Intraluminal Brachytherapy in Oesophageal Cancer

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Introduction

- Intraluminal BT effective and well tolerated
- Delivers tumoricidal doses to superficial lesions while sparing surrounding tissue
- 1980-1990 ILBT was a common treatment option in curative treatment of oesophageal cancer
- RTOG 9207 suggested dose escalation with BT resulted in significant toxicity-high radiation dose to mucosa with no survival benefit
- Use of ILBT gradually declined
- Role in locally advanced,recurrent,non surgical candidates
- Positive oncologic/palliative outcomes can be achieved optimizing BT with 3D CT based treatment planning

Rationale of Brachytherapy in Oesophageal Cancer

- Chemoradiotherapy /Trimodality combining CTRT and surgery standard of care for localised lesions
- High local failure post treatment
- Advance disease at presentation
- Location to nearby critical structures limit delivery of therapeutic dose
- Non surgical candidates
- Elderly and co morbidity
- Recurrent disease after prior external beam radiation therapy
- Dose delivery is dependent upon inverse square law
- Radiation to critical structures (spinal cord,lung,heart) is therefore minimal allowing precise dose delivery in several large fractions
- Easy access by endoscopic procedure

Treatment Goal

- Definitive treatment(boost) for superficial primary tumour for non surgical candidates after CTRT- Limited indications
- New indications are emerging
- Salvage for locally recurrent oesophageal cancer following CTRT +/- surgical resection

- Palliative treatment for patients with advanced/metastatic disease

ABS Guidelines-Selection criteria for definitive brachytherapy

Good candidates

- Primary tumor ≤ 10cm in length
- Tumor confined to oesophageal wall
- Thoracic oesophagus location
- Absence of regional lymph node and distant metastasis

Poor candidates

- Extraoesophageal extension
- Regional LNP
- Tumor involving GE jn and cardia

Contraindications

- Oesophageal fistula
- Cervical location
- Stenosis which cannot be bypassed

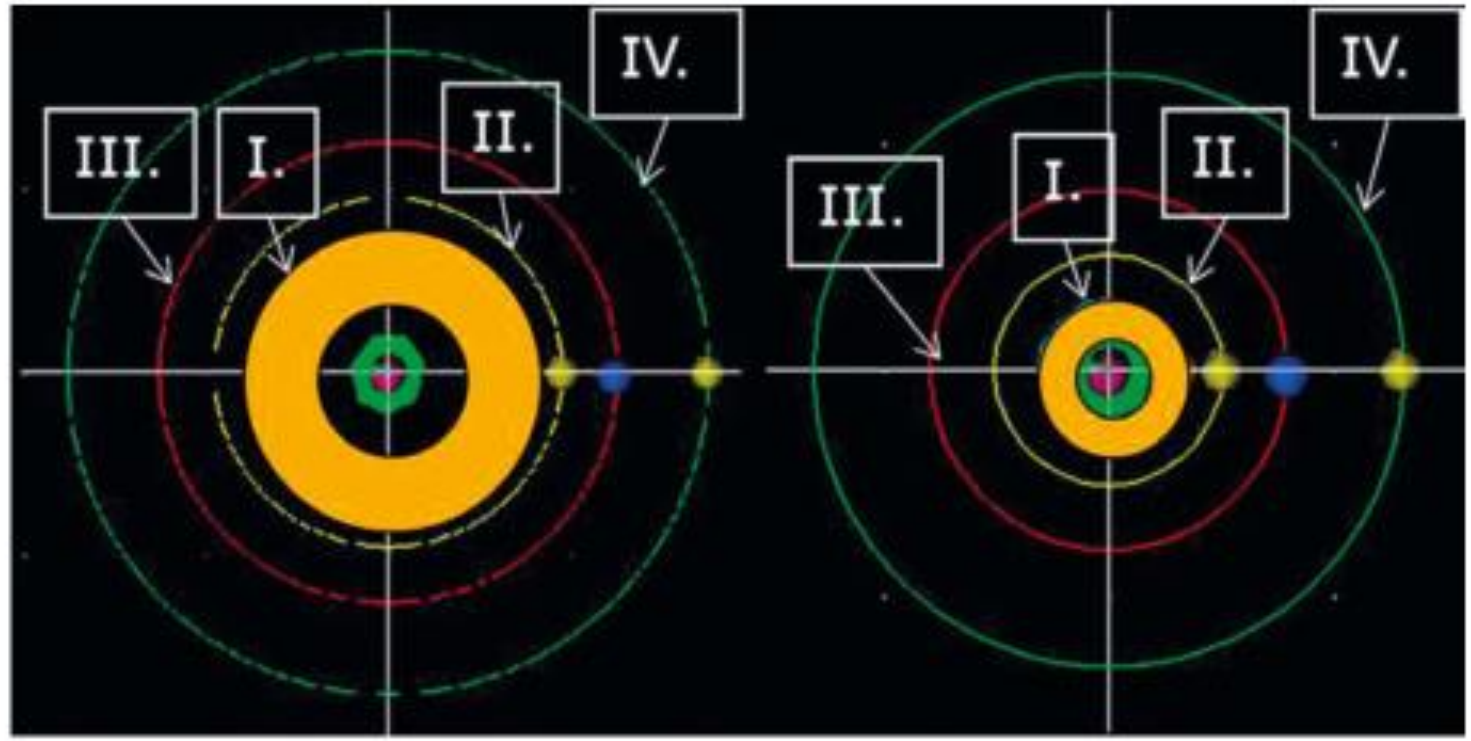
Patient selection and clinical implementation –Modified ABS recommendations

