

AFS 2021 Presidential Lecture:  
The Evolution of FLIP in Motility Diagnostics

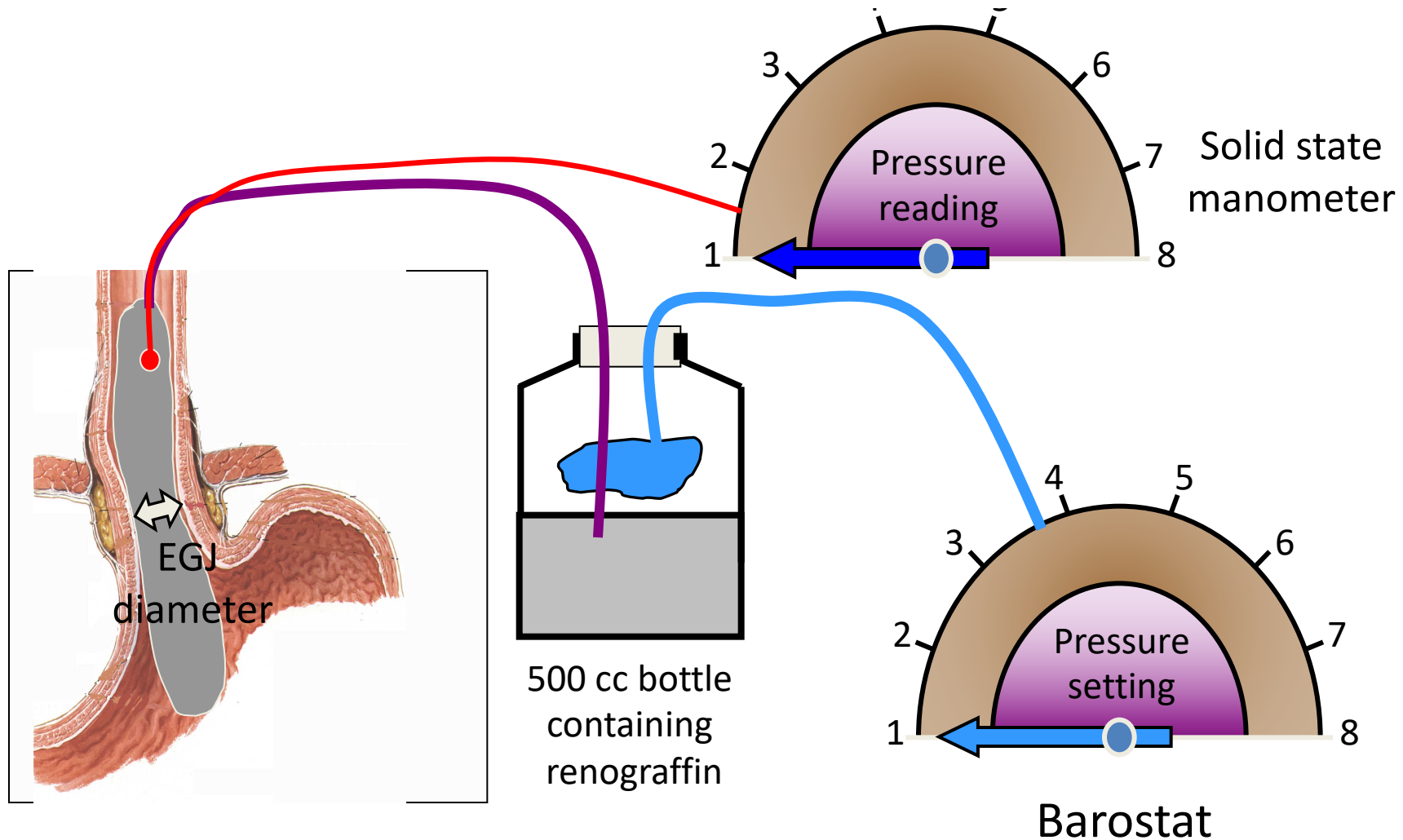
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# Peter J. Kahrilas: Financial Disclosures

- *Consultant:* Ironwood Pharmaceuticals, Reckitt Benchiser, Johnson & Johnson
- *Investment/ownership:* none
- *Speakers Bureau:* none
- *Research grant Support (clinical trials):* Ironwood
- *Patents:* Shared patent on FLIP with Drs Pandolfino and Lin

