GISCoR2014

GISCoR

L'impatto dell'imaging sulla definizione della strategia terapeutica

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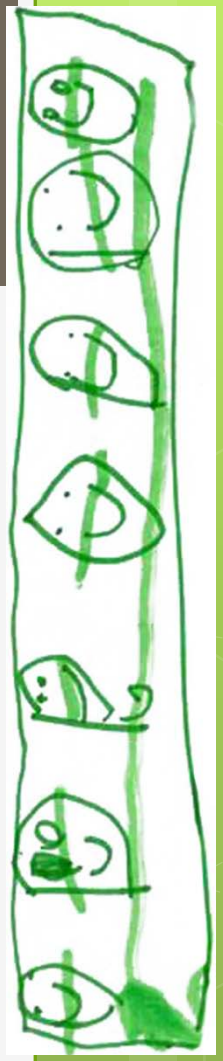
ASMN-IRCCS



Reggio Emilia 14 Novembre 2014

Rectal Cancer

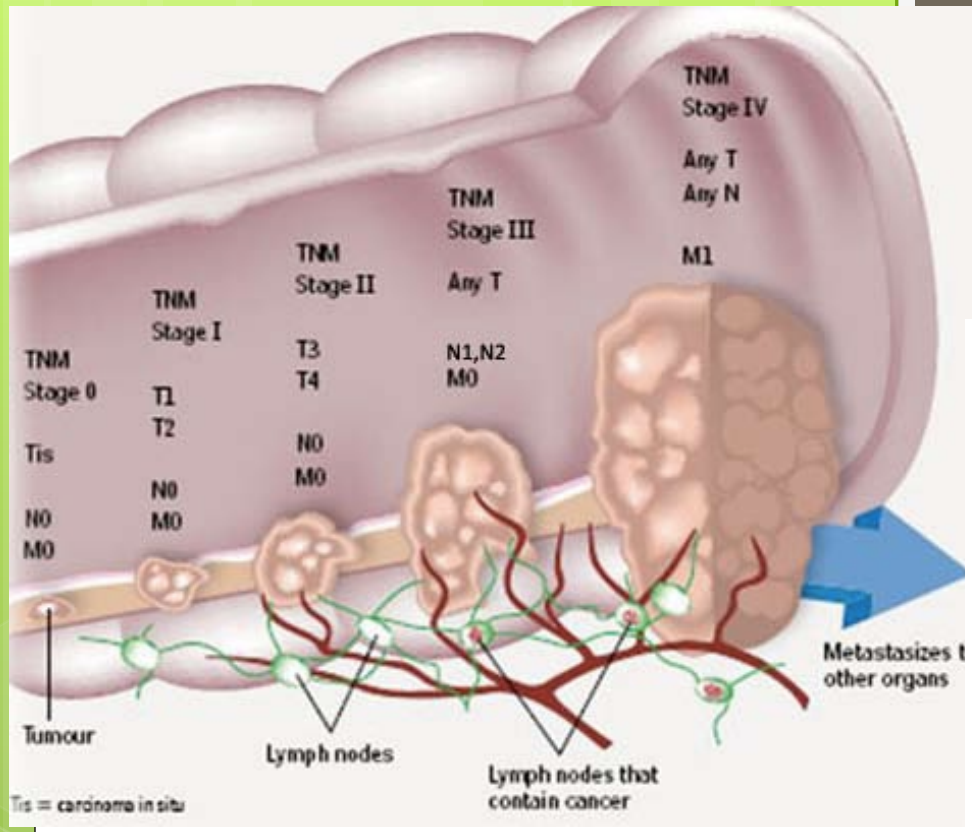


Table 1. Definitions for T, N, M

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[a]
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades through the muscularis propria into the pericolorectal tissues
T4a	Tumor penetrates to the surface of the visceral peritoneum[b]
T4b	Tumor directly invades or is adherent to other organs or structures[b,c]

Regional Lymph Nodes (N)

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 four or more regional lymph nodes
N2a	Metastasis in 4-6 regional lymph nodes
N2b	Metastasis in seven or more regional lymph nodes

Distant Metastasis (M)

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

Table 2. 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	-	-

TNM AJCC-7th edition 2010

Rectal cancer staging is based on 2 principles:

- To define the pertinent anatomy, allowing for surgical planning
- To allow prognostic stage grouping

To select a tailored therapeutic approach in relation to the risk of local or distant recurrence

To reduce overall morbidity from potential overtreatment, while allowing aggressive treatment of high-risk patients

