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**FACULTY OF MEDICAL
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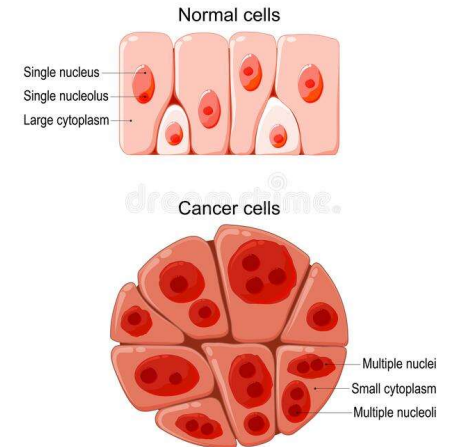
The principles of surgical oncology

Asist. Prof. Marko Spasic

Introduction

- Oncology- the science of tumors (*oncos/logos*)
- Neoplasm - an altered cell population characterized by excessive, uncontrolled and useless proliferation of cell that does not respond to normal control mechanisms nor to the influence of adjacent tissue

Malignant neoplasm





Introduction

- Surgical oncology is a field of medicine that uses surgery to treat cancer and consists of procedures for:
 - diagnosis of malignancy (biopsy)
 - removal of the primary tumor
 - removal of the metastases
 - palliation
- The basis of curative oncological treatment for solid tumors
- The R0 line of tumor resection is the goal of radical cancer surgery
- Multidisciplinary approach to prevention, diagnosis, treatment and rehabilitation of cancer patients.

Multidisciplinary team (MDT)

- Surgical oncologist
- Medical oncologist
- Radiation oncologist
- Reconstructive surgeon
- Pathologist
- Radiologist
- Other specialities (optionally)



Historical facts

- The oldest world document describing cancer comes from Ancient Egypt 1500/1600 BC
- 400 BC, Hippocrates used the Greek term */karcinos* to describe a tumor, calling it “*karkinos*”
- Before the year of 1850 the first attempts of resection of cancer
- 1850-1950 – development of standard surgical resection techniques
- At the end of the 19th century *Rudolf Virchow* recognized that cancer cells arose from normal cells (abnormal proliferation)
- In 1914 *Teodar Boveri* recognized the importance of chromosomal aberrations for the formation of cancer cells





Historical facts

- *Celsus*, a Roman doctor believed that the cancer was an incurable disease and the treatment was often more harmful than the disease itself.
- The century of surgeons (1840-1940) - the development of modern surgical oncology:
 - The discovery of general anesthesia (1840)
 - Antiseptics (1860)
 - Technical progress
- The pioneers of surgical oncology:
 - *Moore* and *Halsted*- radical breast cancer surgery
 - *Kocher*- thyroid surgery
 - *Miles*-abdomino-perineal rectal resection
 - *Dr Christian Albert Theodor Billroth* from Germany, *Dr W. Sampson Handley* from London – gastric surgery

Historical facts

- 1950-1960 – the development of extended radical resection procedures
- In 1953 *Watson* and *Crick* described the structure of DNA, which paved the way for research into the molecular biology of tumors
- 1960-1980 – the examination of the combined approach of cancer treatment
- 1980-2000 – multimodal therapy enables organ preservation and better survival
- 2000 and further on – oncological surgery based on the understanding of the molecular basis and biology of malignant tumors





Types of cancer

Carcinogen - every substance or agents that can induce the development of a malignant disease

- Chemical
- Physical
- Viruses



Chemical carcinogens

Chemical	Predominant Tumor Type
Aflatoxins	Liver cancer
Arsenic	Skin cancer
Benzene	Leukemia
Benzidine	Bladder cancer
Ethylene oxide	Leukemia, lymphoma
Estrogen replacement therapy	Endometrial cancer, breast cancer
Tamoxifen	Endometrial cancer
Tobacco smoke	Lung cancer, oral cancer, pharyngeal cancer, laryngeal cancer, esophageal cancer (squamous cell, pancreatic cancer, bladder cancer, liver cancer, renal cell carcinoma, cervical cancer, leukemia)



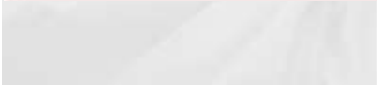
Physical carcinogens

- Ionizing radiation-bone cancer
- Repeated X-ray imaging-cancer of the skin and thyroid gland
- Nuclear ventilation-hematological malignancies (leukemia)



Viruses

Virus	Predominant Tumor Type ^b
Epstein-Barr virus	Burkitt's lymphoma
	Hodgkin's disease
	Immunosuppression-related lymphoma
	Sinonasal angiocentric T-cell lymphoma
	Nasopharyngeal carcinoma
Hepatitis B	Hepatocellular carcinoma
Hepatitis C	Hepatocellular carcinoma
Human immunodeficiency virus-1	Kaposi's sarcoma
	Non-Hodgkin's lymphoma
Human papillomavirus types 16 and 18	Cervical cancer
	Anal cancer
Human T-cell lymphotropic viruses	Adult T-cell leukemia/lymphoma



Definitions

- Primary (or definitive) therapy
 - *en bloc* resection with adequate margins and regional lymph nodes
- Adjuvant therapy
 - Refers to radiation therapy and systemic therapy (chemotherapy, immunotherapy, hormone therapy and combined biological therapy)



Therapy goals

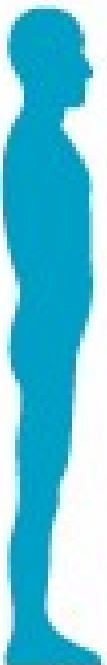
- Primary goal of surgical and radiation therapy: LOCAL AND REGIONAL DISEASE CONTROL
- Primary goal of systemic therapy: SYSTEMIC CONTROL OF DISTANT FOCUSES TO PREVENT METASTASES AND RECURRENCE



Epidemiology


ESTIMATED NEW CASES

MEN:



Prostate	33%
Lung and Bronchus	14%
Colon and Rectum	11%
Urinary Bladder	6%
Melanoma of the Skin	4%
Non-Hodgkin's Lymphoma	4%
Kidney	3%
Oral Cavity	3%
Leukemia	3%
Pancreas	2%
All Other Sites	17%

WOMEN:



Breast	32%
Lung and Bronchus	12%
Colon and Rectum	11%
Uterine Corpus	6%
Ovary	4%
Non-Hodgkin's Lymphoma	3%
Melanoma of the Skin	3%
Thyroid	3%
Pancreas	2%
Urinary Bladder	2%
All Other Sites	20%




Epidemiology


ESTIMATED DEATHS

MEN:

WOMEN:



Lung and Bronchus	31%
Prostate	10%
Colon and Rectum	10%
Pancreas	5%
Non-Hodgkin's Lymphoma	4%
Leukemia	4%
Esophagus	4%
Liver	3%
Urinary Bladder	3%
Kidney	3%
All Other Sites	22%



Lung and Bronchus	25%
Breast	15%
Colon and Rectum	11%
Pancreas	6%
Ovary	5%
Non-Hodgkin's Lymphoma	4%
Leukemia	4%
Uterine Corpus	3%
Brain	2%
Multiple Myeloma	2%
All Other Sites	23%



Epidemiology

Standardized mortality rates
(number per 100.000 population)

Type of cancer	male	female
lungs	79,6	27
stomach	12,9	5,4
colon and rectum	32,3	16,2
prostate	18,4	/
cervix	/	9,1
breasts	/	29,4



** Data for 2016, taken from the Government Program on improving cancer control in the Republic of Serbia for the period 2020-2022.

