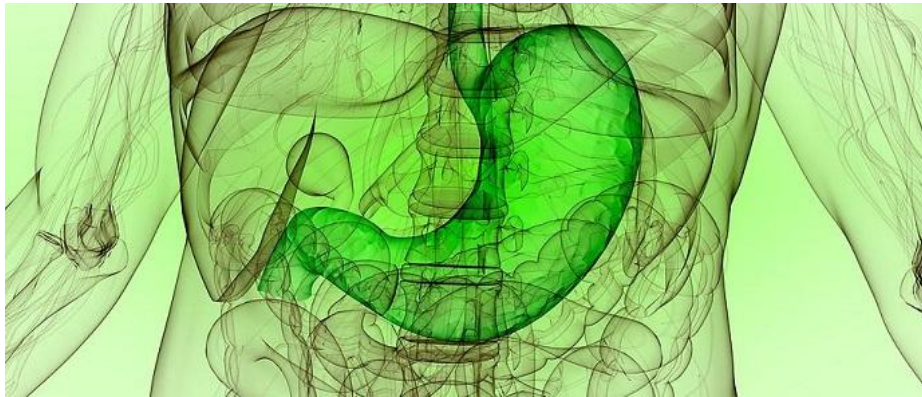


# The most frequent gastrointestinal malignant tumors



R. Němeček  
J. Tomášek, I. Kocáková, I. Kiss,  
R. Obermannová, Š. Tuček

**Masaryk Memorial Cancer  
Institute**

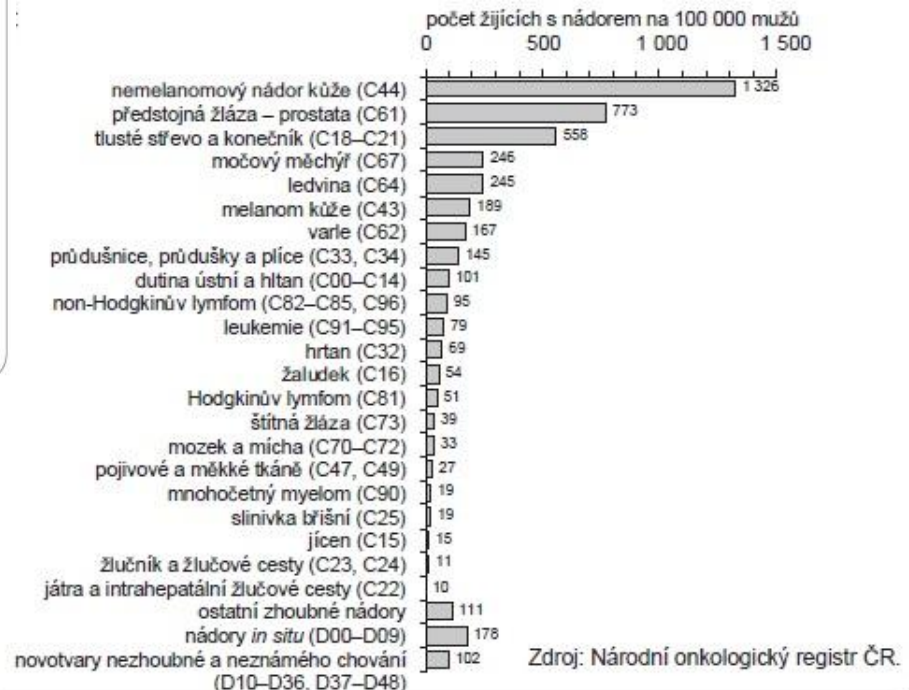
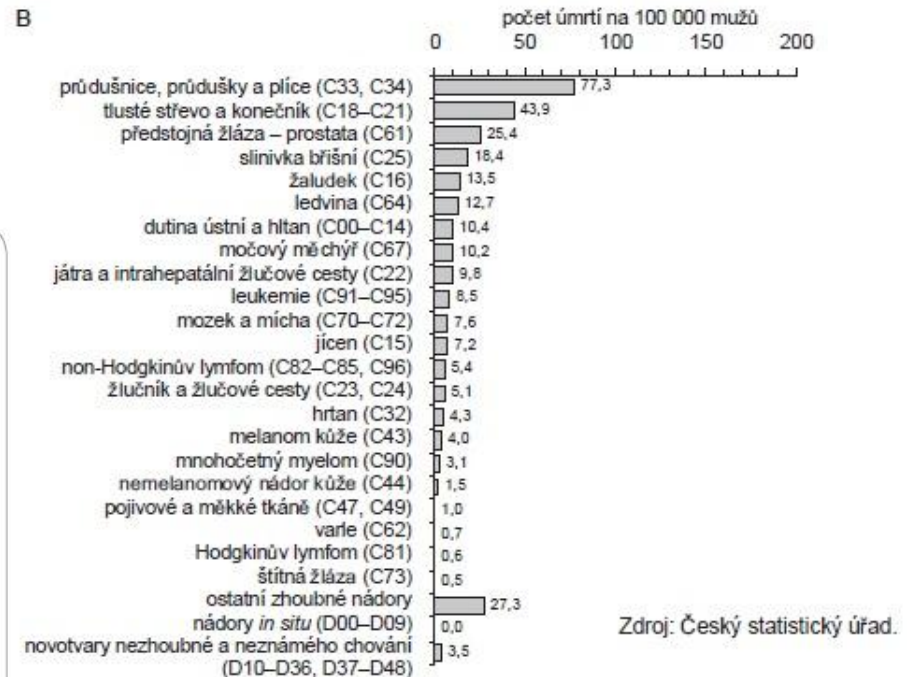
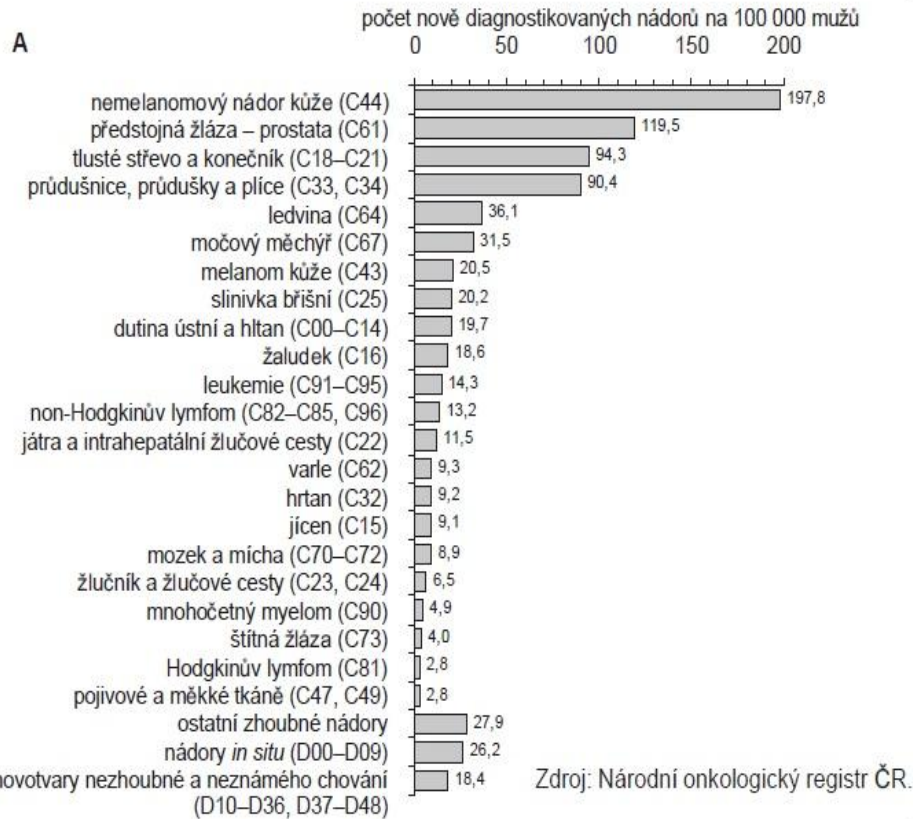
**CLINIC OF COMPREHENSIVE CANCER CARE**

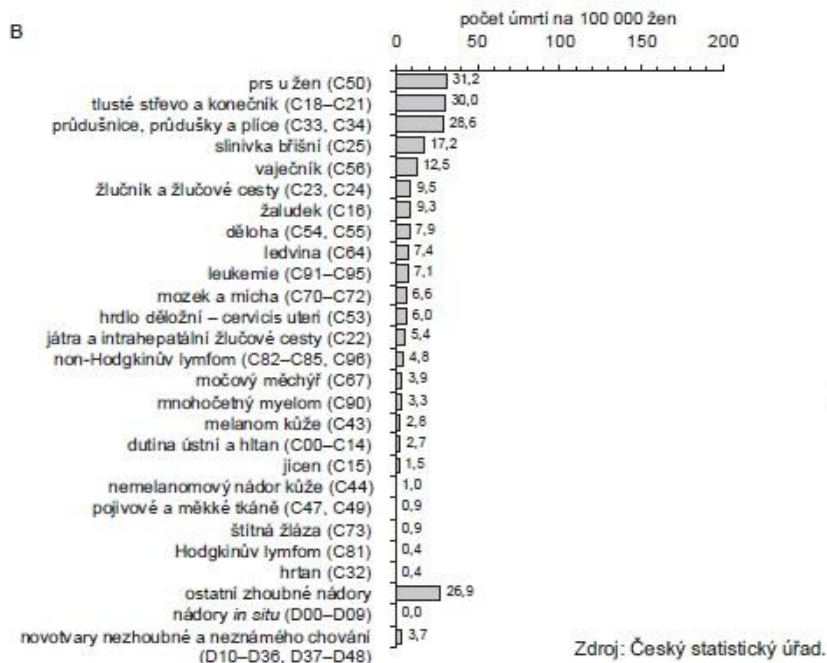
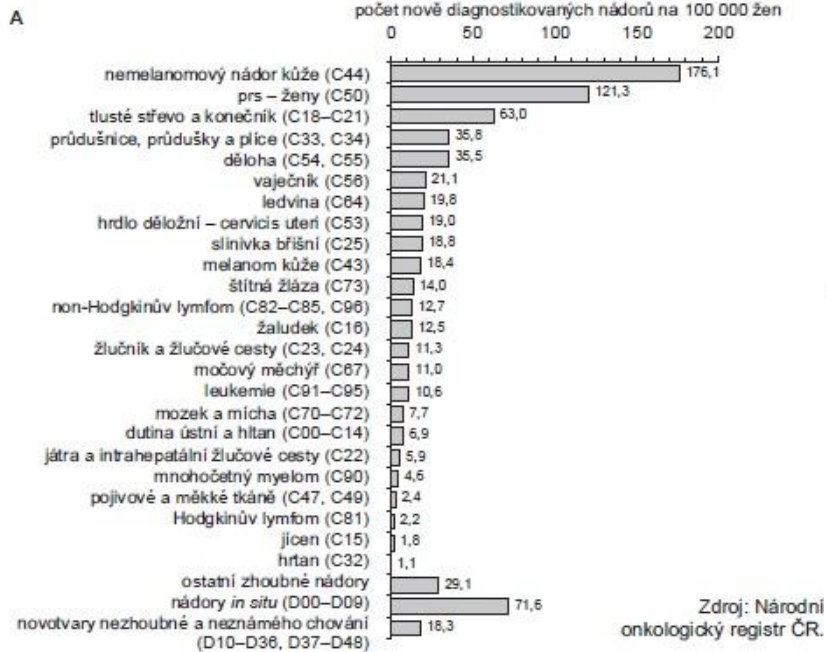
LF MU, Brno



