



COH Phoenix February 23-24, 2024

**Advances and Innovations in Endoscopic Oncology
And Multidisciplinary GI Cancer Care**

Optimal Multidisciplinary GI Cancer Staging Evidence-Based Approach to Rectal Cancer

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Disclosures

- Intuitive Surgery Inc: Proctoring Honoraria
- McGraw-Hill Publisher: Author royalties

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed [Assembly Bill \(AB\) 1195](#), which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed [AB 241](#), which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

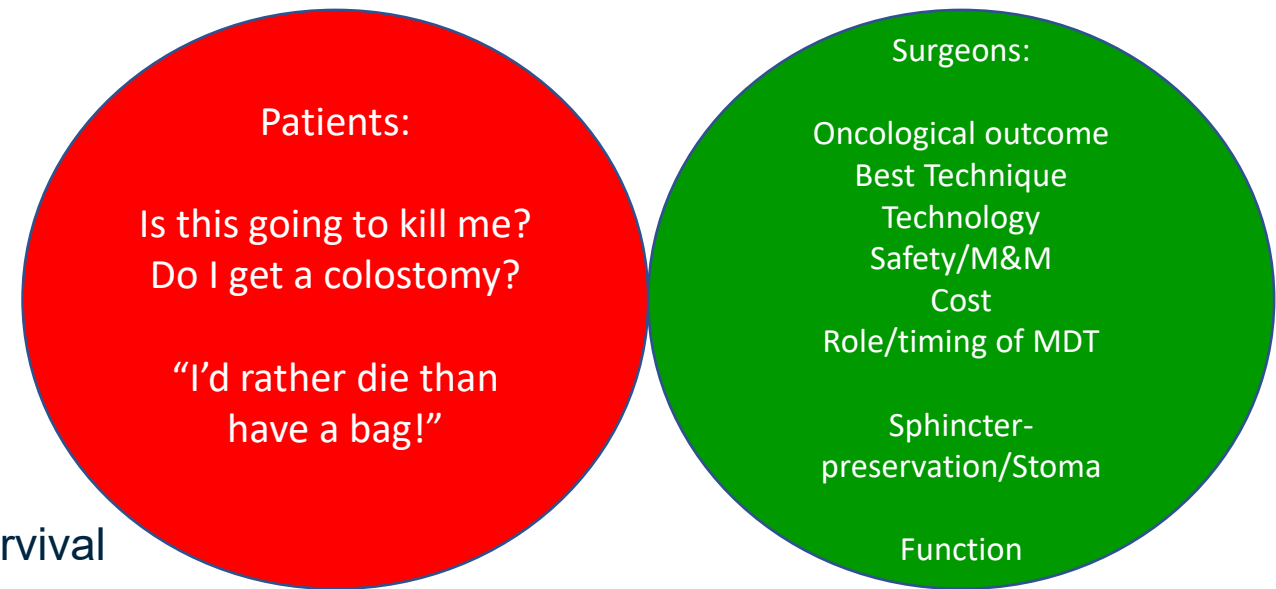
Address how to overcome obstacles to multidisciplinary staging of rectal cancer

Rectal Cancer – Terminology

COLOR II/III
Clinical Complete Response (cCR)
Local Excision
Short-course radiation
Watch & Wait (WW)
MRI staging
ESD
1-2cm
Tumor regression score (TRG)
TATA
LN ≥ 12
Anal verge
Habr-Gama
Lateral Pelvic LN Dissection
FAP "Holy plane"
Stable QoL
Disease (SD)
Colostomy
Dutch trial
Progressive Disease (PD)
1mm
Response Evaluation Criteria in Solid Tumors (RECIST)
Partial Response (PR)
Intact mesorectal envelope
Pathological Complete Response (pCR)
TAMIS
DLI
CRM
TNT
TME
Long-course radiation
IBD
EMR
Sphincter preservation
ELAPE
Stage I
Mesorectum
Obstruction
Distal Resection Margin (DRS)
TaTME
ROLARR
TME
Long-course radiation
IBD
EMR
Stage IV
pCR
APR
TEMS
RLO
12-15cm
Non-inferiority

Purpose of Staging

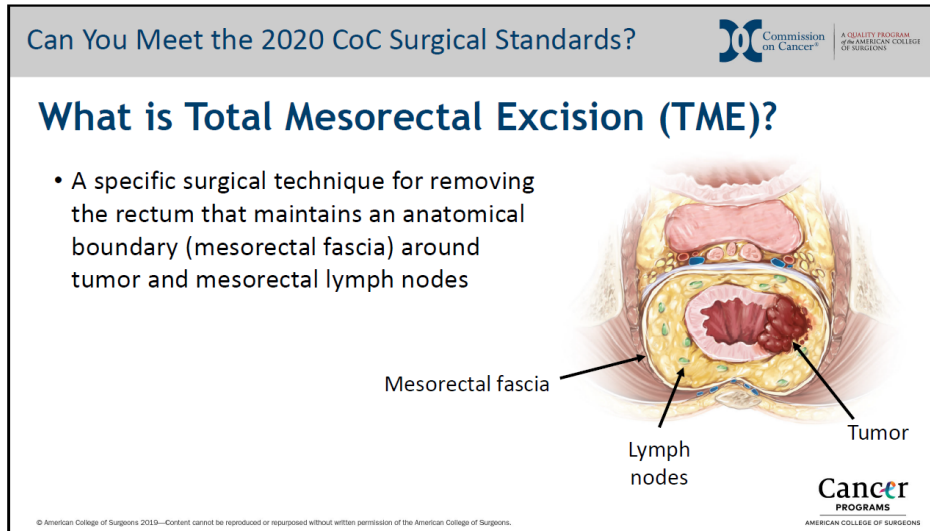
- Establish comparability by means of accurate staging
- Assess treatment strategy in curative intent
 - Surgery alone
 - 1) Abdominal(pelvic surgery
 - 2) Endoluminal surgical intervention (ELSI)
 - Multimodality treatment
 - 1) Standard neoadjuvant → Surgery → Chemo
 - 2) TNT → Surgery
 - 3) PROSPECT → Surgery
- Develop treatment strategy in palliative intent
- Assess probability and function of stoma-free survival
- Monitoring in Watch & Wait
- Assess prognosis



Rectal Cancer - Surgical default

Default = Oncological resection (TME)

- Complete or partial sphincter preservation
- Abdominoperineal resection (permanent colostomy)



Alternatives (in select patients):

- Endoluminal local excision (no lymphadenectomy)
- Watch and wait after neoadjuvant treatment
- Diversion

Default (=first to come to mind, typical choice) ≠ “standard of care”



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OF SURGEONS



Rectal Cancer Surgery – Technique Matters

TME = Specimen-oriented resection under visual control:

- Intact mesorectal compartment (respecting embryological plains, smooth external appearance)
- No specimen waist
- >12 LN
- R0 resection, negative CRM >1mm, adequate proximal and distal margin
- Meticulous MDT documentation including imaging, pathology, pre-treatment testing, genetics ...

N Engl J Med: Local Recurrence Rates with vs w/o XRT 1997 → 2001 (2006)

- Swedish Rectal Cancer Trial (1168 patients): **27%** vs 11%
- Dutch trial (1861 randomized patients 1996-1999):
8.2% vs 2.4% (3 yrs), **10.9%** vs 5.6% (6 years)



