2021 SCSG
GI SYMPOSIUM

Upper Motility/Esophageal Abstracts DDW

John Pandolfino

UC San Diego Health

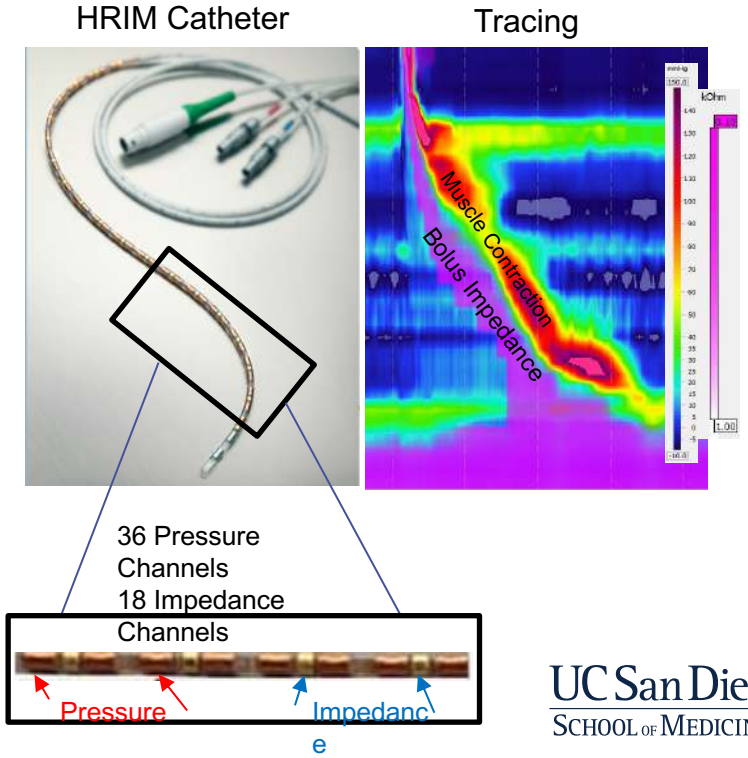
Biomechanical Analysis of Swallow Induced Primary Peristalsis in Patients with EGJOO

Melissa Ledgerwood, Kelvin Mo, Moriah Jewett, Ryan Farzaneh, Vignesh Gandu, Barry Xue, Yinglin Situ, Erica Peng, & Ravinder K. Mittal

DDW 2021

Aim

To determine biomechanical properties of the esophageal wall during peristalsis using luminal CSA (measured from impedance) and pressure from HRIM in normal subjects and patients with EGJOO



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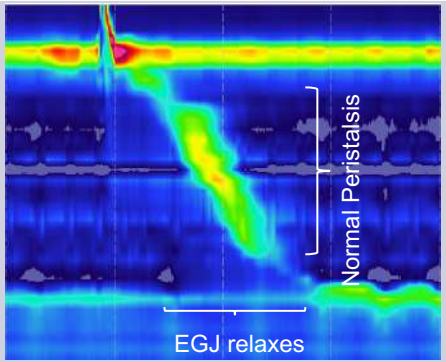
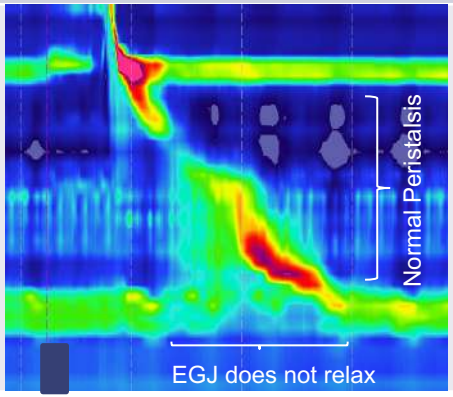
Methods

Subjects: 12 normal healthy asymptomatic subjects and 10 patients with EGJOO. Patients were referred to the UCSD – GI Functional Laboratory for an esophageal manometry study to assess dysphagia symptoms.

Methods: HRIM recording was performed using the standard protocol (10 swallows of 0.5N saline in the supine position), followed by an additional 8-10 swallows of 10ml custom-made viscous gel bolus of 0.5N conductivity were performed in the supine position.

Diagnosis of EGJOO was made from the standard protocol of esophageal manometry using Chicago Classification v3.0. The gel swallows were used to build the tension-area graphs and determine the biomechanical properties of the esophageal wall during peristalsis.

Methods: Study Groups

HRM Example	Groups	Sample Size (# male)	Mean age years (range)	BMI ± SD	Criteria
	**Healthy Normal Controls**	N = 12 (4M)	39.3 (21-65)	22.5 ± 3.1	No dysphagia No history of GI disease or surgery
	**EGJOO Patients***	N = 10 (5M)	62.8 (52-85)	24.5 ± 3.8	Clinical patients with dysphagia (score >1)

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*Used **Chicago Classifications v3.0** This does not use the new 2021 v4.0 (Yadlapati R, Neurogastroenterol Motil, 2021) .

Data Analysis

Modification to HRIM:

Use impedance to obtain **luminal CSA → Deformation**

Neurogastroenterology & Motility

ORIGINAL ARTICLE | Full Access

Novel gel bolus to improve impedance-based measurements of esophageal cross-sectional area during primary peristalsis

Melissa Ledgerwood, Ali Zifan, William Lin, Jesse de Alva, Haojin Chen, Ravinder K. Mittal

First published: 29 December 2020 | https://doi.org/10.1111/nmo.14071

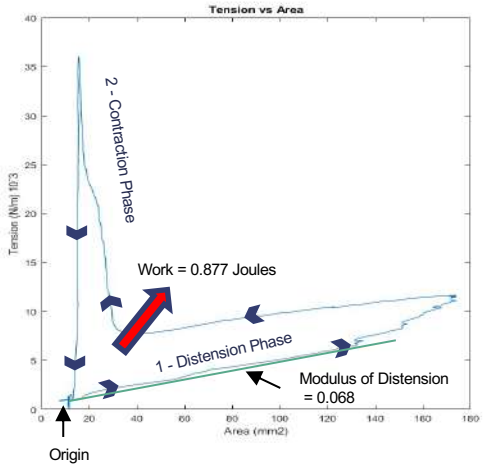
- Mathematically convert impedance value to a cross sectional area (CSA) values.
- The change in CSA is the **deformation** or the stain needed for biomechanics.

