

Endoscopy in Gastric Cancer

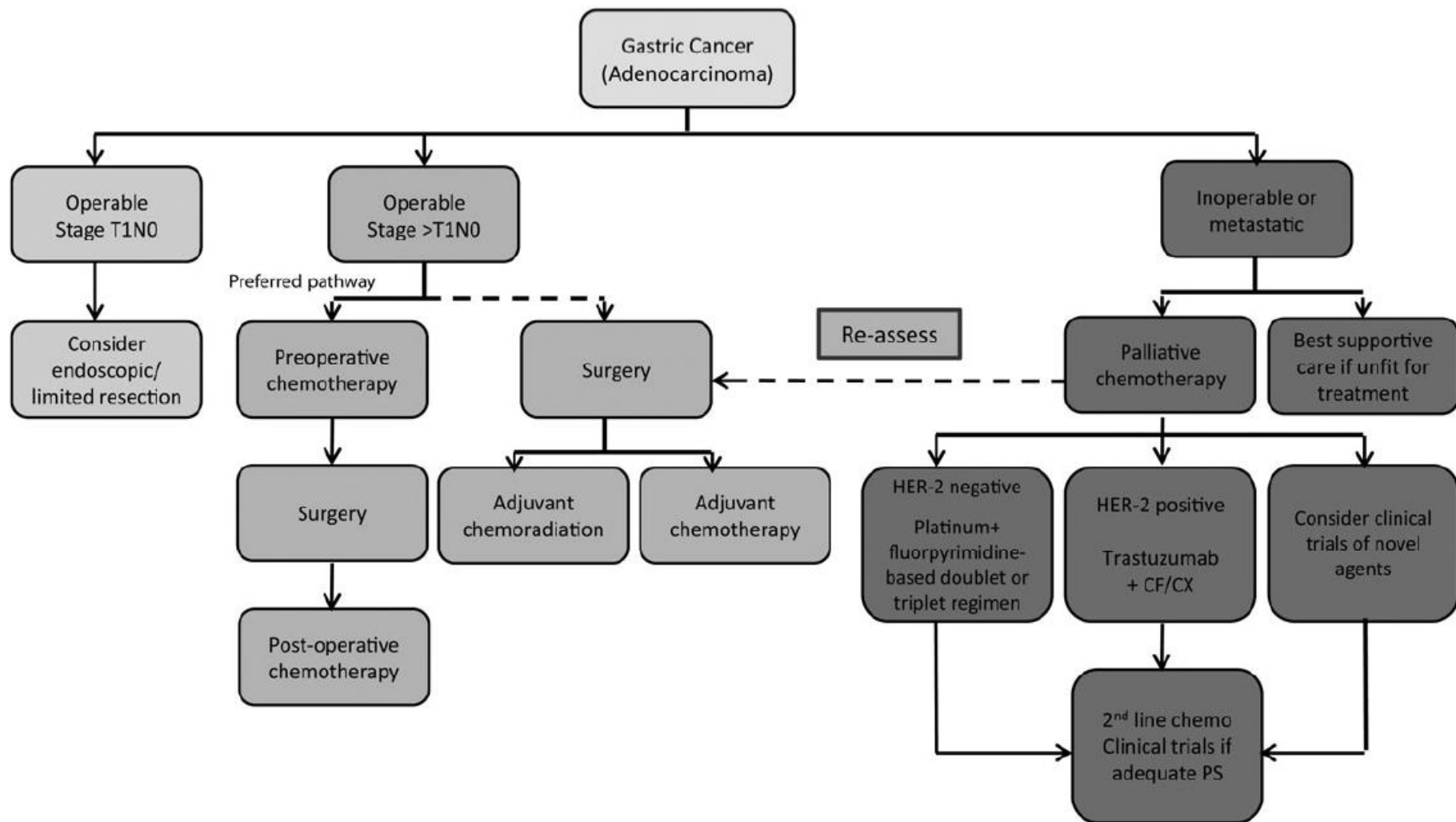
**New Diagnostic and
Therapeutic Techniques
for Individual Treatment Strategies**

**Prof. Dr. Markus Moehler
University Clinic Mainz, Germany**

**DGVS / EORTC / AIO Steering groups
Esophagus-Stomach**

No Disclosures

ESMO Minimal Guidelines





Available at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.ejccancer.info



EJC
EUROPEAN JOURNAL OF CANCER



Highlights of the EORTC St. Gallen International Expert Consensus on the primary therapy of gastric, gastroesophageal and oesophageal cancer – Differential treatment strategies for subtypes of early gastroesophageal cancer

Manfred P. Lutz^{a,*}, John R. Zalcberg^b, Michel Ducreux^c, Jaffer A. Ajani^d, William Allum^e, Daniela Aust^f, Yung-Jue Bang^g, Stefano Cascinu^h, Arnulf Hölscherⁱ, Janusz Jankowski^j, Edwin P.M. Jansen^k, Ralf Kisslich^l, Florian Lordick^m, Christophe Marietteⁿ, Markus Moehler^l, Tsuneo Oyama^o, Arnaud Roth^p, Josef Rueschoff^q, Thomas Ruhstaller^r, Raquel Seruca^s, Michael Stahl^t, Florian Sterzing^u, Eric van Cutsem^v, Ate van der Gaast^w, Jan van Lanschot^x, Marc Ychou^y, Florian Otto^z



German evidence-based guideline on diagnosis and treatment of esophagogastric cancer

124 experts
with review of all national European guidelines

Indication for Endoscopy

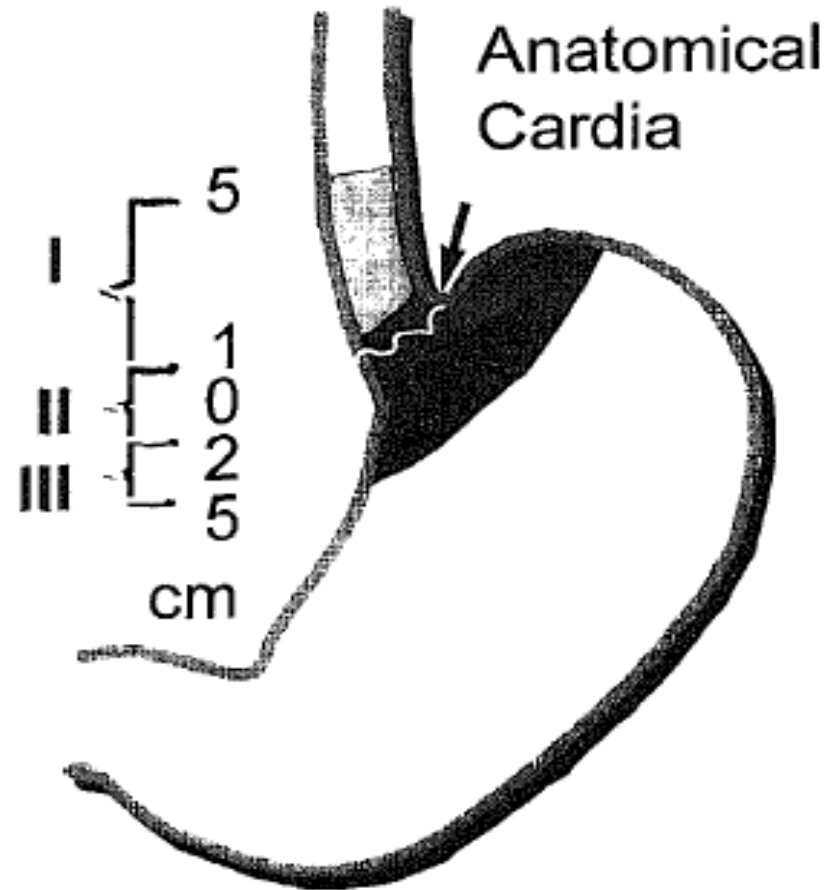
Patients with any of the following alarm symptoms should be referred for early endoscopy with biopsy specimens

- Dysphagia
- Recurrent vomiting
- Anorexia
- Weight loss
- Gastrointestinal bleeding

6-8 Biopsies
should be taken !

Proximal vs Distal Gastric Cancer

Adenocarcinomas
of the esophagogastric
junction (AEG types I-III)



Siewert-Classification

Proximal vs Distal Gastric Cancer

Two distinct patterns

Cardia / GEJ Cancers

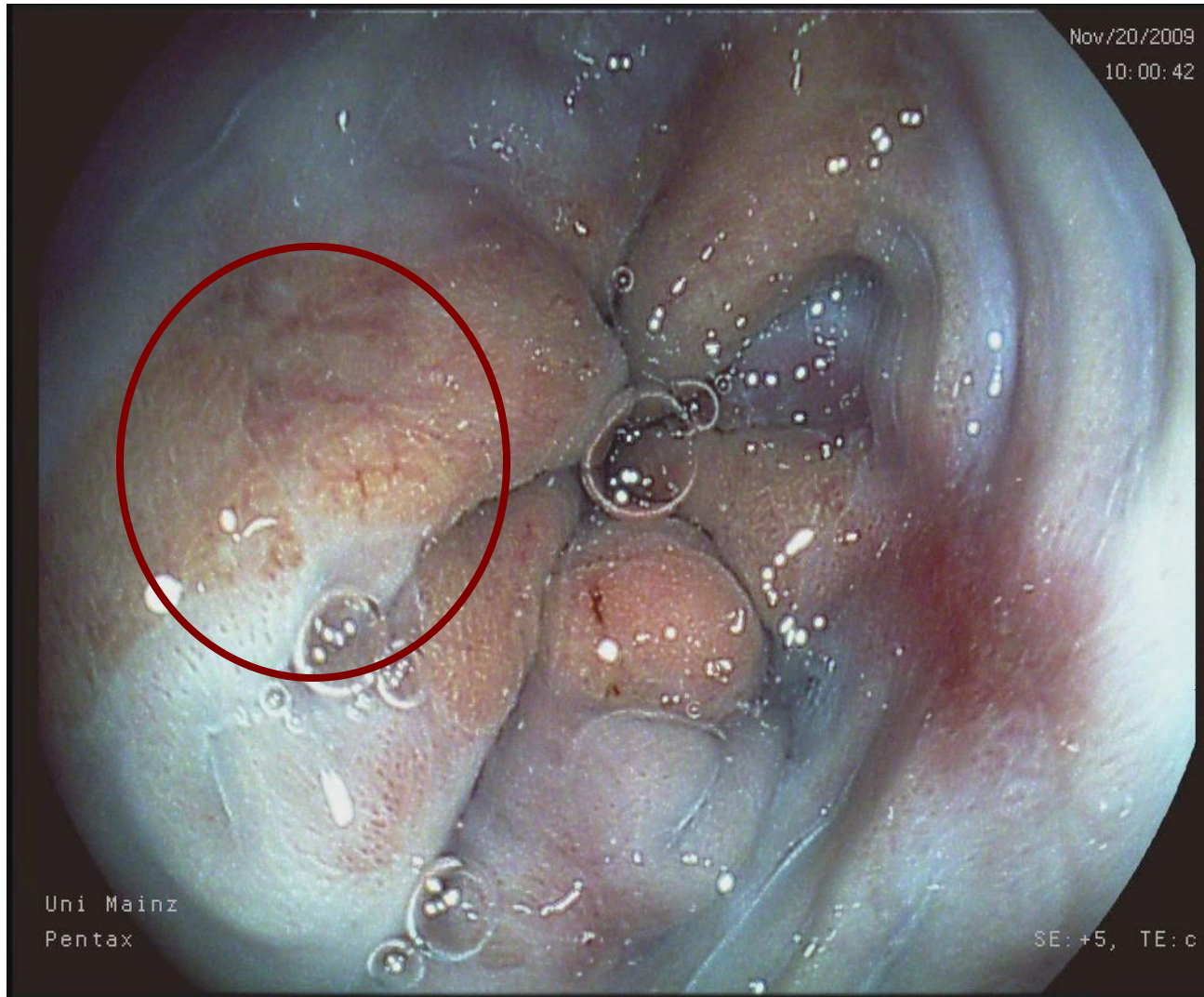
- Male: Female (5:1)
- white: black (2:1)
- wide age range
- Industrialized nations

Non-Cardia Cancers

- Male: Female (2:1)
- white: black (1:4)
- incidence **increases with age** (peak age 60-70)
- ***H. pylori* causative**

Barrett's Tissue

Low risk ?



Barrett's Tissue

Low risk ?