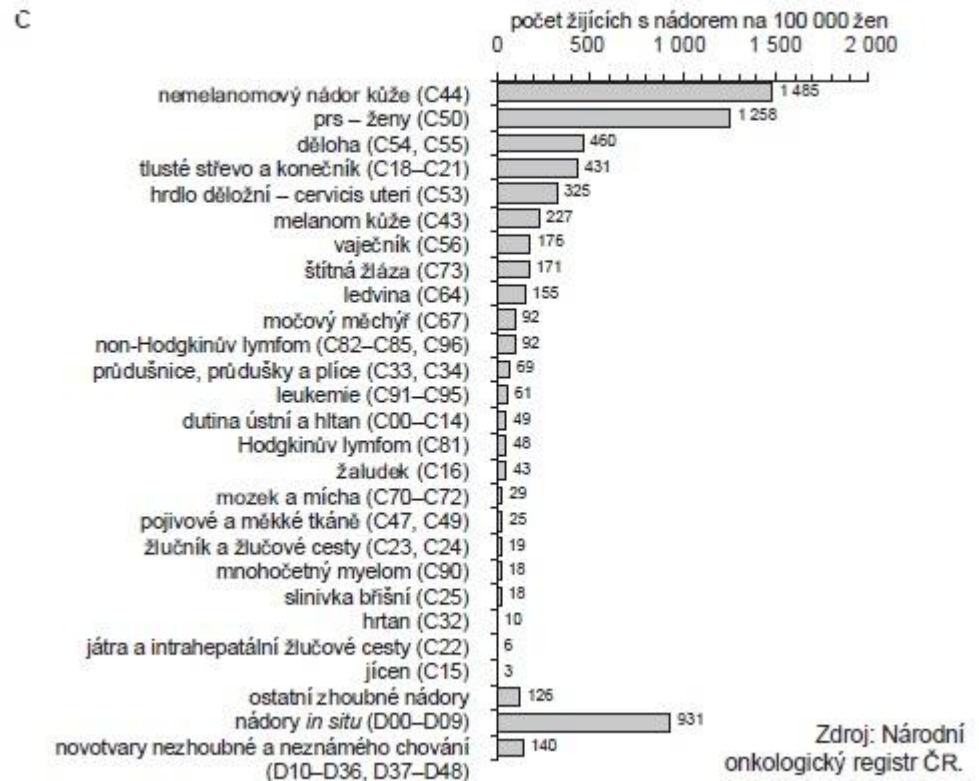
# The most frequent cancers

## - men



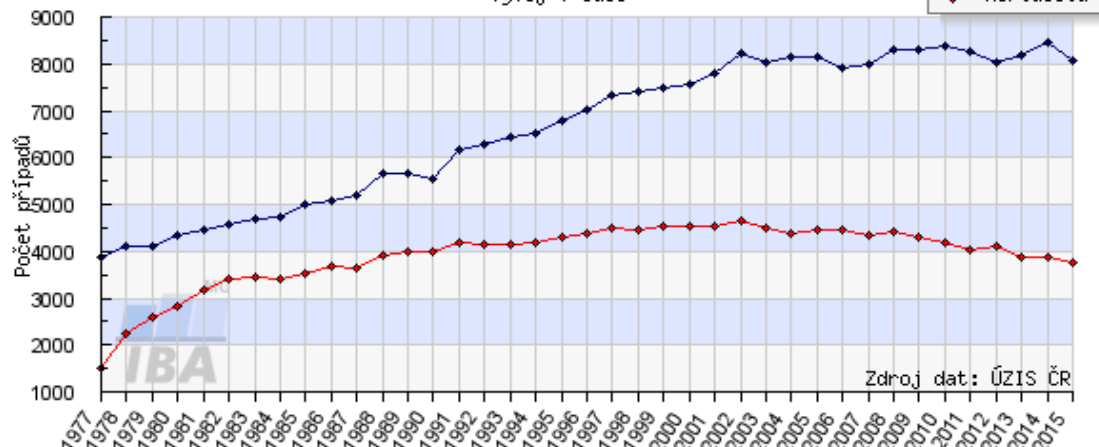


# The most frequent cancers - women



C18-C21 - ZN tlustého střeva a konečníku

Vývoj v čase

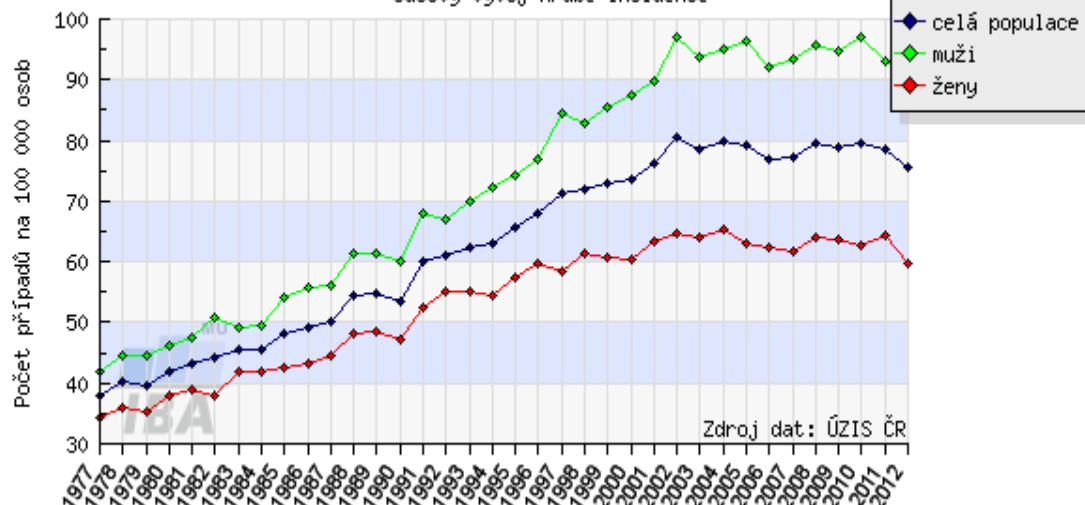


Analyzovaná data: N(inc)=258092, N(mor)=152765

<http://www.svod.cz>

C18-C21 - ZN tlustého střeva a konečníku

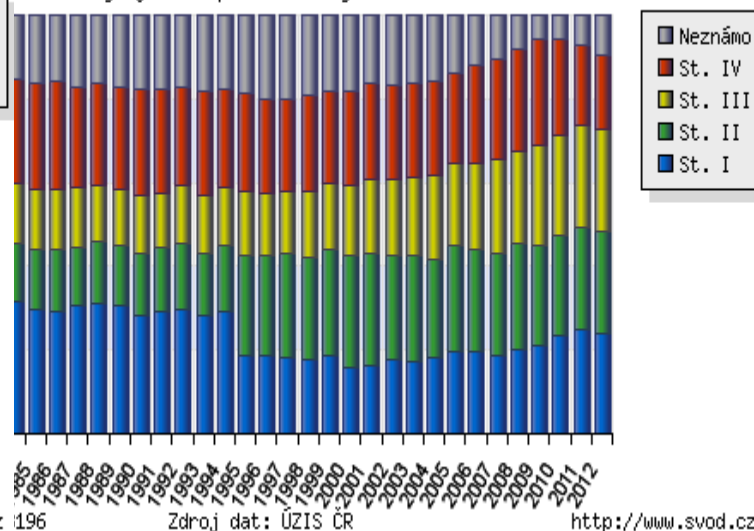
časový vývoj hrubé incidence



<http://www.svod.cz> 196

C18-C21 - ZN tlustého střeva a konečníku

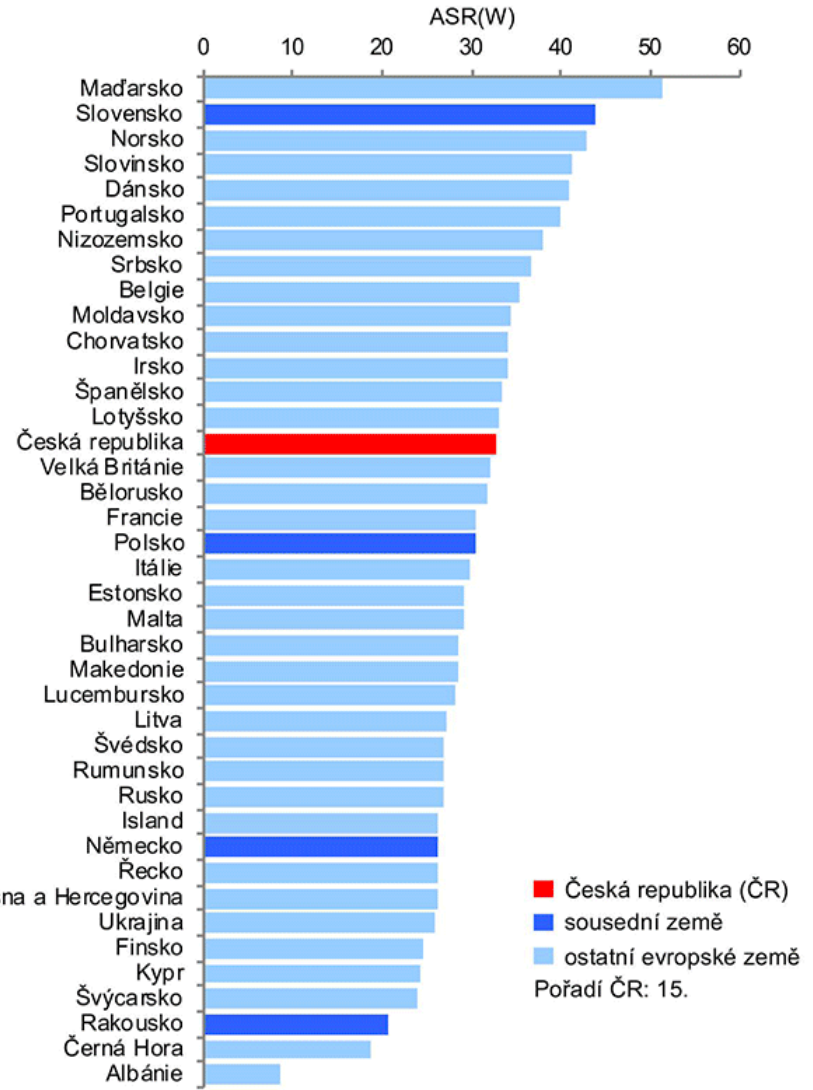
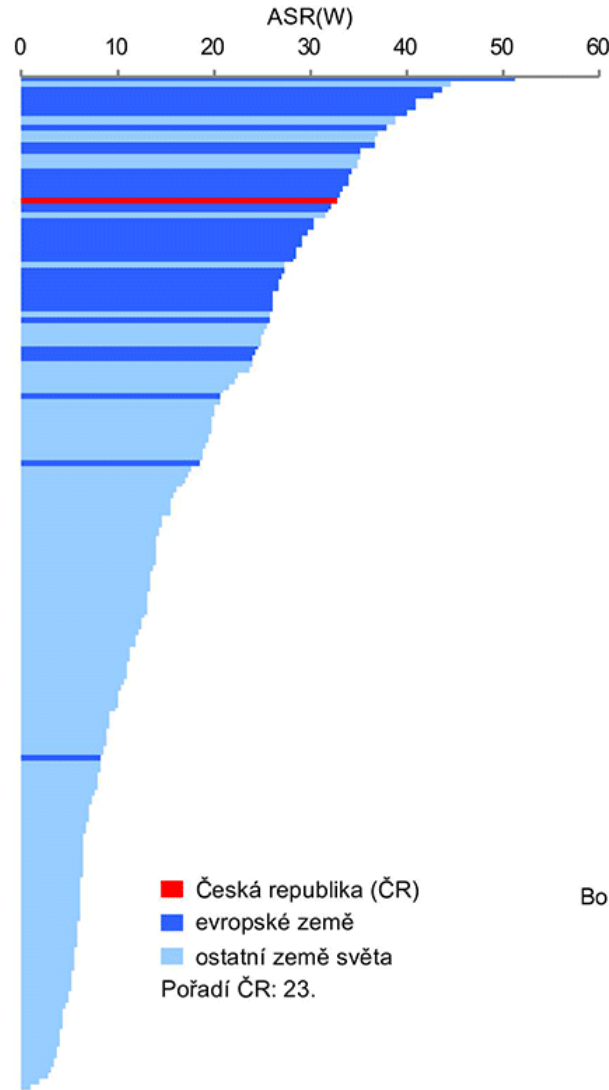
vývoj zastoupení klinických stadií



