A Review of Rectal Cancer

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Disclosures

- No disclosures

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About me..

- Grew up in Southern Illinois-

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About me..

- College- University of Missouri
  - B.S. in Finance and Banking
- Medical School-
  - University of Missouri

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About me..

- Residency-
  - University of Missouri
- Fellowship-
  - Lahey Clinic

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About me..

- Before joining this group…

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Outline

- History of rectal cancer
- Introduction and use of adjuvant and neoadjuvant chemotherapy and radiation
- Current management and controversy
- Future directions of management

Rectal Cancer History

- Pre-modern medicine
  - Rectal cancer was first described and identified in the 13th century
  - Treatment was a colostomy until the 18th and 19 century
    - Originally described around 400 B.C
    - Littre described for rectal cancer in 1710

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Rectal Cancer History

- 1739- Faget described the first operation for rectal cancer
  - Perineal approach
  - Was unsuccessful
- 1826- Lisfranc- first successful excision of a rectal cancer
  - Used a perineal and posterior approach

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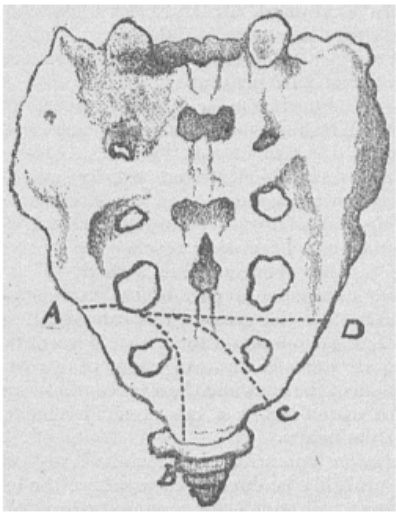
Rectal Cancer History

- 1870s- renewed interest in rectal resections
  - 1883 publication reviewing the first 20 rectal resections
    - Highest tumor was 3 inches above the anal verge
    - 20% mortality
    - Of survivors- 4 were continent, 3 incontinent, 9 unknown
    - 20% disease free survival at 2 yrs

Piechaud T. Traitment du cancer du rectum. Tolmer et Cie, Paris

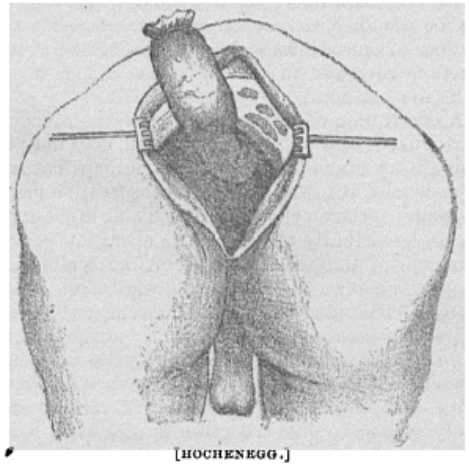
Rectal Cancer History

- 1885- Kraske described a radically different method
  - Better view
  - More space
  - Sacral approach



[HOCHENEGG.]

FIG. I. Showing the amount of bone removed by different operators. AB = Kraske. AC = Hochenegg. AD = Kraske, for extreme cases.



[HOCHENEGG.]

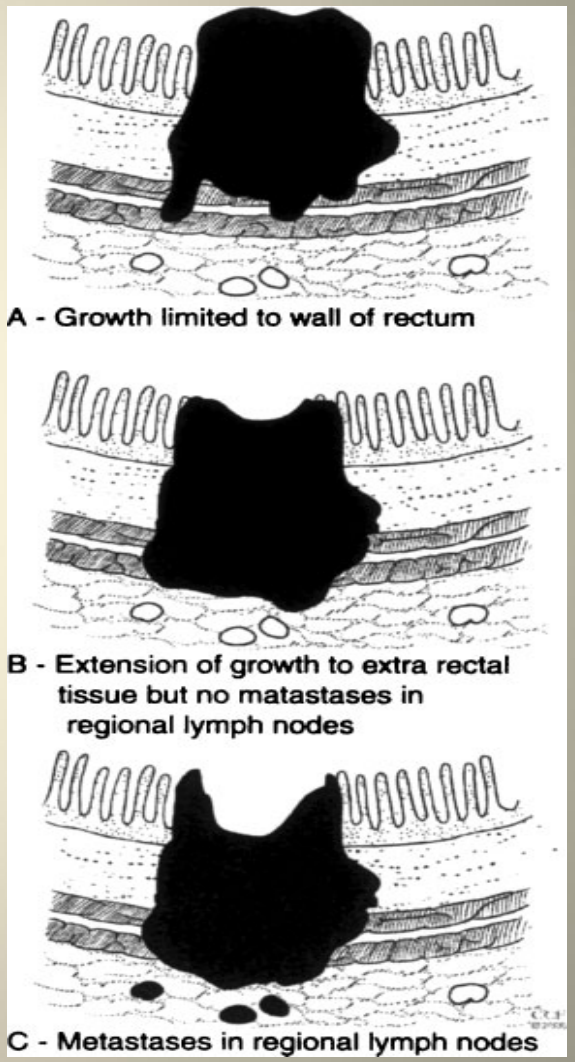
FIG. II. Showing extent of incision and amount of bone removed. Resection partly done, and lower end of bowel brought out through wound.

Rectal Cancer History

- 1894- Czerny combined the Kraske approach with an abdominal approach- first APR
  - Realization of tumor spread outside the primary site- excision of lymphovascular pedicle with tumor
- 1908- modified by Miles
  - Mortality of 42%
- Modifications improved outcomes over the next decades

Rectal Cancer History

- Staging-
  - 1926- Lockhart-Mummery proposed a staging system based on depth of invasion and nodes
  - 1932- Dukes summarized the current staging opinions with an A/B/C system



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Rectal Cancer History

- 1949, 1954, 1963 all saw modifications of the Dukes system
- 1987- American Joint Committee on Cancer introduced the TMN system

Definitions

Primary Tumor (T)

- **TX** Primary tumor cannot be assessed
- **T0** No evidence of primary tumor
- **Tis** Carcinoma in situ: intraepithelial or invasion of lamina propria[1]
- **T1** Tumor invades submucosa
- **T2** Tumor invades muscularis propria
- **T3** Tumor invades through the muscularis propria into pericolorectal tissues
- **T4a** Tumor penetrates to the surface of the visceral peritoneum[2]
- **T4b** Tumor directly invades or is adherent to other organs or structures[2,3]

Regional Lymph Nodes (N)[4]

- **NX** Regional lymph nodes cannot be assessed
- **N0** No regional lymph node metastasis
- **N1** Metastasis in 1–3 regional lymph nodes
- **N1a** Metastasis in one regional lymph node
- **N1b** Metastasis in 2–3 regional lymph nodes
- **N1c** Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis
- **N2** Metastasis in 4 or more regional lymph nodes
- **N2a** Metastasis in 4–6 regional lymph nodes
- **N2b** Metastasis in 7 or more regional lymph nodes

Distant Metastasis (M)

- **M0** No distant metastasis
- **M1** Distant metastasis
- **M1a** Metastasis confined to one organ or site (for example, liver, lung, ovary, nonregional node)
- **M1b** Metastases in more than one organ/site or the peritoneum

ANATOMIC STAGE/PROGNOSTIC GROUPS

Stage	T	N	M	Dukes*	MAC*
0	Tis	N0	M0	–	–
I	T1	N0	M0	A	A
	T2	N0	M0	A	B1
IIA	T3	N0	M0	B	B2
IIB	T4a	N0	M0	B	B2
IIC	T4b	N0	M0	B	B3
IIIA	T1–T2	N1/N1c	M0	C	C1
	T1	N2a	M0	C	C1
IIIB	T3–T4a	N1/N1c	M0	C	C2
	T2–T3	N2a	M0	C	C1/C2
	T1–T2	N2b	M0	C	C1
IIIC	T4a	N2a	M0	C	C2
	T3–T4a	N2b	M0	C	C2
	T4b	N1–N2	M0	C	C3
IVA	Any T	Any N	M1a	–	–
IVB	Any T	Any N	M1b	–	–

NOTE: cTNM is the clinical classification, pTNM is the pathologic classification. The y prefix is used for those cancers that are classified after neoadjuvant pretreatment (for example, ypTNM). Patients who have a complete pathologic response are ypT0N0cM0 that may be similar to Stage Group 0 or I. The r prefix is to be used for those cancers that have recurred after a disease-free interval (rTNM).
* Dukes B is a composite of better (T3 N0 M0) and worse (T4 N0 M0) prognostic groups, as is Dukes C (any T N1 M0 and Any T N2 M0). MAC is the modified Astler-Coller classification.

