

Endoscopic Therapy of Barrett's Esophagus

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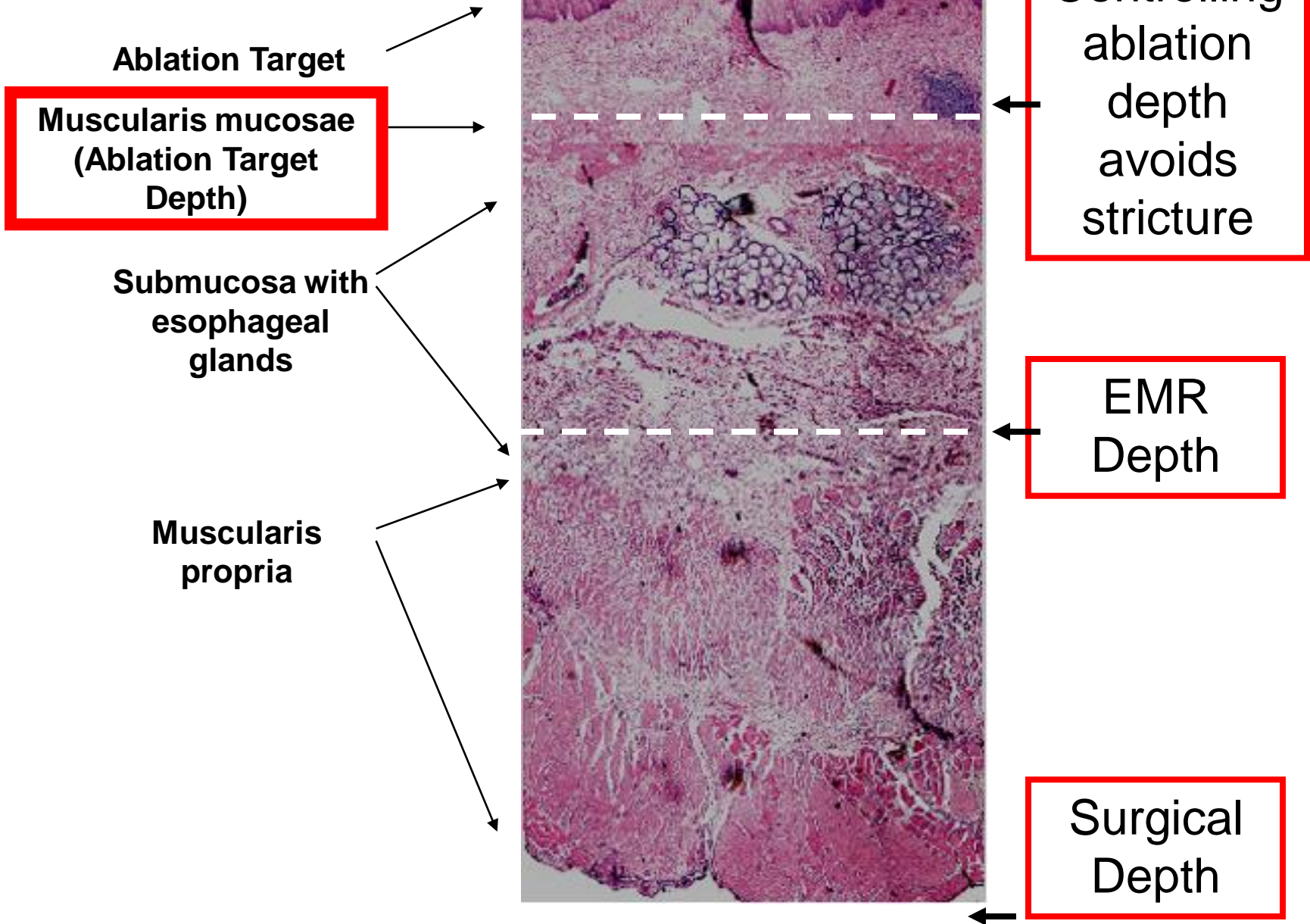
Outline

- Who Should Have Endoscopic Therapy?
 - Possible scenarios
 - BE with nodular disease
 - BE with HGD
 - BE with LGD
 - BE with no dysplasia
 - Squamous disease?
- What does ablation accomplish?
- What are the side effects of ablation?
- What new methodology will be available?

What is ablation?

- Destruction and, ultimately, removal of a cell, epithelium, tissue
- Seminal observation: BE, when ablated in an anacidic milieu, regenerates squamous epithelium
- Mechanism: heating of tissue to the point of vaporization and/or coagulation of proteins
- Endpoint is irreversible cell injury and, ultimately, cell death

