



Esophageal cancer – is combination with surgery (stents) or EBRT a better solution?

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The role of esophageal brachytherapy

- **The role of esophageal brachytherapy**
 - **Curative indications**
 - locally advanced T(2)-3 tumors in combination with external beam radiotherapy
 - especially in bleeding, ulcerating, and/or obstructive tumors



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 - **CONS: relatively high treatment related tox**



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A phase I/II study of external beam radiation, **brachytherapy**, and concurrent chemotherapy for patients with localized carcinoma of the esophagus (Radiation Therapy Oncology Group Study 9207): final report.

Gaspar LE et al. Cancer 2000 Mar 1;88(5):988-95.

Treatment (n=49)

50 grays (Gy) **external beam radiation** (25 fractions given over 5 weeks) followed 2 weeks later by **EB** (either **HDR 5 Gy** during weeks 8, 9, and 10, for a **total of 15 Gy**, or **LDR 20 Gy** during Week 8)

Chemotherapy was given during weeks **1, 5, 8, and 11**, with cisplatin 75 mg/m² and 5-fluorouracil 1000 mg/m²/24 hours in a 96-hour infusion

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Results

Survival rate at 12 months was 49% (estimated median survival of 11 mo.)

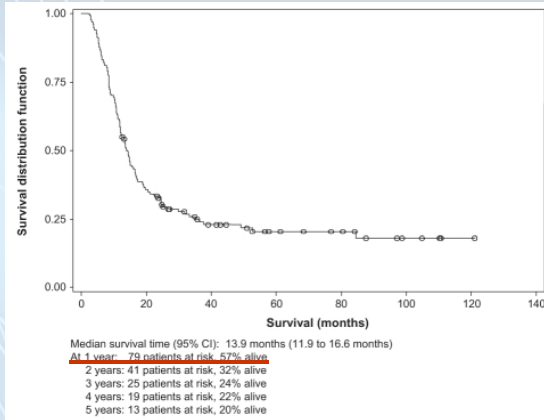
Life-threatening toxicity or treatment-related death occurred in 12 (24%) and 5 (10%) cases, respectively.

Treatment-related esophageal fistulas occurred in **6 cases (12% overall, 14% of patients starting EB)** at 0.5-6.2 months from the first day of brachytherapy, **leading to death in 3 cases (6%)**



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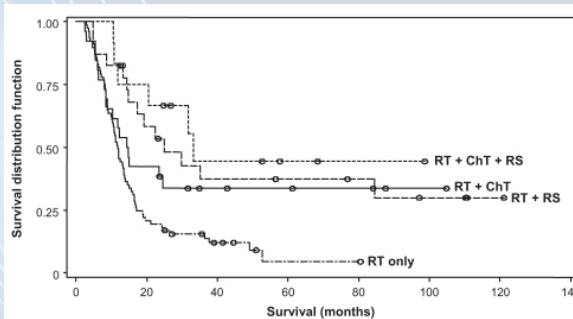


138 consecutive patients treated with radical intent in a single institution (1995-2003)

Agranovich A. et al. Can J Gastroenterol. 2008 Apr;22(4):393-8.

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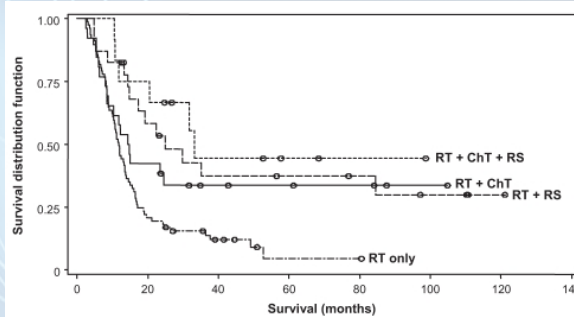
Only combined modality protocols compared favorably with the previously reported results

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Predictors for better survival:

Multimodality treatment regimens (<math><0.0001</math>)

Dose >50 Gy vs. <math><50</math> Gy (0.119)

EBRT + EB vs. EBRT only (0.942)

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Multi-institutional randomized trial of external radiotherapy with and without intraluminal brachytherapy for esophageal cancer in Japan. Japanese Society of Therapeutic Radiology and Oncology (JASTRO) Study Group.