- **Indications curative**
  - Unifocal thoracic adeno- or squamous cancers
  - Maximum length 10 cm
  - No evidence of intra-abdominal or metastatic disease
- **Contraindications**
  - Tracheal or bronchial involvement
  - Cervical esophagus location
  - Stenosis that cannot be bypassed
- **Guiding principles**
  - Applicator should have an external diameter of ≥ 10 mm
  - Avoid giving chemotherapy concurrently
- Brachytherapy **should** follow external beam radiation therapy
- **Dose recommendations** (3-4 weeks after 50-60 Gy EBRT)
- HDR 10-12 Gy in two weekly fractions of 5-6 Gy each

Applicator and Dose prescription

- Applicator should have an external diameter of 6-10 mm
- Narrower(<0.6cmin diameter)deliver significantly higher dose to mucosa
- Larger caliber>1cm associated with perforations
- Dose prescription 1cm from mid source or mid dwell position
- Brachytherapy should follow external beam radiation therapy
- Dose recommendations (3-4 weeks after 50-60 Gy EBRT)
- HDR 10-12 Gy in two weekly fractions of 5-6 Gy each

- Dose distribution in relation to applicator diameter.



Workflow

- Pretreatment preparation

✓Comprehensive evaluation

✓ Applicator preparation and placement

✓Planning imaging

✓Target delineation

- Treatment planning

✓Contouring

✓Catheter reconstruction

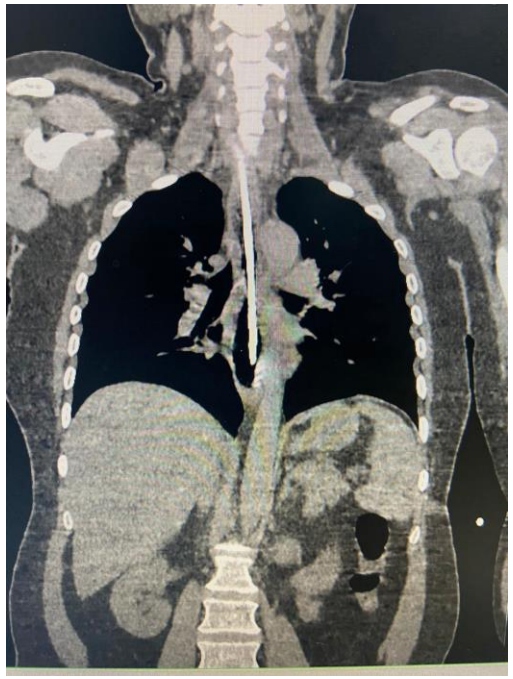
✓Optimization

✓Plan Approval and export

- Treatment delivery

ILBT Technique

- Under sedation, the endoscopy is performed to visualize the tumour, and the proximal and distal borders of the tumour are marked with metal clips
- If there is marked stenosis, a dilation procedure should be performed to allow insertion of an applicator of sufficient diameter (≥ 10 mm)
- If this cannot be achieved in a single session, the brachytherapy should not be attempted and the patient should be scheduled for a second appointment.
- Once insertion of an appropriately sized applicator seems practical, the endoscope is removed leaving a guide wire in situ



- The applicator is then inserted into the oesophagus over the guide wire, and under fluoroscopy, the radiopaque marker ring at its distal end is made to overlie the metal clip marking the distal border of the tumour
- With the applicator position thus defined, it is then secured at the level of the patient's mouth with the help of a bite block
- Under sedation, the patient is then transferred to the CT scanner with the applicator in situ

Treatment planning

- Applicator based
- Reference isodose placed at 5mm tissue depth
- 2cm margin for microscopic disease and spatial inaccuracy of applicator position
- Cylinder shaped target volume,anatomical relations not accounted