M. Ledgerwood, Neurogastroenterol Motil, 2020

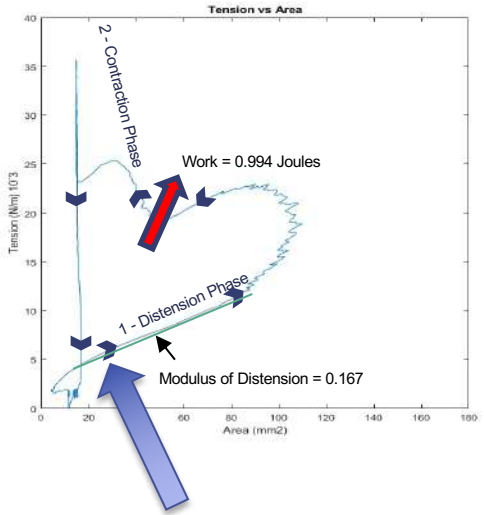
Results: Length-Tension Loop

Tension-Area Loop of Swallow Cycle

Normal



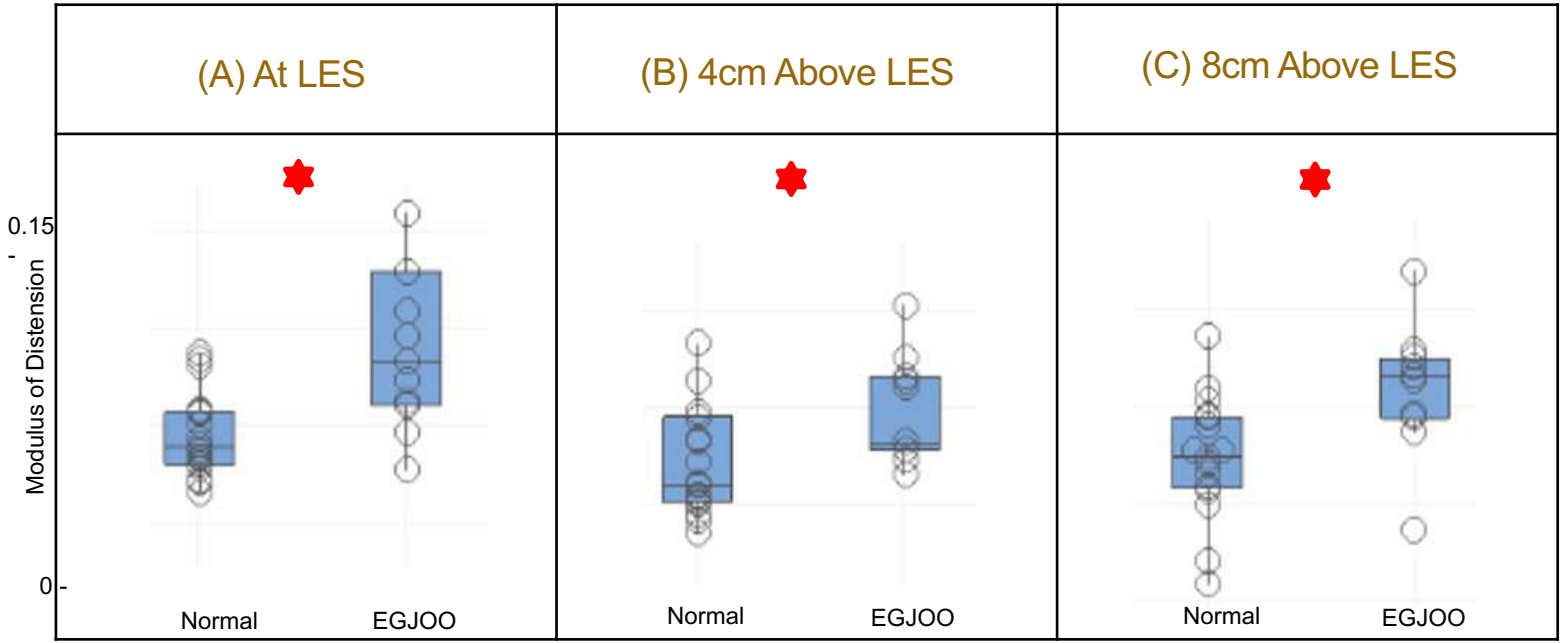
EGJOO



The slope is **steeper** in EGJOO patients
= **stiffer tissue**

- In the Tension – luminal cross sectional area (Tension-Area) loop we see as two limb: **1- Distension** & **2 - Contraction**
- Overall, we found that the healthy normals had a different graph shape than the EGJOO patients
- The slope of the line in the distension section was steeper (modulus of distension greater)
- The modulus of distension is a proxy to the Young's modulus which indicates the stiffness of the tissue.

Results: Young's Modulus at different levels of esophagus



Modulus of Distension / Young's Modulus / Stiffness

was high at all levels of the esophagus from the LES to the mid-esophagus at 8cm above the LES in EGJOO

p≤0.05

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Conclusion

- We present methodology to measure biomechanical properties of the esophageal wall during primary peristalsis using HRIM
- The metrics include peak luminal CSA, intrabolus pressure at the peak CSA, and Modulus of Distension (Young's modulus = a marker of wall rigidity) during the distension phase of peristalsis.
- Patients with EGJOO have different tension-area loops than the healthy pattern. The slope of the tension-area loop is greater in EGJOO patients, compared to normal subjects. A higher modulus was found at the level of LES and 2 locations in the distal esophagus.
- Patients with EGJOO have a stiffer esophageal tissue during the distension phase of peristalsis as compared to healthy subjects.
- The reason for stiffer esophageal wall during the distension phase of peristalsis are not revealed by our study. Possibilities are: 1) impaired inhibitory innervation of muscularis propria, 2) hypertrophy of muscularis propria, 3) fibrosis in the esophageal wall, 4) discoordination between the circular and longitudinal muscle layers.

Intact Esophageal Contractile Reserve is Independently Associated with Improved Pulmonary Function in Interstitial Lung Disease

