Underestimated importance of intraluminal brachytherapy:
bronchus, oesophageal, anorectal and hepatobiliary duct cancer

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Lung cancer
Evolution in brachytherapy...


Ra Cs / Co Ir

? Homeopathy...
1. **Curative intent as a „boost” to EBRT – T1-2 N0-1 M0**
   - LC
   - before EBRT- remission of atelectasis, reclassification.

2. **Alone - definitive brachytherapy for small tumors - T1-2 N0 M0**
   - in patients with occult carcinoma or tumors potentially resectable, with diameter < 2 cm, disqualified for surgery or EBRT (*Japan, USA*).

3. **Postoperative brachytherapy of the bronchial stump after resection with positive resection margins (R2).**

4. **As a boost for minor residual disease within a combined non-surgical radical approach.**

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1. The main indication is treatment of life-threatening complications such as dyspnea, obstructive pneumonia or atelectasis, cough or haemoptysis resulting from endobronchial or endotracheal tumour growth.

2. Treatment of endobronchial or endotracheal recurrent tumour growth in previously irradiated areas or in combination with EBRT for metastatic lung cancers.
1. peripheral location of the tumor,

2. Pancoast tumor (?),

3. location outside of bronchii,

4. contraindication to bronchoscopy (relative).
Reirradiation

1. The aim is to **relieve distress from symptoms** caused by endobronchial recurrences and the restoration of patency of the airway.

2. In order improve the **QoL** it is preferable to use a method that is relatively **easy to perform** and has **minimal complications**.

3. *Removal of the tumour recurrence mass by endoscopic biopsy forceps combined with cryosurgery, electrocautery, or laser ablation can achieve only limited clearance and short – term palliation, because the tumour kinetic is not altered.*

4. Therefore, HDR-BT is the option of treatment endobronchial recurrences tumours which can increase the efficiency of the control of malignant airway obstruction and the duration of palliation.
5. From regard on location of the lesion in some cases brachytherapy is a treatment of choice.

6. In some cases we can repeat this treatment when dyspnea returns. It arises from the fact, that local irradiation is connected with relative good adjacent health tissue sparing.

7. We haven’t often other treatment possibilities, too.
Cross-section CT with izodoses. Two different locations of endobronchial catheter.

High dose in the wall
Isodoses placed on schematically situated right main bronchus and pulmonary artery. Catheter with inserted isotope Ir-192 is located nearby artery wall. In this case irradiation dose, growing constantly with shortening of distance to source, is very high and greater in artery wall than in tumor.

The risk of bronchus and artery wall damage and haemorrhage is high.
Pulmonary arteries and bronchii overlapping each other. The risk of radiation overdose in arteries wall in case of applicator setting nearby artery is great. RPA – right pulmonary artery, LPA – left pulmonary artery, RUL – right upper lobe, RLL – right lower lobe, LLL – left lower lobe, LUL – left upper lobe
CT simulation is recommended for endobronchial BT.

CT planning with 3D target definition is recommended over point prescription for endobronchial BT.

HDR or PDR BT with the ability to optimize dose are recommended over low dose rate BT for endobronchial treatment.

Radical endobronchial BT (alone or as a boost) is recommended generally within confines of clinical trials.

Interstitial seed treatment after sublobar lung resection is recommended generally within the confines of clinical trials.

Postoperative CT planning should be performed for interstitial implants with reporting of dose to organs at risk.
## Summary of updated recommendations

American Brachytherapy Society consensus guidelines for thoracic brachytherapy for lung cancer


### Table 2
The ABS dose recommendations for endobronchial brachytherapy

<table>
<thead>
<tr>
<th>Brachytherapy alone</th>
<th>PDR</th>
<th>30 Gy in one insertion (using pulses that offer biological equivalence to LDR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDR</td>
<td>10 Gy in one fraction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15 Gy in one fraction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>14.2–20 Gy in two fractions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>22.5 Gy in three fractions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 Gy in four fractions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>30 Gy in six fractions (high dose palliation)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Brachytherapy as a boost following EBRT</th>
<th>PDR</th>
<th>15–20 Gy in one insertion (using pulses that offer biologic equivalence to LDR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDR</td>
<td>10-15 Gy in two to three fractions (following up to 60 Gy in 30 fractions)</td>
<td></td>
</tr>
</tbody>
</table>
# Brachytherapy treatment schemas - indications, doses

