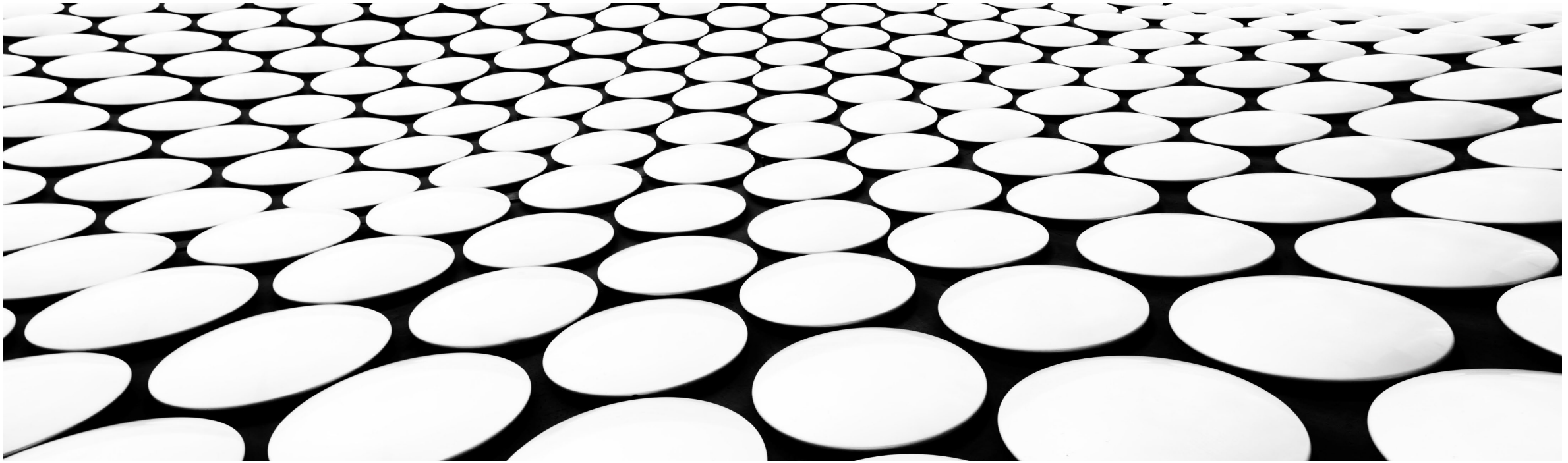
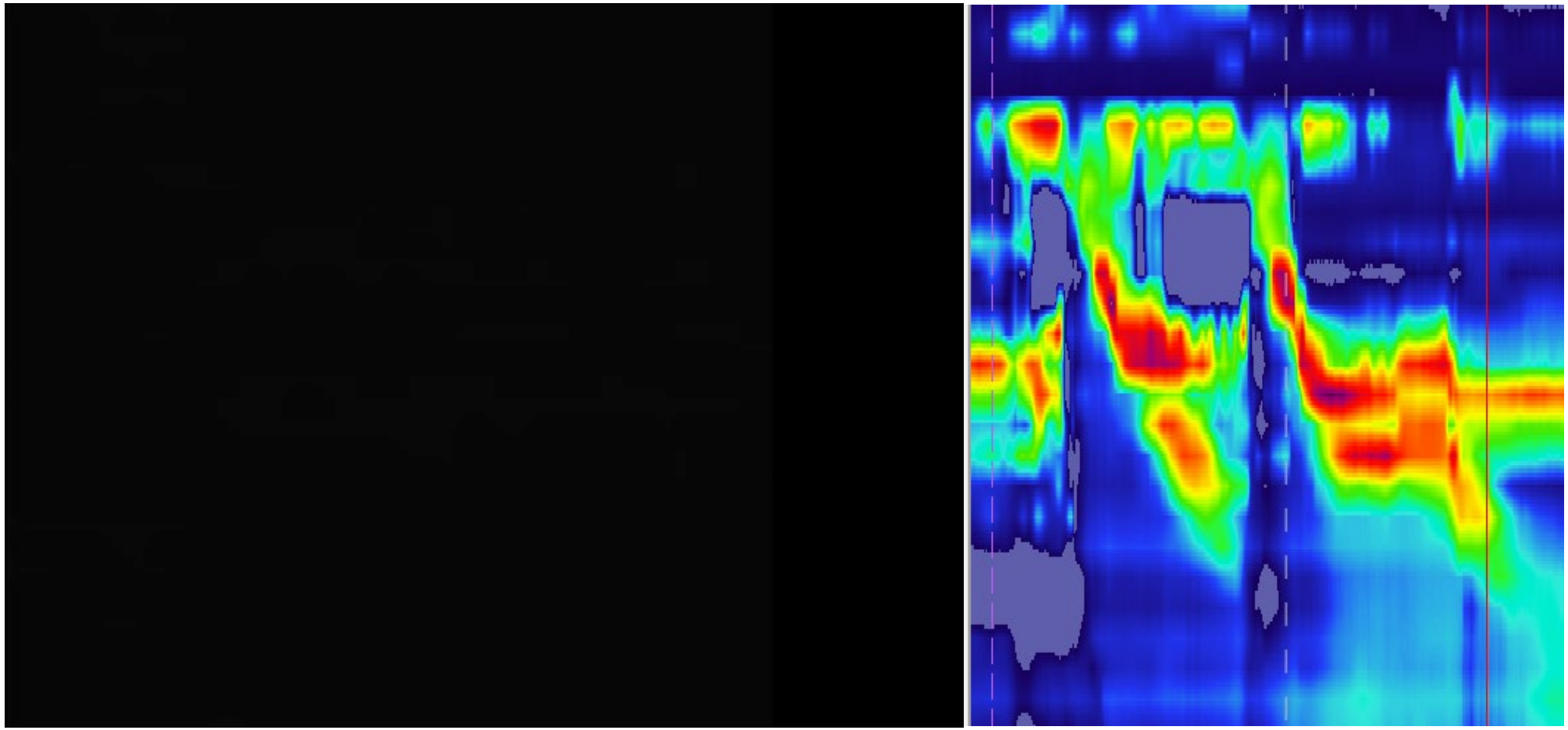
MANAGING HEAD AND NECK CANCER RELATED DYSPHAGIA VIA A RESEARCH PATH