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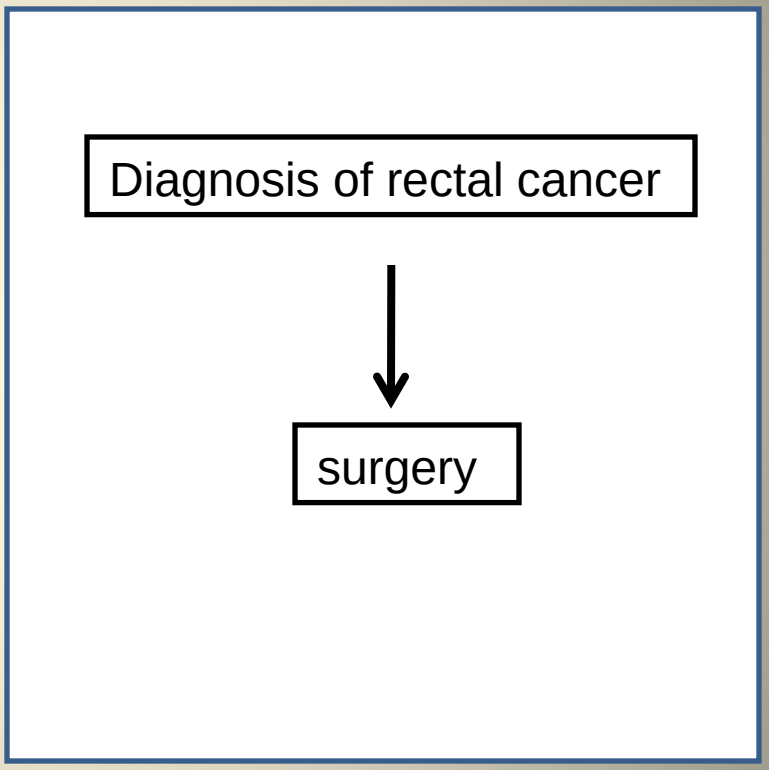
Rectal Cancer History

- Throughout the mid 20th century, rectal cancer continued to be a surgical disease
  - The distal mural resection margin should be 5 cm and is critical to cure
  - All patients with tumors within 10 cm of anal verge require APR



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Rectal Cancer History

- In 1975- Gastrointestinal Study Group Trial comparing surgery to chemo, radiation, or both
- Results
  - Surgery only- 55% recurrence
  - 46% with chemotherapy,
  - 48% with radiation therapy
  - 33% with combined modality

Gastrointestinal Study Group Trial. NEJM 1985;312:1465-1472

Rectal Cancer History

- Additional trials
  - North Central Cancer Treatment Group 79-47-51
  - National Surgical Adjuvant Breast and Bowel Project (NASBP)

Both showed the benefit of postoperative radiation and chemotherapy

Krook JE et al. NEJM 1991;324:709-15
Fisher B et al. J Natl Cancer Inst 1988;80:21-29

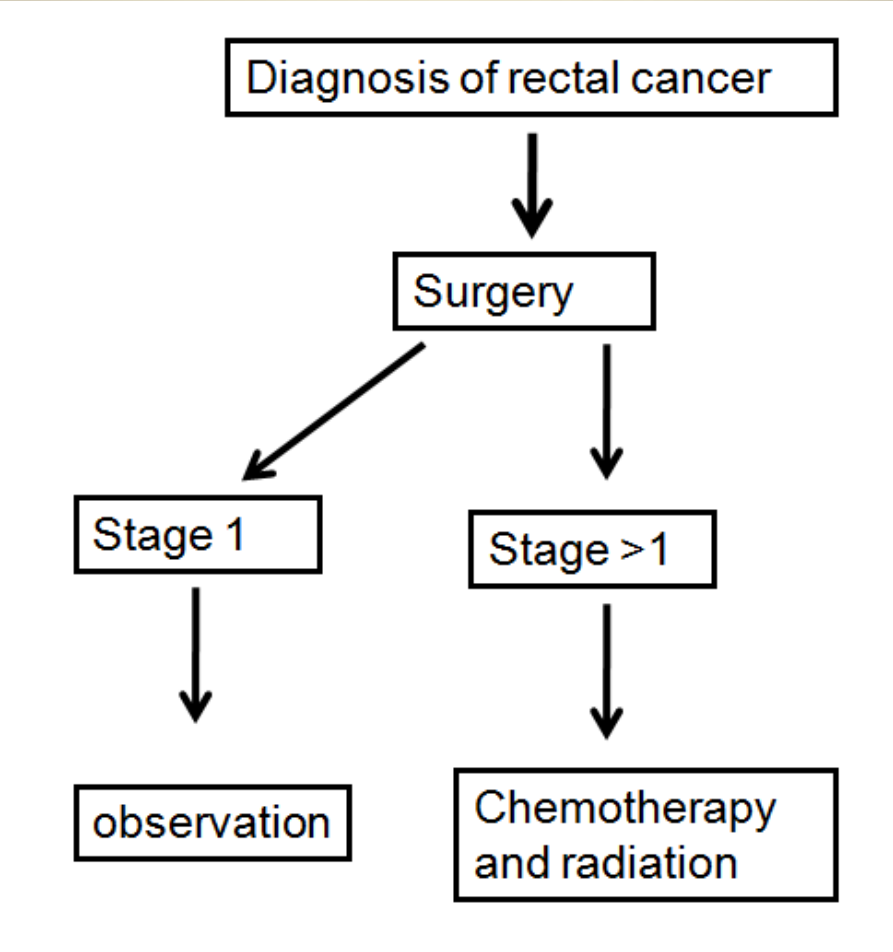
Rectal Cancer History

- In addition- 1980s review of rectal cancer literature
  - Pelvic failure (local failure) of 25-35% in large clinical trials after surgery alone

- NIH Consensus Statement 1990
  - Stage II and III rectal adenocarcinoma should be treated with adjuvant chemoradiotherapy

NIH Consensus Development Panel. JAMA 1990;264:1444-1450

Rectal Cancer Algorithm



Where are we today?

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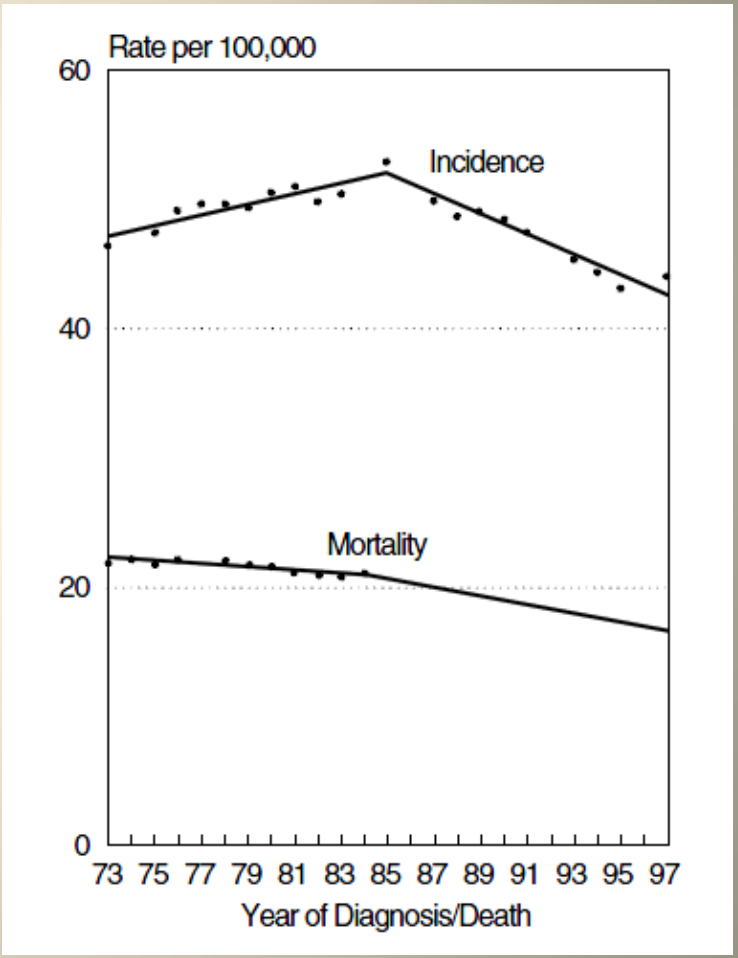
Colon and rectal cancer

Both incidence and deaths from colon and rectal cancer have been declining since the mid-1980's



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Colon and rectal cancer

- Epidemiology:
  - 3rd most prevalence cancer diagnosis
  - 145,000 diagnosed in 2008
  - 2010 estimate- 142,500
    - Estimated over 40,000 diagnosis of rectal cancer
  - Estimated 51,500 deaths in 2010
- Worldwide- responsible for over 650,000 deaths annually

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Rectal Cancer: Goals of Treatment

- Cure
- Avoid Local Pelvic Failure
  - Valuable goal independent of overall survival
  - Surrogate marker for success of pelvic treatment

