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Reirradiation of Lung Cancer: Undervalued Possibility


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Radical treatment (5 -10% of BT patients): Indications

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.

The GEC ESTRO Handbook of Brachytherapy. Gerbaulet A., Potter R., Mazon J-J., Meertens H Van Limbergen E. (eds). ESTRO, Bruksela 2002.



Palliative treatment (>90 % of BT patients): Indications

1. The main indication is treatment of life-threatening complications such a **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.**

The American Brachytherapy Society recommendations for brachytherapy of carcinoma of the lung (2000)

S. Nag, J. F. Kelly, J. L. Horton, R. Komaki, D. Nori

Definitive therapy:

1. HDR dose of 3 fractions of 5 Gy each or 2 fractions of 7.5 Gy each as a boost to 60 Gy in 30 fractions or 45 Gy in 15 fractions EBRT can be used.
2. If endobronchial brachytherapy is **used alone**, doses of 5 fractions of 5 Gy each or 3 fractions of 7.5 Gy each prescribed to 1 cm can be used.
3. The interval between fractions is generally one to two weeks.
4. **Concomitant chemotherapy** should be avoided during brachytherapy unless it is in the context of a clinical trial.
5. The HDR doses should be modified if HDR is used in a treatment regime that includes aggressive **chemotherapy**.
6. **Interstitial brachytherapy** should be considered when endobronchial techniques would be expected to inadequately encompass the tumor.




The American Brachytherapy Society recommendations for brachytherapy of carcinoma of the lung (2000)

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Palliative therapy:

3 fraction of 7.5 Gy or 2 fraction of 10 Gy (HDR)

or

30 Gy (LDR, PDR)  *history*

Brachytherapy treatment schemas - indications, doses

Indications for brachytherapy	I phase	II phase	III phase	IV phase
Radical combined treatment: schema I; clinical stage T1-3 N1-3 M0	Total dose 44 Gy in 22 fr. aa 2 Gy (2 a-p fields)	1 fr. x 6 Gy, ref. point 0.5 - 1 cm	EBRT 16 Gy in 8 fr. (changed fields)	1 fr. x 6 Gy, ref. point 0.5 - 1 cm
Radical combined treatment: schema II; clinical stage T1-3 N1-3 M0	EBRT: total dose 44 Gy in 22 fr. aa 2 Gy (2 a-p fields)	EBRT 16 Gy in 8 fr. (changed fields)	HDR-BT - in 1, 3 and 5 weeks of EBRT - 3 x 10 Gy.	
Radical sole treatment, radiologically occult cancer T1-2N0	Total dose 36 - 42 Gy in 6 - 7 fr. with interval of 4 - 7 days between fractions			
Radical treatment after surgery, R2	After EBRT with total dose of 50 - 60 Gy	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		
Radical treatment: stump infiltration	Sole brachytherapy: 4 fr. of 7.5 - 10 Gy with interval of 4 - 7 days between fractions			
Palliative treatment	30 Gy in 3 fr. of 10 Gy with interval of 4 - 7 days - in patients treated earlier with EBRT - dose > 50 Gy 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 < 50 Gy			
	1 x 10 Gy in case of WHO scale > 2	Sometimes dose can be repeated after few weeks, in cases with clinical remission or visible during bronchoscopy		

Poznań

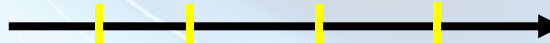
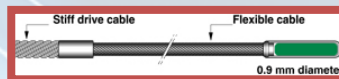
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Contraindications:

1. peripheral location of the tumor,
2. Pancoast tumor (?),
3. pressure - location outside of bronchii,
4. contraindication to bronchoscopy (relative).

Evolution in brachytherapy...



Ra Cs / Co Ir ? Homeopathy...



Re-irradiation – why?

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.

Re-irradiation – why?

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.**



Published results

Author	N	Previous RT	HDR Brachytherapy	Conclusions
Speiser and Spratling 1993				The same palliative effect and OS as in patients treated primarily with palliative intent.
Gauwitz et al. 1992	24	55 Gy	2 fr. x 15 Gy/6mm	Symptomatic relief was obtained in 21/24 (88%), and relief from atelectasis in 15/18 (83%) patients.
Micke et al. 1995	16	50 – 60 Gy	2-4 fr. x 5-6 Gy	The median time of remission was 4 mths, whereas the median OS was 9 mths.
Ornadel et al. 1997	117		1 fr. x 15 Gy	The median OS was 12 mths; no correlation between the total dose of the prior EBRT and the OS or rate of fatal haemoptysis.
Bedwinek et al. 1991	38	> 50 Gy	3 fr. x 6 Gy	76% patients had symptomatic improvement; median duration of symptoms relief was 7.5 mths. Bronchoscopy carried out 3 months after BT revealed that 41% had CR, 41% - PR.
Delclos et al. 1996	81		2 fr. x 15 Gy	The median duration of response was 4.5 mths. 2 fatal complications, which were due to fistula and tracheal malacia.
Taulelle et al. 1998	189	69% - prior EBRT	3-4 fr. x 8-10 Gy	Complete endoscopic response was observed in 54% of patients. The median OS was 7 mths.

Greater Poland Cancer Center material

Criteria for inclusion in this retrospective analysis:

1. history of tracheobronchial carcinoma, bronchogenic or metastatic,
2. the patient must have been previously given HDR-BT (main condition),
3. bronchoscopically documented endobronchial recurrence, producing local symptoms (cough, hemoptysis, dyspnea or obstructive pneumonia),
4. suitable endobronchial location for afterloading catheter placement,
5. general condition according to WHO score ≥ 3 .



Greater Poland Cancer Center material

Decision for repeated brachytherapy was based on:

1. clinical examination,
2. flexible bronchoscopy with precise documentation of the location and the amount of obstruction,
3. supplemented by a chest X-ray,
4. sometimes by CT.

It was important to determine tumour extent as clearly as possible, especially in recurrence of disease in previously irradiated area with high doses.

Greater Poland Cancer Center material

Palliation was the main end-point of our study.



Material and methods

270 patients were treated two or more times using high dose rate brachytherapy in Greater Poland Cancer Center, Poznań, Poland

206 male (76,3%), 64 female (23,7%)

Endobronchial recurrence location:

Endobronchial location	Number of patients	Rate (%)
Trachea	14	5,2
Trachea + main bronchus	34	12,6
Main bronchus	112	41,5
Lobular bronchus	85	31,4
Segmental bronchus	17	6,3
Stump	8	2,9

Material and methods

Clinical data	Number of patients	Rate (%)
Age:		
< 60	66	24,4
60 -70	95	35,2
70 -80	80	29,6
> 80	29	10,7
Sex:		
Male	206	76,3
Female	64	23,7
Histology:		
Squamous cell carcinoma	172	63,7
Adenocarcinoma	27	10
Non small cell carcinoma	14	5,2
Small cell carcinoma	13	4,8
Large cell carcinoma	6	2,2
Undetermined	21	7,7
Metastases	9	3,3
Cell carcinoma	8	2,9
Stage of primary lung cancer :		
I	10	3,7
II	27	10
IIIA	34	12,6
IIIB	104	38,5
IV	51	18,9
Undetermined	44	16,3



Material and methods

Characteristic of given primary treatment modality.

