Ordine dei Medici Chirurghi e degli Odontoiatri della Provincia di Udine
Ente sussidiario dello Stato

ASU FC
Azienda sanitaria universitaria Friuli Centrale

TUMORI FEMMINILI E BRCA: IL PRESENTE PER CAMBIARE IL FUTURO IL PUNTO DI VISTA DEL SENOLOGO

Udine 20 settembre 2023

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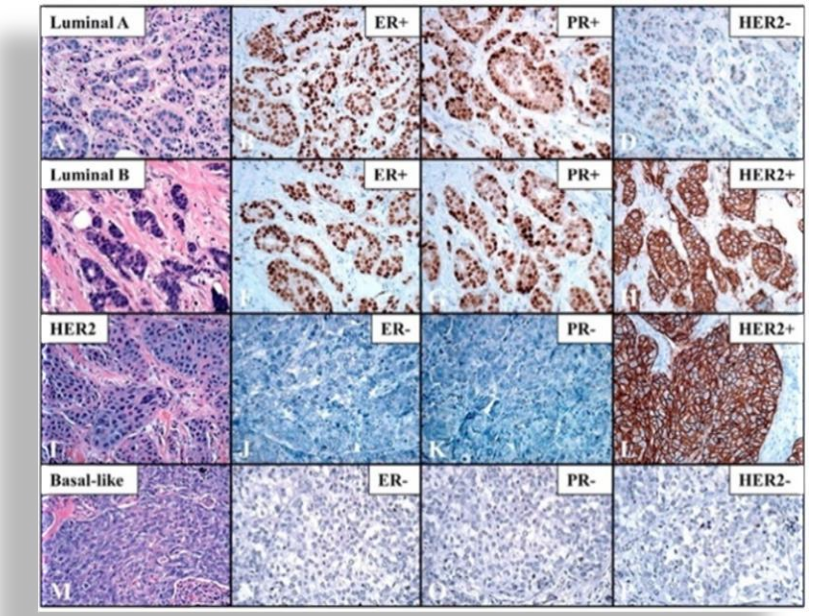
ASUFC – Udine

UNITÀ DI SENOLOGIA
ASUFC

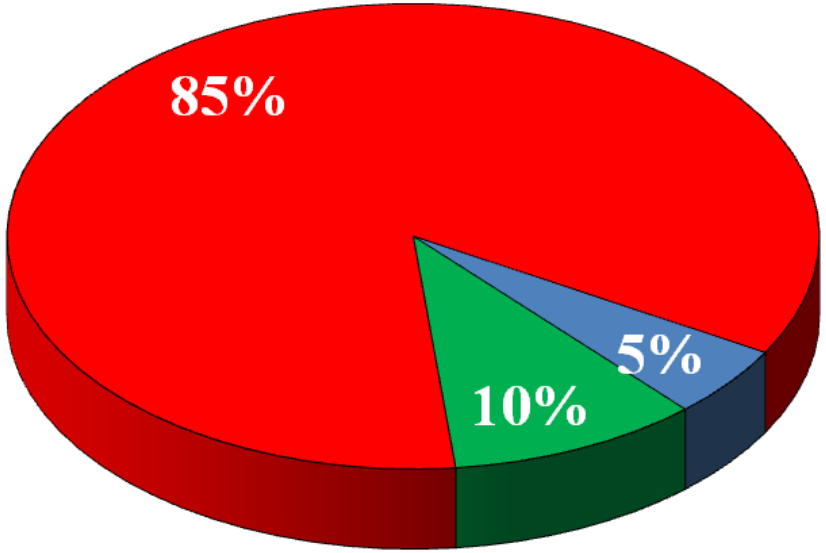
Breast Centres Certification

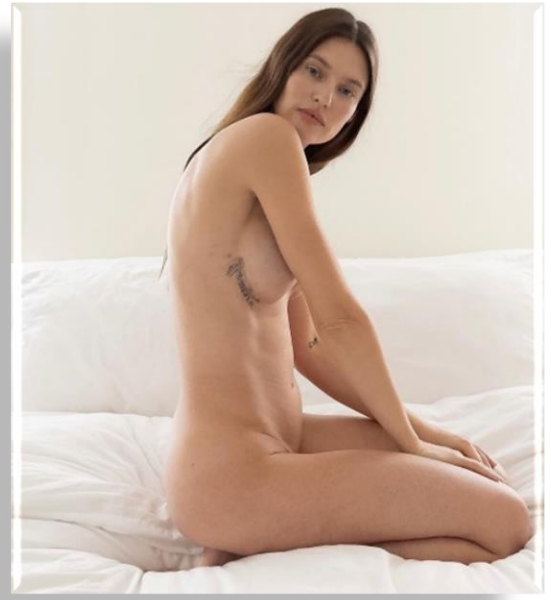
TUMORE DELLA MAMMELLA…
…TANTI TUMORI DIVERSI



