

Breast Cancer in Young Women: Sexuality and Survival

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Case #1: 37 y.o. WF

- Presented in June 2002 with early stage breast cancer
- Underwent mastectomy and simultaneous reconstruction
- Followed by six cycles of CMF chemotherapy at full doses
- Never wanted to come back for follow-up visits
- No evidence of cancer until April, 2005...



Case #1, continued

- Presented ill with bone, liver and brain metastases
- Treated with steroids, whole-brain radiation and chemotherapy
- Tolerated treatment extremely poorly; no response to chemotherapy
- Became very depressed and withdrawn, refused psychiatric intervention and anti-depressants
- Pursued a relentlessly downhill course and died in a few months



Case #2

- 29 y.o. in 2003, found lump in R breast
- Had series of lumpectomies (4) to try to achieve negative margin; ultimately unsuccessful
- Finally underwent mastectomy with delayed reconstruction; 0/9 nodes involved
- Original tumor 1.1 cm; 90% in situ
- ER 70%; PR 20%
- Her-2/neu not overexpressed



Case #2, continued

- Past History:
 - Oral contraceptives for 12 years until 6 months prior to conception
 - Negative family history for breast cancer
- Treated with CMF chemo
- Reconstruction in 8/03
- Became pregnant 11/04
- Uneventful pregnancy; dissuaded from taking oral contraceptives post-partum



Case #2, continued

- Four months after delivery discovered mass in R axilla (ipsilateral to cancer)
- Underwent surgery; 2 masses removed (+); no normal nodal tissue seen
- New tumor Her-2/neu +++; ER+ PR-



Case #2, continued

- Sought second opinion (Dr. Chang)
 - Underwent axillary dissection with more tumor removed; took two attempts to get negative margin; reconstruction preserved
- Treated with Taxotere, Carboplatin, Herceptin; therapy still ongoing
- No evidence of metastases or local recurrence
- 9/06 developed cough and hemoptysis: multiple pulmonary emboli; anticoagulated with improvement
- Herceptin continues
- Throughout treatment has remained upbeat; husband was stationed overseas; reassigned here by military to provide emotional support



Breast Cancer by Age and Stage

Stage	Age group					
	≤40 (%)	41-50 (%)	51-60 (%)	61-70 (%)	71-80 (%)	>80 (%)
Overall	210	515	691	1019	909	443
Stage I	62 (29.5)	201 (39.0)	301 (43.6)	508 (49.9)	435 (47.9)	189 (42.7)
Stage II	112 (53.3)	238 (46.2)	277 (40.1)	345 (33.9)	323 (35.5)	170 (38.4)
Stage III	31 (14.8)	57 (11.1)	61 (8.8)	77 (7.6)	95 (10.5)	53 (12.0)
Stage IV	5 (2.4)	19 (3.7)	52 (7.5)	89 (8.7)	56 (6.2)	31 (7.0)
Unable to be staged						

* Mean age is significantly lower in Stage II disease ($P < 0.001$) compared with the mean age in the other stages.

Disproportionate number of young women
with Stage II disease.

Chung, *CANCER* 77(1):99-103, 1996



Five-Year Disease-Free Survival by Age and Stage

Age (yrs)	% All stages	% Stage I	% Stage II	% Stage III
All ages	64.60 (72.1 ± 0.8)	80.79 (87.4 ± 1.0)	63.15 (69.9 ± 1.2)	36.0 (41.5 ± 2.4)
≤40	60.79 (68.0 ± 3.4)	83.22 (90.3 ± 5.1)	56.09* (39.6 ± 2.2)	16.60* (26.0 ± 5.8)
41-50	73.22 (71.9 ± 1.7)	85.09 (79.3 ± 2.1)	63.87 (52.8 ± 1.7)	44.47 (47.5 ± 6.3)
51-60	66.87 (71.1 ± 1.6)	83.63 (79.5 ± 1.8)	63.53 (70.7 ± 2.7)	39.71 (33.8 ± 4.3)
61-70	71.53 (67.9 ± 1.1)	88.92 (80.9 ± 1.1)	72.44 (70.4 ± .8)	36.73 (32.0 ± 2.5)
71-80	63.11 (63.6 ± 1.3)	77.21 (76.2 ± 1.7)	66.26 (60.3 ± 2.1)	40.48 (41.5 ± 4.5)
>80	39.88* (48.4 ± 2.3)	53.51* (55.3 ± 2.8)	49.91* (49.5 ± 3.5)	22.88* (25.1 ± 6.3)

