HOT TOPICS

Radioterapia Intraoperatoria

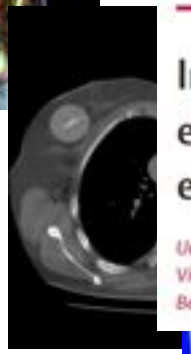
Marina Guenzi

Oncologia Radioterapica Genova

Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial

Lancet 2014; 383: 603–13

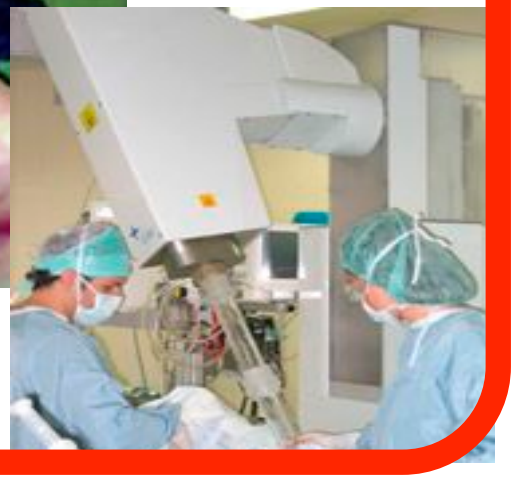
Jayant S Vaidya, Frederik Wenz, Max Bulsara, Jeffrey S Tobias, David J Joseph, Mohammed Keshtgar, Henrik L Flyger, Samuele Massarut, Michael Alvarado, Christobel Saunders, Wolfgang Eiermann, Marinos Metaxas, Elena Sperk, Marc Sütterlin, Douglas Brown, Laura Esserman, Mario Roncadin, Alastair Thompson, John A Dewar, Helle M R Holtveg, Steffi Pigorsch, Mary Falzon, Eleanor Harris, April Matthews, Chris Brew-Graves, Ingrid Potyka, Tammy Corica, Norman R Williams, Michael Baum, on behalf of the TARGIT trialists' group



Lancet Oncol 2013; 14: 1269–77

Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial

Umberto Veronesi, Roberto Orecchia, Patrick Maisonneuve, Giuseppe Viale, Nicole Rotmensz, Claudia Sangalli, Alberto Luini, Paolo Veronesi, Viviana Galimberti, Stefano Zurrida, Maria Cristina Leonardi, Roberto Lazzari, Federica Cattani, Oreste Gentilini, Mattia Intra, Pietro Caldarella, Bettina Ballardini

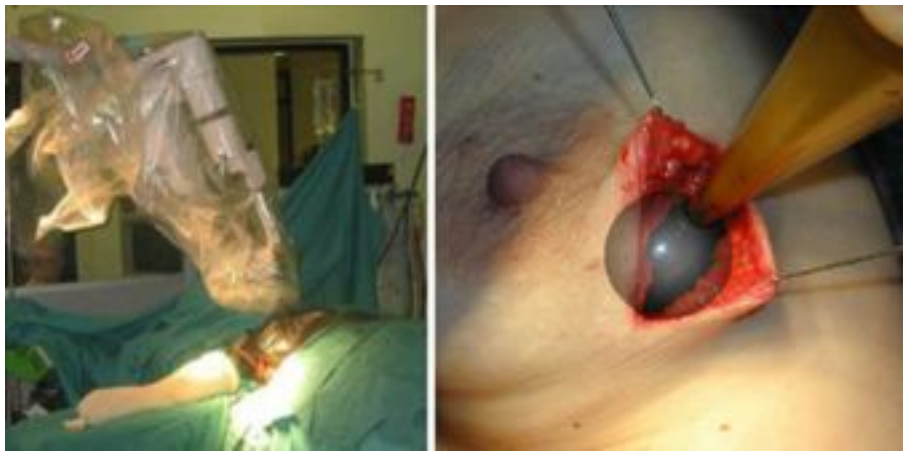


cosa dicono gli autori……

Lancet 2014; 383: 603–13

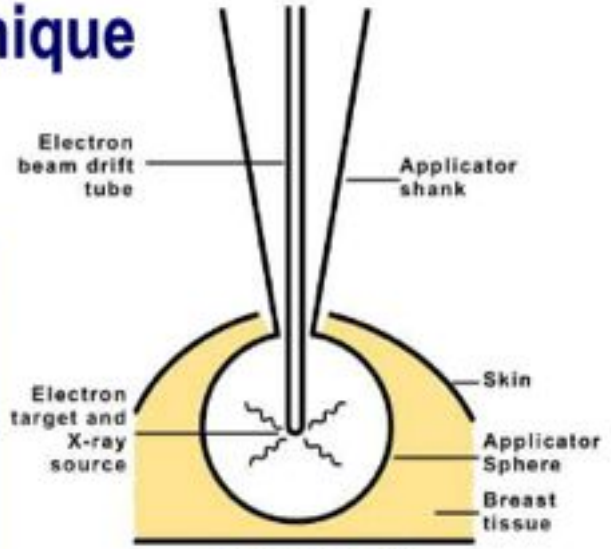
Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial

Jayant S Vaidya, Frederik Wenz, Max Bulsara, Jeffrey S Tobias, David J Joseph, Mohammed Keshtgar, Henrik L Flyger, Samuele Massarut, Michael Alvarado, Christobel Saunders, Wolfgang Eiermann, Marinos Metaxas, Elena Sperk, Marc Sütterlin, Douglas Brown, Laura Esserman, Mario Roncadin, Alastair Thompson, John A Dewar, Helle M R Holtveg, Steffi Pigorsch, Mary Falzon, Eleanor Harris, April Matthews, Chris Brew-Graves, Ingrid Potyka, Tammy Carica, Norman R Williams, Michael Baum, on behalf of the TARGIT trialists' group



San Antonio Breast Cancer Symposium – December 4-8, 2012

The TARGIT Technique



Intrabeam

The dose corresponds to tumour cell density

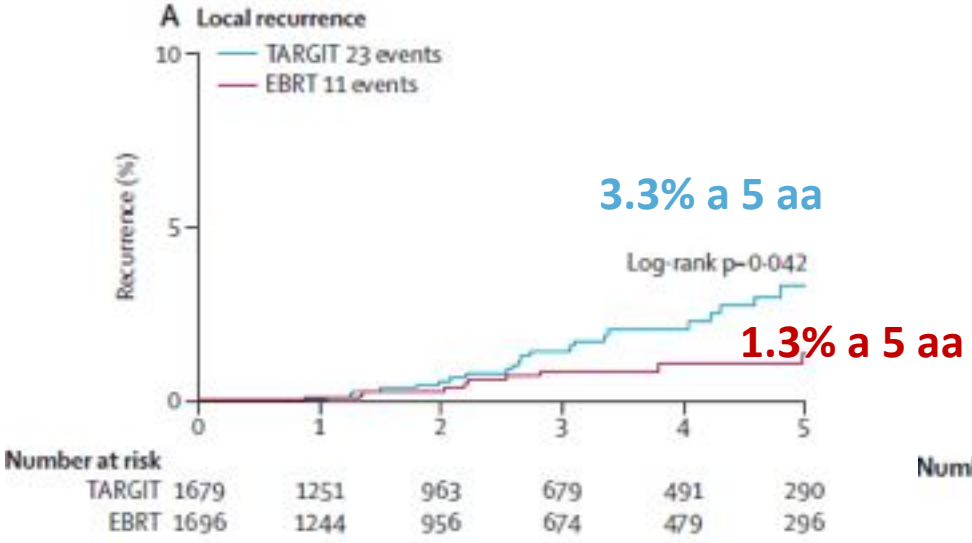
in the initial trial design, randomisation to TARGIT or EBRT group was done before lumpectomy (pre-pathology) (2298 pts)

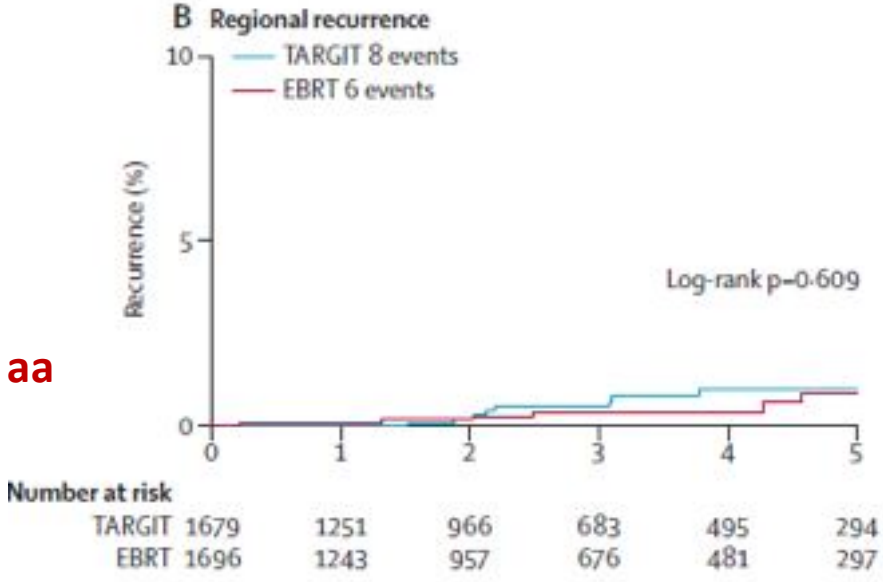
intraoperative radiotherapy as a second procedure by reopening the wound (protocol amendment 2004) (post-pathology) (1153 pts)

3451 pts → median follow-up of 2 years and 5 months
2020 pts→ median follow up of 4 years
1222 pts → median follow up of 5 years.

