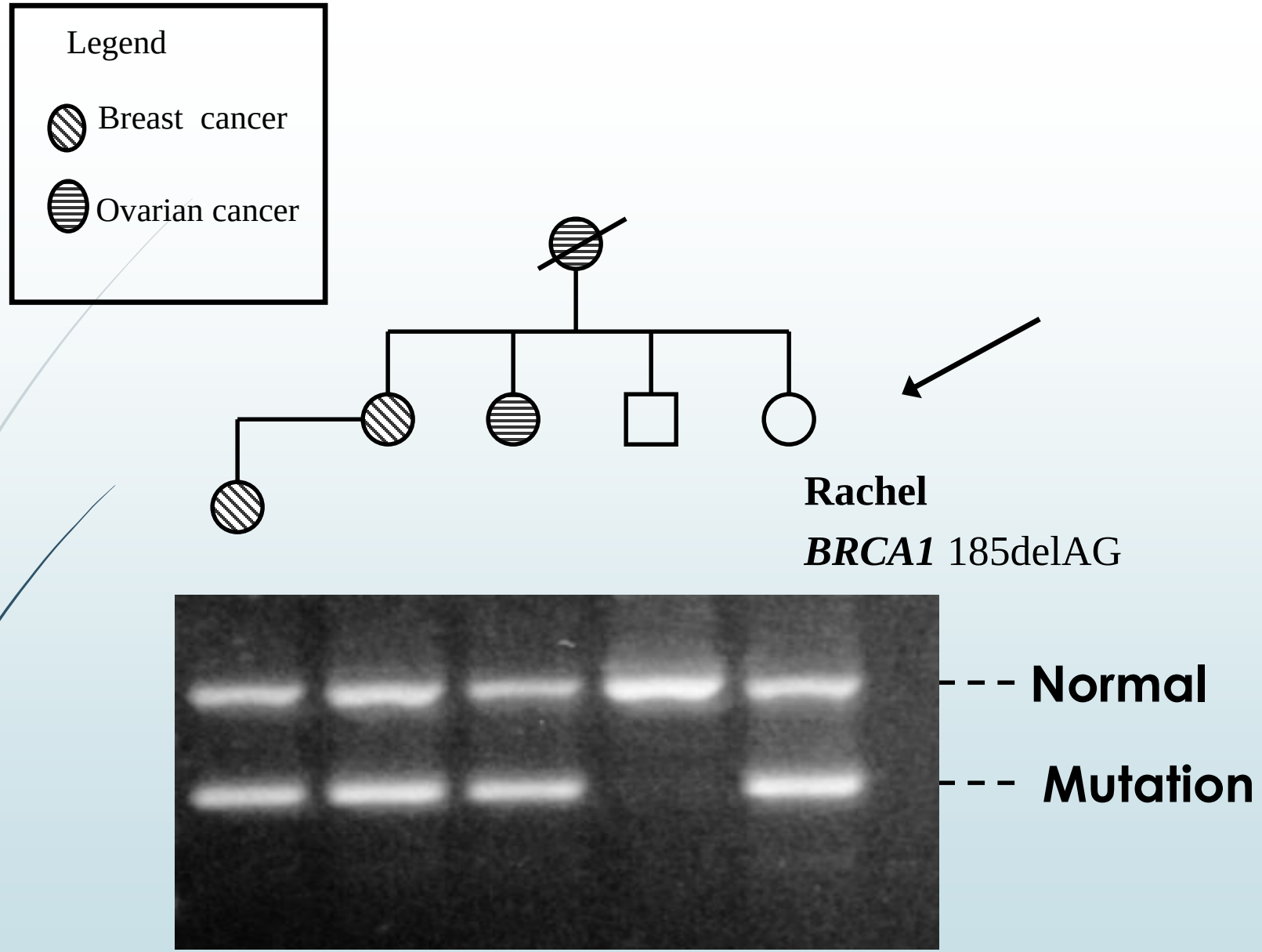
Incontri di aggiornamento del Dipartimento Oncologico

DONNE SANE CON MUTAZIONE BRCA 1-2: COSA FARE?

CHIRURGIA: MASTECTOMIA PROFILATTICA

Dott.ssa Chiara Boccardo

Unità di Chirurgia Senologica
Ospedale Sacro Cuore – Don Calabria


Legend
Breast cancer
Ovarian cancer
Rachel
BRCA1 185delAG
Normal
Mutation

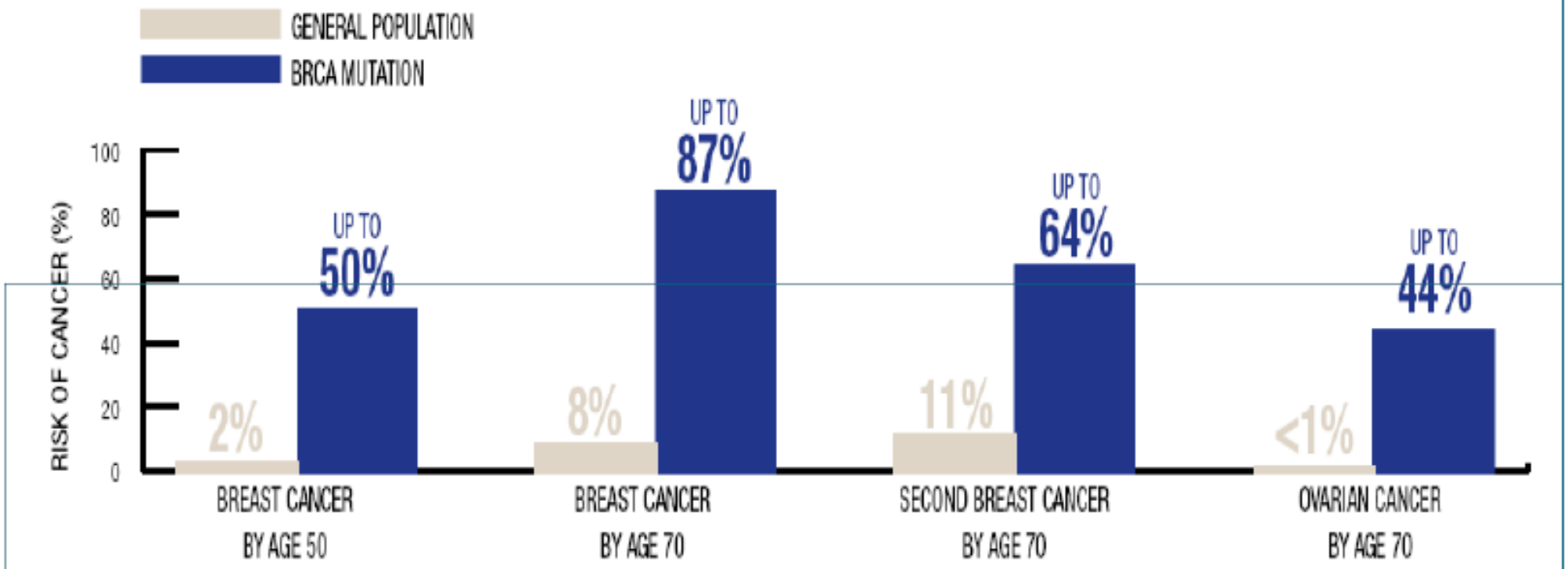
Predicted Mean Cancer Risk to Currently Unaffected *BRCA1/2* Mutation Carriers

