Rectal Carcinoma - staging and restaging – what is relevant?

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Rectal Cancer

- United States 2013:
- 102,480 new cases of colon cancer
- Including 40,340 cases of rectal cancer

- Lifetime risk ~ 2%

TNM Classification of Rectal Cancer

T-Primary tumor

Tx Primary tumor cannot be assessed

T0 No evidence of primary tumor

Tis Carcinoma in situ: intraepithelial or invasion of lamina propria

T1 Tumor invades submucosa

T2 Tumor invades muscularis propria

T3 Tumor invades through muscularis propria into subserosa or into non-peritonealized pericolic or perirectal tissues

T4 Tumor directly invades other organs or structures and/or perforates visceral peritoneum

N-Regional lymph nodes

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Metastasis in one to three regional lymph nodes

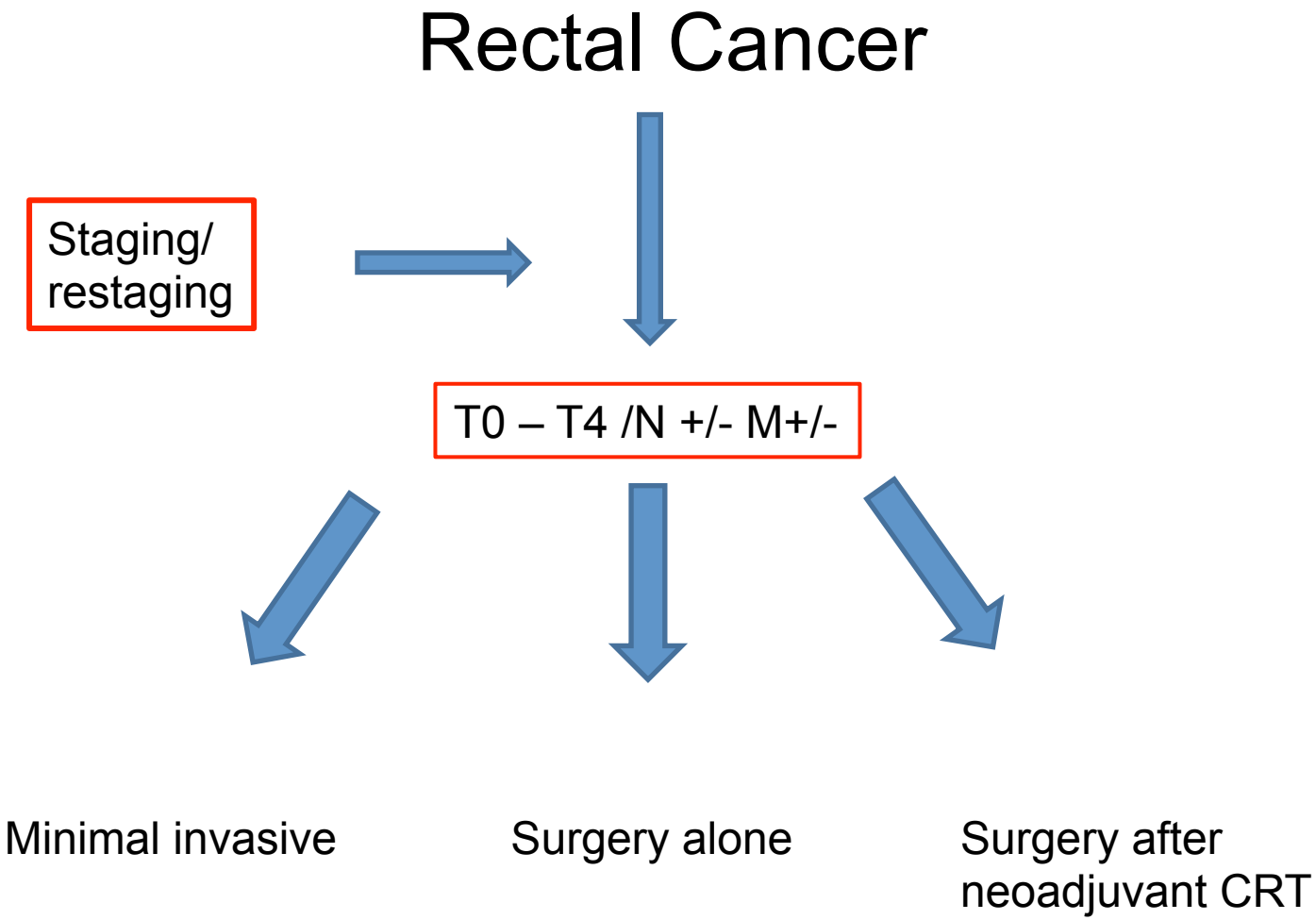
N2 Metastasis in four or more regional lymph nodes

Local treatment

Surgery
+/- neoadjuvant CRT

Neoadjuvant CRT

Rectal cancer

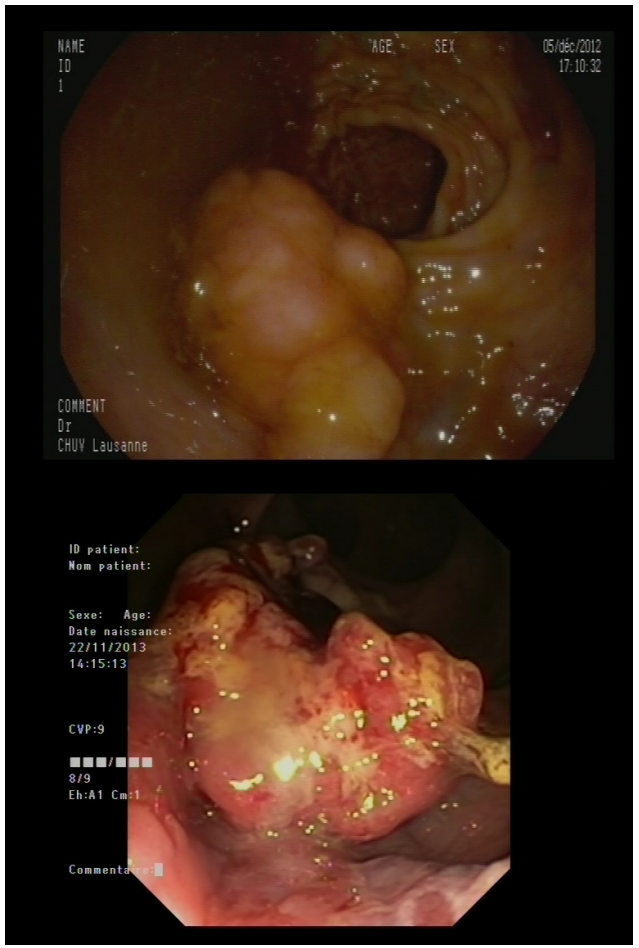


Staging modalities

- Standard Endoscopy
- Biopsies
- EUS
- EUS FNA
- MRI
- CT-scan

Standard Endoscopy and Biopsies

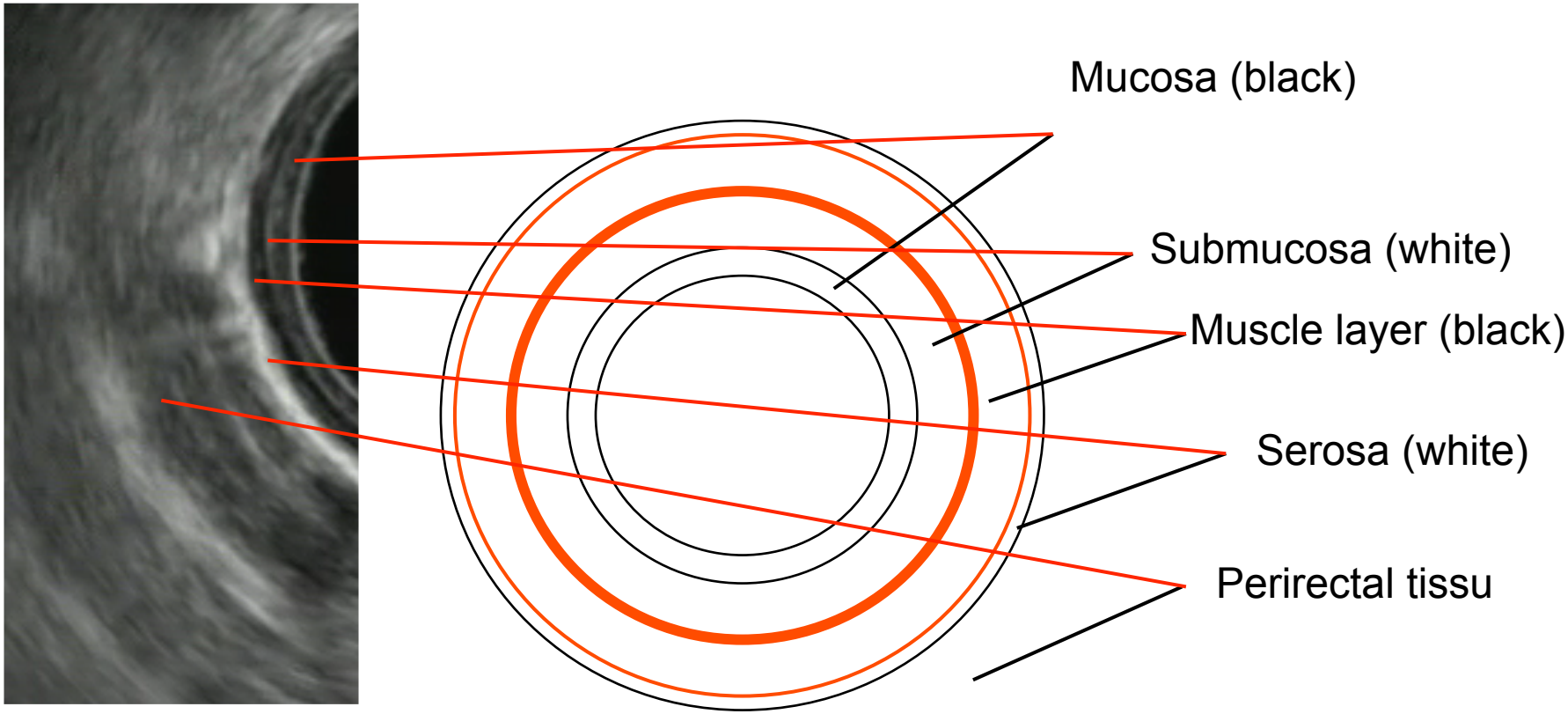
- Localisation of the lesion
- Distance to anal-rectal margin
- Histology:
  - Adenoma
  - Mucosal carcinoma (Tis)
  - Invasive carcinoma: G Typ