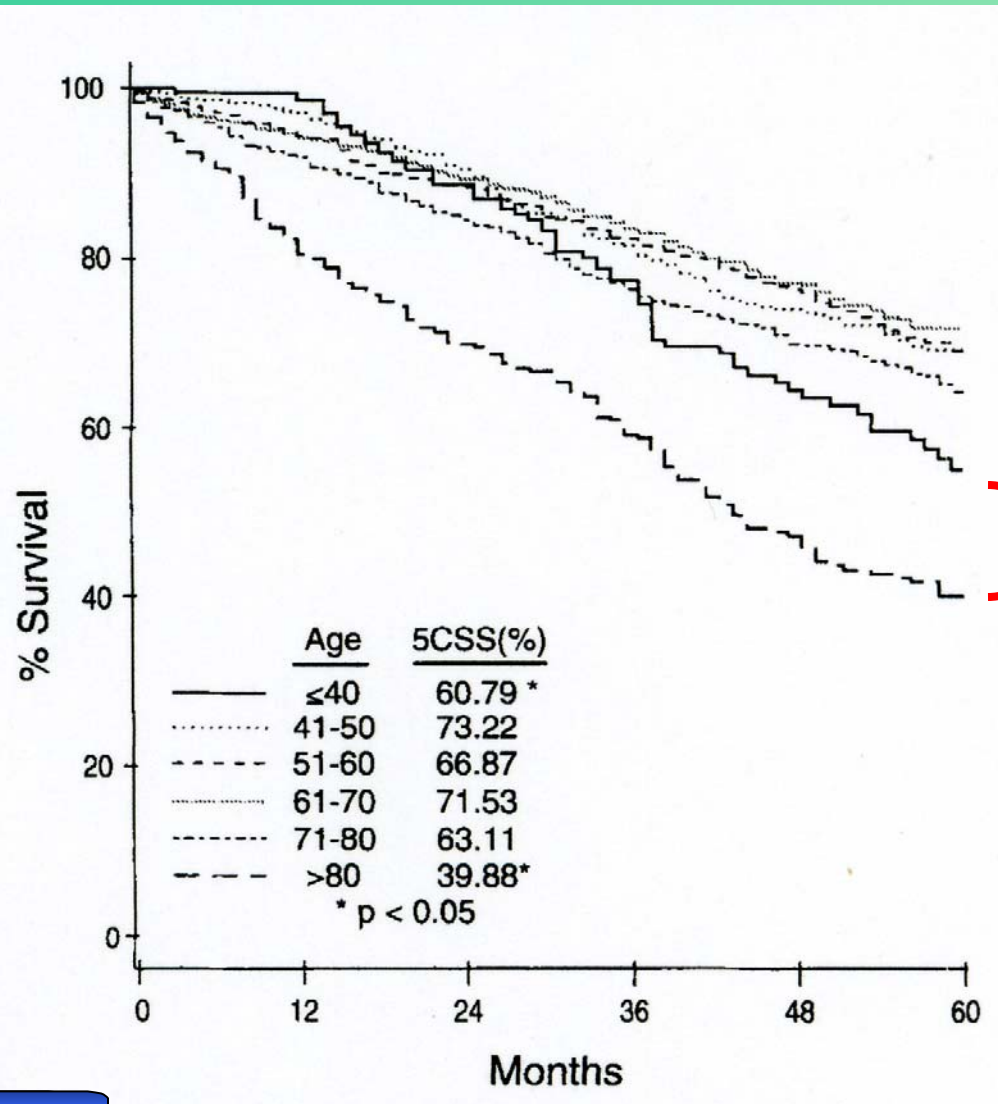
* These groups had a shorter disease free interval than other age groups for each stage ($P < 0.05$). Values within parenthesis reflect disease free interval ± SEM (months).