Treatment	Number of patients	Rate (%)
Previous treatment for recurrent patient :		
Radical treatment:		
1. EBRT + BT as " boost "	61	22,6
2. Surgery + BT	16	5,9
3. Surgery + BT + EBRT	4	1,5
4. EBRT + BT + EBRT	8	2,9
5. EBRT + BT + CHTCH	33	12,2
Palliative treatment:		
1. EBRT + BT	209	77,4
2. EBRT + BT + CHTCH	122	45,2
3. Salvage BT	54	20
4. Salvage BT	33	12,2
Additional treatment for all patients:		
1. EBRT	144	53,3
2. EBRT + CHTCH	65	24
3. EBRT + CHTCH	42	15,6
4. CHTCH	37	13,7
No additional treatment	126	46,6

EBRT = external beam radiotherapy; BT = brachytherapy; CHTCH = chemotherapy

Material and methods

HDR schedule

Brachytherapy procedure:	Number of patients	Rate (%)
At first treatment time:		
3x 7,5 Gy	172	63,7
1x 10 Gy	98	36,3
At second treatment time (8-10 Gy):		
1x	220	81,5
2x	38	14,1
3x	10	3,7
4x	2	0,7
Degree of bronchus obturation at recurrent time:		
< 50 %	22	8,1
>50%	61	22,6
Almost total	84	31,1
Total	91	33,7
Stump	12	4,4



Material and methods

- Single bronchial catheter (French 6) was fixed in bronchus during bronchoscopy, **target volume** included tumor with 1-2 cm margin proximally and distally from tumor.
- Orthogonal **x-ray** were used to verify the position of the catheter and to assist in the treatment planning.
- **Dose of 8 or 10 Gy** was measured 1 cm from catheter axis (8 Gy was given, when previous high EBRT dose over 60 Gy/T was delivered).
- Iryd 192 source with 10 Ci activity was used.
- Patients have undertaken **clinical and endobronchial observation** with rating of local remission and retiring difficulties with breathing, cough and hemoptysis.

Material and methods

- The treatment efficacy was evaluated in **1 to 3 months** after the end of brachytherapy, based on subjective symptomatic attenuation, bronchoscopy and by radiological assessment, depending on patient's clinical situation.
- **Subjective symptomatic relief** was recorded as the patients were asked specific questions about the severity of their symptoms, activity level, and whether their general condition had improved since the last endobronchial treatment.
- Speiser's scale and assessment of **performance status** according to **WHO** score were used.



Material and methods

- **Endoscopic response** were evaluated based on visual intraluminal assessment.
 - **Radiological observation** (x-ray) were performed once in every three months after treatment completion.
- For endoscopic findings:**
- **P** was recorded when increasing size of tumour mass, and/or new cancer focus appeared,
 - **NR** was described for patients without significant tumour regression,
 - **PR** was recorded when there was at least 50 % of reduction in the tumor mass,
 - **CR** was described when there was a total regression of all measurable tumours.

Results:

Symtomatic and endoscopic response to HDR - BT

Response	Number of patients, (%)	P (%)	NR (%)	PR (%)	CR (%)	TR (%)
Symptomatic						
Cough	267 (99)	21 (8)	40 (15)	125 (47)	81 (30)	206 (77)
Dyspnea	243 (90)	26 (11)	32 (13)	145 (60)	40 (16)	185 (76)
Hemoptysis	178 (66)	0 (0)	15 (8)	96 (54)	67 (38)	163 (92)
Pneumonia	124 (46)	4 (3)	12 (10)	76 (62)	32 (26)	102 (82)
Endoscopic	218 (80)	4 (2)	39 (18)	158 (73)	17 (7)	175 (80)

*P = Progression; NR = No Response; PR = Partial Response;
CR = Complete Response; TR = Total Response*



Results:

- 200 (75 %) patients had chest x-rays that showed collapse of one or more lobes or atelectasis due to endobronchial tumour recurrence.
- Out of the 200, **146 (73 %) patients achieved re-aeration**, as defined by decreased atelectasis on subsequent chest x-ray.
- In 54 whose chest x-ray did not change, 15 had definitive symptomatic improvement.

Overall, symptomatic palliation was very satisfactory.

- The majority of the responsive patients enjoyed improved **QoL** and some duration of the palliation.
- The **duration of symptomatic relief**, including complete and partial remission (interval from retiring of symptoms to recurrence of symptoms or death), **ranged from 2 to 14 months with median of 5 months.**

Complications:

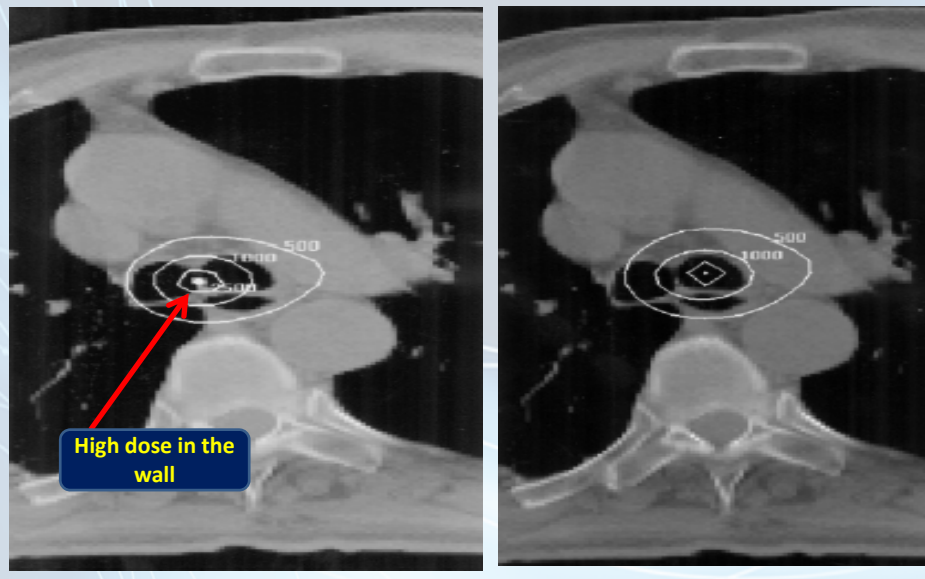
1. **Tolerance of repeated treatment using HDR-BT was good in most of the cases:**
with **superficial mucosal necrosis** observed in **166 pts** and **broncho – oseophageal fistula** recorded in **6 pts**.
2. No patient died as a result of the therapy.
3. There were **two factors** incriminated the complication rate, which were correlated with the development of more sever degree of radiation bronchitis:
 - a. tumour **location** in trachea or main stem bronchus,
 - b. the **dose of radiation** given previously, including total HDR-BT dose plus EBRT dose and fractionation schedule (Mann – Whitney test, $p = 0,002$).



Conclusions:

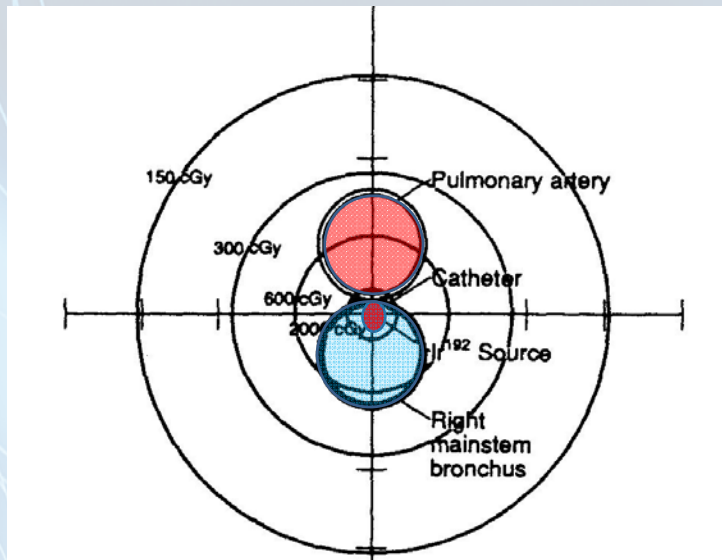
1. Repeated HDR brachytherapy in advanced lung cancer was an efficient method that caused in many patients retiring of the symptoms and improvement of life quality.
2. Prolonged survival was correlated with clinical stage, tumor location, Zubrod – performance status, achieved remission after 1st treatment and interval length between I and II treatment.
3. Repeated HDR brachytherapy up to four times with 10 Gy dosis improved **survival length**.
4. High total dose influenced the growth of the frequency of complications, majority of patients involved a **superficial mucosal necrosis**.

