Carcinoma lobulare

Rappresenta una controindicazione assoluta alla PBI?

IEO
Arc Advanced Radiotherapy Center

Suitable/good	ASTRO	ESTRO
age	≥60 years	>50 years
BRCA1/2mutation	Not present	
histology	IDC or other favorable subtypes	IDC , mucin, tubular, medullary, colloid
ILC	Not allowed	Not allowed
Associated LCIS	allowed	Allowed
DCIS	Pure, not allowed	Not allowed
HG	Any	Any
Tumor size	≤2cm T1	pT1-2 (≤30 mm)
Surgical margin	Negative (≥2mm)	Negative (≥2mm)
Multicentricity	Unicentric	Unicentric
Multifocality	Unifocal total size≤2cm	Unifocal
EIC	Not allowed	Not allowed
LVI	No	Not allowed
ER, PR status	Positive	Any
Nodal status	pN0 (SN Bx orALND)	pN0 (SN bx or ALND)
Neoadjuvant CT	Not allowed	Not allowed

Cautionary/interm	ASTRO	ESTRO
age	50-59 years	>40-50 years years
histology	Invasive lobular	Invasive lobular
ILC	allowed	allowed
Associated LCIS	allowed	Allowed
DCIS	Pure, ≤3cm	allowed
HG	Any	Any
Tumor size	2.1-3.0 cm, T0or T2	pT1-2 (≤30 mm)
Surgical margin	Close (<2mm)	Close (<2mm)
Multicentricity	Unicentric	Unicentric
Multifocality	Unifocal total size 2.1-3.0 cm	Multifocal (limited, within 2cm of index lesion)
EIC	≤3cm	Not allowed
LVI	Limited/focal	Not allowed
ER, PR status	negative	Any
Nodal status	pN0 (SN Bx orALND)	pN1 mi, pN1a (ALND)
Neoadjuvant CT	Not allowed	Not allowed

PRINCIPLES OF RADIATION THERAPY

Whole Breast Radiation:
Target definition includes the majority of the breast tissue, and is best done by both planning. A unifo toxicity are the g such as wedges, modulated radiat positioning. The Gy per fraction, o tumor bed is reco (age < 50, positiv margins). This ca or photon fields. schedules are giv

Chest Wall Radia The target includ drain sites where been reconstruct electrons are app encouraged, in o minimize exposure of these organs. Special consideration should be given to the use of bolus material when photon fields are used, to

Dose is 50 - 50.4 Gy, given as 1.8 - 2.0 Gy fraction size (± scar boost at 2 Gy per fraction to a total dose of approximately 60 Gy); all dose schedules given 5 days per week. If internal mammary lymph nodes are should be given to to the internal diation oncologist. where radiation ode field.

ntrol in selected arable to those wever, is limited participate in tatement from the atients who may be carriers of BRCA al T1N0 ER- l or a favorable d margins should day with ce per day with external beam photon therapy is prescribed to the tumor bed. Other fractionation schemes are currently under investigation.

Accelerated Partial Breast Irradiation (APBI):
Preliminary studies of APBI suggest rates of local control in selected patients with early stage breast cancer may be comparable to those treated with standard whole breast RT. Follow-up, however, is limited and studies are on-going. Patients are encouraged to participate in clinical trials. If not trial eligible, per the consensus statement from the American Society for Radiation Oncology (ASTRO), patients who may be suitable APBI are women 60 y and older who are not carriers of BRCA 1/2 mutation treated with primary surgery for a unifocal T1N0 ER-positive cancer. Histology should be infiltrating ductal or a favorable ductal subtype, not be associated with EIC or LCIS and margins should be negative. 34 Gy in 10 fractions delivered twice per day with brachytherapy or 38.5 Gy in 10 fractions delivered twice per day with external beam photon therapy is prescribed to the tumor bed. Other fractionation schemes are currently under investigation.

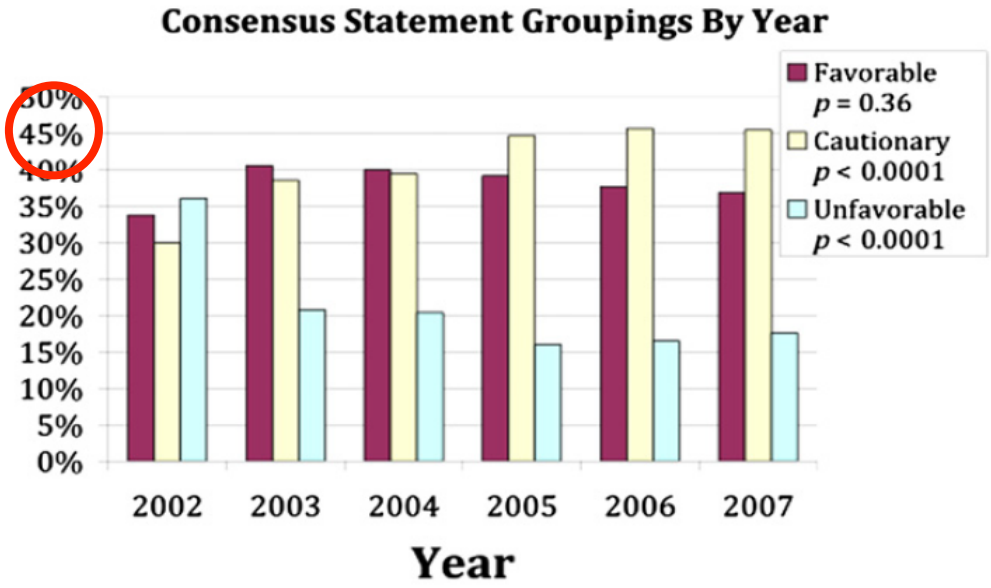
ELSEVIER

BRACHYTHERAPY

Brachytherapy 10 (2011) 479–485

Accelerated partial breast irradiation via brachytherapy: A patterns-of-care analysis with ASTRO consensus statement groupings

Zain A. Husain[1,*], Usama Mahmood[1], Alexandra Hanlon[2], Geoffrey Neuner[1], Robert Buras[3], Katherine Tkaczuk[4], Steven J. Feigenberg[1]



ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 82, No. 2, pp. 674–681, 2012

0360-3016/$ - see front matter

doi:10.1016/j.ijrobp.2010.11.077

CLINICAL INVESTIGATION Breast Cancer

PATIENT PREFERENCES AND PHYSICIAN PRACTICE PATTERNS REGARDING BREAST RADIOTHERAPY

David J. Hoopes, M.D.,* David Kaziska, Ph.D.,† Patrick Chapin, Ph.D.,† Daniel Weed, M.D.,‡ Benjamin D. Smith, M.D.,‖ E. Ronald Hale, M.D., M.P.H.,¶ and Peter A. Johnstone, M.D.‡

Physician practice patterns in BCT (10/2008)		
Technique	**% physicians**	**95%CI**
CF-WBRT	99.1%	98.2-100%
HF-WBRT	43.8%	38.9-48.7%
Balloon -PBI	55.4%	50.6-60.4%
3D-PBI	35.8%	31.2-40.6%
Multicath-PBI	10.8%	7.8-14.0%

55% of physicians do not offer PBI on clinical trials

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

Printed in the USA.
0360-3016/09/$–see front matter

ELSEVIER

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.[¶¶]

Regarding other pathologic features, the Task Force recommended that patients with invasive lobular histology be included in the ''cautionary'' group because the Christie Hospital randomized clinical trial showed that lobular histology was associated with a higher risk of IBTR than was ductal histology among patients treated with APBI (4, 5) and because 6 of the 10 prospective single-arm trials having ≥4 years' follow-up and low recurrence rates excluded patients with lobular histology altogether

Radiotherapy and Oncology 94 (2010) 264–273

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

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)

Csaba Polgár [a,*], Erik Van Limbergen [b], Richard Pötter [c], György Kovács [d], Alfredo Polo [e], Jaroslaw Lyczek [f], Guido Hildebrandt [g], Peter Niehoff [h], Jose Luis Guinot [i], Ferran Guedea [j], Bengt Johansson [k], Oliver J. Ott [l], Tibor Major [a], Vratislav Strnad [l], On behalf of the GEC-ESTRO breast cancer working group

On the other hand, in the current APBI series using careful pathologic assessment of margin status tumour bed BT alone maintained adequate LTC for patients with ILC, too

Based on these considerations, one can conclude that the presence of ILC should not influence decisions regarding local therapy, and patients with ILC can be successfully treated with BCS and APBI. However, to date only few women having ILC have been treated with APBI in prospective studies. Therefore, at this time there is only a limited evidence for the treatment of ILC outside the context of clinical trials.