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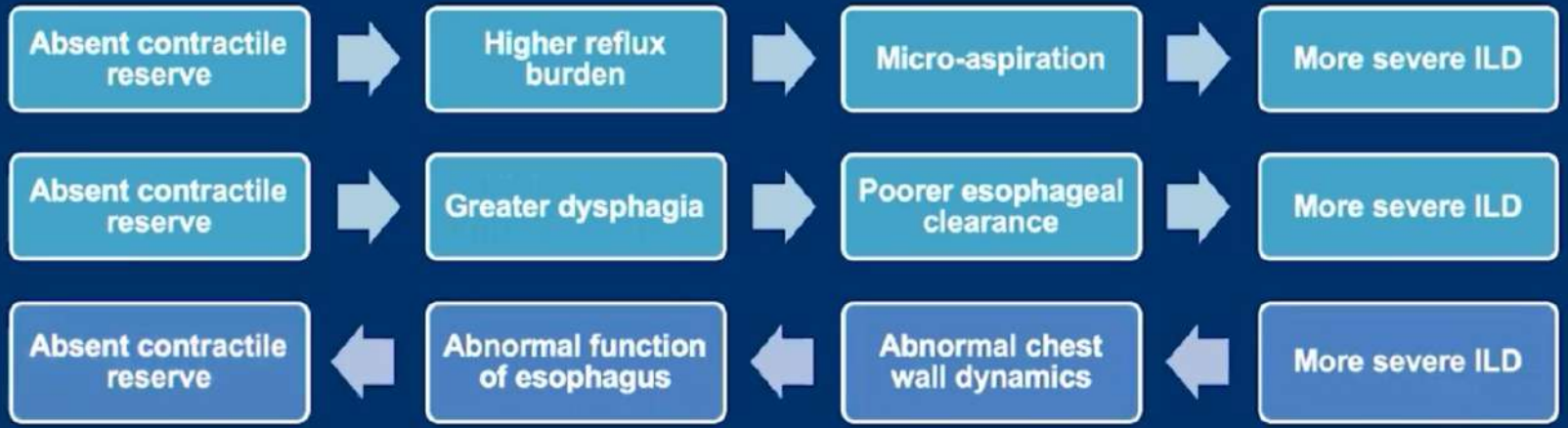
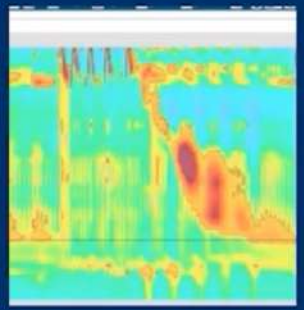
Center for Gastrointestinal Motility
Division of Gastroenterology, Hepatology and Endoscopy
Brigham and Women's Hospital
Harvard Medical School

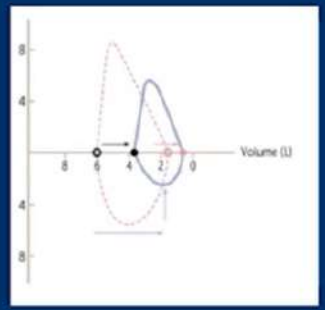
- The role of esophageal contractile reserve in extraesophageal complications is unclear
  - **Does MRS response correlate with pulmonary function in patients with ILD?**



Aim

- To evaluate the relationship between MRS response on HRM and pulmonary function test (PFT) measures in patients with ILD

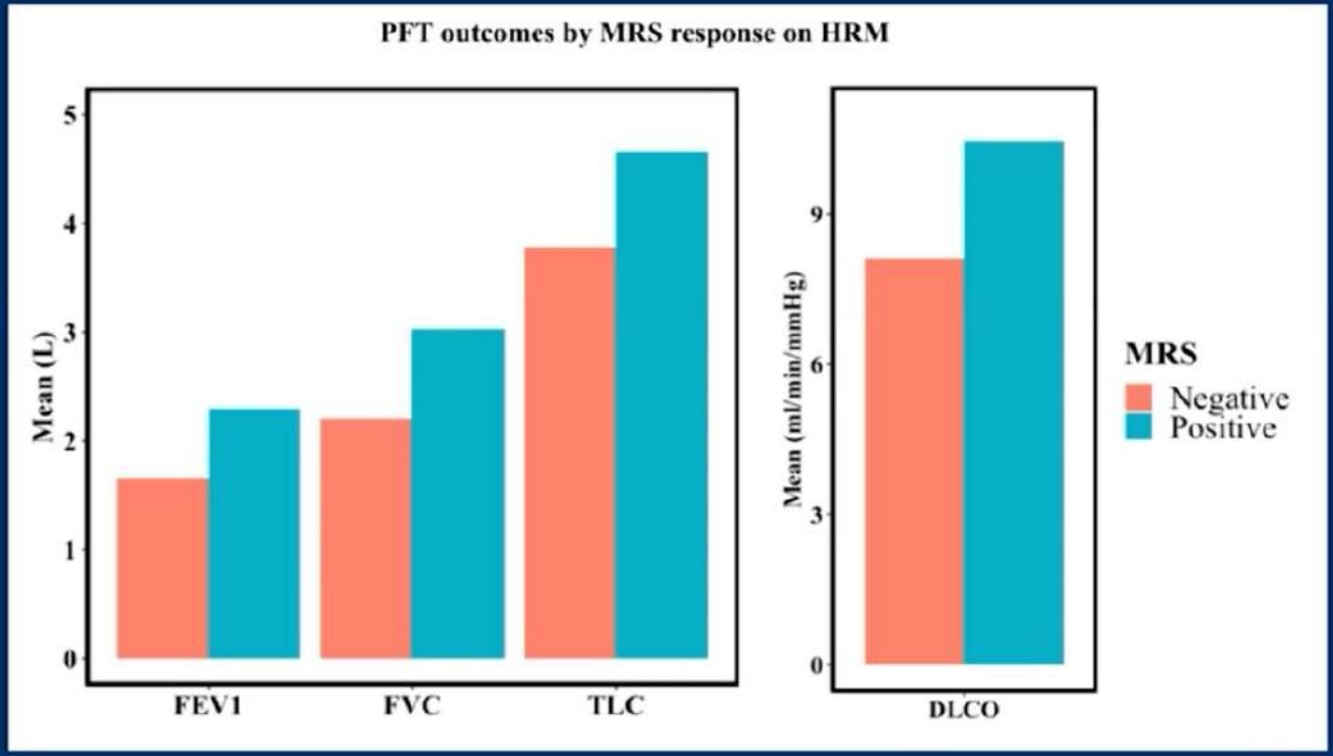




Methods

- Study design:
  - Cohort study
- Inclusion criteria:
  - Consecutive adults with ILD who underwent HRM and impedance-pH as part of routine pre-lung transplant evaluation at a tertiary care institution
- Exclusion criteria
  - Prior anti-reflux or foregut surgery
  - Use of acid suppression within 5 days of testing
  - Incomplete HRM

Results


PFT outcomes by MRS response on HRM
Mean (L)
0
1
2
3
4
5
FEV1
FVC
TLC
Mean (ml/min/mmHg)
0
3
6
9
DLCO
MRS
Negative
Positive

Results

- Multivariable analyses, adjusting for:
  - Age, sex, BMI, smoking history, % failed swallows on HRM, UES pressure, and total # of reflux episodes on MII-pH

Linear regression models	MRS regression coefficient (SE), fully adjusted model	p-value
FEV1 (L)	0.61 (0.21)	0.0051
FEV1 %-predicted	13.89 (6.81)	0.047

Key Clinical Takeaways

- Intact esophageal contractile reserve independently correlated with better lung function among patients with ILD, even after controlling for reflux burden and ineffective motility
  - Supports the potential role of esophageal function in the pathophysiology of ILD
  - Should esophageal function testing, including MRS maneuvers, be more routinely performed in ILD patients?

