

Back to the future

Why more women are having unilateral or bilateral mastectomy for unilateral breast cancer

How inexact risk assessment, fear and indiscriminate use of MRI can return us to the pre-Fisher era of breast cancer care

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Disclosures

I have no disclosures.
I too have no money in Russia.



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67 y/o WF w/ no risk factors for breast cancer
presents w/ clinical T1b N0 M0
ER/PR:+/+,Her2: neg , IDC

Rx plan: Bilateral mastectomy with ipsilat
SNM & PAC placement
Patient requests preop 2nd opinion by medical
oncology w/ Rx plan?

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NCI Consensus Conference- 1991

Endorsed breast conservation as the preferred treatment of early-stage breast cancer

Veronesi et al NEJM 305: 611 (1981)
Fisher et al NEJM 312: 674 (1985)

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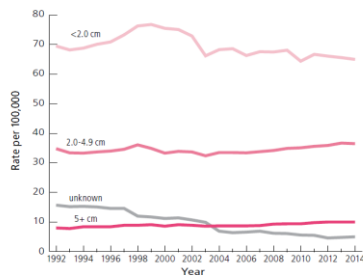
Prospective Randomized Trials: BCT vs. Mastectomy

Trial	Local Recurrence (%)		Survival (%)		F/U Interval
	BCT	M	BCT	M	
NSABP B06 ¹	3	10	46	47	20 years
Milani F	9	2	59	59	20 years
NCP ²	19	6	77	75	10 years
EORTC ³	17	14	54	61	8 years
IGR ⁴	9	14	73	65	15 years
DBC ⁵	3	4	79	82	6 years

¹Fisher et al. *N Engl J Med*. 2002;347:1233-1241. ²Veronesi et al. *N Engl J Med*. 2002;347:1227-1232.
³Wentheiser et al. *CA Cancer J Clin*. 1995;45:83-107. ⁴Kvan Drogen et al. *Natl Cancer Inst Monogr*.
1992;115:15-19. ⁵Swainson et al. *J Clin Oncol*. 1990;12:1550-1554. ⁶Blichstein, Tish et al. *J Natl Cancer Inst Monogr*. 1992;11:19-25.

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Figure 7. Trends in Female Breast Cancer Incidence Rates by Tumor Size, 1992-2014, US

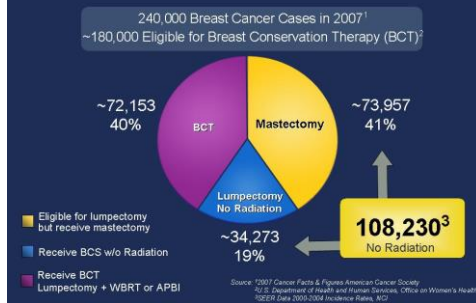


Note: Rates are age adjusted to the 2000 US standard population and adjusted for reporting delays.
Source: 13 SEER Registries, National Cancer Institute, 2017.

American Cancer Society, Inc., Surveillance Research, 2017

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Under-Utilization of BCT



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Why? Many are told they can avoid RT if they undergo mastectomy

"After mastectomy and axillary dissection, radiotherapy reduced both recurrence & breast cancer mortality in women w/ 1-3 positive nodes even w/ systemic therapy use."^{**}

"Many surgeons have inadequate knowledge regarding the role of radiation in breast CA management especially after mastectomy"^{***}

Ref: ^{*}EBCTCG. The Lancet published on line March 19, 2014

^{**}Zou et al. Int J Rad Oncol Biol Phys 87: 1022-1029, 2013

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BCS vs. mastectomy

Luminal A breast CA

LRR @ 10yrs

BCS: 8%

Mastectomy: 8%

Ref: Voduc et al. Breast CA subtypes & the risk of local & regional relapse. J Clin Oncol 28: 1884-2010

Triple negative breast CA

LRR @ 5yrs

BCS: 5%

Mastectomy: 10%

N=768, F/U: 7.8 yrs

Ref: 1. Abdulkarim BS, Cuartero J, Hanson J, et al: Increased risk of locoregional recurrence for women with T1-2N0 triple-negative breast cancer treated with modified radical mastectomy without adjuvant radiation therapy compared with breast-conserving therapy. J Clin Oncol 29:2852-2858, 2011



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Age, breast CA subtype approximation & LRR after BCS

N= 1434

Median f/u: 85 mo.

Luminal A: 0.8%

Luminal B: 2.3%

Her-2 positive: 10.8%

Triple negative: 6.7%

Ref: Arvold et al. JCO 29: 3885-3891, 2011.