Pioneer APBI studies (Polgar, 2010)

Institution	Tech.	Med FU	LR%	Ann. LR%	selection
Utzsoki H.	MDR	12	24	2	T 5 cm, 30%pNx, multifocal, 10% ILC,LVI+, EIC+
Cooktidge H.	EBI	8	12	1.5	T 4.5 cm,41% pN+, LVI+, EIC+
London Reg.Ca.C	HDR	7.6	15	2	T size 4.5 cm, 31% close margin, 15% pN+
Tufts Un.	HDR	7	9.1	1.30	45% close margin, 9% pN+, 55% EIC+,
Guy's H.	LDR	6	37	6.2	T >4cm, 56% positive margin, 44% pN+, 41% EIC+,ILC
Guy'S H.	MDR	6.3	18	2.9	T size 4cm, 43% positive margin, 45% pN+, 14% ILC, LVI+, EIC+
Florence H.	LDR	4.2	6	1.4	T 5cm, 38% pN+, 20% ILC, LVI+, EIC+
Osaka Med C.	HDR	4.3	5	1.15	15% positive margin, 35% EIC, 5% ILC

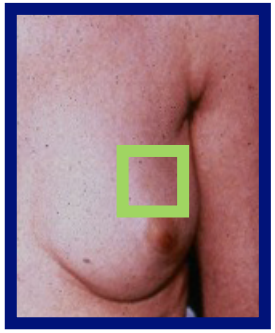
THE CHRISTIE-HOSPITAL TRIAL

Magee 1996

708 (T< 4cm, N0) pts

40 Gy/15 fx

Med 10 MeV, 8cm x 6 cm, 40-42.5 Gy in 8 fx/10 days



Crude breast recurrence by group[a]

Site	LF (n = 353) No. (%)	WF (n = 355) No. (%)
Breast only	21 (6)	13 (4)
Breast and regional nodes	18 (5)	5 (1)
Breast and distant metastases	30 (8.5)	17 (5)
Total	69 (19.5)	35 (10)

Actuarial breast recurrence[a]

Histology	LF No. (%)	WF No. (%)
Invasive ductal carcinoma	44 (22)	24 (12)
Grade 1	5 (13)	1 (<1)
Grade 2	19 (24)	11 (16)
Grade 3	19 (26)	12 (17)
Unknown	1	0
Invasive ductal carcinoma with predominant intraductal component	3 (27)	3 (24)
Intraduct carcinoma	2 (50)	0 (0)
Invasive lobular carcinoma	14 (43)	3 (17)
Mixed lobular and ductal carcinoma	3 (25)	1 (10)
Tubular carcinoma	1 (17)	0 (0)
Mucoid carcinoma	2 (22)	2 (18)
Medullary carcinoma	0 (0)	1 (17)
Lymphovascular invasion		
Yes	11 (36)	8 (25)
No	58 (20)	27 (11)
Unknown	9	7
All histologies	69 (25)	35 (13)

[a]The percentages are actuarial breast recurrence rates at 8 years.

Characteristics	
Median age	52 yrs
T size < 2cm	24%
T size 2-4 cm	76%
G1-G2	43%
G3	28%
EIC	4%
Lobular	9%
Incomplete/ unknown excision	20%
LVI	14%

Magee, 1996

Polgar, 2010, modified

Modern APBI studies with strict selection

Study	Tech	Med FU	LR %	selection
WBH Michigan	LDR/ HDR	9.7	5% 0.52 year	>40,max 3cm, pN0, margin -, ILC excluded
Orebro Med Cen	PDR	7.2	5.9% 0.83 year	≥40, max 4,2 cm, margin -, unifocal, 8% ILC, pN1
HNIO Budapest II	HDR/ EBRT	6.8	4.7% 0.69 year	>40, max 2cm, margin -, unifocal, G1-2, pN1mi, ILC excluded
Ninewells H.	LDR	5.6	0%	>40, max 3,5 cm , unifocal, pN1a, ILC excluded
FDA trial	Balloon	5.2	0	≥45, max 2cm, pN0, margin -, unifocal ,ILC excluded
Kiel-HNIO	Balloon	5	0	≥60, max 2 cm, pN0 , G1-2, margin -,EIC-,LVI-, ILC excluded
University Navarra	HDR	4.4	3.8% 0.86 year	T ≤3cm, margin -, unifocal, pN0, ILC excluded

Hungarian trial

Eligibility criteria

- pT1, pN0-1mi, grade 1–2
- non-lobular breast cancer, no EIC
- negative surgical margins