TME



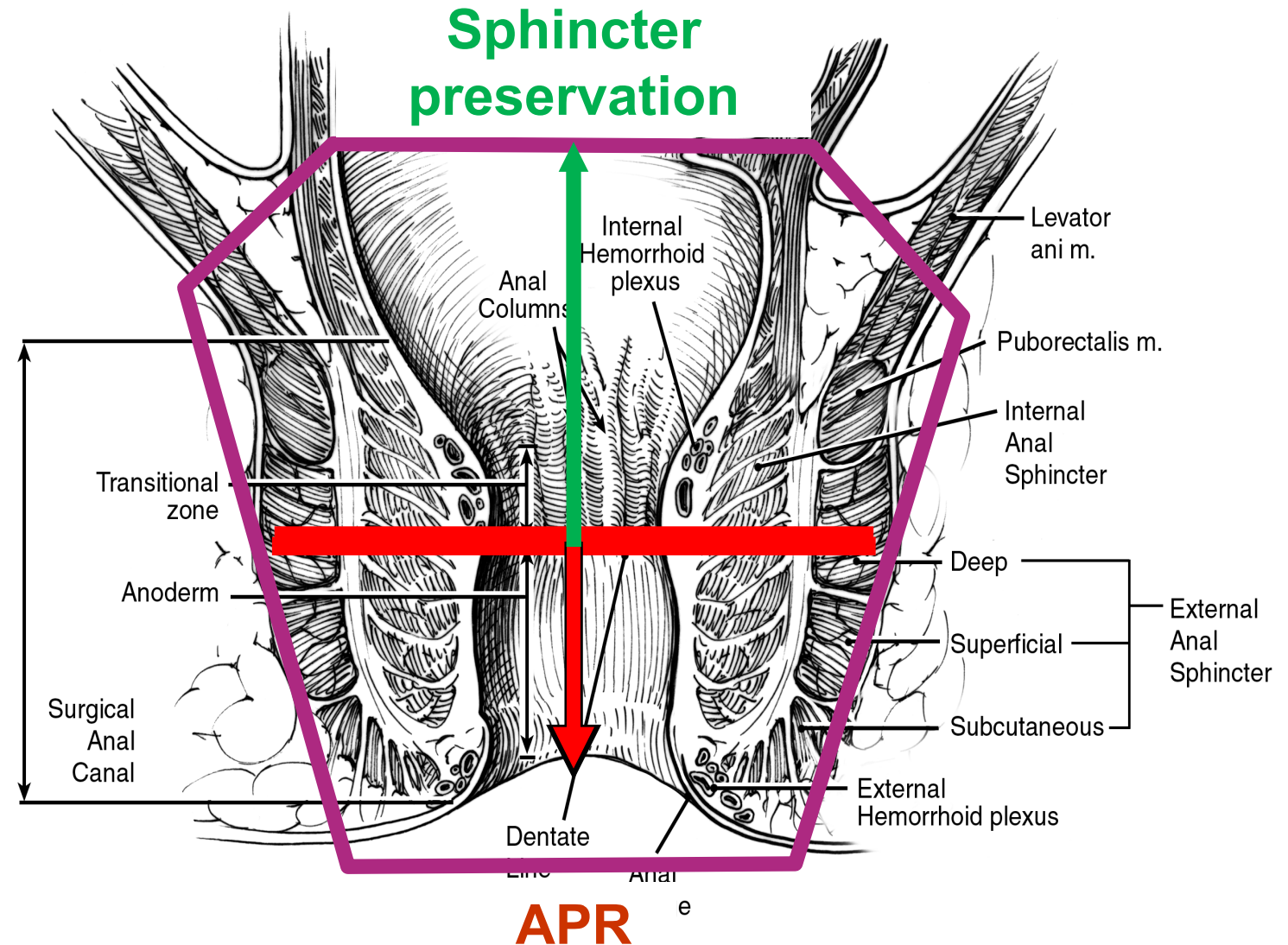
TME as standard

L Pahlman – NEJM 1997
Kapiteijn E – NEJM 2001
Peeters KCMJ – Ann Surg 2007

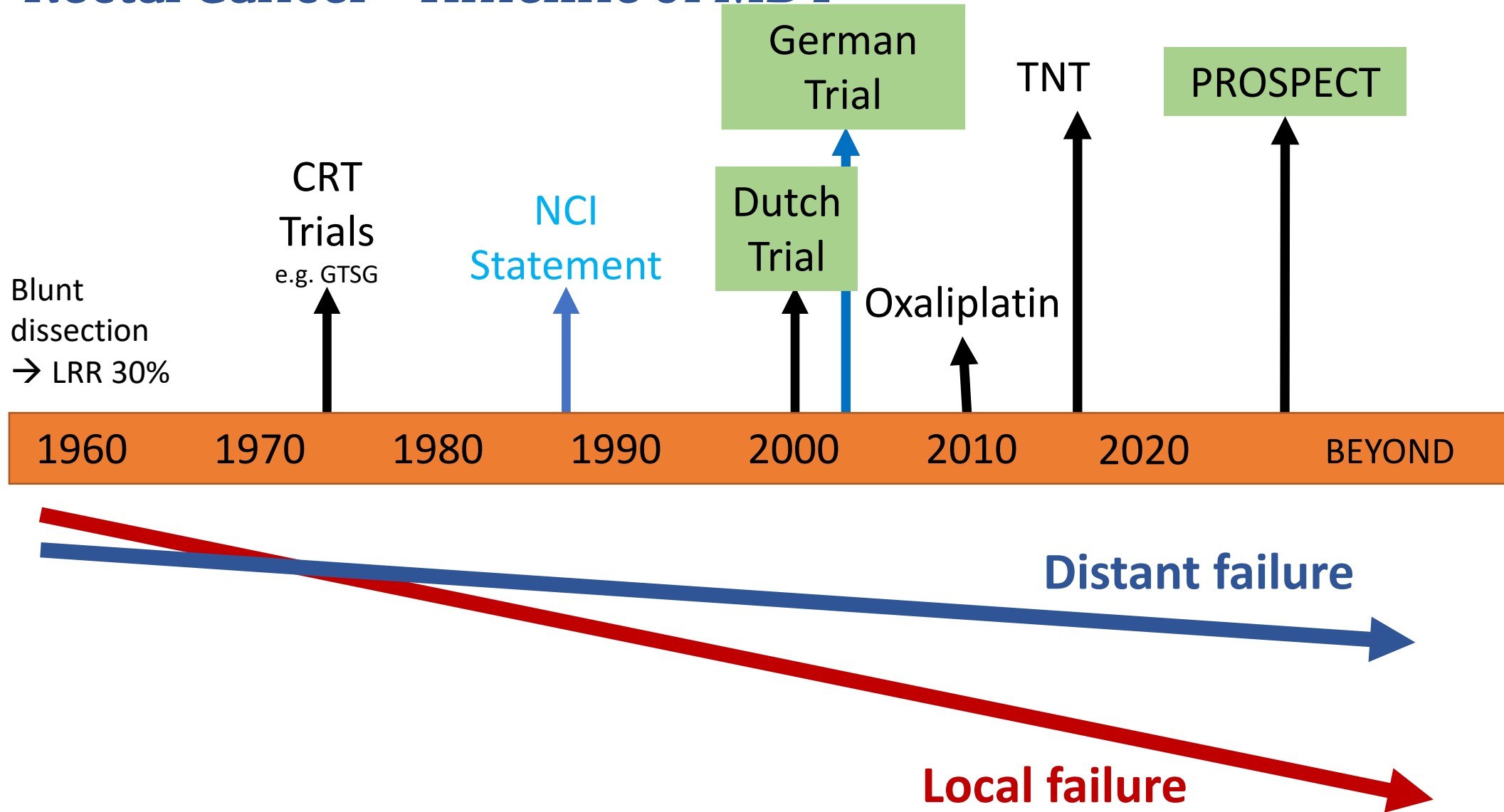
Rectal Cancer Surgery

Extent of surgery depends on:

- Stage / size
- Acuity of presentation
- Level of tumor
- Underlying pan-colonic disease
 - Hereditary cancer
 - IBD
- Patient performance
- Patient input
- **Surgeon's skills**
- **MDT**



Rectal Cancer - Timeline of MDT

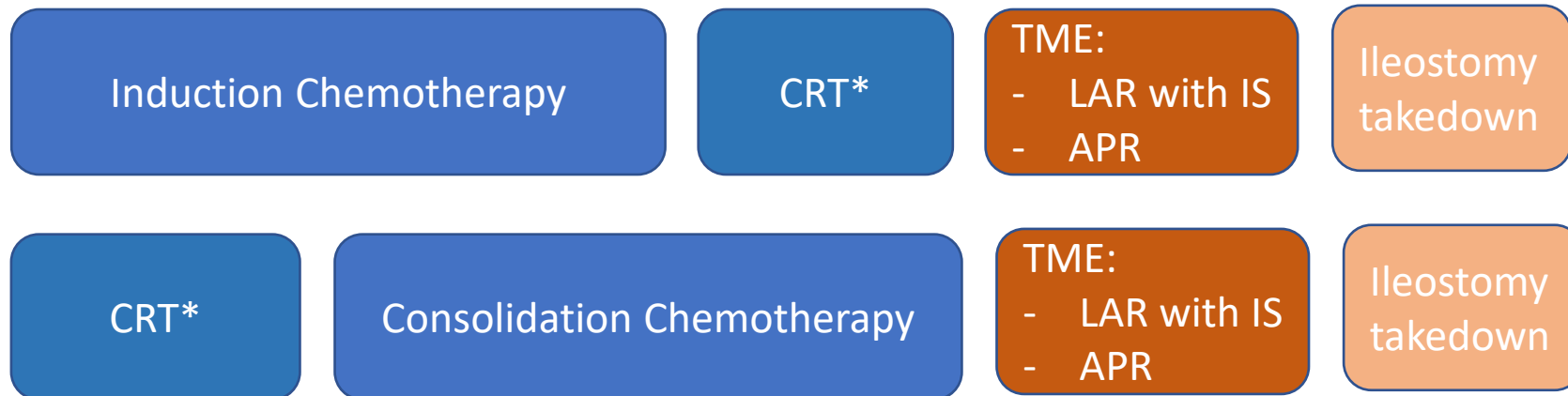


Rectal cancer - Multi-Disciplinary Treatment

➤ Traditional Treatment



➤ Total Neoadjuvant Treatment (TNT)



*CRT: Long-course 50.4 Gy vs short-course 5x5 Gy

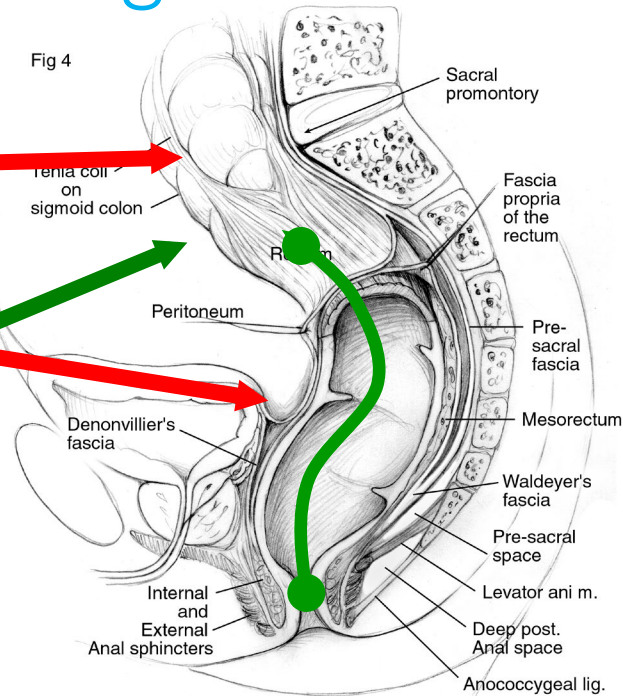
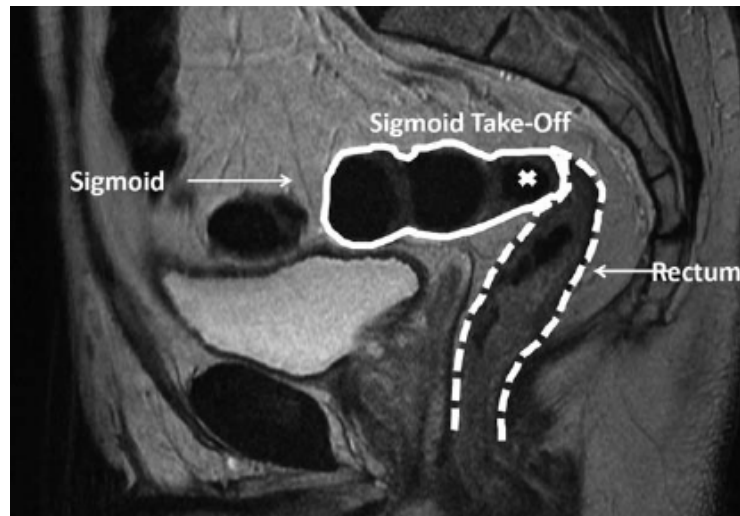
Defining the Rectum – Changing to “the Sigmoid Takeoff”?

➤ Obsolete definitions:

- Sacral promontory
- Peritoneal reflection

➤ USA: 2 most commonly used definitions:

- Coalescence of the tenia
- NCI: rigid 12cm (-15cm) proximal to anal verge



Kaiser AM – Surg Clin N Am. 2002

SURGICAL PERSPECTIVE

Definition of the Rectum

An International, Expert-based Delphi Consensus

*N D'Souza et al – Ann Surg 2019 (Dec)
Mathis KL & Nelson H – Ann Surg 2019*

11 choices:

- MRI most preferred

Validation pending
Ambiguity persistent

Parameters of Staging for Rectal Cancer

- Level of the tumor in relation to pelvic floor and sphincter complex
- TNM stage
- Size and % of involved luminal circumference
- CRM
- mrLRP
- Negative features

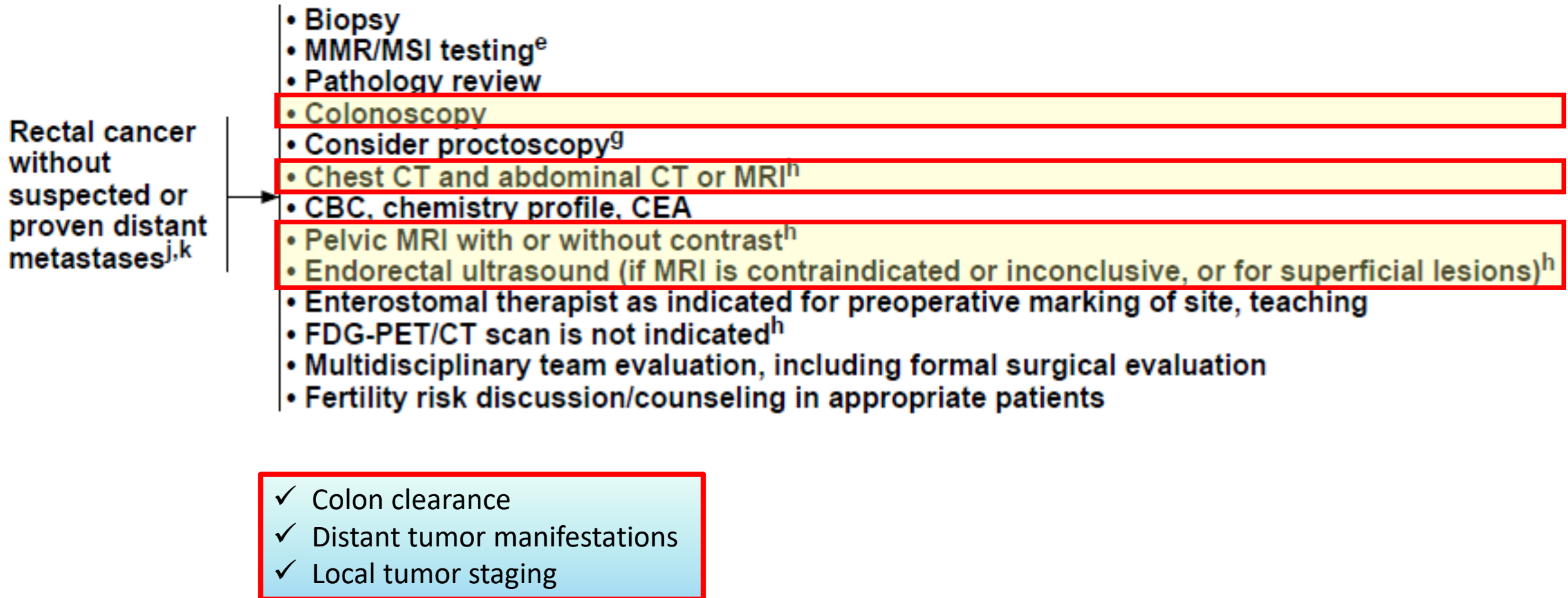
Goal for staging:

Tailored management

Avoid under-treatment

Avoid over-treatment

Rectal cancer treatment starts with staging

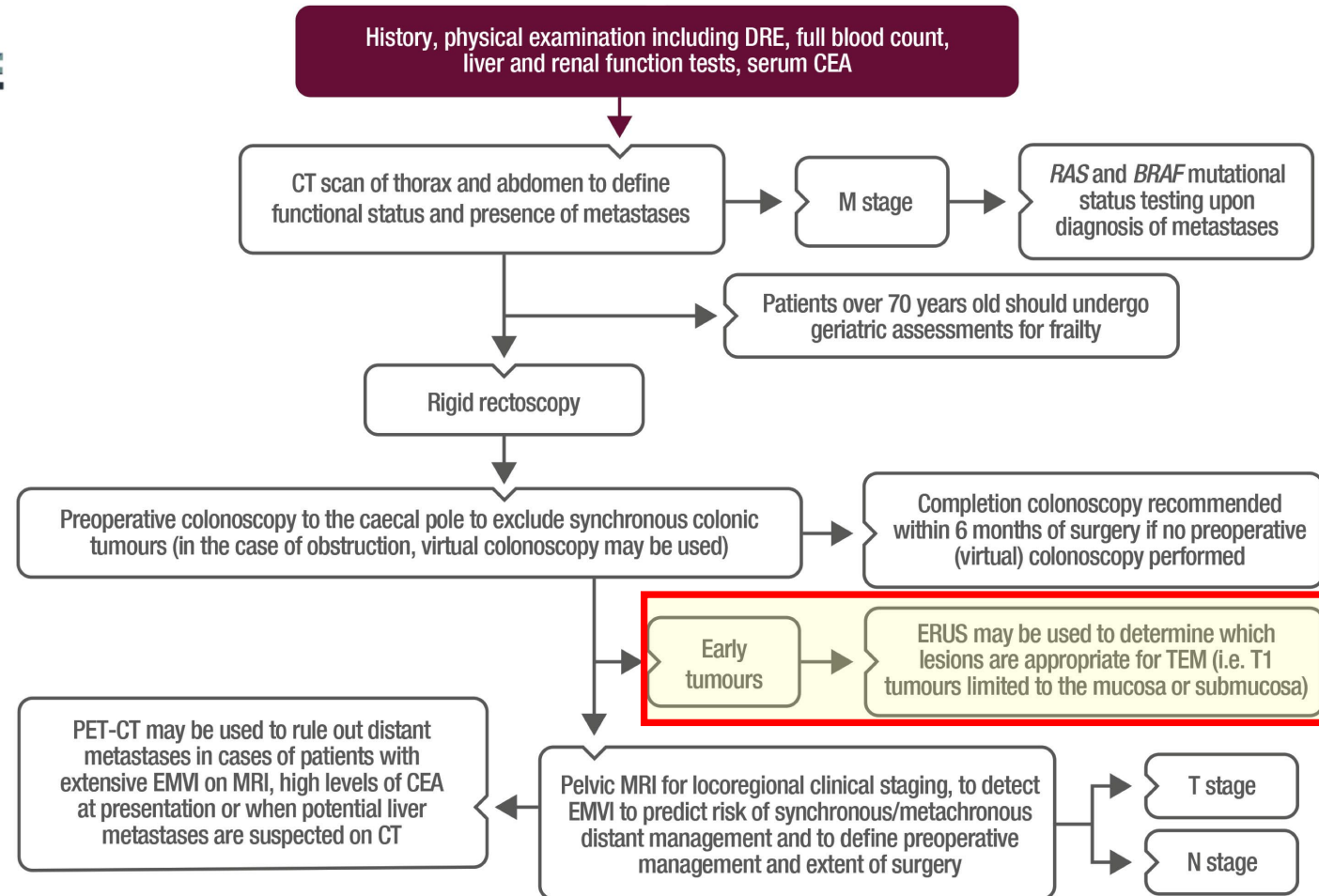


Rectal cancer treatment starts with staging

CLINICAL PRACTICE GUIDELINES

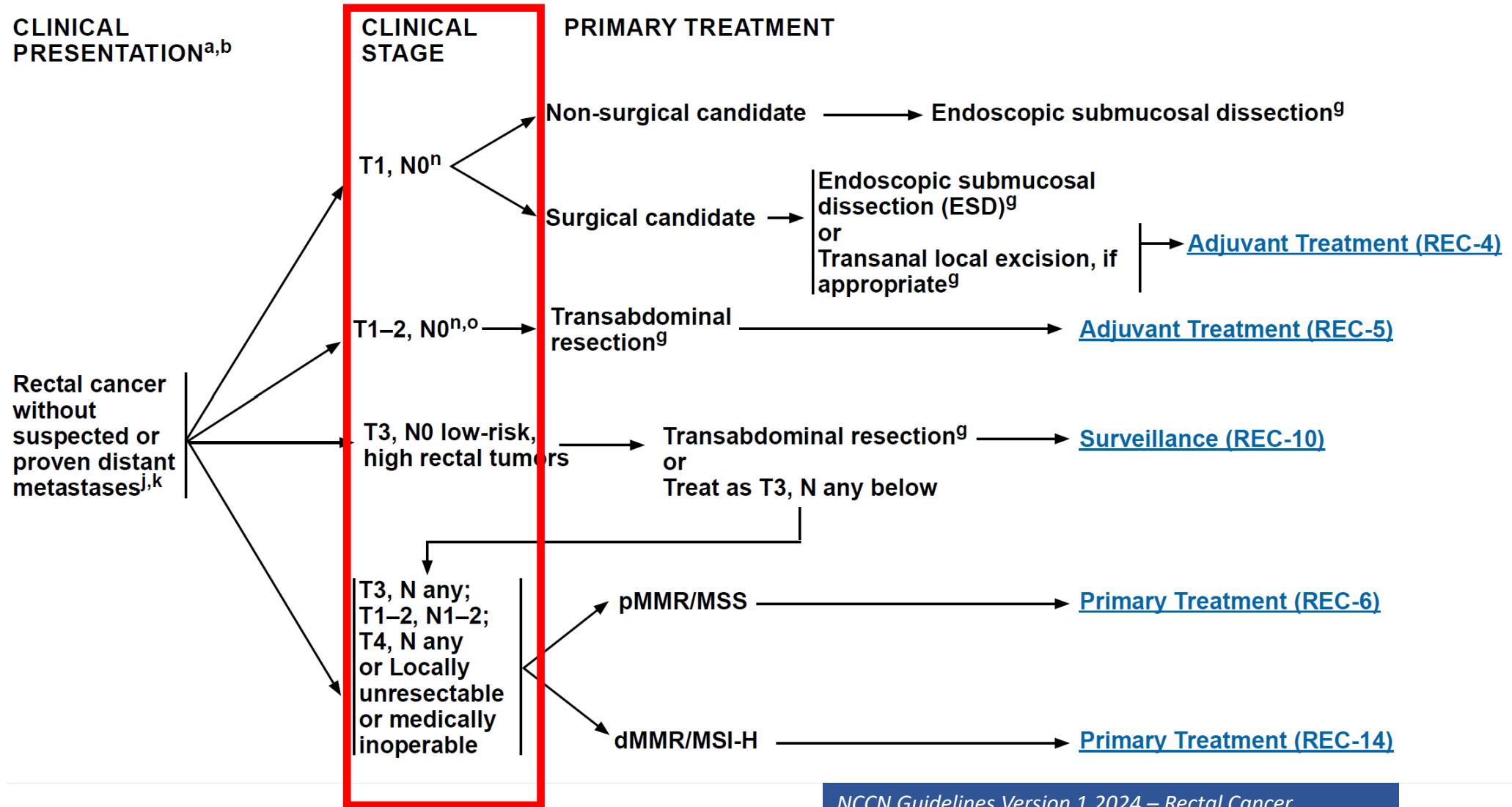
Staging and risk assessment

Management should be by an MDT of radiologists, surgeons, radiation oncologists, medical oncologists and pathologists



© 2018 ESMO. All rights reserved. esmo.org/Guidelines/Gastrointestinal-Cancers/Rectal-Cancer

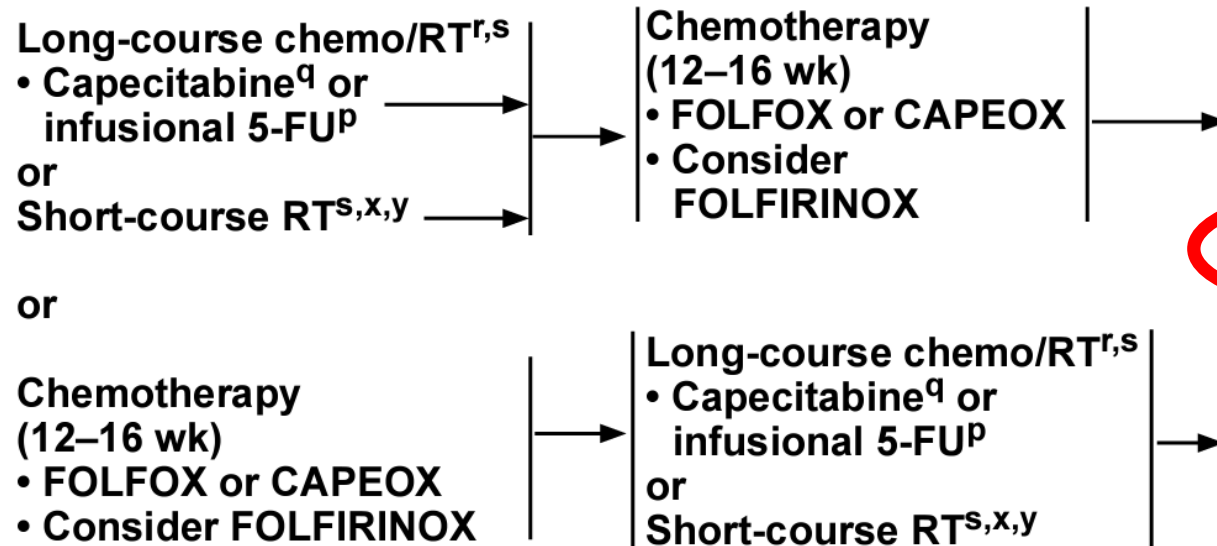
Rectal cancer treatment starts with staging