Metaplasia

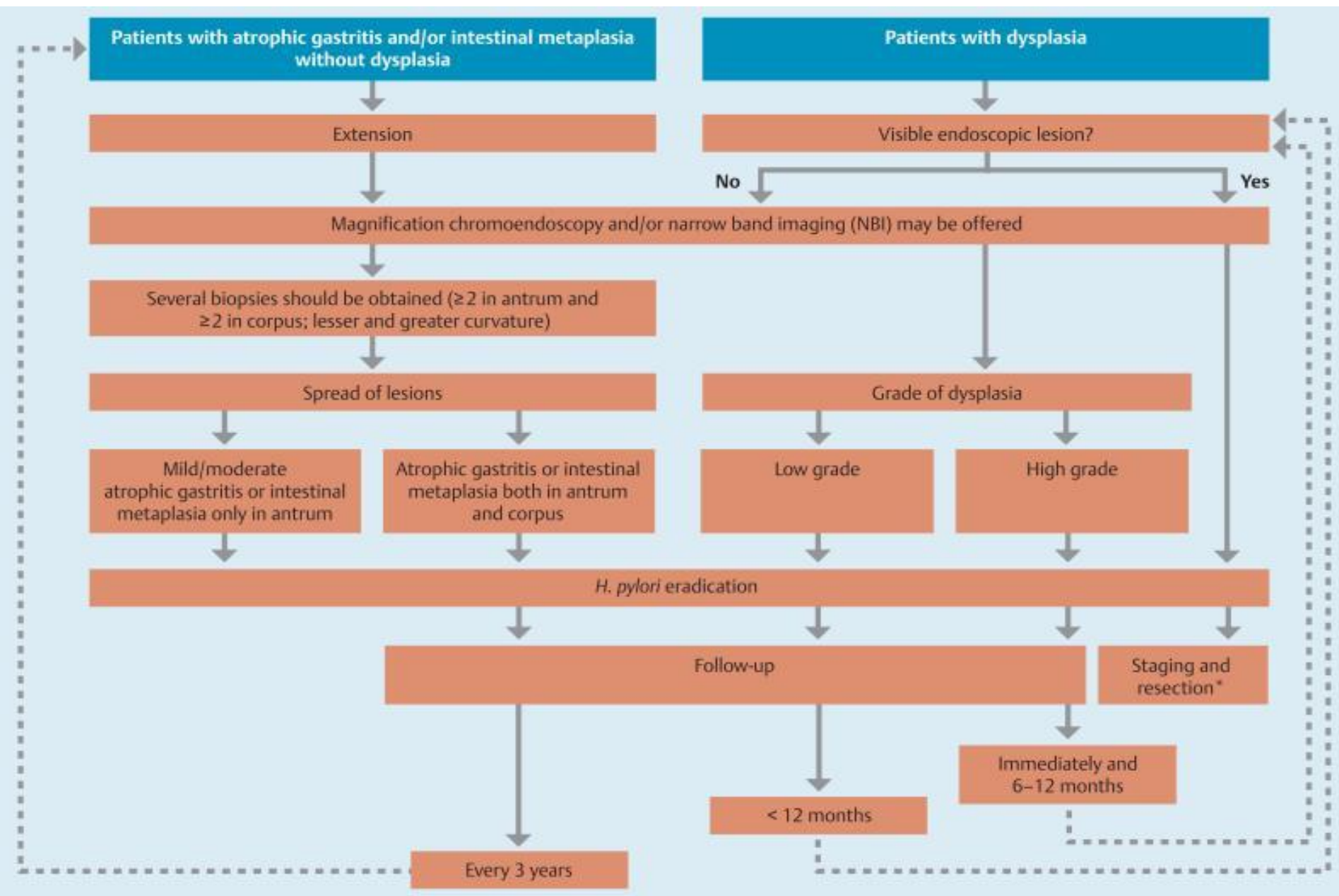
Low-grade Dysplasia

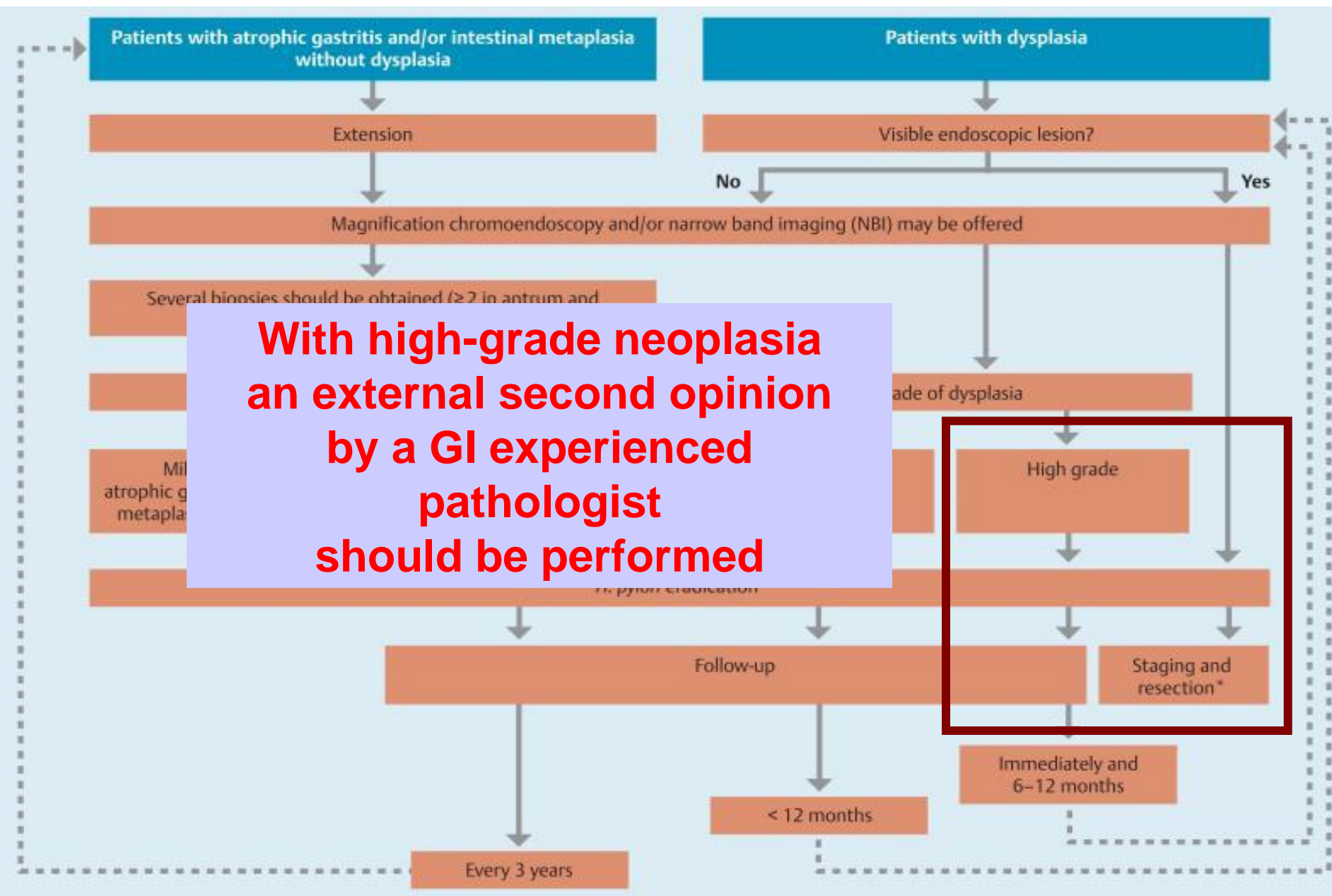
High-grade Dysplasia

Cancer

Management of precancerous conditions and lesions in the stomach (MAPS): guideline from the European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter Study Group (EHSG), European Society of Pathology (ESP), and the Sociedade Portuguesa de Endoscopia Digestiva (SPED).

Dinis-Ribeiro M, Areia M, de Vries AC, Marcos-Pinto R, Monteiro-Soares M, O'Connor A, Pereira C, Pimentel-Nunes P, Correia R, Ensari A, Dumonceau JM, Machado JC, Macedo G, Malfertheiner P, Matysiak-Budnik T, Megraud F, Miki K, O'Morain C, Peek RM, Ponchon T, Ristimaki A, Rembacken B, Carneiro F, Kuipers EJ





How to characterize a Low-Risk Situation

Macroscopic Appearance

use the best Endoscope

EUS

Invasion and LN ?

EMR

Diagnosis and Therapy

How to characterize a Low-Risk Situation

Macroscopic Appearance *use the best Endoscope*

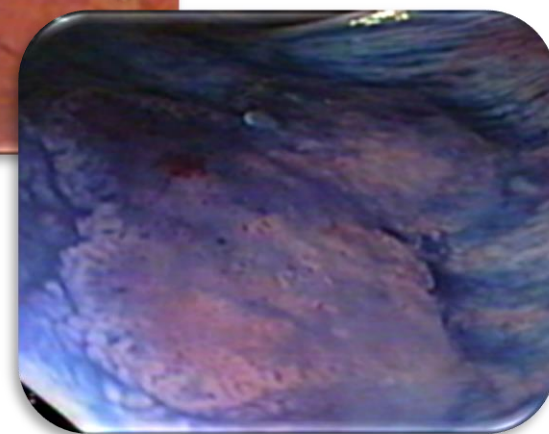
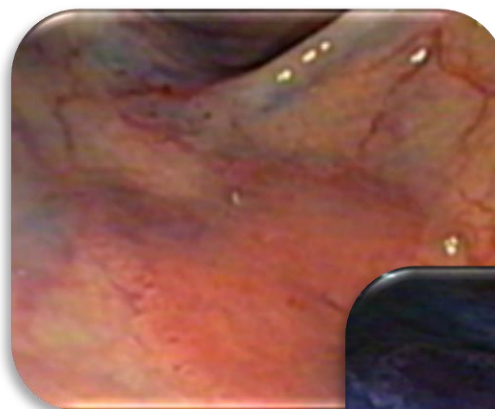


Chromo - Endoscopy

Contrasting Dyes

Indigocarmin 0.2 – 0.4 %

Acetic Acid



Absorptive Dyes

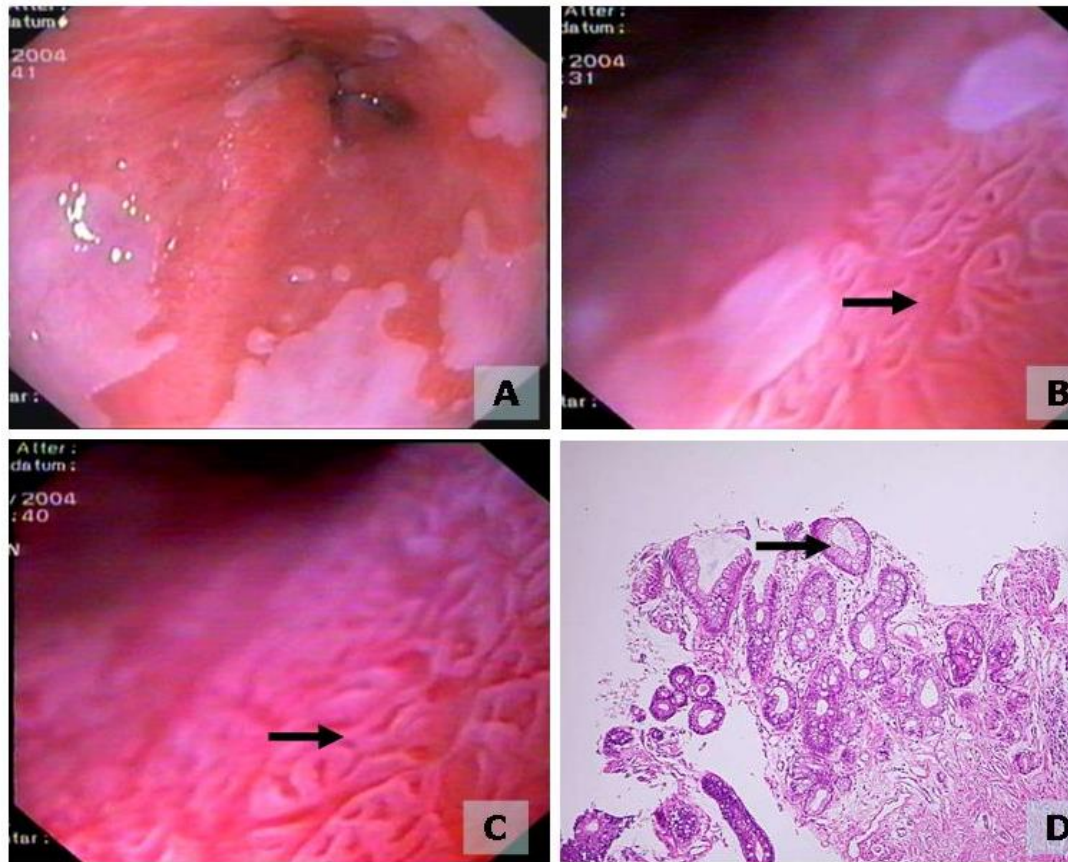
Methylen Blue 0.5 – 1 %

Negative Dyes

Lugol's Solution for
Squamous Lesions



Acetic Acid



Magnification endoscopy after application of Acetic Acid (1.5 %)

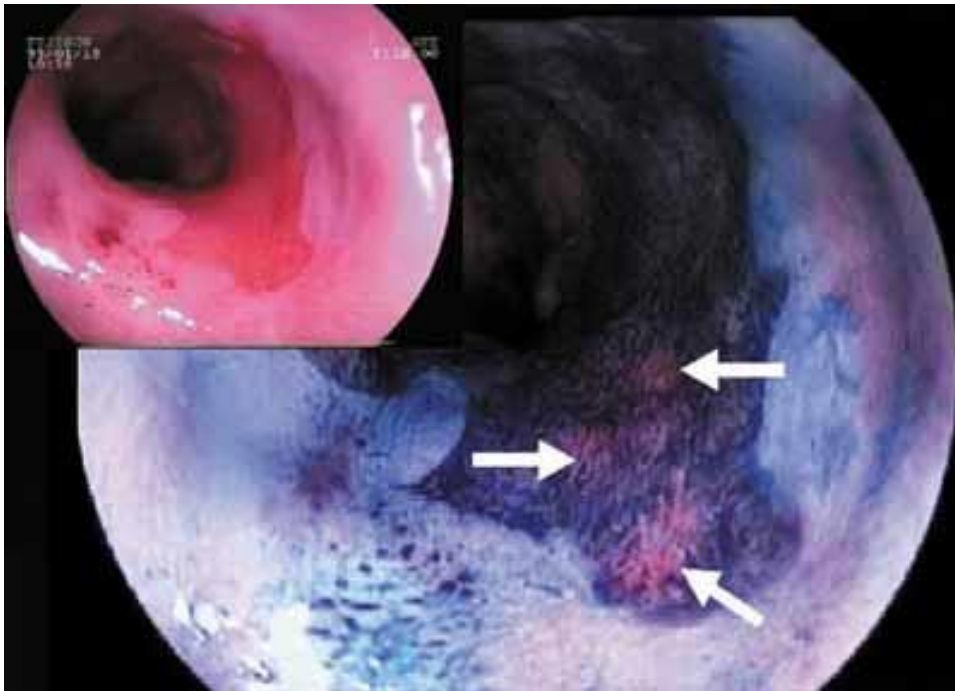
Histological verification of Intestinal Metaplasia with proof of goblet cells (H & E)