Stage of malignant disease

Staging means determining the relative size of the tumor and extension of the malignant disease

- T (0-4)– the size and extension of the primary tumor
- N (0-3)– number and localization of affected regional lymph nodes
- M (0/1) – presence or absence of distant metastases
- Clinical stage– cTNM/TNM
- Pathological stage – pTNM
- Stage after therapy – rTNM (r-re-treatment)
- Stage at autopsy - aTNM



The role of oncological surgery

- Prevention of malignant tumors
- Diagnosis of malignant tumors
- Treatment of malignant tumors





Cancer prevention

Cancer prevention

- Some pathological conditions
- Congenital or genetics characteristics



- High incidence of cancer



Familial adenomatous polyposis (FAP)



- 50% of patients develop colon cancer by the age of 40
- By the age of 70 , all patients develop colon cancer
- Prophylactic proctocolectomy before age 20 to prevent colorectal cancer is suggested to all carrier of APC gene mutation



Ulcerative colitis (UC)

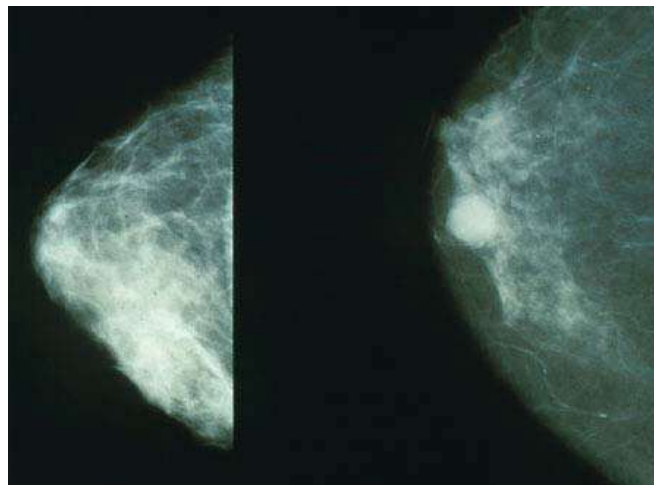


- 40% of people with UC (pancolitis) die as a result of colon cancer
- 3% of children with UC develop colon cancer by the age of 19, and 20% develop cancer during each further decade
- Colectomy is indicated for chronic active form of UC



Breast cancer

- The risk of breast cancer development is higher with a certain group of women
- Genetic analysis of BRCA1 and BRCA2 gene mutation
- Prophylactic mastectomy





Surgery as prevention

- 
- Prophylactic resection to prevent further development of cancer

Pathological condition	Marker	Cure
FAP	APC	Colecetomy
MEN 2	RET	Thyroidectomy
Hereditary breast cancer	BRCA 1,2	Mastectomy
Hereditary ovarian cancer	?	Ovariectomy

Criteria suggestive of hereditary cancer

- Tumor arising earlier than usual
- The presence of bilateral tumor
- The presence of multiple primary tumors
- The presence of a tumor in a gender where it is less common
- Grouping of the same type tumors in several relatives
- Tumors associated with other conditions such as mental retardation or skin changes



Cancer screening

Cancer Site	Population	Test or Procedure	Frequency
Breast	Women, age 20+	Breast self-examination	Monthly, starting at age 20
		Clinical breast examination	Every 3 years, ages 20–39 Annual, starting at age 40
		Mammography	Annual, starting at age 40
Colorectal	Men and women, age 50+	Fecal occult blood test (FOBT)	Annual, starting at age 20
		Flexible sigmoidoscopy	Every 5 years, starting at age 50
		Fecal occult blood test and flexible sigmoidoscopy	Annual FOBT and flexible sigmoidoscopy every 5, years, starting at age 50
		Double-contrast barium enema (DCBE)	DCBE every 5 years, starting at age 50
		Colonoscopy	Colonoscopy every 10 years, starting at age 50
Prostate	Men, age 50+	Digital rectal examination (DRE) and prostate-specific antigen test (PSA)	Offer PSA and DRE annually, starting at age 50, for men who have life expectancy of at least 10 years



Tumor markers

Marker	Cancer	Sensitivity	Specificity
PSA (4 g/L)	Prostate	57–93%	55–68%
CEA	Colorectal	40–47%	90%
	Breast	45%	81%
	Recurrent disease	84%	100%
AFP	Hepatocellular	98%	65%
CA 19-9	Pancreatic	78–90%	95%
CA 27-29	Breast	62%	83%
CA 15-3	Breast	57%	87%



The principles of surgical oncology



The principles of surgical oncology

- For most solid tumors, surgery is the definitive treatment.
- Diagnostic and staging surgery
 - Laparoscopic exploration and biopsy
 - Lymph node *Sampling*
- Primary disease surgery
 - removal of the primary tumor and lymph nodes
- Metastasis surgery
 - Removal of liver, lung, and brain metastases, etc
- Palliative surgery
 - *By – pass* Procedure of the digestive tract
- Surgery of urgent oncological conditions



Cancer diagnosis

Types of oncological surgical procedures

1. Biopsy



- Tissue sampling for accurate pathohistological diagnosis

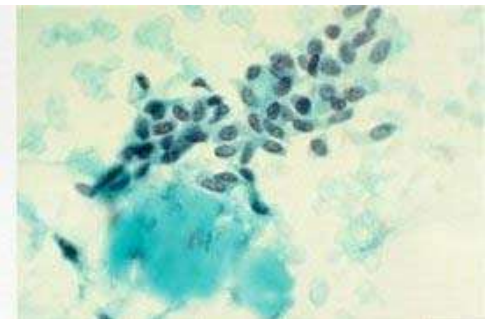
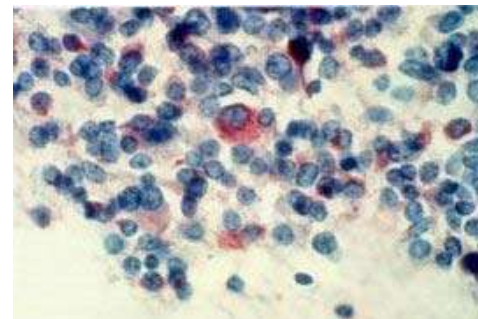


Biopsy

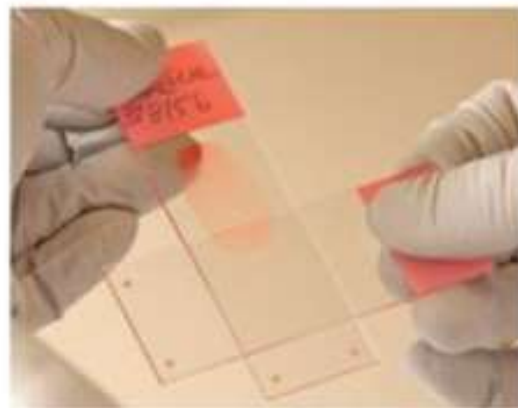
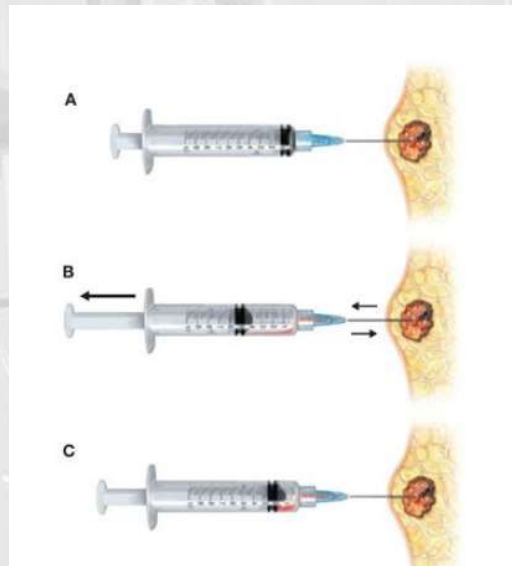
- Aspiration biopsy
- Needle biopsy
- Incisional biopsy
- Excisional biopsy



ASPIRATION BIOPSY



FNA (engl. *Fine Needle Aspiration*, FNA)



Needle (*core*) biopsy



- Core biopsy- a tissue sample that is obtained with the specially designed needle
- Obtaining a tissue sample is sufficient to diagnose most types of tumors
- Sarcomas of soft tissues and bones - difficult to differentiate between benign reparative lesions of malignancy
- Question about tumor spreading along the needle track ???