BRCA1 → BC : 57% (47% - 63%)
OC : 40% (35% - 46%)

BRCA2 → BC : 49% (40% - 57%)
OC : 18% (13% - 23%)

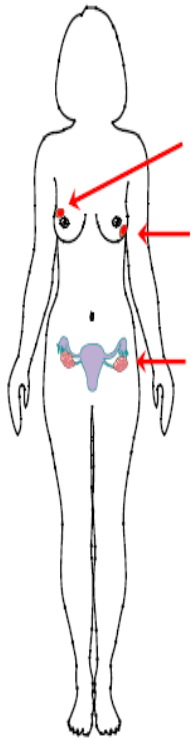
Chen et al JCO 2007

MUTATIONS DRAMATICALLY INCREASE THE RISK OF DEVELOPING CANCER



REDUCE RISK OF HEREDITARY CANCER WITH PROVEN MEDICAL MANAGEMENT

BRCA1-Associated Cancers: Risk by age 70



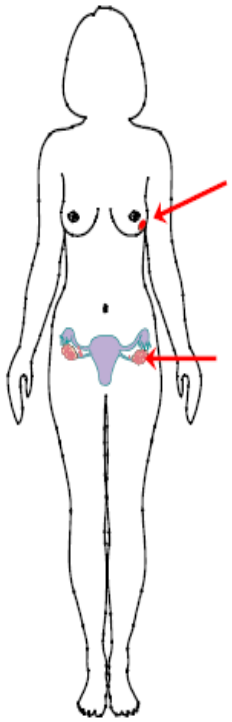
Breast cancer 50-85% (often early age at onset)

Second primary breast cancer 20%-60%

Ovarian cancer 15-45%

Possible increased risk of other cancers (e.g., prostate)

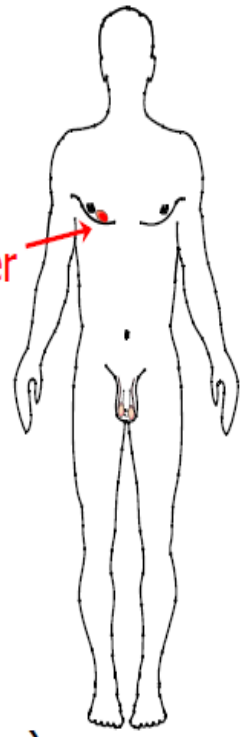
BRCA2-Associated Cancers: Risk by age 70



breast cancer (50-85%)

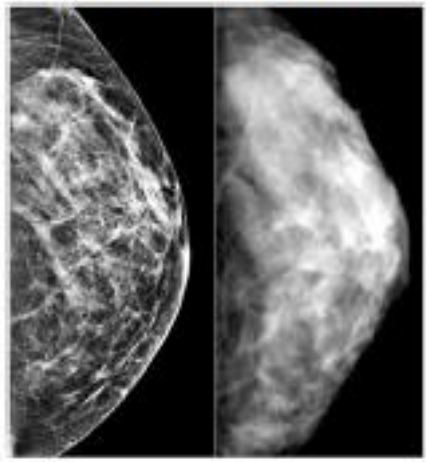
ovarian cancer (10-20%)

male breast cancer (6%)



Increased risk of prostate, laryngeal, and pancreatic cancers (magnitude unknown)