Therefore, the aim of preoperative staging is to accurately differentiate between good and poor prognosis tumors

IL BUONO	• cT1-2 AND cN0	No preop RT
IL BRUTTO	• cT3, expected CRM – • or any suspicious node not	Short
IL CATTIVO	• or tumor encroaching onto sphincterial plane or elevator involvement	Long course CRT
BRUTTO/CATTIVO "borderline"	• rectal cancer appearing unresectable or borderline resectable	Long course CRT

Combined-modality therapy consisting of surgery, radiation therapy, and chemotherapy is recommended for the majority of patients with stage II or stage III rectal cancer

Compared to postop (C)RT, the preop (C)RT is associated with a superior overall compliance rate, an improved rate of local control, reduced toxicity, an increased rate of sphincter preservation (?)

Do not offer preop (C)RT solely to facilitate sphincter-saving surgery

Main disadvantage: possibility of overtreating early-stage tumors

Even with improvements in preoperative staging techniques, the risk of over or under-staging disease has not been eliminated

Post-op CRT is recommended when stage I rectal cancer is upstaged to stage II or III after pathologic review of the surgical specimen

Selection of Patients for Preop Treatment Based on P… …c Features

The assessment of morphologic feature… …the resected rectal specimen remains the … …tic stratification

These features include a…

1. depth of spre…
2. circum… …)
3. …MVi)
4. …
5. pe… …oration

Can diagnostic imaging provide us with informations about prognostic features?

Modalities of Local Staging

Intraluminal Endoscopic Ultrasound (EUS)

Very accurate for early-stage low tumors (T1 and T2), with a sensitivity of 94% and specificity of 86% but performs less well in cases of advanced rectal cancer (*Garcia-Aguilar 2000*)

EUS can detect lymph nodes >5 mm in size; but an estimated 50% of metastatic lymph node associated with rectal cancer is smaller than 5 mm, so the sensitivity of EUS is limited

The mesorectum and the peritoneum cannot be visualized by EUS, so the CRM status and degree of peritoneal involevment cannot be determined

None information about extramural venous invasion

CT Scanning for M

European Journal of Cancer (2014) 50, 1.e1–1.e34

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Position Paper

EURECCA colorectal: Multidisciplinary management: European consensus conference colon & rectum ☆

MRI

European Journal of Cancer (2014) 50, 1.e1–1.e34

Available at www.sciencedirect.com

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Position Paper

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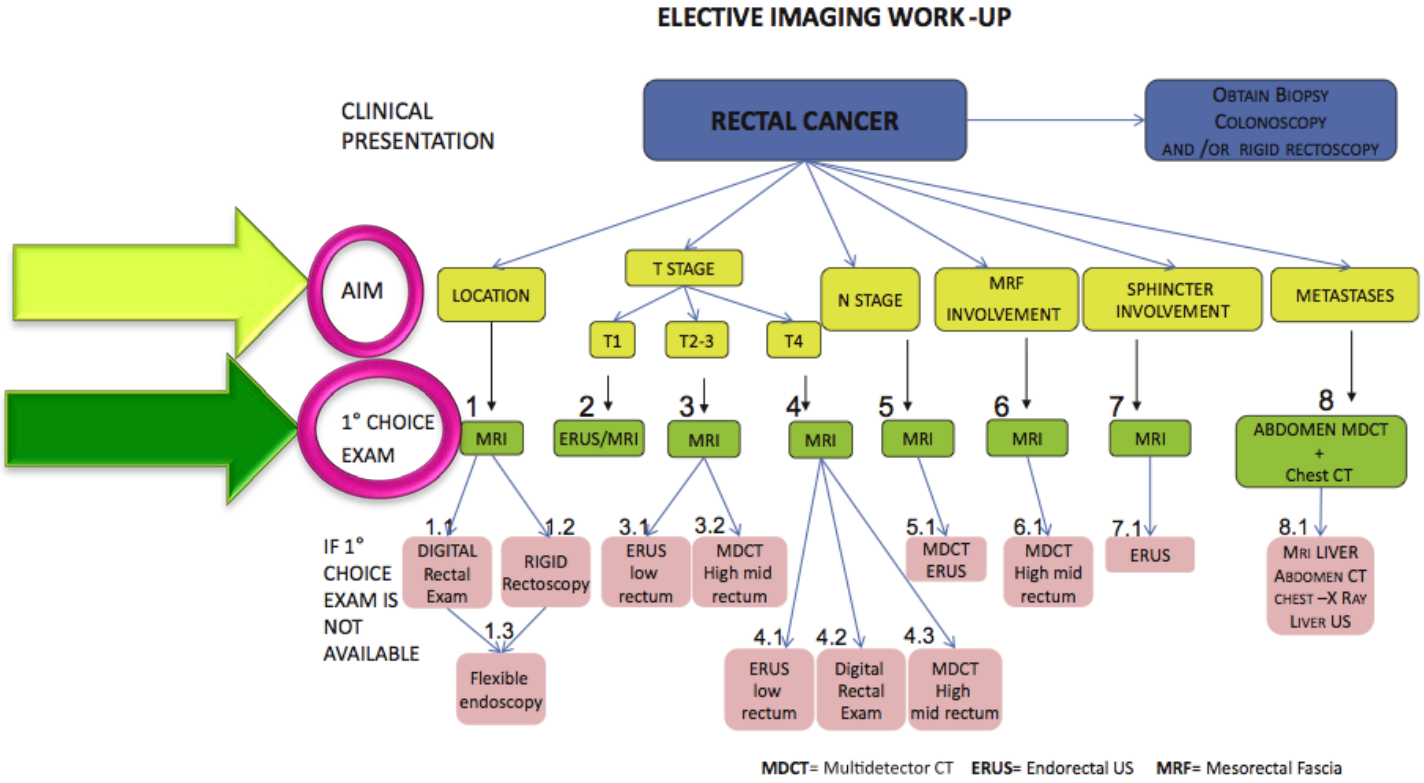


