



2° CONGRESSO NAZIONALE
Verso la medicina genere specifica

LA DONNA E LA COPPIA DOPO L'ETÀ FERTILE

La salute che cambia:
prevenzione, stili di vita, fragilità

19 - 20 settembre 2018

HOTEL MICHELANGELO • MILANO

Tumore al seno: update nella prevenzione, nella diagnosi precoce e nel trattamento

Paolo Veronesi



IEO

Istituto Europeo di Oncologia



UNIVERSITÀ DEGLI STUDI DI MILANO



Classificazione funzionale sec. Shephard

distingue quattro età in base al declino delle capacità e dell'autosufficienza, in assenza di patologia

- **Età media (dai 40 ai 65 anni);** si ha un peggioramento delle funzioni globali che va dal 10 al 30% rispetto al valore di picco registrato nell'uomo adulto
- **Età anziana (dai 65 ai 75 anni) (terza età);** si ha un ulteriore indebolimento funzionale senza però gravi compromissioni dell'equilibrio organico globale
- **Età molto anziana (dai 76 agli 85 anni) (quarta età);** la perdita funzionale intacca il normale svolgimento delle attività quotidiane, pur non minando l'autonomia
- **Età anziana estrema (oltre gli 85 anni) (longevi);** si ricorre spesso a qualche forma di assistenza istituzionale o domiciliare

L'INCIDENZA DEI TUMORI IN ITALIA

Nel 2017 in Italia sono stati diagnosticati circa 365.000 nuovi casi di tumore

189.600 (54%) negli uomini e 176.200 (46%) nelle donne

nuove diagnosi di tumore in Italia

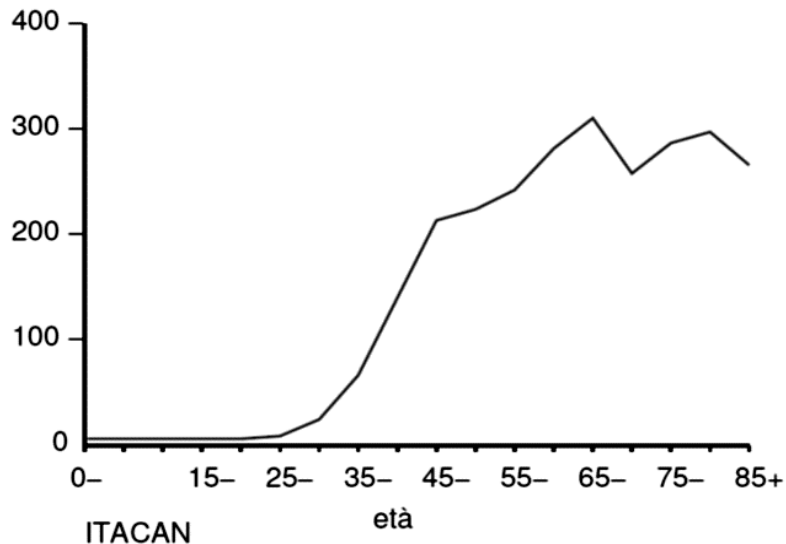
tumore	UOMINI	DONNE
Colon-retto	29.500	22.900
Mammella	500	50.000
Polmone	27.800	13.500
Prostata	35.000	
Vescica	21.400	5.200

Frequenza tumore seno per fascia di età

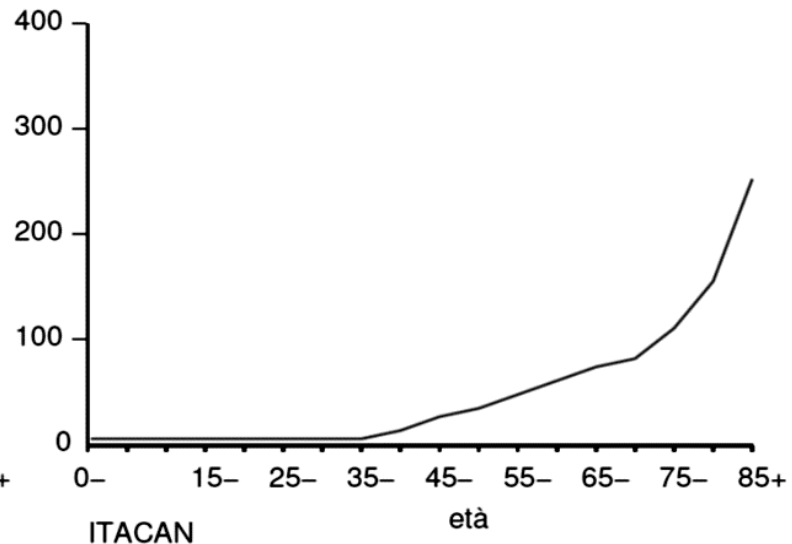
ETA'		
0-49	50-69	70+
Mammella (42%)	Mammella (36%)	Mammella (22%)

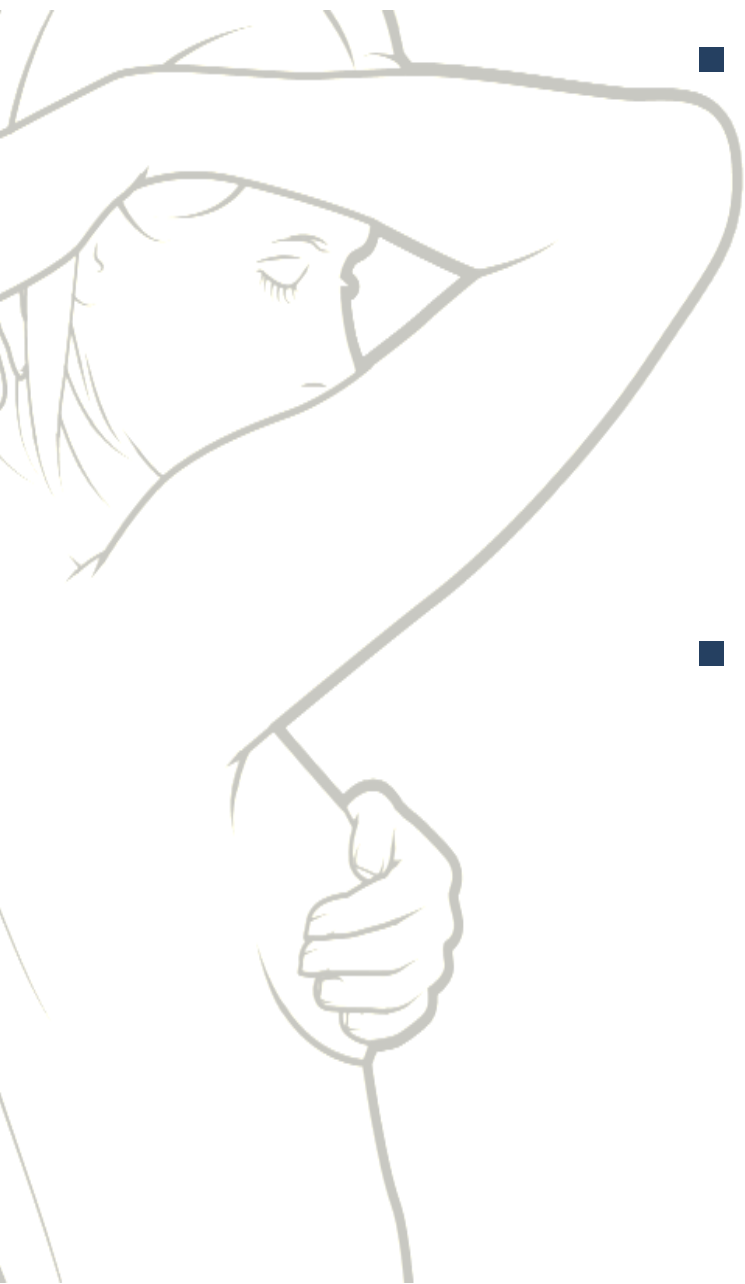
Incidenza - Mortalità

Tassi età-specifici per 100 000
Incidenza (2005–2009)



Tassi età-specifici per 100 000
Mortalità (2005–2009)





- Il carcinoma della mammella è il tumore più frequente fra le donne, per incidenza (oltre 50.000 casi anno) e mortalità (8.000 decessi anno)
- Mentre la **mortalità** è in calo a partire dagli anni '90, l'**incidenza** è in lieve ma costante aumento, forse come conseguenza, in parte, del diffondersi della diagnosi precoce

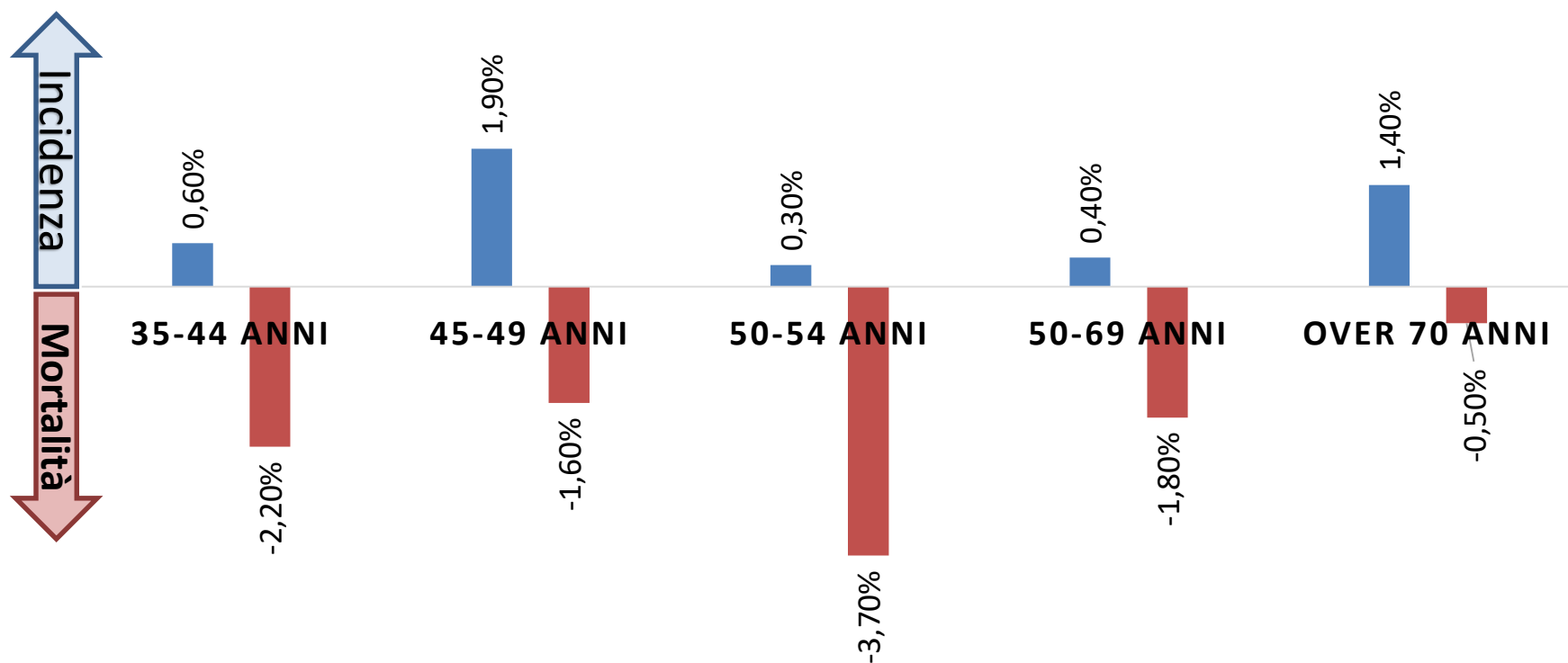
35-44 anni: l'incidenza aumenta lievemente dello 0,6%, la mortalità cala del 2,2%

45-49 anni: l'incidenza aumenta dell'1,9%; la mortalità si abbassa dell'1,6% l'anno.

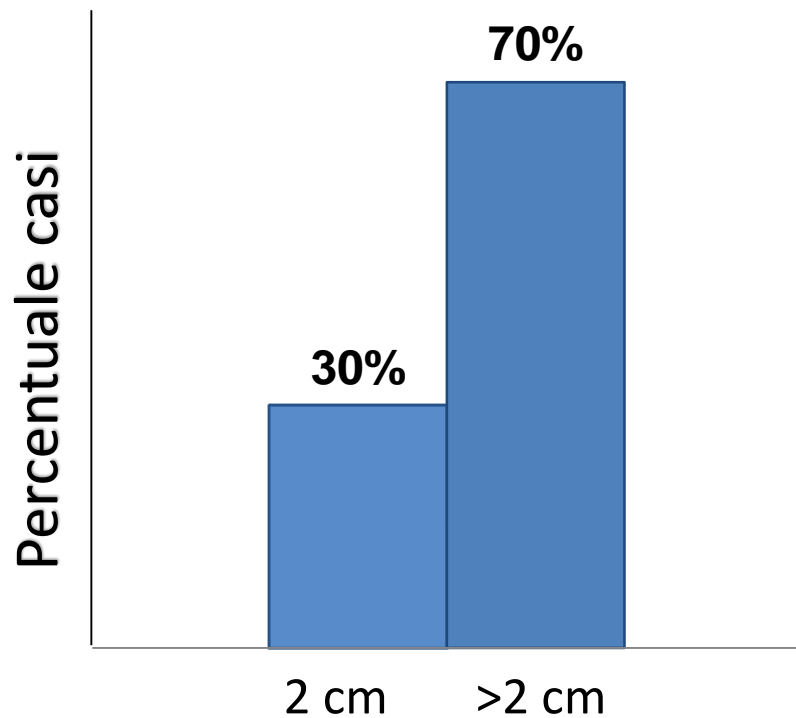
50-54 anni: L'incidenza è sostanzialmente stabile (+0,3%); la mortalità si abbassa del 3,7%

50-69 anni: incidenza stabile (0,4%); la mortalità cala dell'1,8% l'anno.

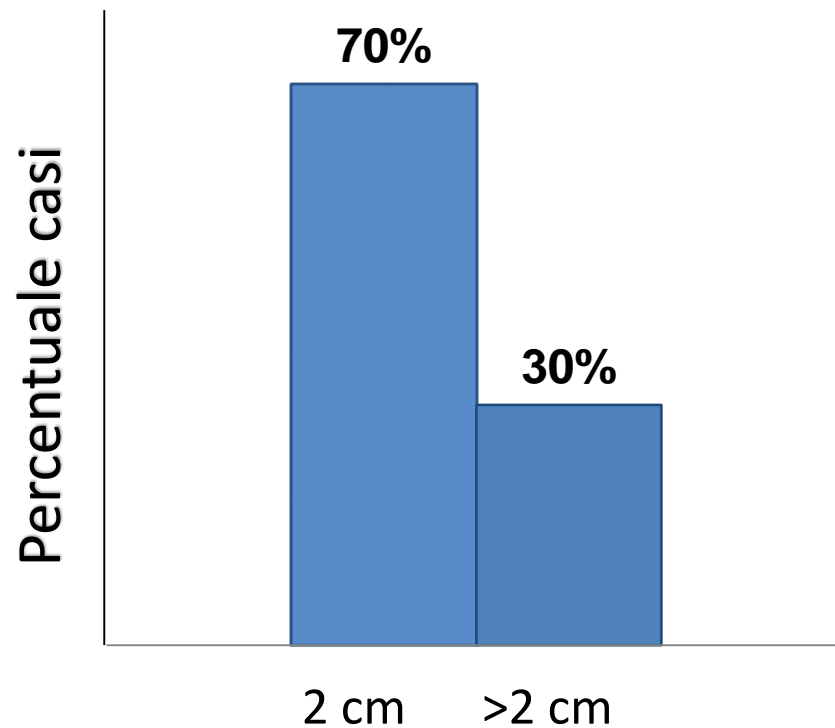
Over 70: l'incidenza aumenta dell'1,4%; la mortalità è sostanzialmente stabile (+0,5%).