Key Clinical Takeaways

- Post-lung transplant aspirations, dysphagia, dysmotility, and reflux are common and have been associated with allograft injury
  - Vagal manipulation or injury may play a role
  - Given associations between negative MRS and dysphagia post-anti-reflux surgery, MRS testing may be an adjunct prognostic tool during lung transplant evaluation to stratify for post-transplant complications

Atkins ZB et al. *J Heart Lung Transplant* 2007
Murthy R *J Heart Lung Transplant* 2015
Stoikes N et al. *Surg Endosc* 2012

FLIP Topography Demonstrates Higher Rate of Retrograde Contractions and Dose-Dependent Reduction in Esophagogastric Junction Distensibility in Chronic Opioid Patients

Diana L. Snyder MD, Michael D. Crowell PhD, Jennifer L. Horsley-Silva MD, Allon Khan MD, Francisco C. Ramirez MD, and Marcelo F. Vela MD

Division of Gastroenterology and Hepatology, Mayo Clinic, Scottsdale, Arizona

Background

- Chronic opioid use is associated with esophageal dysmotility due to impaired inhibitory signaling in the esophagus
- This is termed opioid-induced esophageal dysfunction (OIED)

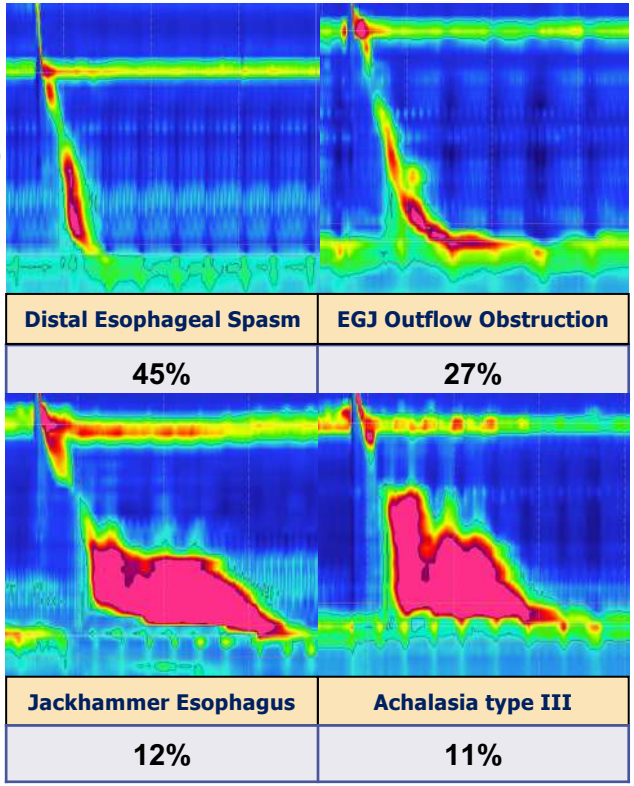
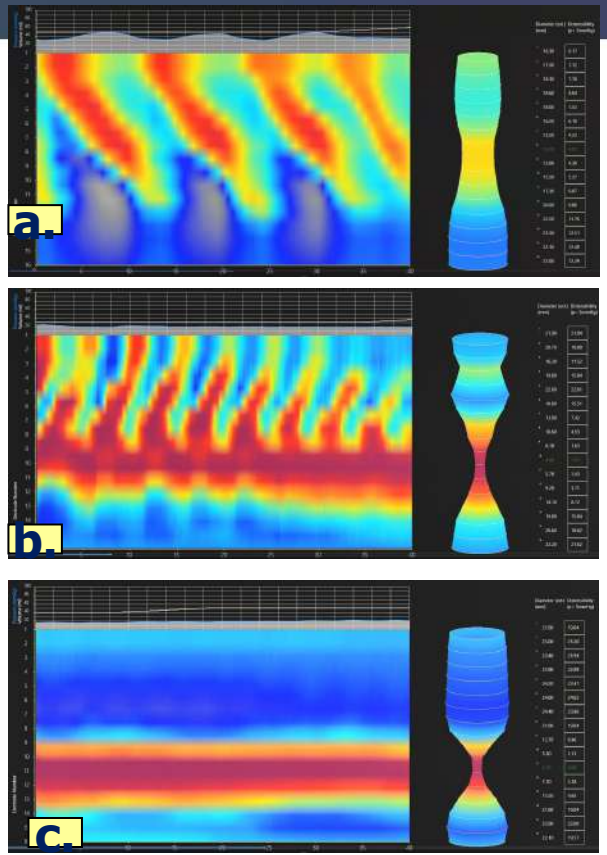


Figure redrawn from Ratuapli et al. AJG 2015, Snyder et al. AJG 2019

Background

- Functional lumen imaging probe (FLIP) during endoscopy evaluates:
  - EGJ distensibility
  - Esophageal body contraction pattern during distension-induced secondary peristalsis
- FLIP findings have not been studied in chronic opioid users
- FLIP may serve as screening tool for OIED



Methods

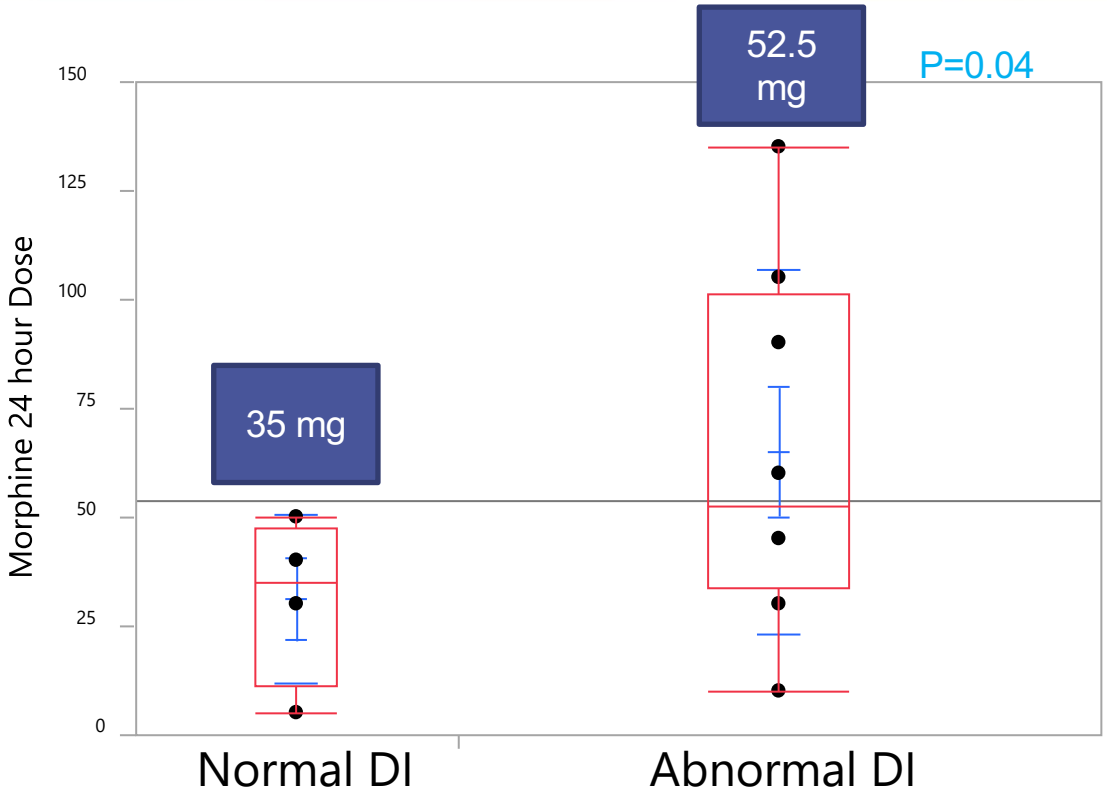
- Retrospective analysis of FLIP studies evaluating esophageal symptoms in chronic opioid users (>3 months) compared to control patients not on opioids
- Exclusions: prior gastroesophageal surgery, pneumatic dilation, esophageal botulinum toxin within 6 months of FLIP, stricture, achalasia type I or II
- FLIP topography completed during propofol-sedated endoscopy with a 16 cm balloon
  - Secondary peristaltic response assessed at 30-40-50-60 ml classified as:
    - Repetitive antegrade contractions (RACs)
    - Repetitive retrograde contractions (RRCs)
    - Diminished/disordered contractile response
    - Absent contractility
  - Median EGJ distensibility index calculated at 60 ml (abnormal <3 mm^2/mmHg)
- Opioid type and dose converted to 24-hour morphine equivalent dose