Intrinsic subtype	Clinicopathologic surrogate definition						Type of therapy
		ER	PR	HER2	Ki-67	Recurrence risk[a]	
Luminal A	Luminal A-like	+	+[b]	–	Low <14%	Low (if available)	Endocrine therapy is often used alone Cytotoxic therapy may be added
Luminal B	Luminal B-like[c] (HER2-negative)	+	– or low	–	High	High (if available)	Endocrine therapy for all patients, cytotoxic therapy for most
	Luminal B-like (HER2-positive)	+	Any	Over-expressed or amplified	Any	NA	Cytotoxics+anti-HER2+endocrine therapy
ErbB-2 overexpression	HER2-positive (non-luminal)	Absent	Absent	Over-expressed or amplified	NA	NA	Cytotoxics+anti-HER2
Basal-like	Triple negative (ductal)	–	–	–	NA	NA	Cytotoxics

EPIDEMIOLOGIA





TUMORI SPORADICI

TUMORI FAMILIARI

TUMORI GENETICI

TUMORE DELLA MAMMELLA E BRCA

Lifetime risk di carcinoma mammario 60-80% (BRCA1) e 40-70% (BRCA2)

BRCA1: Tumori più aggressivi e in età più precoce, più spesso bilaterali, triple-negative, G3

BRCA2: luminal B

Prognosi peggiore nelle pz con BRCA1

	Mutazione di BRCA1	Mutazione di BRCA2
Rischio di carcinoma mammario	72% (95% CI, 65% - 79%)	69% (95% CI, 61% - 77%)
Rischio di carcinoma ovarico	44% (95% CI, 36% - 53%)	17% (95% CI, 11% - 25%)

AIOM 2021

MAMMELLA CONTROLATERALE

Tabella 25. Rischio età specifico di tumore della mammella controlaterale dopo la prima diagnosi (*Modificata da Kuchenbaecker KB, JAMA 2017*[4])

Anni dopo la prima diagnosi	Rischio di tumore mammario controlaterale	
	BRCA1(DS)	BRCA2 (DS)
< 5	0,13 (0,06)	0,08 (0,06)
>5-10	0,23 (0,07)	0,16 (0,09)
>10-15	0,32 (0,08)	0,21 (0,09)
>15-20	0,40 (0,10)	0,26 (0,13)
>20-45	0,53 (0,18)	0,65 (0,73)