1980



2018



PREVENZIONE PRIMARIA

Un'oncia di prevenzione vale una libbra di cure
-Benjamin Franklin-

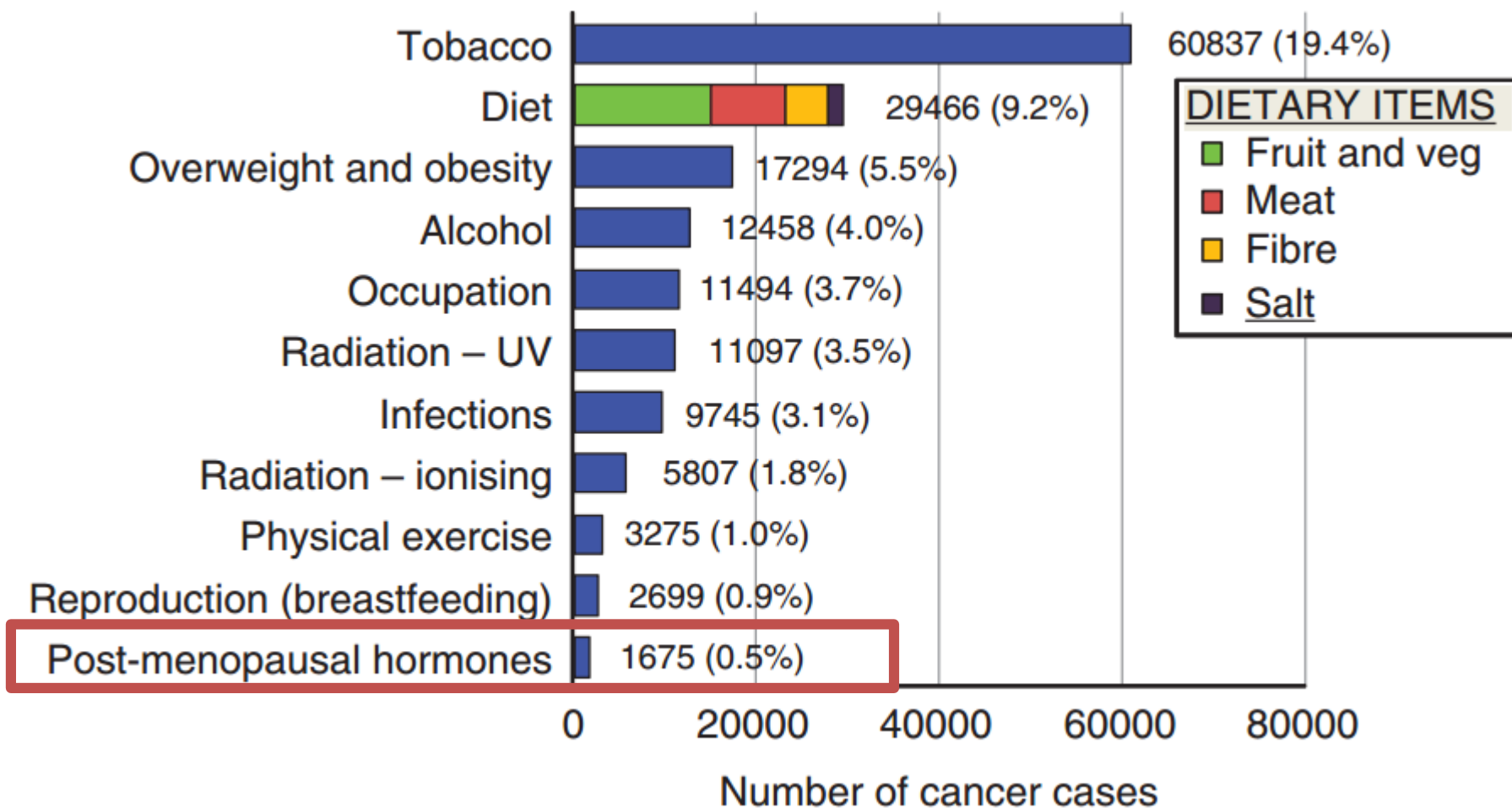
IMPEDIRE LO SVILUPPO DELLA MALATTIA



RIMOZIONE DELLE CAUSE e

*adozione di stili di vita che riducano il
rischio*

Number and Percentage of Cancer Cases in the UK Attributable to Different Exposures

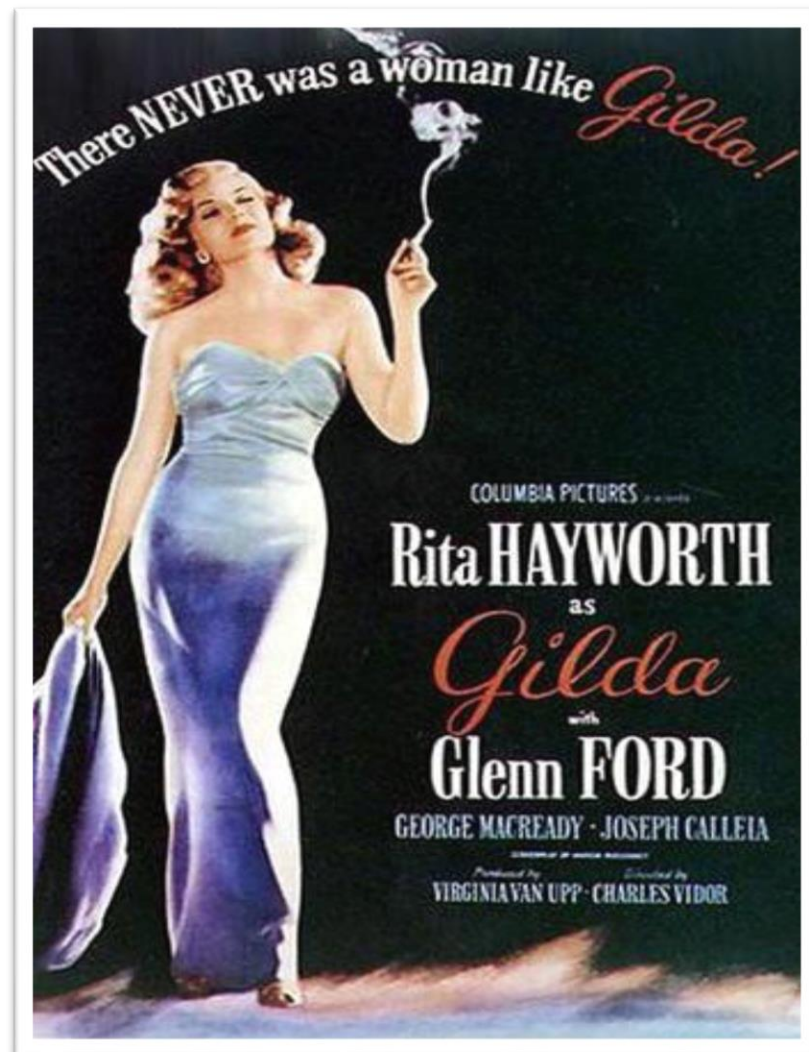


Migliorando lo stile di vita

- Secondo alcune stime, si potrebbe prevenire circa un terzo di tutti i tumori maligni modificando o eliminando i principali fattori di rischio, quali:
 - ✓ **tabagismo**
 - ✓ **eccesso ponderale**
 - ✓ **scarsa assunzione di frutta e verdura**
 - ✓ **sedentarietà**
 - ✓ **consumo di alcool**

Il fumo nella donna

- La mortalità per tumore al polmone è diminuita del 15% nei maschi, ma è aumentata del 30% nelle donne



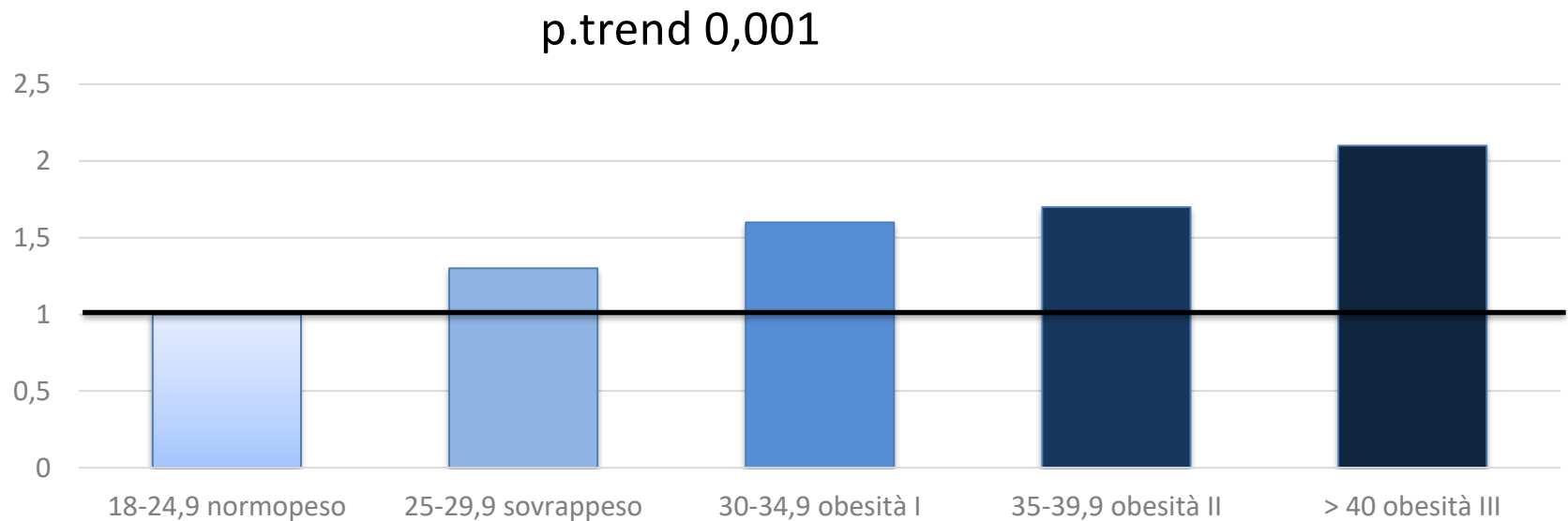
LA “SINDROME METABOLICA”

E' una condizione clinica che raggruppa un insieme di fattori che coalizzati sono i precursori di malattie cardiovascolari, diabete e patologie tumorali



RISCHIO DI MORTE PER TUMORE MAMMARIO DONNE IN POSTMENOPAUSA IN FUNZIONE ALL'INDICE DI MASSA CORPOREA

Cancer Prevention Study (USA): coorte di 495.977 donne, età media 57 anni, seguite per 16 anni (*Calle et al, N Engl J Med 2003*)



CORRETTA ALIMENTAZIONE

- Assumere almeno cinque porzioni al giorno di frutta e verdura
- E' utile consumare molte crucifere (rape, cavolfiore, cavolini di Bruxelles, cavolo)
- Limitare gli zuccheri raffinati, che hanno l'effetto di innalzare l'insulina nel sangue a favore di zuccheri grezzi ed amidi
- Limitare il consumo di grassi di origine animale



Cosa succede se eseguiamo un'adeguata attività fisica in post-menopausa

Regoliamo il metabolismo, aiutando a diminuire la massa grassa, e la glicemia



Regoliamo la produzione ormonale, soprattutto gli ormoni steroidei e sessuali

Randomized Trial of a Telephone-Based Weight Loss Intervention in Postmenopausal Women With Breast Cancer Receiving Letrozole: The LISA Trial

Pamela J. Goodwin, Roanne J. Segal, Michael Vallis, Jennifer A. Ligibel, Gregory R. Pond, André Robitoux, George L. Blackburn, Brian Findlay, Julie R. Galloway, Som Mukherjee, Mark Levine, and Kathleen I. Pritchard

See accompanying editorial on page 2197

Pamela J. Goodwin, Lunenburg, Tanenbaum Research Institute, Mount Sinai Hospital and Princess Margaret Hospital; Kathleen I. Pritchard, Sunnybrook Odette Cancer Center; Pamela J. Goodwin and Kathleen I. Pritchard, University of Toronto, Toronto; Roanne J. Segal, Ottawa Hospital Regional Cancer Center, University of Ottawa, Ottawa; Gregory R. Pond, Som Mukherjee, and Mark Levine, Juravinski Hospital and Cancer Center, Brian Find-

ABSTRACT

Purpose

Obesity is associated with poor outcomes in women with operable breast cancer. Lifestyle interventions (LIs) that help women reduce their weight may improve outcomes.

Patients and Methods

We conducted a multicenter randomized trial comparing mail-based delivery of general health information alone or combined with a 24-month standardized, telephone-based LI that included diet (500 to 1,000 kcal per day deficit) and physical activity (150 to 200 minutes of moderate-intensity physical activity per week) goals to achieve weight loss (up to 10%). Women receiving

DEFINITIVE guide to how you can save money

Daily workout could beat disease

EXERCISE SLASHES RISK OF BREAST CANCER

WOMEN who exercise energetically for an hour a day can cut their risk of breast cancer—regardless of their weight or age.

Researchers say that those who exercise vigorously for an hour a day reduce their chances of the disease by 11 per cent.

Exercising for longer will increase protection further still compared with the

By Jenny Hooper
Medical Correspondent

West African women, according to findings released at the European Breast Cancer Conference in Glasgow.

Researchers examined results from 21 studies involving more than four million women.

They found women of any age or size who exercise for an hour a day cut their risk of breast cancer by 11 per cent.

Turn to Page 2

SPRING CLEAN YOUR FINANCES

Race on to flee poor pensions

As the pension industry faces a crisis of confidence, many investors are turning to private equity funds. But what are the risks? A new report from the UK's Financial Conduct Authority (FCA) warns that private equity funds can be "highly volatile" and "subject to significant fluctuations in value". The FCA also notes that private equity funds can be "difficult to diversify" and "may be subject to significant fluctuations in value".

UK troops the clear Iraqi debt

UK troops the clear Iraqi debt. The UK government has announced that it will not pay the Iraqi debt. This is a significant move, as the UK has been one of the few countries to not pay the debt. The UK government has announced that it will not pay the Iraqi debt. This is a significant move, as the UK has been one of the few countries to not pay the debt.