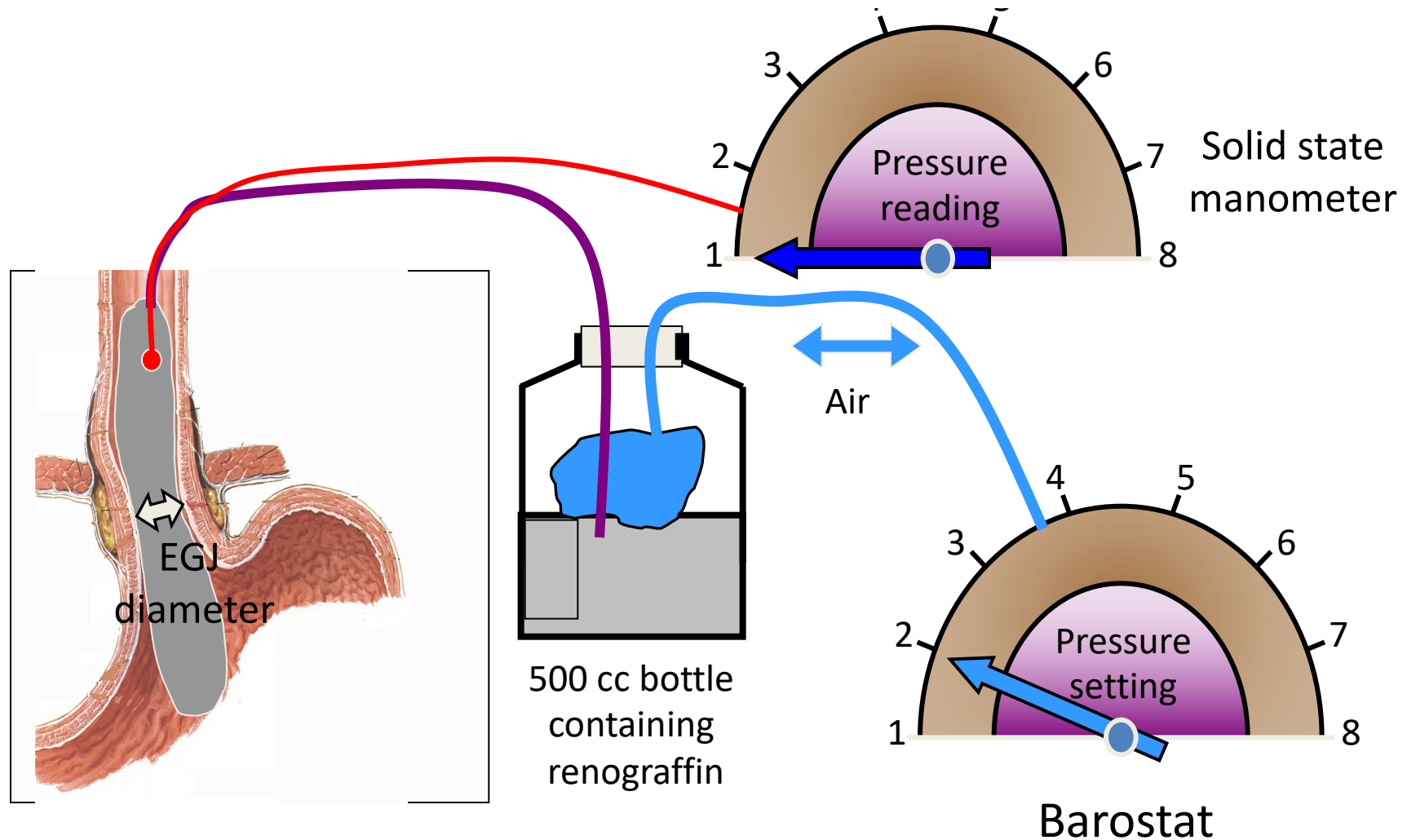
# Hydrostat: a Modified Barostat

*The impetus for FLIP technology*



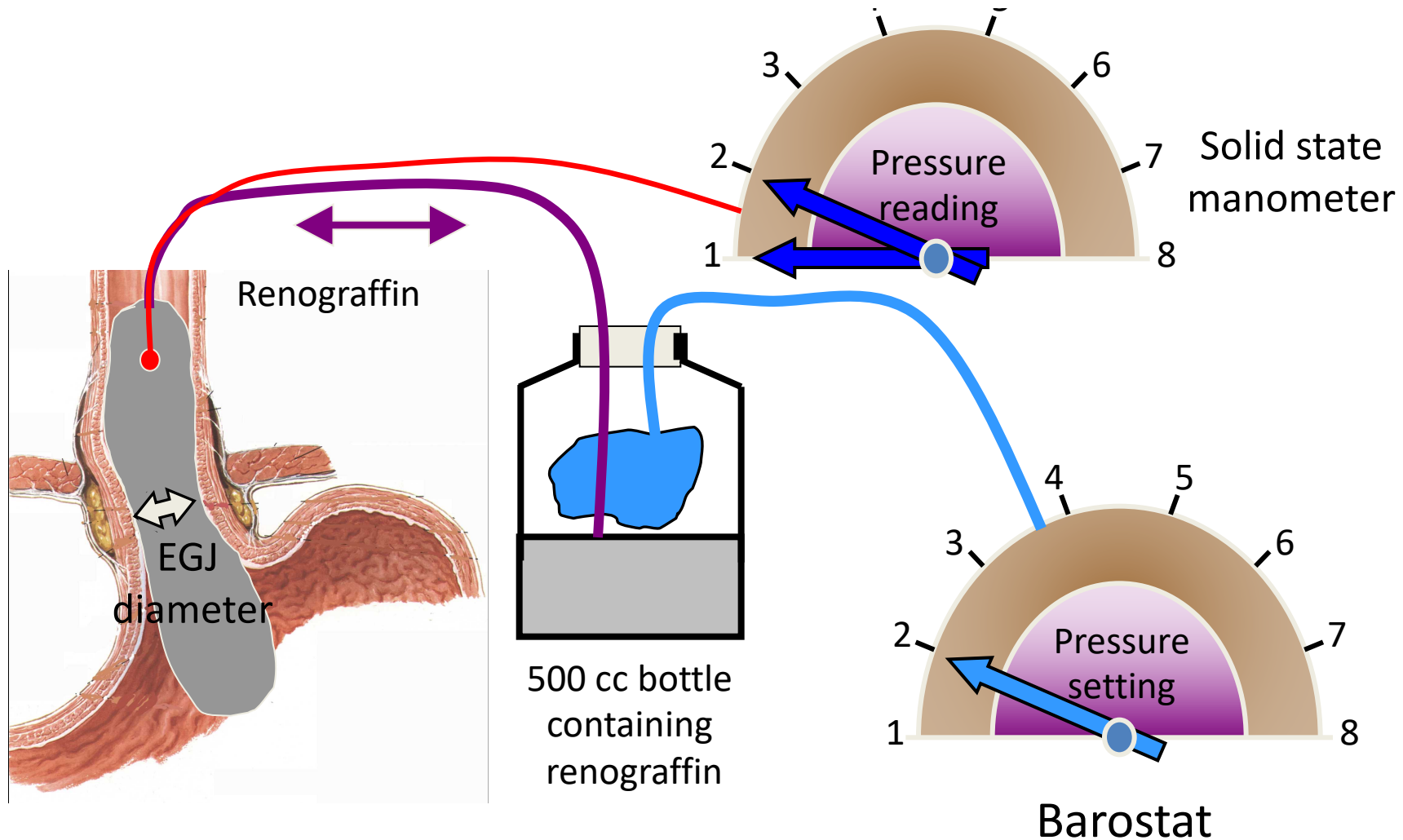
# Hydrostat: a Modified Barostat

*The impetus for FLIP technology*

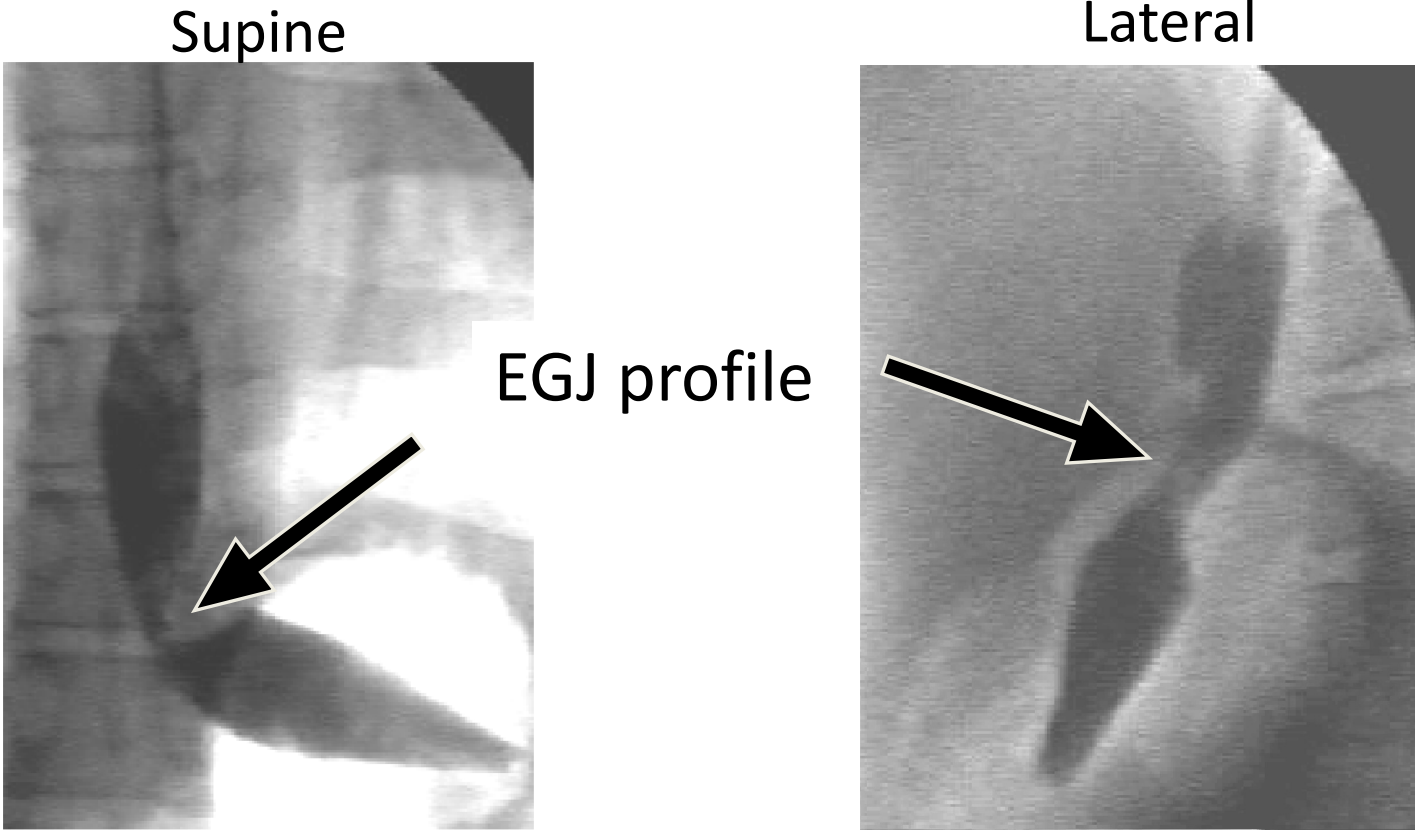


# Hydrostat: a Modified Barostat

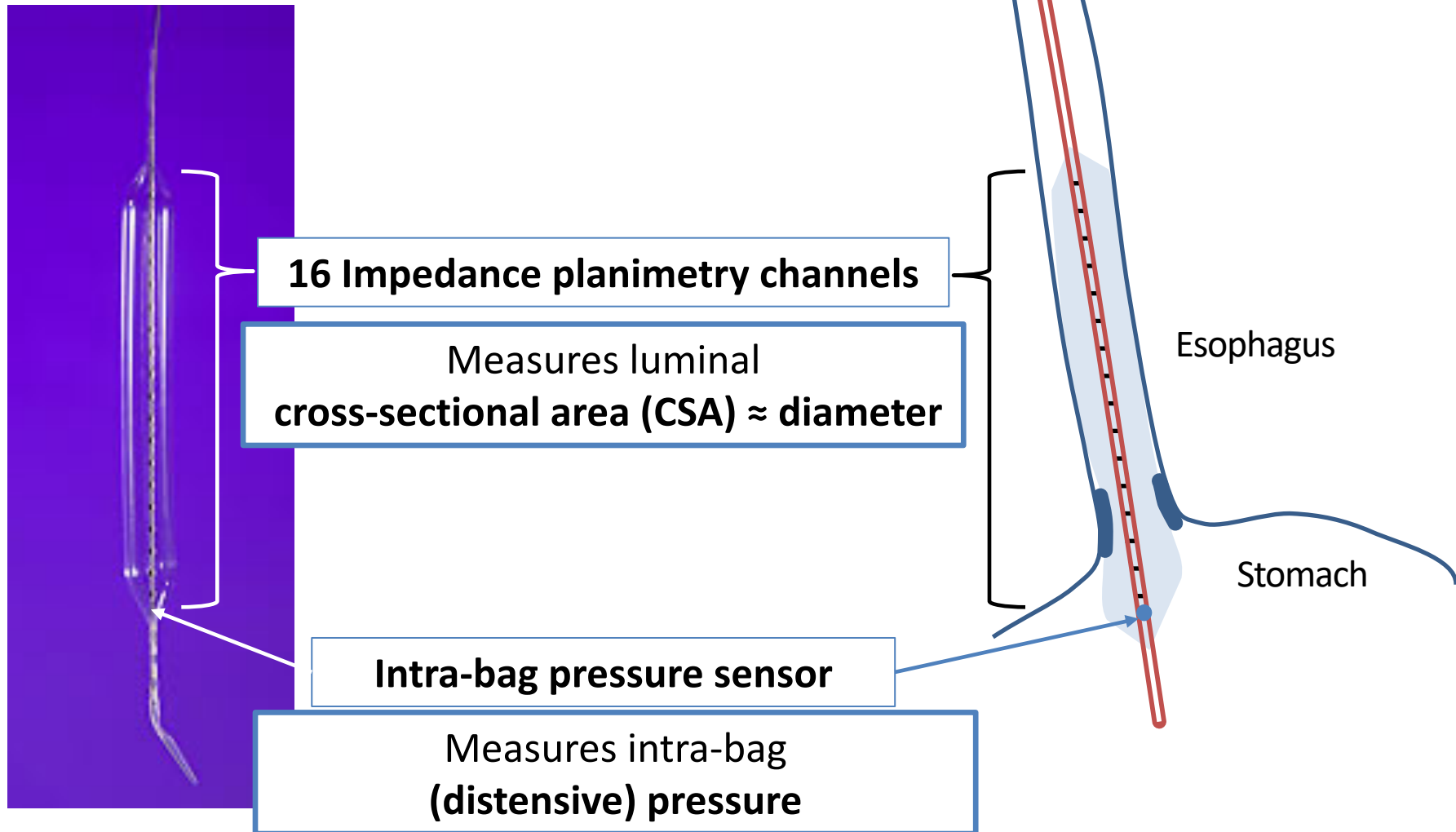
*The impetus for FLIP technology*



# Fluoroscopic images of Hydrostat:normal subject

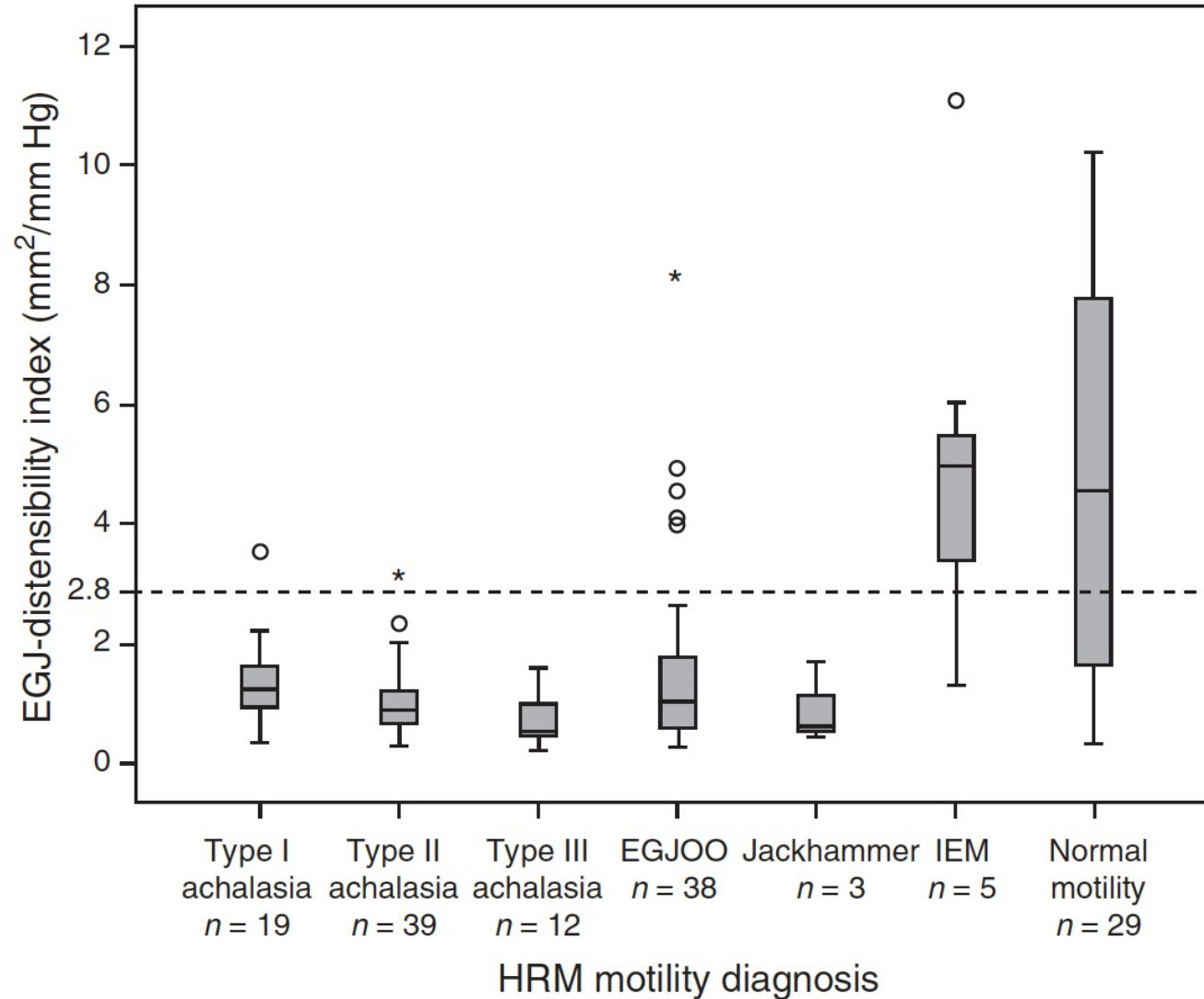


# Functional lumen imaging probe (FLIP)



# EGJ distensibility index as criterion for achalasia

*Lower limit of normal = 2.8 mm<sup>2</sup>/mmHg*





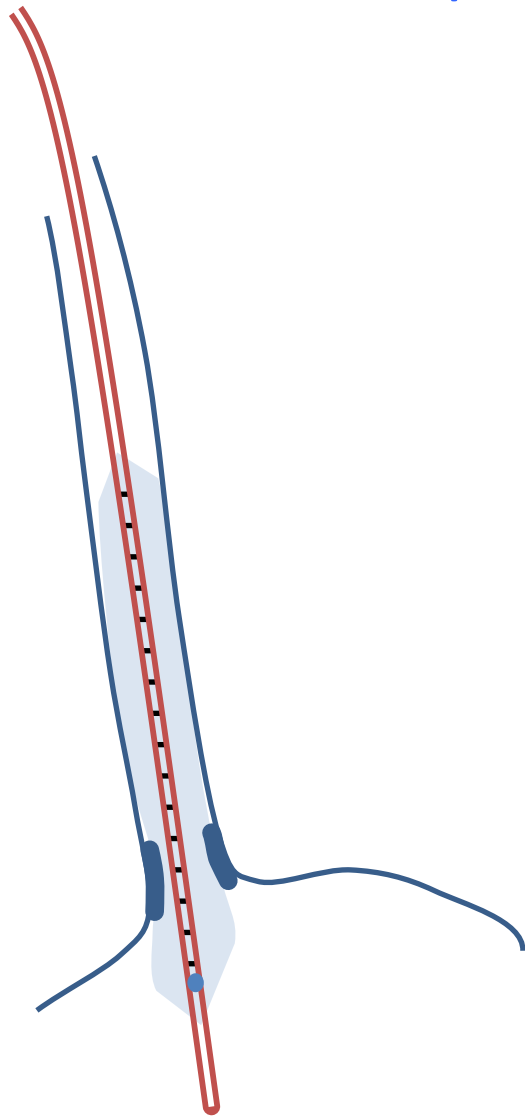
# FLIP in the evaluation of dysphagia and EMDs

## *Applications*

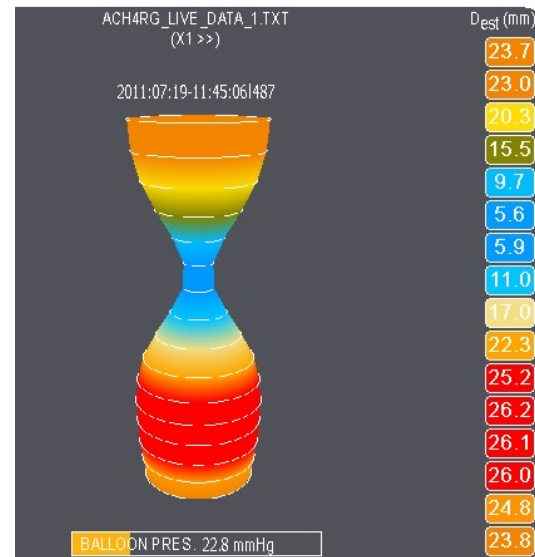
- Achalasia diagnosis and subtyping
  - Motility assessment in lieu of manometry

