Endobronchial Intra- Luminal Brachytherapy (ILT)

Dr Hamid Sheikh, Consultant in Clinical Oncology

The Christie Hospital
Manchester

The Christie NHS
NHS Foundation Trust

DISCLOSURE OF INTEREST

Endobronchial
Intra- Luminal Brachytherapy
(ILT)

Dr Hamid Sheikh
Clinical Oncologist, The Christie

I have no disclosures to make

ESMO

Overview

- Background & evidence
- Technique
- Case Studies
- Twin-line applications
- Summary

What is brachytherapy

- Radioactive source placed within or close proximity to tumour
- Geometric advantage, relative sparing of normal tissues
- Non-uniform radiation field
- Lower dose rate further away → differential cell killing
- Precise source placement to irradiate small volumes

Types of brachytherapy

- Interstitial, eg prostate
- Intracavity, eg cervix, bronchus
- Surface applications (moulds), eg skin

History of ILT

- 1921 Yankhauer inserted radium capsules (radon-222) via rigid scope

- 1964 Henschke developed remote after-loading with iridium-192. need for GA

History of ILT

- 1980s remote afterloading via plastic catheter tube inserted by flexible bronchoscopy
- Iridum-192 HDR by microselectron

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Endobronchial therapies

- Surgical:
  - Neodymium-YAG laser debulking
  - Tracheo-bronchial stents
  - Cryotherapy
- Medical:
  - Photodynamic therapy
- ILT (+/- EXBRT)

Indications : Radical

- Radical (3 successive weekly fractions):
  - Superficial T1N0M0 NSCLC
  - CIS biopsy proven and limited in extent
  - Localised tumour rec at surgical RM

- NSCLC prior to radical EXBRT to re-expand lung (single fraction)

Indications : Palliative

- Palliative (single fraction): (+/- EBXRT)
  - Symptomatic endoluminal disease NSCLC
  - Endobronchial metastasis from distant primary
  - Direct invasion from malignant node
  - Post debulk +/- stent insertion

- SOB due to collapse
- Haemoptysis
- Intractable cough

Dose & Fractionation

Disease site	Technique	External Beam Dose	Brachytherapy prescription
Lung Radical	HDR MicroSelectron ILT (prescribed to 10mm)	No previous XRT	800-1000cGy weekly x 3
Lung Radical	HDR MicroSelectron ILT (prescribed to 10mm)	No previous XRT	Re-inflation before radical XRT 500 – 1000cGy x 1
Lung Palliative	HDR MicroSelectron ILT (prescribed to 10mm)	No previous palliative XRT	1000 – 1500cGy x 1
Lung Palliative	HDR MicroSelectron ILT (prescribed to 10mm)	Previous palliative XRT	1000 – 1500cGy x 1
Lung Palliative	HDR MicroSelectron ILT (prescribed to 10mm)	Previous radical XRT	500 – 750cGy x 1

Effective in Palliation

- Christie series, n=50
- Haemoptysis relieved in 24/28 pts (86%)
- SOB relieved in 21/33 pts (64%)
- Cough relieved in 9/18 pts (50%)
- Radiological collapse resolved in 11/24 pts

Intraluminal irradiation for the palliation of lung cancer with the high dose rate micro-Selectron.
Burt PA; O'Driscoll BR; Notley HM; Barber PV; Stout R. Thorax 1990 Oct;45(10):765-8.

Effective as Radical

- n= 106 patients not eligible for surgery or EXBRT
  - 43 relapse after surgery, 27 relapse after EXBRT, 36 early lung cancer poor lung FTs
- 6 x weekly 5 or 7 Gy
- CR rate at 3 mths was 59%
- 3YS and 5YS 47.4 and 24%
- 5 toxic deaths (2 MFH, 3 bronchial necrosis).
- long-term cause-specific survival 50% - ‘could be considered curative’.

- Long-term results of endobronchial brachytherapy: A curative treatment? Hennequin C, Bleichner O, Trédaniel J, Quero L, Sergent G, Zalcman G, Maylin C. Int J Radiat Oncol Biol Phys. 2007;67(2):425.

Effective as Radical

- n=226 (1991-2004)
- 24-35Gy in 4-6 fractions
- 94% complete endoscopic resp at 3mths
- 2YS 57%, 5YS 29% (81%, 56% cancer specific)
- 5% MFH, 20% late bronchitis, 3.5% necrosis

- High-dose-rate brachytherapy for non-small-cell lung carcinoma: a retrospective study of 226 patients. Aumont-le Guilcher M, Prevost B, Sunyach MP, Peiffert D, Maingon P, Thomas L, Williaume D, Begue M, Lerouge D, Campion L, Mahe MA. Int J Radiat Oncol Biol Phys. 2011;79(4):1112.

Christie Radical case series

- 1997-2007, n=37
  - M:F 32:3
  - Ages 46 – 81 (mean 67, median 66)

Histology	no
Squamous cell ca	19
CiS	8
NSCLC	2
Adenoca	1
Adenoid Cystic	1
Clear cell	1
Unknown	4

- MS 15.5 months, 2YS 38.5%
- MFH rate 8%

Palliate by ILT or EXBRT ?

- Christie RCT 1989-93, n=99 randomised
- 1° endpt symptom relief, acute & late SE, QoL scores
- Better Sx relief with XRT but more acute morbidity
- Better duration relief with XRT (28% had ILT median 304 days later) than ILT (51% had XRT median 125 days later)
- MS 287 vs 250 days

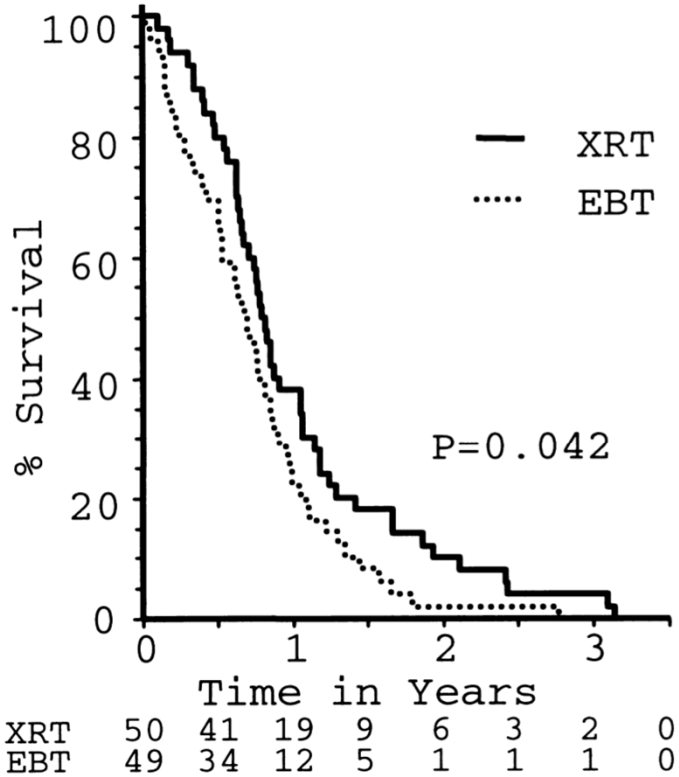


Fig. 1. Percentage crude survival by initial treatment. XRT $n = 50$. EBT $n = 49$.

XRT preferred to ILT as initial treatment in better PS pts → better palliation and OS

Stout, Barber, Burt et al, R+O 2000 (56), 323-327

Laser alone?

- Laser + ILT vs laser alone

- Survival of patients undergoing Nd:YAG laser therapy compared with Nd:YAG laser therapy and brachytherapy for malignant airway disease. Shea JM, Allen RP, Tharratt RS, Chan AL, Siefkin AD. Chest. 1993;103(4):1028.

ILT Cochrane Meta-analysis

- 13 RCTs
- EXBRT alone is more effective for palliation than ILT alone.
- No conclusive results that ILT plus EXBRT improved symptom relief over EXBRT alone. No conclusive evidence to recommend ILT with EXBRT, chemotherapy or Nd-YAG laser.
- For patients previously treated by EXBRT who are symptomatic from recurrent endobronchial central obstruction, ILT may be considered

Palliative endobronchial brachytherapy for non-small cell lung cancer. Cardona AF; Reveiz L; Ospina EG; Ospina V; Yepes A. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD004284.

Cautions

- Medically unfit for bronchoscopy
- Bulky disease needing surgical airway management
- Extrinsic compression
- Proximity to major vessel
- Invasion into adjacent organ → risk fistulation
- Heavily pre-irradiated or laser debulked

Complications

- Epistaxis, haemorrhage
- Chest infection
- Hypoxia
- Cardiac
- Pneumothorax
- Bleeding
- Treatment related
  - Radiation bronchitis possibly → stenosis
  - fistulation
  - MFH

Christie morbidity data

- 1988-92, n=406
- 32 pts died of MFH. Risk factors were 20Gy as opposed to 15Gy, 2nd ILT in same area first, prior laser treatment
- MFH peaked 9-12 mths after ILT

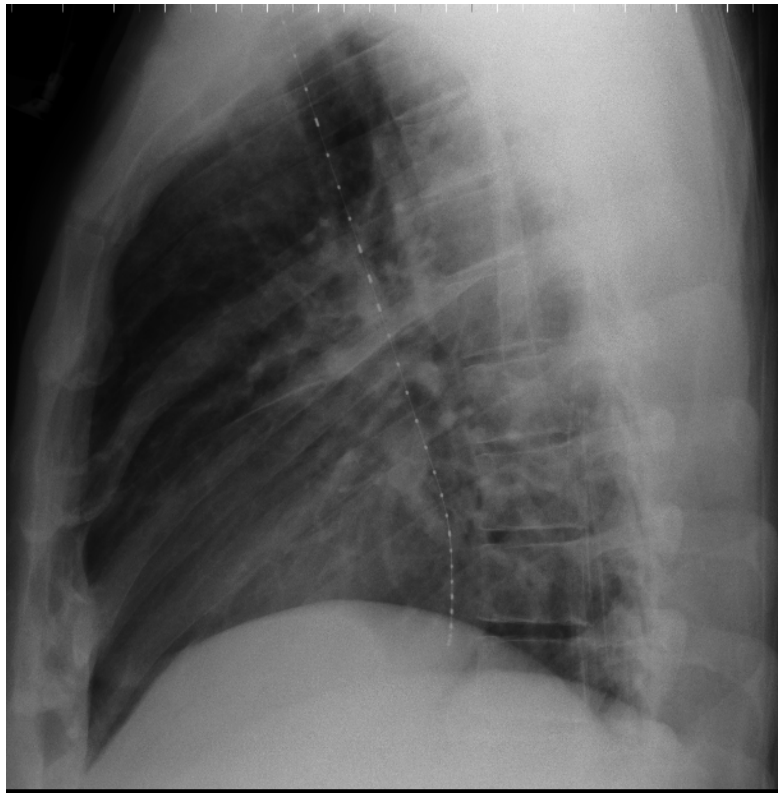
- Radiother Oncol. 1996 May;39(2):105-16. Massive haemoptysis death and other morbidity associated with high dose rate intraluminal radiotherapy for carcinoma of the bronchus. Gollins SW, Ryder WD, Burt PA, Barber PV, Stout R.