Results

- 17 chronic opioid patients and 20 control patients
- No difference in BMI, age and sex

FLIP Findings	Chronic Opioid Patients	Controls	P value
RRCs	29%	0%	P=0.014
Mean DI	2.58	2.96	P=0.54
Abnormal DI	59%	55%	P=1.00

Results


52.5 mg
P=0.04
35 mg
Morphine 24 hour Dose
150
125
100
75
50
25
0
Normal DI
Abnormal DI

Key Take-Away

- This is the first study to evaluate DI and esophageal contractility by FLIP in chronic opioid users
- RRCs are associated with DES, achalasia type III and EGJOO
- Since RRCs were more frequent in opioid users, this supports an association between opioids and these motor abnormalities of impaired inhibition
- Significantly higher morphine equivalent dose in opioid users with low DI suggests opioids impair EGJ relaxation in a dose-dependent manner
- Pending larger study confirmation, FLIP may serve to screen for OIED

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Comparative Performance of High Resolution Manometry, Barium Esophagram, and Ambulatory pH Monitoring in Obese Individuals Undergoing Pre-Operative Evaluation for Bariatric Surgery

Fady Youssef[1,]; Priya Sharma[2], Madeline Greytak[1], Rena Yadlapati[1]

[1]Division of Gastroenterology, University of California San Diego, La Jolla, California; [2,]Department of Medicine, University of California San Diego, La Jolla, California

Background:

- Esophageal physiologic testing performed as pre-operative evaluation for bariatric surgery may include esophageal high resolution manometry (HRM), barium esophagram (BE), and/or ambulatory reflux monitoring (ARM)
- Reliability and clinical value of these modalities in pre-operative evaluation is not well understood

Research Aim

- To compare physiologic findings between HRM, BE, and ambulatory reflux monitoring in patients with obesity (BMI > 35kg/m2) undergoing pre-operative evaluation for bariatric surgery

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Methods: Study Design & Subjects

- **Study Design:** Retrospective single center study conducted over 12 months (February 2019 to February 2020)
- **Subjects:** Individuals with BMI > 35 kg/m^2 undergoing pre-operative evaluation for bariatric surgery
  - All underwent high resolution esophageal manometry
  - HRM metrics included hiatal hernia, median integrated relaxation pressure (IRP), distal latency, and manometric diagnosis

Methods: Outcomes & Analysis

- **Primary Outcome:**
  - HRM metrics were compared to BE findings of hiatal hernia, delayed transit of barium tablet, and presence of tertiary contractions
  - Acid exposure time on ambulatory reflux monitoring off acid suppression was compared to presence of gastro-esophageal reflux on BE
- **Statistical Analysis:**
  - Receiver operating characteristics and area under the curve (AUC) were assessed

Results

Of the 300 individuals, 247 underwent both HRM and BE

		BE (n = 247)	ARM (n = 53)
Age (years) (SD)		45.8 (13.3)	47.9 (12.0)
Gender, N (%)	Men	56 (22.7%)	13 (24.5%)
	Women	191 (77.3%)	40 (75.5%)
BMI (SD)		45.8 (8.7)	43.9 (9.6)
Tobacco, N, (%)	Never	148 (59.9%)	33 (62.3%)
	Former	76 (30.8%)	15 (28.3%)
	Current	21 (8.5%)	5 (9.4%)
	Unknown	2 (0.8%)	0 (0%)
Alcohol, N (%)	Never	108 (43.7%)	27 (50.9%)
	Social	114 (46.2%)	23 (43.4%)
	Heavy	19 (7.7%)	3 (5.7%)
	Unknown	6 (2.4%)	0 (0%)
Diabetes, N (%)		91 (36.8%)	17 (32.1%)
Hypertension, N (%)		138 (55.9%)	33 (63.5%)
GERD, N (%)		92 (37.2%)	45 (84.9%)
PPI, N (%)		106 (42.9%)	42 (79.2%)
Opiates, N (%)		46 (11.4%)	8 (15.1%)
Symptomatic, N (%)		158 (64.0%)	49 (92.5%)
Hiatal Hernia, N (%)		70 (35.7%)	20 (39.2%)

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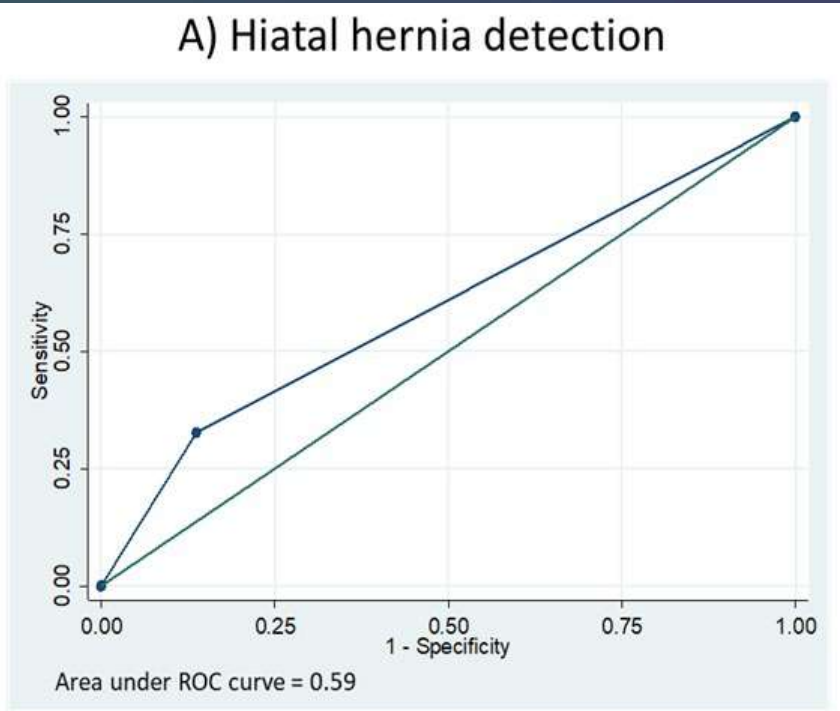
Results