SORVEGLIANZA



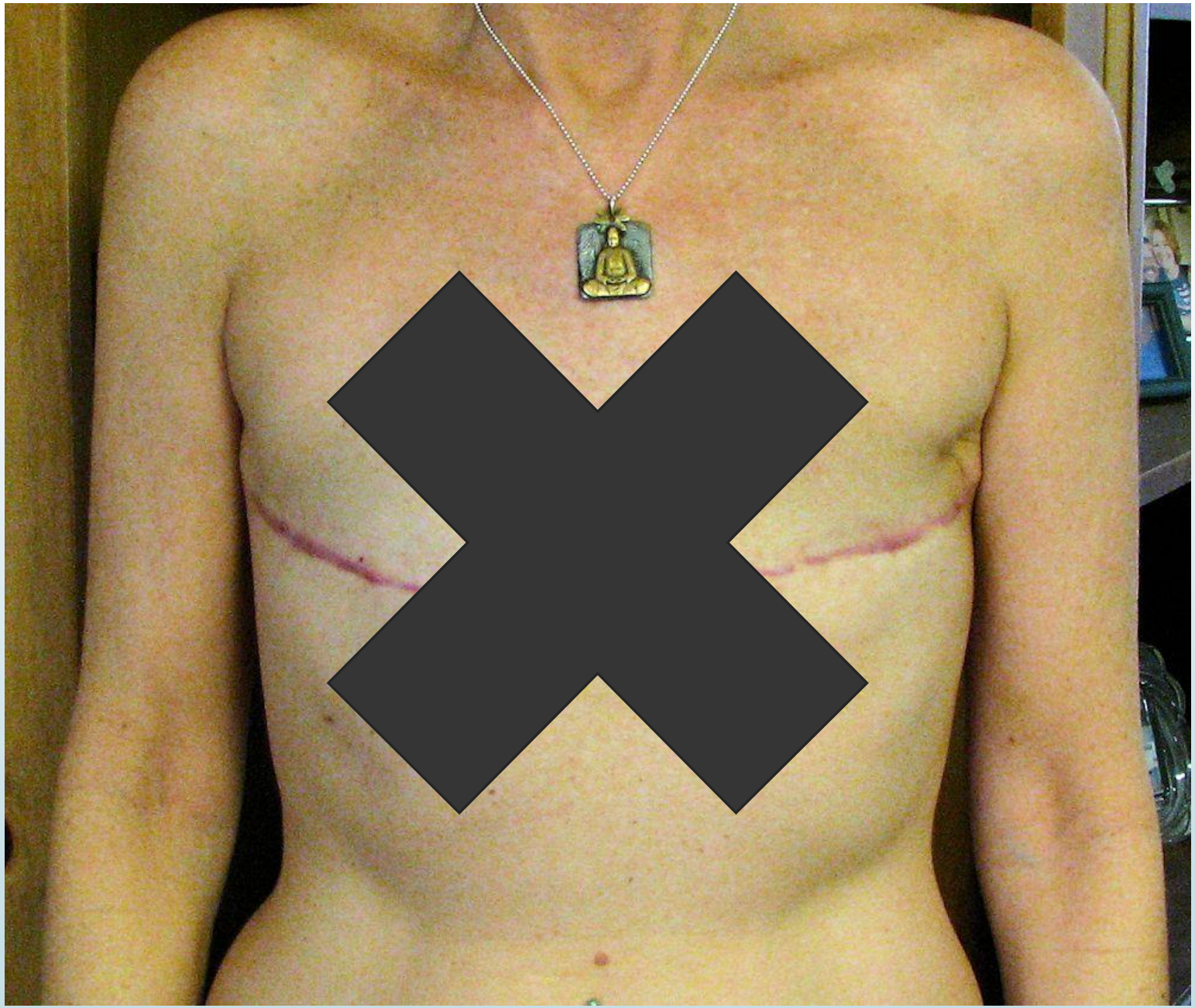
CHEMOPREVENZION

CHIRURGIA

BRCA

WHICH SURGERY?

- ~~TOTAL BILATERAL MASTECTOMY~~
- SKIN SPARING MASTECTOMY: Removal 95-99% of breast tissue
- NIPPLE SPARING MASTECTOMY : Removal 95% of breast tissue