Median FU→ 29 months

primary outcome: local recurrence





TARGIT-A trial

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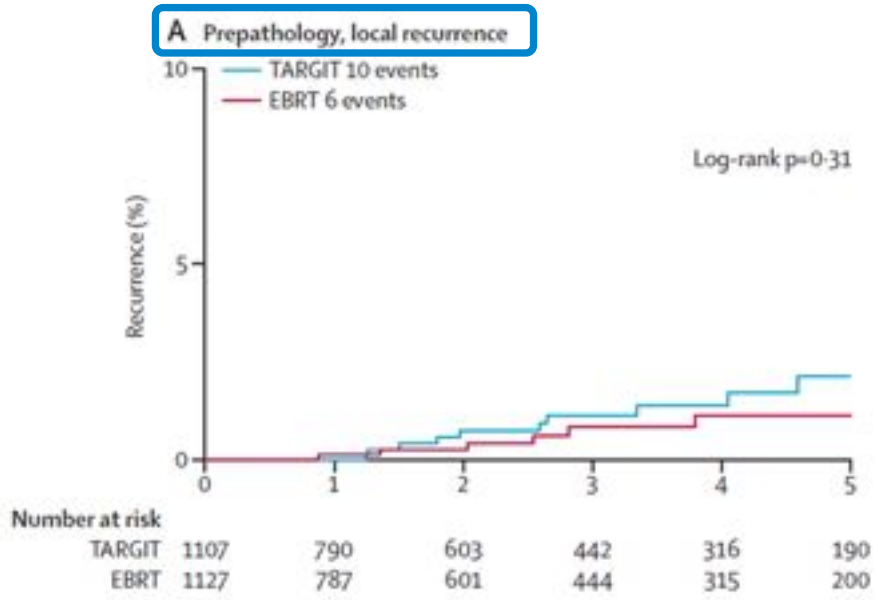
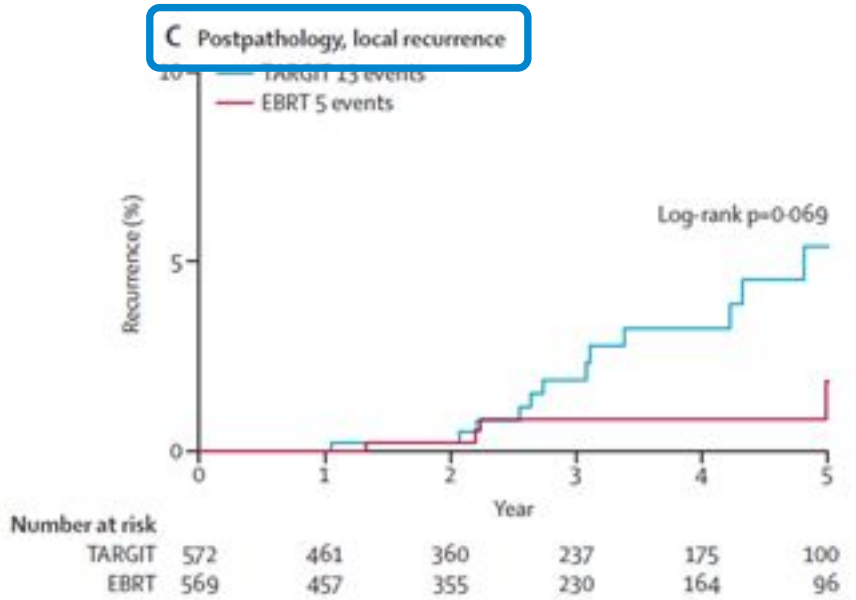




TARGIT-A trial

secondary outcomes:

toxicity

overall survival (breast-cancer deaths / non-breast cancer deaths)

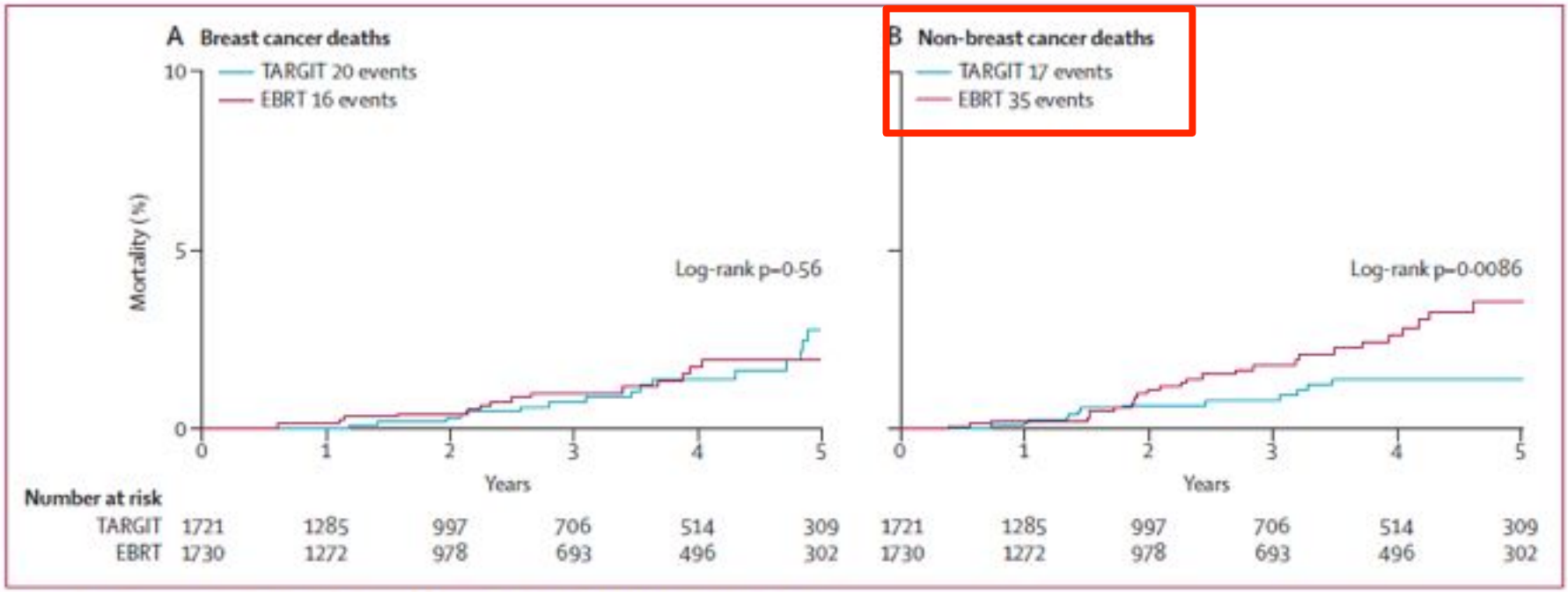


Figure 1: **Kaplan-Meier analysis of breast cancer deaths and non-breast-cancer deaths**
(A) Breast cancer. (B) Non-breast-cancer. TARGIT=targeted intraoperative radiotherapy. EBRT=external beam radiotherapy.

Although an increase in cardiovascular deaths related to radiotherapy has not previously become apparent for 7–10 years a large study that included patients treated until 2001, has shown that significant radiotherapy-related cardiac toxicity is apparent within the first 4 years.

S. Darby 2013

	TARGIT	EBRT
Other cancers	8	16
Cardiovascular causes		
Cardiac*	2	8
Stroke	0	2
Ischaemic bowel	0	1
Other†	7	8
Total	17	35

5-year risk 1·4% for TARGIT versus 3·5% for EBRT; log-rank p=0·0086. TARGIT=targeted intraoperative radiotherapy. EBRT=external beam radiotherapy. *Included one "sudden death at home" in EBRT group. †TARGIT: two diabetes, one renal failure, one liver failure, one sepsis, one Alzheimer's disease, one unknown; EBRT: one myelopathy, one perforated bowel, one pneumonia, one old age, four unknown.

Table 2: Causes of death other than breast cancer in all patients

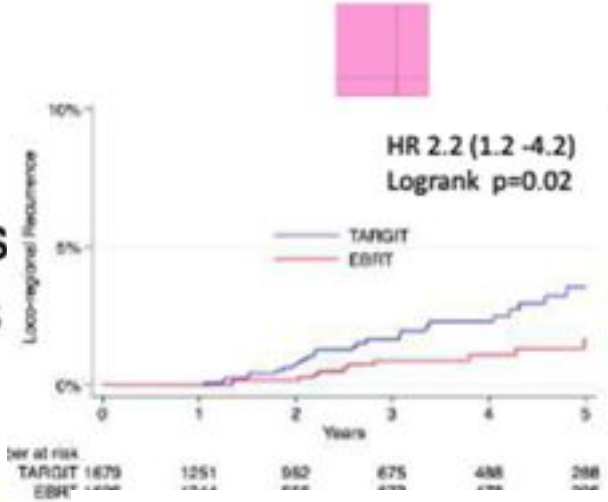
Table 3. Percentage Increase in the Rate of Major Coronary Events per Gray, According to Time since Radiotherapy.

Time since Radiotherapy*	No. of Case Patients	No. of Controls	Increase in Rate of Major Coronary Events (95% CI)†
			% increase/Gy
0 to 4 yr	206	328	16.3 (3.0 to 64.3)
5 to 9 yr	216	296	15.5 (2.5 to 63.3)
10 to 19 yr	323	388	1.2 (−2.2 to 8.5)
≥20 yr	218	193	8.2 (0.4 to 26.6)
0 to ≥20 yr	963	1205	7.4 (2.9 to 14.5)

Conclusion 1

Primary end point

All patients



The absolute difference in ipsilateral breas
recurrence between TARGIT and EBRT is

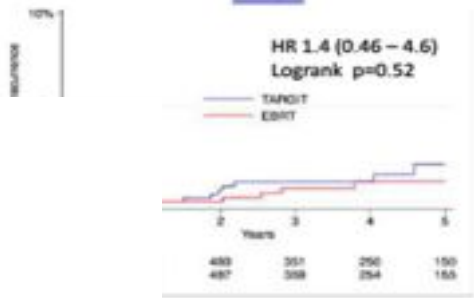
Selezione !!!

TARGIT *minus*

difference (95%CI

For unselected patients 2.0% (0.32 – 3.

Prepathology PgR+ve



How to select patients for TARGIT?

- Cautiously
- Fulfill the eligibility criteria for the TARGIT-A trial
- Preferred option:
  Concurrent TARGIT in PgR +ve patients
- Add external beam radiotherapy if adverse prognostic factors are present

Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial

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Lancet 2014; 383: 603–13

quali commenti.

Breast Cancer Res Treat (2014) 144:371–378
DOI 10.1007/s10549-014-2881-2

CLINICAL TRIAL

Application of a decision analytic framework for adoption of clinical trial results: are the data regarding TARGIT-A IORT ready for prime time?

L. J. Esserman · M. D. Alvarado · R. J. Howe · A. J. Mohan · B. Harrison · C. Park · C. O'Donoghue · E. M. Ozanne

Confidence in trial results	•**Comparison of results and peak hazards to similar trials suggest the TARGIT-A 4-year results are stable** •Local recurrence rate for IORT within range of similar trials •Peak hazard reached at 2-3yrs and no second peak expected
Potential adverse impact of early adoption (if results do not hold)	•**No impact on life expectancy for wide range of the local recurrence rate for IORT** •At an IORT local recurrence rate of 10%, only 0.002 fewer expected life-years (less than one day) compared to EBRT •Frequency of major toxicities similar between treatments
Potential adverse impact of failure to adopt early (if results do hold)	•**$1,7 billion opportunity cost of waiting an additional five years to adopt IORT** •IORT and No Radiation are preferred strategies compared to EBRT (offer similar life expectancy, but cost less) •EBRT costs an additional $1467 in indirect costs per patient

Applying an evaluative framework for the adoption of clinical trial results to the TARGIT-A IORT therapy trial results in the assessment that the trial results are stable, early adoption would lead to minimal adverse impact, and substantially less resource use.

