


**Radiation Therapy for
Gastro-esophageal Cancer**

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The logo for UNC Lineberger Comprehensive Cancer Center, featuring the letters 'UNC' in a large, bold font above the text 'N.C. CANCER HOSPITAL' and 'LINEBERGER COMPREHENSIVE CANCER CENTER'.

DISCLOSURES

NONE

Terminology

- Substantial confusion as to biology related to site of origin of tumors in the stomach and esophagus
- Epidemiology of classical esophageal, gastric and GE junction cancers are distinct
- Clinical trials have been designed for gastric or esophageal cancers with variable numbers of patients with GE junction tumors included

Terminology

- Unclear relevance of many published studies to true GE junction tumors
 - Recent gastric trials have generally included primarily classical gastric cancers, with about 20-25% of GE junction cancers
 - Recent esophageal trials from the US have included a majority of patients with GE junction adenocarcinomas
 - These trials may be more reflective of appropriate management strategies

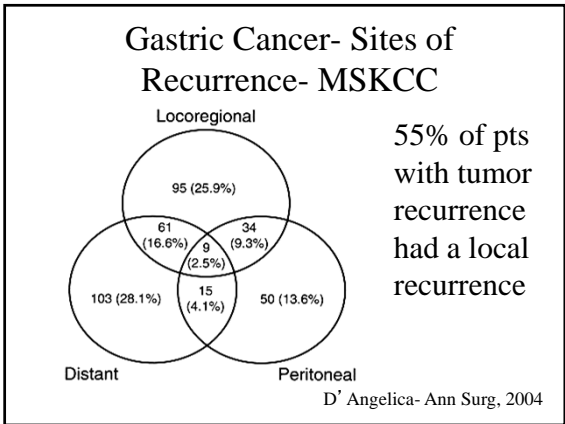
GASTRIC CARCINOMA - MGH

STAGE	TOTAL LOCAL-REGIONAL FAILURE	LOCAL-REGIONAL FAILURE ALONE
A	0	0
B1	3/16 (19%)	1/16 (6%)
B2	6/12 (50%)	1/12 (8%)
B3	2/5	0
C1	4/17 (24%)	2/17 (12%)
C2	16/44 (36%)	10/44 (23%)
C3	18/32 (56%)	7/32 (22%)

University of Minnesota Re-operation Series

Stage	Number failed	Local-regional failure	Local-regional failure alone
B	10/12 (83%)	9/12 (75%)	4/12 (33%)
C	68/89 (76%)	59/89 (66%)	17/89 (19%)

Gunderson



Gastric Cancer- Sites of Recurrence- MSKCC

Local Regional- 199 patients

- Lymph nodes 48%
- Anastomosis 32%
- Gastric bed 20%

Distant - 188 patients

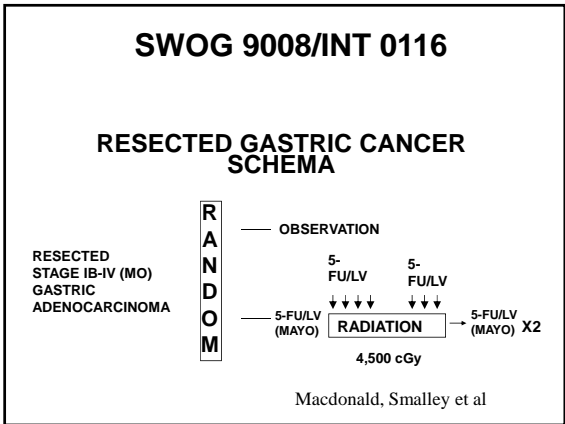
- Liver 37%
- Lung 16%
- Bone 16%
- Lymph nodes 14%
- Brain 6%

D' Angelica- Ann Surg, 2004

Gastric Cardia

- Surgery vs preoperative radiation therapy
- Limited radiation fields
- 5- year survival- 20% vs 30%
- Local failure- 52% vs 39%
- Distant metastases- no difference