# FLIP assessment of EGJ in achalasia

*Complementary test in diagnosis and outcome assessment*

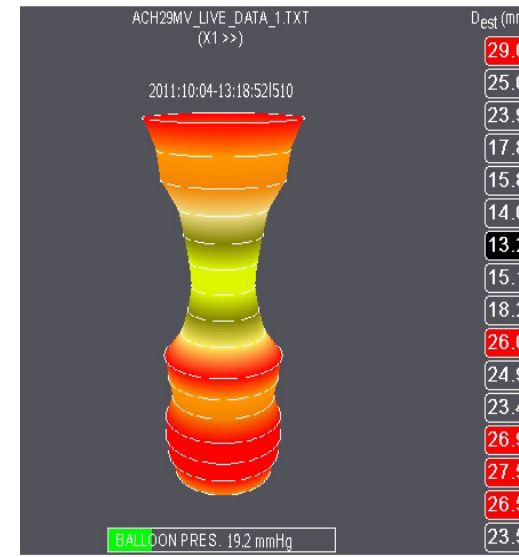


## Untreated



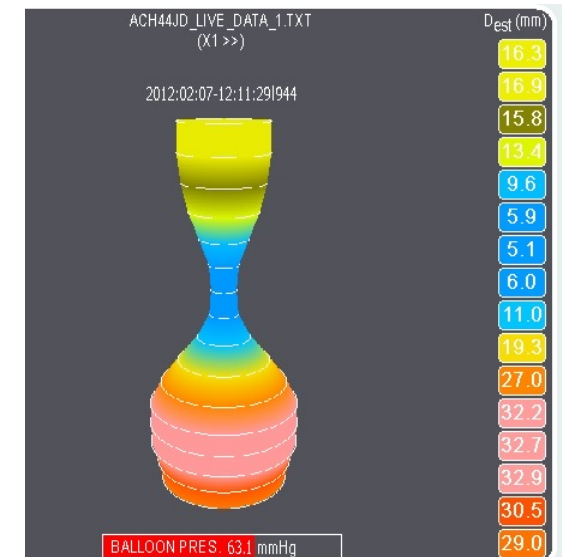
Volume: 40 ml  
CSA= 24 mm<sup>2</sup>  
Pressure =22.8 mmHg  
EGJ distensibility index=1.05

## Good Response



Volume: 40 ml  
CSA= 137 mm<sup>2</sup>  
Pressure =19.2 mmHg  
EGJ distensibility index = 7.1

## Poor Response

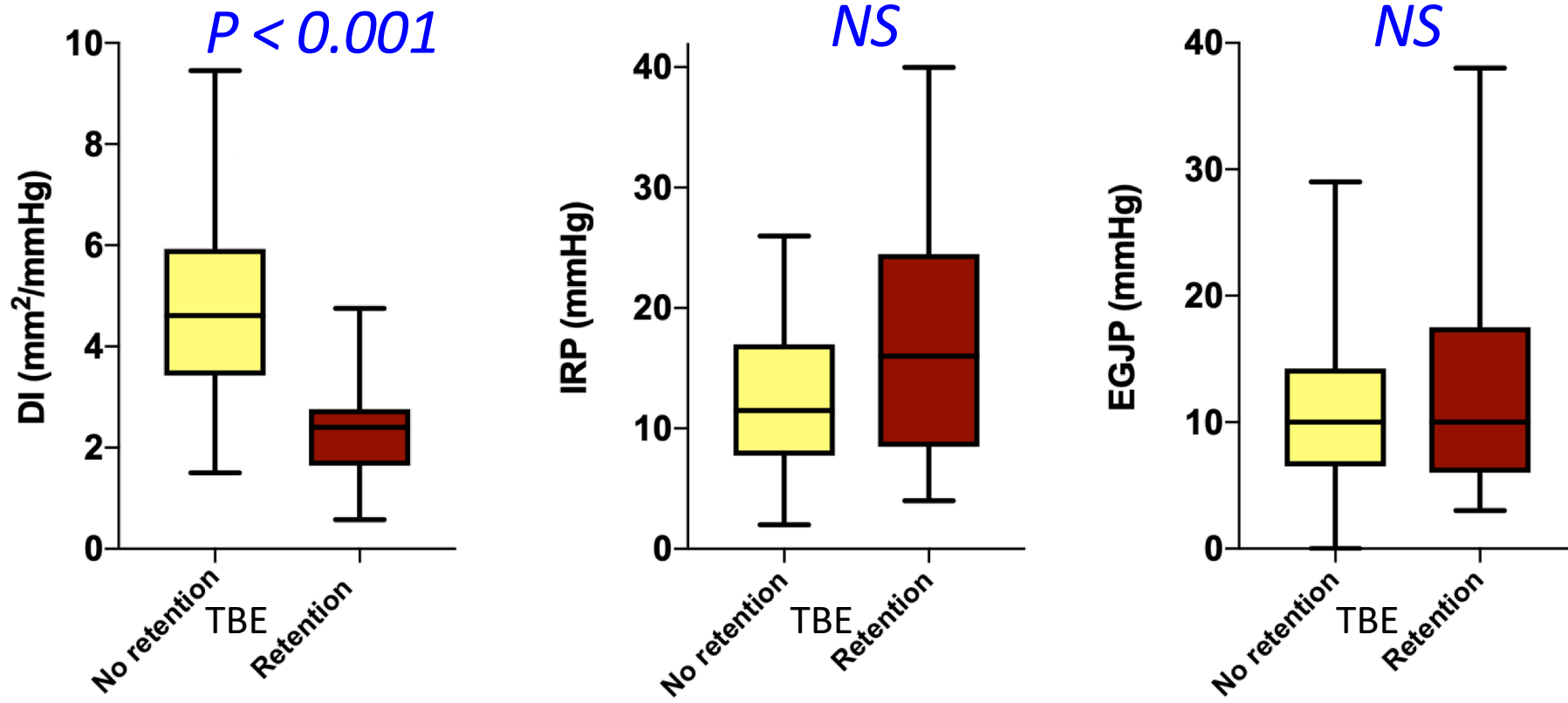


Volume: 40 ml  
CSA= 21 mm<sup>2</sup>  
Pressure =63.1 mmHg  
EGJ distensibility index = 0.33

# Assessment of treatment response in achalasia

*FLIP vs HRM: 52 pts 13 (4-204) mo after treatment*

EGJ-DI better associated with outcome than IRP or LES pressure

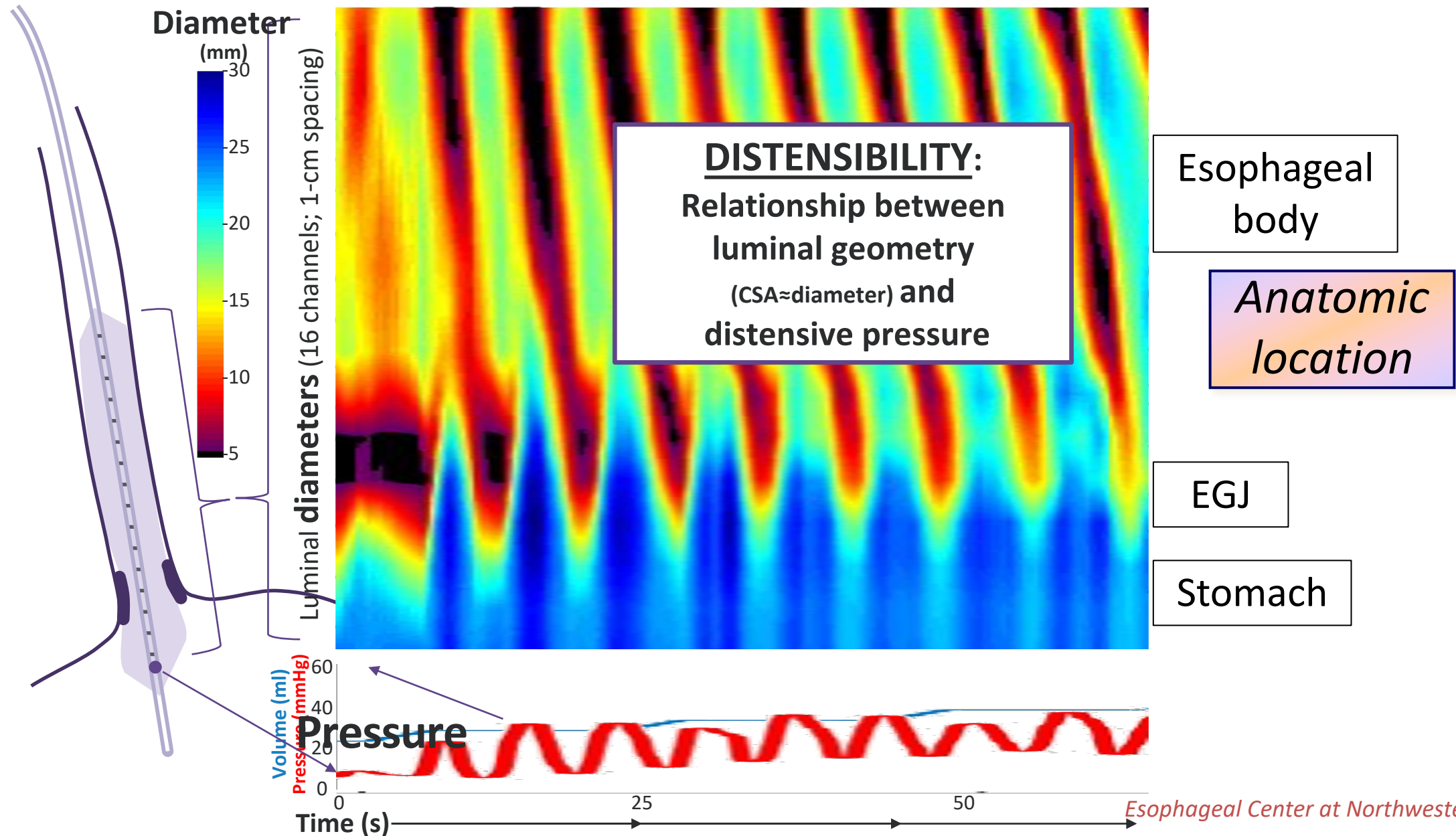


# FLIP in the evaluation of dysphagia and EMDs

## *Applications*

- Achalasia diagnosis and subtyping
  - Motility assessment in lieu of manometry
- Achalasia treatment assessment
  - Intraoperative
  - Recurrence

# FLIP Panometry: esophageal *diameter* topography



# FLIP in the evaluation of dysphagia and EMDs

## *Applications*

- Achalasia diagnosis and subtyping
  - Motility assessment in lieu of manometry
- Achalasia treatment assessment
  - Intraoperative
  - Recurrence
- Functional assessment of EGJ outflow obstruction

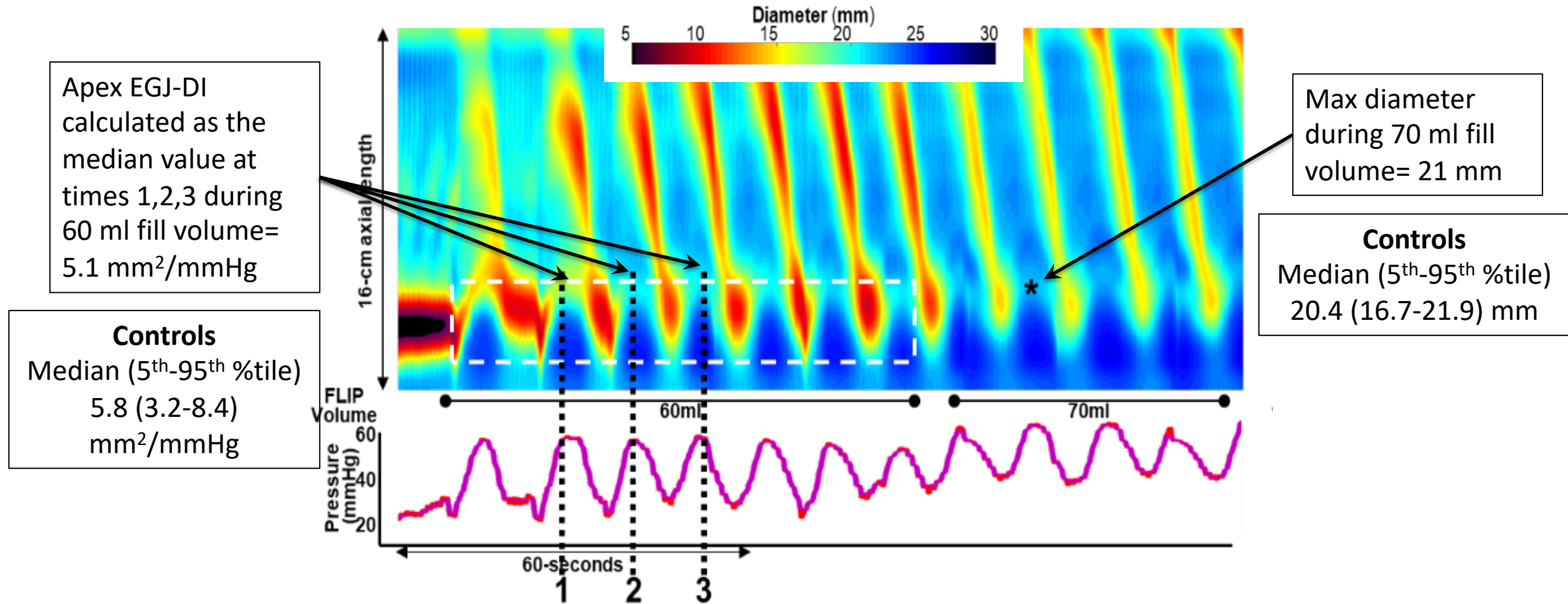
# Flip Panometry Assessment of EGJ Obstruction

## *Methodology*

- 687 patients (245 with outflow obstruction on HRM, 314 nl on HRM, 128 inconclusive) and 35 controls with FLIP and HRM studies included
- Flip data exported and analyzed with open source software:  
<http://www.wklytics.com/nmgi>
- Two metrics: Distensibility index (DI) at 60 ml and Max EGJ diameter achieved at 60ml or 70ml
  - Areas of dry catheter artifact excluded