Okawa T et al. Int J Radiat Oncol Biol Phys 1999 Oct 1;45(3):623-8

Treatment (n=103):

After 60 Gy stratified into 2 groups: external irradiation boost of 10 Gy versus HDR or LDR EB 10 Gy (2 x 5 Gy) once-weekly schedule, reference dose at depth of 5 mm of the esophageal submucosa)

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Results:

Overall survival rate was 20.3% at 5 years

Cause-specific survival rate was **31.8% at 5 years** (27% in the external irradiation alone group and 38% in intraluminal brachytherapy combined group, $p = 0.385$)

Interestingly: CSS in TU 5 cm or less tumor length 64% at 5 years in EBRT + EB versus 31.5% in EBRT alone ($p = 0.025$), and trend in T1-2, no difference T3-4

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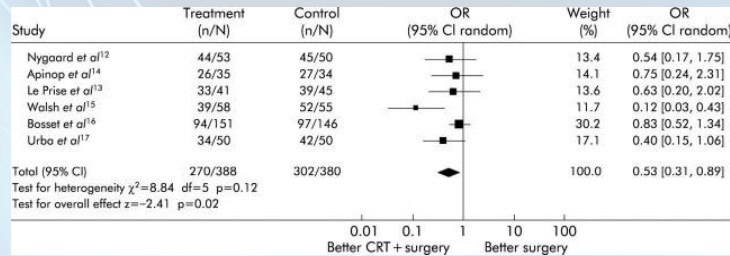
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 - Curative indications
 - Lessons learned
 - 1. Yes – very effective in terms of local control
 - 2. Yes – very effective in terms of controlling symptoms
 - 3. No – not adding benefit in survival (CSS benefit in small TUs?)
 - 4. However, please be careful with late toxicity
 - » Especially fistula and stenosis



The role of esophageal brachytherapy

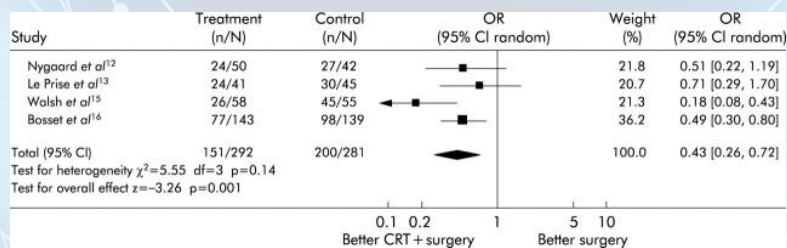
- The role of esophageal brachytherapy (EB)
 - Curative indications
 - Additional aspects – Meta-analysis (3 Y mortality)



Fiorica F et al. Gut. Jul 2004; 53(7): 925–930.

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 - Additional aspects – Meta-analysis (effect of treatment on downstaging)

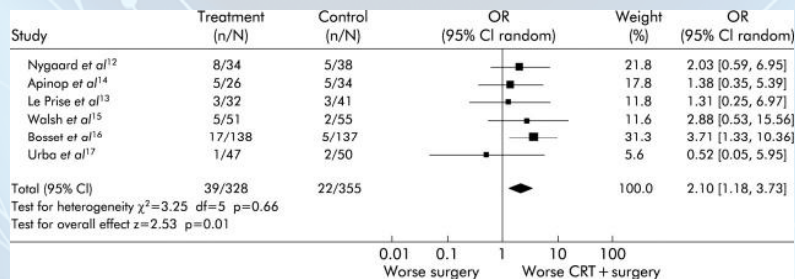


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 - Additional aspects – Meta-analysis (effect of treatment on postoperative mortality)



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 - Palliative indications

Stent insertion or endoluminal brachytherapy as palliation of patients with advanced cancer of the esophagus and gastroesophageal junction. Results of a randomized, controlled clinical trial.

Bergquist H et al. Dis Esophagus 2005;18(3):131-9.