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BCS vs. MRM in trials w/ contemporary RT & systemic therapy

Recent studies of BCS vs. MRM for T1-2 N0-1 M0 breast cancer in young and old women confirm that:

1. Even for women under age 40 lumpectomy and radiation with appropriate systemic therapy is equivalent to or slightly better than mastectomy with loco-regional failure rates of 4.6% and 8.5% at 5 years and 8.5% and 10.8% respectively for BCS vs. mastectomy.
2. BCS is more effective than mastectomy for triple negative breast cancers with LRR rates of 4% vs. 10% respectively with mean follow-up of 7.8 years.

Buckley et al., 2011 Breast CA Symp.
Abstr 70, Sept 8, 2011
Mahmoud et al., 2011 Breast CA Symp.
Abstr 85, Sept 8, 2011
Abich Karim et al. JCO 29:2852-58, 2011



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**Hwang et al. Survival after BCS & mastectomy for early stage breast CA. Cancer 119: 1402-1411, 2013.

[illegible]

BCT: Breast conservation treatment; CPM: Contralateral prophylactic mastectomy; ASBS: American Society of Breast Surgeons

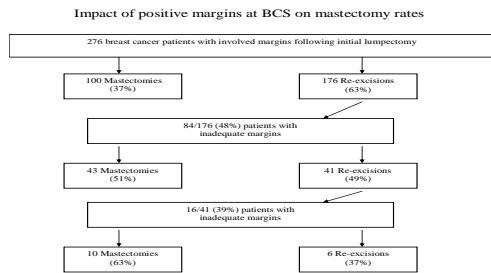


Fig. 1 Treatment course of 276 breast cancer patients who required multiple re-excisions or mastectomy following initial breast conservation with inadequate margins.

Cellini C, et al (2005) *The American Journal of Surgery* 189:662-666

Table 1
Local recurrence as a function of surgical margin in patients with invasive breast carcinoma treated with breast conservation therapy

Margin assessment	Author (reference)	No. of patients	Follow-up (months)	Local recurrence (%)	Positive Margin
Positive versus negative ¹	Franklin et al., 1997 (18)	48	40	3	18
	Hossein et al., 1997 (19)	300	40	3	13
	Burke et al., 1995 (21)	306	40	3	11
	Chambers et al., 1994 (22)	312	40	3	15
	Wang et al., 1994	312	40	3	9
	Vaccaro et al., 1992 (24)	289	70	3	17
	van Donge et al., 1992 (25)	414	100	3	20
	Veronesi et al., 1990 (16)	436	120	3	19
	Clarke et al., 1988 (27)	436	120	3	19
	Al-Sayid et al., 1986 (28)	422	120	3	19
Negative <1 mm	Franklin et al., 1997 (18)	184	40	0	16
	Hossein et al., 1997 (19)	184	40	0	16
	Burke et al., 1995 (21)	184	40	0	16
	Chambers et al., 1994 (22)	184	40	0	16
	Wang et al., 1994 (23)	184	40	0	16
	Vaccaro et al., 1992 (24)	184	70	0	16
	van Donge et al., 1992 (25)	184	100	0	16
	Veronesi et al., 1990 (16)	184	120	0	16
	Clarke et al., 1988 (27)	184	120	0	16
	Al-Sayid et al., 1986 (28)	184	120	0	16
Negative >1 mm	Franklin et al., 1997 (18)	184	40	3	16
	Hossein et al., 1997 (19)	184	40	3	16
	Burke et al., 1995 (21)	184	40	3	16
	Chambers et al., 1994 (22)	184	40	3	16
	Wang et al., 1994 (23)	184	40	3	16
	Vaccaro et al., 1992 (24)	184	70	3	16
	van Donge et al., 1992 (25)	184	100	3	16
	Veronesi et al., 1990 (16)	184	120	3	16
	Clarke et al., 1988 (27)	184	120	3	16
	Al-Sayid et al., 1986 (28)	184	120	3	16
Negative >2 mm	Franklin et al., 1997 (18)	184	40	3	16
	Hossein et al., 1997 (19)	184	40	3	16
	Burke et al., 1995 (21)	184	40	3	16
	Chambers et al., 1994 (22)	184	40	3	16
	Wang et al., 1994 (23)	184	40	3	16
	Vaccaro et al., 1992 (24)	184	70	3	16
	van Donge et al., 1992 (25)	184	100	3	16
	Veronesi et al., 1990 (16)	184	120	3	16
	Clarke et al., 1988 (27)	184	120	3	16
	Al-Sayid et al., 1986 (28)	184	120	3	16
Negative >3 mm	Franklin et al., 1997 (18)	184	40	3	16
	Hossein et al., 1997 (19)	184	40	3	16
	Burke et al., 1995 (21)	184	40	3	16
	Chambers et al., 1994 (22)	184	40	3	16
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	Clarke et al., 1988 (27)	184	120	3	16
	Al-Sayid et al., 1986 (28)	184	120	3	16
Negative >5 mm	Franklin et al., 1997 (18)	184	40	3	16
	Hossein et al., 1997 (19)	184	40	3	16
	Burke et al., 1995 (21)	184	40	3	16
	Chambers et al., 1994 (22)	184	40	3	16
	Wang et al., 1994 (23)	184	40	3	16
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	Veronesi et al., 1990 (16)	184	120	3	16
	Clarke et al., 1988 (27)	184	120	3	16
	Al-Sayid et al., 1986 (28)	184	120	3	16
Microscopic	Franklin et al., 1997 (18)	184	40	3	16
	Hossein et al., 1997 (19)	184	40	3	16
	Burke et al., 1995 (21)	184	40	3	16
	Chambers et al., 1994 (22)	184	40	3	16
	Wang et al., 1994 (23)	184	40	3	16
	Vaccaro et al., 1992 (24)	184	70	3	16
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¹Positive versus negative: all patients with positive margins were included in the analysis.