<http://www.svod.cz>

# CRC:

**Incidence zhubných nádorů tlustého střeva a konečníku (C18–C21) u obou pohlaví v mezinárodním srovnání.**  
 ASR(W) – počet nově diagnostikovaných nádorů na 100 000 osob věkově standardizovaný na světový věkový standard.



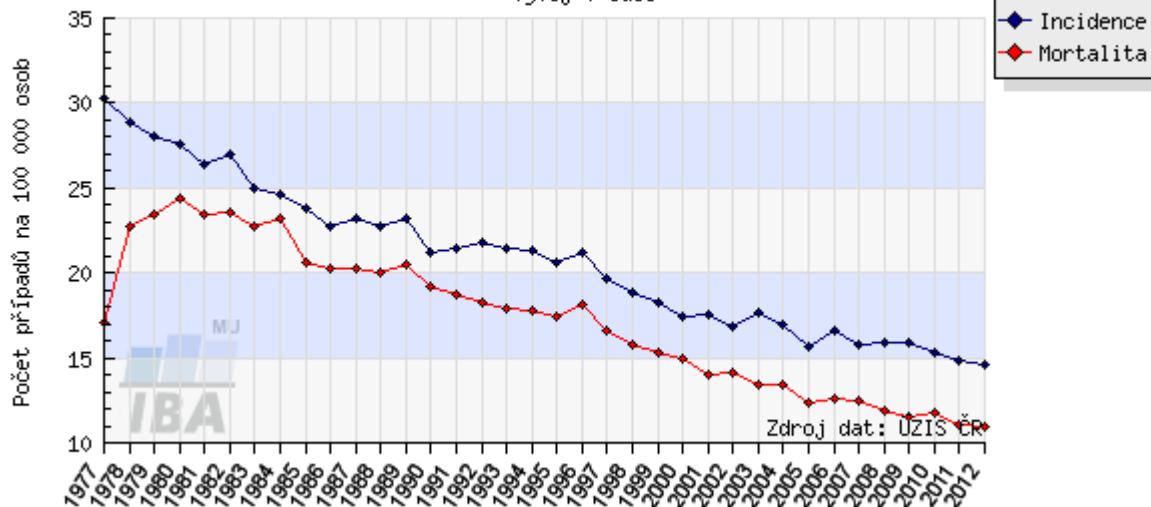
Zdroj: Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, Znaor A, Soerjomataram I, Bray F (2018). Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Available from: <https://gco.iarc.fr/today>, accessed on 4 October 2018.

