GI Alliance

Advancing GI Patient Care 2021

SATURDAY, JULY 24, 2021

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This program is supported by an educational grant from
AbbVie, Janssen Biotech, Inc., Mallinckrodt Pharmaceuticals and Pfizer Inc.

Contemporary Management of Rectal Cancer

Farshid Araghizadeh, MD, MBA, FASCRS

Southlake, TX

Rectal Cancer

- Background & Epidemiology
- Concepts in Staging & Treatment
- Evolution of Surgical Management
- Future Directions

ACS – 2021 Facts & Figures

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2021 Estimates

Estimated New Cases

Male			Female		
Prostate	248,530	26%	Breast	281,550	30%
Lung & bronchus	119,100	12%	Lung & bronchus	116,660	13%
Colon & rectum	79,520	8%	Colon & rectum	69,980	8%
Urinary bladder	64,280	7%	Uterine corpus	66,570	7%
Melanoma of the skin	62,260	6%	Melanoma of the skin	43,850	5%
Kidney & renal pelvis	48,780	5%	Non-Hodgkin lymphoma	35,930	4%
Non-Hodgkin lymphoma	45,630	5%	Thyroid	32,130	3%
Oral cavity & pharynx	38,800	4%	Pancreas	28,480	3%
Leukemia	35,530	4%	Kidney & renal pelvis	27,300	3%
Pancreas	31,950	3%	Leukemia	25,560	3%
All sites	**970,250**		**All sites**	**927,910**	

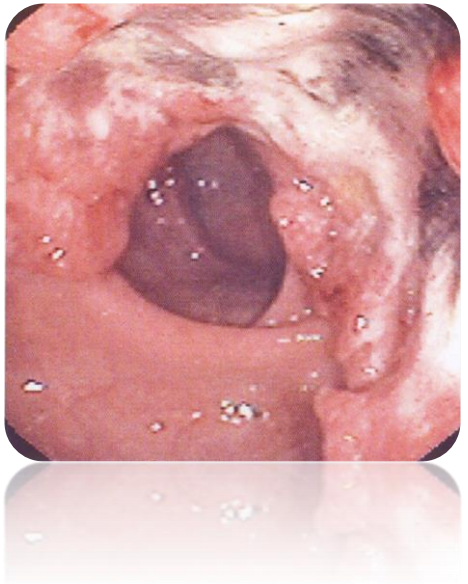
Estimated Deaths

Male			Female		
Lung & bronchus	69,410	22%	Lung & bronchus	62,470	22%
Prostate	34,130	11%	Breast	43,600	15%
Colon & rectum	28,520	9%	Colon & rectum	24,460	8%
Pancreas	25,270	8%	Pancreas	22,950	8%
Liver & intrahepatic bile duct	20,300	6%	Ovary	13,770	5%
Leukemia	13,900	4%	Uterine corpus	12,940	4%
Esophagus	12,410	4%	Liver & intrahepatic bile duct	9,930	3%
Urinary bladder	12,260	4%	Leukemia	9,760	3%
Non-Hodgkin lymphoma	12,170	4%	Non-Hodgkin lymphoma	8,550	3%
Brain & other nervous system	10,500	3%	Brain & other nervous system	8,100	3%
All sites	**319,420**		**All sites**	**289,150**	

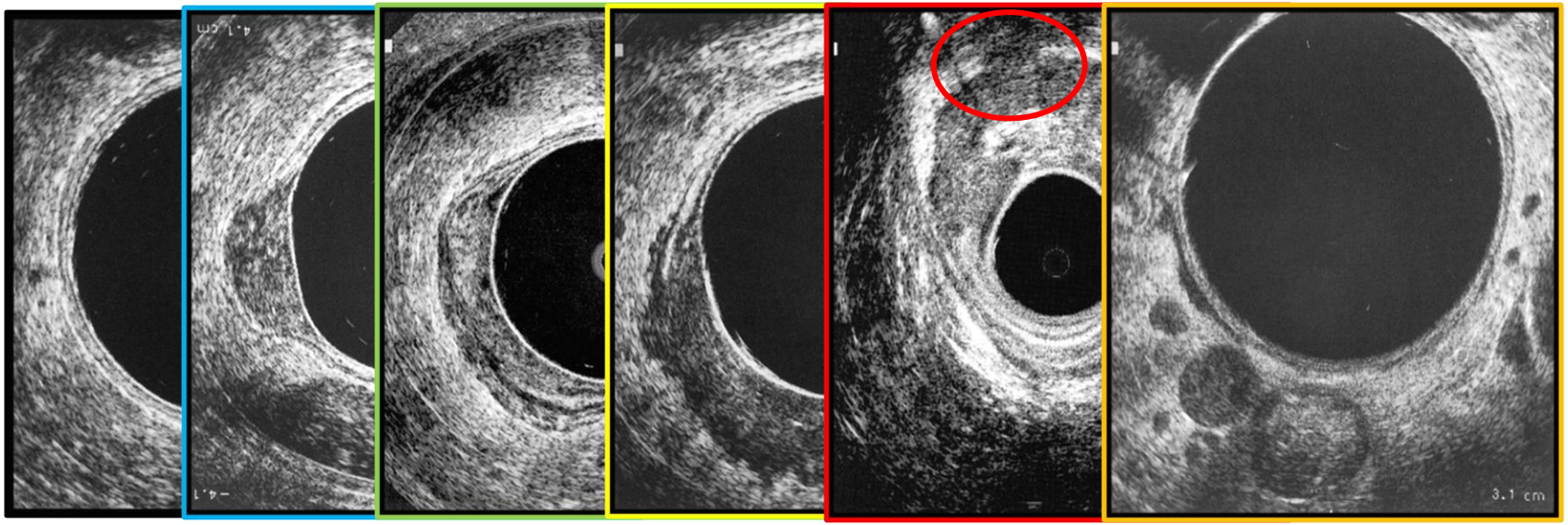
Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