Guided biopsies

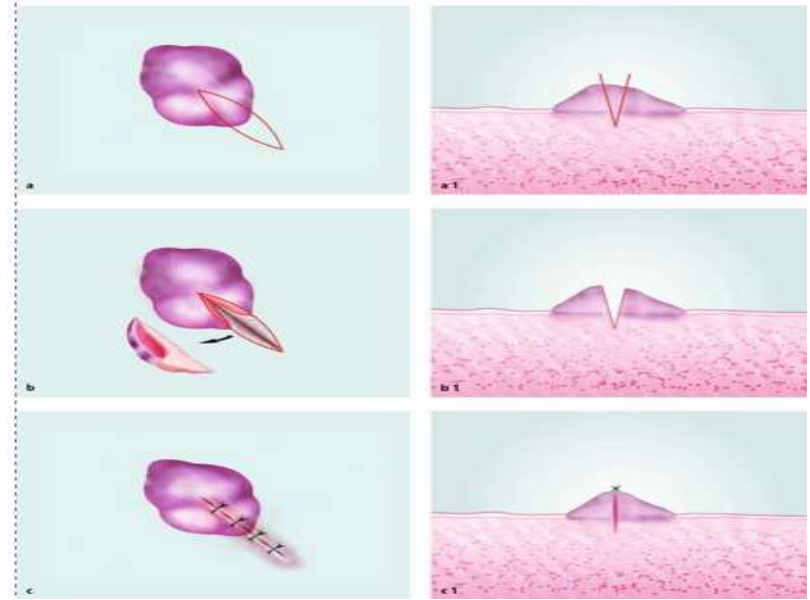


US guided



CT guided

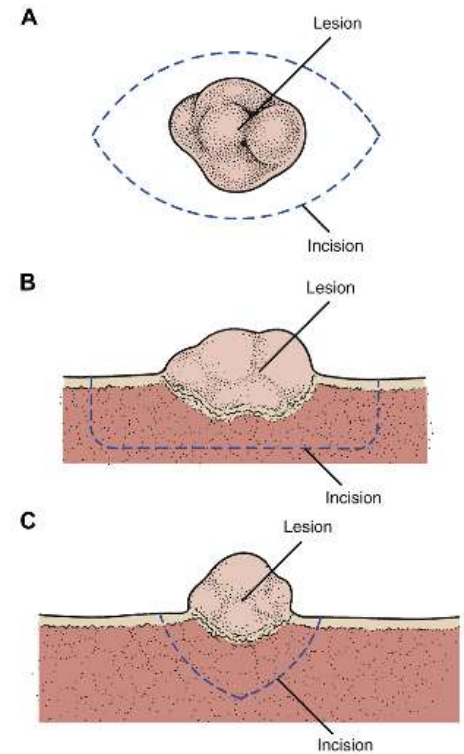
Incisional biopsy



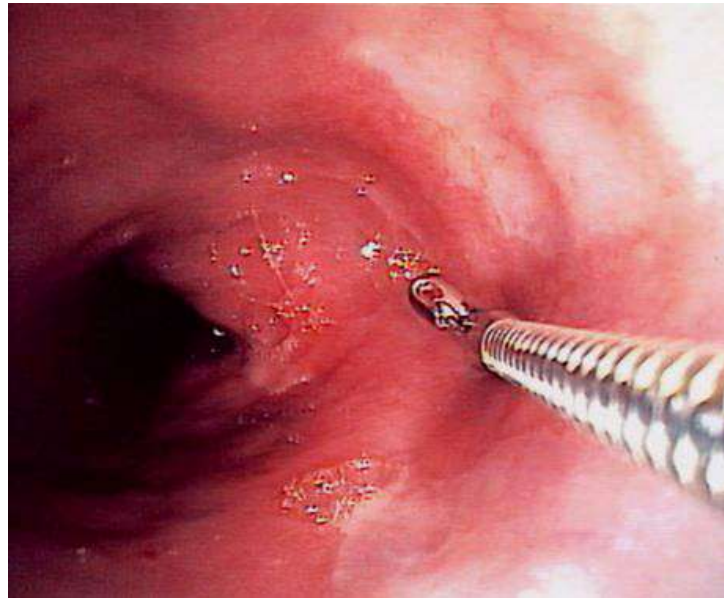
- Removal of a smaller sample of tissue from the edges of larger tumor mass
- Diagnosis of larger tumor masses whose removal indicates complicated surgical procedures than simple excision of indicated tumor
- The best way to diagnose sarcomas of soft tissues and bones

Excisional biopsy

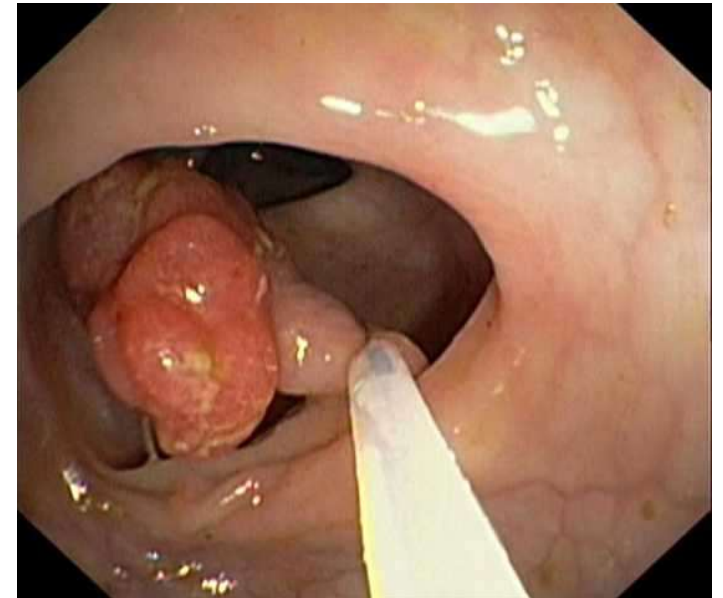
- Excision of the whole suspicious tumor tissue
- The procedure of choice for most tumors if it does not interfere with the plan of the final surgical procedures
- For example: Lymph node biopsy



Endoscopic biopsy



Incisional



Excisional




Principles of surgical biopsy

- Scars- can be removed permanently using surgical procedure
- Avoid tissue contamination during the procedure
- Take multiple samples simultaneously
- Sufficient tissue
- Mark parts of the tumor for easier orientation of the pathologist
- Tumor labeling for neoadjuvant radiation



