13th Winter Cancer Symposium, Rio Grande, Puerto Rico

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ONCOPLASTIC SURGERY

• INTRA OPERATIVE RADIO THERAPY- IORT





• ONCOPLASTIC SURGERY

 Combines the principles of oncologic resection with the advantages of plastic reconstruction to obtain the best possible cosmetic results without compromising the oncologic resection. • INTRA OPERATIVE RADIO THERAPY- IORT





ONCOPLASTIC SURGERY

- INTRA OPERATIVE RADIO THERAPY- IORT
 - Direct delivery of the planed radiation dose into the tumor cavity at the time of surgery.
 - May be used as a single treatment or as a tumor bed boost followed by subsequent WBRT

















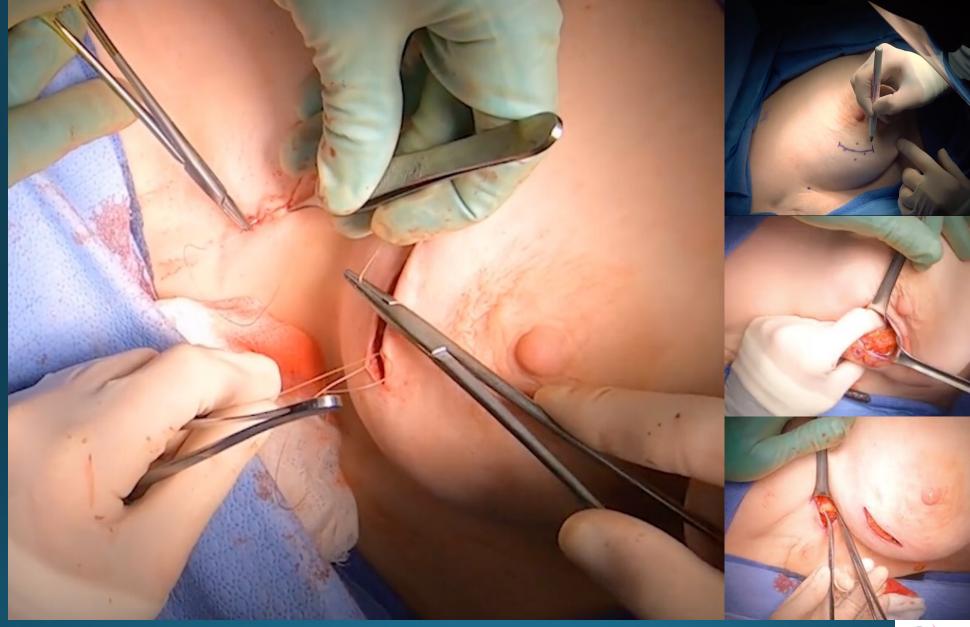
















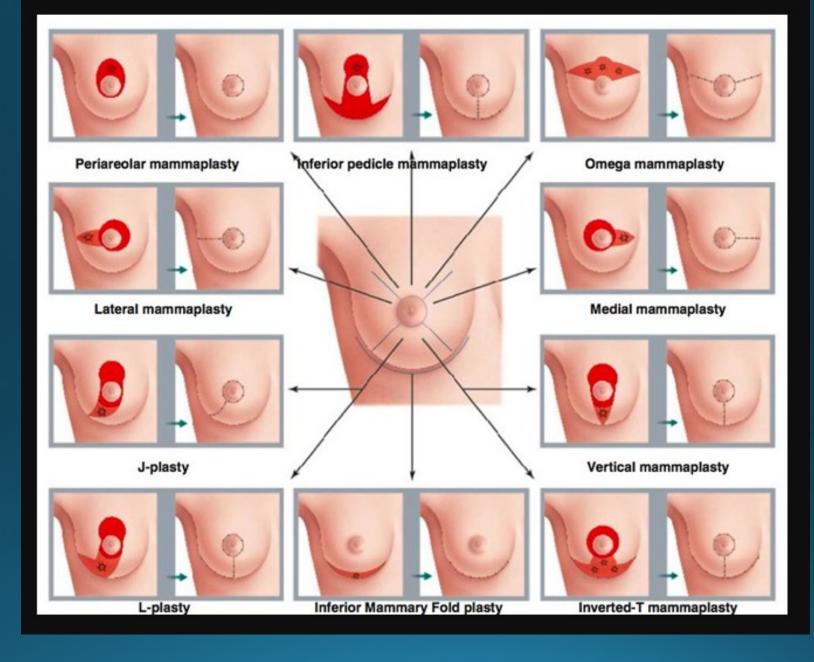








Oncoplastic resection options depending on tumor localization







ONCOPLASTIC BREAST SURGERY CLASSIFICATION

Technique	Classification/ Definition	Examples	
Volume displacement	Level 1: <20% breast tissue removed	Local tissue rearrangement	
	tissue temoveu	Crescent mastopexy	
	Level 2: 20–50% of breast tissue removed	Reduction mammoplasty	
Volume replacement	> 50% of breast tissue removed	Implant-based reconstruction	
		Local/regional flap reconstruction	
		Thoracodorsal artery perforator, etc	





Quick basics of radiotherapy

- Photons- completely pass through tissues
 - when used, they must be angled to traverse the target tissue only so as to avoid critical normal tissue
- Electrons- traverse only to a specific depth
 - Can be targeted to tailor the tissues of interest





Quick basics of radiotherapy

- Whole breast radiotherapy WBRT
- Accelerated partial breast irradiation- APBI
- External beam radiotherapy- EBRT
- Brachytherapy
- Intraoperative Radiation Therapy- IORT





Intra Operative Radiation Therapy-IORT

- GOAL
 - Provide a non-inferior option to patients with early stage breast cancer