Ann Surg Oncol
DOI 10.1245/s10434-014-3999-5

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

REVIEW ARTICLE – BREAST ONCOLOGY

Intraoperative Radiation Therapy: A Critical Analysis of the ELIOT and TARGIT Trials. Part 2—TARGIT

Melvin J. Silverstein, MD[1,2], Gerd Fastner, MD[3], Sergio Maluta, MD[4], Roland Reitsamer, MD[5], Donald A. Goer, PhD[6], Frank Vicini, MD[7], and David Wazer, MD[8,9]

ASTRO GUIDELINE

LIMITATIONS OF THE AMERICAN SOCIETY OF THERAPEUTIC RADIOLOGY AND ONCOLOGY CONSENSUS PANEL GUIDELINES ON THE USE OF ACCELERATED PARTIAL BREAST IRRADIATION

Radiotherapy and Oncology

GEC-ESTRO Recommendations

Patient selection for accelerated partial-breast irradiation (APBI) after breast-conserving surgery: Recommendations of the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) breast cancer working group based on clinical evidence (2009)

The TARGIT-A trial, like the ELIOT Trial, included pts that today would not be considered the best choice for APBI.

TARGIT-A has contributed to our understanding….

With 29 months of median follow-up, the TARGIT Data are still immature

FOLLOW UP

- Also they said peak recurrences for breast cancer occur in years 2 and 3, offering in support that no recurrences were seen in year 4.

At that time, critics expressed concern mainly about the immaturity of the datas

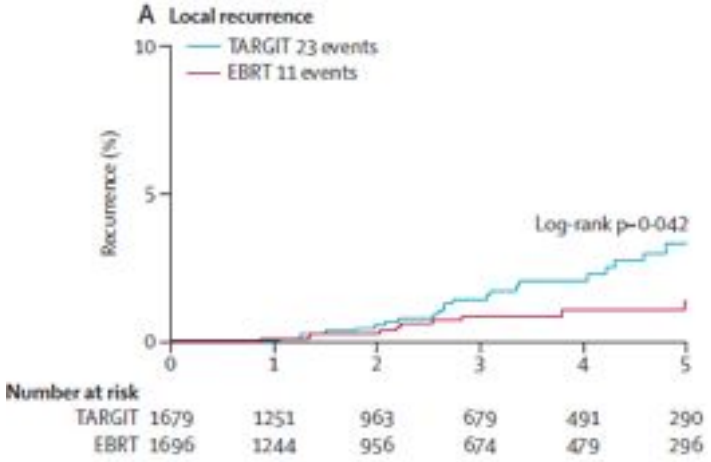
FOLLOW UP

Accrual and randomization of 1,219 additional patients continued until June 2012, increasing the Trial population to 3,451 patients, resulting in a median follow-up of just 29 months.

The TARGIT-A update shows recurrences in both the TARGIT and EBRT groups in year 4.

Only 18 % of patients had a FU of 5 years in the TARGIT-A update

>90% ER+
65% →OT
..delay recurrences

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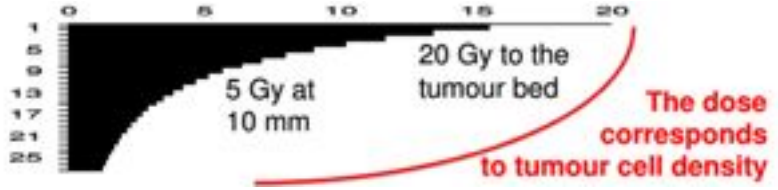
PRE PATHOLOGY
POST PATHOLOGY → Higher local recurrences

↓

- delay in wound fluid suppression of tumor cells,
- a geometric miss when inserting the applicator postsurgery

The volume of tissue irradiated with the TARGIT technique is of concern because dose decreases rapidly with distance from the applicator surface.

Even assuming favorable radiobiological equivalence, only **tissue within a few mm of the applicator surface** receives as much as a 50-Gy EBRT equivalent dose.



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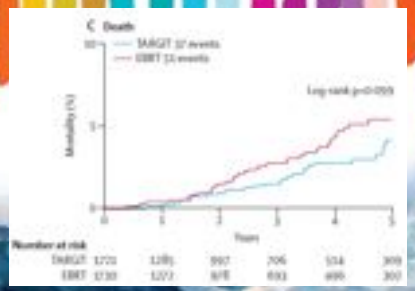
TRIAL MULTICENTRICC

The variability of standards from center to center makes it more difficult to identify which cohort of women might benefit from this treatment strategy



Causes of death as reported in TARGIT-A update

Harness, 2014
Yarnolds, 2014
Mackenzie, 2014

	All deaths	
	TARGIT	EBRT
Breast cancer	20	16
Other cancers	8	16
Cardiac death	2	8
Strokes	0	2
Ischemic bowel	0	1
Other deaths	7	8
Total	37	51

Ann Surg Oncol
DOI 10.1245/s10434-014-3999-5

Annals of
SURGICAL ONCOLOGY
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REVIEW ARTICLE – BREAST ONCOLOGY

Conclusioni.....

Intraoperative Radiation Therapy: A Critical Analysis of the ELIOT and TARGIT Trials. Part 2—TARGIT

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- the TARGIT-A trial included **patients** that today would **not** be considered **the best choice for APBI**.

- **data are still immature**

until the data are more mature, 50-kV patients should be treated **under strict institutional protocols.**

Breast Cancer Res Treat (2014) 147:221–222
DOI 10.1007/s10549-014-3032-5

LETTER TO THE EDITOR

Altri autori….
la fretta fa danno…

Haste makes waste: Are the data regarding TARGIT-A IORT ready for prime time?

Orit Kaidar-Person · Philip Poortmans · Suzanne Klimberg · Joanne Haviland · Birgitte Offersen · Riccardo Audisio · John Yarnold

follow-up in the TARGIT-A trial is immature→
longer follow-up is required to truly understand the recurrence pattern and effectiveness of this treatment.

The authors' assumption that the peak of local recurrence is within 3 years is not consistent with the reports of long-term follow-up of low-risk breast cancer patients

In the TARGIT-A study, of those who received the experimental treatment, 15.2 % (239 of 1,571) received both TARGIT and EBRT

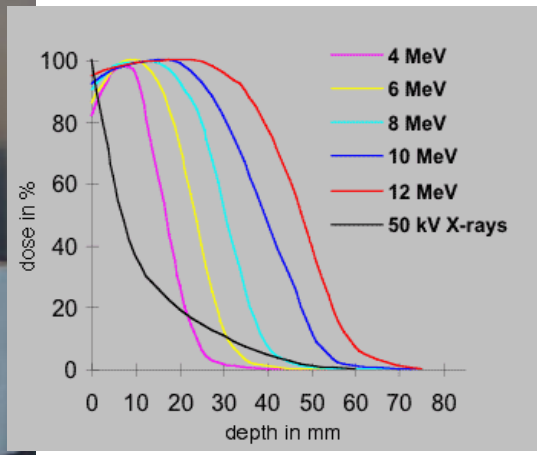
Conclusioni……

When long-term results are available……

it is likely there will be a higher overall recurrence rate for TARGIT when compared with EBRT, but we may **be able to select** subgroups of favorable patients where this difference is small and acceptable.

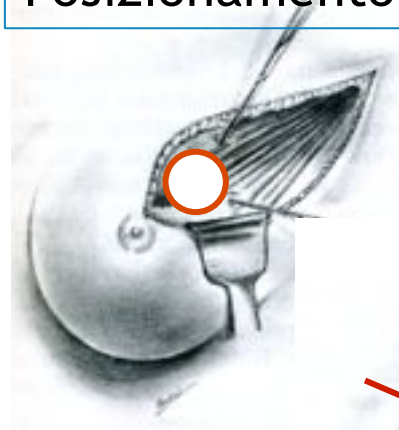
How much additional risk of local recurrence is **acceptable will vary with patients and the situation** in which they find themselves

IOERT



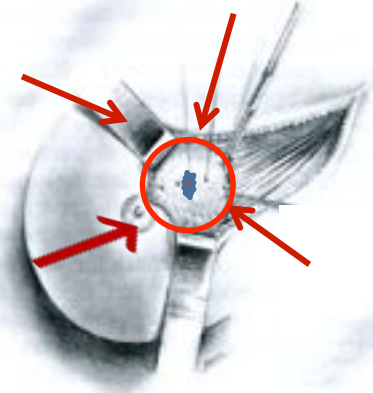
Elettroni di energia nominale compresa tra 3 e 12 MeV, ad un rateo di dose molto elevato (6–30 Gy per minuto), così da rendere brevissimo il tempo necessario per l'erogazione della dose prescritta, 21 Gy. (2 minuti)

Asportazione neoplasia
Scollamento dei lembi
Posizionamento disco



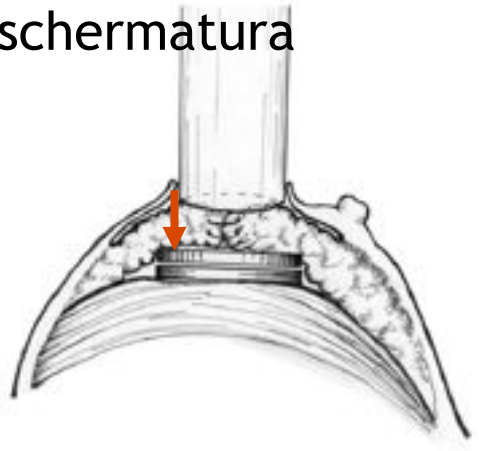
IOERT

Avvicinamento dei lembi
Intorno alla neoplasia, di quel quadrante
a costituire il **CTV**