Technique : Localisation

- Bronchoscopy
- Epidural catheter
- Adrenaline
- 2mm diameter applicator via biopsy channel
- Applicator secured to nose
- Guidewire changed to a RMW

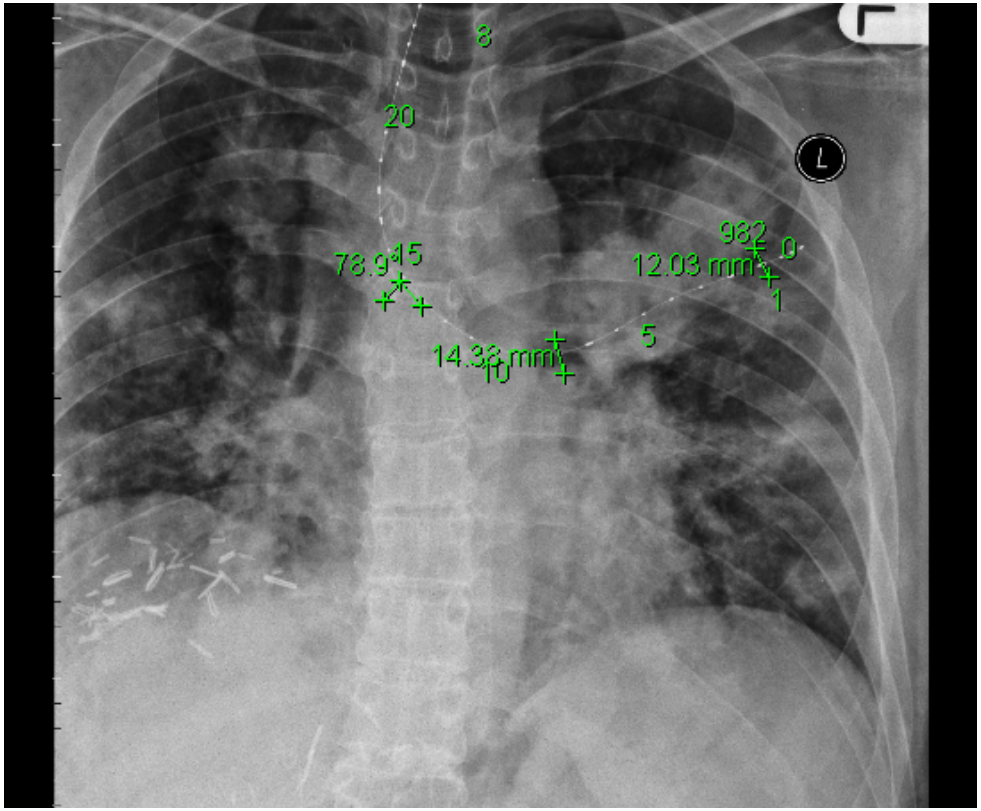
Technique – RT planning

- AP & Lat CXR to verify catheter position
- Oncologist localises treatment volume on CXR using 1cm scale on RMW
- Length and prescription dose determine dwell time at 5mm increments
- Treatment prescribed and microselectron machine programed



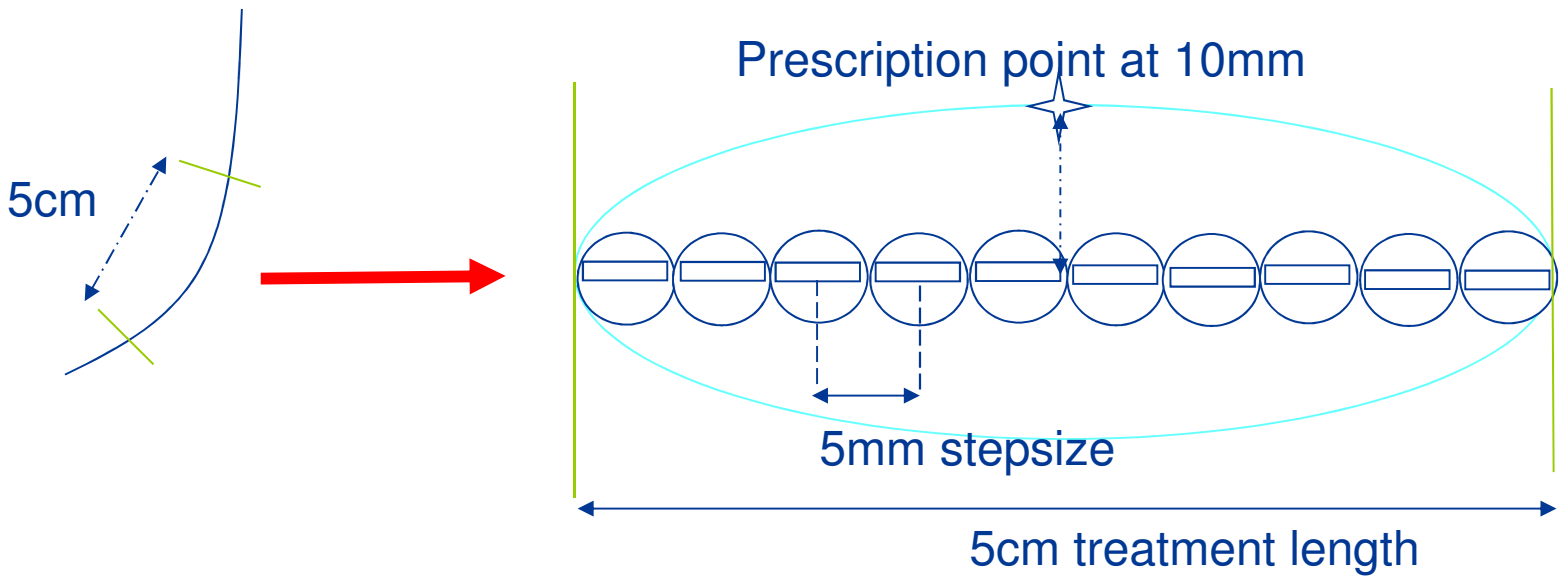
Treatment “Planning”

- Oncologist localises treatment volume on CXR based on bronchoscopy findings
- 1cm scale on Radiographic marker wire (RMW)
- Length and prescription dose determine
- Treatment parameters calculated by hand by 3 independent people



Standard line source plan

- Dwell time is the same for each source position
- 5mm stepsize between dwells
- Cigar shaped 100% dose distribution
- 10.5 cm^3 treated - Small area - Large dose



Dwell times from BT.4.22

Table 1. Dwell times for Source Serial Number D36E4576
(Reference Strength: 10.58 µGy.s^{-1} on 9th November 2012 at 15:00)

Doses prescribed at 10 mm from axis

Lengths (cm)	Dwell times (in seconds) for: -			
	750cGy	800cGy	1000cGy	1500cGy
4	14.6	15.6	19.5	29.2
5	13.7	14.6	18.3	27.4
6	13.1	14.0	17.5	26.3
7	12.8	13.6	17.0	25.5
8 or 9	12.4	13.2	16.5	24.8
10 to 12	12.1	12.9	16.1	24.1
13 to 17	11.8	12.6	15.7	23.5
18 to 24	11.6	12.3	15.4	23.1

Table 2. Decay correction factors – *November 2012 to February 2013*

14 November 2012	1.048
21 November 2012	1.119
28 November 2012	1.195
05 December 2012	1.276
12 December 2012	1.363

Time per dwell

=14.6* 1.363

=19.9s

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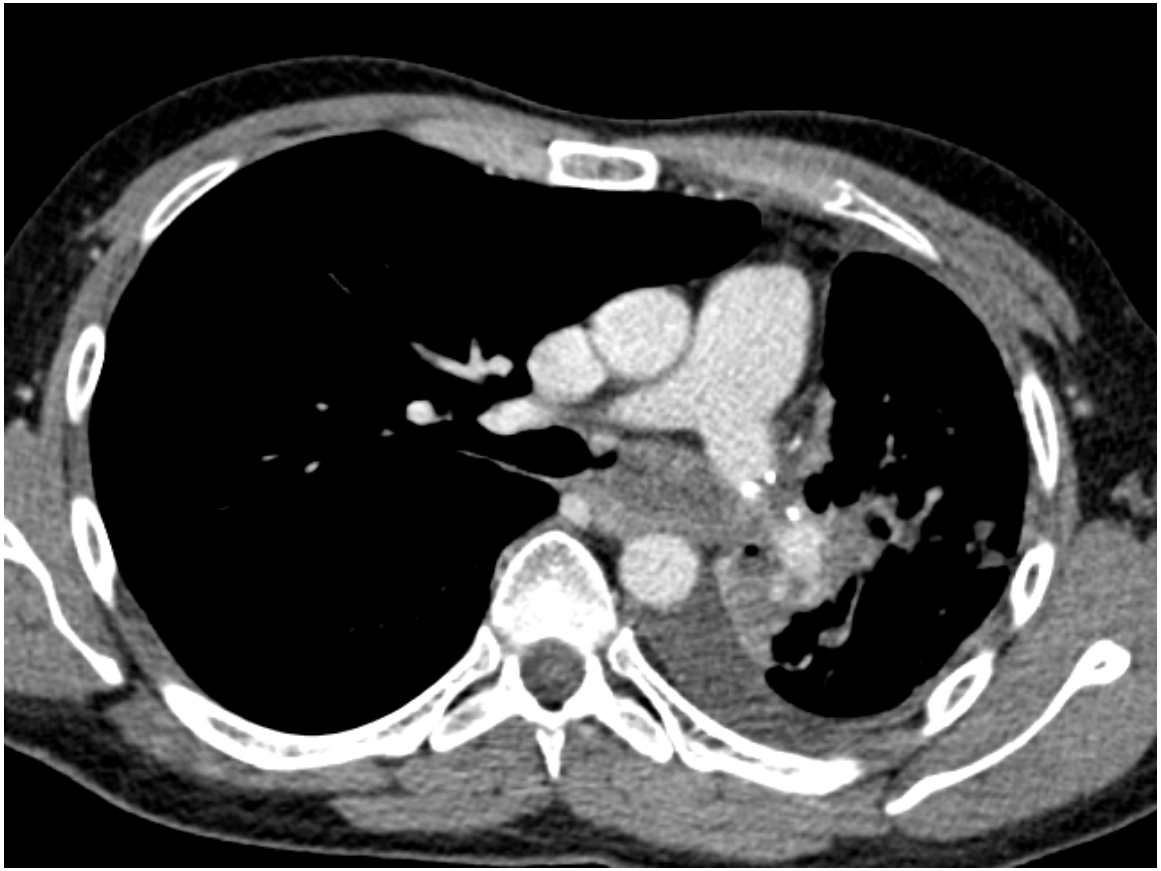
Case

- 42 yo man
- PT2a N2 R0 adenocarcinoma – LUL lobectomy 6/2016. extra capsular spread at stations 5 & 10
- EGFR, ALK-1 neg
- adjuvant chemo completed 8/2016
- declined participation into LUNGART trial

Case

- Recurrence 11/2017
- Airway debulking 12/2017
- referred to med onc for palliative systemic therapy options, ? immunotherapy trial.
- PS 1. PDL-1 95% TPS
- Abdominal and shoulder skin mets rapid evolution



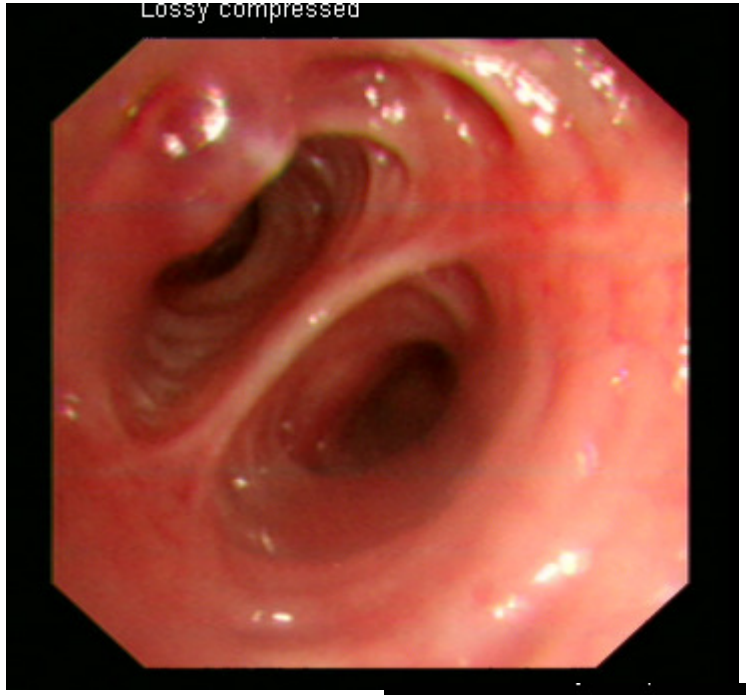
Options?