Human Esophagus

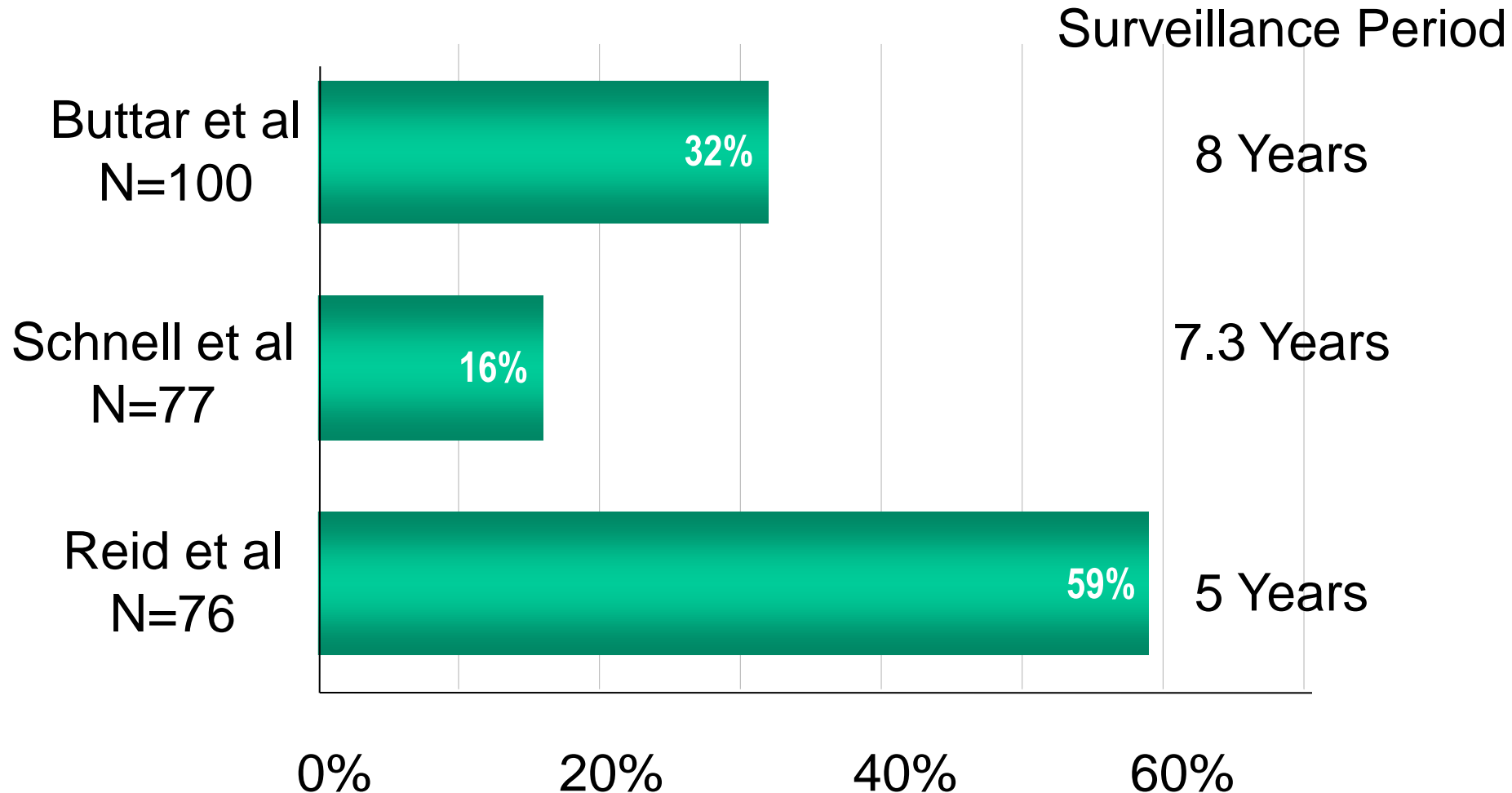


Who Should Have Ablative Therapy?

The Case for Ablation in HGD

- The risk of progression of the lesion is high
- The risk of a metachronous cancer is substantial
- The competing strategy (surgery) is morbid
- Patients are often more comfortable with a proactive strategy
- Some data to suggest a decreased cancer risk

