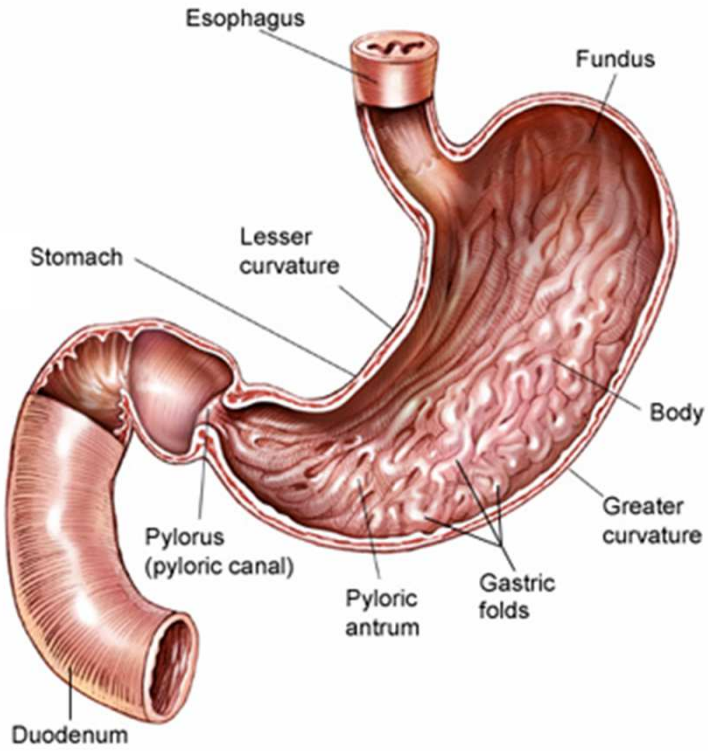
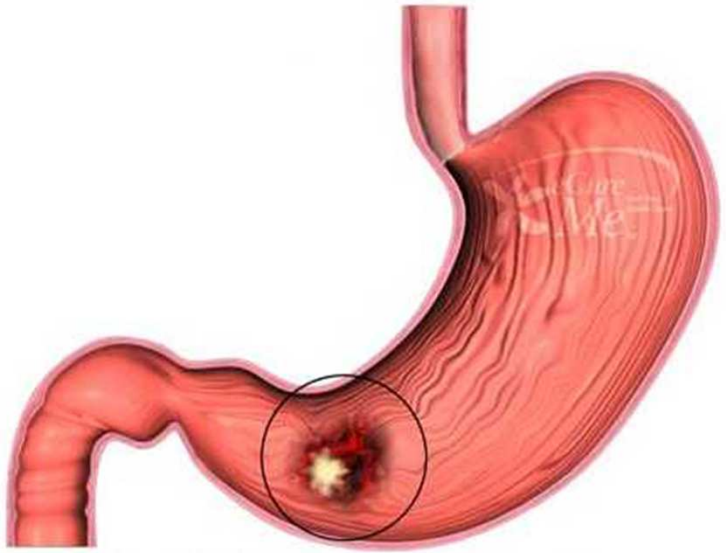
Stomach (Gastric) Cancer





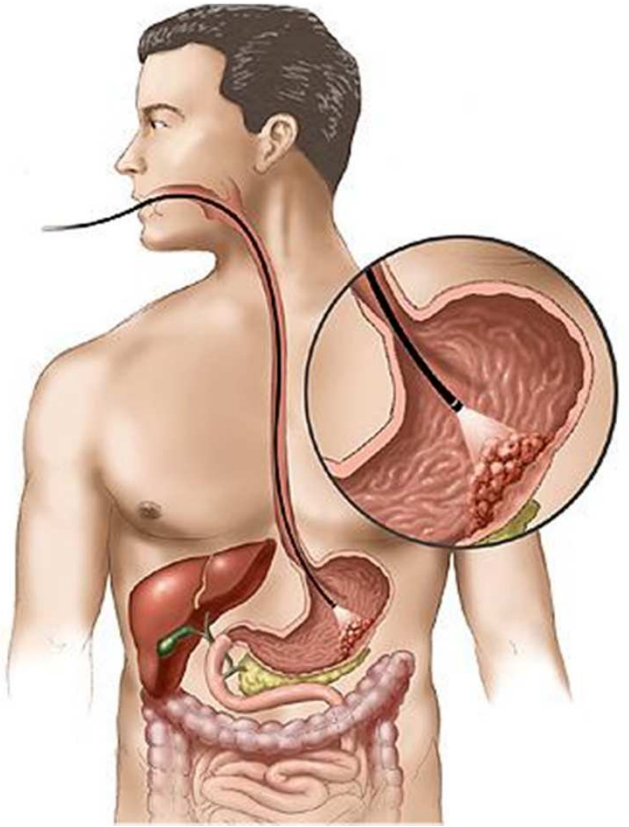
Prof. M K Mahajan
ACDT & RC Bathinda

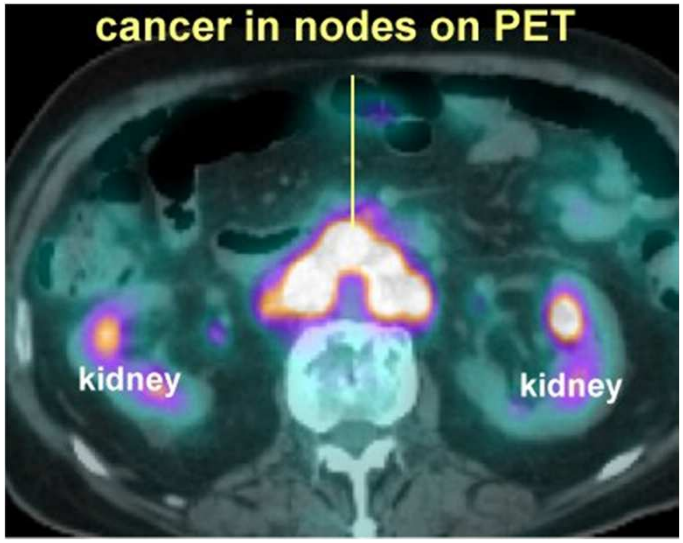
Gastric Cancer

Role of Radiation

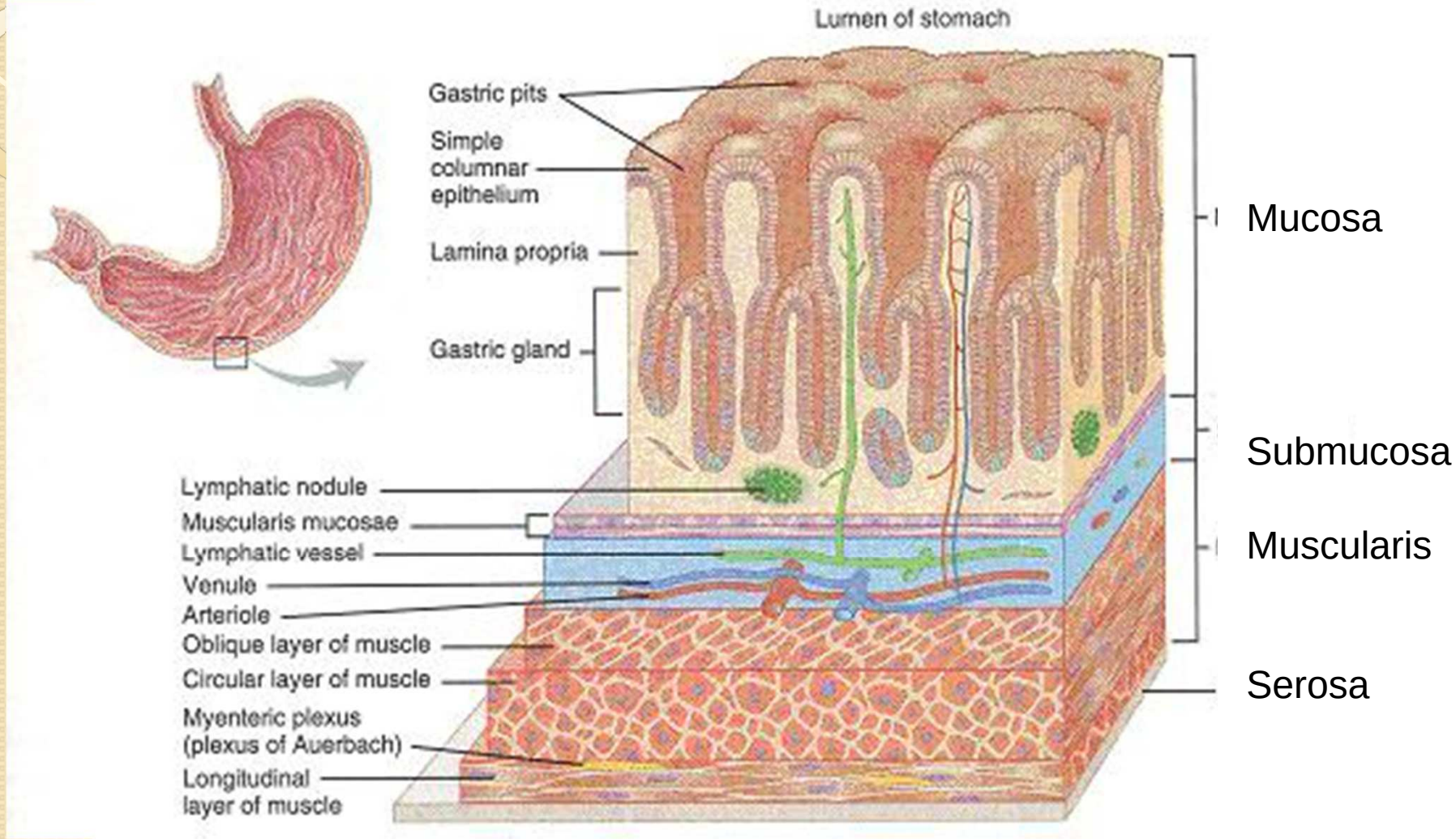
WORKUP

- H&P
- Upper GI endoscopy and biopsy[a]
- Chest/abdominal CT with oral and IV contrast
- Pelvic CT as clinically indicated
- PET-CT evaluation if no evidence of M1 disease[b]
- CBC and chemistry profile
- Endoscopic ultrasound (EUS) if no evidence of M1 disease (preferred).
- Endoscopic mucosal resection (EMR) may contribute to accurate staging of early stage cancers[c]
- Nutritional assessment and counseling
- Biopsy of metastatic disease as clinically indicated
- HER2-neu testing if metastatic adenocarcinoma is documented/ suspected[d]
- Smoking cessation advice, counseling and pharmacotherapy[e]