<table>
<thead>
<tr>
<th>Indications for brachytherapy</th>
<th>I phase</th>
<th>II phase</th>
<th>III phase</th>
<th>IV phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radical combined treatment:</strong> schema I; clinical stage T1-3 N1-3 M0</td>
<td>Total dose 44 Gy in 22 fr. aa 2 Gy (2 a-p fields)</td>
<td>1 fr. x 6 Gy, ref. point 0.5 - 1 cm</td>
<td>EBRT 16 Gy in 8 fr. (changed fields)</td>
<td>1 fr. x 6 Gy, ref. point 0.5 - 1 cm</td>
</tr>
<tr>
<td><strong>Radical combined treatment:</strong> schema II; clinical stage T1-3 N1-3 M0</td>
<td>EBRT: total dose 44 Gy in 22 fr. aa 2 Gy (2 a-p fields)</td>
<td>EBRT 16 Gy in 8 fr. (changed fields)</td>
<td>HDR-BT - in 1, 3 and 5 weeks of EBRT – 3 x 10 Gy.</td>
<td></td>
</tr>
<tr>
<td><strong>Radical sole treatment,</strong> radiologically occult cancer T1-2N0</td>
<td>Total dose 36 - 42 Gy in 6 - 7 fr. with interval of 4 - 7 days between fractions</td>
<td>To consider increasing the total use using HDR-BT HDR. Fr. dose from 1 x 6 Gy till 3 fr. x 6 Gy (18 Gy), depending on EBRT dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Radical treatment after surgery, R2</strong></td>
<td>After EBRT with total dose of 50 - 60 Gy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Radical treatment:</strong> stump infiltration</td>
<td>Sole brachytherapy: 4 fr. of 7.5 – 10 Gy with interval of 4 - 7 days between fractions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Palliative treatment</strong></td>
<td>18 Gy in 3 fr. of 6 Gy with interval of 4 -7 days – in patients treated earlier with EBRT – dose &gt; 50 Gy</td>
<td>22,5 Gy in 3 fr. of 7.5 Gy Gy with interval of 4 -7 days – in patients not irradiated or treated earlier with EBRT – dose &lt; 50 Gy</td>
<td>1 x 10 Gy in case of WHO scale &gt; 2</td>
<td>Sometimes dose can be repeated after few weeks, in cases with clinical remission or visible during bronchoscopy</td>
</tr>
</tbody>
</table>
Material – Greater Poland Cancer Centre
Tumor infiltrating carina and both main bronchi before application and after application of two brachytherapy catheters. In this cases irradiated area includes carina and both main bronchi.
Examples of brachytherapy – tumor localized in main bronchus, French 6 (5) catheter placed in bronchus close by, scale on catheter (n cm) useful for treatment planning visible.
Tumor infiltrating carina and both main bronchi before application and after application of two brachytherapy catheters. In this cases irradiated area includes carina and both main bronchi.
Late radiation injury
Late radiation injury
Late radiation injury
Late radiation injury
Treatment planning - X-ray, catheter with marker inside
Rak płuc
– cewnik z markerem, oskrzele główne i górnopłatowe prawe, zdjęcie a

[Image: X-ray of the chest with a marker and a catheter]
Treatment planning - X-ray, catheter with marker inside
Obustronny rak płuca – 2 cewniki z markerami, oskrzele główne prawe i lewe, zdjęcie a
Esophageal cancer
>60% patients with esophageal cancer

palliative treatment

• clinical stage - locally advanced or metastatic disease,
• other diseases,
• cachexia.
Esophageal cancer

Aim of brachytherapy:

• Restoration of patency of the esophagus.