Of the 300 individuals, 247 underwent both HRM and BE

- Hiatal hernia: 49 (20%) on HRM with HH ≥ 1.0 cm vs 43 (17%) on BE
- Compared to HRM, BE had AUC 0.59 (95% CI 0.52, 0.67) with 33% sensitivity and 86% specificity for identifying hiatal hernia



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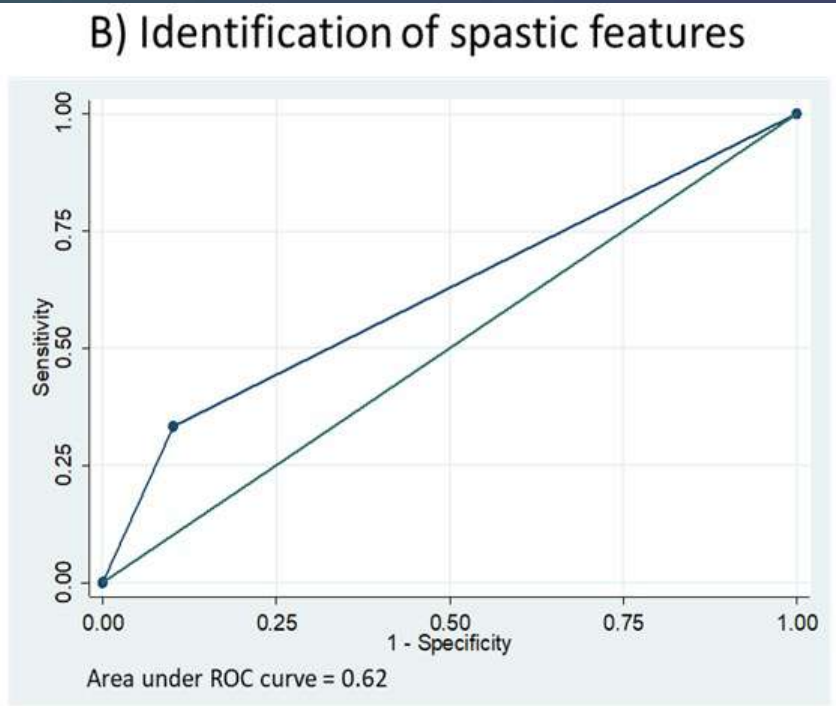
Results

Of the 300 individuals, 247 underwent both HRM and BE

- –Obstructive physiology, 48 individuals had HRM and BE with a tablet
- –Of the 14 with an elevated IRP on HRM, only 1 (7%) had a tablet lodge on BE
- –Compared to HRM detection of ≥20% premature contractions, BE had an AUC of 0.62 (95% CI 0.50, 0.73) for identifying tertiary contractions with 33% sensitivity and 90% specificity



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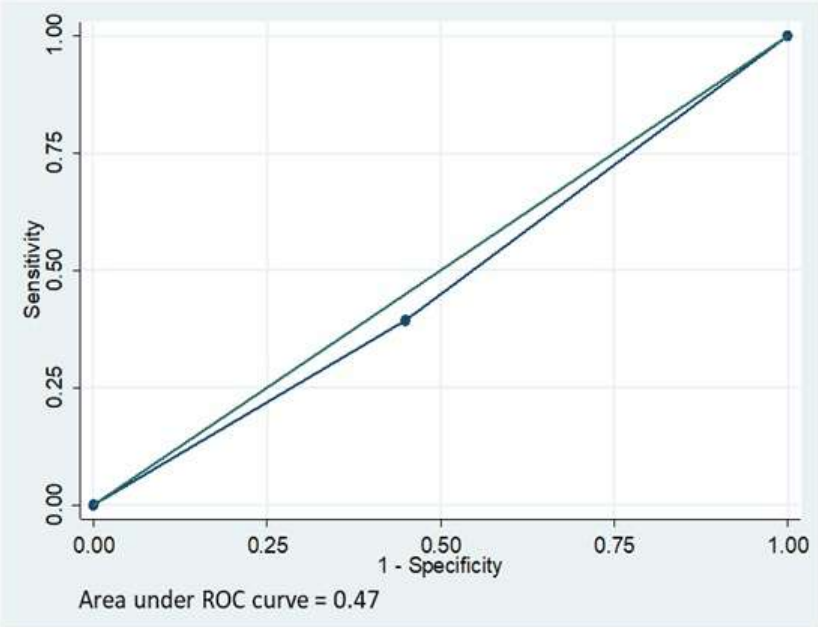
Results

Of the 300 individuals, 53 underwent both BE and ARM off acid suppression

- Compared to GERD identified on ambulatory reflux monitoring (defined as an acid exposure time >4.0% on reflux monitoring), the AUC for BE identification of gastro-esophageal reflux was 0.47 (95% CI 0.33, 0.61) with 39% sensitivity and 55% specificity

C) Gastro-esophageal reflux detection



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Conclusion

- Comparisons of esophageal physiologic testing characteristics among a cohort of individuals with obesity identified that barium esophagram is highly specific for detection of hiatal hernia or spasticity against the gold standard of high-resolution manometry, though poorly sensitive
- Barium esophagram has suboptimal sensitivity and specificity for identification of gastro-esophageal reflux against the gold standard of ambulatory reflux monitoring
- Further studies are needed to determine the optimal method to evaluate esophageal physiology and candidacy for bariatric surgery

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Classification of Functional Dysphagia in Adults Using Deep Structured Learning of Esophageal Intraluminal Electrical Admittance Measurements

Ali Zifan, Pudan Xu, Ravinder K Mittal

Division of Gastroenterology, Department of Medicine

UC San Diego, CA, USA

DDW 2021

May 21-23 | VIRTUAL

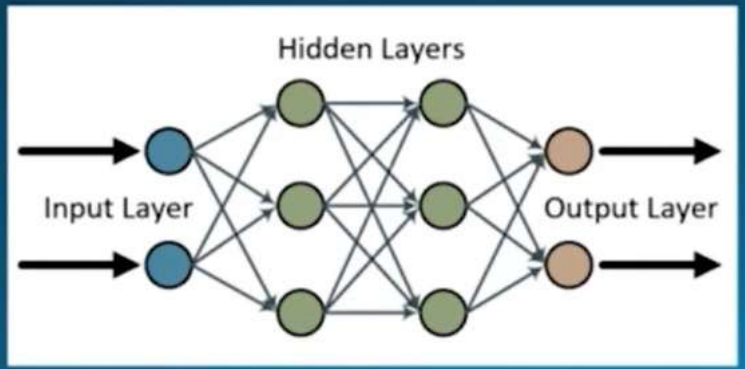
Aim

- We investigate objectively and quantitatively, whether patients with Functional Dysphagia have differences in distension patterns during peristalsis as compared to Normal subjects.