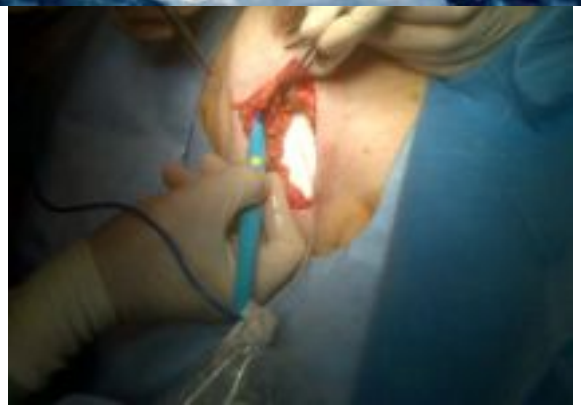


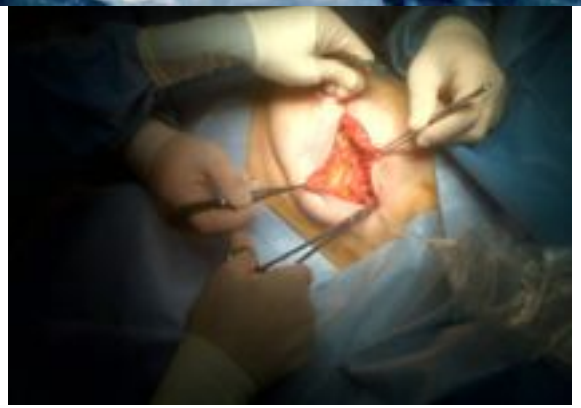
Posizionamento del collimatore
La sutura provvisoria al centro
del collimatore

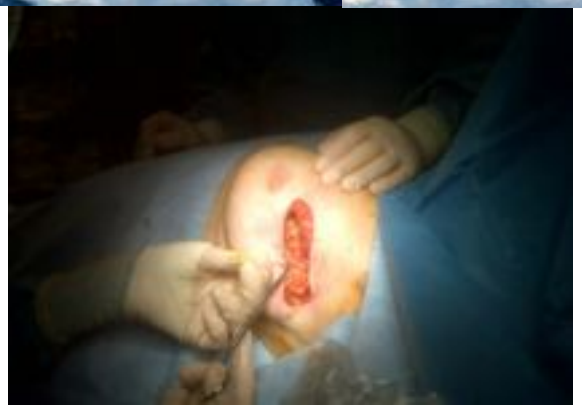
Verifica del corretto posizionamento del disco di schermatura

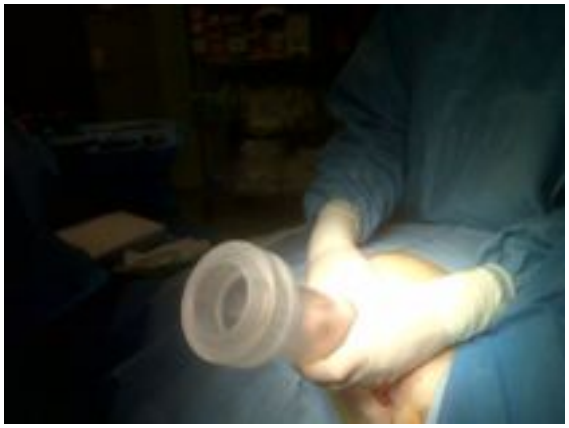


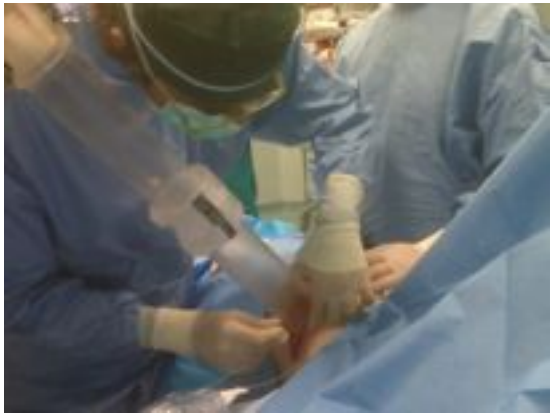
Importanza della tecnica e della collaborazione interdisciplinare

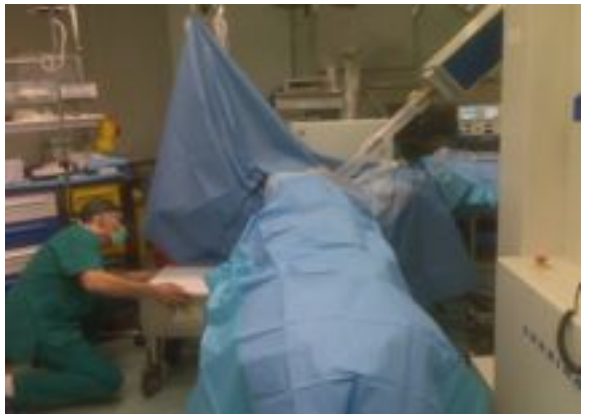




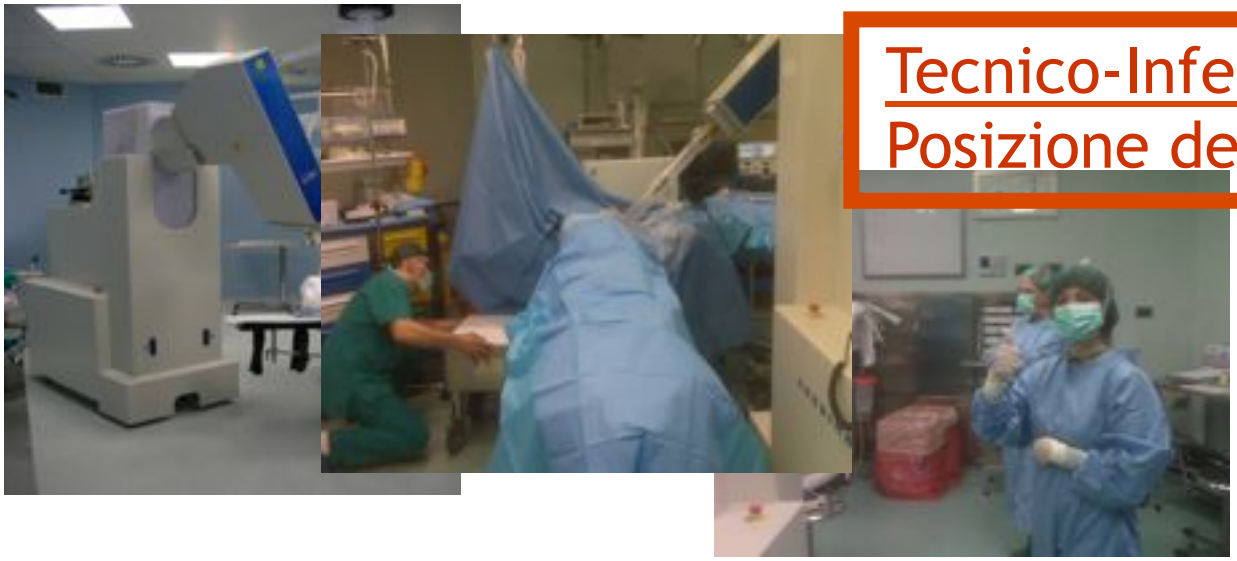




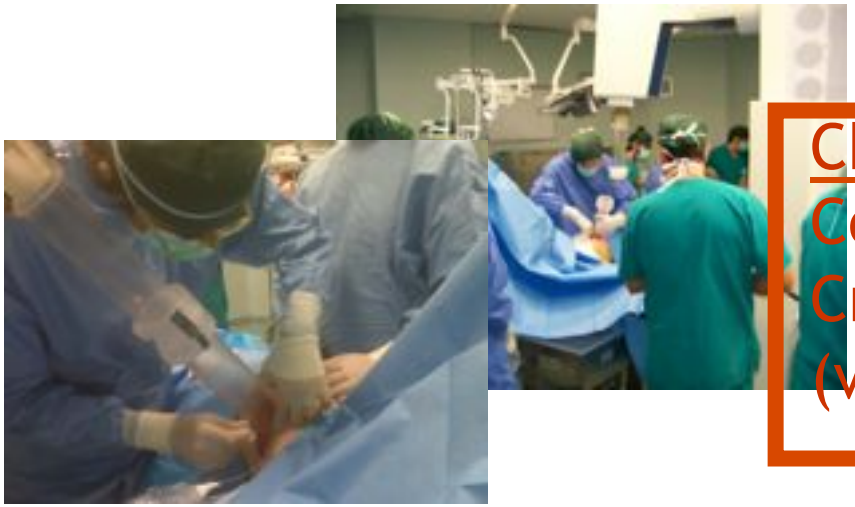




Selezione delle pazienti
Collaborazione e rispetto
Aderenza a programmi di QA

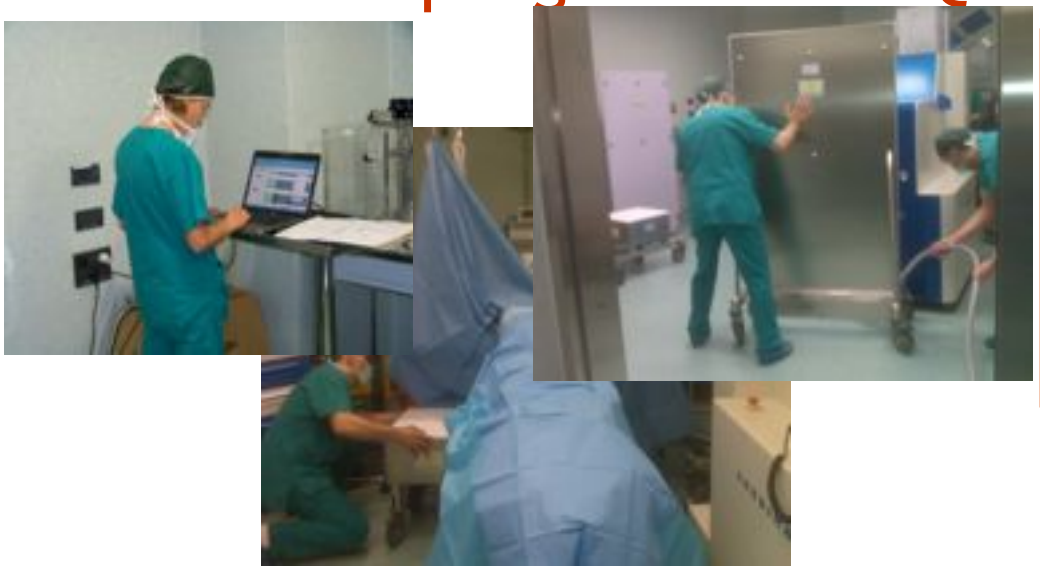


<u>Tecnico-Infermiere di sala:</u>
Posizione del tavolo operatorio



<u>Chirurgo - Oncologo Radioterapista:</u>
Confezionamento del CTV
Criteri di scelta del collimatore
(volume e sede nodulo, volume seno

