Surgery for Colorectal Tumors

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THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

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THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center

Disclosures

- Up To Date® (author)

Objectives

- Oncologic Principles
  - Surgical
  - Combined modality therapy and benchmark outcomes
- Tailoring local therapy
  - Minimal access surgery
  - Change surgery in context of multimodality therapy?

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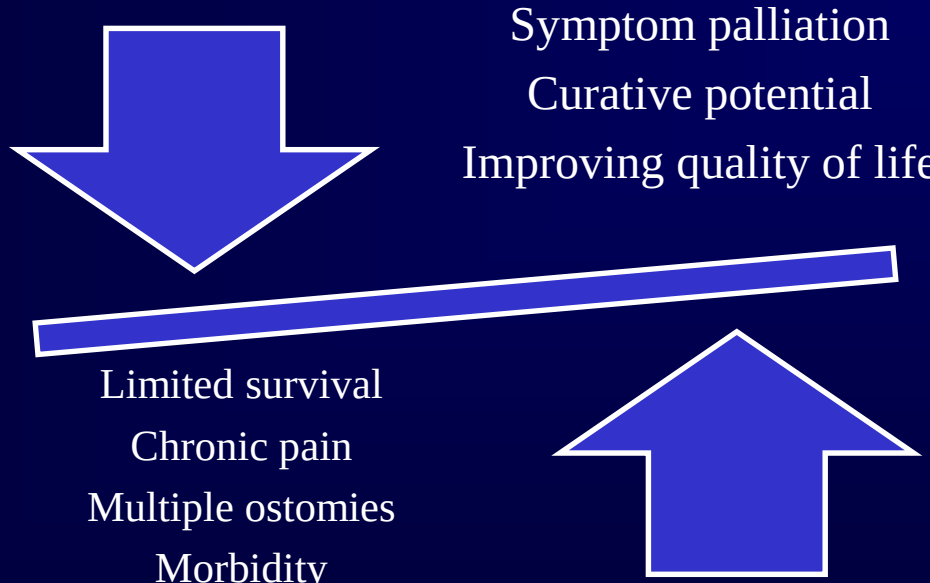
Colorectal Cancer
Treatment Principles

- Surgery as primary treatment for loco-regional disease
  - Remove tumor with adequate margins
  - Treatment of lymph nodes
  - En bloc resection of adjacent organs
    - Restoration of organ integrity if possible
      - – Sphincter preservation
      - – Bladder preservation

Extended Surgical Procedures in Cancer
Complex Problems



CAN resect vs. **SHOULD** resect

Surgical Principles Colon Cancer

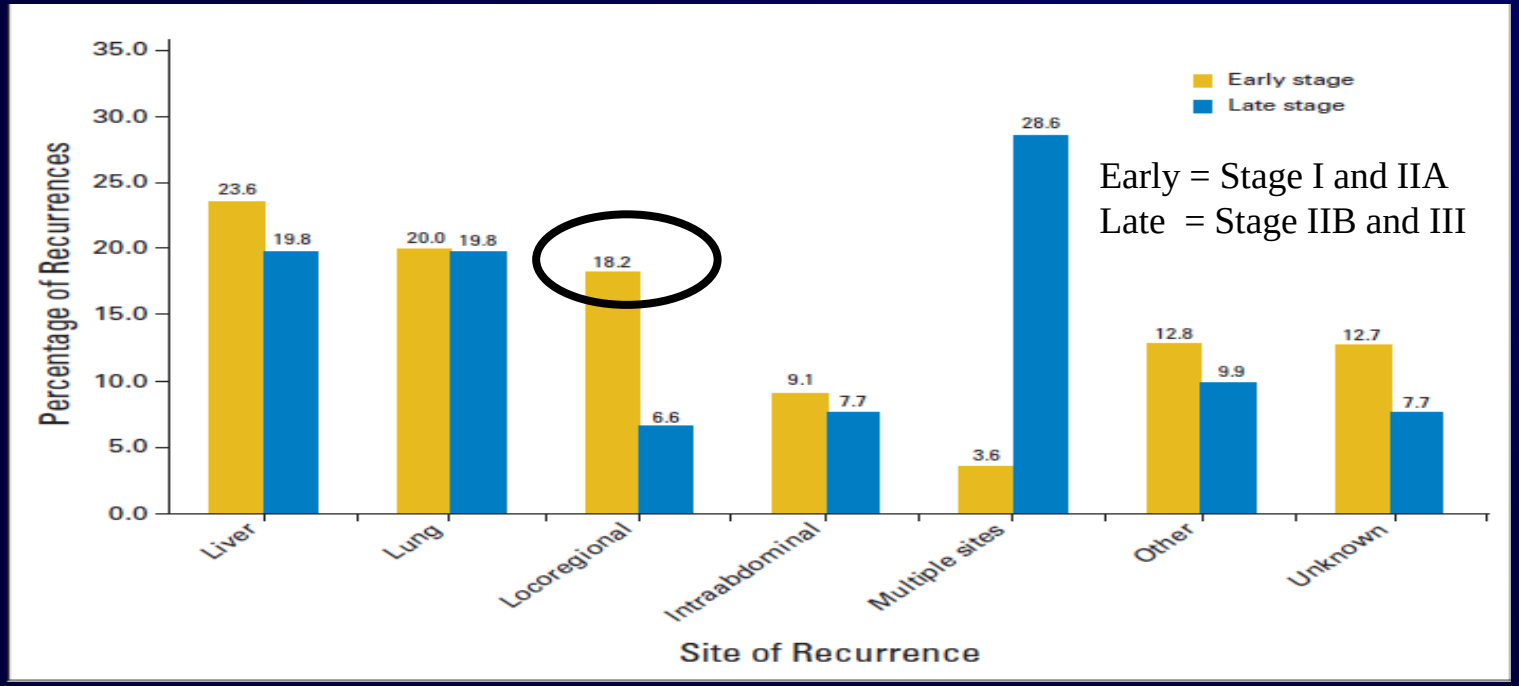
Extent and Integrity of Resection

- NIH Consensus 2001
  - Lymph node resection should extend to the level of the origin of the primary feeding vessel…be radical and en bloc.

