Impact of Positive Margin Re-excision on Median 5-Year Follow-Up Results in an International Single Arm Prospective Trial Evaluating Early-Stage Breast Cancer Patients Treated with Intra-Operative Electronic Brachytherapy

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Dr. Schwartzberg is a trial consultant for Xoft, Elekta.

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XOFT IORT Steering Committee Meeting – January 28, 2012

Co-Chairs:

- Helena Chang MD – Breast Surgeon, UCLA, Los Angeles, CA
- Nisar Syed MD – Radiation Oncologist, MemorialCare Hospital, Long Beach, CA

Membership:

- Elayne Arterbery MD
- Charles Cox MD
- Jeffrey Demanes MD
- William Dooley MD
- Olga Ivanov MD
- Joshua Petit MD
- Barbara Schwartzberg MD

Consultants:

- Lowell Rogers MD
- Anil Sharma MD

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-ExBRT TRIAL-

A Safety and Efficacy Study of Intra-Operative Radiation Therapy (IORT) Using the Xoft® Axxent® eBx ® System at the Time of Breast Conservation Surgery for Early-Stage Breast Cancer

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OBJECTIVE

A single arm prospective multi-institution trial was designed to determine the efficacy and outcome of intra-operative radiation therapy (IORT) using disposable balloon electronic brachytherapy at the time of lumpectomy for early-stage breast cancer.

The primary endpoint was ipsilateral breast tumor recurrences (defined as recurrence in the lumpectomy cavity/index quadrant) at median 5-year follow-up.

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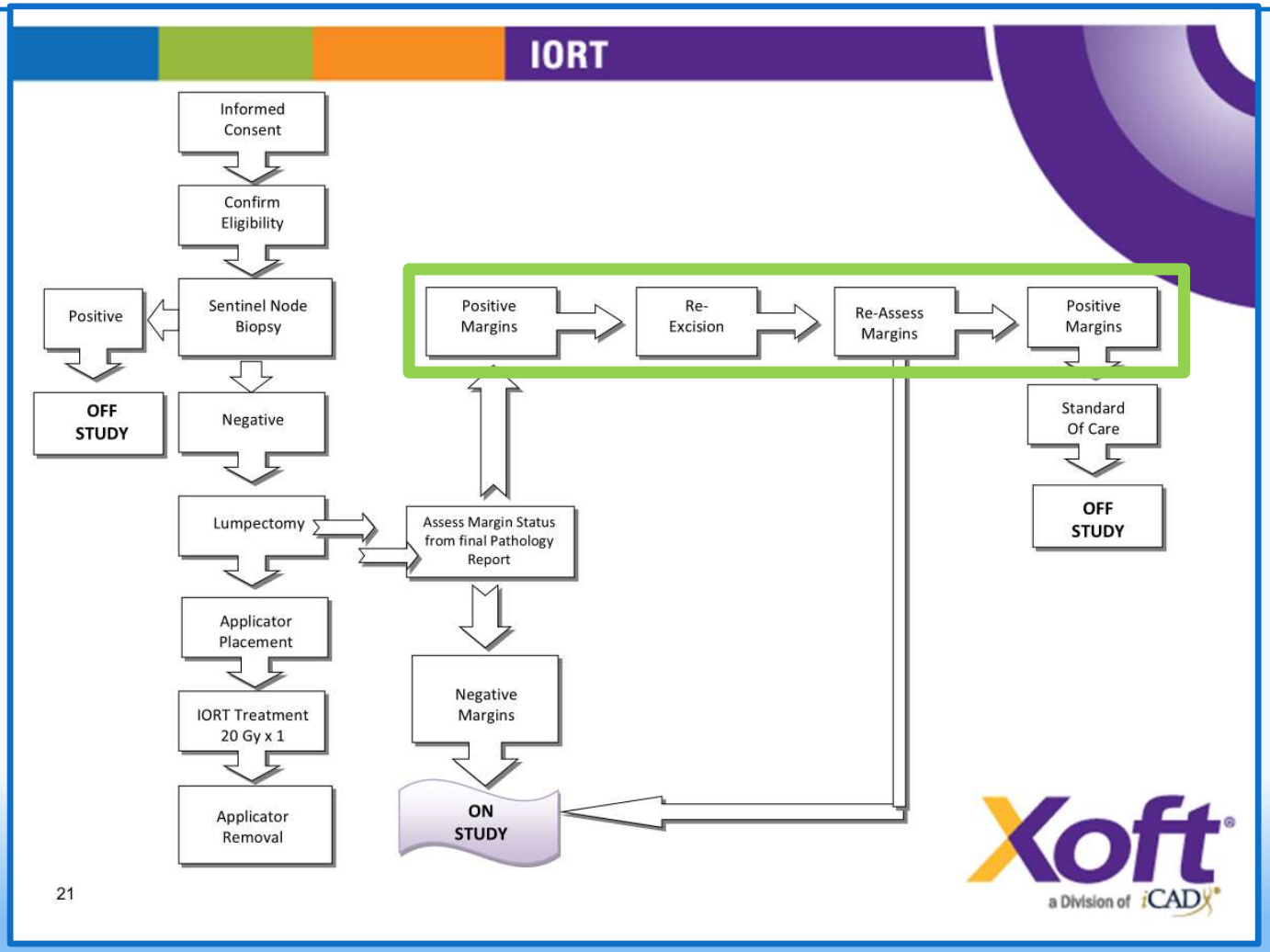