How the other Stones called L'Wren Yoko

CLINICAL ONCOLOGY

ORIGINAL REPORT

Randomized Exercise Trial of Aromatase Inhibitor–Induced Arthralgia in Breast Cancer Survivors

Melinda L. Irwin, Brenda Cartmel, Cary Gross, Elizabeth Ercolano, Fangyong Li, Xiaopan Yao, Martha Fiellin, Scott Capozza, Marianna Rothbard, Yang Zhou, Maura Harrigan, Tara Sanft, Kathryn Schmitz, Tuhina Neogi, Dawn Hershman, and Jennifer Ligibel

ABSTRACT

Purpose

Arthralgia occurs in up to 50% of breast cancer survivors treated with aromatase inhibitors (AIs) and is the most common reason for poor AI adherence. We conducted, in 121 breast cancer survivors receiving an AI and reporting arthralgia, a yearlong randomized trial of the impact of exercise versus usual care on arthralgia severity.

Patients and Methods

Eligibility criteria included receiving an AI for at least 6 months, reporting ≥ 3 of 10 for worst joint pain on the Brief Pain Inventory (BPI), and reporting < 90 minutes per week of aerobic exercise and no strength training. Participants were randomly assigned to exercise (150 minutes per week of aerobic exercise and supervised strength training twice per week) or usual care. The BPI, Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index, and Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire were completed at baseline and at 3, 6, 9, and 12 months. Intervention effects were evaluated using mixed-model repeated measures analysis, with change at 12 months as the primary end point.

Results

Over 12 months, women randomly assigned to exercise ($n = 61$) attended 70% (\pm standard deviation [SD], 28%) of resistance training sessions and increased their exercise by 159 (\pm SD, 136) minutes per week. Worst joint pain scores decreased by 1.6 points (29%) at 12 months among women randomly assigned to exercise versus a 0.2-point increase (3%) among those receiving usual care ($n = 60$; $P < .001$). Pain severity and interference, as well as DASH and WOMAC pain scores, also decreased significantly at 12 months in women randomly assigned to exercise, compared with increases for those receiving usual care (all $P < .001$).

Conclusion

Exercise led to improvement in AI-induced arthralgia in previously inactive breast cancer survivors.

Fare sport in post menopausa riduce il rischio di tumore al seno

**L'attività fisica è un'arma importantissima di prevenzione
per il tumore al seno**

Fattori di rischio

- **Obesità ed eccessivo accumulo di adipe addominale**
- **Alto indice glicemico**
- **Alterato equilibrio ormonale**



Studio InForma

Promuovere la perdita di peso con la dieta ed esercizio fisico nelle donne in sovrappeso con tumore al seno: uno studio di intervento randomizzato a quattro bracci

Gnagnarella et al *Trials* (2016) 17:363
DOI 10.1186/s13063-016-1487-x


Trials

STUDY PROTOCOL

Open Access

Promoting weight loss through diet and exercise in overweight or obese breast cancer survivors (InForma): study protocol for a randomized controlled trial



Patrizia Gnagnarella^{1*} , Daniele Dragà¹, Federica Baggi², Maria Claudia Simoncini², Annarita Sabbatini³, Ketti Mazzocco^{4,5}, Fabio Domenico Bassi⁶, Gabriella Pravettoni^{4,5} and Patrick Maisonneuve¹

FATTORI DI RISCHIO

Fattori genetico-costituzionali:

Età

Familiarità

Fattori comportamentali:

Radiazioni ionizzanti

Attività fisica

Dieta, alcool

Fattori legati alla vita riproduttiva:

Durata vita fertile

Gravidanza

Allattamento

Terapie ormonali

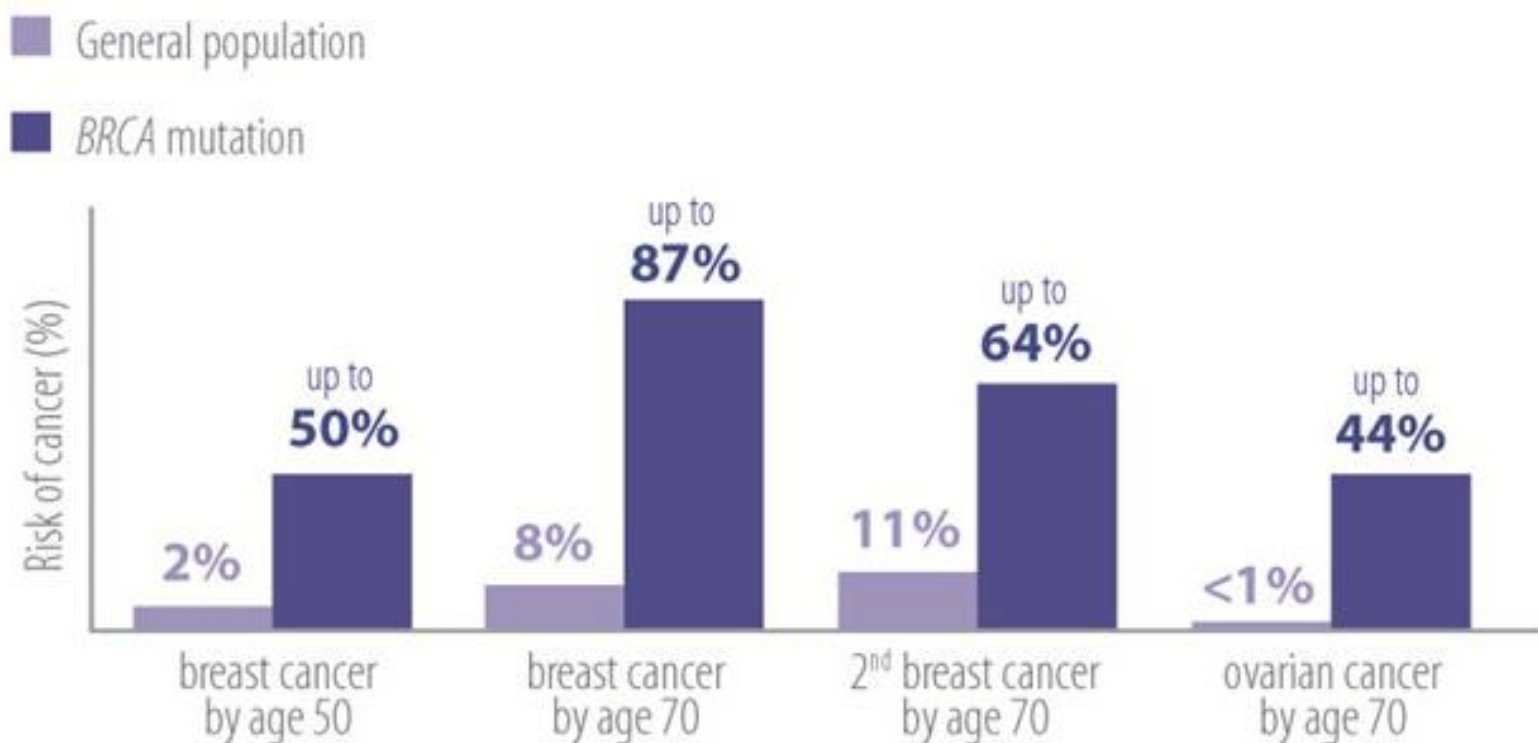
Pregresso tumore mammario

FAMIGLIE AD ALTO RISCHIO

- Precoce età di insorgenza
- Bilateralità e multifocalità
- >2 parenti di I° grado malati (mammella e ovaio)

BRCA1

RISCHIO DI TUMORE MAMMARIO



FAMIGLIE AD ALTO RISCHIO

TEST GENTICO POSITIVO

- Interventi chirurgici profilattici
- Chemioprevenzione
- Stretto follow-up (Diagnosi precoce)

PREVENZIONE SECONDARIA

LIMITARE GLI EFFETTI DELLA
MALATTIA



DIAGNOSI PRECOCE



Diagnosi Precoce



Aumentata probabilità di guarigione



Corretto utilizzo delle metodiche diagnostiche

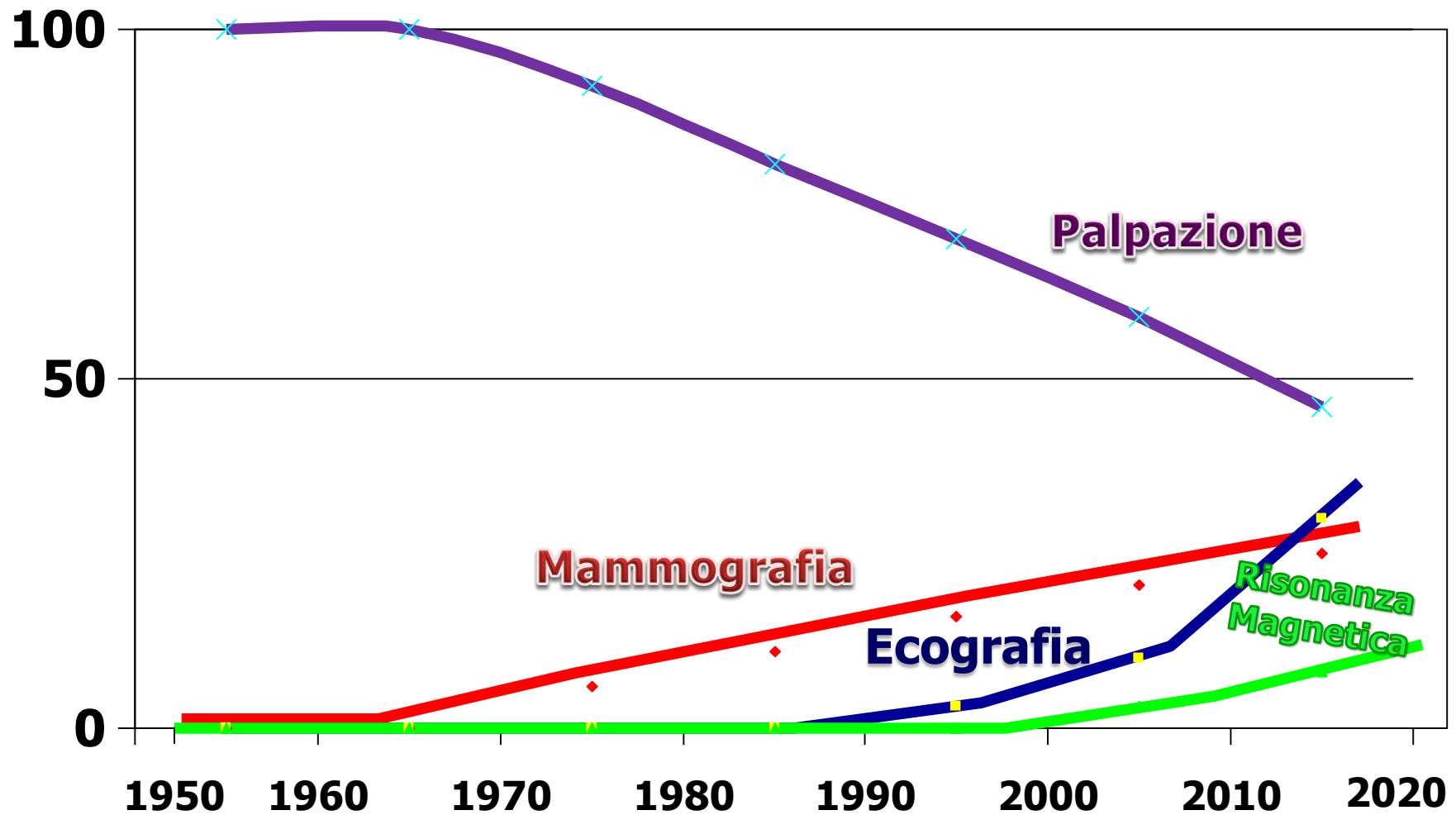


Chirurgia mirata e rispettosa della femminilità e dell'immagine corporea ed efficacia delle cure