Rectal Cancer

- Evaluation
  - History & physical examination
  - Lab evaluation – CEA level
  - Endoscopy
    - Total Colonoscopy
    - Rigid proctosigmoidoscopy
  - Imaging
    - Endorectal Ultrasound (ERUS)
    - MRI
    - CT scan & PET/CT scan

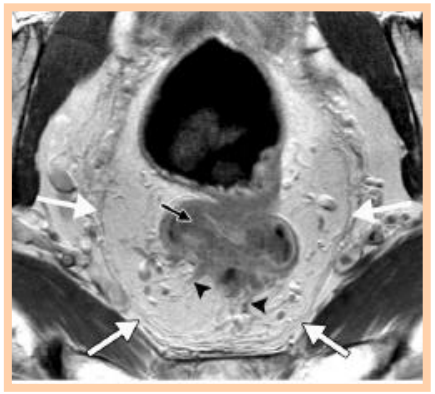


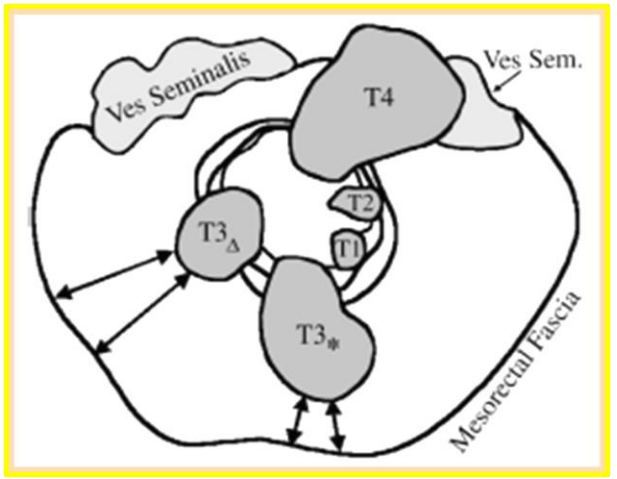
Rectal Cancer Staging – ERUS



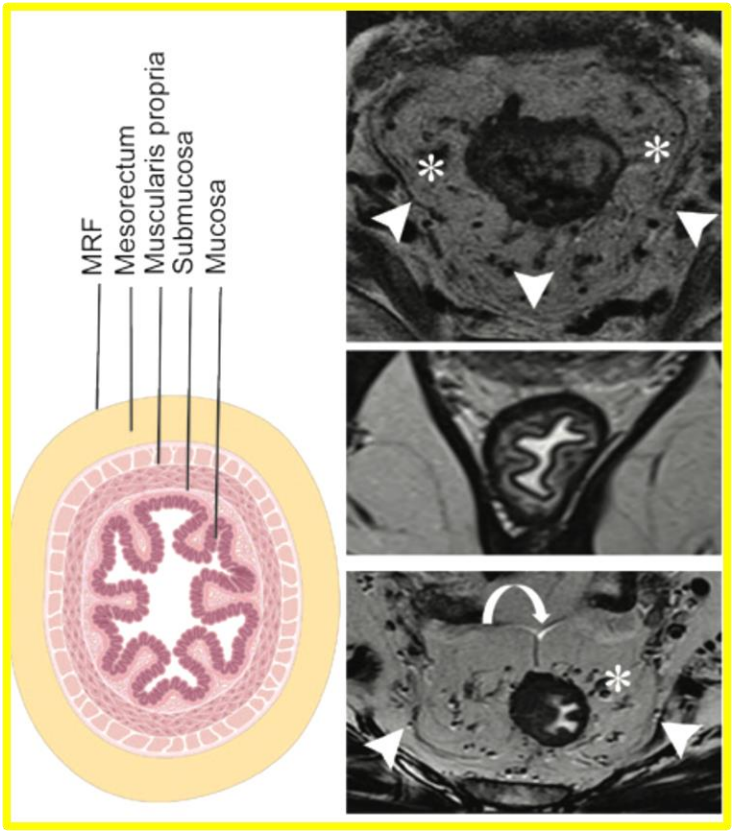
Rectal Cancer Staging – MRI

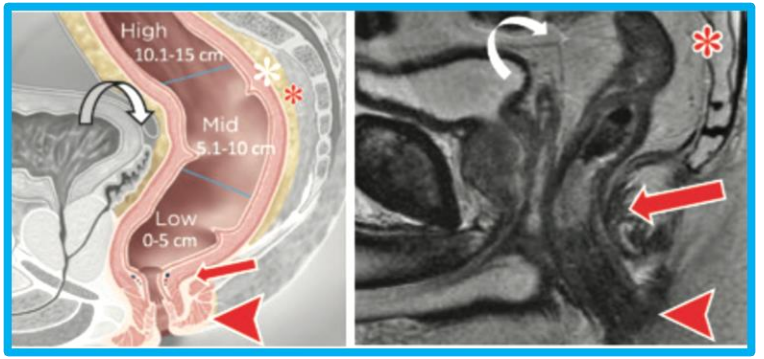
- ***Phased array coils***
- ***High spatial Resolution***
- ***Large field of view***