Fig. 4. Elective imaging work up algorithm for rectal cancer. Almost all imaging decisions achieved large consensus with exception of the two lesser choice exam decisions. Moderate consensus was achieved on imaging step 1.1 and moderate consensus on step 3.1.

Selection of Patients for Preop Treatr… …Features

The assessment of morpl… …he resected rectal specim… … stratification

These fe…

1…

4.

1. Lo… …tion

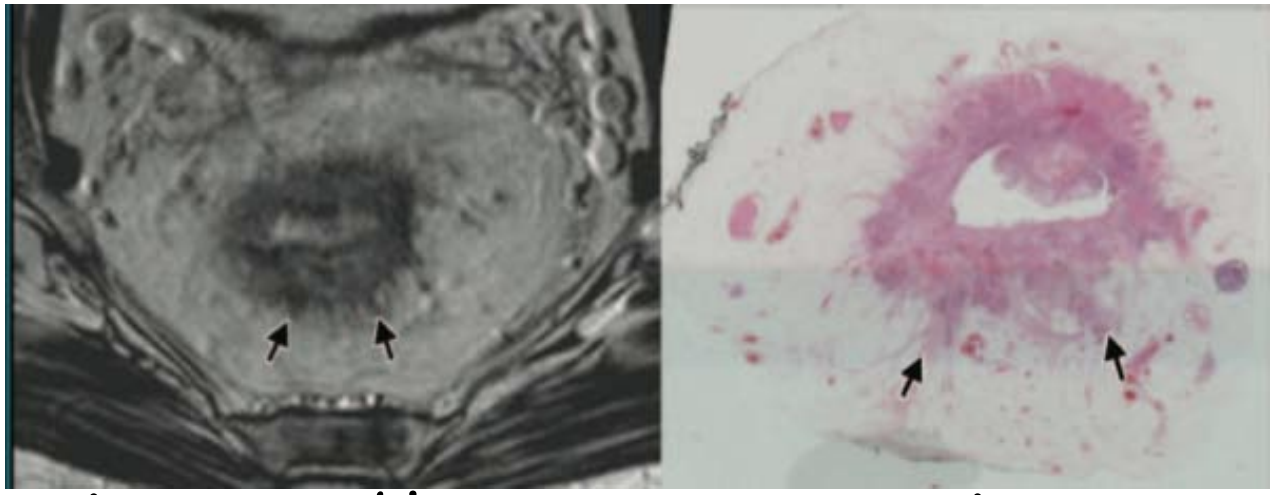
RMN provides us with informations on each of the prognostic features AND provides a guide for the choice of treatment strategy

Extramural tumor depth

study	# pts	stage	treatments	results
MERCURY *Radiology 2007*	679	any stage	various approaches	MR is accurate to measure Extramural depth

- MRI is equivalent to histology in measurement of extramural depth
- T with extension into the mesorectum >5 mm have lower 5 y survival
  - This is independent of lymph node involvement

Sensitivities 71-91% Specificities of 78-100%



MRI imaging can enable accurate preoperative prognostication

Extramural tumor depth

Since the maximal extramural depth of spread, from the outer edge of muscularis propria to the outermost edge of the tumour, correlates with cancer specific survival, clinical stage T3 rectal cancers should be subclassified as depicted in table

T3 subclassification based on MRI from the rectal wall into the mesorectal fat.

mrT3a	Tumour extends <1 mm beyond muscularis propria
mrT3b	Tumour extends 1–5 mm beyond muscularis propria
mrT3c	Tumour extends >6–15 mm beyond muscularis propria
mrT3d	Tumour extends >15 mm beyond muscularis propria

The mr prefix denotes the staging is based upon MRI.