Much worse 5-yr DFS

Much shorter DFI



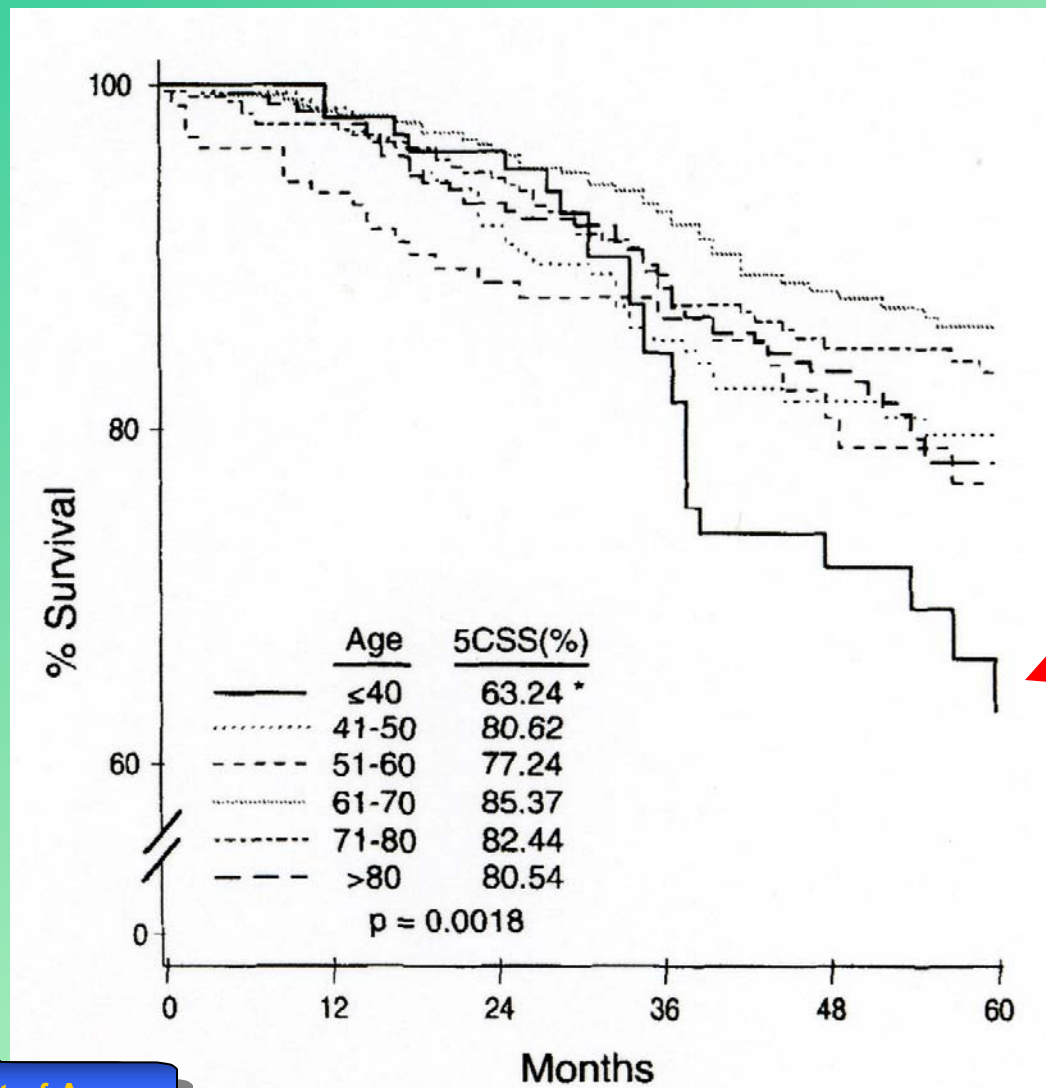
Disease-Free Survival by Age



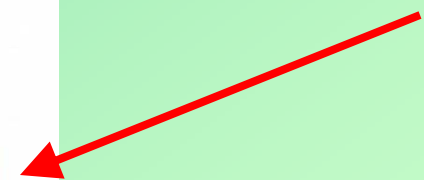
Only women over 80 do worse



Cancer-Specific Survival for Stage II Breast Cancer



Very bad outcome in young women with Stage II



Treatment by Age Group: Why the Elderly did so Badly

Treatment	≤40	41-50	51-60	61-70	71-80	>80
Local						
L	10.6	12.3	16.9	16.5	20.8	35.5
AND	0.0	0.6	0.1	0.2	0.0	0.0
LAND + RT	26.7	24.3	25.2	20.5	12.6	4.1
MRM	62.8	62.5	57.3	62.3	66.1	54.7
No Tx	0.0	0.4	0.4	0.5	1.3	5.6
Data available:	3722					
Chemotherapy						
Yes	59.4	45.6	29.7	16.3	9.2	3.5
No	40.6	54.4	70.3	83.7	90.8	96.5