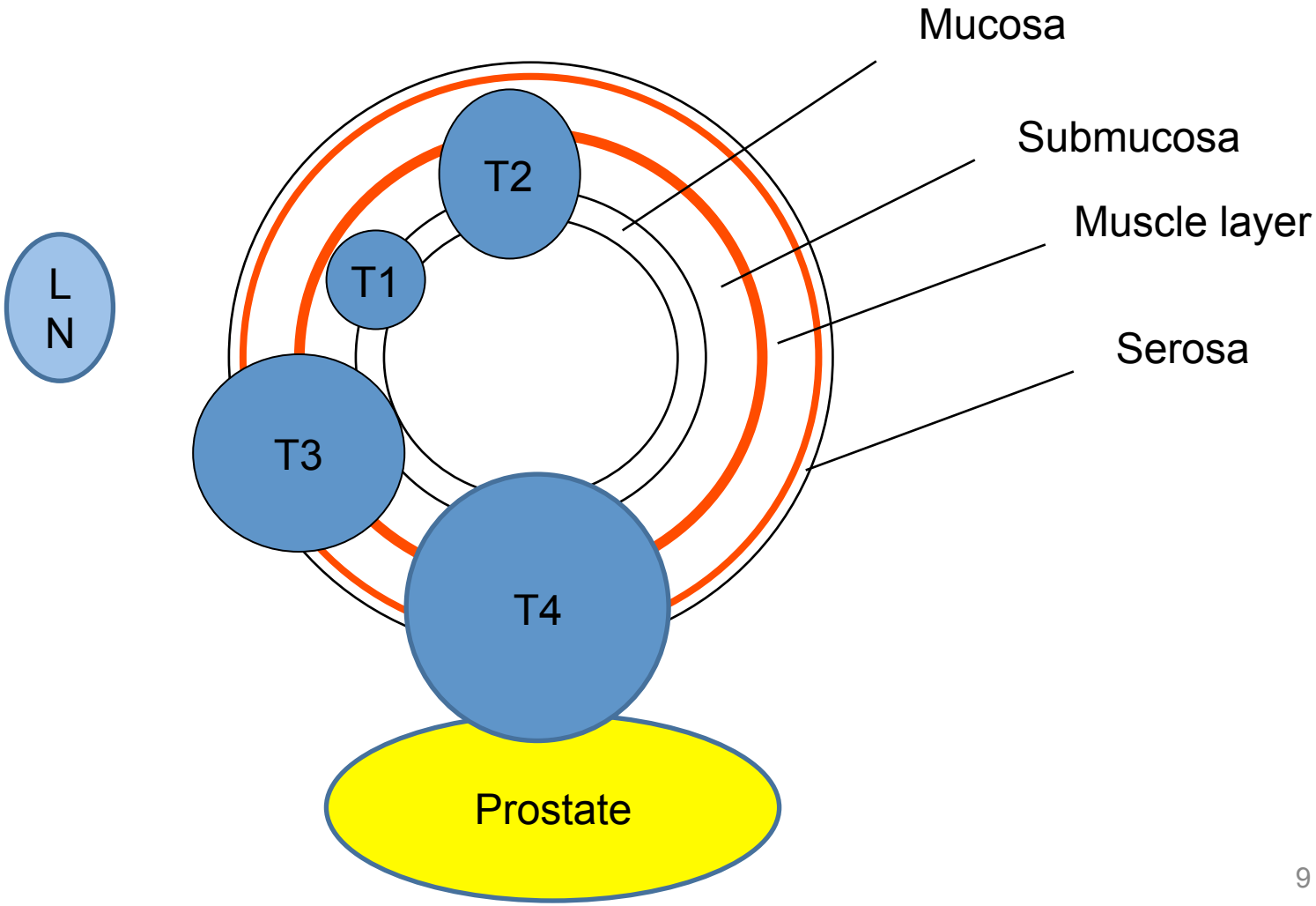
EUS

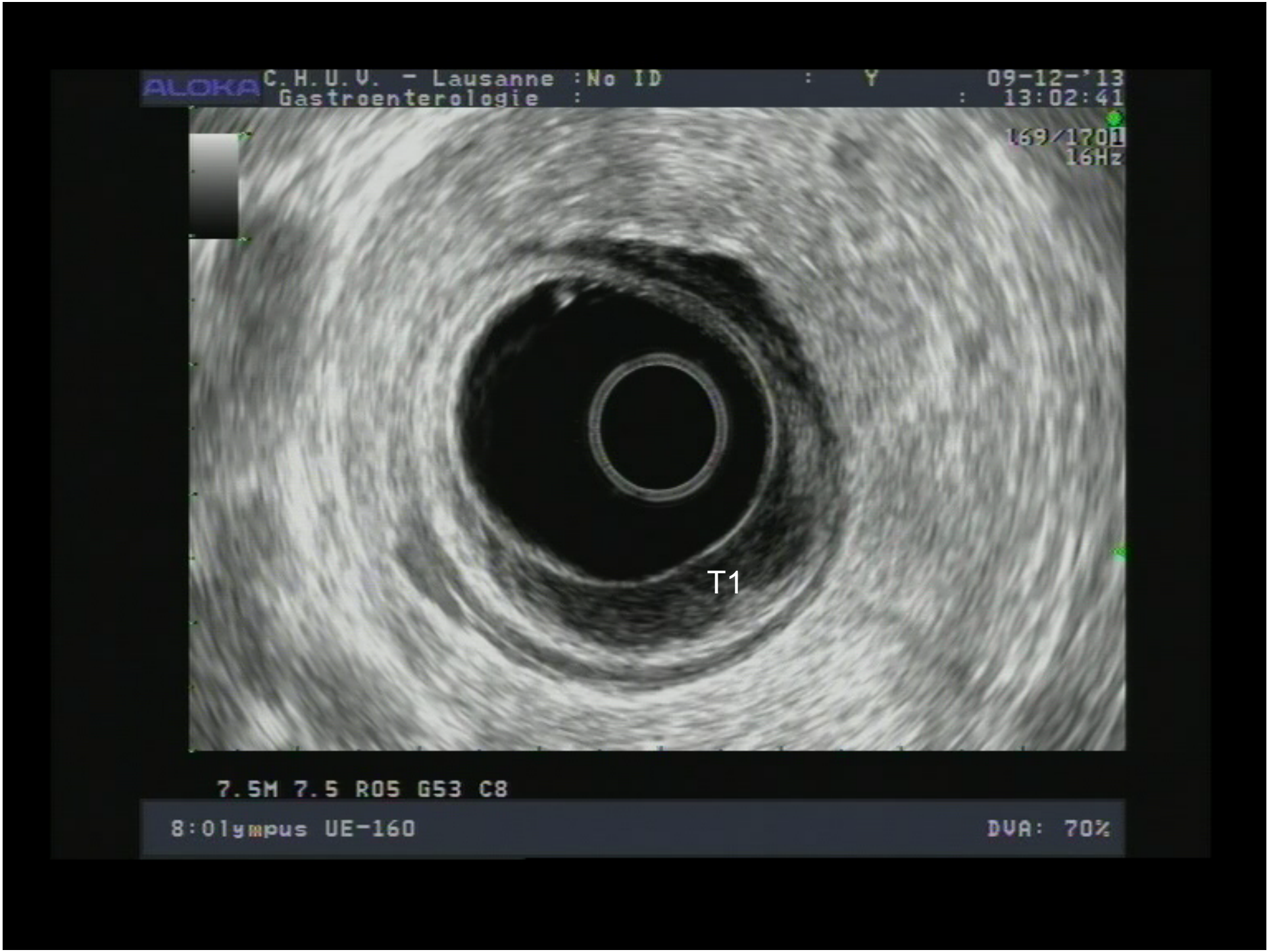
- Localisation of the lesion
- Distance to anal-rectal margin
- T stage
- N Stage
- FNA of suspect LN