TIMOTHY M MCCULLOCH

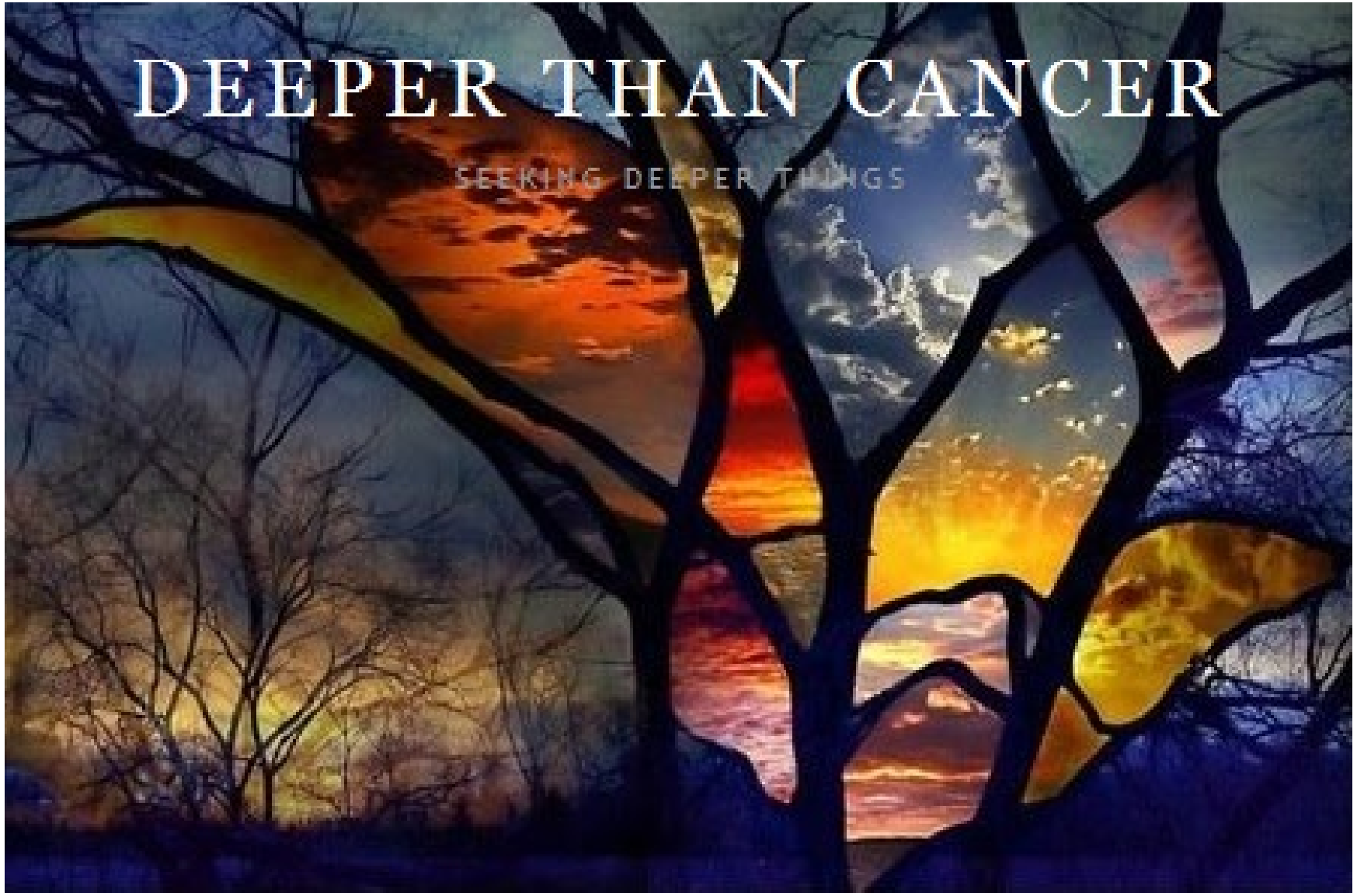


NO CONFLICTS OF INTEREST

56 Y/O T3 N2 TONGUE BASE
S/P TORS AND NECK WITH POST OP XRT



TOXICITY OF CHEMO-RADS



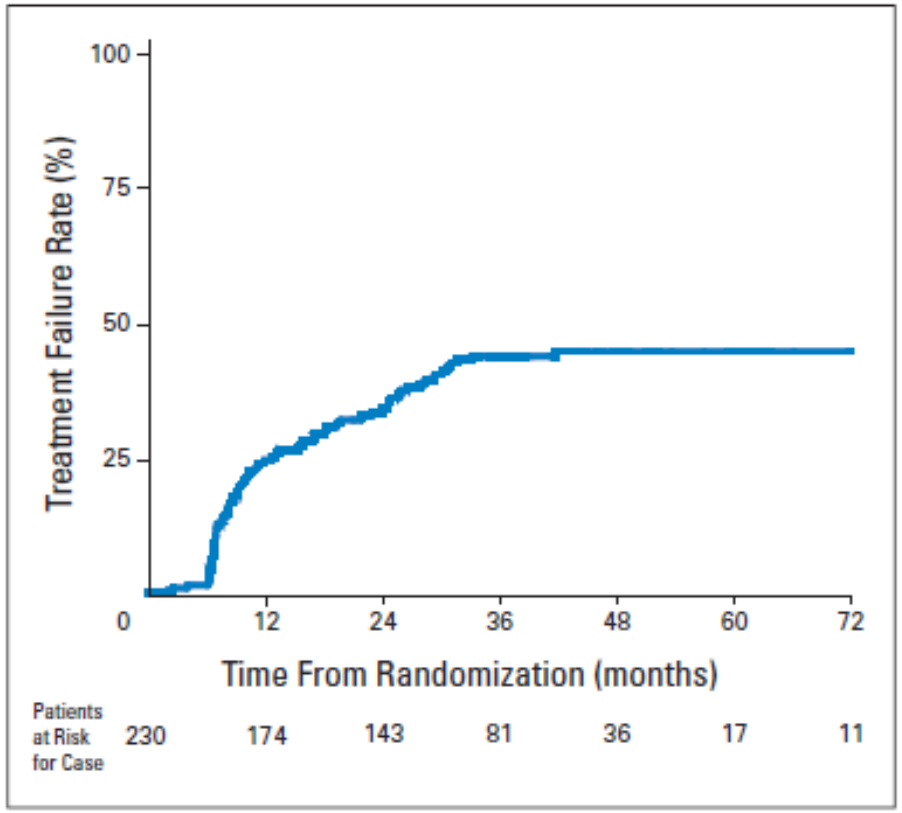
Another major event today...my first two course meal...I had a bowl of Campbells Cream of Chicken Soup followed by Cherry Jello. I actually had a slight sensation of taste for both, though I had to strain out the teensy-weensy chunks of chicken in the soup, and rinse my mouth repeatedly after each course. Now, my repertoire of food is up to three items...(eggs, soup and jello). I've had sips of other beverages, attempts to eat other food, but usually one sip or one small bite shouts "NOT YET."

INCIDENCE OF TOXICITIES

- **Machtay** et al: analysis of late larynx/pharynx toxicity
  - 3 RTOG trials including chemotherapy and RT
- 230 patients with sufficient recurrence-free survival
- **43% had a severe late toxicity**
  - Age > 70
  - T3/4 stage
  - Larynx / hypopharynx primary

INCIDENCE OF TOXICITIES

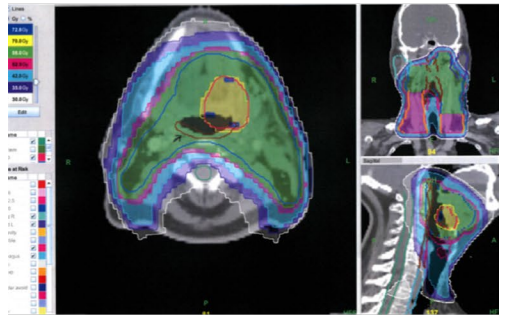
- G tube dependence: 29 (13%)
  - At 2 years
- Pharynx toxicity: 63 (27%)
- Larynx toxicity: 28 (12%)
- Other: 4
  - Infection, fistula



INCIDENCE OF TOXICITIES

- Rutten et al., 2011
  - Chemoradiation for stage 3/4 HNSCC
  - 84% reported impaired diet at ~ 4 years
- Maclean et al., 2009
  - 72% of patients report subjective dysphagia after total laryngectomy

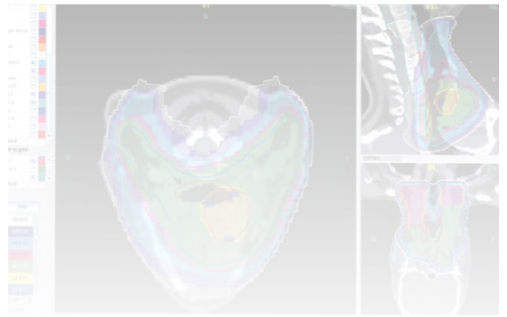
MINIMIZING TOXICITIES



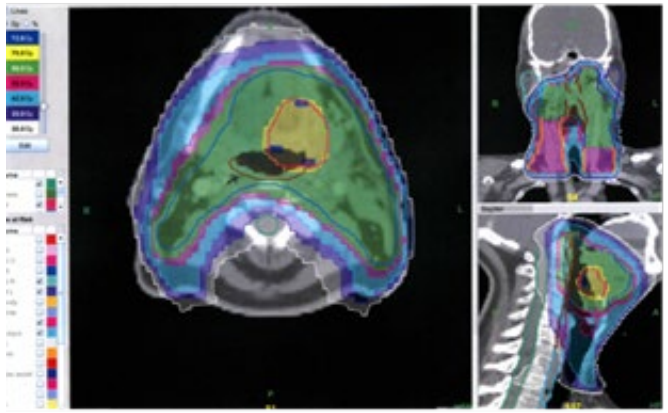
- Lower treatment dose
- IMRT/IGRT/altered fractionation

  Possibility of salivary-sparing plans /reduction of chronic toxicity

- Surgery for cure to avoid XRT



MINIMIZING TOXICITIES



- IMRT for oropharynx cancer, Eisbruch et al.
- Limitation of dose to constrictors, parotids, larynx
  - Correlates with swallow evaluation outcomes
  - Correlates with quality of life (historical control)

DARS zone

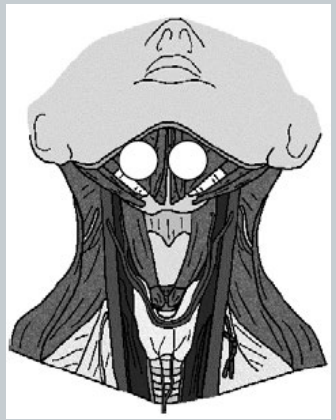
MINIMIZING TOXICITIES

- Mucositis
- Post treatment hyposalivation and Xerostomia
- Pain

SAN FRANCISCO 2005

THE EFFICACY OF ELECTRICAL STIMULATION FOR DYSPHAGIA IN HEAD & NECK CANCER PATIENTS

- Randomized clinical trail
- Subjected with moderate to sever dsyphagia
  - (PAS score of 4 or greater)
- 3 months or more post CRT or RT treatment of head and neck cancer
- Aggressive swallow therapy with NMES vs. Aggressive swallow therapy with Sham stim



INTERVENTIONS

Protocol of at home therapy post training
2 session a day – 6 days a week – for 12 weeks

9 minute stretching protocol followed by a 60 swallow therapy session with the device

Patients performed 60 sequential swallows, where they were given 4 seconds to initiate and execute a swallow, and then 12 seconds to rest. This protocol was typically performed in 16-20 minutes.					
10 Super-supraglottic Swallows	10 Regular Swallows	10 Mendelssohn Swallows	10 Regular Swallows	10 Effortful Swallows	10 Regular Swallows

RCT (2007-2012)

170 HNC patients enrolled

All had (C)RT as their primary modality treatment

Inclusion criterion – moderate to severe dysphagia
at time of enrollment

2 treatment arms

Aggressive swallow exercises + electrical stimulation (experimental group)

Aggressive swallow exercises + sham estim (control)

Home program; 2x/day for 30 min, 6 days/week, 3 months

STUDY RESULTS

Out of more than 488 patients screened for possible eligibility, 170 subjects were enrolled and randomized in the study. 116 were allocated to the active NMES plus exercise group while 54 were assigned to the sham NMES plus exercise group

(Complete data was available of 64 active and 16 sham subjects)

- The sham NMES + exercise group scored better (lower) than the Active NMES + exercise for PAS total ($p = 0.03$) and for PAS of thin liquid ($p = 0.01$).
- The Sham NMES group showed significant improvement in total PAS score, moving from a mean of 5.48 to 4.91 ($p = 0.05$).