• Relief of dysphagia - a fast, reliable and durable, represents the main need of oesophageal cancer patients.
Treatment approaches providing adequate and rapid palliation of symptomatic disease presentation (‘passage and pain’):

- self-expanding stents,
- broadening — dilatators, balloons,
- radiotherapy (external beam, EBRT),
- brachytherapy,
- chemotherapy,
- laser therapy (Nd:YAG),
- elektrocaugulation — argon,
- photodynamic therapy.
Polish Oncology Union - recommendations

Clinical stage III (T4), IV

Restoration of patency:
1. broadening with dilatators,
2. broadening with balloons,
3. laser thermal ablative therapy,
4. photodynamic therapy.

1. self-expanding stents,
2. anastomosis, gastrostomy

1. Radiotherapy (EBRT),
2. brachytherapy
All attempts improving crude survival time have to be cautiously balanced against the need for local control and maintenance of adequate Quality of Life.
• may provide the most immediate and stable symptomatic alleviation, but is associated with substantial procedural risks,

• less invasive approaches such as balloon dilation, stenting and laser thermal ablative therapy are alternative well-established methods.

In parallel to these local endoscopic approaches, radiotherapy has a clearly proven value.

Its specific advantages comprise:

• the shortness of treatment time,
• a low treatment-related morbidity,
• causal effectiveness.

Among patients for whom definitive treatment with curative intent is not possible, palliation can be achieved with radiation therapy in approximately 75%.

It is better to pursue immediate irradiation for palliation than to await the development of more severe symptoms, because immediate irradiation produces a greater and more lasting palliation than the alternatives.

[Radiation Oncology, 9th Edition - Rationale, Technique, Results By James D. Cox, MD, FACR and Kie Kian Ang, MD, PhD, 2009]
The **efficacy of radiotherapy** is underlined by results from several prospective – and even randomized – **trials**. **Stenting vs local radiotherapy**

Two randomized studies:

- The larger trial, a Dutch multicentre study commenced in 1999, randomized 209 patients to either **stent placement vs single-dose HDR brachytherapy (12 Gy)**.
- There was no difference in terms of **median survival** ($p = 0.23$).
- Although stenting provided the most rapid relief from dysphagia, no significant difference in terms of **persistent or recurrent dysphagia** was seen after 6 months ($p = 0.81$).
- At that time, a **quality of life assessment** clearly favoured **brachytherapy** which was also associated with fewer treatment-related complications.
- **Thus, the authors recommended brachytherapy as primary palliative measure.**

EBRT vs brachytherapy

• no randomized trial is available directly comparing brachytherapy and EBRT
  
  both approaches may be used to treat somewhat distinct patterns of disease.
  
• bulky disease with lymph node masses will be preferably palliated by EBRT,

• whereas plane circumferentially growing tumours are ideal for an BT.
The addition of EBRT (30 Gy in 10 fractions) to HDR (16 Gy in 2 fractions) showed no further advantage in terms of symptom-free and overall survival. Thus, in case of tumours suitable for an endoluminal approach, HDR brachytherapy alone may offer sustained symptomatic relief with a minimum of expense and inconvenience.

With respect to brachytherapy, a South African trial compared **two different fractionation** concepts of HDR intraluminal brachytherapy

- 232 patients,
- unresectable oesophageal cancer, were randomized to:
  1. 18 Gy in 3 fractions
  2. 16 Gy in 2 fractions.
- **No significant difference** in efficacy was found between both groups (p < 0.05).
- **Overall dysphagia-free survival was 7.9 months** with satisfying treatment acceptance and tolerance.

Brachytherapy

- High concentrated dose in tumor,
- Sparing of surrounded health tissues (Organs at Risk),
  - Short treatment time,
  - Outpatient treatment.
Clinical Investigation

AMERICAN BRACHYTHERAPY SOCIETY (ABS) CONSENSUS GUIDELINES FOR BRACHYTHERAPY OF ESOPHAGEAL CANCER

Laurie E. Gaspar, M.D.,* Subir Nag, M.D.,† Arnold Herskovic, M.D.,‡ Rao Mantravadi, M.D.,§ Burton Speiser, M.D.‖ and the Clinical Research Committee, American Brachytherapy Society, Philadelphia, PA
Table 2. Suggested schema for definitive external beam radiation and esophageal brachytherapy