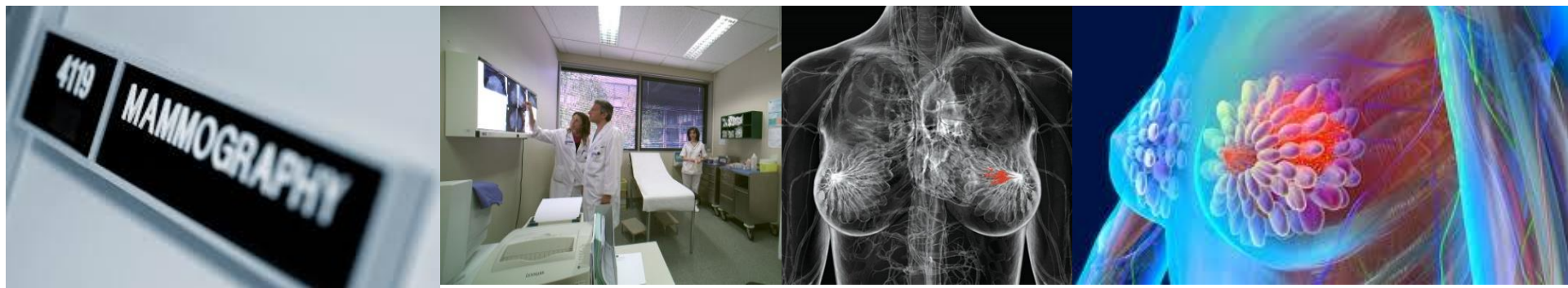
Prevenzione Secondaria

Anticipazione Diagnostica e Nuovi Modelli di Cura

Come viene scoperto il tumore al seno

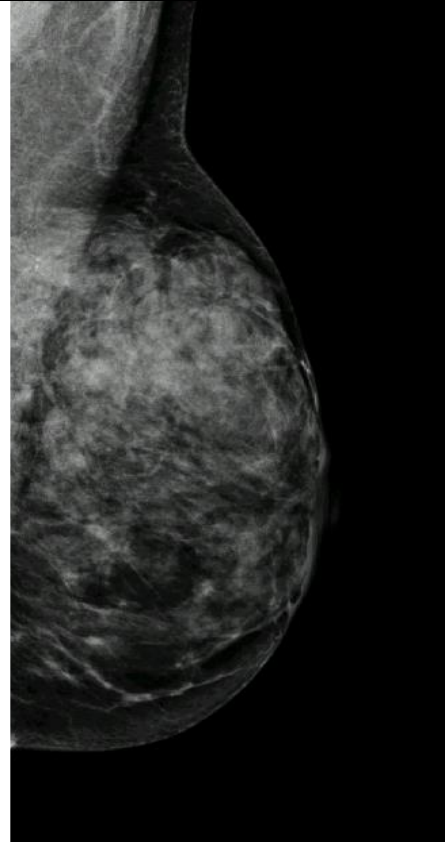


Rivoluzione delle Immagini

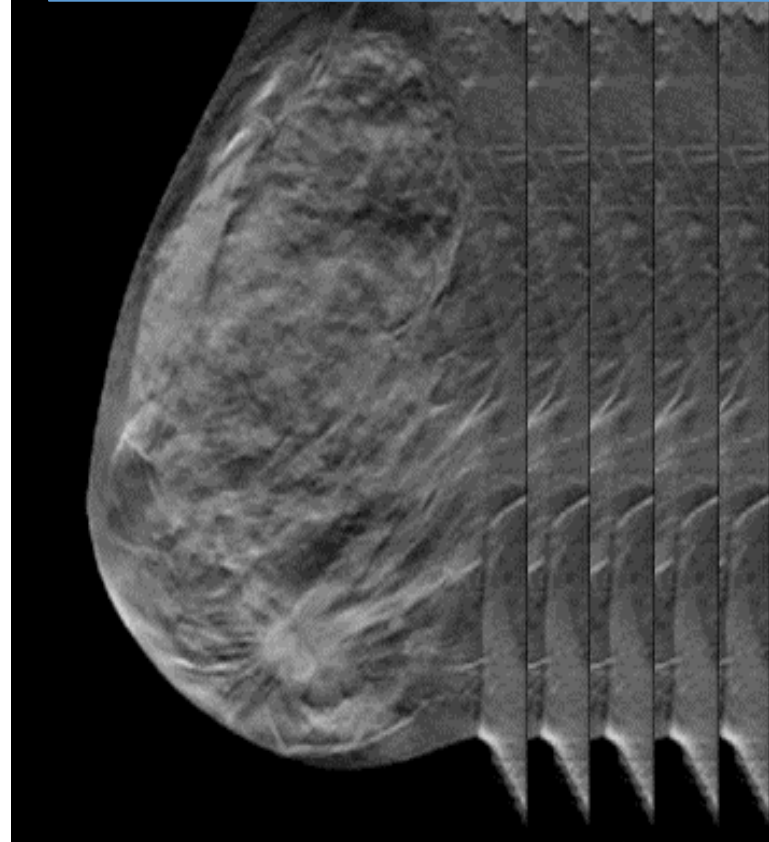


La TOMOSINTESI permette di vedere **‘dentro’** e non solo **‘attraverso’**

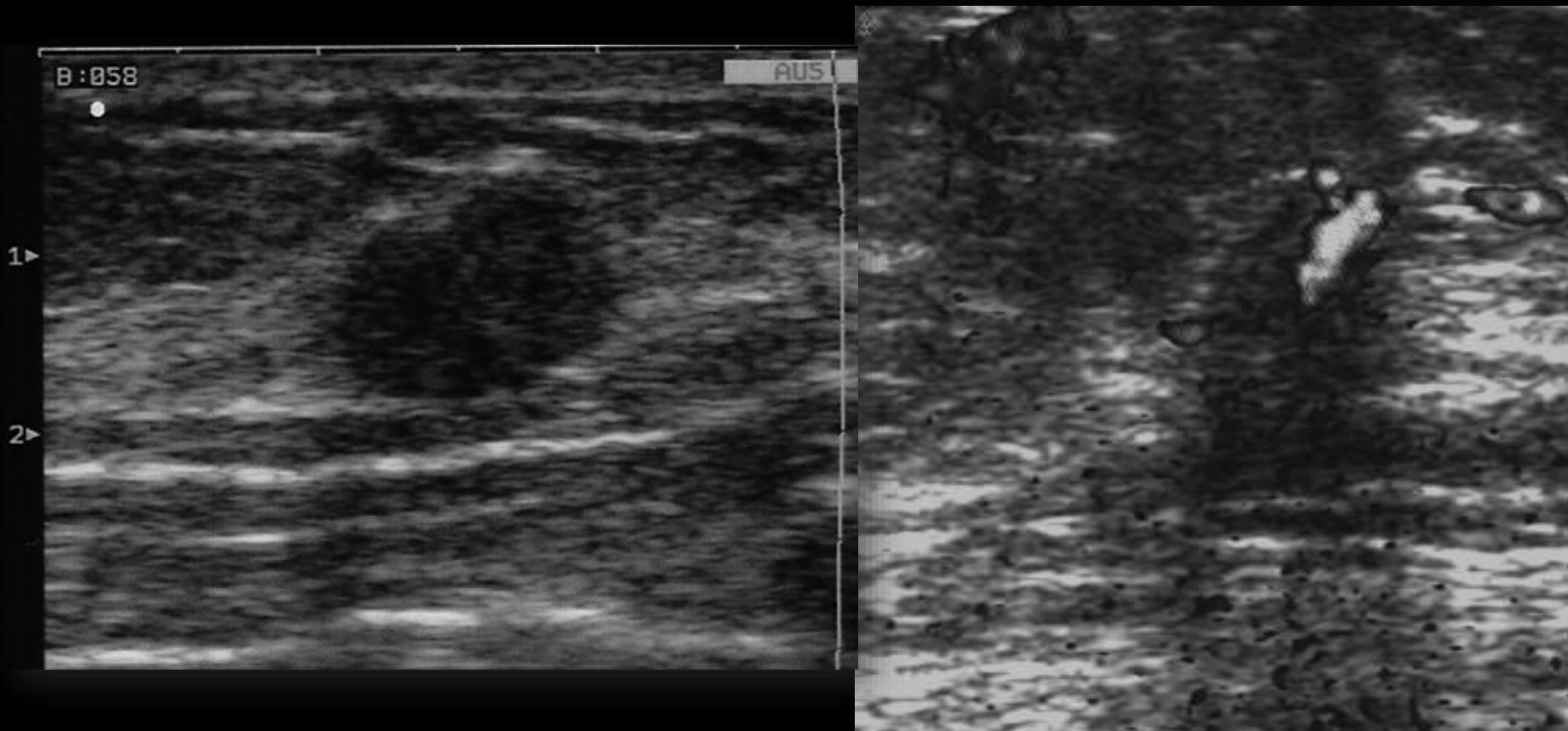
mammografia



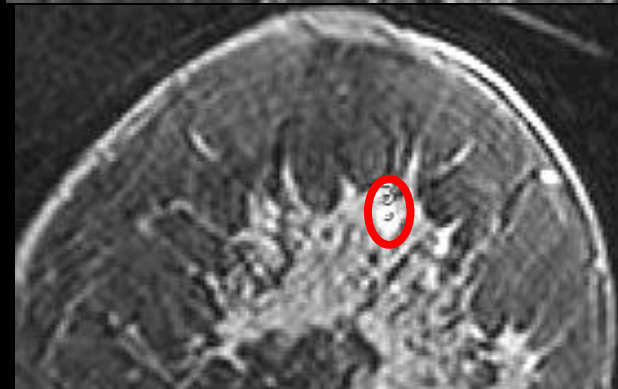
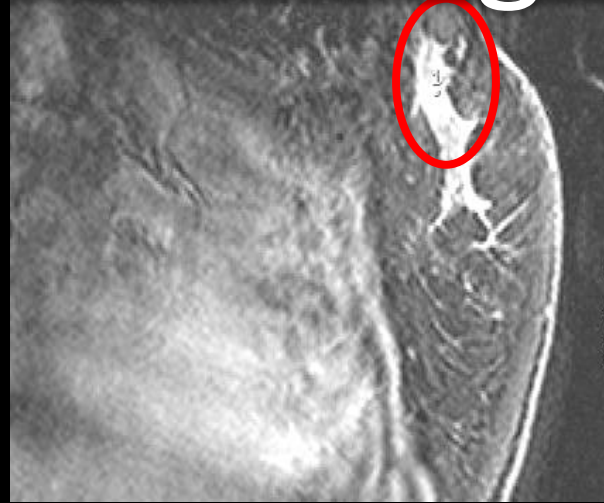
tomosintesi