EUS: what we can see



EUS: Staging TN

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Gastroenterologie :
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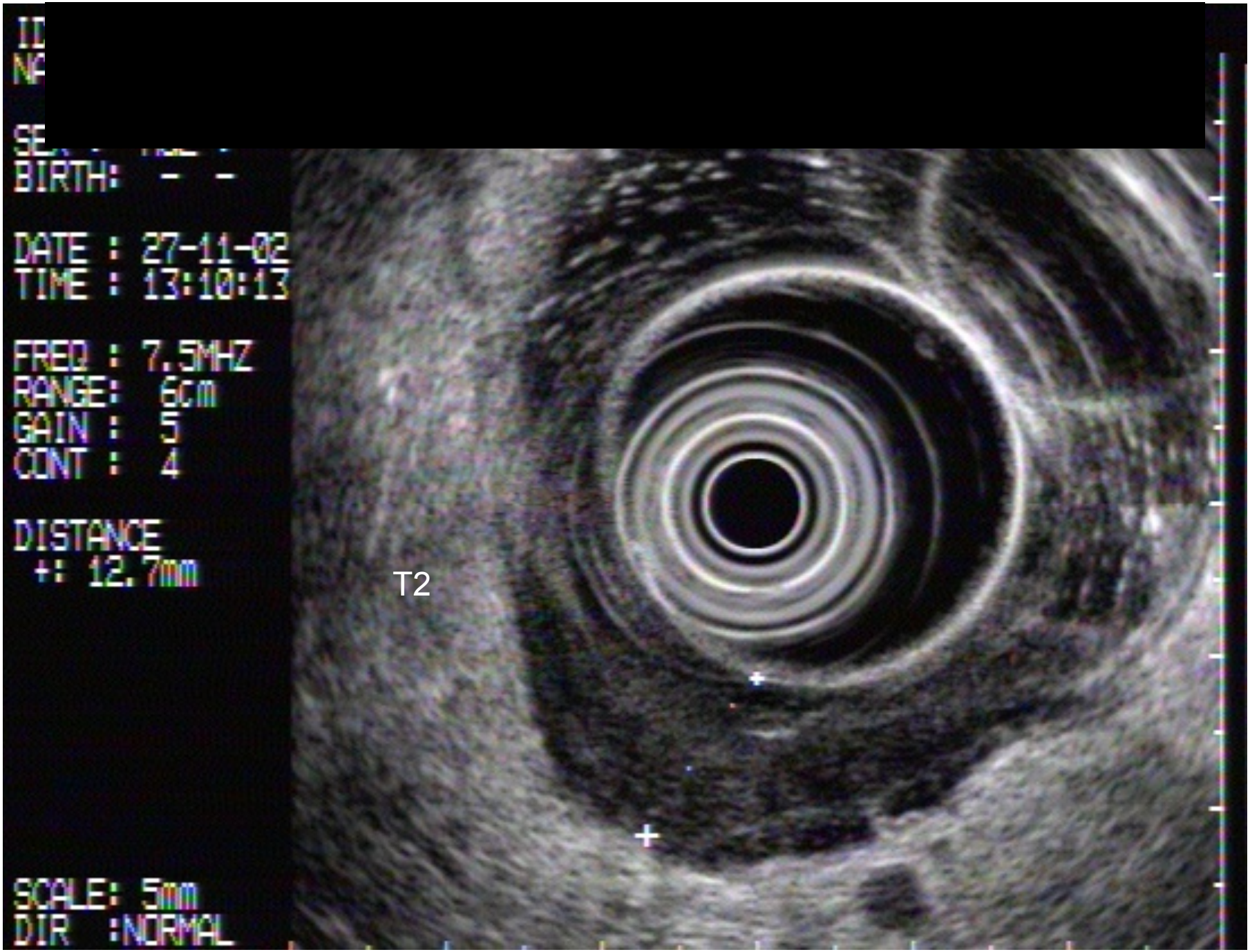
169/1701
16Hz
T1
7.5M 7.5 R05 G53 C8
8:Olympus UE-160
DVA: 70%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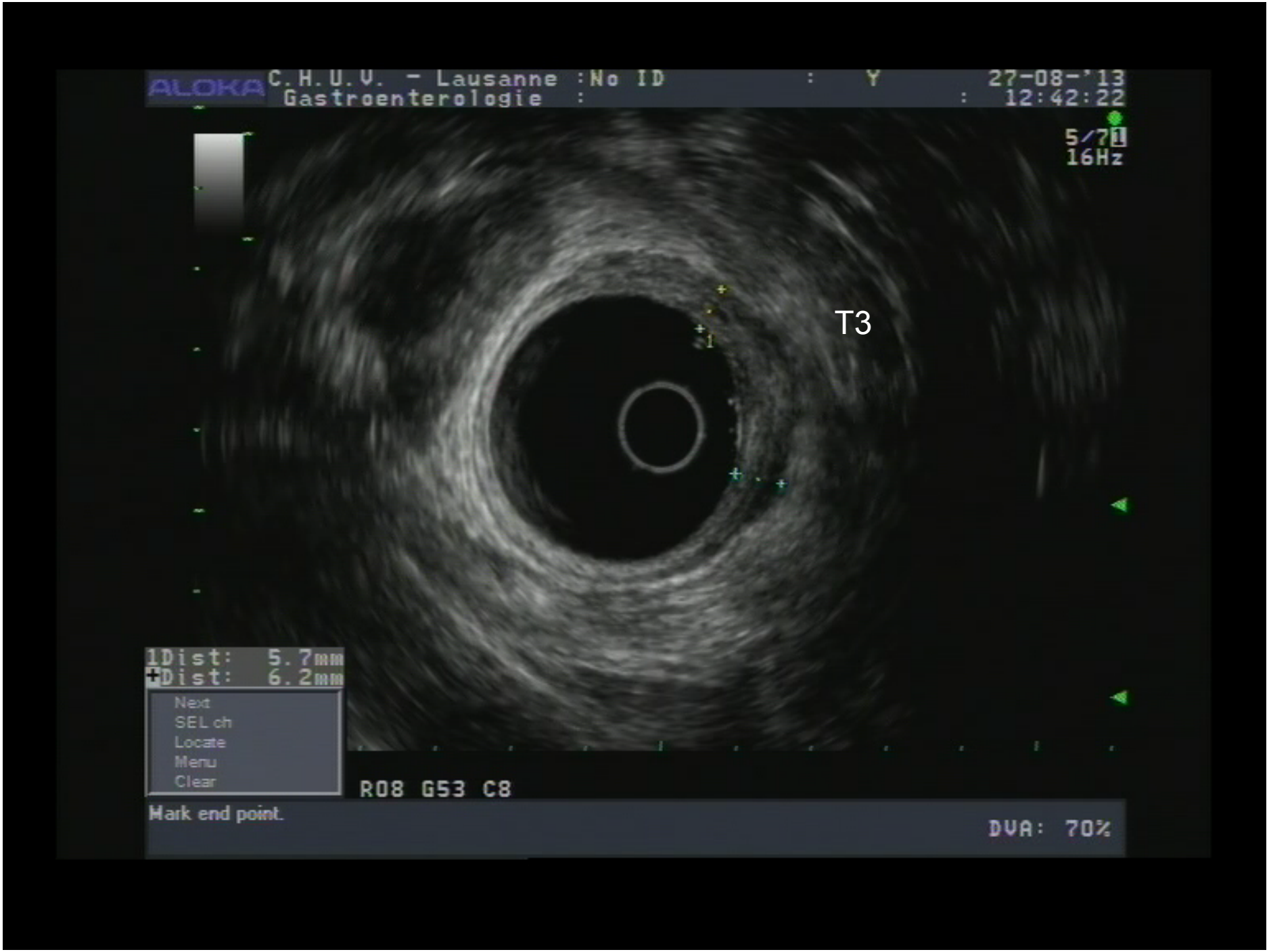
CONT : 4
DISTANCE
+: 12.7mm
T2
SCALE: 5mm
DIR :NORMAL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12:42:22
5/7
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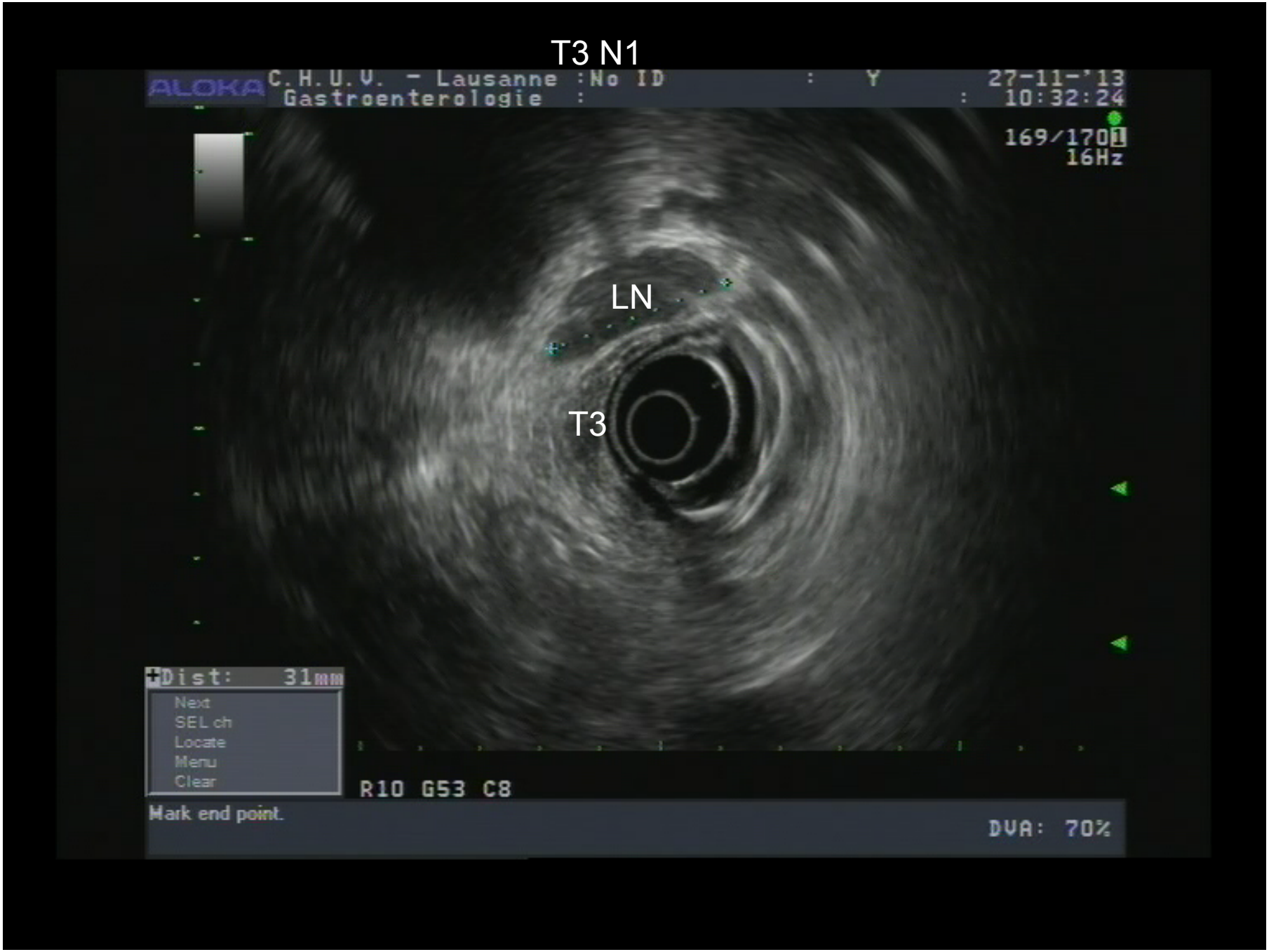
T3
1Dist: 5.7mm
+Dist: 6.2mm
Next
SEL ch
Locate
Menu
Clear
R08 G53 C8
Mark end point.
DVA: 70%