- National Comprehensive Cancer Network (NCCN)
  - Patients considered to be N0 but who have <12 lymph nodes examined are suboptimally staged and should be considered in the high-risk group for adjuvant chemotherapy.

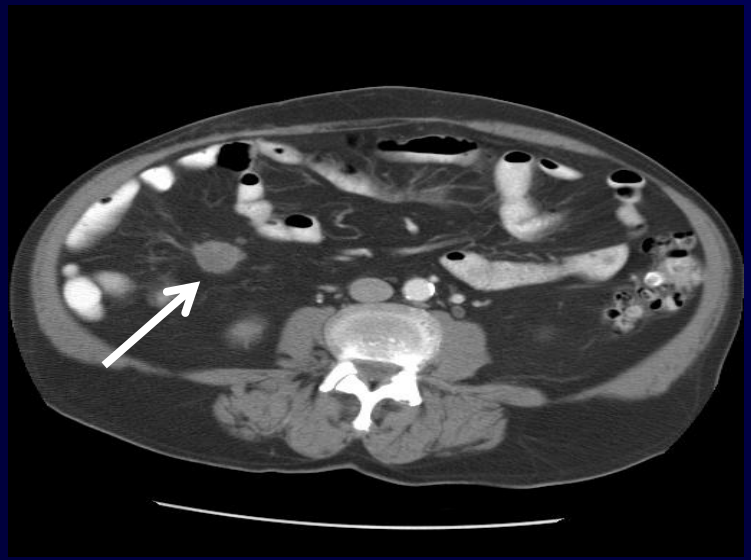
Nelson H, et al. J Natl Cancer Inst 2001; 93:583-596.
http://www.nccn.org/professionals/physician_gls/PDF/colon.pdf

Surgical Standards Colon Cancer Patterns of Recurrence COST Trial



Vassiliki L, et al J Clin Oncol 2009; 27:3671-3676.

Ileocolic LN Recurrence/Persistence



Complete Mesocolic Excision and Central Vascular Ligation

Old Concepts New Terminology

(Turnbull, Stearns and Schottenfeld, Bokey, Enker)

Standardized surgery for colonic cancer: complete mesocolic excision and central ligation – technical notes and outcome

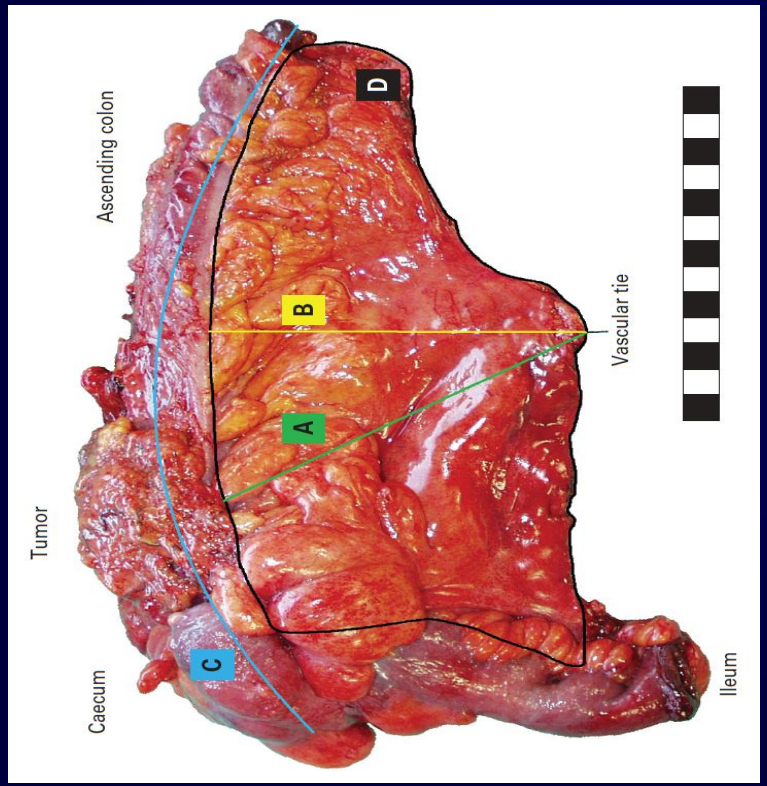
W. Hohenberger*, K. Weber*, K. Matzel*, T. Papadopoulos† and S. Merkel*

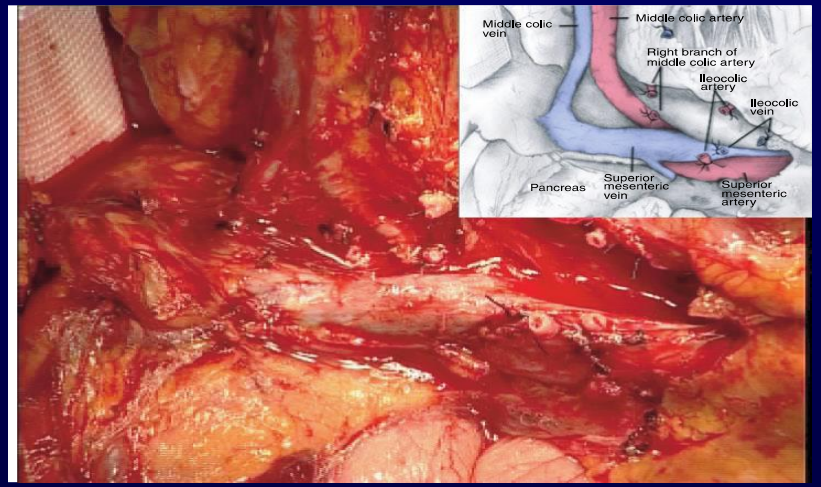
*Department of Surgery, University Hospital, Erlangen, Germany and †Department of Pathology, Vivantes Humboldt Hospital, Berlin, Germany

- Sharp dissection of the visceral plane from the retroperitoneal one aiming to avoid breach of the visceral fascia layer
- Origin of colonic arteries exposed and tied centrally at their origin ensuring maximum LN harvest

Hohenberger W, et al. Colorectal Dis 2008; 11; 354-365.