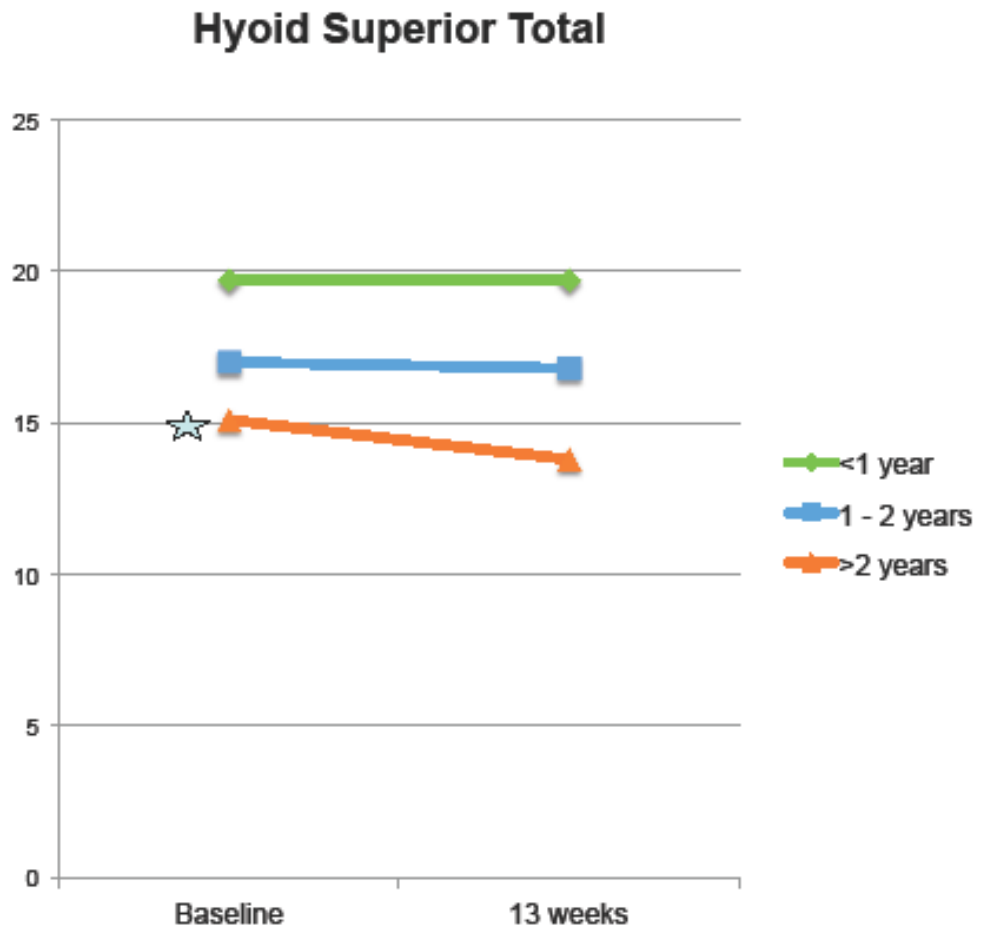
  (In clinical terms, a difference of less than 1 PAS score is of marginal significance)

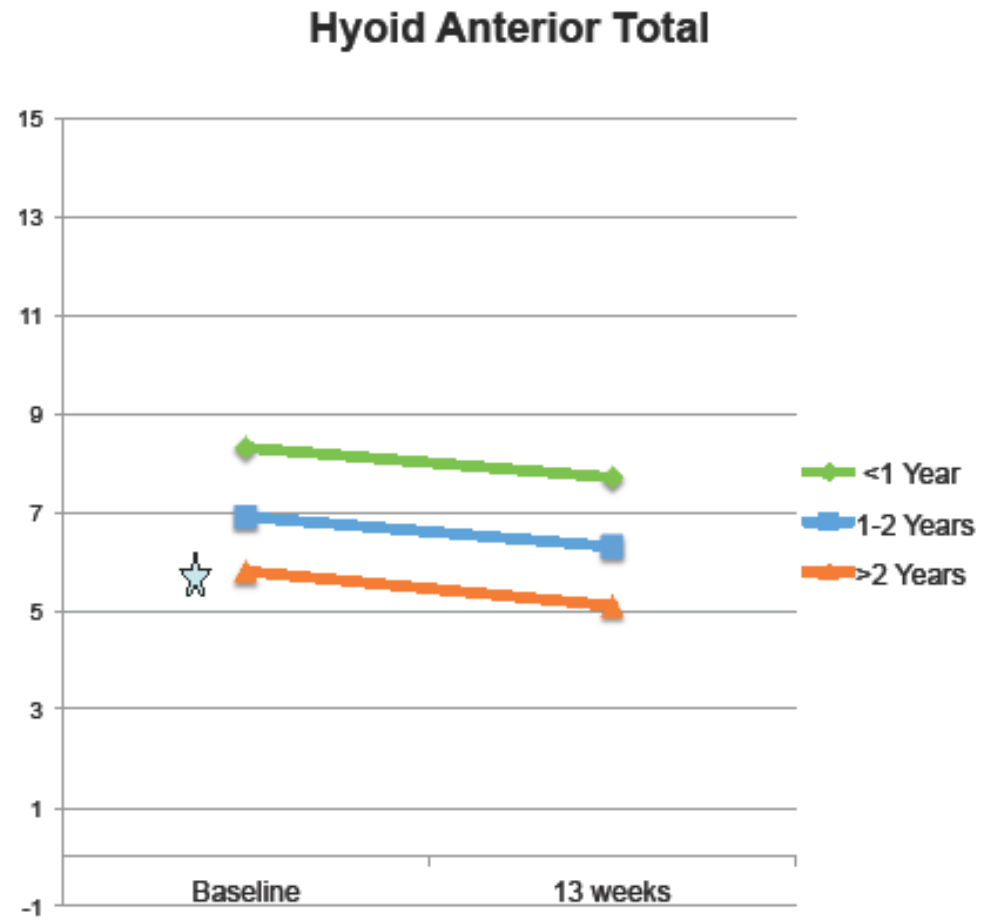
- None of the other primary outcome measures showed a significant difference between the 2 groups.

- Hyoid anterior movement, showed a significant decline over time when both groups were combined ($p = .04$).

  (hyoid excursion was 6.91cm at baseline and 6.26cm at week 13).