Cross-section CT – izodose picture. Two different locations of catheter

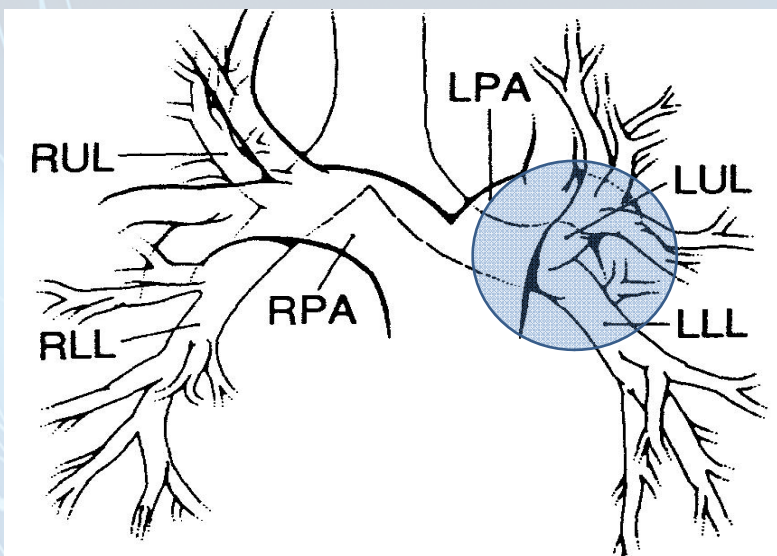




Isodoses placed on schematically situated right main bronchus and pulmonary artery. Catheter with inserted isotope Ir-192 is located nearby artery wall. In this case **irradiation dose, growing constantly with shortening of distance to source, is very high and greater in artery wall than in tumor.**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

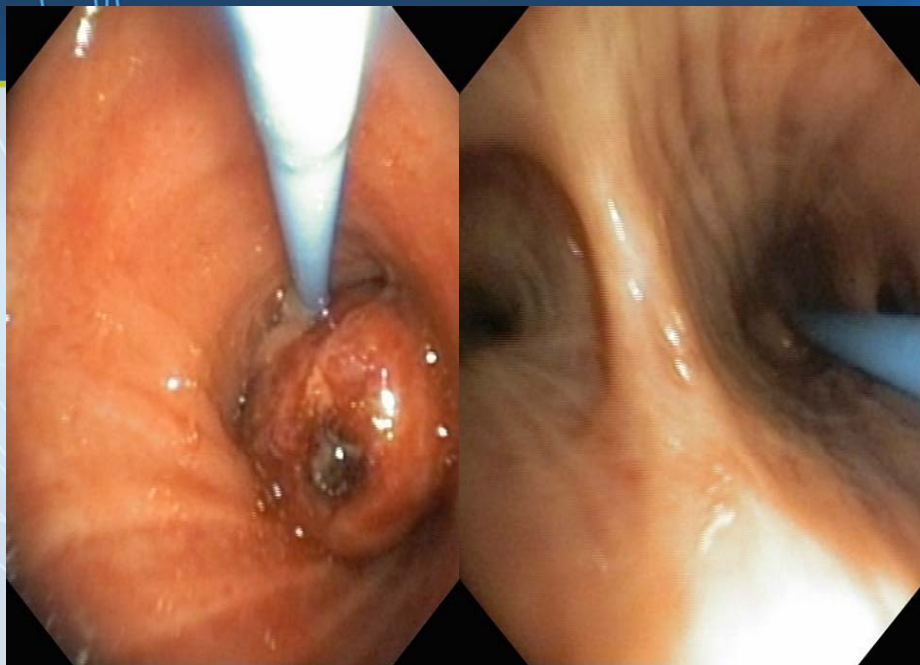
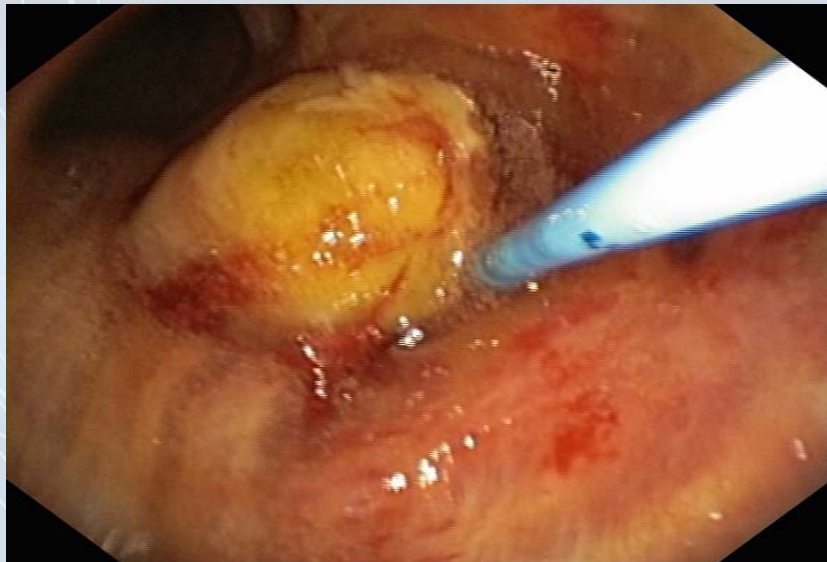


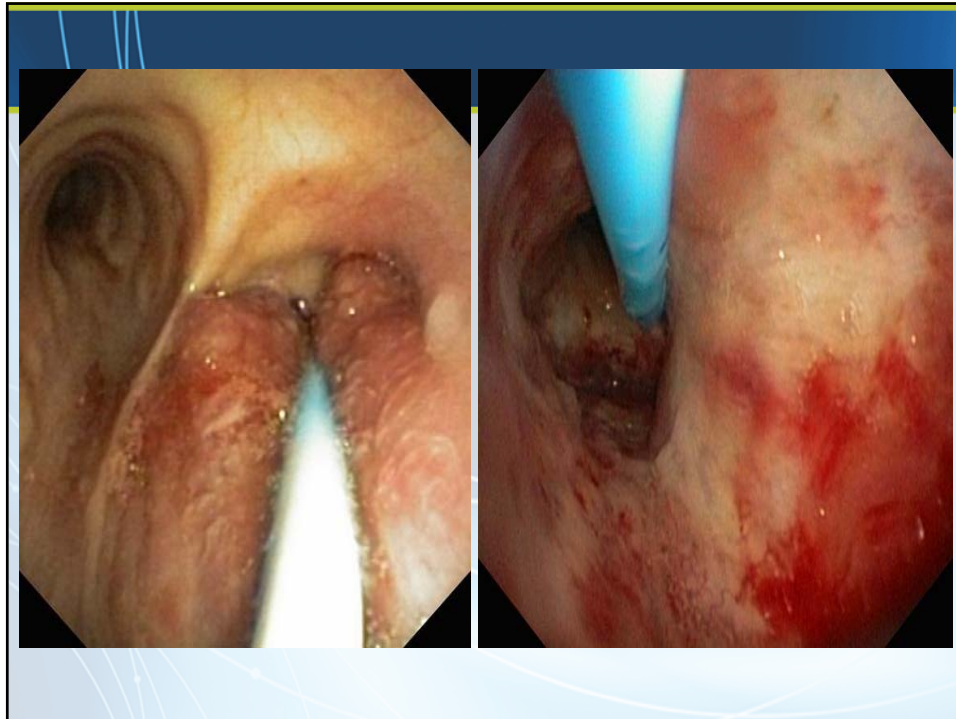
Pulmonary arteries and bronchii overlapping each other. The risk of radiation overdose in arteries wall in case of applicator setting near-by artery is great. RPA – right pulmonary artery, LPA – left pulmonary artery, RUL – right upper lobe, RLL – right lower lobe, LLL – left lower lobe, LUL – left upper lobe