ExBRT: Investigators and Site Locations

A.M. Nisar Syed, MD Memorial Care Long Beach Medical Center, Long Beach, CA - **PRINCIPAL INVESTIGATOR**
Barbara Schwartzberg, MD Schwartzberg Center for Minimally Invasive Surgery, Santa Rosa, CA
Albert Chang, MD David Geffen School of Medicine at UCLA, Los Angeles, CA
Shawndeep Tung, MD Cancer Research Collaborations, Inc. Breastlink, Orange, CA
Ajay Bhatnagar, MD Cancer Treatment Services, Casa Grande, AZ
Sophia Rahman, MD Diablo Valley Oncology Hematology Medical Group, Pleasant Hill, CA
Todd Cockerham, MD Sarah Cannon Cancer Center at Parkridge Medical Center, Chattanooga, TN
Virginia Osborn, MD Exeter Hospital, Exeter, NH
Robert Cohen, MD Sentara Northern Virginia, Norfolk, VA
Wesley Hodge, MD Advent Health Florida Hospital, Orlando, FL
Christina Lopez-Penalver, MD Miami Cancer Institute at Baptist Health, Inc., Miami, FL
Bapsi Chakravarthy, MD Vanderbilt University Medical Center, Nashville, TN
Veronica Jones, MD City of Hope National Medical Center, Duarte, CA
William Dooley, MD Oklahoma University Medical Center, Oklahoma City, OK
Chika Madu, MD Staten Island University Hospital, Staten Island, NY
Seth Reiner, MD Swedish Medical Center, Englewood, CO
Atsuko Okabe, MD MedStar Franklin Square Medical Center, Bel Air, MD
Maen Farha, MD MedStar Good Samaritan, Baltimore, MD
Paulo Costa, MD Clinica de Radioterapia do Porto, Porto, Portugal
Andrea Madrigrano, MD Rush University Medical Center, Chicago, IL
Christopher Morrison, MD University of Arizona, Tucson, AZ
Geoffrey Neuner, MD Greater Baltimore Medical Center, Towson, MD
Craig Wengler, MD Cleveland Clinic Martin Health Medical Center, Stuart, FL
Byron Stephens MD Lutheran Health Network Lutheran Medical Group, Fort Wayne, IN
Steven David, MD Monash Health/Peter MacCallum Centre, Melbourne, VIC, Australia
Katayoon Toosie, MD Tri-City Medical Center, Oceanside, CA

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ExBRT Inclusion Criteria

- Women ≥ 40 years old
- Infiltrating ductal carcinoma (IDC)
- Ductal carcinoma in situ (DCIS)
- Single lesion ≤ 3.0 cm
- No lymphovascular invasion
- No extensive intraductal component
- cN0
- No neo-adjuvant therapy

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ExBRT Trial Enrollment

Enrollment period:	**May 2012 – July 2018**
Total subjects enrolled in ExBRT trial:	**1399 patients**
Enrolled subjects excluded from ExBRT trial:	**200 patients**
Pre-IORT treatment withdrawal from trial:	94 patients
Intra-operative findings of lymph node positivity:	49 patients
Inadequate intra-operative balloon surface-to-skin distance:	45 patients
Intra-operative balloon-to-cavity non-conformance:	8 patients
Persistent intra-operative positive margins:	3 patients
Informed Consent technicality:	1 patient

FINAL ExBRT TRIAL ENROLLMENT: 1199 PATIENTS

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2017 ASTRO APBI SUITABILITY CRITERIA