# Gastric cancer:

**5th most common malignancy worldwide.**  
**3rd most common cause of death from malignancy worldwide**

C16 - ZN žaludku

Vývoj v čase

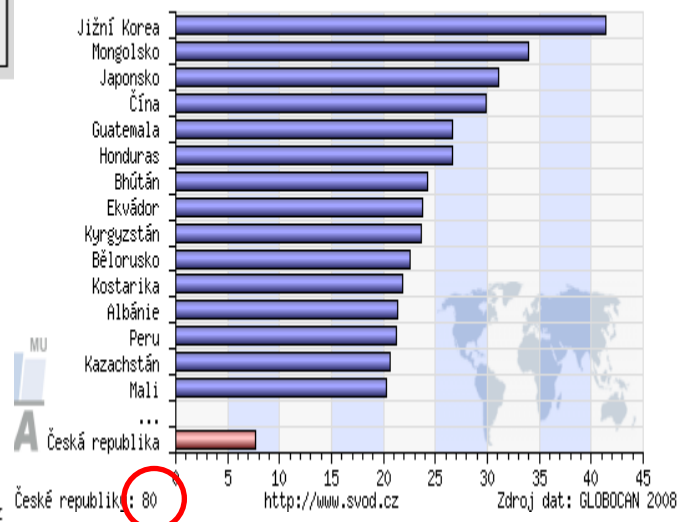


Analyzovaná data: N(inc)=77462, N(mor)=64207

<http://www.svod.cz>

C16 - Žaludek

srovnání incidence v ČR s ostatními zeměmi světa, ASR - světový standard



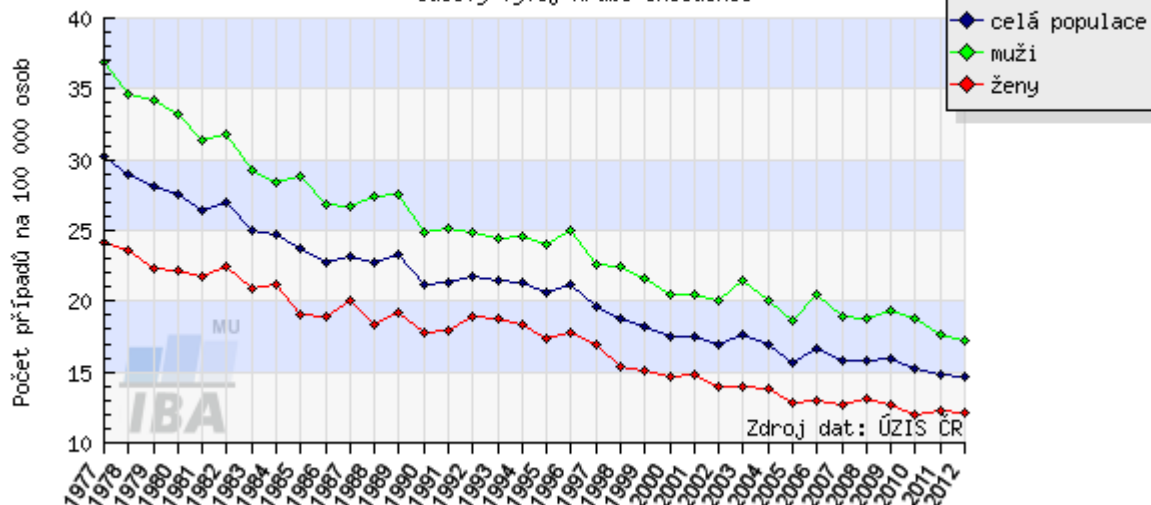
České republiky: 80

<http://www.svod.cz>

Zdroj dat: GLOBOCAN 2008

C16 - ZN žaludku

časový vývoj hrubé incidence

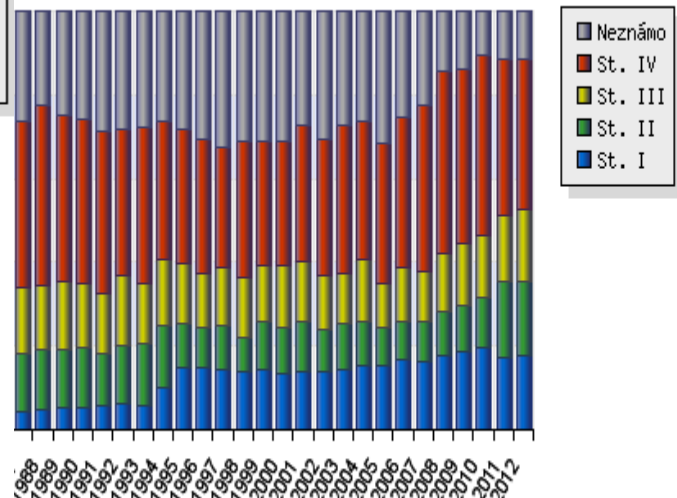


Zdroj dat: ÚZIS ČR

<http://www.svod.cz>

C16 - ZN žaludku

vývoj zastoupení klinických stadií



Zdroj dat: ÚZIS ČR

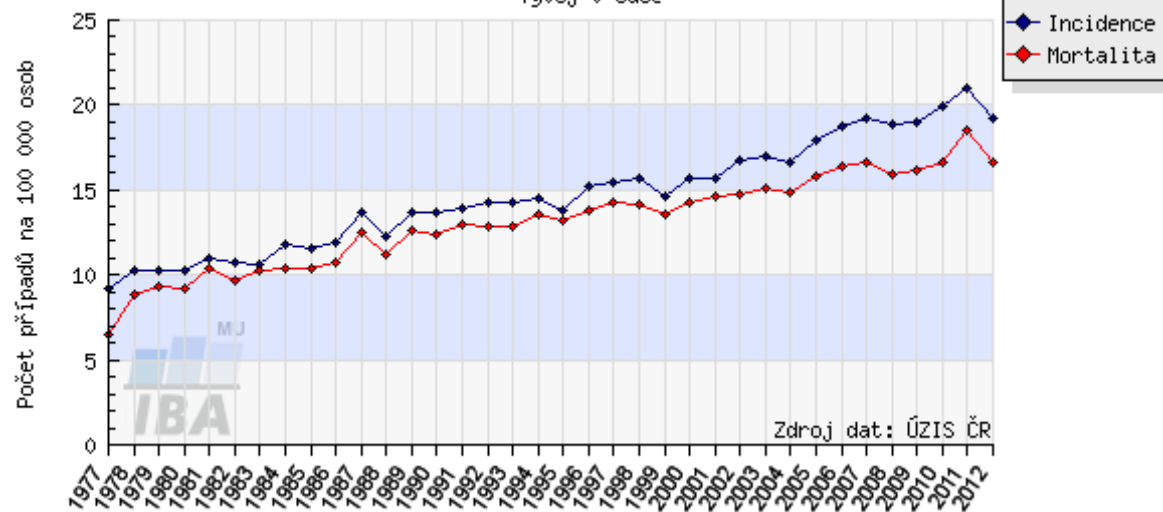
<http://www.svod.cz>

# Pancreatic cancer

4th most common cause of death from malignancy worldwide

C25 - ZN slinivky břišní

Vývoj v čase

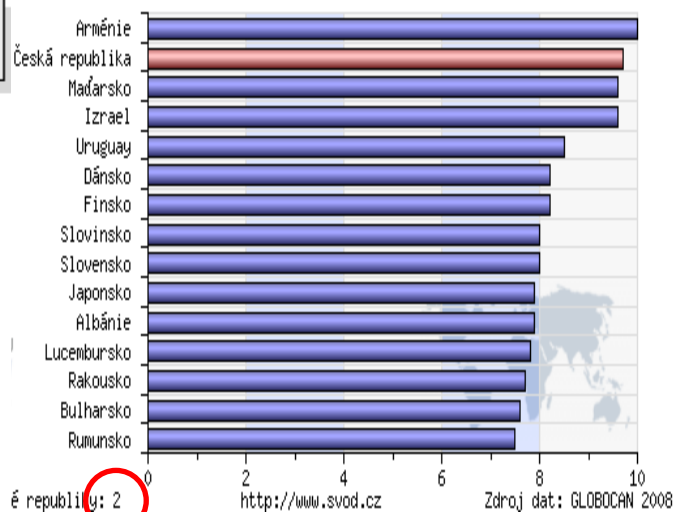


Analyzovaná data: N(inc)=54546, N(mor)=48757

<http://www.svod.cz>

C25 - Slinivka břišní

srovnání incidence v ČR s ostatními zeměmi světa, ASR - světový standard



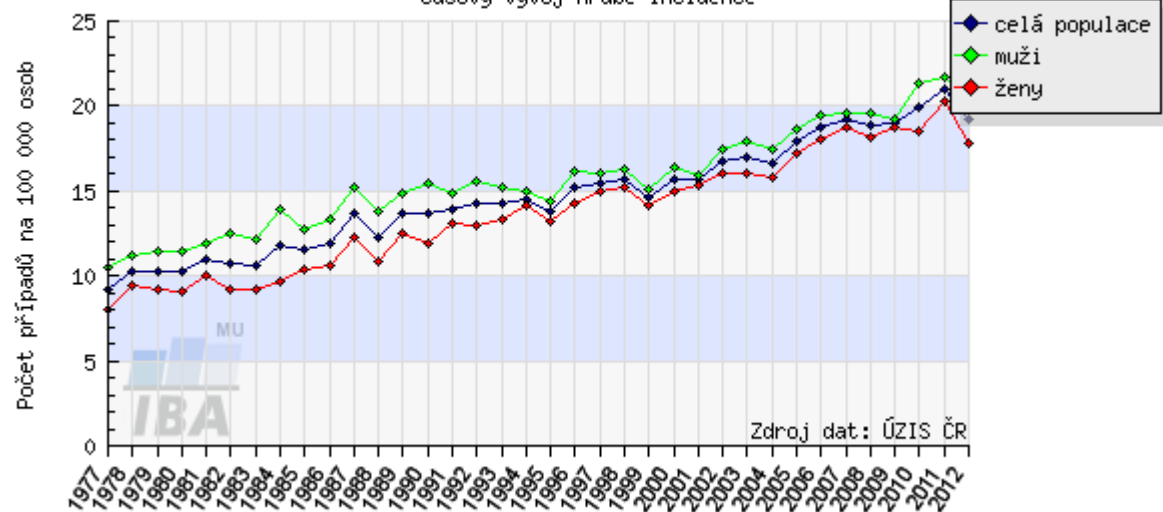
Česká republika: 2

<http://www.svod.cz>

Zdroj dat: GLOBOCAN 2008

C25 - ZN slinivky břišní

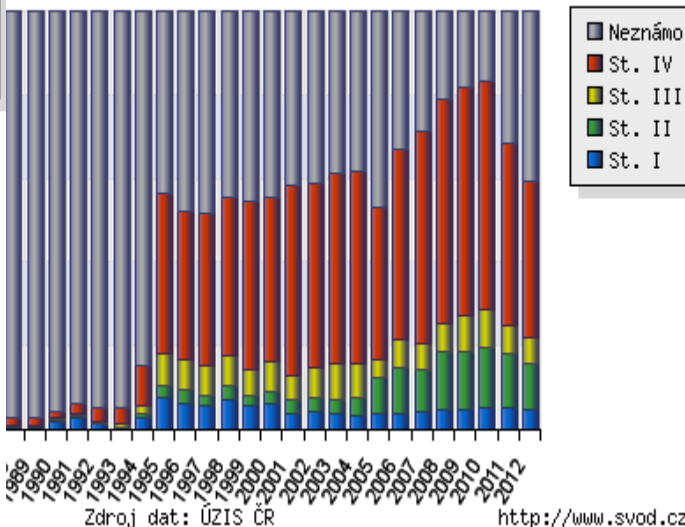
časový vývoj hrubé incidence



<http://www.svod.cz>

C25 - ZN slinivky břišní

vývoj zastoupení klinických stadií



<http://www.svod.cz>

# **Gastrointestinal malignancies**

## **clinical symptoms**



# CRC:

## Colon:

- blood in the stool, episodes of rectal bleeding  
(more common in right sided bowel cancers)
  - asymptomatic patients - screening – faecal occult blood test
- changing of bowel habits - worsening constipation, alternation of constipation and diarrhea  
(more common in left sided bowel cancers)



## Rectal cancer

- tenesmus

## General symptoms:

- fatigue, weakness, anemia, loss of appetite, unintended weight loss, cramping or abdominal pain ...

# Gastric cancer:

- **often asymptomatic / nonspecific symptoms**



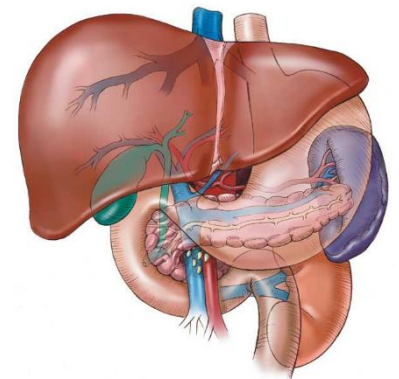
- upper abdominal pain, nausea, heartburn, vomiting
- sense of fullness in the upper abdomen after the eating of a small portion of meal
- loss of appetite (meat disgust)
- weight loss, fatigue...

- bleeding → haematemesis, melena
- anemia → fatigue, weakness, dyspnea...

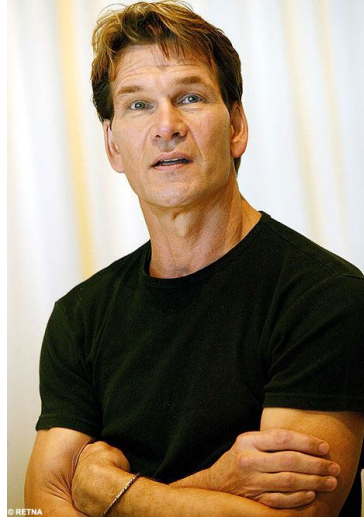


# Pancreatic cancer:

- **NO SYMPTOMS** in early stages
- **typically diagnosed in advanced stage !!!**
- pain in the upper abdomen or back
- **obstructive jaundice**
  - skin, pale stool, dark urine
- fatigue, weakness
- unexplained weight loss
- nausea, vomiting ....(duodenal obstruction)
- diabetes mellitus ...



# Difference?



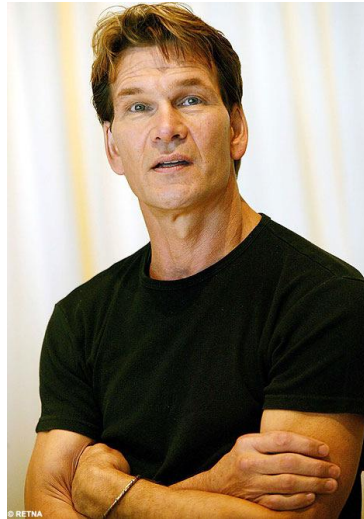
**12months**

**vs.**

**7 years**



# Pancreatic cancer (Ductal adenocarcinoma)




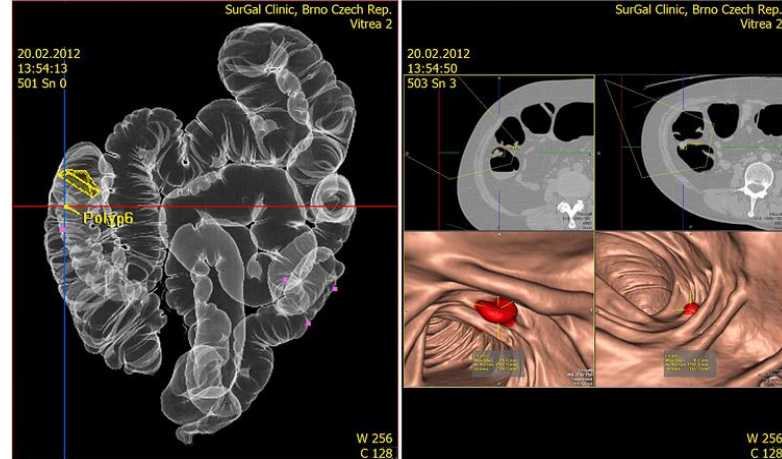
**Pancreatic neuroendocrine  
tumors**  
(3-5% pancreatic malignancies)



# Diagnostic methods

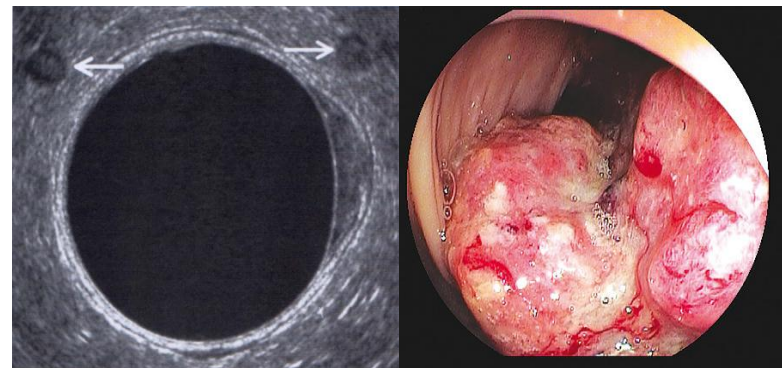
# CRC:

Colonoscopy, sigmoideoscopy  
(rectoscopy)  
biopsy  histology



## Staging (extent of disease): TNM

- abdominal and pelvic CT
- chest CT or chest X-ray
- preoperative staging of rectal cancer
  - **pelvic MRI** and/or **endoscopic ultrasound**
- tumor markers: CEA, CA 19-9



## Medical history, physical examination

Blood count, biochemistry, urinalysis



# Gastric cancer:

- Gastroscopy  
biopsy → histology

## Staging: TNM

- abdominal and pelvic CT
- chest CT or chest X-ray
- tumor markers: CEA, CA 72-4
- History, physical examination
- Lab. tests: CBC , Blood Chemistry, Urinalysis



Obr. 1. CT břicha a malé pánve, ložiska jaterní před zahájením léčby.