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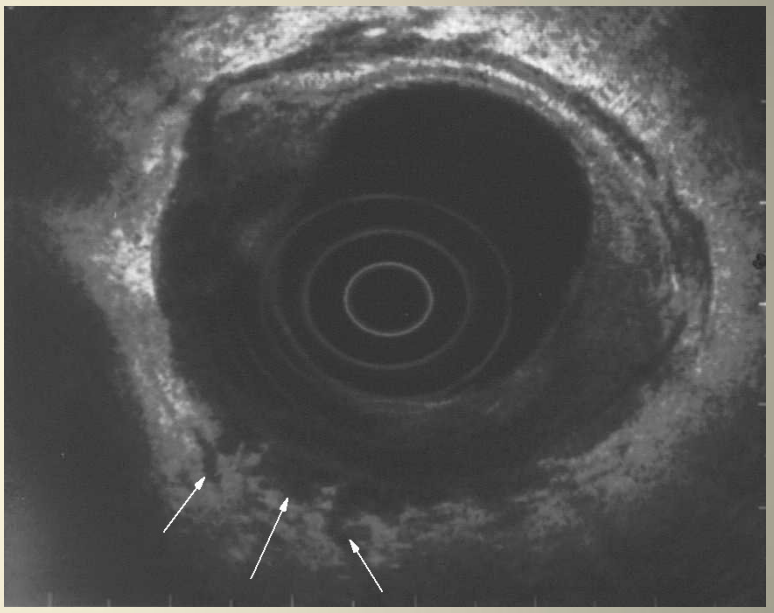
Rectal Cancer Staging

- Pre-op work-up
  - Very important for rectal cancer, as stage effects treatment
    - Physical exam
    - Colonoscopy- evaluate for other polyps/cancers
    - CEA level
    - CXR
    - CT scan of abd/pelvis
    - **Endorectal ultrasound or MRI**

Rectal Cancer Staging

- Endorectal Ultrasound
  - 81-95% accuracy distinguishing between T1/T2 cancers and T3 cancers
  - Overall 60-90% accuracy for T stage
  - ~60% accuracy at nodal staging
  - Cons- learning curve



Solomon MJ et al. Dis Colon Rectum 1993;36:200-5
Kim NK et al. Dis Colon Rectum 1999;42:770-5

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Rectal Cancer Staging

- MRI
  - 70-81% accuracy when using an EndoCoil
  - Nodal accuracy of ~60-70%

Golfieri R et al. Radiol Med 1993;85:779-83

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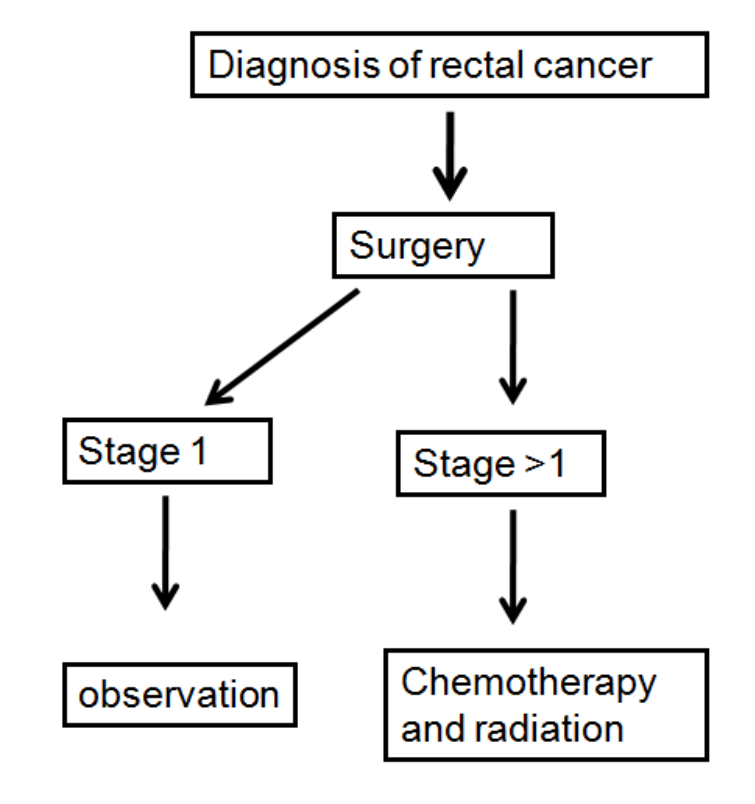
Rectal Cancer Staging

- Why stage?
  - T status and N status matter



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Rectal Cancer

Treatment options

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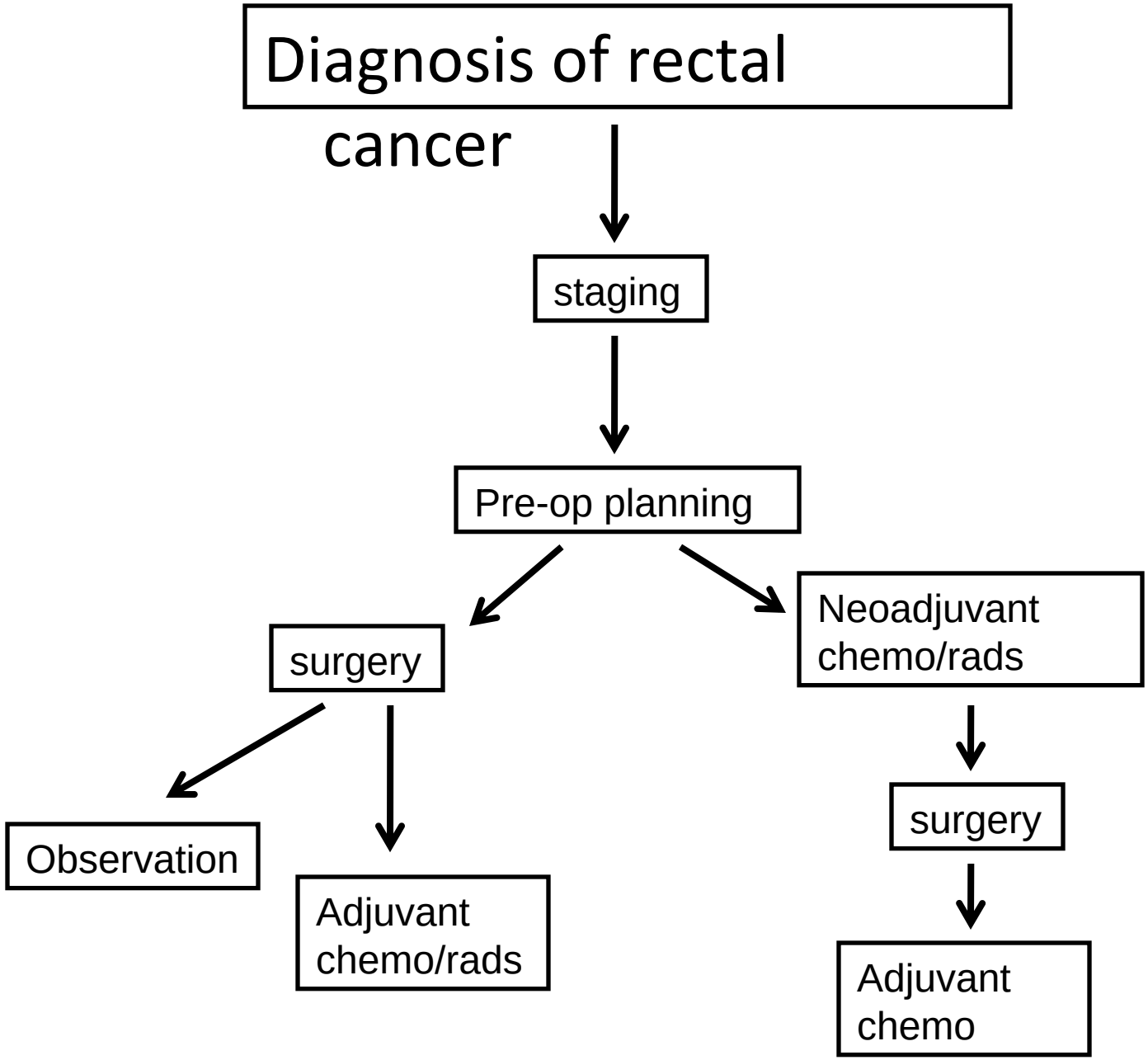

Diagnosis of rectal cancer
staging
Pre-op planning
surgery
Neoadjuvant chemo/rads
Observation
Adjuvant chemo/rads
surgery
Adjuvant chemo