²Local recurrence: 1.5% with locally positive margins, 2.8% with extensively positive margins.

³Local recurrence: 1.5% with locally positive margins, 2.7% with extensively positive margins.

⁴Negative margin defined as no microscopic focus of tumor within inked margins.

Singleton, S.R. (2002) *The American Journal of Surgery* 184:383-393.

Recurrence and Margin Width

For the last time, what is the correct margin for BCS?

Positive margins still account for a 2-fold increase in IBTR rates

The absence of tumor on the inked margin is no worse than increasing margin width

Increasing margin width does not reduce the rate of IBTR

Ref: Moran, et al. SSO-RTOG consensus guideline on margins for BCS w/ WBRT in stages I-II invasive breast CA. (A meta-analysis of 33 studies) JCO on line Feb 10, 2014.

Preoperative Breast MRI for decreasing margin positive rates at BCS- not what we wished it would be.

-Margin positive rates at BCS in USA vary from <10% to 68%

COMICE Trial: Margin positive rate was 19% for patients undergoing preoperative MRI & Mammogram vs. Mammogram alone.

MONET Trial: Re-excision rates were 34% in the MRI group vs. 12% in the non-MRI group yet the number of conversions to mastectomy did not differ.

European Society of Radiology Meta-analysis, N=10,811: conversion to mastectomy was appropriate on pathologic exam in 12.8% and inappropriate in 6.3% of patients.

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REPORTED IMPACT ON SURGICAL PLANNING IN WOMEN WHO HAD ROUTINE ASSESSMENT VERSUS THOSE WHO ALSO HAD MRI FROM STUDIES OF WOMEN PLANNED FOR BREAST-CONSERVATION SURGERY

	Surgical Outcome	Did not Have MRI	Had MRI	P
		No. (%) with Outcome	No. (%) with Outcome	
Turnbull ^{1,2} (COMICE)	Reoperation/Re-excision	156/807 (19.3)	153/816 (18.8)	.77
Pengel ³	Positive margins	35/180 (19.4)	22/159 (13.8)	.17
Bleicher ²⁶	Positive margins (adjusted for T classification)	33/239 (13.8)	11/51 (21.6)	.2

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Preoperative Breast MRI for decreasing margin positive rates at BCS- not what we wished it would be.

MRI overestimates tumor size in 11-70% of patients

MRI underestimates tumor size in 10-56% of patients

Ref: 1) Behjatnia et al. Int J Clin Exp Path 3: 303-309, 2010. 2) Onesti, et al. Am J Surg 196: 844-850, 2008. 3) Bleicher, R.J. JCO 32: 370-371, 2014.

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MRI

Does it reduce local recurrence when used to select patients for breast conservation?

Solin's retrospective report of 756 patients treated with BCS included 215 staged with MRI & mammography and 541 staged with mammography alone. After 8 years:

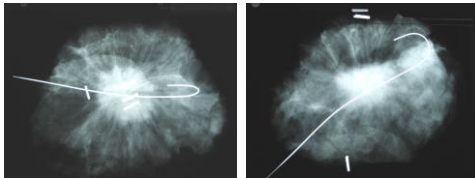
- 1) LR was 4% in those staged w/o MRI
- 2) LR was 3% in those staged w/ MRI
- 3) If these were biologically significant, second cancers identified by MRI would have led to LR rates of 11% to 30%

Solin, et al., JCO 26: 386-391 (2008)



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The only aspect of BCS totally controlled by the surgeon is margin clearance



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Impact of positive margins at BCS on mastectomy rates

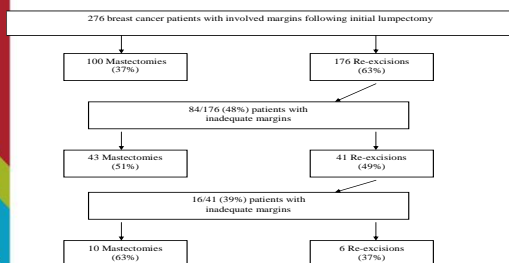


Fig. 1 Treatment course of 276 breast cancer patients who required multiple re-excisions or mastectomy following initial breast conservation with inadequate margins.