AIOM 2021

Mammografia ogni 2 anni

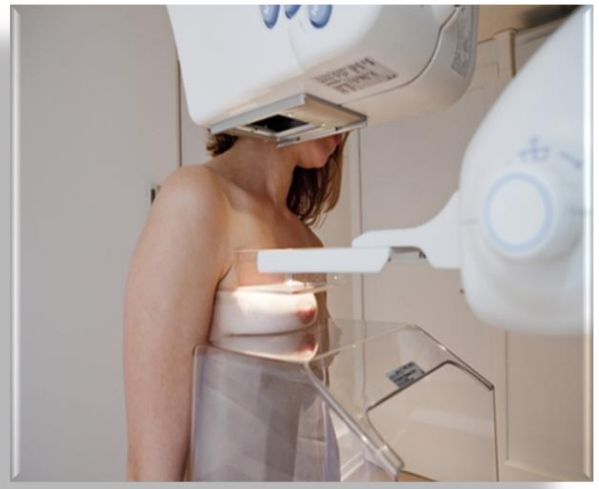
45 – 74 anni

Secondo livello

Ecografia, Tomosintesi

Ulteriori approfondimenti

Agobiopsia, RMM, CEM



SCREENING IN DONNE AD ALTO RISCHIO

Visita clinica ogni 6 -12 mesi a partire dai 25 anni

25-29 aa

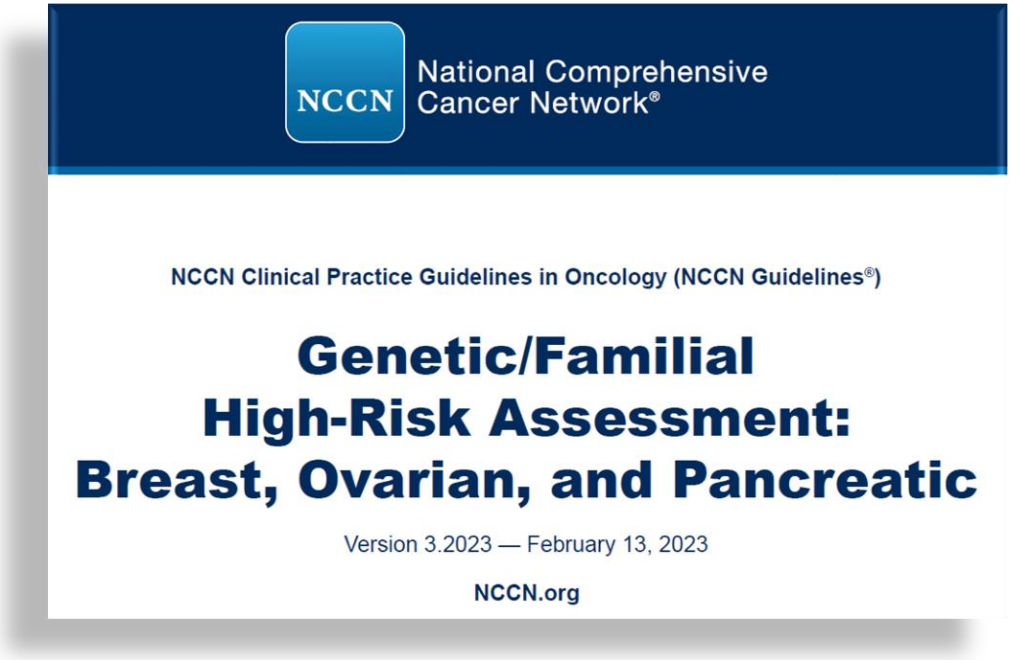
RMM annuale

30-75 aa

Mx e RMM annuali

> 75 aa

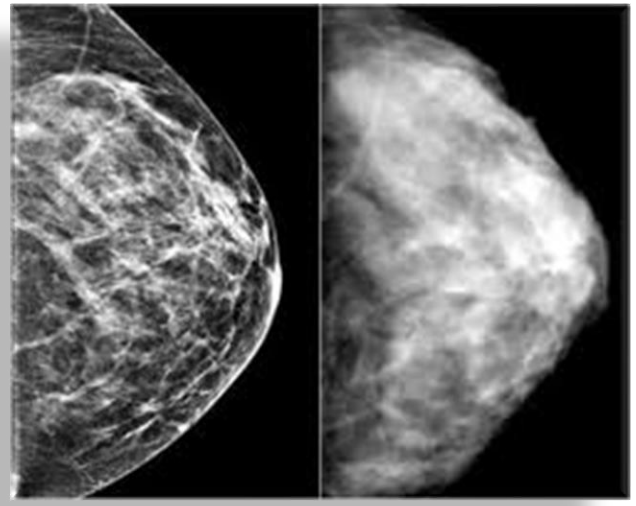
Screening personalizzato

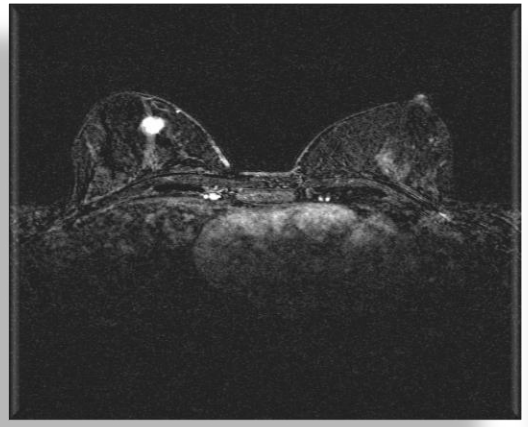


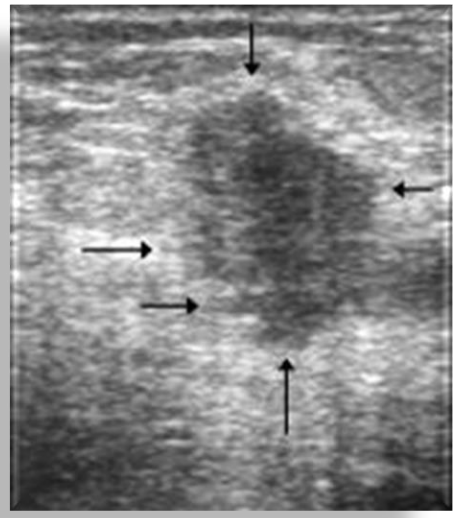
Author	MRI		Mammography		Combined MRI and Mammography	
	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Vreemann S et al., 2018[41]	63%	95%	45%	98%	66%	94%
Cortesi L et al, 2006 [42]	100%	NR	50%	NR	NR	NR
Leach MO et al, 2005 [43]	77%	81%	40%	93%	94%	77%
Le-Petross HT et al, 2011 [44]	92%	87%	NR	82%	NR	NR
Rijnsburger AJ et al, 2010 [45]	77%*	89.7%	35.5%*	94.6%	NR	NR