Zhang- IJROBP- 1998



SWOG 9008/INT 0116

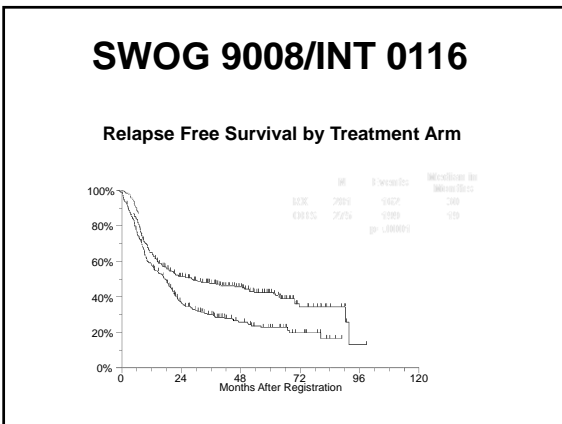
BASELINE DISEASE CHARACTERISTICS

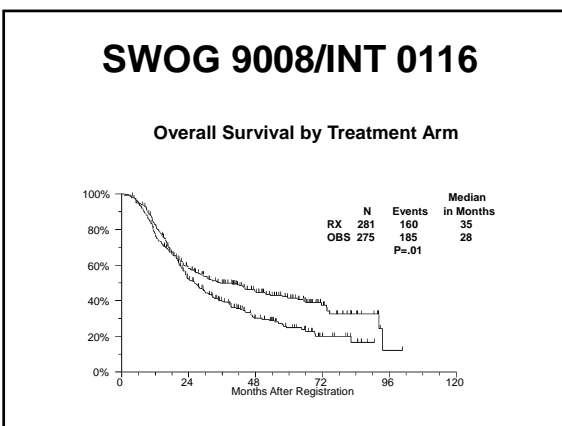
	<u>OBS(275)</u>	<u>RX(281)</u>
T-STAGE		
%T1-T2	31%	31%
% T3	61%	62%
% T4	8%	6%
NO. + NODES		
% None	16%	14%
% 1-3	41%	42%
% 4+	43%	43%

SWOG 9008/INT 0116

BASELINE DISEASE CHARACTERISTICS

	<u>OBS(275)</u>	<u>RX(281)</u>
LOCATION OF PRIMARY		
Antrum	56%	53%
Corpus	25%	24%
Cardia	18%	21%
Multicentric	0.4%	2%





SWOG 9008/INT 0116

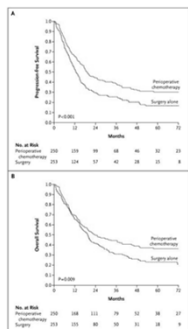
Sites of recurrence

	<u>obs (n=176)</u>	<u>rx (n=112)</u>
local	51	21
regional	126	76
distant	32	36

MAGIC Trial

- 3 cycles ECF preoperatively
- Surgical resection
- 3 cycles ECF postoperatively
- ECF
 - Epirubicin- 50 mg/m²/d, d1
 - Cisplatin- 60 mg/m²/d, d1
 - 5-FU- 200 mg/m²/d x 21 d
- Approximately 25% of patients with GE junction or esophageal cancer
- No obvious difference in outcome on site of primary

Progression-free and Overall Survival



Cunningham D et al. N Engl J Med 2006;355:11-20

Patterns of Failure

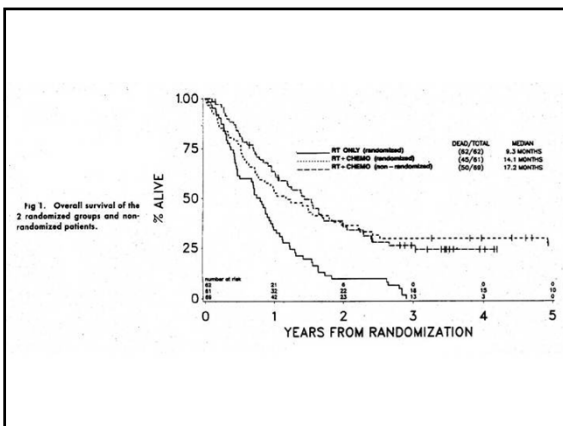
	Local Recurrence	Distant metastases
Control	20.6%	36.8%
Peri-operative chemotherapy	14.4%	24.4%