T3 N1
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Gastroenterologie :
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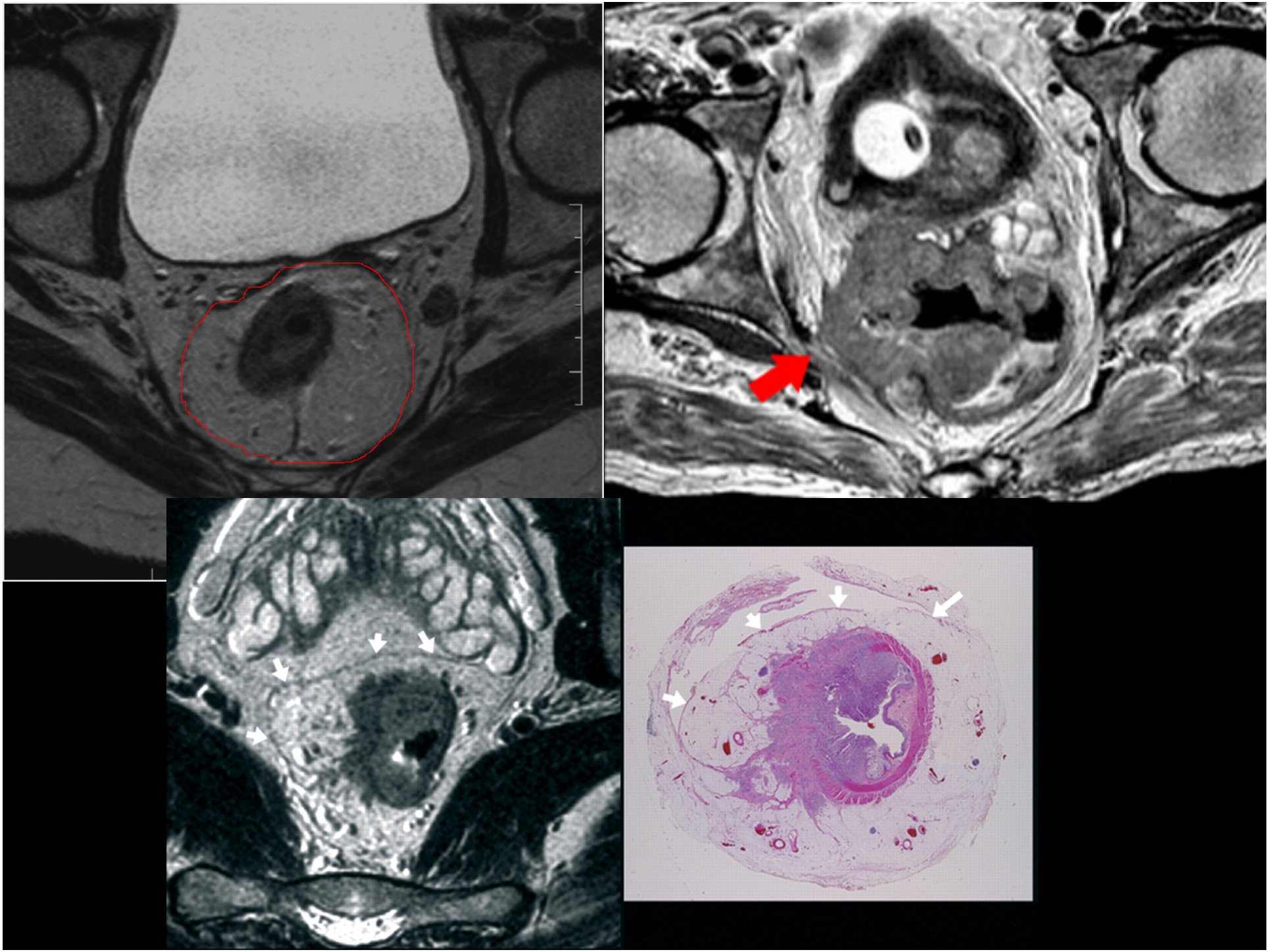
169/170
16Hz
LN
T3
Dist: 31mm
Next
SEL ch
Locate
Menu
Clear
R10 G53 C8
Mark end point.
DVA: 70%

MRI

- Localisation of the lesion
- Distance to anal-rectal margin
- T stage (not T1)
- N stage
- M staging
- Correlation tumor and LN with mesorectal fascia



CT - scan

- M staging: thoraco-abdominal-pelvin
- (T stage)
- (N stage)

PET - scan

- N+ or N-

ASGE: State of the Art

Staging

	EUS		MRI		CT	
	Sens	Spec	Sens	Spec	Sens	Spec
T 0 -3	80-96	75-98	82-94	69-76	79	78
N +/-	67	78	66	76	55	74

Restaging after CRT

	EUS		MRI		CT	
	Accuracy		Accuracy		Accuracy	
T	27		34	-	37	-
N +/-	65		68		62	

Staging TN rectal cancer EUS/CT/MRI

TABLE 3
Summary Estimates of Sensitivity and Specificity for Endoluminal US, CT, and MR Imaging in the Staging of Rectal Cancer

Stage	Imaging Modality	Sensitivity (%)	Specificity (%)
Muscularis propria invasion	EUS	94 (90, 97)	86 (80, 90)
	CT	NA	NA
	MR imaging	94 (89, 97)	69 (52, 82)*
Perirectal tissue invasion	EUS	90 (88, 92)	75 (69, 81)
	CT	79 (74, 84)*	78 (73, 83)
	MR imaging	82 (74, 87)*	76 (65, 84)
Adjacent organ invasion	EUS	70 (62, 77)	97 (96, 98)
	CT	72 (64, 79)	96 (95, 97)
	MR imaging	74 (63, 83)	96 (95, 97)
Lymph node involvement	EUS	67 (60, 73)	78 (71, 84)
	CT	55 (43, 67)	74 (67, 80)
	MR imaging	66 (54, 76)	76 (59, 87)

Note.—Numbers in parentheses are 95% CIs. EUS = endoluminal US, NA = not applicable.
* Significantly lower than EUS.

Meta- Analysis Bipat Radiology 2004

EUS and MRI: T and N Staging

N= 90 prospective study

TABLE 3. Positive and negative predictive values obtained by EUS and MRI in estimating T stage in rectal tumors

	T1		T2		T3		T4	
	PPV, % (95% CI)	NPV, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
EUS	73 (39-94)	99 (93-100)	52 (28-74)	83 (72-91)	77 (63-87)	73 (54-88)	0 (NP)	95 (88-99)
MRI	0 (NP)	90 (81-95)	50 (31-69)	91 (81-97)	90 (78-97)	74 (57-87)	50 (16-84)	100 (80-100)

PPV, Positive predictive value; *CI*, confidence interval; *NPV*, negative predictive value; *MRI*, magnetic resonance imaging; *NP*, not possible because at least 1 variable in each 2-way table on which measures of association are computed is a constant.

TABLE 4. Performance characteristics of EUS and MRI for the detection of positive lymph nodes in rectal tumors

	Se, % (95% CI)	Sp, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Acc, % (95% CI)
EUS	41 (22-61)	89 (72-98)	79 (49-95)	61 (44-76)	65 (51-78)
MRI	71 (51-87)	86 (67-96)	83 (63-95)	75 (57-88)	79 (65-88)
P	NP	NS			NS

MRI, Magnetic resonance imaging; *Se*, sensitivity; *CI*, confidence interval; *Sp*, specificity; *PPV*, positive predictive value; *NPV*, negative predictive value; *Acc*, accuracy; *MRI*, magnetic resonance imaging; *NP*, not possible because at least 1 variable in each 2-way table on which measures of association are computed is a constant; *NS*, not significant.