# Flip Panometry Assessment of EGJ Obstruction

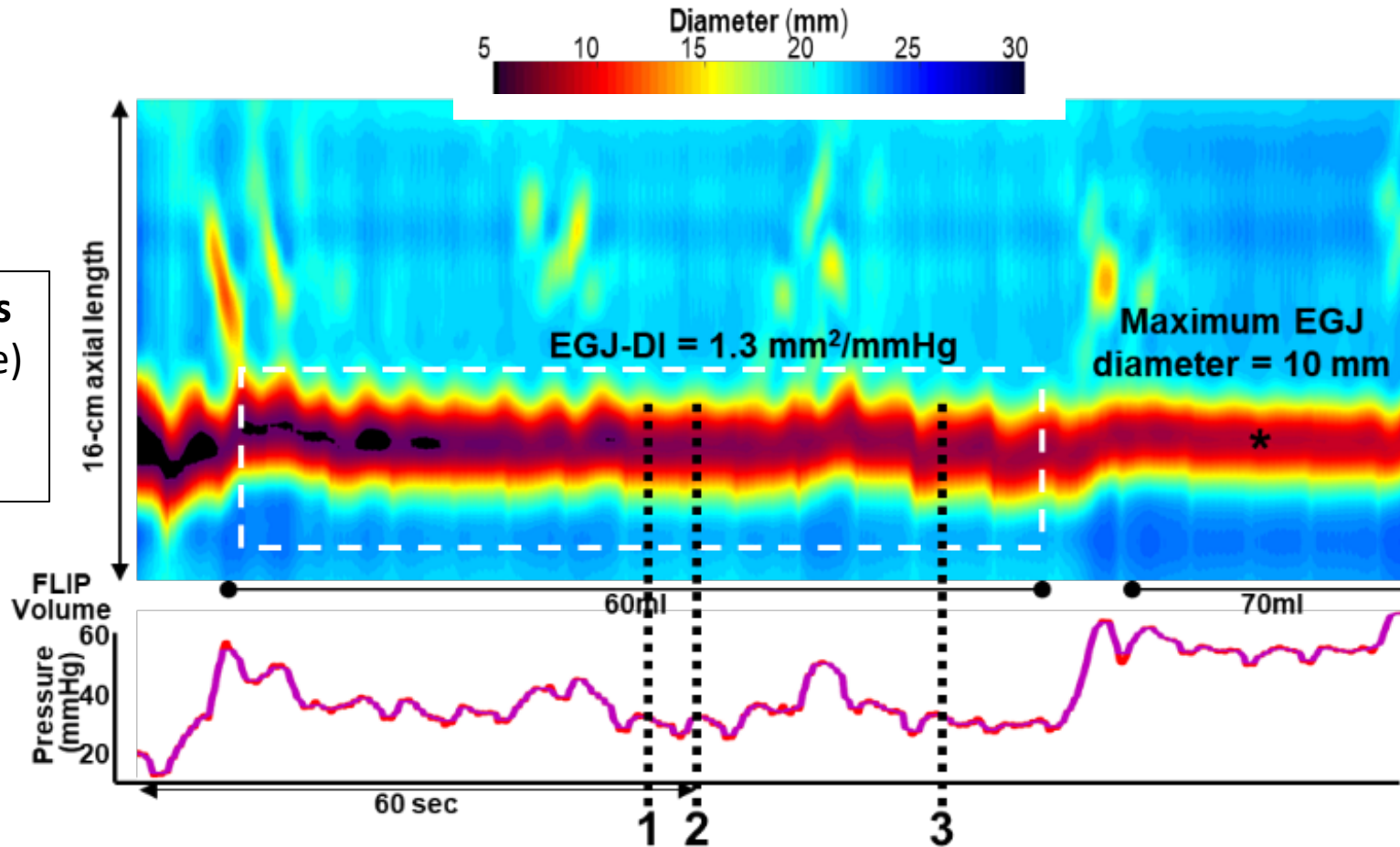
## Determining Distensibility Index (EGJ-DI) and Max diameter- normal





# Flip Panometry Assessment of EGJ Obstruction

## *Distensibility Index (DI) and Max diameter- Achalasia*

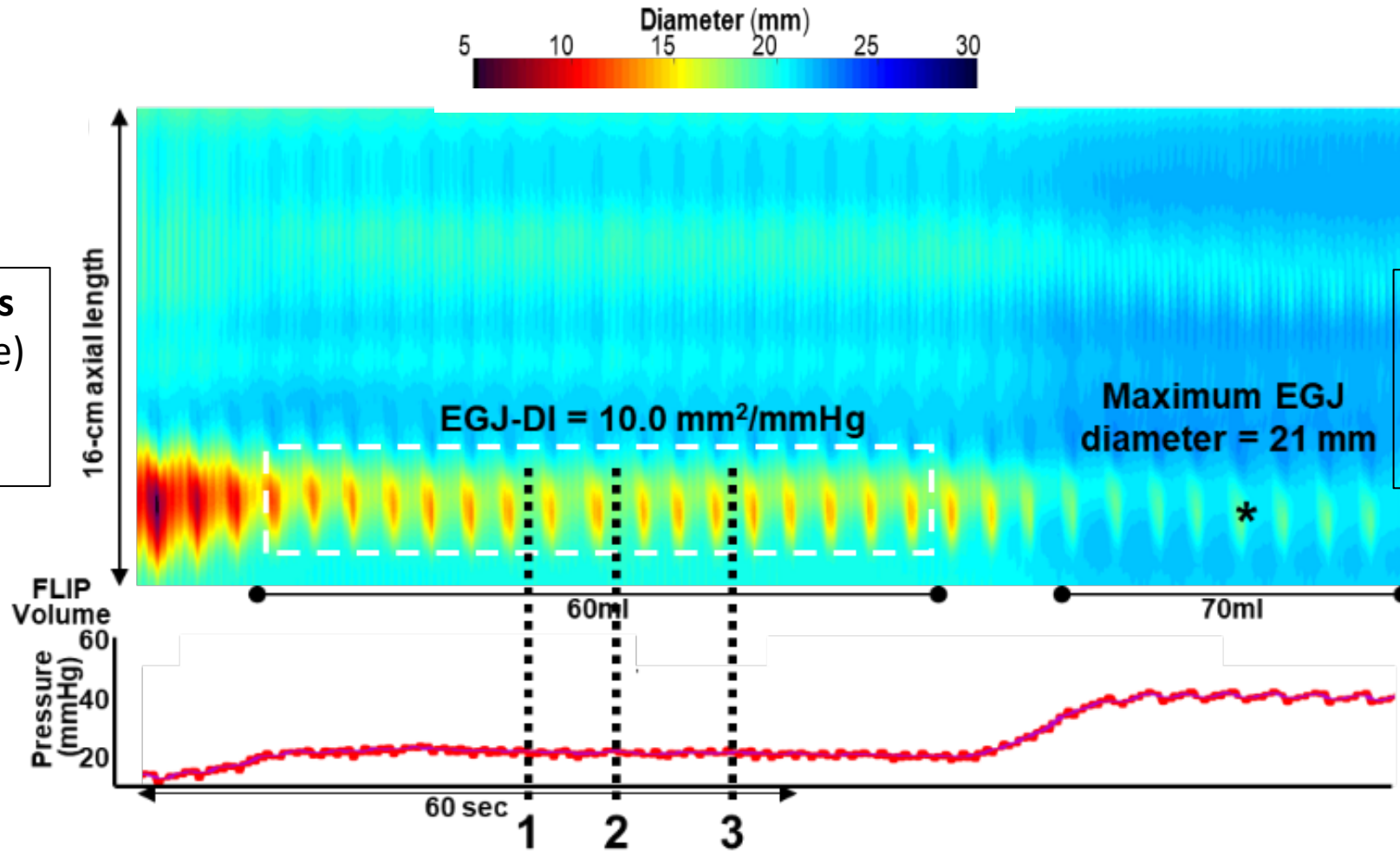


**Apex EGJ-DI Controls**  
Median (5<sup>th</sup>-95<sup>th</sup> %tile)  
5.8 (3.2-8.4)  
mm<sup>2</sup>/mmHg

**Max Diameter Controls**  
Median (5<sup>th</sup>-95<sup>th</sup> %tile)  
20.4 (16.7-21.9) mm

# Flip Panometry Assessment of EGJ Obstruction

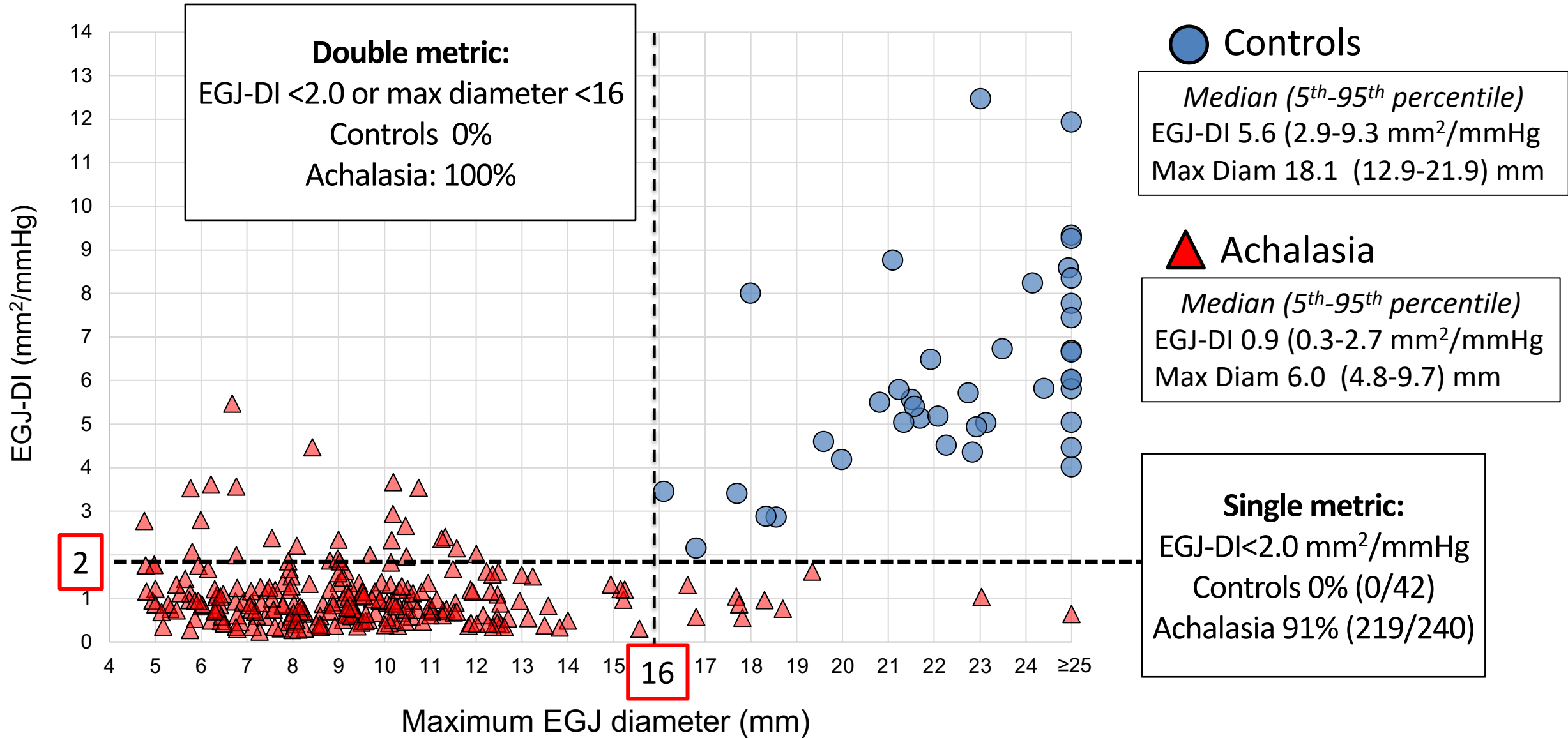
## *Distensibility Index (DI) and Max diameter- Scleroderma*