- BENEFITS
 - Shorter duration of tx
 - Decreased RT effect to the rest of the breast
 - Improved cosmesis
 - Reduced cost
 - IMPROVED NON-BREAST RELATED MORTALITY??
- DISADVANTAGES
 - Controversial long term results
 - Not for everyone
 - Limited availability





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PRACTICE GUIDELINE | ARTICLES IN PRESS

Partial Breast Irradiation for Patients With Early-Stage Invasive Breast Cancer or Ductal Carcinoma In Situ: An ASTRO Clinical Practice Guideline

Simona F. Shaitelman, MD, EdM 😕 ■ Bethany M. Anderson, MD • Douglas W. Arthur, MD • ...

Shaveta Vinayak, MD • Timothy Whelan, BM BCh • Janice A. Lyons, MD • Show all authors

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Major guidelines for APBI

Criteria	American Society of Breast Surgeons	ASTRO/ NCCN	ESTR O
Age	> 45	≥ 50	≥ 50
Histology	All and DCIS >50 No LVSI	IDC, DCIS (under conditions)	IDC, DCIS
Receptor Status	ER/PR +/-	ER+	
Tumor Size	≤ 3cm	≤ 2cm Inv 2,5 TIS	≤ 3cm
Node Status	NO	NO	NO
Margins	Negative	Negative	Negative
	2018	2023	2020





Intra Operative Radiation Therapy-IORT

- ELIOT TRIAL (miniaturized electron beam accelerator)
 - Arch Surg. 2003 Nov;138(11):1253-6.
 - Lancet Oncol. 2013;14:1269–1277
 - Lancet Oncol 2021 Apr 09
- TARGIT-A TRIAL (miniaturized low energy X-ray applicator)
 - Lancet Oncol. 2004;5(3):165
 - *Lancet.* 2010;376:91–102
 - BMJ 2020;370:m2836





ELIOT and TARGIT-A Study Comparison

Subject	ELIOT	TARGIT-A
Whole number in	1305	3451
Number of centers	Single in Milan	33 centers in 11 countries
Time	2000 - 2007	2000 - 2012
Number of IORT group	651	1721
Number of EBRT group	654	1730
EBRT after IORT	Exclude	15.2%
Radiation type	Electron	X-ray
Applicator	4-8 cm diameter (cylindrical)	1.5 - 5 cm diameter (spherical)
Energy	4 - 12 MeV	50 kV
Time	3 - 5 minutes	20 - 45 minutes
Dose	21 Gy	20 Gy at surface