Fernandes-Esparrach Gastrointestinal endoascopy 2011

Under/Overstaging MRI/EUS

TABLE 6. Comparison of cases overstaged and understaged by EUS and MRI

	All cases (N = 90)	T1 (n = 9)	T2 (n = 22)	T3 (n = 55)	T4 (n = 4)
EUS					
Understaging	16	0	4	8	4
Overstaging	8	1	7	0	0
MRI					
Understaging	6	0	0	6	0
Overstaging	18	9	5	4	0

MRI, Magnetic resonance imaging.

Fernandes-Esparrach Gastrointestinal endoscopy 2011

Staging CT for colorectal cancer

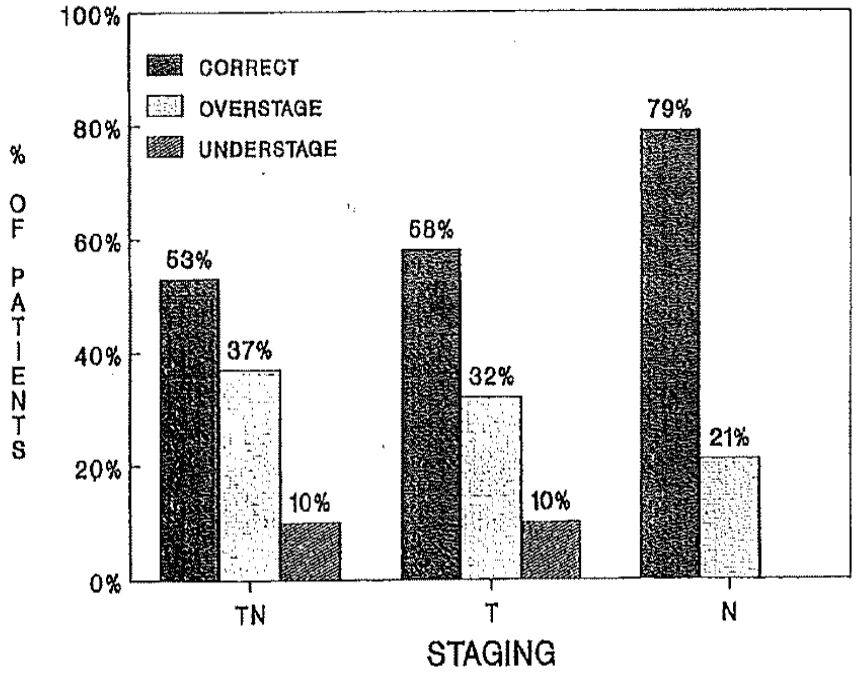


Figure 2. Accuracy of TN, T, and N staging of rectal cancers using CT scan *before* radiation therapy as compared with pathologic specimen.

Fleshmann Dis colon rectum 1992

TNM Classification of Rectal Cancer

T-Primary tumor

Tx Primary tumor cannot be assessed

T0 No evidence of primary tumor

Tis Carcinoma in situ: intraepithelial or invasion of lamina propria

T1 Tumor invades submucosa

Local treatment

T2 Tumor invades muscularis propria

T3 Tumor invades through muscularis propria into subserosa or into non-peritonealized pericolic or perirectal tissues

T4 Tumor directly invades other organs or structures and/or perforates visceral peritoneum

Surgery
+/- neoadjuvant
CRT (> T 3b)

N-Regional lymph nodes

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Metastasis in one to three regional lymph nodes

N2 Metastasis in four or more regional lymph nodes

Neoadjuvant
CRT (> N 0)

Key questions

- T 1 N0 or > T1
  - Endosocopic or TEM
- T2 /T3a > T3a
  - Surgery alone or CRT and surgery
- N0 or N+
  - N+ neoadjuvant CRT

Accuracy of EUS: T1cancer

- In 5/30 non-diagnostic, 1 overstaged
  → accuracy 83%

Koebrugge B. J Clinical Ultrasound 2010

- N=81 TEM 26% pTis overstaged uT1
  41% of T1 understaged Tis

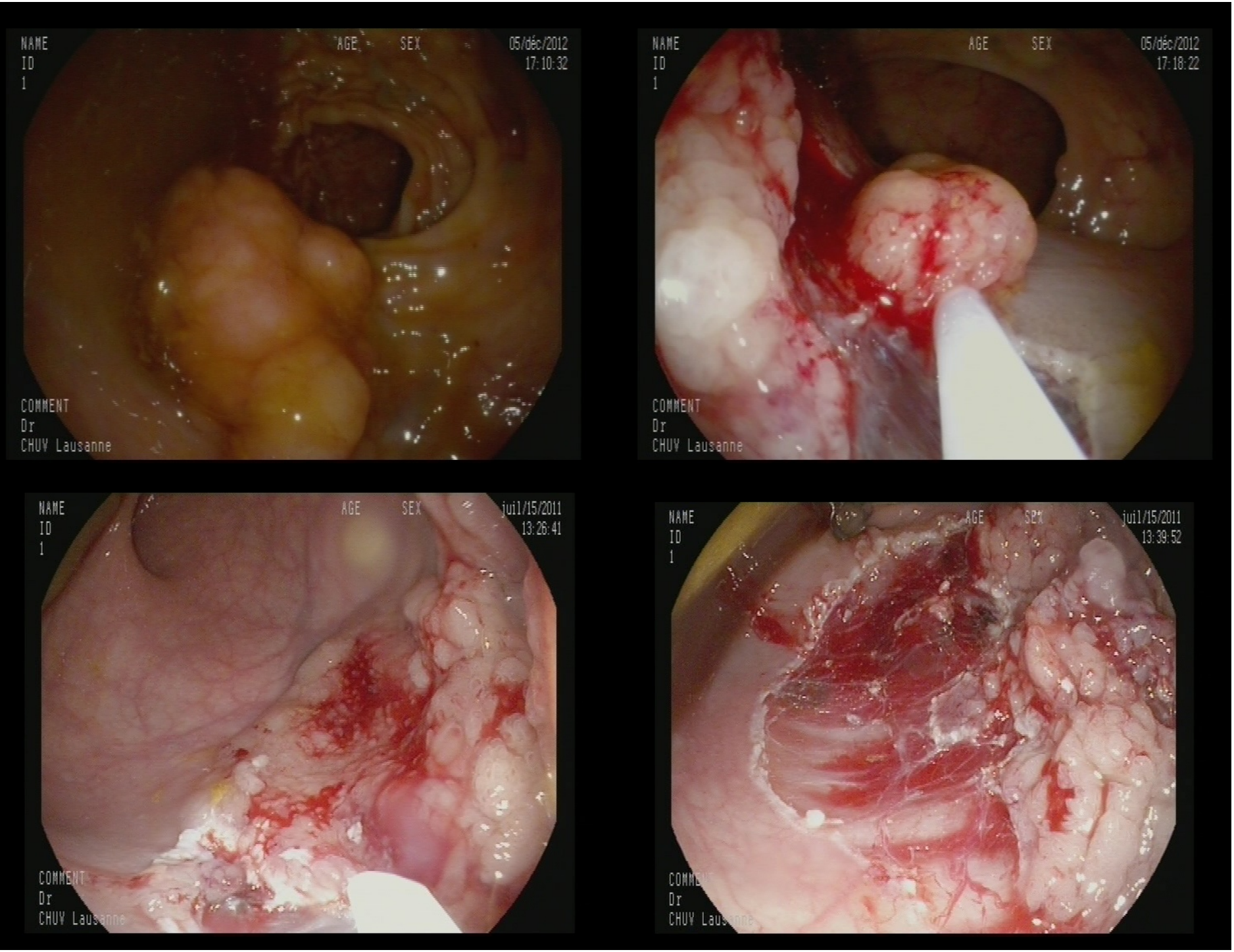
(MRI: identification of T1 impossible)

Zorcolo L. Surg Endosc 2009

Rectal cancer

- Treatment modalities:
- Endoscopic:
  - Mucosectomy
  - Submucosal resection
- Surgical:
  - TEM
  - TME, RAB +/- neoadjuvant CRT

Minimal invasive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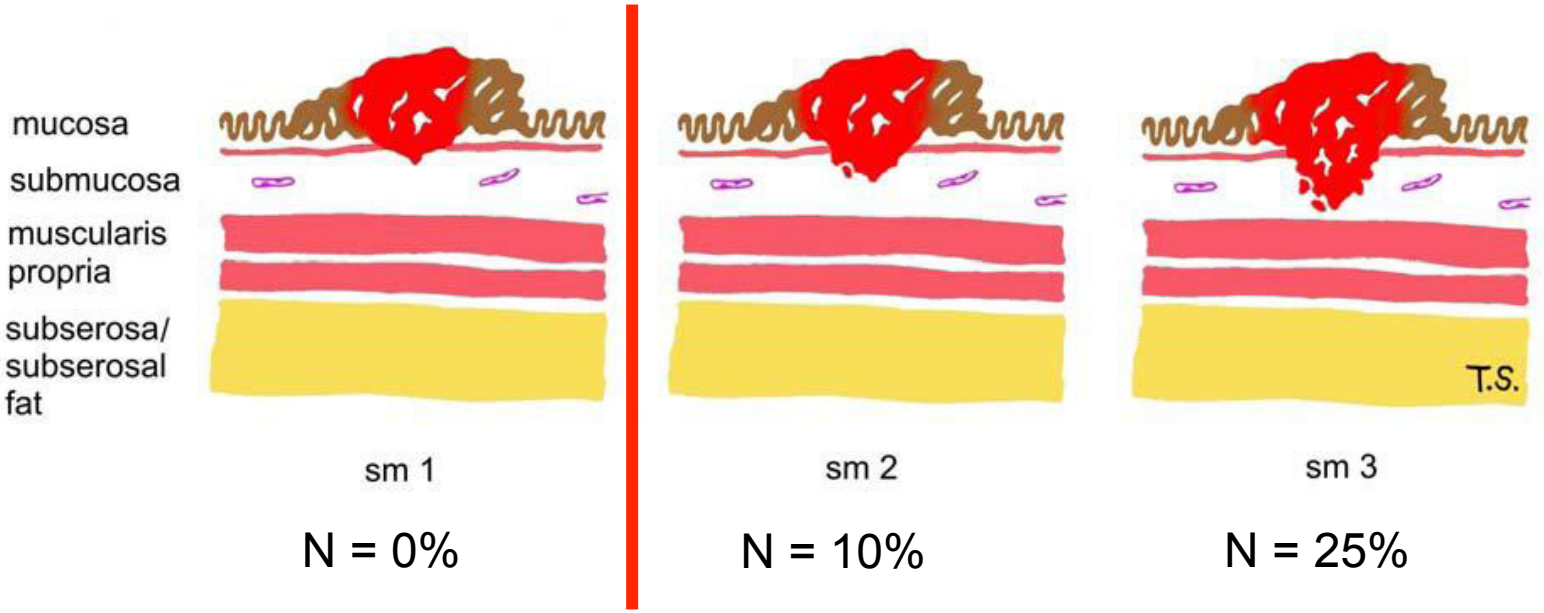
Côlon: Kikuchi classification