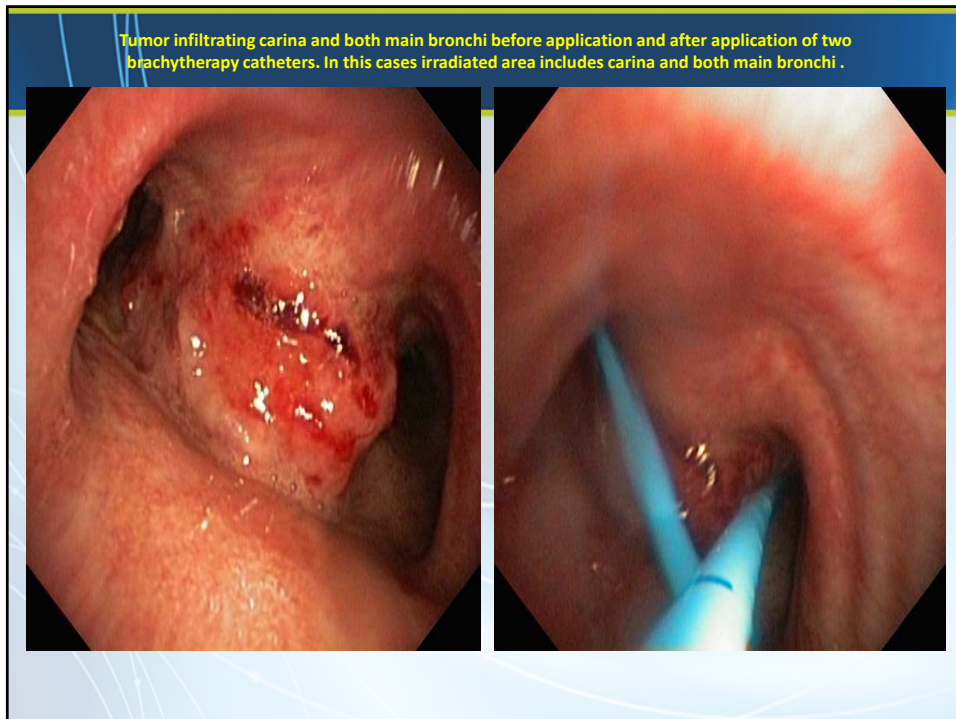


Material – Greater Poland Cancer Centre



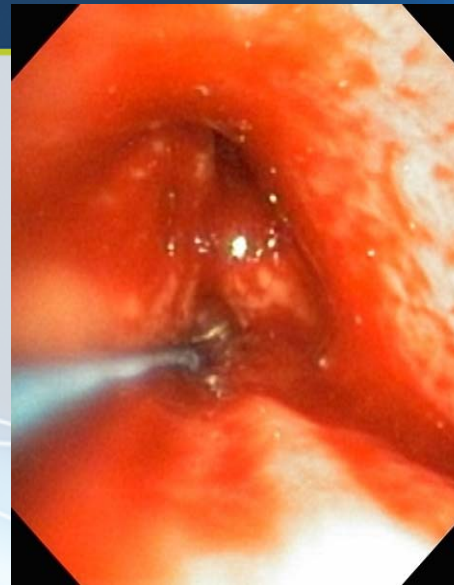
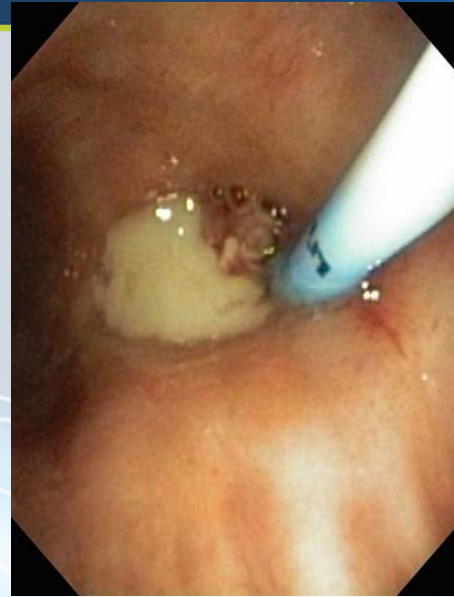


Tumor infiltrating carina and both main bronchi before application and after application of two brachytherapy catheters. In this cases irradiated area includes carina and both main bronchi .



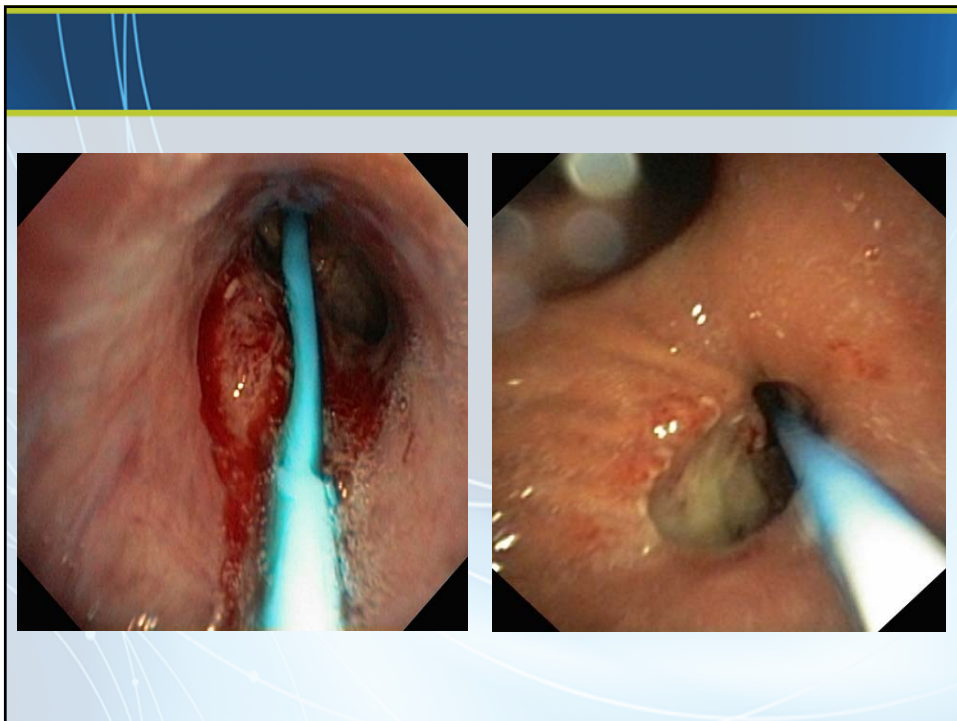
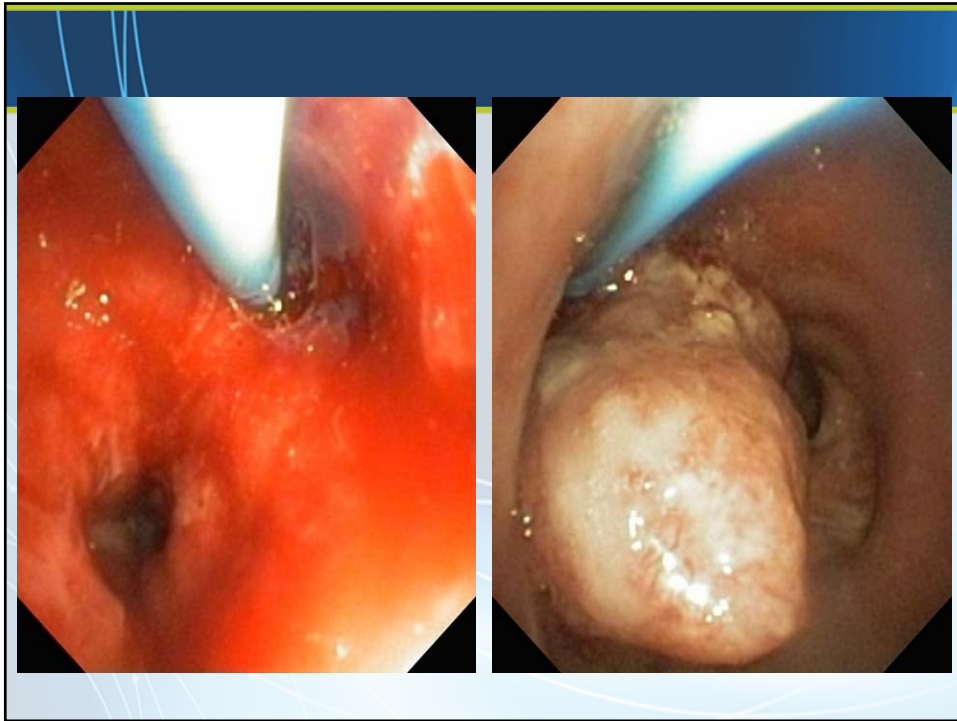