(Sahlgrenska University Hospital, Göteborg, Sweden)

Treatment (n=65):

Ultraflex expandable stent or HDR endoluminal brachytherapy with 7 Gy x 3 given in 2-4 weeks

Endpoints: Clinical assessment and health-related quality of life (HRQL) were measured at inclusion and 1, 3, 6, 9 and 12 months later



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Results (n=65):

For stent group significantly better HRQL scores for dysphagia ($P < 0.05$) at the 1-month follow-up, **but most other HRQL scores, including functioning and symptom scales deteriorated.**

Among brachytherapy-treated patients, improvement was found for the dysphagia-related scores **at 3-months follow-up.**

No Δ in median survival

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 - Palliative indications – **confirmed by RCT's**

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

Homs MY et al. Lancet 2004 Oct 23-29;364(9444):1497-504. (Erasmus MC/University Medical Centre Rotterdam, Netherlands)

Treatment / Results (n=209):

Stent placement (n=108) or single-dose (12 Gy) brachytherapy (n=101)

Dysphagia improved more rapidly after stent placement than after brachytherapy, **but long-term relief of dysphagia was better after brachytherapy.**

Stent placement had more complications (36 [33%] of 108 vs. 21 [21%] of 101; $p=0.02$).

Groups did not differ for persistent or recurrent dysphagia ($p=0.81$), or for median survival ($p=0.23$).



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 - Palliative indications
 - **EB is very effective in improving dysphagia**
 - **ED effect is longer lasting**
 - However, insertion of self-expandable metal stents offers a more instant relief

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 - **Logical question: can we combine stent insertion and single high-dose brachytherapy ?**
 - Aim: Both 1/ prompt effect (stent), and 2/ more long-lasting relief of dysphagia and a better health-related quality of life (HRQL) – effect of brachytherapy



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Combined stent insertion and single high-dose brachytherapy in patients with advanced esophageal cancer - results of a prospective safety study.

Bergquist H et al. Dis Esophagus 2012 Jul;25(5):410-5.

(Sahlgrenska University Hospital, Gothenburg, Sweden)

Treatment (n=12):

Stent insertion followed by a single dose (12 Gy) of brachytherapy

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(Sahlgrenska University Hospital, Gothenburg, Sweden)

Results:

Relief of dysphagia was achieved in the majority of cases (10/11, $P < 0.05$), but HRQL did not improve except for dysphagia-related items.

Only minor adverse events, including chest pain, reflux, and restenosis, were reported. The median survival time after inclusion was 6.6 months



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Combination of biodegradable stent placement and single-dose brachytherapy is associated with an unacceptably high complication rate in the treatment of dysphagia from esophageal cancer.

Hirdes MM et al. Gastrointest Endosc 2012 Aug;76(2):267-74.

(University Medical Center Utrecht, the Netherlands)

Treatment (n=19):

Single-dose brachytherapy (12 Gy) on day 1 followed by **biodegradable stent placement on day 2**

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Results (n=19):

Positive - 1/ Dysphagia scores decreased significantly from a median of 3 (IQR 3-4) to a median of 1 (IQR 0-3) after 1 month (P < .001). + 2/ adequate luminal patency in 17 patients (89%)



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Results (n=19):

Negative - In 9 patients (47%), major intervention-related complications (severe retrosternal pain with or without vomiting [n = 6], hematemesis [n = 1], recurrent dysphagia [n = 2].

Conclusions and Acknowledgments

- **Conclusions**
 - Esophageal brachytherapy (EB) is very effective in terms of local tumor control
 - EB (8-10 Gy, 2 x 4-5 Gy once-weekly schedule) may be used as *alternative boost procedure in experienced hands after 50 (-60) Gy EBRT*
 - However, combination of higher doses (15-20 Gy?) or with chemotherapy? – maybe unsafe and toxic
 - Patient selection for ED boost remains unsolved: bleeding/ulcerating/obstructing TUs, < 5 cm length?
 - ED for palliation in dysphagia is standard treatment (long-lasting effect + more pronounced HRQoL benefit (combination with stent maybe unsafe?))

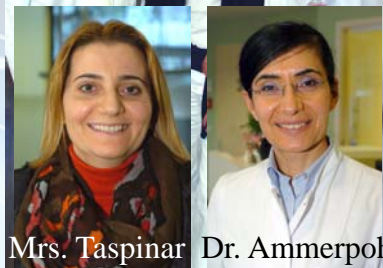


Conclusions and Acknowledgments

- Acknowledgments to the brachy team!



Katja Polz Dr. Hepp



Mrs. Taspinar Dr. Ammerpohl

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- Many thanks for invitation and your attention !