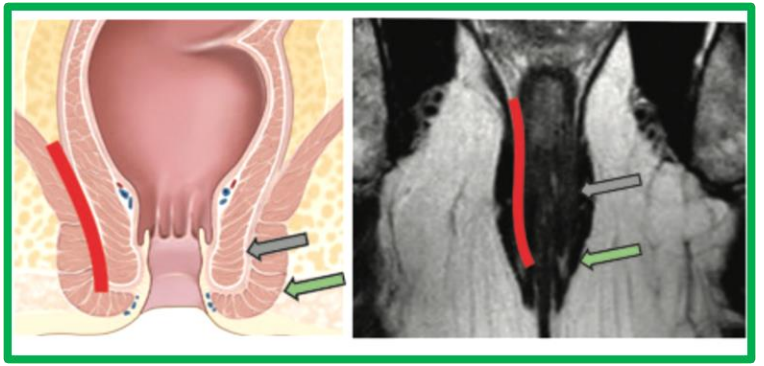




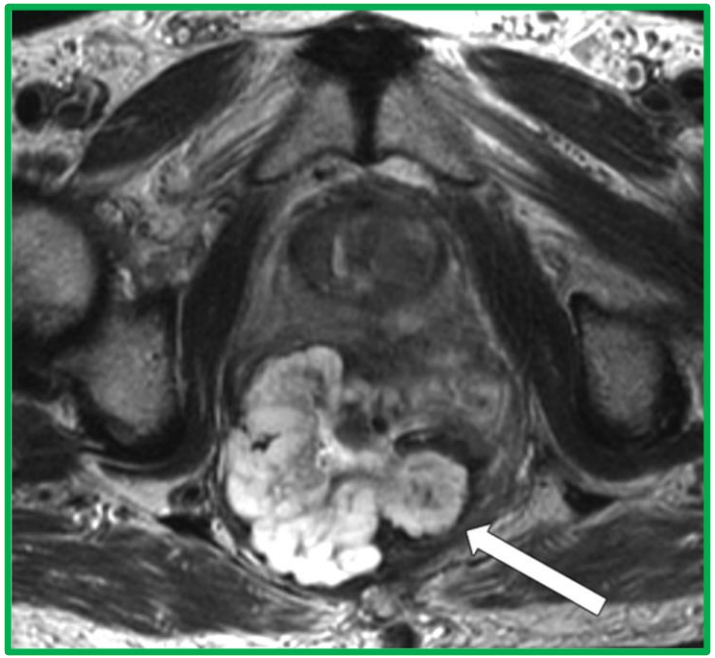
Rectal Cancer Staging – MRI

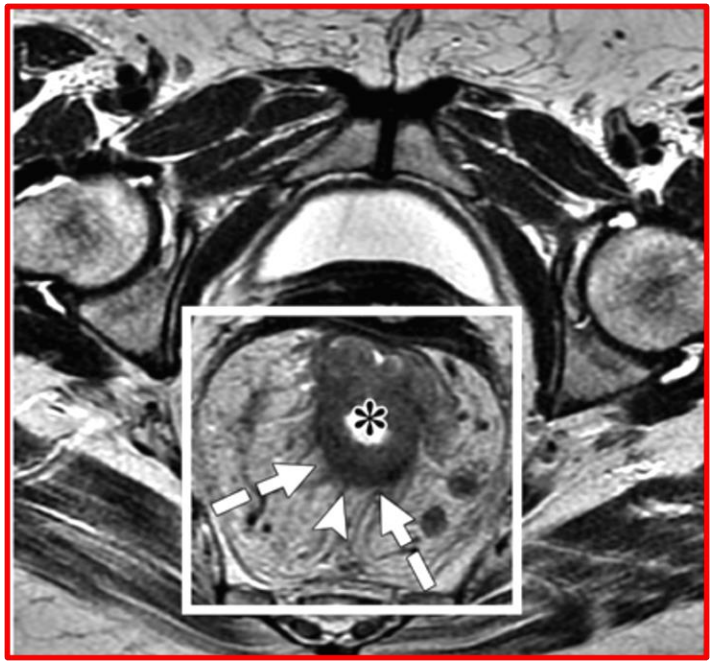




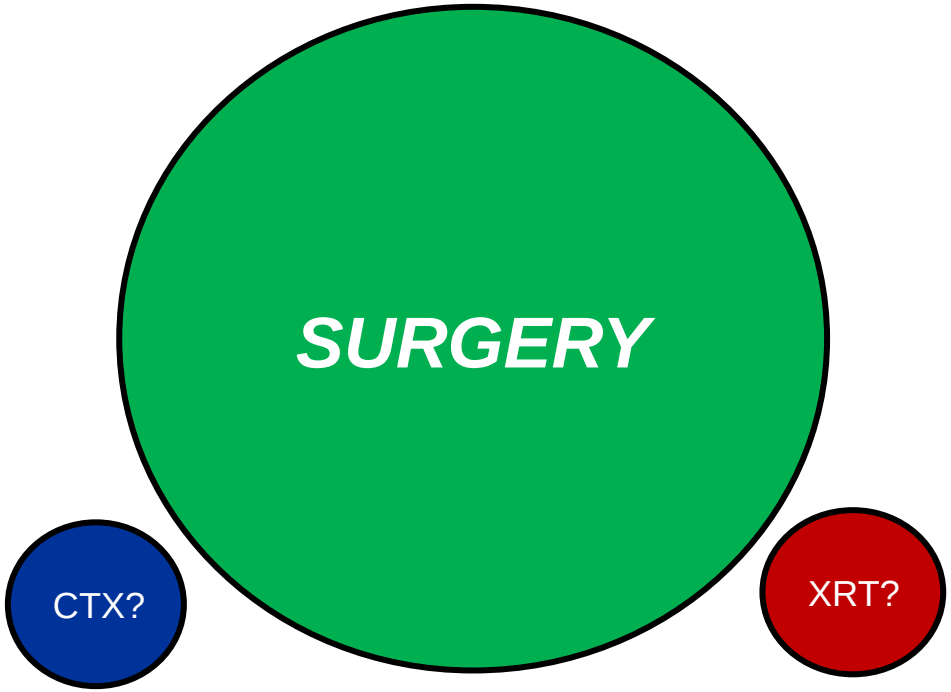


Rectal Cancer Staging – MRI

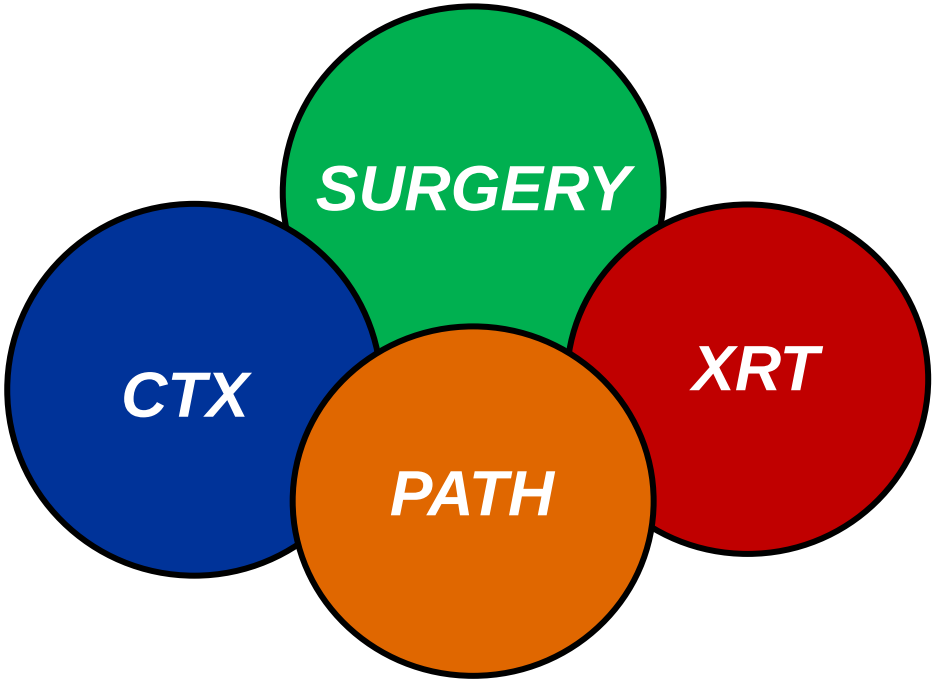




Treatment of Rectal Cancer – 1980



Treatment of Rectal Cancer – 2021



Chemoradiotherapy for Rectal Cancer

Pre-operative (Neoadjuvant) CRT

Advantages

- Tumor Downstaging
- Increased rates of restorative proctectomy
- Improved patient compliance
- Final stage may predict survival

Disadvantages

- Exposing patients who may not need it
- Sphincter damage
- Anastomotic problems
- Difficulty in surgical resection

Chemoradiotherapy for Rectal Cancer

Post-operative (Adjuvant) CRT

Advantages

- Improved patient selection