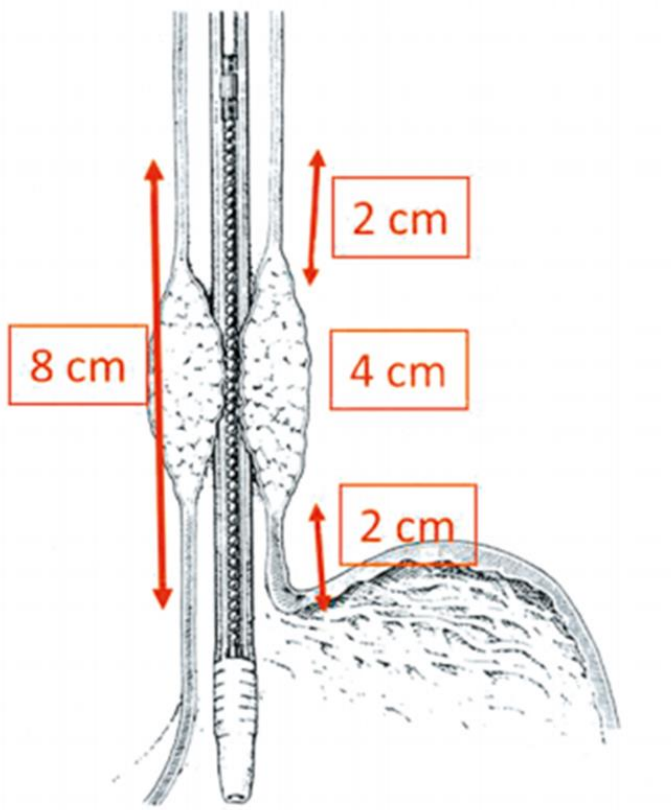
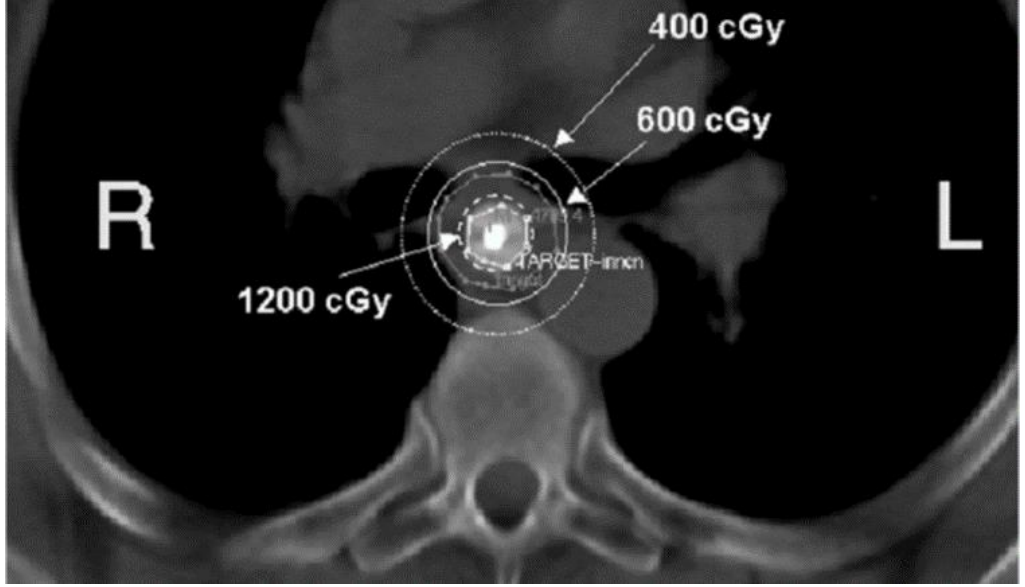
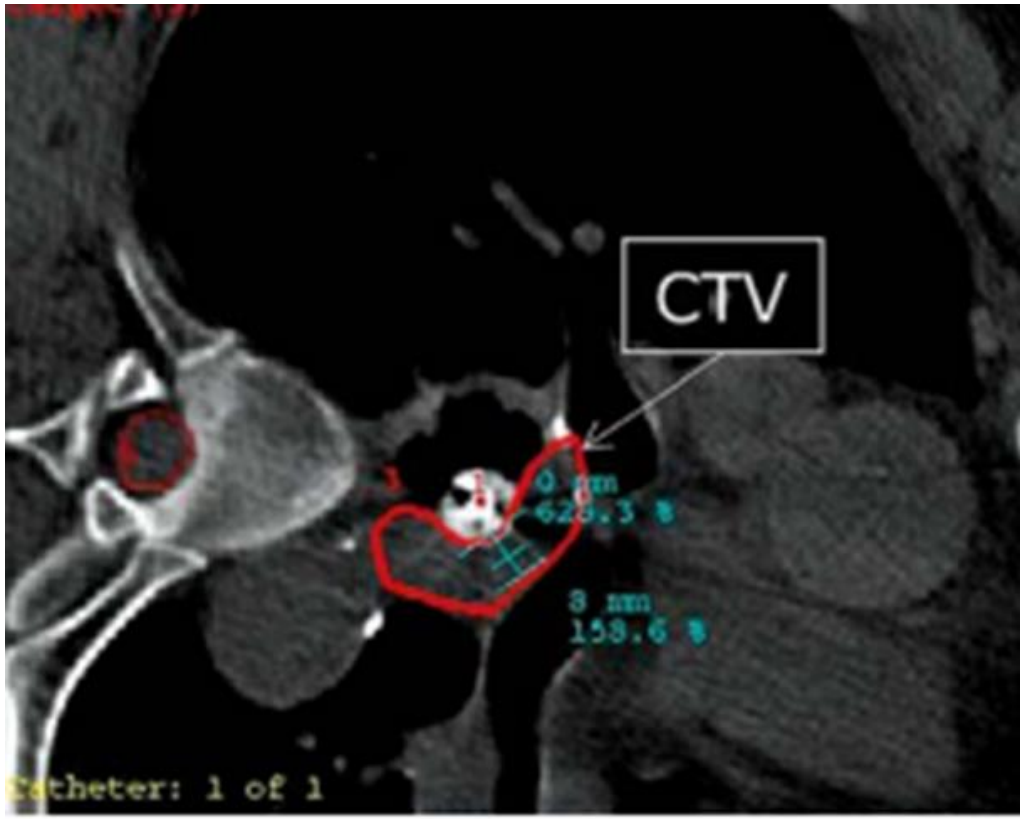