**Only Invasive cancer*

AIOM 2021

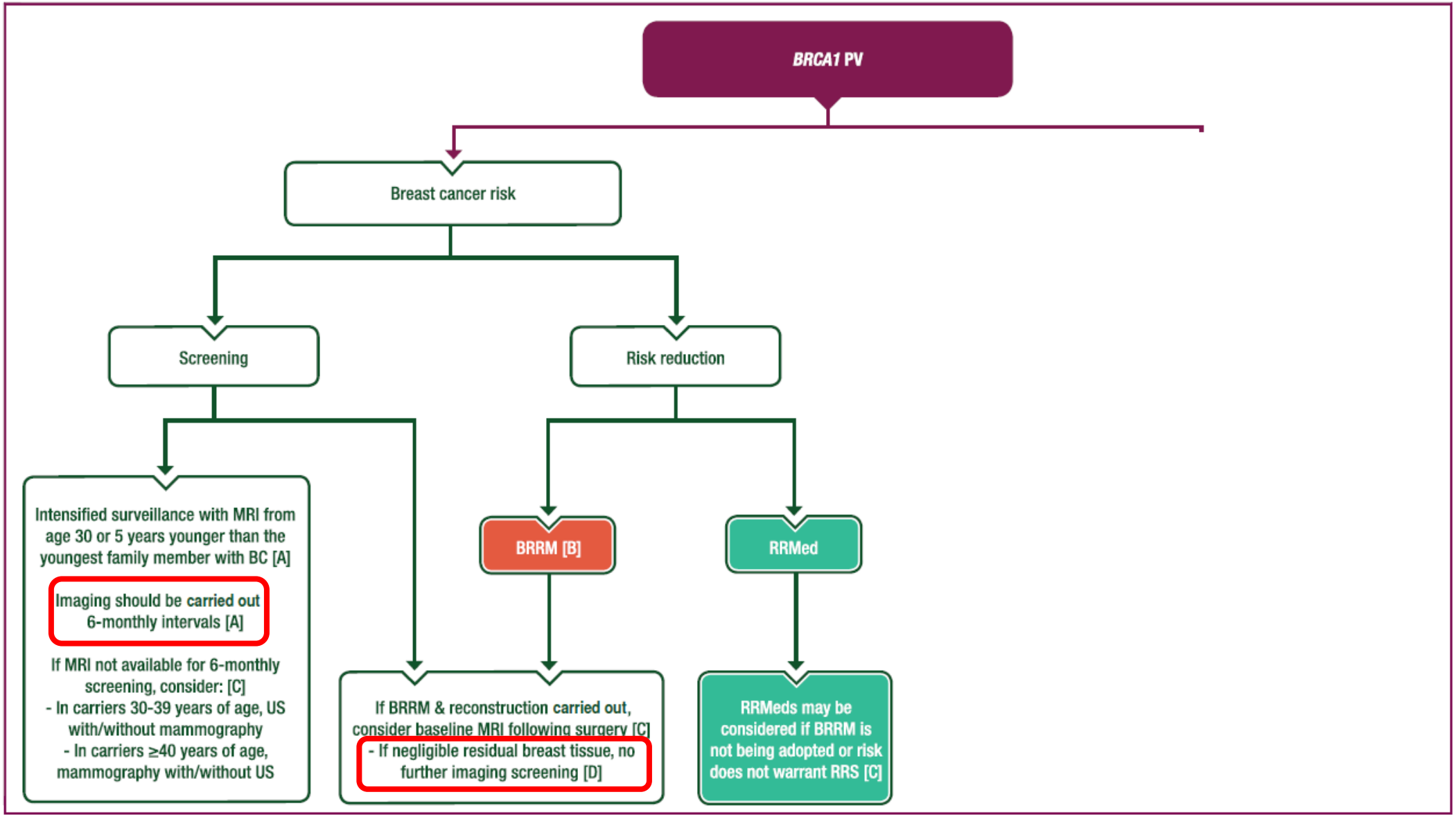




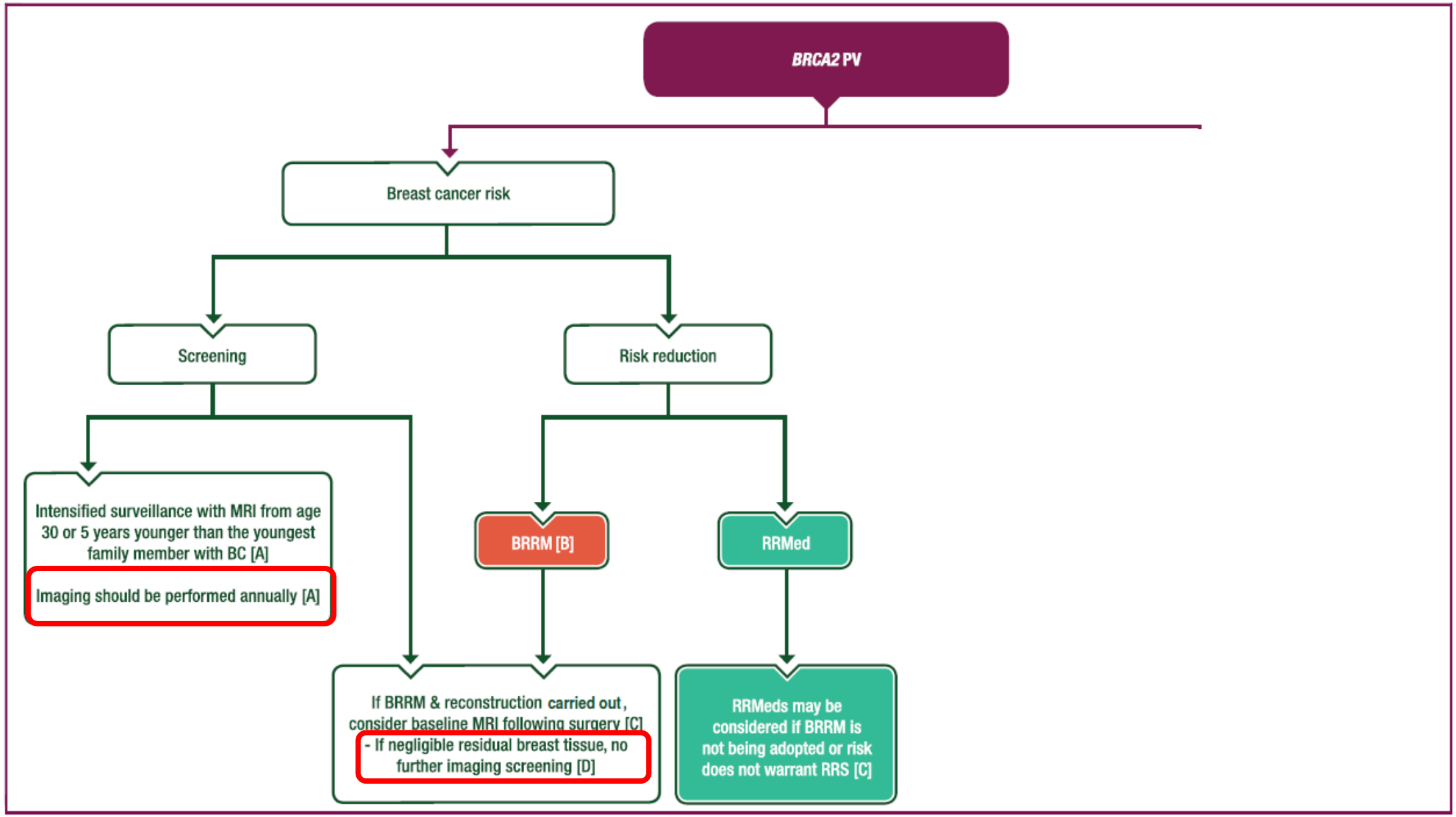


Ecografia mammaria

Utile ma non standardizzata



ESMO Guidelines, 2023



ESMO Guidelines, 2023

THIS ARTICLE HAS BEEN UPDATED BY AN ASCO RAPID RECOMMENDATION

Management of Hereditary Breast Cancer: American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Guideline

2020

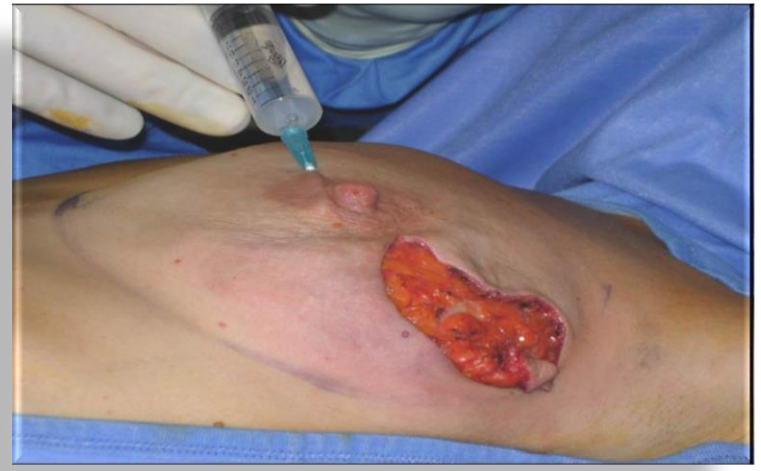
Women with breast cancer who have a *BRCA1/2* mutation	
Local therapy recommendations	
Index/current cancer	Germline *BRCA* status should not preclude a patient with newly diagnosed breast cancer otherwise eligible for BCT from receiving BCT.
	Surgical management of the index malignancy (BCT *v* ipsilateral therapeutic and CRRM) in *BRCA1/2* mutation carriers should be discussed, considering the increased risk of CBC and possible increased risk of an ipsilateral new primary breast cancer compared with noncarriers.
	For women with newly diagnosed breast cancer undergoing mastectomy who have a deleterious mutation in *BRCA1/2*, nipple-sparing mastectomy is a reasonable oncologic approach to consider in appropriately selected patients.