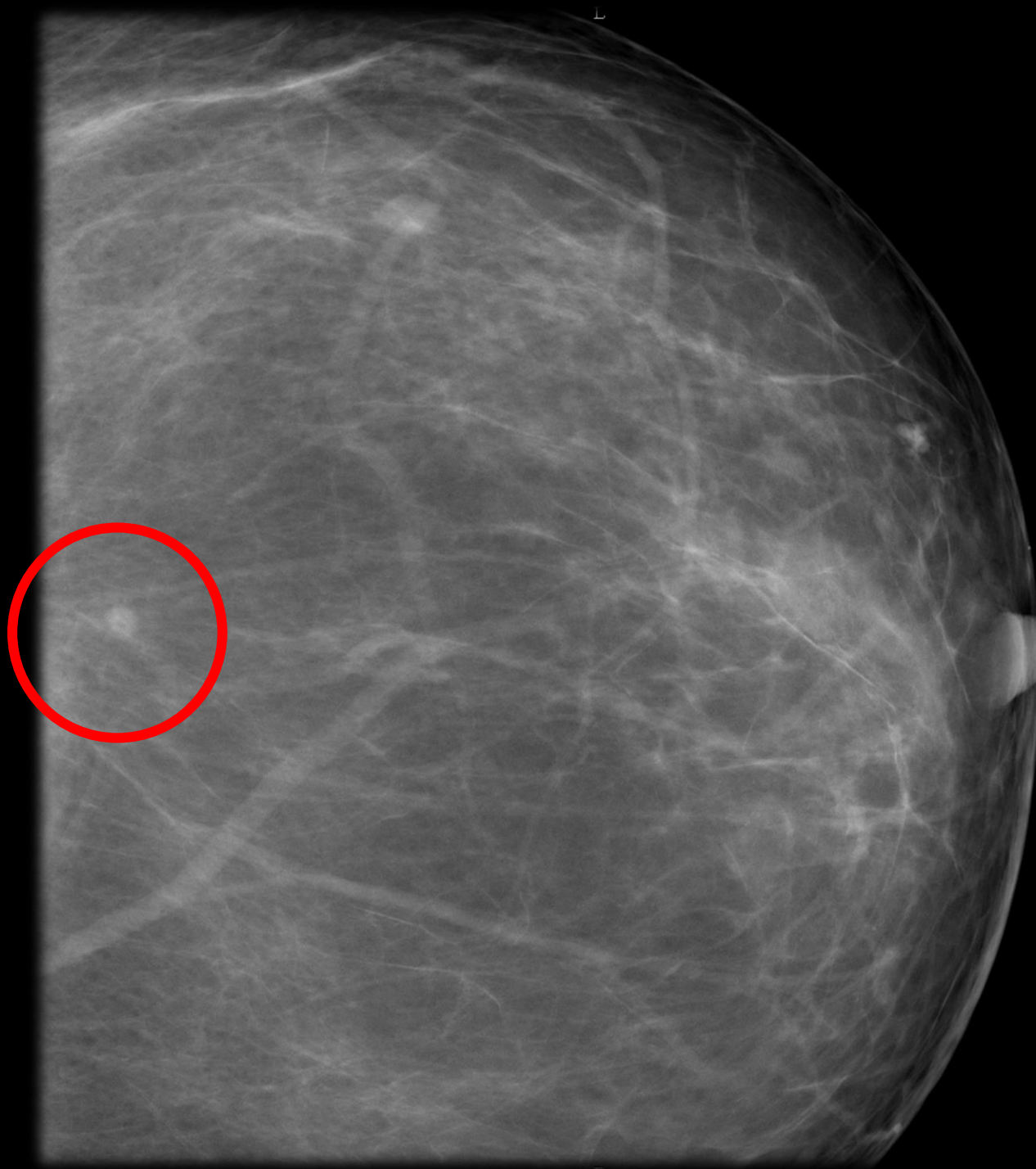


Ecografia



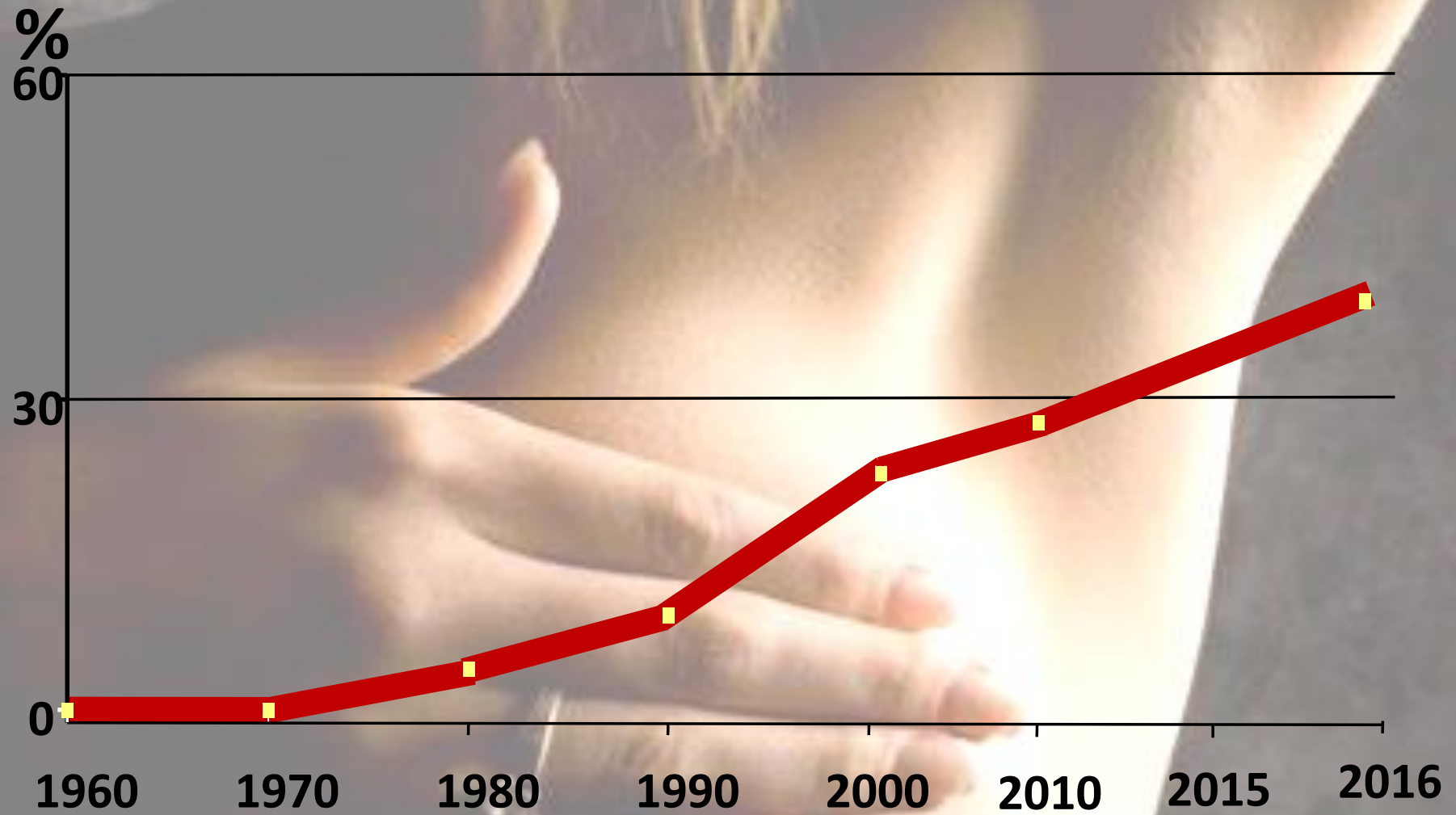
Risonanza Magnetica





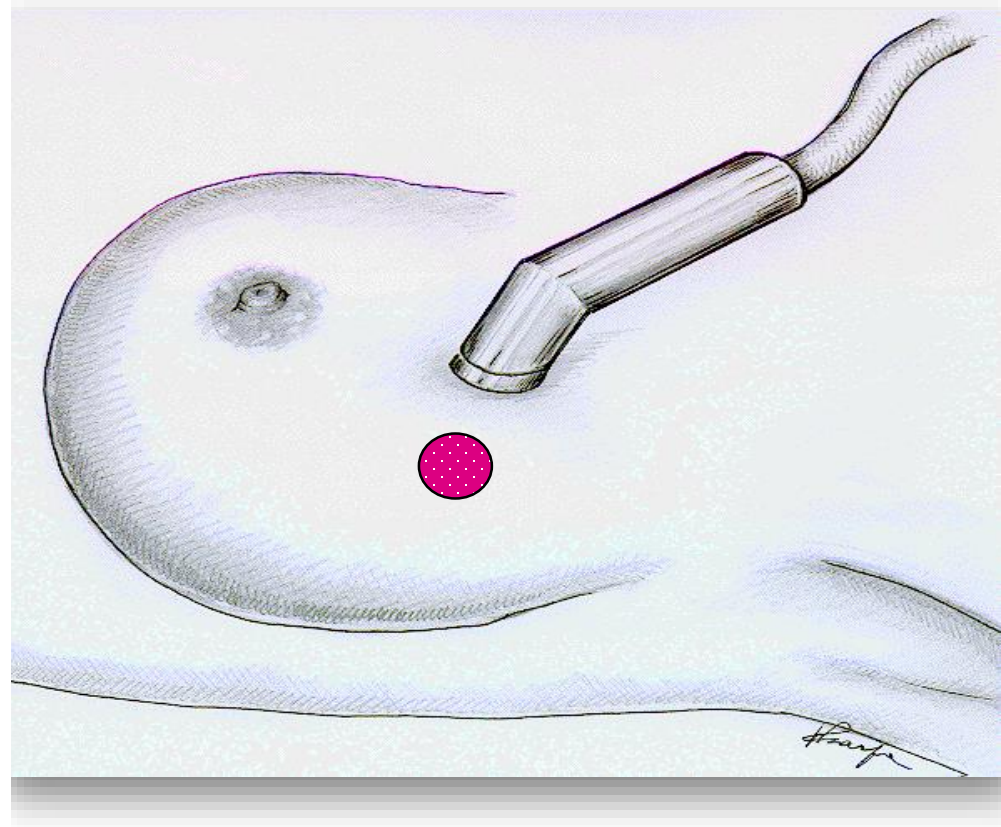
La diffusione su larga scala degli
esami di screening e la
maggiore consapevolezza della
popolazione femminile hanno
portato a diagnosticare un
numero sempre maggiore di
lesioni non palpabili

Tumore non palpabile della mammella

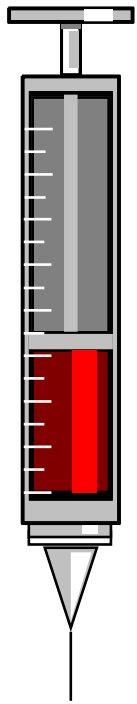


R.O.L.L.

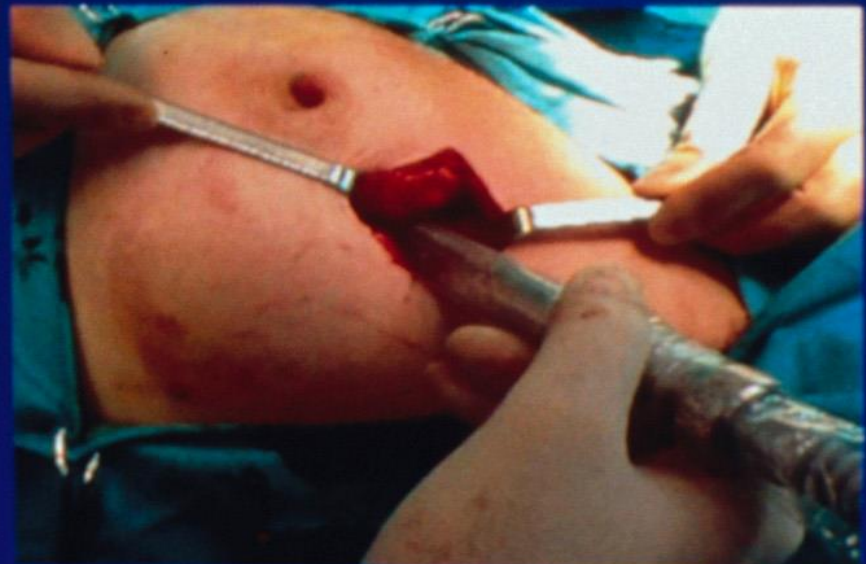
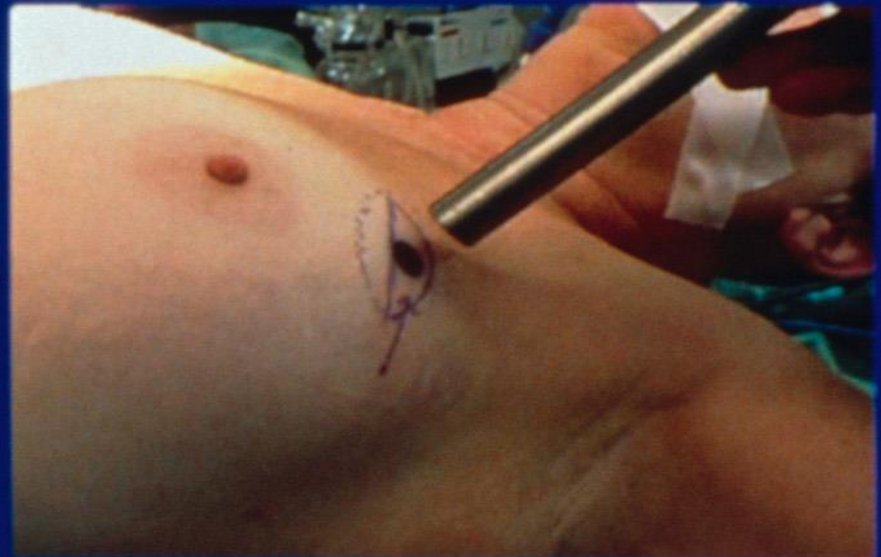
Radioguided
Occult
Lesion
Localization

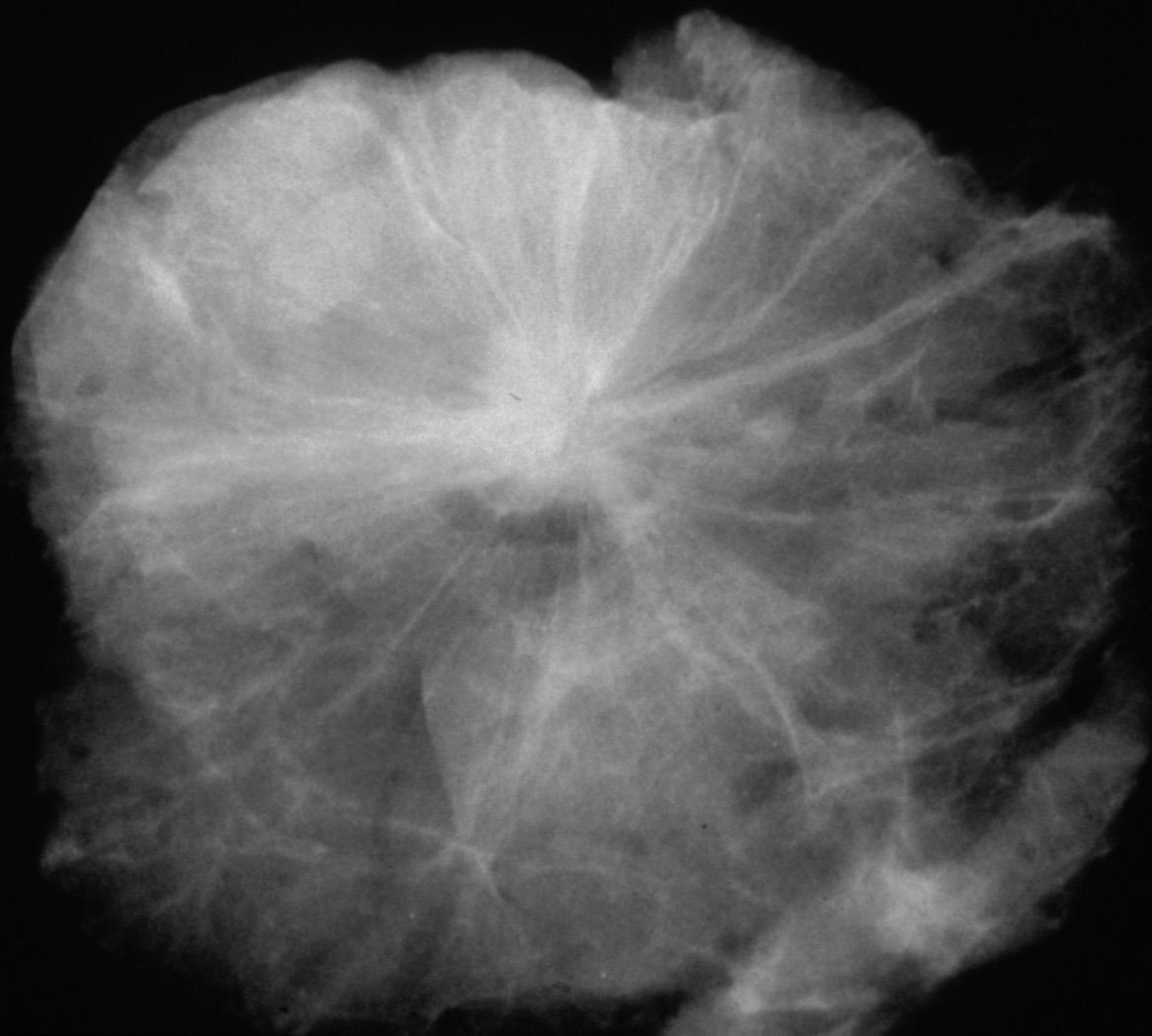


Localizzazione radioguidata delle lesioni occulte (R.O.L.L.)



0.05mg. di macroaggregati di albumina serica (diametro di 10-150 micron) identificati con TC 99 iniettati nella lesione con guida stereotassica o ecografica





Nonpalpable Breast Carcinomas: Long-Term Evaluation of
1,258 Cases

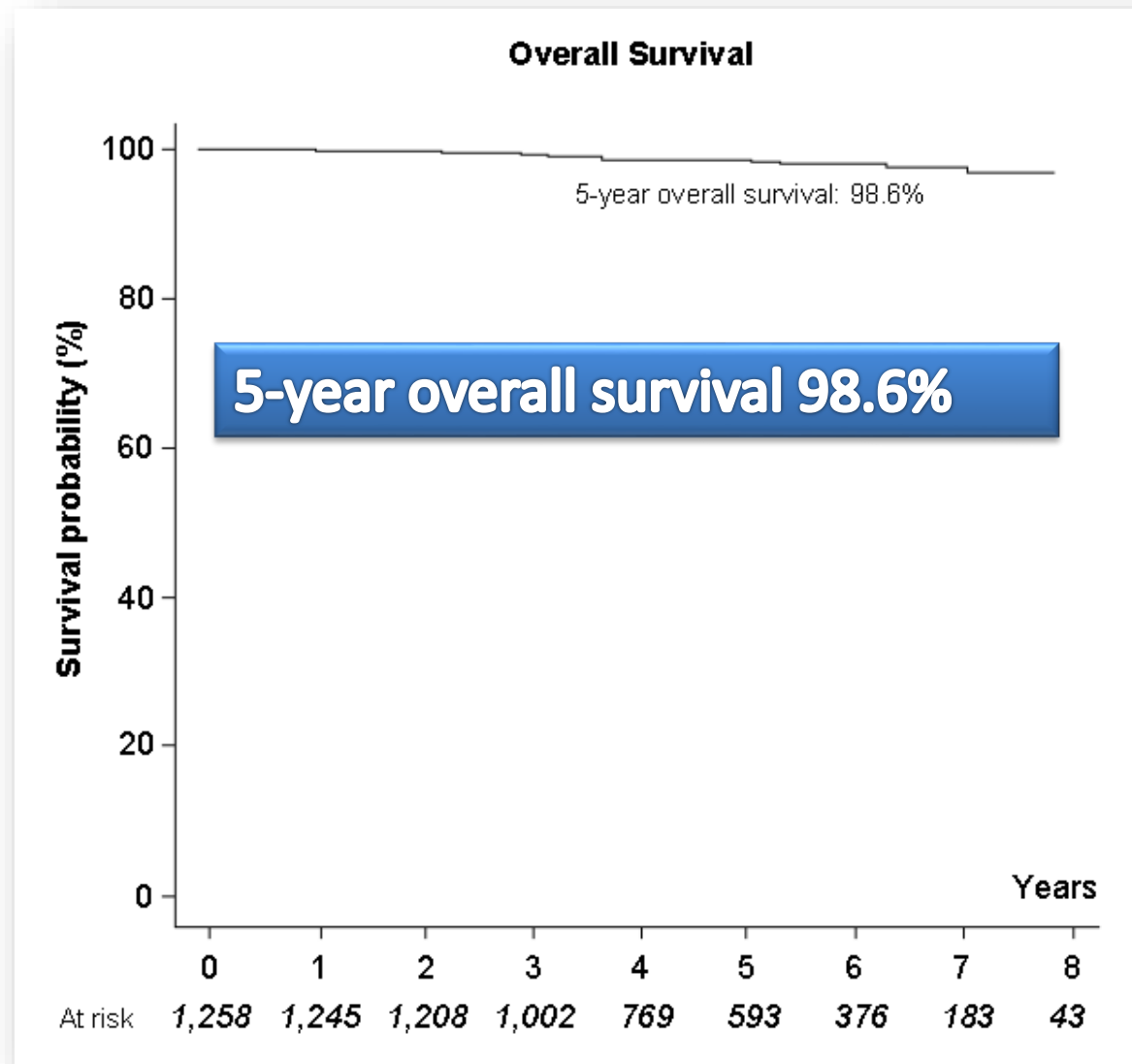
UMBERTO VERONESI,^a ALBERTO LUINI,^b EDOARDO BOTTERI,^c STEFANO ZURRIDA,^{b,d} SIMONETTA MONTI,^b
VIVIANA GALIMBERTI,^b ENRICO CASSANO,^e ANTONIO LATRONICO,^e MARIA PIZZAMIGLIO,^e
GIUSEPPE VIALE,^{d,f} DARIO VEZZOLI,^g NICOLE ROTMENSZ,^c SIMONA MUSMECI,^b FABIO BASSI,^b
LOREDANA BURGOA,^b PATRICK MAISONNEUVE,^c GIOVANNI PAGANELLI,^h PAOLO VERONESI^{b,d}

^aIEO European Institute of Oncology, Milan, Italy; ^bDivisions of Senology and ^cEpidemiology and
Biostatistics, IEO European Institute of Oncology, Milan, Italy; ^dUniversity of Milan School of Medicine,
Milan, Italy; ^eBreast Radiology Unit, ^fDivision of Pathology, ^gDivision of Anaesthesiology, and ^hDivision of
Nuclear Medicine, IEO European Institute of Oncology, Milan, Italy