Fig. 4. Diagram showing definition of the target volume using the applicator-based approach to treatment planning

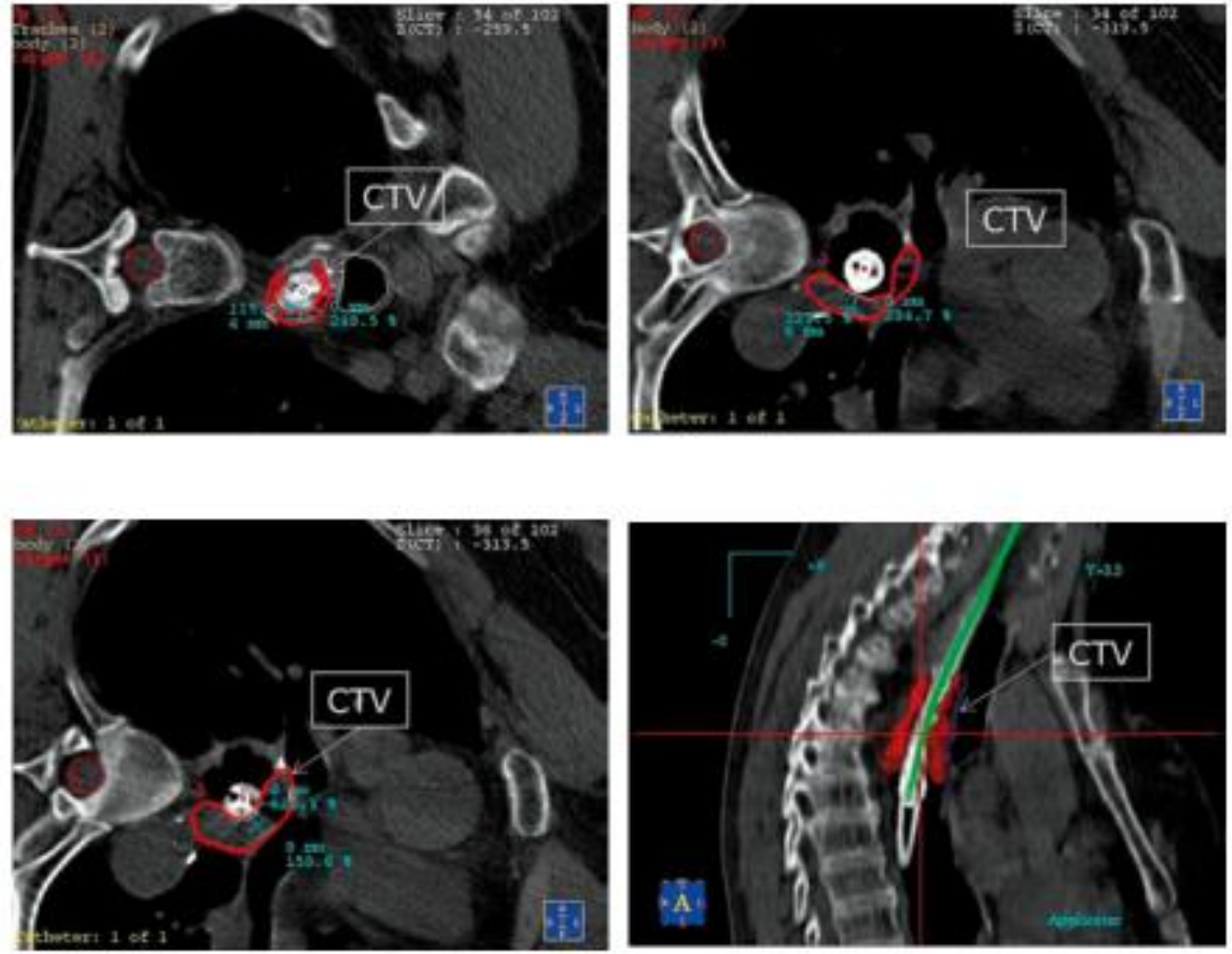


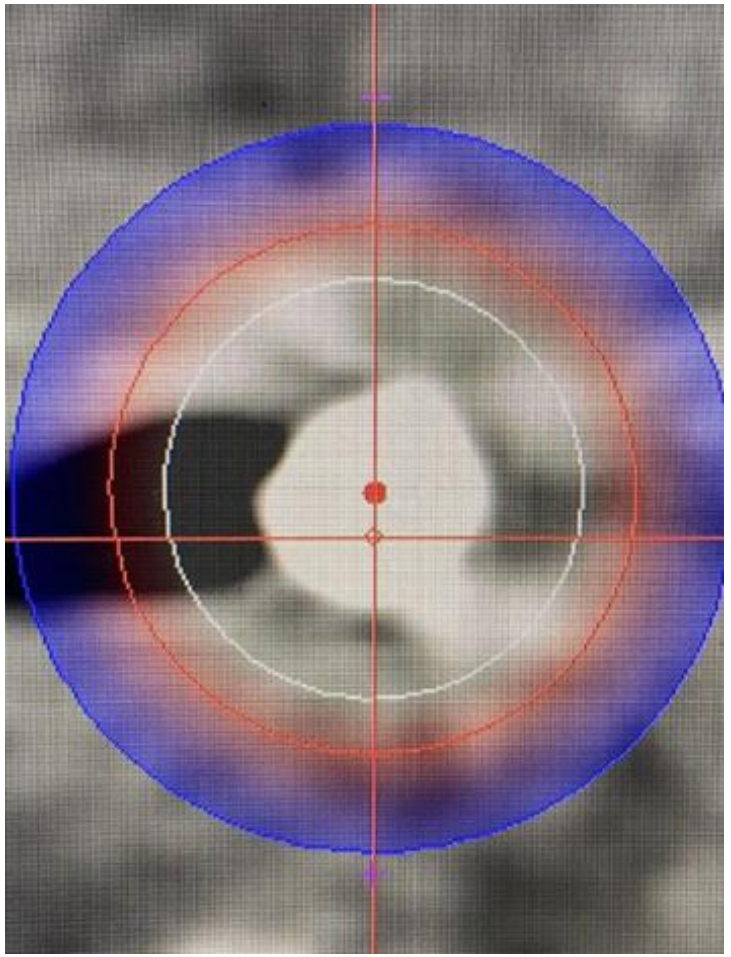


Treatment Planning

- CT based treatment planning
- CTV & OAR contoured