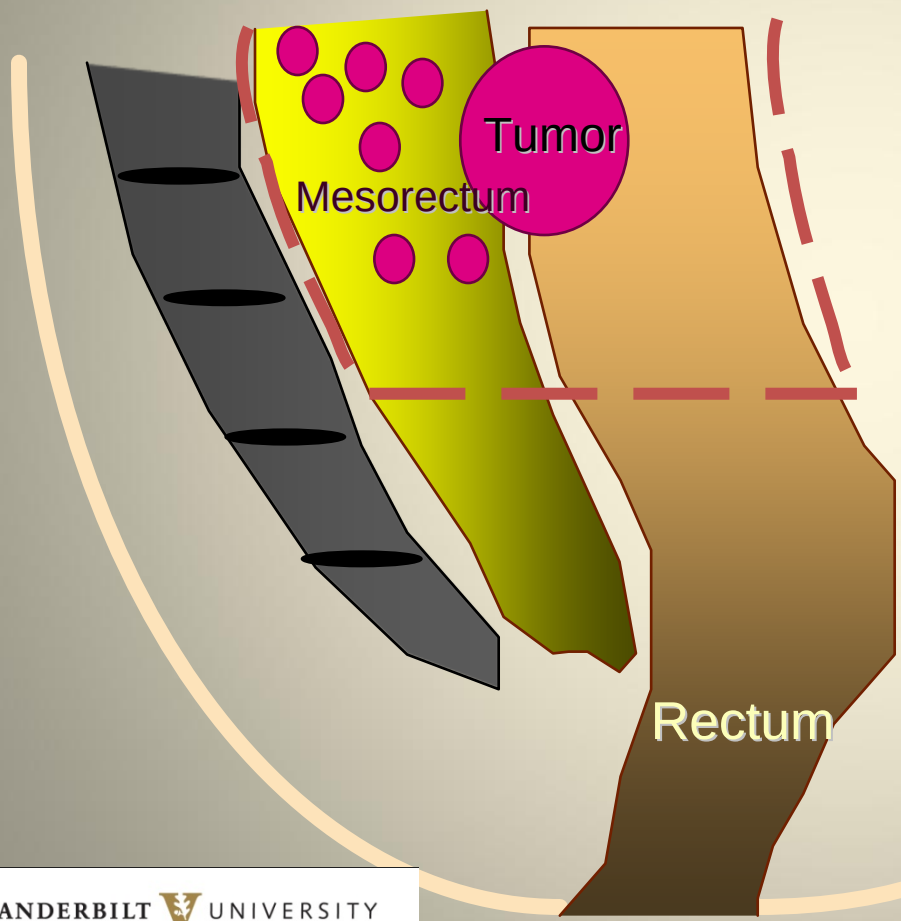
Adjuvant Therapy

- Due to the 1990 consensus statement
  - Significant research developed
    - Better chemotherapeutic agents
    - Improved radiation techniques
    - Adding “sensitizing” chemotherapy to radiation

Neoadjuvant therapy

- Developed from an increase in morbidity seen in postoperative chemoradiation treatments
  - Hypothesis
    - More effective= better local control= better survival
    - Increase the rate of curative resection
    - Decrease the rates of radiation injury

Neoadjuvant Therapy: Benefits



- Shrink tumor prior to removal
  - Downsizing
  - Downstaging
- Sterilize margins prior to pelvic dissection
- More effective than postop XRT
  - oxygenated field
- Better functional result
  - Radiate only one side of anastomosis
- More patients complete treatment course

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Preop vs. Postop Chemoradiotherapy

- German rectal cancer trial 2004

	Preop XRT	Postop XRT
patients	405	392
Local pelvic failure	6%	12%
Survival	No difference	
Anastomotic leak	No difference	
Toxicity (acute)	Lower	Higher
Toxicity (late)	Lower	Higher

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Swedish Rectal Cancer Trial

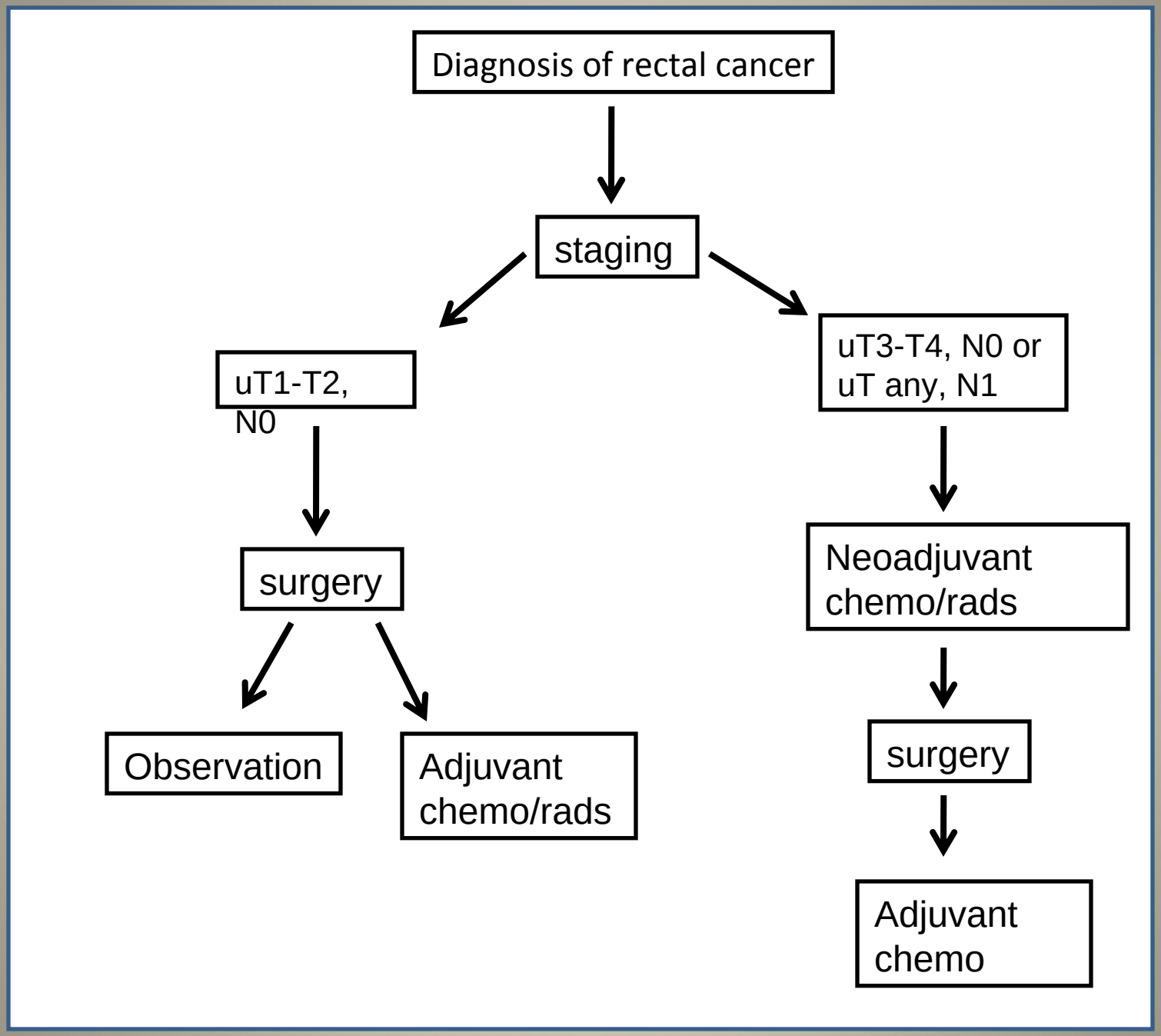
- Pre-op Radiation vs. surgery alone
- Local Pelvic Failure 5 years

	2500 cGy + Surgery		Surgery Alone
Total	9%	p<0.001	26%

- Survival at 5 years

	2500 cGy + Surgery		Surgery Alone
Total	38%	p=0.008	30%

Survival and Local Control benefits persist at 13 year analysis


Diagnosis of rectal cancer
staging
uT1-T2, N0
uT3-T4, N0 or uT any, N1
surgery
Neoadjuvant chemo/rads
Observation
Adjuvant chemo/rads
surgery
Adjuvant chemo

Rectal Cancer Surgery

Surgery was evolving-

- "sphincter sparing operations"
  - From 1989-2001
    - 10% decrease in APRs being performed in the US
    - Pt were 28% more likely to have a sphincter sparing procedure in 2001 than in 1989
    - Colorectal training programs were preforming LAR 3 times as much than APRs for rectal cancer

Abraham Ns et al. Aliment Pharmacol Ther 2005;21:35-41
Schoetz DJ et al. J Am Coll Surg 206;203:322-327

Rectal Cancer Surgery

- At the same time- realization that not all surgery is created equal
  - "Total mesorectal excision"

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TME

- 1980s- pelvic failure rates of 25-35%
- Concept of TME- complete surgical removal of the perirectal soft tissue envelope, using sharp

  instruments under direct vision
- Prospective studies showed a decrease to 5% pelvic failure rates

Heald RJ et al. Lancet 1986;1:1479–82
MacFarlane JK, Ryall RD, Heald RJ. Lancet 1993;341:457–60
Cecil TD et al. Dis Colon Rectum 2004;47:1145–50.
Faerden AE, et al. Dis Colon Rectum 2005;48:2224–31.