Cancer treatment

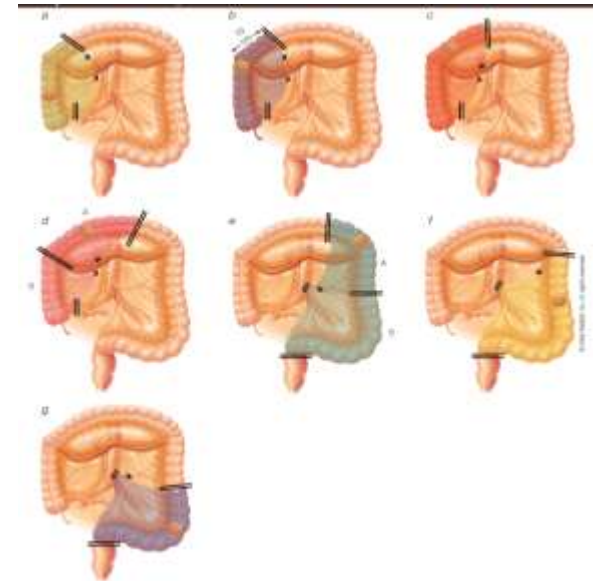


Types of oncological surgical procedures

- The principles of resection of malignant disease are based on
 - the surgical goal
 - the functional importance of the affected organ
 - the ability to reconstruct the affected and surrounding organs
- Removal of local structures where the tumor invasion is present
- Preoperative non-adjuvant therapy
- R2, R1 and R0 resection
- R1 resection is connected to a bad treatment outcome and a higher rate of local recurrence (30%)

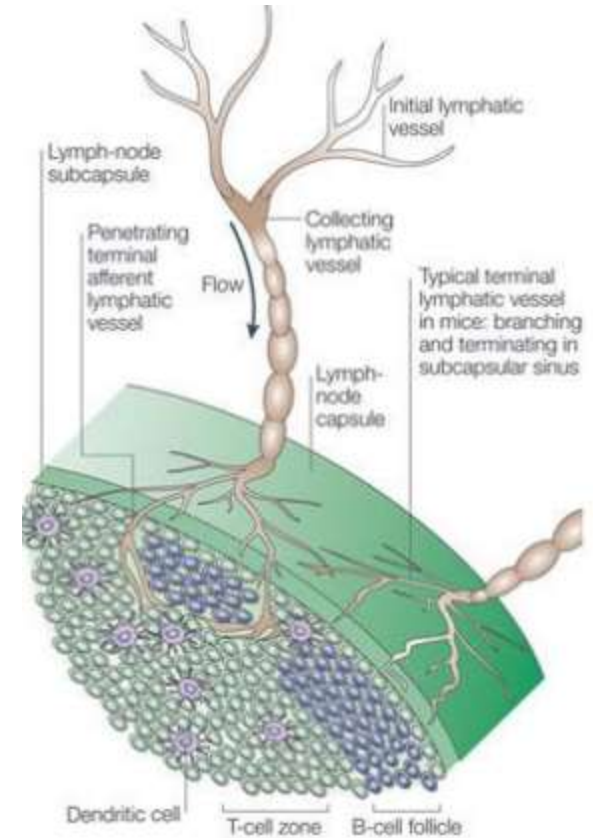
Resection margins

- Tumor biology
- Location
- In general 1cm of margin is the minimum
- The goal is to reduce the possibility of local recurrence

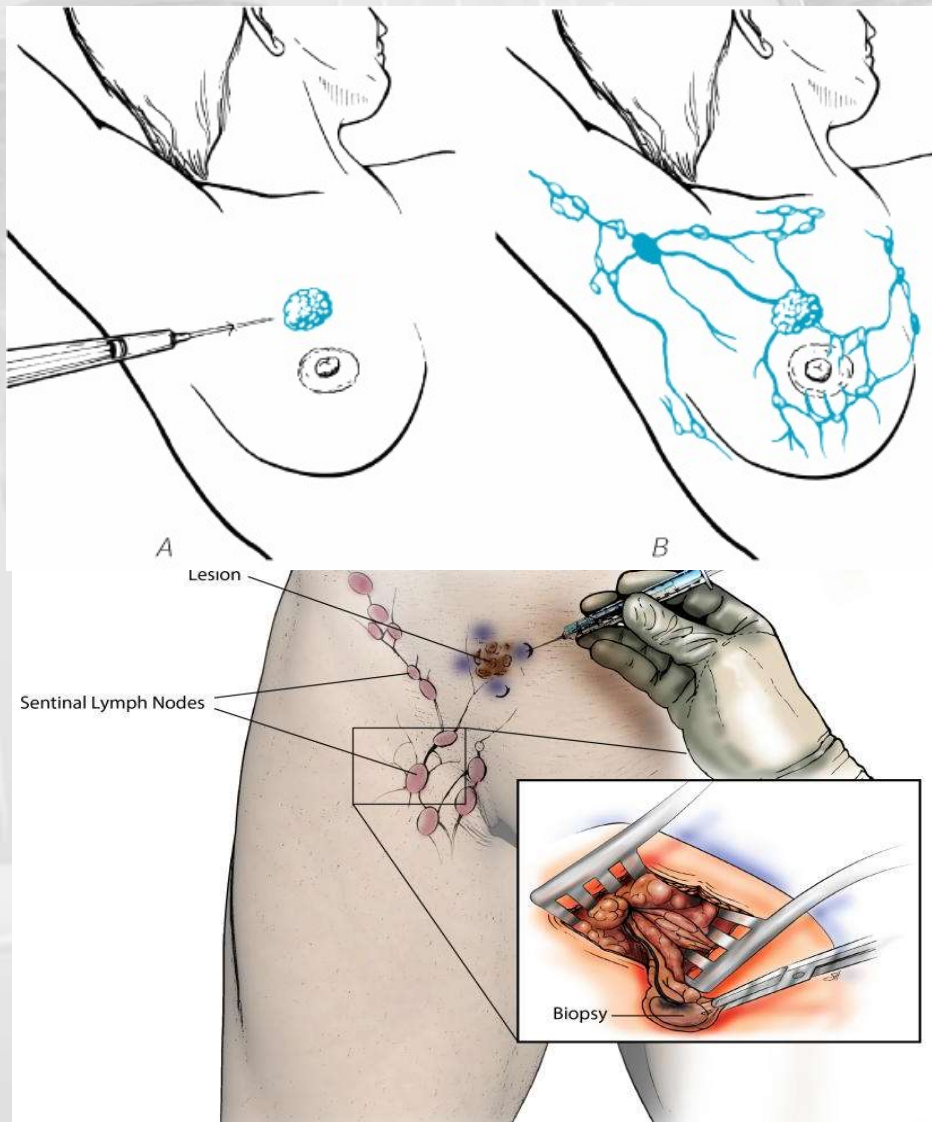


Lymphadenectomy

- Roles of the lymph node:
 - Antigen recognition
 - Not filters
 - Most tumor cells pass through the lymph node
 - Rare tumor cells give regional metastases in the lymph nodes
 - Indicators of survival



- Lymph node mapping and *sentinel* lymph node biopsy





The “*no touch*” principle

- This principle is based on the concept of direct contact and manipulation of tumor during resection that can lead to the increase of local implantation and embolization of tumor cells
- Theoretically, metastatic potential of the primary lesion would be enhanced by the mechanical extrusion of tumor cells into the local lymphatic and vascular space
- This theory may be valid for tumors that are directly spread into the venous system (e.g. renal cell tumors with extension to the vena cava) or those that extensively involve local venous drainage (e.g. large hepatocellular carcinoma)



The “*no touch*” principle

- It has been proven that extensive palpation and manipulation of a colorectal tumor leads to a direct spillage of tumor cells into the lumen of the colon
- One of the ways to reduce this risk was ligation of the proximal and distal lumen of the colon segment with the tumor
- These areas are then included in the resection limiting the contract of the tumor cells with the planned anastomoses