Methylen Blue

Detection of Inflammatory & Dysplastic Areas

Shifted Core-Plasma Reaction in inflammatory or dysplastic cells

→ *Lower reception of Methylen blue*



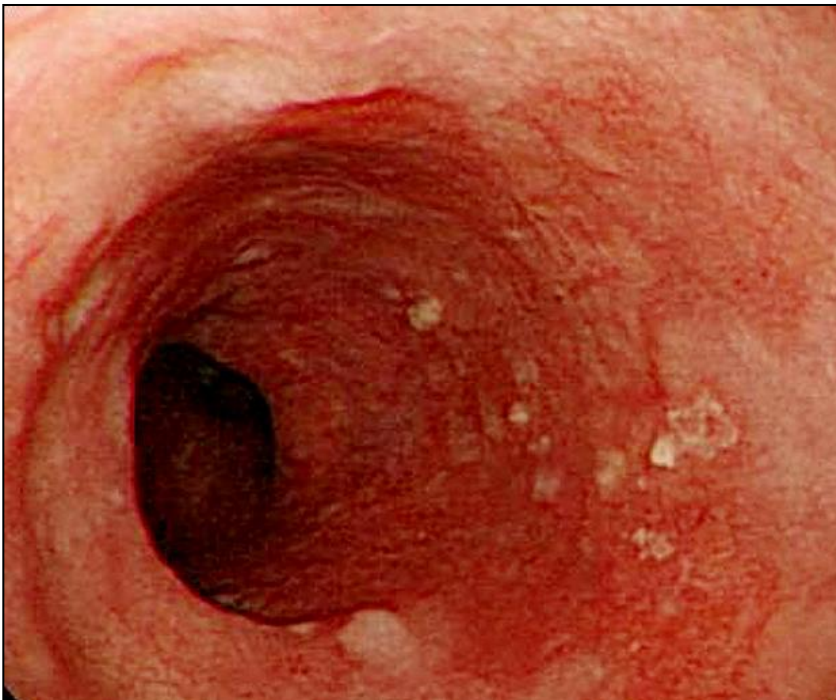
*Methylene blue-directed biopsies
improve detection of intestinal
metaplasia and dysplasia in
Barrett's esophagus*

(12% vs. 6% $p=0.004$)

Dysplastic area in Barrett's Esophagus

Squamous Cell Cancer of the Esophagus

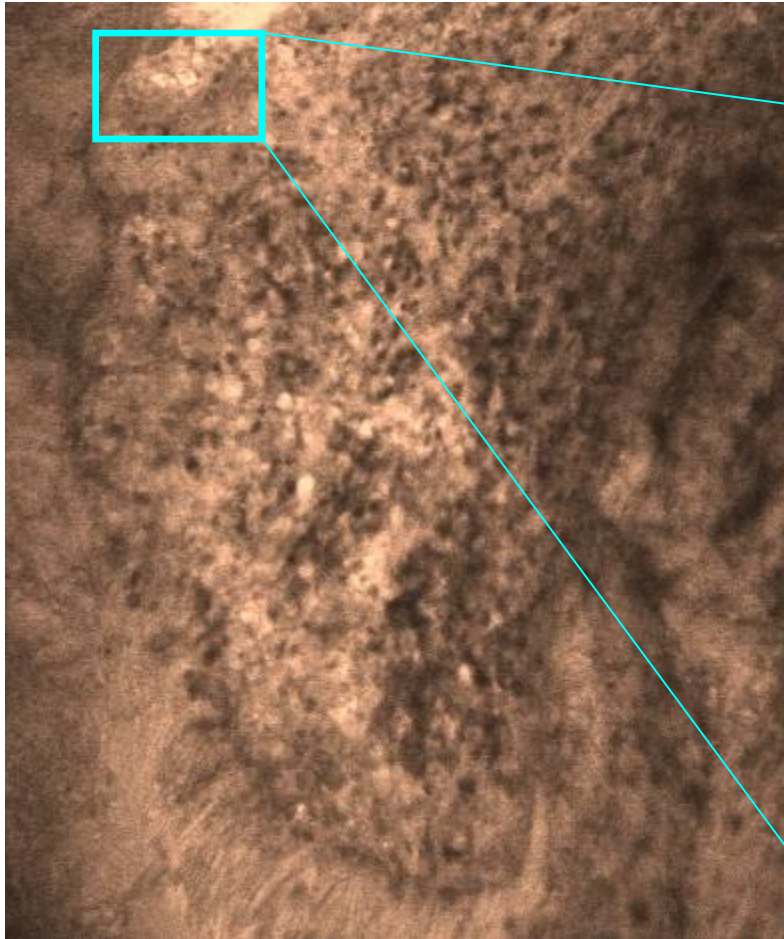
Lugol's Solution



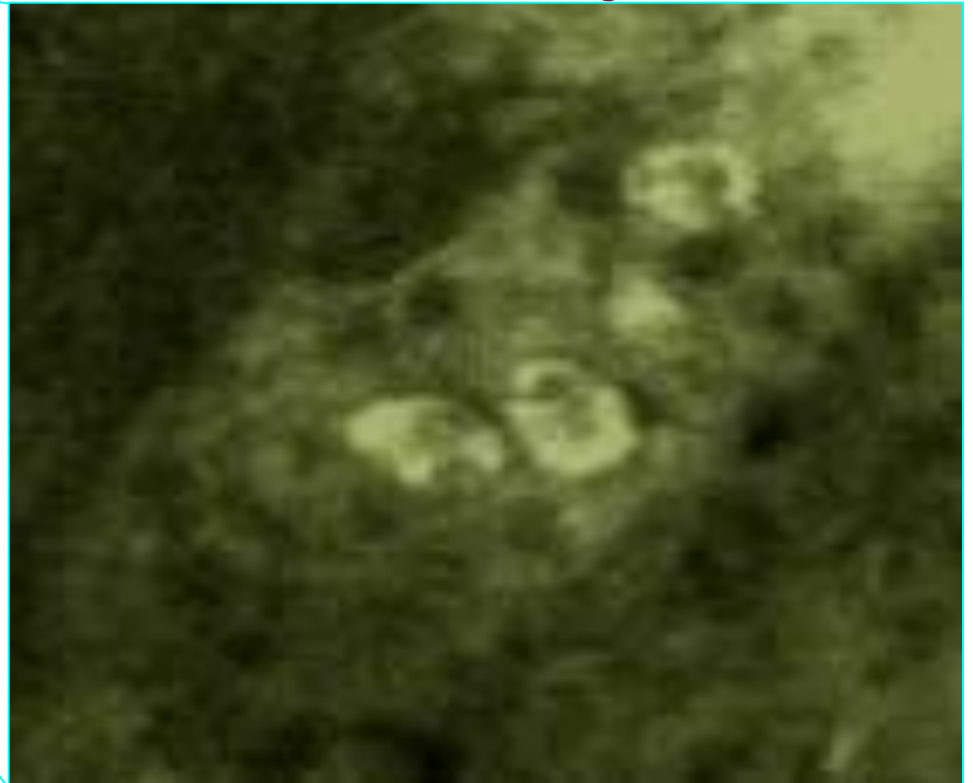
Early Ca Type II b + a

Molecular in vivo imaging ?

Targeting of EGFR in gastric cancer



human-murine xenograft model:



How to characterize a Low-Risk Situation

Macroscopic Appearance

use the best Endoscope

EUS

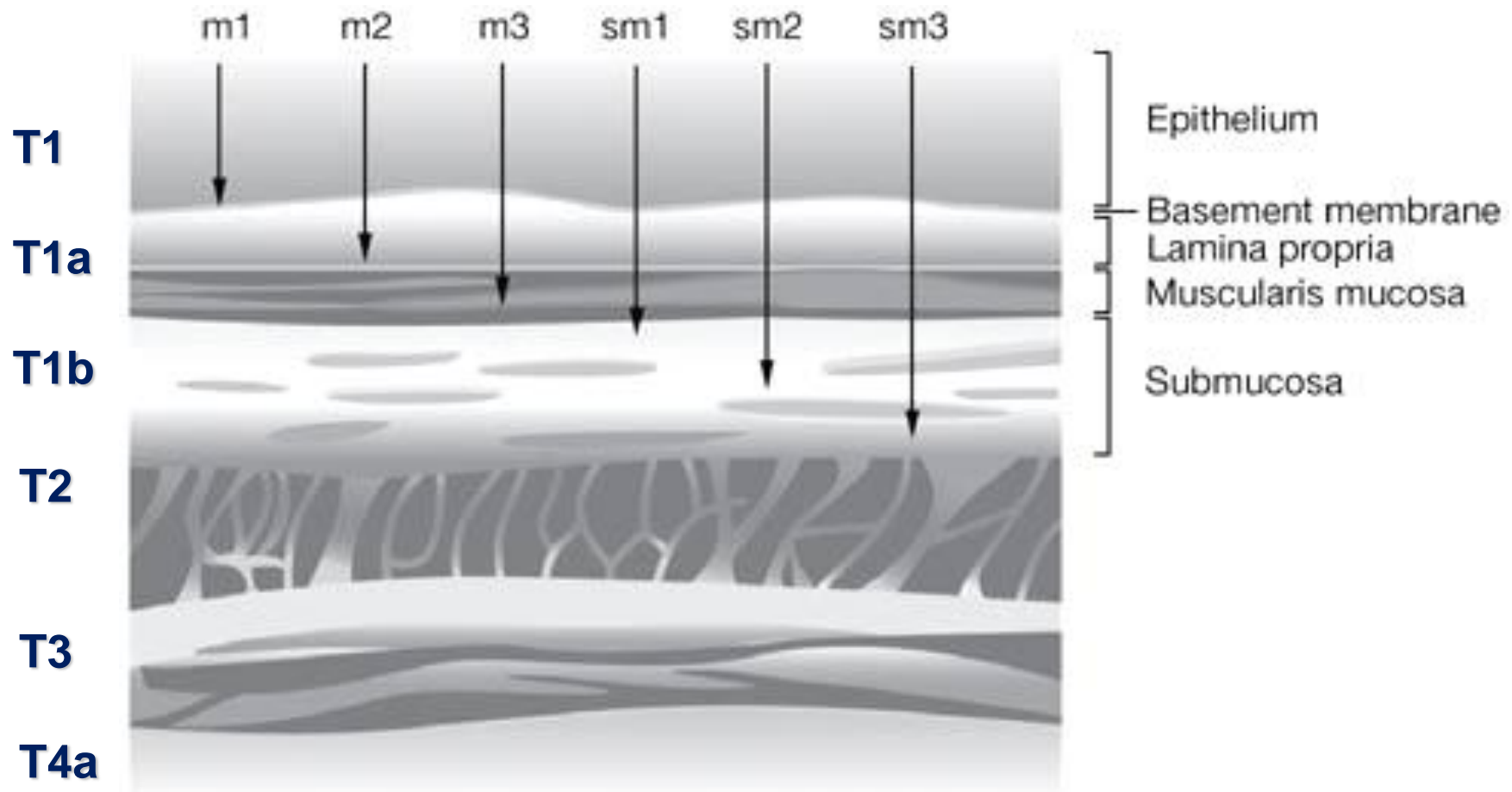
Invasion and LN ?