- We use esophageal electrical admittance(inverse of electrical impedance), and a surrogate of distension as input features to deep learning neural networks, which mimic human learning in the brain to discern between the two groups.

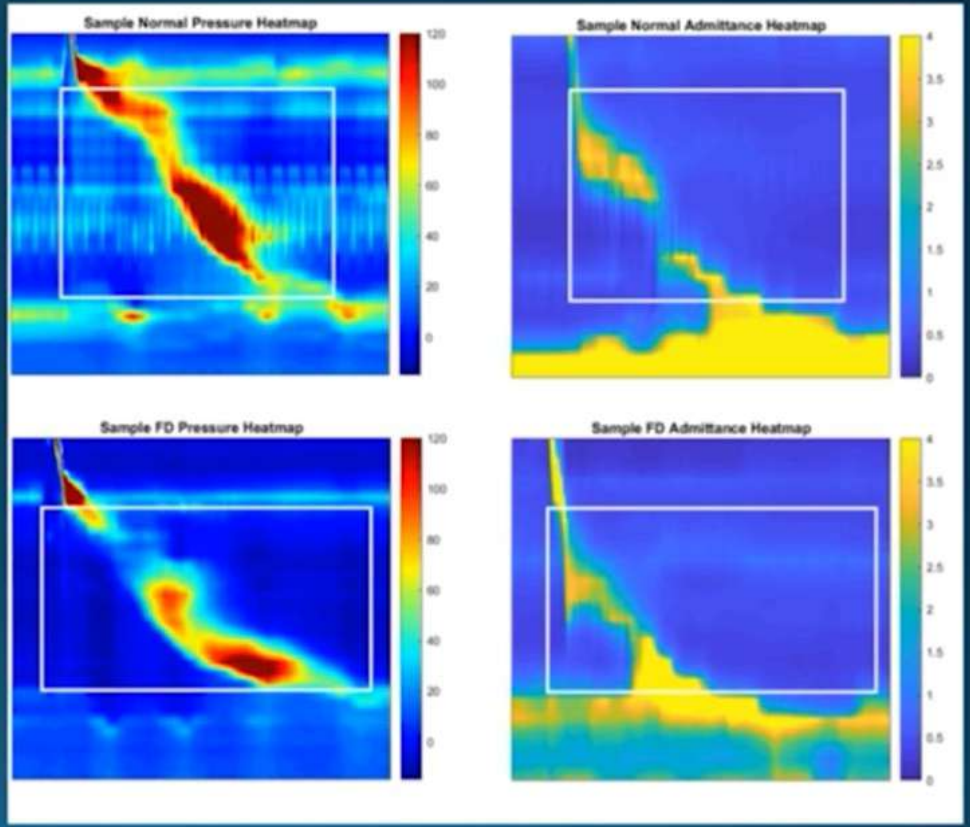
ANN

- ANN posess a large number of processing elements called nodes/neurons which operate in parallel.
- Neurons are connected with others by connection link.
- Each link is associated with weights which contain information about the input signal.
- Each neuron has an internal state of its own which is a function of the inputs that neuron receives- Activation level



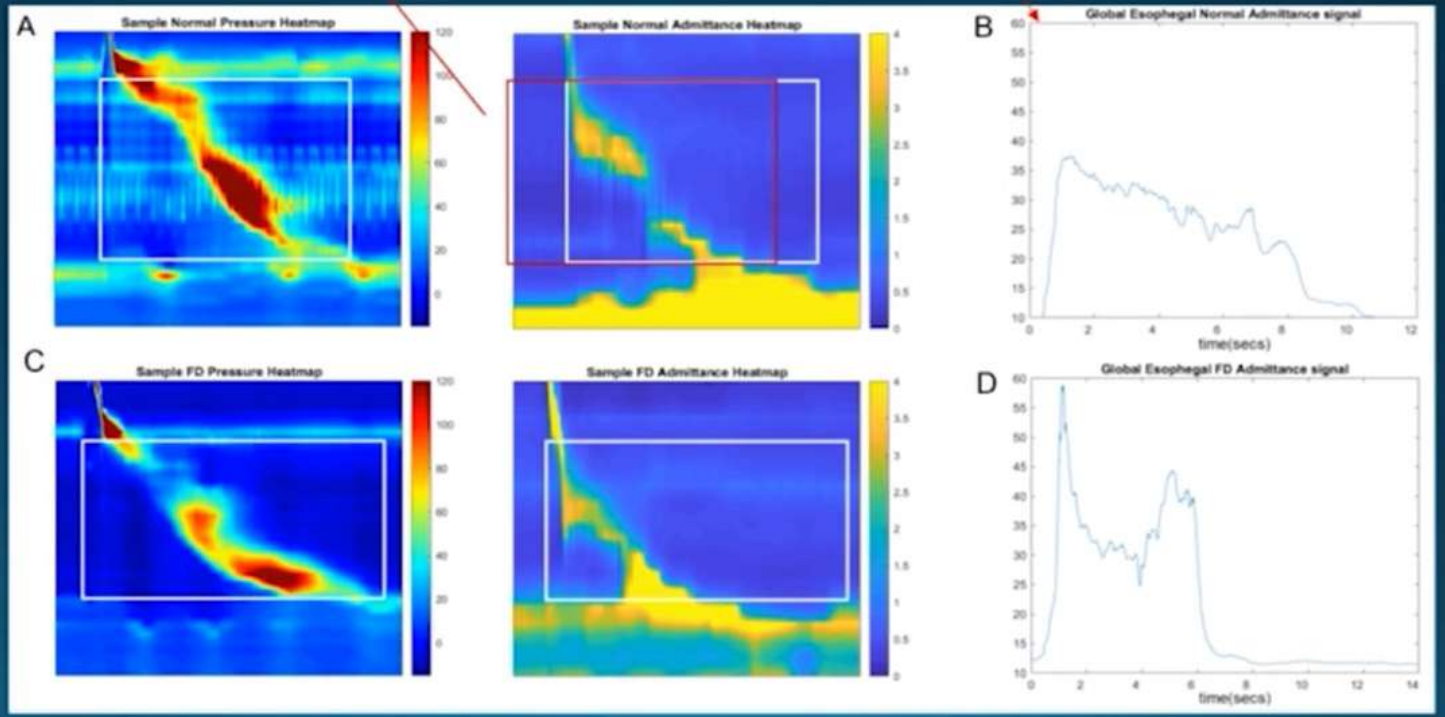
Methods

- High-resolution manometry-impedance experiments, were conducted on 27 asymptomatic normal, and 27 FD patients (Brief Esophageal Dysphagia Questionnaire, BEDQ>10) using 10ml, 0.5N saline.
- To account for inter-swallow variability, 4 swallows per subject was chosen.
- Next, signals falling inside the region between the upper edge of the LES and lower edge of the UES were used for subsequent analysis.