Types of cancer and localization



Selection of the adequate local therapy of cancer



Melanoma

- Definite surgery with adequate margins width is the appropriate modality of local therapy:
 - 1 cm margin for $<1\text{mm}$ lesion depth
 - 2 cm margin for $>1\text{mm}$ lesion depth
 - SLN biopsy for $>1\text{mm}$ primary lesion depth
 - Metastases in SLN – Radical dissection of lymph nodes



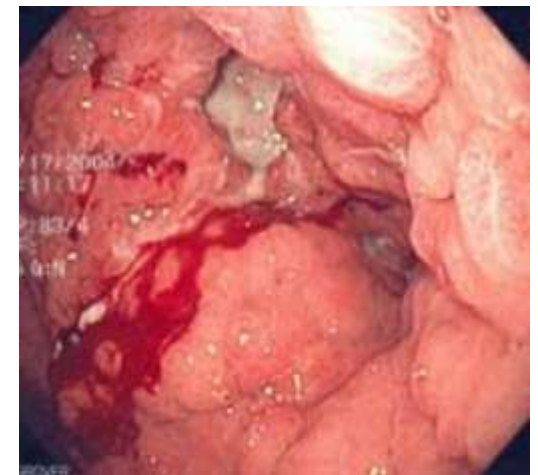
Colorectal cancer

- 5 cm margins
- 1 cm for low rectal cancer after chemo-radiation
- Remove the main vascular pedicle with lymph nodes
- Similar survival laparoscopy vs open surgery

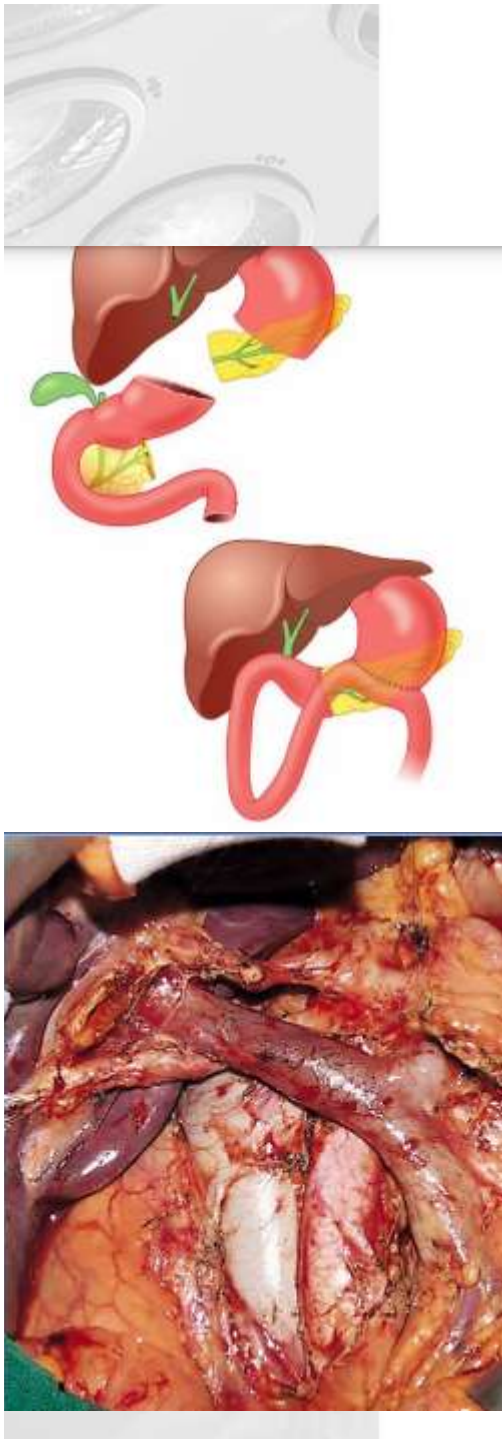


Stomach cancer

- 5 cm margins
- Remove the main of vascular pedicle with lymph nodes
- Splenectomy is not indicated
- D2 dissections - no benefit in survival



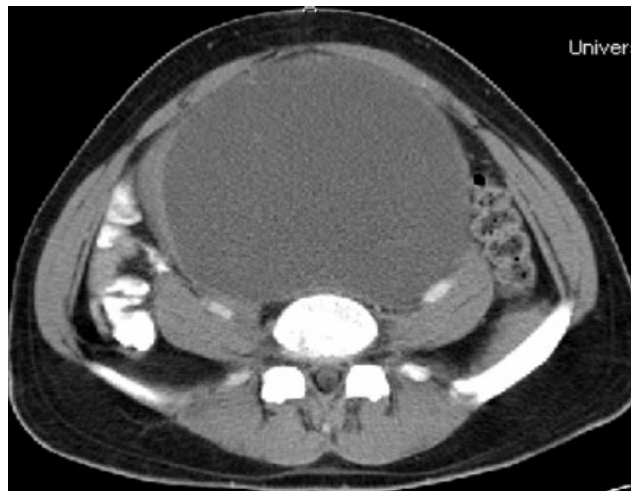
Pancreatic cancer



- Resectability- as assessed by the surgeon
- Contraindications include infiltration of the celiac trunk, superior mesenteric and hepatic arteries
- Relative contraindications include infiltration of portal veins or positive lymph nodes

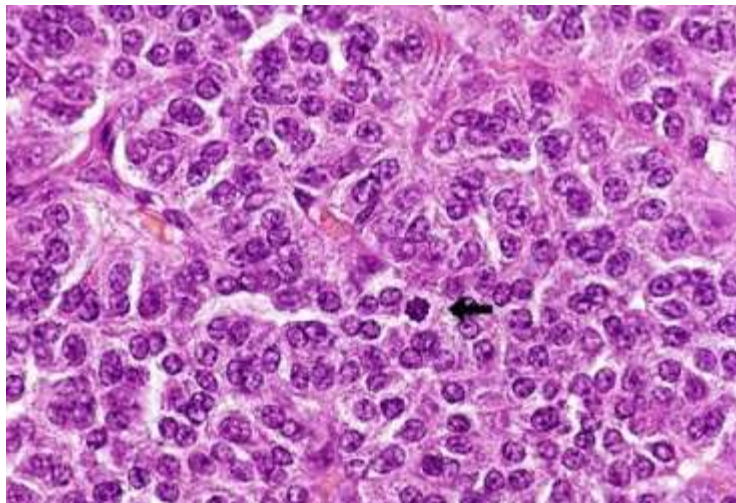
Sarcomas

- Margins 1-2cm
- Preservation of neurovascular structure
- No need for lymphadenectomy
- Radiation reduces local recurrence
- Chemotherapy- limited effect