How to characterize a Low-Risk Situation

| | |
|-----|---|
| T1 | Lamina propria, submucosa |
| T1a | Lamina propria and muscularis mucosae |
| T1b | Submucosa |
| T2 | Muscularis propria |
| T3 | Subserosa (<u>was</u> T2b) |
| T4a | Perforated Serosa (<u>was</u> T3) |
| T4b | Neighboring Structures |
| N1 | 1 to 2 Lymph Nodes |
| N2 | 3 to 6 Lymph Nodes (<u>was</u> N1) |
| N3a | 7 to 15 Lymph Nodes (<u>was</u> N2) |
| N3b | 16 or more Lymph Nodes (<u>was</u> N3) |

***T- und N-Categories of
Tumors of the Stomach
(UICC 2010)***

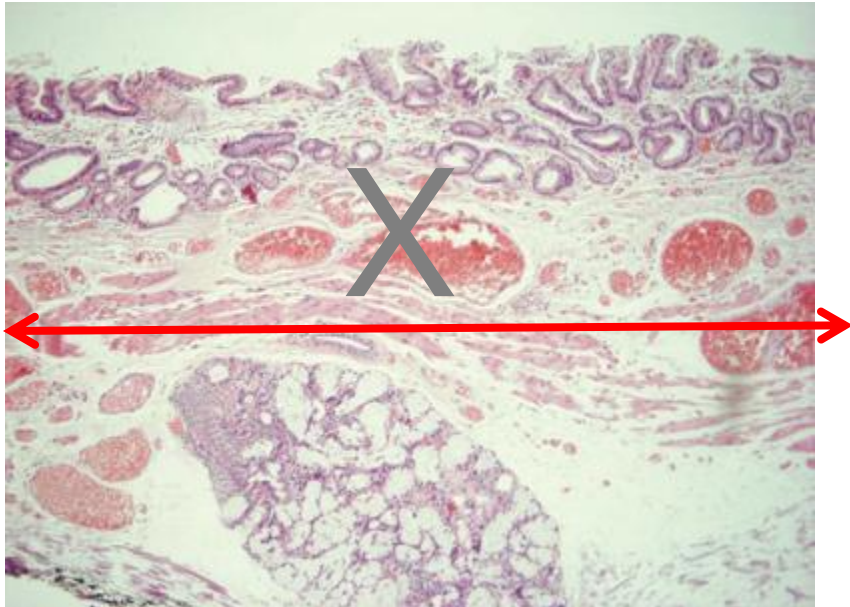
How to characterize a Low-Risk Situation



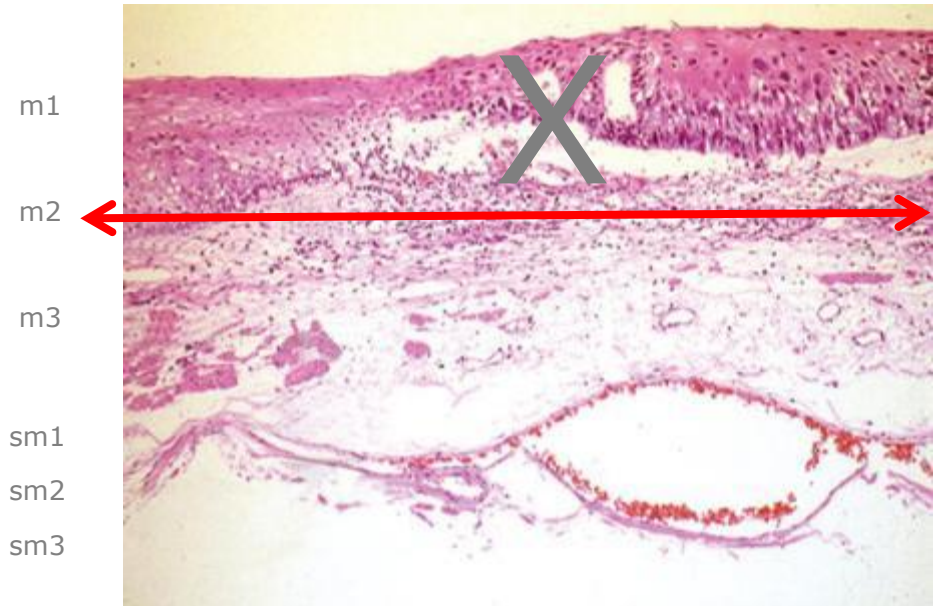
How to characterize a Low-Risk Situation

Low risk: 0-5%

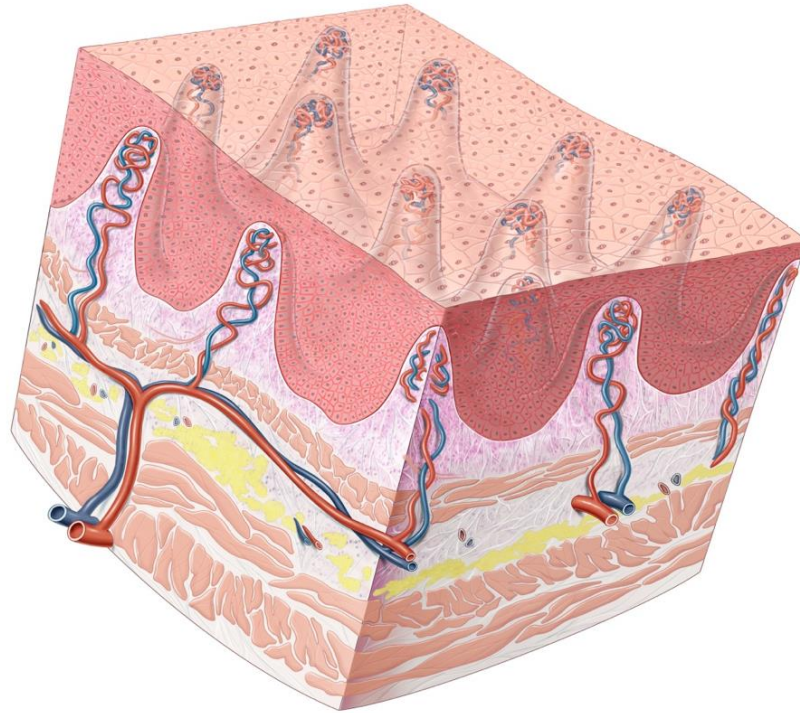
Barrett's Ca (Adenocarcinoma)



Squamous Cell Carcinoma



How to characterize a Low-Risk Situation

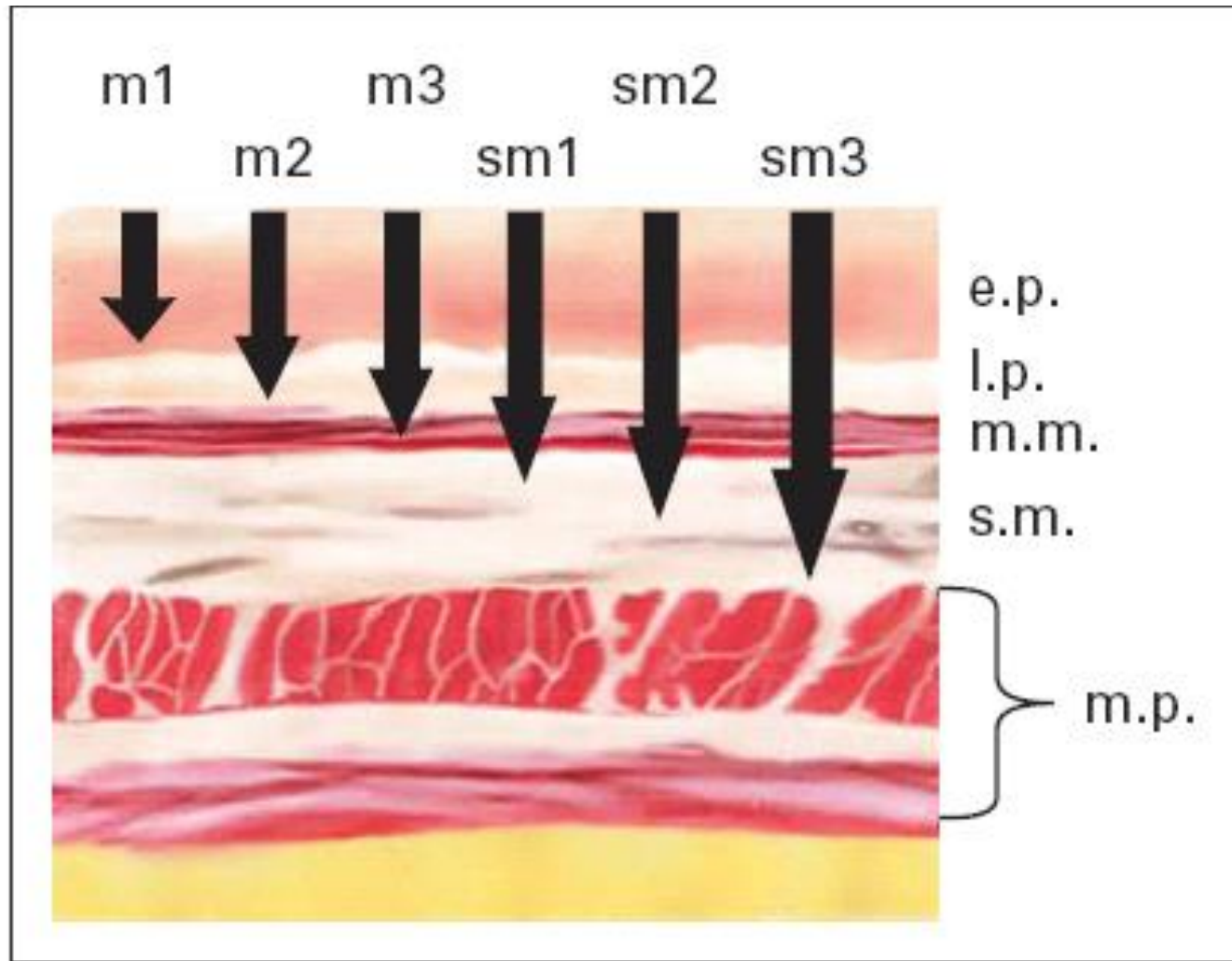


Be careful with Squamous Epithelium:

Structure of Mucosa and Submucosa has a
higher risk for LN involvement !

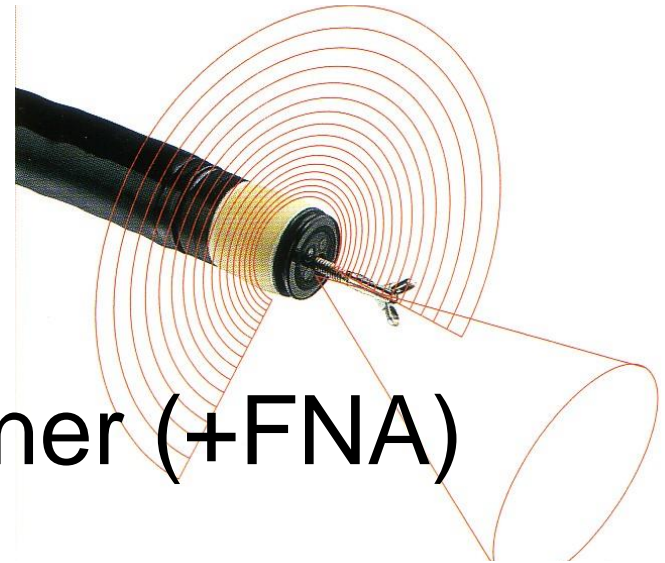
Lymph node metastases

mucosal 2% - submucosal 20%

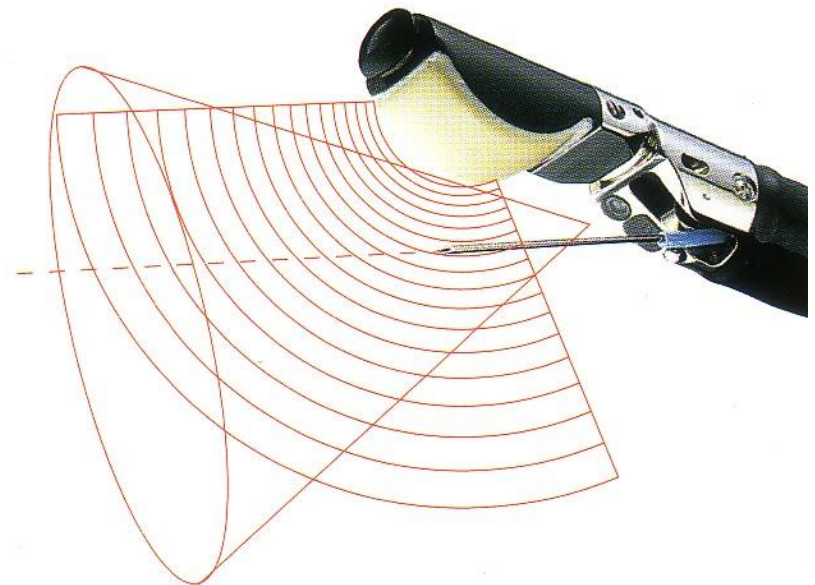


Endosonography (EUS)

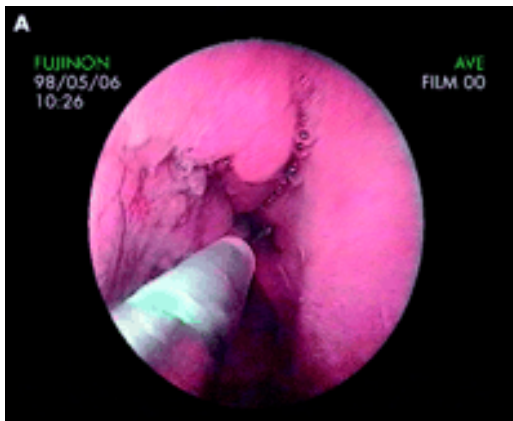
1. Radial Scanner



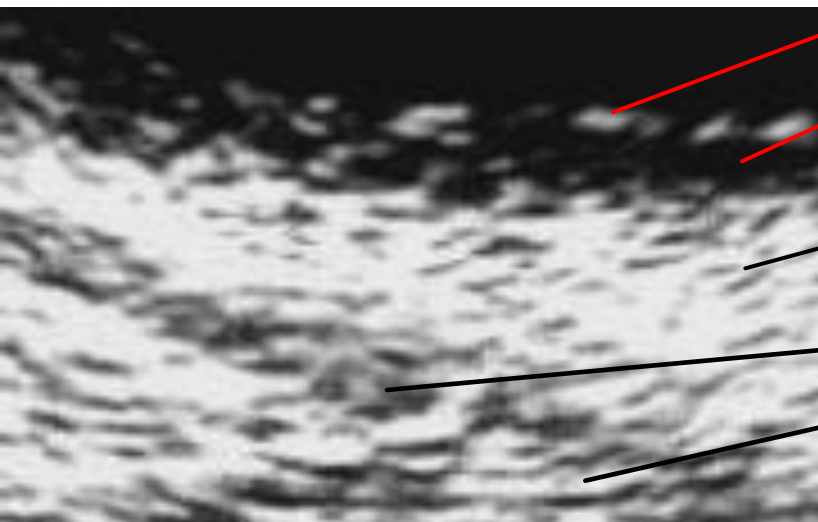
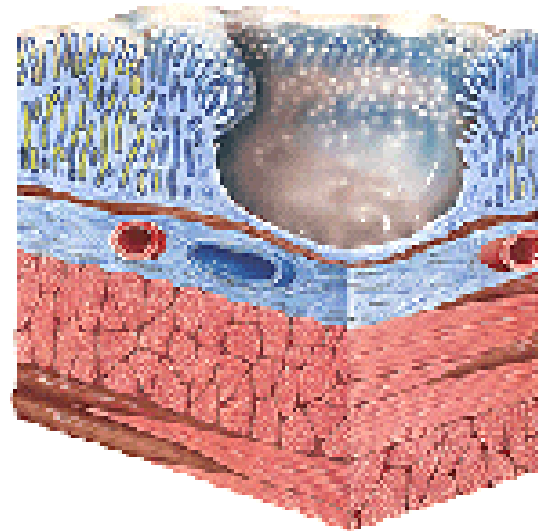
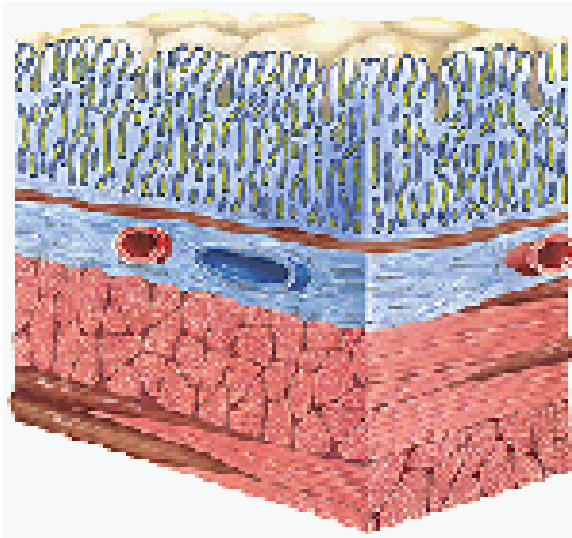
2. Longitudinal Scanner (+FNA)