Proctectomy for Rectal Cancer: Margins

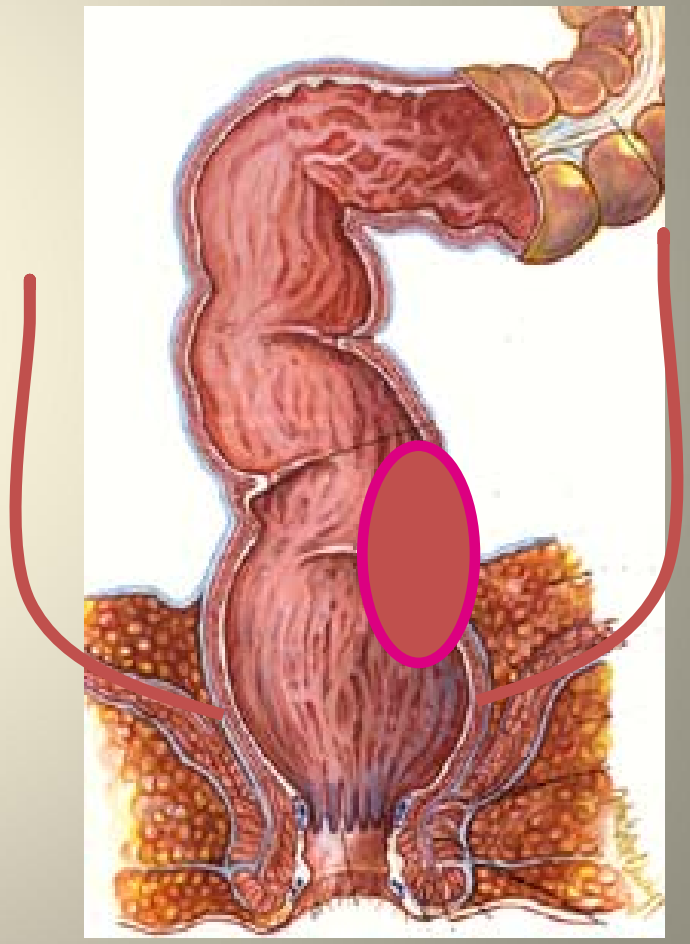
- Distal Mural Resection Margin
  - 1-2 cm
  - Tumors do not spread longitudinally in wall of rectum

Dukes C. Proc R Soc Med. 1943

- Radial Margin
  - Critical to ensure complete tumor removal
  - Pathologists must measure and report

Quirke et al. Lancet. 1986

- Mesorectal Margin



Kodner IJ. CIBA Symposium. 1989

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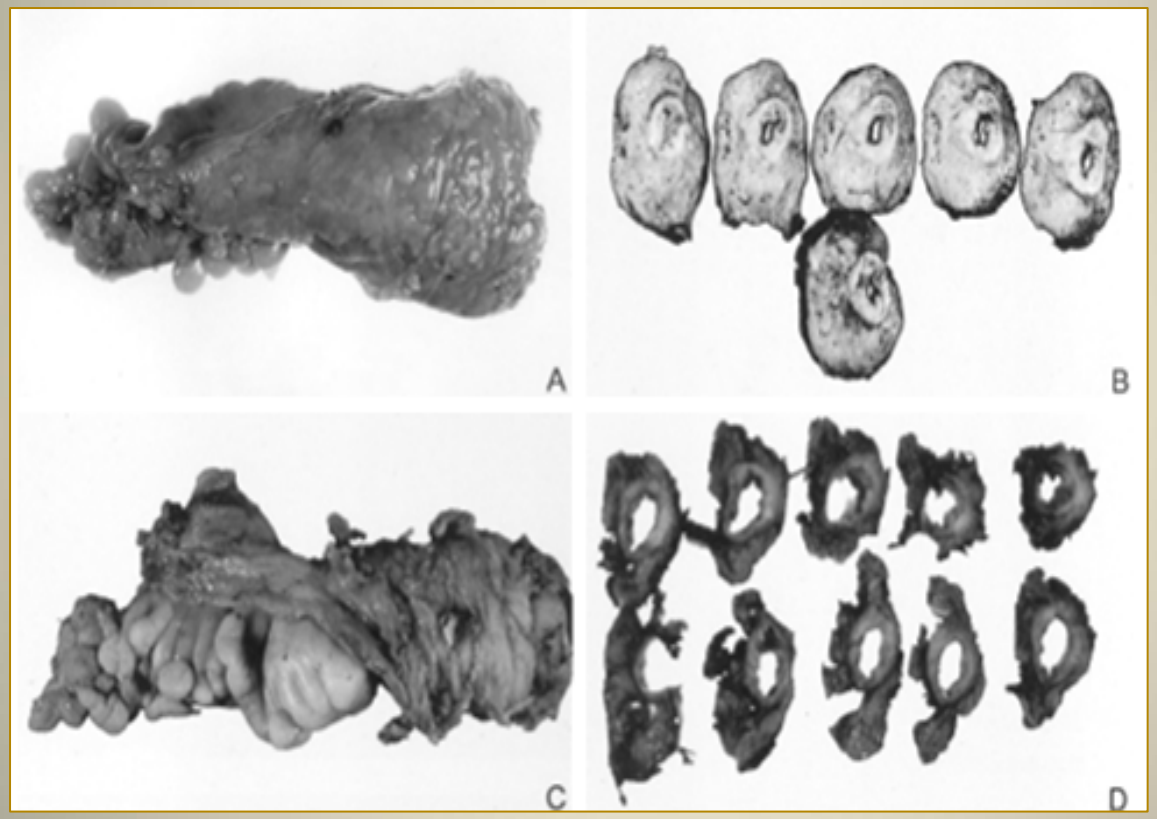
TME



Maslekar S, et al. Dis Colon Rectum 2007;50:168-175 (Hull)

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TME

- Mesorectal Grade Correlates with Pelvic Failure Rate

Table 1 Grading of quality and completeness of the mesorectum in a total mesorectal excision specimen

	Mesorectum	Defects	Coning	CRM
Complete	Intact, smooth	Not deeper than 5 mm	None	Smooth, regular
Nearly complete	Moderate bulk, irregular	No visible muscularis propria	Moderate	Irregular
Incomplete	Little bulk	Down to muscularis propria	Moderate–marked	Irregular

Both the specimen as a whole (fresh) and cross-sectional slices (fixed) are examined in order to make an adequate interpretation.
CRM, circumferential radial margin.

Parfitt JR, et al. J Clin Pathol 2007;60:849–855

Maslekar S, et al. Dis Colon Rectum 2007;50:168-175 (Hull)

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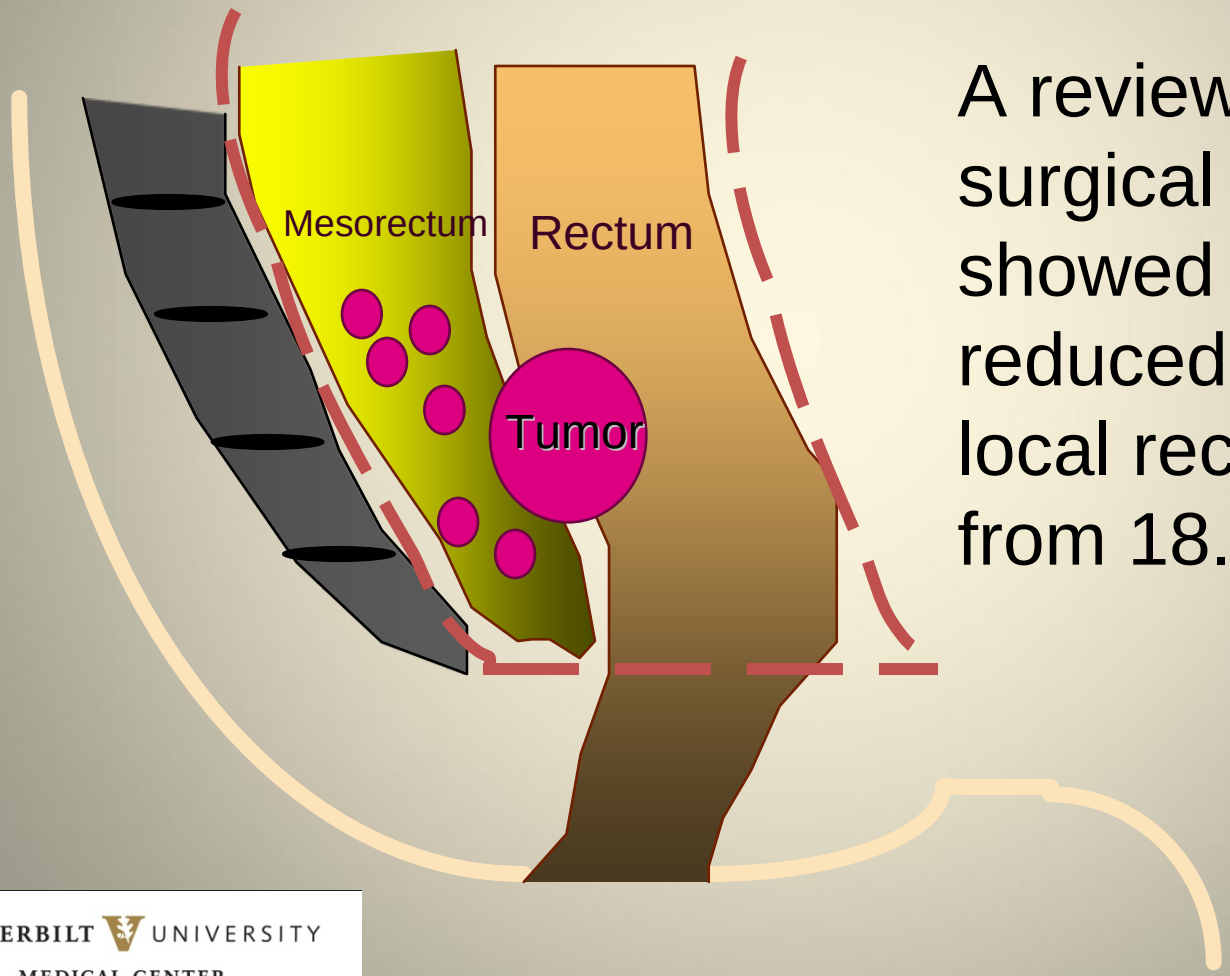
Total Mesorectal Excision