Data available:	3701					
Hormonal therapy						
Yes	22.4	22.7	39.8	42.4	50.7	50.1
No	77.6	77.3	60.2	57.6	49.24	49.9
Data available:	3701					

L: lumpectomy; AND: axillary node dissection; LAND + RT: lumpectomy, axillary node dissection, and radiotherapy to affected breast; MRM: modified radical mastectomy; No Tx: no treatment beyond biopsy; Chemotherapy: adjuvant therapy with CAF or CMF; Hormonal therapy: adjuvant therapy with tamoxifen.



Population-based Study from Australia*

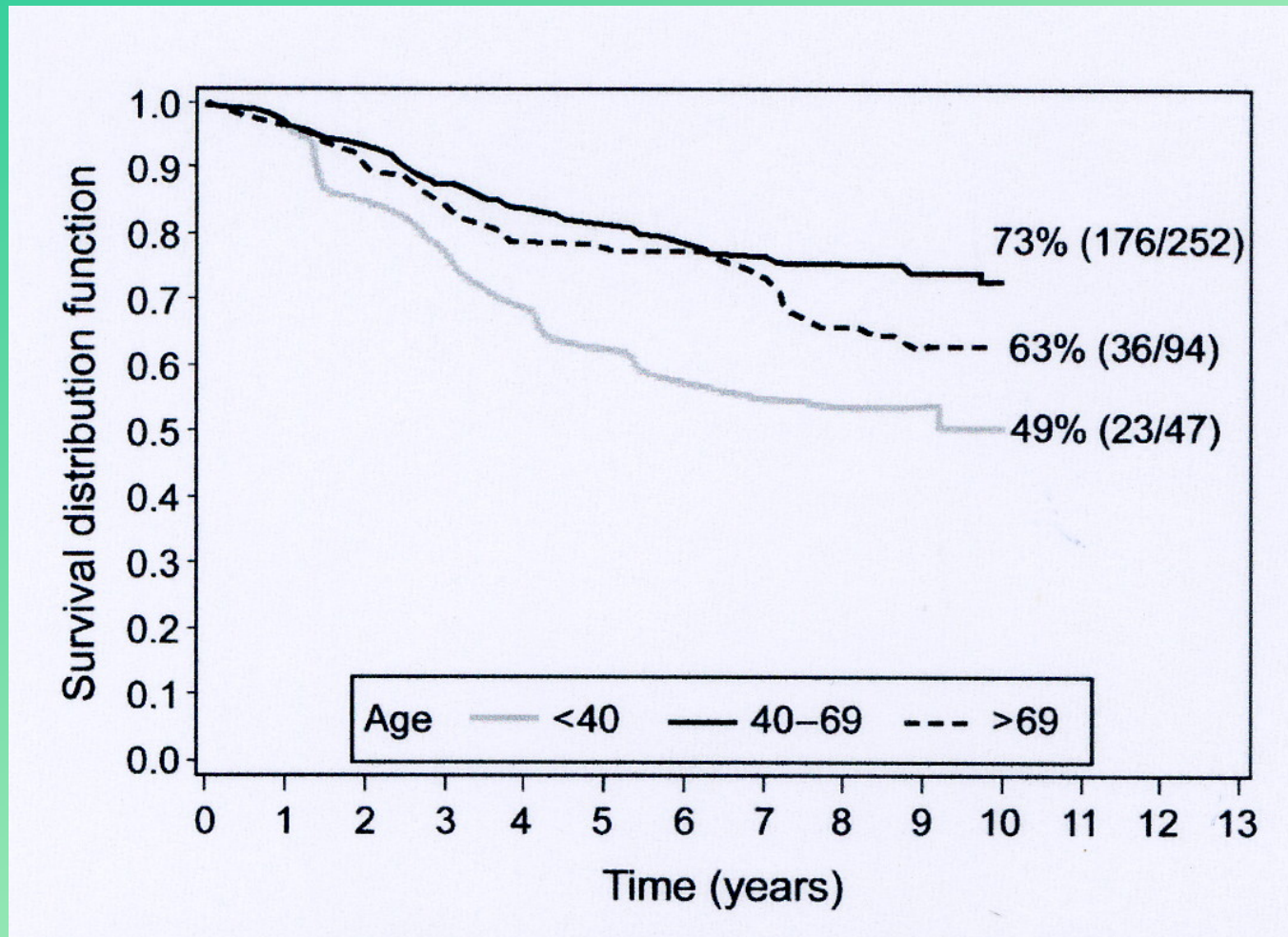
- n=393 women diagnosed in 1992
 - Long follow-up
- Breakdown by age:
 - 47 < 40y.o.
 - 252 40-69y.o.
 - 94 >69y.o.