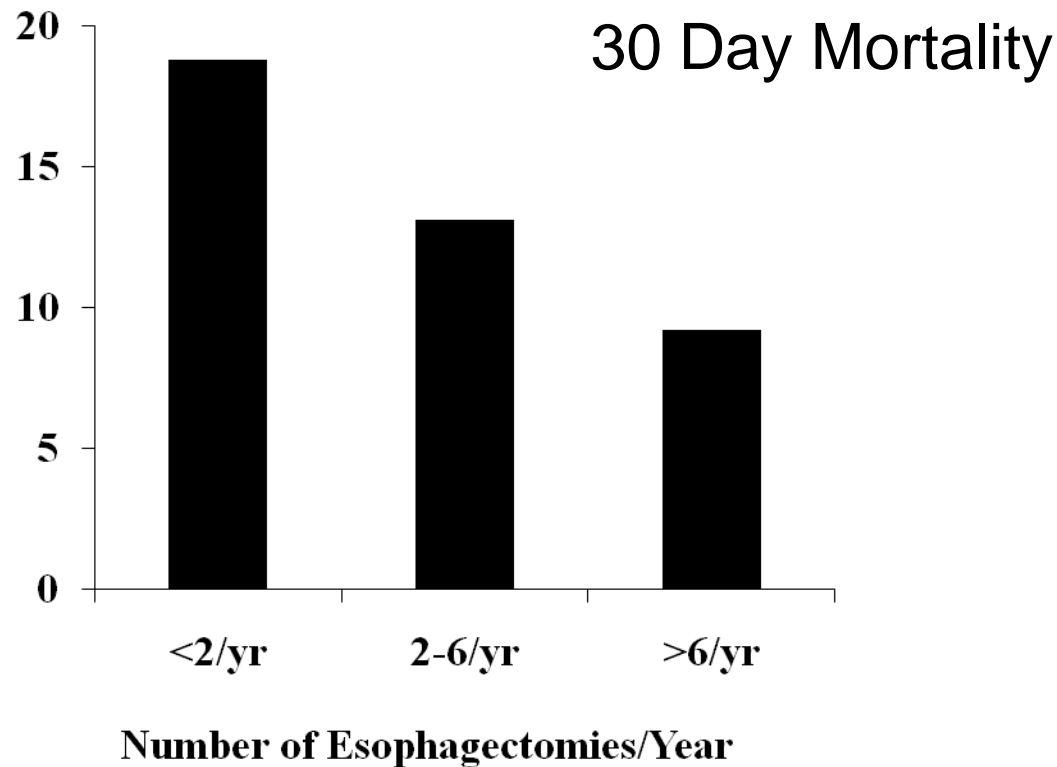
Progression to Cancer



7 Reid et al. Am J Gastro 2000;95:1669-1676.
Buttar et al. Gastro 2001;120:1630-1639.

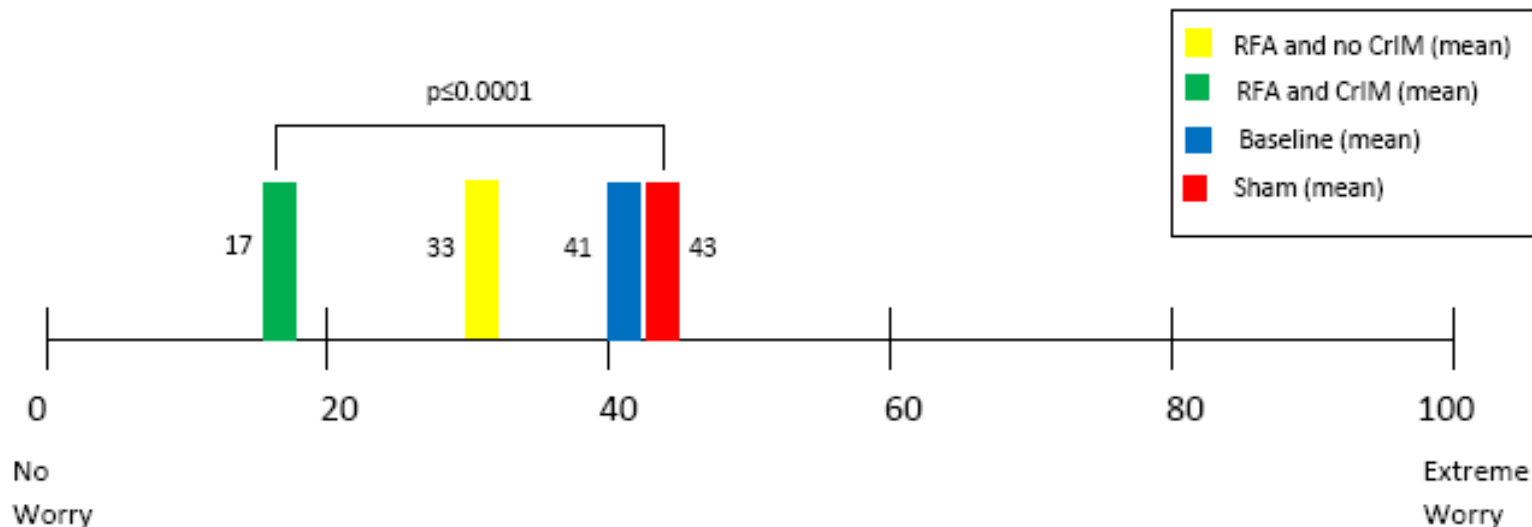
Schnell et al. Gastro 2001; 120:1607-1619.

What is the Risk of Death with Esophagectomy?



Patients Prefer an Active Approach to Dysplastic BE

Indicate the degree to which you worry about the present condition of your esophagus.



So ablation seems reasonable for HGD...

- What about lesser forms of dysplasia and metaplasia (LGD, Indefinite, ND-BE)?
 - Given lower rates of progression here, side effects and costs of therapy become important
 - No data showing diminished cancer risk in these patient populations

How Benign is Low-Grade Dysplasia?

- 147 subjects with a diagnosis of LGD made in a community practice in the Netherlands
- Path reviewed by 2 expert pathologists
 - Disagreements resolved by consensus
- 85% of cases were down-graded
- In the 15% who were not, the incidence rate of HGD or EAC was 13.4%/pt-yr (mean f/u: 51 months)

Isn't the Risk of Cancer too Low to ND-BE Justify Intervention?

The risk of cancer in any single year is low for those with ND-BE. The NNT to prevent one cancer in a given year is 1/250.