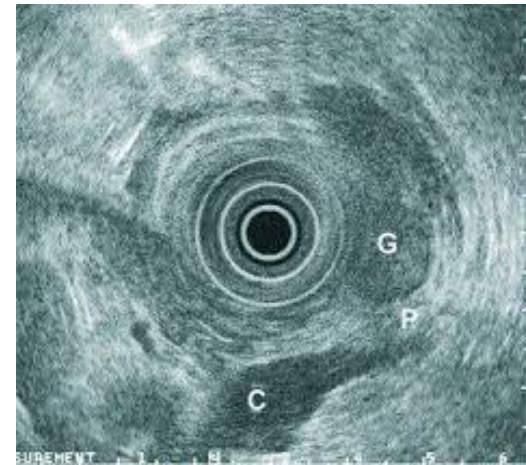


# Pancreatic cancer

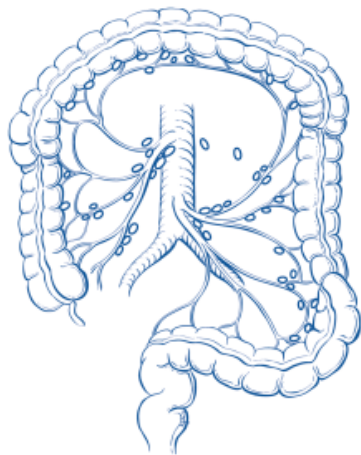
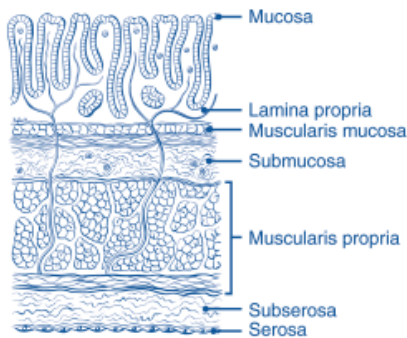
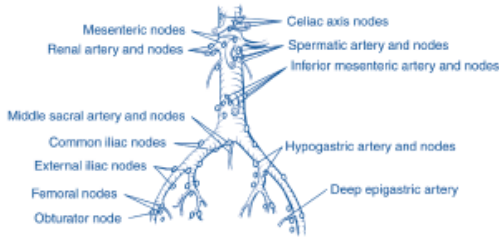
- **endoscopic ultrasound (EUS)**
  - **F**ine **N**eedle **A**spiration **B**iopsy (cytology)
- **ERCP** – individual cases

## Staging: TNM

- abdominal and pelvic CT
- chest CT or chest X-ray
- tumor markers: CEA, CA 19-9
- History, physical examination
- Lab. tests: CBC , Blood Chemistry, Urinalysis



# Colon and Rectum Cancer Staging



## Definitions

### Primary Tumor (T)

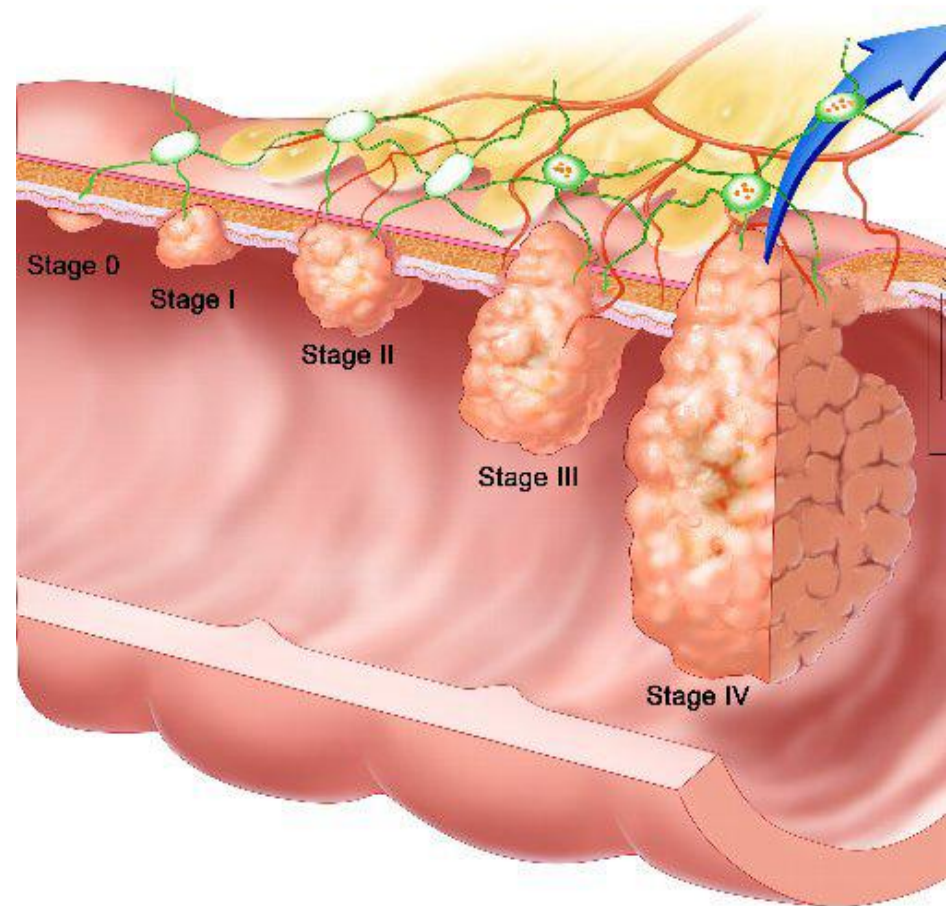
- TX** Primary tumor cannot be assessed
- T0** No evidence of primary tumor
- Tis** Carcinoma in situ: intraepithelial or invasion of lamina propria<sup>1</sup>
- T1** Tumor invades submucosa
- T2** Tumor invades muscularis propria
- T3** Tumor invades through the muscularis propria into pericolorectal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

### Regional Lymph Nodes (N)<sup>4</sup>

- 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



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.

# TNM classification:

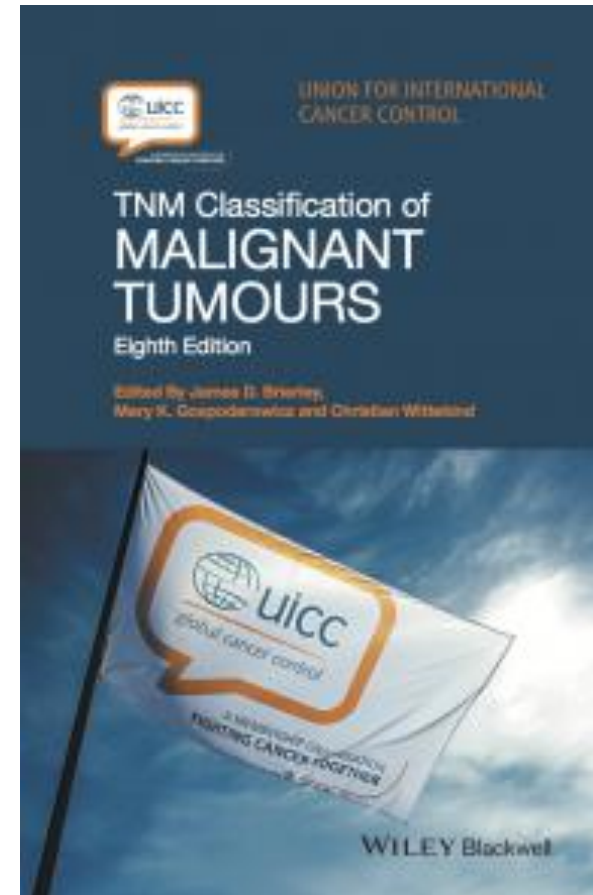
Stadium I = small tumor, mostly N0, always M0

Stadium IV = M1

Stadium II a III = inbetween

e.g. CRC:

- St. II – T3,T4 a N0
- St. III –any T , N+



# **Histology**

# ADENOCARCINOMA

= neoplasia of epithelial tissue (glandular origin)

## CRC

- intestinal, mucinous ...
- testing : MSI (early stages) / RAS status (metastatic)

## Gastric cancer – Lauren classification:

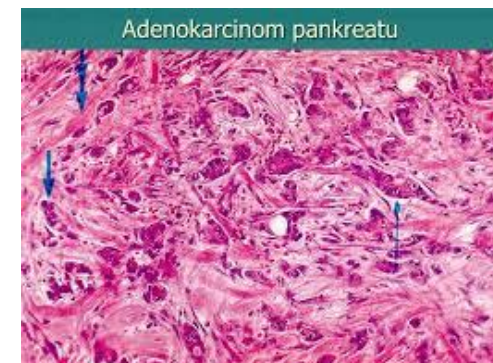
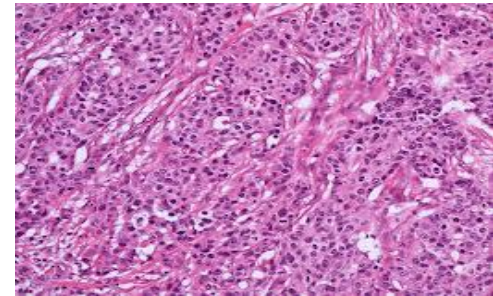
- intestinal type (better prognosis)
- diffuse type (worse prognosis)
- testing: HER2 in advanced stages

## Pancreatic cancer

- ductal adenocarcinoma (mostly)

**GRADING** = degree of differentiation = aggressiveness

G1- well differentiated    x    G3 - poorly differentiated



**Treatment: Surgery**

# CRC - resection :

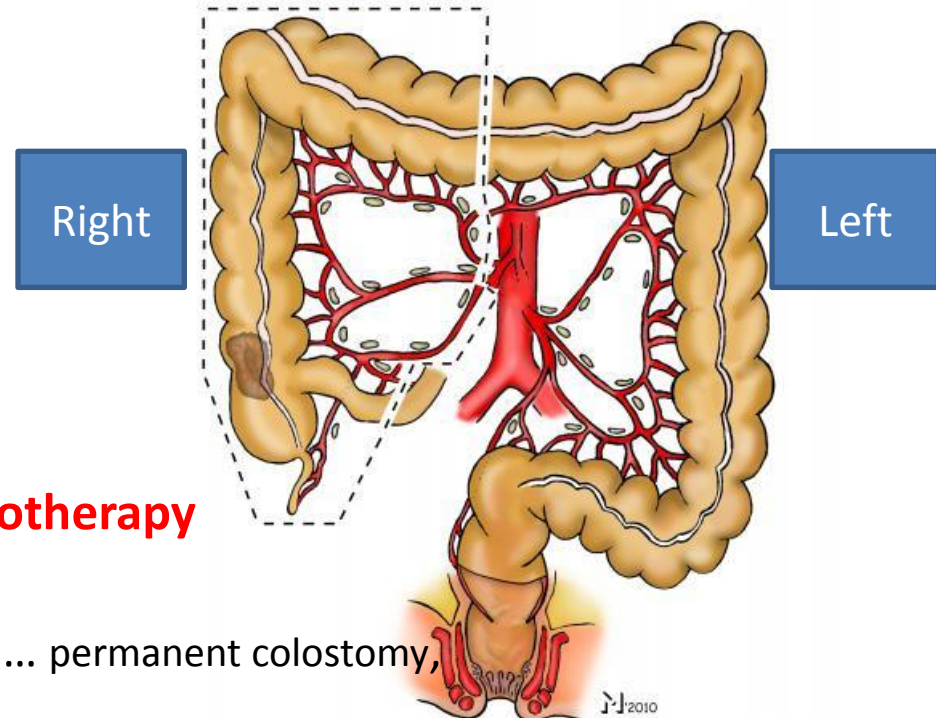
- complete surgical removal with adequate margins, mesocolon dissection (minimal count of dissected lymph nodes = 12)