Cellini C, et al (2005) The American Journal of Surgery 189:662-666



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Fate of BCS candidate w/ positive margins at initial surgery

63% go on to unilateral mastectomy to clear margins

81% of those requesting BCS converted to bilat mastectomy after margin positive BCS

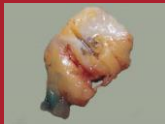
King, et al. Clinical management factors contribute to the decision for CPM. JCO 29: 2158-2164, 2011.



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Radioactive Seed Localization (RSL)

The Nebraska Medical Center



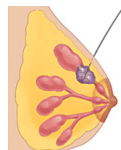
University of Nebraska Medical Center
Nebraska Medicine

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Wire Localization

Wire localization (WL) of nonpalpable lesions has been the standard method used to identify the location of the lesion

In WL, a metal wire (8 gauge) is guided by ultrasound or mammography to mark the site



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Wire Localization Shortcomings

- Entry site of wire is often not at the ideal location for incision by the surgeon, leading to unnecessary dissection & suboptimal cosmetic results
- Wire must be placed on the day of the operation, meaning coordination of scheduling of radiology & surgical procedures
- Most important disadvantage is the inaccuracy of localizing the target lesion



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Radioactive Seed Localization (RSL)

In the RSL procedure, a small radioactive iodine-125 (I-125) seed is implanted at the site of the lesion (using an 18 gauge biopsy needle).



I-125 seeds (looks like mechanical pencil lead)

The "point source" more clearly identifies the center of the mass. The surgeon uses a special radiation detector to pinpoint the seed & lesion. Because the I-125 seed remains radioactive for some time, surgical excision of the lesion can be performed up to several days after seed implantation.



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RSL Overview – Seed Placement

Authorized user will implant seed into breast using either mammography or ultrasound



Seed Implantation using Ultrasound

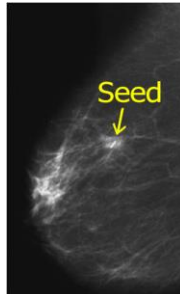


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RSL Overview – Seed Placement

Breast is imaged to verify placement of seed

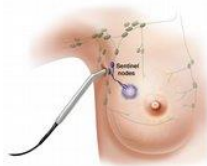
Mammography staff will write the word "SEED" directly on the skin of the patient's breast that contains the seed(s) & will include the # of seeds implanted (e.g., "1 SEED")



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Sentinel Node Biopsy

If sentinel node procedure is also being performed concurrently with RSL, the sentinel node procedure will typically be performed first.



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Seed/Lesion Removal

Surgical team reviews location of I-125 seed during pre-op surgical site marking & confirms verbally during surgical time-out

Set Neoprobe to I-125 and locate seed

Perform incision to remove tissue/seed. Do NOT dissect with scissors in order to avoid damaging the seed

Use Neoprobe to ensure I-125 radioactivity confined to the removed specimen



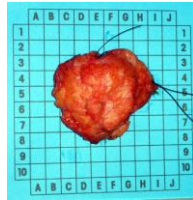
Using the gamma probe to re-orient to the position of the radioactive seed during dissection.

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Seed/Lesion Removal

Specimen must be radiographed to verify that the seed has been removed

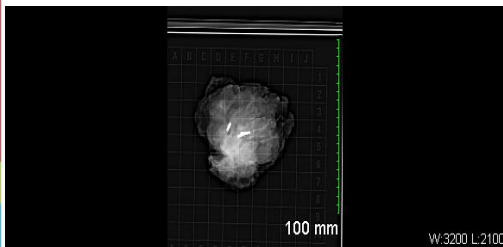
Radiograph is performed using the Hologic cabinet x-ray specimen unit in the OR



Specimen placed on Grid for radiograph

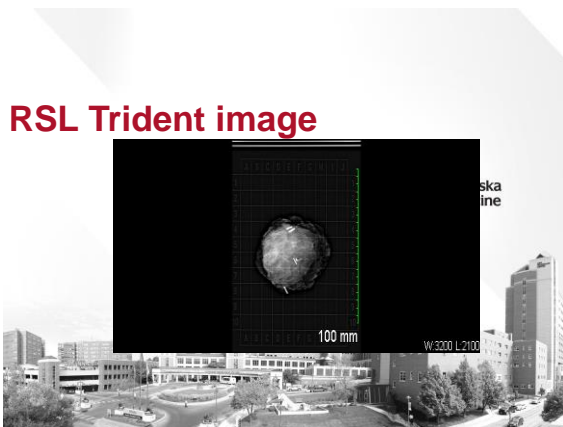


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RSL Trident image



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Radioactive seed localization (RSL) in the treatment of non-palpable breast cancer: Systematic review & meta-analysis

The results of this meta-analysis demonstrate a statistically significant benefit of RSL over the gold standard wire localization in terms of involved margin status, re-operation rates & reduced operative time.