1. Pembrolizumab
2. Clinical trial
3. Palliative RT
4. More airway debulking
5. Gemcitabine/ carboplatin

Case

- ILT attempt 1/2018 failed. Central occlusive disease
- Referred airway debulking
- Died 2 weeks later before could be debulked.
- CXR- cannonball mets

Case Studies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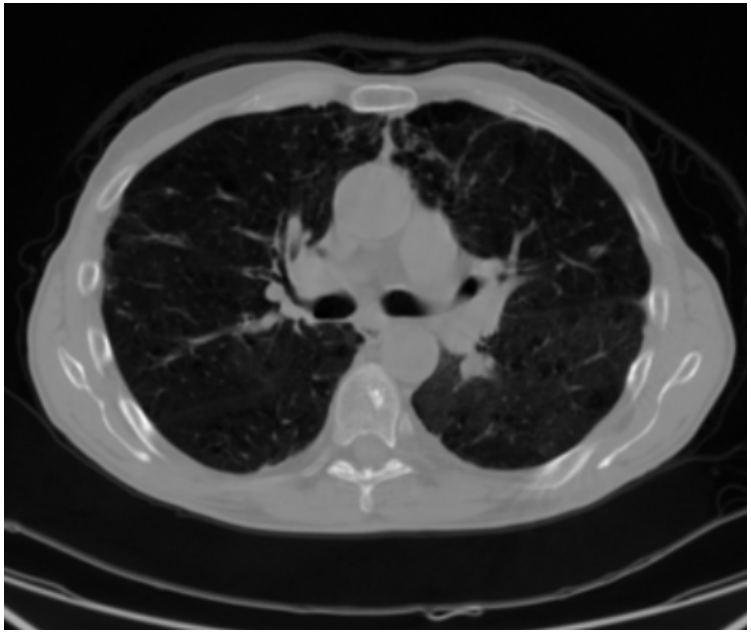

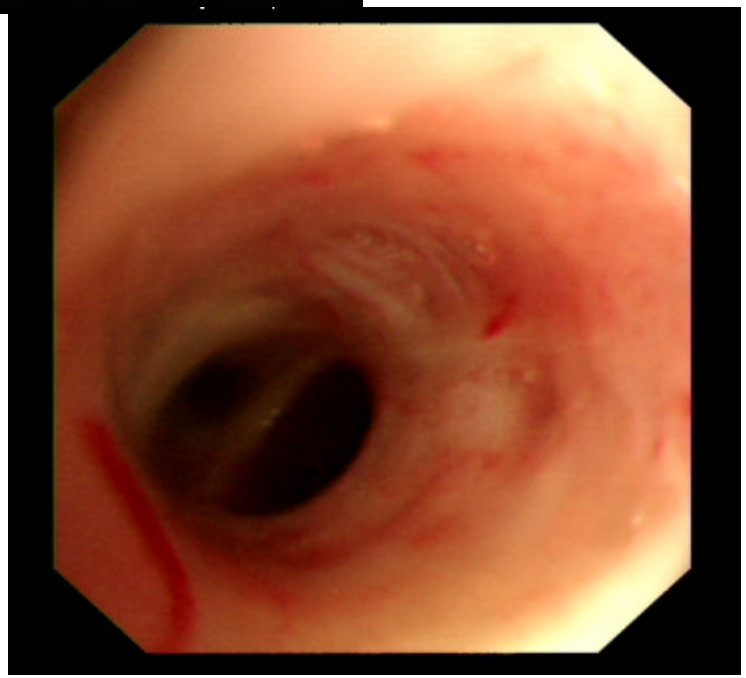

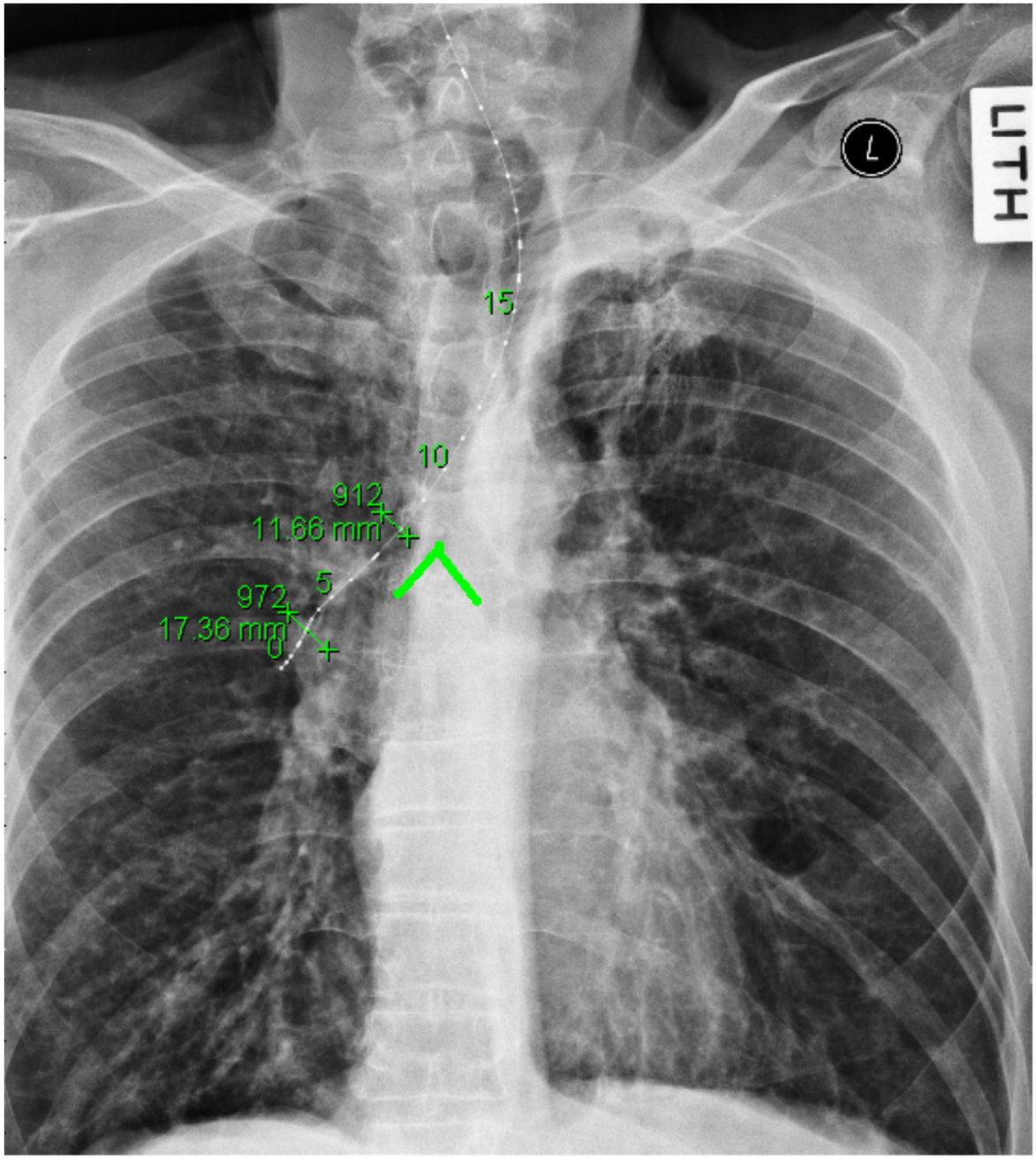

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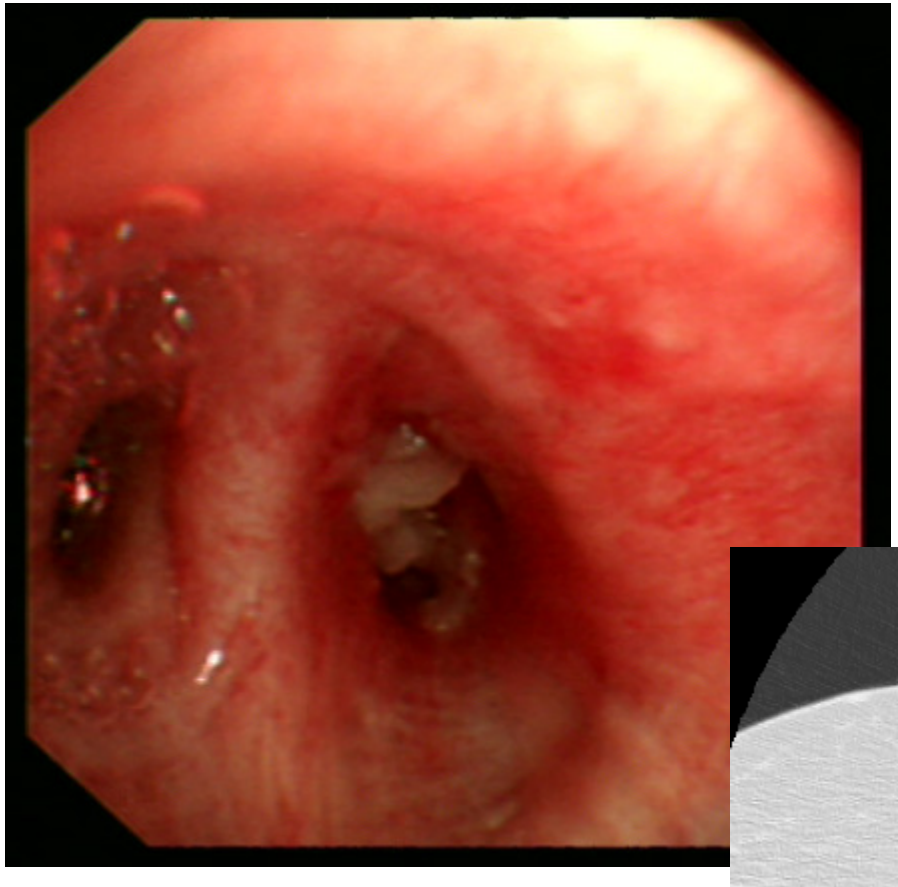