	For women with breast cancer who are treated with BCT or with mastectomy for whom postmastectomy RT is considered, RT should not be withheld because of mutation status, except for mutations in *TP53* (see Recommendation 6.3, which states that irradiation of the intact breast is contraindicated in *TP53* carriers). There is no evidence of a significant increase in toxicity or CBC related to radiation exposure among patients with a mutation in a *BRCA1/2*
Contralateral risk-reducing mastectomy (CRRM)	For women with breast cancer who have a BRCA1/2 mutation, CRRM should be discussed. CRRM is associated with a decreased risk of CBC; there is insufficient evidence for improved survival. The following factors should be considered for assessing risk of CBC and the role of risk-reducing mastectomy: -Age at diagnosis (the strongest predictor of future contralateral breast cancer) -Family history of breast cancer -Overall prognosis from this or other cancers (eg, ovarian) -Ability of patient to undergo appropriate breast surveillance (MRI) -Comorbidities -Life expectancy
	For patients with breast cancer with a deleterious germline *BRCA1/2* mutation interested in risk-reducing contralateral mastectomy, physicians should discuss the option of nipple-sparing mastectomy as a reasonable oncologic option.
	BRCA1/2 mutation carriers who do not have bilateral mastectomy should undergo high-risk breast screening of remaining breast tissue with annual mammogram and MRI.