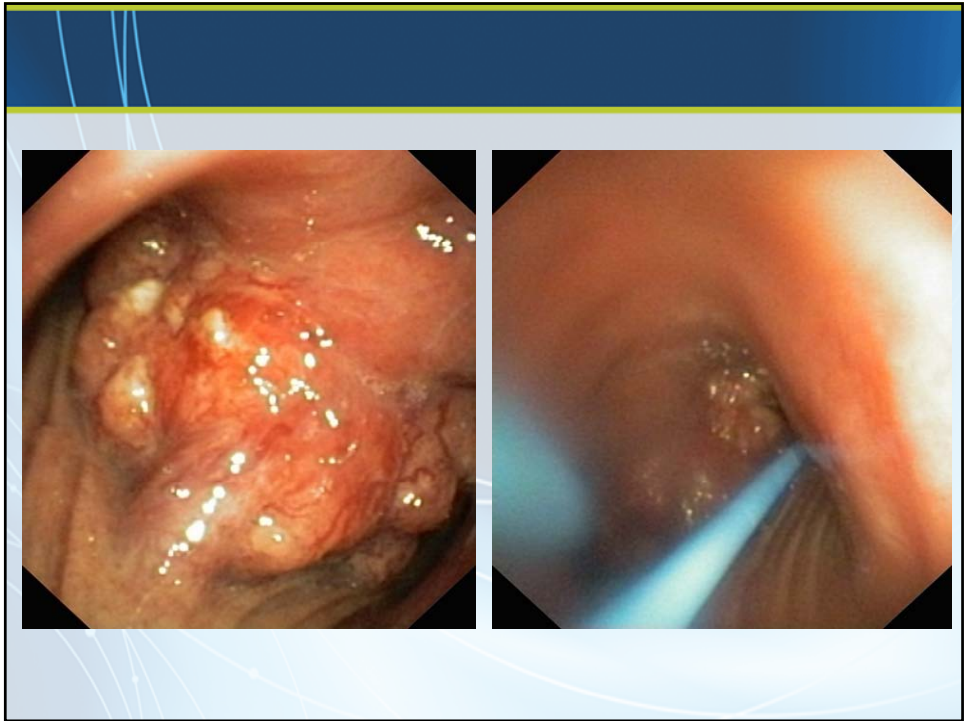
Examples of brachytherapy – tumor localized in main bronchus, French 6 (5) catheter placed in bronchus close by, scale on catheter (in cm) useful for treatment planning visible .



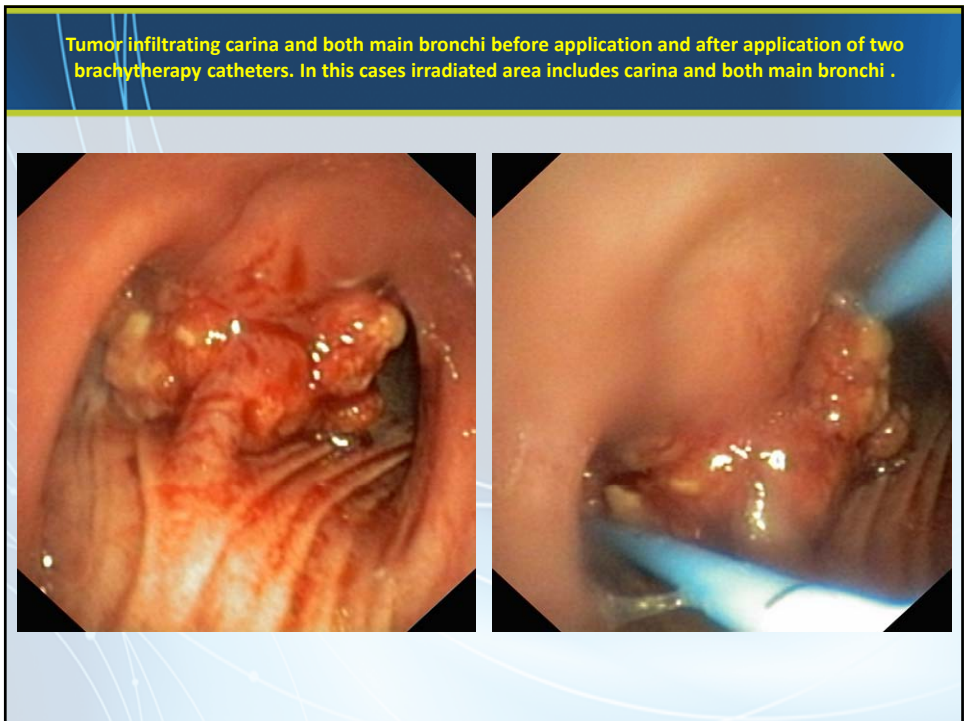
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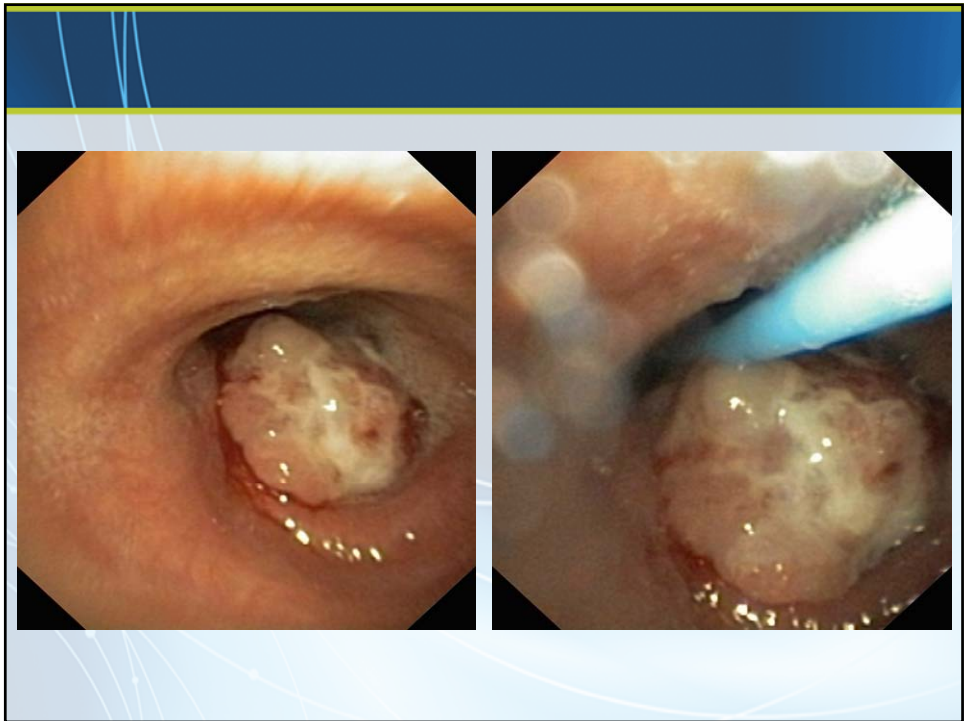
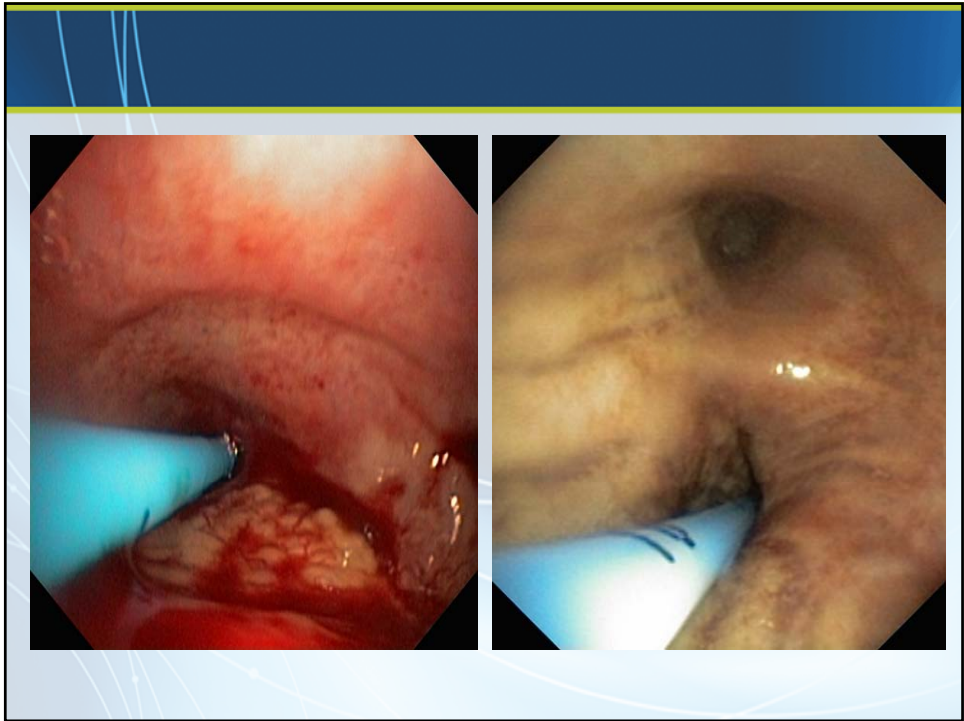
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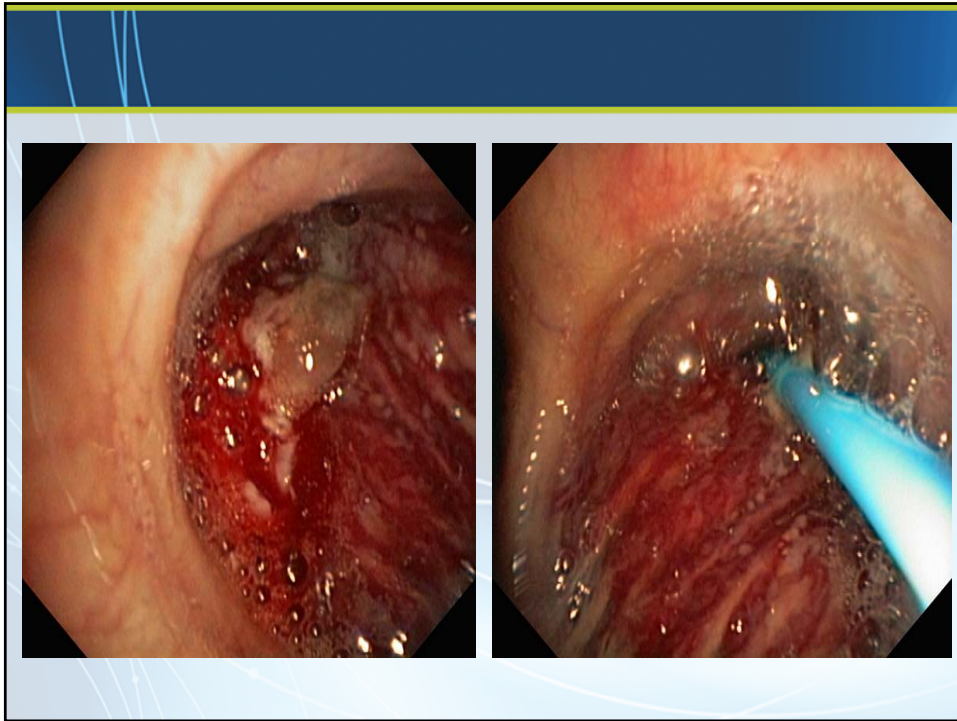