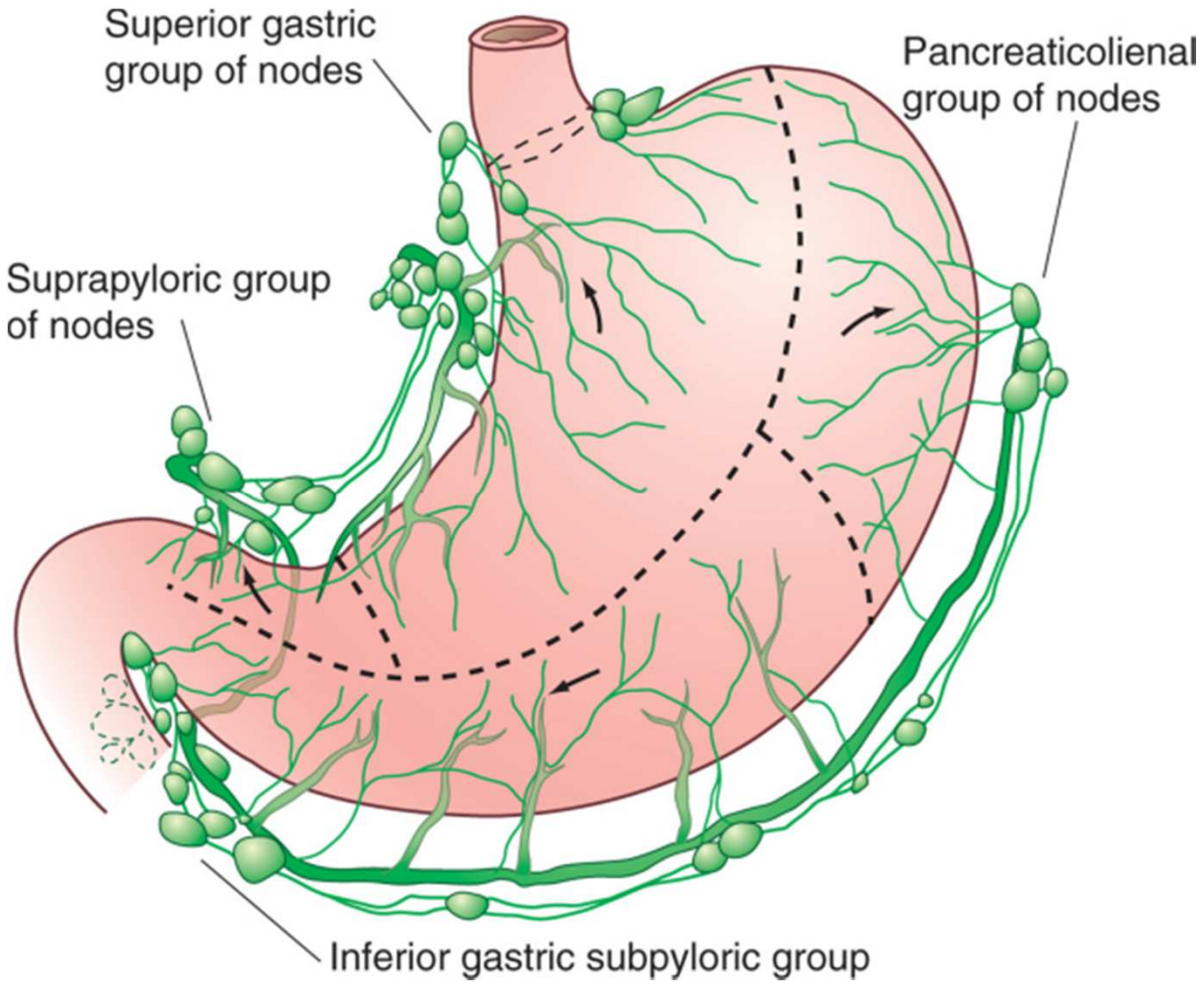




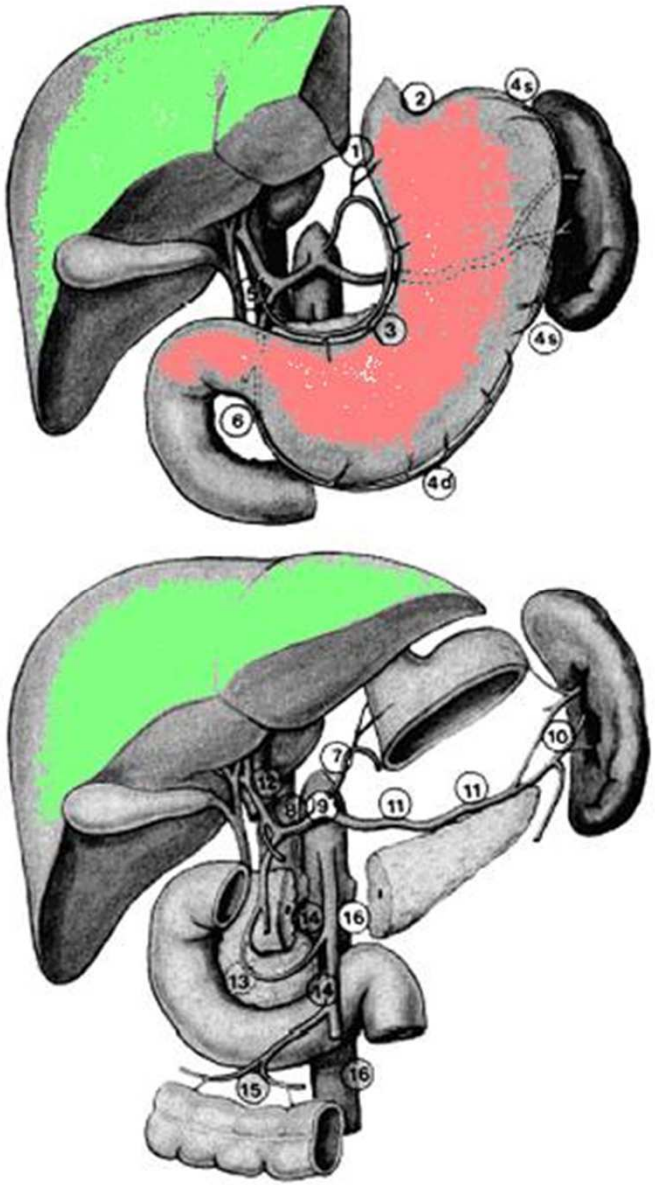
Layers of the Stomach



Stomach and Regional Lymph Nodes



Stomach and Regional Lymph Nodes



Gastric cancer lymph node stations. Lymph node stations surrounding the stomach: 1, right cardial nodes; 2, left cardial nodes; 3, nodes along the lesser curvature; 4, nodes along the greater curvature; 5, suprapyloric nodes; 6, infrapyloric nodes; 7, nodes along the left gastric artery; 8, nodes along the common hepatic artery; 9, nodes around the celiac axis; 10, nodes at the splenic hilus; 11, nodes along the splenic artery; 12, nodes in the hepatoduodenal ligament; 13, nodes at the posterior aspect of the pancreas head; 14, nodes at the root of the mesentery; 15, nodes in the mesocolon of the transverse colon; 16, para-aortic nodes.

T (tumor) Stage

Primary Tumor (T)

TX Primary tumor cannot be assessed
T0 No evidence of primary tumor
Tis Carcinoma in situ: intraepithelial tumor without invasion of the lamina propria
T1 Tumor invades lamina propria, muscularis mucosae or submucosa
T1a Tumor invades lamina propria or muscularis mucosae
T1b Tumor invades submucosa
T2 Tumor invades muscularis propria*
T3 Tumor penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures**,***
T4 Tumor invades serosa (visceral peritoneum) or adjacent structures**,***
T4a Tumor invades serosa (visceral peritoneum)
T4b Tumor invades adjacent structures

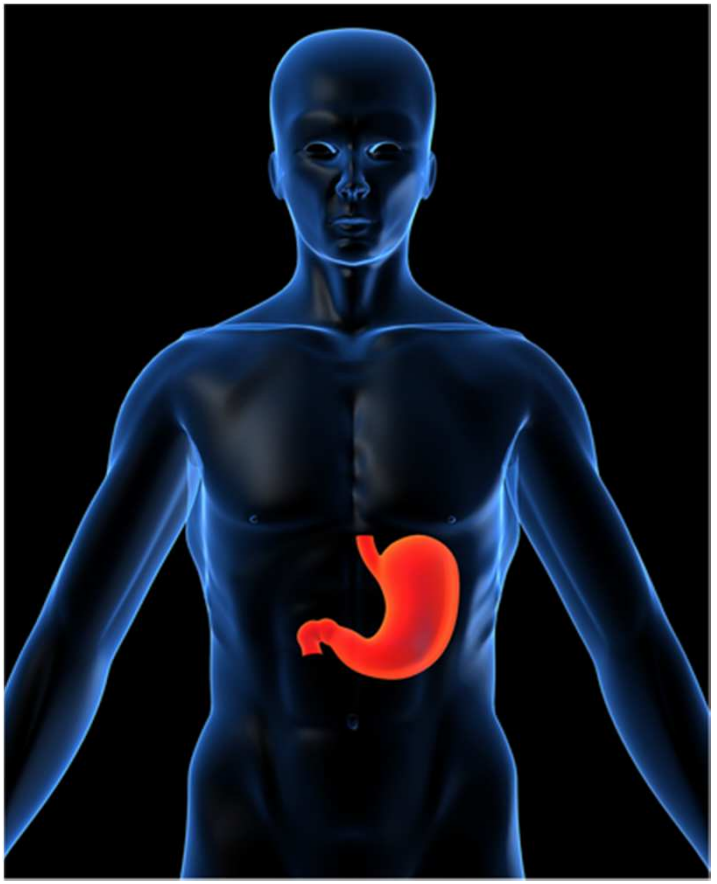
N (lymph node) Stage

Regional Lymph Nodes (N)