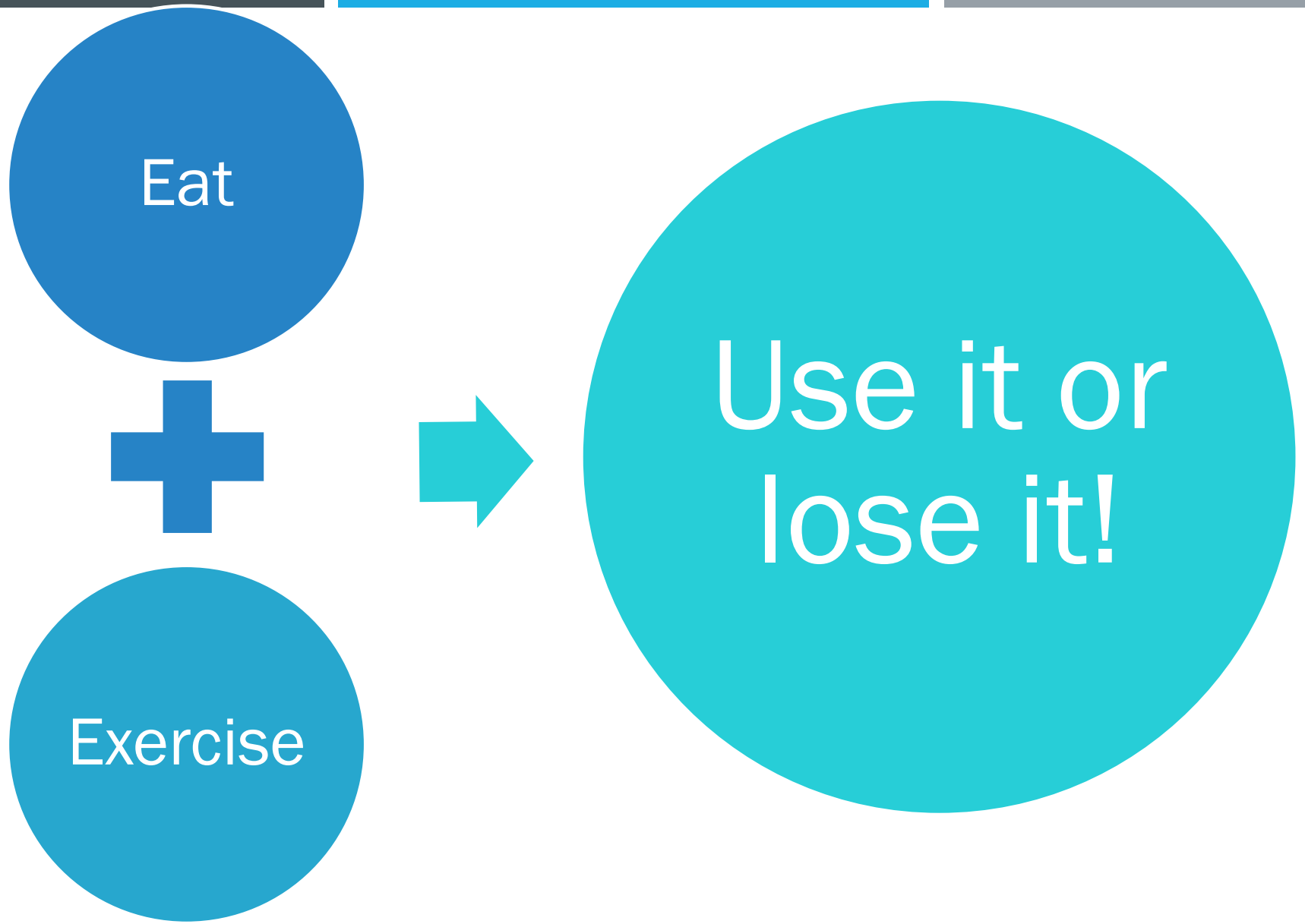
- No other swallow measures showed a significant difference over time.



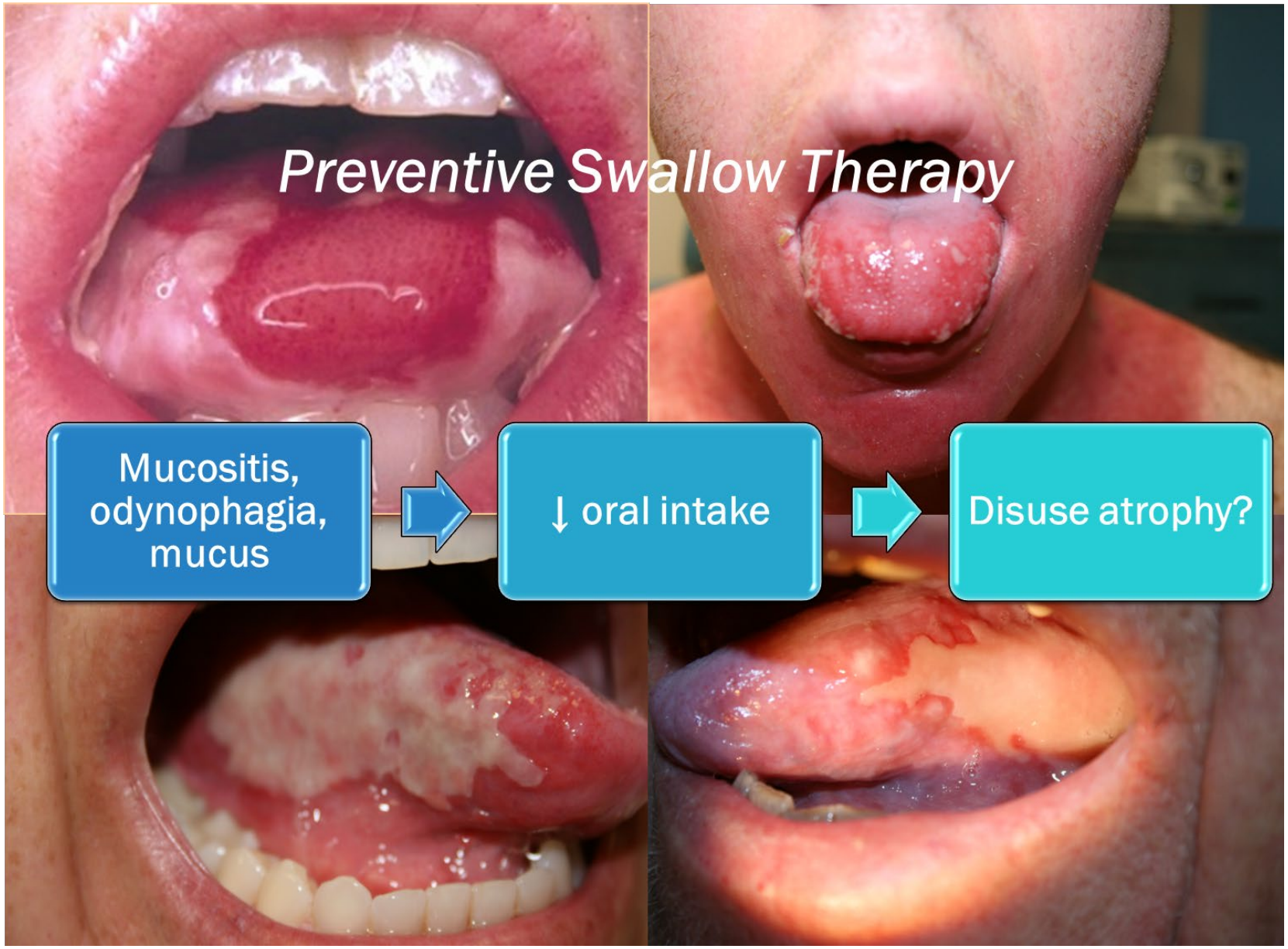


BOSTON UNIVERSITY

Preventive swallowing therapy



Preventive Swallow Therapy



EVIDENCE FOR PROACTIVE SWALLOWING THERAPY: *EXERCISE*

Study		Outcomes
UAB	Retrospective	Superior **MDADI** (swallow-related QOL)[1] Better **BOT & epiglottic** movement[2]
MDACC	Retrospective	Shorter **duration PEG** (OPC & HP)[3] Adherence improves **MDADI** (swallow-related QOL)[4]
UF	RCT	Significant preservation **muscle mass by MRI**[5]
Dutch	RCT	Improved **mouth opening**[6]
Mt Sinai	RCT	Superior **diet** levels (3-6M after CRT)[7]

1. Kulbersh BD et al, *Lscope* (2006)
2. Carrol WR et al, *Lscope* (2008)
3. Bhayani M et al, *Head Neck* (2013)
4. Shinn E et al, *Head Neck* (2013)
1. Carnaby-Mann G et al, *IJROBP* (2012)
2. Van der Molen L et al, *Dysphagia* (2011)
3. Kotz T et al, *Arch Oto-HNS* (2012)

EVIDENCE FOR PROACTIVE SWALLOWING THERAPY: *EAT*

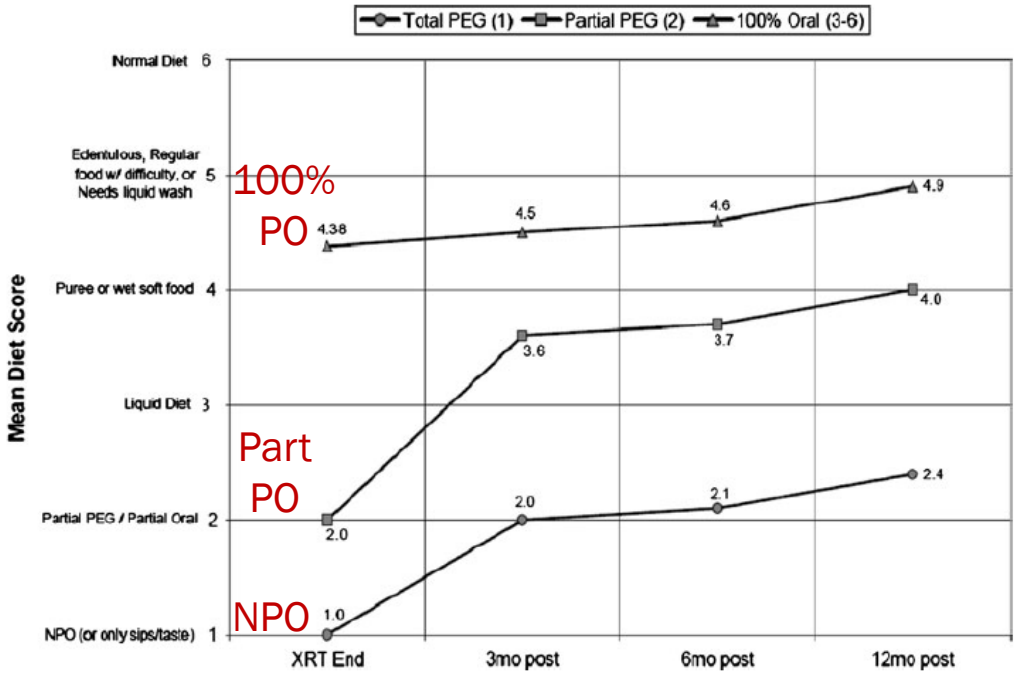


TABLE III.
Potential Dysphagia Risk Factors Assessed by ANCOVA.