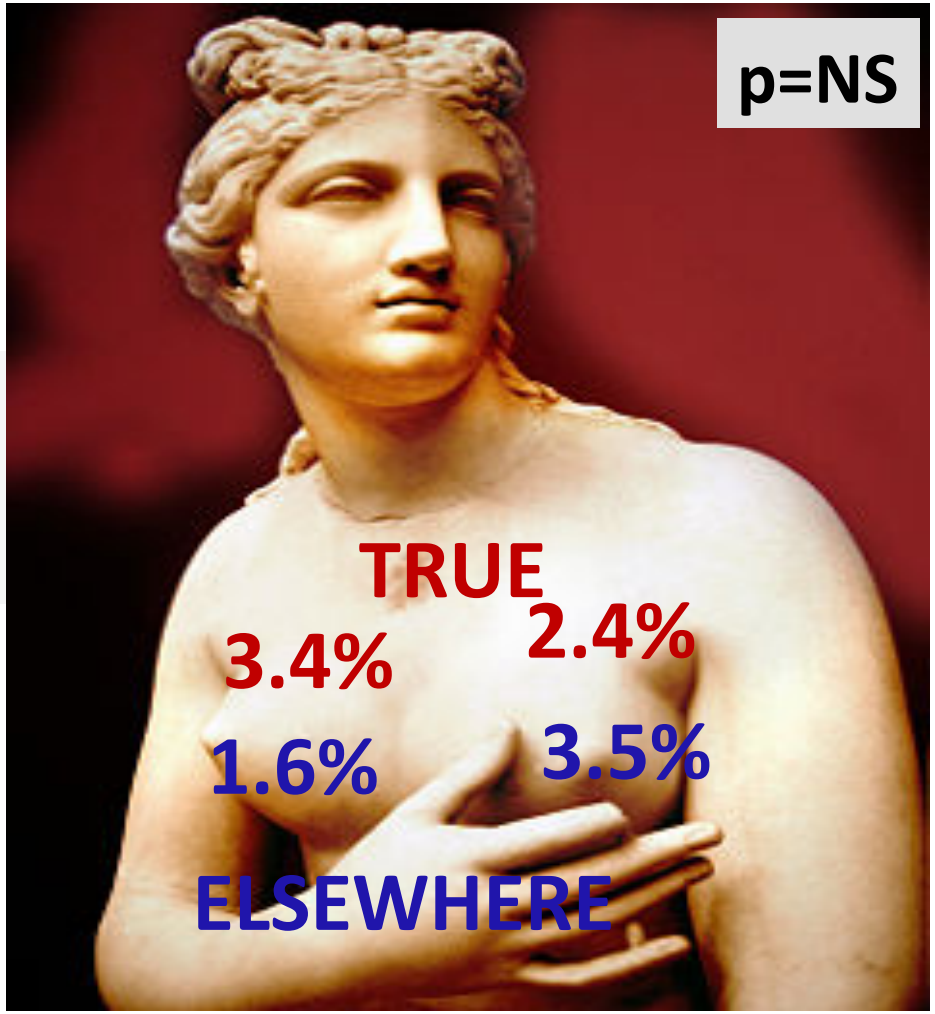
RT WB

arm 130 pts

10-year LR

5.1%

CLBC 6.4%



PBI

arm 128 pts

10-year LR

5.9%

CLBC 8.3%

Polgar 2013

www.thelancet.com Vol 382 Published online November 11, 2013

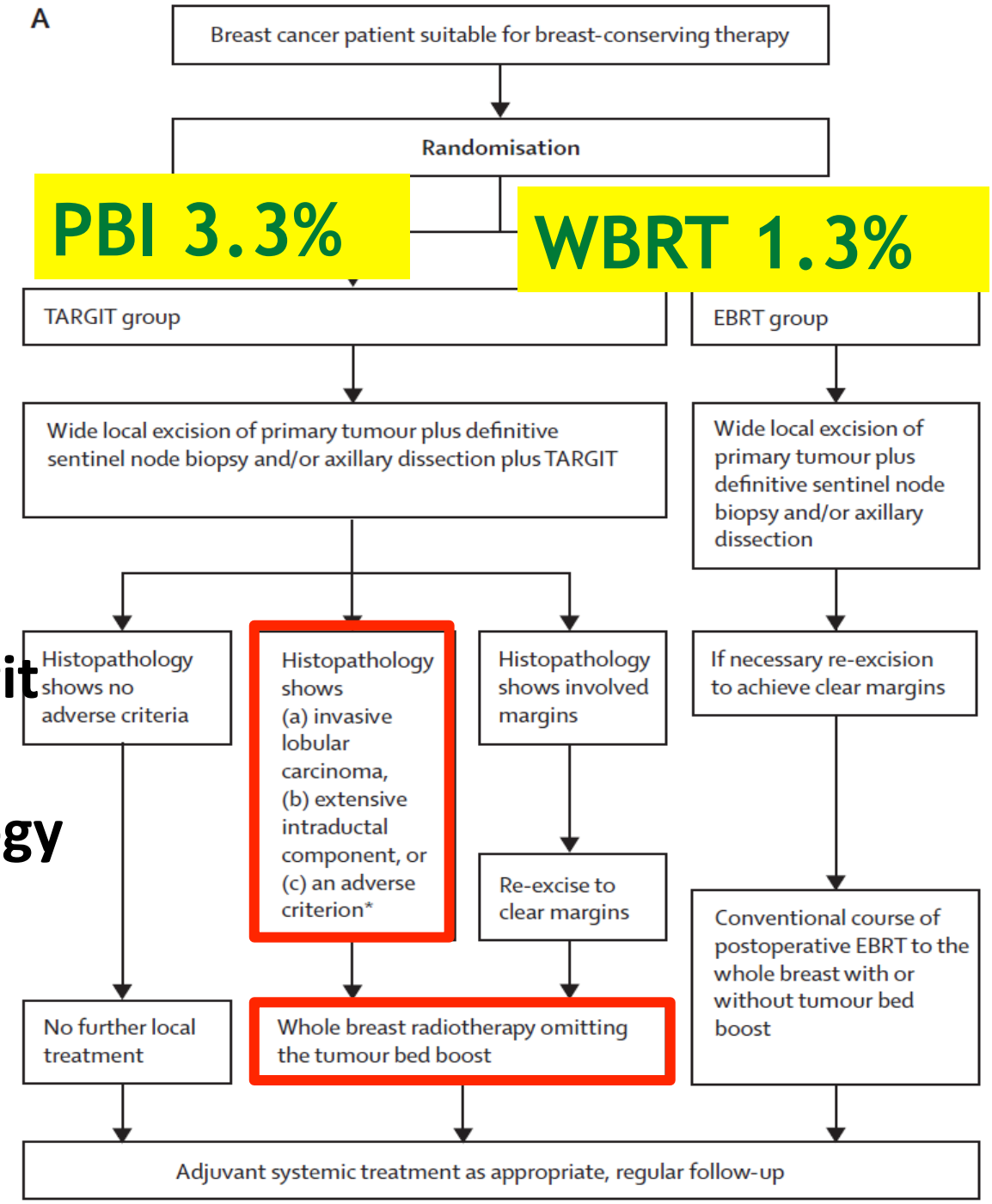
Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial

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 Corica, Norman R Williams, Michael Baum, on behalf of the TARGIT trialists' group

- **Intention to treatment**

15% randomized to Targit received WBRT because of adverse histopathology

med FU 43 months



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Brachytherapy 12 (2013) 267–277

BRACHYTHERAPY

The American Brachytherapy Society consensus statement for accelerated partial breast irradiation

Chirag Shah[1,2], Frank Vicini[3], David E. Wazer[4,5], Douglas Arthur[6], Rakesh R. Patel[7,*]

[1]Department of Radiation Oncology, Washington University School of Medicine, Saint Louis, MO

American Brachytherapy Society acceptable criteria for accelerated partial breast irradiation

Criteria	2013
Age	≥50 y old
Size	≤3 cm
Histology	All invasive subtypes and DCIS
Estrogen receptor	Positive/negative
Surgical margins	Negative
Lymphovascular space invasion	Not present
Nodal status	Negative

ILC

Not previously included in AMERICAN BRACHYTHERAPY SOCIETY BREAST BRACHYTHERAPY TASK GROUP, February, 2007

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Brachytherapy 12 (2013) 267–277

BRACHYTHERAPY

The American Brachytherapy Society consensus statement for accelerated partial breast irradiation

Chirag Shah[1,2], Frank Vicini[3], David E. Wazer[4,5], Douglas Arthur[6], Rakesh R. Patel[7,*]

[1]Department of Radiation Oncology, Washington University School of Medicine, Saint Louis, MO

With regard to lobular histology, there remains a paucity of data specifically addressing the use of APBI in patients with this invasive carcinoma subtype.

Because no modern series have been published documenting higher rates of IBTR for ILCs and multiple series using WBI have found comparable outcomes between IDCs and ILCs, it was the consensus opinion that lobular carcinomas should be considered acceptable for treatment (76–79). Again, implicit in this recommendation is the acknowledgment that further data from Phase III trials (and other prospective data) will be needed to conclusively establish the efficacy of APBI in patients with ILC.

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 80, No. 1, pp. 17–24, 2011

0360-3016/$–see front matter

doi:10.1016/j.ijrobp.2010.01.020

CLINICAL INVESTIGATION **Breast**

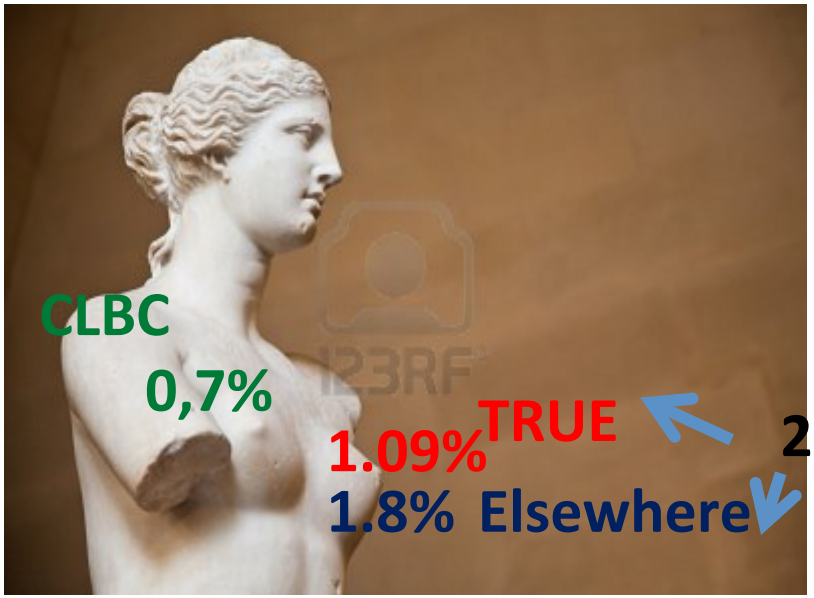
ACCELERATED PARTIAL BREAST IRRADIATION: 5-YEAR RESULTS OF THE GERMAN-AUSTRIAN MULTICENTER PHASE II TRIAL USING INTERSTITIAL MULTICATHETER BRACHYTHERAPY ALONE AFTER BREAST-CONSERVING SURGERY

Vratislav Strnad, M.D.,* Guido Hildebrandt, M.D.,†‡ Richard Pötter, M.D.,§ Josef Hammer, M.D.,¶ Marion Hindemith, M.D.,† Alexandra Resch, M.D.,§ Kurt Spiegl, M.D.,¶ Michael Lotter, Ph.D.,* Wolfgang Uter, M.D.,‖ Mayada Bani,** Rolf-Dieter Kortmann, M.D.,† Matthias W. Beckmann, M.D.,** Rainer Fietkau, M.D.,* and Oliver J. Ott, M.D.*

274 patients, med FU

ASTRO o ESTRO "good"	
age	≥35
grade	G1-G2
Tumor size	≤ 3cm
Surgical margin	neg
Multicentricity	no
Multifocality	no
EIC	no
LVI	no
ER, PR status	Any positive
Nodal status	N0

Med age 60.5



sion analysis or log rank test. In detail: tumor size, tumor grade (G1 vs. G2 vs. G3), histology (lobular histology vs. nonlobular histology), ER status, and mode of brachytherapy (HDR vs. PDR) had no significant association with local recurrence, disease-free survival, or overall survival. Also from

Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 4, pp. e547–e551, 2011

0360-3016/$ - see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2011.04.050

CLINICAL INVESTIGATION **Breast**

CLINICAL OUTCOMES USING ACCELERATED PARTIAL BREAST IRRADIATION IN PATIENTS WITH INVASIVE LOBULAR CARCINOMA

Chirag Shah, M.D., J. Ben Wilkinson, M.D., Simona Shaitelman, M.D., Inga Grills, M.D., Michelle Wallace, R.N., Christina Mitchell, R.N., and Frank Vicini, M.D.