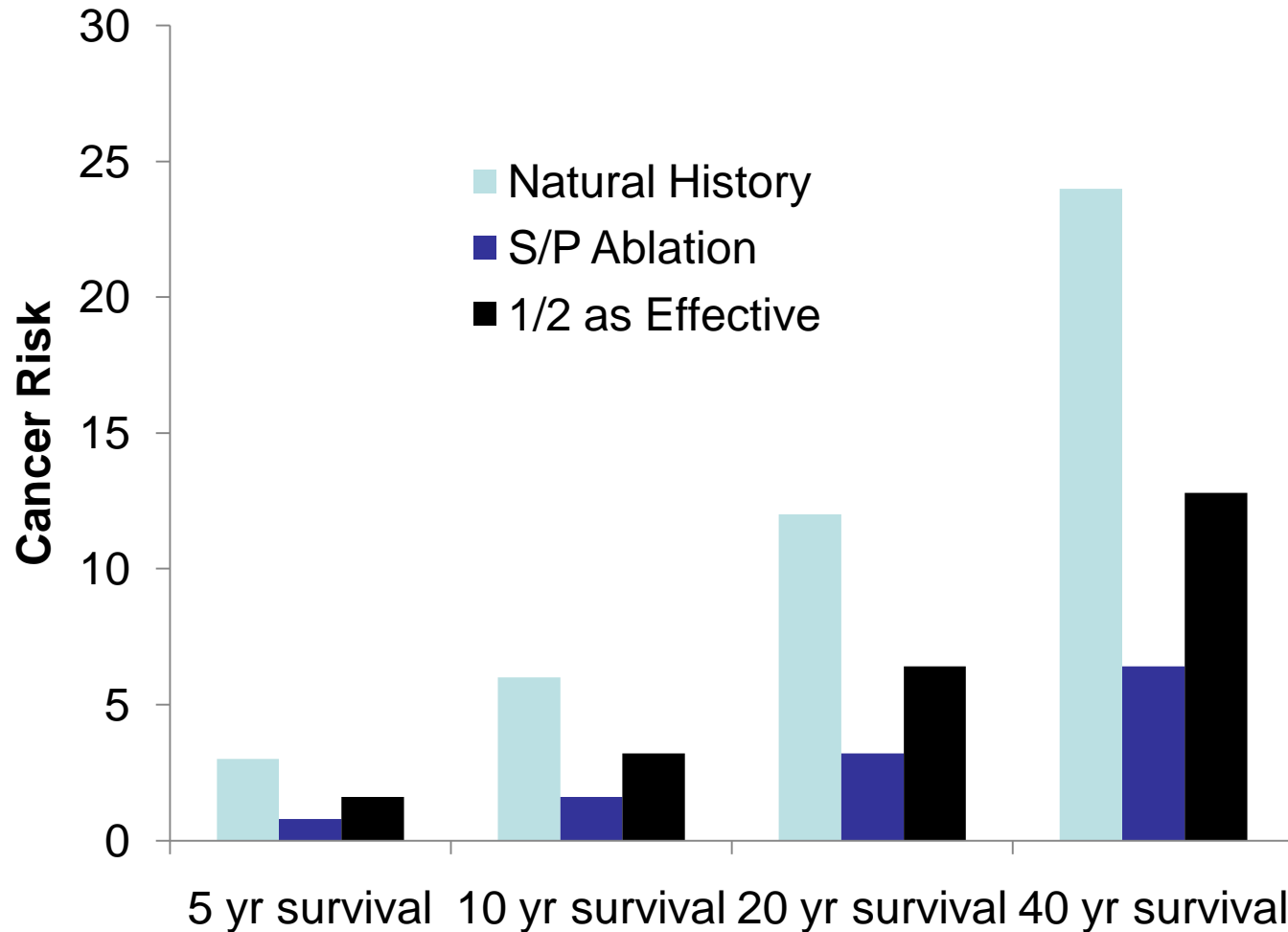
Consider a 40 yo male w/ ND-BE....

- Such an individual may have 40-50 yrs of life expectancy in 2010
- If risks are linear, compounding 0.5% over this time yields an overall cancer risk of 20-25%
- Single year NNT's are irrelevant
 - Ablation is illogical for someone with a short life expectancy
- The real questions are what the lifetime cancer risk for the individual is, and how much it could be lowered with ablation?