Circumferential resection margin

VOLUME 32 · NUMBER 1 · JANUARY 1 2014

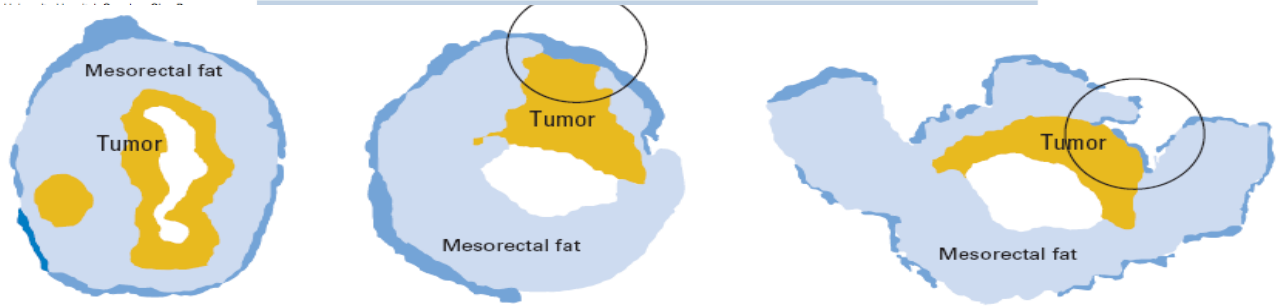
JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Preoperative Magnetic Resonance Imaging Assessment of Circumferential Resection Margin Predicts Disease-Free Survival and Local Recurrence: 5-Year Follow-Up Results of the MERCURY Study

Fiona G.M. Taylor, Philip Quirke, Richard J. Heald, Brendan J. Moran, Lennart Blomqvist, Ian R. Swift, David Sebag-Montefiore, Paris Tekkis, and Gina Brown

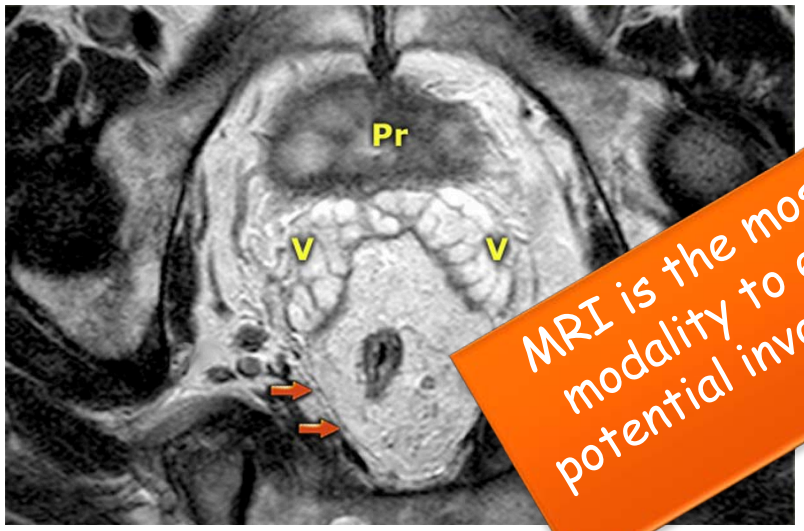
Listen to the podcast by Dr Tepper at www.jco.org/podcasts