Department of Radiation Oncology, Beaumont Cancer Institute, Oakland University William Beaumont School of Medicine, Royal Oak, MI

	ILC (n = 16)	IDC (n = 410)	p value
Age at diagnosis			0.09
Mean (y)	70.9	66.2	
Range	46–87	41–93	
Tumor size (mm)			0.03*
Mean	14.1	10.9	
Range	1–32	1–35	
ER +	12 (75.0%)	303 (73.9%)	0.95
PR +	9 (56.2%)	203 (49.5%)	0.85
Margins			0.006*
Negative	12 (80.0%)	307 (84.6%)	
Positive	3 (20.0%)	14 (3.9%)	
Close	0 (0%)	42 (11.6%)	
T-Stage			0.01*
T1	12 (75.0%)	336 (91.3%)	
T2	4 (25.0%)	32 (8.7%)	
Lymph node status			<0.001*
Node negative	14 (87.5%)	367 (89.5%)	
Node positive	0 (0%)	39 (9.5%)	
Unknown/not sampled	2 (12.5%)	4 (1.0%)	
Adjuvant hormonal therapy	9 (75.0%)	196 (52.0%)	0.11
Adjuvant chemotherapy	2 (15.0%)	46 (22.0%)	0.57
APBI type			0.09
Interstitial	3 (18.8%)	173 (47.0%)	
Balloon-based	8 (50.0%)	118 (32.1%)	
3D-CRT	5 (31.2%)	77 (20.9%)	
Follow up (y)			<0.001*
Mean	3.4	6.8	
Range	0.1–6.1	0.1–16.9	

Med FU 3.8 years

Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 4, pp. e547–e551, 2011

0360-3016/$ - see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2011.04.050

CLINICAL INVESTIGATION **Breast**

CLINICAL OUTCOMES USING ACCELERATED PARTIAL BREAST IRRADIATION IN PATIENTS WITH INVASIVE LOBULAR CARCINOMA

Chirag Shah, M.D., J. Ben Wilkinson, M.D., Simona Shaitelman, M.D., Inga Grills, M.D., Michelle Wallace, R.N., Christina Mitchell, R.N., and Frank Vicini, M.D.

Department of Radiation Oncology, Beaumont Cancer Institute, Oakland University William Beaumont School of Medicine, Royal Oak, MI

5-year actuarial	ILC ($n = 16$)	IDC ($n = 410$)	p value
LR	0%	2.5%	0.59
RR	0%	0.7%	0.80
DFS	100%	94%	0.43
DM	0%	3.5%	0.54
CSS	100%	97%	0.59
OS	92%	89%	0.88

Conclusions:

These findings suggest that ILC histology should not in and of itself be considered a negative prognostic factor for the optimal application of APBI.

Ann Surg Oncol (2012) 19:553–559
DOI 10.1245/s10434-011-1941-7

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

ORIGINAL ARTICLE – BREAST ONCOLOGY

A Single-Institution Review of Accelerated Partial Breast Irradiation in Patients Considered "Cautionary" by the American Society for Radiation Oncology

Tari S. Stull, MD[1], M. Catherine Goodwin, MD[1], Edward J. Gracely, PhD[2], Michael R. Chernick, PhD[3], Richard J. Carella, MD[4], Thomas G. Frazier, MD[1], and Andrea V. Barrio, MD[1]

109 patients,med FU 3 years

Variable	Hazard ratio [95% CI]	*P*
Age 50–59 years	0.57 [0.06–5.11]	0.61
Tumor size 2.1–3.0 cm[a]	– No event	0.48
Close margins	2.69 [0.45–16.16]	0.28
Focal LVI	3.94 [0.44–35.35]	0.22
ER-negative	2.87 [0.48–17.18]	0.25
ILC[a]	– No event	0.43
DCIS[a]	– No event	0.041

ILC 5.4%

3-year actuarial IBTR rate was 1.8%

no association between cautionary criteria and risk of local and distant relapse

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 79, No. 4, pp. 977–984, 2011

0360-3016/$–see front matter

doi:10.1016/j.ijrobp.2009.12.047

ASTRO GUIDELINE

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

FRANK VICINI, M.D.,* DOUGLAS ARTHUR, M.D.,† DAVID WAZER, M.D.,‡ PETER CHEN, M.D.,* CHRISTINA MITCHELL, R.N.,* MICHELLE WALLACE, R.N.,* LARRY KESTIN, M.D.,* AND HONG YE, M.S.*

Table 5. Risk of 10-year local recurrence vs. ASTRO group and treatment type

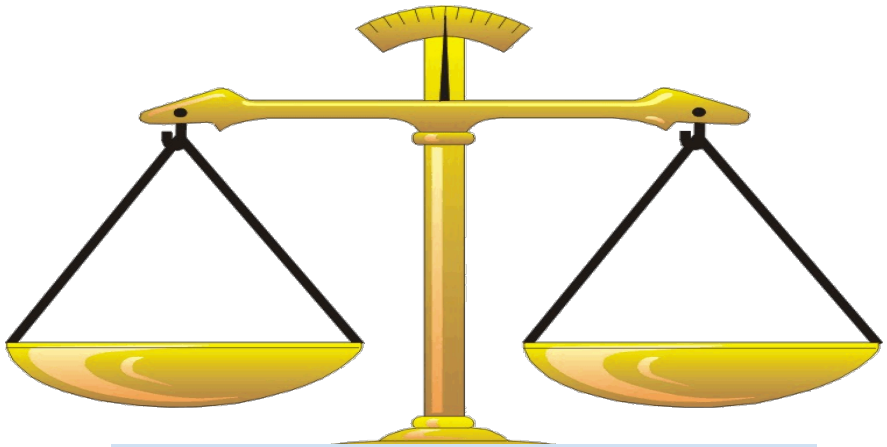
ASTRO grouping	All patients (n = 398)	APBI patients (n = 199)	EBRT matched (n = 199)	p Value
Suitable (n = 176)	3.3%	2.6%	4.1%	0.544
Cautionary (n = 132)	3.9%	7.8%	1.2%	0.080
Unsuitable (n = 90)	5.5%	2.5%	8.4%	0.758
p Value	0.709	0.858	0.382	

No difference in LR, RNF and DM

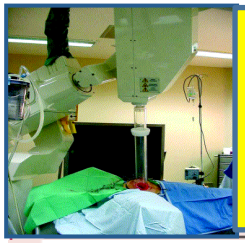
regardless of histology

ELIOT PHASE III trial:

PBI 4.4% vs. WBRT 0.4%



LOBULAR HISTOLOGY



ELIOT TRIAL

	Patients (n/N)	IBTR 5-year event rate (95% CI)	Log-rank p value*
Histology			
Ductal	28/524	4·5% (2·6–6·5)	..
Lobular	3/53	4·6% (0·0–10·8)	..
Ductal and lobular	2/17	6·3% (0·0–18·1)	..
Other	2/53	2·1% (0·0– 6·1)	0·69

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D-13-01374R1
S1470-2045(13)70497-2
Embargo: [add date when known]

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

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 Ciocca · Roberta Lazzari · Pietro Caldarella · Nicole Rotmensz · Claudia Sangalli · Daniele Sances · Patrick Maisonneuve

