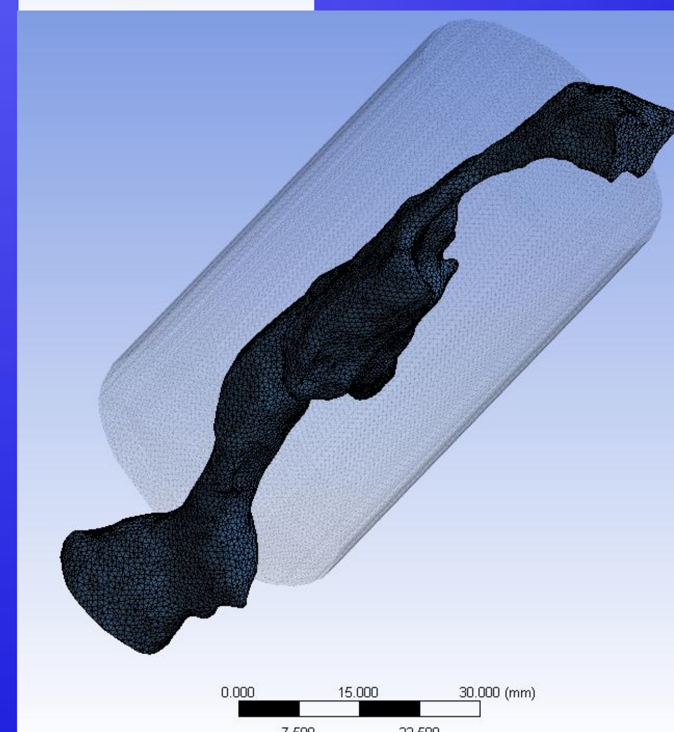
ROADMAP :: FSI MODELING :: 3D Case





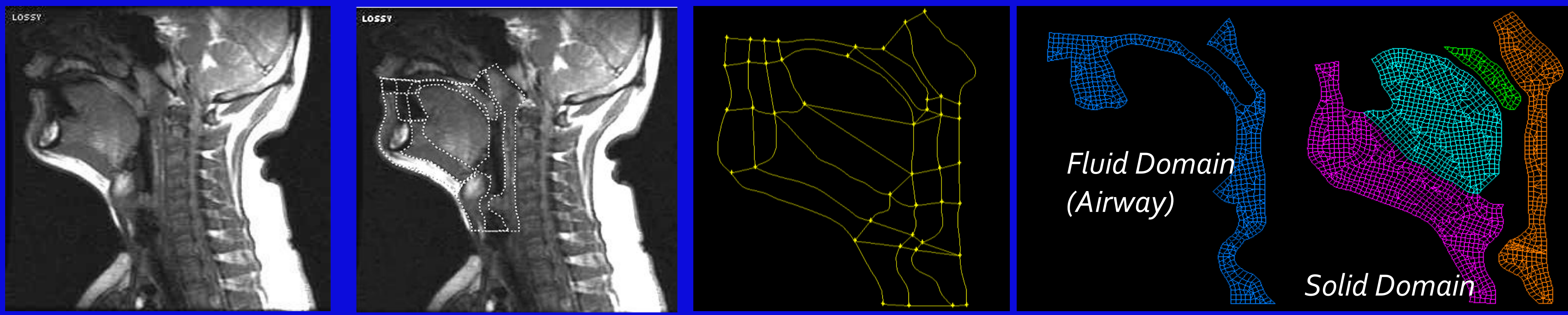






STEP 1

Fluid Structure Interaction (FSI) Methodology



Sagittal Image → **Boundary Identification** → **Model Reconstruction** → **Domain Discretization** → **FSI Solver**

❑ Airway was assumed rigid in previous studies. We are addressing here this limitation.

DYMOSA Aims

- Aim 1: Collect data characterizing upper airway anatomy, tissue compliance and collapsibility
- Aim 2: Generate and validate individualized dynamic FSI model for each child

DYMOSA Aims

- Aim 3: Use the validated dynamic computational model to tailor each patient's surgery and better predict surgical outcomes
- Virtual surgery
  - See effects of virtual surgery: How does surgery on one area of the airway change airway collapse in the rest of the airway?

Long Term Goal

Improve surgical outcomes

- Sleep abnormalities may continue to be a concern throughout the child's life
- Need to continue to observe for changes in sleep patterns as child grows, especially if there are large weight gains

- With more children being evaluated for and diagnosed with OSA, more research will go towards developing better treatments