- Avoidance of XRT complications

Disadvantages

- Less compliance
- Radiation exposure to small bowel
- Post-op complication delay treatment

Chemoradiotherapy for Rectal Cancer

NIH consensus conference – 1990

Adjuvant therapy for patients with colon & rectal cancer*

Combined post-operative chemoradiation therapy for patients with pT3 and/or Node positive rectal cancer (stage II & III)

**JAMA*. 1990. (264)11: 1444-50.

Chemoradiotherapy for Rectal Cancer

- *German Rectal Cancer Trial**
  - 421 patients: neoadjuvant CRT vs.
  - 402 patients: adjuvant CRT
  - 5040 cGY XRT + CTX
  - Overall survival
    - 76% – neoadjuvant group
    - 74% – adjuvant group
  - Local recurrence – (P<0.006)
    - 6% – neoadjuvant group
    - 13% – adjuvant group

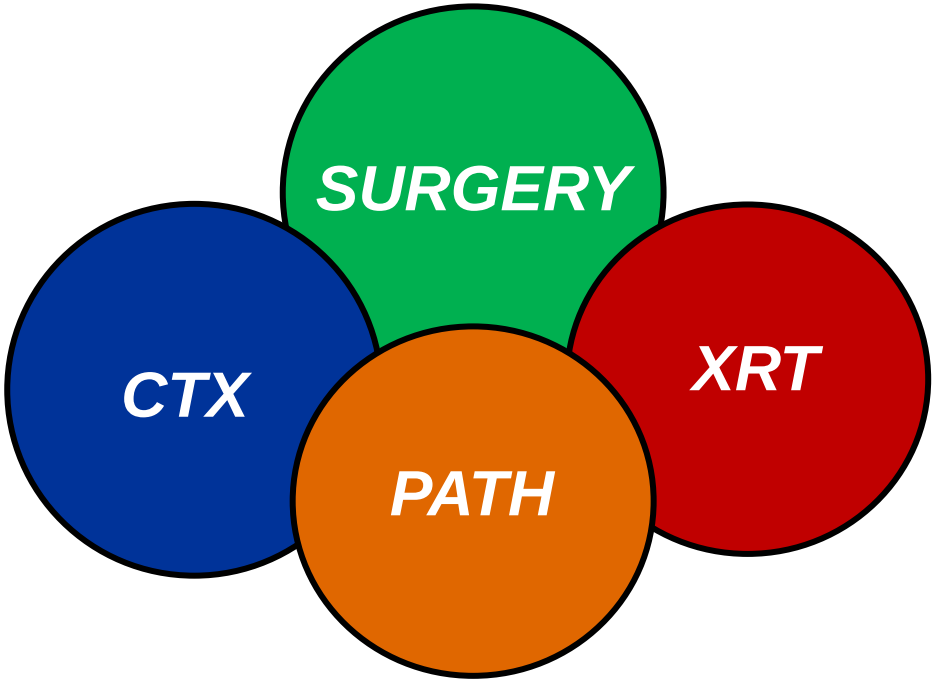
*Sauer R et al. *NEJM*. 2004.