NX Regional lymph node(s) cannot be assessed
N0 No regional lymph node metastasis§
N1 Metastasis in 1 - 2 regional lymph nodes
N2 Metastasis in 3 - 6 regional lymph nodes
N3 Metastasis in seven or more regional lymph nodes
N3a Metastasis in 7 - 15 regional lymph nodes
N3b Metastasis in 16 or more regional lymph nodes

TNM Stage

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
	T1	N1	M0
Stage IIA	T3	N0	M0
	T2	N1	M0
	T1	N2	M0
Stage IIB	T4a	N0	M0
	T3	N1	M0
	T2	N2	M0
	T1	N3	M0
Stage IIIA	T4a	N1	M0
	T3	N2	M0
	T2	N3	M0
Stage IIIB	T4b	N0	M0
	T4b	N1	M0
	T4a	N2	M0
	T3	N3	M0
Stage IIIC	T4b	N2	M0
	T4b	N3	M0
	T4a	N3	M0
Stage IV	Any T	Any N	M1



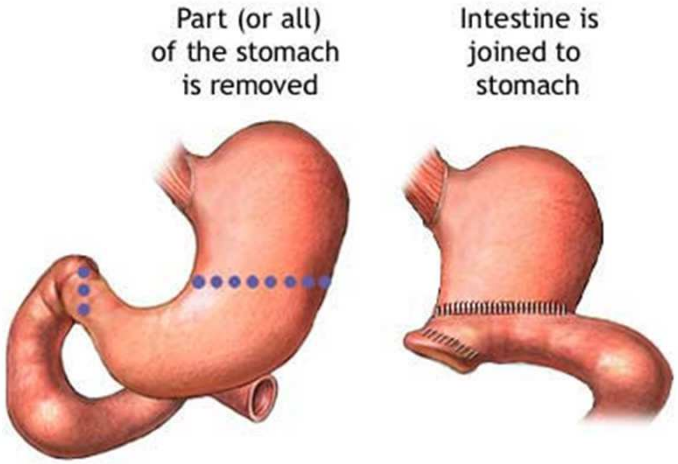
5 Year Survival by Stage

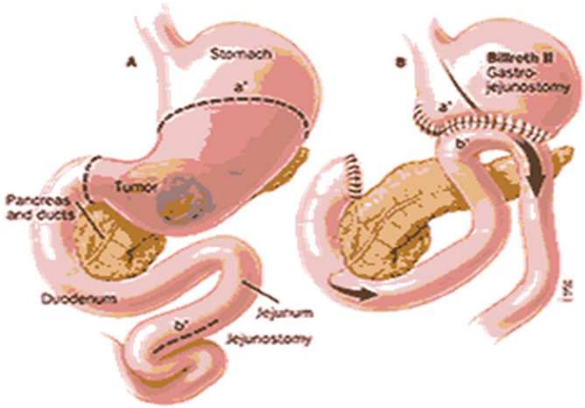
IA	70.8%
IB	57.4%
IIA	45.5%
IIB	32.8%
IIIA	19.8%
IIIB	14.0%
IIIC	9.2%
IV	4.0%

Primary Treatment of Gastric Cancer is Surgery

Resectable tumors

- Tis or T1 tumors limited to mucosa (T1a) may be candidates for endoscopic mucosal resection (in experienced centers)
- T1b-T3 : Adequate gastric resection to achieve negative microscopic margins (typically ≥ 4 cm from gross tumor).
  - Distal gastrectomy
  - Subtotal gastrectomy
  - Total gastrectomy
- T4 tumors require en bloc resection of involved structures

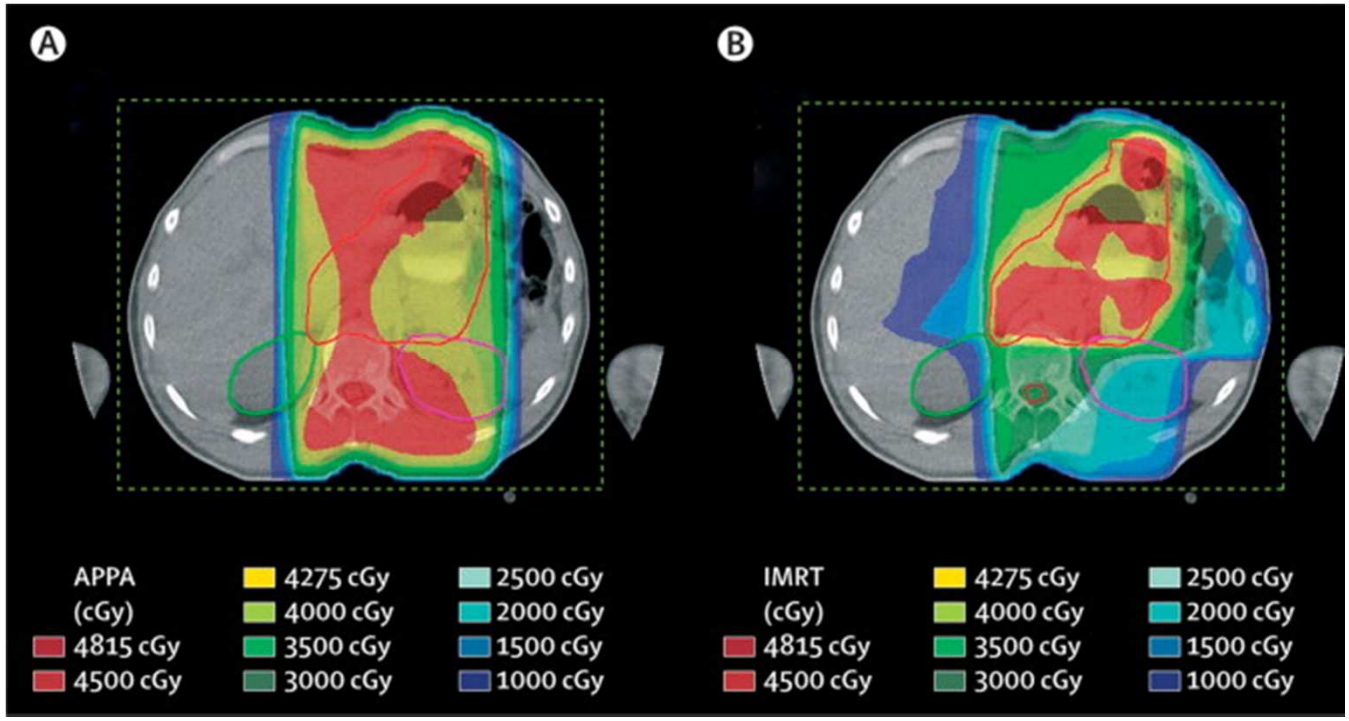




Operable gastric cancer- Treatment options

- NACT → Surgery → Adjuvant chemo
- Surgery → adjuvant Chemo-RT

Role for radiation in the treatment of gastric cancer



Conventional radiation

IMRT radiation

High risk of a local relapse after surgery

Patterns of failure after "curative" resection of gastric cancer

Pattern of failure	Incidence in total patient group (%)		
	Clinical (3)	Reoperation (2)*	Autopsy 4, 5, 33, 34, 35
Locoregional	38	67	80–93
Peritoneal seeding	23	41	30–50
Localized		19	
Diffuse		22	
Distant metastases	52	22	49

Site of a local relapse after surgery

Pattern of locoregional failure after resection of gastric cancer

Failure area	Incidence (%)		
	Clinical*	Reoperation†	Autopsy‡
Gastric bed	21	54	52–68
Anastomosis or stumps	25	26	54–60
Abdominal or stab wound		5	
Lymph node(s)	8	42	52

Post Operative or PreOp Radiation for Gastric Cancer

Local relapse (PostOp Trial, British Stomach Cancer Group, Lancet. 1994 May 28;343(8909):1309-12)

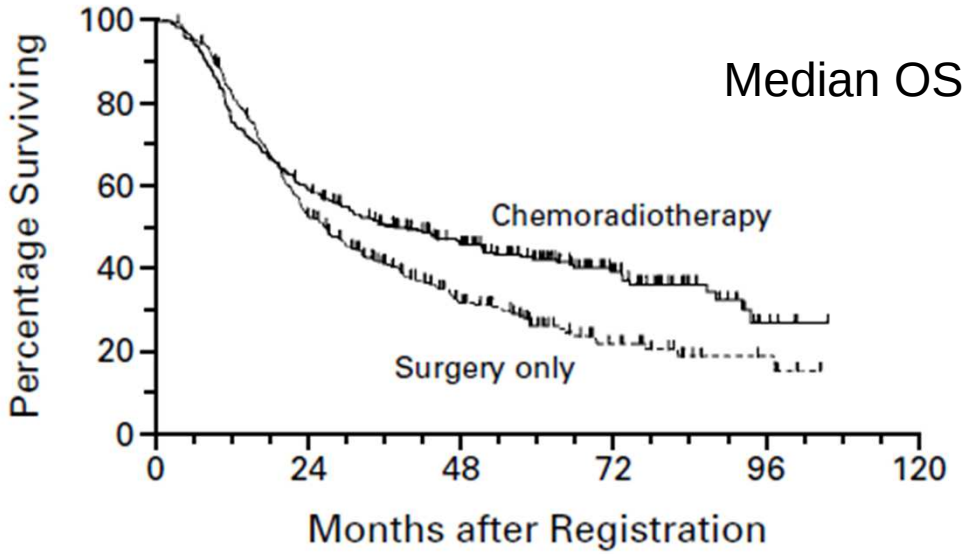
surgery alone (27%)
surgery plus radiation (10%)
surgery plus chemotherapy (19%)

Survival (PreOp Trial by Zhang Int J Radiat Oncol Biol Phys. 1998 Dec 1;42(5):929-34)

surgery alone (20%)
radiation then surgery (30%)

US-Intergroup trial design

- Phase 111 trial – 2 arms(T3,T4,N+)
  - Arm : surgery
  - Arm2: surgery +adjuvant chemo RT



Median OS : 36m vs. 26m

N Engl J Med, Vol. 345, No. 10 · September 6, 2001 · www.nejm.org ·

Chemo-radiation - toxicity

TABLE 3. MAJOR TOXIC EFFECTS OF CHEMORADIOTHERAPY.*

TYPE OF TOXIC EFFECT	NO. OF PATIENTS (%)
Hematologic	148 (54)
Gastrointestinal	89 (33)
Influenza-like	25 (9)
Infection	16 (6)
Neurologic	12 (4)
Cardiovascular	11 (4)
Pain	9 (3)
Metabolic	5 (2)
Hepatic	4 (1)
Lung-related	3 (1)
Death†	3 (1)

*Major toxic effects were defined as those of grade 3 or higher. Data are for the 273 patients who received chemoradiotherapy.