Cunningham, NEJM, 2006

Esophageal Cancer

- Squamous or adeno, no mets
- RT alone- 6400 cGy
- RT + chemo
 - 5-FU 1000 mg/m² x 4 d, d 1-4 x 4 cycles
 - Cis-platin- 75 mg/m², d 1 x 4 cycles
 - RT- 5000 cGy

Herskovic, NEJM, 1992



Patterns of Failure- Herskovic, NEJM - 1992

First Failure	RT Only (%)	RT + CT-randomized (%)	RT + CT-non-randomized (%)
None	11	36	26
Local Persistence	37	25	28
Local-Regional Only	18	15	20
Local/Reg/Distant	13	5	6
Total Local Regional	68%	45%	54%

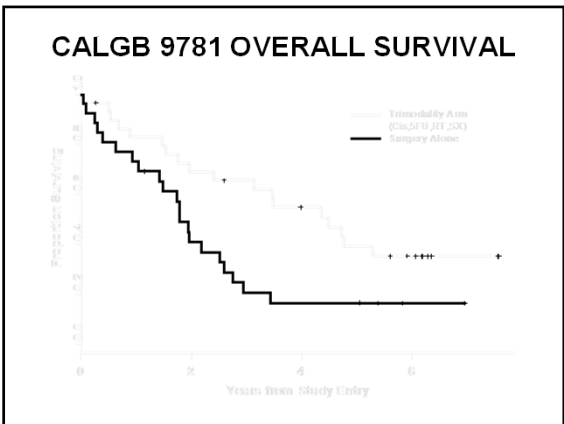
**CALGB 9781-
Chemo/RT + Surg vs Surg alone**

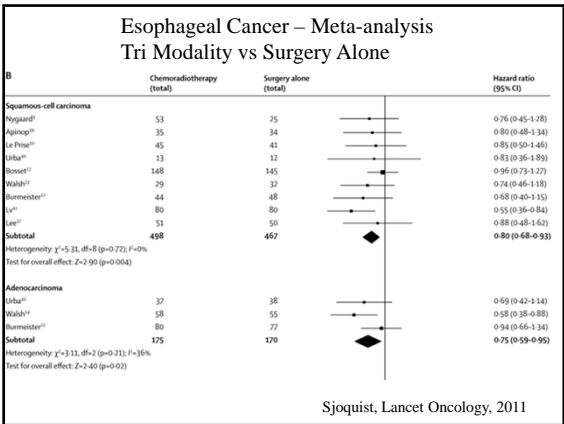
STAGE I, II, III esophageal cancer

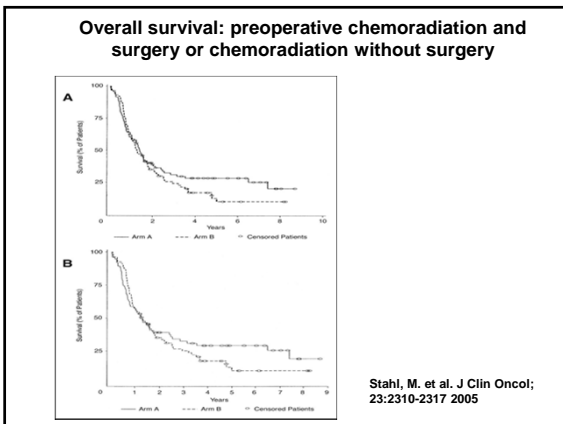
5FU-1000mg/m² x 4 d
cisplatin- 100 mg/m² Surgery alone
Chemo weeks 1 and 5