- Dose constraints D90 V100 respected
- Allows varaiation shape size of reference isodose in all directions improving tumor coverage and sparing of OAR

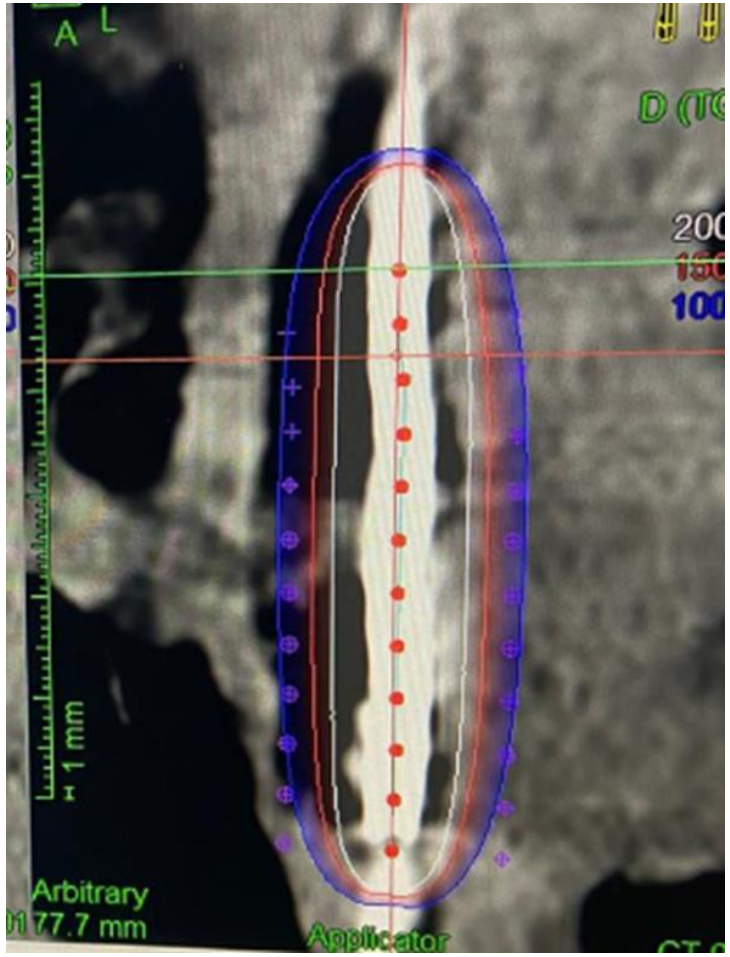
Planning CT scan with applicator in situ showing anatomical relations and contours of the CTV