†One patient died from a cardiac event, one from sepsis complicating myelosuppression, and one from pulmonary fibrosis.

N Engl J Med, Vol. 345, No. 10 · September 6, 2001 · www.nejm.org ·

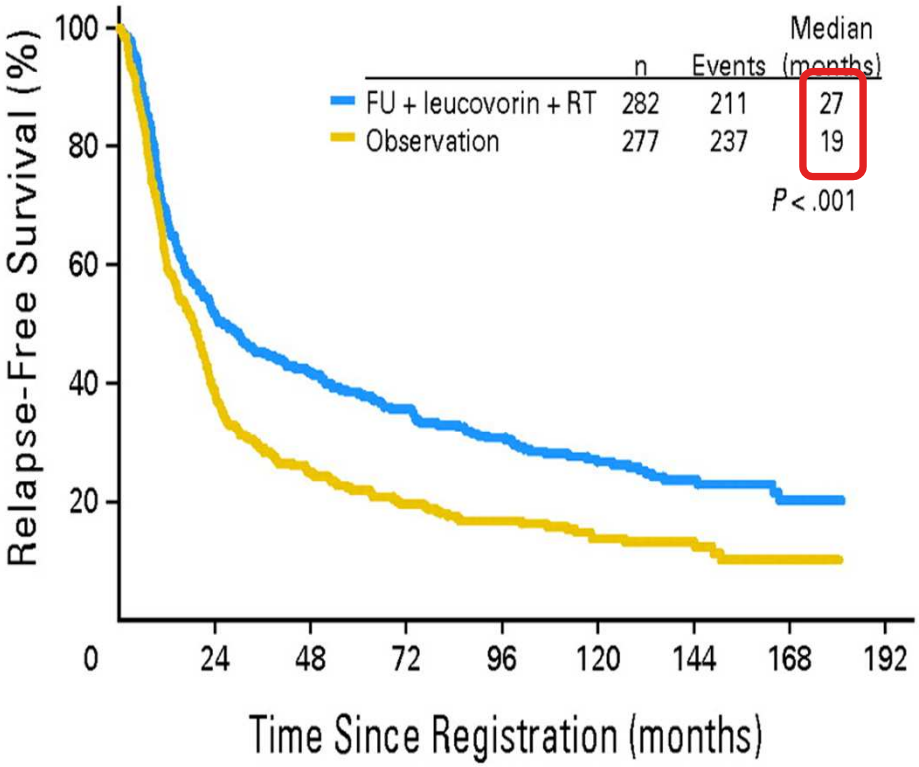
VOLUME 30 · NUMBER 19 · JULY 1 2012

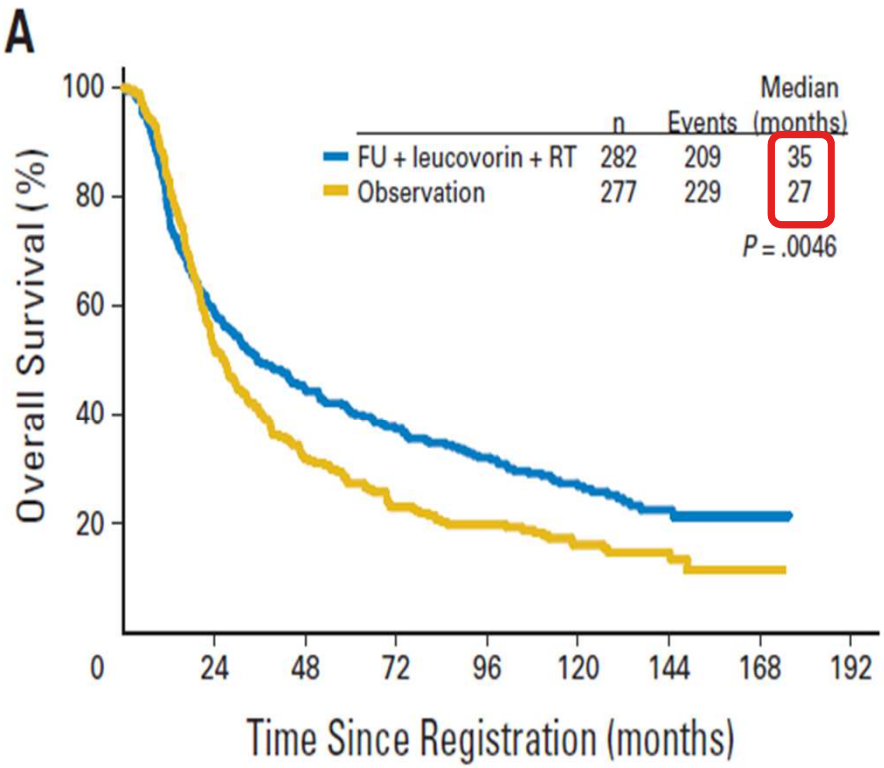
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Updated Analysis of SWOG-Directed Intergroup Study 0116: A Phase III Trial of Adjuvant Radiochemotherapy Versus Observation After Curative Gastric Cancer Resection

Stephen R. Smalley, Jacqueline K. Benedetti, Daniel G. Haller, Scott A. Hundahl, Norman C. Estes, Jaffer A. Ajani, Leonard L. Gunderson, Bryan Goldman, James A. Martenson, J. Milburn Jessup, Grant N. Stemmermann,† Charles D. Blanke, and John S. Macdonald





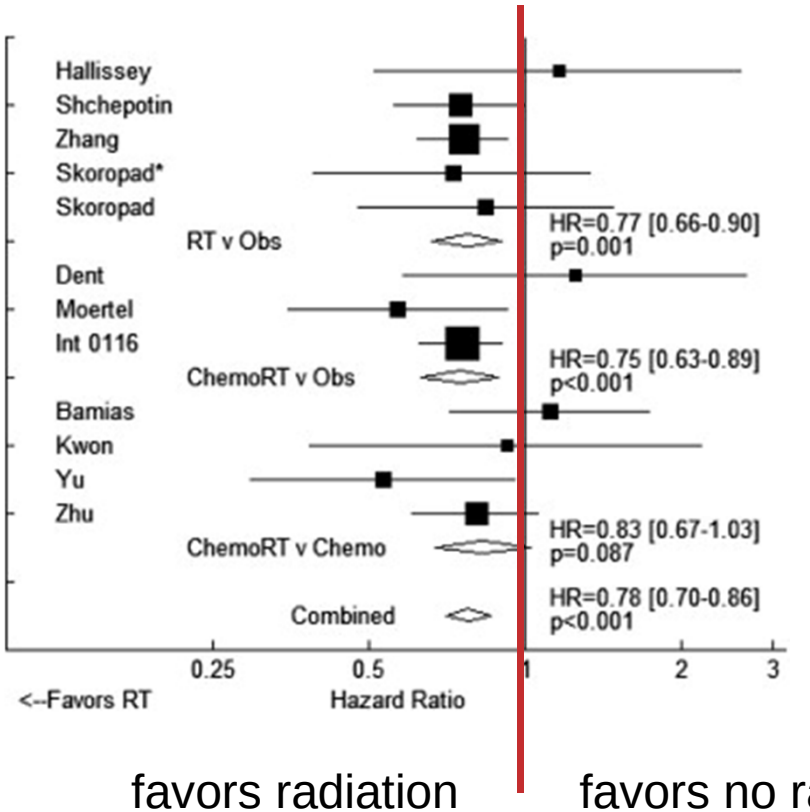
Survival after radiotherapy in gastric cancer: systematic review and meta-analysis.

Radiotherapy had a significant impact on 5-year survival. Using an intent to treat (ITT) and a Per Protocol (PP) analysis, the overall 5-year RR was 1.26 and 1.31 respectively. (**Survival improved by 26 to 31%)**

This meta-analysis showed a statistically significant 5-year survival benefit with the addition of radiotherapy in patients with resectable gastric cancer.

Radiother Oncol. 2009 Aug;92(2):176-83

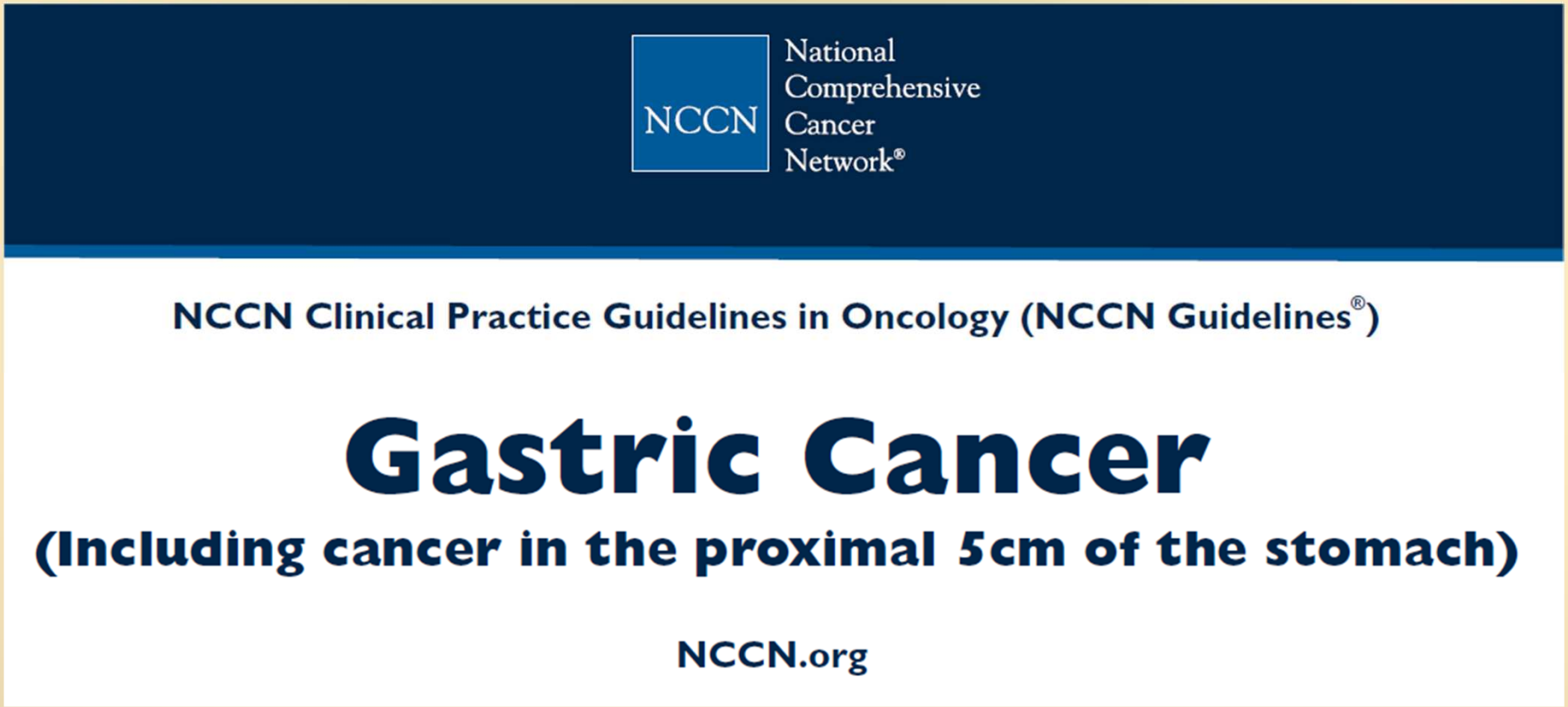
Impact of adjuvant radiation therapy (RT) on overall survival (OS) – meta-analysis