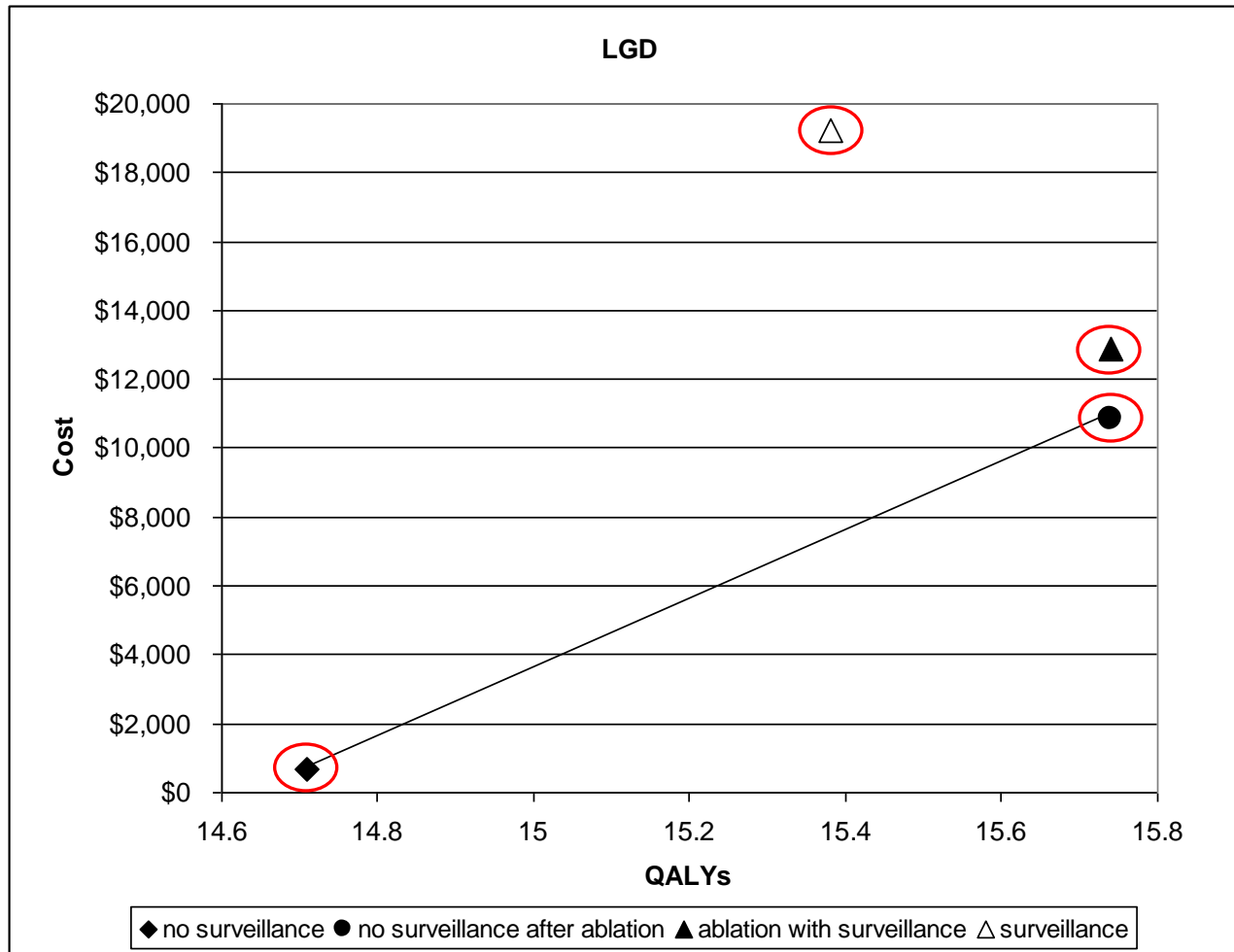
We Don't Have Good Data on the Longterm Protective Effect of Ablation

- But we can make some estimate of the effect of endoscopic ablation and compare it to natural history studies
- Risk from natural history studies: 6/1000
- Risk from meta-analysis of ablation: 1.6/1000

Using these data, let's play some hypotheticals...