**Apex EGJ-DI Controls**  
Median (5<sup>th</sup>-95<sup>th</sup> %tile)  
5.8 (3.2-8.4)  
mm<sup>2</sup>/mmHg

**Max Diameter Controls**  
Median (5<sup>th</sup>-95<sup>th</sup> %tile)  
20.4 (16.7-21.9) mm

# Reduced EGJ distensibility in achalasia



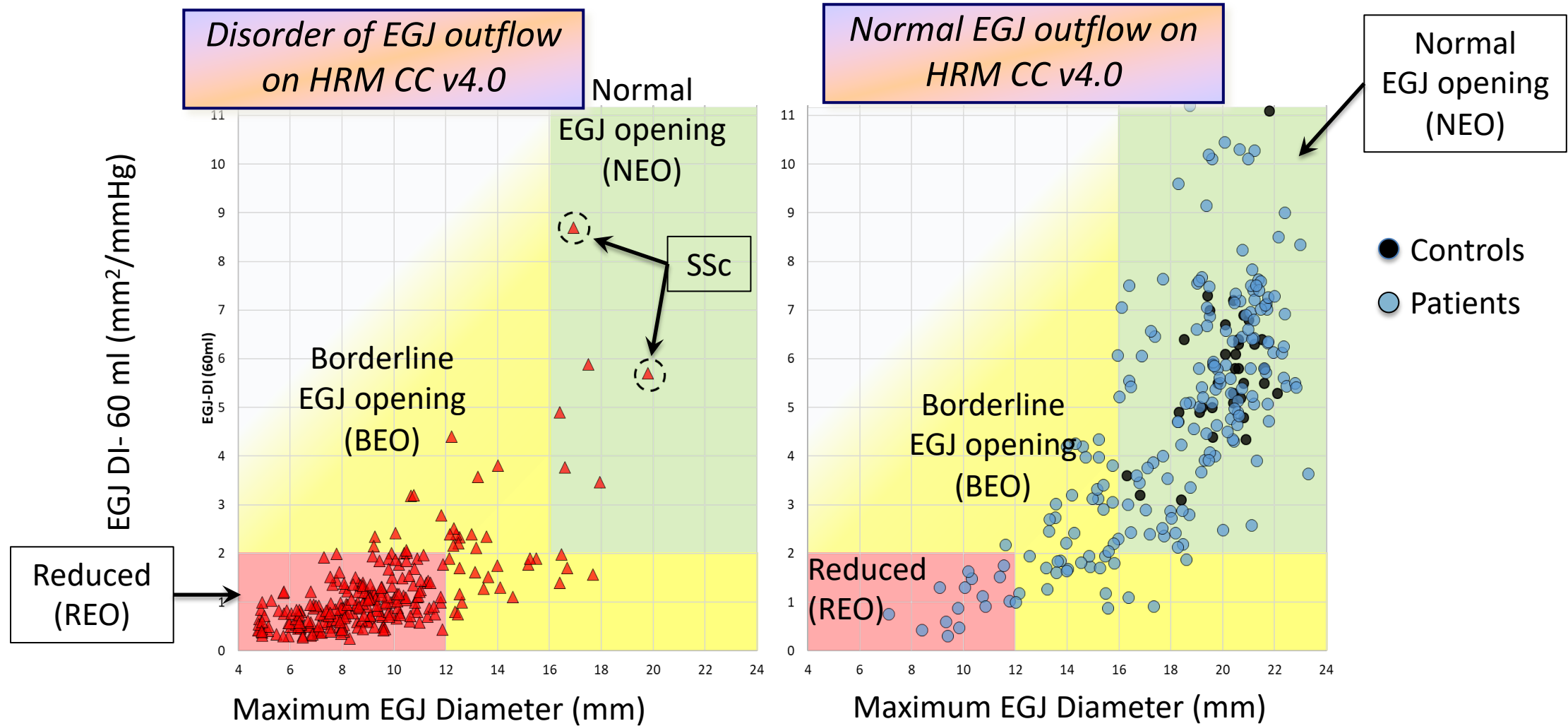
# Flip Panometry Classification of EGJ Obstruction

*Based on 687 patients and 35 controls*

- Normal EGJ Outflow (NEO)= EGJ-DI  $\geq 2\text{mm}^2/\text{mmHg}$  *and* Max diameter  $\geq 16$  mm
- Borderline EGJ Outflow (BEO)= EGJ-DI  $< 2\text{mm}^2/\text{mmHg}$  *or* Max diameter  $< 16$  mm
- Reduced EGJ Outflow (REO)= EGJ-DI  $< 2\text{mm}^2/\text{mmHg}$  *and* Max diameter  $< 12$  mm

# Flip Panometry Assessment of EGJ Obstruction vs HRM diagnosis of Disordered EGJ Outflow

687 patients and 35 controls



# Flip Panometry Classification of EGJ Obstruction

*Based on 687 patients and 35 controls*

- Normal EGJ Outflow (NEO)= EGJ-DI  $\geq 2\text{mm}^2/\text{mmHg}$  *and* Max diameter  $\geq 16$  mm
- Borderline EGJ Outflow (BEO)= EGJ-DI  $< 2\text{mm}^2/\text{mmHg}$  *or* Max diameter  $< 16$  mm
- Reduced EGJ Outflow (REO)= EGJ-DI  $< 2\text{mm}^2/\text{mmHg}$  *and* Max diameter  $< 12$  mm

*Among the 241 patients with REO,  
86% had a conclusive HRM disorder of EGJ outflow per CCv4.0*

*Among the 203 patients with NEO,  
99% had normal HRM EGJ outflow per CCv4.0*

# FLIP in the evaluation of dysphagia and EMDs

## *Applications*

- Achalasia diagnosis and subtyping
  - Motility assessment in lieu of manometry
- Achalasia treatment assessment
  - Intraoperative
  - Recurrence
- Functional assessment of EGJ outflow obstruction
- Functional assessment of secondary peristalsis

# Flip Panometry Assessment of Peristalsis

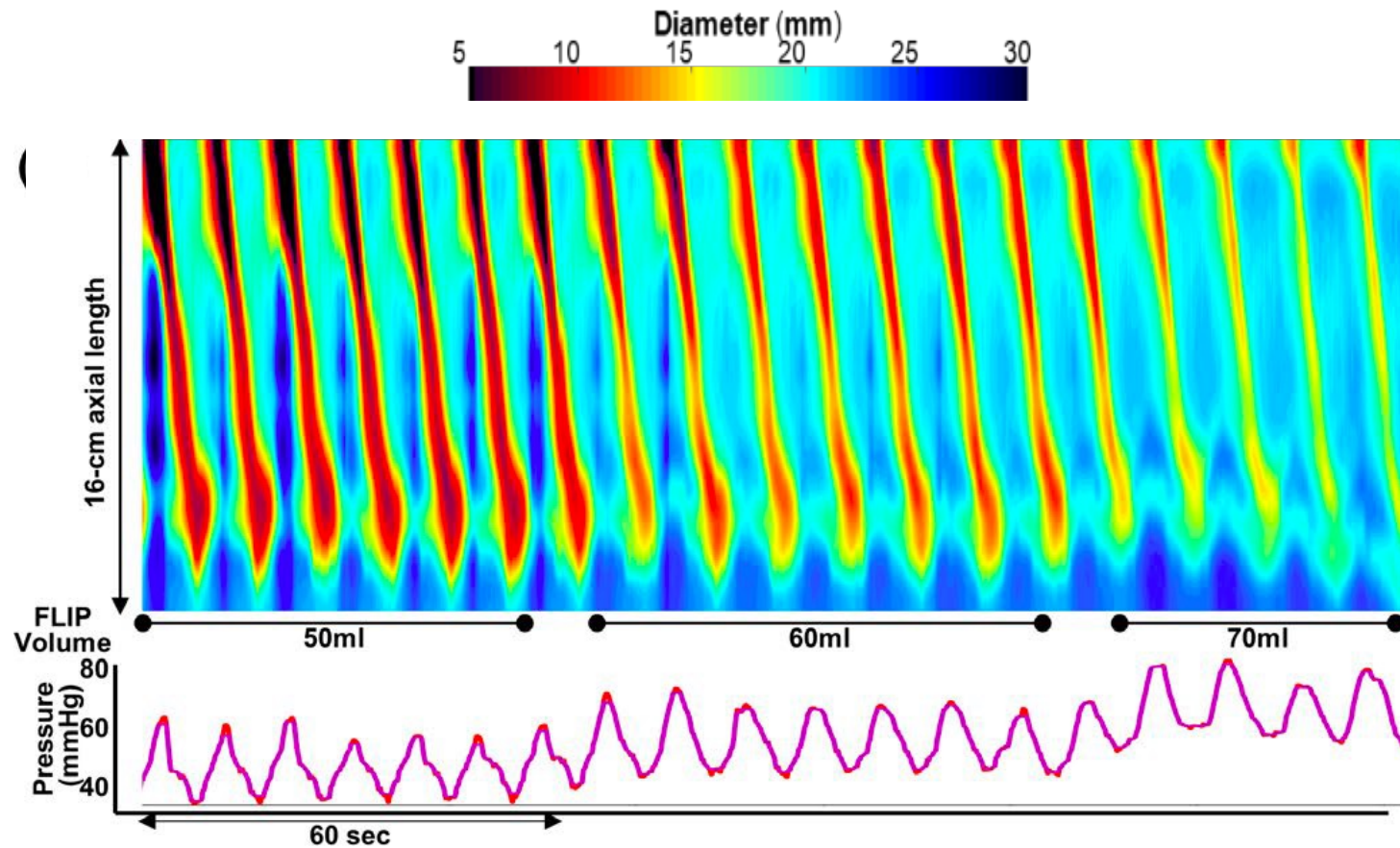
## *Methodology*

- 706 patients (245 with achalasia 1-3 on HRM, 178 nl on HRM) and 35 controls (3 with IEM) with FLIP and HRM studies included
- Flip data exported and analyzed with open source software:  
<http://www.wklytics.com/nmgi>
- 50-70 ml volumes evaluated for contractile response (CR) patterns
  - Normal Contractile Response (NCR)
  - Borderline Contractile Response (BCR)
  - Impaired/Disordered Contractile Response (IDCR)
  - Spastic Reactive Contractile Response (SRCR)
- Studies read blindly by 4 authors and 3 trained outside reviewers



# Flip Panometry Assessment of Peristalsis

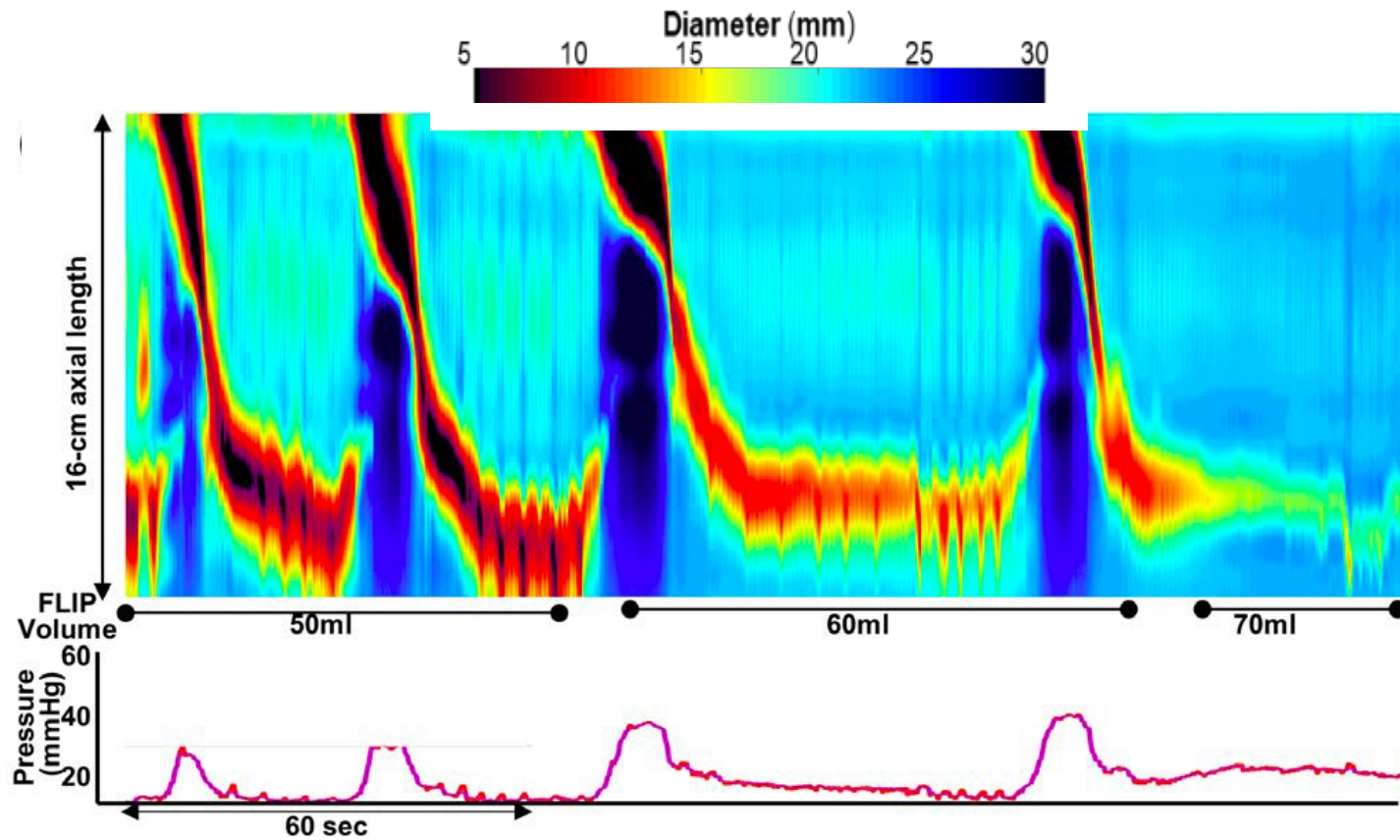
## *Methodology- Normal Contractile Response (NCR)*



*RACs- repetitive antegrade contractions of > 6 contractions, ≥6 axial length, occurring at a rate of 6±3 contractions per minute- rule of 6s*