WHICH SURGERY?

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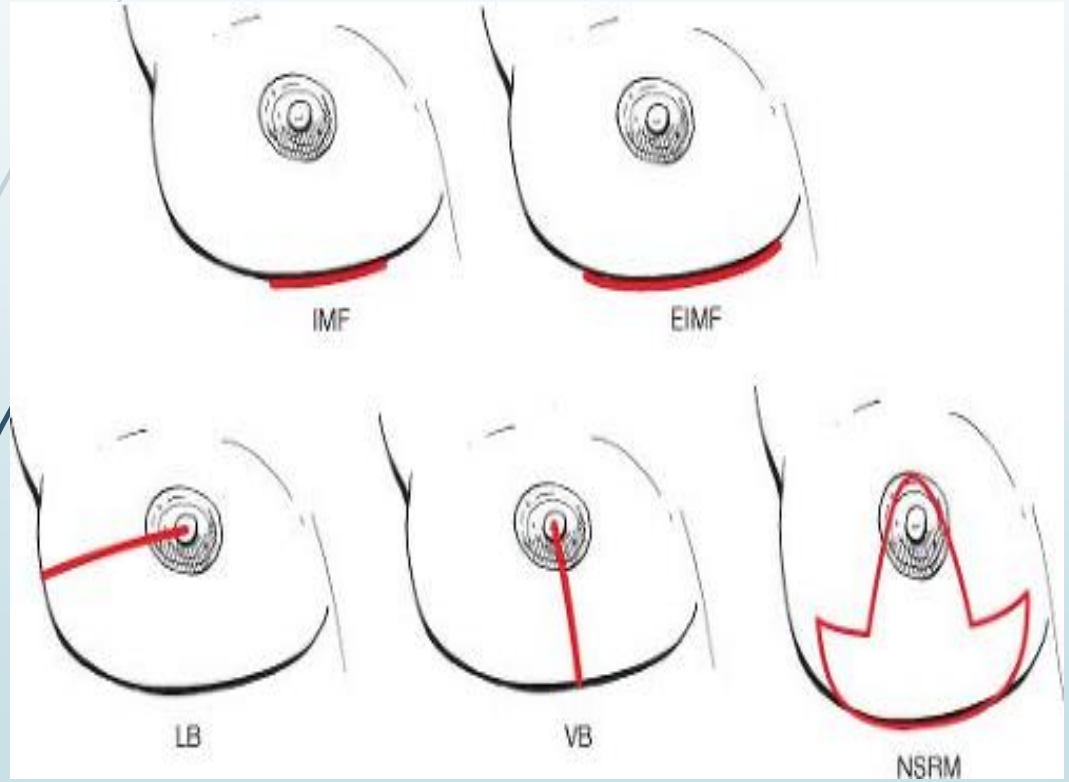
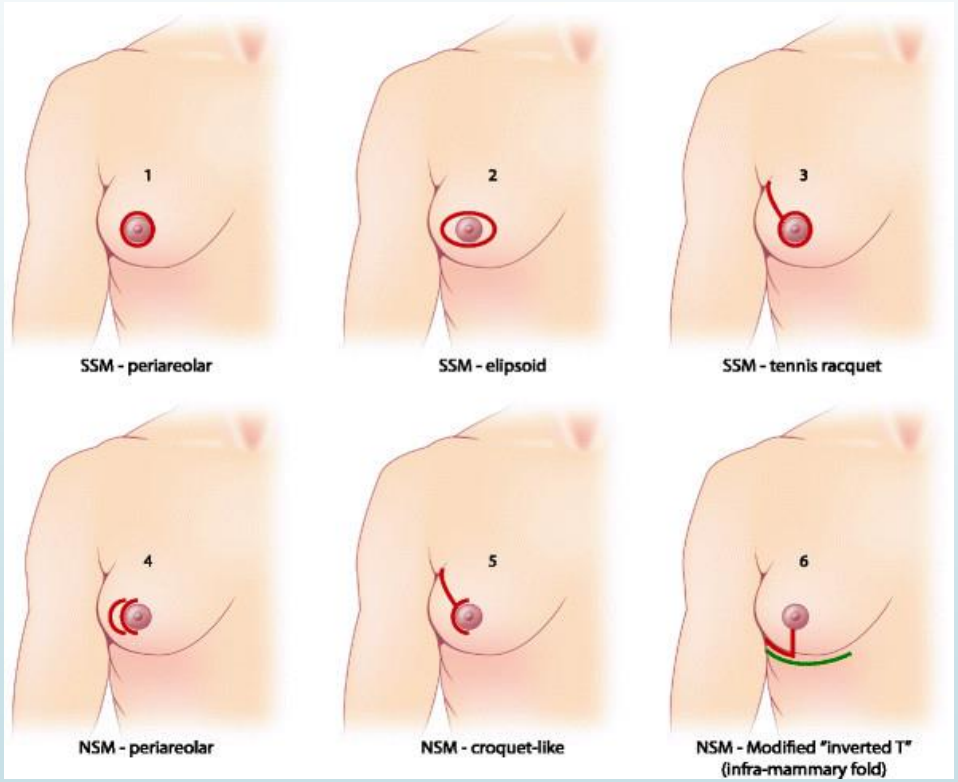
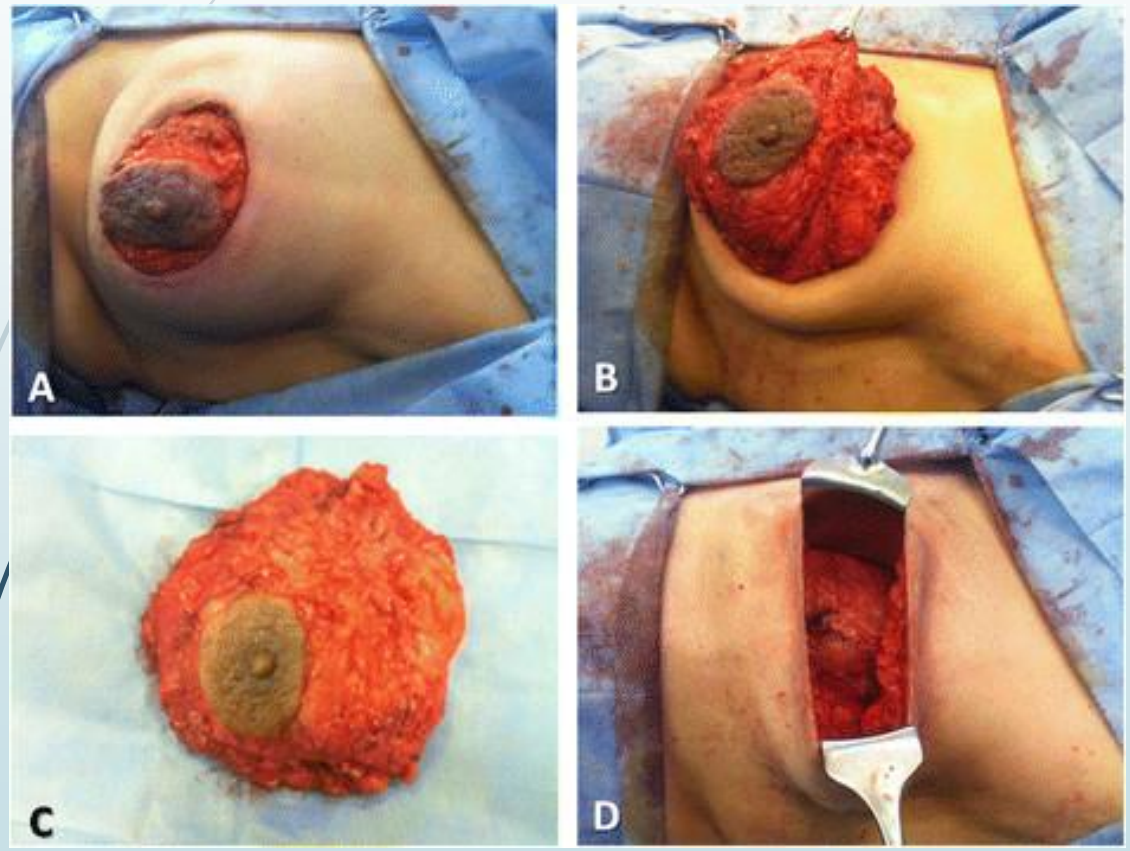
WHICH SURGERY?