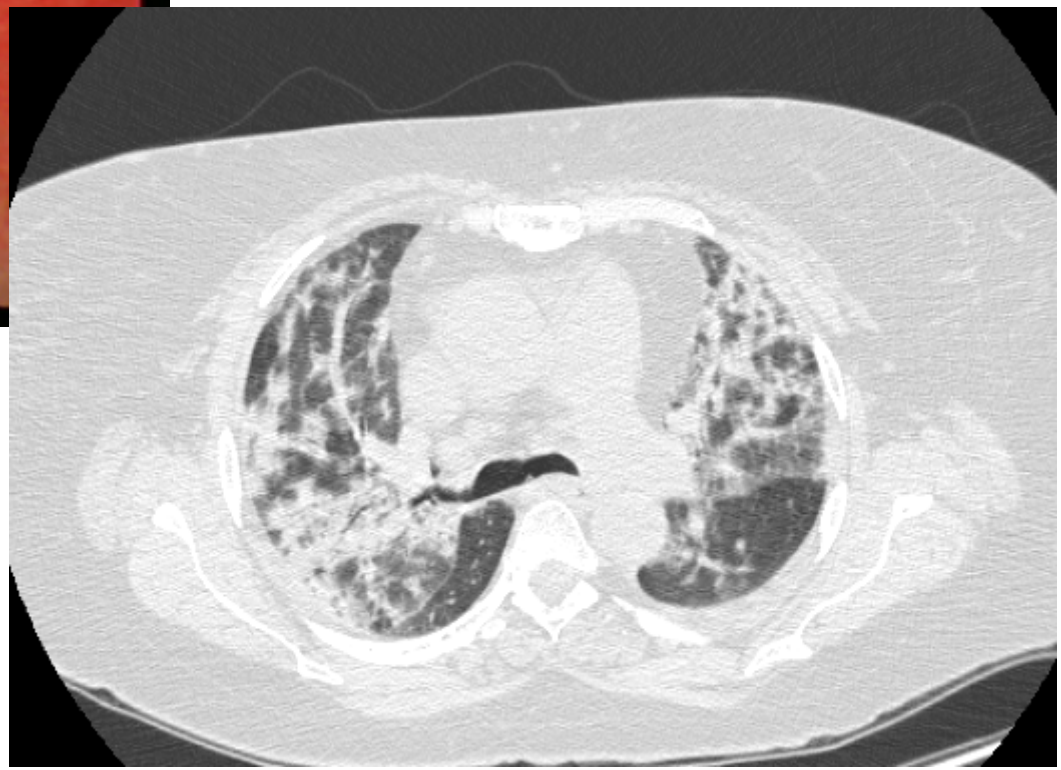

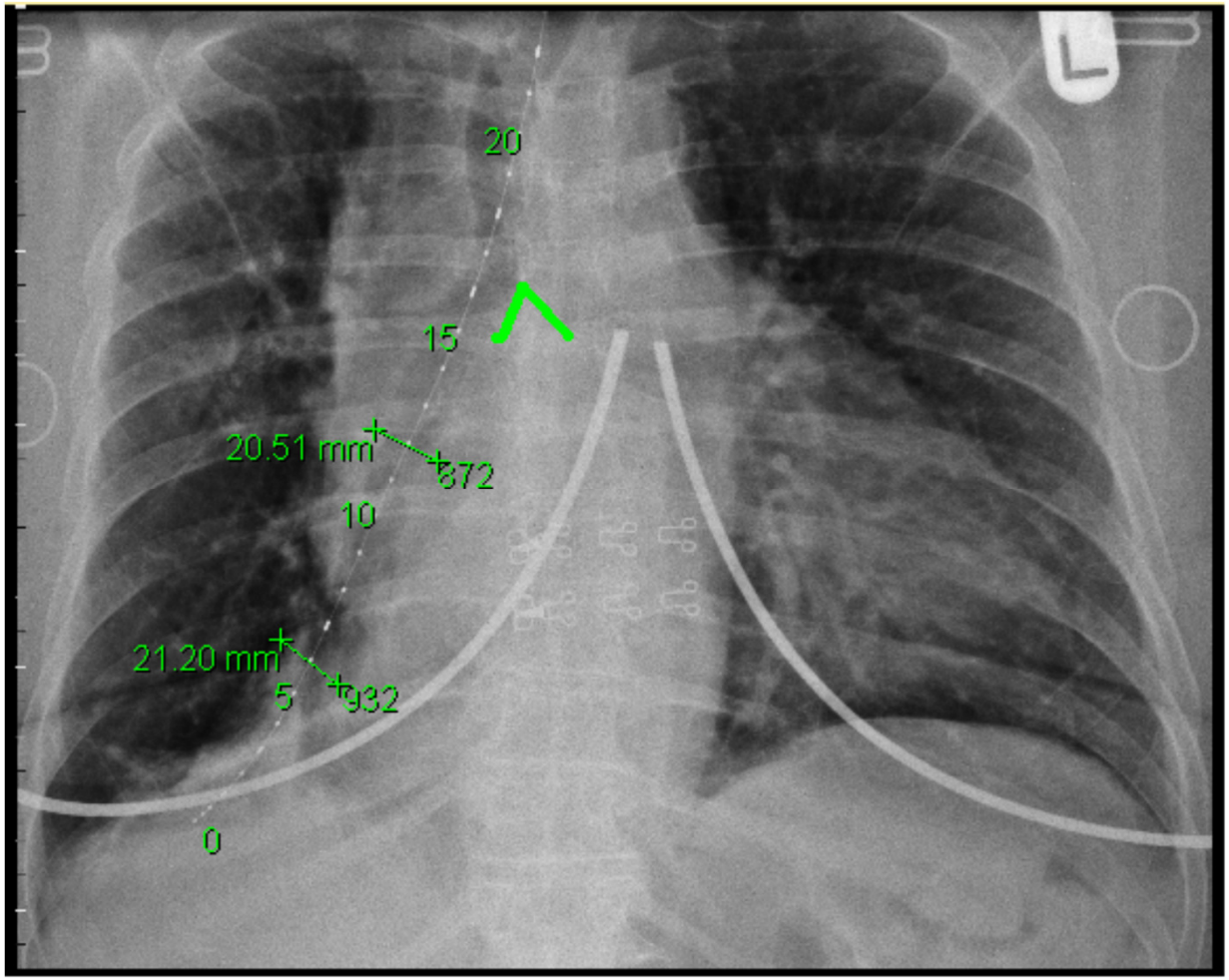

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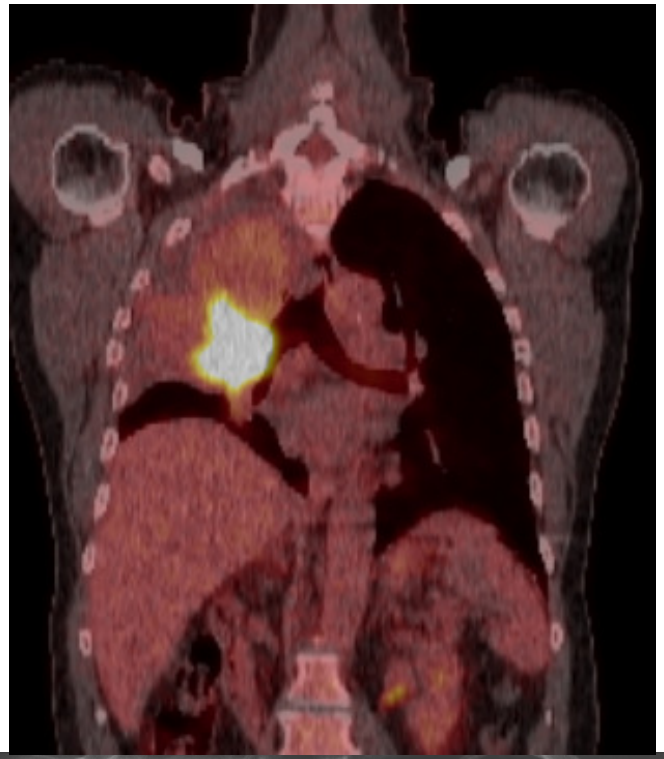