Age	<40	40-69	>69
Tumor Size			
T1	47	48	33
T2	28	29	36
T3	2	2	1
T4	10	8	12
Unknown	13	13	18
Nodal status			
0	47	46	32
1-3	23	23	8
>3	17	14	11
Unknown	13	17	49

Tumor size was about the same across the board; nodal status was only slightly worse in younger women



Survival by Age



Differences in survival not explained by tumor size or nodal status



BRCA 1 and 2 Mutations in Young Women with Breast Cancer

- Overall incidence of mutation in general breast cancer population is 3%
- In one study* of 89 women under 40 with breast cancer, 8 had BRCA 1 or 2 mutation (3X general population)
- Relative risk of 5.5 in this group of developing contralateral breast cancer in first 8 years after diagnosis
- Has implications for management, even though by current guidelines most of these women would not have been candidates for testing



Clinicopathologic Features of Breast Cancer in Young Women

Clinicopathologic feature	Bertheau et al., 1998 ¹⁴	Gajdos et al., 2000 ⁴	Colleoni et al., 2002 ¹³	Jimor et al., 2002 ²¹	Shavers et al., 2003 ⁹	Current study
Age range (yrs)	0-35	21-35	< 35	≤ 35	15-34	23-30
Lymph node involvement (%)	61	51	60	49	59	74
ER positive (%)	NA	48	61	20	36	45
PR positive (%)	NA	38	1	NA	33	36
HER-2/ <i>neu</i> positive (%)	26	NA	40	NA	NA	44
p53 positive (%)	22	NA	NA	NA	NA	50

ER: estrogen receptor; NA: not available; PR: progesterone receptor.