**External beam radiation:**
- 45–50 Gy in 1.8–2.0-Gy fractions, five fractions/week, weeks 1–5

**Brachytherapy**
- HDR — total dose of 10 Gy, 5 Gy/fraction, one fraction/week, starting 2–3 weeks following completion of external beam
- LDR — total dose of 20 Gy, single course, 0.4–1.0 Gy/hr, starting 2–3 weeks from completion of external beam

* All doses specified 1 cm from midsource or mid-dwell position.
Table 3. Suggested schema for external beam radiation and brachytherapy* in the palliative treatment of esophageal cancer

(a) Recurrent after external beam radiation or short life expectancy

**Brachytherapy:**
- HDR — total dose of 10–14 Gy, one or two fractions
- LDR — total dose of 20–40 Gy, one or two fractions, 0.4–1.0 Gy/hr

(b) No previous external beam radiation

**External beam radiation:**
- 30–40 Gy in 2–3-Gy fractions

**Brachytherapy:**
- HDR — 10–14 Gy, one or two fractions
- LDR — total dose of 20–25 Gy, single course, 0.4–1.0 Gy/hr

(c) No previous external beam radiation, life expectancy greater than 6 months

**External beam radiation:**
- 45–50 Gy in 1.8–2.0-Gy fractions, five fractions per week, weeks 1–5

**Brachytherapy:**
- HDR — total dose of 10 Gy, 5 Gy/fraction, one fraction/week, starting 2–3 weeks from completion of external beam
- LDR — total dose of 20 Gy, single course, 0.4–1.0 Gy/hr, starting 2–3 weeks from completion of external beam

* All doses specified 1 cm from midsource or mid-dwell position.
Applicators

- Endoscopic
- Manual
Poznań, Greater Poland Cancer Center – brachytherapy treatment schemas

• WHO 3-4, poor condition
  Dose 10 Gy / 1 fraction / 1 cm form axis

• WHO < 3, better condition
  Total Dose 22.5 Gy / 3 fractions / 1 cm
Poznań, Greater Poland Cancer Center – EBRT treatment schemas

- 20 Gy / 4-5 fractions
- 30 Gy / 10 fractions
- 44 Gy / 22 fractions

When BT added:
- pause 1-2 week
- + 10-15 Gy / 1-2 fractions
PTV = tumor length + 2cm proximally and distally
PTV = tumor length + 2cm proximally and distally
Marker used for planning
PTV = prothesis length + 2cm proximally and distally
2D Treatment Plan - example
Rapid dose fall – advantages of brachytherapy
Endoscopic image of a patient with a malignant esophageal lesion

(a) Isodose lines of the brachytherapy treatment planning are shown on CT image (b) and on a corresponding endoscopic ultrasound image (c).

Isodose values in cGy are reported on the extreme right; outlined structures are the target volume (red), the aorta (cyan), the lungs (dark yellow), the vertebral body (light brown), the spinal cord (purple), and the trachea (blue).
Brachytherapy - complications

• Acute mucositis ~ 80%
  • Fistula 5 – 10%
  • Ulceration ~ 30%
• Chronic mucositis, stenosis 10 – 30%
  • Bleedings – rarely
  • Perforation - rarely
Nutrition

- An important part of palliative treatment of patients with esophageal cancer is the longest possible to maintain a satisfactory nutritional indicators.

- Nutritional therapy in patients with esophageal cancer should be based on the situation through the application of methods of oral feeding, enteral or parenteral administration.
Treatment of recurrence is dependent on the primary method of treatment.

In patients with local recurrence after primary surgical treatment should consider the possibility of chemo or radiation therapy, taking into account their clinical status and tolerability rescue capabilities.

Occurrence of subsequent tumor recurrence and distant metastasis is an indication for palliative treatment according to the previously mentioned principles and take the best available symptomatic treatment.
Bile duct cancer
Biliary Duct Cancer

- **Biliary tract cancers** consist of cancer of the gallbladder, the **bile ducts**, and the ampulla of Vater,

  **Bile ducts:**
  - intrahepatic,
  - perihilar,
  - distal extrahepatic biliary tree,

- They are highly lethal because most are locally advanced at presentation,

- Gallbladder cancer – 2/3 of these cancer patients,
bile duct cancer – 1/3.
Cholangiocarcinoma is a rare tumor in developed countries; there are approximately 5,000 cases per year in the United States.