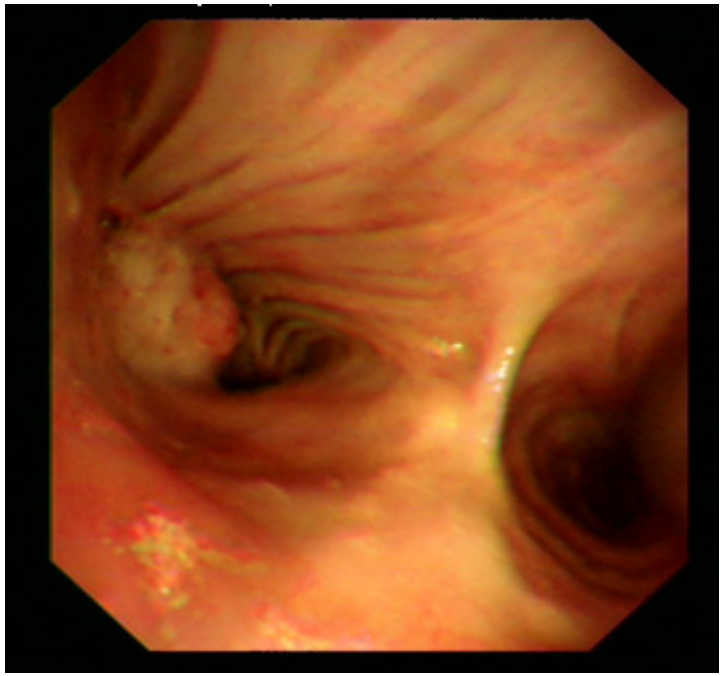

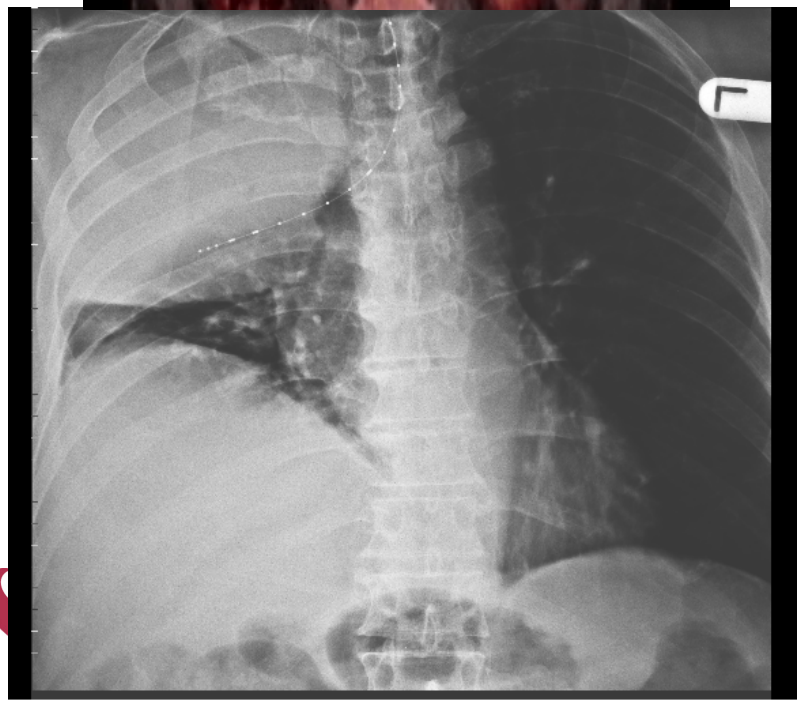

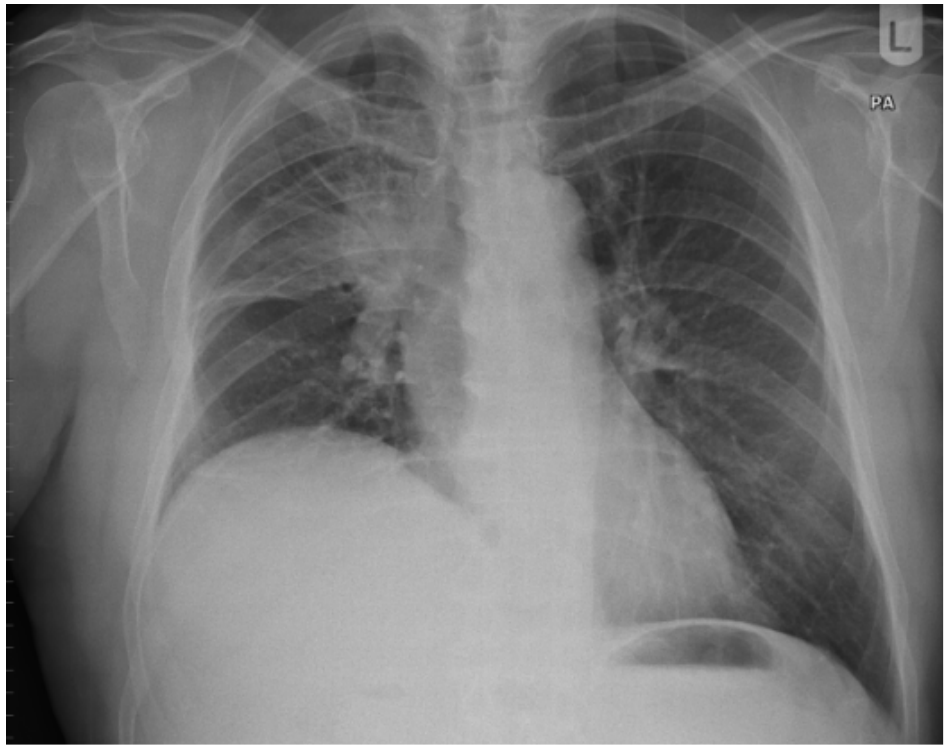
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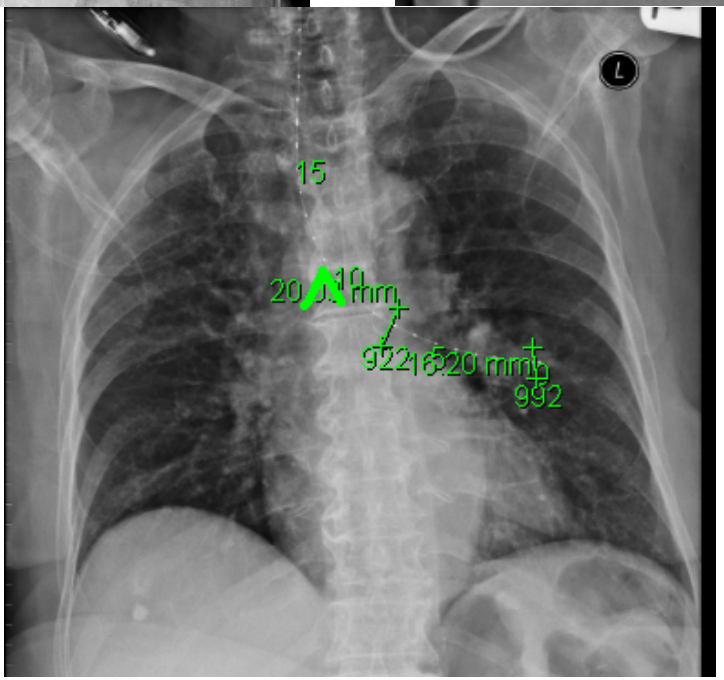

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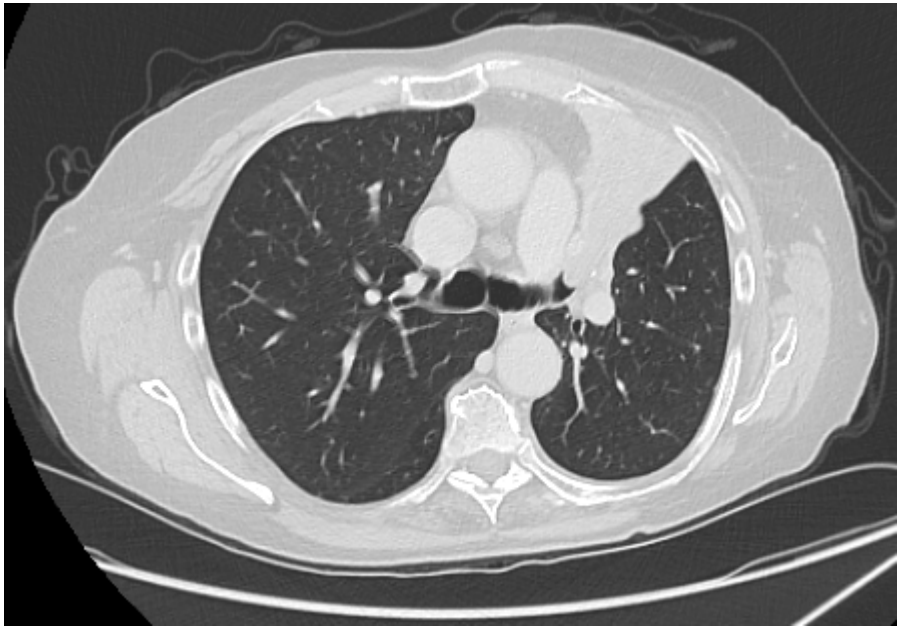

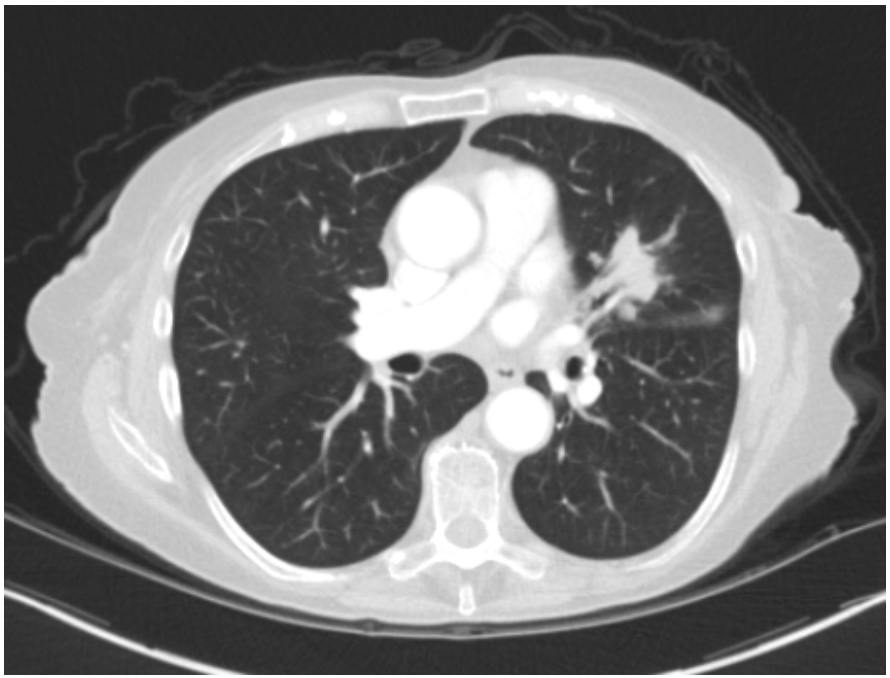

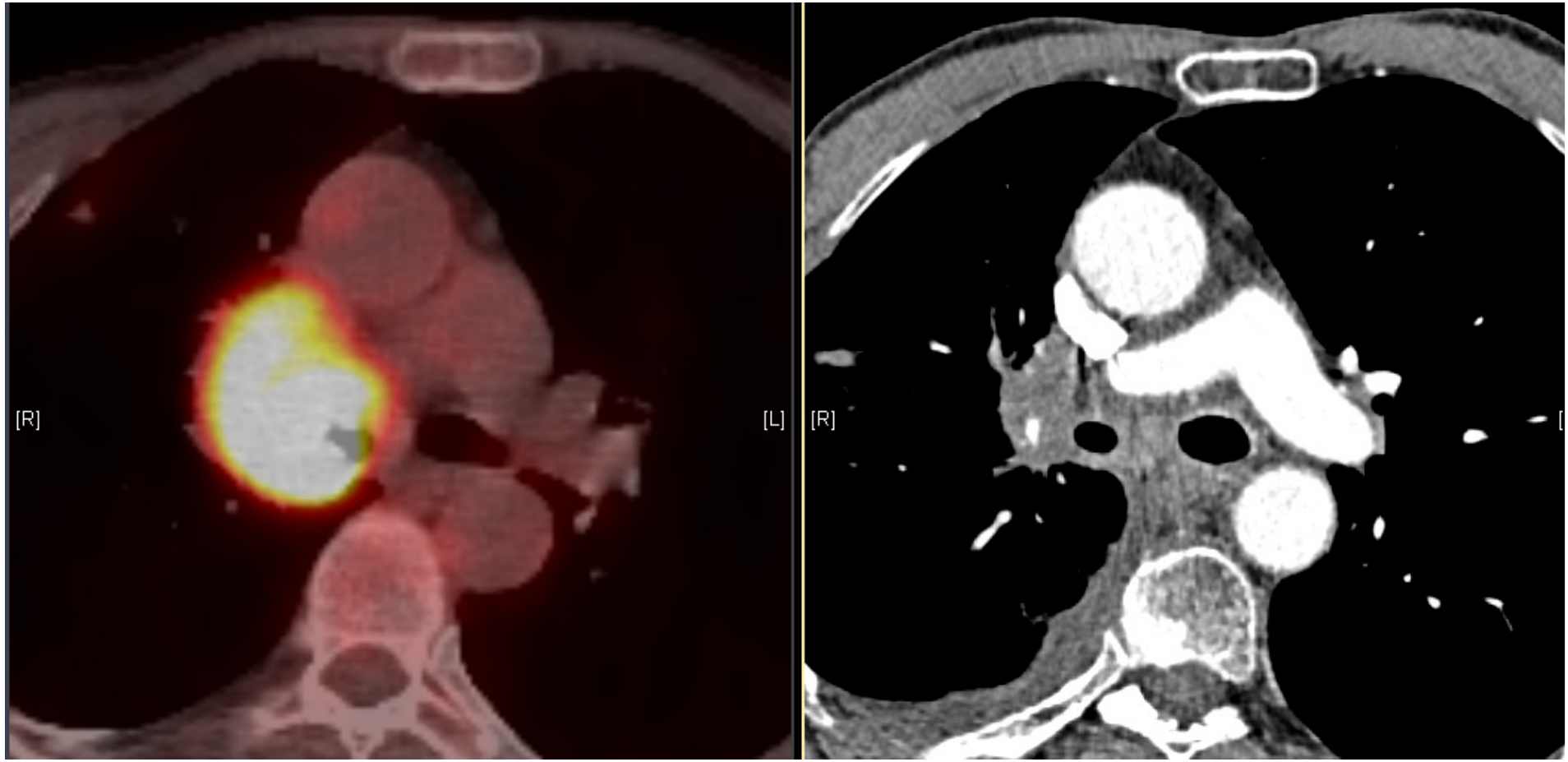
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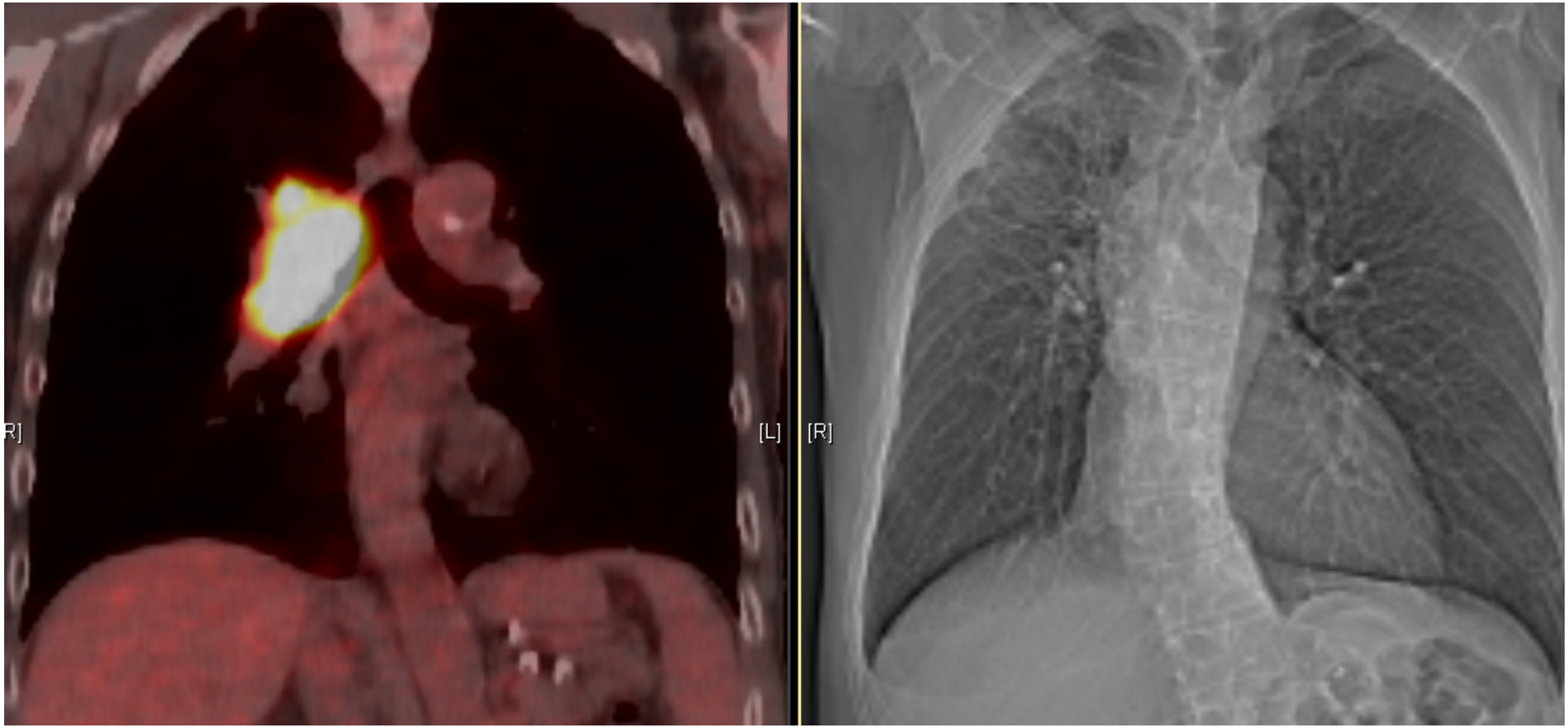
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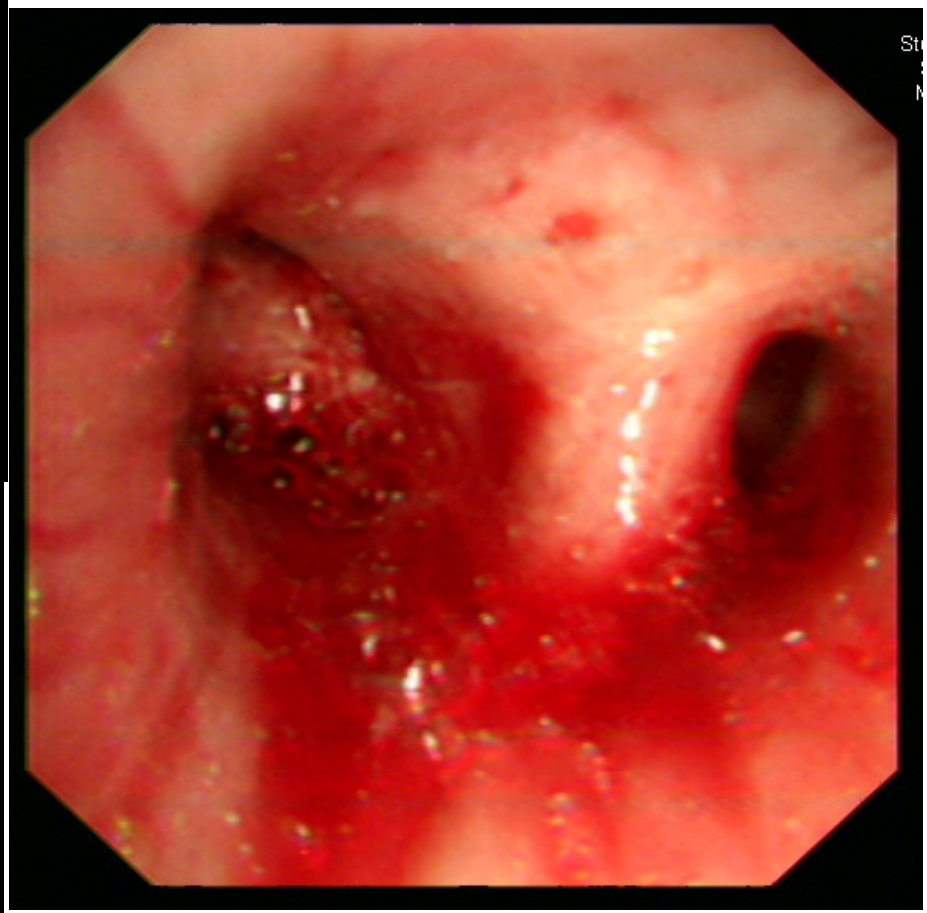