Ref: Ahmed M, Douek M. The Breast 22: 383-388, 2013.



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Christy, et al. Preop chemo decreases need for re-excision of breast CA 2-4 cm in diameter. Ann Surg Onc 16: 697-702, 2009.

For tumors between 2 and 4 cm, preoperative chemotherapy is associated with a significantly decreased rate of re-excision following lumpectomy. This not only results in fewer mastectomies, but also avoids the morbidity and inferior cosmetic results associated with a re-excision lumpectomy.



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Can MRI help in the routine management of the non high risk patient?

If equivalent OS of BCS & mastectomy for ESBC was established well before MRI was invented, can it help to improve BCS rates?

Let us look at the evidence...



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Histologic Multifocality of TIS, T1-2 Breast Carcinomas Implications for Clinical Trials of Breast Conserving Surgery

-If tumors 2cm or less were removed with a margin of 4cm. ...about 5% of patients would harbor invasive tumor in the remaining breast. In another 5% of the cases DCIS may remain behind.” *

*Holland R, et al. Histologic multifocality of Tis, T1-2 breast carcinomas. Implications for clinical trials of breast conserving surgery Cancer 56: 979-990, 1985



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MRI

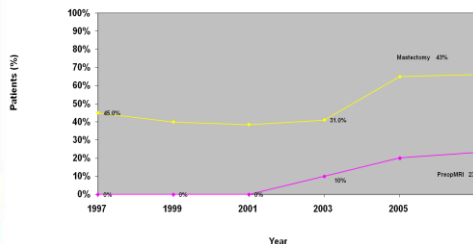
- Is able to identify some of these other cancer!! Surprised?
- Not all of those detected can be found by serial sectioning in the manner of Holland
- Many of those found by serial sectioning are not identified by MRI thus NOT reducing the recurrence rate to zero
- Yes, it can find 11-31% additional lesions in the same breast. Yet, LRR in BCS & mastectomy are ~3-5%

Sardanelli, et al AJR 183: 1149 (2004)



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MRI & Decrease in BCS



The recent rise in the proportion of early-stage patients undergoing mastectomy (2003-2006) appears to correspond to a rise in the proportion obtaining preoperative MRI.
Katipamula R, ASCO 2008, abstr 509



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Mastectomy Rates & MRI Use

No MRI – 29%

Negative MRI – 39%*

Positive MRI (no biopsy) – 51%**

Positive MRI (w/ biopsy) – 54%**

Positive MRI (positive biopsy) – 82%***

*Many have something else on MRI.

**Only 3% have a second CA!

***Why not 100%

Miller B, Abbott A, Tuttle T. The influence of preop MRI on breast cancer treatment. Ann Surg Onc (2012) 19: 536-540.

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How to address the impact of MRI on current BCS

- Biopsy all second lesions identified
- Recognize that it is only ~90% sensitive
- At least 50% of second lesions are DCIS
- In the community most second lesions are not confirmed by biopsy before the change in recommendation from BCS to mastectomy is made
- Systemic chemotherapy and hormonal therapy reduce local recurrence rates to 1-3% in patients receiving RT for BCS

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MRI

Does it reduce local recurrence when used to select patients for breast conservation?

Solin's retrospective report of 756 patients treated with BCS included 215 staged with MRI & mammography and 541 staged with mammography alone. After 8 years:

- 1) LR was 4% in those staged w/o MRI
- 2) LR was 3% in those staged w/ MRI
- 3) If these were biologically significant, second cancers identified by MRI would have led to LR rates of 11% to 30%

Solin, et al., JCO 26: 386-391 (2008)

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How to address the impact of MRI on current BCS

- Informed consent takes time and effort to allay the fears of most patients
- Long standing clinical data on BCS refutes the significance of new MRI findings
- Remind patients that local failure after mastectomy is still 8% in node negative women not receiving post op radiation
- Local failure after mastectomy in node positive patients was 27.6% in patients not receiving radiation or systemic therapy

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Indications for breast MRI use

- 1) BRCA carriers
- 2) Women w/ a palpable mass w/ a normal mammogram & U/S
- 3) Pre & post evaluation when using preop chemotherapy
- 4) Women w/ occult breast CA – palpable axillary nodes & normal mammogram (0.4% of breast CA)
- 5) Paget's w/ normal mammogram
- 6) Women w/ implants

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What about the other breast?