Fiona G.M. Taylor and Ian R. Swift, Mayday

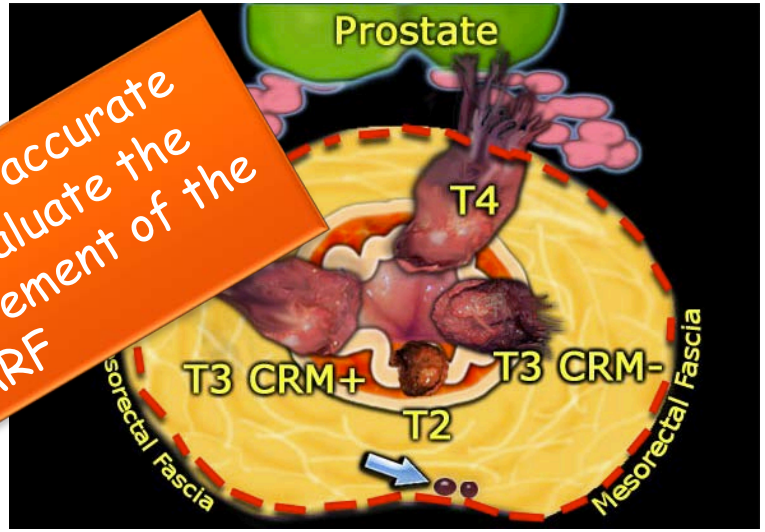


If the MRF is involved or if the tumour extends to a point within 1 mm from the MRF, there is a clear risk that CRM will be involved after surgery if only a TME is performed

Circumferential resection margin



MRI is the most accurate modality to evaluate the potential involvement of the MRF



Since pre-op RT-CRT is more efficient and less toxic than post-op therapy, it has become increasingly important to evaluate the risk of MRF+ before the surgery

Of the preoperative features, the relationship of the tumour to the MRF has emerged as one of the most powerful predictors of outcome in terms of local recurrence, development of DM, survival

Extramural venous invasion(EMVI)

- Presence of malignant cells within the endothelial blood vessels beyond the muscularis propria
- It can occur in up to 50% of rectal cancer patients
- EMVI can be identified pre-operatively on MRI with reasonable accuracy
- EMVI is a poor prognostic factor for overall survival and local recurrence
- The poor prognostic value on overall survival and local recurrence of EMVI is independent of tumour stage

Lymph node status

15-42% of pts have small <5 mm mesorectal patologic lymph nodes

- Identifying nodal disease is **still a diagnostic problem**
- Although lymph node size is not accurate for defining N metastases, nodes of >8 mm are suspicious for nodal involvement on CT, MRI and EUS

- The most reliable method of positively identifying nodal metastases is based on morphological features such as the presence of a round shape, heterogeneity within the lymph node and/or irregularity of the borders of the lymph node due to capsular penetration by malignancy

Lymph node status

The overall accuracy of N-staging is low but MRI is the preferred examination for nodal staging

FNA is not recommended for nodal staging

FDG/PET has shown disappointing results for N-staging in rectal cancer, especially in the mesorectum in the presence of a bulky tumour

Two more relavant information…….

✧ Tumor location

MRI is accurate in measuring the distance between the ano-rectal junction and the distal part of the tumor; is accurate for the tumor length

✧ Sphinteric infiltration

MRI is reliable in assessing sphinteric infiltration, is the preferred method

Annals of Surgery • Volume 253, Number 4, April 2011

Preoperative High-resolution Magnetic Resonance Imaging Can Identify Good Prognosis Stage I, II, and III Rectal Cancer Best Managed by Surgery Alone

Fiona G.M Taylor, MBBS, FMRCS, Philip Quirke, PhD, BM, FRCPath†, Richard J Heald, MB, Bch, FRCS‡, Brendan Moran, MB, Bchir, FRCSI‡, Lennart Blomqvist, MD, PhD§, Ian Swift, MS, FRCS, FICS*, David J Sebag-Montefiore, FRCP, FRCR¶, Paris Tekkis, BMBS, MD, FRCS**, and Gina Brown, MBBS, MD, FRCR†† for the MERCURY study group*

122 of 374 patients followed up in the MERCURY study were defined as "good prognosis" stage III or less on MRI

MRI feature	Good prognosis	Poor prognosis
CRM	>1mm clear	<1mm involved
Low rectal <5cm	intersphincteric plane clear of tumor	intersphincteric plane involved by tumor
T stage	T1/T2, T3a<1mm, T3b, 1-5mm extramural spread	T3c>5mm extramural spread, T4
EMVI	negative	positive
N stage	any	any

The routine policy was primary surgery alone in MRI-predicted stage I, II and in MRI "good prognosis" stage III

Results: 5y-OS: 68% 5y-DFS: 85% LR: 3%

CONCLUSIONS: The preoperative identification of good prognosis tumors using MRI will allow stratification of patients and better targeting of preoperative therapy. This study confirms the ability of MRI to select patients who are likely to have a good outcome with primary surgery alone.

Scenario of ongoing research *supported by the multimodal imaging*

Radiotherapy intensification

Dose escalation

Treatment de-intensification

No surgery for complete clinical response?