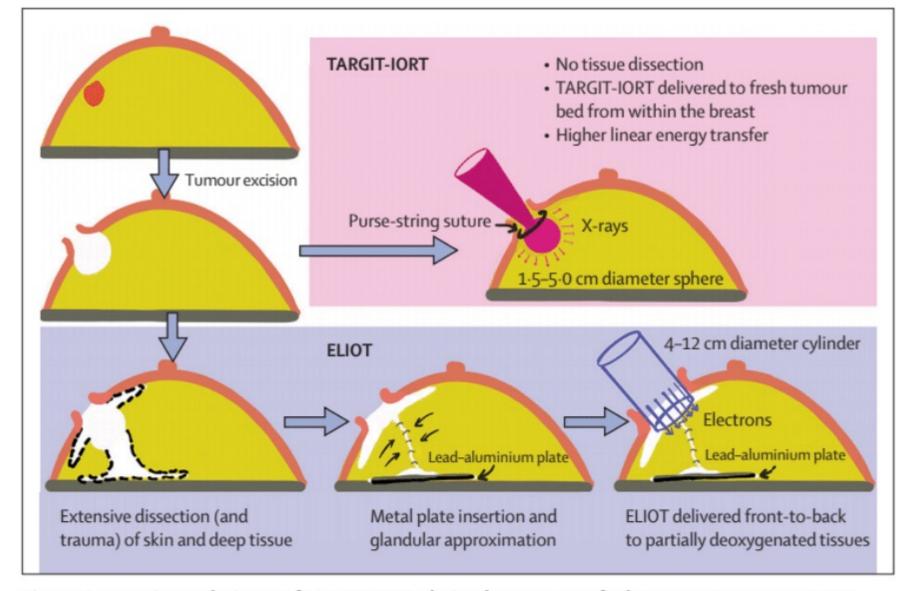


Figure: Contrasting techniques of TARGIT-IORT (during lumpectomy for breast cancer) versus ELIOT ELIOT=electron intraoperative radiotherapy. TARGIT-IORT=targeted intraoperative radiotherapy.





ELIOT TRIAL

- Single-centre, randomised, phase 3 equivalence trial was done at the European Institute of Oncology (Milan, Italy). Eligible women, aged 48-75 years with a clinical diagnosis of a unicentric breast carcinoma with an ultrasound diameter not exceeding 25 mm, clinically negative axillary lymph nodes, and who were suitable for breast-conserving surgery
- Randomly assigned to receive post-operative WBI with conventional fractionation (50 Gy given as 25 fractions of 2 Gy, plus a 10 Gy boost), or 21 Gy intraoperative radiotherapy with electrons (ELIOT) in a single dose to the tumour bed during surgery
- The primary endpoint was the occurrence of IBTR.
- Overall survival was the secondary endpoint.
- The cumulative incidence of IBTR events and overall survival were assessed at 5, 10, and 15 years of follow-up





ELIOT TRIALRandomization schema

1305 patients enrolled and randomly assigned 654 assigned to WBI 651 assigned to ELIOT 53 excluded during or after surgery 66 excluded during or after surgery 35 ineligible 50 ineligible 19 benign or in-situ tumour 15 benign or in-situ tumour 12 multifocal disease 17 multifocal disease 1 tumour size > 2.5 cm* 10 tumour size >2.5 cm* 4 metastatic disease 3 other reasons† 18 protocol violations 4 other reasons† 16 patients refused assigned 16 protocol violations 1 patient refused assigned treatment 1 radical mastectomy treatment 1 radiotherapy not done for severe 14 dysfunction of intraoperative radiotherapy machine cardiomyopathy 1 intraoperative radiotherapy not done under local anaesthesia 601 patients in per-protocol population 585 patients in per-protocol population 654 patients in intention-to-treat population 651 patients in intention-to-treat population