	Suitable	Cautionary	Unsuitable
Age	≥50 years	40-49 years	<40 years
Tumor size	≤2 cm	2.1-3.0cm	>3cm
Stage	Tis or T1	T2	T3,T4
Margins	Negative	Close	Positive (ink on tumor)
Grade	Any	Any	Any
ER status	Positive	Negative	Negative
Multicentricity	None		Present
pN0	pN0		pN1,2,3
Histology	IDC	ILC	
	DCIS low/intermediate grade ≤ 2.5 cm	DCIS ≤ 3 cm	DCIS > 3cm
N stage	pN0		pN1,2,3

Correa, et al. Prac Rad Oncol 2017

Impact of Positive Margin Re-excision on Median 5-Year Follow-Up Results in an International Single Arm Prospective Trial Evaluating Early-Stage Breast Cancer Patients Treated with Intra-Operative Electronic Brachytherapy

2017 ASTRO APBI Categories

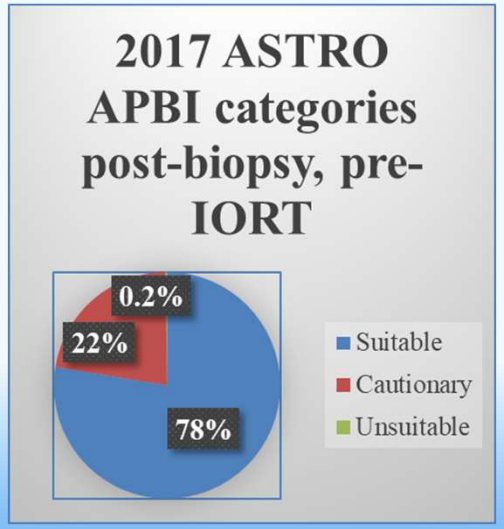
Post-biopsy, pre-IORT

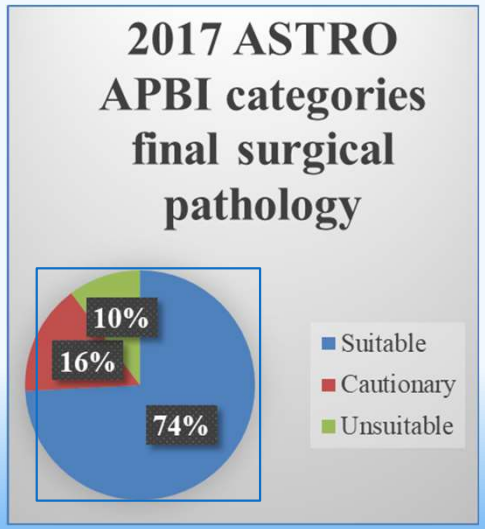
Suitable	**930 patients (77.6%)**
Cautionary	**266 patients (22.2%)**
Unsuitable	**3 patients (0.2%)**

2017 ASTRO APBI Categories

Surgical pathology

Suitable	**890 patients (74.2%)**
Cautionary	**187 patients (15.6%)**
Unsuitable	**122 patients (10.2%)**





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93 (7.8%) patients were Unsuitable due to positive margins on surgical pathology.

Patients who refused re-excision	**21**
Patients who underwent re-excision per protocol:	**72**
Patients who obtained negative margins with re-excision:	**70**
Patients with persistent positive margins:	**2**
Second re-excision plus WBXT	1
Mastectomy	1
TOTAL:	**93**