1 Radiotherapy intensification

Dose escalation

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Radiotherapy and Oncology xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

Impact of radiotherapy boost on pathological complete response in patients with locally advanced rectal cancer: A systematic review and meta-analysis

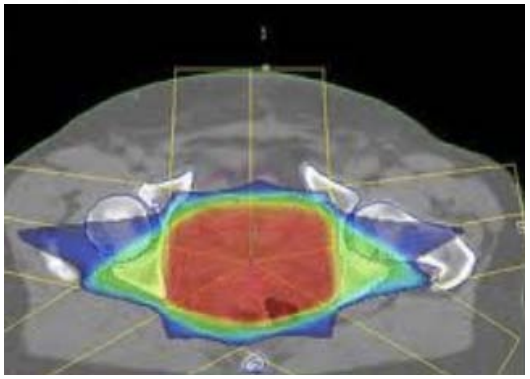
Johannes Peter Maarten Burbach [a,*,1], Annemarie Maria den Harder [b,1], Martijn Intven [a], Marco van Vulpen [a], Helena Marieke Verkooijen [c], Onne Reerink [a]

[a] *Department of Radiation Oncology;* [b] *Department of Radiology; and* [c] *Trial Bureau Imaging Division, University Medical Center, Utrecht, The Netherlands*

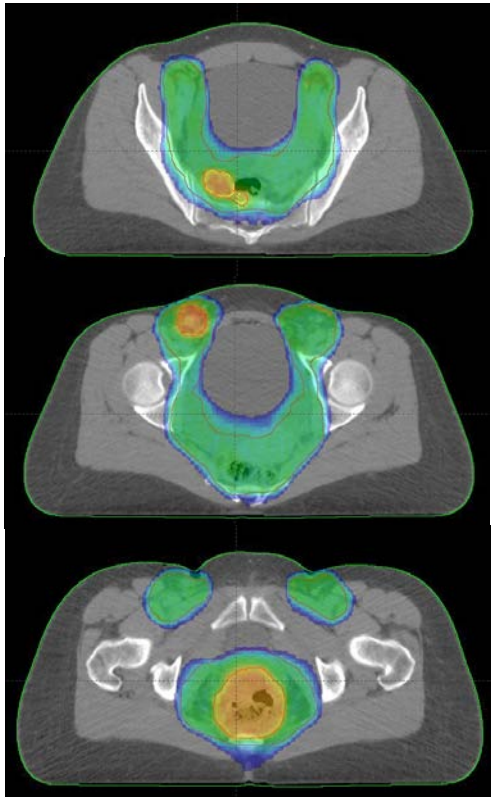
Conclusion: Dose escalation above 60 Gy for locally advanced rectal cancer results in high pCR-rates and acceptable early toxicity. This observation needs to be further investigated within larger randomized controlled phase 3 trials in the future.