A review of 51 surgical series showed that TME reduced the median local recurrence rate from 18.5 to 7.1%.

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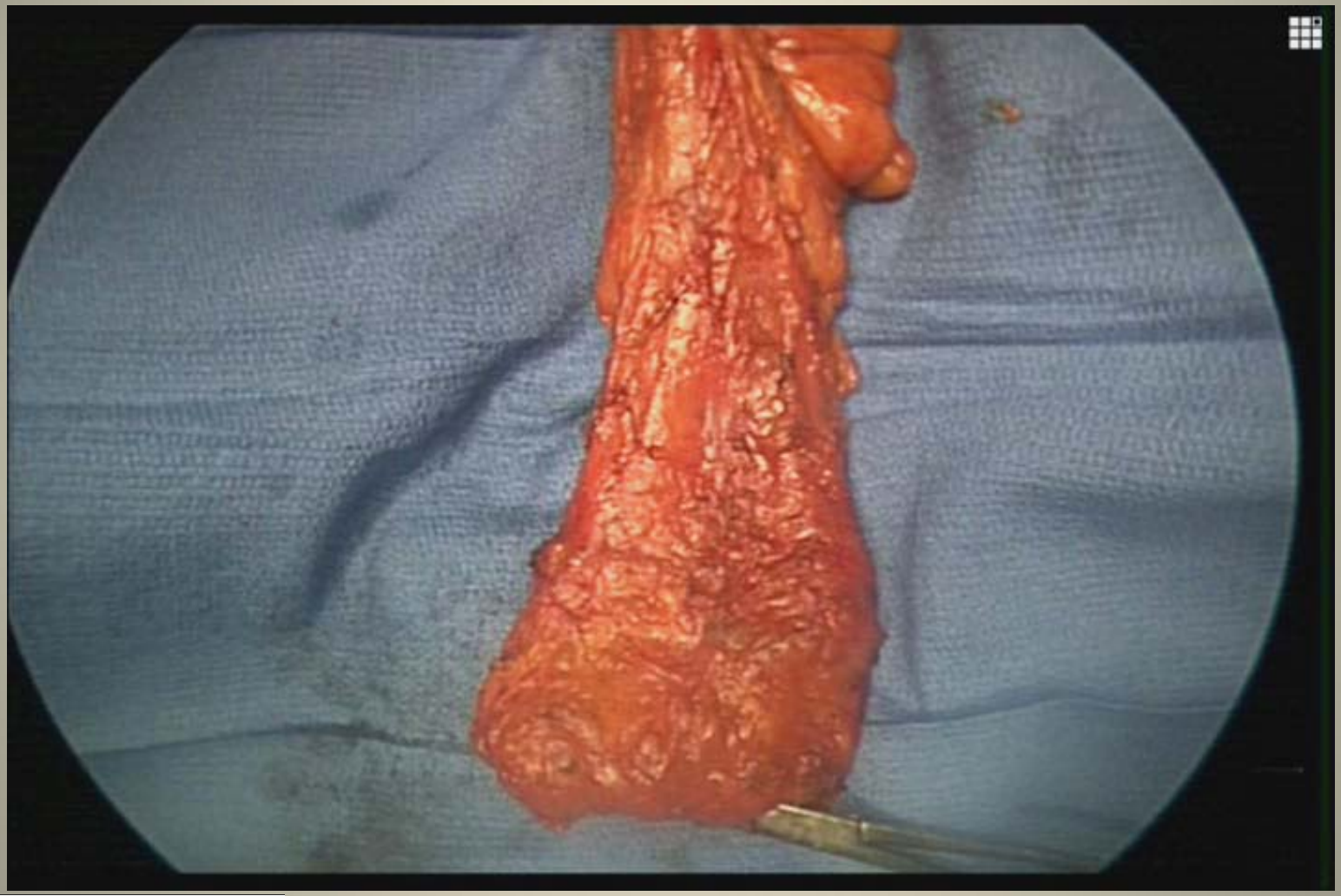
Total Mesorectal Excision



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Dutch Rectal Cancer Trial

- Prospective, Randomized, n=1748
- 2500 cGy preop XRT vs. surgery alone (TME)

- Local pelvic failure

2500 cGy + Surgery	Surgery	
2.4%	8.3%	2 years
5.8%	11.4%	5 years

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Laparoscopy for Rectal Cancer

- Laparoscopic vs. open resection for rectal cancer
  - Principles of TME-
    - Complete removal of perirectal envelope
    - Sharp dissection
    - Direct visualization
- 1 major trial, 1 underway

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UK MRC CLASICC Trial

- Prospective, randomized, experienced surgeons, colon and rectum
- n=794 overall
- n=242 rectal

- Disease free survival and local control (3 years)
  - No difference between laparoscopic and open

  - Local failure

	open	lap
• Anterior resection	7%	8%
• APR	21%	15%

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UK MRC CLASICC Trial: Concerns

- Conversion rate
  - Colectomy: 25%, and dropped
  - Proctectomy: 34%, and remained high
- Positive radial margin
  - Laparoscopic 12%
  - Open 6% (p=0.19)

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Jayne DG et al. J Clin Oncol 2007;25:3061-8

ACOSOG Z6051 trial

- American College of Surgeons Oncology Group
- 650 pts, randomized, multi-center trial of open vs. HALS resection for rectal cancer

- Currently enrolling

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Rectal Cancer Surgery

- Does local therapy have a role?
  - Less invasive, minimal morbidity and mortality
  - Must maintain goals of therapy
    - Cure
    - Local control
    - QOL factor

Rectal Cancer Surgery

- Multiple options tried
  - Two most accepted
    - Transanal resection
    - Transanal endoscopic microsurgery (TEM)
- Both accepted for unresectable polyps

Local Therapy Results

- Transanal
  - Early studies showed 4-13% local failure rate at 4 years
  - University of Minnesota-
    - Transanal local failure- 18% T1, 47% T2
      - Radical surgery pts- 0% T1, 6% T2
  - Cleveland Clinic-
    - Transanal local failure- 23% T1
- Results not explained by expected percentage of nodal disease in patient population

Local Therapy

- Failure of local therapy For T1= 18%
- Failure of local therapy of T2=47%

Table 2 Incidence of Positive Lymph Nodes in Relation to Tumor Characteristics and Pathological Findings

Tumor Characteristic	Positive Lymph Node (%)
Stage	
T1	0–12
T2	12–28
T3	36–67
Size	
< 2 cm	29
< 3 cm	17–31
< 4 cm	33–50
Differentiation	
Well	25
Moderate	33
Poor	77

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TEMS

- Due to the observed failure of transanal excision, TEMS was developed
  - Better surgery=better results= decreased local failure
- Benefits of TEM vs. transanal
  - Better visualization
  - Able to address lesions from anus to rectosigmoid junction

TEM Results

- TEM results for T1 are better, except in "high risk" cancers
- In poorly matched reviews, was called "equivalent" to radical surgery

Table 2 TEM in pT1 rectal adenocarcinomas: oncological results

Authors	No. of patients	Local recurrence rate (%)	5-year survival rate (%)
Borschitz (2006) [21]	Low-risk – 89	6	89[a]
	High-risk – 21	39	93[b]
Heintz (1998) [19]	Low-risk – 46	4.3	79
	High-risk – 12	33	62
Floyd (2006) [28]	53	7.5	100
Lee (2003) [23]	52	4.1	100
Stipa (2006) [22]	48[c]	8.7	100
Bretagnol (2007) [30]	31	9.6	81
Winde (1996) [20]	24	4.2	96