Not Significant ($P \geq .05$)	Significant
Age	Speech pathology consultation ($P = .005$)
Time since treatment	NPO > 2 weeks ($P = .002$)
Sex	Lower SF-36 Mental Health Subscore ($P = .002$)
Race (white vs. nonwhite)	
T-stage	
Tumor site	
History of reflux	
Current tobacco use	
Current alcohol use	
Dentition (teeth/dentures vs. none)	
Body mass index	
SF-36 Bodily Pain Subscale score	
Education (H.S. diploma/equivalent vs. none)	

ANCOVA = analysis of covariance; SF = Short-Form; NPO = nothing by mouth.

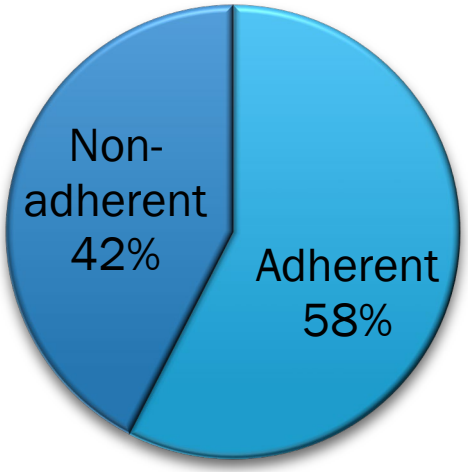
MDADI scores $\bar{x}$ 4.7± 3.4 yrs

Langmore S et al, *Dysphagia* (2012)
Gillespie B et al, *Lscope* (2004)

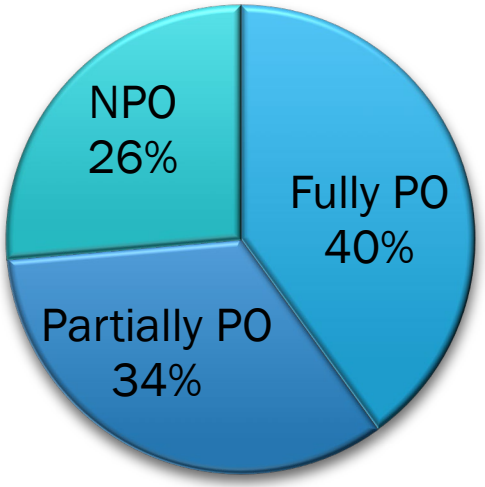
Exercise

USE IT OR LOSE IT: THE MDACC EXPERIENCE

- N = 497 (458 OPC, 39 HP)
- Curative RT ± chemo

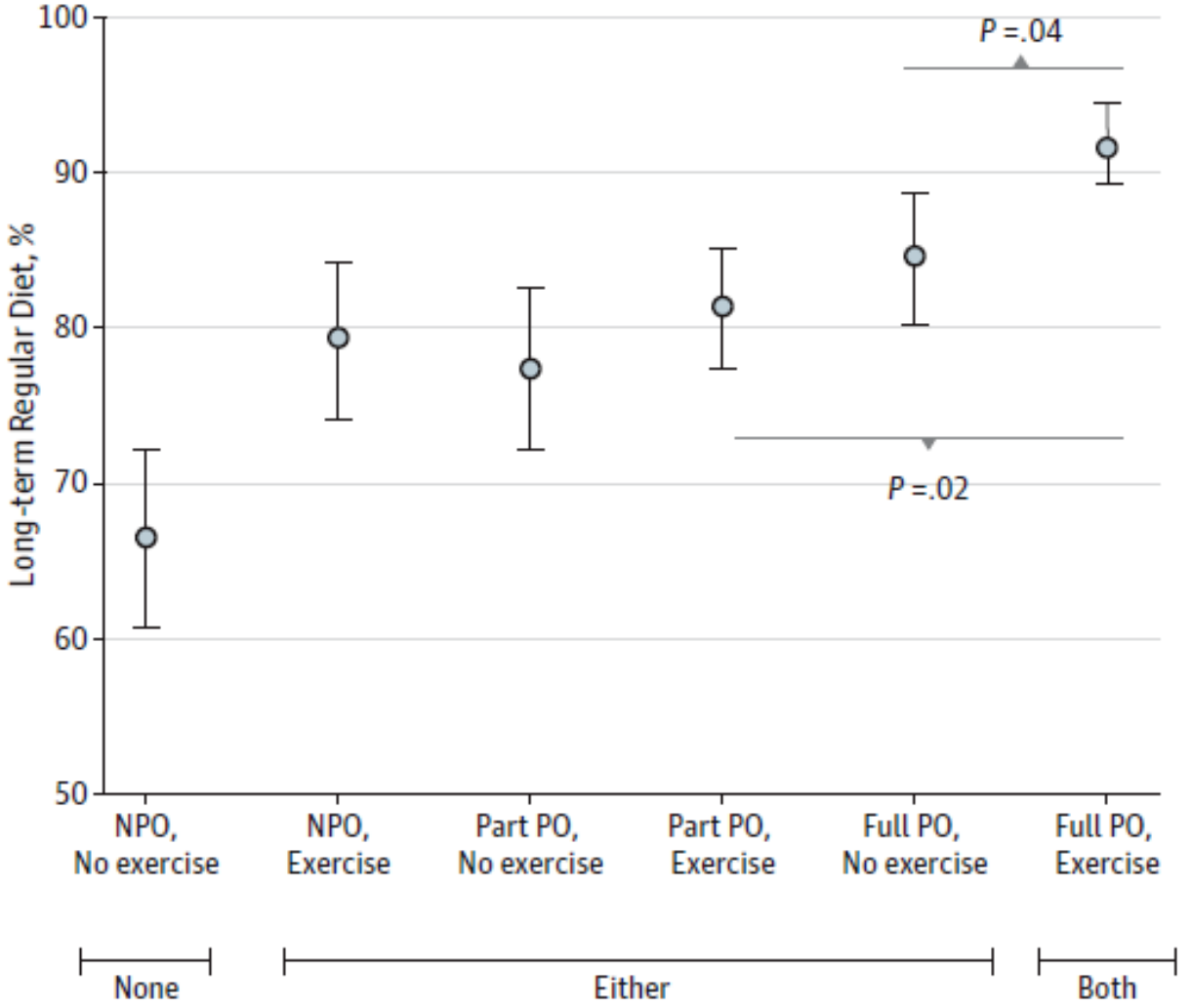


Eat



Hutcheson, Bhayani, Beadle, Gold, Shinn Lai, Lewin. *JAMA-OtoHNS* (2013)

LONG-TERM DIET
BY EAT & EXERCISE



Greater proportions of patients who performed swallowing exercises and/or maintained PO throughout treatment ate a regular diet at the conclusion of radiotherapy or chemoradiotherapy (*P* = .01). NPO indicates no oral intake; PO,