Selezione delle pazienti
Collaborazione e rispetto
Aderenza a programmi di QA



Fisico-Tecnico:
Posizionamento delle schermature mobili

Fisico - Oncologo Radioterapista
identificazione energia ottimale
Valutazione della dose “misurata” ed eventuale correzione delle UM

Breast Cancer Res Treat (2010) 124:141–151
DOI 10.1007/s10549-010-1115-5

Istituto Europeo di Oncologia
Istituto di Ricovero e Cura a Carattere Scientifico

CLINICAL TRIAL

Intraoperative radiotherapy during breast conserving surgery: a study on 1,822 cases treated with electrons

Umberto Veronesi · Roberto Orecchia · Alberto Luini · Viviana Galimberti · Stefano Zurrida · Mattia Intra · Paolo Veronesi · Paolo Arnone · Maria Cristina Leonardi · Mario Ciocca · Roberta Lazzari · Pietro Caldarella · Nicole Rotmensz · Claudia Sangalli · Daniele Sances · Patrick Maisonneuve

cosa dicono gli autori……

Table 3 First unfavourable event and deaths

	N	%	Annual rate (%)
First event			
True local recurrence	42	2.3	0.77
Ipsilateral breast cancer	24	1.3	0.44
Regional metastasis	18	1.0	0.33
Contralateral carcinoma	19	1.0	0.35
Distant metastasis	26	1.4	0.47
Other carcinoma	33	1.8	0.60
Death as first event	11	0.6	0.20
Any first event[a]	171	9.4	3.12
Deaths			
Deaths due to breast cancer	28	1.5	0.46
Deaths due to other causes	12	0.7	0.20
Unspecified cause of death	6	0.3	0.10
Any cause of death	46	2.5	0.76

[a] One patient developed simultaneously distant metastasis and contralateral breast cancer and another patients axillary metastasis and contralateral breast cancer

mean follow-up of 36.1 months,

4.6% in breast relapse

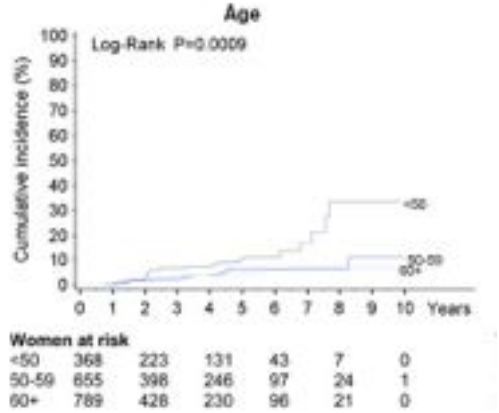
Table 2 Side effects among 1,822 patients

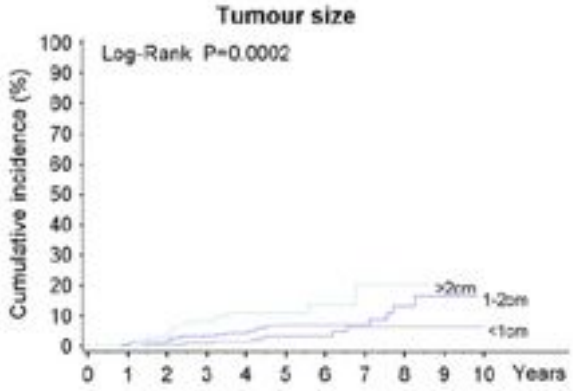
Side effects	*N*	%
Mild fibrosis	32	1.8
Severe fibrosis	2	0.1
Lyponecrosis	78	4.2
Haematoma	101	5.5
Oedema	24	1.3
Pain	13	0.7
Wound infection	24	1.3
Sieroma	235	12.9
No side effect	1434	78.7
1 Side effect	292	16.0
2 Side effects	76	4.2
3 Side effects	16	0.9
4 Side effects	3	0.2
5 Side effects	1	<0.1

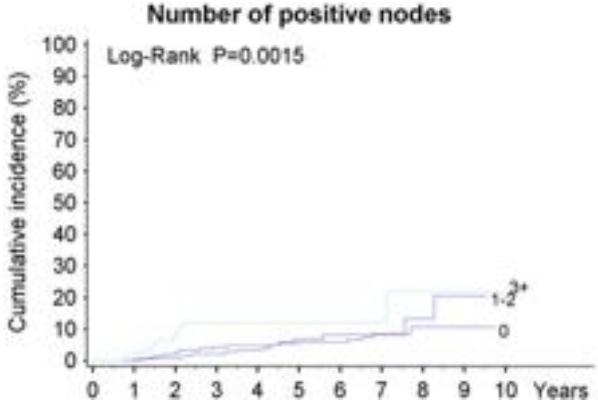
Breast Cancer Res Treat (2010) 124:141–151
DOI 10.1007/s10549-010-1115-5

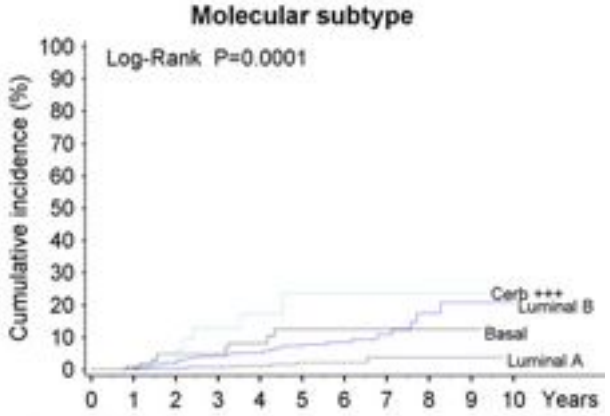
CLINICAL TRIAL

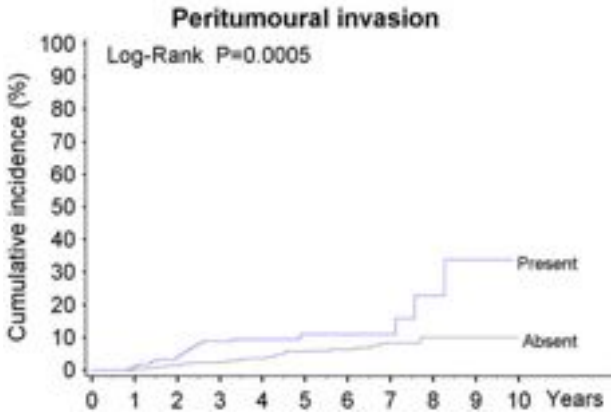
Intraoperative radiotherapy during breast conserving surgery: a study on 1,822 cases treated with electrons

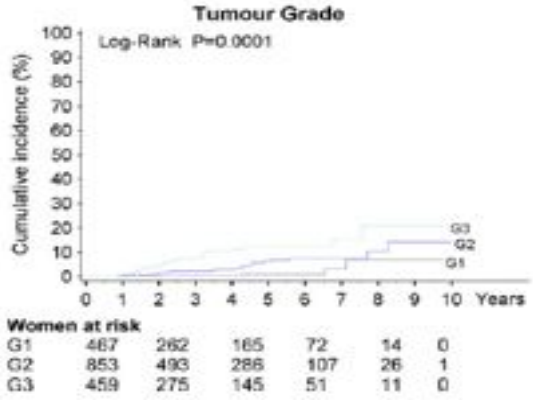












2011

Istituto Europeo di Oncologia

Istituto di Ricovero e Cura a Carattere Scientifico

International Journal of Radiation Oncology biology • physics

Clinical Investigation: Breast cancer

How Do the ASTRO Consensus Statement Guidelines for the Application of Accelerated Partial Breast Irradiation Fit Intraoperative Radiotherapy? A Retrospective Analysis of Patients Treated at the European Institute of Oncology

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 74, No. 4, pp. 987–1001, 2009

0360-3016/09/$–see front matter

doi:10.1016/j.ijrobp.2009.02.031

CONSENSUS STATEMENT

ACCELERATED PARTIAL BREAST IRRADIATION CONSENSUS STATEMENT FROM THE AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO)

Benjamin D. Smith, M.D.,[*] Douglas W. Arthur, M.D.,[†] Thomas A. Buchholz, M.D.,[†] Bruce G. Haffty, M.D.,[‡] Carol A. Hahn, M.D.,[‖] Patricia H. Hardenbergh, M.D.,[¶] Thomas B. Julian, M.D.,[#] Lawrence B. Marks, M.D.,[**] Dorin A. Todor, Ph.D.,[‡] Frank A. Vicini, M.D.,[††] Timothy J. Whelan, M.D.,[‡‡] Julia White, M.D.,[§§] Jennifer Y. Wo, M.D.,[‖‖] and Jay R. Harris, M.D.[¶¶]

Table 1 Criteria defining suitability for accelerated partial breast irradiation according to the American Society for Radiation Oncology (ASTRO) consensus statements

	294 ASTRO guidelines		812
	Suitable	Cautionary	Unsuitable
Patient factors		691	
Age, years	≥60	50–59	<50
BRCA1/2 mutation	Absent	Absent	Present
Pathologic factors			
Tumor size, cm	≤2	2.1–3.0	>3
pT	pT1	pT0 or pT2	pT3–pT4
Margins	Negative	Close	Positive
Grade	Any	Any	Any
LVI	No	Limited/focal	Extensive
ER status	Positive	Negative	Any
Multicentricity	Uncentric	Unicentric	Present
Multifocality	Unifocal	Unifocal	Multifocal
Histology	Invasive ductal*	Invasive lobular	Any
Pure DCIS	Not allowed	≤3 cm	>3 cm
EIC	Not allowed	≤3 cm	>3 cm
Nodal factors			
Nodal stage	pN0 (i^-,i^+)	pN0 (i^-,i^+)	pN1, pN2, pN3
Nodal surgery	SNB or ALND	SNB or ALND	Not performed
Treatment factors			
Neoadjuvant therapy	Not allowed	Not allowed	Yes

at least one of the unsuitable characteristics

The main reasons:

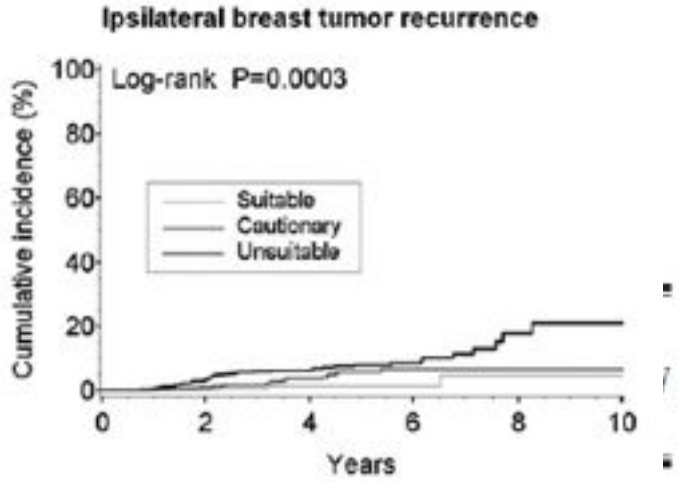
- **lymph node +,**
- **age <50 years,**
- **LVI,**
- **extended or prevalent EIC.**

International Journal of Radiation Oncology biology • physics

All the 1,822 cases except for 25 could be classified according to ASTRO CS:

294 patients into the **suitable** group, → **LR 1,5%**
691 patients into the **cautionary** group, → **LR 4,4%**
812 patients into the **unsuitable** group. → **LR 8,8%**

5-year rate of ipsilateral breast recurrence ($p = 0.0003$).



Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial

Umberto Veronesi, Roberto Orecchia, Patrick Maisonneuve, Giuseppe Viale, Nicole Rotmensz, Claudia Sangalli, Alberto Luini, Paolo Veronesi, Viviana Galimberti, Stefano Zurrida, Maria Cristina Leonardi, Roberta Lazzari, Federica Cattani, Oreste Gentilini, Mattia Intra, Pietro Caldarella, Bettina Ballardini

cosa dicono gli autori……

2000 → 2007

www.thelancet.com/oncology Published online November 11, 2013

Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial

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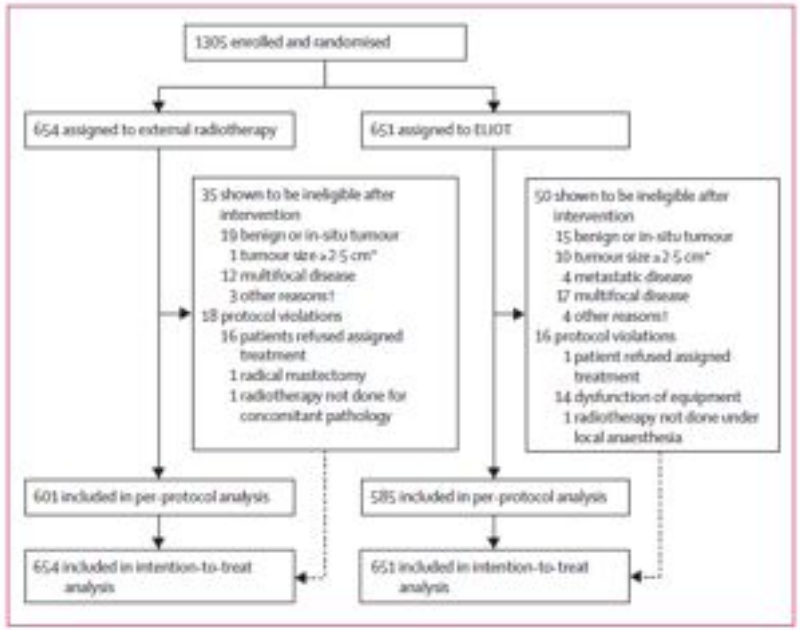


women aged 48–75 years with early breast cancer

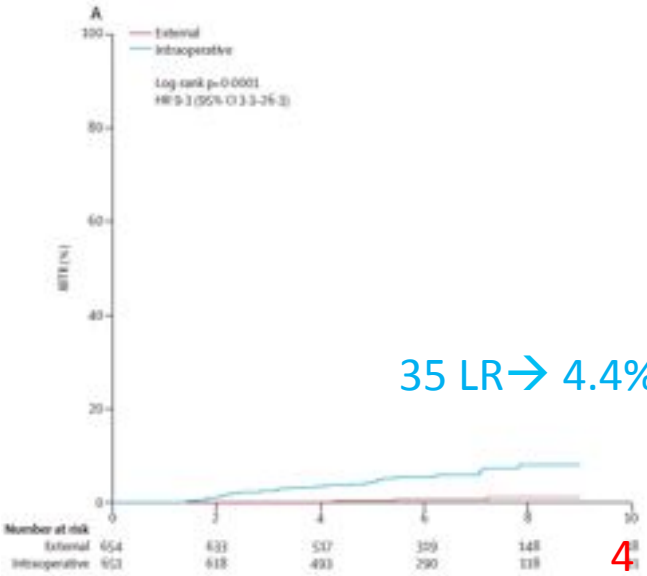
a maximum tumour diameter of up to 2. 5 cm

suitable for breast-conserving surgery

This was an equivalence trial; the prespecified equivalence margin was local recurrence of 7.5% in the intraoperative radiotherapy group

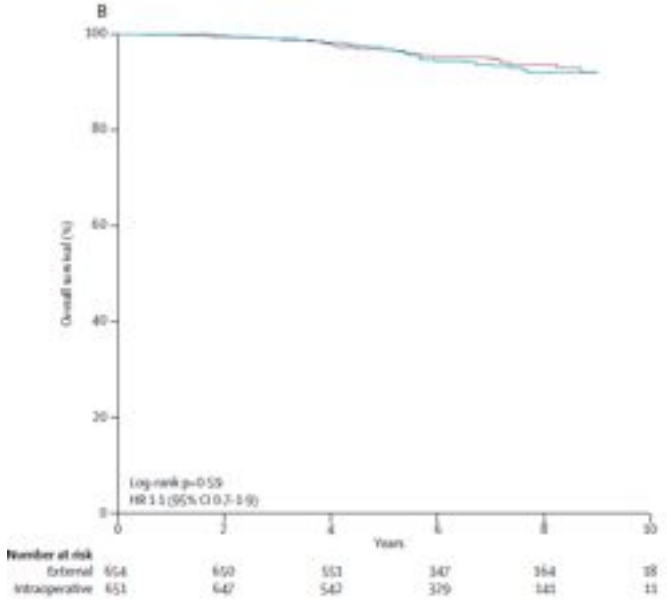
medium FU of 5. 8 years

true recurrences →2.5%*vs* 0.4%
new tumours→ 1.9% *vs* 0%



35 LR→ 4.4% a 5 aa

4 LR→ 0.4% a 5 aa



Trial

progettato anni fa

prima della pubblicazione dei criteri ESTRO/ ASTRO

prima che fossero disponibili dati sulla IORT con e-

quando le LR dopo chirurgia conservativa +RT→3-20%

criteri age >48 anni; nodulo <2.5cm; American Brachytherapy Society
American Society Breast Surgeons

controindicazioni : DCIS; multifocalità; T>2.5 cm; M+;

NON è Intention to treat→ tutte le pazienti hanno realmente ricevuto il trattamento del braccio di randomizzazione

Veronesi, 2013

	External radiotherapy	Intraoperative radiotherapy with electrons
Age*		
48–49 years	43 (7%)	44 (7%)
50–59 years	267 (41%)	286 (44%)
60–69 years	269 (41%)	259 (40%)
≥70 years	75 (11%)	62 (10%)
Histology†		
Ductal	514 (79%)	524 (81%)
Lobular	57 (9%)	53 (8%)
Ductal and lobular	21 (3%)	17 (3%)
Other	55 (9%)	53 (8%)
Pathological size‡		
≤1 cm	194 (30%)	199 (31%)
1–1·5 cm	235 (36%)	243 (38%)
1·5–2 cm	115 (18%)	120 (19%)
>2 cm	103 (16%)	83 (13%)
Number of positive nodes†		
None	471 (73%)	478 (74%)
1–3	138 (21%)	138 (21%)
≥4	38 (6%)	31 (5%)

51%→<59aa

32% →>1.5cm

26%→ N+

	External radiotherapy	Intraoperative radiotherapy with electrons
Tumour grade§		
G1	160 (25%)	196 (31%)
G2	328 (52%)	305 (48%)
G3	145 (23%)	129 (20%)
Oestrogen receptor¶		
Negative	56 (9%)	63 (10%)
Positive	589 (91%)	583 (90%)
Progesterone receptor‖		
Negative	132 (20%)	158 (24%)
Positive	512 (80%)	487 (76%)
Proliferative index (Ki-67)**		
<14%	242 (38%)	263 (41%)
14–20%	138 (21%)	138 (21%)
>20%	265 (41%)	244 (38%)
Molecular subtype¶		
Luminal A	237 (37%)	256 (40%)
Luminal B	352 (55%)	327 (51%)
HER2 positive (non-luminal)	24 (4%)	20 (3%)
Triple negative	32 (5%)	43 (7%)

20%→G3

38%→>20 ki67

61% →cl molecolare sfavorevole

5-year IBTR exceeded **10%** in patients with

large (>2 cm) tumours,
four or more positive lymph nodes,
poorly differentiated (grade 3) tumours,
oestrogen-receptor negative tumours,
triple-negative breast tumours

Overall, **5-year** occurrence of **IBTR** was **1.5%** for selected low risk pts

- The logical conclusion is that IOERT should be restricted to suitable patients

- One option would be to use preoperative criteria such as tumour size, breast volume, age of the patient, and pathological and biological studies of preoperative biopsy specimens to help with identifying suitable patients

- Another possibility would be to treat all patients with full-dose IOERT during surgery and, after final categorisation, to give additional external whole breast irradiation to patients at high risk of local recurrence

Veronesi, 2013

Ann Surg Oncol (2014) 21:3787–3792
DOI 10.1245/s10434-014-3998-6

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

REVIEW ARTICLE – BREAST ONCOLOGY

Intraoperative Radiation Therapy: A Critical Analysis of the ELIOT and TARGIT Trials. Part 1—ELIOT

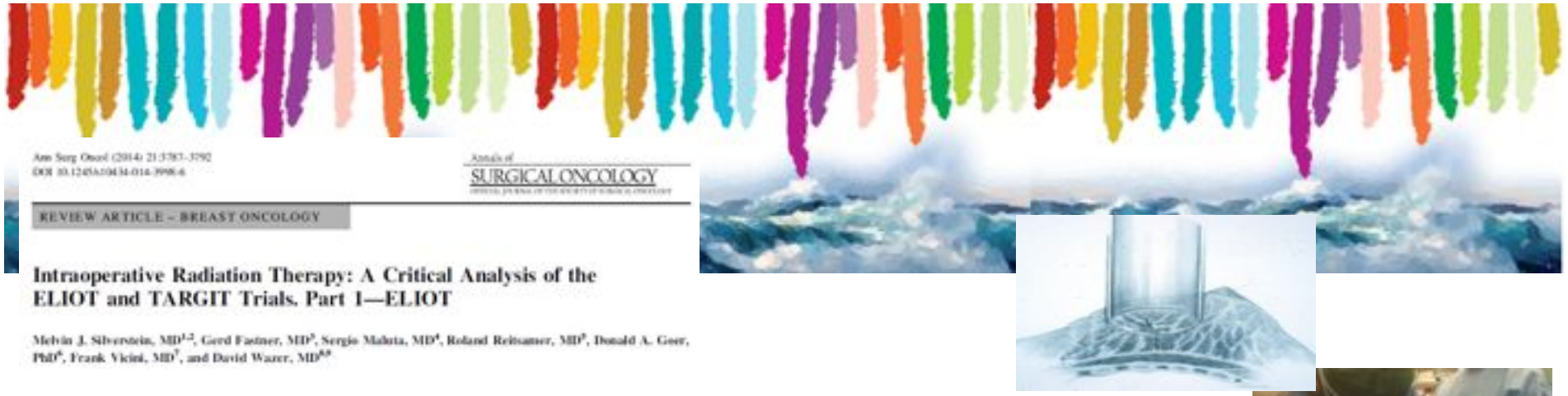
Melvin J. Silverstein, MD[1,2], Gerd Fastner, MD[3], Sergio Maluta, MD[4], Roland Reitsa[illegible]er, MD, Don[illegible]d [illegible]. G[illegible]er, PhD[6], Frank Vicini, MD[7], and David Wazer, MD[8,9]

quali commenti

Analysis of the results began 5 years after accrual of the last patient

. . .