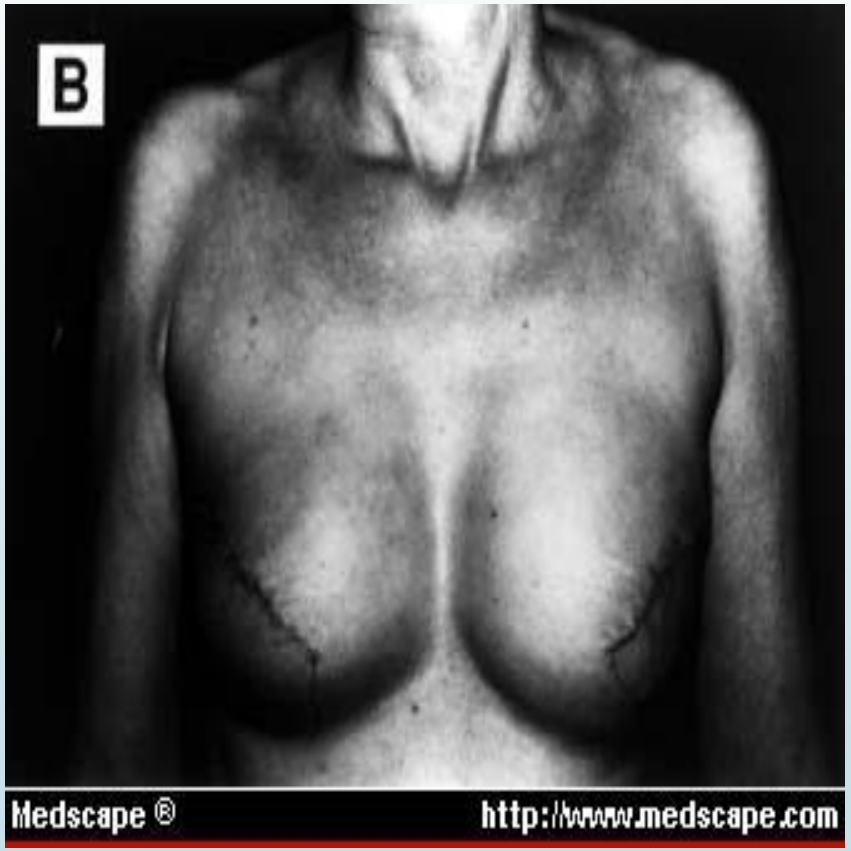
INCISIONS


IMF
EIMF
LB
VB
NSRM

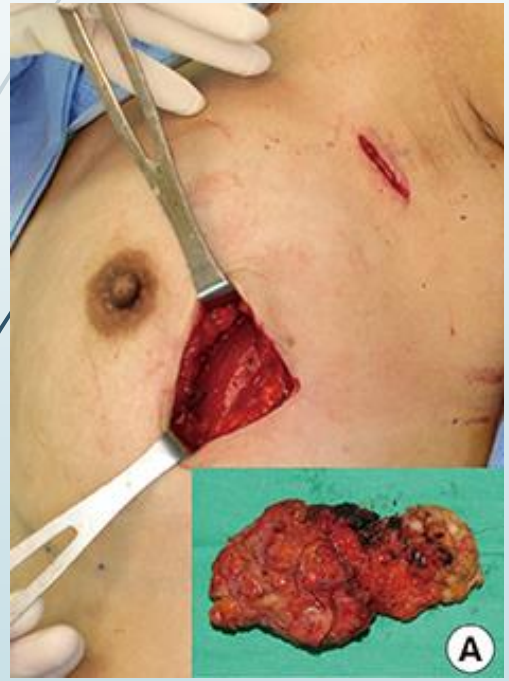

1
2
3
SSM - periareolar
SSM - elipsoid
SSM - tennis racquet
4
5
6
NSM - periareolar
NSM - croquet-like
NSM - Modified "inverted T"
(infra-mammary fold)

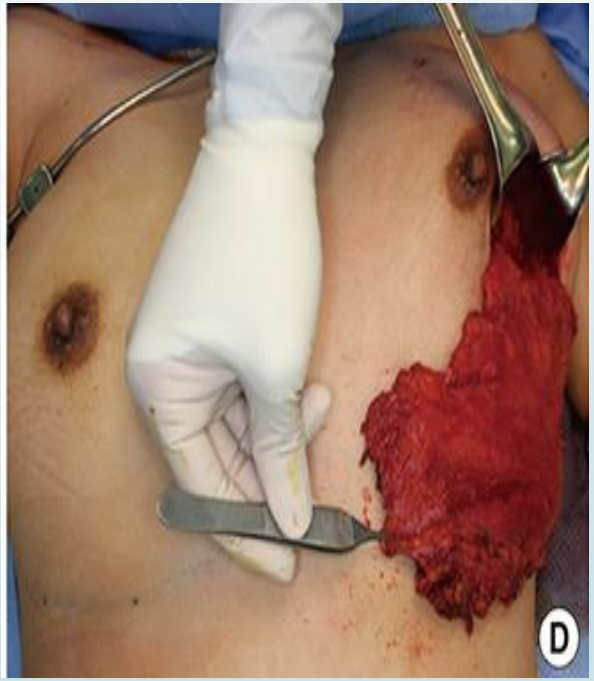
SKIN SPARING MASTECTOMY



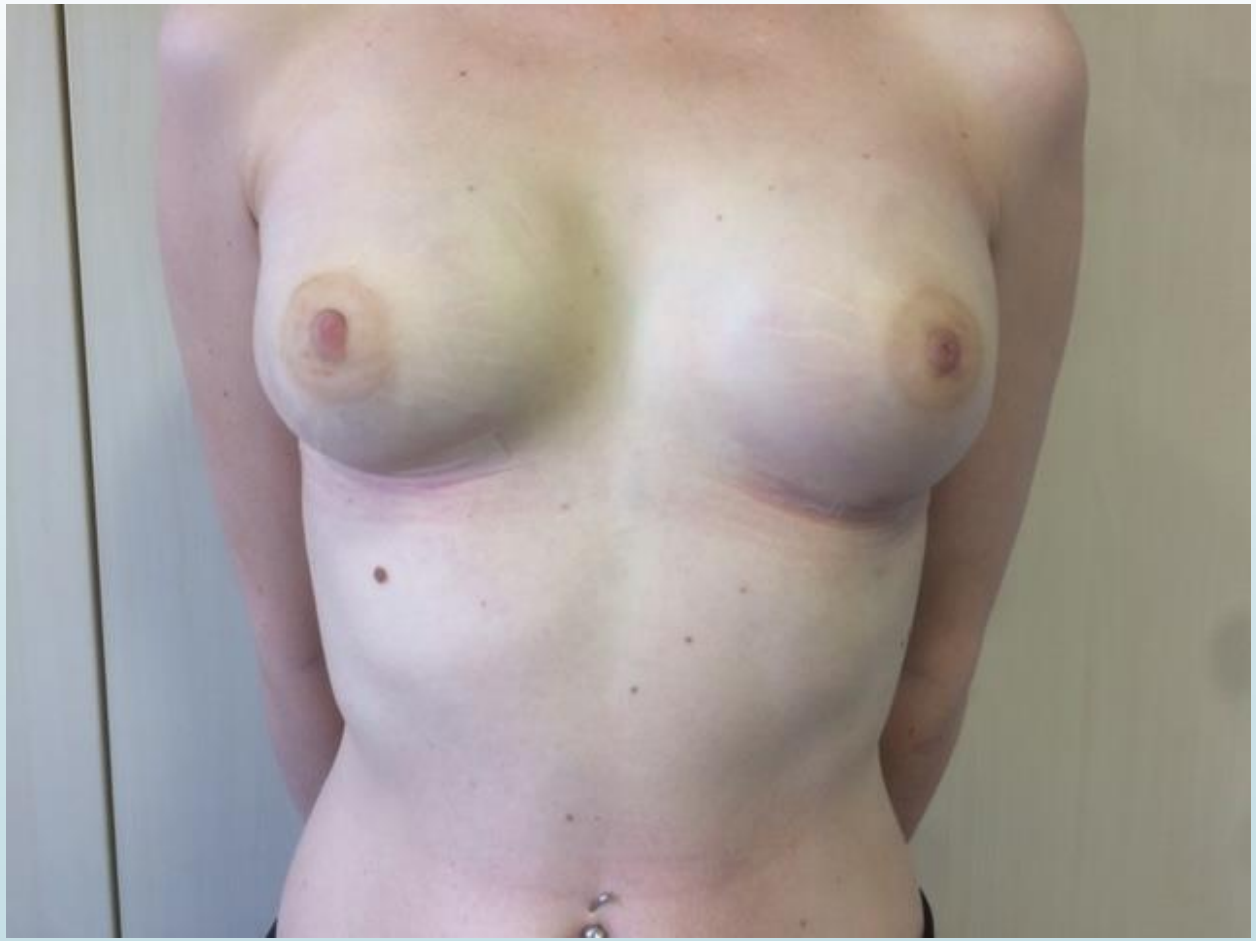


NIPPLE SPARING MASTECTOMY





NIPPLE SPARING MASTECTOMY



Courtesy of Chirurgia Plastica Negrar

Prophylactic Mastectomy in Patients at High Risk: Is There a Role for Sentinel Lymph Node Biopsy?

