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Brachytherapy ■ (2018) ■

BRACHYTHERAPY

# Endoluminal high-dose-rate brachytherapy for locally recurrent or persistent esophageal cancer

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**ABSTRACT**

**PURPOSE:** Management of locally recurrent or persistent esophageal cancer (EC) after standard chemoradiation is challenging. This study updates our experience of treating medically inoperable EC patients with endoluminal high-dose-rate brachytherapy (EHDRBT) including the patients treated with a novel multiballoon channel centering esophageal applicator.

**METHODS AND MATERIALS:** Thirty-three consecutive patients with early-stage primary ($n$ = 7), posttreatment persistent ($n$ = 7), and recurrent ($n$ = 19) EC treated with EHDRBT at our institution were included. Median dose and treatment lengths were 14 Gy (range 10−17.5 Gy) and 6 cm (3.5−9.0 cm), respectively. Endoscopy and biopsy were performed 3 months after EHDRBT and then every 3−6 months thereafter.

**RESULTS:** Median followup was 17.4 months (range 5.0−88.3). Grade 1 and 2 toxicities were observed in 13 (44.8%) and 11 (37.9%) patients, respectively. Grade 3 toxicity (tracheoesophageal fistula) was observed in 1 patient who had previously received two courses of external beam radiotherapy as well as a stent insertion. Median overall survival (OS) for entire cohort was 20.9 months, and 1-year OS was 78%. Complete response was achieved in 58.6% of patients with median time to failure and 1-year disease-free survival of 10.3 months (range 5.4−28.2) and 27%, respectively.

**CONCLUSIONS:** For medically inoperable patients with early-stage primary or local posttreatment residual or recurrent EC, EHDRBT is a well-tolerated treatment option with minimal Grade ≥3 toxicity. Brachytherapy in our hands continues to be a safe treatment option. Although 58.6% of patients achieved a complete response and the OS of this cohort is relatively good, long-term local control and cure remains a challenge. 

*Keywords:* Early stage; Recurrent; Esophageal cancer; Brachytherapy; High-dose-rate

## Introduction

Patients with recurrent or persistent esophageal cancer (EC) after standard chemoradiation have limited treatment options, especially those who are medically inoperable. Endoluminal high-dose-rate brachytherapy (EHDRBT) can play a significant role in management of EC because of its ability to deliver high doses of radiation to the tumor with relative sparing of surrounding normal tissues (1−8). In the setting of prior radiation therapy, this localized delivery of dose is especially important as further external beam radiation may potentially expose nearby normal tissues such as the lung, heart, and spinal cord to significant additional dose.

The rapid dose falloff typical of brachytherapy, however, has disadvantages as well, as the dose delivered to the mucosal surface can be much higher (often two- to three-

Received 3 November 2017; received in revised form 16 January 2018; accepted 24 January 2018.

Conflict of interest: The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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1538-4721/$ - see front matter 
https://doi.org/10.1016/j.brachy.2018.01.010

fold higher) than that delivered to the prescription depth (8). Furthermore, when using narrow catheters, the uncertainty of channel position within the lumen of the esophagus may result in a much higher dose to the portion of esophagus nearest the radiation source, potentially resulting in higher risk of severe toxicity such as fistula. We have now introduced a novel multiballoon channel centering esophageal applicator (MBCEA) (Bionix Medical, Toledo, OH) into our clinical practice (Fig. 1a). This applicator has five independently controlled balloons, and each balloon can be inflated up to 2-cm diameter, a larger diameter than can be achieved with older techniques. The applicator has 5-mm shaft diameter with central source lumen, which can also be used for placement over a guidewire. Because of the inverse-square relationship of radiation dose vs. distance from source, the larger effective diameter of the MBCEA provides a better ratio of prescription dose vs. mucosal dose compared to smaller diameter applicators, such as bougie catheters.