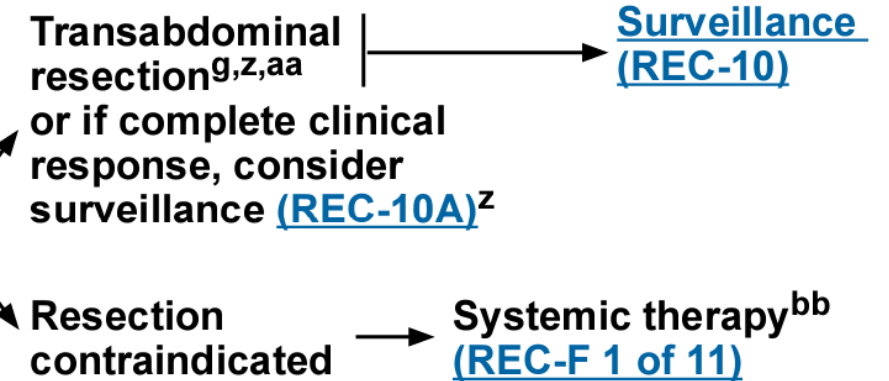
NCCN Guidelines Version 1.2024 – Rectal Cancer

Rectal cancer treatment starts with staging

TOTAL NEOADJUVANT THERAPY^w



PRIMARY TREATMENT



Rectal Cancer Staging

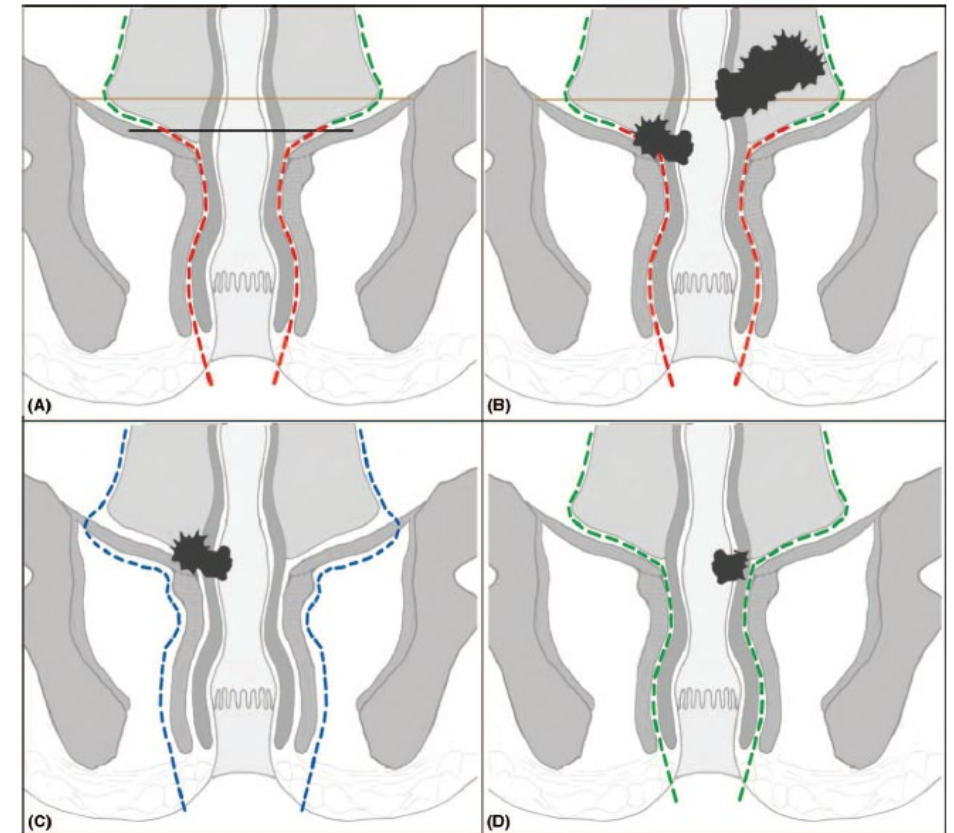
- Clinical local exam
- Full colonic evaluation
- CT chest/abdomen/ pelvis with oral/iv (poss rectal contrast)

- Pelvic MRI with rectal contrast:
 - Nodal disease
 - CRM
 - EMVI
 - Depth of EMI ($>5\text{mm}$ vs $\leq 5\text{mm}$)
 - mrLRP ($<6\text{cm}$)

- Optional:
 - ERUS: early lesions
 - PET: not routine, only specific indication

Prospective Validation of a Low Rectal Cancer Magnetic Resonance Imaging Staging System and Development of a Local Recurrence Risk Stratification Model

The MERCURY II Study



Battersby NJ, ..., Brown G – Ann Surg 2016

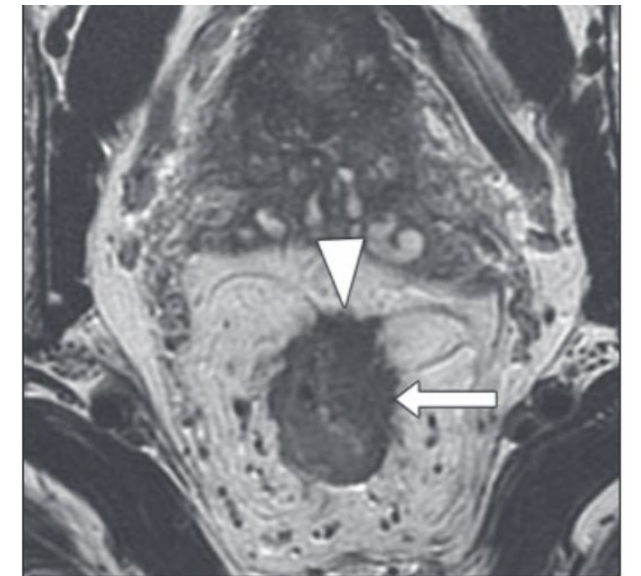
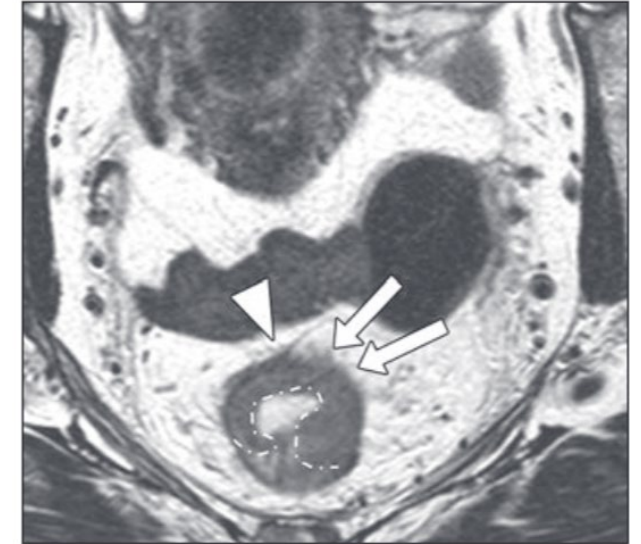
Rectal Cancer Staging

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- Pelvic MRI with rectal contrast:

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- CRM
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- Depth of EMI ($>5\text{mm}$ vs $\leq 5\text{mm}$)
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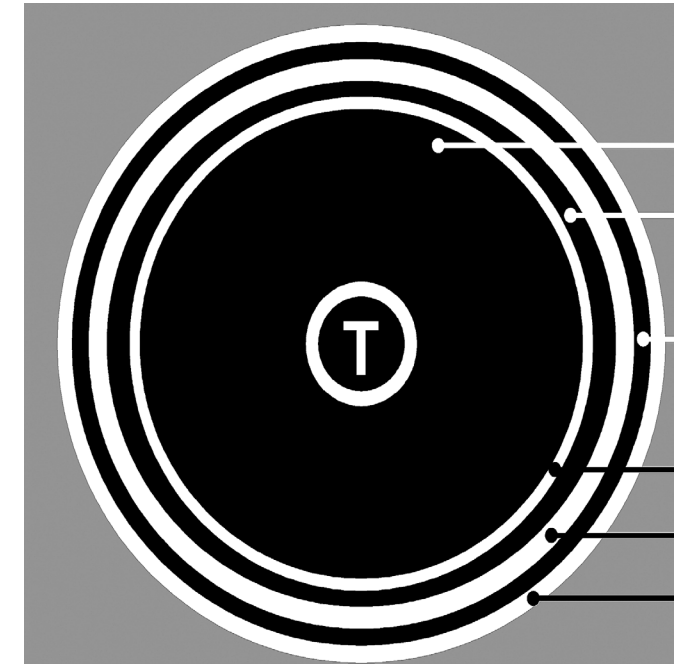
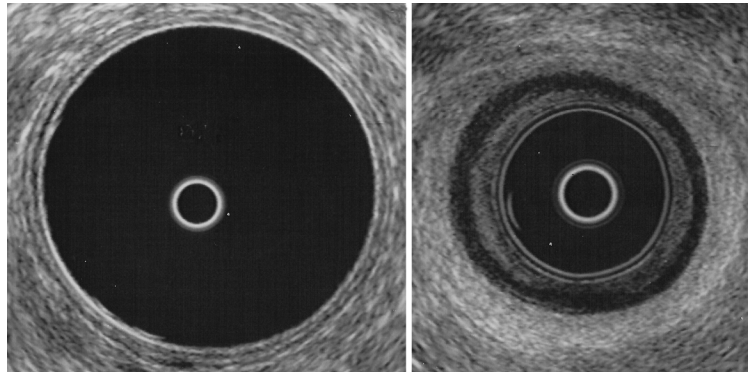


Kaur H – Am J Roentgenol 2021

Rectal Cancer Staging - ERUS

Primary lesion: distortion of the rectal wall; depth, axial and circumferential size:

- uT0 or T1: thickening of black-2, intact of white-2.
- uT2: interruption of white-2, no indentation into white-3.
- uT3: interruption of white-2, indentation of tumor fingers into white-3.
- uT4: blurring of the plane toward prostate, distortion of sphincter complex.