Chemoradiotherapy for Rectal Cancer

- Short course XRT vs. Chemoradiation
  - 12 modern randomized trials
    - Neoadjuvant XRT (without CTX)
    - All use low to moderate doses of XRT
    - Most show a reduction in local recurrence
    - *Swedish Rectal Cancer Trial** – survival benefit
    - 38% vs. 30 % (P=0.008)
- Short course CRT vs. Long course CRT**
  - No difference – LR or survival

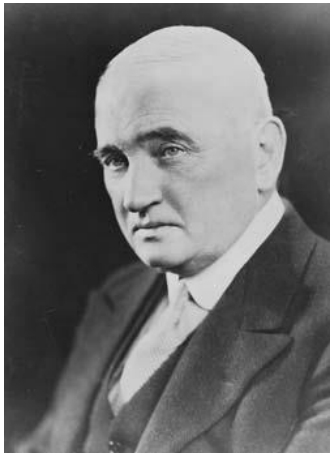
*Birgisson H et al. *J Clin Oncol*. 2005; **Bujko K et al. *Br J Surg*. 2006.

Treatment of Rectal Cancer – 2021



Surgery for Rectal Cancer

- Radical excision
  - Pain
  - Damage to GU organs
  - Bone/neurologic destruction
  - Perineal sepsis
  - Stoma!



"…a calm, unhurried atmosphere about the theater which made the whole performance see at first somewhat slow and where there was economy of movement and effortless ease which only experience and skill could bring about..."

Lancet. 1908. sir W. Ernest Miles.

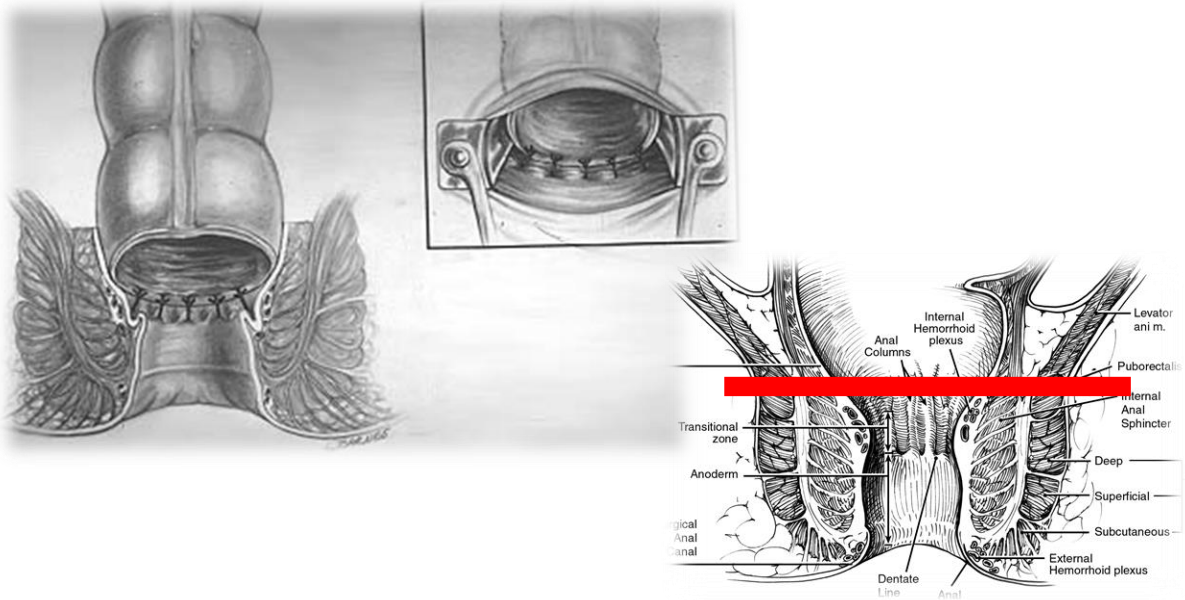
Surgery for Rectal Cancer

- Equivalence of sphincter preservation to AP excision[1,2]
- ***NSABP –*** No difference in disease-free & overall survival with hand-sewn vs. stapled anastomoses[3]
- Acceptable minimum distal margin[4] – ?
  - Intramural spread of rectal cancer <1 cm
  - Distal margins of 1 cm do not compromise oncologic outcome[5]

[1]Beahrs OH. *Surg Gyn Obstet.* 1966; [2]Chodoff RJ. *Am J Proctol.* 1967; [3]Wolmark N et al. *Dis Colon & Rectum.* 1986;
[5]Moore HG. *Ann Surg Onc*. 2003.