3. Mini probes



Endosonography (EUS)



Admission reflex

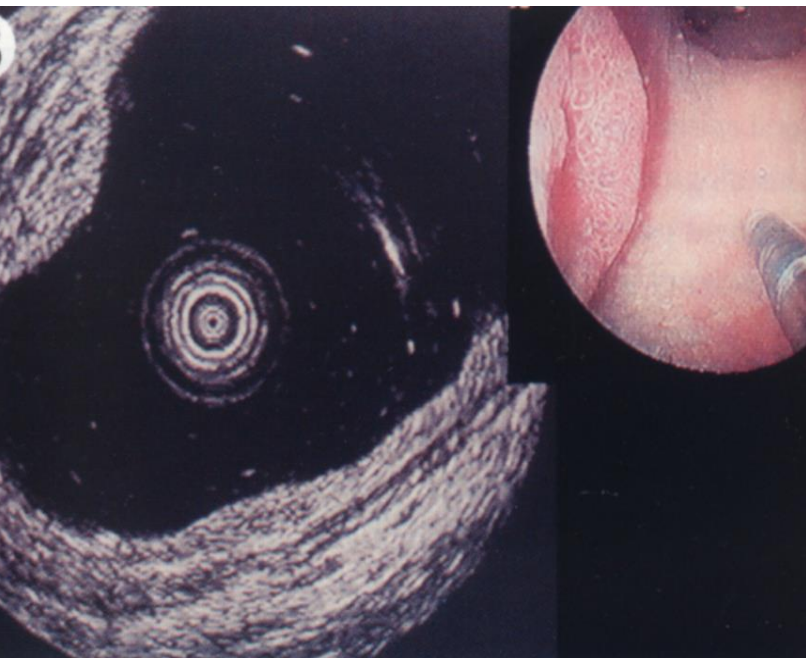
Mucosa

Submucosa

Muscularis

Serosa

5-7,5 MHz



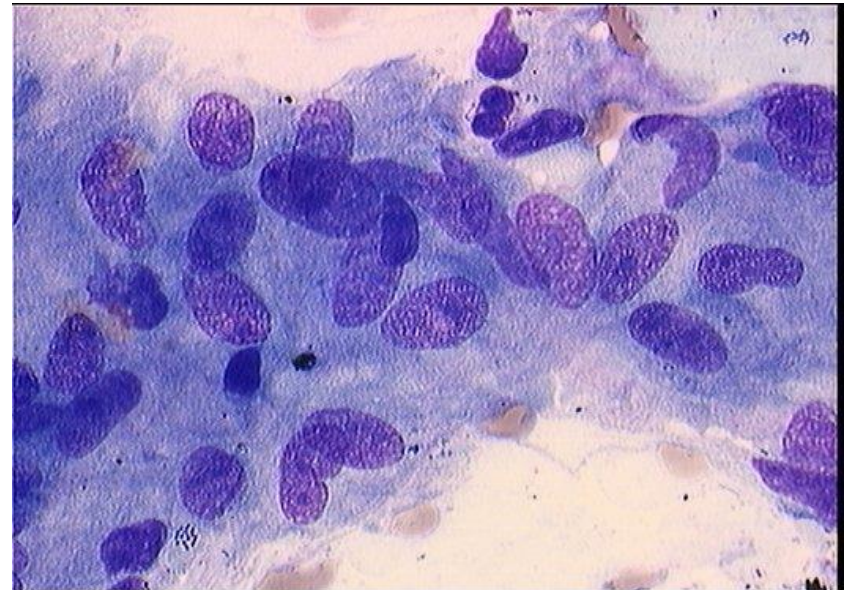
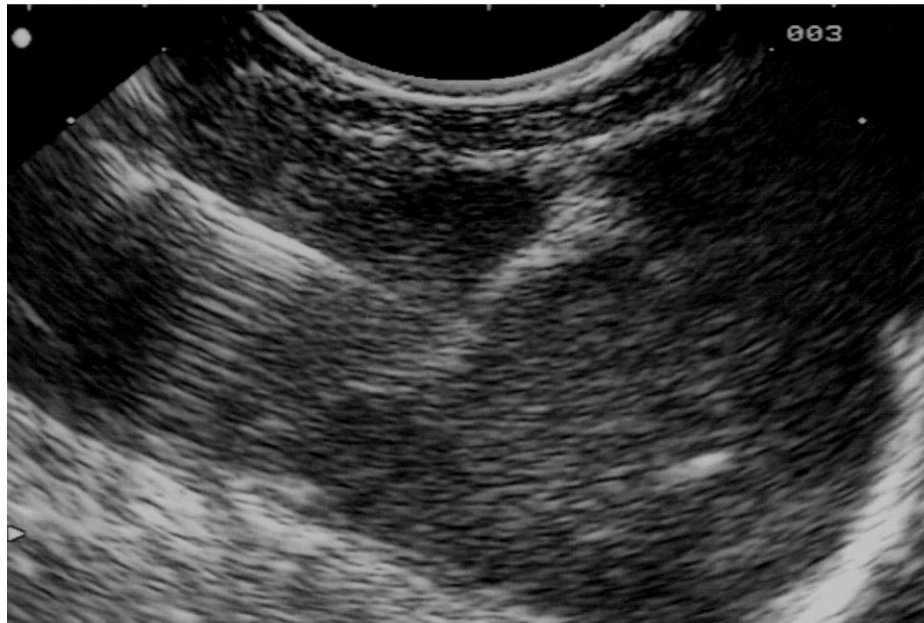
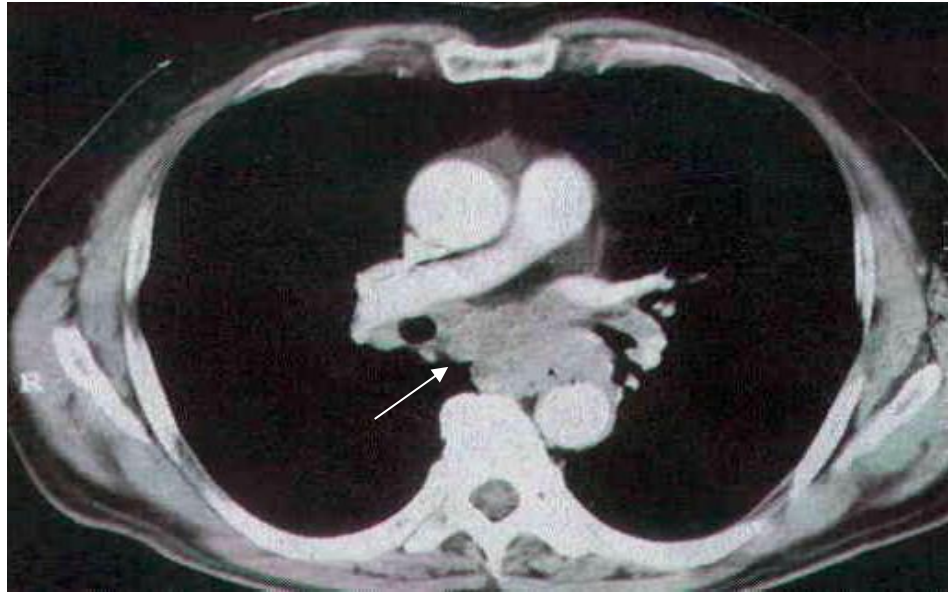
Endosonography (EUS)

Early cancers T1 m
Mucosal Resection



EUS + FNP:
cytological puncture
93% vs 70% ($p=0.02$)

Endosonography (EUS)

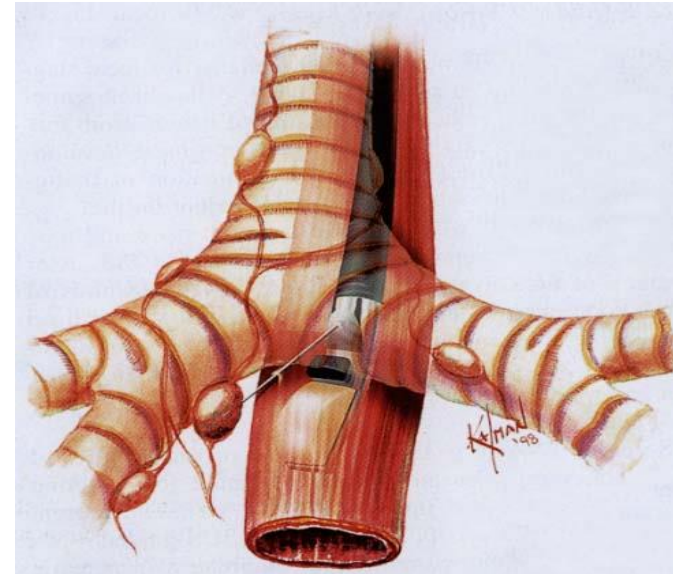
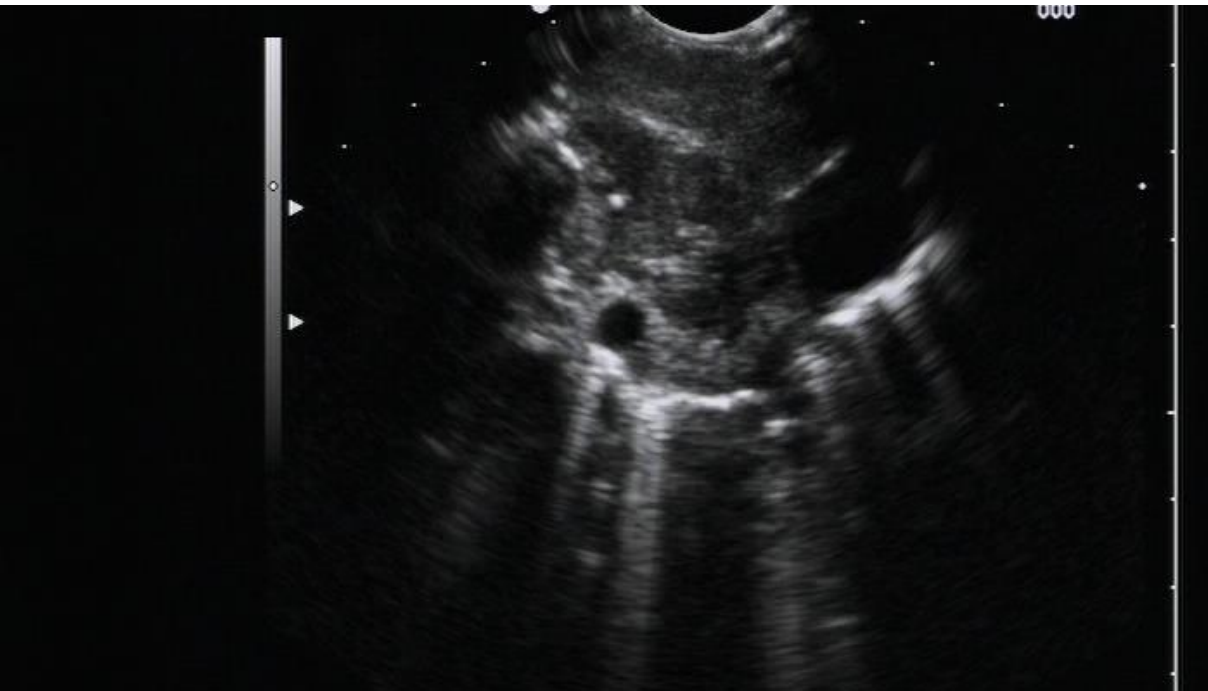


Endosonography (EUS)

> 20 Studies with > 1250 Patients

Sensitivity 0.61–1 (median 0.90)

Specificity 0.71–1 (median 1.00)



Moehler et al.,
Z Gastroenterol 2011

Endosonography (EUS)

.. *should be* used
complementary to CT

for early esophagogastric cancers
and

for selection of patients
in perioperative therapy.