Cave: G3

Key questions

- T 1 N0 or > T1
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- N0 or N+
  - N+ neoadjuvant CRT

Rectal cancer

- Treatment modalities:
- Endoscopic:
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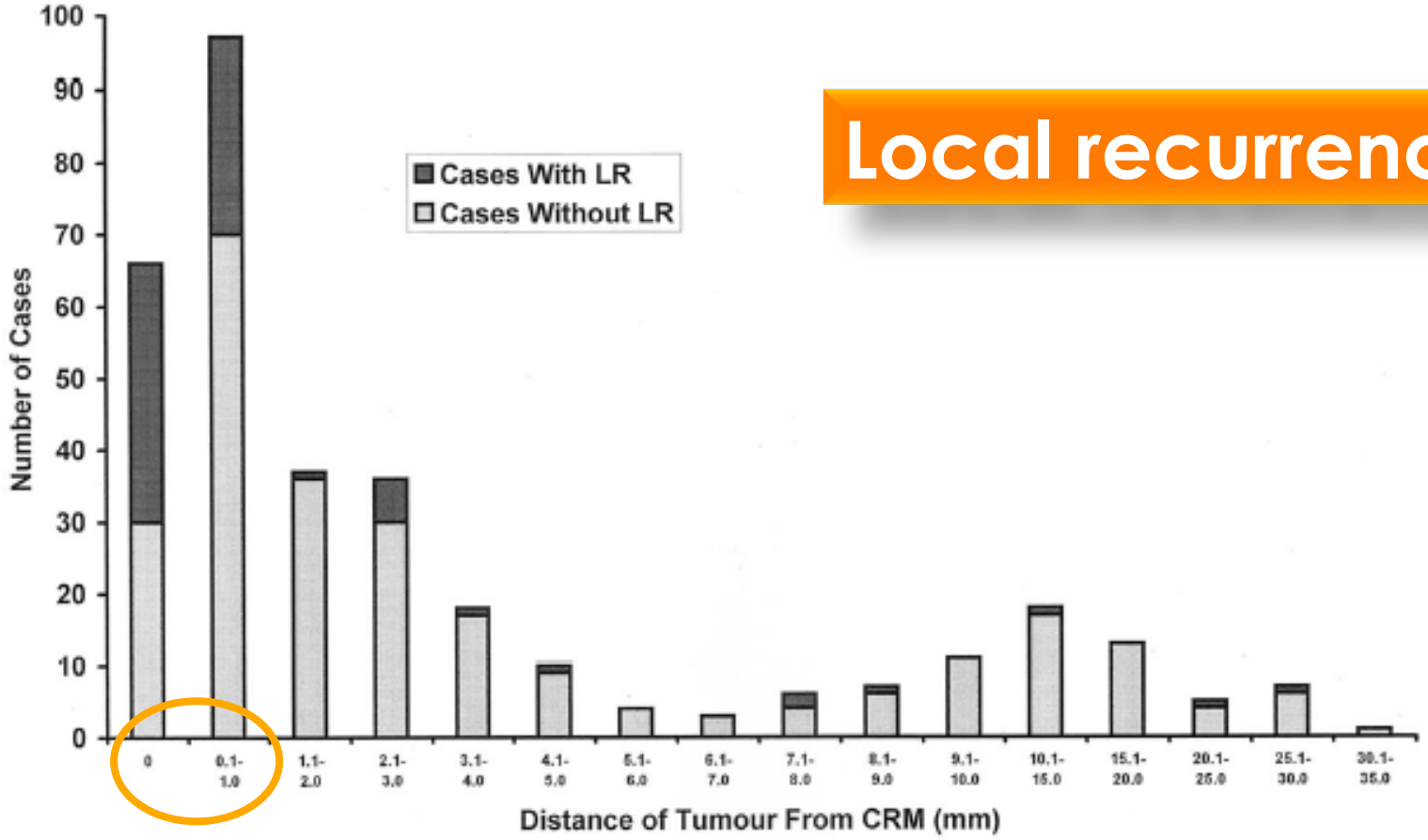
  - Submucosal resection
- Surgical:
  - TEM
  - TME, RAB +/- neoadjuvant CRT

CRM (Circumferential Resection Margin)

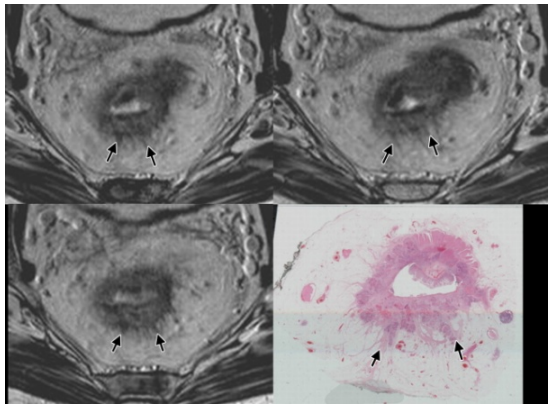


Local recurrence

Birbeck KF. Ann Surg 2002

EMD (Extra Mural Spread)

295 pts (UK, N, Se, Ger)
Only surgery or short-term RT



- **Difference EMD:**
  MR vs. Pathology = Mean -0.05mm

- **<5mm : 85% 5yrs SV**
- **>5mm : 54% 5yrs SV**

MERCURY Study Group, Radiology 2007

EUS and MRI: T Staging

N= 90 prospective study

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	T1		T2		T3		T4	
	PPV, % (95% CI)	NPV, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
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Fernandes-Esparrach Gastrointestinal Endoscopy 2011

MRI in T staging: T2 – T3 b

Table 1

MR versus Histopathologic Assessment of Tumor Stage in 311 Patients Who Underwent Primary Surgery

	Histopathologic Depth of Invasion								
MR Tumor Stage	pT0	pT1	pT2	pT3a	pT3b	pT3c	pT3d	pT4	Total
T0	3	0	0	0	0	0	0	0	3
T1	2	1	3	2	0	0	0	0	8
T2	7	12	39	24	25	6	0	4	117
T3a	1	2	13	10	11	0	0	1	38
T3b	1	4	16	13	26	13	0	3	76
T3c	0	0	0	7	14	17	3	1	42
T3d	0	0	0	0	0	3	1	0	4
T4	0	0	1	0	0	4	2	5	12
Data not available	0	0	0	0	0	0	0	0	11
Total	14	19	72	56	76	43	6	14	311

Note.—Data are numbers of patients. Weighted κ with quadratic (Fleiss-Cohen) weights = 0.54 (95% CI: 0.43, 0.63). Observed weighted agreement = 96%.

Understaging MRI: 36/155 (23%)

Mercury Study Radiology 2007

Key questions

- T 1 N0 or > T1
  - Endosocopic or TEM
- T2 /T3a > T3a
  - Surgery alone or CRT and surgery
- N0 or N+
  - N+ neoadjuvant CRT

EUS and MRI: N - Staging

N= 90 prospective study

TABLE 4. Performance characteristics of EUS and MRI for the detection of positive lymph nodes in rectal tumors

