

Science Brief—Cervical Cancer

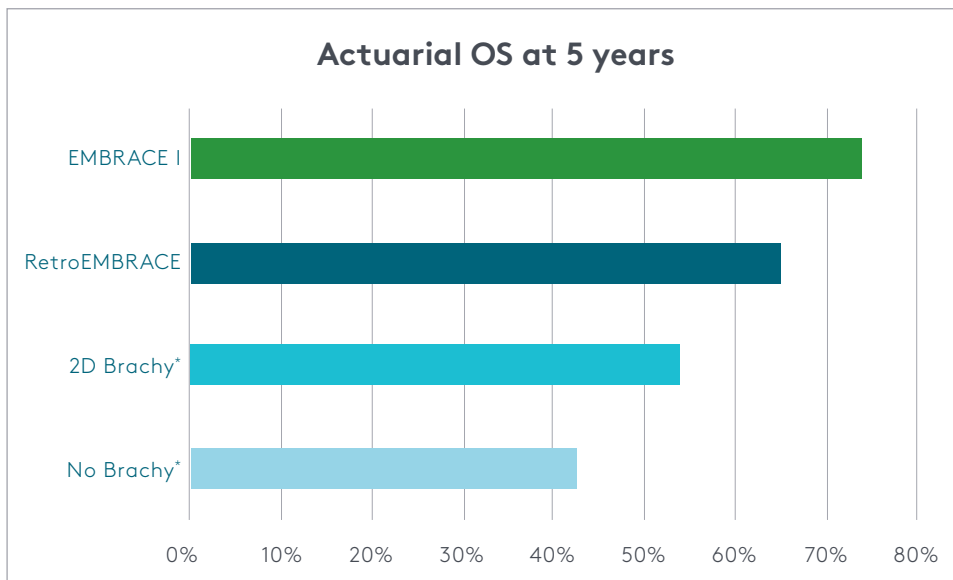
EMBRACE

Image-guided intensity modulated **E**xternal beam radiochemotherapy and **M**RI-based adaptive **BRA**chytherapy in locally advanced **C**ervical Cancer, multicenter prospective cohort studies

Introduction

EMBRACE, Image-guided intensity modulated **E**xternal beam radiochemotherapy and **M**RI-based adaptive **B**RAchytherapy in locally advanced **C**ervical Cancer, multicenter prospective cohort studies

The overall local control across all stages was unprecedented¹



RetroEMBRACE Study data published in 2016 have shown over 10% survival benefit of 4D Image Guided Adapted Brachytherapy (IGABT) over conventional 2D Brachytherapy in locally advanced cervical cancer (LACC).³

The EMBRACE I study published in April 2021 found further improved local control (LC) and overall survival (OS) at 5 years over RetroEMBRACE in LACC.¹

*extrapolated from²

Background and objective

In order to evaluate the outcome of IGABT in a multicenter setting, the GEC-ESTRO GYN network launched the "International study on MRI-based brachytherapy in cervical cancer" (EMBRACE I) in 2008.⁴

- The excellent outcome of IGABT has been demonstrated in several mono-institutional reports, as well as in the RetroEMBRACE (study closed in 2008).^{3,4}
- The purpose of RetroEMBRACE was to compile retrospective IGABT outcome data until mature prospective data became available e.g. from the EMBRACE I study.⁷
- EMBRACE I was a prospective observational study including external beam (45–50 Gy) and MRI-based IGABT. The study closed in 2015 with the accrual of 1,416 patients.⁴

Main findings

- Actuarial OS at 5 years has improved from 65% (RetroEMBRACE) to 74% (95% CI of 72–77) (EMBRACE I).^{1,3}
- Actuarial LC at 5 years has improved from 89% (RetroEMBRACE) to 92% (95% CI of 90–93) (EMBRACE I).^{1,4}
- RetroEMBRACE demonstrated that use of intracavitary/interstitial (IC/IS) brachytherapy in large tumors significantly increased LC in tumors with a high-risk clinical target volume (HRCTV) of $\geq 30 \text{ cm}^3$ at the time of first brachytherapy, without increasing morbidity.^{4,5}
- 43% of patients in EMBRACE I were treated with a combination of intracavitary and interstitial treatment techniques,¹ preliminary data for EMBRACE II show this likely to increase to >70%.⁶
- Brachytherapy associated actuarial grade 3 or worse morbidity such as fistulae, ureteric strictures, vaginal stenoses seem limited in EMBRACE I (3.2%, 2.9%, and 4%) and are especially low for patients with stage I to II diseases.¹

Material and Methods

- Contouring and dose reporting in EMBRACE I done according to GEC-ESTRO guidelines/ICRU 89 report; dose prescription done according to institutional guidelines.¹
- During accrual in EMBRACE I, dose effect relationship was demonstrated based on RetroEMBRACE data, and planning aims (soft and hard constraints) for the target were developed. These were subsequently incorporated in EMBRACE I protocol.⁷ The ability to reach dose constraints for both targets and OAR relies on a change of practice, which mainly involves increased use of IC/IS brachytherapy.⁴
- Based on data from EMBRACE I, dose effect-relationship was demonstrated for varied morbidity end points, therefore soft and hard constraints were recommended for organ at risk (OAR).⁸

Discussion

- MRI-based IGABT represents a paradigm shift for the treatment of LACC that affects clinical practice and should be used as guidance for future studies of treatment for this type of cancer.⁴

Conclusion

- There is a potential for further improvement for patients with advanced local disease including pelvic wall involvement and for patients with asymmetric HRCTV at the time of brachytherapy using more complex applicators for combined intracavitary/interstitial brachytherapy.⁹
- The results of EMBRACE I provide the clinical evidence for MRI-guided IGABT as being the new gold-standard IGABT of LACC to be implemented across the world, replacing the traditional two-dimensional point A concept.¹

Outlook

- Access to MRI is limited by its availability, logistics and financial implications. Use of alternative imaging like CT and ultrasound (US) for IGABT has been attempted. To arrive at a systematic, uniform, and international approach for CT based definition and contouring of target structures, GEC-ESTRO, IBS, and ABS agreed to jointly develop such recommendations based on concepts and terms as published in the ICRU Report 89.¹⁰
- The hypothesis of EMBRACE II is further improvement of locoregional and systemic control at 5 years over EMBRACE I with better OS,³ and it aims to benchmark a low incidence of intermediate and major morbidity as well as a high level of quality of life with application of advanced EBRT, BT and chemotherapy.¹¹

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Elekta Offices

Elekta AB

Box 7593
SE-103 93
Stockholm, Sweden

T +46 8 587 254 00
F +46 8 587 255 00

Europe

T +46 8 587 254 00
F +46 8 587 255 00

Turkey, India, Middle East & Africa

T +90 216 474 3500
F +90 216 474 3406

North & Central America including the Caribbean

T +1 770 300 9725
F +1 770 448 6338

South America & Cuba

T +55 11 5054 4550
F +55 11 5054 4568

Asia Pacific

T +852 2891 2208
F +852 2575 7133

Japan

T +81 3 6722 3800
F +81 3 6436 4231

China

T +86 10 5669 2800
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