Complete Mesocolic Excision





West NP, et al. J Clin Oncol 2010; 28:272-278.
Hohenberger W, et al. Colorectal Dis 2008; 11: 354-365.

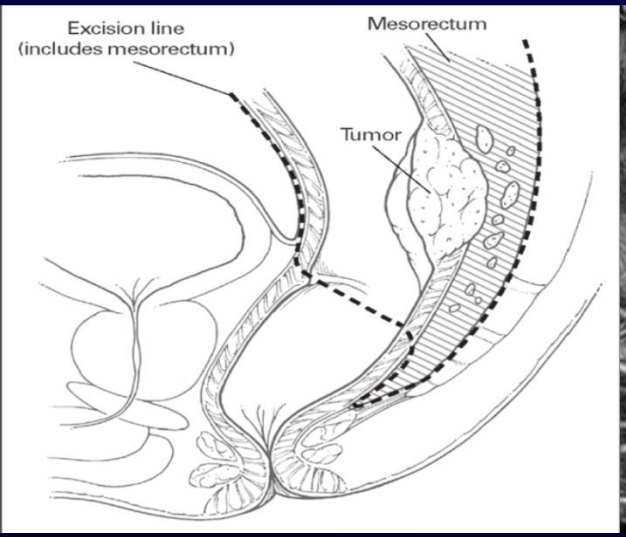
Rectal Cancer
Adjuvant and Neoadjuvant Chemoradiation
The Facts:

- **Good News =**
  - Local Recurrence < 10%
- **Bad News =**
  - Distant Metastases ≈ 25%

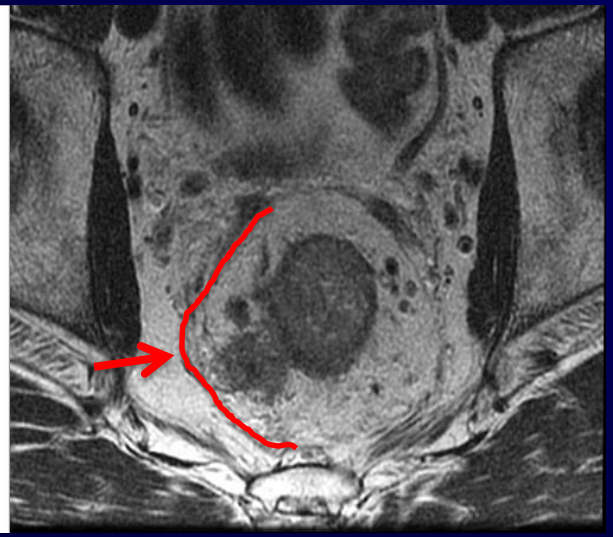
Do not make up for poor surgery

Optimal Local Control

Extent and Integrity of the Resection



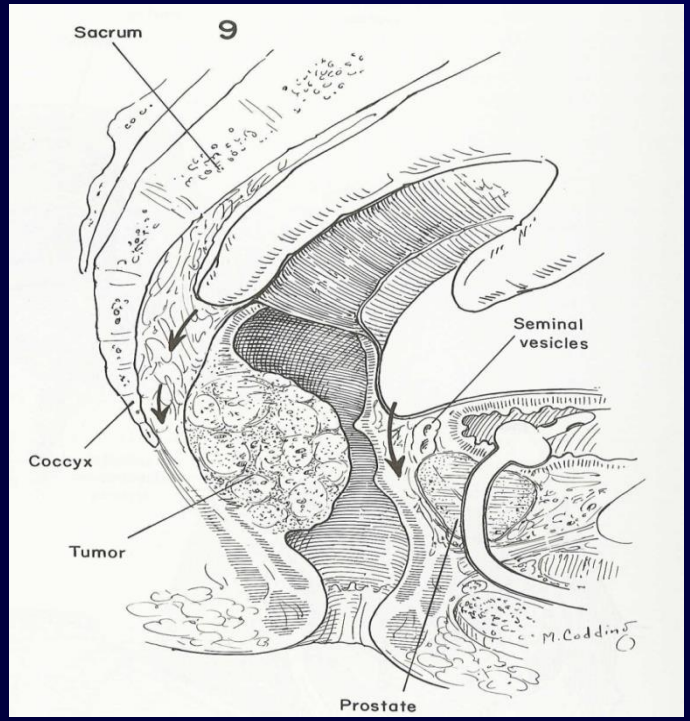
TME



Circumferential Resection Margin (CRM)

Regional Lymphadenectomy

Why does surgery for rectal cancer fail?