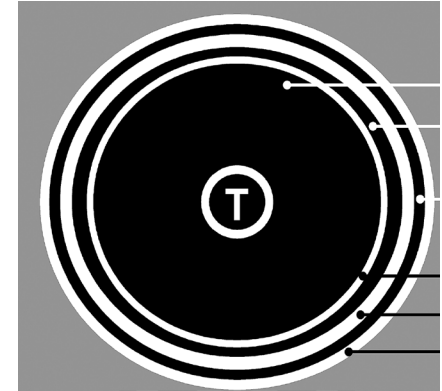
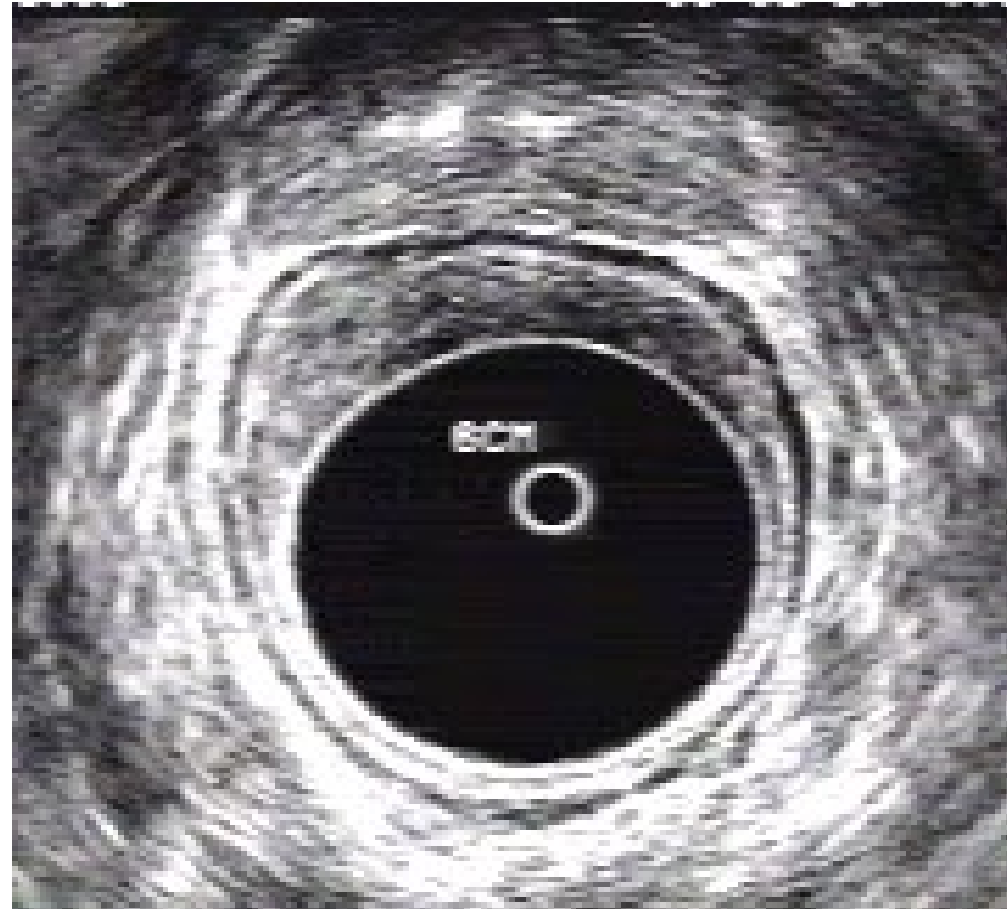


From: Kaiser AM – MGH Manual Colorectal Surgery

Rectal Cancer Staging - ERUS

Thickening of hypoechogenic first black-1 layer

Intact middle white line

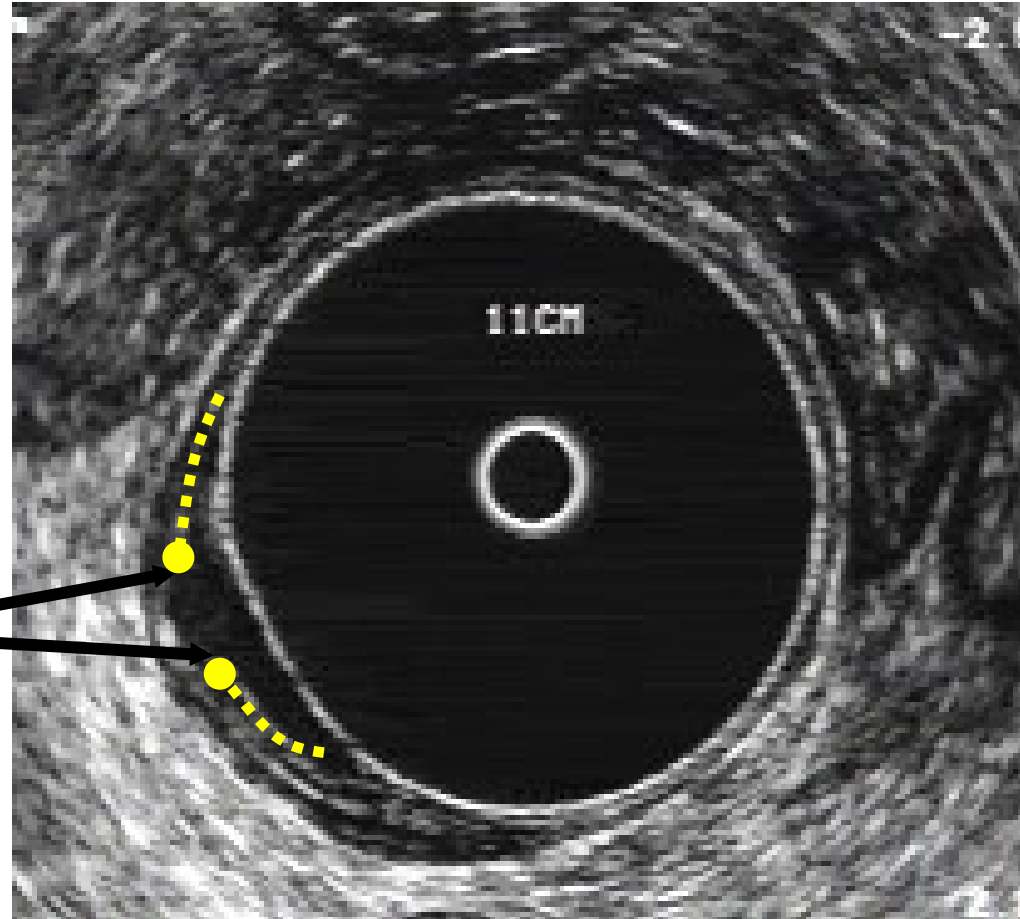


Adeno-Ca in anterior quadrant,
consistent with uTiS/T1 uN0

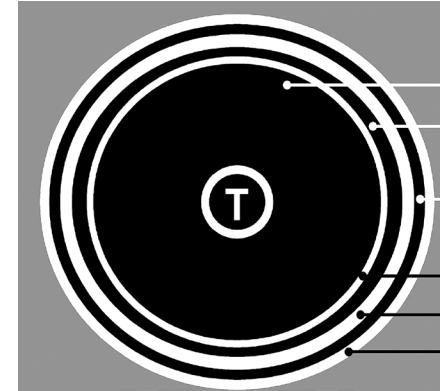
From: Kaiser AM – MGH Manual Colorectal Surgery

Rectal Cancer Staging - ERUS

Central interruption
of middle white line



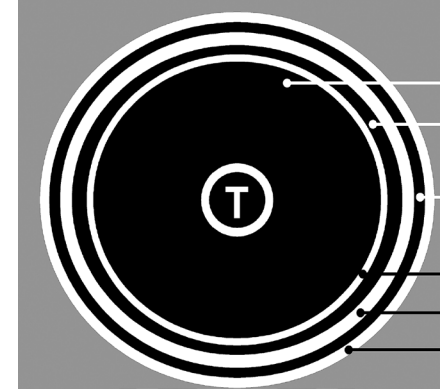
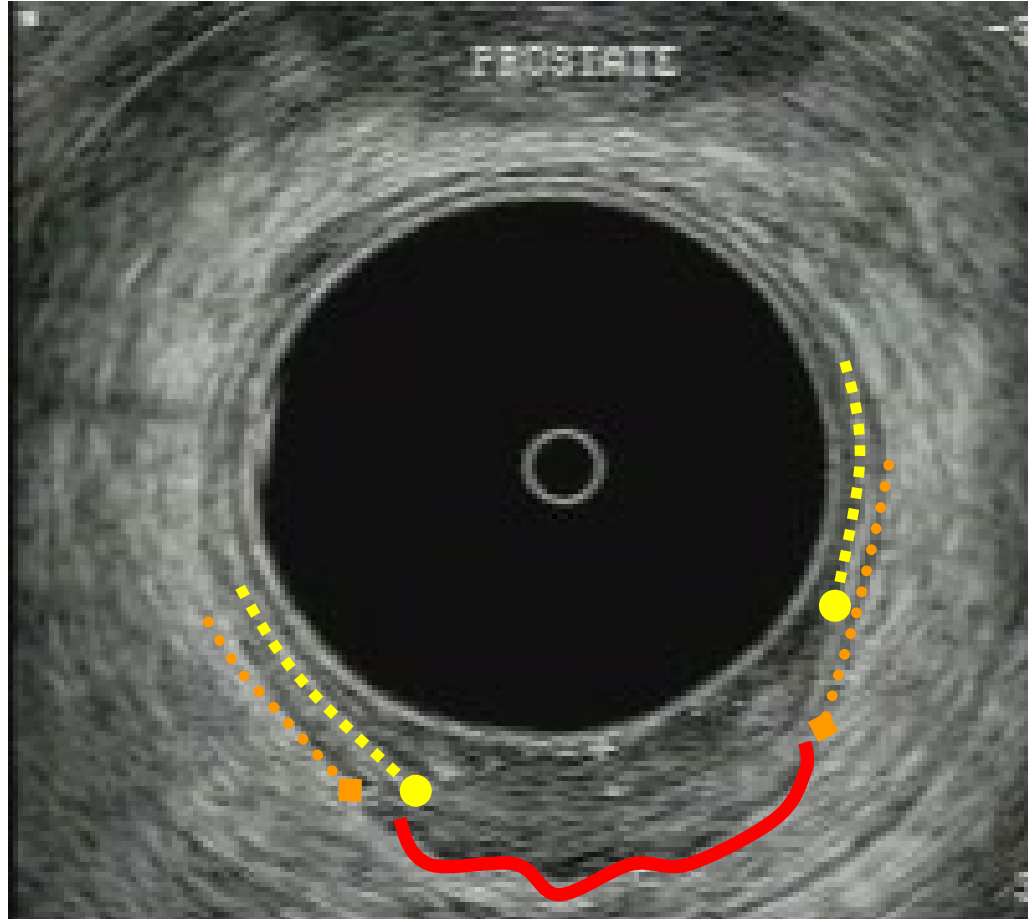
Adeno-Ca in right posterior quadrant,
consistent with uT2 uN0



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Rectal Cancer Staging - ERUS