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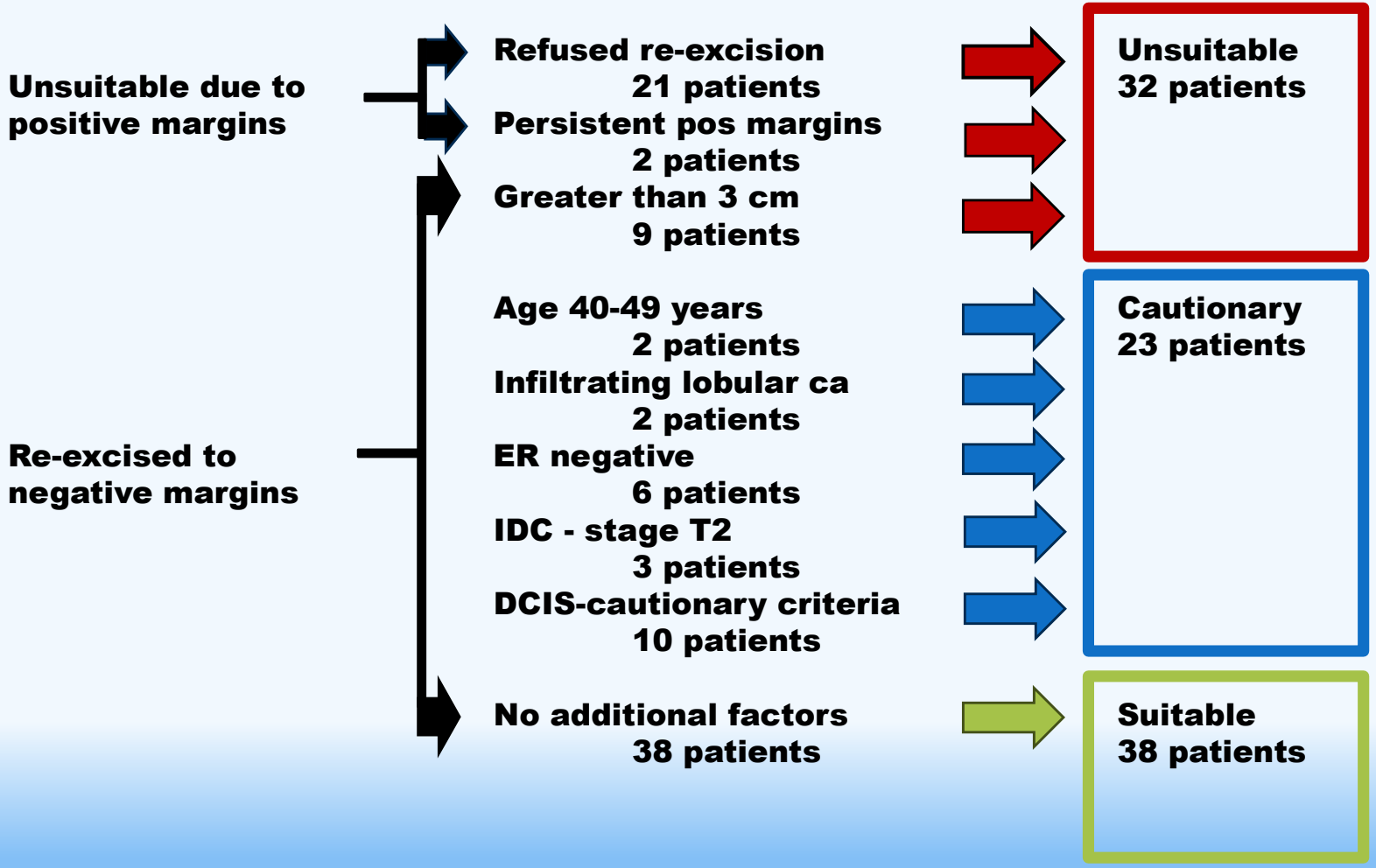

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Post-biopsy, pre-IORT

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2017 ASTRO APBI Categories

Surgical pathology

Suitable	890 patients (74.2%)
Cautionary	187 patients (15.6%)
Unsuitable	122 patients (10.2%)

2017 ATRO APBI Categories

Adjusted for treatment of positive margins

Suitable	928 patients (77.4%)
Cautionary	210 patients (17.5%)
Unsuitable	61 patients (5.1%)

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Treatment of Unsuitable Patients with Positive Margins

Treatment	N
IORT, (+) margins, re-excision	54
IORT, (+) margins, re-excision, WBXT	10
IORT, (+) margins, no re-excision	16
IORT, (+) margins, no re-excision, WBXT	5
IORT, (+) margins, mastectomy	6
IORT, (+) margins, re-excision, WBXT, mastectomy	2
TOTAL	93

17 patients (12 with re-excision and 5 without re-excision) received WBXT

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ExBRT TRIAL IBTR RESULTS AT MEDIAN 5-YEAR FOLLOW-UP

- 42 IBTR -

2017 ASTRO APBI criteria

IBTR - Post-biopsy, pre-IORT

Suitable	28 IBTR
Cautionary	14 IBTR
Unsuitable	0 IBTR

IBTR – Final surgical pathology

Suitable	25 IBTR
Cautionary	12 IBTR
Unsuitable	5 IBTR

IBTR Statistics

Suitable	2.8%	(95% CI = 1.7, 3.9)
Cautionary	6.4%	(95% CI = 2.9, 9.9)
Unsuitable	4.1%	(95% CI = 0.6, 7.6)