# Flip Panometry Assessment of Peristalsis

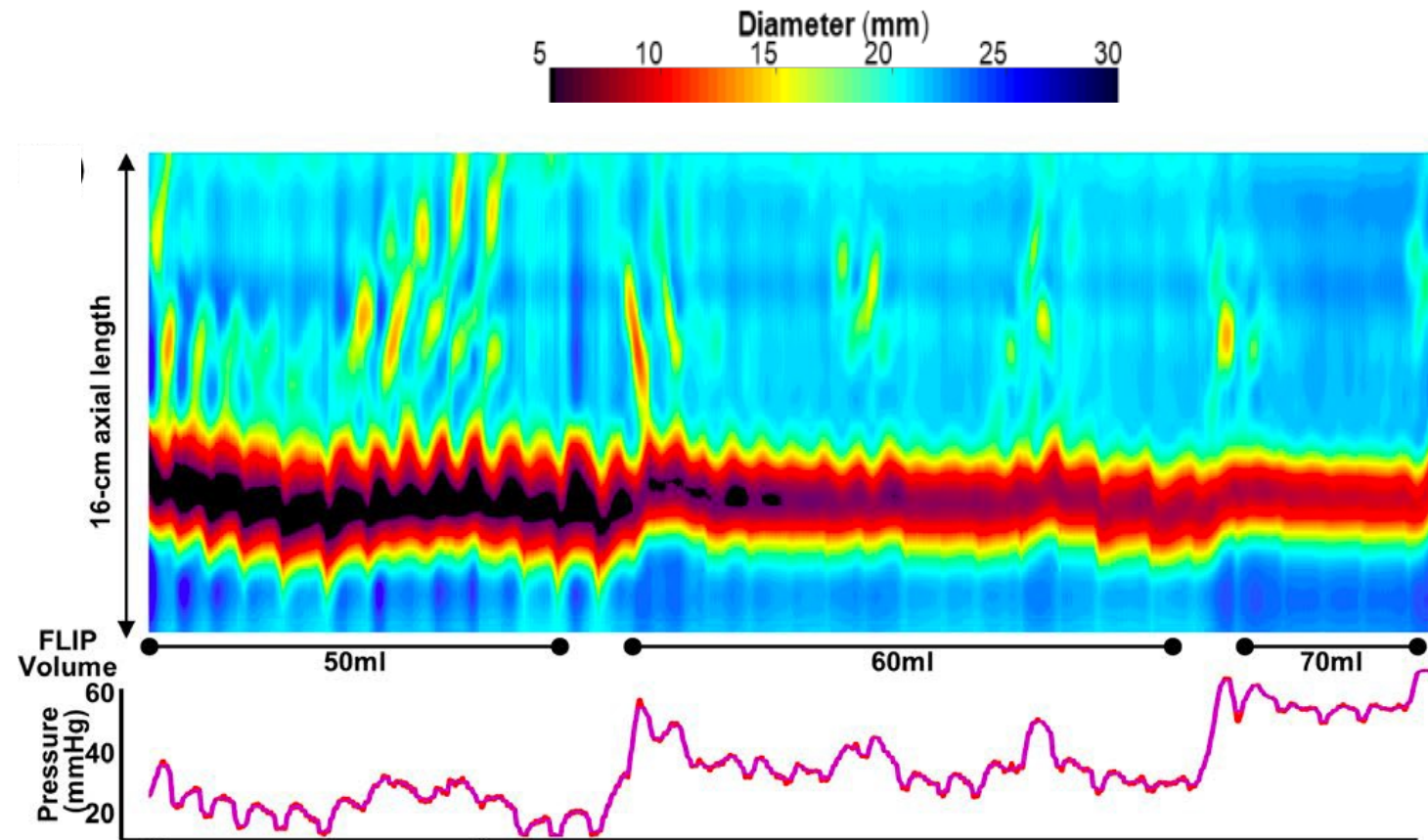
## *Methodology- Borderline Contractile Response (BCR)*



*BCR- distinct antegrade contractions but not meeting the rule of 6s- this example had IEM on HRM*

# Flip Panometry Assessment of Peristalsis

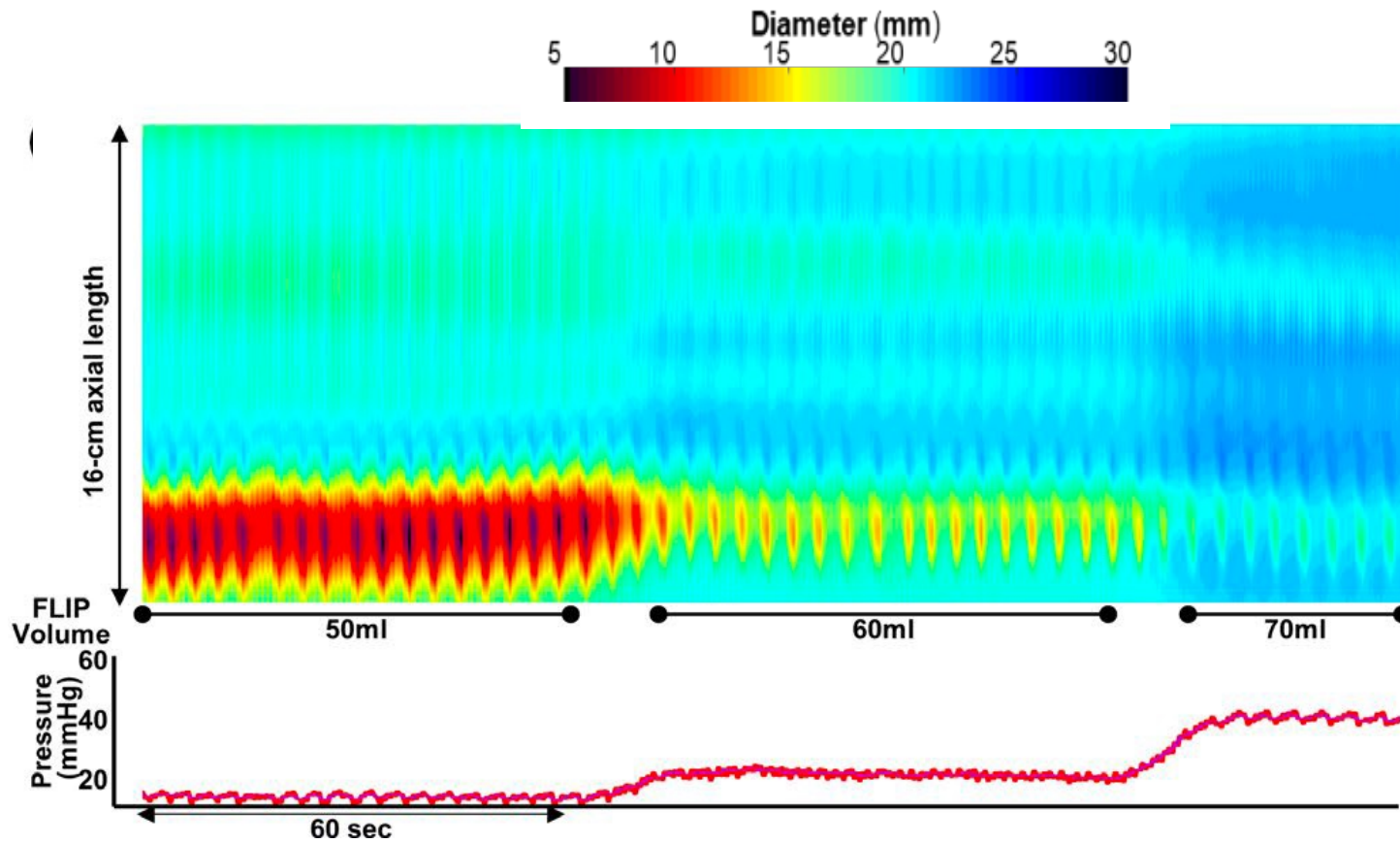
## *Methodology- Impaired/Disordered Contractile Response (IDCR)*



*IDCR- no distinct antegrade contractions , RRCs, SOC*

# Flip Panometry Assessment of Peristalsis

## *Methodology- Absent Contractile Response (ACR)*

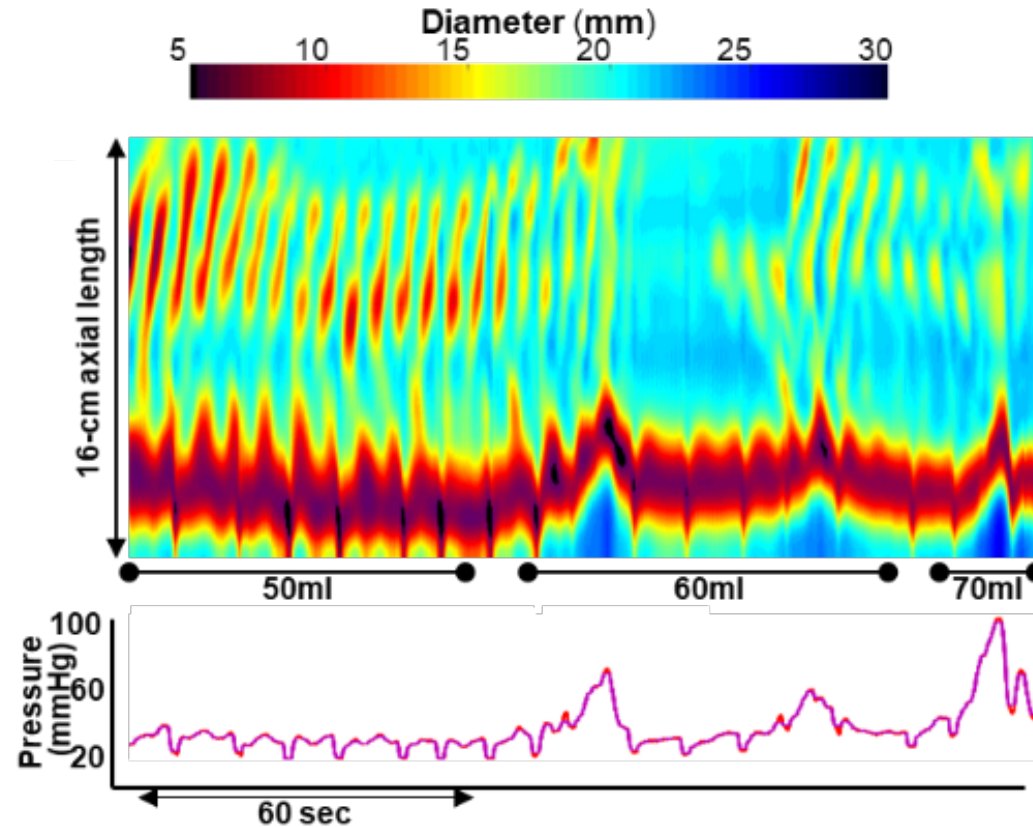


*ACR- no contractile activity in the esophageal body*

# Flip Panometry Assessment of Peristalsis

## *Spastic Reactive Contractile Response- RRCs*

**Controls**  
None observed

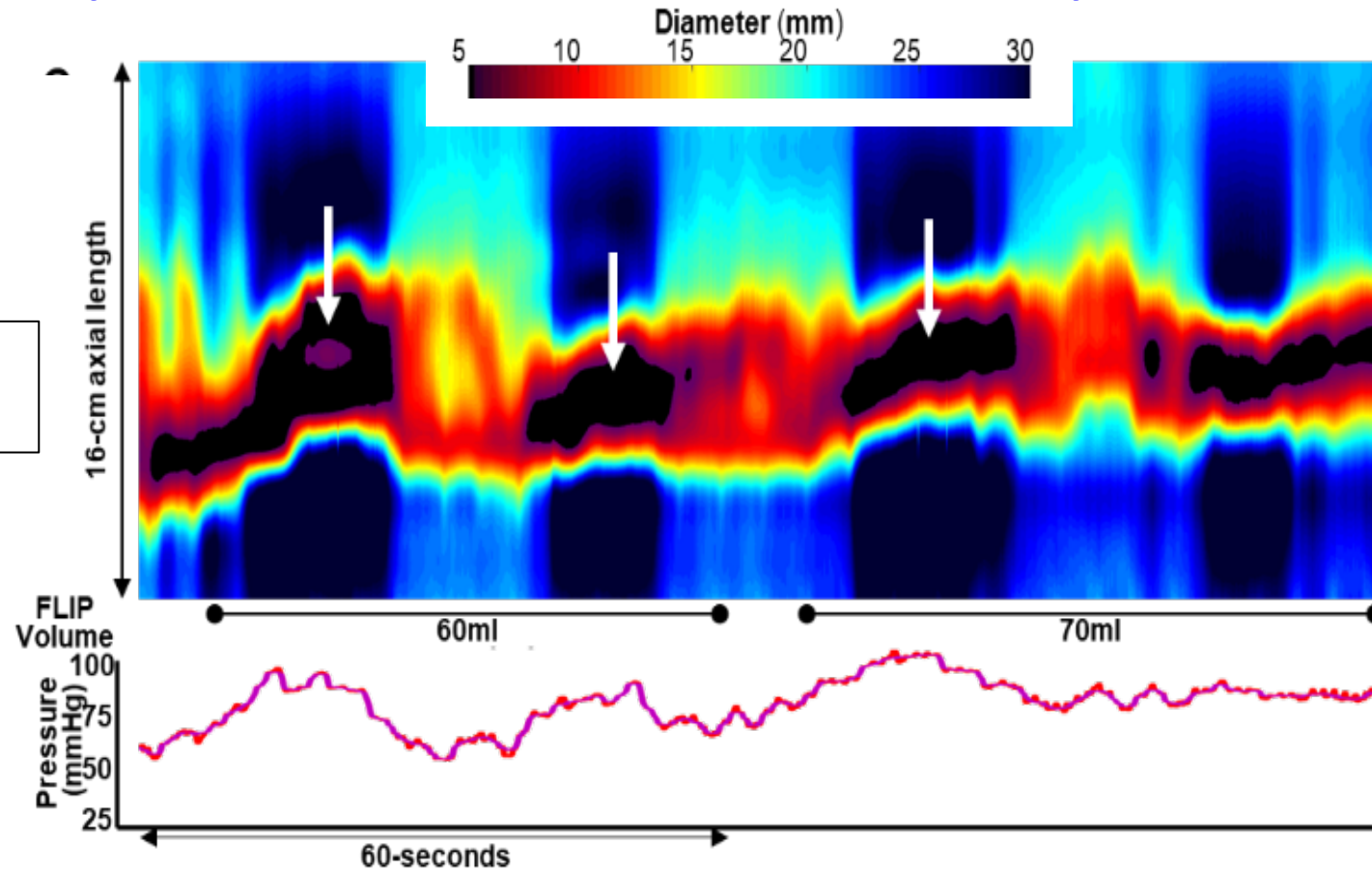


*RRCs- repetitive retrograde contractions of  $\geq 6$  axial length occurring at a rate of  $>9$  contractions per minute- this example had type III achalasia on HRM*