	ELIOT	Out-trial ELIOT
Tumor size <1-2 cm Tumor size >2	86% 13%	85 15% (up to 5 cm)
Tumor Type IDC TumorType ILC	81% 8%	78% 11%
Tumor grade G1-G2 Tumor grade G3	79% 20%	72% 25%
Age <50 51-59 >60	7% 44% 50%	20% 36% 43%
EIC Present EIC Absent	50% 50%	48% 52%
Nodes status Negative Nodes status Positive	74% 26% (5% 3+)	71% 28% (8% 3+)
ER Positive ER Negative	90% 10%	89% 11%

International Journal of Radiation Oncology biology • physics
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Clinical Investigation: Breast Cancer

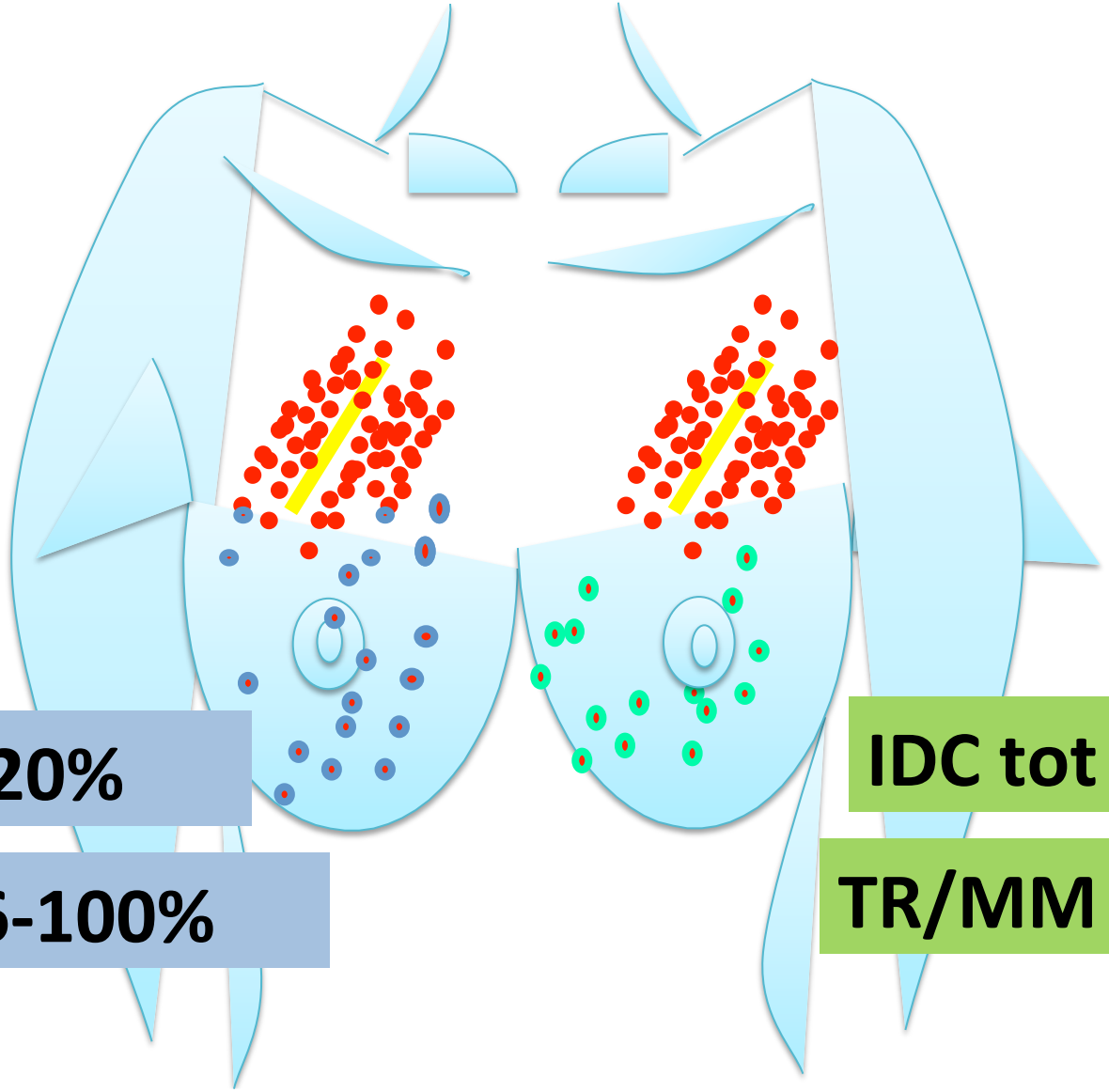
How Do the ASTRO Consensus Statement Guidelines for the Application of Accelerated Partial Breast Irradiation Fit Intraoperative Radiotherapy? A Retrospective Analysis of Patients Treated at the European Institute of Oncology

Maria Cristina Leonardi, M.D.,* Patrick Maisonneuve, Ing.,† Mauro Giuseppe Mastropasqua, M.D.,‡ Anna Morra, M.D.,* Roberta Lazzari, M.D.,* Nicole Rotmensz, M.Sc.,† Claudia Sangalli, D.M.,§ Alberto Luini, M.D.,§ Umberto Veronesi, M.D.,¶ and Roberto Orecchia, M.D.*,‖

Table 5 Multivariate analysis of clinical outcomes for patients with breast cancer treated with full-dose intraoperative radiotherapy with electrons categorized according to the American Society for Radiation Oncology (ASTRO) consensus statements

Variable	Ipsilateral breast tumor recurrence		Regional lymph node failure		Distant metastases	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Histology						
Ductal	1.00		1.00		1.00	
Lobular	1.97 (1.00–3.90)	0.05	–	–	1.58 (0.45–5.55)	0.48
Other histologies	0.79 (0.25–2.50)	0.69	–	–	0.92 (0.16–5.21)	0.92

QUART: similar local control
similar site of failure within the breast



● ILC

● IDC

ILC tot 3-20%

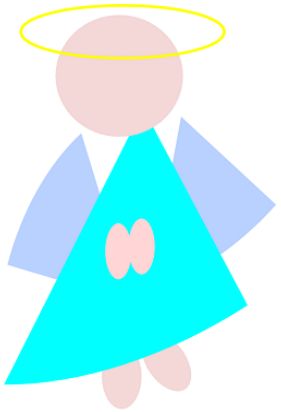
TR/MM 86-100%

IDC tot 5-22%

TR/MM 71-80%

Favorable prognostic profile

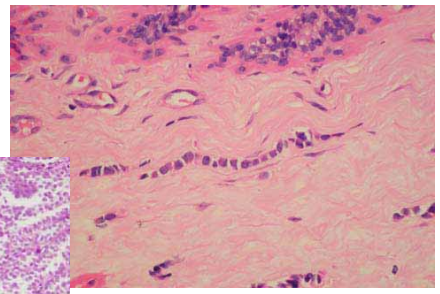
- High level of expression of hormonal receptors
- No overexpression of HER2-neu receptor
- Low grade
- Low proliferation index
- No vascular invasion
- Good response to hormonal therapy
- Older age

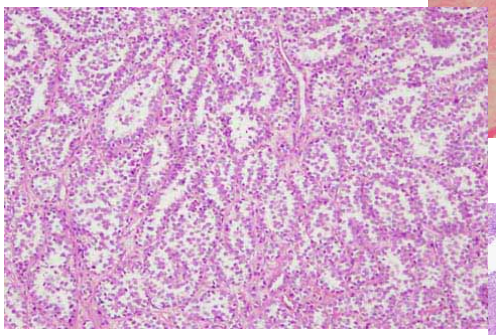


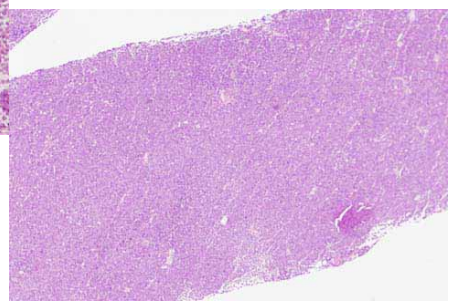
Large T size

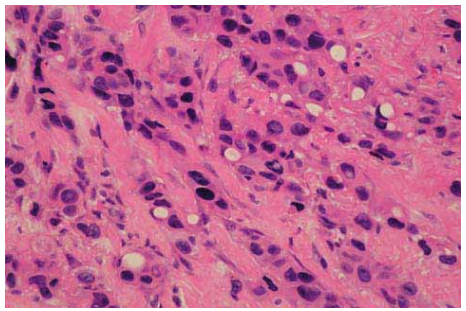
Lobular carcinoma variants

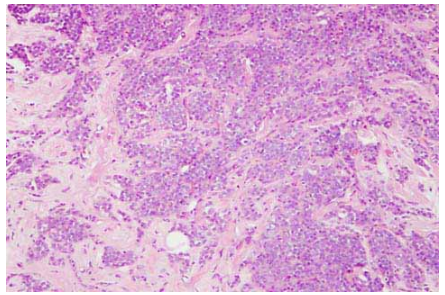
- Tubulo-lobular
- Alveolar
- Solid
- Pleomorphic
- Mixed