For the 23 % of the ELIOT patients who were ASTRO suitable for APBI, the IBTR was 1.5 % at 5 years and equivalent to the IBTR for the EBRT-suitable patients.



LR→14 of 35 (40 %) "elsewhere" recurrences

It is important non only….

- to define **patients at low risk** of harboring microscopic disease beyond the tumor site

- but also to define the **proper coverage of the tumor bed**

proper coverage of the tumor bed

~~4 cm~~
5 cm
6 cm
7 cm
8 cm

It has been estimated that, depending on the energy, a 4-cm applicator covers at most only 55 % of the clinical treatment volume (“CTV”) to the 90 % prescription dose.

Kreketov, 2014

To ensure uniform coverage of microscopic residual disease, the IOERT applicator should have a circumferential dimension at least 1.5 to 2 cm larger than the maximum tumor dimension.

SURGICAL ONCOLOGY

REVIEW ARTICLE – BREAST ONCOLOGY

Intraoperative Radiation Therapy: A Critical Analysis of the ELIOT and TARGIT Trials. Part 1—ELIOT

Melvin J. Silverstein, MD[1,2], Gerd Fastner, MD[2], Sergio Maluta, MD[3], Roland Reitsamer, MD[2], Donald A. Goer, PhD[4], Frank Vicini, MD[5], and David Wazer, MD[6,7]

TABLE 3 Reported guidelines at the EIO for low-risk IOERT Group

Age	≥60 years
Tumor size	<2 cm
Applicator size	6 cm minimum, 5 cm occasionally
Grade	G1/G2
ER status	ER+
Proliferative index	Ki-67 < 20
Biology	Luminal A
Lobular CA	Only with MRI assessment

As reported at ISIORT 2012, Baveno, Italy, and with permission of Springer Science & Business Media[24]

Taccuino IORT Mammella

Istruzioni operative

Associazione Italiana di Radioterapia Oncologica

Gruppo di Studio: IORT

Coordinatori: Dott. L. Tomio e Dott. M Guenzi

Revisionato per il Gruppo di Lavoro IORT:
M. Alessandro (SC Radioterapia oncologica, Citta di Castello); D. Beldì (SCDU Radioterapia, A.O.U. Ospedale Maggiore della Carità, Novara); F. Berti (UO Radioterapia e MN, Ist. Oncologico Veneto, Padova); M. Benedetti (UO Radioterapia, Ospedale Infermi, Rimini), M. Calabrese (Senologia Radiologica, A.O.U. IRCCS San Martino- IST, Genova); L.F. Cazzaniga (UO Radioterapia oncologica, A.O. Papa Giovanni XXIII, Bergamo); M.G. Cesaro (UO Radioterapia oncologica, Osp. Cà Foncello, Treviso); C. Fillini (SC Radioterapia oncologica, A.O. S.Croce e Carle, Cuneo); P. Fenaroli (UO Chirurgia Senologica, A.O. Papa Giovanni XXIII, Bergamo); G. Gritti (UO Radioterapia oncologica, A.O. Papa Giovanni XXIII, Bergamo); G. Ivaldi (UO Radioterapia, IRCCS Fondazione Maugeri, Pavia); R. Lazzari (Divisione di Radioterapia Istituto Oncologico Europeo, Milano); N. Marciai (U.O. Radioterapia, A.O., Verona); L. Menegotti (Fisica Sanitaria, Osp. S. Chiara, Trento); M. Pellegrini (Servizio di Senologia, APSS, Trento); F. Perini (UO Radioterapia, Ospedale Infermi, Rimini); M. Ricci (Anatomia Patologica, Ospedale Infermi, Rimini); A. Rosso (UOC Radioterapia, ARNAS Garibaldi; Catania); A. Stefanelli (U.O. Radioterapia oncologica, A.O.U. Arcispedale s.Anna, Ferrara).

Taccuino IORT Mammella

Istruzioni operative

Associazione Italiana di Radioterapia Oncologica

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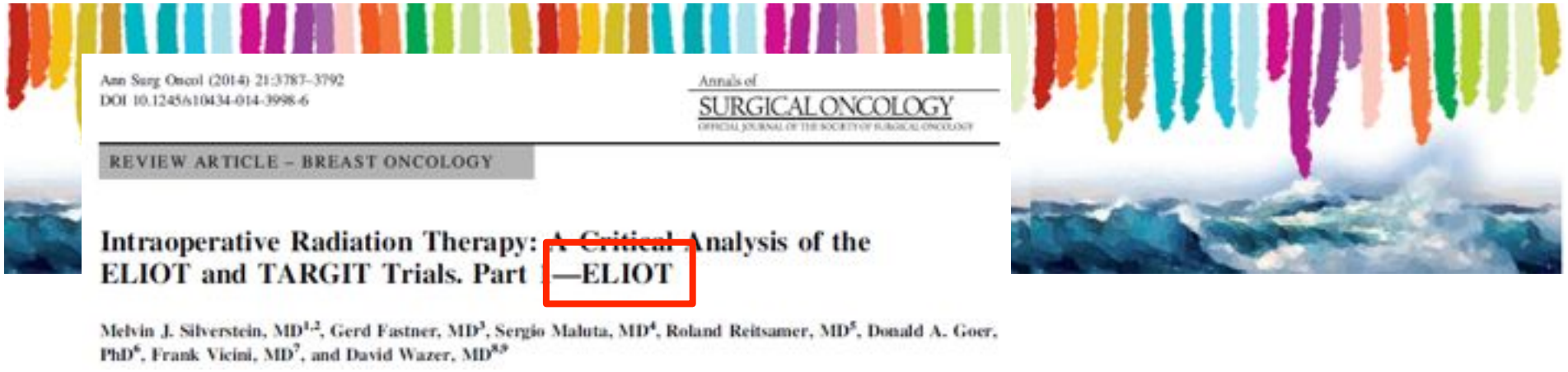
INDICAZIONI e CONTROINDICAZIONI
VALUTAZIONE PRE CHIRURGICA
CONSENSO INFORMATO
STEP in SALA OPERATORIA
FOLLOW UP

Scelta e Posizionamento del collimatore:

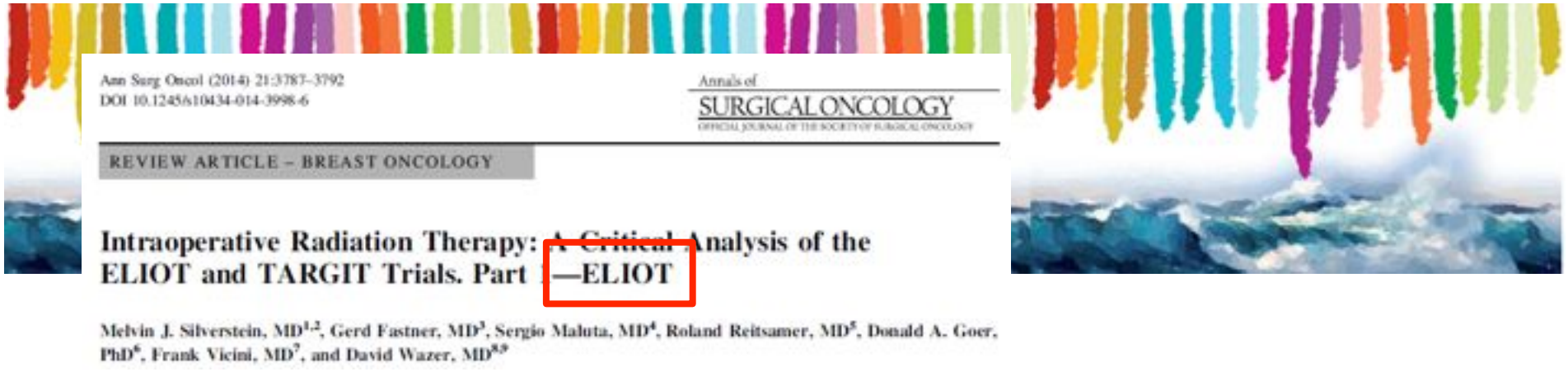
Si ritiene opportuno l'utilizzo di **collimatori di diametro superiore ai 4 cm**, considerando comunque il diametro della neoplasia e la sede della stessa nella mammella.

Si ritiene opportuno **evitare l'erniazione** del tessuto ghiandolare all'interno del collimatore con l'ausilio di dischi di plexiglass o materiale plastico, dopo opportuna valutazione dosimetrica.



The ELIOT trial has contributed to our understanding of whether a single-dose treatment using electrons may be possible.

The Trial included some high-risk patients that today would not be considered a good choice for APBI.



It appears, however, that IOERT APBI may have a subset of low-risk women

ASTRO suitable,
ELIOT Low Risk,
Luminal A

for whom IOERT could be effective, with a recurrence rate in the 2 % range at 5 years.

In spite of a 5.8-year median follow-up, the ELIOT data are still early and single-fraction IOERT patients should be treated under strict institutional protocols.

When long-term results are available, it is likely there will be a higher overall recurrence rate for IOERT when compared with EBRT, but **we should be able to select subgroups of favorable patients** where this difference is small and acceptable.