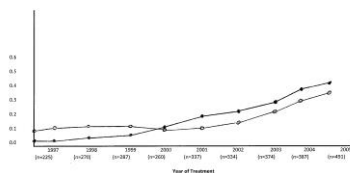


Fig 1. Rates of contralateral prophylactic mastectomy (CPM) and use of magnetic resonance imaging (MRI) as a diagnostic by year of surgery.

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Who are these women ?

- Young, married, employed women
- Caucasian
- Positive family history of breast cancer-58%
- Have undergone breast MRI- 44% had CPM due to a never biopsied MRI finding w/ <3% positive finding
- Offered simultaneous breast reconstruction
- Less than 29% undergo BRCA testing & many proceeded to CPM w/ known negative BRCA test

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What is the incidence of synchronous contra-lateral invasive breast cancer in non-BRCA carriers?

1%
~5% may have DCIS

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Age at Diagnosis for First Breast Cancer (years)	ER-Positive First Cancer		ER-Negative First Cancer	
	Per 100/Year	95% CI	Per 100/Year	95% CI
20-29	0.45	0.30 to 0.80	1.28	0.88 to 1.64
30-34	0.31	0.25 to 0.37	0.85	0.68 to 1.02
35-39	0.25	0.20 to 0.28	0.64	0.50 to 0.74
40-49	0.24	0.21 to 0.26	0.53	0.44 to 0.61
50-59	0.24	0.22 to 0.27	0.47	0.39 to 0.54
60-64	0.26	0.24 to 0.29	0.43	0.36 to 0.52
65-69	0.30	0.27 to 0.33	0.45	0.38 to 0.52
70-74	0.24	0.20 to 0.27	0.47	0.39 to 0.55
75-79	0.35	0.32 to 0.40	0.51	0.42 to 0.59
80-84	0.27	0.23 to 0.41	0.55	0.45 to 0.64
75-79	0.33	0.29 to 0.36	0.60	0.47 to 0.73
80-84	0.35	0.27 to 0.52	0.63	0.48 to 0.85

Abbreviation: ER, estrogen receptor.
*Estimated using the Poisson regression model with adjustment for time since first breast cancer diagnosis.

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Contralateral Prophylactic Mastectomy for Unilateral Breast Cancer (n=152,755)
 Tuttle, et al (2007) J Co 25 (33):5203-5209

Age (Years)	BCS		Unilateral Mastectomy		CPM
	No. of Patients	%	No. of Patients	%	%
<	88,326	57.8	59,460	38.9	7.7
18-39	4,694	49.9	4,136	43.7	13.2
40-49	17,610	56.4	12,011	38.5	11.8
50-59	25,371	59.9	14,916	35.7	9.2
60-69	21,855	59.9	13,853	37.9	5.4
70-79	18,796	55.6	14,544	43.1	2.9

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Back to the future-Why women with a single breast cancer are getting bilateral mastectomy

- The most common reasons given by patients for pursuing this course is a doctor's recommendation & fear
- MRI use delayed definitive treatment by more than 2 weeks (which is good!)
- 81% of those requesting BCS converted to bilat mastectomy after margin positive BCS
- New reconstruction options may contribute to this trend

Ref: Silva, E. Breast Conserving Surgery versus Mastectomy for Early-Stage Breast Cancer: Could Patient Choice Lead to an Inferior Outcome? *The Breast Journal* 20: 7-69, 2014.
 King, et al. Clinical management factors contribute to the decision for CPM. *JCO* 29: 2158-2164, 2011.

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Increased post op complications of bilat mastectomy w/o breast reconstruction

N=4219

Unilat mastect: 88%, Bilat mastect: 12%

Wound complications: 2.9% vs. 5.8%

All complications @ 30d: 4.2% vs. 7.6%

HR: 1.9

Ref: Increased Post op complications in bilateral mastectomy patients compared to unilateral

mastectomy: An analysis of NSQIP database. *Annals Surg Onc* 20: 3212-3217, 2013

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The problem of the contra-lateral breast

SEER data on 134,501 patients with breast cancer showed a 3% incidence of contralateral breast cancer at 5 years. Int J Radiat Oncol Biol Phys 56: 1038-1045, 2003.

The contra-lateral risk of breast cancer is cut by 50-60% in women treated w/ systemic chemo & hormonal ablation

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The problem of the contra-lateral breast

Question #1:

What is the chance of developing a 2nd cancer in the opposite breast?

Answer: 0.5%/yr with a max of 2.3% to 3.9% @ 10 years

Question #2:

Will removing the normal contra-lateral breast improve my survival from my primary cancer?

Answer: No, your outcome is determined by the stage of your primary cancer

Khan S. JCO: 26(16): 2132-2135. (2011)
Gao et al., J Radiat Onc Biol Phys 56: 1038 (2003)

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The problem of the contra-lateral breast

What can be done to manage the contra-lateral risk?