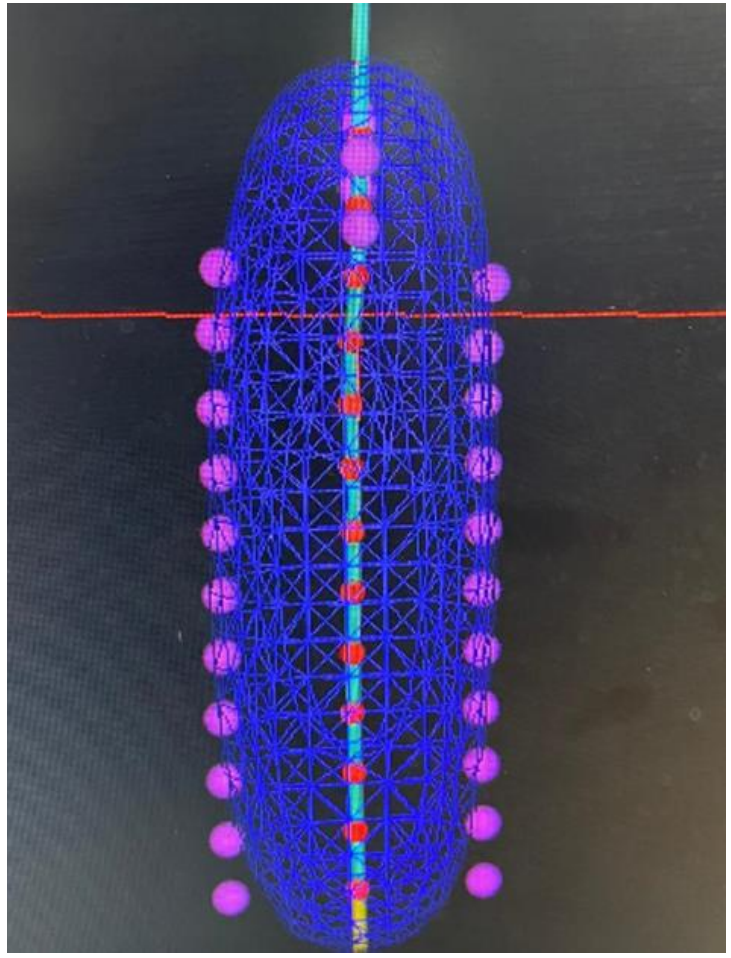




Catheter reconstruction and normalization

Treatment Planning





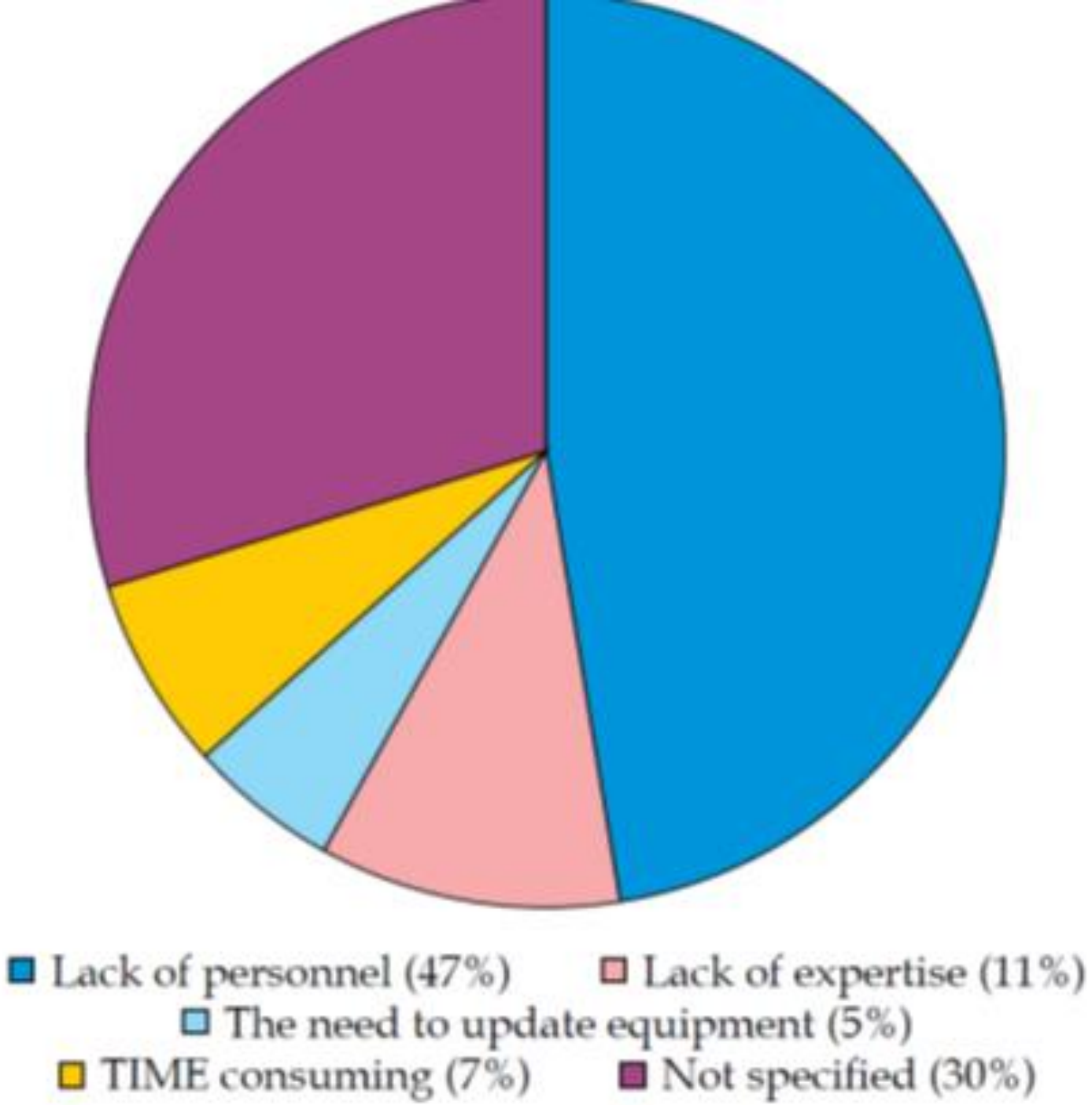
- Catheter points
- 3D reconstruction and dose distribution