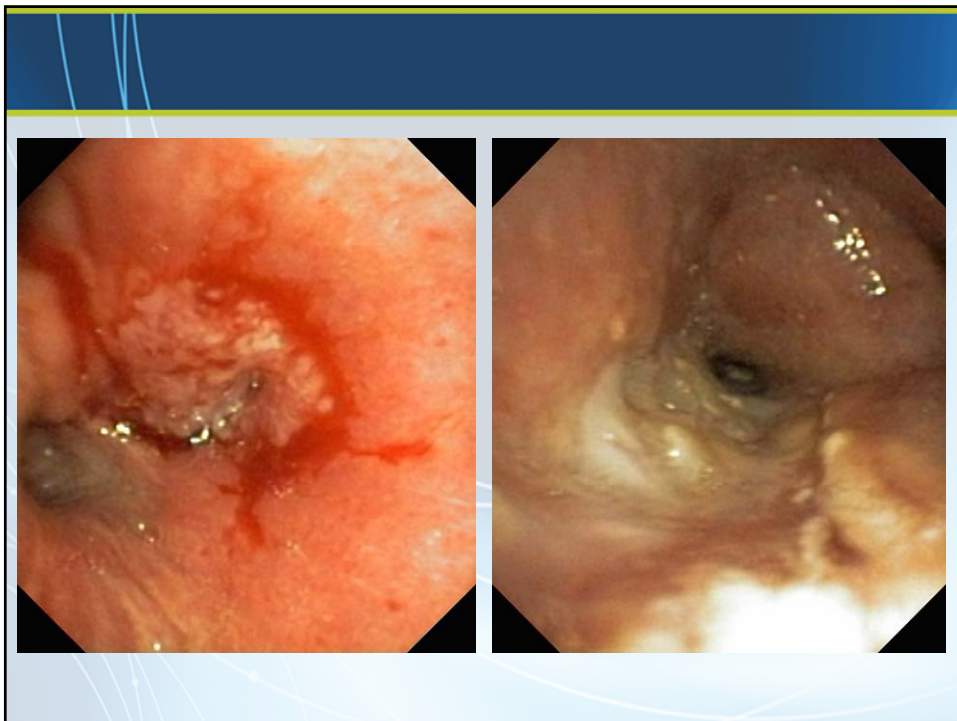
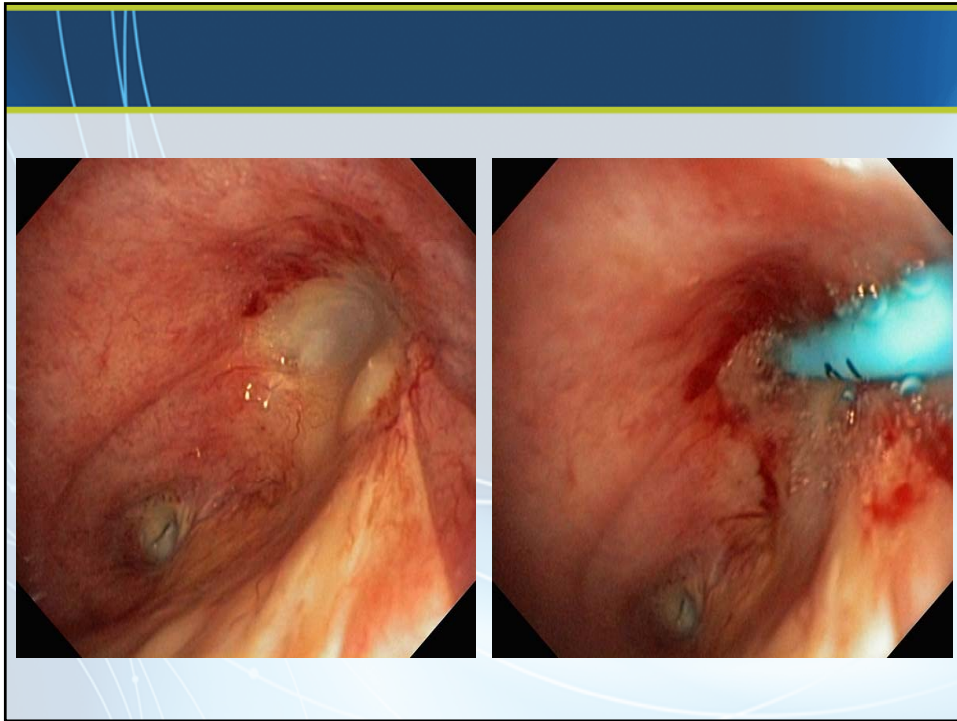


Tumor infiltrating carina and both main bronchi before application and after application of two brachytherapy catheters. In this cases irradiated area includes carina and both main bronchi .