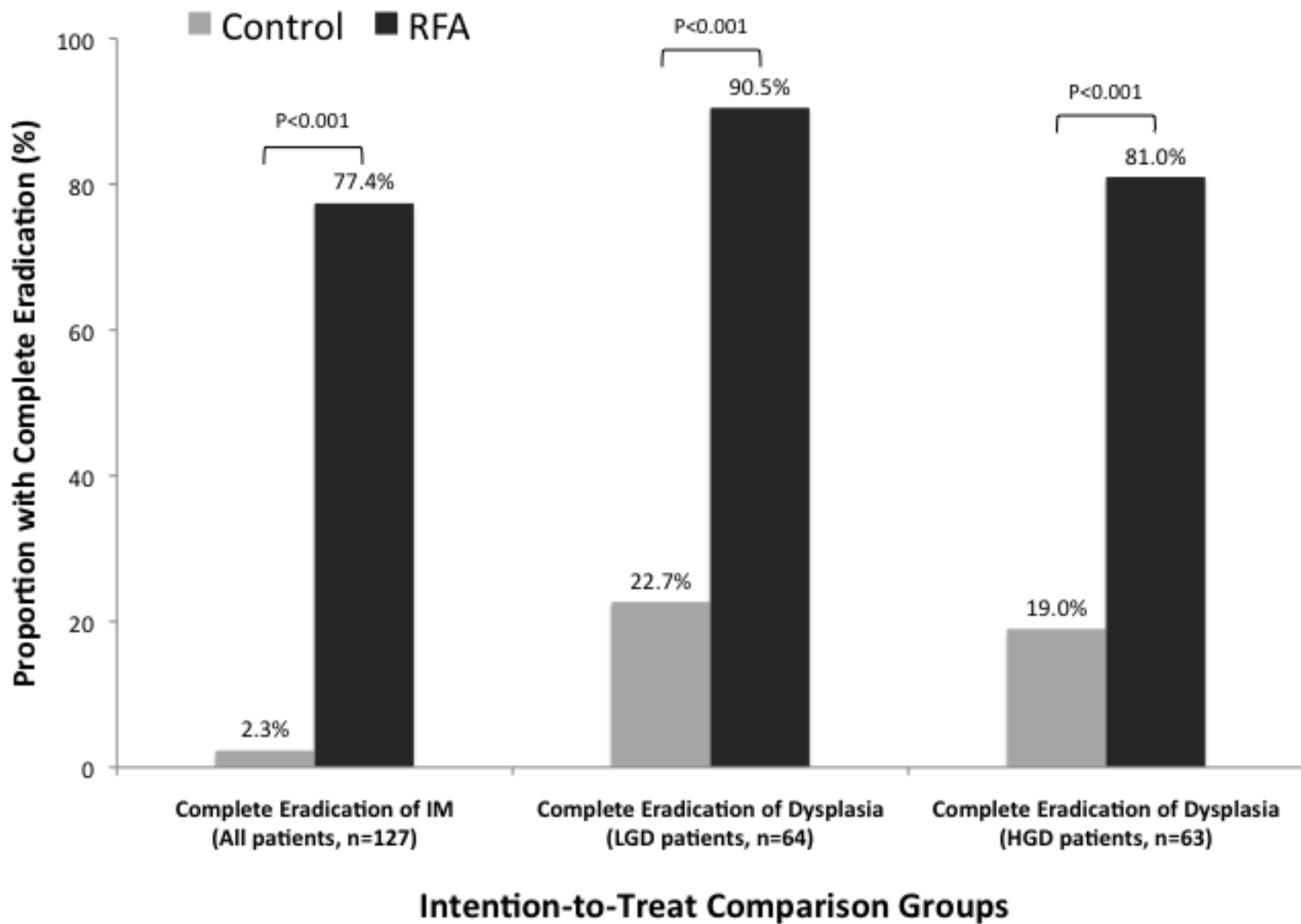


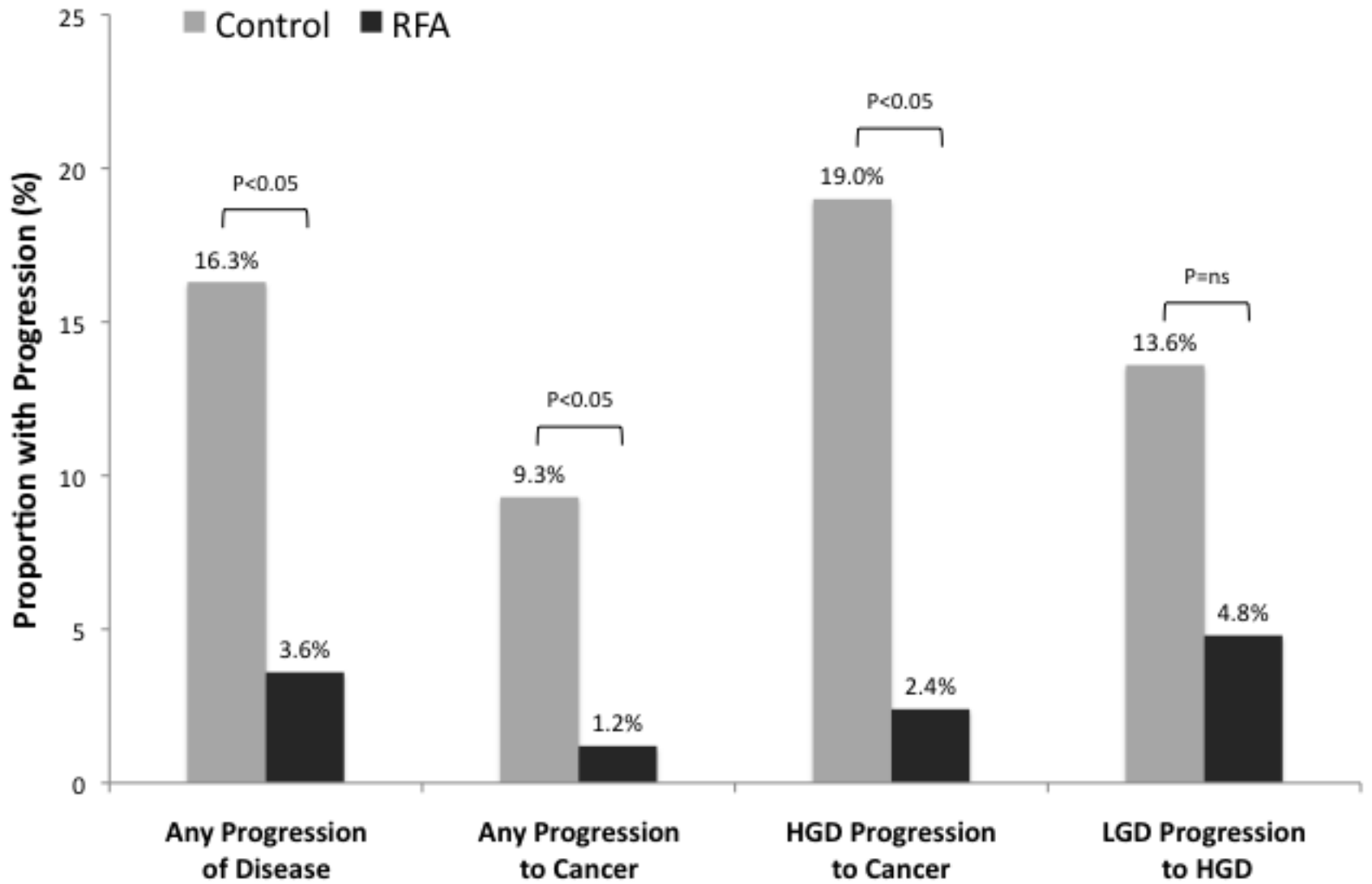
Ablation of Lesser Forms of Dysplasia Might be Effective and Cost-Effective