- **Poland**: (2011) gallbladder 1207
  bile ducts and ampulla of Vater 627

- It is one of the most common cancers in endemic areas of developing countries, as high as 87 per 100,000 people in northeast Thailand.

- Cholangiocarcinoma accounts for about 20% of the primary liver cancer in Western countries, and <10% in Asian nations that are endemic for HCC.
### Biliary Duct Cancer

#### Diagnostic Work-Up for Carcinoma of the Bile Duct

<table>
<thead>
<tr>
<th>General</th>
<th>Radiographic studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>❖ History,</td>
<td>Standard</td>
</tr>
<tr>
<td>❖ Physical examination,</td>
<td>❖ Computed tomography scan,</td>
</tr>
<tr>
<td>❖ Laboratory studies:</td>
<td>❖ Ultrasonography,</td>
</tr>
<tr>
<td>• Complete blood cell counts,</td>
<td>❖ Transhepatic cholangiography,</td>
</tr>
<tr>
<td>• Blood chemistry profile to include liver function studies,</td>
<td>❖ Endoscopic retrograde cholangiopancreatography.</td>
</tr>
<tr>
<td>• Tumor markers: CA 19-9, CEA.</td>
<td>Optional</td>
</tr>
<tr>
<td></td>
<td>❖ Endoscopic ultrasound,</td>
</tr>
<tr>
<td></td>
<td>❖ Magnetic resonance cholangiopancreatography,</td>
</tr>
<tr>
<td></td>
<td>❖ Dynamic computed tomography scan,</td>
</tr>
<tr>
<td></td>
<td>❖ Arteriography.</td>
</tr>
</tbody>
</table>
Biliary Duct Cancer

• **Surgical excision** of all detectable biliary tract cancers is associated with improvement in long-term survival,

• Ampulla of Vater location – **better prognosis,**

• Klatskin tumor (intrahepatic, perihilar) – **worse prognosis,**

• For **unresectable tumors**, the purpose of treatment is to palliate symptoms such as obstructive **jaundice**, biliary tract infection, pain, and ascites,

**Brachytherapy can be one of the treatments of choice.**
The only curative treatment is radical surgical excision,

However, because of the propensity of cholangiocarcinomas to invade the hepatic artery, portal vein and other vital structures this is only feasible in 10 to 15% of cases and is associated with an operative mortality of 5 to 10%.

Effective palliation is achieved by biliary decompression.

This is carried out either surgically by using bypass procedures such as hepaticojejunostomy or nonoperatively by endoscopic or percutaneous insertion of biliary endoprotheses.

Indications for brachytherapy include all malignant strictures of the bile duct which can be cannulated.

Patients should be fit enough for the procedure and have been reviewed to confirm that they are not suitable for resection.

Combined treatment is possible in patients who are in reasonably good condition; it is usual to combine brachytherapy (BT) with external beam radiation therapy (EBRT)
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Indications</th>
<th>Applicator</th>
<th>Ref. Point (CTV)</th>
<th>Pulse dose</th>
<th>Pulse frequency</th>
<th>Total dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radical</td>
<td>Inoperable tumors, combined with EBRT (40 Gy)</td>
<td>French 5</td>
<td>1.0 - 2.0 cm</td>
<td>0.5 - 0.8 Gy</td>
<td>every 1 h (recommended)</td>
<td>2-3 fractions of 20.0 Gy</td>
</tr>
<tr>
<td>Radical after surgery</td>
<td>After non radical resection</td>
<td>French 5</td>
<td>0.5 - 2.0 cm</td>
<td>0.5 - 0.8 Gy</td>
<td>every 1 h</td>
<td>40 - 50.0 Gy</td>
</tr>
<tr>
<td>Palliative</td>
<td>Obstructive jaundice</td>
<td>French 5</td>
<td>1.0 - 2.0 cm</td>
<td>0.5 - 1.0 Gy</td>
<td>every 1 h</td>
<td>20 - 40.0 Gy</td>
</tr>
</tbody>
</table>
Tumor visible during cholangioendoscopy
Tumor visible during cholangiorenoscopy
Prothesis in bile duct
"Rendez – Vous„ - steps