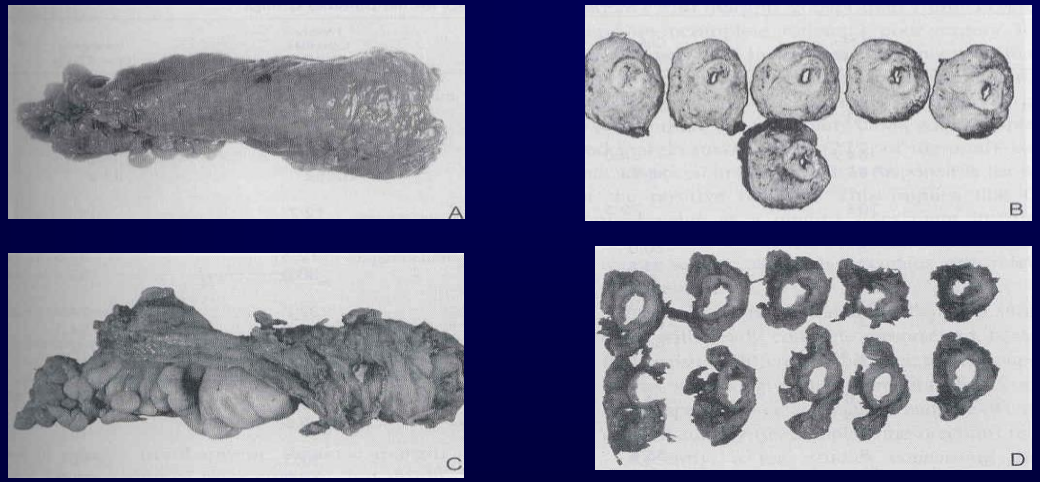


Technical Failure Results in Treatment Failure

Zollinger & Zollinger, Atlas of Surgical Operations 7th ed 1993

Rectal Cancer
Local Recurrence

- The main cause of local recurrence after rectal cancer surgery is incomplete removal of the lateral or circumferential tumor spread.

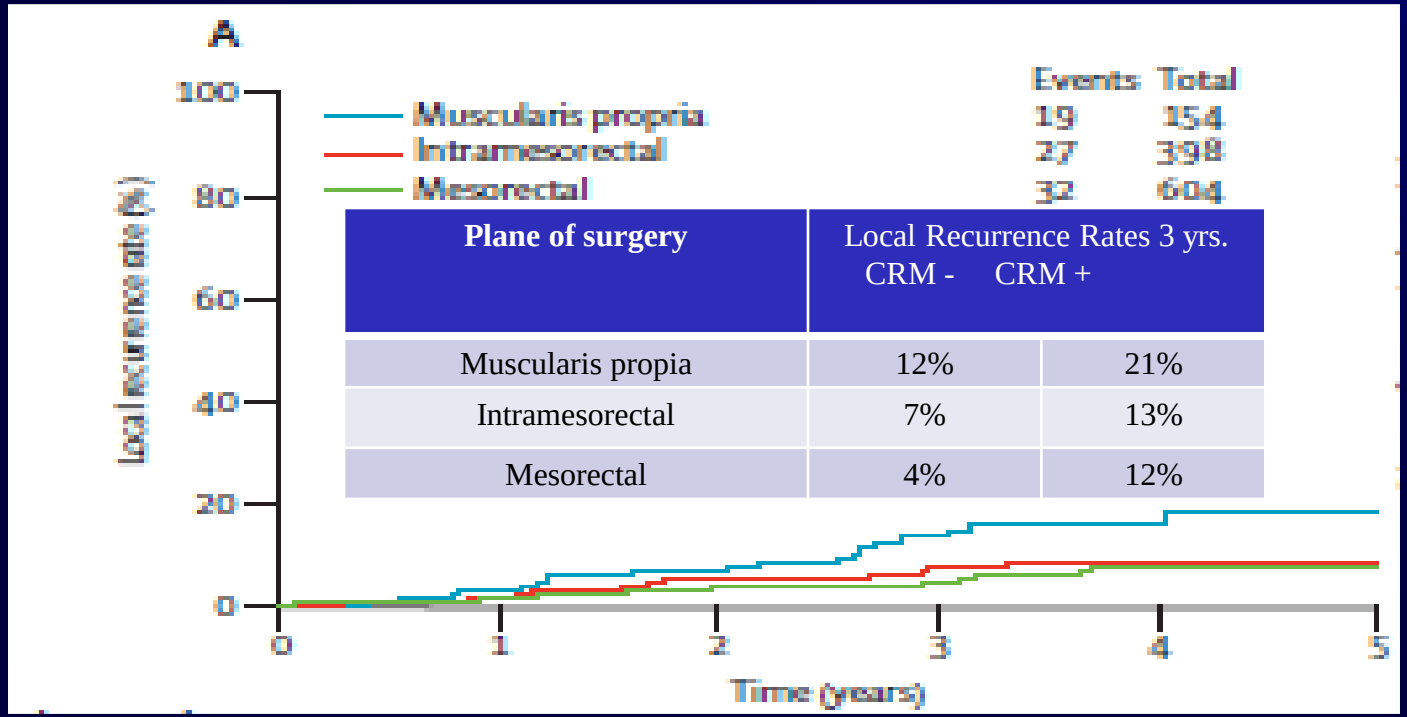


Photos from Nagtegaal ID, et al. J Clin Oncol 2002; 20:1729-1734.

Optimal Surgical Quality

MRC C07/NCIC CTG CO16

Routine XRT + TME vs. TME + selective CXRT involved CRM



Plane of surgery	Local Recurrence Rates 3 yrs. CRM -	CRM +
Muscularis propria	12%	21%
Intramesorectal	7%	13%
Mesorectal	4%	12%

Quirke P, et al. Lancet 2009; 373: 821-28.