# Flip Panometry Assessment of Peristalsis

## *Spastic Reactive Contractile Response- SLESC*

**Controls**  
None observed



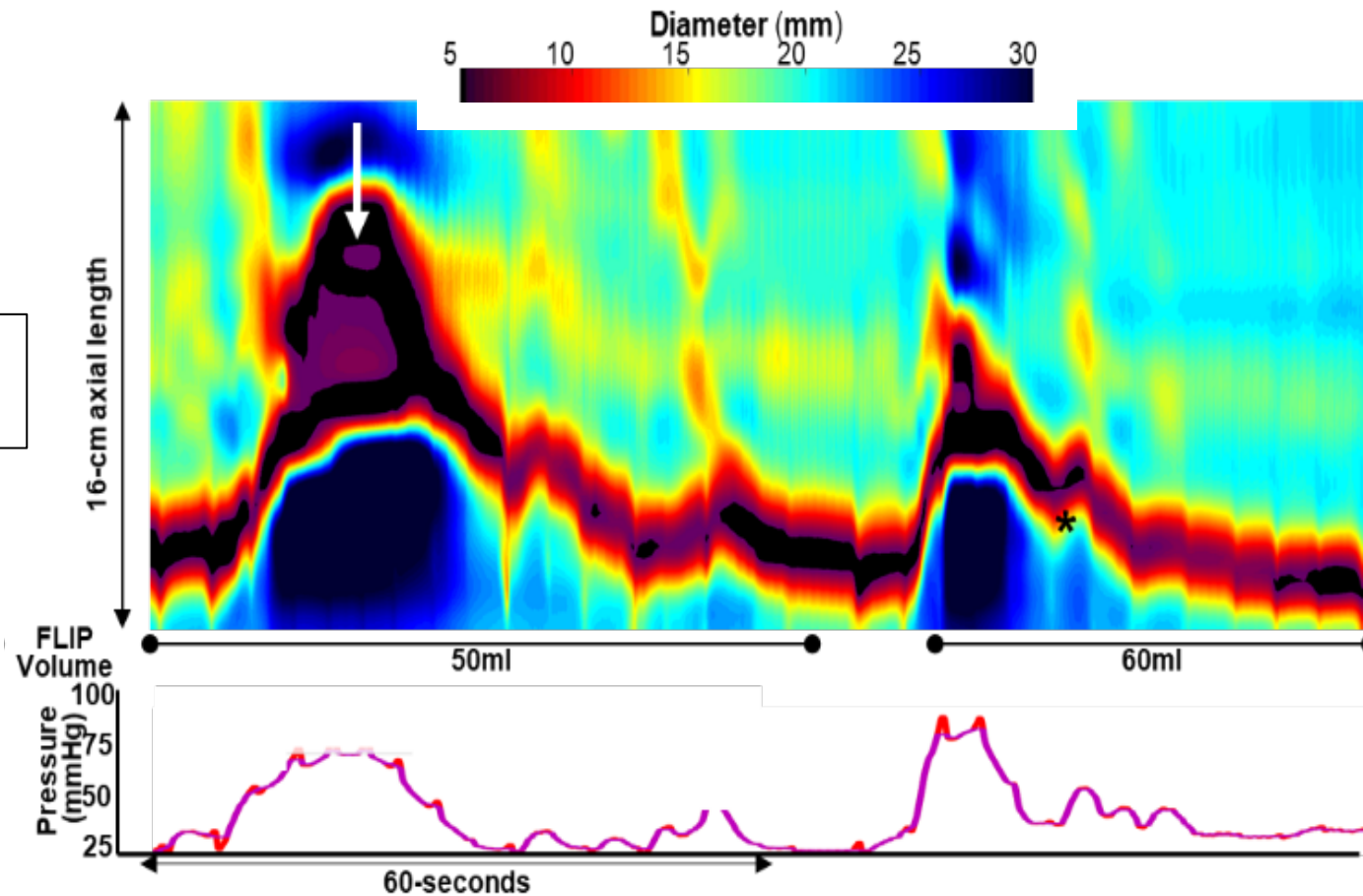
- Patients**
- 7% overall
  - 32% with epiphrenic had SLESC or SOC
  - Hiatal hernia more frequent with SLESC or SOC (30% vs 19%)

*Sustained LES Contraction (-SLESC)- sustained reduced LES diameter with increased FLIP pressure for >5s independent of esophageal body contraction- this example had hypercontractility and small HH on HRM*

# Flip Panometry Assessment of Peristalsis

## *Spastic Reactive Contractile Response- SOC*

**Controls**  
None observed

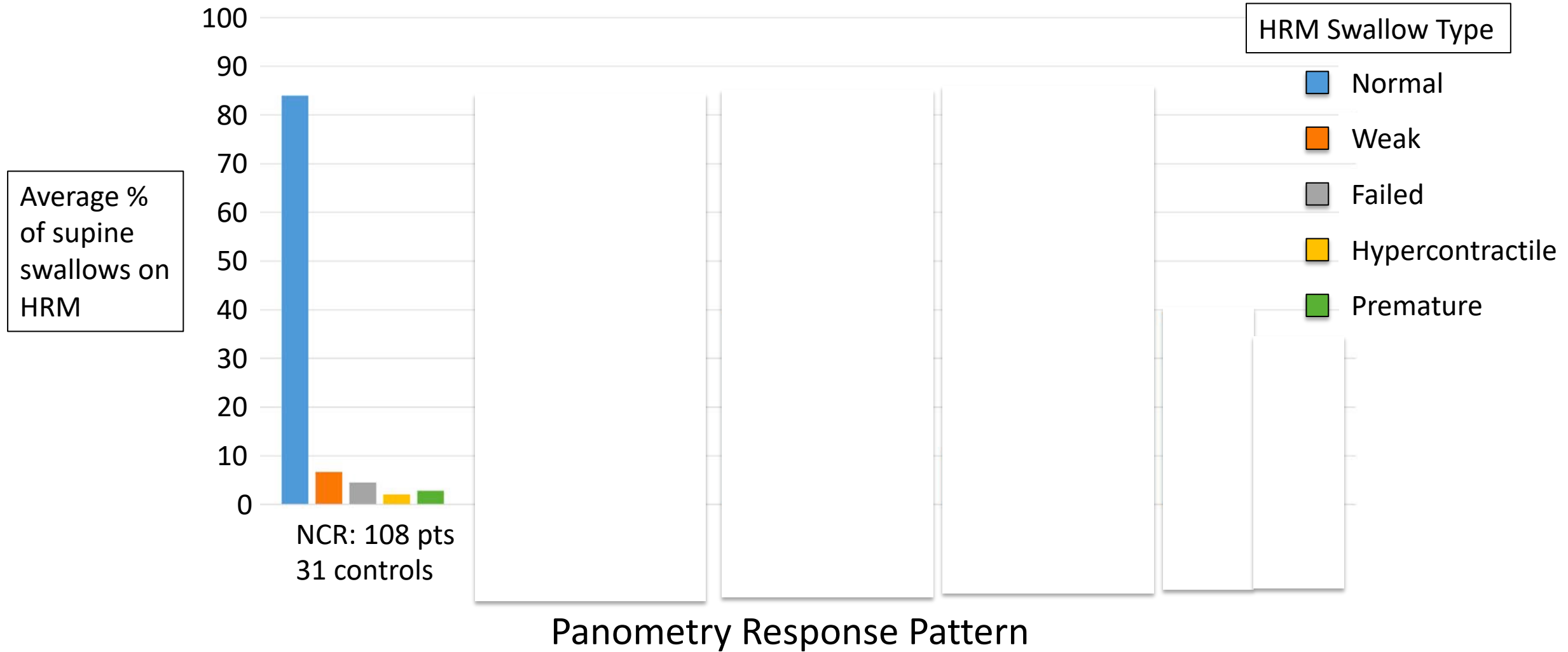


**Patients**

- 4% overall
- 32% with epiphrenic tic had SLESC or SOC
- Hiatal hernia more frequent with SLESC or SOC (30% vs 19%)

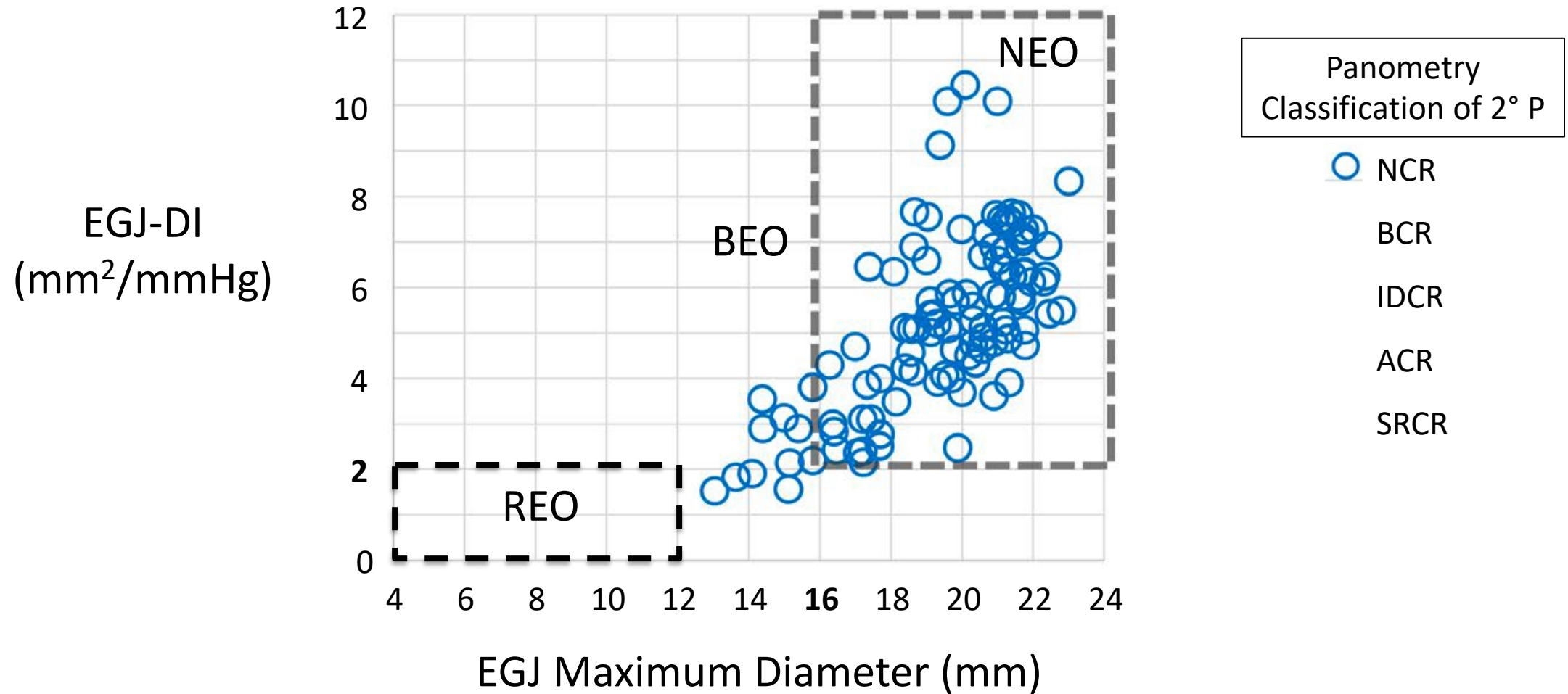
*Sustained Occluding Contraction (SOC)- non-propagating occluding contraction in continuity with the EGJ for >10s – this example had type III achalasia on HRM*