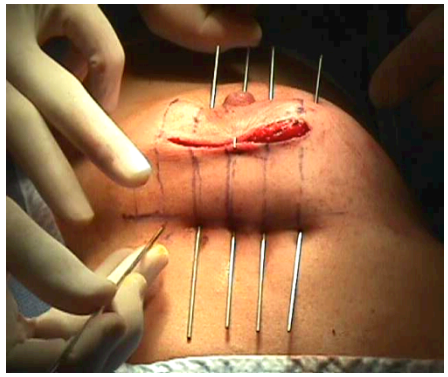
Should more aggressive variants as plemorphic subtype be excluded from PBI?

Breastpathology.info

The Breast Journal, Volume 7, Number 2, 2001 91–96

Breast Conservation Therapy with Tumor Bed Irradiation Alone in a Selected Group of Patients with Stage I Breast Cancer

Leela Krishnan, MS, MD,* William R. Jewell, MD,†
Ossama W. Tawfik, MD, PhD,‡ and Engikolai C. Krishnan, MS, MD†
*Departments of *Radiation Oncology, †Surgery, and ‡Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, Kansas*



	No. of patients
Histology	
Infiltrating ductal	14
Infiltrating tubular	4
Infiltrating ductal and tubular	2
Infiltrating lobular	3
Invasive colloid	1
Invasive mucinous	1
T size	
T1a	3
T1b	11
T1c	11
Grade	
I	15
II	7

≥60 anni

≤2 cm

pN0

LDR 20-25 Gy,
FU 47 months
no local relapse

Exclusion criteria

nonclassic lobular carcinoma

LCIS

Breast Cancer Res Treat (2012) 133:713–723
DOI 10.1007/s10549-012-2002-z

CLINICAL TRIAL

Invasive lobular breast cancer: subtypes and outcome

Monica Iorfida · Eugenio Maiorano · Enrico Orvieto · Patrick Maisonneuve · Luca Bottiglieri · Nicole Rotmensz · Emilia Montagna · Silvia Dellapasqua · Paolo Veronesi · Viviana Galimberti · Alberto Luini · Aron Goldhirsch · Marco Colleoni · Giuseppe Viale

After mastectomy or BCS + WBRT

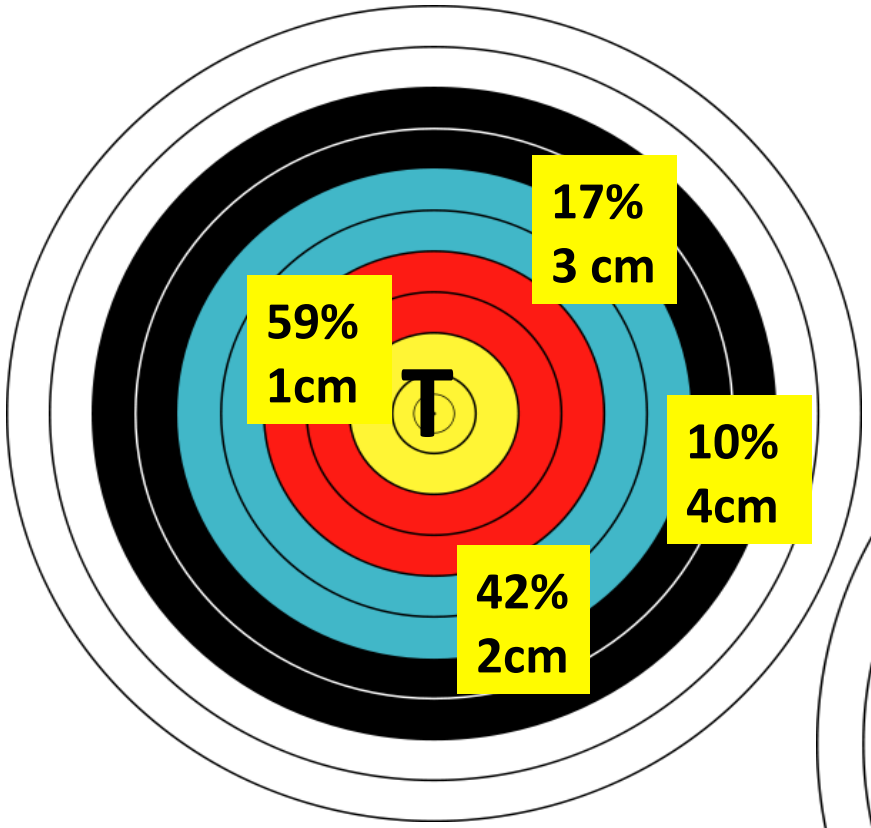
Multivariate analysis in 981 patients with primary lobular breast cancer treated at the European Institute of Oncology between 1994 and 2005

	Loco-regional relapse	Distant metastasis	Contralateral breast cancer	Disease-free survival	Breast cancer specific survival	Overall survival
Histological subtype						
Classic	1.00	1.00	1.00	1.00	1.00	1.00
Alveolar	1.30 (0.69–2.46)	1.50 (0.84–2.68)	1.27 (0.39–4.11)	1.38 (0.94–2.05)	1.26 (0.64–2.47)	1.41 (0.80–2.48)
Solid	1.85 (0.91–3.78)	1.73 (0.98–3.06)	1.45 (0.38–5.50)	**1.92 (1.29–2.88)**	1.91 (0.96–3.79)	**2.44 (1.39–4.29)**
Mixed, non-classic	1.40 (0.68–2.87)	1.21 (0.67–2.18)	2.42 (0.74–7.92)	1.40 (0.93–2.13)	1.85 (0.96–3.58)	**1.99 (1.12–3.53)**
Trabecular	0.64 (0.09–4.80)	1.10 (0.33–3.67)	–	0.87 (0.32–2.41)	0.85 (0.11–6.41)	0.70 (0.10–5.22)