Risultati

1.258 pazienti trattate con ROLL
dal 2000 al 2006 con diagnosi
finale di carcinoma invasivo

1.258 casi identificati solo con indagini strumentali



la ricerca di un trattamento chirurgico ottimale per il tumore al seno



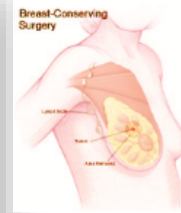
Mastectomia
Radicale
(HALSTED)



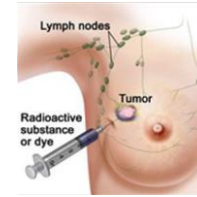
Mastectomia
Radicale Estesa
(URBAN)



U. VERONESI E
B. FISHER



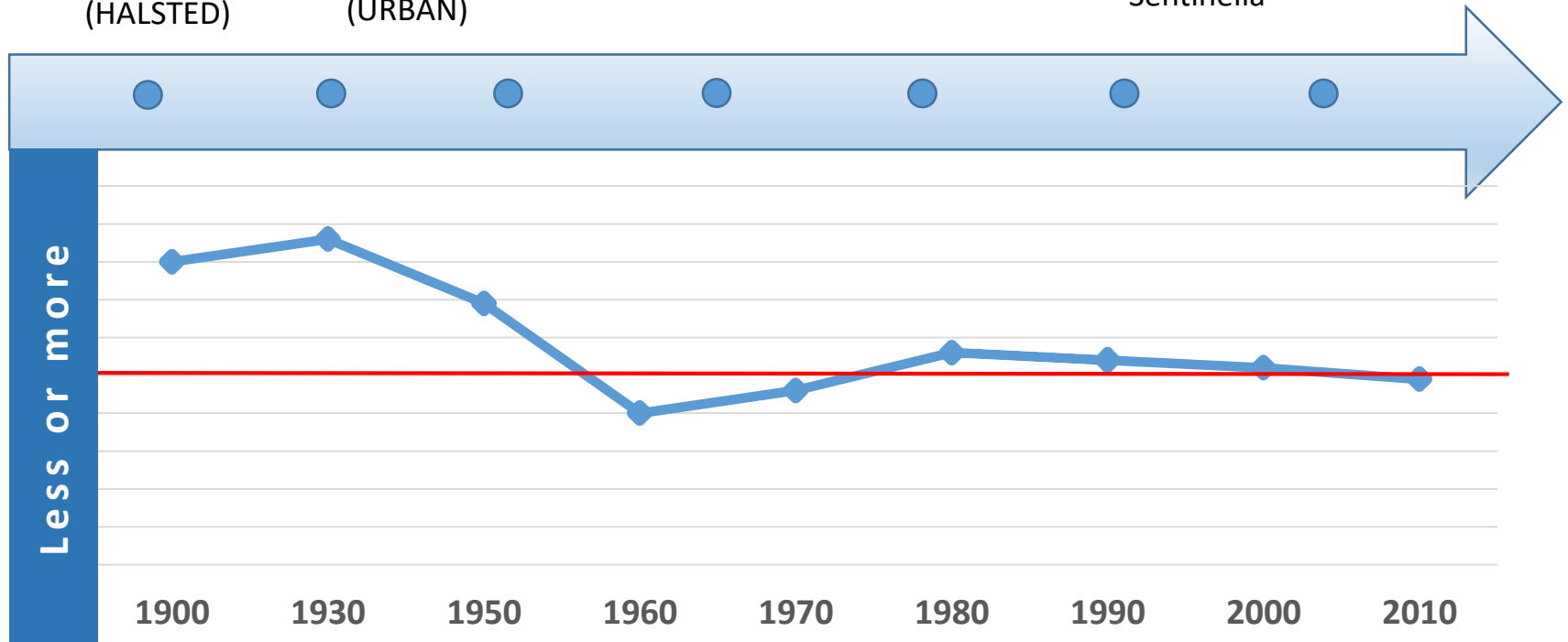
Chirurgia
Conservativa



Biopsia
Linfonodo
Sentinella



2011
(GIULIANO)



Mastectomia Radicale estesa vs Chirurgia Conservativa





Invasive cancer Milan Trial at 20 years

Operation	# pts	LR	Breast CA-specific survival
Radical Mastectomy	349	2.3%	76%
Quad/ALND plus RT	352	8.8%	74%

Cambio di paradigma nella chirurgia conservativa della mammella

■ Negli ultimi anni il concetto di chirurgia conservativa dell'organo si è evoluto nel senso di conservazione dell'immagine e della funzionalità corporea, anche in caso di necessaria asportazione della ghiandola mammaria



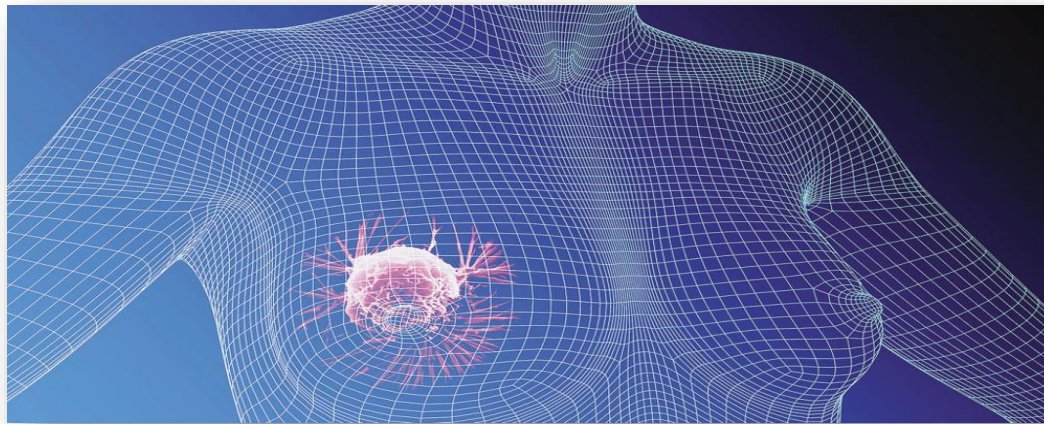
**Chirurgia conservativa o
ricostruttiva**

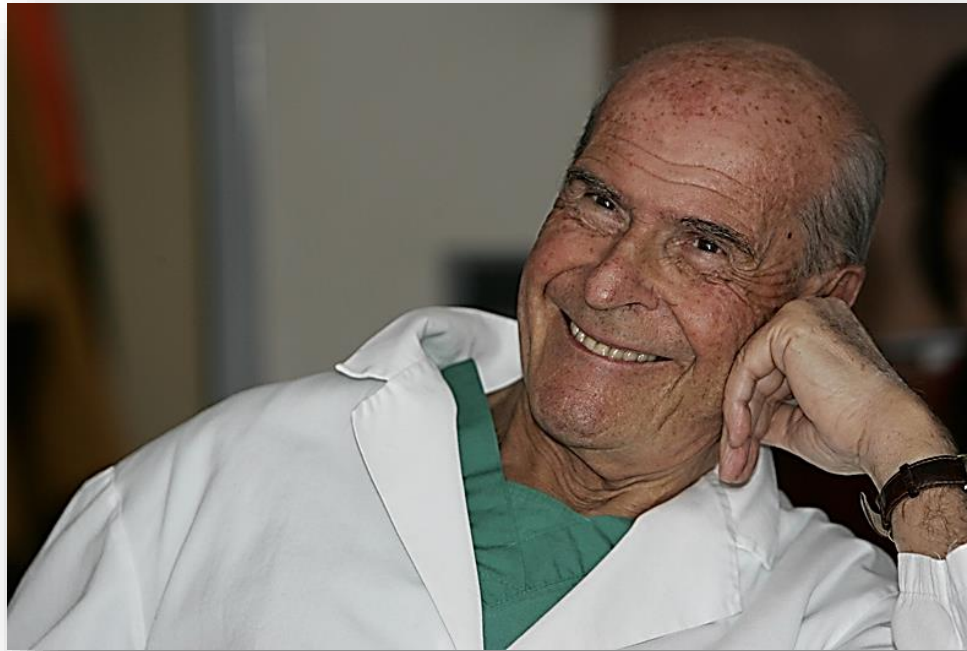


**Conservazione dei
linfonodi ascellari**

TRATTAMENTO CHIRURGICO

- Chirurgia conservativa e ricostruttiva
- Conservazione linfonodi ascellari



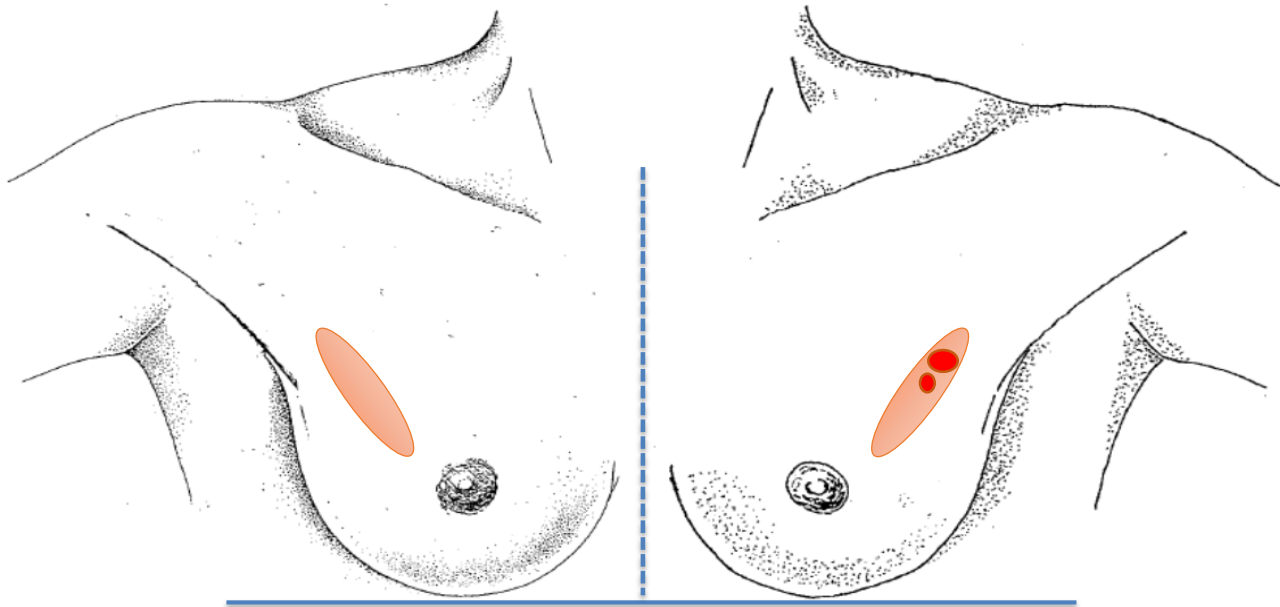


Negli anni 90' Umberto Veronesi ha introdotto il concetto di “*mirror quadrantectomy*” sviluppato in seguito in un progetto più ampio con lo scopo di allargare la resezione del seno colpito riducendo di conseguenza le dimensioni di quello opposto.

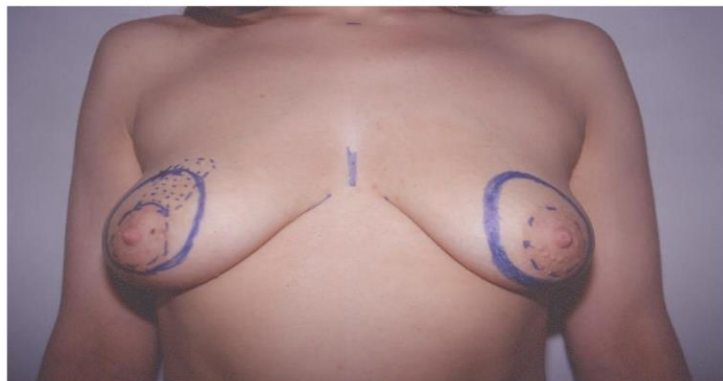
Con questa nuova strategia la conservazione del seno è stata applicata anche a pazienti con tumori fino a 5 cm di diametro purchè le dimensioni del seno lo permettano

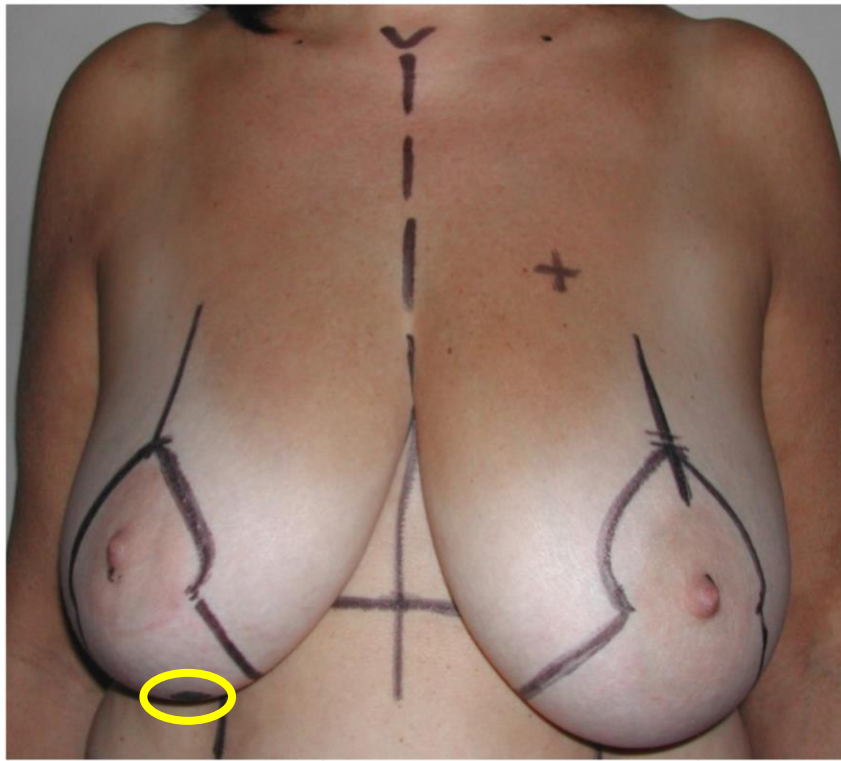
«mirror quadrantectomy»

- Migliore risultato estetico, rendendo il seno simmetrico
- Informazioni sullo stato della mammella controlaterale
- Riduzione dell'incidenza di tumore al seno controlaterale - circa il 50% dei carcinomi controlaterale appare nello stesso quadrante come tumore primario
- Soddisfazione psicologica delle pazienti