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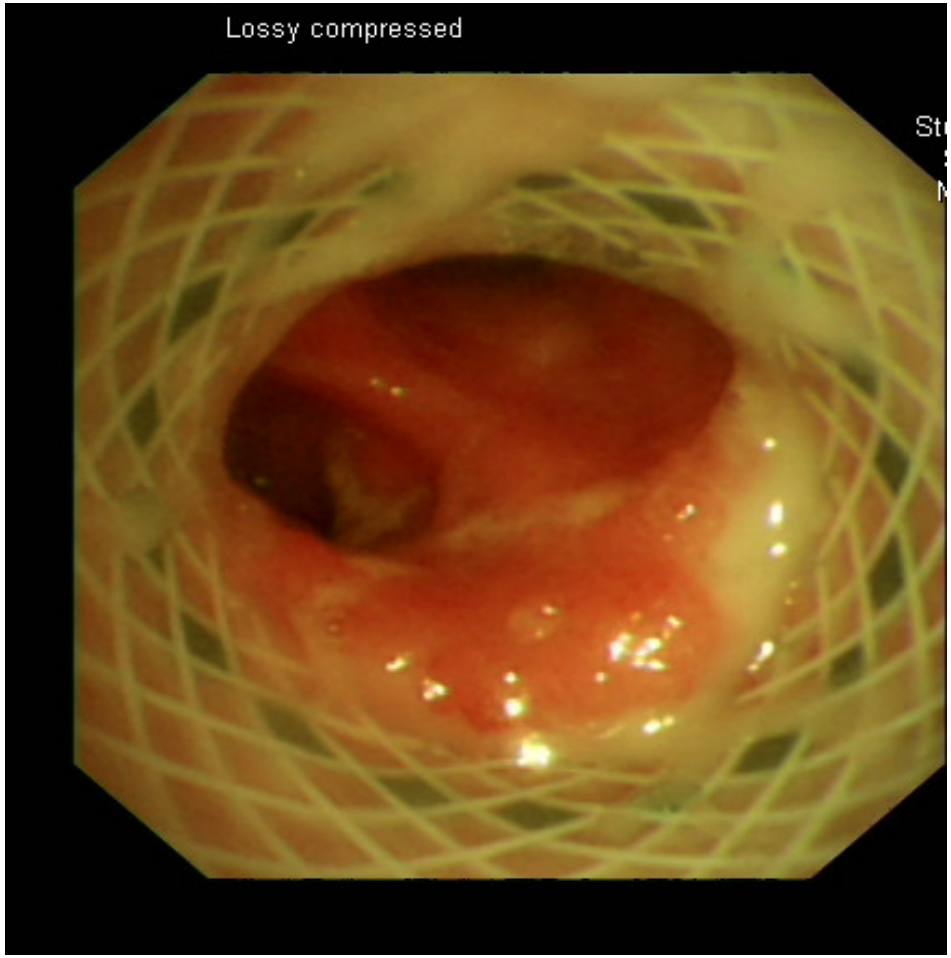
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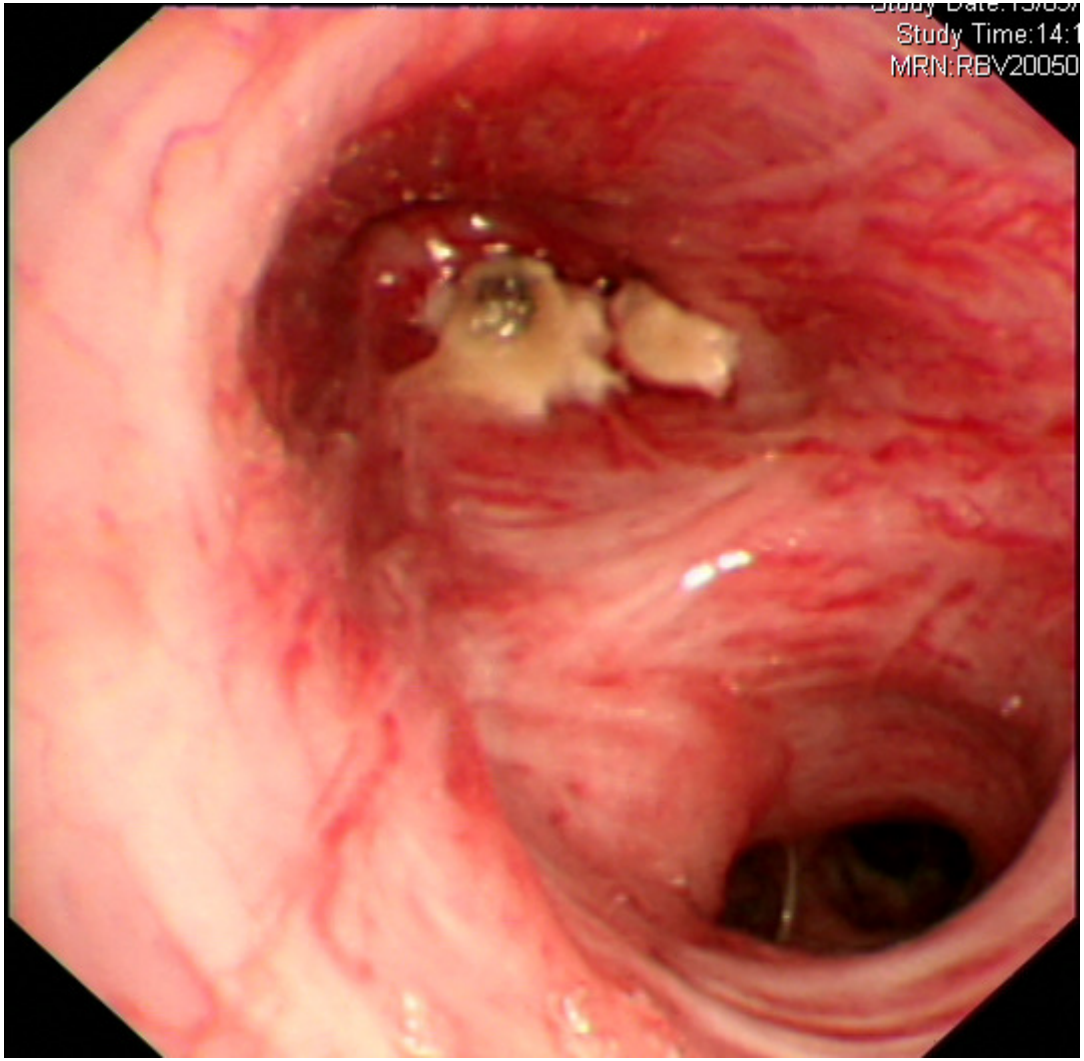
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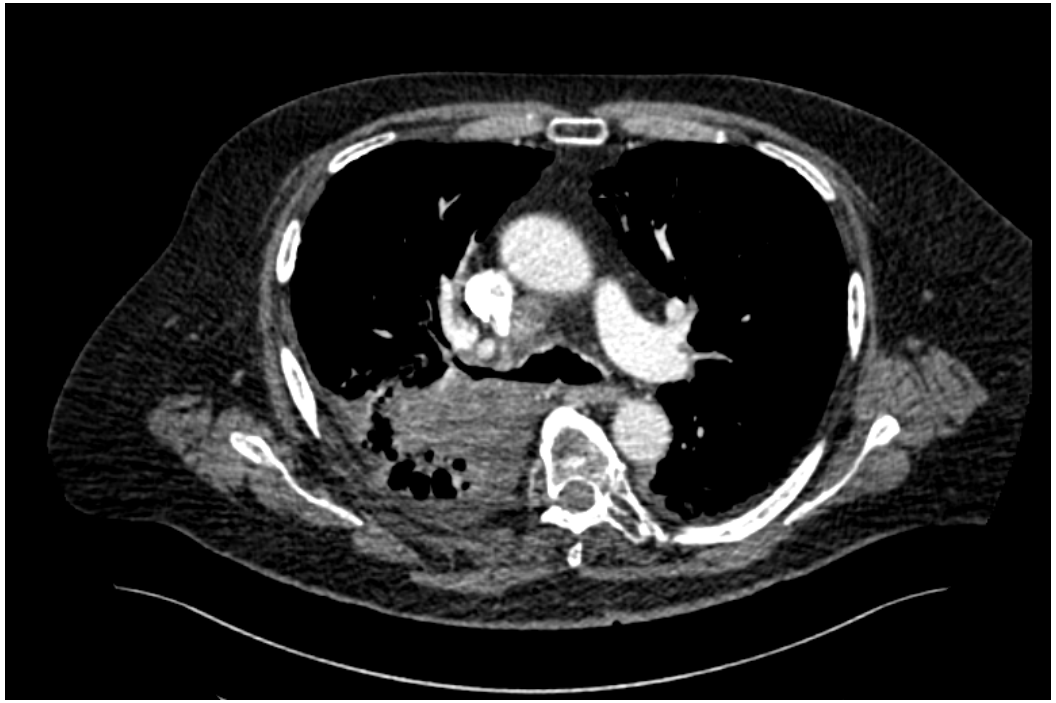
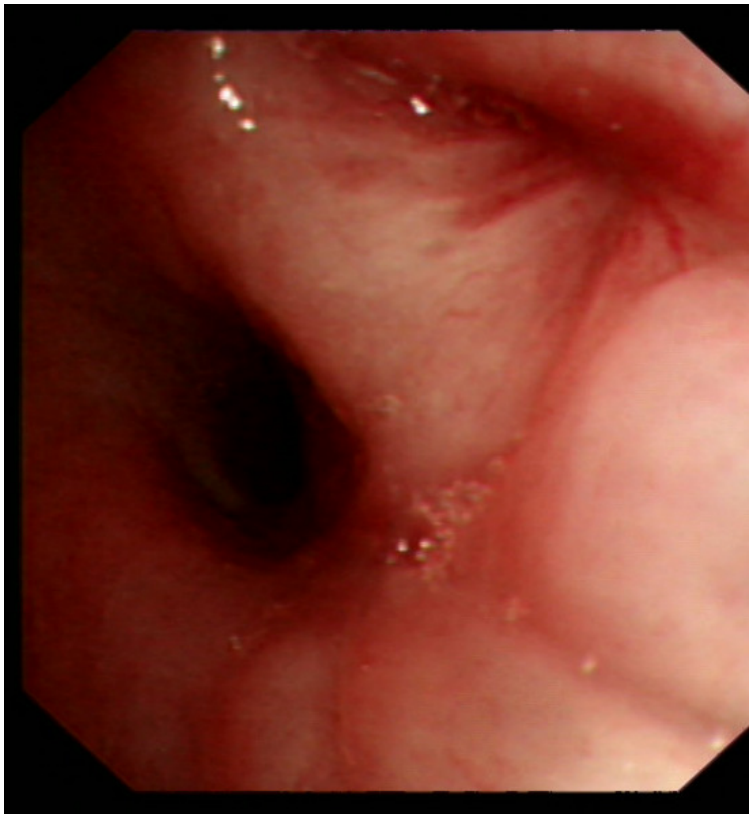
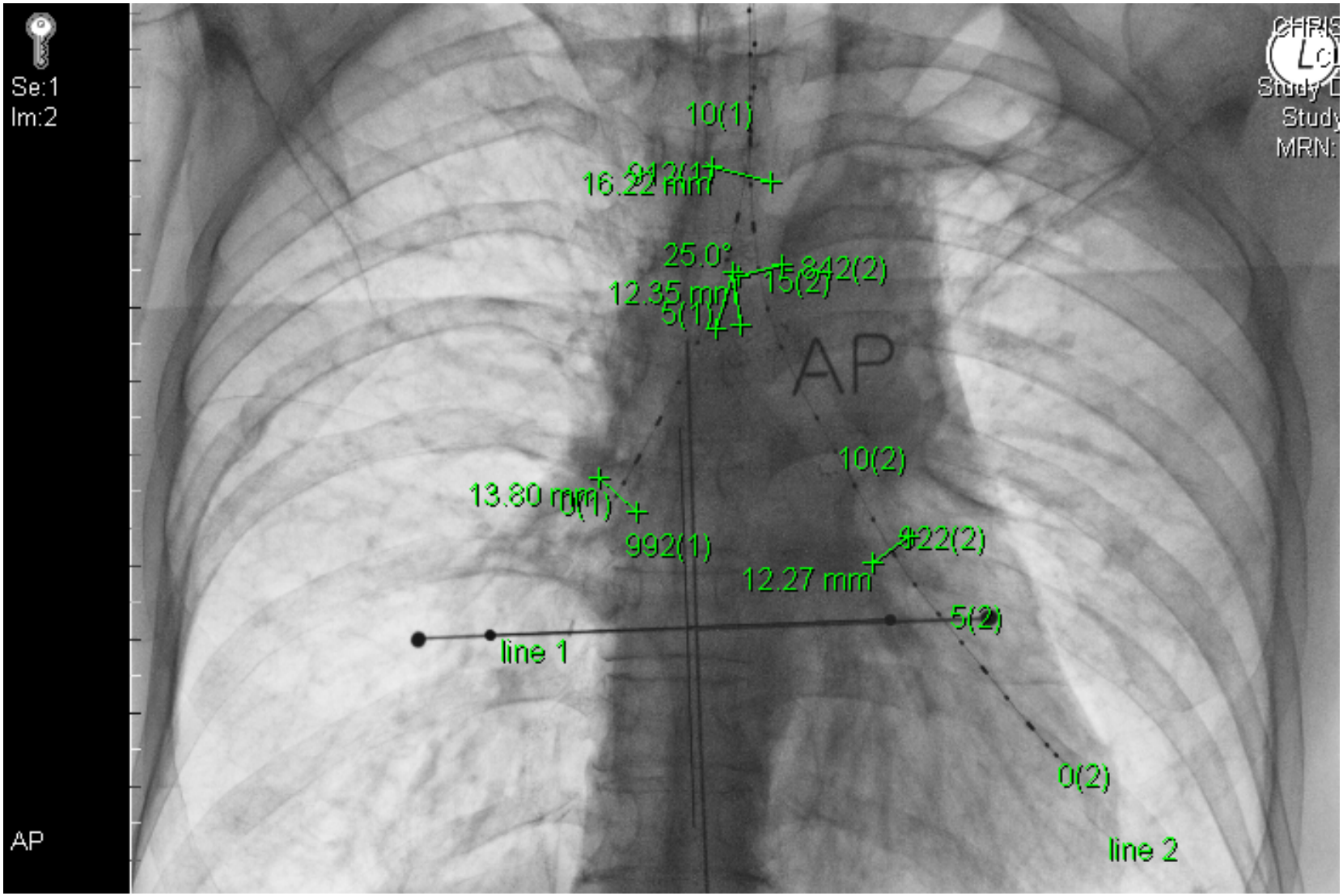