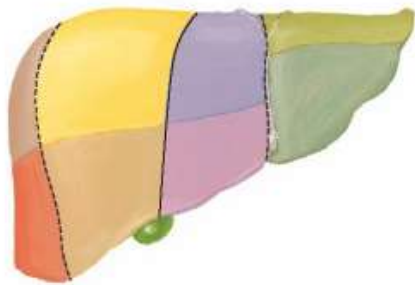


Carcinoids

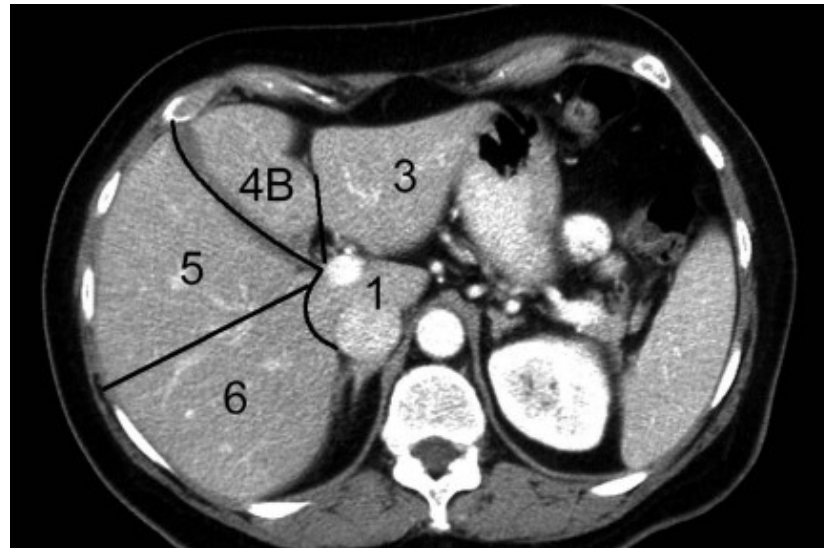
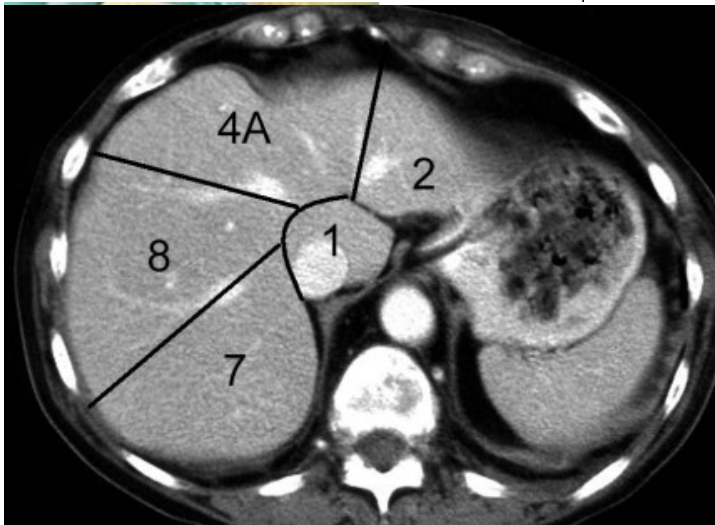
- Slow- growing lesions
- Surgery for symptoms of obstruction , hormonal stimulation
- Cytoreductive surgery
- <1 cm- remove only the tumor
- >2 cm – remove both tumor and lymph nodes



Liver tumors



- Primary vs metastatic
- Resectability:
 - Surgeon's assessment
 - Defined by what remains (not by what can be removed)



Rhabdomyosarcoma

- Use of neo-adjuvant therapy
 - Only surgery followed by 5-year survival
10-20%
 - Neo-adjuvant chemoradiation, 5-year survival
80%



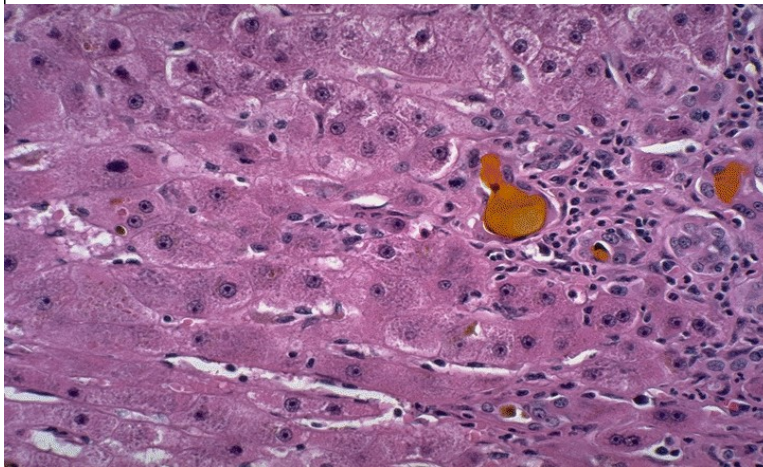
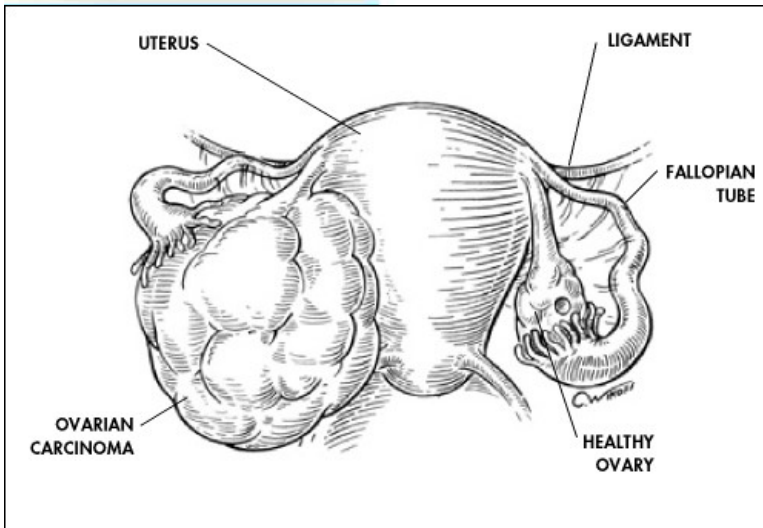


Cancer surgery and resectability

- Assessment of resectability based on:
 - evaluation of tumor characteristics with the help of diagnostic tests
 - existence of local and/or distant disease
 - age
 - comorbidity
 - functional status and laboratory findings
 - risk-benefit of surgery



Ovarian cancer

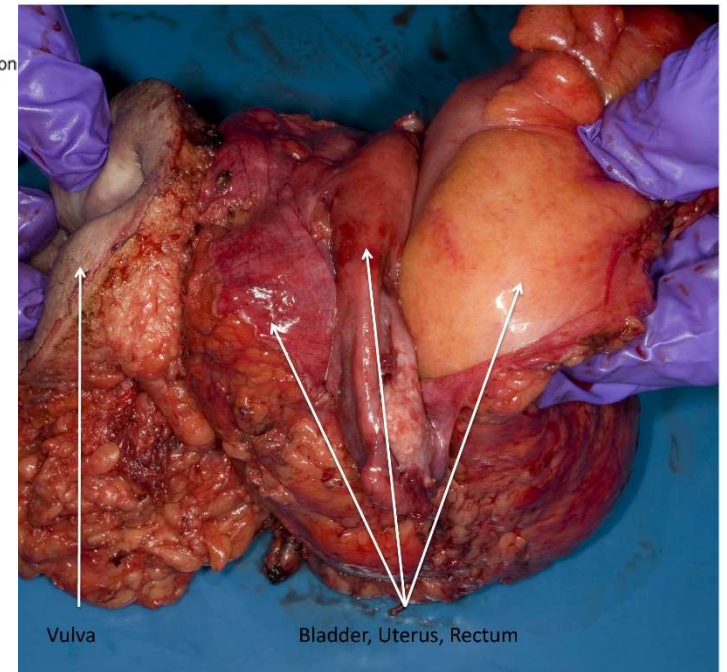
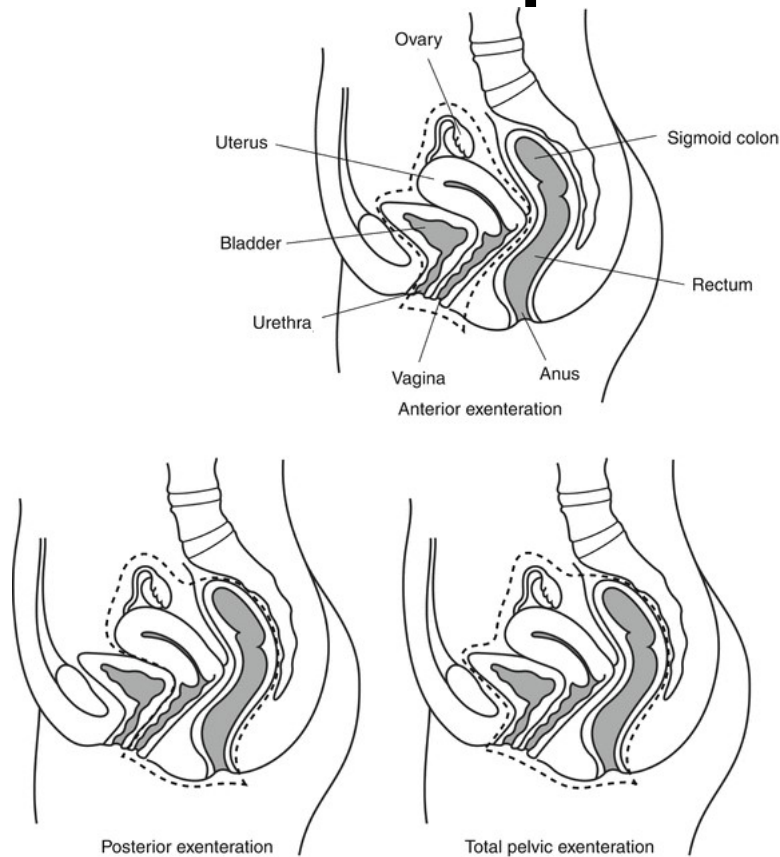