We previously reported on the use of EHDRBT on 14 patients with good clinical outcome (freedom from local failure [LF] and overall survival [OS] at 18 months were 46% and 73%, respectively) and limited acute toxicity using a bougie applicator (9). In this series, our aim was to evaluate and update our institutional experience with EHDRBT, including the patients treated with the novel MBCEA.

## Methods

### *Patient selection*

An EHDRBT procedure was developed at our institution to treat patients with (*1*) recurrent or residual EC after chemoradiation or endoscopic mucosal resection and (*2*) early-stage primary tumors, who are not good surgical candidates. Between August 2008 and October 2015, 28 patients with EC were treated using a bougie catheter. After November 2015, 5 patients were treated with a novel MBCEA (Fig. 1).

### *Brachytherapy procedure*

Brachytherapy procedure and workflow with bougie applicator have been previously described (9). Briefly, after induction and intubation of the patient, upper gastrointestinal endoscopy was performed to visualize the esophageal tumor. The superior and inferior extent of the tumor was identified, and radio-opaque markers were placed on the overlying skin of the chest wall using fluoroscopy, unless the lesion was previously implanted with an internal radiopaque fiducial marker at the time of prior staging endoscopic ultrasound procedure. A guidewire was then placed into the esophagus, after which the endoscope is removed. A bougie catheter (generally 14-mm diameter; Varian Medical Systems, Inc., Palo Alto, CA) was passed over the guidewire, and the guidewire was removed. Dummy wires were placed in the central catheter, and position was verified with plain radiograph.

The procedure with MBCEA has similar workflow but with some modifications. After placement of guidewire into the esophagus as previously described, brachytherapy applicator is gently inserted over the guidewire, such that the target (tumor plus 1−1.5 cm craniocaudal margin) is situated within the length of the treatment area of the applicator. The balloons are then individually inflated with 4 cc of 10% Omnipaque solution to achieve a 2-cm diameter of each balloon. The position of the applicator is confirmed with a plain radiograph and adjustments made as necessary by deflating/reinflating balloons until a satisfactory position is achieved. Subsequently, the patient is transferred to obtain a three-dimensional image data set with CT simulation and treatment planning.

### *Treatment planning and delivery*

With bougie catheter, treatment was planned and delivered with plain radiographs. Dose was prescribed to median depth of 7 mm (range 4−10 mm) from the surface, with prescription depth determined on the basis of clinical assessment of tumor thickness. A treatment plan was generated to provide the specified dose, generally limiting the mucosal surface dose to 8−10 Gy. The treatment planning system used was ABACUS v3.1 (Varian, previously Isotopen-Technik Dr. Sauerwein, Haan, Germany), and the plan is independently checked.

With the MBCEA applicator, the contours of the target (tumor plus margin), nontarget esophagus, heart, and gastroesophageal junction are drawn on the CT scan data set, and a plan is generated using BrachyVision software (Varian Brachytherapy, Charlottesville, VA) with the following planning criteria: target $V_{100}$ (volume receiving 100% of dose) $>$ 90% and $D_{0.3}$ cc (maximum dose to 0.3 cc of volume) $\leq$12 Gy/fraction. The target volume included 1−1.5 cm of additional margin beyond the cranial and caudal extent of the endoscopically visualized tumor. In some cases, for deeply situated target volumes, because of the limitation of a high surface dose using the bougie applicator, prescribed dose at depth was reduced to preserve the mucosal dose limit. Target prescription dose was 15 Gy. The patient is then connected to a GammaMed Plus remote afterloader (Varian), the room is cleared, and treatment is delivered.

Treatments were delivered in three fractions over 3 weeks, 7 days apart. When feasible, patients ($n$ = 24) were instructed to take capecitabine for radiosensitization during the 3 weeks of EHDRBT treatment (weekdays only).

### *Assessment and followup*

Patients were followed up with a physical examination, CT scan, and upper gastrointestinal endoscopies every