Twin Line Treatments

- Used to treat adjacent lengths of airway
- Bronchoscopy procedure as per single lines.
- A RMW is placed in each catheter, with different markings to enable distinction.



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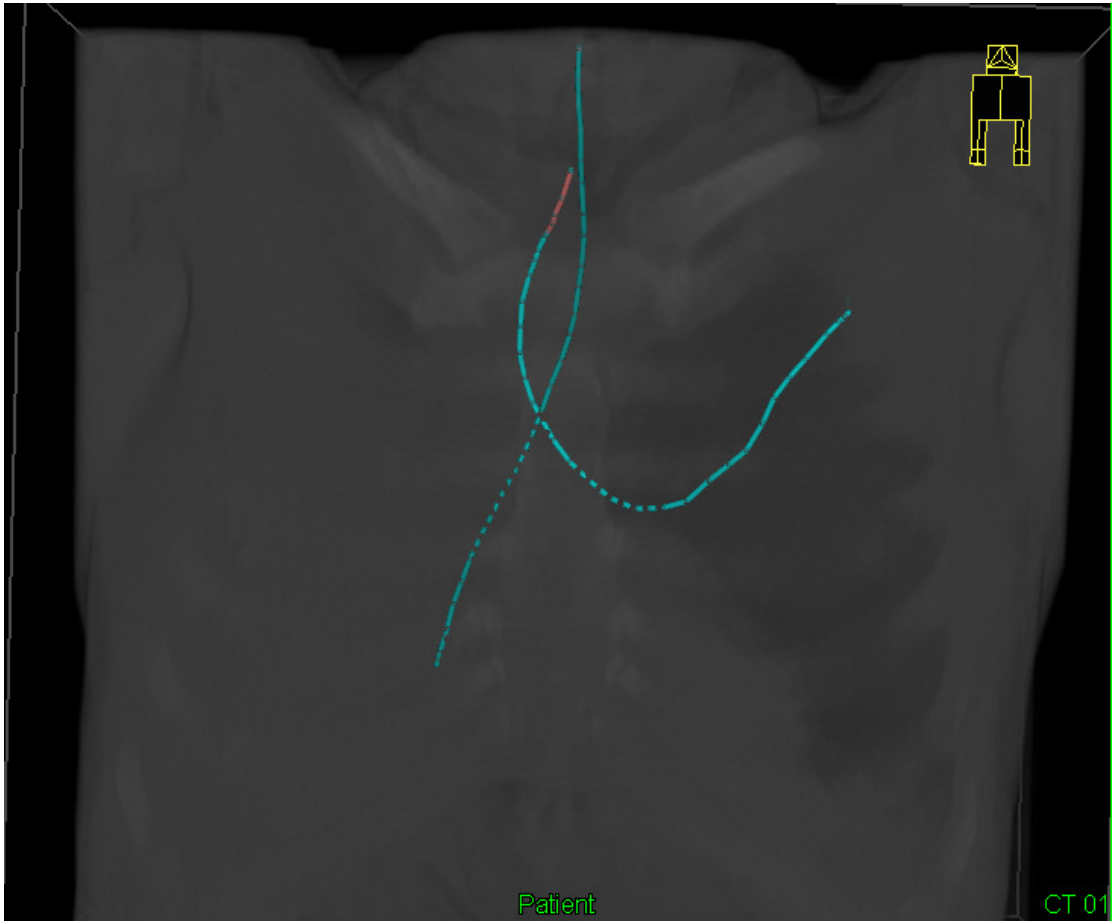
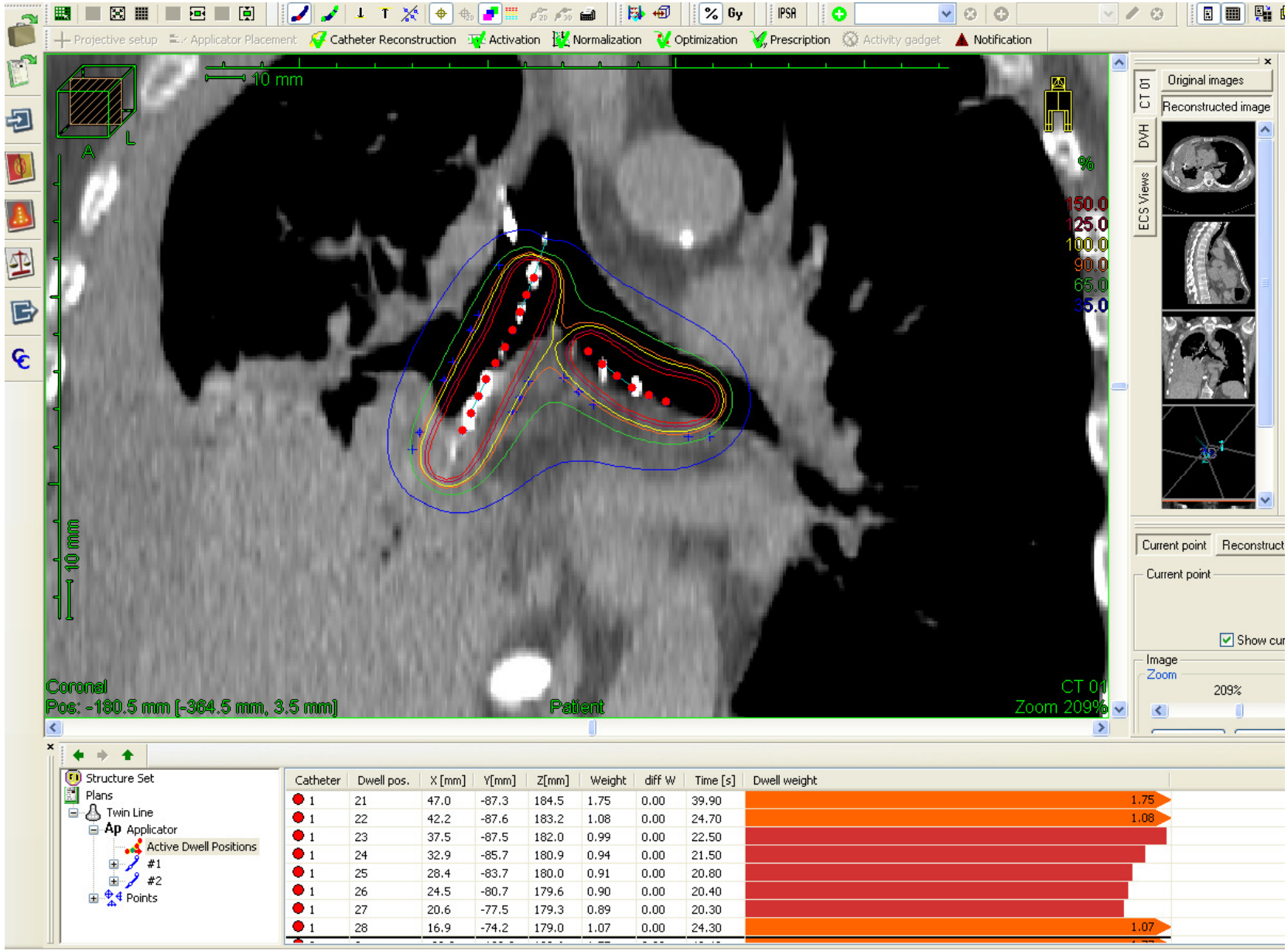
3D Planning