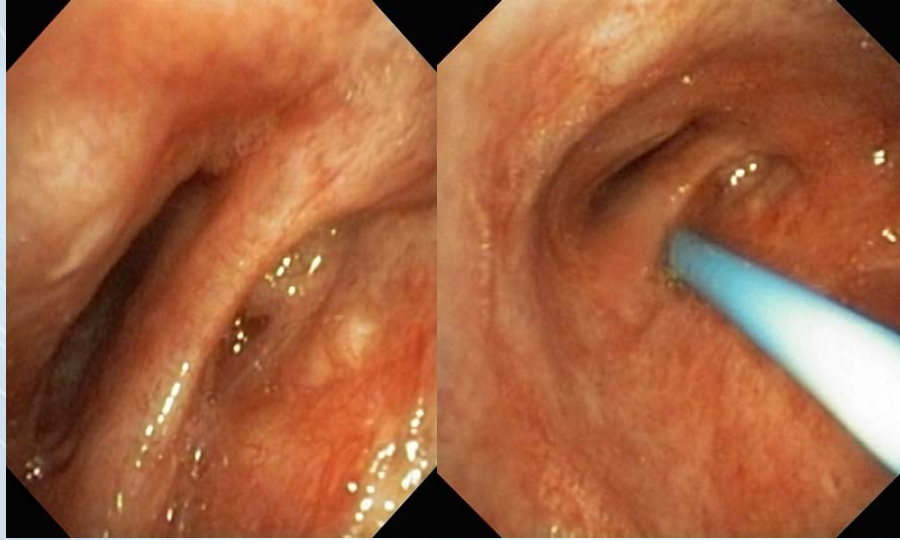




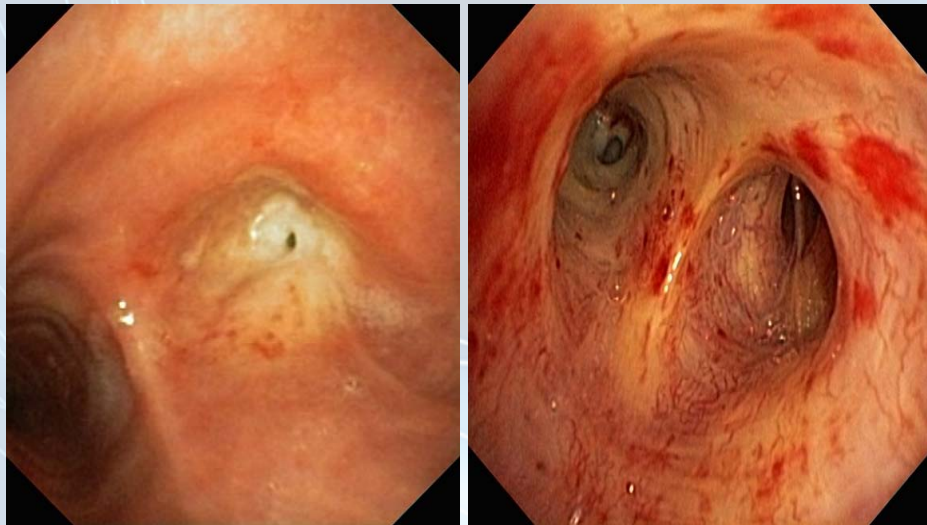




Stump

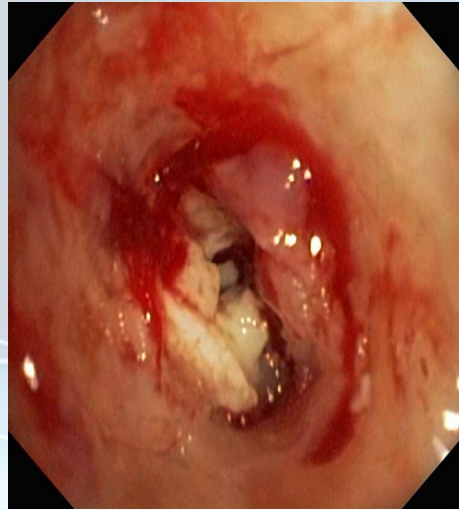


Late radiation injury





Late radiation injury

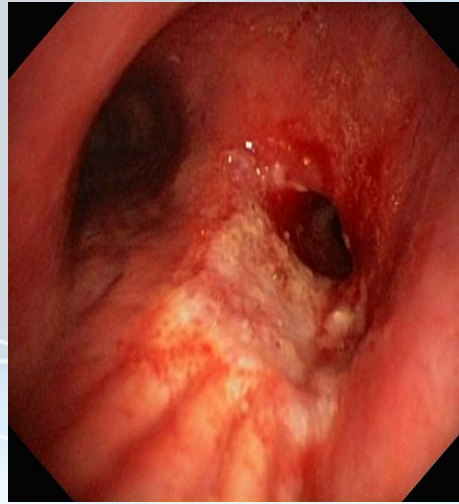
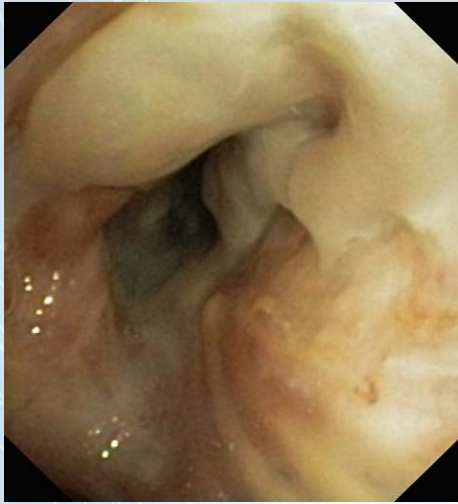