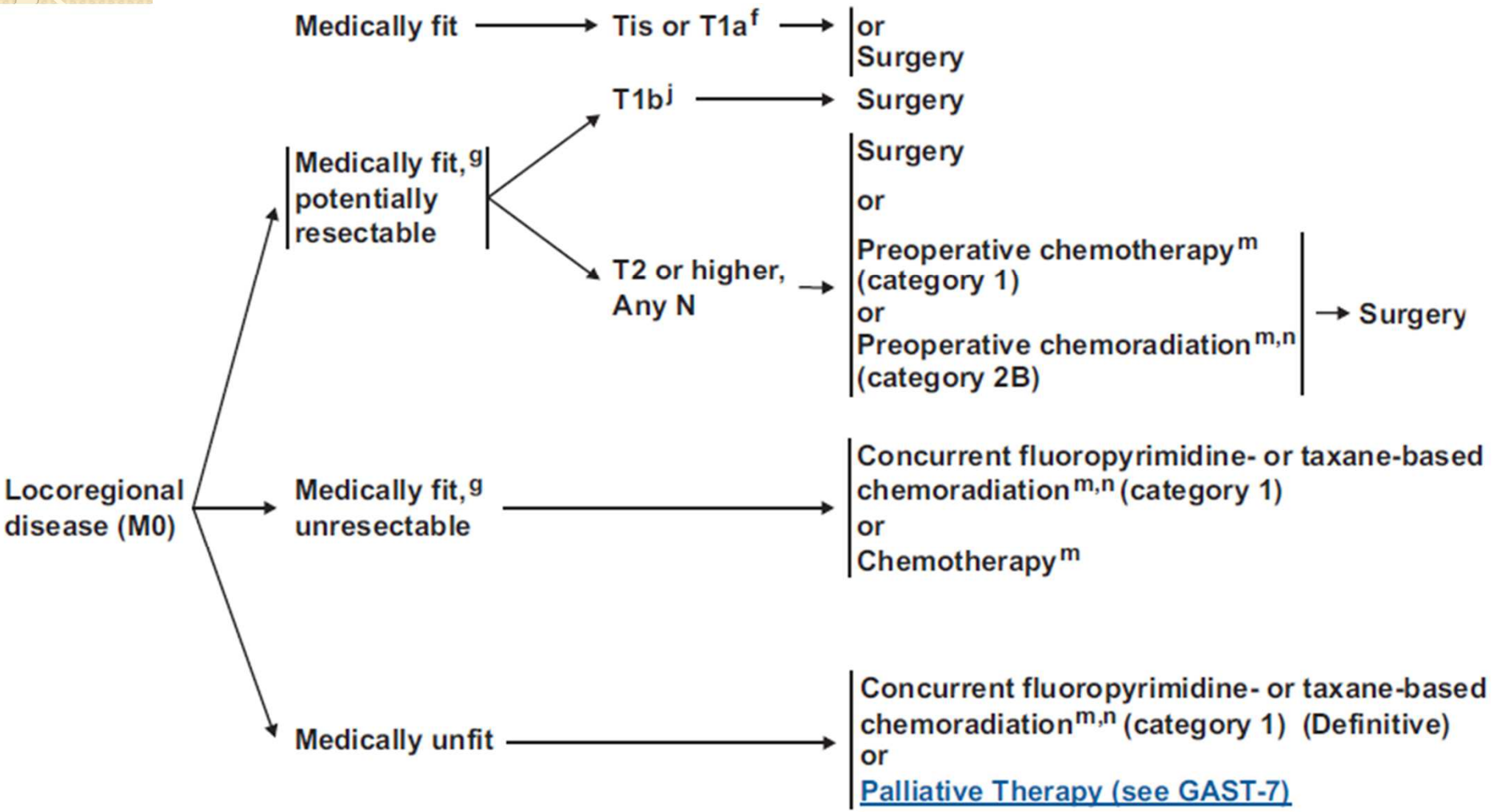
favors radiation favors no radiation

Hazard ratios (HR) for each trial are represented by squares, the size of each square represents the weight of that trial in the meta-analysis, and the horizontal line crossing the square represents the 95% confidence interval. Diamonds represent the estimated overall effect based on meta-analysis. *Included intraoperative radiation therapy.

NCCN.org


NCCN
National
Comprehensive
Cancer
Network®
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)
Gastric Cancer
(Including cancer in the proximal 5cm of the stomach)
NCCN.org