Vijayashree Murthy,[1] Ronald S. Chamberlain[1,2,3]

Table 5 Clinical Arguments for and Against the Adoption of SLNB in PM

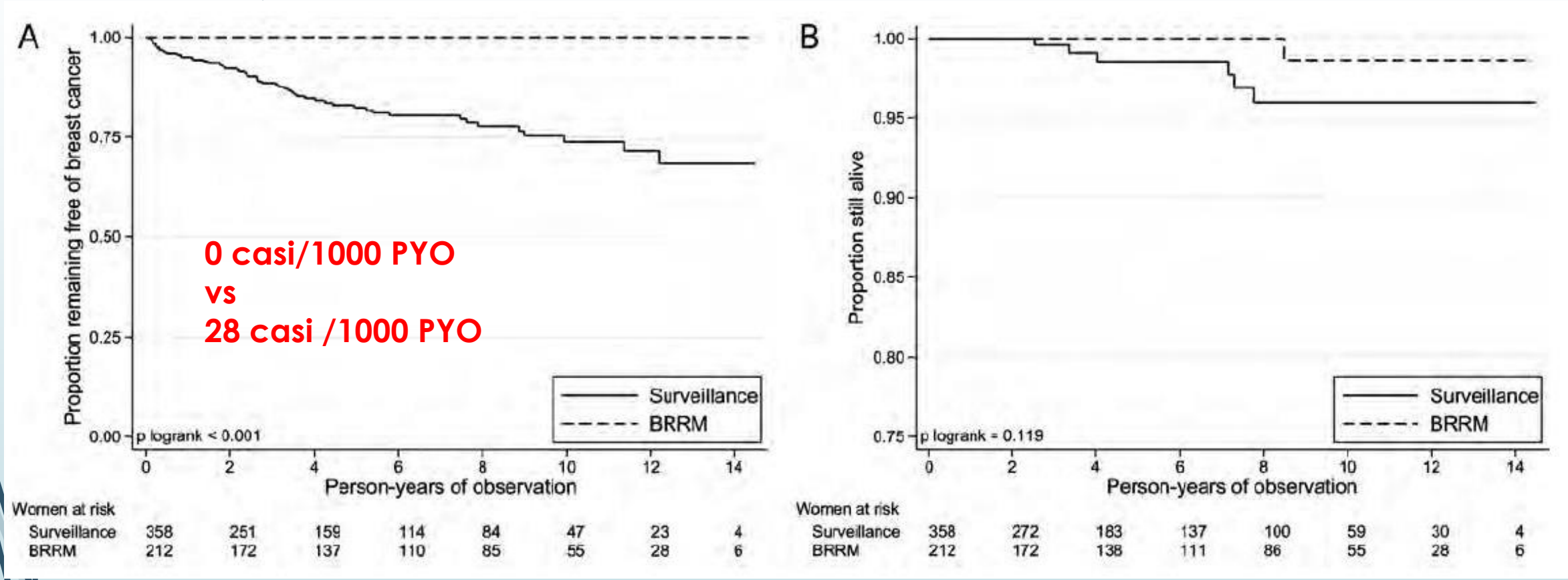
Arguments Supporting the Adoption of SLNB in PM	Arguments Against the Adoption of SLNB in PM
1. SLNB is associated with low morbidity and cannot be reliably performed after mastectomy (due to disrupted lymphatics) should an occult malignancy be detected.	1. The true positive nodal yield of SLNB in CPM and pure bilateral PM is unknown.
2. Incidence of occult malignancy in CPM is up to 5%-15%, therefore, SLNB will stage the axilla adequately and avoid the need for ALND in these patients.	2. Despite a 5%-15% occult malignancy in PM specimens, these are typically early lesions (T1mic or T1) and the yield of SLNB in this setting is almost zero.
3. Incidence of contralateral axillary metastases in locally advanced and recurrent breast cancer is 3.5%-5%.	3. CPM has been proven to increase DFS and OS in patients with ipsilateral breast cancer; however, the utility of SLNB to further improve the results on the PM side is unproven.
4. SLNB performed at the time of PM results in decreased surgical procedures and anesthesia risk and provide significant patient advantages.	4. Increased operative time and cost (operating room time, frozen section, and immunohistochemistry) are not justified for a procedure with such a low yield.
5. SLNB may be performed through a single incision if done at the time of mastectomy.	5. No defined or standard operative technique or intraoperative assessment of SLN has been established in the PM setting.
6. Concurrent SLNB decreases treatment delays in case an occult malignancy is found in the prophylactic breast specimen.	6. ACSOG-Z0011 trial concluded that observation of the axilla in a SLNB positive patient with known breast malignancy does not yield inferior result, if this is true then SLNB in a prophylactic setting would be overtreatment.
	7. Complications of SLNB include limb paresthesias, lymphedema, anaphylaxis to patent blue dye and failure to map the SLN.
	8. The role of MRI to predict disease in the contralateral breast and axilla needs more investigation and may avoid unnecessary axillary procedures and morbidity.

BILATERAL PROPHYLACTIC MASTECTOMY: OUTCOMES

Strategia	Relative reduction in the risk of developing BC
Risk-reducing bilateral mastectomy	>90%
Risk-reducing bilateral salpingo – oophorectomy (premenopausal)	Up to 50%
Risk reducinc medication SERMS Aromatase inhibitors	 38% >50%
Screening (MX and MRI)	NA

Domcheck Sm JAMA 2010; Cuzick J, Lancet 2013; Cardoso F Eur J Cancer 2012

BILATERAL PROPHYLACTIC MASTECTOMY



0 casi/1000 PYO
vs
28 casi /1000 PYO

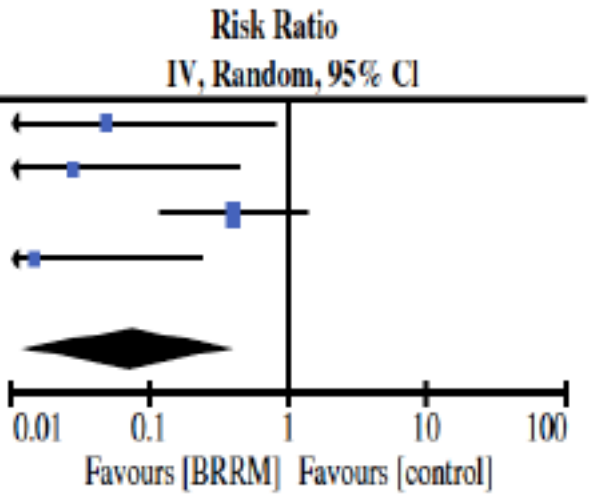
Heemskerk-Gerritsen, Ann Oncol 2013

BILATERAL PROPHYLACTIC MASTECTOMY

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI	Year
Meijers–Heijboer 2001	–3.0181	1.4453	20.9%	0.05 [0.00, 0.83]	2001
Domchek 2010	–3.5719	1.4161	21.4%	0.03 [0.00, 0.45]	2010
Skyttc 2011	–0.8865	0.617	36.3%	0.41 [0.12, 1.38]	2011
Hemskerk–Gerritsen 2013	–4.2229	1.4177	21.4%	0.01 [0.00, 0.24]	2013
Total (95% CI)			**100.0%**	**0.07 [0.01, 0.44]**	