Inadomi JM et al. Gastroenterology 2009.

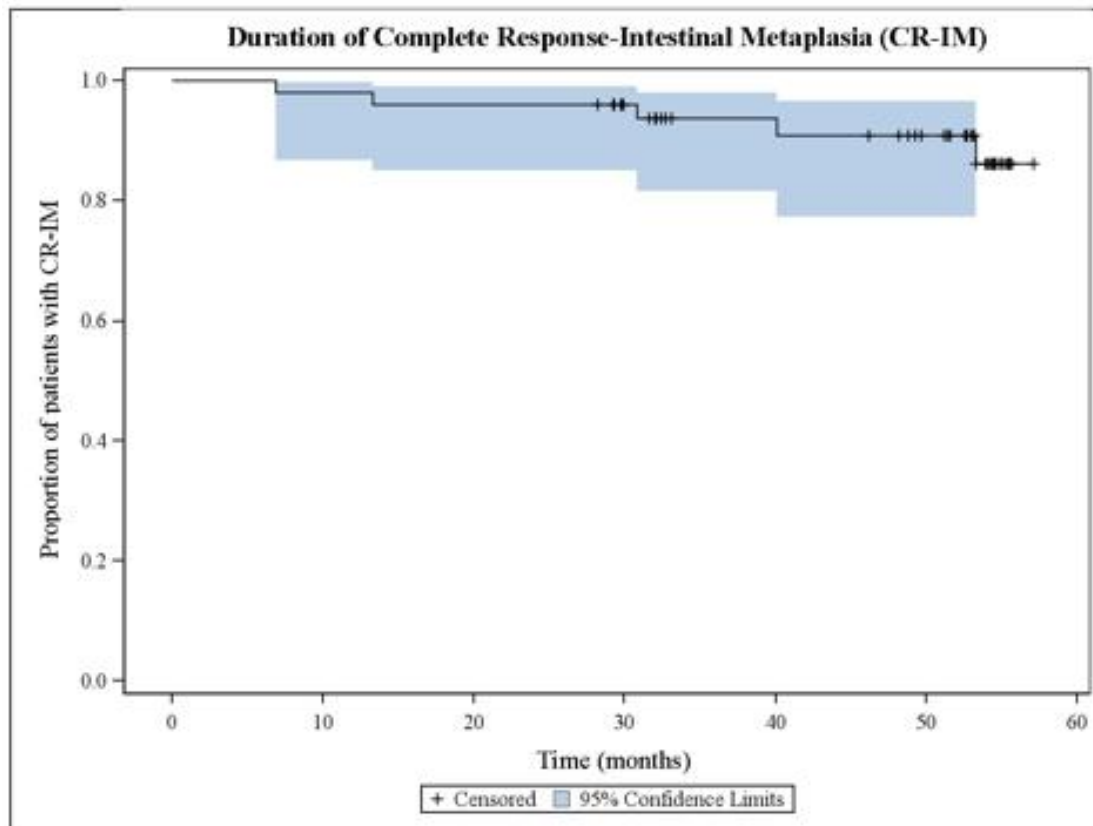
What Can Be Accomplished?





What About Durability?

Reversion Appears Durable in the ND-BE Population out to 5 Yrs



What are the True Risks with Ablation?

- Chest Pain
 - Pretty much everyone gets some
 - 23/100 on a VAS in recent RCT
 - Resolves on average by a week or so
- Bleeding
- Perforation
- Stricture
- Buried BE