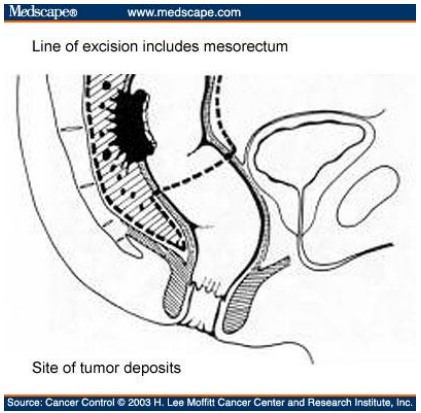
Surgery for Rectal Cancer

When radical proctectomy is required, we can almost always save the anus



Surgery for Rectal Cancer

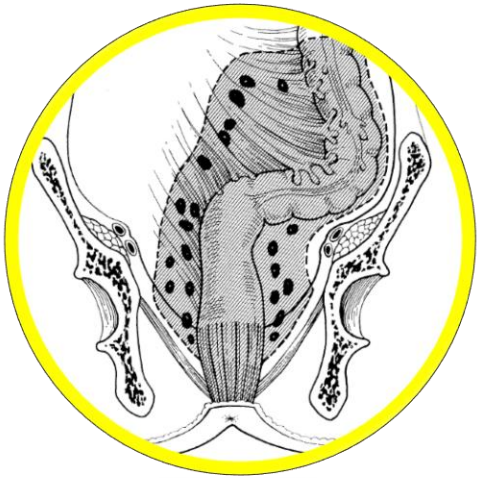
- 113 consecutive patients who underwent TME
- Rectal cancers down to 4 cm from AV
- 2 year follow up – 0% local recurrence
- 5 year follow up
  - 3.7% local recurrence
  - Overall survival – 87.5%
  - Disease-free survival – 81.7%



*Heald RJ et al. *Br J Surg.* 1982. 69: 613.

Surgery for Rectal Cancer

- Total Mesorectal Excision (TME)
  - Mesorectum is a site of occult nodal metastases
  - Foci of carcinoma frequently detected in the mesorectum below and away from the tumor
  - Progressive narrowing of the pelvis



Surgery for Rectal Cancer

- Circumferential Resection Margins (CRM)
  - 85% local recurrence rate with CRM positivity *vs.* 3% if CRM negative[1]
  - CRM positive local recurrence – independent of TNM stage
  - CRM < 2 mm – local recurrence rate 16% *vs.* 6%[2]

[1]Quirke J. *Lancet.* 1986; [2]Natagagal et al. *Am J Surg Pathol.* 2002.

Surgery for Rectal Cancer

WHAT ABOUT MINIMALLY INVASIVE PROCTECTOMY?

Laparoscopy for Colon Cancer

ORIGINAL ARTICLES

Laparoscopic Colectomy for Cancer Is Not Inferior to Open Surgery Based on 5-Year Data From the COST Study Group Trial

James Fleshman, MD, Daniel J. Sargent, PhD,† Erin Green, BS,† Mehran Anvari, MD,‡ Steven J. Stryker, MD,§ Robert W. Beart, Jr, MD,¶ Michael Hellinger, MD,‖ Richard Flanagan, Jr, MD,** Walter Peters, MD,†† and Heidi Nelson, MD,§§ for The Clinical Outcomes of Surgical Therapy Study Group††*

Laparoscopic colorectal surgery: summary of the current evidence

EMAD H ALY

Fowler & White. 1991.

Laparoscopy for Rectal Cancer

- ***Potential Advantages***
  - Smaller incisions; faster recovery
  - Use of capnoperitoneum
  - Unobstructed views of the pelvis
- ***Challenges & Concerns***
  - Exposure – !!!
    - Experienced assistant is essential
  - Localization of the tumor
  - Limitations of current devices
    - Difficulty in rectal transection
  - 2 – D visualization
  - Surgeon Tremor
  - Poor ergonomics

Laparoscopy for Rectal Cancer

Short Term Outcomes

Table 4. Operative outcomes for laparoscopic versus open resection of rectal cancer in major randomized trials and meta-analyses

Trial	Assigned Group	No. of Patients	Conversion Rate (%)	Operative Time (min)	Estimated Blood Loss (mL)	Lymph Node Count (mean)	Positive CRM Rate (%)
COLOR II[25]	Laparoscopy	739	17	240	200	13	10
	Open	364		188	400	14	10
CLASICC[8]	Laparoscopy	230	34	180	—	8	16
	Open	113		135	—	7	14
Meta-analyses							
Arezzo[71]	Laparoscopy	2087	13	219	—	—	—
	Open	2452		175	—	—	—

Laparoscopy for Rectal Cancer

LONG-TERM OUTCOMES

Non-inferiority Trials

Original Investigation

Effect of Laparoscopic-Assisted Resection vs Open Resection of Stage II or III Rectal Cancer on Pathologic Outcomes
The ACOSOG Z6051 Randomized Clinical Trial

Original Investigation

Effect of Laparoscopic-Assisted Resection vs Open Resection on Pathological Outcomes in Rectal Cancer
The ALaCaRT Randomized Clinical Trial

JAMA. 2015.