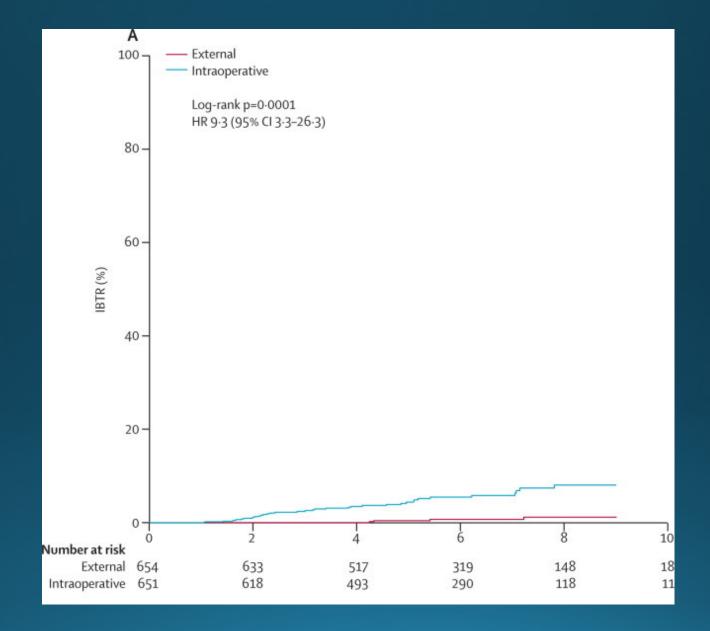
Lancet Oncol 2021 Apr 09





ELIOT TRIAL-

Ipsilateral breast tumor recurrence ELIOT- 11% WBRT- 2% p= 0.0001



Lancet Oncol 2021 Apr 09

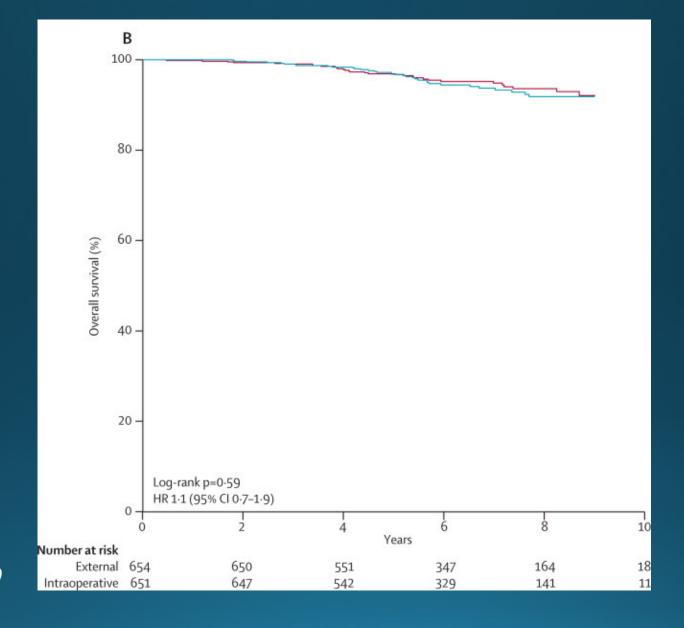




ELIOTTRIAL-

Overall survival ELIOT- 90.7% WBRT- 92.7%

p = 0.59



Lancet Oncol 2021 Apr 09





ELIOTTRIAL-

shielding disc being placed beneath the target parenchyma and above the muscle







TARGIT-ATRIAL

- Objective- To determine whether risk adapted intraoperative radiotherapy, delivered as a single dose during lumpectomy is noninferior to postoperative whole breast external beam radiotherapy for early breast cancer.
- Design- Prospective, open label, randomized controlled clinical trial.
- Setting- 32 centers in 10 countries in the United Kingdom, Europe, Australia, the United States, and Canada.
- Participants- 2298 women >44 years with invasive ductal carcinoma up to 3.5 cm in size, cNo-N1, eligible for breast conservation and randomized before lumpectomy.





The TARGIT - A trial

In the randomised TARGIT-A trial, two policies of local radiation treatment after breast cancer surgery are compared:

Breast cancer patient (>=45 years) suitable for breast conserving surgery

Randomisation

TARGIT group (A)

Single dose of TARGIT with Intrabeam

+

If high risk* add EBRT (45-50Gy) no boost (in ~15%)

*pre-specified criteria e.g., unsuspected lobular carcinoma, lymphovascular invasion, etc

EBRT group (B)

External Beam Radiotherapy (EBRT)