US, location of gallbladder, bile ducts, upper abdomen status
Local analgesia
X-ray, location of needle in bile ducts
fluoroscopy, location of needle in bile ducts
Preparing for guide-wire insertion in bile ducts
Guide-wire insertion in bile ducts
Fluoroscopy control of guide-wire insertion
Flexible catheter is inserted into the biliary tree to appropriate depths, under fluoroscopic control.
8F catheter (or 10F) insertion in bile ducts
Drain patency check
Rinsing
Cholangography
French 5 catheter (dark blue) ready for brachytherapy, inserted in 10 Ff catheter (light blue)
Applicator 5F inside of 10F catheter, marker visible
Irradiated length = CTV + 1 cm

Applicator 5F inside of 10F catheter, marker visible
Applicator 5F inside of 10F catheter, marker visible
Prothesis in obturated bile ducts
Prothesis and French 5 catheter for brachytherapy, marker inside
Anorectal cancer
Anorectal cancer
For limited size rectal cancer (T1, small T2), brachytherapy alone offers an alternative to radical surgery and leads to excellent results without major morbidity.

In advanced rectal cancer a brachytherapy boost either with contact X-ray brachytherapy (Papillon) or HDR rectal endoluminal brachytherapy can increase the chance of complete clinical response.
Rectal brachytherapy can also be used as a **palliative treatment** for locally advanced inoperable disease to control symptoms.

Tumour characteristics such as size (thickness and length), configuration and growth pattern (exophytic or infiltrative) are essential for selecting the appropriate form of brachytherapy whether contact X-ray, endoluminal or interstitial.

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The clinical target volume (CTV) in limited size tumours (<3cm), suitable for x-ray contact brachytherapy (Papillon) or for endoluminal brachytherapy, is the gross tumour itself (GTV) with a margin of 5mm around the tumour (CTV).

CTV=PTV.
Dose, Dose Rate and Fractionation:

Contact x-ray brachytherapy (Papillon):

- radical BT alone, 3 fr. of 30 Gy are given with one fraction every 2 weeks resulting in a total physical dose of 3 x 30 Gy.
Dose, Dose Rate and Fractionation:

**HDR endoluminal brachytherapy:**

- Pre-operative brachytherapy alone is given in 4 daily fr. with 6.5 Gy per fr. (target depth dose) resulting in a physical overall dose of 4 x 6.5 Gy.

- HDR BT as a boost after EBRT - A dose per fraction of 7-10 Gy in 3 fr. given at weekly intervals.

Dose, Dose Rate and Fractionation:

Interstitial BT dose

- The dose for interstitial HDR brachytherapy is 4.5Gy in 3 fr. over 24 hours. This delivers the equivalent dose of 20 Gy (EQD2) as a boost following EBRT.
Dose, Dose Rate and Fractionation:

**Palliative BT dose**

- Palliative brachytherapy is given using a single line source with cylinder (POVA) postoperative vaginal type applicator or endobronchial tube.
- The dose of 10Gy at 10mm from the surface of the applicator or from the perpendicular midpoint of the line source is prescribed to control symptoms such as bleeding.
Anal cancer - summary

Indications:

1. Curative treatment:
   1. T1 – sole brachytherapy (BT) or external beam (EBRT) + BT
   2. T2 – EBRT + BT
   3. T3 – EBRT + Chtch + BT

Conditions

1. Tumors infiltrating less than 2/3 of the circumference of the anus
2. N0 (extremely small nodes in the anal area possible to acquire the 85% isodose)
3. M0
2. Palliative treatment:

1. Inoperable recurrence,
2. Recurrence after EBRT,

Treatment of recurrence - after partial cytoreduction or without surgery

3. Anal margin tumors:

1. Rarely, after EBRT – „boost”
Contraindications:

1. No regression after initial chemoradiotherapy,

2. Tumors infiltrating more than 2/3 of the circumference of the anus – high risk of necrosis and stenosis,

3. T4 tumors,

4. N1, in some cases after individual decision combined treatment is possible (chemoradiotherapy _ brachytherapy).
Thank you