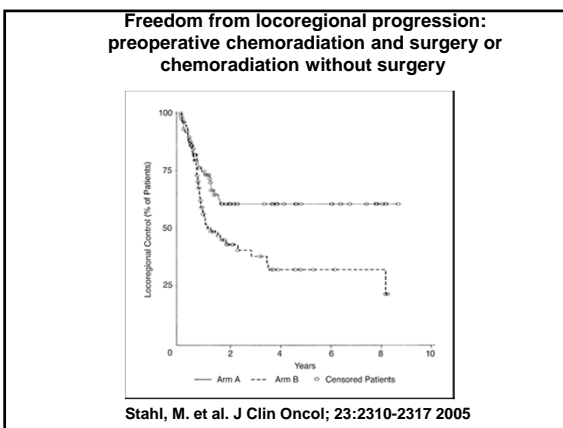
Radiation therapy (50.4 Gy)
concurrent with
chemotherapy

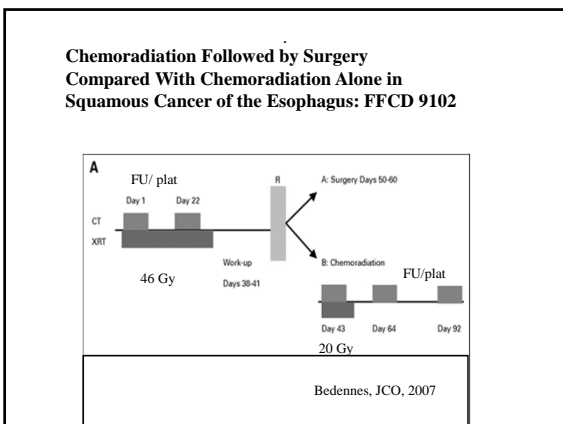
Surgery-3-8 wks later











Radiation Therapy Technique

- Treat celiac axis nodes if this does not require a large field extension
- Proximal and distal margins on esophageal lesion are arbitrary
 - Generally recommend 3-5 cm
- Treat para-esophageal nodes in the primary field
- Minimize cardiac and pulmonary irradiation
- Keep spinal cord dose to ≤ 45 Gy
- Concurrent chemotherapy based on
 - FU
 - Irinotecan
 - Platinum

Radiation Therapy Technique

- Fields should be primarily AP-PA to minimize pulmonary dose
 - IMRT should be used with caution, especially in preoperative setting
- Off cord for a small percentage of dose
 - Laterals
 - Obliques
- Emphasis should be on the likely surgical margins in para-esophageal soft tissue

Radiation Therapy Technique

- 45 Gy/180 cGy/fx to initial field
- 5.4 Gy cone down
- Liver- Mean dose < 25 Gy
 - 60% of liver ≤ 30 Gy
- Heart- Entire heart < 30 Gy
 - 50% of heart < 40 Gy
- Lung- $< 20\%$ of lung receiving 30 Gy

Radiation Therapy Technique-Problems

- **Cervical esophageal cancers**
 - IMRT is often useful
 - Difficult to meet constraints with standard fields
- **Postoperative radiation therapy (especially transhiatal esophagectomy)**
 - Difficult to treat entire field without excessive morbidity
 - Often need to treat highest risk area, which may be the tumor bed, not the anastomosis
- **Strongly prefer preoperative RT**

GE Junction cancers

- Local control remains a clinical issue in both gastric and esophageal cancer patients
- Radiation therapy, with concurrent chemotherapy, decreases local failure in both gastric and esophageal cancer
- Treatment regimens with radiation therapy improve survival in both gastric and esophageal cancer
- Radiation therapy remains an important component of the management of GE junction carcinomas

GE Junction Cancers

- The value of chemotherapy in gastric cancer in no way minimizes the value of radiation therapy
- Clinical trials are needed to optimize the combination of the therapeutic modalities
- Need to define which patients are at highest risk for local and systemic failure
- We must improve our understanding of the biology of GE junction tumors