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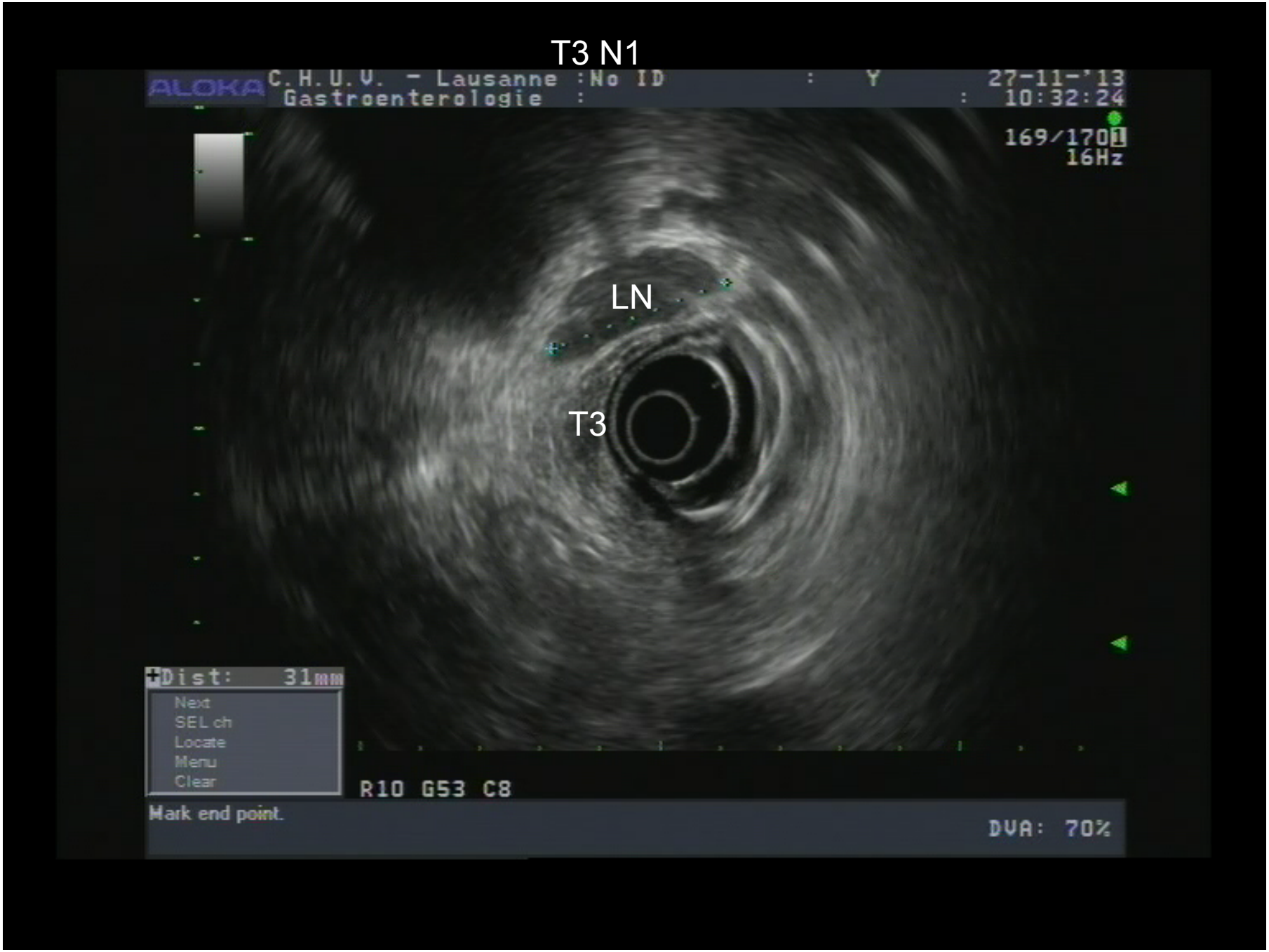
P	NP	NS			NS

MRI, Magnetic resonance imaging; *Se*, sensitivity; *CI*, confidence interval; *Sp*, specificity; *PPV*, positive predictive value; *NPV*, negative predictive value; *Acc*, accuracy; *MRI*, magnetic resonance imaging; *NP*, not possible because at least 1 variable in each 2-way table on which measures of association are computed is a constant; *NS*, not significant.

Fernandes-Esparrach Gastrointestinal Endoscopy 2011


T3 N1
ALOKA
C.H.U.V. - Lausanne :No ID : Y
Gastroenterologie :
27-11-'13
10:32:24
169/170
16Hz
LN
T3
Dist: 31mm
Next
SEL ch
Locate
Menu
Clear
R10 G53 C8
Mark end point.
DVA: 70%

EUS: N-staging

Table 2 Comparison between ERUS and pathological N staging

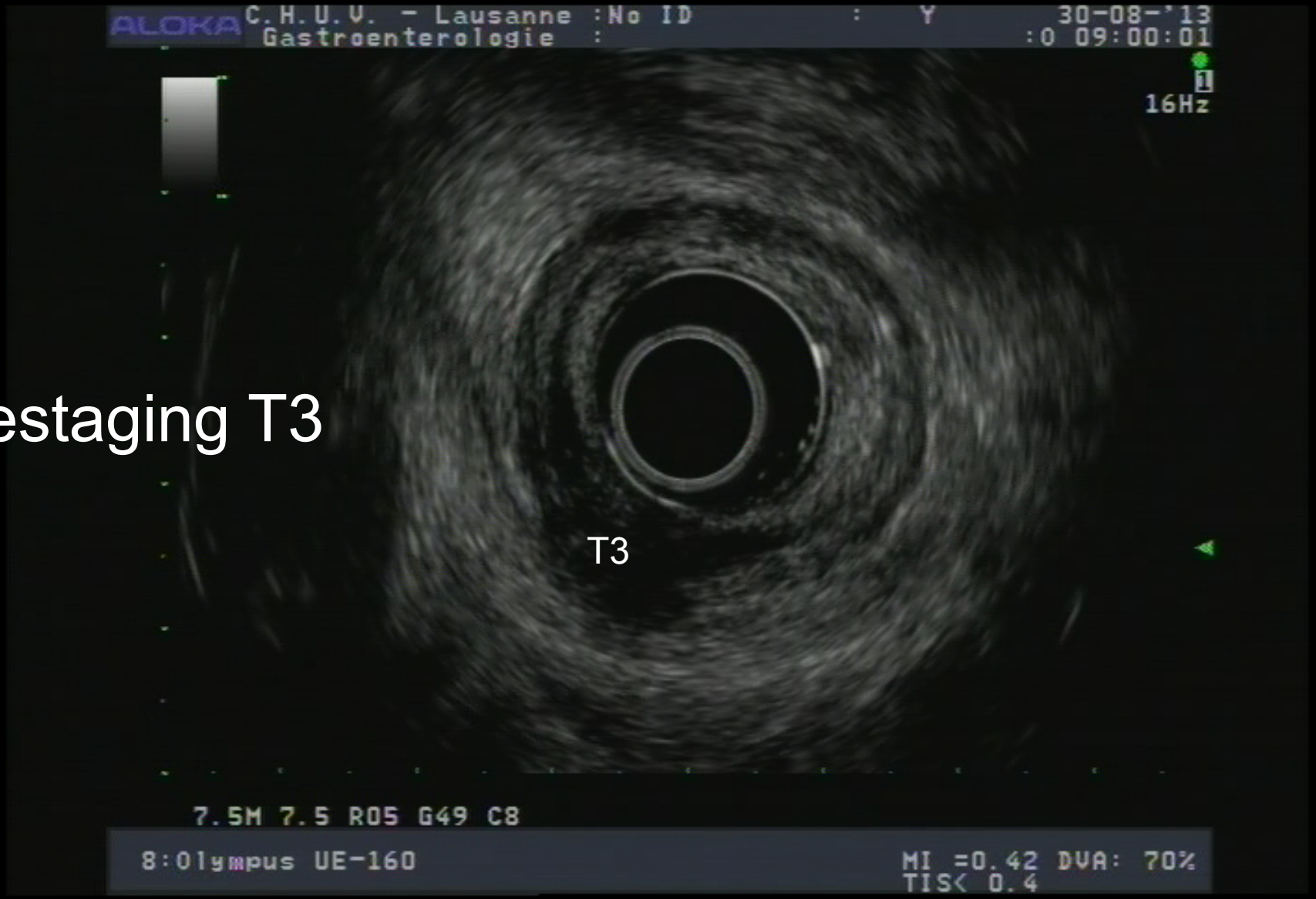
N stage	Pathology stage			Total (*n*)	Overstaged (%)	Understaged (%)	Accuracy (%)
ERUS	pN0	pN1	pN2				
uN0	21	5	0	26	–	19	81
uN1	9	6	3	18	50	–	50
Total	30	11	3	44	20	11	68