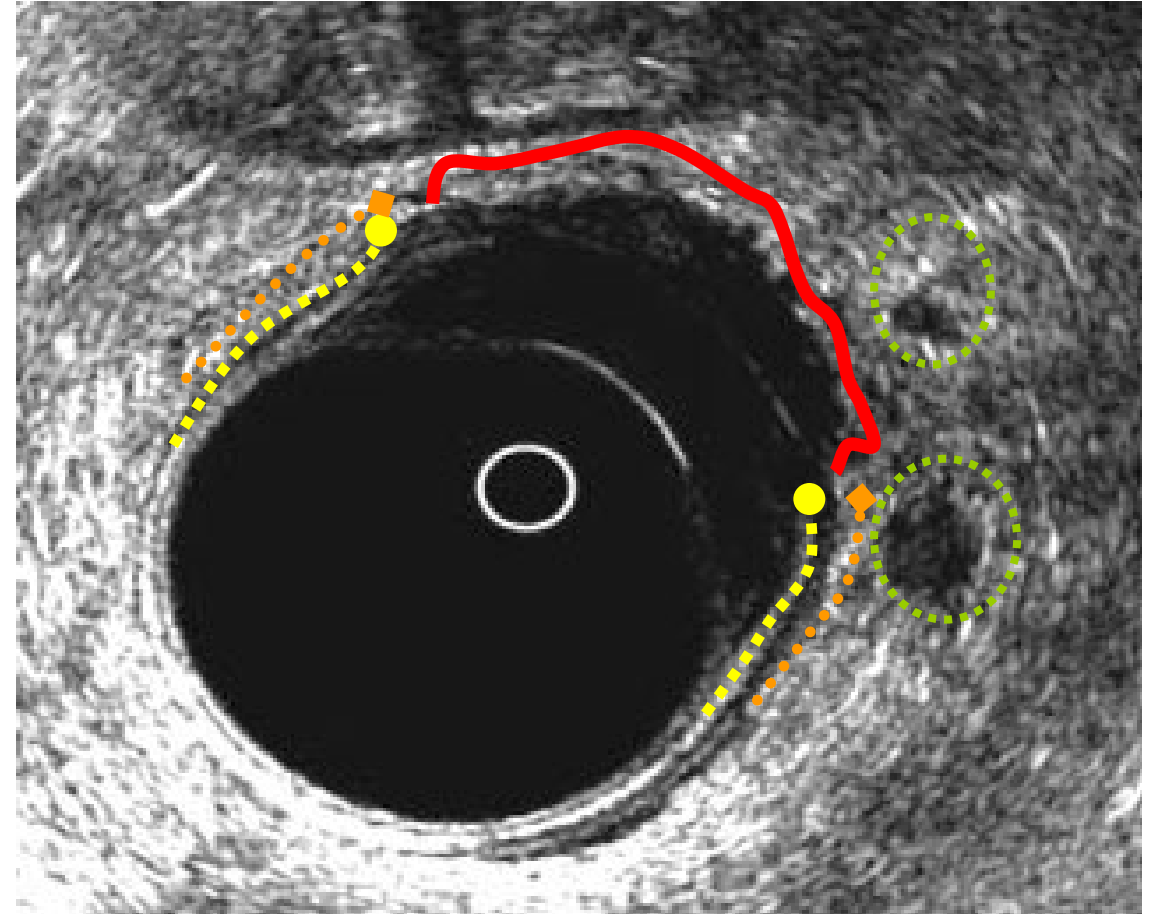
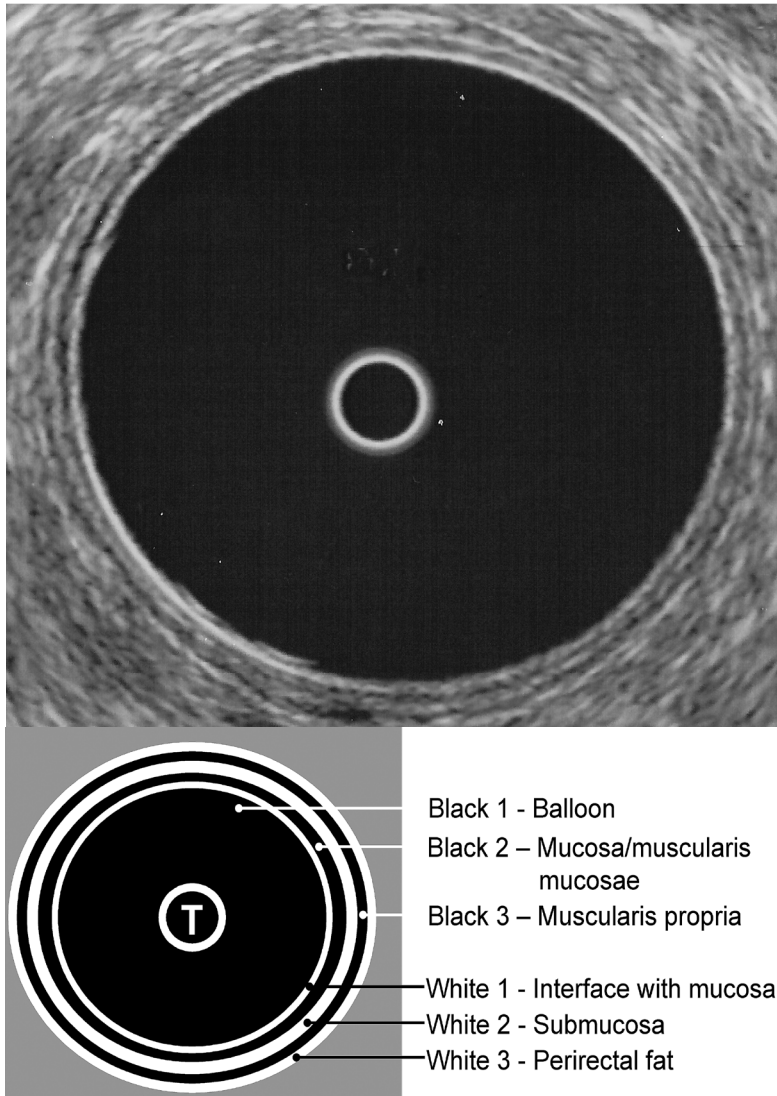
Interruption of white-2
Indentation of tumor
fingers into white-3



Adeno-Ca in posterior quadrant,
consistent with uT3 uN0

From: Kaiser AM – MGH Manual Colorectal Surgery

Rectal Cancer Staging - ERUS



From: Kaiser AM – MGH Manual Colorectal Surgery

Local Staging Modalities - Accuracy

ERUS: excellent for T-stage (small to medium size)

- Better detail:
 - ✓ Small/early tumors
 - ✓ Sphincter complex
- Limitations: operator-dependent , artifacts, high tumors, very large tumors, obstruction/stricture

MRI:

- Better detail on:
 - ✓ Large tumors
 - ✓ CRM, threatened margins
 - ✓ EMVI
- Limitations:
 - ✓ Blurred planes after tattooing?
 - ✓ Post radiation?
 - ✓ Over staging/under staging

Bipat S - Radiology 2004
MERCURY Study Group - BMJ 2006
Detering R – BJS 2020

	T-Stage (%)	N-Stage (%)
ERUS	87 (80 - 96)	75 (70 - 85)
CT	72 (60 – 80)	70 (50 - 85)
MRI	65 (55 - 95)	82 (72 -95)

Table 2 Clinical versus pathological tumour category assignment by MRI alone, including local excisions

	pT1	pT2	pT3	pT4	Total
cT1	656	197	85	4	942
cT2	792	2191	1311	52	4346
Total	1448	2388	1396	56	5288

Table 3 Clinical versus pathological nodal staging by MRI alone

	pN0	pN1	pN2	pNx	Total
cN0	2733	672	178	32	3615
cN1	524	311	89	6	930
cN2	46	15	18	0	79
cNx	36	24	3	4	67
Total	3339	1022	288	42	4691*

Local Staging Modalities - Accuracy

MRI cT1–2 rectal cancer staging accuracy: a population-based study

R. Detering¹, S. E. van Oostendorp³, V. M. Meyer⁷, S. van Dieren², A. C. R. K. Bos⁹, J. W. T. Dekker¹¹, O. Reerink⁸, J. H. T. M. van Waesberghe⁴, C. A. M. Marijnen⁵, L. M. G. Moons¹⁰, R. G. H. Beets-Tan⁶, R. Hompes¹, H. L. van Westreenen⁷, P. J. Tanis¹ and J. B. Tuynman³, on behalf of the Dutch ColoRectal Audit Group*

- 5539 patients with cT1–2 rectal cancer □ correlation with pathology:
 - pT1: 55% over staged by MRI, 31% by MRI+ERUS
 - pT2: understaged in 27% and 9%, respectively
 - pT1N0: correctly staged in only 30%, 70% over staged as cT2N0 (58%) or cT1-2 N1 (12%)

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Tumour category, including local excisions					
cT1	69.0 (59.7, 77.2)	72.6 (64.3, 79.9)	68.4 (61.6, 74.5)	73.1 (67.1, 78.5)	70.9 (64.9, 76.5)
cT2	72.1 (62.8, 80.2)	61.4 (52.8, 69.5)	59.7 (53.8, 65.3)	73.5 (66.7, 79.4)	66.1 (59.9, 72.0)
Node category					
cN0	90.6 (83.8, 95.2)	10.7 (2.3, 28.2)	80.9 (78.6, 83.0)	21.4 (7.5, 47.7)	75.2 (67.3, 82.0)
cN1	4.3 (0.1, 22.0)	91.0 (84.4, 95.4)	8.3 (1.2, 40.1)	83.5 (82.0, 84.8)	77.2 (69.6, 83.8)
cN2	20.0 (0.5, 71.6)	99.3 (96.1, 99.9)	50.0 (6.8, 93.2)	97.2 (95.7, 98.2)	96.6 (92.1, 98.9)

Detering R – BJS 2020

Circumferential Radial Margin (CRM)

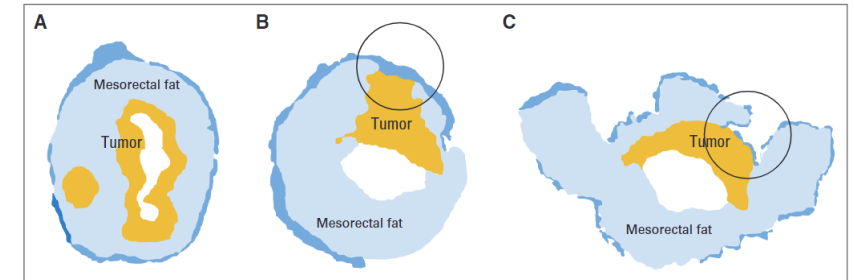
➤ CRM = Single most critical predictor of failure of local and systemic control

- NCCTG study (1979-92): CRM only evaluated in 21%: <1mm CRM → 25% LRR vs >1mm CRM → 3% LRR

Adams IJ – Lancet 1994

- MRC CR07 trial (SCRT+TME vs TME + selective adjuvant radiation): Adjuvant treatment will not improve the situation after the fact:

- 1) 1156 patients 1998-2002 with resectable rectal cancer
- 2) 11% CRM+



- 3-yr f/u: LRR 4% for mesorectal, 7% for intramesorectal, and 13% for muscularis propria resection plane
- Benefit of short-course preoperative radiotherapy: No difference in the three plane of surgery groups
- Short-course preoperative radiotherapy + resection in mesorectal plane had a 3-year local recurrence rate of only 1%.

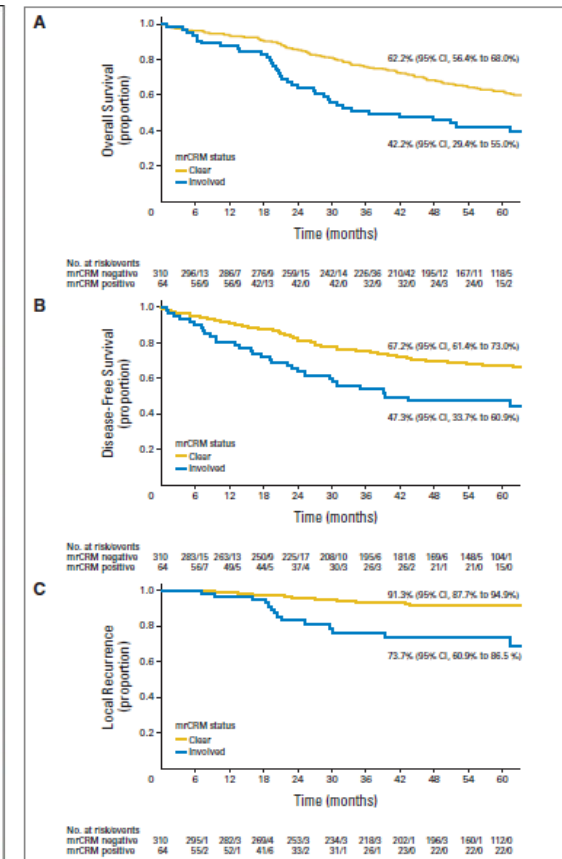
Sebag-Montefiore D – JCO 2006
Nagtegaal ID – JCO 2008
Quirke P – Lancet 2009

Circumferential Radial Margin (CRM)

- CRM = Single most critical predictor of failure of local and systemic control
- Single most critical predictor of failure: 5 yr data from MERCURY study (G Brown):
 - 374 patients with preoperative high-resolution magnetic resonance imaging (MRI)
 - CRM assessment:

- 1) >1mm
- 2) <1mm

OS	62% (-)	vs	42% (+)
DFS	67% (-)	vs	47% (+)
LR-free:	91% (-)	vs	74% (+)



Circumferential Radial Margin (CRM)

MERCURY II:

- 2008-2012: prospective, observational multicenter study
- 279 patients with adeno CA ≤ 6 cm from AV

Increased risk of CRM+:

- Anterior location
- <4cm from AV
- mrLRP safe vs unsafe
- mrEMVI status +

TABLE 6. The Predicted Risk (%) of pCRM Involvement in Patients With Low Rectal Cancer According to the Four Key MRI Assessed Risk Factors*

		MRI Predicted Involved CRM (mrLRP†)			
		‘SAFE’		‘UNSAFE’	
		Tumour Height (Distance from Anal Verge)			
		≥ 4cm	<4cm	≥ 4cm	< 4cm
mrEMVI Status	Tumour Site‡				
Negative	Not Anterior	1	4	4	13
Negative	Anterior	3	10	11	29
Positive	Not Anterior	4	13	14	35
Positive	Anterior	11	30	31	60

The risk of pCRM involvement: green, low risk <5%; amber, intermediate risk 5–15%; red, high risk >15%. The probabilities are calculated from the multivariate model (Table 5), all values are reported as a predicted percentage (%) risk of pCRM involvement (n = 279).