1 Radiotherapy intensification

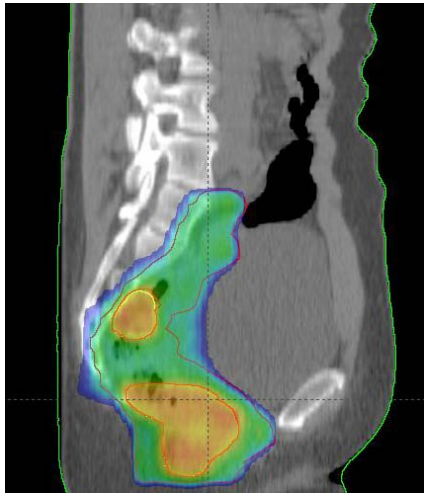
Dose escalation

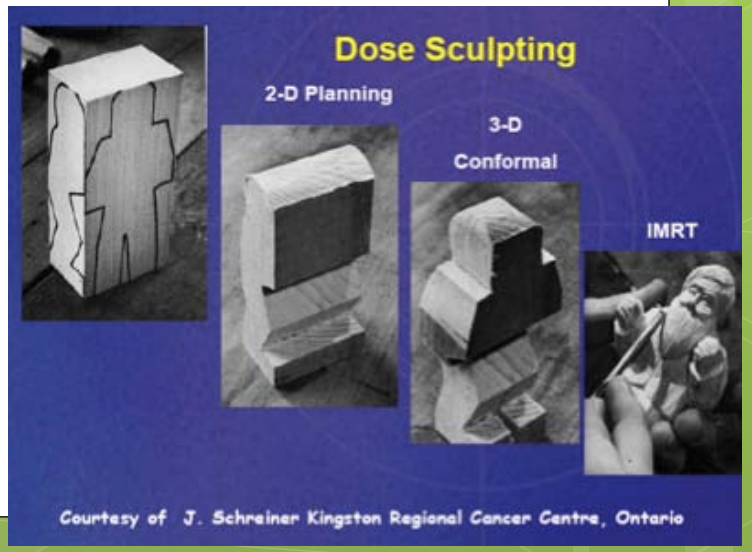


3D CRT



IMRT





Multimodality Imaging

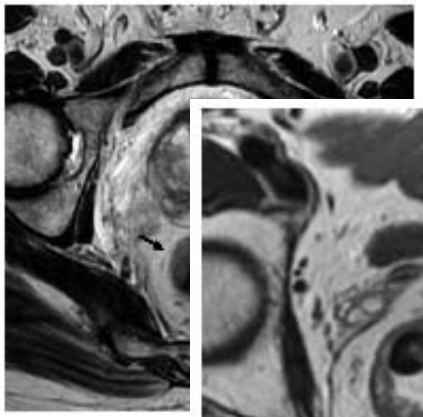


Fig. 1 T2 stage rectal tu
anterolateral rectal wall mass
seen as disruption of the high
The fat planes around the
invasion are seen.

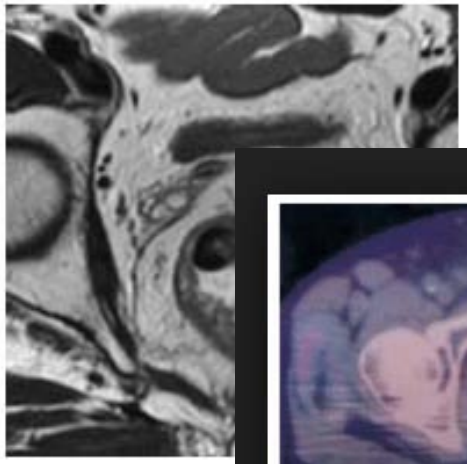


Fig. 2 T3 stage rectal tumor:
rectal wall mass that extends int
causing its stranding. A perire
(arrow head)

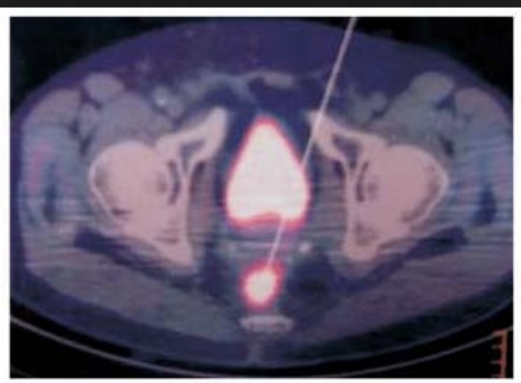
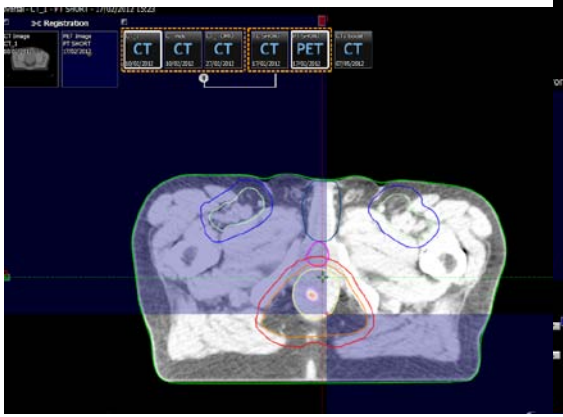
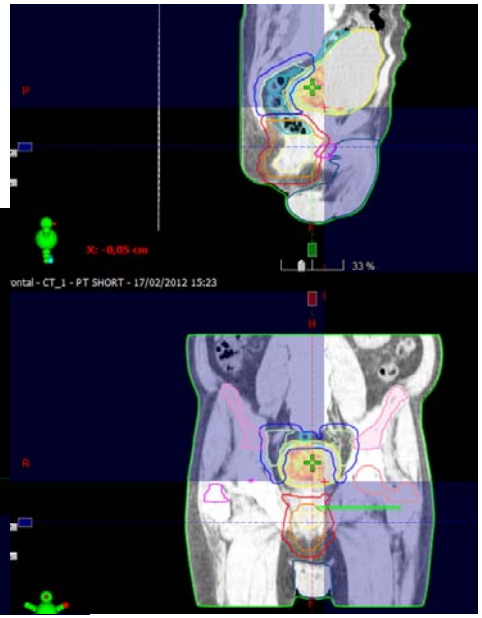