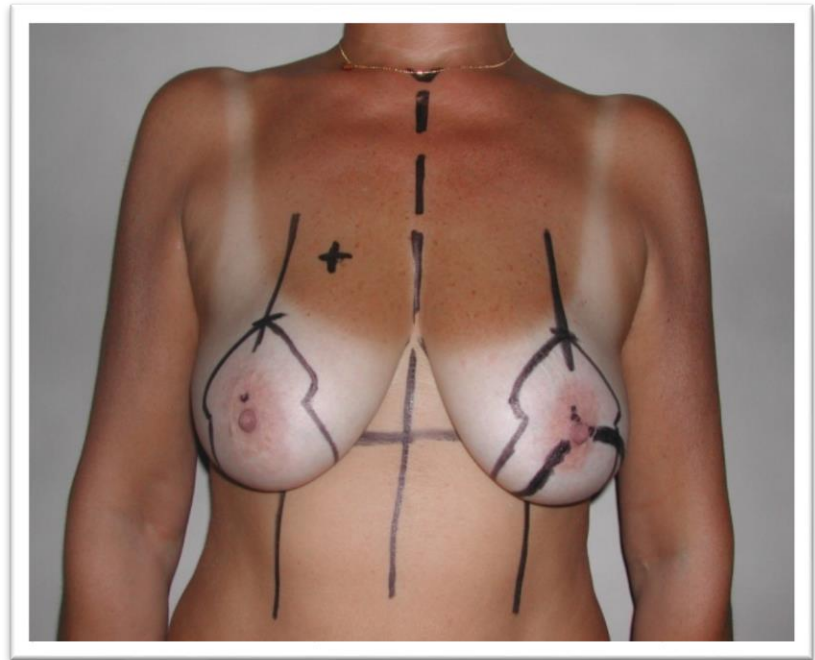


La «Mirror Quadrantectomy» è stato il seme che ha fatto germogliare una nuova e ormai diffusa disciplina: **la Chirurgia “Oncoplastica”**

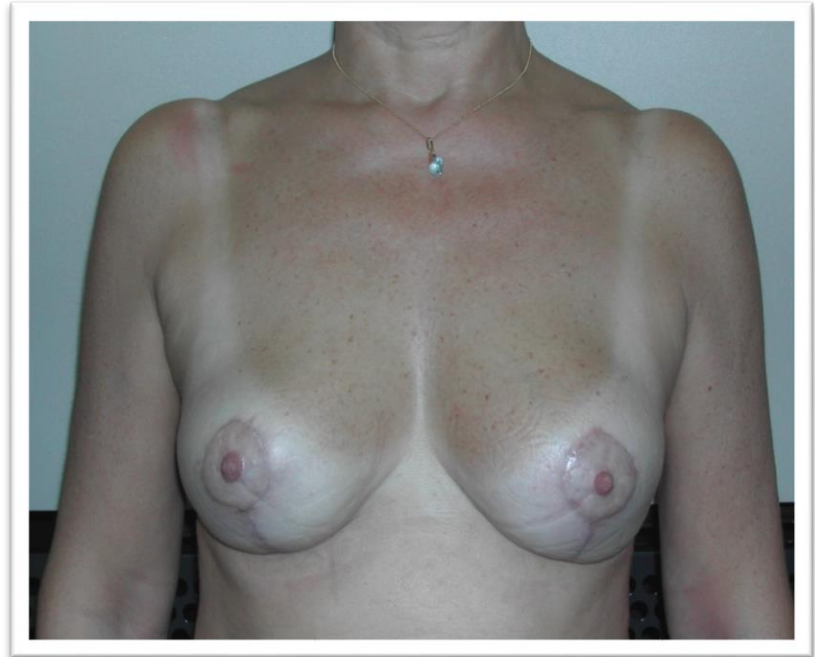


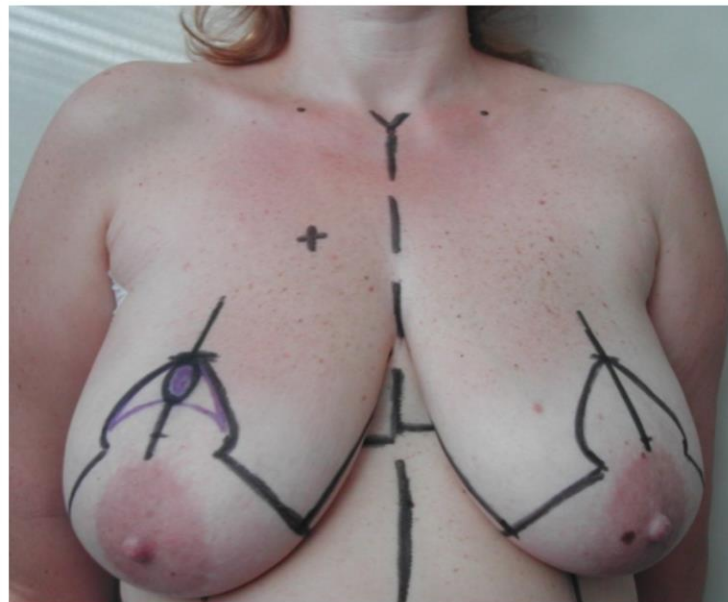


Inferior quadrants: unfavourable tumor location



**Large
tumors/inferior
quadrants**





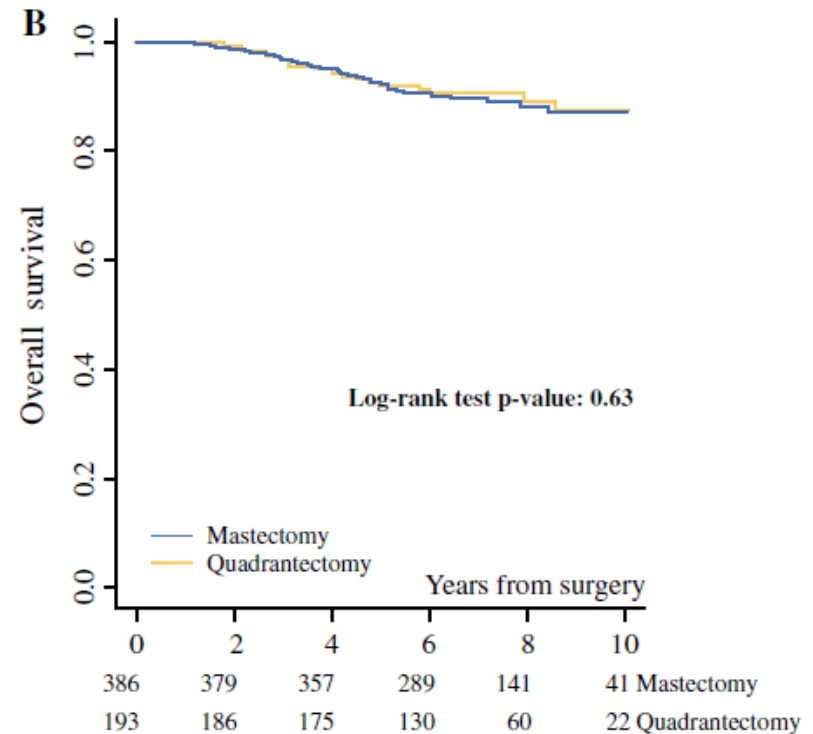
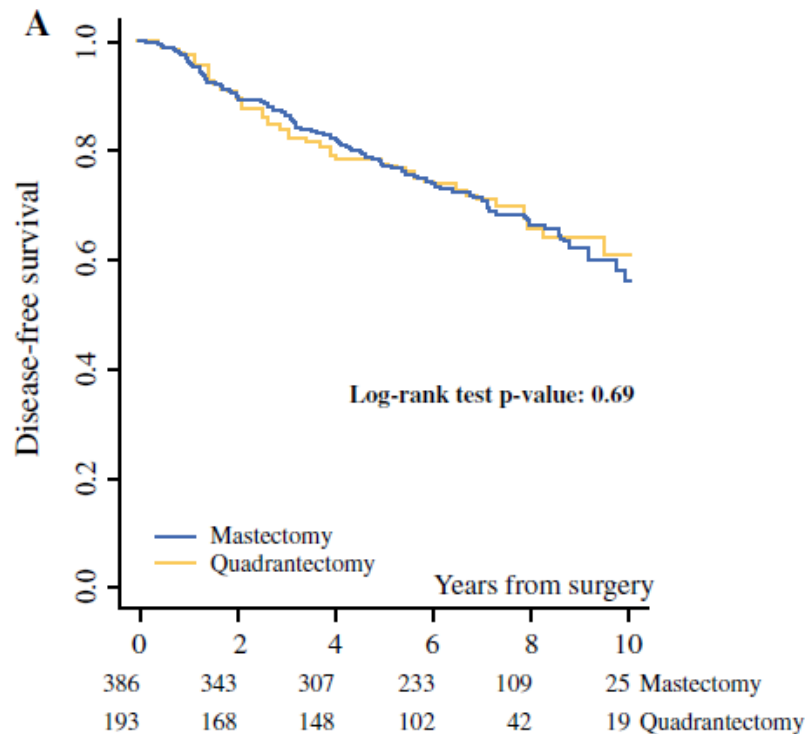


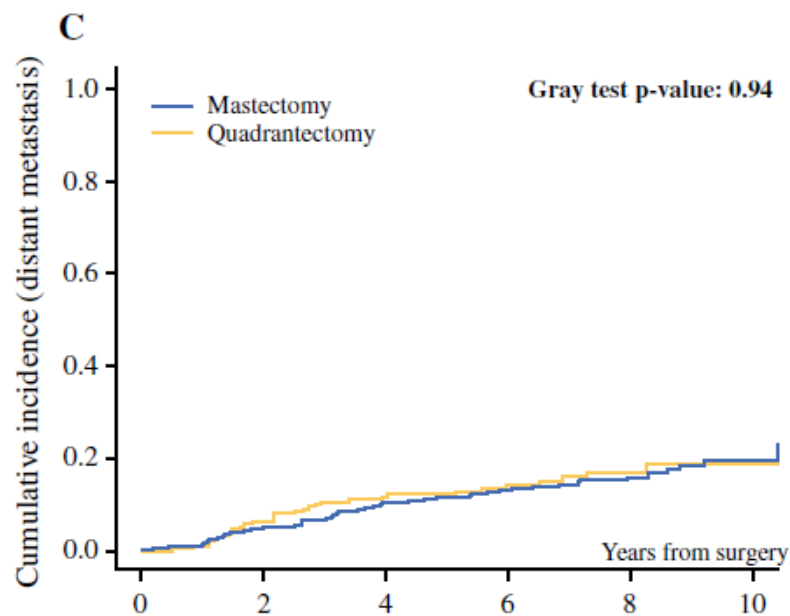
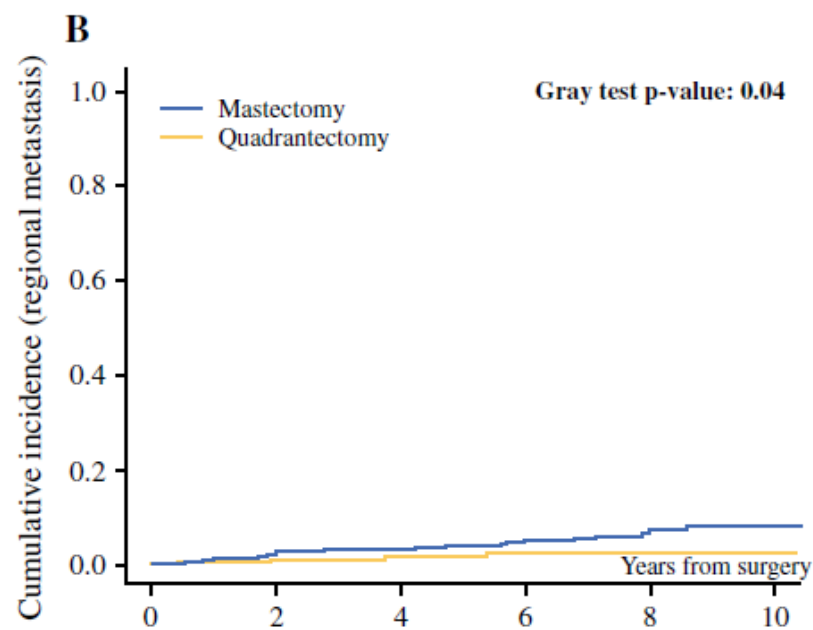
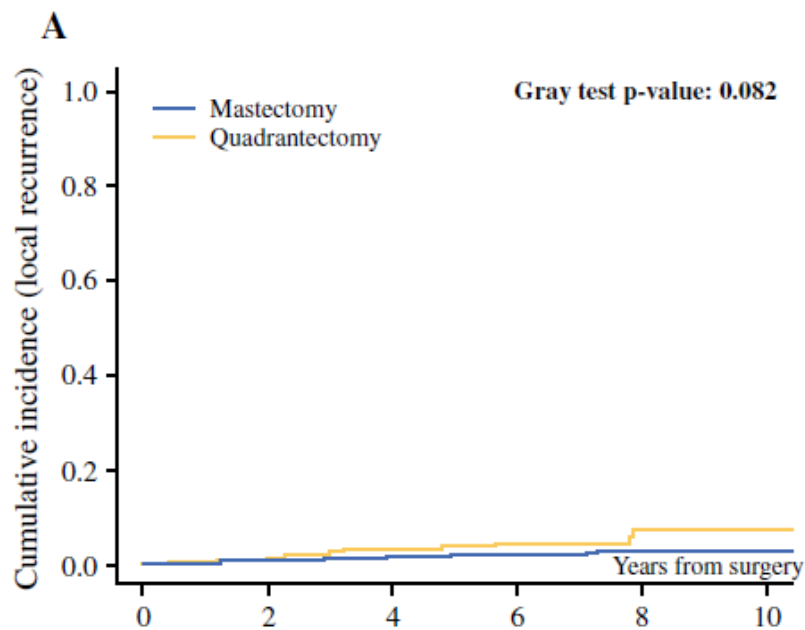
ORIGINAL ARTICLE – BREAST ONCOLOGY

Oncoplastic Breast-Conserving Surgery for Tumors Larger than 2 Centimeters: Is it Oncologically Safe? A Matched-Cohort Analysis

Francesca De Lorenzi, MD, PhD¹, Pietro Loschi, MD¹, Vincenzo Bagnardi, PhD^{2,3}, Nicole Rotmensz, MSc², Gabriel Hubner, MD¹, Giovanni Mazzarol, MD⁴, Roberto Orecchia, MD⁵, Viviana Galimberti, MD⁶, Paolo Veronesi, MD⁶, Marco Angelo Colleoni, MD⁷, Antonio Toesca, MD⁶, Nickolas Peradze, MD⁶, and Rietjens Mario, MD, PhD¹