Can brachytherapy be properly considered in the clinical practice? Trilogy project: The vision of the AIRO (Italian Association of Radiotherapy and Clinical Oncology) Interventional Radiotherapy study group

Luca Tagliaferri, MD, PhD[1], Andrea Vavassori, MD[2], Valentina Lancellotta, MD[1], Vitaliana De Sanctis, MD[3], Fernando Barbera, MD[4], Vincenzo Fusco, MD[5], Cristiana Vidali, MD[6], Bruno Fionda, MD[1], Giuseppe Colloca, MD[1], Maria Antonietta Gambacorta, MD, PhD[1,7], Cynthia Aristei, MD[8], Renzo Corvò, MD[9], Stefano Maria Magrini, MD[4]

Brachytherapy be considered as important tool and integrated with other therapeutic strategies

J Contemp Brachytherapy 2020

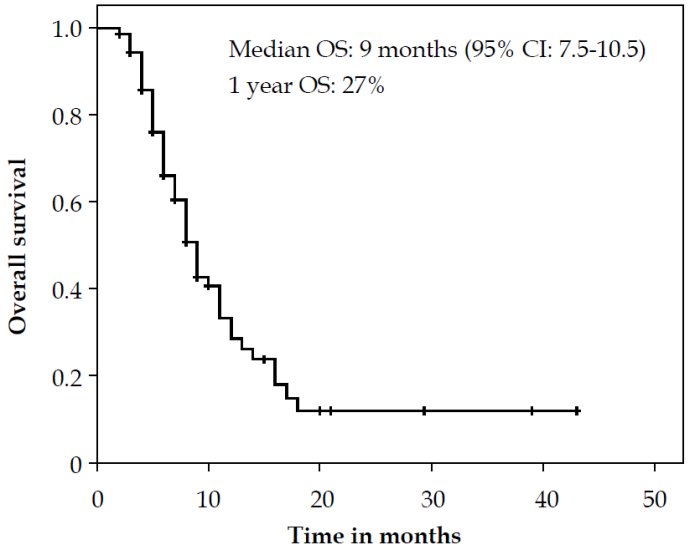


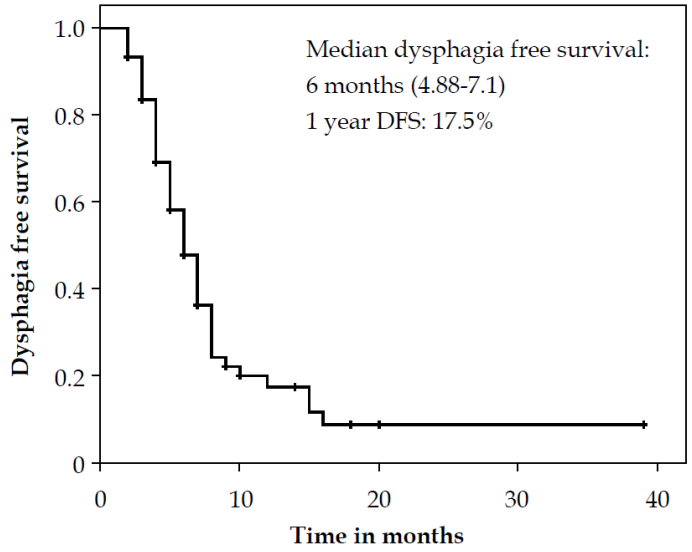
Reasons for not using available brachytherapy equipment

Is there a role of ILBT as boost following EBRT ?

Author	*n*	EBRT dose	iBT dose	Local control	Overall survival
Mujis *et al.*	62	60 Gy	12 Gy (2 fractions)	45% (3y)	11% (5y)
Murakami *et al.* (2011)	87	50-61 Gy	10 Gy (4-5 fraction)	49-75% (5y)	31-84% (5y)
Tamaki *et al.* (2011)	54	56-60 Gy	10 Gy (2 fractions) 9 Gy (3 fractions)	79% (5y)	61% (5y)
Gaspar *et al.*; phase I/II – RTOG 9207 trial (2000)	49	50 Gy	10-15 Gy (2-3 fractions)		49% (1y)
Yorozu *et al.* (1999)	169	40-61 Gy	8-24 Gy (2-4 fractions)	40-80% (2y)	20-70% (2y)
Okawa *et al.*; phase III trial (1999)	103	60 Gy	10 Gy (2 fractions)		20% (5y)
Kumar *et al.* (1993)	75	40-55 Gy	8-10 Gy 10-12 Gy 12-15 Gy	38% (1y)	39% (1y)