Endoscopic Therapy of Early Cancer

Low Risk Situation

Operation

Morbidity 18-48%

Mortality 2-20%

**reduced
Life Quality**

Endoscopic Resection

Morbidity 1-3%

Mortality 0%

Organ-preserving

Endoscopic Therapy of Early Cancer

Indication for EMR

Superficial cancers that are confined to the mucosa (T1aN0M0) can be dealt with in accordance with the following criteria for endoscopic resection

- Lesions <2 cm in size sublim types
- Lesions of <1 cm in size in flat types
- Histological differentiation grade (G1/G2)
- No macroscopic ulceration
- Invasion limited to the mucosa
- No residual invasive disease after EMR

Endoscopic Therapy of Early Cancer

Indication for EMR

| Depth Histology | Mucosal Cancer | | | | Submucosal Cancer | |
|--------------------|----------------------------|---|---|---|---|---|
| | No Ulceration | | Ulcerated | | SM1 | SM2 |
| | ≤ 20 | > 20 | ≤ 30 | > 30 | ≤ 30 | Any Size |
| Intestinal | Guideline criteria for EMR | Expanded criteria for EMR | Expanded criteria for EMR | Surgery (gastrectomy + lymph node dissection) | Expanded criteria for EMR | Surgery (gastrectomy + lymph node dissection) |
| Diffuse | Consider surgery | Surgery (gastrectomy + lymph node dissection) | Surgery (gastrectomy + lymph node dissection) | Surgery (gastrectomy + lymph node dissection) | Surgery (gastrectomy + lymph node dissection) | Surgery (gastrectomy + lymph node dissection) |

Guideline criteria for EMR

Consider surgery

Expanded criteria for EMR

Surgery (gastrectomy + lymph node dissection)

Endoscopic Therapy of Early Cancer

Oncological Criteria are essential

R0 Resection !!!