[a]10-year cancer-free survival
[b]10-year cancer-free survival after reoperation
[c]Includes Tis and T2 lesions

Dias et al. Tech coloproctol. 13:105-111 (2009)

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TEMs Results

- T2 lesions-
  - Lee et al- TEM- 19.4% local failure rate, vs. 9%
  - Borschitz et al.- TEM 29% local failure
    - 50% failure in the subset with “high risk features”
  - Overall TEMS not standard therapy for T2 lesions

TEMs and neoadjuvant Tx

- Lezoche et al-
  - 103 pts with T2, T3 NO cancer
  - Neoadjuvant treatment
  - Then TEM for surgical treatment
- Local failure rate- 5% at 55 months
- Cancer specific survival was 89% at 90 months

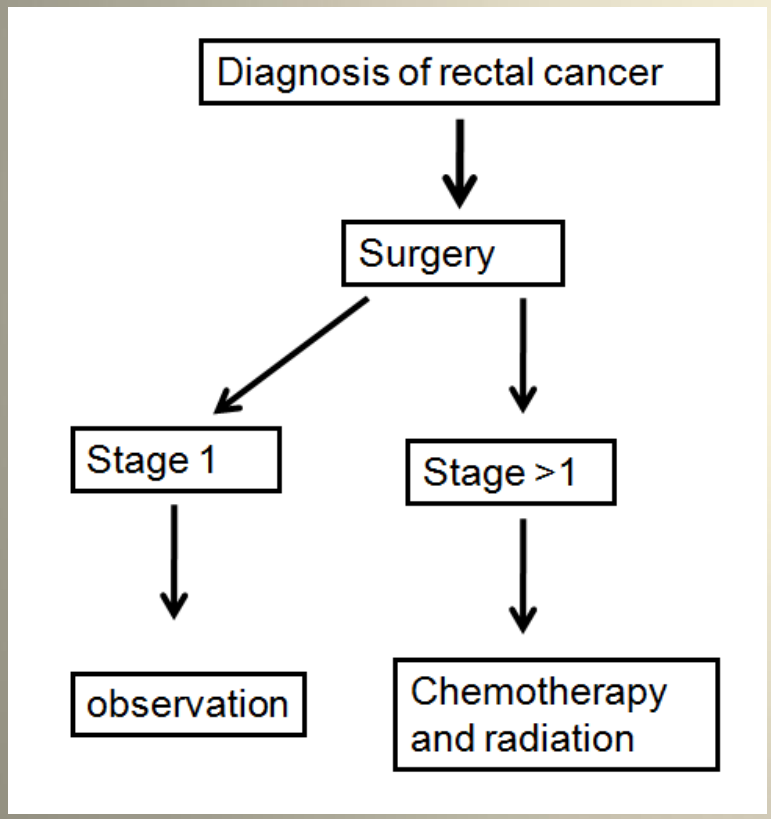
TEMs and neoadjuvant Tx

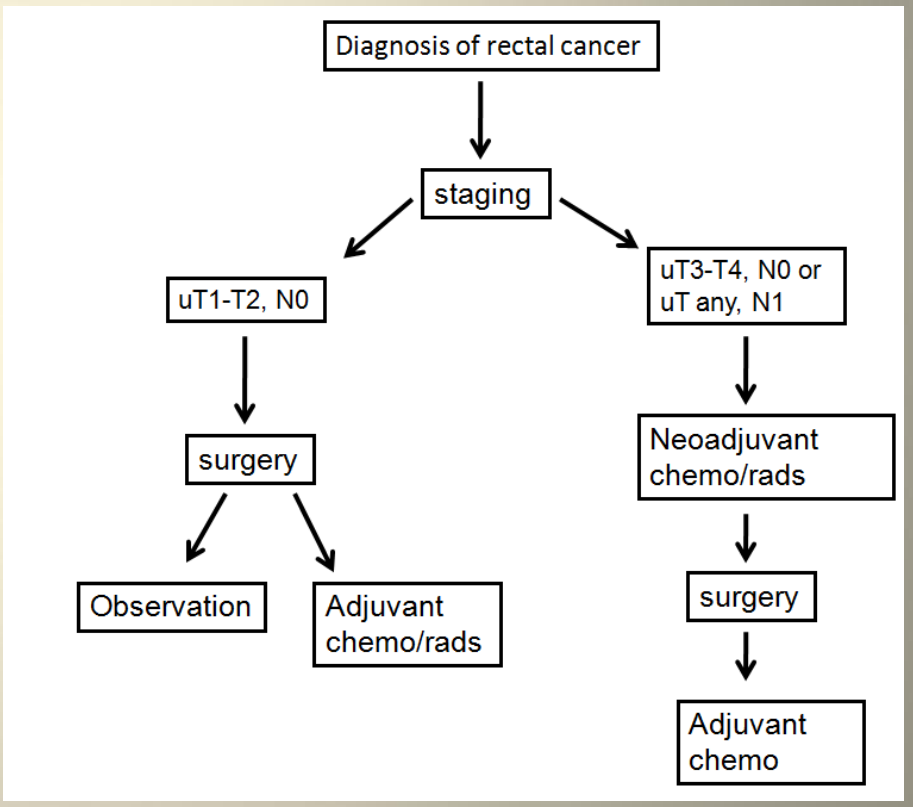
- Radiation is not free
  - Local excision + Radiotherapy
    - Rectum left in situ: fibrosis, poor compliance
  - Neoadjuvant Radiotherapy + Proctectomy/Coloanal
    - Native rectum removed
- Functional outcomes no different comparing local excision and radiation to proctectomy and coloanal anastomosis

Akbari R, Read TE et al. ASCRS. 2008

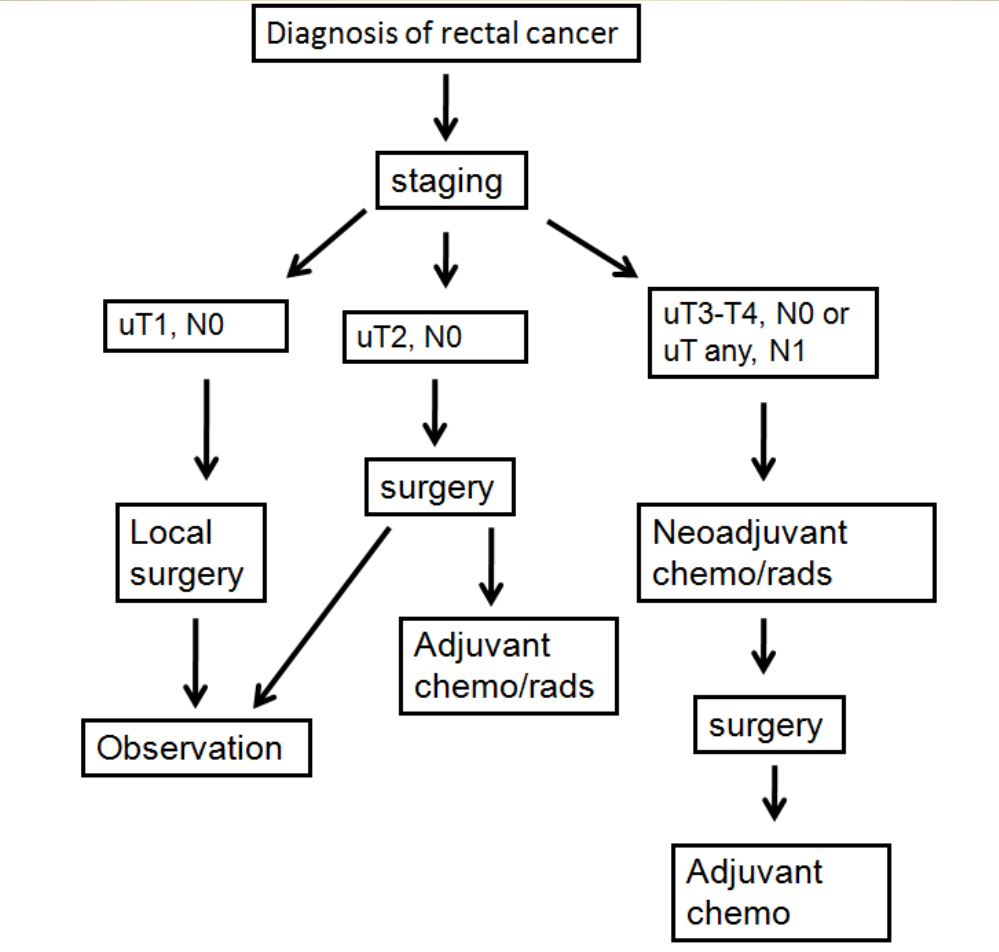
How do we currently treat rectal cancer?