- 3D brachytherapy planning system

Oncentra
By Nucletron

- The catheters are reconstructed on the CT scan and the clinician marks the distal and proximal extent of the treatment for each line





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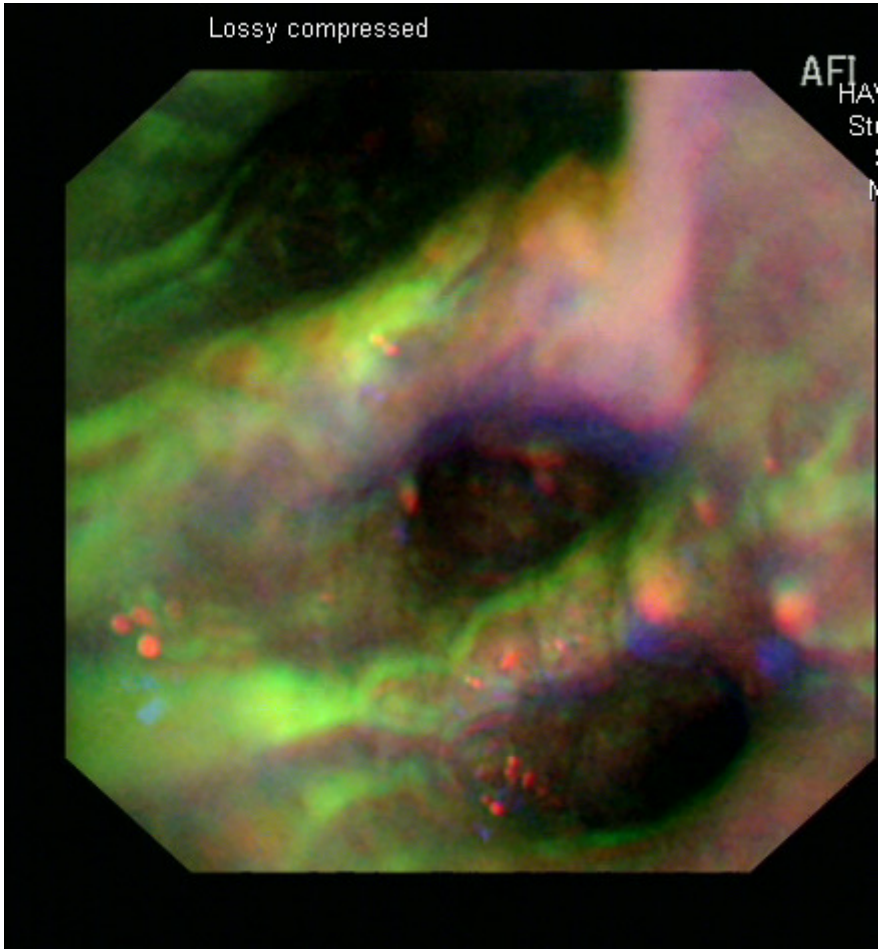
Airway MDT

- tertiary service for pre-treated patients:
  - Recurrence vs fibrosis
  - Biopsies for genetic testing or trials
  - Washings for infection
- ‘medical airway team’ to complement surgical airway team
  - combined specialist input of radiation oncologist and resp medicine, with technical physics team

Fluorescence Bronchoscopy

- Dysplasia, CIS, and microinvasive ca – fluoresce differently when exposed to approp wavelength light – this difference can be detected
- Varying reports on specificity / sensitivity, needs validation



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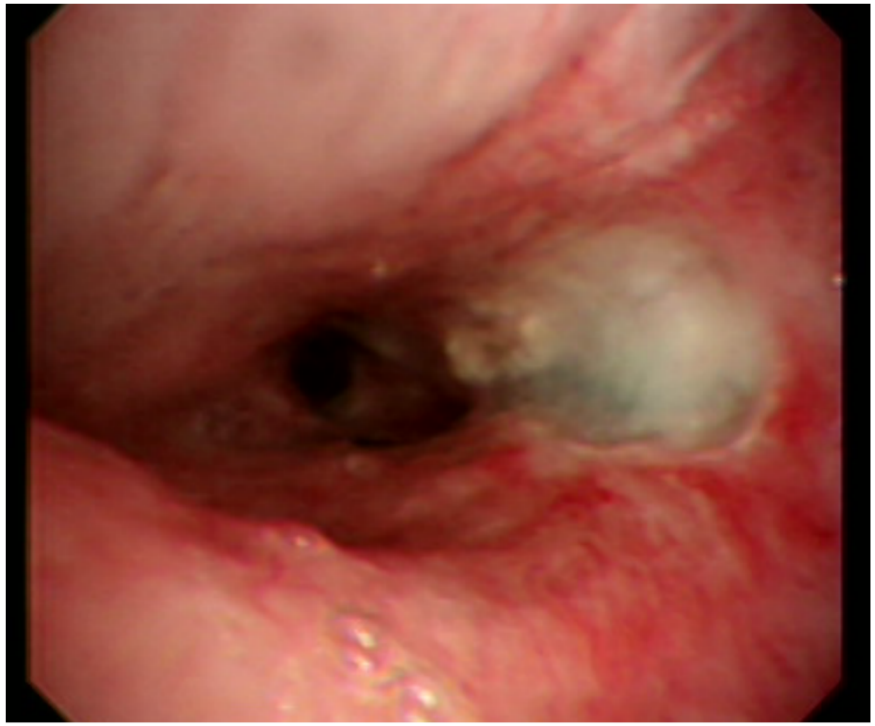

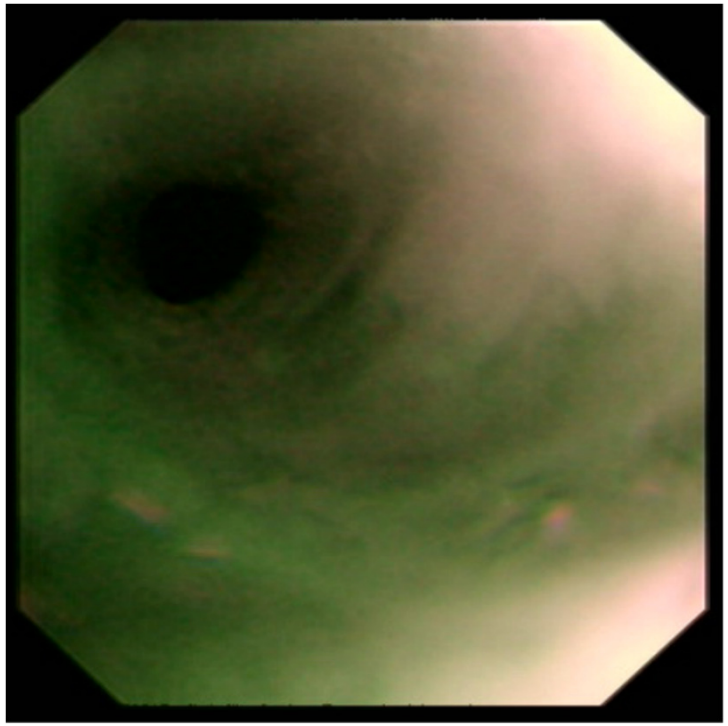

1) Left upper lobe segmentectomy for PT1a N0 NSCLC 9/14

2) RLL apical segment squamous cell ca radical ILT 11/14

3) Post radiation ulcer in RBI

Centre devices

- balloons, cages, or sheaths, can be employed to maintain the radioactive source within the centre of the bronchial lumen and avoid dose inhomogeneity

Summary

- Consider ILT for patients with symptomatic endo-luminal disease
- Palliatively:
  - adjunct to chemo
  - +/- EXBRT
  - following surgical airway Mx
  - relapse following previous chemo/ RT
- Radically:
  - early stage/ CIS limited to airway
  - as prelude to EXBRT if collapse
  - ? For +ve bronchial RM
  - ?? For non-resectable carcinoid

Summary

indication

- located in trachea, MB or LL (accessible)
- intrinsic tumour essential, some extrinsic compression and submucosal infiltration
- Lumen wide enough to accept catheter
- Survival expected >3 months

Relative contra-indication

- High grade airway obstruction
- Close proximity to large BV/ invasion
- Destruction of bronchial wall/ fistulation
- Unfit for bronchoscopy

Dr Hamid Sheikh **07515 358361**
Dr Clara Chan **07771 957119**

Hamid.sheikh@christie.nhs.uk
Clara.chan@christie.nhs.uk

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