horizontal

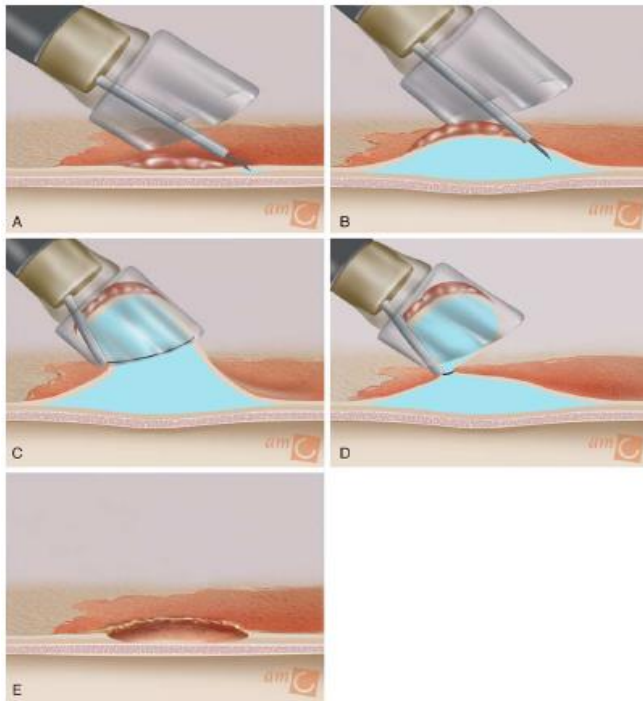


vertical



Endoscopic Therapy of Early Cancer

Endoscopic mucosal resection: EMR

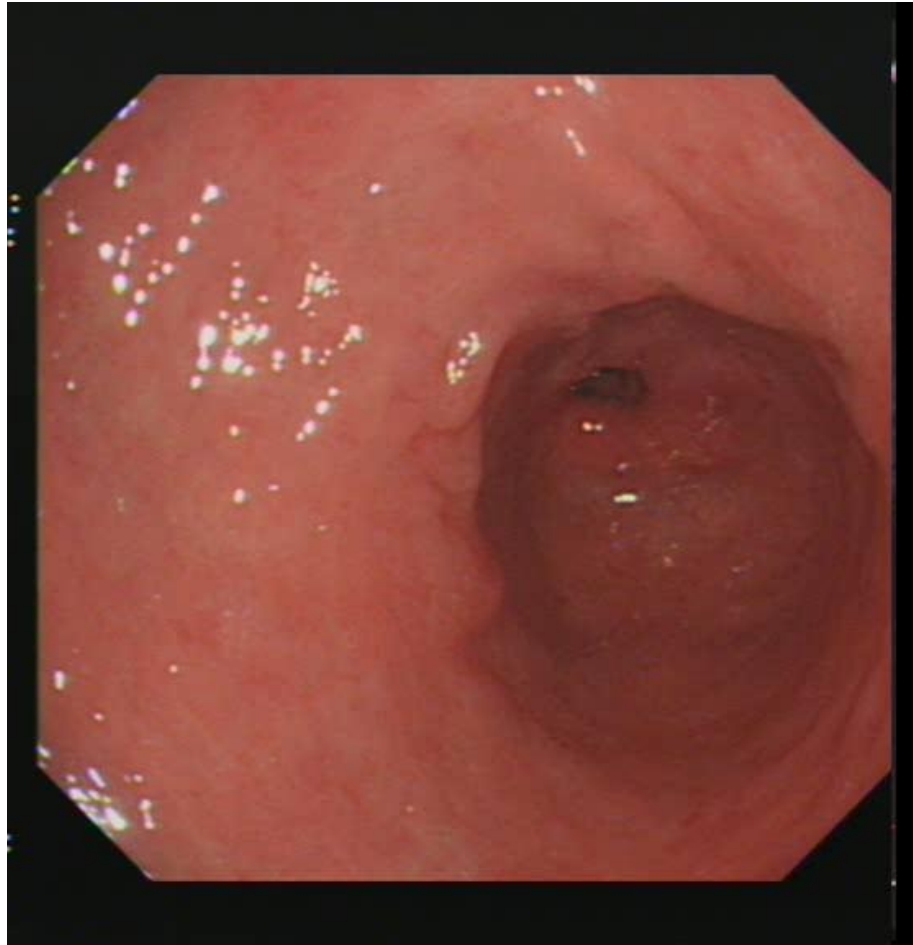


“suck-and-cut” technique

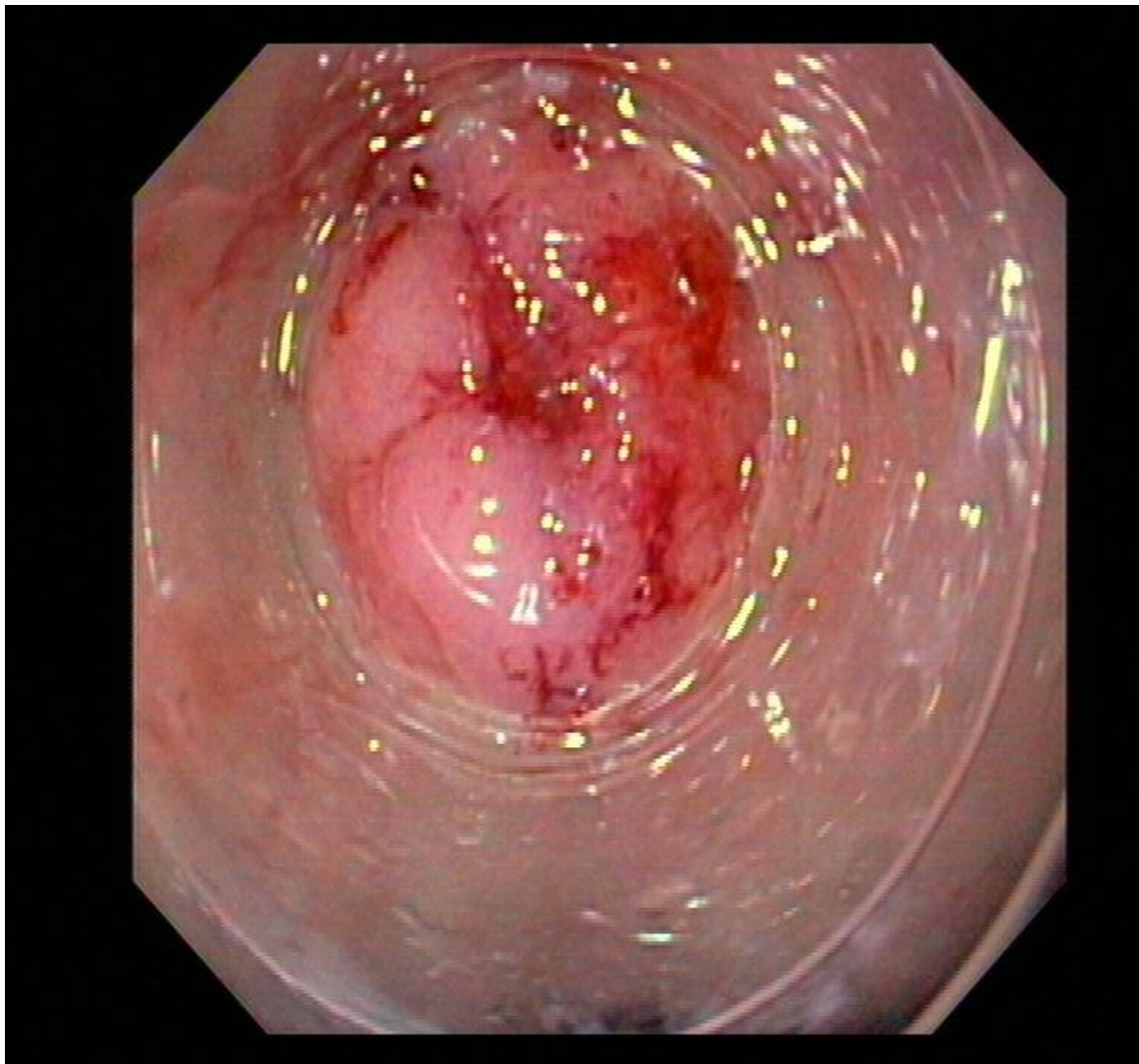


Multiband Mucosectomy: MBM

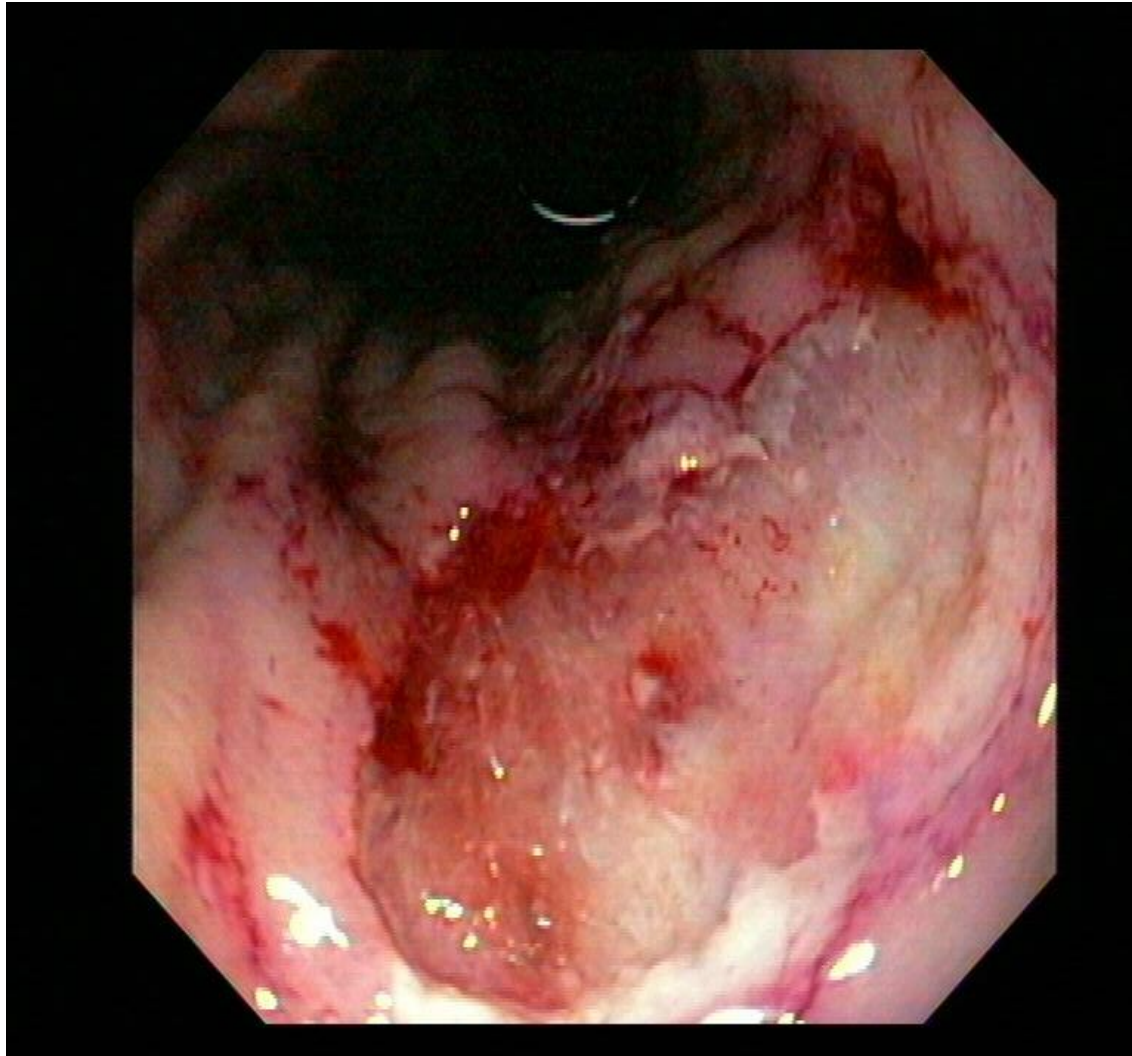
EMR



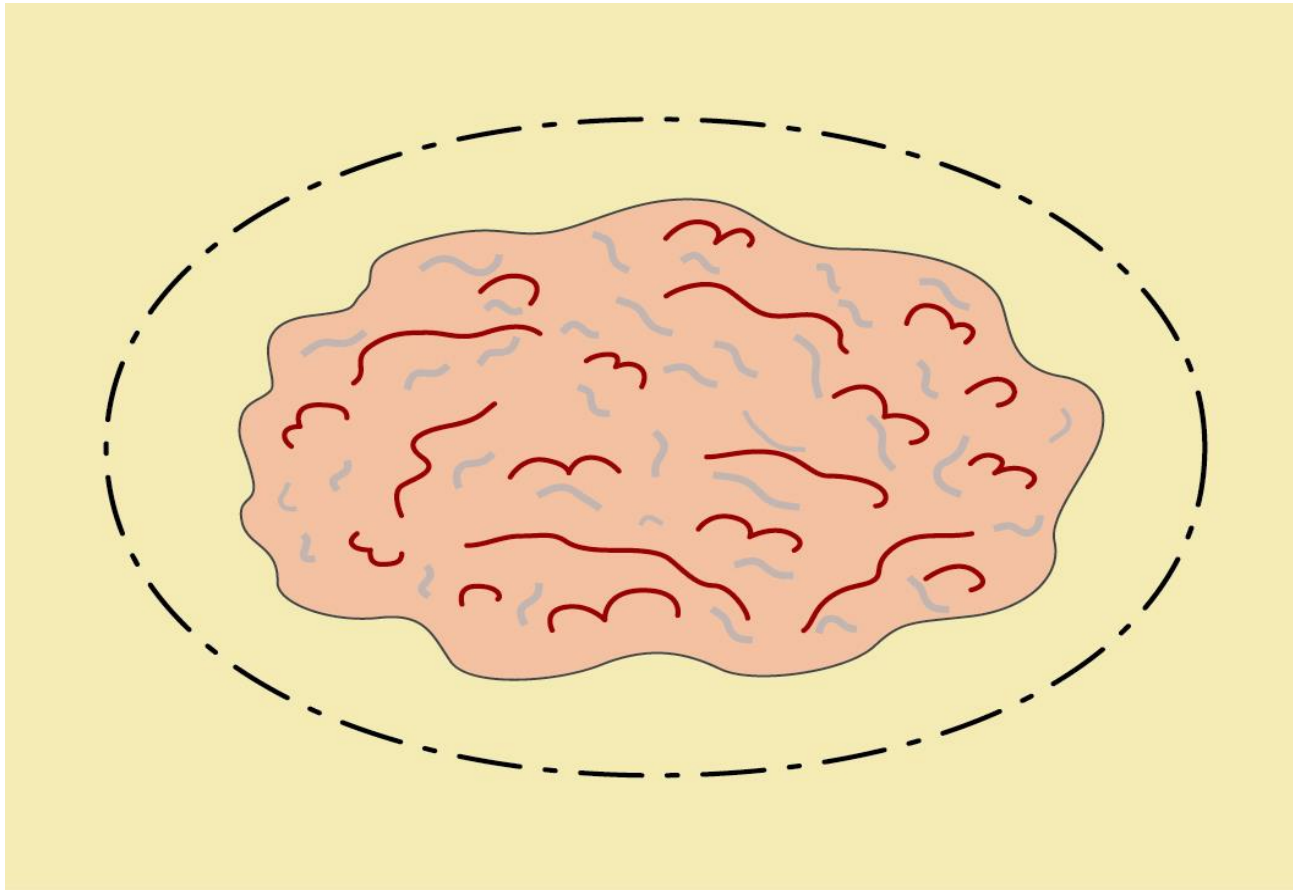
EMR



EMR

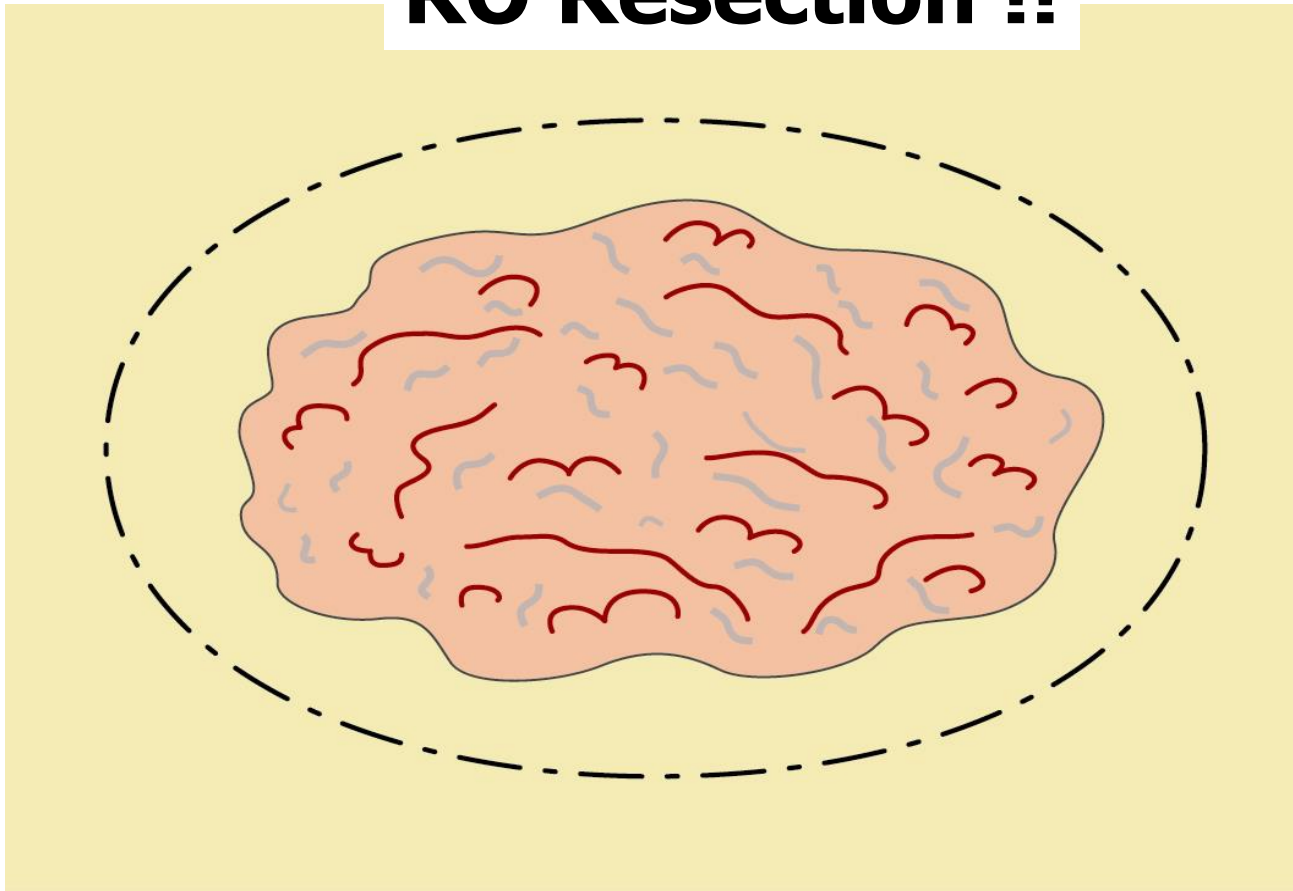


Oncologically adequate therapy

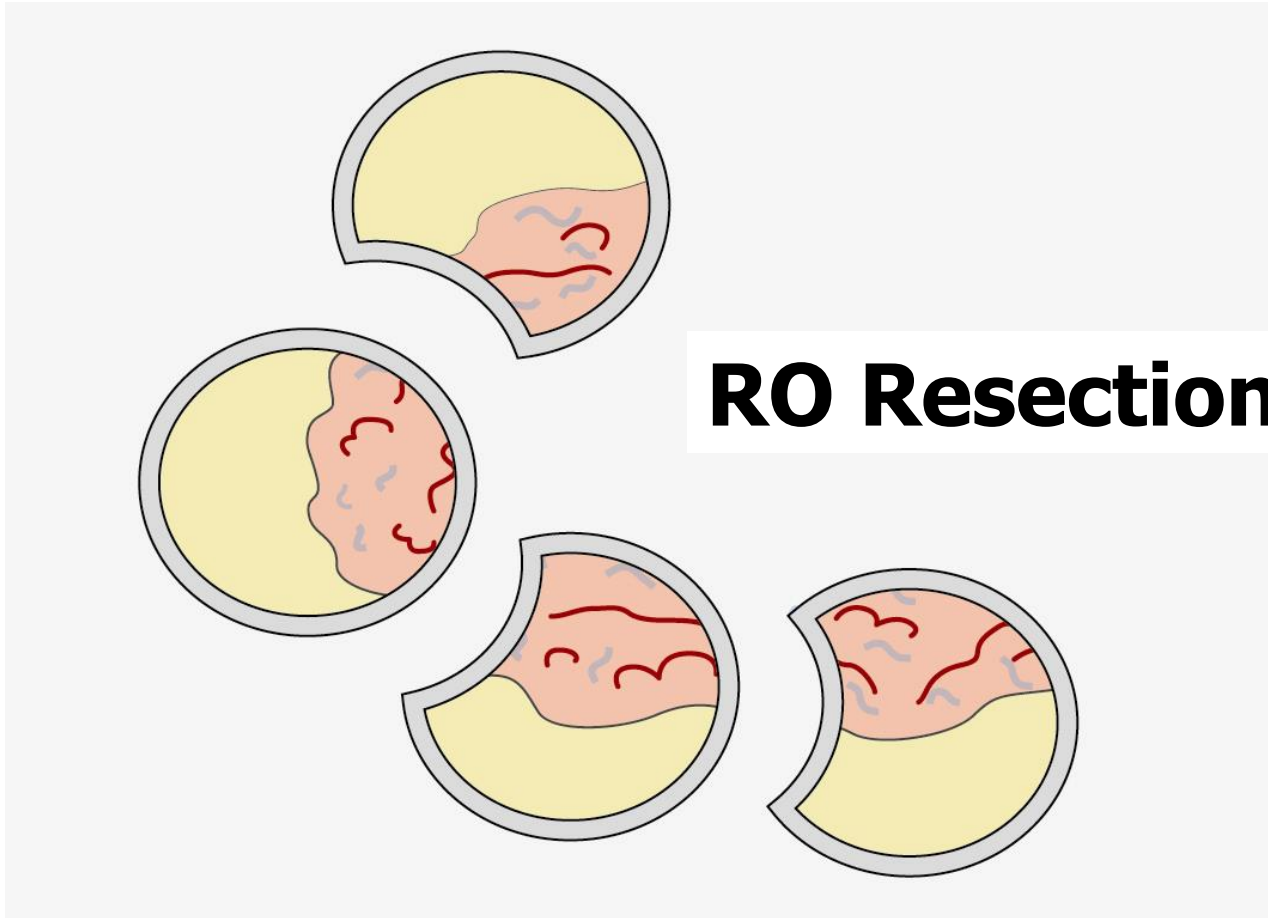


Oncologically adequate therapy

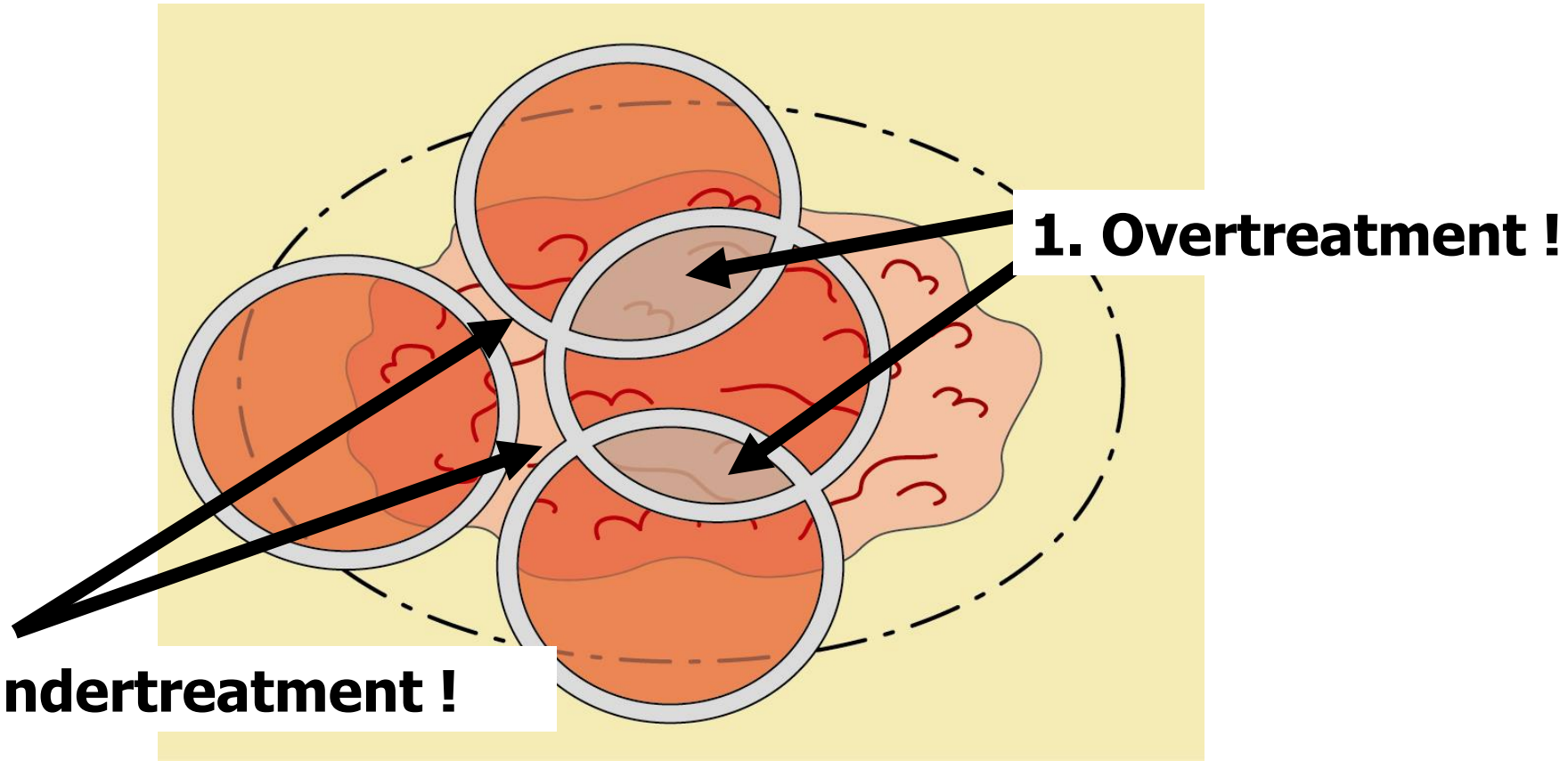
R0 Resection !!