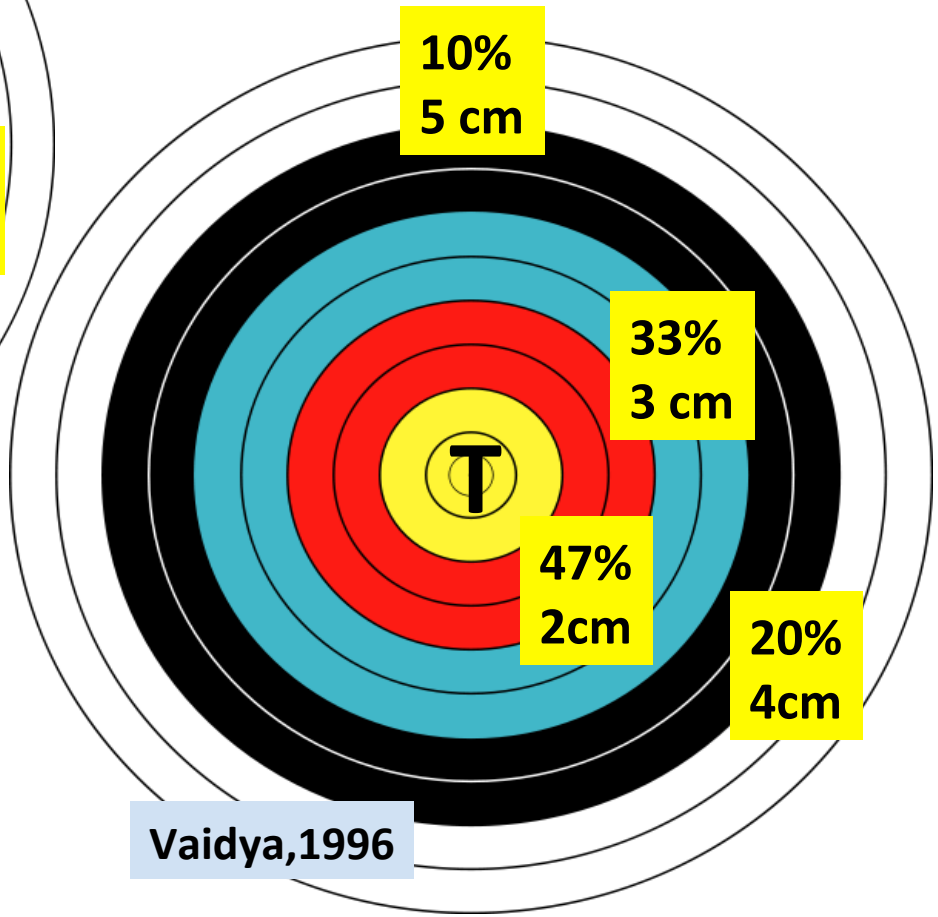
THE PATHOLOGY OF INVASIVE BREAST CANCER

A Syllabus Derived from Findings of the National Surgical Adjuvant Breast Project (Protocol No. 4)

EDWIN R. FISHER, MD,* REMIGIO M. GREGORIO, MD,* AND BERNARD FISHER, MD,† WITH THE ASSISTANCE OF CAROL REDMOND, ScD,† FRANK VELLIOS, MD,§ AND SHELDON C. SOMMERS, MD,§ AND COOPERATING INVESTIGATORS



Holland, 1985



Vaidya,1996

Tumoral microscopic foci beyond excision site

Breast Cancer Res Treat (2009) 117:211–214
DOI 10.1007/s10549-008-0112-4

Lack of prognostic significance of "classic" lobular breast carcinoma: a matched, single institution series

Giuseppe Viale · Nicole Rotmensz · Patrick Maisonneuve · Enrico Orvieto · Eugenio Maiorano · Viviana Galimberti · Alberto Luini · Marco Colleoni · Aron Goldhirsch · Alan S. Coates

	All patients	Classical		*P*-value
		Ductal	Lobular	
Multifocality				
Monofocal	465 (77.2%)	256	209	
Multifocal	137 (22.8%)	45	92	**<0.0001**
Number of positive nodes				
None	366 (60.8%)	193	173	
1–3	141 (23.4%)	78	63	
4–10	43 (7.1%)	23	20	
>10	28 (4.7%)	5	23	**0.001**[a]
pNx	24 (4.0%)	2	22	
Tumor grade				
Grade 1	319 (53.0%)	145	174	
Grade 2	283 (47.0%)	156	127	**0.022**
Proliferative fraction				
ki67 labeling index <20%	471 (78.2%)	222	249	
ki67 labeling index ≥20%	129 (21.4%)	79	50	**0.005**
Unknown	2 (0.3%)	0	2	

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

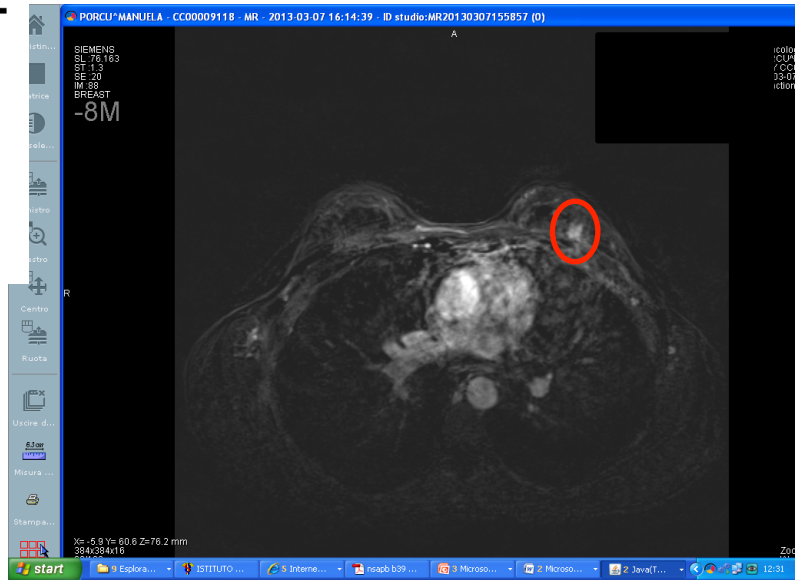
Printed in the USA.
0360-3016/09/$–see front matter

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.¶¶



Consensus statement. Patients treated with APBI should undergo standard imaging assessment, which typically includes diagnostic mammography and breast ultrasonography

At present there are insufficient data to justify routine use of breast magnetic resonance imaging (MRI) in patients selected for APBI.

Original Article

Preoperative Breast Magnetic Resonance Imaging in Early Breast Cancer

Implications for Partial Breast Irradiation

Rahul D. Tendulkar, MD[1], Melanie Chellman-Jeffers, MD[2], Lisa A. Rybicki, MS[3], Alice Rim, MD[2], Ashwin Kotwal[1], Roger Macklis, MD[1], and Betty B. Obi, MD[1]

Tumor factors associated with occult ipsilateral disease

	Ipsilateral Biopsy-proven Tumor	%
Age, y		*P*=.17
<50	2/65	3%
50-69	9/148	6%
≥70	0/47	0%
Menopausal status		*P*=.76
Premenopausal	3/68	4%
Perimenopausal	1/12	8%
Postmenopausal	7/178	4%
Index histology		*P*=.043
DCIS	2/63	3%
IDC	5/157	3%
ILC	3/17	18%
Mixed/other	1/23	4%
Clinical T stage		*P*=.64
cT0	3/73	4%
cT1	8/169	5%
cT2	0/18	0%
Pathological T stage		*P*=.038
pTis	2/63	3%
pT1	5/166	3%
pT2	4/31	13%
Pathological N stage		*P*=.06
pN0-Nx	5/158	3%
pN1	4/39	10%

18% vs 3%, p 0.004

MF/MC (MX occult) in 14%-31%

Breast Cancer Res Treat (2008) 107:1–14
DOI 10.1007/s10549-007-9528-5

REVIEW

MRI compared to conventional diagnostic work-up in the detection and evaluation of invasive lobular carcinoma of the breast: a review of existing literature

Ritse M. Mann · Yvonne L. Hoogeveen · Johan G. Blickman · Carla Boetes

- More accurate **extent** of ILC than MX (above all in pT1)
- Greater **sensitivity** than MX in detecting multifocality and multicentricity (MX sensitivity 57%-81% ; US sensitivity 68%-87%)
- Tumor foci identified in 15% to 37% of ipsilateral breasts
- (changed strategies in 10% to 31% of cases)

Tendulkar, 2009: Our data suggest that, if APBI is being considered for an individual patient with ILC, a pretreatment breast MRI may prove valuable in excluding additional disease.

Breast Cancer Res Treat (2012) 133:713–723
DOI 10.1007/s10549-012-2002-z

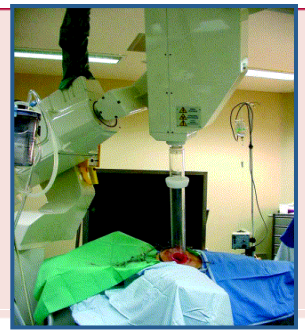
CLINICAL TRIAL

Invasive lobular breast cancer: subtypes and outcome

Monica Iorfida · Eugenio Maiorano · Enrico Orvieto · Patrick Maisonneuve · Luca Bottiglieri · Nicole Rotmensz · Emilia Montagna · Silvia Dellapasqua · Paolo Veronesi · Viviana Galimberti · Alberto Luini · Aron Goldhirsch · Marco Colleoni · Giuseppe Viale

981 pts

	Total	Classic	Alveolar	Solid	Mixed, non-classic	Trabecular
Molecular subtype						
Luminal A	342	255	36	13	28	10
Luminal B	476	197	78	80	93	28
HER2 positive	4	–	–	–	4	–
Triple negative	15	5	1	2	7	–