Heterogeneity. $Tau^2 = 1.95$; $Chi^2 = 7.37$, df = 3 (P = 0.06); $I^2 = 59\%$

Test for overall effect: Z = 2.85 (P = 0.004)



Meta-analysis of four prospective studies, including 2635 patients, demonstrated a significant risk reduction of breast cancer incidence in BRCA1 and BRCA2 mutation carriers receiving BRRM (HR 0.07; 95 % CI 0.01-0.44; p = 0.004).

De Felice et al, Ann Surg Oncol. 2015

DRAWBACKS PROPHYLACTIC MASTECTOMY

- Irreversible
- **Risk reduced but not cancelled**
- Post operative complications
- Psychological impact

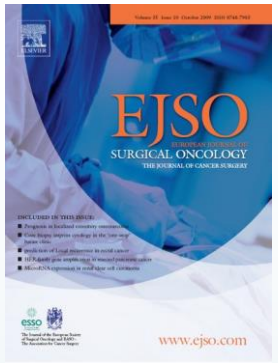
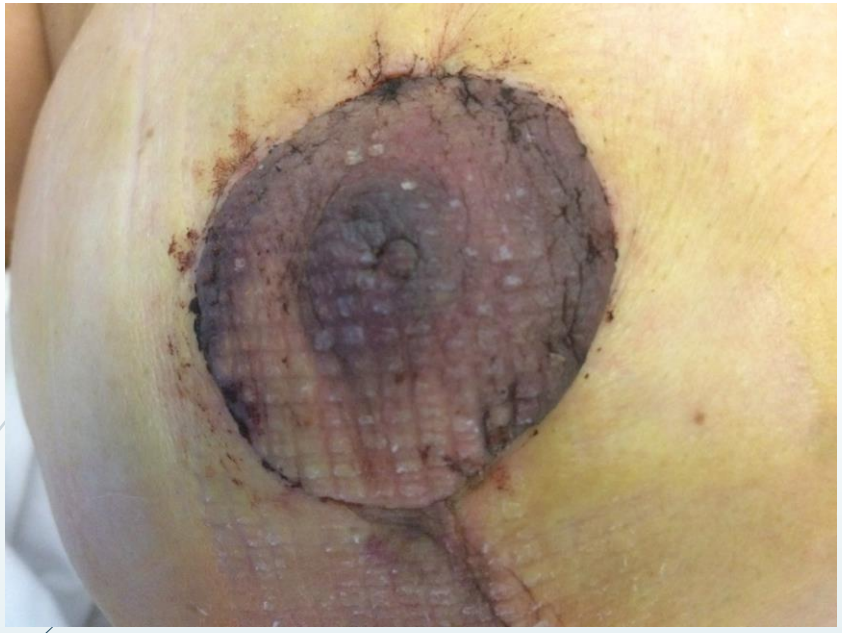


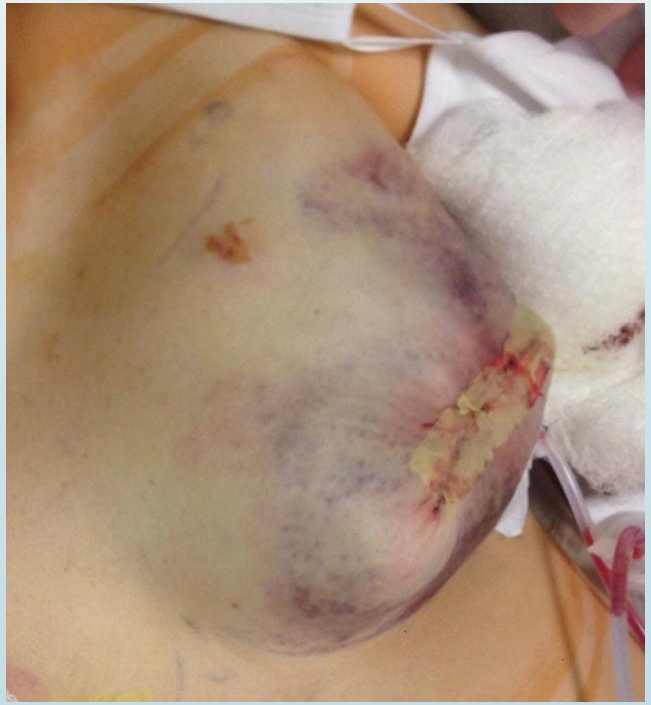
Table 1
Complications of mastectomy.

Seroma formations (25–60%)
Wound infections (2.8–15%)
Skin flap necrosis (1–22%)
Hematoma (2%)
Complications of implants
Prosthesis infection (0.5–2%)
Capsular contraction (3–5% up to 30% depending on type of implants)
Device failure and rupture (10%)
Complications of autologous tissue reconstruction
Flap necrosis (1–3%)
Wound infection (4–8%)
Functional impairment (variable)
Abdominal hernias (20%)

Boccardo C et al. EJSO 2016

COMPLICATIONS





ANY DOUBTS?