MEETING MULTIDISCIPLINARE

Discussione

- Pazienti mutate
- Pazienti ad alto rischio

CHIRURGIA RISK-REDUCING



Efficace in caso di mutazione di BRCA
Da valutare in caso di TP53, PTEN, STK11, CDH1, PALB2

Riduzione RR del 90%
Beneficio ridotto oltre i 55 aa

Riduzione incidenza e rischio di morte per tumore mammario (Cochrane 2010)

Riduzione del rischio del 50% anche con annessiectomia preventiva (BRCA1>BRCA2, in particolare < 40 aa)

AIOM 2021, ESMO 2023

CRITERI DI SCELTA

Valutare risk-reducing mastectomy in base a:

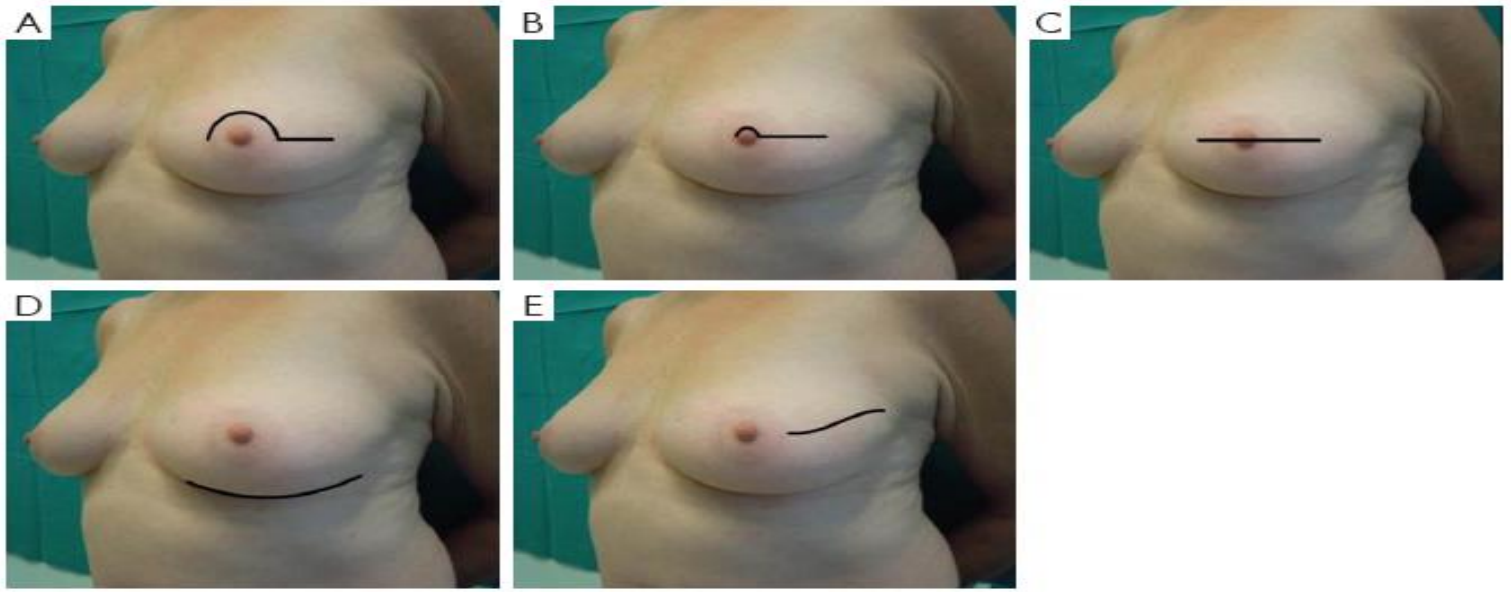
2020

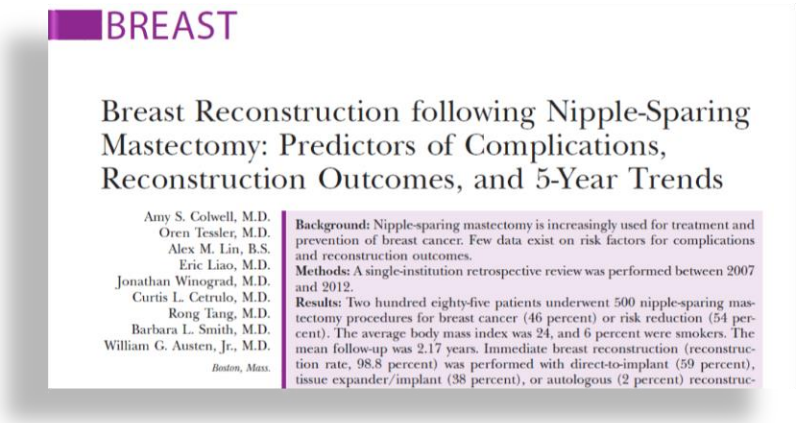
Età
Familiarità per carcinoma mammario
Prognosi di ev altre neoplasie (es: tumore ovarico)
Comorbidità e aspettativa di vita
Compliance al follow-up radiologico
- vs chirurgia
- vs farmaco-prevenzione

CHIRURGIA RISK-REDUCING

Mastectomia nipple-sparing bilaterale

Ricostruzione protesica





BREAST

Breast Reconstruction following Nipple-Sparing Mastectomy: Predictors of Complications, Reconstruction Outcomes, and 5-Year Trends

Amy S. Colwell, M.D.
Oren Tessler, M.D.
Alex M. Lin, B.S.
Eric Liao, M.D.
Jonathan Winograd, M.D.
Curtis L. Cetrulo, M.D.
Rong Tang, M.D.
Barbara L. Smith, M.D.
William G. Austen, Jr., M.D.
Boston, Mass.