## Colon: **immediately**

- hemicolectomy
  - right
  - left

## Rectum: **following neoadjuvant chemotherapy**

- LAR = low anterior resection
- Abdominoperineal amputation (Miles) ... permanent colostomy, higher rate of sexual and urinary dysfunction



**Primarily metastatic patients without symptoms of intestinal obstruction:  
no surgery but systemic treatment immediately!**

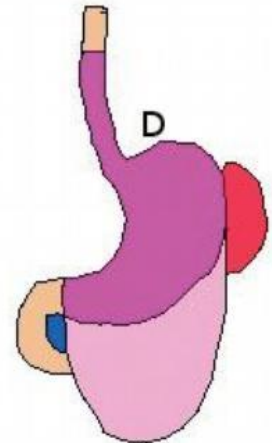
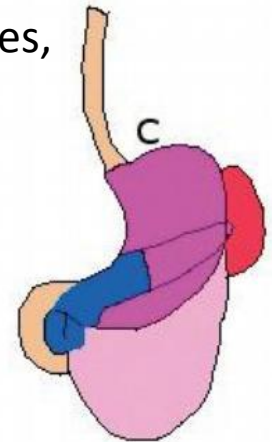
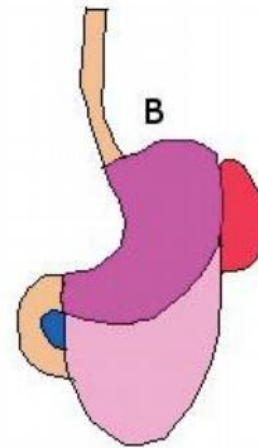
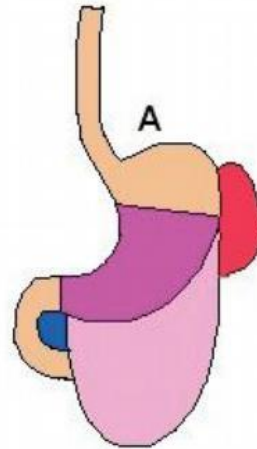
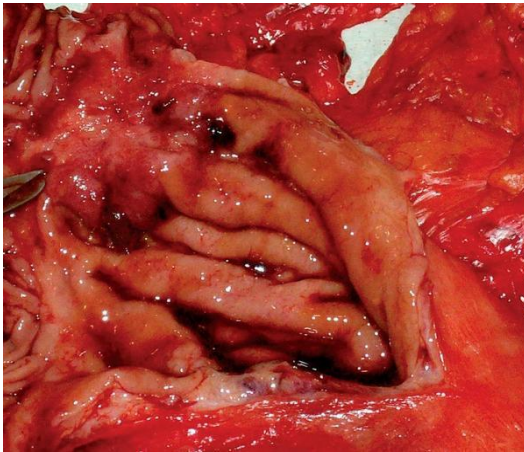
# Gastric cancer :

- R0 resection = histologically negative margins

D1 lymphadenectomy includes only nodes adjacent to the stomach

D2 lymphadenectomy (hepatic, left gastric, celiac, and splenic arteries, as well as those in the splenic hilum)

- **Diffuse type** – total gastrectomy



- **Intestinal type** - subtotal (partial) gastrectomy (min 5cm proximal and distal)



# Pancreatic cancer :

Resectability < 20% cases

Head of the pancreas :

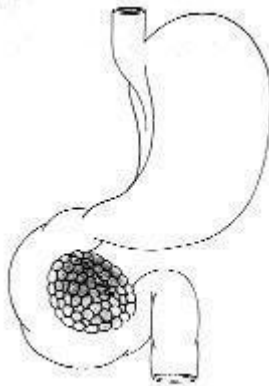
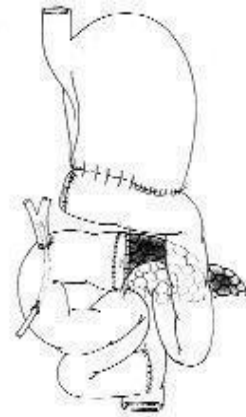
- **Whipple surgery** (hemipancreatoduodenectomy)  
= remove part of the pancreas, part of the small intestine and the gallbladder.

Body of the pancreas:

- total pancreatectomy

Tail of the pancreas:

- distal pancreatectomy



# **Oncological therapy**

- localized stage

# CRC:

## Colon cancer:

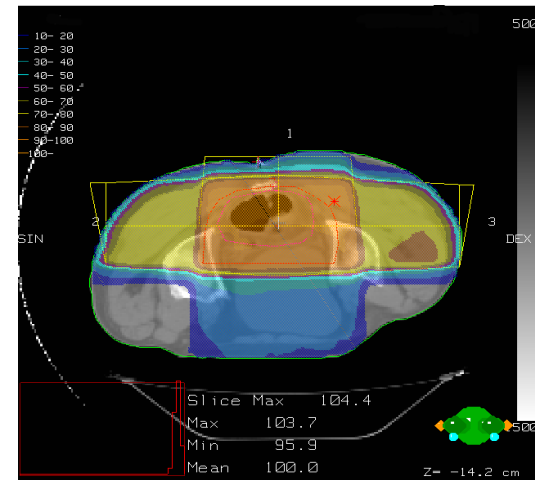
- **adjuvant chemotherapy (CHT) for 6 months** in stage III and in high risk patients with stage II CRC (low risk st. II only 3 months or no CHT)
- CHT : continuous administration of **5-FU** more effective than bolus –FU
- **Capecitabine** = oral prodrug of 5-FU
- Addint oxaliplatine (FOLFOX4) demonstrated a significant improvement of prognosis in stage III colon cancer patients

- **No radiotherapy !!!**



## Rectal cancer:

- **neoadjuvant concomitant chemo-radiotherapy (CH-RT) in risk patients**  
T3, T4 and/or N+ (EUS or MRI)  
RT 50Gy throughout 5 weeks + capecitabine
- **Surgery should be performed 6 to 8 weeks** after completion of chemoradiation
- adjuvant chemotherapy



# Neoadjuvant (preoperative) radiation therapy in rectal cancer

## Preoperative radiation therapy advantages:

- tumor down-staging
- increase chance of resectability  
(possibly permitting the use of a sphincter-sparing procedure)
- decrease the risk of local recurrence
- preoperative radiation therapy works better in well-oxygenated tissues prior to surgery

# Gastric cancer: various treatment options

## **Neoadjuvant chemotherapy :**

- downstaging of the disease to increase the chance of resectability
- decrease micrometastatic disease burden prior to surgery
- reduce the rate of local and distant recurrences
- improve survival

## **Perioperative chemotherapy:**

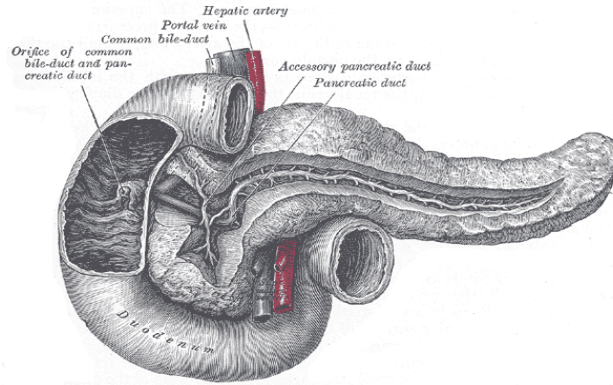
**FLOT regimen (5-FU + LV + oxaliplatin + docetaxel)**

**FLOT...FLOT...FLOT... FLOT... surgery... FLOT... FLOT...FLOT...FLOT**

(or **FOLFOX** – in case of frailty patients)

**Adjuvant radiotherapy** was associated with improvements in both overall and relapse-free survival and reduction in locoregional failure, but significant toxicity. Today – **CHT = preferred option!**

# Pancreatic cancer :



- adjuvant CHT (gemcitabine) .... total duration 5-6months
- since 2018 – adjuvant CHT **FOLFIRINOX** (FU + oxaliplatin + irinotecan)
- adjuvant chemoradiotherapy – 5-FU based (recently used only rarely)
- Risk of relapse .... up to 80-100% !!



**Oncological treatment  
of  
advanced /metastatic disease**

# Metastatic CRC:

- **Metastasis: liver, lung, peritoneal .... local relapse**
- **Metastatic disease regimens: 5-FU or capecitabine**
  - in combination with **irinotecan** (FOLFIRI regimen)
  - in combination with **oxaliplatin** (FOLFOX / XELOX regimen)

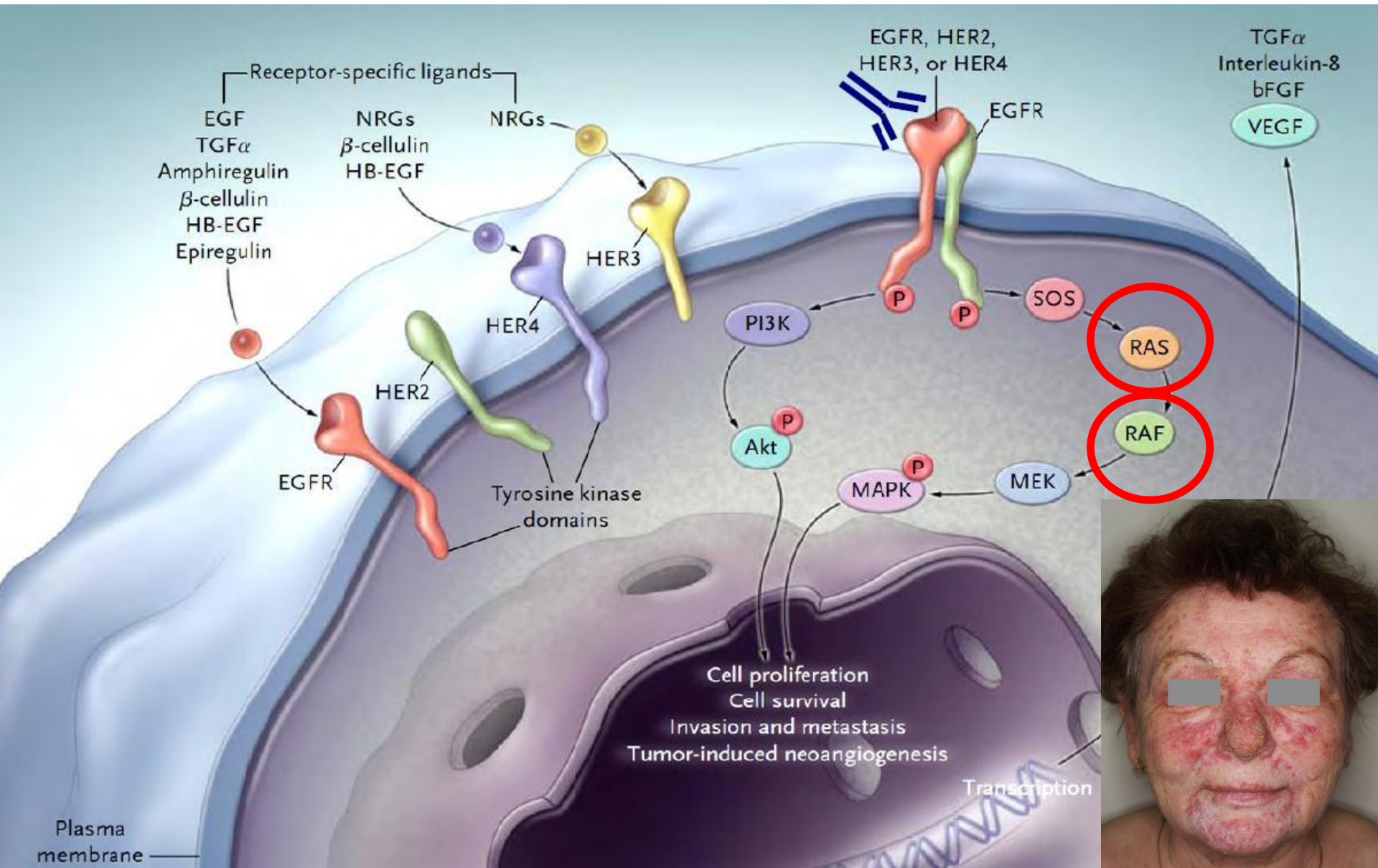
## Terms:

- „palliative“ x „curative“ therapy x „best supportive care “
- „cycle o chemotherapy“ x line of therapy“ („1st, 2nd, 3rd...“)
- Targeted therapy:
  - anti EGFR – cetuximab, panitumumab
  - anti VEGF – bevacizumab, aflibercept, ramucirumab
  - multitargeted tyrosine kinase inhibitor : regorafenib
- Rectal cancer : palliative radiotherapy



# Epidermal growth factor receptor (EGFR):

Monoclonal antibodies **cetuximab** and **panitumumab**



# Vascular endothelial growth factor (VEGF):

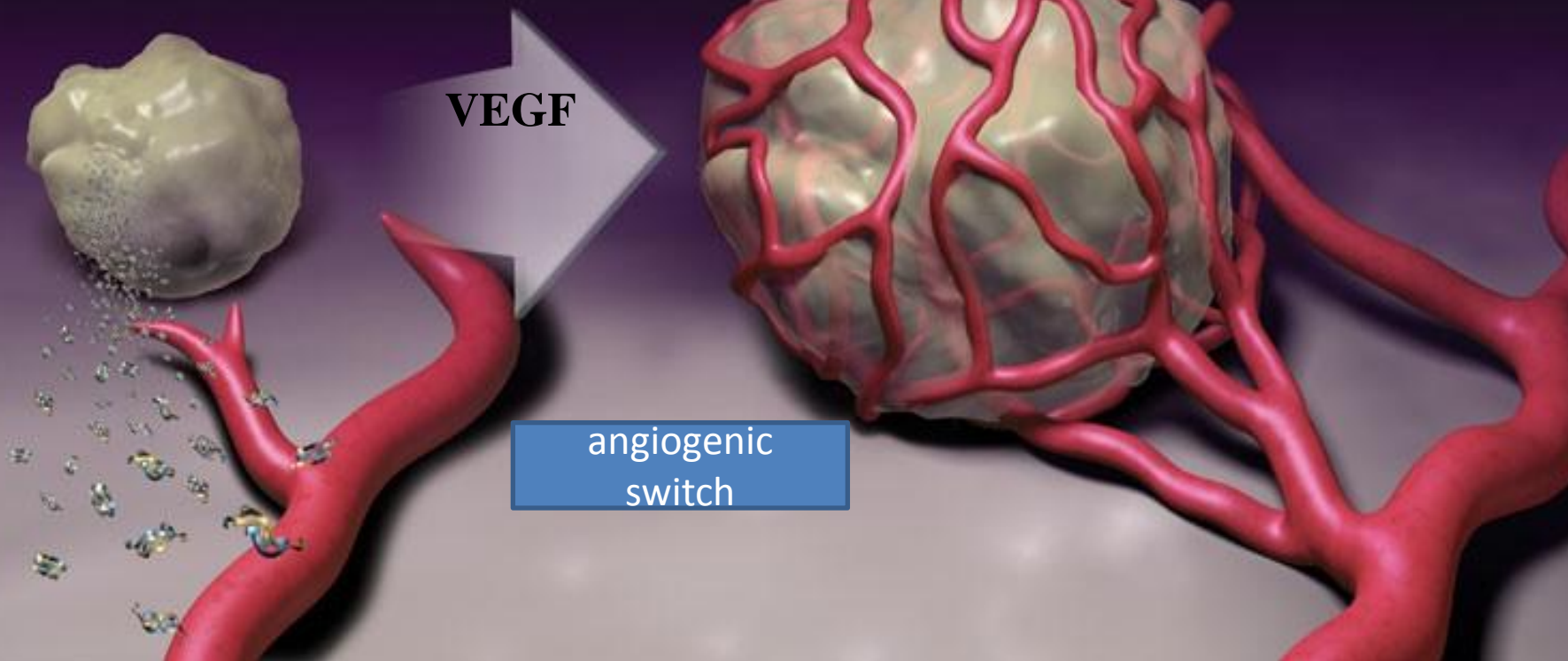
**bevacizumab, aflibercept, ramucirumab**