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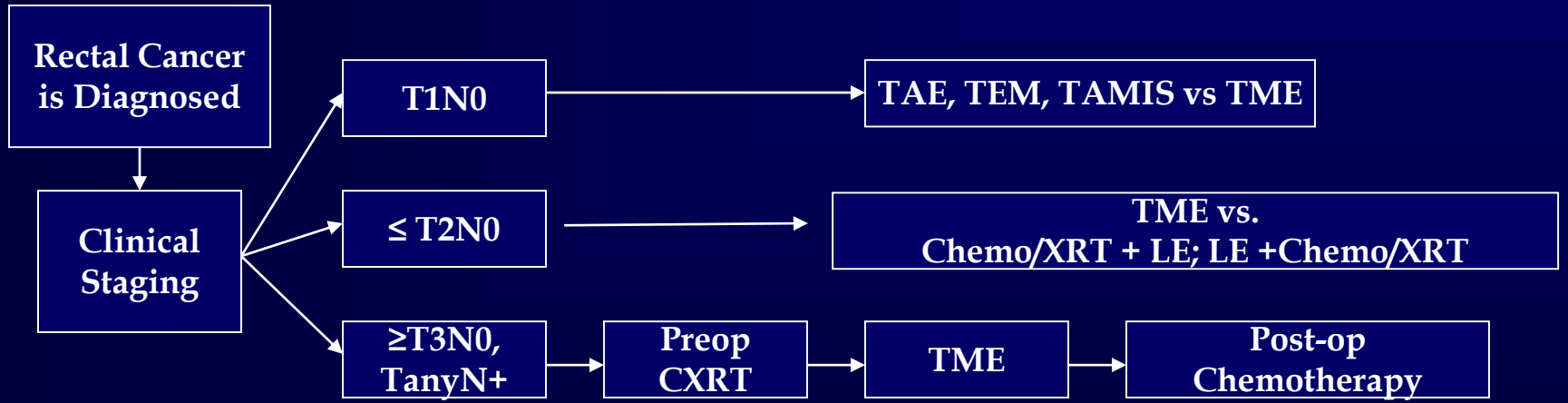
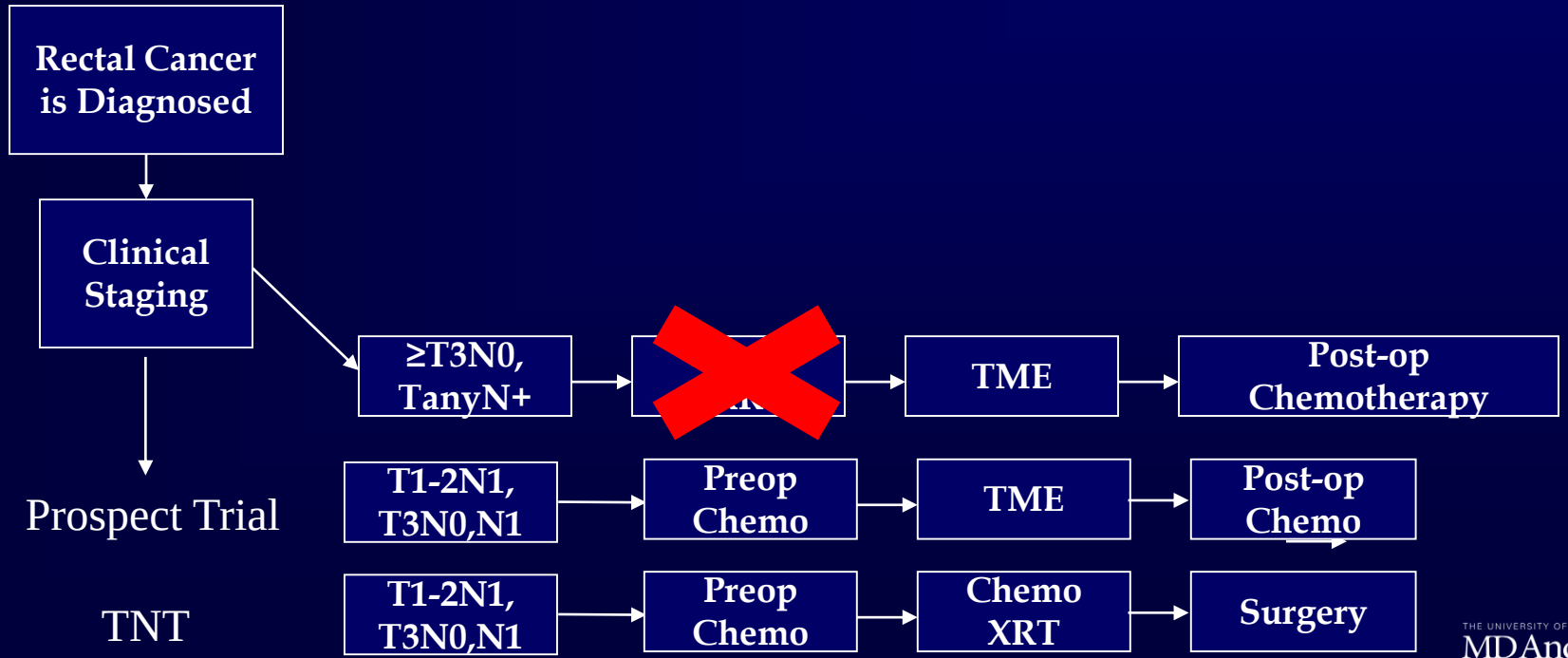
Rectal Cancer Treatment 2018



Rectal cancer treatment…the future in selected patients?



Neoadjuvant treatment response and outcomes MDACC

n=725 f/u median 65 mos	Complete response (n=131)	Intermediate response (n=210)	Poor response (n=384)
Local recurrence only	0	3 (1.4)	17 (4.4)
Systemic recurrence only	8 (6.2)	19(9)	87(22.7)
Local + systemic	1 (0.8)	2 (1)	16 (4.2)

Park IJ, et al. J Clin Oncol 2012; 30:1770-1776.

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Systemic recurrence only	8 (6.2)	19(9)	87(22.7)
Local + systemic	1 (0.8)	2 (1)	16 (4.2)
Survival			
5-yr DFS	90.5%	78.7%	58.5%
5-yr OS	93.4%	87%	77.3%

Park IJ, et al. J Clin Oncol 2012; 30:1770-1776.