FNA ! / PET-scan

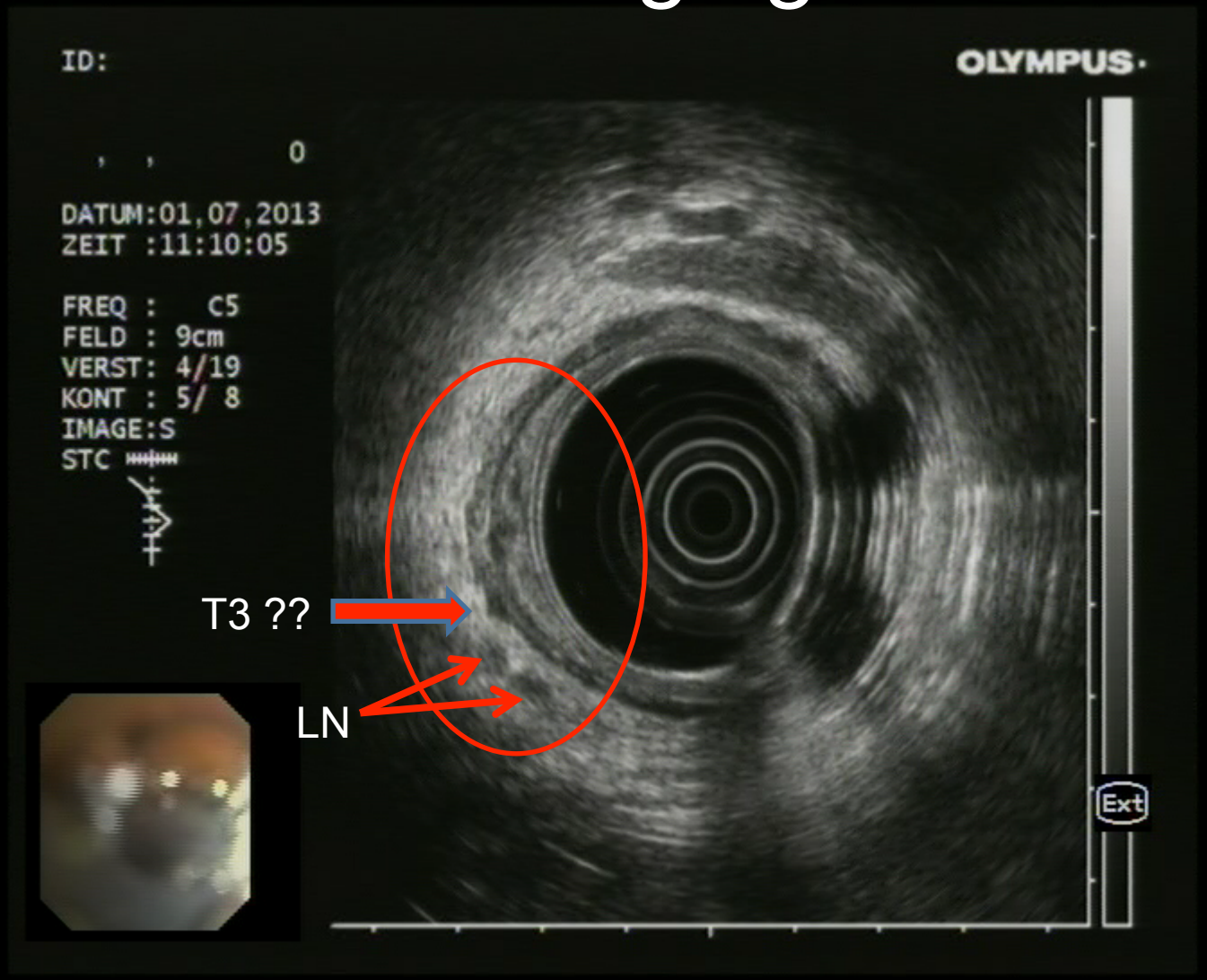
Radovanivic Surg Endosc 2008

Restaging of Rectal Cancer After CRT

Restaging T3



Restaging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KONT : 5/ 8
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T3 ??
LN
Ext

EUS: Restaging T post CRT

N=82

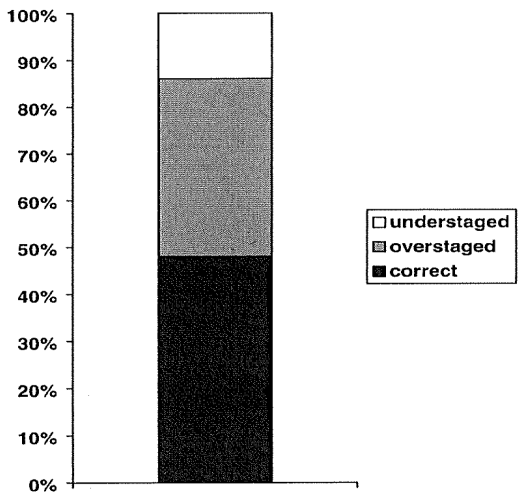


Figure 1. T-staging accuracy for restaging after neoadjuvant chemoradiation, with percentages correctly staged (solid), overstaged (gray), understaged (white).

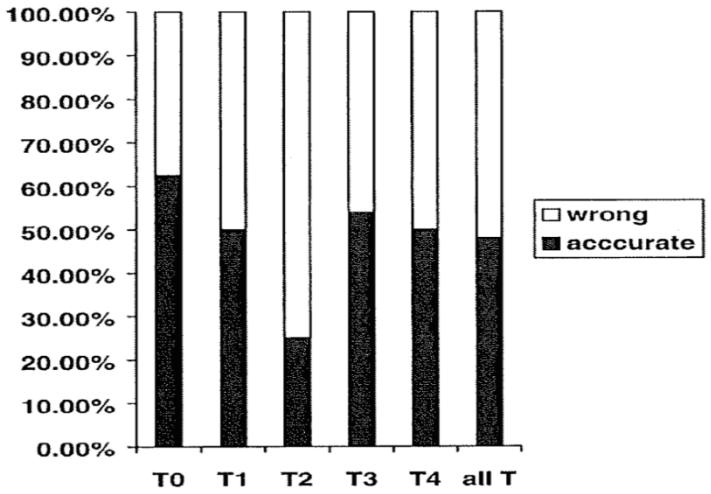


Figure 2. T-staging accuracy of restaging after neoadjuvant chemoradiation (black bars) for the individual T-stages and composite for all stages. The white bars represent the entire group.

Vangunas Am J Gastro 2003

TABLE 4. Comparison between EUS post-CRT and pathological N stage

EUS N stage	*Pathology stage*		*Total*	*Understaged*	*Overstaged*
	pN0	*pN+*	*n*	*n (%)*	*n (%)*
uN0	**146**	46	160	46 (28)	0 (0)
uN+	14	**29**	43	0 (0)	14 (32)
Total	160	75	235	46 (19)	14 (6)

Sensitivity, 39%; specificity, 91%; PPV, 67%; NPV, 76%.

EUS = endoscopic ultrasound; CRT = chemoradiation; PPV = positive predictive value; NPV = negative predictive value.

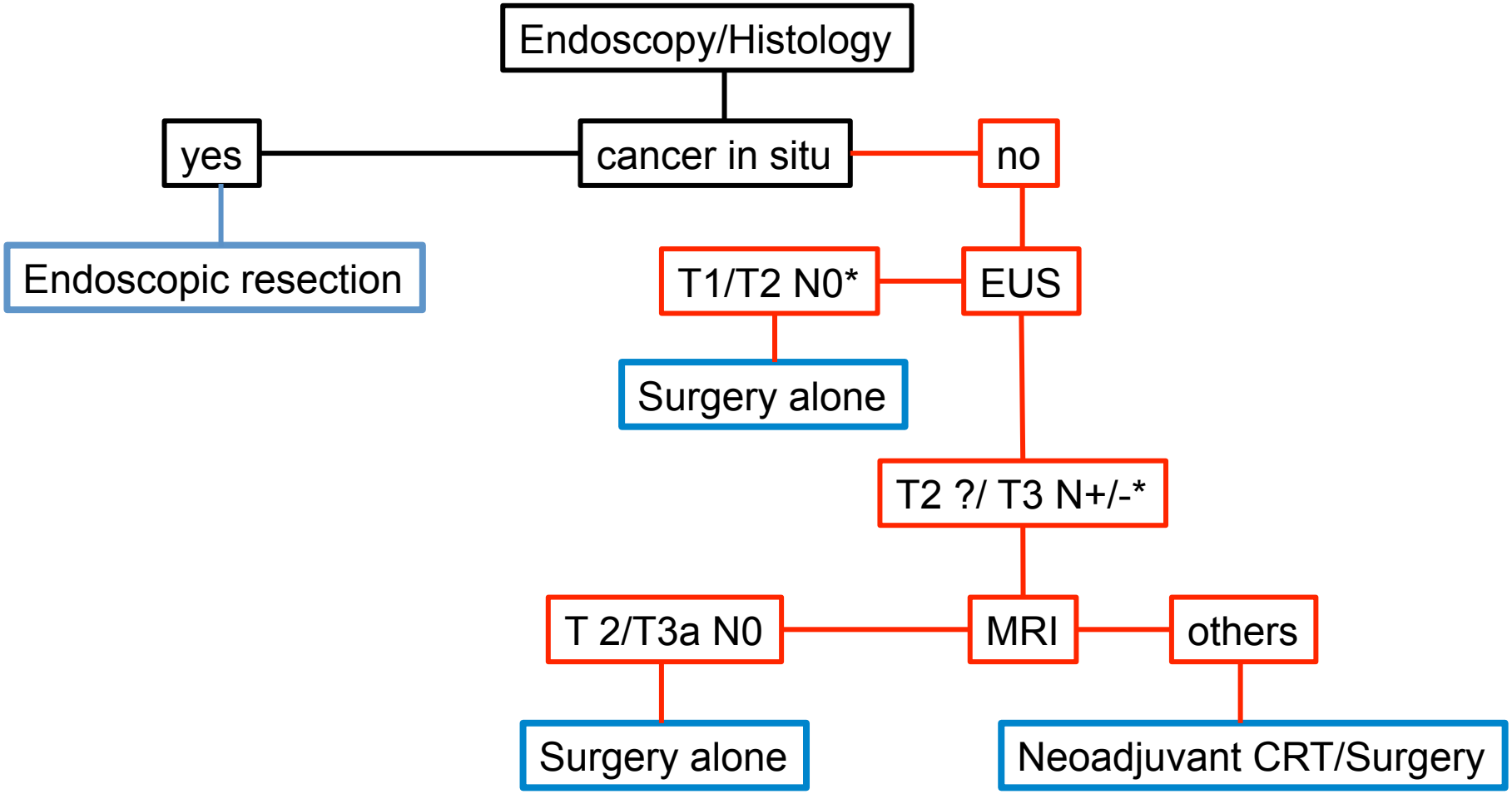
Pastor Dis colon rectum 2011

Advantages / Disadvantages

- EUS
- Pos:
  - Tis /T1
- Neg:
  - Extramural spread
  - Mesorectal fascia
  - Localisation LN
  - Restaging
- Staging early lesions

- MRI
- Pos:
  - Extramural spread
  - Mesorectal fascia
  - Localisation LN
- Neg:
  - T1
  - Restaging
- Staging advanced lesions

Staging Algorithme



* CT M-staging

PET-scan/ EUS FNA : N?