Overall, the results of the ELIOT Trial are reasonably mature and encouraging

Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial

Jayant S Vaidya, Lancet 2014; 383: 603–13

median follow-up of 29 months

the 5-year LR → 3.3 % and 1.3 %,
p = .042.

low risk **group→ prepathology /PGR +**

Selezione delle pazienti candidabili

Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial

Umberto Veronesi, Lancet Oncol 2013; 14: 1269–77

median follow-up of 5.8 years

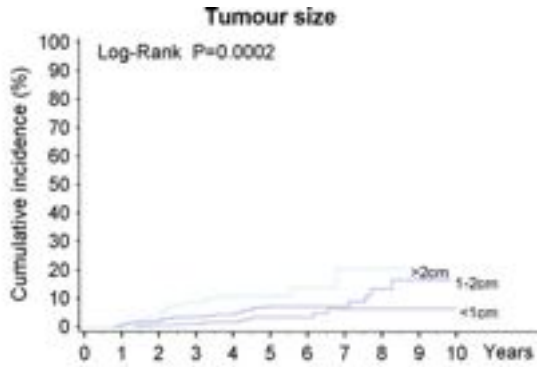
the 5-year LR→ 4.4 % vs 0.4 %,
p = .0001

low-risk **ELIOT group** →5-year LR 1.5 %

TARGIT-A vs ELIOT

12% versus 14% were 2 cm or bigger
17% versus 26% were node positive
15% versus 20% were grade 3

making comparisons difficult.

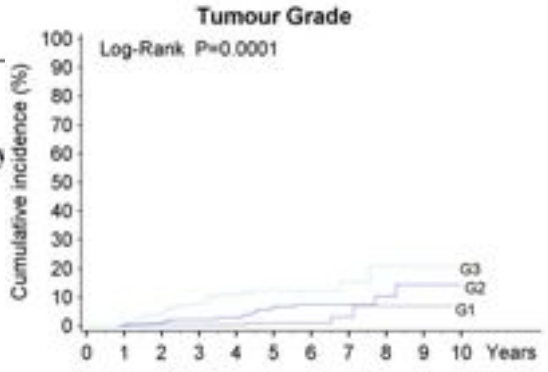


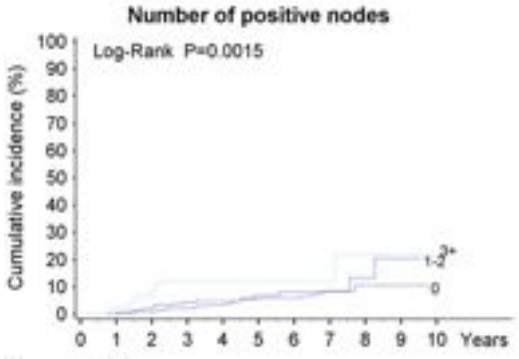
Breast Cancer Res Treat (2010) 124:141–151
DOI 10.1007/s10549-010-1115-5

CLINICAL TRIAL

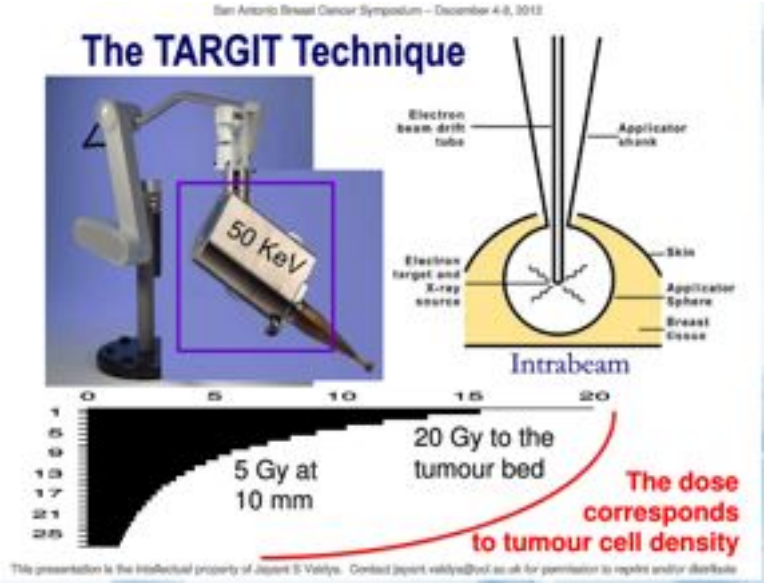
Intraoperative radiotherapy during breast conserving surgery a study on 1,822 cases treated with electrons

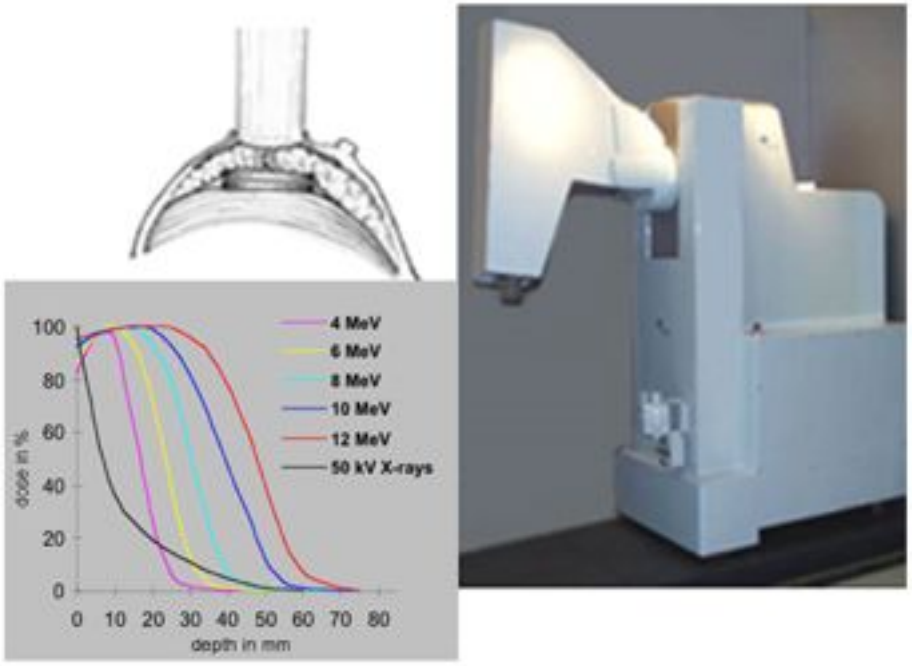
Umberto Veronesi · Roberto Orecchia · Alberto Luini · Viviana Galimberti · Stefano Zurrida · Mattia Intra · Paolo Veronesi · Paolo Arnone · Maria Cristina Leonardi · Mario Cioca · Roberta Lazzari · Pietro Caldarella · Nicole Rotmensz · Claudia Sangalli · Daniele Sances · Patrick Maisonneuve





TARGIT-A vs ELIOT





TARGIT-A	vs	ELIOT
Multicentrico		Monocentrico
2000→ 2012: 3451 pz		2000→ 2007: 1305 pz
FU		FU
Risk adapted RT 15% anche ERT		NON è Intention to treat→ tutte le pazienti hanno ricevuto il trattamento del braccio di randomizzazione

Intraoperative Radiotherapy in Breast Conserving Surgery

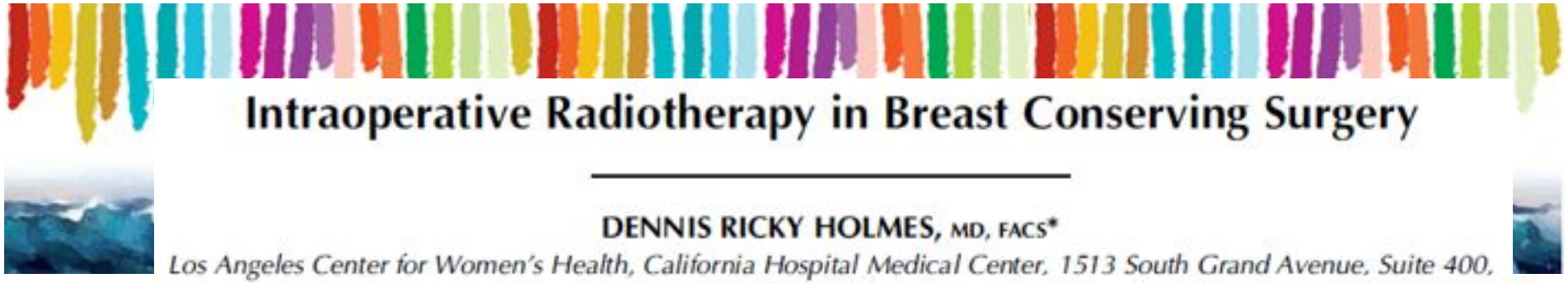
Journal of Surgical Oncology 2014;110:68–74

DENNIS RICKY HOLMES, MD, FACS*

Los Angeles Center for Women's Health, California Hospital Medical Center, 1513 South Grand Avenue, Suite 400, Los Angeles, California 90015

Intraoperative radiotherapy is a novel intervention capable of significantly

reducing the inconvenience,
morbidity,
cost of breast radiotherapy.



Intraoperative Radiotherapy in Breast Conserving Surgery

DENNIS RICKY HOLMES, MD, FACS*
Los Angeles Center for Women's Health, California Hospital Medical Center, 1513 South Grand Avenue, Suite 400, Los Angeles, Californ

Journal of Surgical Oncology 2014;110:68–74

The TARGIT A and ELIOT trials **show IORT to be as safe and effective as standard radiotherapy** for

post-menopausal women
with low to intermediate grade,
lymph node negative
invasive ductal carcinoma lacking high-risk features

A recent patient preference study showed that most breast cancer patients would choose IORT over WB-EBRT even if it were associated with a 10-year 2.3% higher absolute risk of local recurrence

Breast Cancer Res Treat (2014) 143:135–140
DOI 10.1007/s10549-013-2782-9

CLINICAL TRIAL

Patient preferences regarding intraoperative versus external beam radiotherapy following breast-conserving surgery

Michael D. Alvarado · Jay Conolly · Catherine Park · Theadora Sakata · Aron J. Mohan · Brittany L. Harrison · Mitchell Hayes · Laura J. Esserman · Elissa M. Ozanne

Ulteriore follow up per confermare o meno i dati attuali di entrambi gli studi

Controllo di malattia sembra essere adeguato in pazienti accuratamente selezionate

La metodica migliora la qualità di vita della paziente

Ottimizza la gestione delle risorse dei centri

La IORT non è ancora considerabile uno standard e deve essere attuato nell'ambito di attenti protocolli di istituto

Sapendo di dover offrire una attenta

- selezione delle pazienti (ASTRO-ESTRO)
- tecnica accurata
- consenso informato !