*median: 671 days

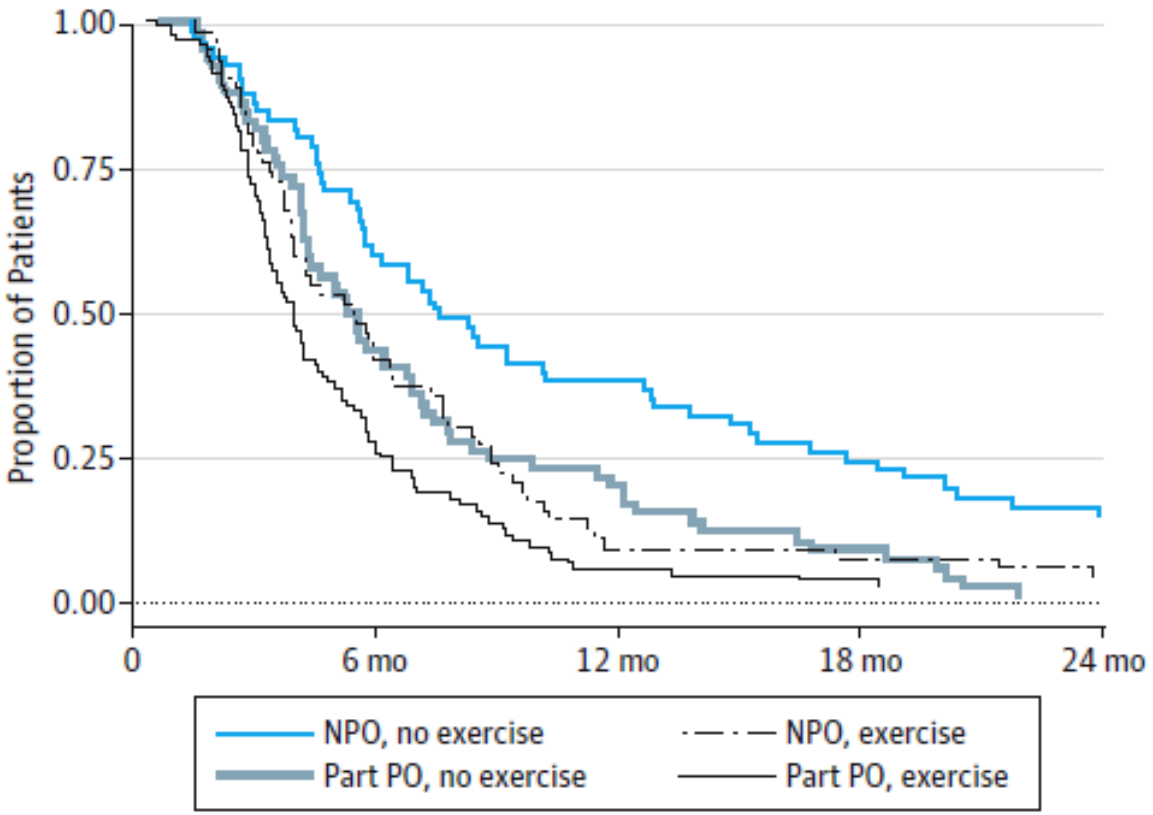
Hutcheson, Bhayani, Beadle, Gold, Shinn, Lai, Lewin. *JAMA-OtoHNS* (2013)

Duration PEG

by EAT & EXERCISE

Eat	Exercise	Median duration (days)
NPO	-	222
Part	-	157
NPO	+	151
Part	+	111

Figure 2. Duration of Gastrostomy Dependence by Swallowing Groups



Among the 313 patients who received a gastrostomy tube, exercise adherence and maintenance of some PO at the end of treatment was associated with significantly shorter duration of gastrostomy dependence ($P = .03$).

Hutcheson, Bhayani, Beadle, Gold, Shinn, Lai, Lewin. *JAMA-OtoHNS* (2013)

Independent effects?
Eat & Exercise

Table 4. Multivariable Models: Long-term Diet and Duration of Gastrostomy Dependence by Eat and Exercise

Variable	Duration of Gastrostomy Dependence			Diet After RT or CRT		
	Median (Range), Days PEG[a]	Coefficient (95% CI)	*P* Value	Regular Diet, No. (%)[b]	Adjusted Odds Ratio (95% CI)	*P* Value
Eat[c]						
NPO status	183 (0-1716)			94 (73)	1 [Ref]	
Partial PO status	120 (0-2029)	95.4 (−143.7 to −47.1)	<.001	132 (79)	1.2 (0.8 to 2.9)	.23
Full PO status	...	...		176 (88)	2.0 (1.0 to 4.6)	.045
Exercise						
Nonadherent	113 (0-1594)			160 (76)	1 [Ref]	
Adherent	68 (0-1815)	−06.0 (−182.8 to −29.2)	.007	242 (85)	4.0 (1.9 to 6.4)	<.001

Original Investigation

Eat and Exercise During Radiotherapy or Chemoradiotherapy for Pharyngeal Cancers

Use It or Lose It

JAMA-Oto HNS (2013)

Katherine A. Hutcheson, PhD; Mihir K. Bhayani, MD; Beth M. Beadle, MD, PhD; Kathryn A. Gold, MD; Eileen H. Shinn, PhD; Stephen Y. Lai, MD, PhD; Jan Lewin, PhD

PREVENTIVE THERAPY:
USE IT OR LOSE IT!!

EAT
OR
EXERCISE?

Independent, positive effects of ***eat*** and ***exercise*** during nonsurgical treatment

Best outcomes in patients who ***eat*** and ***exercise*** during treatment

Outcomes worst in those who neither ***eat*** nor ***exercise***

Swallowing (*eat & exercise*) feasible during (chemo)RT

Pre-treatment swallowing therapy is an important component of multidisciplinary care during (chemo)RT

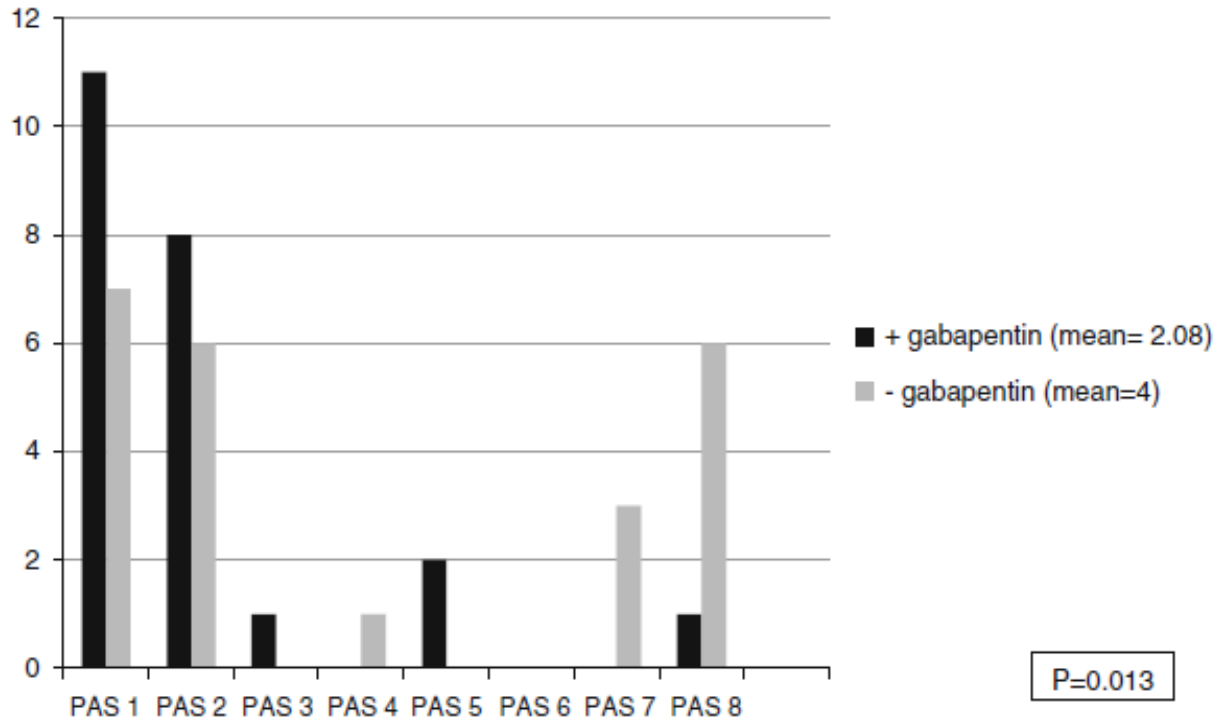
Dysphagia
DOI 10.1007/s00455-014-9521-1

ORIGINAL ARTICLE

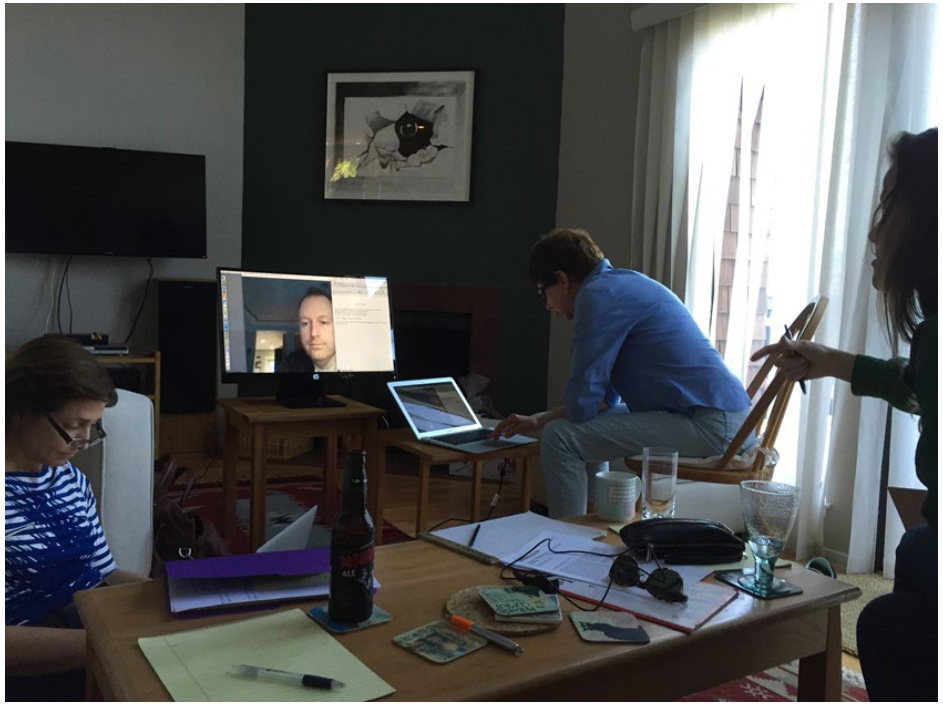
Effect of Gabapentin on Swallowing During and After Chemoradiation for Oropharyngeal Squamous Cell Cancer