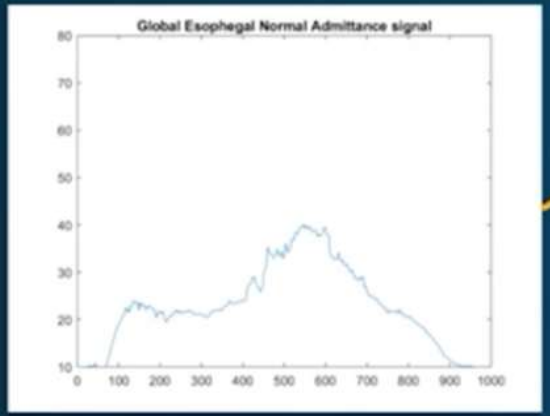


- Next, signals falling inside the region between the upper edge of the LES and lower edge of the UES were used for subsequent analysis.
- The resulting images (10secs from pharyngeal opening) were normalized to the mean esophageal length, and then summed across channels to results in a global esophageal signal for all subjects.

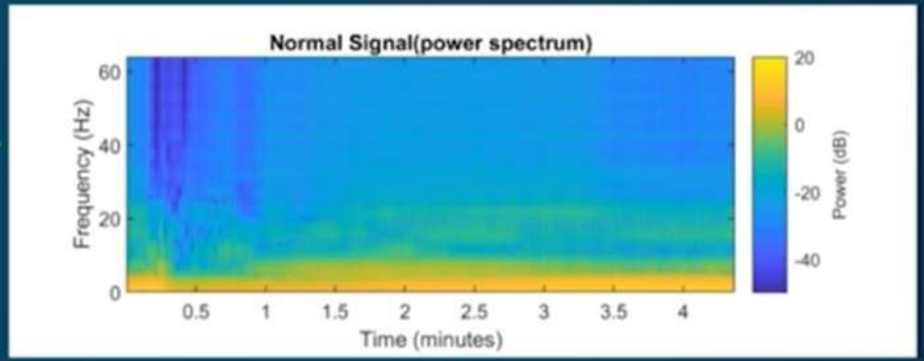
- Next, time-frequency features(i.e., spectral entropy) was extracted from the former signals to train the DLNN



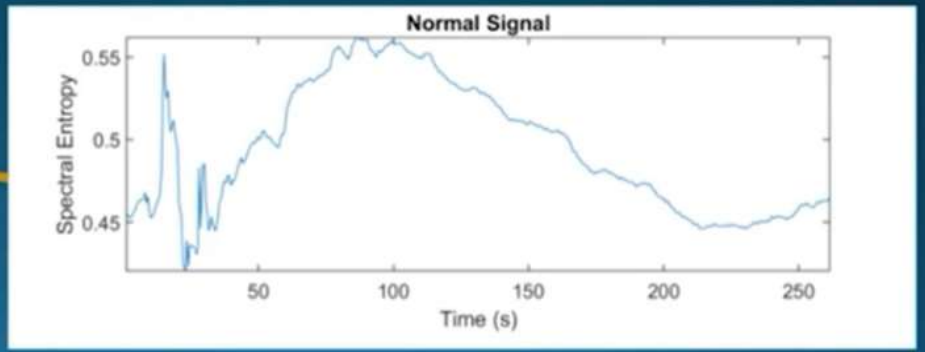
Esophageal Admittance Sum (Normal)



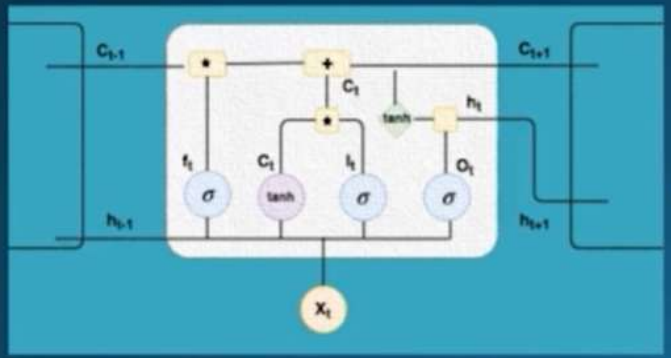
Power Spectrum

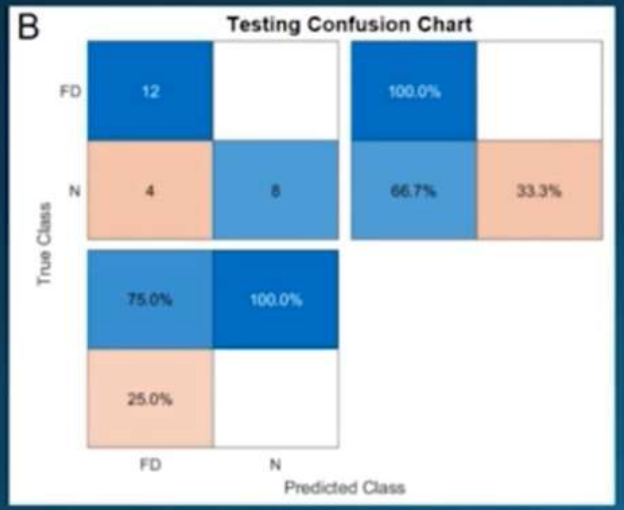


Spectral Entropy



LSTM Network





Results

- Training the LSTM network using admittance time-frequency moment features, resulted in an overall accuracy of 95.83% for training set and 83.33% for testing (120 hidden units per layer, Mini batch size=80, learning rate= 0.01).

- Positive predictive values (PPV) of 99% in training and 100% during testing for FD, and PPV of 92.7% and 66.7% for normals, in training and testing, respectively.

- True positive rates (TPR) of 93.1% and 75% for FD during training and testing. The TPR values were 98.9% and 100% for normal in training and testing, respectively.

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