Cosa vi spinge a fare test genetico brca1 e 2

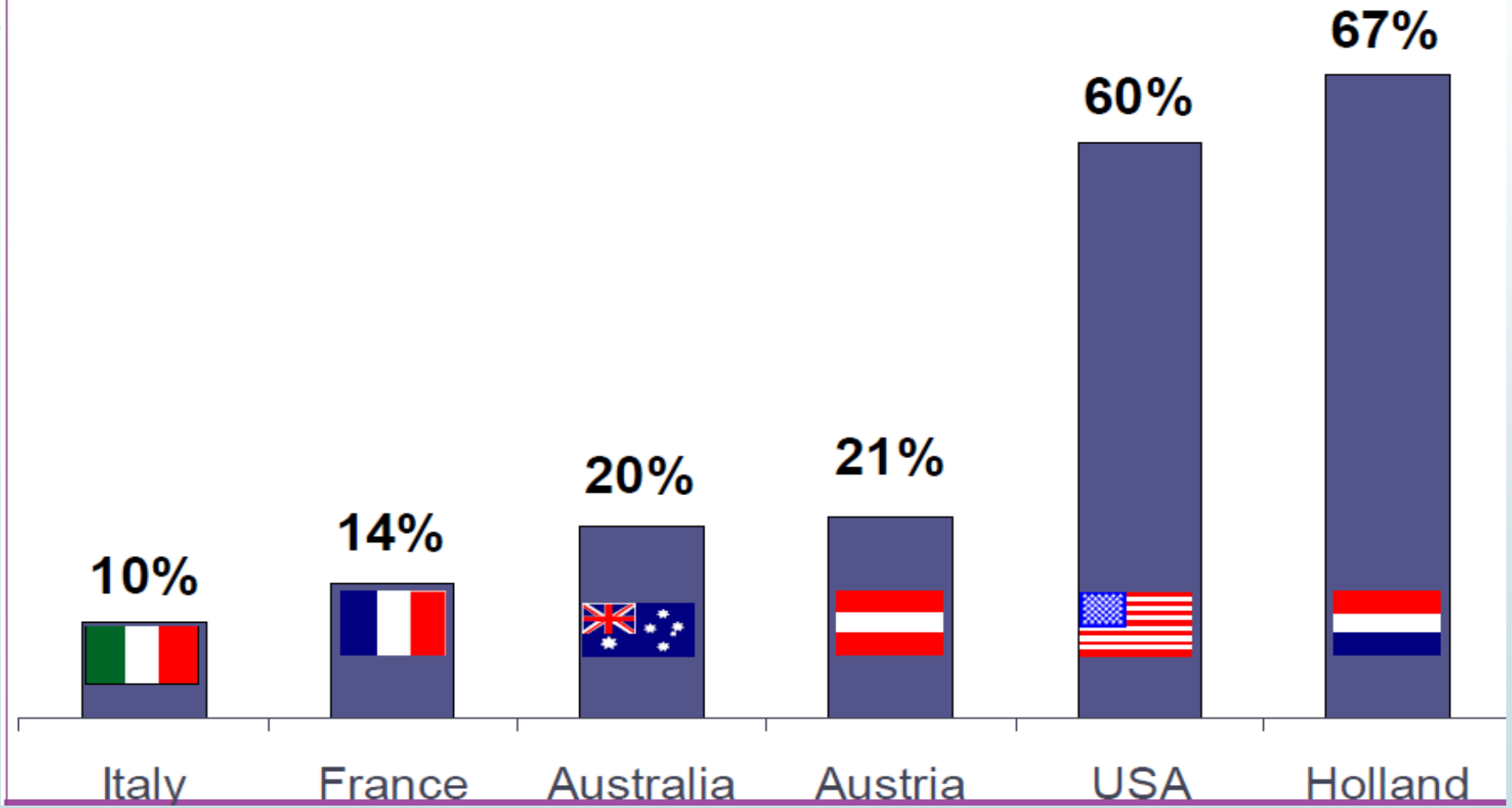
da:brioches1

Ciao meravigliose, ho una domandina da porvi: cosa vi spinge a fare il test genetico BRCA1e2 ?.nel senso che io vorrei farlo ma ho paura della risposta e nel caso di positività? ok è vero meglio togliersi le tette piuttosto che riaffrontare operazione, chemio, radio e tutto ci che ne comporta.ma alla fine siamo donne perbaccoinsomma sono molto combattuta..
Qualcuna può aiutarmi????

per me la voglia di crescere la bambina è stata determinante nell'aver scelto di fare il test genetico...positivo al brca1 dopo un ca al seno a soli 27 anni, poi ho fatto la mastectomia bilaterale profilattica e non sono pentita per nulla, il 21maggioi è nato Francesco Gabriele. adesso faccio molti controlli alle ovaie che prima o poi asporterò'. sai secondo me il test genetico serve per anticipare la bestiaccia per arrivare prima noi di lei un abbraccio

Mary 7720

Acceptability of prophylactic mastectomy



Metcalfe KA Int J Cancer 2008

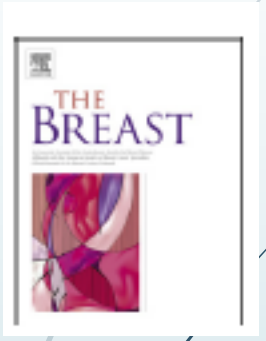
PSYCHO-ONCOLOGY
Psycho-Oncology **9**: 462–472 (2000)

CLINICAL FOLLOW-UP AFTER BILATERAL RISK REDUCING ('PROPHYLACTIC') MASTECTOMY: MENTAL HEALTH AND BODY IMAGE OUTCOMES

PENELOPE HOPWOOD[a,*], ANDREW LEE[a], ANDREW SHENTON[b], ANDREW BAILDAM[c], ANNE BRAIN[d], FIONA LALLOO[e], GARETH EVANS[e] and ANTHONY HOWELL[d]
[a] *The CRC Psychological Medicine Group, Christie Hospital NHS Trust, Manchester, UK*
[b] *Family History Clinic, Kinnaird Road, Withington, Manchester, UK*
[c] *Withington Hospital, Nell Lane, Manchester, UK*
[d] *Christie Hospital NHS Trust, Manchester, UK*
[e] *St Mary's Hospital, Manchester, UK*

- **For the majority of women there is no evidence of significant mental health or body image problems in the first 3 years following Bilateral Prophylactic Mastectomy (BPM), but women who have complications warrant additional psychological help. Careful pre-operative preparation and long-term monitoring are advocated in this new field of cancer prevention**

PSYCHOLOGICAL IMPACT OF BILATERAL PROPHYLACTIC MASTECTOMY



- The literature strongly suggests women want more information surrounding BPM, particularly related to the after effects of the surgery, and the impact on their psychological wellbeing

Glassey et al The Breast 2016

- No negative effects on anxiety, depression, and quality of life were found. Anxiety and social activities improved. Negative impact on sexuality and body image was reported.

Brandberg et al JCO 2008

IN CONCLUSIONE

Mastectomia profilattica bilaterale

Riduzione del Rischio

Impatto psicologico
Esiti chirurgici