40-56 Gy in 15-25 Fr

+/-

Boost

10-16 Gy in 5-8 Fr





Pre-Pathology Recruitment

TARGIT-A trial

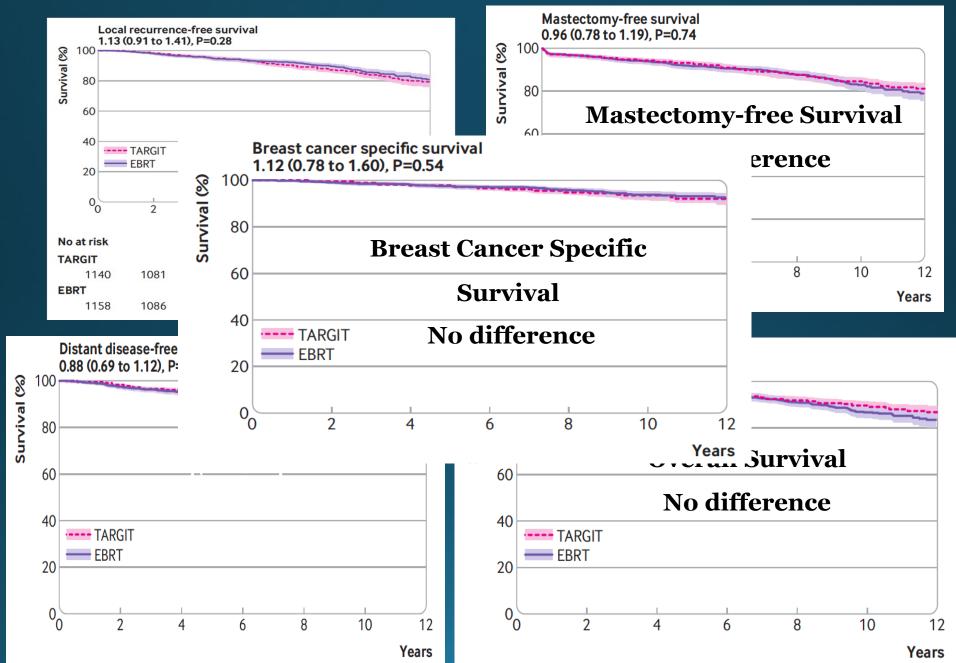
(2298) Eligibility Age ≥45 years Diagnosis established by needle biopsy Unifocal invasive ductal carcinoma preferably ≤3.5 cm, cN0-N1 (MRI not required) Breast conserving surgery feasible Randomise 1158 1140 Risk adapted radiotherapy Conventional radiotherapy TARGIT-IORT focused to tumour bed and delivered Standard fractionated whole breast in single dose with Intrabeam during lumpectomy EBRT over three to six weeks If high risk factors are found on final pathology, supplemental EBRT recommended

BMJ 2020;370:m2836





Local Recurrence Free Survival 12yrs



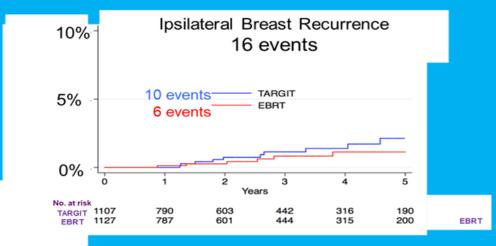




TARGIT-A trial

Primary endpoint LRR

Pre-pathology (Immediate) n=2298



Difference 1% (-0.6-2.7) p=0.31

Non-inferiority Statistical Design, ≤2.5%

BMJ 2020;370:m2836





Puerto Rico Data

- IORT available at Hospital Oncológico Isaac González Martínez since December 2022
- 18 patients treated
- Staging: pT1 and T2a, all No
- One patient required completion WBRT

Thanks to Dr. Julio Diaz who provided these facts





Doubts and other considerations

- Positive margins
- Younger patients
- DCIS
- Recurrence rates
- Omit radiotherapy altogether?
 - 10-year outcomes of the PRIME II omission of radiotherapy was associated with an increased incidence of local recurrence but had no detrimental effect on distant recurrence as the first event or overall survival (OS)
- Ready for prime time?





Doubts and other considerations

- Positive margins
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- Omit radiotherapy altogether?
 - 10-year outcomes of the PRIME II omission of radiotherapy was associated with an increased incidence of local recurrence but had no detrimental effect on distant recurrence as the first event or overall survival (OS)
- Ready for prime time? **BUT NOT YET!**







TAKE HOME MESSAGE

- IORT is not yet standard therapy for radiotherapy at the time of BCS but if selected, it can be used in conjunction with oncoplastic resection.
- Review of the two main randomized trials (TARGIT-A and ELIOT)
 demonstrates conflicting evidence as to breast cancer patients treated
 with IORT having a higher risk of local recurrence (LR).
- <u>However</u>, patients with <u>low-risk features</u> and IORT performed at the time of surgery had <u>similar rates</u> of LR at 5 years, with longer follow-up needed.
- IORT as a boost is promising, and studies are ongoing
- IORT is now available in Puerto Rico at the Hospital Oncologico Isaac Gonzalez Martinez (further information available through Dr. Edna Mora MD FACS)





!Gracias por su atención!