# HRM vs FLIP Panometry Classification of Peristalsis

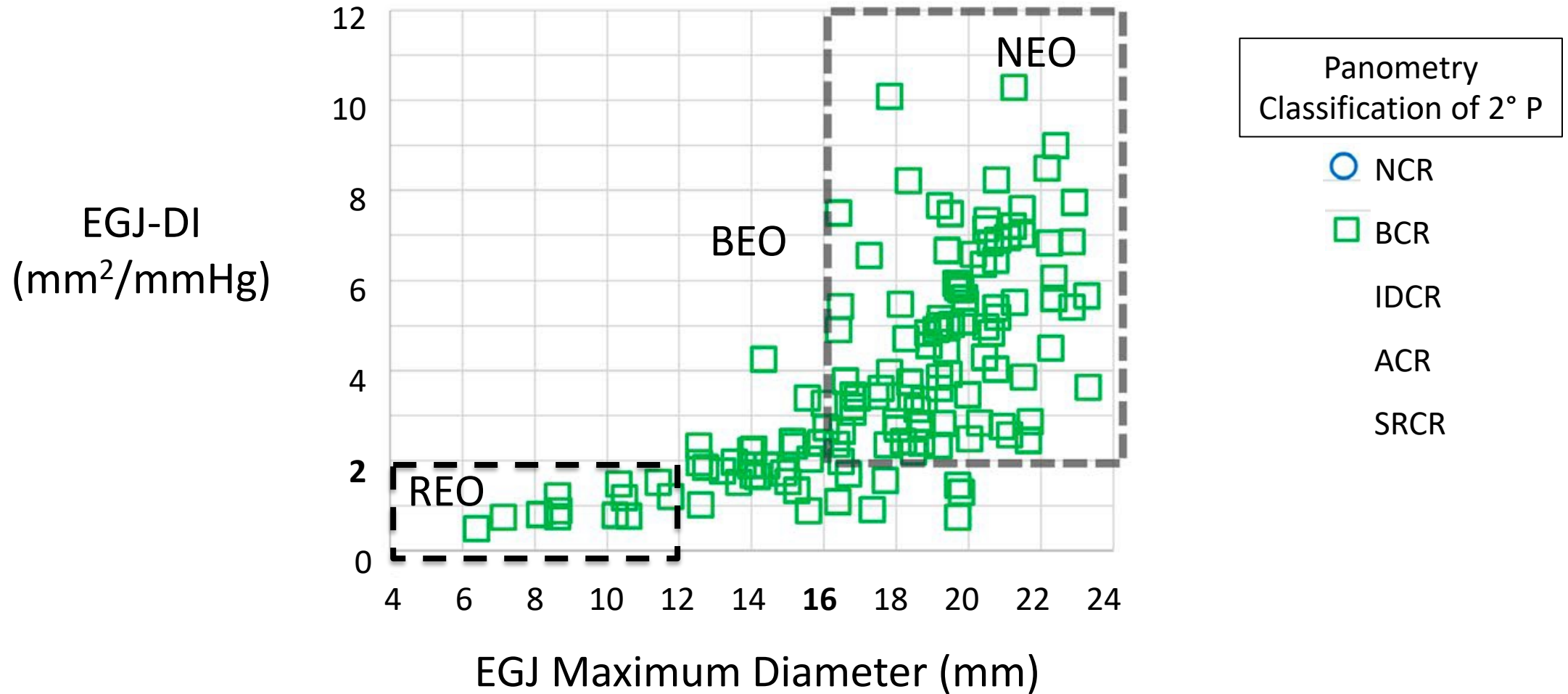




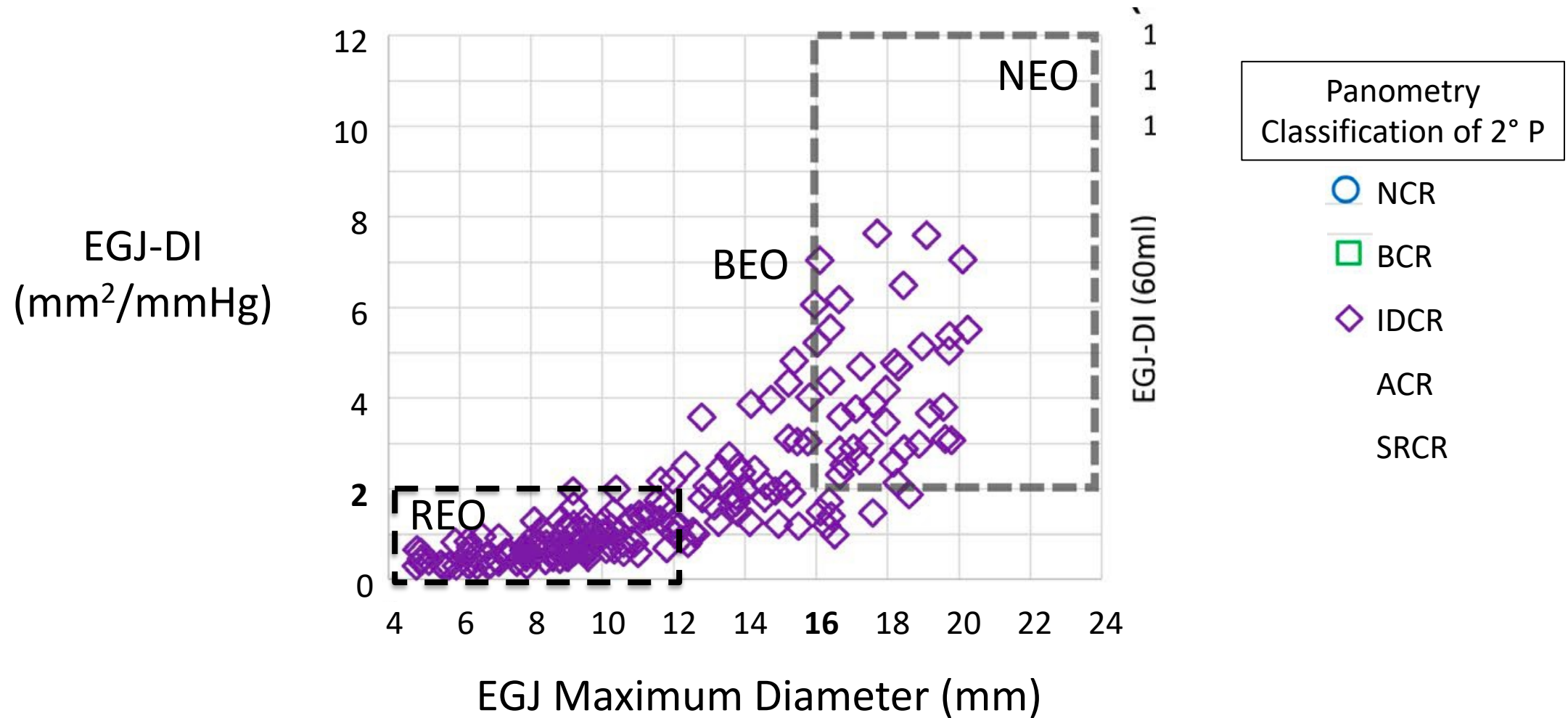
# Panometry Assessment of EGJ Obstruction among Contractile Response Classifications: Normal Contractile Response (NCR)



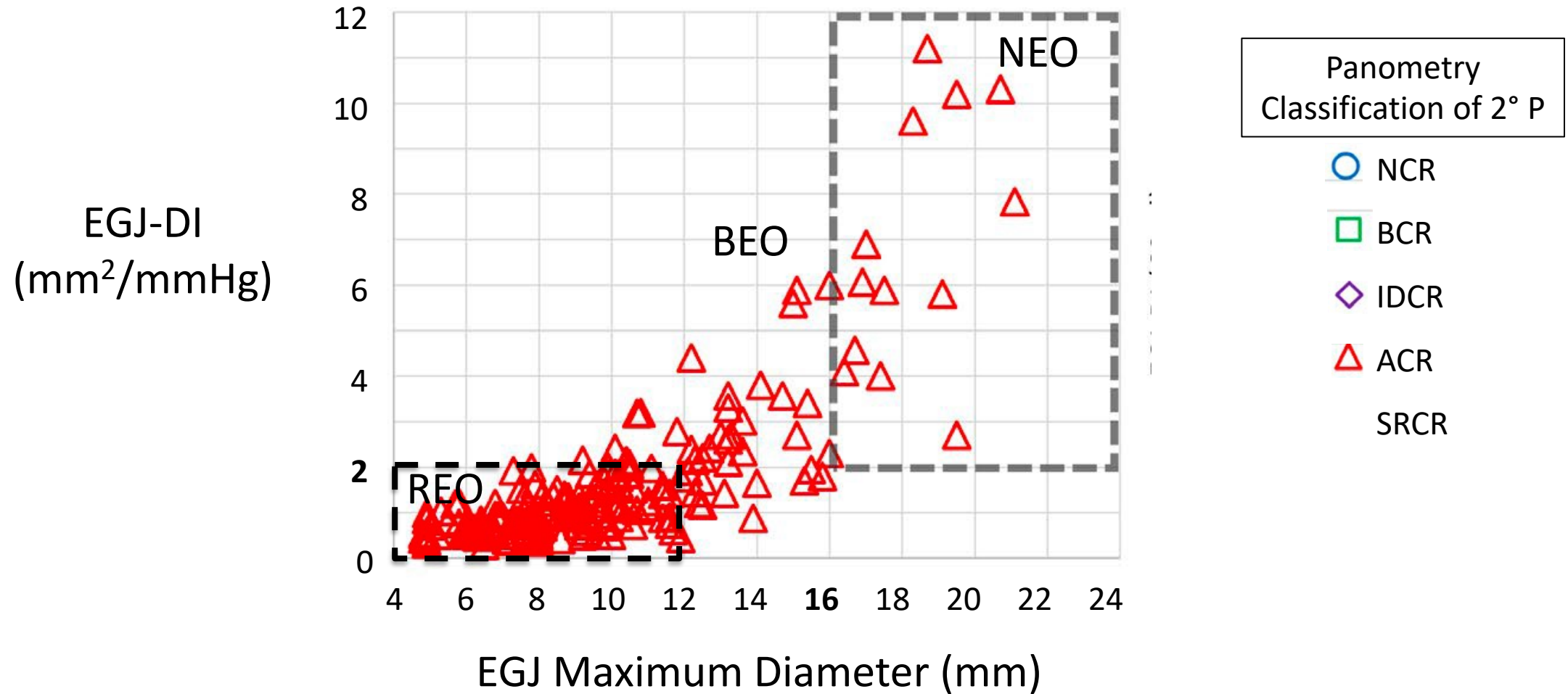
# Panometry Assessment of EGJ Obstruction among Contractile Response Classifications: Borderline Contractile Response (BCR)



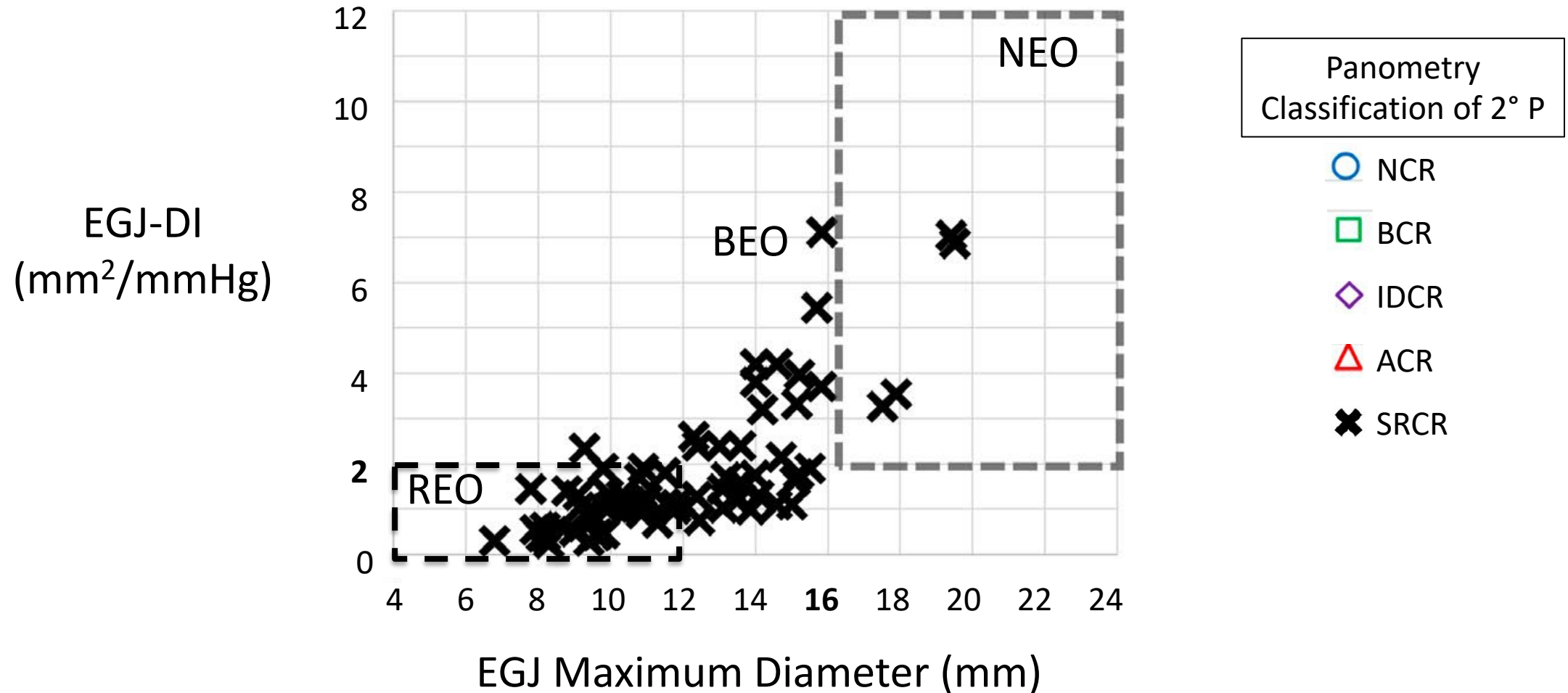
# Panometry Assessment of EGJ Obstruction among Contractile Response Classifications: Impaired/Disordered Contractile Response (IDCR)



# Panometry Assessment of EGJ Obstruction among Contractile Response Classifications: Absent Contractile Response (ACR)



# Panometry Assessment of EGJ Obstruction among Contractile Response Classifications: Spastic-Reactive Contractile Response (SRCR)



# Flip Panometry Classification of 2° Peristalsis

*Based on 706 patients and 35 controls*

- Transition from normality (NCR with RACs) to abnormality (BCR, ACR) paralleling 1° peristaltic function assessed on HRM (normal, IEM, absent contractility)
  - Some discordance is observed: Panometry detects non-occluding contractions
- Abnormal spastic motor contractions (IDCR, SRCR) are observed
  - SOCs are better than RRCs to differentiate spastic (type III) and non-spastic achalasia
  - RRCs, SOCs, and sLESCs are observed in patients with spastic motor findings on HRM, hiatus hernia, and epiphrenic diverticula suggesting that when seen, these merit further evaluation
- HRM and FLIP Panometry are complementary evaluations of esophageal motor function

*A normal contractile response on FLIP panometry in the setting of a normal endoscopy effectively excludes achalasia*

# FLIP in the evaluation of dysphagia and EMDs

## *Conclusions*

- Easily done in conjunction with sedated endoscopy
- Equal to (or better than) HRM in detecting achalasia
- Objective measure of treatment efficacy in achalasia
- Provides functional assessment of EGJOO irrespective of IRP
- Potential to replace HRM in the detection of EMDs