ILBT in combination with EBRT for palliation in oesophageal cancer





- 148 patients advanced/metastatic disease
- Treated with 8Gy× 2 fractions followed by EBRT
- 47% had improved dysphagia scores
- Complications 36.4%-Stricture (27%)Fistula(5.4%) Bleeding(4%)
- *Laskar et al J Contemp Brachytherapy 2015*

Brachytherapy in palliative setting

Author	*n*	Compared with	iBT dose
Rosenblatt *et al.* (2010)	219	± EBRT (30 Gy in 10 fractions)	16 Gy (2 fractions)
Rupinski *et al.*, randomized trial (2011)	87	Photodynamic therapy	12 Gy (1 fraction)
Bergquist *et al.*, randomized trial (2005)	65	Stent	21 Gy (3 fractions)
Homs *et al.*, randomized trial (2004)	209	Stent	12 Gy (1 fraction)

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

Brachytherapy for the palliation of dysphagia owing to esophageal cancer: A systematic review and meta-analysis of prospective studies

Lorenzo Fuccio [a,*], Daniele Mandolesi [a], Andrea Farioli [a], Cesare Hassan [b], Leonardo Frazzoni [a], Alessandra Guido [c], Nicola de Bortoli [d], Savino Cilla [e], Chiara Pierantoni [a], Francesco Saverio Violante [a], Franco Bazzoli [a], Alessandro Repici [f], Alessio Giuseppe Morganti [c]

Brachytherapy as an alternative to stent placement.Effective safe Underuse not justified

DysFS 86.9% and 67.2% after 1 and 6 months respectively

Stenosis in 12% Fistula 8.3%

Single-dose brachytherapy versus metal stent placement for the palliation of dysphagia from oesophageal cancer: multicentre randomised trial

*Marjolein Y V Homs, Ewout W Steyerberg, Wilhelmina M H Eijkenboom, Hugo W Tilanus, Lukas J A Stalpers, Joep F W M Bartelsman, Jan J B van Lanschot, Harm K Wijrdeman, Chris J J Mulder, Janny G Reinders, Henk Boot, Berthe M P Aleman, Ernst J Kuipers, Peter D Siersema, for the Dutch SIREC study group**

Stent placement vs single-dose (12 Gy) brachytherapy

	BRACHYTHERAPY	STENT
DYSPHAGIA	More long term effect in relief of symptoms	Rapid improved but effect not prolonged
COMPLICATIONS	21%	33%- (Increased late hemorrhage)

Role of palliative Interventional Radiotherapy in oesophageal cancer for dysphagia free survival

- Systematic review to examine efficacy of palliative brachytherapy in oesophageal cancer compared with other treatment modalityfor dysphagia free survival
- 554 articles
- 905 patients
- Median DyFS 99 days in brachytherapy group
- Grade 3-4 toxicity(Fistula and stenosis)8.3%and 12.1%
- Median survival 175.5.days

AIRO review Brachytherapy 19(2020)

ELSEVIER

Check for updates

BRACHYTHERAPY

Brachytherapy 19 (2020) 390–400

COVID-19

Proposed brachytherapy recommendations (practical implementation, indications, and dose fractionation) during COVID-19 pandemic

Disease site	Indication	Practical implementation considerations during pandemic	Common dose/fractionation	Suggested dose/ fractionation during pandemic	References
Esophageal cancer	Palliative	Avoid brachytherapy until pandemic resolves/resources become available due to increased risk of staff exposure from droplets. Consider short-course EBRT	Intraluminal HDR monotherapy: 12 Gy × 1 fraction, prescribed to 5–10 mm from source axis (50,51), or 7–7.5 Gy at 10 mm from source axis × 3 fractions (50) Intraluminal HDR with EBRT: 8 Gy at 10 mm × 2 fractions, once weekly combined with EBRT (52), or 10 Gy at 10 mm × 1 fraction or 7 Gy at 10 mm × 2 fractions, combined with EBRT (53)		1. Netherlands multicenter, Homs *et al.* PMID 15500894 (50) 2. Systematic review, Fuccio *et al.* PMID 28104297 (51) 3. IAEA, Rosenblatt *et al.* PMID: 20950882 (52) 4. ABS Guidelines, Gaspar *et al.* PMID: 9212013 (53)
	Re-irradiation	Avoid brachytherapy until pandemic resolves/resources become available due to increased risk of staff exposure from droplets. Consider conformal EBRT.	Intraluminal HDR monotherapy: 5–7 Gy at 5 mm × 5–6 fractions (54), or 10–17.5 Gy at tumor depth in 3 fractions (limit mucosa to ≤ 12 Gy per fraction) (55)		1. Saint Louis Hospital, Paris, Wong Hee Kam *et al.* PMID 25906950 (54) 2. Memorial Sloan Kettering Cancer Center, New York, Taggar *et al.* PMID 29496425 (55)

Take home message

- Intraluminal BT plays an important role in treatment of oesophageal tumors
- Highly effective and relatively safe
- Indications of BT boost limited however newer indications are emerging
- Palliative brachytherapy useful to reduce dysphagia,pain and bleeding alone or in combination with EBRT or stenting
- Patient selection, applicator diameter, dose specification,prescription sequencing with EBRT and chemotherapy are important issues and contribute to efficacy or toxicity