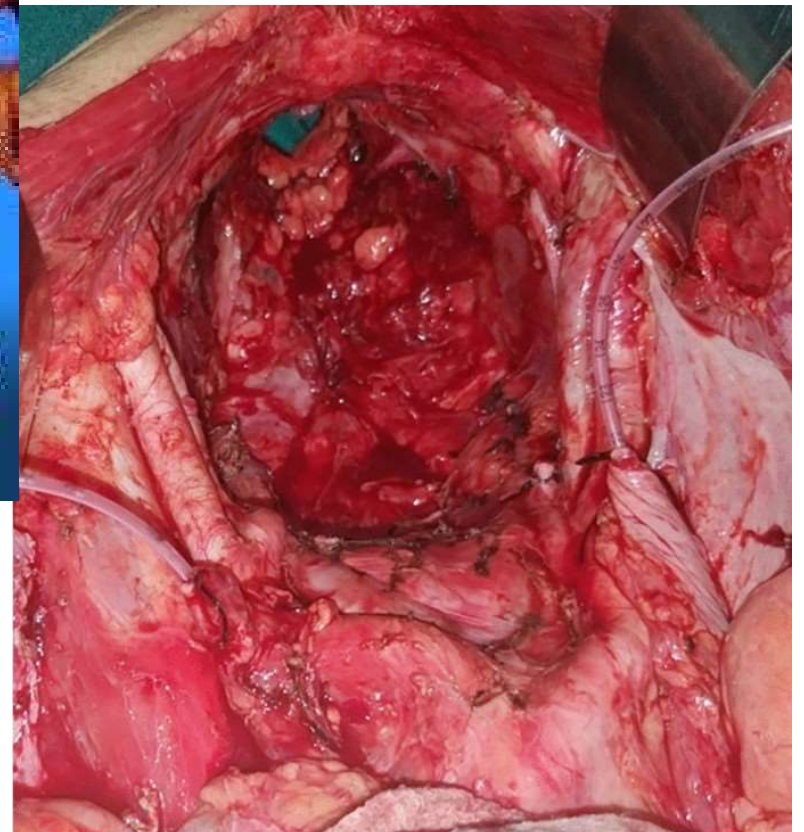
Burkitt lymph

Cytoreductive surgery

- Extensive local spread of cancer is contraindication for radical intervention
- Partial surgical resection of a tumor mass in certain types of cancer improves the effectiveness of other treatment modalities in the control of residual unresectable tumor
- It is considered that intraperitoneal chemotherapy is not effective in eradication of lesions larger than 2.5cm
- It is achieved by a process peritonectomies and en-block resection of visceral organs, where it is necessary
- It is combined with HIPEC - *Hyperthermic Intraperitoneal Chemotherapy*

Exeresis of small pelvis








Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

- Isolated peritoneal metastases in advanced colorectal cancer
- Patient selections:
 - Good general health condition
 - Limited intraperitoneal dissemination (*peritoneal cancer index*, $PCI < 20$)
 - Limited small bowel involvement
 - No extra- abdominal metastases



Types of surgicaloncological procedures

Metastases extirpation surgery

- Previously metastatic disease-contraindication for surgery
- Metastases- systemic disease
- “*seed and soil*” hypothesis: prediction of metastases and limited number of metastases - complete surgical extirpation can cure certain patients
- The combination of metastasectomy and effective chemotherapeutics significantly prolongs survival



Metastases surgery

- Selection of patients for metastasectomy:
 - The primary tumor must be controlled
 - Metastases are limited to one organ
 - Limited number of metastases
 - There is no better therapeutic option like effective chemotherapy for certain number of tumor:
 - Resection of local recurrence and cytoreductive surgery with intraperitoneal chemotherapy- for peritoneal metastases of ovarian or appendix cancer



Palliative surgery

Palliative surgery - intervention to reduce disease symptoms and improve life quality

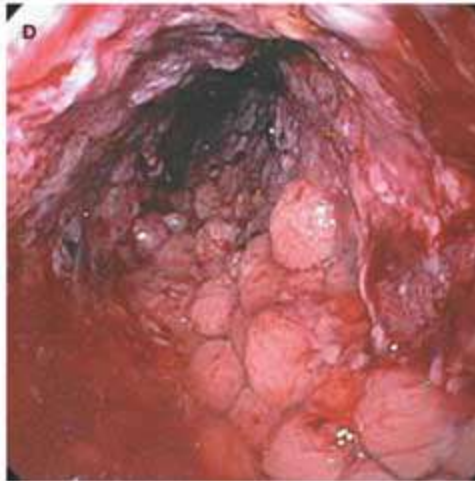
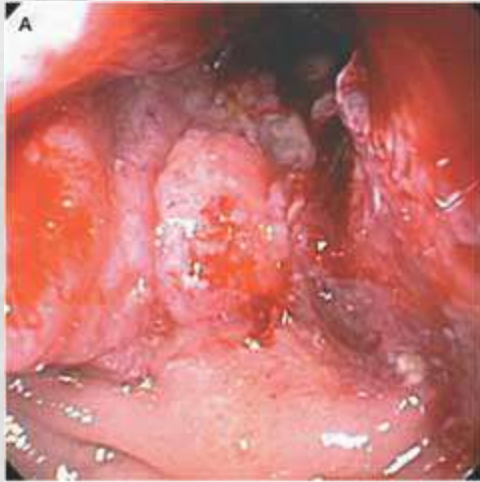
- To lessen the pain
- To remove the obstruction (bowel, ureter, bile ducts,...)
- To control bleeding
- To solve perforation, fistula
- These procedures are performed to relieve symptoms , but not to cure patients
- To improve the quality of life
- Prophylactic palliation prevention of occurrence symptoms that cannot be controlled later
- Minimal invasive procedures