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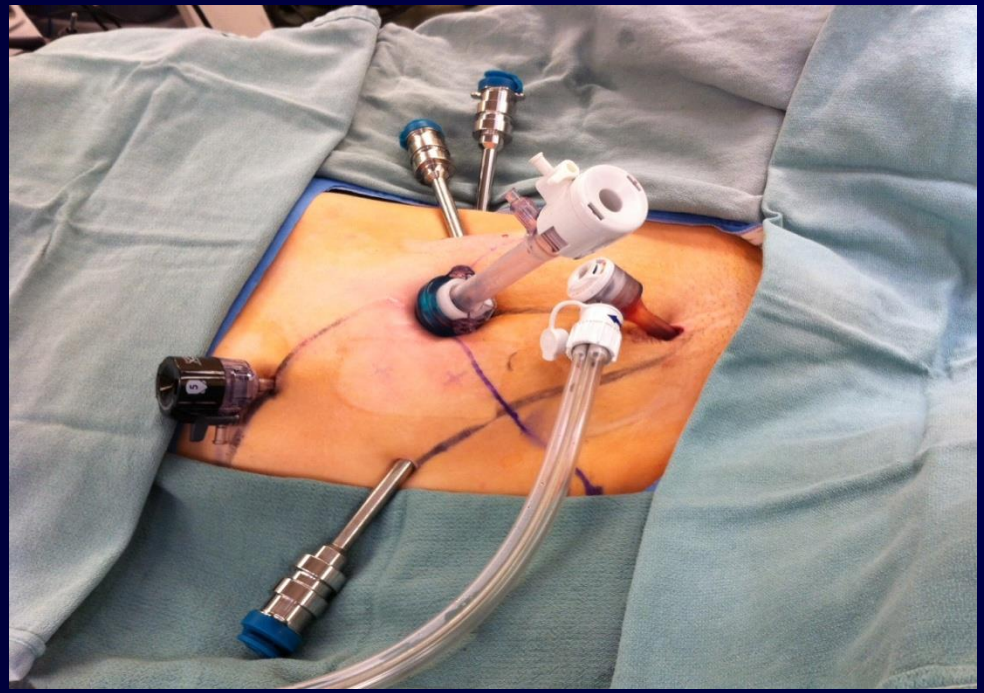
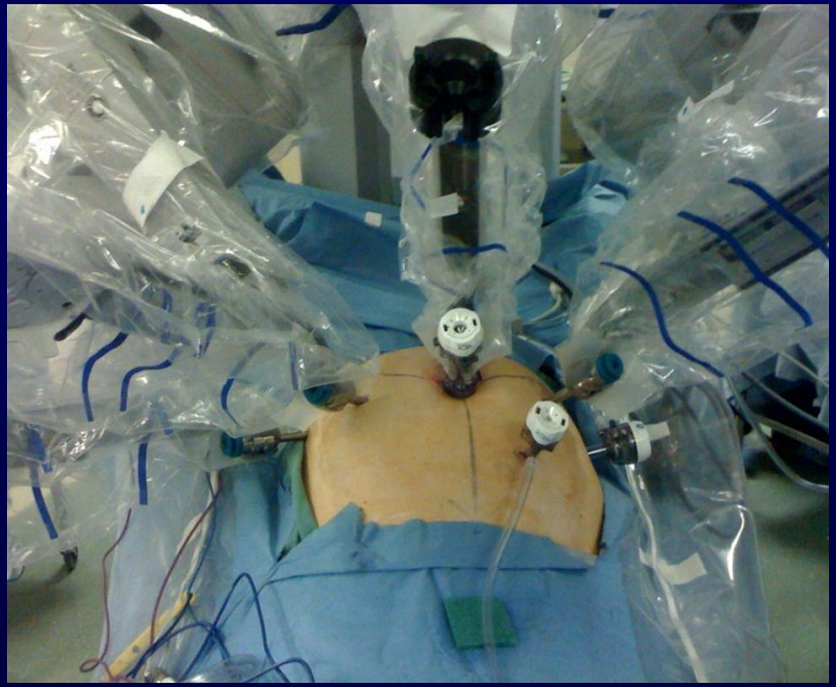
Current Techniques in Rectal Cancer Surgery





Courtesy Y. Nancy You, MD

Laparoscopy in Colorectal Cancer

- Randomized trials
  - COST (Colon and Rectal)
  - CLASICC (Colon and Rectal)
  - COLOR II (Rectal)
  - COREAN (Rectal)

- Results:
  - Oncologic outcomes similar (Colon and Rectal)[1,2,3]
    - DFS, OS, CRM positivity, Distal Margin
  - Short term benefits favor laparoscopy (Colon and Rectal)[1,2,3]
    - LOS, return of bowel function
  - Quality of life (Colon Cancer)[4,5]
    - Minimal differences between techniques
  - No differences in functional outcomes (Rectal Cancer)[6]

1. Fleshman J, et al. Ann Surg 2007; 246:655-664.
2. Green BL, et al. Br J Surg 2013; 100:75-82.
3. van der Pas MHGM, et al. Lancet Oncol, 2013; 14:210-218. Bonjer HJ, et al. NEJM 2015; 372:1324-1332.
4. Weeks JC, et al. JAMA 2002; 16:321-328.
5. Stucky CC, et al. Ann Surg Onc, 2011; 18:2422-2431.
6. Andersson J, et al. Br J Surg, 2014; 101:1272-1279.
7. Yeong SY, et al. Lancet Oncol 2014; 15:767-764.