Piece-meal resection



Piece-meal resection




Endoscopic Therapy of Early Cancer


Japanese Guidelines

| Depth Histology | Mucosal Cancer | | | | Submucosal Cancer | |
|--------------------|----------------|------|-----------|------|-------------------|----------|
| | No Ulceration | | Ulcerated | | SM1 | SM2 |
| | ≤ 20 | > 20 | ≤ 30 | > 30 | ≤ 30 | Any Size |
| Intestinal | | | | | | |
| Diffuse | | | | | | |

 Guideline criteria for EMR

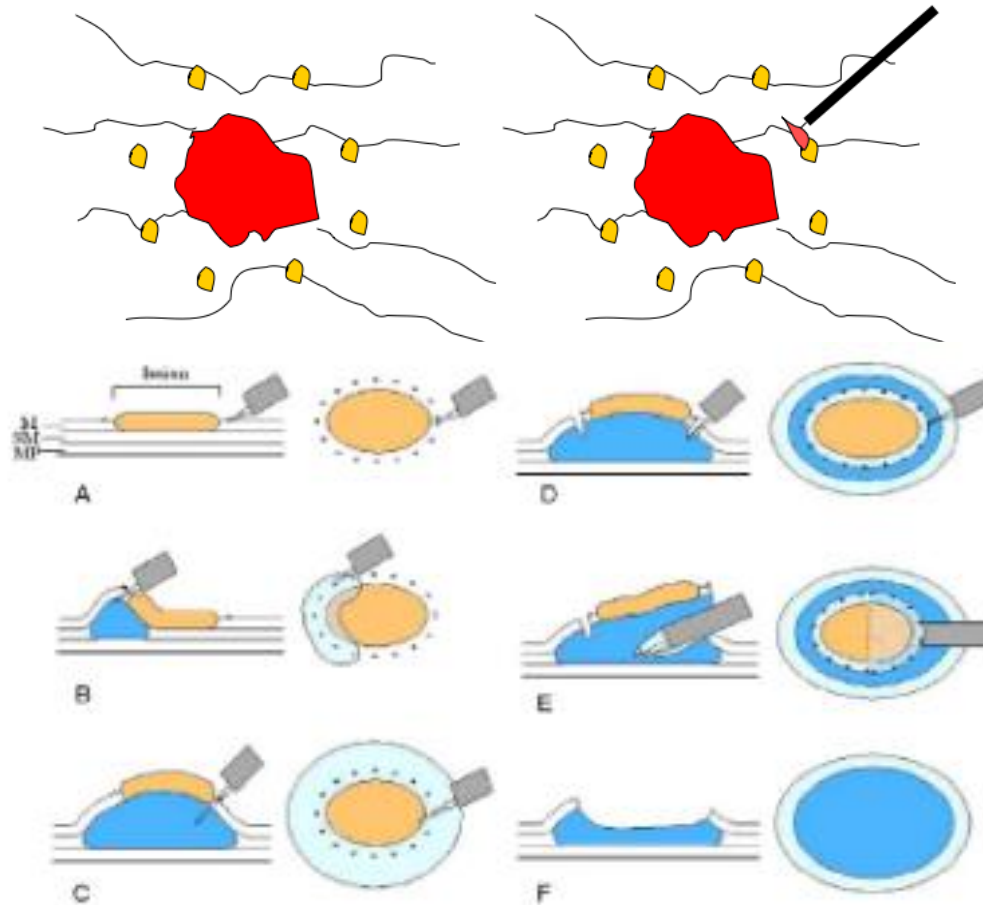
 Expanded criteria for EMR

 Consider surgery

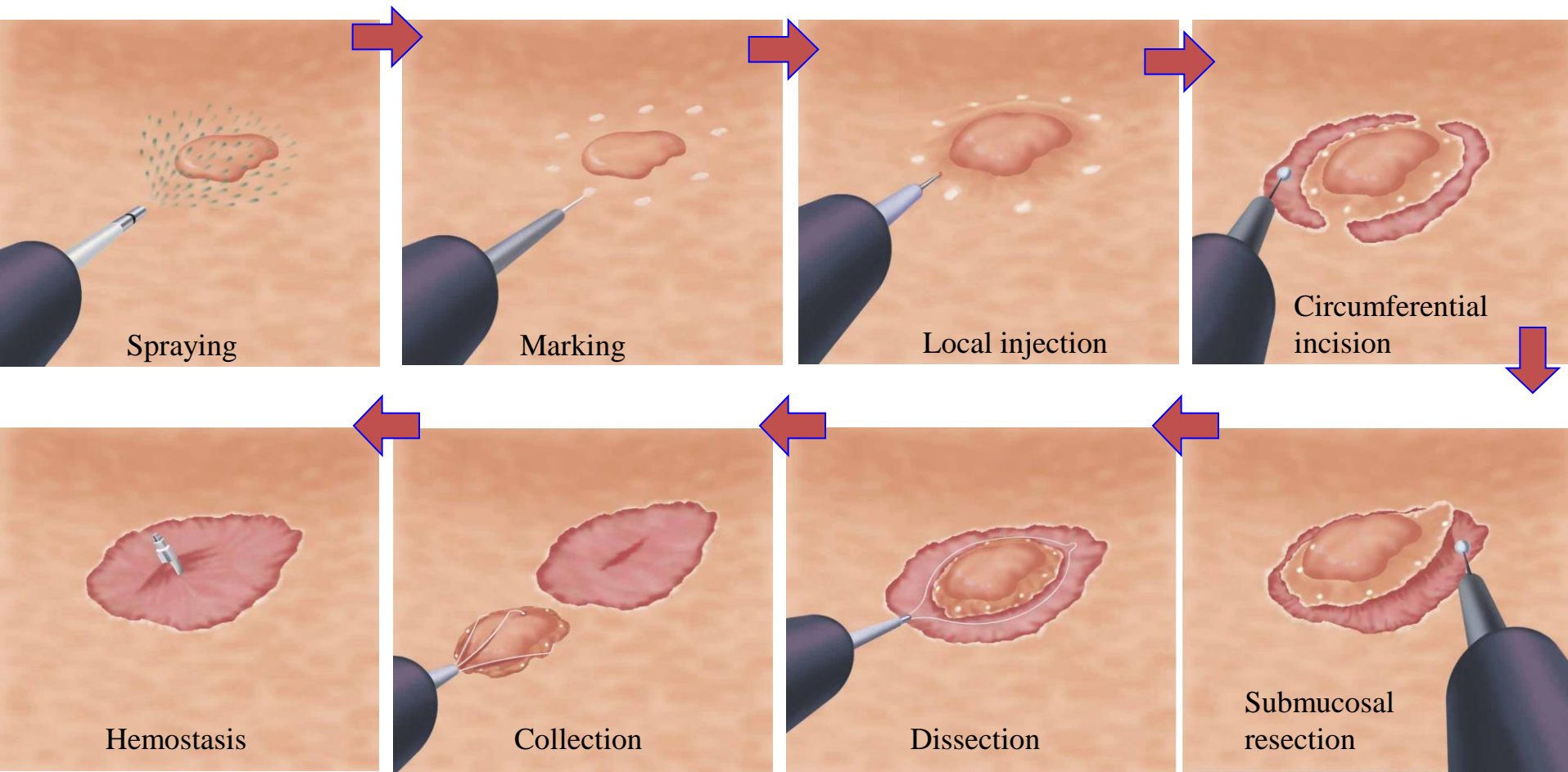
 Surgery (gastrectomy + lymph node dissection)

Endoscopic Therapy of Early Cancer

Endoscopic mucosal resection: ESD



ESD



ESD for tumors with *Expanded criteria*

EMR

ESD

p

En bloc resection rates

| | | | |
|----------|-----------------|-----------------|-------|
| all size | 708/790 (89.6%) | 418/458 (91.3%) | 0.345 |
| ≤ 20mm | 607/660 (90.2%) | 267/292 (92.1%) | 0.783 |
| >20 mm | 101/130 (77.7%) | 151/166 (91.0%) | 0.001 |

complete resection rates

| | | | |
|----------|-----------------|-----------------|-------|
| all size | 371/465 (79.5%) | 315/369 (85.5%) | 0.036 |
| ≤ 20mm | 291/338 (86.1%) | 192/215 (86.1%) | 0.256 |
| >20 mm | 37/77 (48.1%) | 102/146 (70.1%) | 0.001 |

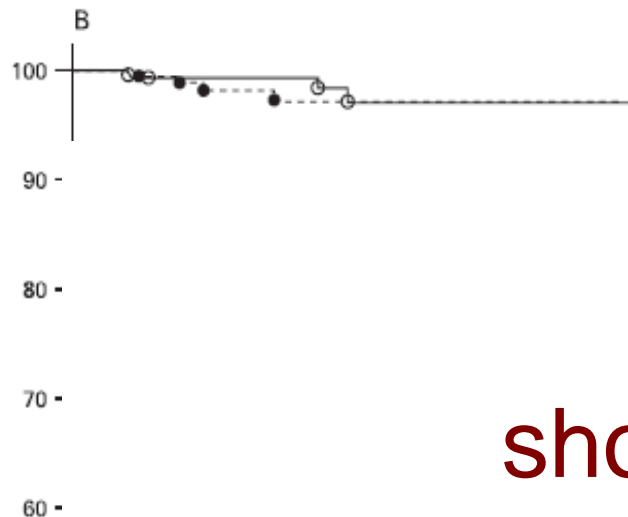
Kim WJ , DDW 2009 / 2010 # 422

The result of EMR and ESD of gastric tumors over 15 years

ESD for tumors with *Expanded criteria*

Table 4 Comparison of clinicopathological parameters of early gastric cancer lesions that fulfilled the standard guideline criteria (standard group) with those that did not meet the guideline criteria but fulfilled the expanded inclusion criteria (expanded group)

| Group (number) | Standard group (302) | Expanded group (208) | p Value |
|------------------------|----------------------|----------------------|---------|
| Median age, range | 72, 44–88 | 73, 38–92 | NS |
| Gender, F:M | 88:214 | 57:151 | NS |
| Macroscopic appearance | | | NS |
| Elevated | 155 | 114 | |
| Flat/depressed | 146 | 94 | |
| Unknown | 1 | | |
| Tumour size | | | p<0.001 |
| <20 mm | 202 | 150 | |



EMR and ESD
should be performed
only by endoscopists in centers
with appropriate expertise !!

Indications for Endoscopic Therapy

Esophagus

- T1m Squamous Cell Cancer
- T1m Barrett Carcinoma
- HGD in Barrett Esophagus

Stomach

- T1m Adeno Carcinoma
- Adenoma
- Carcinoids

Endoscopic follow-up after EMR/ESD

| | |
|-------------------------------------|---|
| 48. | Consensus based recommendation |
| Level of Evidence GCP | <p>Patients who were treated with endoscopic resection should receive endoscopic surveillance.</p> <p>A follow-up endoscopy should be performed every 3 months in the first year, then every 6 months during the second year and then annually.</p> |
| Vote in Plenum | Strong Consensus |

LEITLINIENPROGRAMM ONKOLOGIE



Endoscopic Therapy of Early Cancer

Summary

| Depth Histology | Mucosal Cancer | | | | Submucosal Cancer | |
|--------------------|----------------|--------|-----------|--------|-------------------|----------|
| | No Ulceration | | Ulcerated | | SM1 | SM2 |
| | ≤ 20 | > 20 | ≤ 30 | > 30 | ≤ 30 | Any Size |
| Intestinal | Blue | Yellow | Yellow | Orange | Yellow | Orange |
| Diffuse | Red | Orange | Orange | Orange | Orange | Orange |

Blue Guideline criteria for EMR

Yellow Expanded criteria for EMR

Red Consider surgery

Orange Surgery (gastrectomy + lymph node dissection)

Endoscopy in Gastric Cancer

New Diagnostic and
Therapeutic Techniques
for Individual Treatment Strategies

Prof. Dr. Markus Moehler
University Clinic Mainz, Germany

Thank you for your attention