Figura 2 - *Aspecto do PET-CT (corte transversal) de doente com recidiva pélvica de adenocarcinoma retal.*

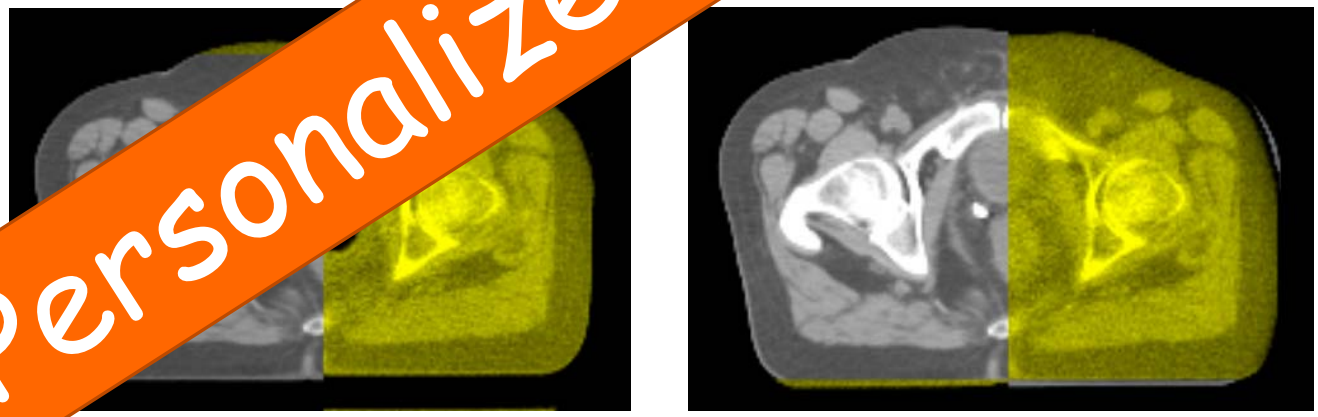
Registration images





1 Radiotherapy intensification

Dose escalation



Personalized treatment

Set-up control before delivery

2 Treatment de-intensification

No surgery for complete clinical response?

Neoadjuvant therapy and surgery contributes markedly to poorer functional outcomes and secondary complications

The impressive incidence of pCR in recent trials raises the possibility of selecting pts with a cCR atfer preopertive treatment to avoid surgery

WATCH AND WAIT POLICY

TABLE 1. Selected Series of Reports of Nonoperative Approach in Rectal Cancer Treated by CRT

References (Institution)	Patients Treated	Follow-up (mo)	cCR (n [%])	Outcomes		
				Locoregional Failure	Disease-free Survival	Overall Survival
Habr-Gama et al[16] (Brazil)	265	57	71 (26.8)	2/71 (2.8%)	83% (5 y)	88% (5 y)
Habr-Gama et al[18] (Brazil)	361	60	99 (27.4)	5/99 (5%)	85% (5 y)	93% (5 y)
Habr-Gama et al[19] (Brazil)	360	NS	99 (27.5)	6/99 (6%)	NS	NS
Habr-Gama et al[20] (Brazil)	173	65	67 (39)	8/173 (4.6%)	72% (5 y)	96% (5 y)
Maas et al[22] (The Netherlands)	192	35±23 (Mean)	21 (11)	1/21 (5%)	89% (2 y)	100% (2 y)
Dalton et al[23] (England)	49	26	12 (24)	Biopsy negative: all NED Biopsy positive: 2/6 distant failure		
Smith et al[24] (MSKCC)	265	28	32 (12)	6/32 (19%)	88% (2 y)	96% (2 y)

cCR indicates clinical complete response; CRT, chemoradiation; MSKCC, Memorial Sloan-Kettering Cancer Center; NED, no evidence of disease, NS, not stated.

2 Treatment de-intensification

No surgery for complete clinical response?

Can Surgery be Avoided After Preoperative Chemoradiation for Rectal Cancer in the Era of Organ Preservation? Current Review of Literature

Sheema Chawla, MD, Alan W. Katz, MD, MPH,† Stephen M. Rauh, MD,‡ and John R. T. Monson, MD, FRCS, FACS§*

- Collected data show a high recurrence in the first 12 months, patients following the watch and wait approach should be monitored intensively in the first year
- At present, the evidence supporting this treatment is limited
- Results from prospective studies and trials using modern imaging techniques will be essential to guide oncologists in the selection of appropriate patients for nonoperative management of rectal cancer after CRT

Grazie per l'Attenzione