Laparoscopy in Rectal Cancer

ACOSOG Z6051	Laparoscopic Resection (n = 240)	Open Resection (n = 222)	Difference, % (95% CI)	*P* Value
CRM >1 mm or distance = NA	87.9 (83.8 to 92.0)	92.3 (88.8 to 95.8)	[illegible] to 0.98)	.11[b]
Distal margin negative	98.3 (96.7 to 99.95)	98.2 (96.5 to 99.9)	[illegible] (−2.3 to 2.5)	.91[b]
Complete or nearly complete total mesorectal excision	92.1 (88.7 to 95.5)	95.1 (92.3 to 97.9)	−3.0 (−7.4 to 1.5)	.20[b]
Successful resection[d]				
Modified intent to treat	81.7 (76.8 to 86.[illegible])	[illegible]9 (82.5 to 91.4)	−5.3 (−10.8 to ∞)[c]	.41
Per protocol[e]	81.7 (76.5 to [illegible])	86.9 (82.5 to 91.4)	−5.3 (−11.0 to ∞)[c]	.41

ALaCaRT	Laparoscopic Rectal Resection (n = 238)	Open Laparotomy and Rectal Resection (n = 235)	Risk Difference, % (95% CI)	*P* Value
Primary Outcome				
No. (%) with negative circumferential and distal margins and complete total mesorectal excision	194 (82)	208 (89)	−7.0 (−12.4 to ∞)	.38[a]

Unable to show NON-INFERIORITY

1. Fleshman J, et al. JAMA 2015; 314:1346-1335.
2. Stevenson, et al, JAMA, 2015; 314:1356-1363.

Current Evidence for Robotic Surgery in Rectal Cancer

- Early data suggests:
  - Technically feasible with low conversion rate[1,2]
  - Immediate oncologic principles maintained (CRM, distal margin)[1,2,3]
  - Possible improved local recurrence[2]
  - Similar 5 yr DF and OS[2]
  - Potential for improved urologic/sexual outcomes[4]

- Randomized trial: Robotic vs. Laparoscopic rectal surgery (ROLARR)[5]
  - No difference in conversion (12% vs 8%)
  - No difference in short term oncologic outcomes

1. Hellan M, Ann Surg Oncol, 2015; 22:2151-2158.
2. Ghezzi TL, Eur J Surg Oncol, 2014; 40:1072-1079.
3. Park IJ, et al. Dis Colon Rectum 2012; 55:228-233. Sammour T et al Ann. Surg 2018.
4. Borholm M, et al. Colorectal Dis 2014 2015; 17:375-381.
5. Jayne D, et al. JAMA 2017; 318:1569-1580.

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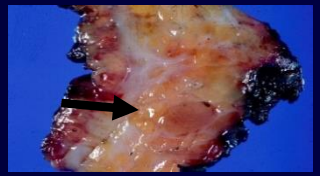
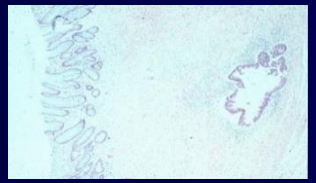
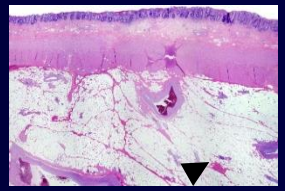
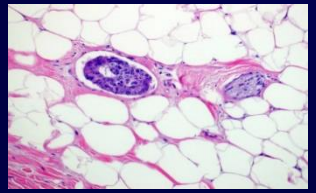
Complete Clinical Response

Lymph nodes, LVI









Rectal Adenocarcioma

Nodal Status after Neoadjuvant Chemoradiation

	MDACC n = 219*	MSKCC n= 187	Wash U./ Western PA n – 644	Padova n = 235	International EUS T3N0 n = 188	MDACC n = 420**
ypT0	9%	7%	2%	2%	3%	12%
ypT1	20%	8%	4%	15%	7%	10%
ypT2	23%	22%	23%	17%	20%	30%
ypT3		37%	47%	38%	} 36%	58%
ypT4		67%	48%	33%		50%

Bedrosian I et al. J Gastrointest Surg 2004; 8:56-63.
Stipa F, et al. Ann Surg Oncol 2004; 11:187-191.
Read TE, et al. Dis Colon & Rectum 2004; 47:825-831.
Puccinelli S, et al. Ann Surg Oncol 2005; 12:111-116.
Guillem J et al. J Clin Oncol 2008; 26:368-373.
420 patients RB (Mar 2017) N+,Jd0-1

* n= 122 pT0-pT2

Watch and Wait

Int J Radiat Oncol Biophys 2014; 88:822-828.

International Journal of Radiation Oncology biology • physics

www.redjournal.org

Clinical Investigation

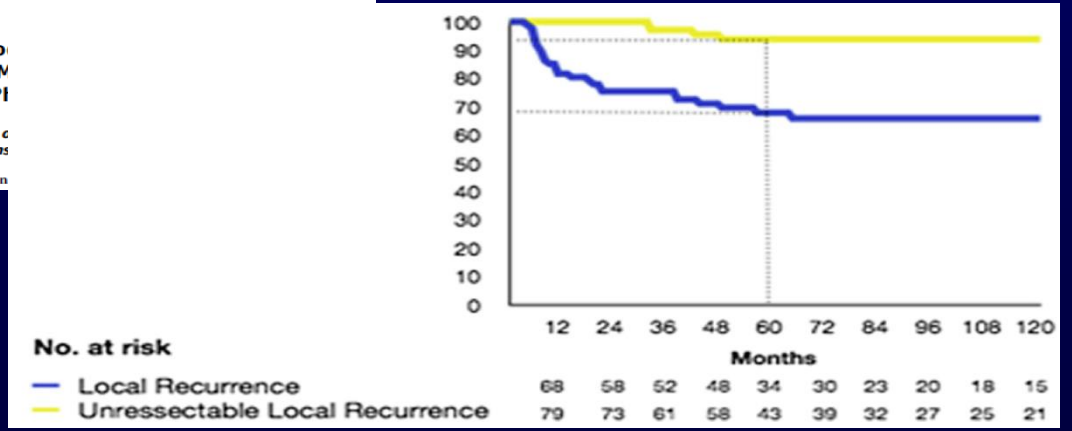
Local Recurrence After Complete Clinical Response and Watch and Wait in Rectal Cancer After Neoadjuvant Chemoradiation: Impact of Salvage Therapy on Local Disease Control

Angelita Habr-Gama, MD, PhD,*,† Joaquim Gama-Ro
Guilherme P. São Julião, MD,*,‡ Igor Proscurshim, M
Patricio B. Lynn, MD,* and Rodrigo O. Perez, MD, Ph