ELIOT TRIAL

	Patients (n/N)	IBTR 5-year event rate (95% CI)	Log-rank p value*
Molecular subtype			
Luminal A	7/256	1·4% (0·0–3·0)	..
Luminal B	20/327	4·9% (2·4–7·4)	..
HER2-positive (non-luminal)	1/20	5·9% (0·0–17·1)	..
Triple negative	7/43	18·9% (6·1–31·7)	0·001

	Patients (n/N)	IBTR 5-year event rate (95% CI)	Log-rank p value*
Proliferative index (Ki-67)			
<14%	8/263	1·8% (0·0–3·5)	..
14–20%	5/138	1·5% (0·0–3·6)	..
>20%	22/244	9·1% (5·1–13·1)	0·002

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

CLINICAL TRIAL

ELIOT out 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

	All patients	True local recurrences			Second ipsilateral cancer		
	N	*N*	%	Annual rate (%)	*N*	%	Annual rate (%)
Molecular subtype[a]							
Luminal A	648	3	0.46	0.15	4	0.62	0.20
Luminal B	977	28	2.87	0.96	16	1.64	0.55
Cerb+++	53	6	11.32	3.88	0	–	–
Basal	137	5	3.65	1.19	4	2.92	0.95

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 77, No. 5, pp. 1296–1302, 2010

0360-3016/$–see front matter

doi:10.1016/j.ijrobp.2009.12.011

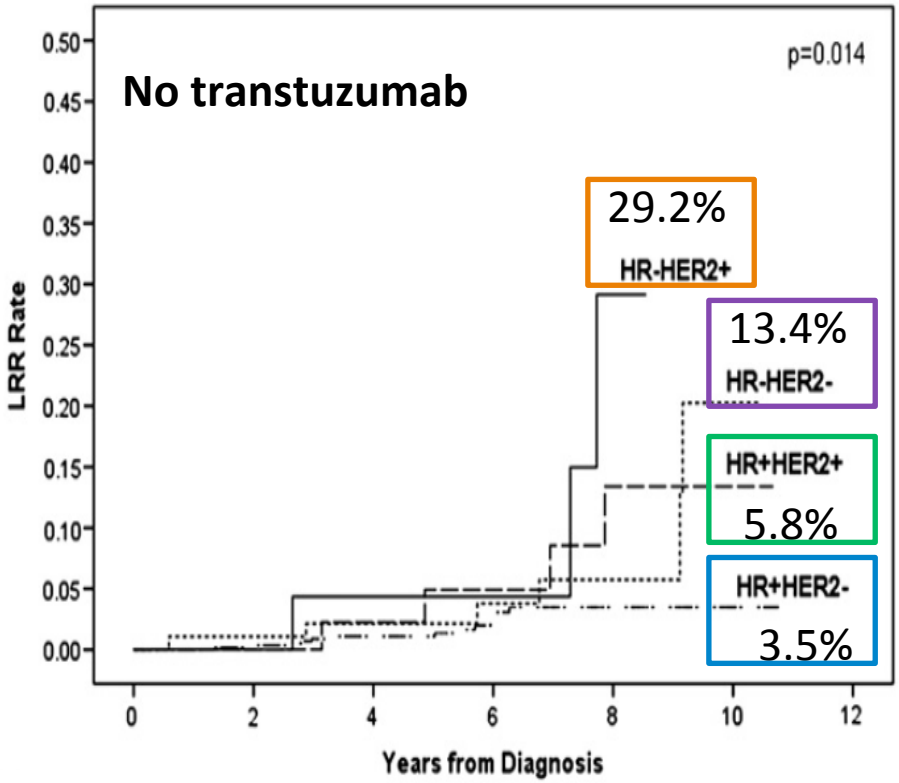
CLINICAL INVESTIGATION Breast

ESTROGEN/PROGESTERONE RECEPTOR NEGATIVITY AND HER2 POSITIVITY PREDICT LOCOREGIONAL RECURRENCE IN PATIENTS WITH T1a,bN0 BREAST CANCER

Jeffrey M. Albert, M.D.,* Ana M. Gonzalez-Angulo, M.D.,† Merih Guray, M.D.,‡ Aysegul Sahin, M.D.,‡ Eric A. Strom, M.D.,* Welela Tereffe, M.D.,* Wendy A. Woodward, M.D., Ph.D.,* Susan L. Tucker, Ph.D.,§ Kelly K. Hunt, M.D.,¶ Gabriel N. Hortobagyi, M.D.,† and Thomas A. Buchholz, M.D.*

Table 3. Multivariate analysis*

Variable	Hazard ratio	95% Confidence interval	*p*
HER2+ vs. HER2–	3.13	1.23–7.92	.016
Close/positive vs. free margins	5.02	1.86–13.58	.001
ER–/PR– vs. ER+ and/or PR+	2.37	1.02–5.51	.046
Lobular vs. other histologic features	4.75	1.63–13.84	.004



Overall 8-year LRR rate was 5.9% (26/756) after BCT with WBRT or mastectomy

HR negativity and HER2 positivity increase the LRR risk in $T1_{a,b}$ N0

International Journal of Radiation Oncology biology • physics
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Clinical Investigation: Breast Cancer

Impact of the Number of Cautionary and/or Unsuitable Risk Factors on Outcomes After Accelerated Partial Breast Irradiation

Jessica Wobb, MD,* J. Ben Wilkinson, MD,* Chirag Shah, MD,†
Christina Mitchell, RN,* Michelle Wallace, RN,* Hong Ye, MS,*
Jannifer Stromberg, MD,* Inga Grills, MD,* and Peter Y. Chen, MD, FACR*

*Department of Radiation Oncology, Beaumont Cancer Institute, Oakland University William Beaumont School of Medicine, Royal Oak, Michigan; and †Department of Radiation Oncology, Washington University School of Medicine, St. Louis, Missouri

Five-year outcomes by number of risk factors (cautionary n = 343; unsuitable n = 109)

	Cautionary			Unsuitable		
Outcome	1 (n = 228)	2+ (n = 115)	*P*	1 (n = 96)	2+ (n = 13)	*P*
IBTR	0.6	2.0	.03	2.2	7.7	.30
CLTR	2.2	0	.11	3.1	0	.44
RR	0	0	—	1.7	7.7	.05
DM	1.5	6.5	.02	4.9	7.7	.53
DFS	98	92	<.01	94	85	.21
CSS	98	97	.44	96	91	.08
OS	89	91	.32	93	84	.01

APBI vs WBRT phase III trials

Trial	PBI technique	ILC
TARGIT	Intraop photons	YES (+WBRT)
ELIOT	Intraop electrons	YES
GEC-ESTRO	HDR/PDR BRT	YES
NSABP-B-39/ RTOG-0413	HDR BRT/MammoSite BT/ 3D CRT	YES
RAPID	3D CRT	NO
IMPORT LOW	IMRT	NO
IRMA	3D CRT	YES
Univ.of Florence	IMRT	YES
HUNGARIAN	HDR BT/ext. electrons	NO

Suitable/good	ASTRO	ESTRO
age	≥60 years	>50 years
BRCA1/2mutation	Not present	
histology	IDC or other favorable subtypes	IDC , mucin, tubular, medullary, colloid
ILC	allowed	Allowed
Associated LCIS	allowed	Allowed
DCIS	Pure, not allowed	Not allowed
HG	Any	Any
Tumor size	≤2cm T1	pT1-2 (≤30 mm)
Surgical margin	Negative (≥2mm)	Negative (≥2mm)
Multicentricity	Unicentric	Unicentric
Multifocality	Unifocal total size≤2cm	Unifocal
EIC	Not allowed	Not allowed
LVI	No	Not allowed
ER, PR status	Positive	Any
Nodal status	pN0 (SN Bx orALND)	pN0 (SN bx or ALND)
Neoadjuvant CT	Not allowed	Not allowed

Is lobular carcinoma an absolute contraindication to PBI?

NO

Radiotherapy and Oncology 106 (2013) 1–4

Contents lists available at SciVerse ScienceDirect

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journal homepage: www.thegreenjournal.com

Commentary

Infiltrating lobular breast cancer: Truly a separate entity! Consequences for radiation therapy

Philip M.P. Poortmans [a,*], Marc Bollet [b], Erik Van Limbergen [c]

Based on these data, one could conclude that the presence of ILC should not influence decisions regarding local therapy, and patients over 50 years, with ILC smaller than 3 cm, might be offered APBI after wide tumour excision with negative section margins. However, at this time there is only limited evidence

THANK YOU!