- 1) Assess informative value of screening mammogram
- 2) Design personalized screening strategy accordingly (MRI- yes why not?, U/S, q. 6 mo. Exam)
- 3) Consider proactive strategies (Tamoxifen, Raloxifen, exercise and diet- they work!!)

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The problem of the contra-lateral breast

If contra-lateral prophylactic mastectomy was a sound strategy for women at normal risk there would be no women in the USA with breast cancer with any endogenous breasts

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Incidence of contralateral primary vs. ipsilateral recurrence or metastases (N=2965)

- 1) Incidence of CBC: 0.5% is 17X less than the
 - 2) Incidence of distant metastases: 7% and 7X less than the
 - 3) Incidence of loco-regional recurrence: 3%
 - 4) Incidence of distant metastases in patients undergoing CPM: 4% at 4 yrs
 - 5) Only 29% of women had readily available genetic testing
- Conclusion: prognosis is determined by index lesion**

Ref: King et al. JCO 29: 2158-2164, 2011.

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67 y/o WF w/ no risk factors for breast cancer presents w/ clinical T1b N0 M0 ER/PR +/+ ,Her2 - , IDC

Rx plan: bilat^{eral} mastectomy with ipsilat SNM & PAC placement

Pt requests preop 2nd opinion by medical oncology with Rx plan ?

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Your answer

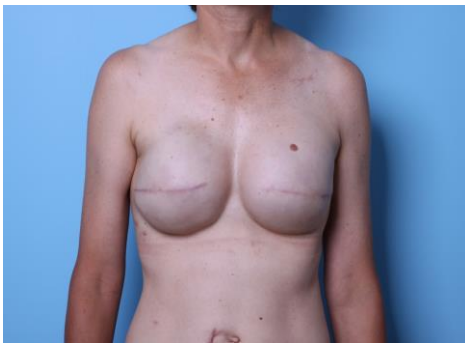
- 1) Ipsilateral mastectomy, SNM, and contra-lateral prophylactic mastectomy
- 2) Ipsilateral BCS, SNM and post operative radiotherapy after bilateral MRI staging
- 3) Ipsilateral BCS, SNM and post operative radiotherapy w/o bilateral MRI staging
- 4) Ipsilateral BCS, SNM and post operative radiotherapy w/ accelerated partial breast irradiation

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What options a there for the outlying patient : The surgeon as psychiatrist?

Can a psycho-oncologist help?
 Do we treat breasts w/ cancer or patients w/ breast CA?
 Are other risk reducing strategies an alternative to CPM?
 From an ethical standpoint does preventive mastectomy warrant the traditional mutilating procedure when NSSM is and should be the preferred approach?

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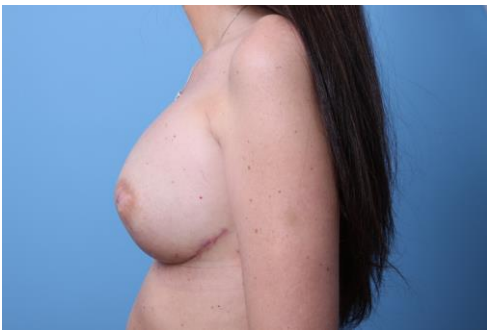


8/16/2012

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Thank you.

Questions?

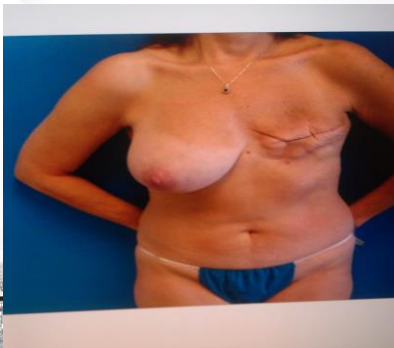
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Is BCS safe for women < 40?

- 1) Exclude BRCA carriers first
- 2) No benefit for MRM over BCS
- 3) Contralateral breast CA risk: 2% for non-BRCA carriers, 13% for BRCA carriers, 23% for triple negative patients

Giuliano et al 2017

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Understanding Microscopic Disease Extension in Different Age Populations

Two contemporary pathology publications reporting on disease extension from edge of lesion in patients treated with mastectomy or quadrantectomy:

- Imamura¹
 - Pt age: 40 – 64 years
 - Maximum distance of extension = 8.32 mm.
 - Pt age: > 64 years
 - Maximum distance of extension = 5.28 mm.
- Ohtake²
 - Patient age: ≥ 50 years
 - Maximum distance of disease extension = 6.7 – 7.7 mm.

¹Imamura et al. Breast Cancer Res Treat. 2003;82:177-184.
²Ohtake et al. Cancer. 1995;75:32-45.