Laparoscopy for Rectal Cancer

LONG-TERM OUTCOMES

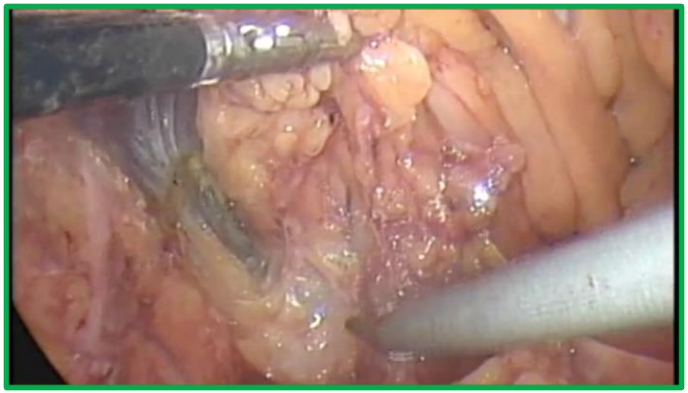
ACOSOG Z6051 & ALaCaRT

Neither trial was able to establish non-inferiority with respect to laparoscopic resection of rectal cancer

"…Although the overall quality of surgery was high, these findings do not provide sufficient evidence for the routine use of laparoscopic proctectomy for locally advanced rectal cancer."

Laparoscopy for Rectal Cancer

- ***Challenges & Concerns***
  - Exposure – !!!
  - Localization of the tumor
  - Limitations of current devices
  - 2-D visualization
  - Surgeon Tremor
  - Poor ergonomics

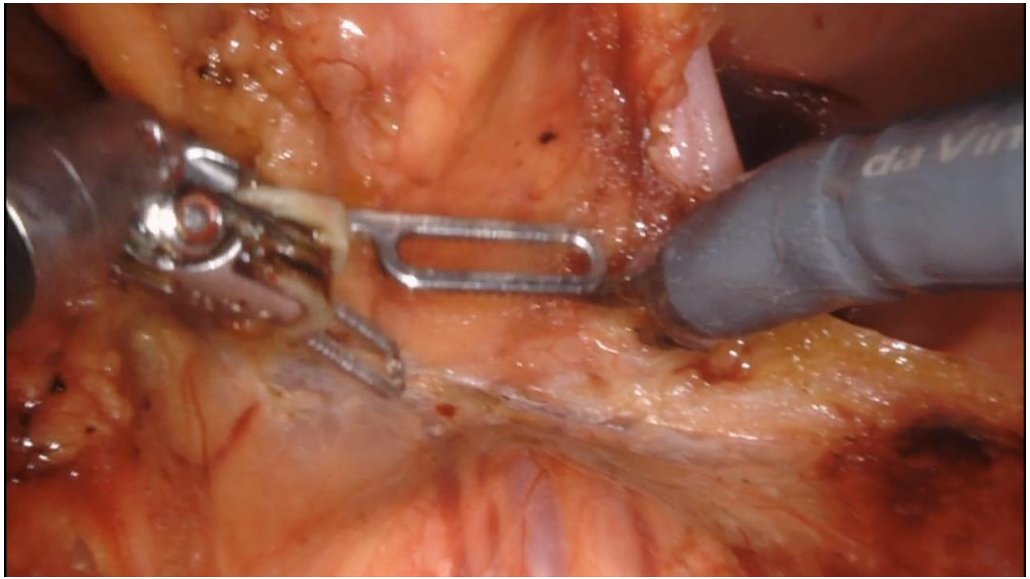


Are the inferior results of laparoscopic proctectomy due to the laparoscopic platform itself?

Robotics for Rectal Cancer

- ***Robotic surgery – DaVinci***
  - 3 – D, HD vision
  - 7 degrees of freedom
  - Enhanced ergonomics
  - Tremor filtration
  - Superior dexterity
  - Improved maneuverability in pelvis
  - Improved retraction with a fixed arm

Robotics for Rectal Cancer



Do these advantages translate to a benefit for patients?

Robotics for Rectal Cancer

Effect of Robotic-Assisted vs Conventional Laparoscopic Surgery on Risk of Conversion to Open Laparotomy Among Patients Undergoing Resection for Rectal Cancer

The ROLARR Randomized Clinical Trial

- 471 patients – 237 RTME & 234 LTME
  - Adequacy of lymphadenectomy
  - Involvement of CRM
  - 30 day mortality

  No statistically significant advantages for robotic TME

Surgery for Rectal Cancer

Transanal Total Mesorectal Excision (Ta-TME)

Surgery for Rectal Cancer

- Avoidance of radical proctectomy
  - Improve function
    - Avoidance of anterior resection syndrome
  - Reduce need for fecal diversion
  - Less morbidity & mortality

Treatment of Rectal Cancer

OBSERVATION (WATCH & WAIT) FOLLOWING NEOADJUVANT CRT

“IS IT SAFE?”

MARATHON MAN, 1976

Observation of Rectal Cancer After CRT

- Largest series
  - 361 patients: Tumor within 7 cm from AV
  - CRT: 5040 cGY + 5-FU/folinic acid
  - 8 weeks after completion of CRT
    - DRE, proctoscopy/bx, CT scan & CXR
  - Small, suspicious ulcer – full excisional bx

*Habr-Gama et al. *J Gastrointestinal Surgery*. 2006.

Observation of Rectal Cancer After CRT

- Results:
  - 122 patients had a cCR at first assessment
  - At 12 months
    - 27% had a ***sustained*** clinical response – **Stage c0**
  - Mean follow up – 60 months
    - 13% recurrence
    - 5 endoluminal, 7 systemic; 1 combined
    - OS – 93% and DFS – 85%

*Habr-Gama et al. *J Gastrointestinal Surgery*. 2006.