Surgery or PreOp Chemo or Chemo-RT then Surgery



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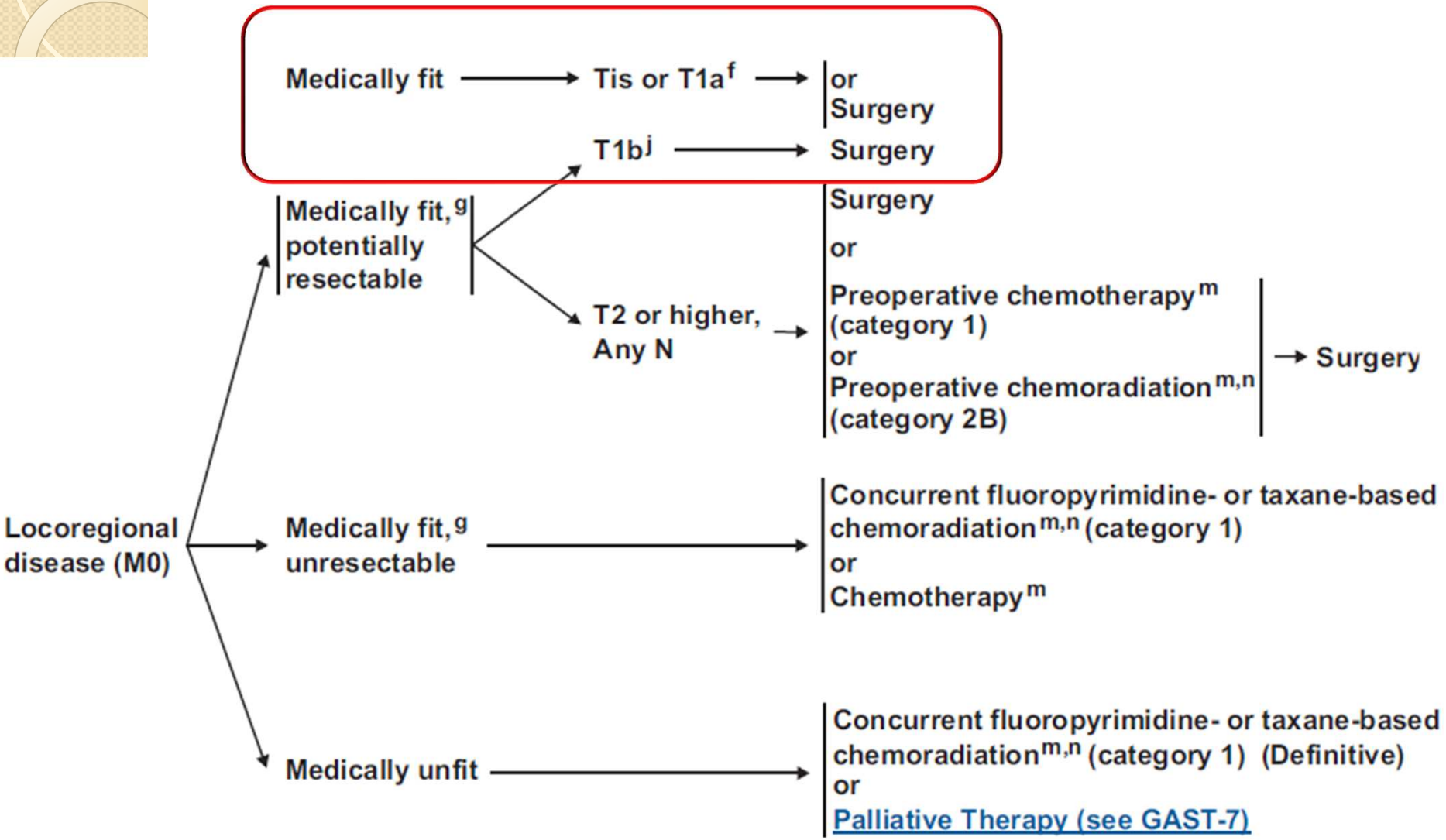
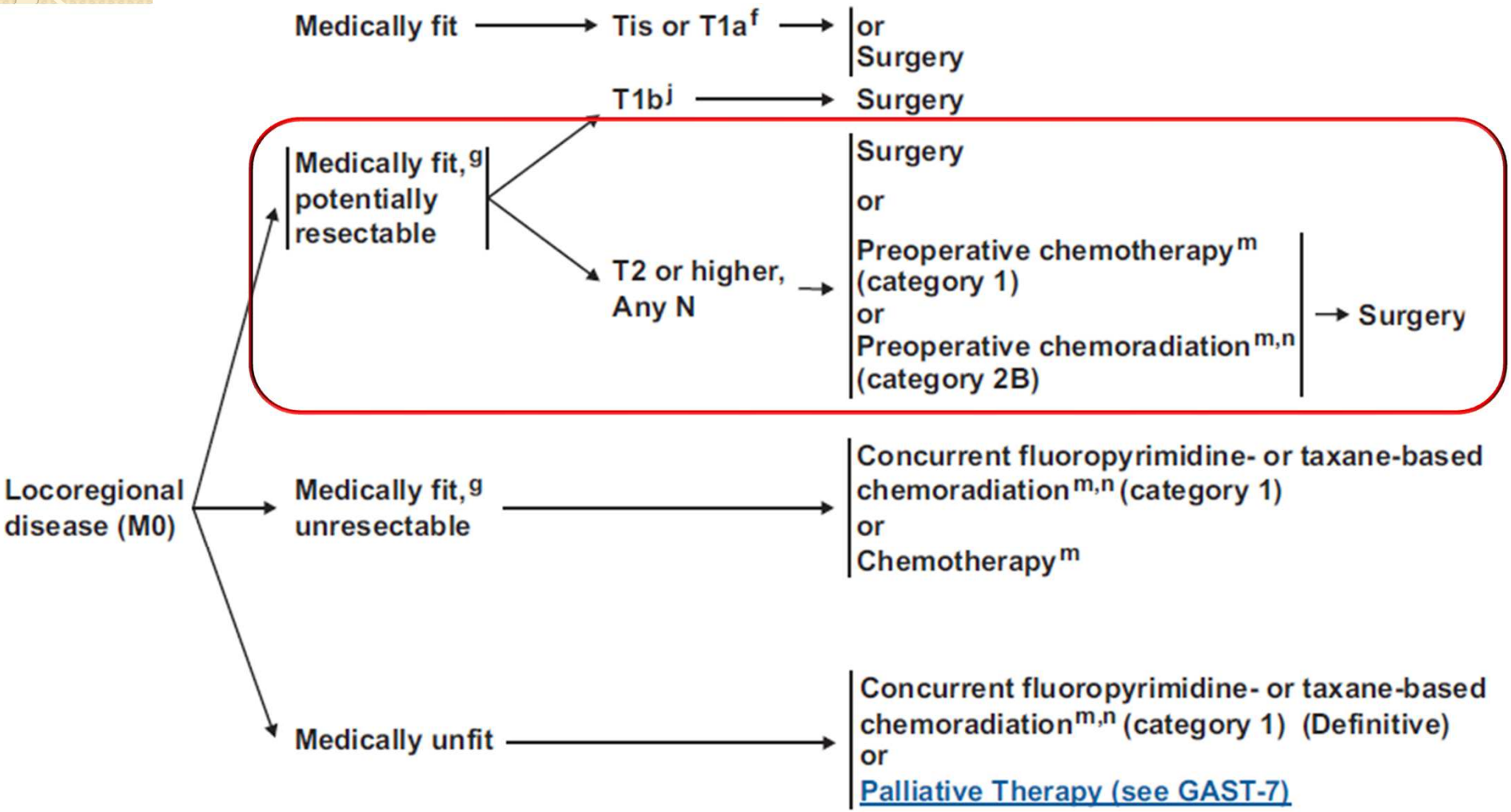
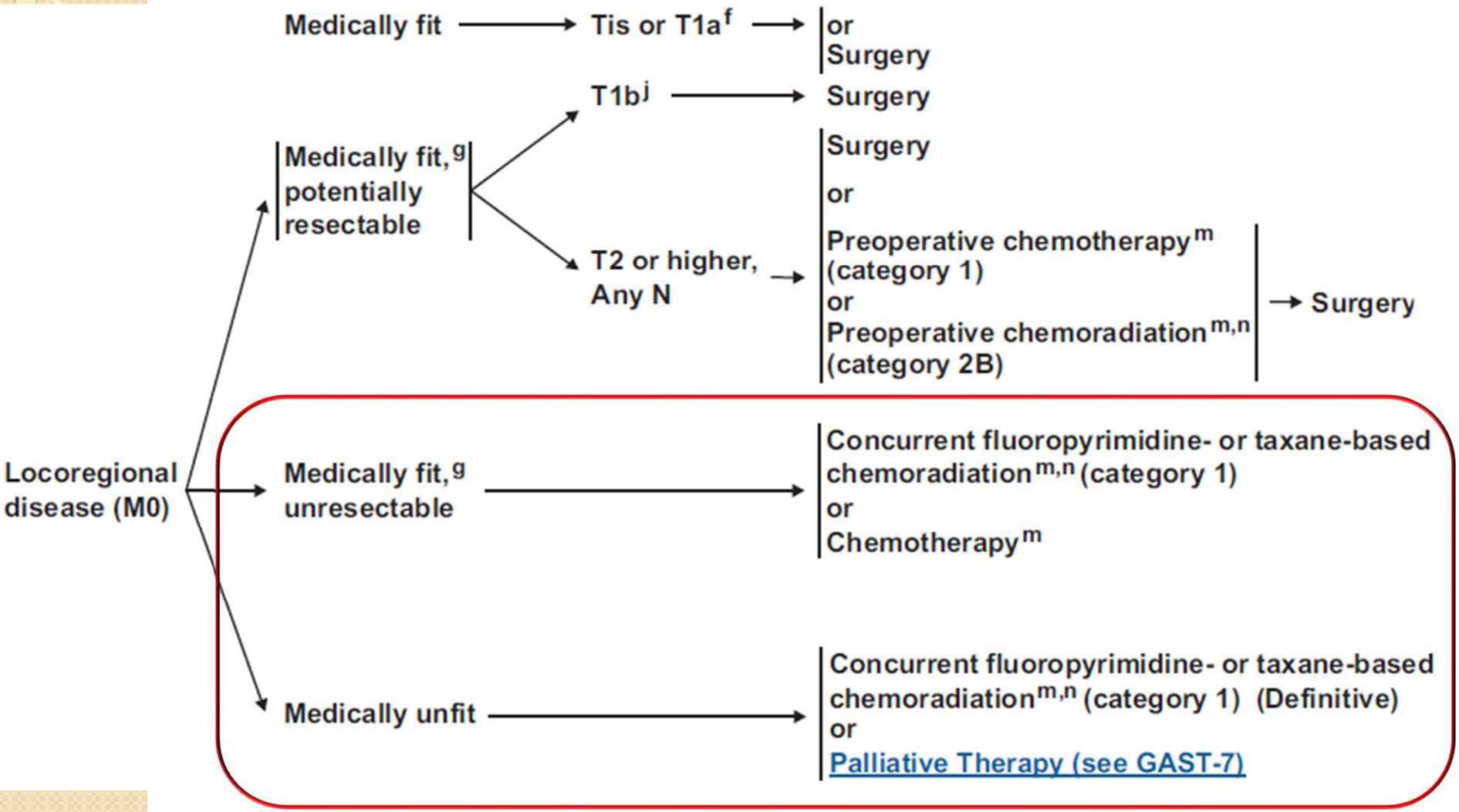


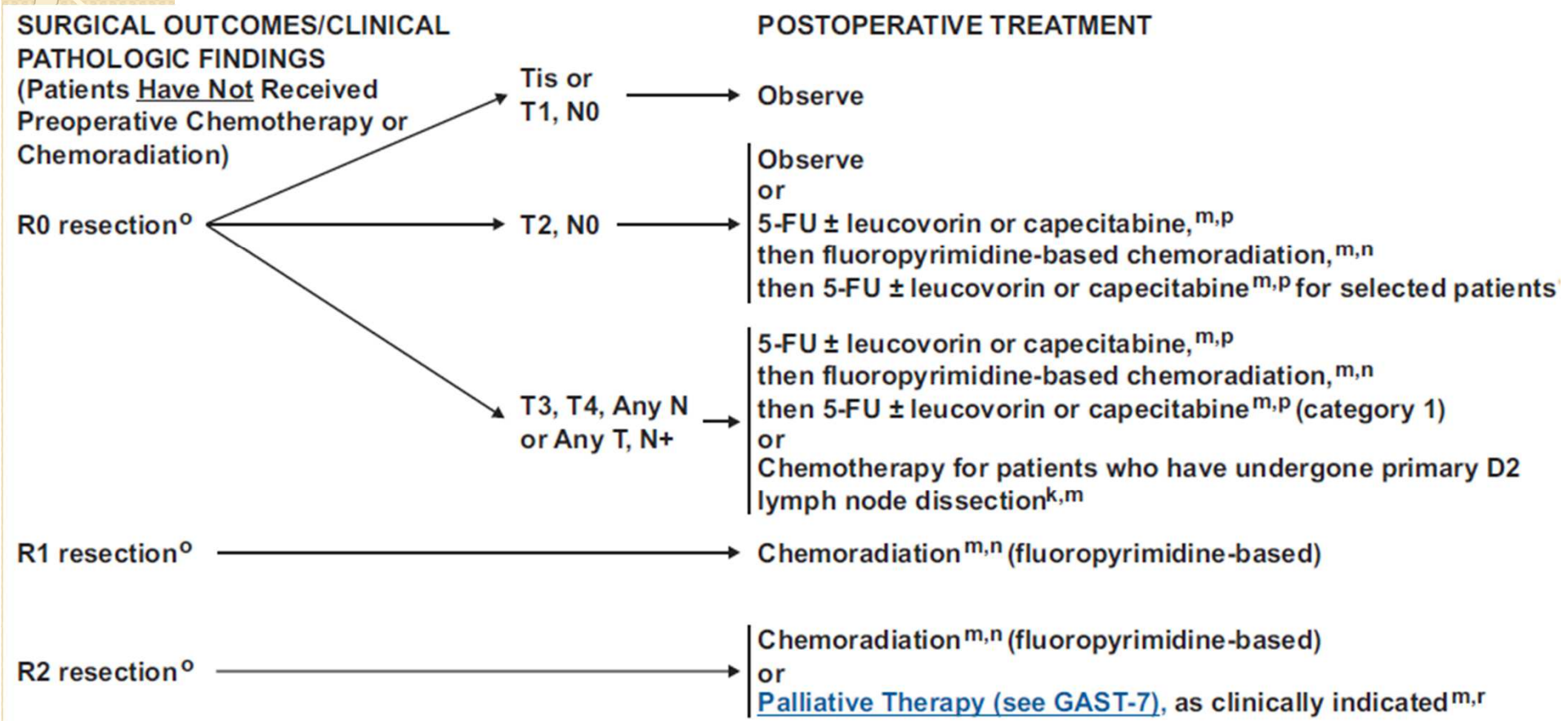
Surgery or PreOp Chemo or Chemo-RT then Surgery