Paliation: Pain

- Analgetics
- Nerve block
- Epidural block
- Celiac ganglion block (lead by ultrasound)



Palliation: Obstruction- Stent



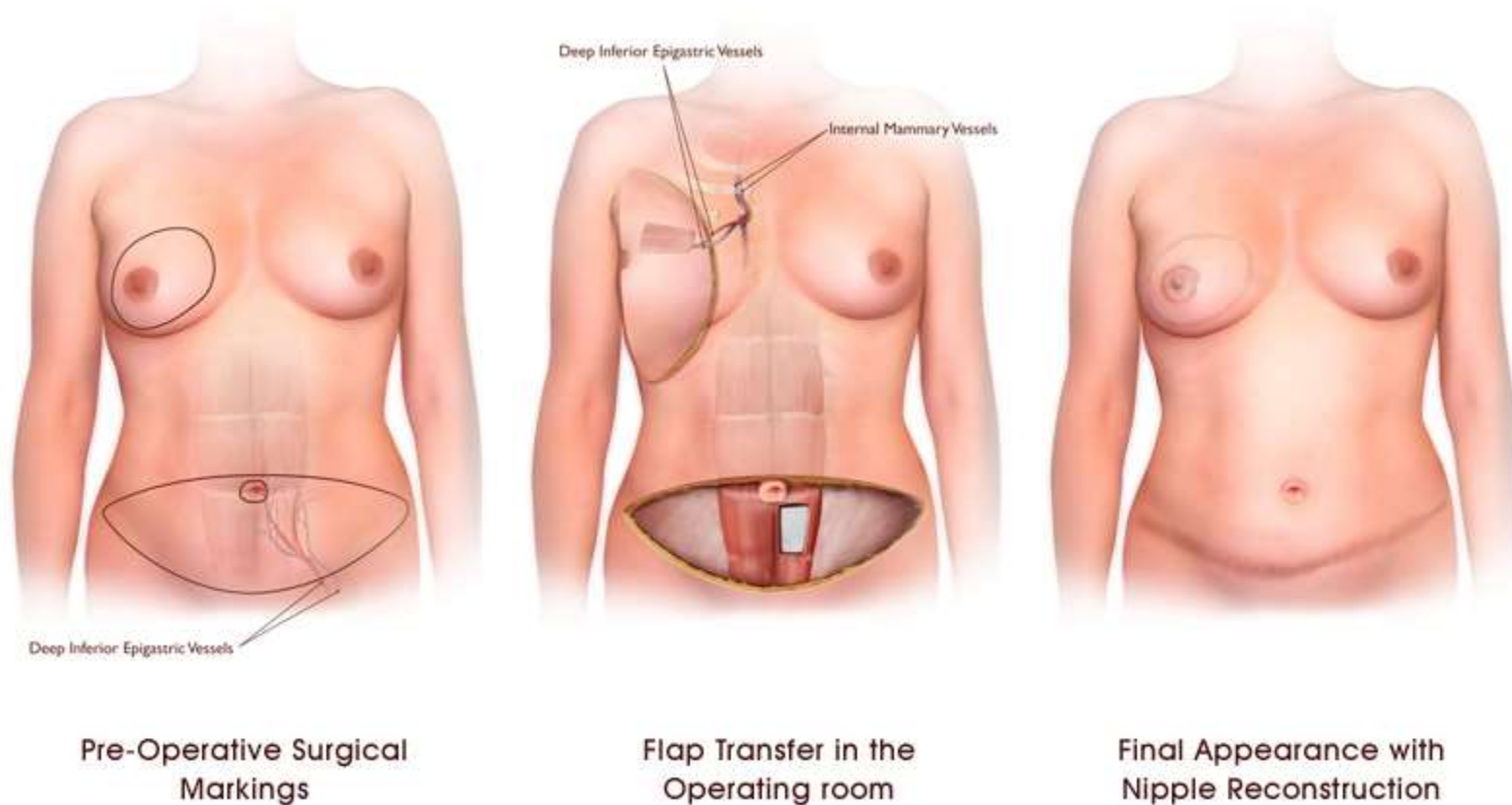


Reconstructive surgery

- All tumor surgery are followed by some degree of reconstruction
 - By surgical oncologist (anastomosis)
 - Complex reconstructions (vascular surgeon, plastic surgeon)
- Improves function and cosmetic reasons
- Free flaps and microvascular surgery of resected and irradiated tissue

Reconstruction and rehabilitation

TRAM Free Flap Reconstruction



Emergency surgical oncology conditions

- Massive bleeding
- Abscesses
- Perforations of hollow organs
- Threatening destruction of vital organs



The future of oncological surgery

"Targeted therapy"

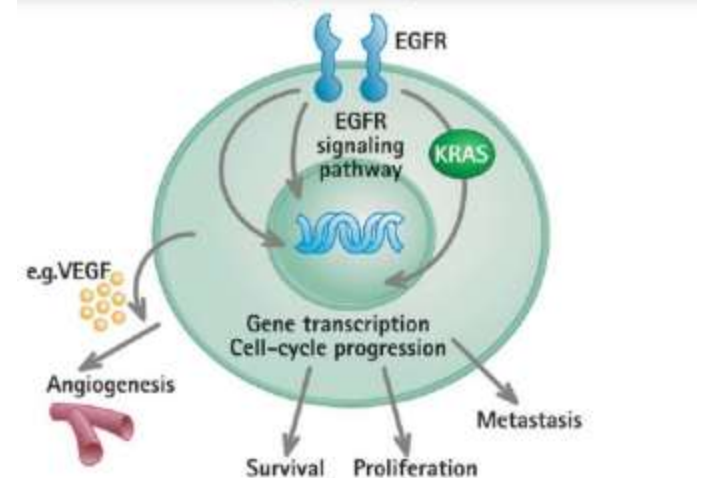
- Paradigm of gastrointestinal stromal tumors (GISTs)
 - Mutations of sTK (tyrosine kinase) is a growth signal
 - Imatinib (*Gleevec*®) is a drug that blocks the mentioned signaling pathway
 - It is indicated for metastatic disease and high risk of resectio
 - It changed the natural course of this disease



Future of oncological surgery

“Personalized therapy”

- The example of status KRAS in colorectal cancer
- *Cetuximab* (Erbix) and *panitumumab* (Vectibix) are monoclonal antibodies that block epidermal growth factor
- in metastatic disease
- Mutations in the KRAS gene without the effects of the mentioned biological therapy
- Status of the KRAS gene in patients with liver metastasis



The future of oncological surgery

- Past

Radical resections

- Present

Conservative resections

- Future

?



History of Surgical Oncology

Radical Surgery



Time

Watch & Wait



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‡*



ARTICLE

Long-term Outcome of an Organ Preservation Program After Neoadjuvant Treatment for Rectal Cancer

Milou H. Martens, Monique Maas, Luc A. Heijnen, Doenja M. J. Lambregts, Jeroen W. A. Leijtens, Laurents P. S. Stassen, Stephanie O. Breukink, Christiaan Hoff, Eric J. Belgers, Jarmo Melenhorst, Rob Jansen, Jeroen Buijsen, Ton G. M. Hoofwijk, Regina G. H. Beets-Tan, Geerard L. Beets



Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study

*Maxime J M van der Valk, Denise E Hilling, Esther Bastiaannet, Elma Meershoek-Klein Kranenbarg, Geerard L Beets, Nuno L Figueiredo, Angelita Habr-Gama, Rodrigo O Perez, Andrew G Renehan, Cornelis J H van de Velde, and the IWWD Consortium**



Thank you for your attention!



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