Treatment of Rectal Cancer

- Locally Advanced Rectal Cancer (LARC)
  - Neoadjuvant CRT → Radical Surgery → CTX
- Alternative Approach
  - CTX → Neoadjuvant CRT → Surgery

Total Neoadjuvant Therapy (TNT)

Total Neoadjuvant Therapy – TNT

- Meta-analysis[1]
  - 2416 Patients
  - 1206 – received TNT
  - pCR – 29.9% TNT group
  - pCR – 14.9% Standard group

TNT a promising strategy in achieving pCR – Long term studies needed to assess effect on local recurrence & Overall survival

[1]Kasi A et al. *JAMA*. 2020.

Observation of Rectal Cancer After CRT

- New set of challenges
  - Tumor assessment extremely difficult
  - Risk of residual mural cancer & metastases in the mesorectum – ?
  - Clinical relevance of these residual nests of cancer – ?

Local Excision for Rectal Cancer

- Curative resection
  - Size ≤ 3 cm
  - Less than 1/3 of the circumference
  - Freely mobile
  - Pre-op ERUS: uT1 or (selected) uT2
  - Well or moderately well-differentiated tumors
  - No LVI

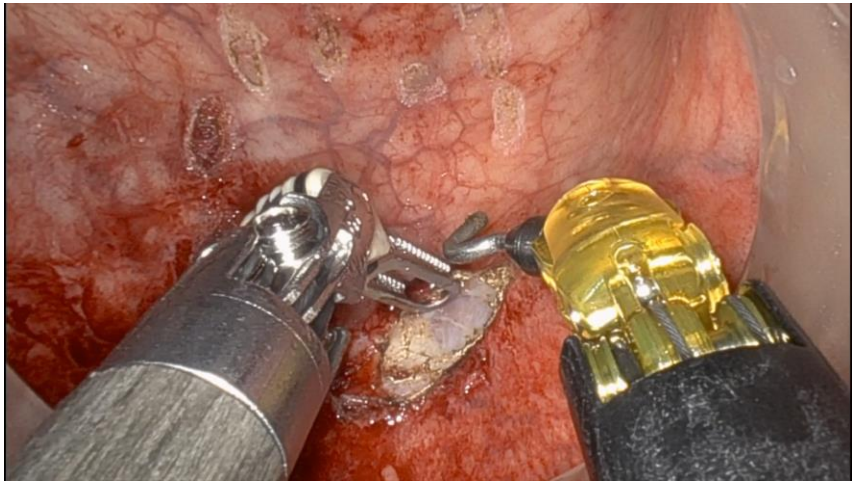
Local Excision for Rectal Cancer

- Long-term survival after local excision for T1 rectal cancer
  - 282 patients: 1985 – 2006
    - 145 radical proctectomy
    - 137 – Transanal excision
    - LVI & differentiation were similar
    - Local recurrence – median follow up 5.6 years
      - 2.7% - radical resection
      - 13.2% - TAE

Disease specific survival – inferior in TAE

*Nash G et al. *Dis Colon & Rectum*. 2009.

Local Excision for Rectal Cancer

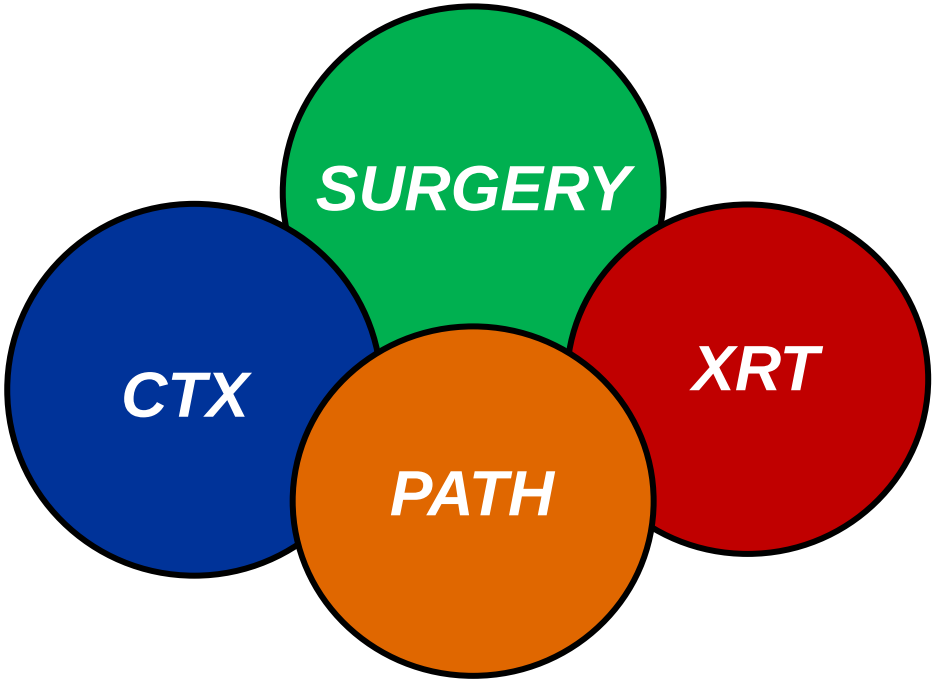


- ***Malignant***
  - Polyp
  - T1-2 Cancer
  - Palliative
  - Carcinoid
- ***Benign***
  - Strictures
  - Fistulae

Treatment of *Rectal Cancer*

Is rectal cancer the new anal cancer?

Treatment of Rectal Cancer – 2021



Summary

- Management of rectal cancer remains a significant challenge
- Neoadjuvant CRT is preferred to adjuvant therapy
- Radical proctectomy with TME remains the standard for most patients
- Some patients may be candidates for less radical surgery or observation
- Best informed decisions are made via a multidisciplinary approach