Heather M. Starmer · WuYang Yang · Raju Raval · Christine G. Gourin · Marian Richardson · Rachit Kumar · Bronwyn Jones · Todd McNutt · Sierra Cheng · Harry Quon

- N = 46 OPC
- Matched case/control
- Prophylactic gabapentin during CRT
- ***Significantly less***:
  - Pain
  - PEG utilization
  - PEG duration
  - Aspiration (per MBS)



FOLLOW UP GRANT PLANNING MEETINGS 2017



THE TO DO LIST FOR PCORI GRANT FEB 2018

PRO-ACTIVE

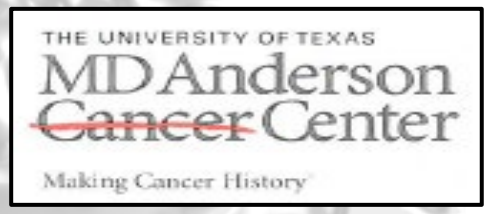
PROPHYL**ACT**IC SWALLOW **I**NTER**VE**NTION FOR PATIENTS RECEIVING RT FOR HNC

Rosemary Martino, PhD (co-PI)

Kate Hutcheson, PhD (co-PI)

Funding: pcori | Patient-Centered Outcomes Research Institute


UHN
Princess
Margaret
Cancer Centre


THE UNIVERSITY OF TEXAS
MD Anderson
Cancer Center
Making Cancer History


Hôpital général juif
Jewish General Hospital


London Health Sciences Centre


BU
Boston University School of Medicine


Mount
Sinai
Beth Israel


DEPARTMENT OF
Surgery

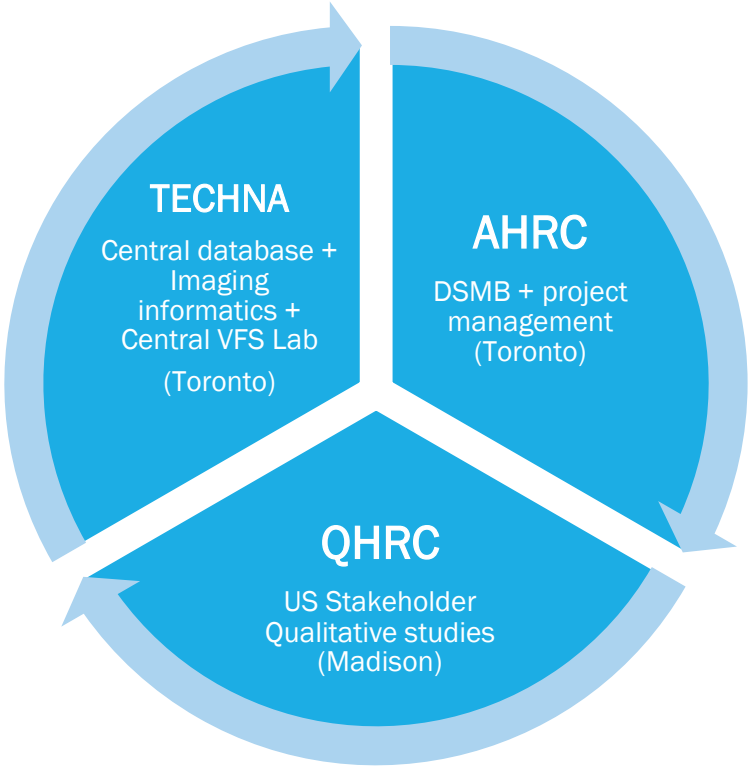

QHRC


AHRC
Applied Health Research Centre


TECHNA

ORGANIZATIONS

Organization	Site PI
Princess Margaret Cancer Centre, Toronto, ON, CAD	Rosemary, Martino, PhD (co-PI)
University of Texas MD Anderson Cancer Center, Houston, TX, USA	Katherine A. Hutcheson, PhD (co-PI)
University of Wisconsin Hospitals and Clinics, Madison, WI, USA	Timothy McCulloch, MD
Boston University Medical Center, Boston, MA, USA	Susan Langmore, PhD
Mount Sinai Beth Israel Health System, New York, NY, USA	Cathy Lazarus, PhD
London Health Sciences Centre, London, Ontario, CAD	David Palma, MD, PhD, Julie Theurer, PhD
Jewish General Hospital, Montreal, Quebec, CAD	Khalil Sultanem, MD



PATIENT ELIGIBILITY

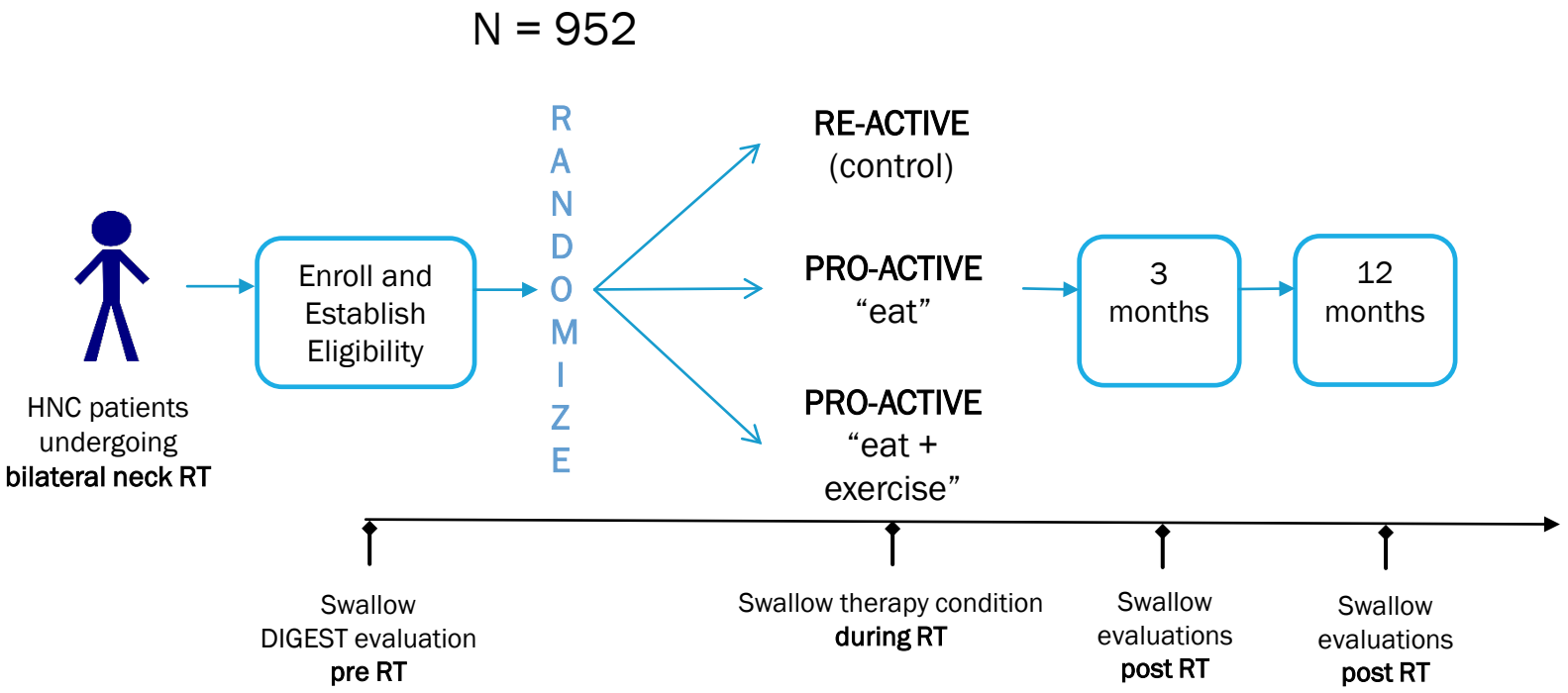
Any patient for whom the following decisional dilemma exists:
"*is there a benefit to proactive swallowing therapy during RT?*"