Rectal Cancer Algorithm





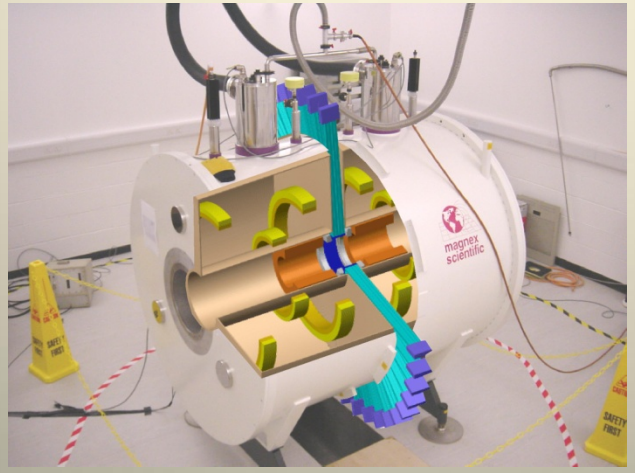
Rectal Cancer Algorithm



What is the future of rectal cancer?

Staging

- MR/PET- increased detection of nodal disease
- Genetic analysis- better risk stratification of tumors that are more likely to have nodal/metastatic spread
- ??



Kim SK, et al. European Journal of Cancer. 45(12):2103-9, 2009 Aug.

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Surgery

ORIGINAL CONTRIBUTION

Total Mesorectal Excision for Rectal Cancer: The Potential Advantage of Robotic Assistance

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PURPOSE: The purpose of this study was to analyze the safety, feasibility, and efficacy of the da Vinci S HD robotic system in mesorectal excision for rectal adenocarcinoma, with the aim to identify areas of potential advantage for the robot in this procedure.

METHODS: This study was conducted as a retrospective review of a prospectively maintained database of 44 consecutive cases of robot-assisted mesorectal excision for rectal adenocarcinoma performed between August 2005 and February 2010. Patient demographics, perioperative outcomes, and complications were evaluated and compared with similar published reports and relevant literature.

RESULTS: There were 28 (63.6%) men and 16 (36.4%) women, with a mean age of 63 years. The majority of patients were either overweight or obese and 88.7% of lesions were in the mid or low rectum. We performed 36 low anterior resections (6 intersphincteric) and 8 abdominoperineal resections with a median blood loss of 150 mL (range, 50–1000), a median operative time of 347 minutes (range, 155–510), and a median length of stay of 5 days (range, 3–36). The median lymph node yield was 14 (range, 5–45) and the circumferential resection margin was negative in all patients. We had 1 distal margin positivity (2.7%), 2 anastomotic leaks (5.6%), 1 death (2.7%), and 2 conversions (4.5%) to the open approach. No robot-associated morbidity occurred in this series.

CONCLUSIONS: This series compares favorably with similar published reports with regard to the safety and feasibility of robotic assistance in total mesorectal excision for rectal cancer. The lower conversion rates reported for robotic rectal resection compared with laparoscopy require validation in large randomized trials.

KEY WORDS: Robotic surgery; da Vinci robot; Robot-assisted surgery; Total mesorectal excision; Rectal cancer; Obesity.

The past few years have seen the rapid acceptance and utilization of robotic assistance in a variety of surgical specialties.[1] This is because the da Vinci robotic system offers a number of advantages compared with conventional laparoscopy, greatly enhancing surgical dexterity and precision. The surgeon is comfortably seated at the console and is empowered with 7 degrees of freedom through endowristed instruments that are controlled by ergonomically designed finger grips.

In pelvic procedures, the restricted degrees of freedom of current laparoscopic instruments make retraction and precise dissection cumbersome and time consuming. It is here that the endowristed instruments, 3-dimensional imaging, and fixed third-arm retraction of the da Vinci robotic system are most beneficial, making pelvic surgery ideally suited for robotic assistance.

Unlike other surgical specialties, the majority of colorectal procedures involve more than one abdominal quadrant. This limits the application of the da Vinci robot, which, in its current version, has a limited range of movement of the arms for a fixed position of the robotic cart. A

Financial Disclosures: Dr Prasad received honoraria from Intuitive Surgical, Ethicon, and Covidien and fellowships from Ethicon and Covidien. The remaining authors have no relevant disclosures.

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Dis Colon and Rectum, 12/2010

Treatments

- Better chemotherapy agents
  - Sensitizers for radiotherapy
- Short course radiation therapy pre-op
- Elimination of traditional “whole pelvis” radiation for radiotherapy aimed at the rectum/mesorectum

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Future of rectal cancer

- Algorithm gets more “individualized” and more complex
- Better staging=less invasive surgery
- Expanded use of neoadjuvant therapies

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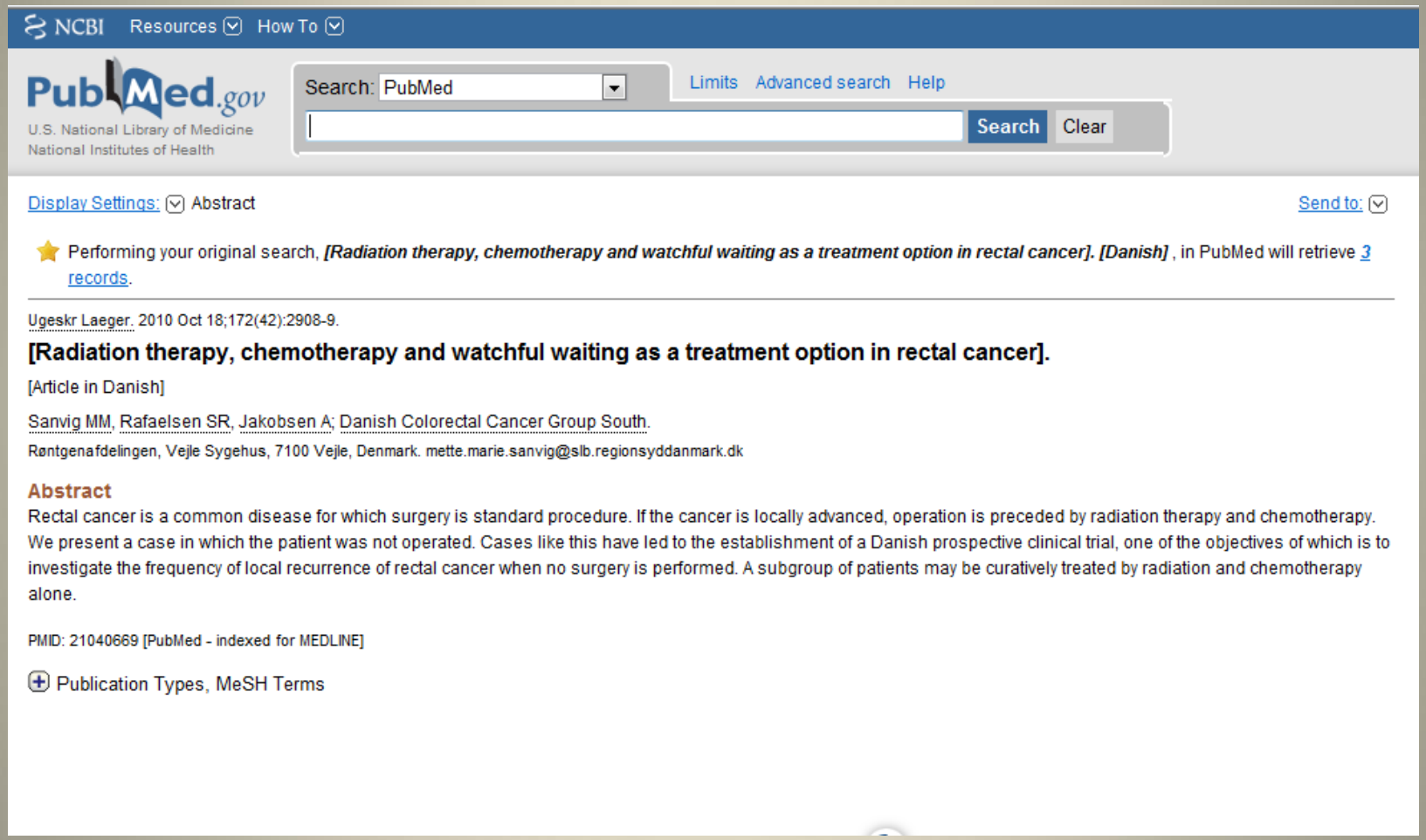
Crazy?



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Ugeskr Laeger. 2010 Oct 18;172(42):2908-9.

[Radiation therapy, chemotherapy and watchful waiting as a treatment option in rectal cancer].

[Article in Danish]

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Abstract

Rectal cancer is a common disease for which surgery is standard procedure. If the cancer is locally advanced, operation is preceded by radiation therapy and chemotherapy. We present a case in which the patient was not operated. Cases like this have led to the establishment of a Danish prospective clinical trial, one of the objectives of which is to investigate the frequency of local recurrence of rectal cancer when no surgery is performed. A subgroup of patients may be curatively treated by radiation and chemotherapy alone.

PMID: 21040669 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms

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