Maru et al (M.D. Anderson series):
CANCER 103:900-5, 2005

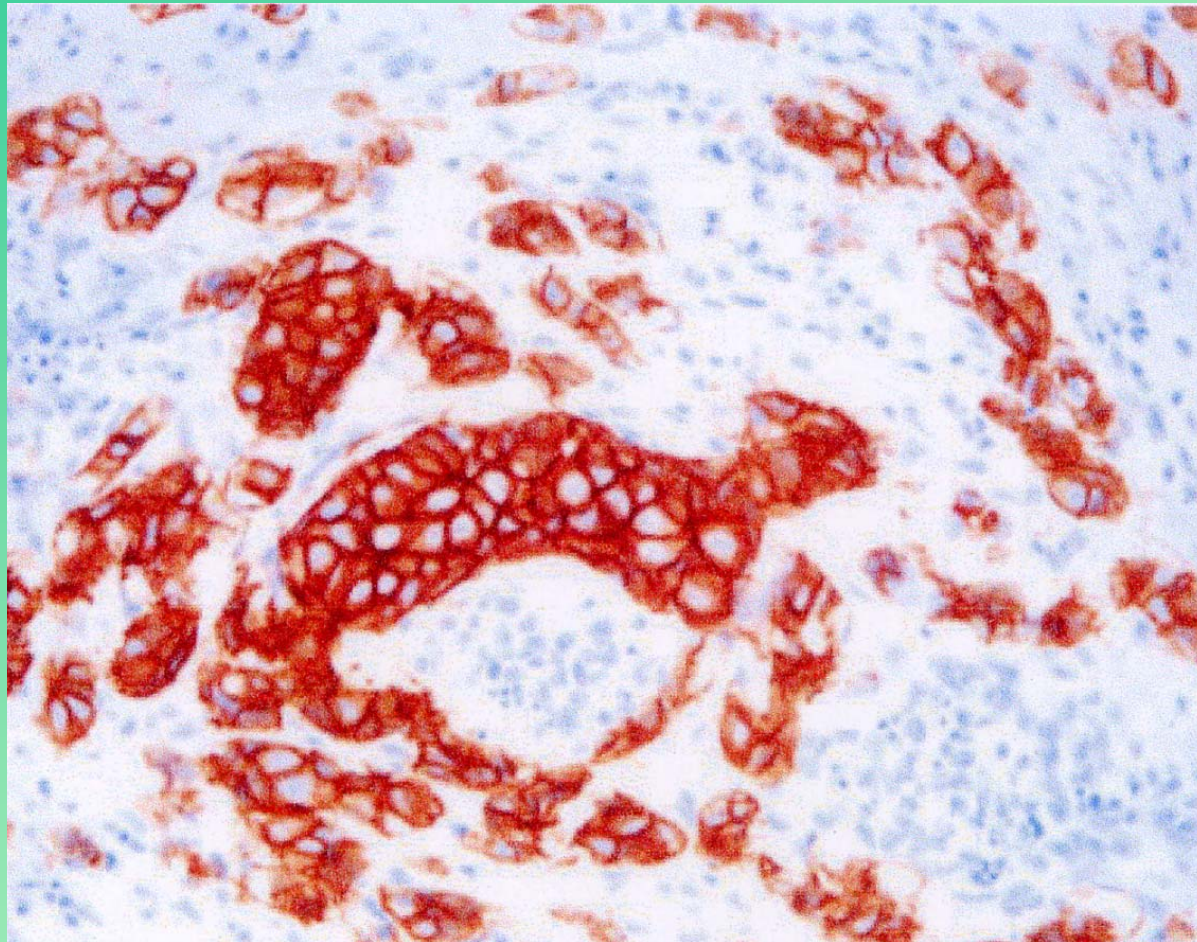


Clinicopathologic Features of Breast Cancer in Young Women

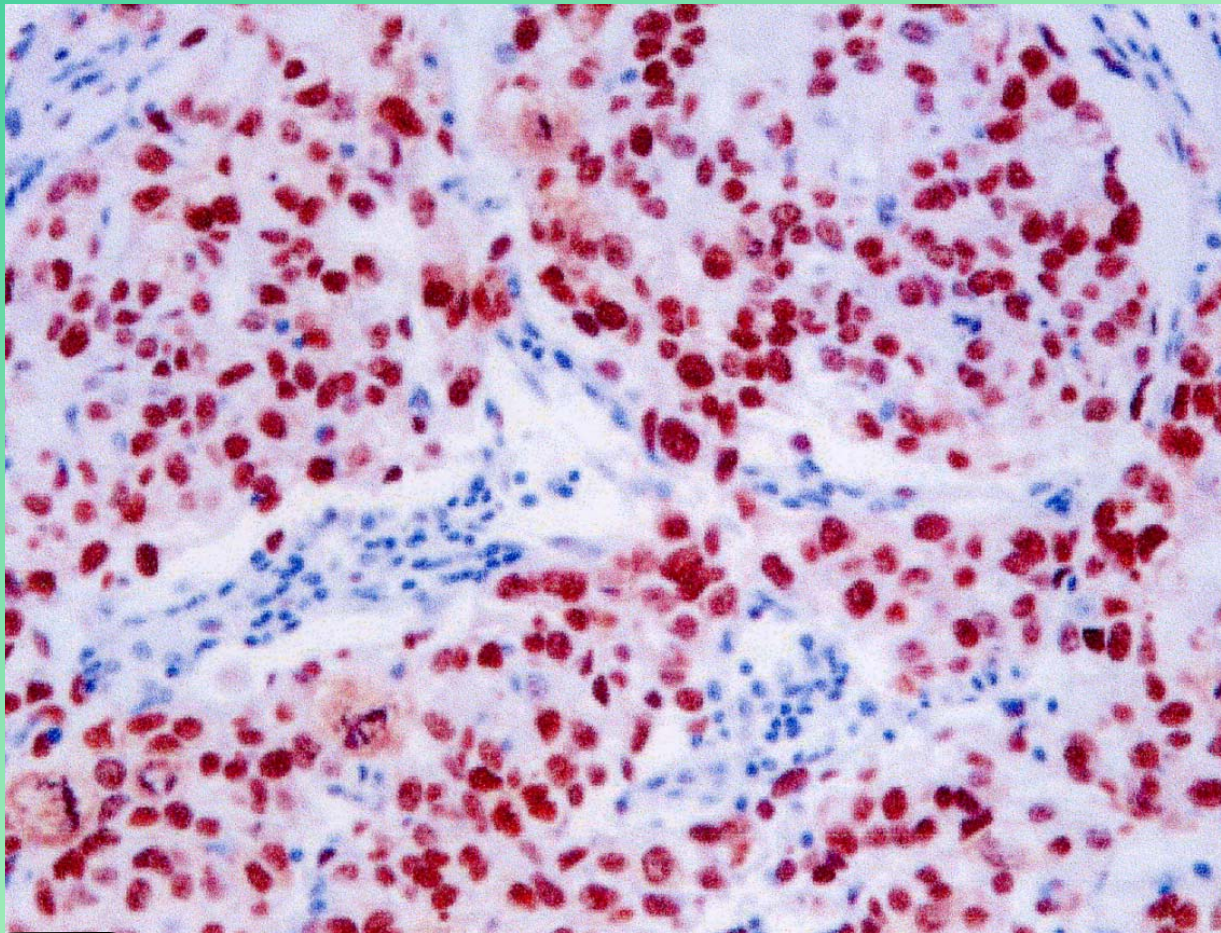
Clinicopathologic feature	Current study	
Age range (yrs)	23–30	
Lymph node involvement (%)	74	<50
ER positive (%)	45	
PR positive (%)	36	
HER-2/ <i>neu</i> positive (%)	44	30
p53 positive (%)	50	35

All three above parameters predict for poor outcome and are much higher in this group than in all women with breast cancer

Her-2/neu Positivity (3+) predicted for lymph-node involvement in Maru study



Nuclear staining for p53 protein accumulation in tumor cells



Her-2/neu and p53 Overexpression by Lymph Node Status^a

Lymph node status	HER-2/ <i>neu</i> status				P53 status	
	IHC		FISH		Positive (<i>n</i> = 22)	Negative (<i>n</i> = 22)
	Positive (<i>n</i> = 18) ^b	Negative (<i>n</i> = 23) ^c	Positive (<i>n</i> = 10) ^d	Negative (<i>n</i> = 30) ^e		
N0	2	9	0	10	5	7
N1 or N2	16	14	10	20	17	15
<i>P</i> value	0.044		0.035		0.5	

IHC: immunohistochemistry; FISH: fluorescence in situ hybridization.

^a Data shown are the numbers of patients.

^b Two plus and 3+ positive by IHC.

^c Zero and 1+ negative by IHC.

^d Amplification of the Her-2/*neu* gene.

^e No amplification of the HER-2/*neu* gene or 0 and 1+ by IHC.

Her-2/neu is somewhat more predictive of nodal status than p53



Prognosis: Conclusions

- Young women with breast cancer do somewhat worse than women of other age groups except the very old
- Difference not entirely explained by difference in stage at diagnosis
- Markers of tumor aggressiveness are more frequent in young women



Social Security is the Third Rail of Politics*

- Touching the third rail is fraught with hazard
- It's what makes the trains go



*Charles Stein, *Boston Globe* February 25, 1996.



Social Security is the Third Rail of Politics*

- Touching the third rail is fraught with hazard
- It's what makes the trains go
- One could argue....
 - ***Sex is the third rail of Oncology***
- Tossing caution to the winds: Let's talk about what happens to your sex life when you get cancer...