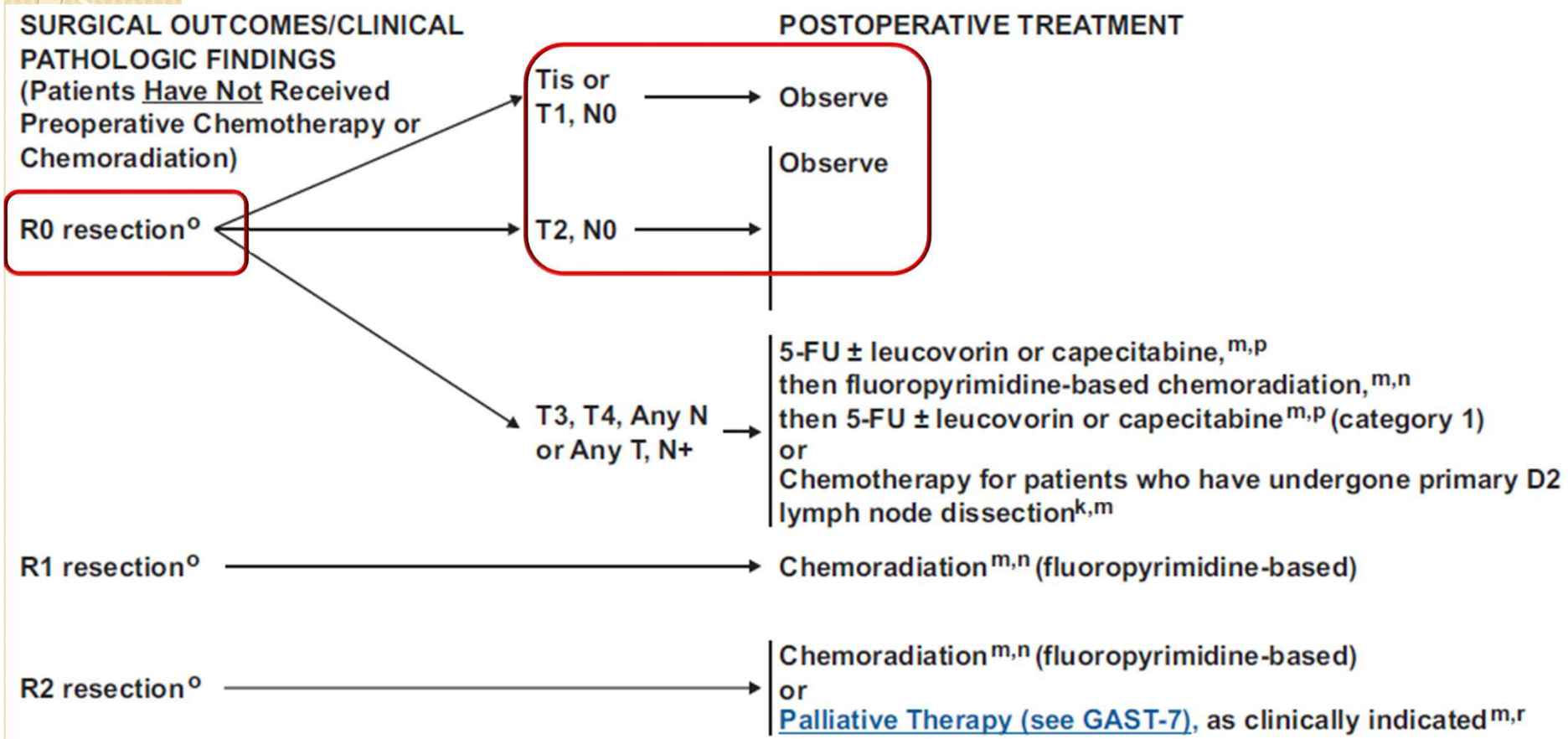
Surgery or PreOp Chemo or Chemo-RT then Surgery



Surgery or PostOp Chemo or Chemo-RT then Surgery

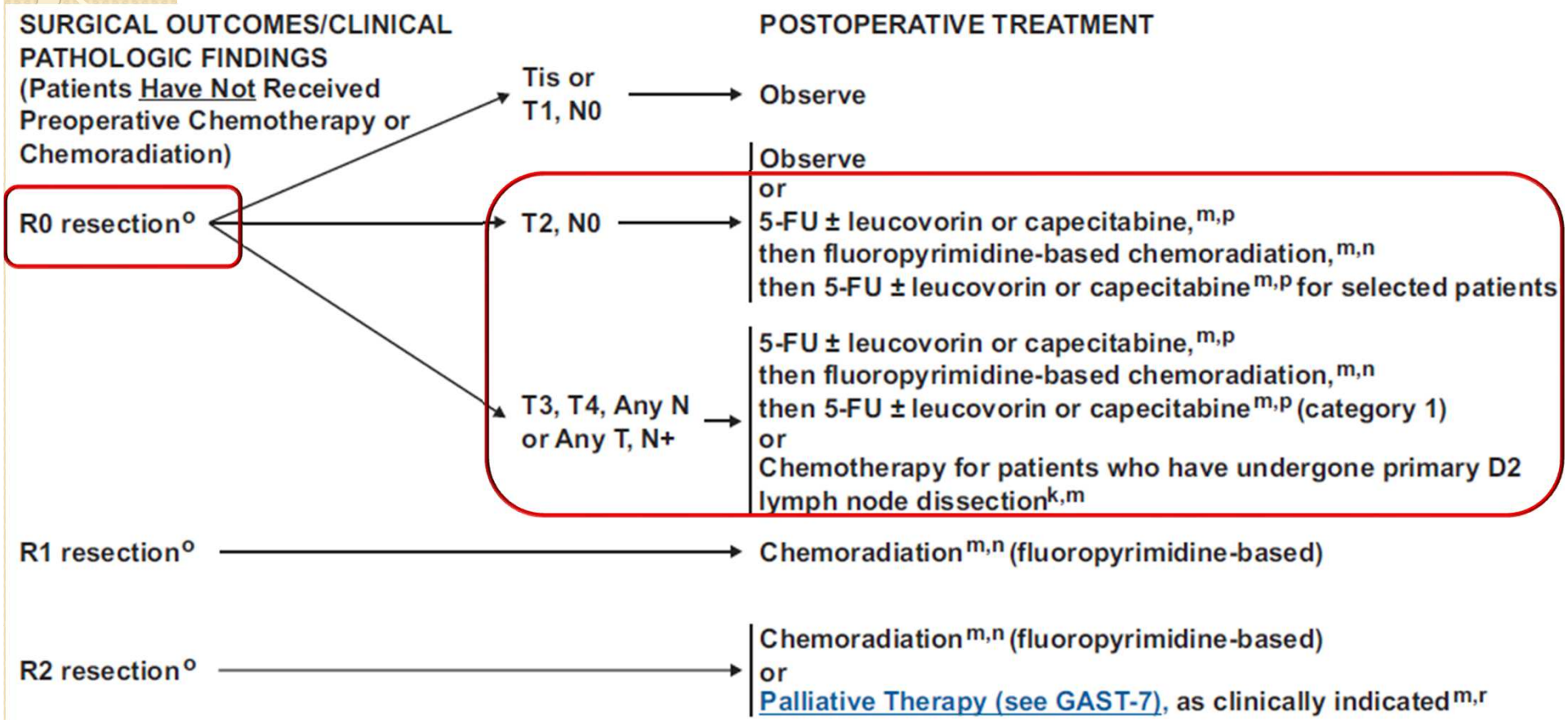


Surgery or PostOp Chemo or Chemo-RT then Surgery



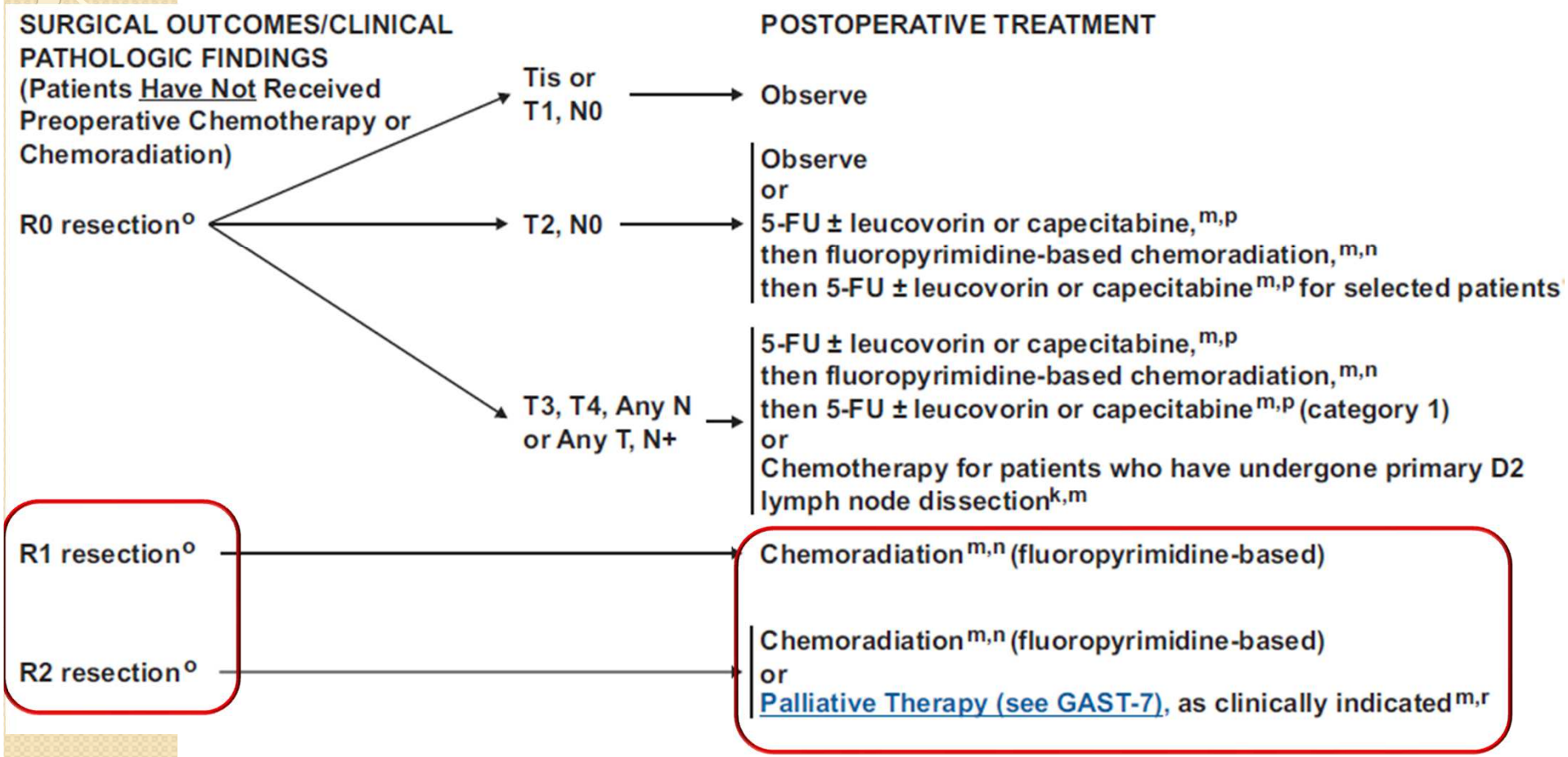
R0 = complete resection with negative margins