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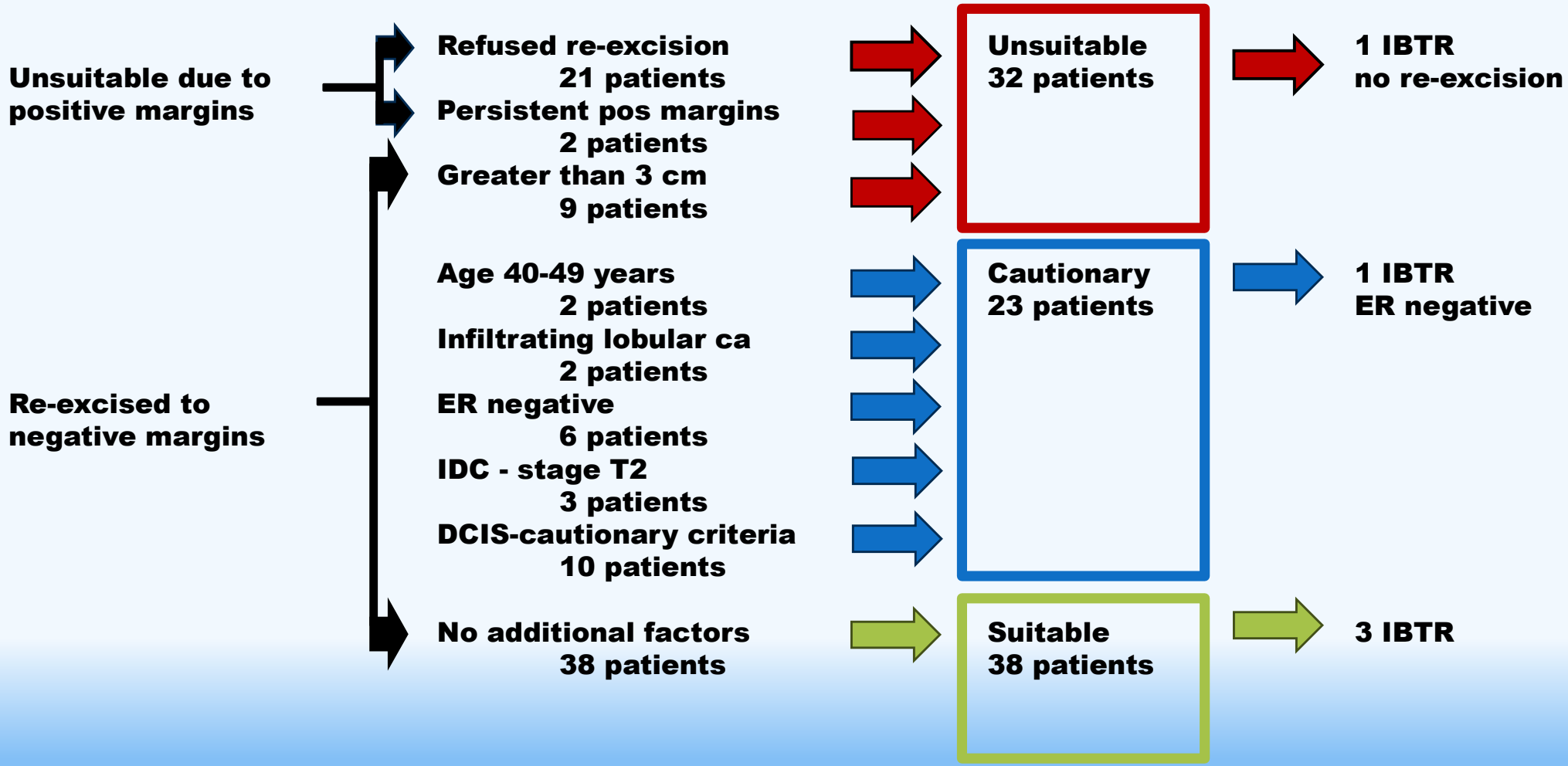

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-ExBRT TRIAL-

MEDIAN FOLLOW-UP: 5.0 YEARS

IBTR: 42 of 1199 PATIENTS

3.50%

(95% CI = 2.5, 4.5)

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Patients with post-IORT positive margins: IBTR of 5.4%

Patients with post-IORT negative margins: IBTR of 3.3%

Not statistically significant (p=0.307)

Odds ratio: 1.69 (95%CI = 0.65, 4.40)

The 1 breast cancer-related death did not have positive margins.

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CONCLUSIONS

At median 5-year follow-up, early-stage breast cancer patients successfully treated with single 20 Gy fraction IORT using disposable balloon electronic brachytherapy demonstrated a low IBTR consistent with published reports.

Unsuitable patients with positive margins were easily dealt with by re-excision with a small IBTR increase which was not statistically significant.

Future trials should be created with enough statistical power to investigate this subset as a primary endpoint.

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THANK YOU