*Charles Stein, *Boston Globe* February 25, 1996.



The Unspoken Question

Is there sex after cancer?

Sexual dysfunction in breast cancer patients

- One half of all women treated will experience long term sexual dysfunction.

Sexual dysfunction manifests as:

- Decreased desire
- Arousal difficulties
- Anorgasmia
- Dyspareunia

Etiology of sexual dysfunction

1. Physical

- Post Surgical Changes
- Premature Menopause
- Post Radiation Changes

Post Surgical Changes

- Decreased Nipple or surrounding skin sensation—inability to experience arousal through breast stimulation
- Lymphedema secondary to axillary node dissection—responsible for pain , swelling and poor body image
- Changes notably less in breast conservation surgery than mastectomy—
Schover et al. 1997

Premature Menopause

- Signs of estrogen depletion are significant and distressing to all phases of sexuality.
 - Vaginal dryness and decreased sensation with accompanying dyspareunia
 - Decreased androgens—ovary contributes 50% circulating testosterone—significant decline in desire, diminished sexual energy and fantasy—Kaplan et al., 1992.
 - Hot flashes, sleep disturbances and mood changes

Premature menopause, continued

- Symptoms of premature menopause worse than those of natural menopause—Moore, 2001
- In general the younger the patient, the more severe the symptoms—likely due to higher endogenous estrogen levels

Etiology of sexual dysfunction

2. Psychological

- Self esteem/ body image
- Prior Sexual Health
- Lack of Information and support
- Coping Skills /Previous Mental Health

Self Esteem/Body Image

- Extremely narrow impact of breast conservation on sexual satisfaction or desire.
- Improved body image –no difference in incidence of sexual dysfunction or marital satisfaction—Schover et al.
- One half of all women reported dissatisfaction with body image post treatment in both mastectomy and conservation group

Self Esteem/Body Image

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Prior Sexual Health

- The most important predictor of post surgical sexual satisfaction—Dow-1995.

Lack of information and support

- 25 percent of women reported communication problems with the doctor.
- Most common barrier is either the patients or the providers discomfort in addressing these issues—i.e. the “dreaded third rail”
- Time constraints-managed care setting, critical treatment plans –sexual health deemed a low priority

Etiology of sexual dysfunction

3. Pharmacological

- Chemotherapeutic agents—nausea, weight gain, fatigue, premature menopause
- Antidepressants –decreased libido, anorgasmia
- Aromatase inhibitors, tamoxifen—hot flashes, vaginal dryness and pain

Etiology of sexual dysfunction

4. Relational

- Resuming sexual intercourse rapidly is key in restoring relationship balance.
- One third of patients report partners are “overprotective” and afraid of hurting them
- Important caveat to caregiver to give permission to resume relations.

Etiology of sexual dysfunction

4. Relational

- Outcome of single women much worse.
- One half report they would not tell a date about their cancer.
- one third report they were afraid to initiate a relationship—Schover-1991

Treatment of Sexual Dysfunction

- Multidisciplinary Approach: PLISSIT model
 - Permission—open ended questions—“some women have changes in their sex lives after surgery—has this been an issue for you?”
 - Limited information—web sites ,pamphlets
 - Specific Suggestions—Lubricants, sensate focus techniques, hormone replacement therapy—a double edged sword
 - Intensive Therapy— referral to a trained sex therapist—AASECT.org

Pharmaceutical Treatment

- Vagifem/femring for atrophic vaginitis—needed blessing of oncologist and informed consent
- Testosterone/androgen replacement for decreased libido/ sensation—Kaplan reported significant increased desire and sensation with androgen replacement—methyltestosterone does not aromatize to estrogen
- Effexor/ssris for vasomotor symptoms

Conclusions

- Breast cancer diagnosis damages sexual health in many ways.
- Younger patients often most affected.
- RECOGNITION , DISCUSSION AND ADMISSION OF THESE quality of life issues crucial to successful treatment.
- In era of managed care, utilize physician extenders, nurses for sensitive time occupying discussions—some patients more comfortable with extenders than primary oncologist for these talks.

Questions for either speaker?