*The data are based on the preoperative MRI. This would be the posttreatment MRI for patients who received preoperative therapy.

[†]mrLRP, MRI assessment of low rectal cancer plane (a 'safe' mrLRP implies that the mesorectal fascia and intersphincteric planes are clear of tumor).

[‡]The quadrant of tumor invasion.

Proposed MRI Criteria of Good Prognosis Stages I, II, III

Poor tumor features

T4, T3c
Stage III
Bulky tumors

MRI features:

- CRM <1mm
- extramural venous invasion (EMVI)
- lymphovascular invasion
- pelvic side wall involvement

Low rectal cancer:

- down-staging → increased sphincter preservation?
- possibility of complete response → avoidance of surgery

Poor tumor features

→ Favor neoadjuvant radiation

Low risk tumors

- Upper third of the rectum
- CRM > 1cm
- T3a, T3b
- N0, LVI-
- Small tumor volume
- Absence of EMVI, absence of T3c

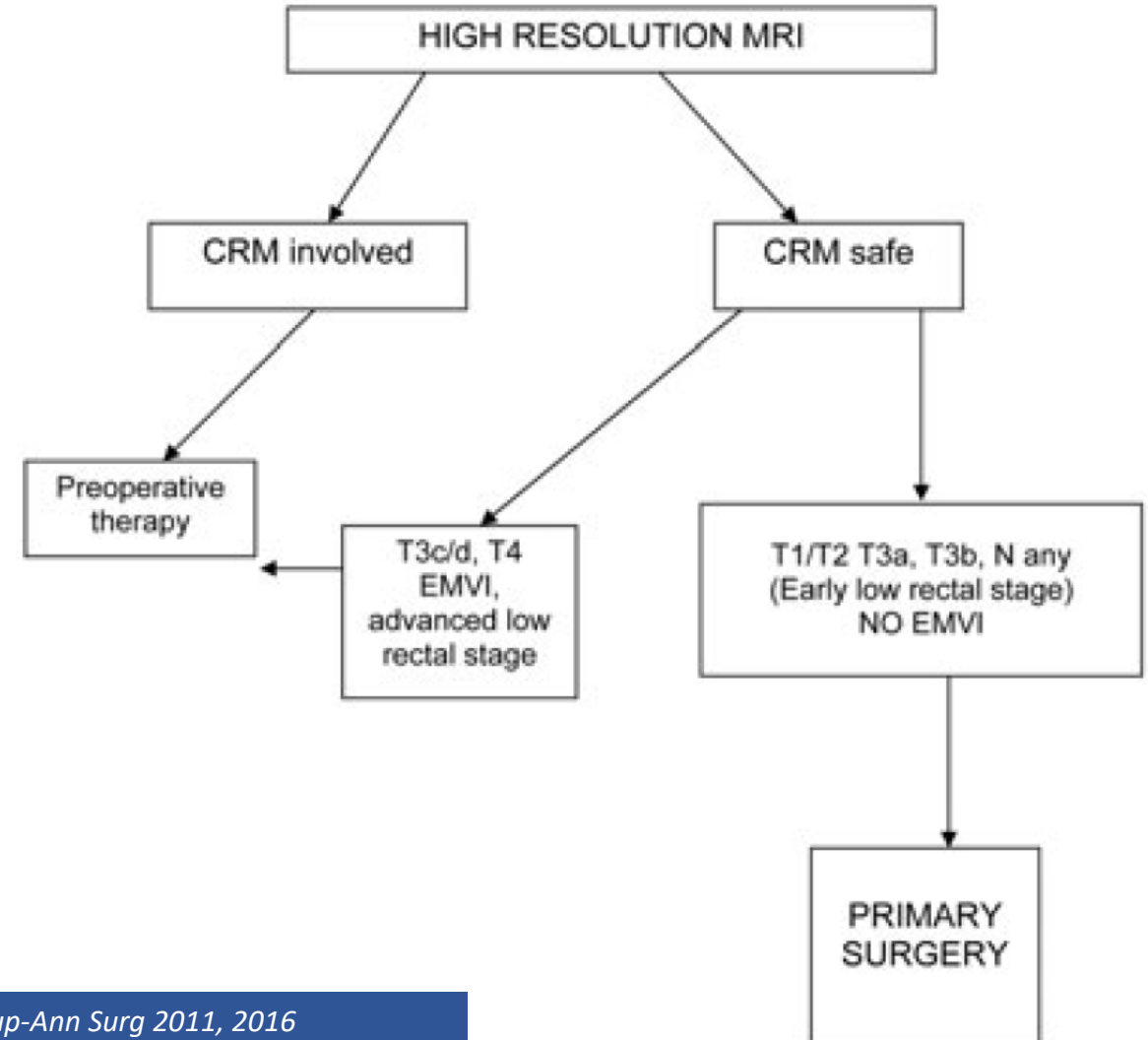
Surgery first → selective adjuvant CRT if negative features present

MERCURY Study Group-Ann Surg 2011, 2016

Proposed MRI Criteria of Good Prognosis Stages I, II, III

MERCURY trial:

- 354/408 (87%) with clear CRM
 - Accuracy of negative margins 94%
 - Accuracy after NCRT 74%
- 5 year outcomes:
 - Overall survival 85%
 - Disease-free survival 68%
 - Local recurrence rate 3%



MERCURY Study Group-Ann Surg 2011, 2016

Proposed MRI Criteria → Risk Categories

TABLE 1: Summary of Prognostic Criteria in MERCURY, OCUM, and QuickSilver Studies and NCCN Guidelines

Prognostic Criteria	MERCURY [21]	OCUM [3]	QuickSilver [20]	Current NCCN Guidelines [5]
Features of good prognosis group (patient proceeds directly to surgery)	CRM: > 1 mm ^a Low rectum: clear ISP T1, T2, or T3 (< 5 mm ^b) EMVI: negative	CRM: > 1 mm ^a	CRM: > 1 mm ^a T2 or T3 (< 5 mm ^b) EMVI: negative or equivocal	CRM: NA T1 or T2
Features of poor prognosis group (patient undergoes nCRT before surgery)	CRM: < 1 mm Low rectum: ISP involved T3 (> 5 mm ^b) or T4 EMVI: positive	CRM: < 1 mm Low rectum: T3 or T4 Mid or high rectum: T4a or T4b	CRM: < 1 mm Low rectum: ISP involved T3 (> 5 mm ^b) or T4 EMVI: positive Lateral pelvic nodes	T3 or T4 Node positive EMVI: NA
Mesorectal node status	NA	NA	NA	Patients with N+ disease receive nCRT
LR in good prognosis group (or direct surgery group)	3.3% of patients at 5 y	2.2% of patients at 3 y	NA	NA

Note—MERCURY = Magnetic Resonance Imaging and Rectal Cancer European Equivalence Study Group, OCUM = Optimierte Chirurgie Und MRT (Optimized Surgery and MRI-Based Multimodal Therapy), NCCN = National Comprehensive Cancer Network, CRM = circumferential resection margin, NA = not assessed, ISP = intersphincteric plane, EMVI = extramural vascular invasion, nCRT = neoadjuvant chemoradiation therapy, LR = local recurrence.

^aFor CRM, values represent tumor distance from CRM.

^bFor T3, values in parentheses represent tumor extent beyond muscularis propria.

➤ **Prognostic features on MRI include tumor location, T category, CRM, EMVI status**

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Proposed MRI Criteria → Risk Categories

TABLE 2: Risk-Adapted Treatment of Rectal Cancer

Prognostic Feature on MRI	Low Risk (Good Prognosis or Early Stage)	Intermediate Risk	High Risk (Poor or Bad Prognosis)	Very High Risk (Very Poor Prognosis, Advanced Stage, or Ugly)
Tumor location	Low or mid or high rectum	Low or mid rectum	Low or mid rectum	NA
T category and depth of invasion beyond MP	T1 or T2 if low rectum ^a T1, T2, or T3 (< 5 mm ^b) if mid or high rectum	T3 (< 5 mm ^b) if low or mid rectum	T3 (> 6–15 mm ^b)	Any T4a or T4b
MRF ^c	MRF clear	MRF clear	Any tumor with MRF threatened	Any tumor with MRF involved
Nodal stage	N0 N1 in high rectal tumors	N1 or N2	N1 or N2	Lateral pelvic nodes involved
EMVI	Negative	Negative	Positive	Positive
Treatment options	TME surgery	TME surgery nCRT followed by TME surgery	nCRT followed by TME surgery	nCRT followed by TME surgery More extended surgery

Note—The approach set out in this table relies on information from the 2017 European Society for Medical Oncology (ESMO) Practice Guidelines as described in Glynn-Jones et al. [10]. NA = not applicable, MP = muscularis propria, MRF = mesorectal fascia, EMVI = extramural vascular invasion, TME = total mesorectal excision, nCRT = neoadjuvant chemoradiation therapy.

^aMajority of low rectal tumors fall in intermediate- and high-risk groups.

^bFor T3, values in parentheses represent tumor extent beyond MP.

^cMRF is used instead of circumferential resection margin in ESMO 2017 practice guidelines.