Systematic Review of Complications with RFA

Author	Year	No. patients	Average follow-up	Strictures	Perforations	Chest pain	Bleeding	Hospitalizations	Buried glands
Sharma et al ²¹	2009	63	24 mo	1 (2%)	0 (0%)	NA	1 (2%)	0 (0%)	0 (0%)
Pouw et al ²²	2009	24	22 mo	1 (4%)	1 (4%)	1 (4%)	1 (4%)	0 (0%)	0 (0%)
Velanovich ²³	2009	66	12 mo	4 (6%)	0 (0%)	NA	0 (0%)	0 (0%)	NA
Shaheen et al ¹⁷	2009	84	12 mo	5 (6%)	0 (0%)	2 (2%)	1 (1%)	2 (2%)	*
Eldaif et al ²⁴	2009	27	2 mo	0 (0%)	0 (0%)	NA	NA	NA	0 (0%)
Vassiliou et al ²⁵	2009	25	20 mo	2 (8%)	0 (0%)	2 (8%)	1 (4%)	0 (0%)	0 (0%)
Ganz et al ²⁶	2008	142	12 mo	1 (1%)	0 (0%)	NA	NA	NA	0 (0%)
Gondrie et al ²⁷	2008	12	14 mo	1 (8%)	0 (0%)	NA	0 (0%)	0 (0%)	0 (0%)
Fleischer et al ^{18†}	2008	70	30 mo	0 (0%)	0 (0%)	12 (17%)	1 (1%)	0 (0%)	0 (0%)
Hernandez et al ²⁸	2008	10	12 mo	0 (0%)	0 (0%)	NA	0 (0%)	0 (0%)	1 (10%)‡
Sharma et al ²⁹	2008	10	24 mo	0 (0%)	0 (0%)	N/A	1 (10%)	1 (10%)	0 (0%)
Gondrie et al ³⁰	2008	11	14 mo	0 (0%)	0 (0%)	NA	0 (0%)	0 (0%)	0 (0%)
Sharma et al ³¹	2007	100	12 mo	0 (0%)	0 (0%)	12 (12%)	1 (1%)	0 (0%)	0 (0%)
Roorda et al ³²	2007	13	12 mo	0 (0%)	0 (0%)	3 (23%)	0 (0%)	0 (0%)	0 (0%)

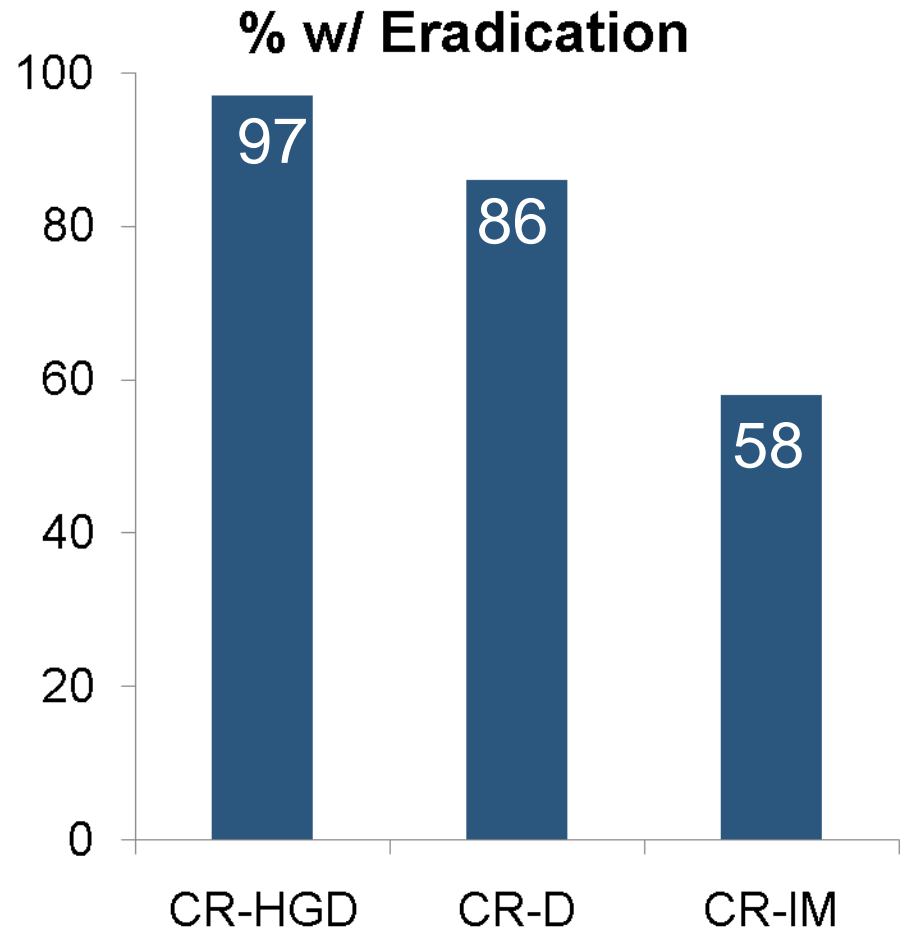
Given the relatively short-term nature of data after ablation, it is unwise currently to cease surveillance endoscopy after ablative therapy.

Evolving Technology in BE



Cryotherapy in HGD: An Initial Report

- 98 subjects w/ HGD treated at 10 institutions
 - 61 completed Rx, 27 ongoing
- 281 total procedures
 - 4.0/pt
- No perfs, no buried glands, no bleeds or chest pain requiring hospitalization
- One progression to CA



Shaheen NJ et al. DDW 2009.

Summary

- For Nodular Disease and HGD, endoscopic therapy with EMR and RFA, respectively, seem straightforward
- The current “hot topic” is LGD
 - Not crazy to consider ablation here
 - Still significant holes in our data
 - Space for shared decision-making between doc and patient
- For ND-BE, the conceptual underpinnings for treatment exist
 - Again, no data substantiating decreased cancer risk
 - Pragmatically, most of these patients have the luxury of time
 - For that reason, we are generally counseling no ablation presently, as data accrue