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"Elsewhere" Failures

- Incidence of failures outside of tumor bed in randomized trials comparing lumpectomy with or without postoperative irradiation.¹

Trial	Median fu (mo)	Surgery Alone		Surgery Plus RT	
		N	%	N	%
NSABP-B06	125	17 / 636	2.7	24/829	3.8
Milam	39	4 / 223	1.5	0/294	0
Ontario	43	15 / 421	3.5	4/416	1.0
JCRT	116	-	-	27/874	2.8

- The data suggest WBRT does not protect against new disease development elsewhere in the breast.

¹Baglan et al. Int J Radiat Oncol Biol Phys. 2001;50:1003-1011.

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PROXIMA
THERAPEUTICS, INC.

Prospective Randomized Trials of Lumpectomy +/- Radiotherapy

-Updated Results-

Trial	% of Patients With Recurrence		% Reduction Recurrence (CS vs. CS + RT)
	CS Alone	CS + RT	
NSABP B-06*	36	12	67
Milam*3	24	6	75
Scottish	25	6	76
Uppsala-Orebro*	24	9	63
Ontario	35	11	69
English	35	13	63

* Recently Updated

1987, 2004 Rev. A

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Table 3 PATHOLOGIC TYPE OF MALIGNANT FOCI MISSED ON MAMMOGRAPHY AND DYNAMIC MRI IN PATHOLOGY-CONTROLLED STUDIES IN 99 BREASTS

Pathologic Type	Mammography	MRI
Invasive	45	18
IDC	20	8
ILC	17	7
IDC + ILC	5	1
Other	3 ^a	2 ^b
In-situ	19	18
DCIS	17	16
LCIS	2	2
Total	64	36

Note: IDC = invasive ductal carcinoma, ILC = invasive lobular carcinoma, DCIS = ductal carcinoma in-situ, LCIS = lobular carcinoma in-situ.

^aEndolymphatic carcinoma (n=2), metaplastic carcinoma (n=1)

^bEndolymphatic carcinoma (n=2)

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Table 2 FOCUS-BY-FOCUS ANALYSIS OF DIAGNOSTIC PERFORMANCE OF MAMMOGRAPHY AND DYNAMIC MRI IN PATHOLOGY-CONTROLLED STUDIES IN 99 BREASTS

Features	Mammography	MRI	P
True positive	124	152	-
False negative	64	36	-
Overall sensitivity	66% (124/188)	81% (152/188)	<0.001 ^a
Sensitivity for invasive foci	72% (113/158)	89% (140/158)	<0.001 ^a
Sensitivity for in-situ foci	37% (11/30)	40% (12/30)	NS ^a
Invasive-noninvasive ratio of false-negative	2.4 (45/19)	1.0 (18/18)	0.043 ^b
Diameter of false-negative (mm)			
Mean ± SD	10.9 ± 18.2	5.6 ± 4.5	0.033 ^c
Median	8.0	5.0	-
Range	0.5 – 130.0	0.5 – 15.0	-
False-positives	40	70	-
Positive predictive values	76% (124/164)	68% (152/222)	NS ^b

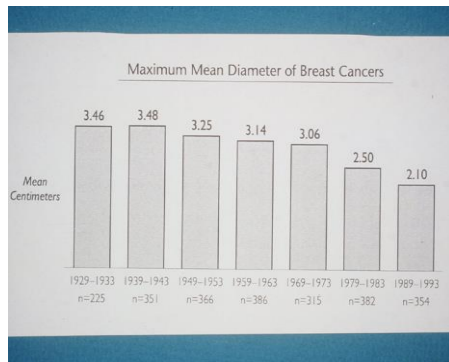
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Table 5 SENSITIVITY AND POSITIVE PREDICTIVE VALUE OF MAMMOGRAPHY AND MRI IN DETECTING 1988 MALIGNANT FOCI IN 99 BREASTS FOR DIFFERENT PATTERNS ON MAMMOGRAPHY

Statistics	Fatty Breasts			Scattered Fibroglandular, Heterogeneously Dense, and Extremely Dense Patterns				Total		
	Mammography	MRI	P	Mammography	MRI	P		Mammography	MRI	P
Sensitivity	75% (56/75)	80% (60/75)	NS	60% (66/113)	81% (62/113)	<0.001		66% (124/188)	81% (152/188)	<0.001
Positive predictive value	73% (56/77)			78% (66/87)	71% (62/130)	NS		76% (124/164)	68% (152/222)	NS

Note: McNemar test was used for comparisons of sensitivity and chi square test for comparisons of positive predictive values. NS = not significant.

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Why one must read critically!

"CPM is associated with a small improvement in 5 year breast cancer survival in young women with early stage ER negative breast cancer." Bedrosian et al. JNCI 102: 401-409, 2010.

"There is no conclusive evidence to show that CPM confers a survival advantage" Yao et al. Breast CA Res Treat: 142: 465-476, 2013.

But... You must know that...

OS is determined by distant relapse inherent to stage at presentation not by CPM removing the cancer you never had!

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