- **Age** - 18 years and older
- **Cancer** - head and neck
- **Treatment** – planned bilateral RT >60 Gy
- **Dysphagia** – grade 0-1 (per MBS DIGEST)

PRO-ACTIVE

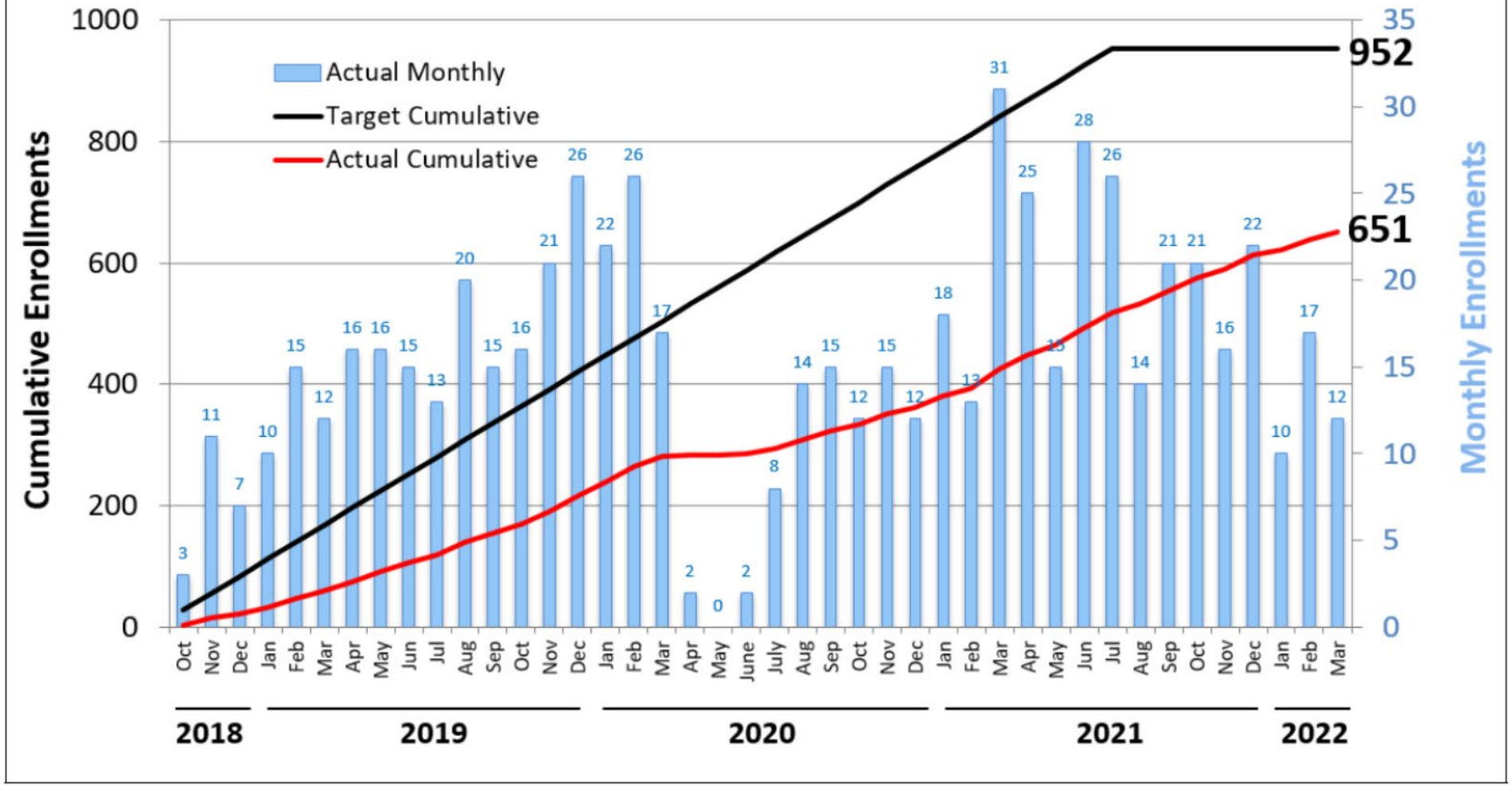
Comparing the Effectiveness of Prophylactic Swallow Intervention for Patients Receiving Radiotherapy for HNC

PCORI Award (2018 – 2023)



https://www.pcori.org/research-results/2017/pro-active-comparing-effectiveness-prophylactic-swallow-intervention-patients

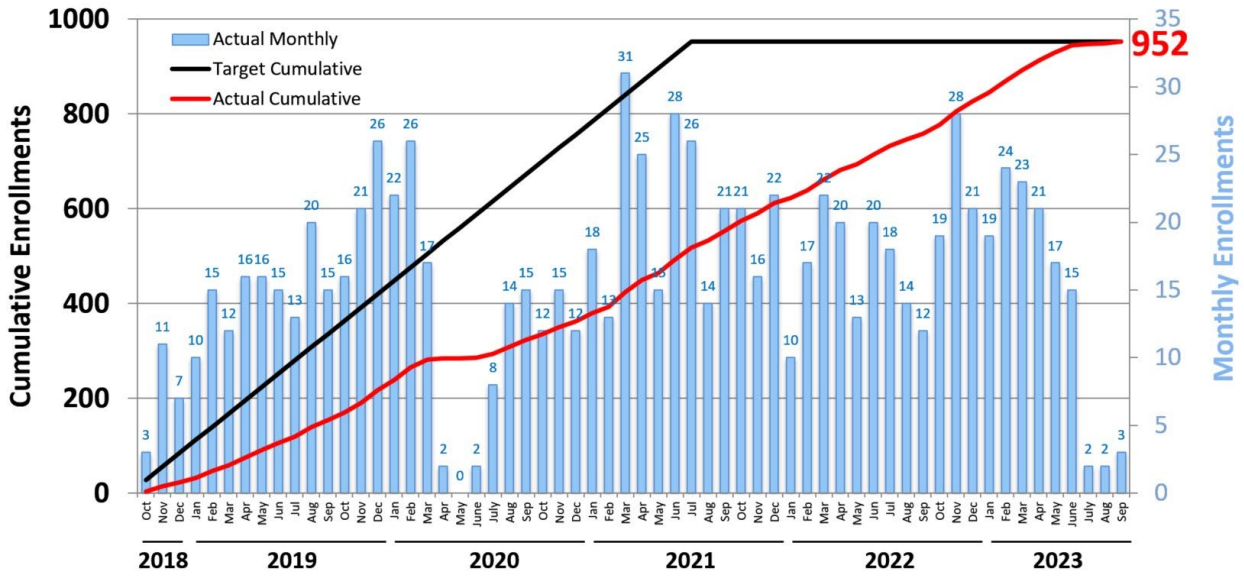
Overall Study Enrollment (as of Mar 18, 2022)

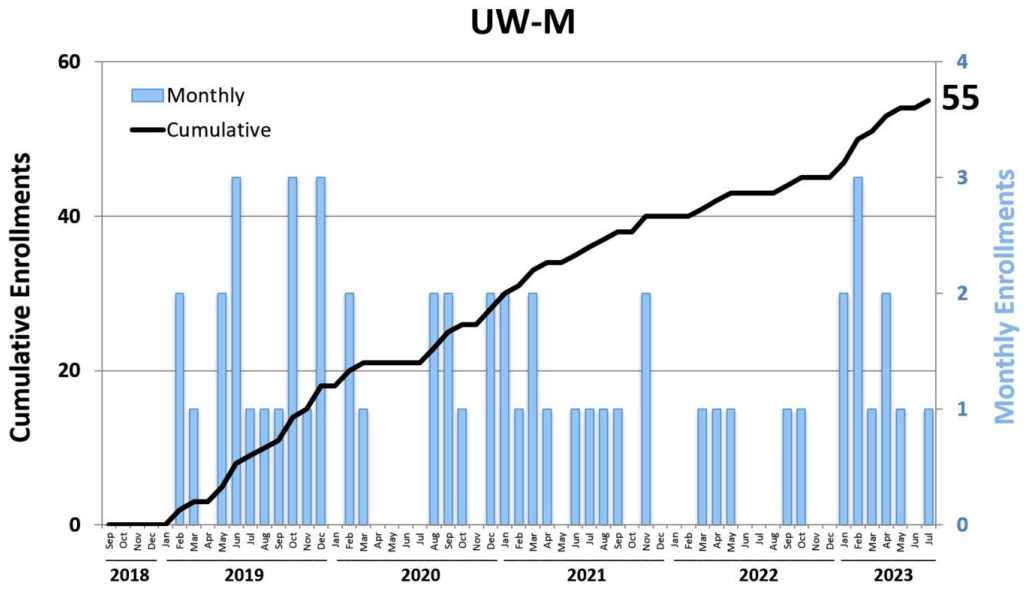


Trial Randomization Progress: 68%

651 / 952

FINAL ENROLLMENT





MID-TRIAL MEETINGS


Helpful Suggestions
X-Y-Z 60
U 54