Late radiation injury

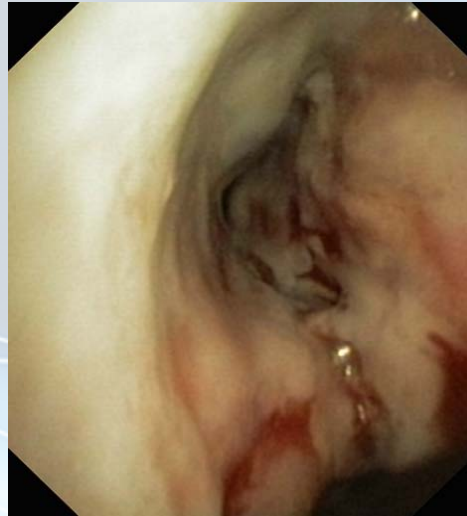




Late radiation injury

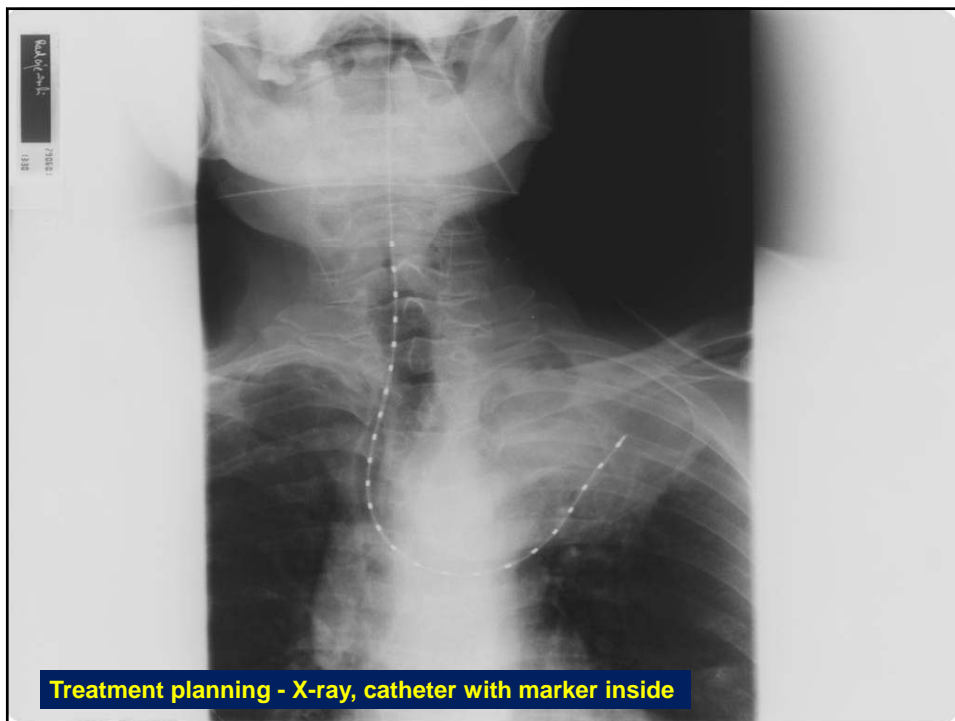
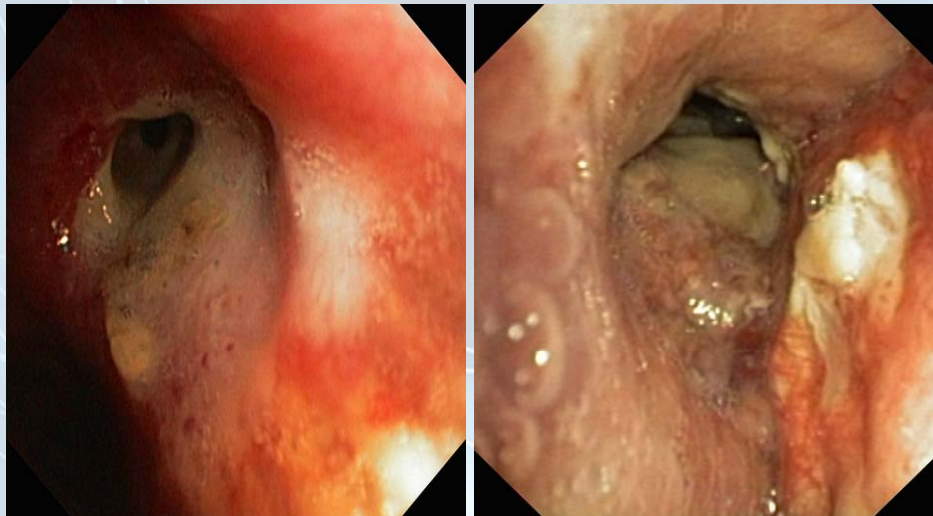


Late radiation injury

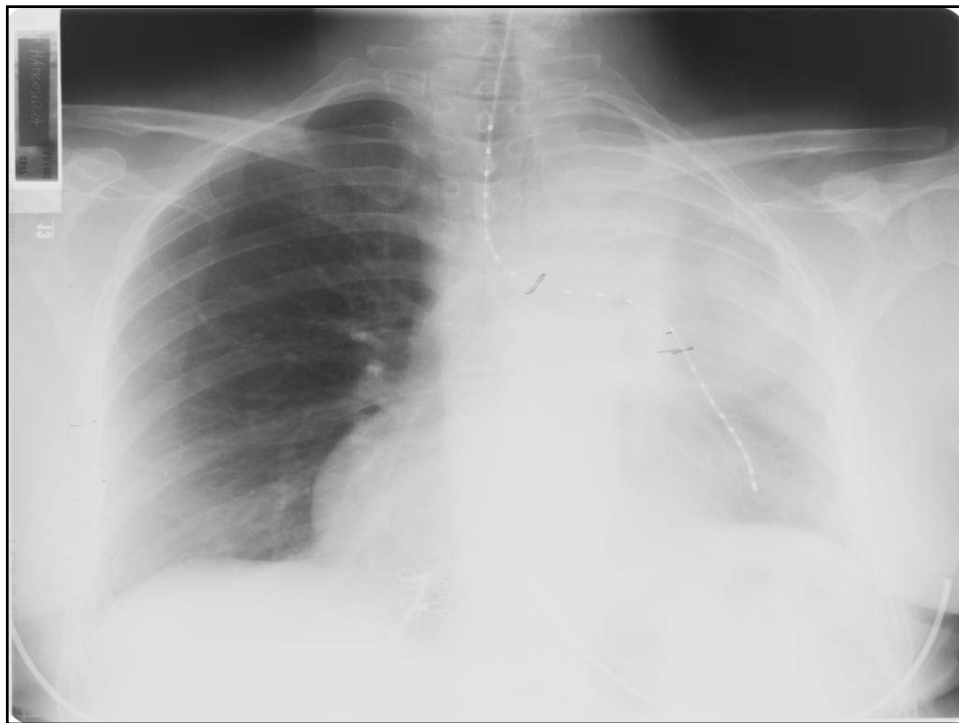


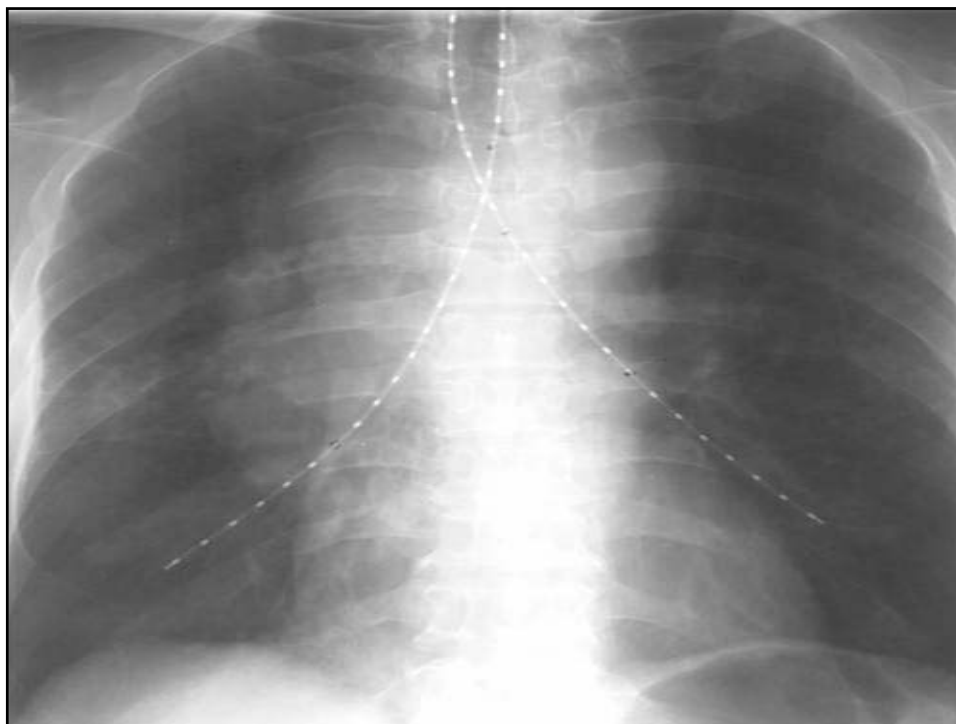


Late radiation injury



Treatment planning - X-ray, catheter with marker inside





Movie – brachytherapy application

Henryk

27/05/2014
08:12:09
Gr:Norm. Ex:A1
Media: ■■■





Thank you