*Angelita and Joaquim Gama Institute; †University of São Paulo School o
University of São Paulo School of Medicine, São Paulo, Brazil; §Ludwig Ins

Received Oct 15, 2013, and in revised form Nov 29, 2013. Accepted for publication

- N=98/183
- 5-year local recurrence=31%
- 93% salvaged
- 78% organ preservation



International Watch & Wait Database (IWWD) ASCO GI 2017

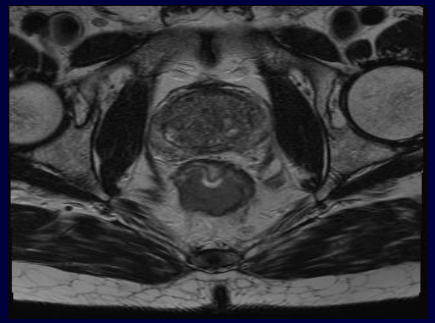
- International Multicenter Observational Study
- 775 patients; 11 countries; 35 participating institutions
  - 679 (90%) included due to a cCR;
    - incomplete response or other reasons for watch and wait excluded
  - Median follow-up 2.6 yrs. (range 0-24)
  - 90% neoadjuvant chemoradiation

van der Valk M et al. J Clin Oncol 2017; 35 (suppl 4S; abstract 521)

International Watch & Wait Database (IWWD) ASCO GI 2017

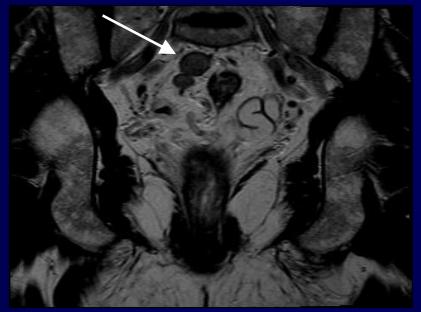
- 167 pts. (25%) local regrowth
  - 84% of these occurred in years 1-2 of follow-up
    - 96% (n=161) located endoluminal
    - 4% (n= 7) in regional LN
- 49 pts. (7%) distant metastases
- 3-yr overall survival 91% in all pts.
  - 87% in pts. with tumor regrowth.

van der Valk M et al. J Clin Oncol 2017; 35 (suppl 4S; abstract 521)



Pre treatment

26 mos. post CRT



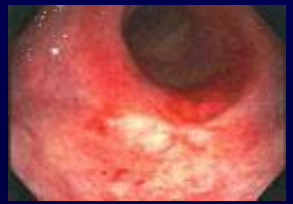
pre treatment

26 most post CRT

Pre treatment

2 mos. post CRT

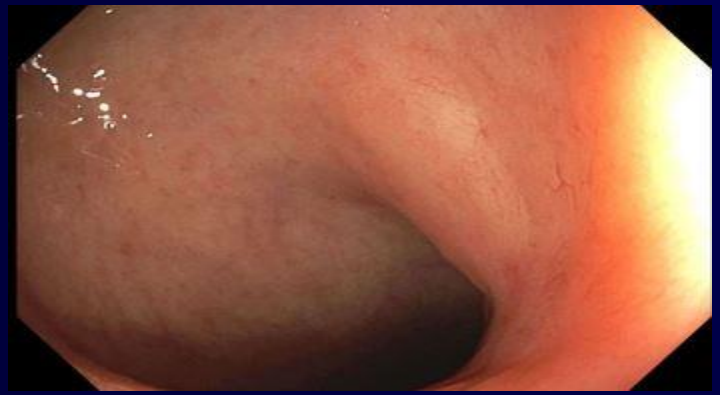
9 mos post CRT



21 mos. post CRT

26 most post CRT

Tumor Regrowth after Watch and Wait



9 months post CXRT

12 mos. Post CXRT (3 mos post last eval.)

RB Watch and Wait Patients

- 2003-2018 patients with cCR after neoadjuvant CXRT
- 19 patients, 17 males 2 female
- Median age 63 yrs (range 42-75)
  - Median distance anal verge 5 cm (1.5-12)
- MRI or EUS
  - 14 T3, 10 N+, 4Nx, 1M1
- Circumference median 25% (15-80%)
- CEA median 1.8 ng/mL (0.8-88.4*)
- 50.4 Gy + capecitabine; (1) 5-FU CI
- 18/19 adjuvant chemo

RB Watch and Wait Patients

- median follow-up of 24.7 months (range 1.7-142.6 mos.)
  - 3/19 tumor regrowth at primary site
    - 1 refused surgery in spite of + LN
      - Later salvaged ypT3N2
      - rypT3N0M0 and rypT2N0M0
  - 1/19 mesorectal recurrence salvaged
    - Alive 142.6 mos. liver, lung, bone metastases
  - 1/19 lung metastases salvaged
    - Alive 137 mos. NED
  - 1/19 with lateral LN involved refused rectal surgery
  - 1/19 lung mets at dx alive cCR at primary 39 mos.

Surgery for Colorectal Tumors
Conclusions

- Optimal local control
  - High quality surgery to begin with
  - Multimodality therapy (benefit/toxicities)

- Tailor local therapies
  - Mimimally invasive surgery
    - post op benefits and long term results
  - Patient selection is key to tailor extent of surgery in context of multimodality therapy

Acknowledgements

- Brian Bednarski, MD
- George Chang, MD
- Craig Messick, MD
- Paul Nickerson, MD
- John Skibber, MD
- Y. Nancy You, MD

Rectal Adenocarcinoma

“What has been omitted during surgery for the primary tumor has been lost forever”

Anonymous

RJ Heald, Rio de Janeiro 1998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Gracias por su atención
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MD Anderson Cancer Center
R. Lee Clark Clinic
Margaret and Ben Love Clinic
Charles A. LeMaistre Clinic