Background: Nipple-sparing mastectomy is increasingly used for treatment and prevention of breast cancer. Few data exist on risk factors for complications and reconstruction outcomes.
Methods: A single-institution retrospective review was performed between 2007 and 2012.
Results: Two hundred eighty-five patients underwent 500 nipple-sparing mastectomy procedures for breast cancer (46 percent) or risk reduction (54 percent). The average body mass index was 24, and 6 percent were smokers. The mean follow-up was 2.17 years. Immediate breast reconstruction (reconstruction rate, 98.8 percent) was performed with direct-to-implant (59 percent), tissue expander/implant (38 percent), or autologous (2 percent) reconstruc-

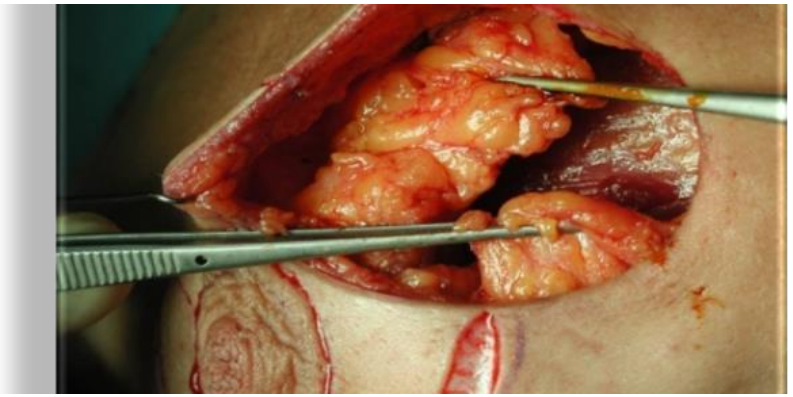
NEOPLASIA MAMMARIA IN BRCA MUTATA

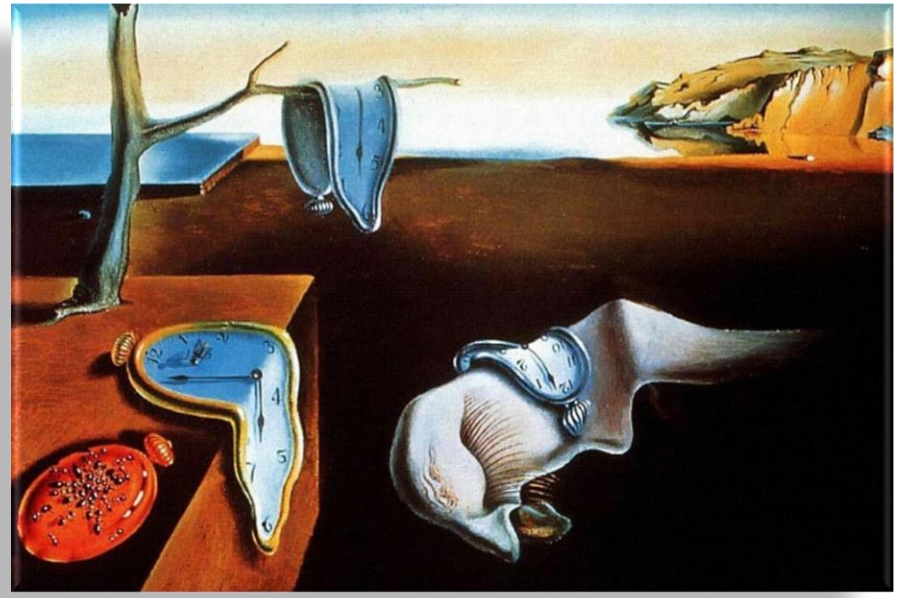
Considerare mastectomia omolaterale + controlaterale preventiva

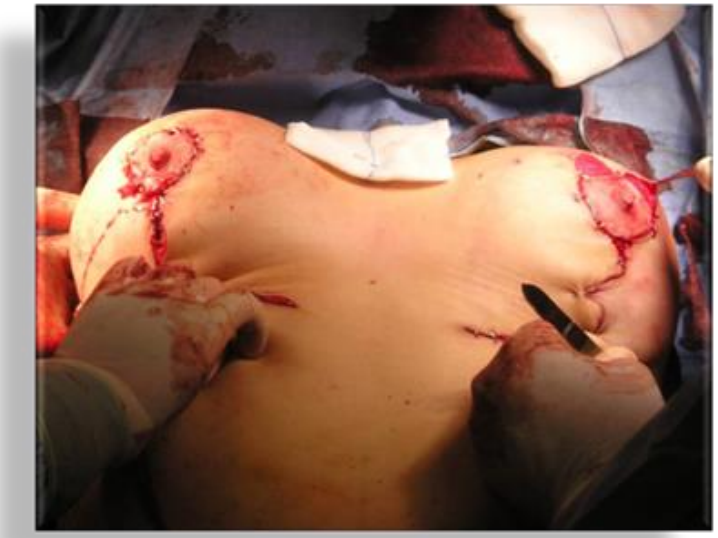
Chirurgia conservativa + RT può comunque essere offerta