Surgery or PostOp Chemo or Chemo-RT then Surgery

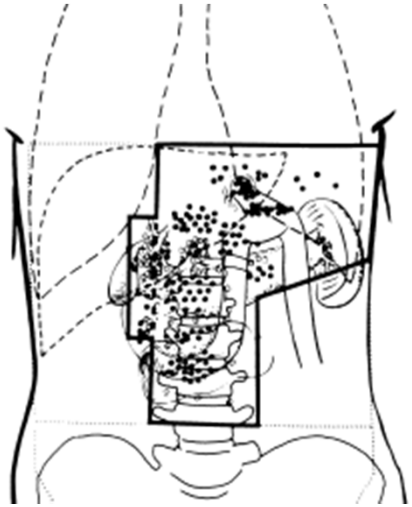


High Risk Features: poor diff or high grade, lymphovascular or perineural invasion or age <50y

Surgery or PostOp Chemo or Chemo-RT then Surgery

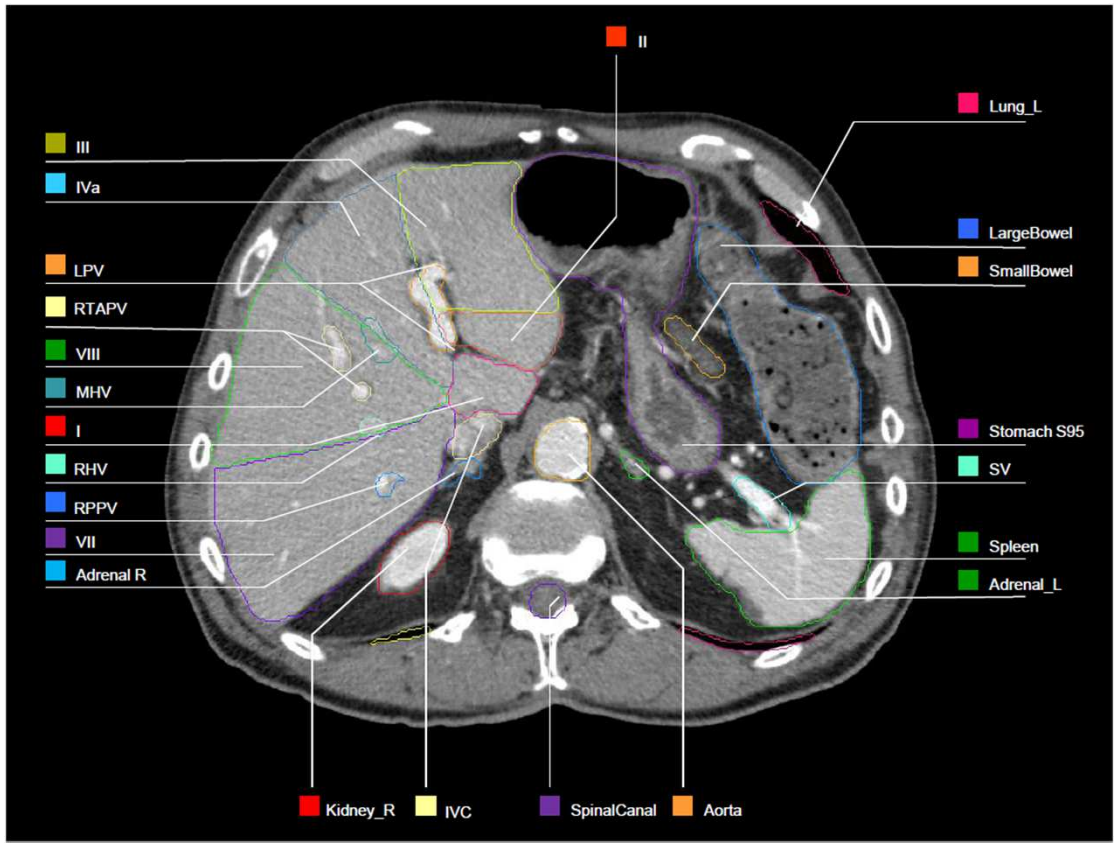


R1 = resection with + microscopic margins
R2 = resection with macroscopic (visible) cancer left behind



Radiation Technique for Gastric Cancer

RTOG®
RADIATION THERAPY ONCOLOGY GROUP



Contouring Atlases

- Anorectal
- Brachial Plexus Contouring Atlas
- Breast Cancer Atlas
- Female RTOG Normal Pelvis Atlas
- GYN
- H & N Atlases
- Hippocampal Sparing
- Male RTOG Normal Pelvis Atlas
- Pancreas Atlas
- Prostate Pelvic Lymph Nodes
- Prostate Post-Op
- RTOG Extremity Soft Tissue Sarcoma Atlas
- Lung Atlas
- Upper Abdominal Normal Organ Contouring Consensus

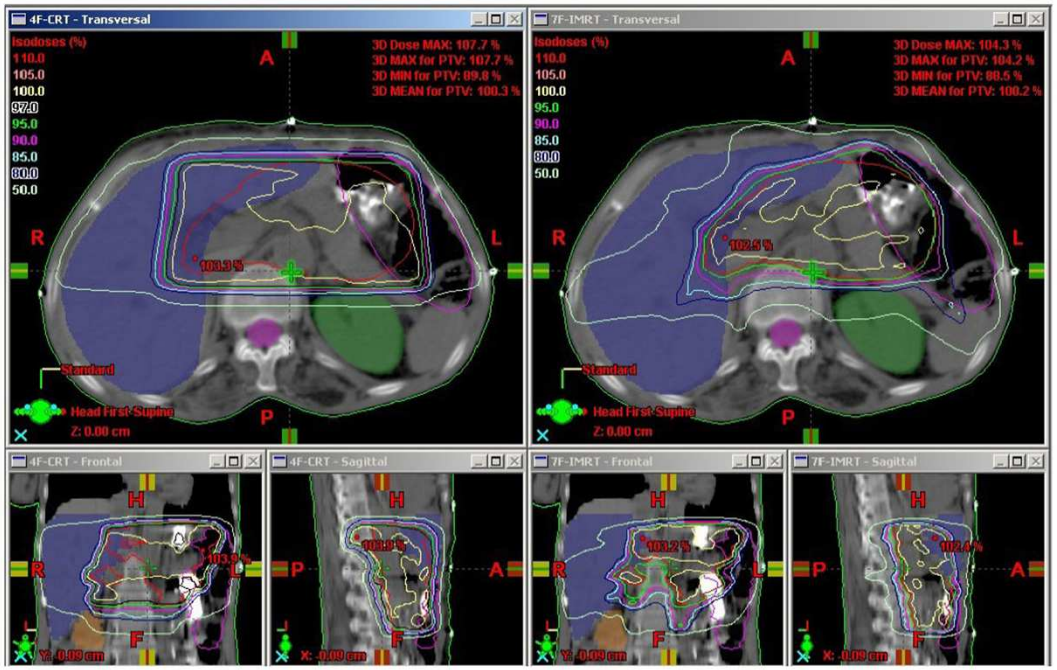
Radiation Guidelines

Dose

- 45-50.4 Gy (1.8 Gy/day)

Blocking

- Custom blocking is necessary to reduce unnecessary dose to normal structures including liver (60% of liver < 30 Gy), kidneys (at least 2/3 of one kidney < 20 Gy), spinal cord (< 45 Gy), heart (1/3 of heart < 50 Gy, effort should be made to keep the left ventricle doses to a minimum) and lungs.[a]



Clinical benefit of palliative radiation therapy in advanced gastric cancer.

Department of Radiation Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas 77030, USA.

The rates of control for bleeding, (70%) dysphagia/obstruction (81%) and pain (86%)

These symptoms were controlled without additional interventions for a median of 70%, 81%, and 49% of the patient's remaining life, respectively.

Patients receiving CRT had a trend towards better median overall survival than those receiving RT alone (6.7 vs. 2.4 months,).

Lower radiation dose (<41 Gy predicted for poorer local control (6-month local control 70% vs. 100%,

Acta Oncol. 2008;47(3):421-7.

The role of palliative radiation therapy in symptomatic locally advanced gastric cancer.

Department of Radiation Oncology, The Cancer Institute, National University Hospital, Singapore.

The majority of patients received 30 Gy/10 fractions . Median survival was 145 days, actuarial 12-month survival 8%.

A total of 54.3% with bleeding responded (median duration of response of 140 days), 25% with obstruction responded (median duration of response of 102 days), and 25% with pain responded (median duration of response of 105 days)

Int J Radiat Oncol Biol Phys. 2007 Feb 1;67(2):385-8. Epub 2006 Nov 21

Conclusion

- Adjuvant Chemo-Radiation has improved outcome after surgery.
- The normal tissues need to be spared using modern techniques like 3D-CRT / IMRT / IGRT.
- Multidisciplinary approach to be adopted.
- Extent of resection and performance status – key to success.

Thank you