➤ Prognostic features on MRI include tumor location, T category, CRM, EMVI status

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2023: PROSPECT Protocol

Appropriate

AdenoCA of the rectum
Stages II/III: T3 N0 and T1-3 N1
Location: mid to upper rectum

Adult (≥ 18 years of age)
Normal operability
Intellectually competent
Compliant

PS: Prior pelvic radiation: per default no further radiation indicated

Proceed with default surgery

Consideration of chemoradiation (short course vs long course) if:

- near complete response \rightarrow cCR attainable ($>90\%$ response)
- response $<20\%$
- dose-limiting side effects with FOLFOX
- refusal of surgery
- positive post-resection margins

Exclusion

Other pathology than mid/upper rectal adenoCA

T4 lesions
N2 (≥ 4 LN)
Bulky tumors

Threatened circumferential margin ($< 3\text{mm}$)

- By primary tumor
- By peripheral mesorectal lymph nodes (MERCURY data)

Lateral pelvic lymph nodes

Relative contraindications:

- Pan-colonic disease (FAP, multicentric tumors, ulcerative colitis, Crohn colitis)?
- Inability to perform pelvic MRI
- Inability to tolerate FOLFOX

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Preoperative Treatment of Locally Advanced Rectal Cancer

Deborah Schrag, M.D., M.P.H., Qian Shi, Ph.D., Martin R. Weiser, M.D.,

Schrag D – NEJM 2023

Local control

The role of Watch & Wait

Watch and Wait (Habr-Gama Approach)

➤ pCR

- German trial: 8%

➤ Habr-Gama 2004: 265 pts

- cCR 27% → W&W
- iCR 73% → Surg → 8.3% pCR
- 5 yr OS and DSF:
 - 1) Surg: 88% and 83%, respectively
 - 2) W&W: 100% and 92%

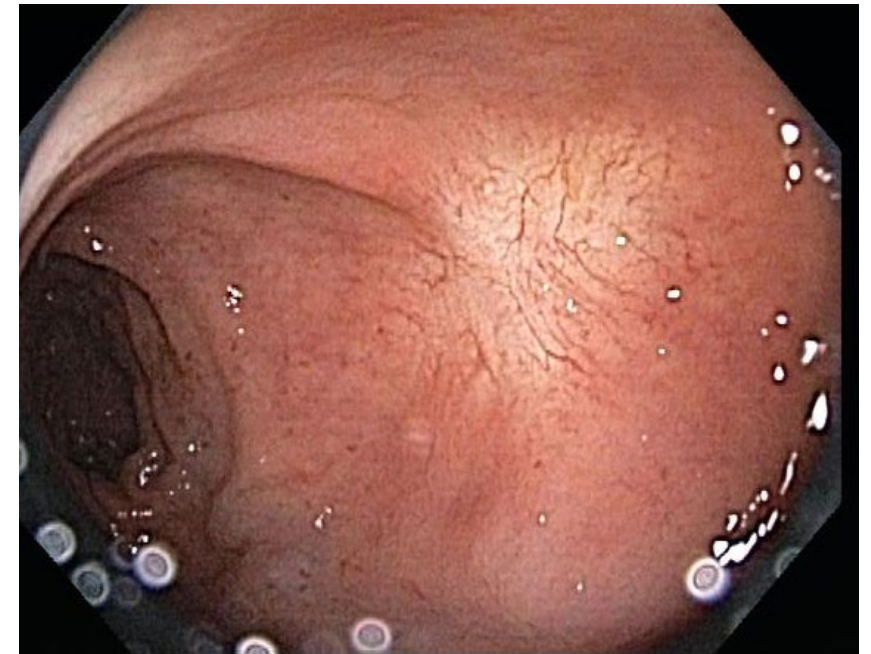
pCR = favorable prognosis, 10-25% after LCRT Criteria:

- ✓ Inert flat non-ulcerated mucosa, maybe some telangiectasias
- ✓ No palpatory, endoscopic, radiological residua
- ✓ Compliant patient → frequent surveillance

Operative Versus Nonoperative Treatment for Stage 0
Distal Rectal Cancer Following Chemoradiation Therapy

Long-term Results

Angelita Habr-Gama, MD, Rodrigo Oliva Perez, MD,* Wladimir Nadalin, MD,†
Jorge Sabbaga, MD,† Ulysses Ribeiro Jr, MD,‡ Afonso Henrique Silva e Sousa Jr, MD,*
Fábio Guilherme Campos, MD,* Desidério Roberto Kiss, MD,* and Joaquim Gama-Rodrigues, MD,‡*



Habr-Gama A – Ann Surg 2004

Watch and Wait (COH)



cCR:

- ✓ Inert flat non-ulcerated mucosa, maybe some telangiectasias
- ✓ No palpatory, endoscopic, radiological residua
- ✓ Compliant patient → frequent surveillance

COH – Internal SOP

Watch and Wait (COH)

Months	3	6	9	12	15	18	21	24	30	36	42	48	54	60
Clinical/DRE	●	●	●	●		●		●	●	●		●		●
Labs incl CEA	●	●	●	●		●		●	●	●		●		●
Flex/rigid sig	●	●	●			●		● / C		●		●		●
Colonoscopy				●				Interval to be determined on findings ----->						
CT CAP		●		●		●		●		●		●		●
MRI pelvis	●		●		●		●		●	●		●		●
ctDNA														

cCR:

- ✓ Inert flat non-ulcerated mucosa, maybe some telangiectasias
- ✓ No palpatory, endoscopic, radiological residua
- ✓ Compliant patient → frequent surveillance

COH – Internal SOP

Watch and Wait (Habr-Gama Approach)

	cCR N (%)	Follow-up (months)	Local failure	Salvaged after local failure	Systemic recurrence	DFS ^c	OS ^c	Stoma-free survival ^c
Habr-Gama 2004	71 (27%)	57	3%	100%	4%	92%	100%	
Habr-Gama 2006	122 (34%)	60	24%	100%	6%	85% 5yr	93% 5yr	
Habr-Gama 2013	47 (68%)	56	26%	92%	17%	72% 3yr	90% 3yr	88%
Habr-Gama 2014	90 (49%)	60	31%	78%	13–18%	68% 5yr	91% 5yr CSS	78%
Mass 2011	21 (11%)	25	5%	100%	Unknown	89% 2yr	100% 2yr	
Ayloor Seshadri 2013	23	72	30%	Unknown	Unknown	Unknown	Unknown	87%
Smith 2012	32	28	19%	100%	9%	88% 2yr	96% 2yr	
Applet 2015	40 (78%)	24	26%	100%	8%	58% 2yr	100% 2yr	78% 2y
Li 2015	122 (14%)	60	7%	100%	3%	90% 5yr	100% 5yr	
Smith 2015	18	68	6%	100%	6%	89% 5yr	100% 5yr	
Renehan 2016	129	33	34%	88%	5.5%	Unknown	96% 3yr	74% 3y
Martens 2016	85	41	15%	100%	3.5%	81% 3yr	97% 3yr	92%

<http://www.iwwd.org/>



International Watch & Wait database

Watch and Wait (NEJM)

➤ Phase 2 study with single-agent anti-PD-1 monoclonal antibody dostarlimab every 3 weeks for 6 months in MMRd stage II/III rectal adenocarcinoma:

- 100% cCR at 6 months
- No progression to CRT or surgery during 6-25 months f/u

Concerns:

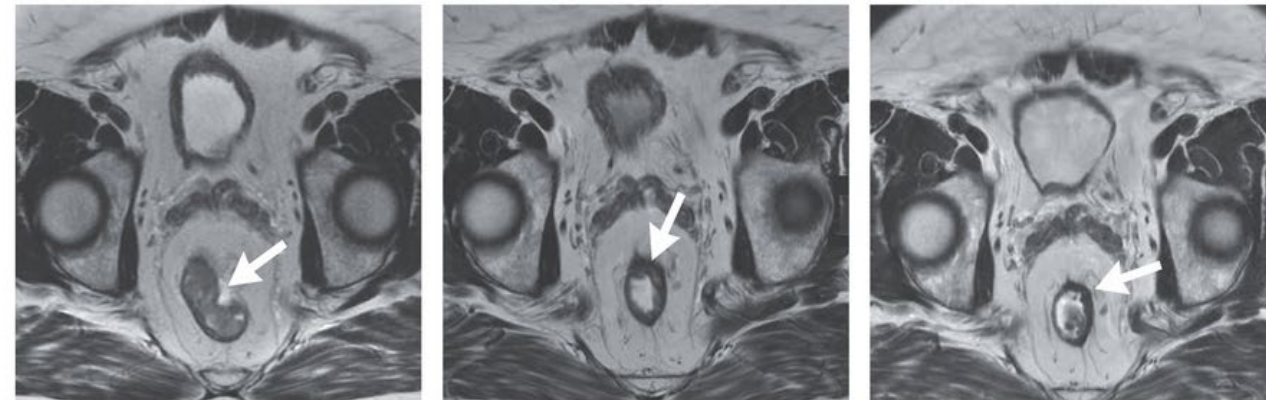
Would not have passed COH criteria for cCR

- ✓ Tumor area not consistent with cCR
- ✓ Area with deformities, likely induration
- ✓ At 3 and 6 months: PET avidity
- ✓ At 3 and 6 months: MRI lesion

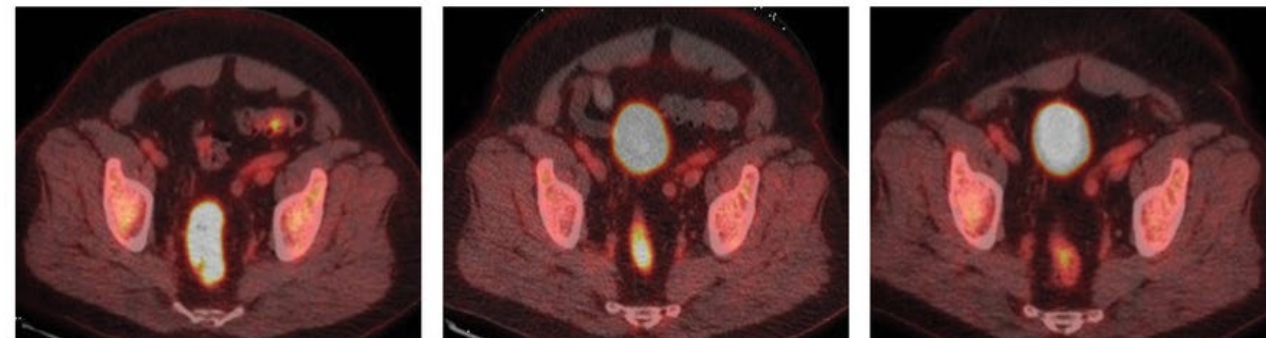
Endoscopy



Rectal MRI



PET



Cercek A – NEMJ 2022

Watch and Wait (Habr-Gama Approach)

Uncertainties about W&W:

- LRR: 3% or 50-60%?? → ~30%
- Majority of LRR <24 months
- Definitive assessment limited:
 - MRI Tumor regression grade (mrTRG)
 - Endoluminal vs nodal CR?
 - Local excision? → Severe wound healing problems
 - Circulating tDNA?

- Higher pCR with:
 - ✓ Longer wait? → higher risk of systemic failure?
 - ✓ Intensified chemoradiation?
 - ✓ TNT?
- Justifiable to radiate stage I disease to avoid surgery?

Neoadjuvant Therapy for Rectal Cancer: Histologic Response of the Primary Tumor Predicts Nodal Status

Thomas E. Read, M.D.,^{1,2} Jose E. Andujar, M.D.,² Philip F. Caushaj, M.D.,² Douglas R. Johnston, B.A.,² David W. Dietz, M.D.,¹ Robert J. Myerson, M.D., Ph.D.,³ James W. Fleshman, M.D.,¹ Elisa H. Birnbaum, M.D.,¹ Matthew G. Mutch, M.D.,¹ Ira J. Kodner, M.D.¹

Is T Classification Still Correlated with Lymph Node Status after Preoperative Chemoradiotherapy for Rectal Cancer?

	ypN+
ypT0	2
ypT1	4-8
ypT2	17-23
ypT3	47-49
ypT4	43-48

Read TE – DCR 2004
Kim DW – Cancer 2006

Summary – Staging for Rectal Cancer

- Staging defines risk categories and allows for treatment algorithms
- Accurate staging and restaging is key to tailored management with minimized over- and under-treatment
- Local staging consists of clinical exam, endoscopy, MRI, possible ERUS
- MERCURY trial, W&W and PROSPECT protocol have changed the landscape and require even more emphasis of staging and re-staging

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