Considerare tipo di neoplasia ed eventuali terapie adiuvanti/neoadiuvanti

Timing







ESMO Guidelines 2023, ASCO 2020

ESENZIONE SU ESAMI

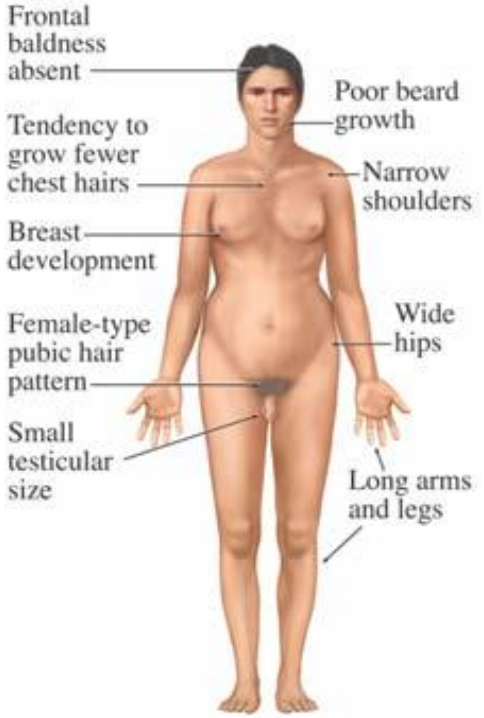
Esenzione D97/D99 in caso di mutazione BRCA1-2

Campania, Emilia Romagna, Lazio, Lombardia, Piemonte, Sicilia, Toscana, Veneto, Province Autonome di Trento e Bolzano, Liguria

Prestazioni comprese e non comprese

PRESTAZIONI
VISITA SENOLOGICA (PRIMA VISITA)
VISITA SENOLOGICA (CONTROLLO)
MAMMOGRAFIA BILATERALE
ECOGRAFIA MAMMELLA BILATERALE
RMN MAMMELLA BILATERALE CON E SENZA CONTRASTO
VISITA GINECOLOGICA (PRIMA VISITA)
VISITA GINECOLOGICA (CONTROLLO)
ECOGRAFIA TRANSVAGINALE
CA 125 (ANTIGENE CARBOIDRATICO 125)

MASCHIO BRCA



BRCA-2

Rischio aumenta in caso di ginecomastia (RR 9.8)

e sd di Klinefelter (RR 24.7)

Esame clinico annuale dai 35 aa

Ev Mx/Eco annuale dai 50 aa, in particolare nei pz con BRCA-2

Non indicazioni a chirurgia preventiva

RR carcinoma prostatico, PSA annuale dai 40 aa

NCCN 2023, ESMO Guidelines, 2023

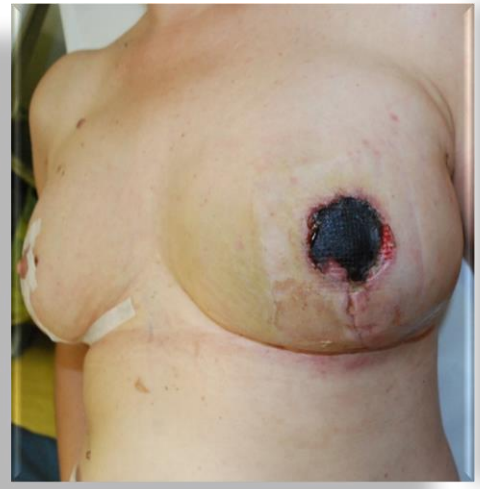
CONCLUSIONI

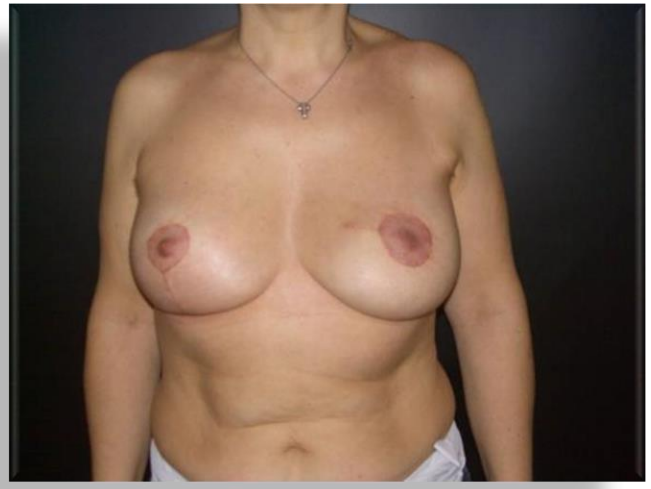
Chirurgia profilattica/esito

Timing

MMD

Decisione consapevole





"*La mammectomia profilattica riduce il rischio di sviluppare carcinoma mammario nelle pazienti BRCA+ dell'95-100%"*

Rebbek Tr et al *J Clin Oncol* (2007) 22:1055-1062