**Small tumor (1–2mm)**

- avascular

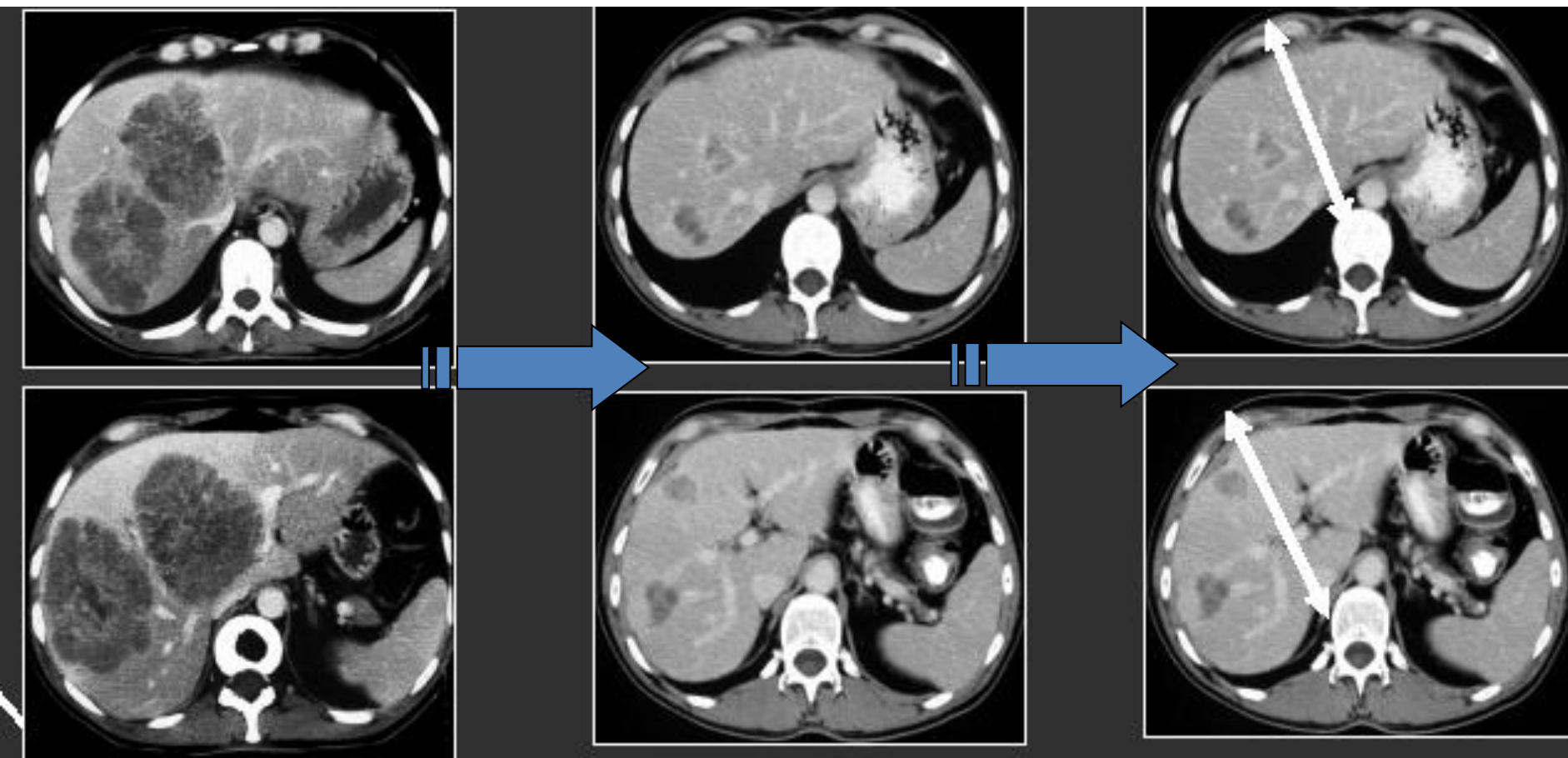
**Larger tumor**

- vascular
- potential to metastasize



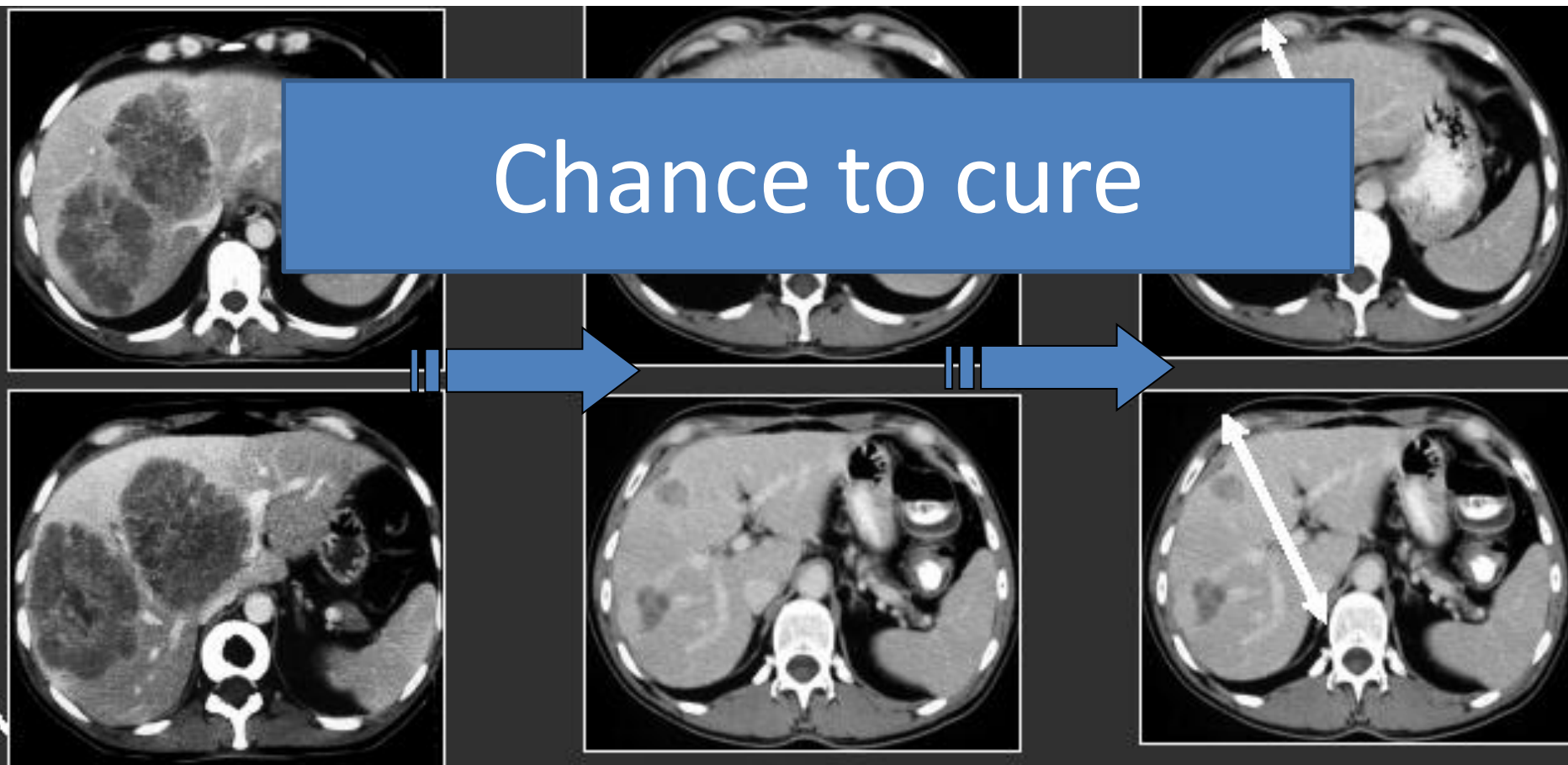
**Curative-intent resections of liver metastases have significantly improved long-term survival, with acceptable postoperative morbidity, including older patients.**

Effect of neoadjuvant chemotherapy/targeted anti-EGFR therapy in patients with initially unresectable colorectal liver metastases.



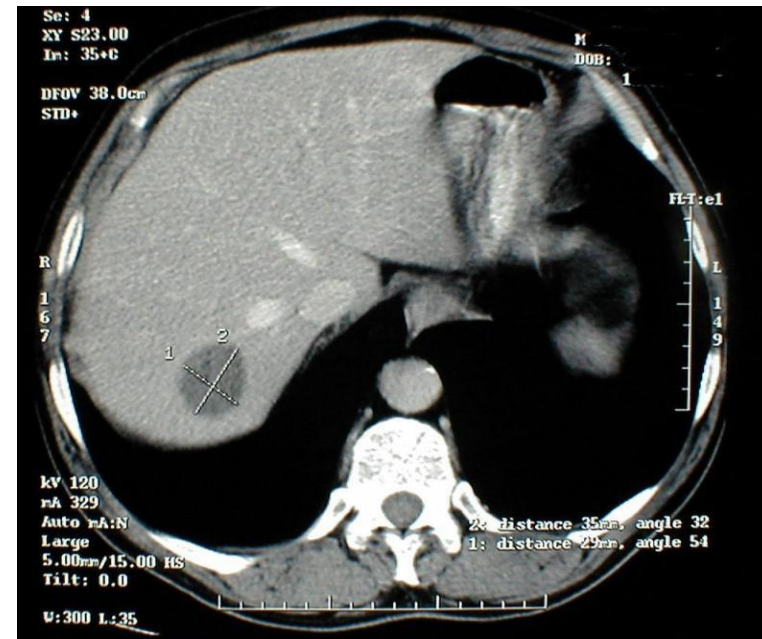
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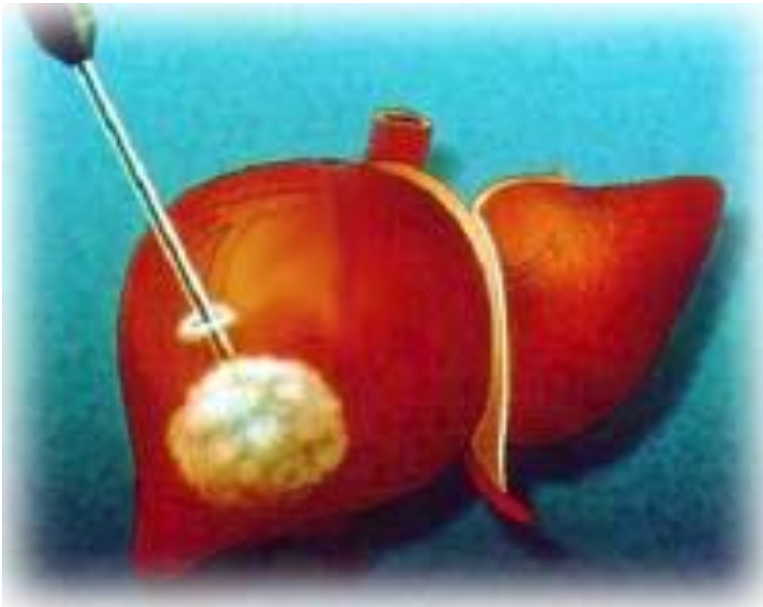
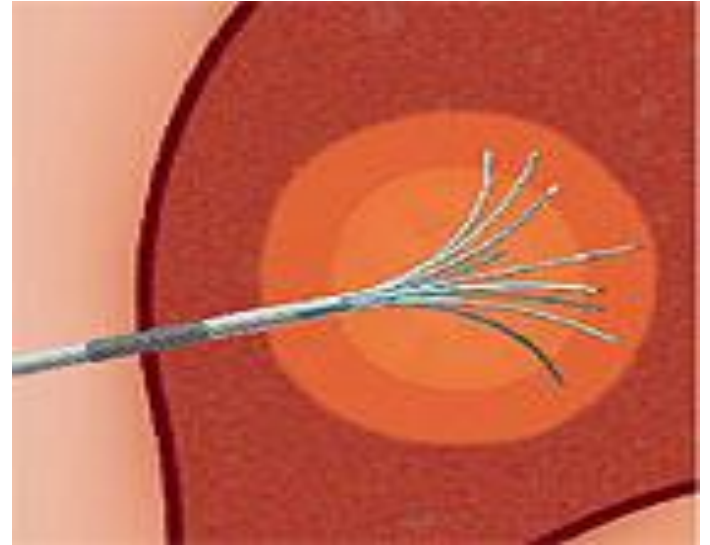
# Liver metastases treatment

- **Surgery** - the only potentially curative treatment
- Local ablative techniques:
  - Radiofrequency ablation (RFA)
  - Microwave ablation (MWA)
  - Cryosurgery
  - Percutaneous ethanol injection (PEI)
- chemoembolization (TACE)
- intra-arterial chemotherapy infusion (liver)
- stereotactic radiotherapy (SBRT)



# Liver ablation methods

- Radiofrequency ablation (RFA)
- Microwave ablation (MWA)
- Cryosurgery
- Percutaneous ethanol injection (PEI)



# Gastric cancer - advanced unresectable /metastatic:

- Surgical procedures with palliative intent: wide local excision, partial gastrectomy, total gastrectomy, gastrointestinal anastomosis, and bypass
- palliative CHT : **5-FU, cisplatin or oxaliplatin based** (DDP/FU/FA or FOLFOX )  
**epirubicin, docetaxel**
- **Second line : taxans** (paklitaxel / docetaxel) or **irinotekan**
- Targeted therapy:
  - **anti HER2 – trastuzumab (Herceptin) (1st line)**  
(HER2 positive – cca 20% patients)
  - **anti VEGF – ramucirumab (2nd line)**

# Pancreatic cancer - advanced unresectable /metastatic :

1. **5-FU +oxaliplatine + irinotecan** (FOLFIRINOX regimen)
  2. **Gemcitabine + nab-paclitaxel** albumin-bound nanoparticle formulation
  3. **Gemcitabin monotherapy (worse PS, less toxicity)**
- Targeted therapy:
    - anti-EGFR: erlotinib ..... minimal benefit ... not used !!
  - Radiotherapy - palliative , locally advanced tumor
  - **Best Supportive Care (BSC) ..... optimal therapy in many patients**
  - very poor prognosis

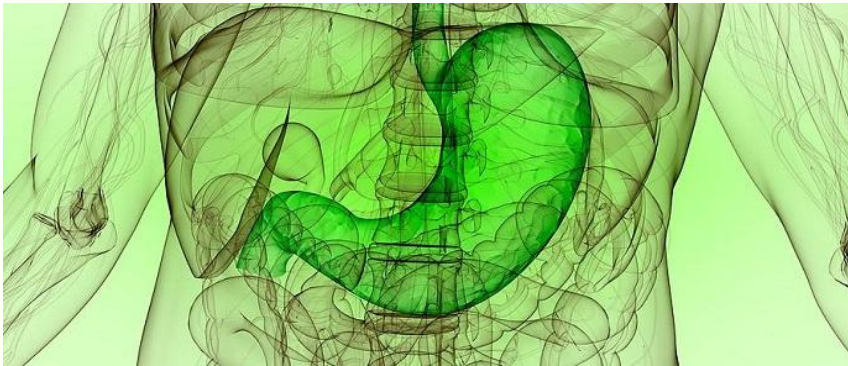


# The prognosis of metastatic disease

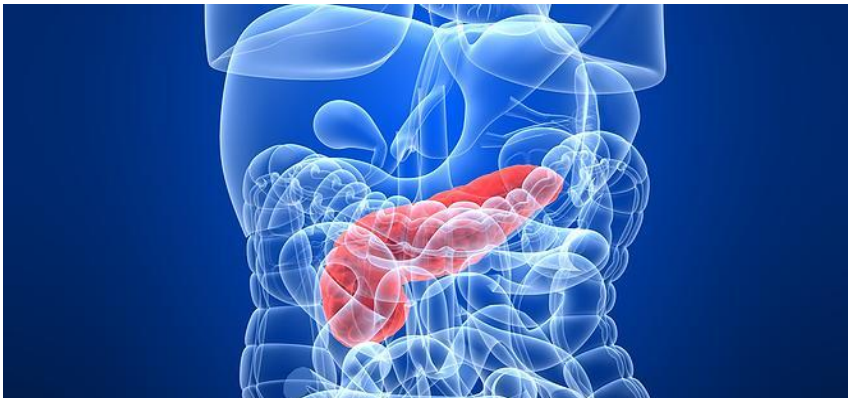


**Median overall survival**  
**(otherwise in good condition, best treatment)**

**24 – 30 months**



**8- 16 months**



**6- 12 months**

Thank you for  
your attention