Survival rates of the two groups





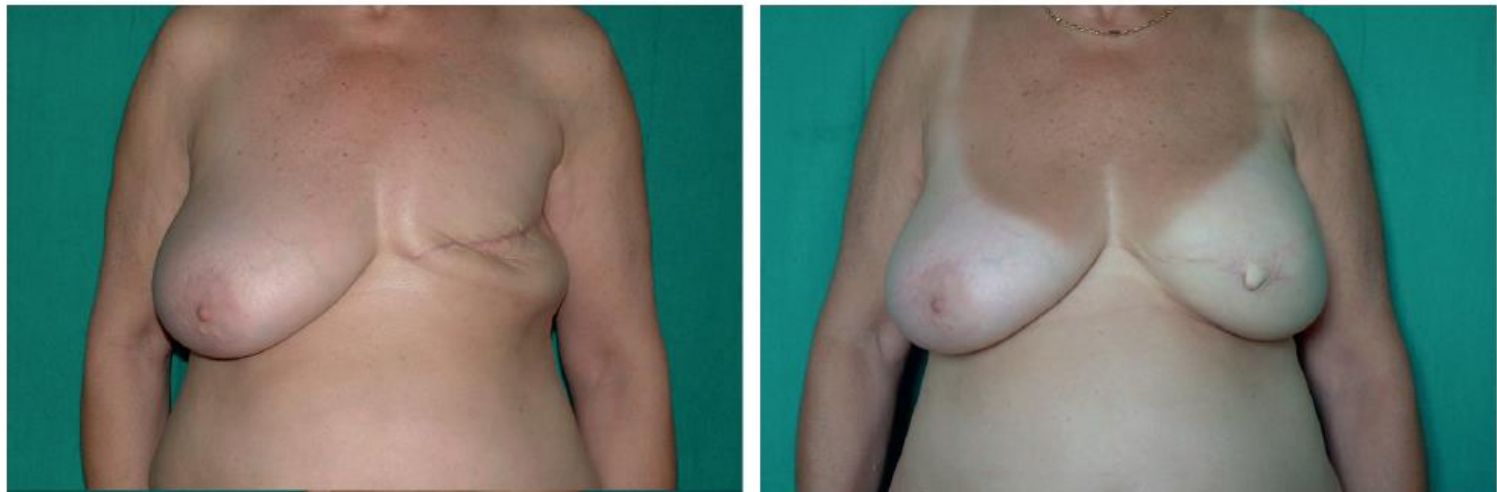
Cumulative incidence of local recurrence (a), regional metastasis (b), and distant metastasis (c) by group

One-stage breast reconstruction techniques in elderly patients to preserve quality of life

M. MARUCCIA¹, M. MAZZOCCHI², L.A. DESSY¹, M.G. ONESTI¹

¹Department of Surgery "P. Valdoni", Unit of Plastic and Reconstructive Surgery Sapienza University, Rome, Italy

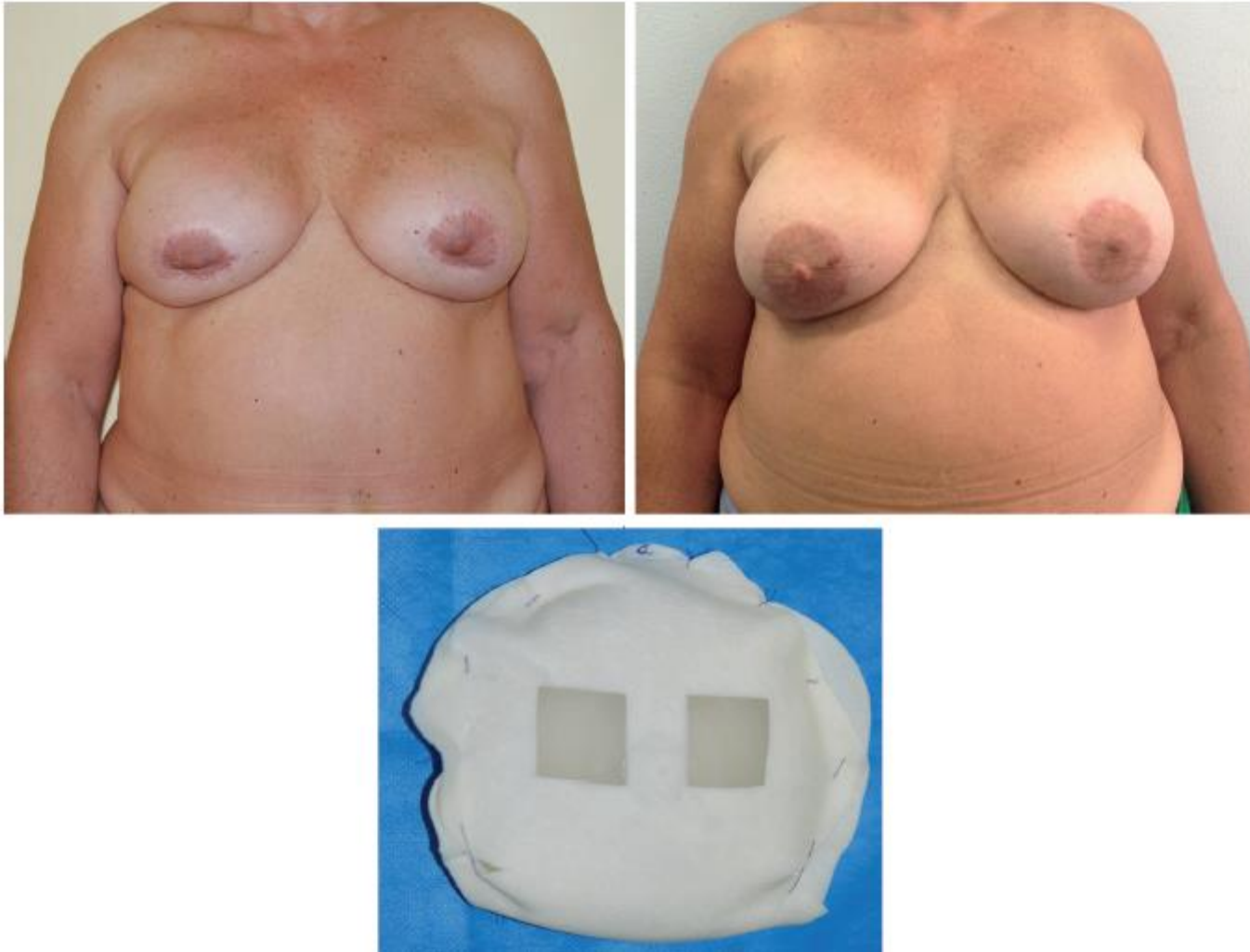
²Department of Plastic and Reconstructive Surgery, University of Perugia, Perugia, Italy



Preoperative image of the outcomes of radical mastectomy of a 72-year-old patient. **(B)** Patient underwent a breast reconstruction with permanent inflatable expanders in a sub-muscular position (Group A) and nipple reconstruction with local flap 6 months later (1-year follow-up).



(A) Image of a 67-year-old patient with ductal breast bilateral cancer. Right hematoma caused by trauma from biopsy. **(B)** This elderly woman underwent nipple skin sparing mastectomy and immediate breast reconstruction with Acellular Dermal Matrix and sub-muscular implant (1-year follow-up).



(A) Image of a 75-year-old patient with capsular contracture after nipple sparing mastectomy and reconstruction with sub-muscular implant 32 years ago. **(B)** Outcomes of capsulectomy and breast reconstruction with Braxon® Acellular Dermal Matrix and subcutaneous implant (18-month follow-up) (Group C). **(C)** Posterior view of the Braxon® Acellular Dermal Matrix with implant.

A total of 840 women underwent breast reconstruction, of whom 138 elderly women received one-stage breast reconstruction. There were 118 cases (85.5%) of monolateral reconstructions and 20 cases (14.5%) of bilateral reconstructions, resulting in 138 breast reconstructions. These were performed with permanent inflatable expanders in the sub-muscular position (Group A, n= 50), with acellular dermal matrix and partial sub-muscular anatomic implant (Group B, n= 50), and with Braxon® acellular dermal matrix and anatomic implant with muscle-sparing technique (Group C, n= 38). The EORTC questionnaires showed the best results in Group C regarding the quality of life

Table II. Quality of life (QLQ-C30).

Variable	Mean score		
	Group A (no. = 50)	Group B (no. = 50)	Group C (no. = 38)
Global health status	47	48.5	54
Functioning domains	45.5	46	49.5
Symptoms	35	28	22

Table III. Quality of life (QLQ-BR23).

Variable	Mean score		
	Group A (no. = 50)	Group B (no. = 50)	Group C (no. = 38)
Functioning domains	61	63	71
Symptoms	42	39.5	29

Radioterapia intraoperatoria

Riduzione della Radioterapia



RT esterna frazionata

vs.

Dose intera RT intraoperatoria (ELIOT, 21Gy)

Risultato



ELIOT Dose completa
(21Gy) o BOOST
(12Gy) somministrata
in tre minuti



SCELTA IDEALE DEI PAZIENTI

- Età e stato menopausale
- Dimensione e focalità del tumore (MRI, tomosintesi)
- Caratteristiche biologiche (biopsia preoperatoria)
- Stato dei linfonodi (PET, SLNB)
- Profilo genetico (MammaPrint, Oncotype)

FAST-LIKE nelle pazienti in post menopausa

- ***Schema***

- 5.7 Gy in 5 frazioni (28.5 Gy) 1 volta a settimana per 5 settimane (≥ 65 anni , T1-T3 N0-N1, problematiche logistiche/cliniche)

- ***Tecnica***

- IMRT
- 3D convenzionale

Studio in collaborazione con Psico-Oncologia sulla QoL



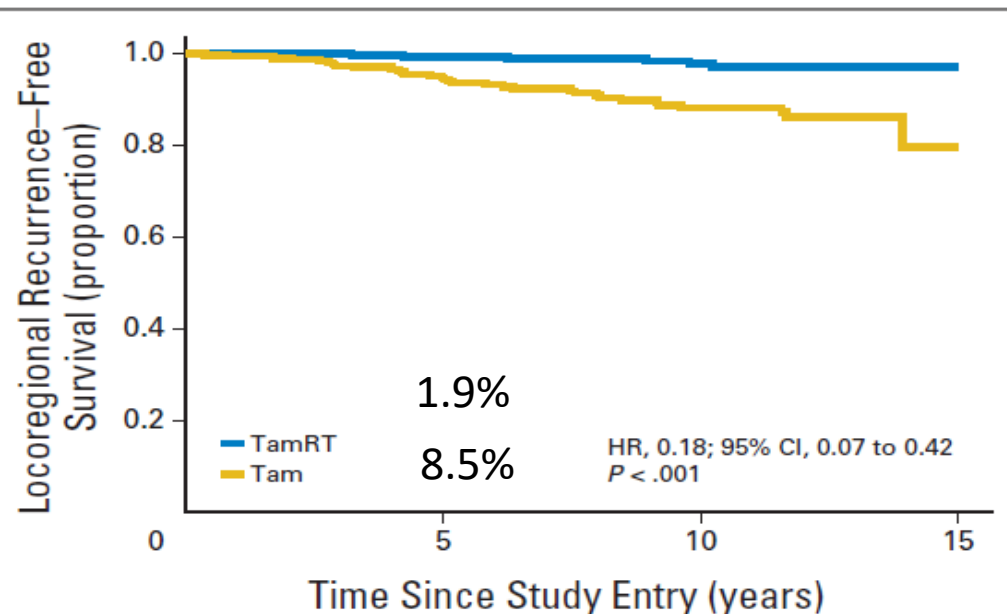
9 · JULY 1 2013

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Lumpectomy Plus Tamoxifen With or Without Irradiation in Women Age 70 Years or Older With Early Breast Cancer: Long-Term Follow-Up of CALGB 9343

Kevin S. Hughes, Lauren A. Schnaper, Jennifer R. Bellon, Constance T. Cirincione, Donald A. Berry,
Beryl McCormick, Hyman B. Muss, Barbara L. Smith, Clifford A. Hudis, Eric P. Winer, and William C. Wood



No. at risk

TamRT	317	261	162	7
Tam	319	243	144	2

SEMPRE DISCUSSIONE AMBULATORIALE

Nessun trattamento, se profilo biologico ed istologico favorevole

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

SEPTEMBER 2, 2004

VOL. 351 NO. 10

Tamoxifen with or without Breast Irradiation in Women 50 Years of Age or Older with Early Breast Cancer

Anthony W. Fyles, M.D., David R. McCready, M.D., Lee A. Manchul, M.D., Maureen E. Trudeau, M.D.,
Patricia Merante, R.N., Melania Pintilie, M.Sc., Lorna M. Weir, M.D., and Ivo A. Olivetto, M.D.

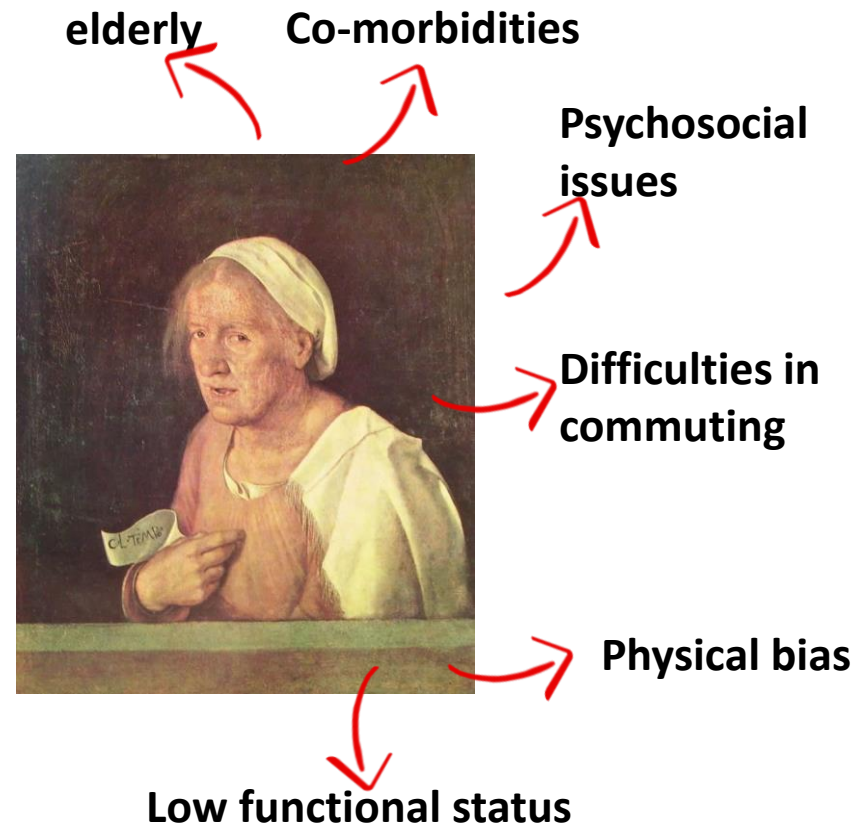
**T1N0:
9.9% (TAM) vs. 4.4% (TAM+ RT)
FU 8 aa (Update 2006)**

5-fraction schedule: once a week

**5.7 Gy-6.5 Gy to WB once a wk x 5 wks
± SEQ/SIB boost of 6.5 Gy x 1-5 fr**

Features from literature (Maher, Rostom, Baillet, Ortholan, Kirowa, Dragun, Monten, Martin, Rovea)

age	Mean 73 (50-81)
N° pts	Mean 155 (30-367)
FU	mean 46 months (36-93)
T stage	T1-T2: mean 77%; T3-T4: mean 23%
N stage	N0: 57%-100%
LC	Mean 87% (>80% for T1-2; ~60% for T3, <i>Maher 1995</i>)
OS	Mean 85.5%
Acute tox	G≥2 12-43%
Late tox	G1-G2: 22-36%; G3<5%
cosmesis	Good/excellent: 77%-86% Change in appearance; 23%-45%





Trattamento ipofrazionato whole breast a fasci esterni

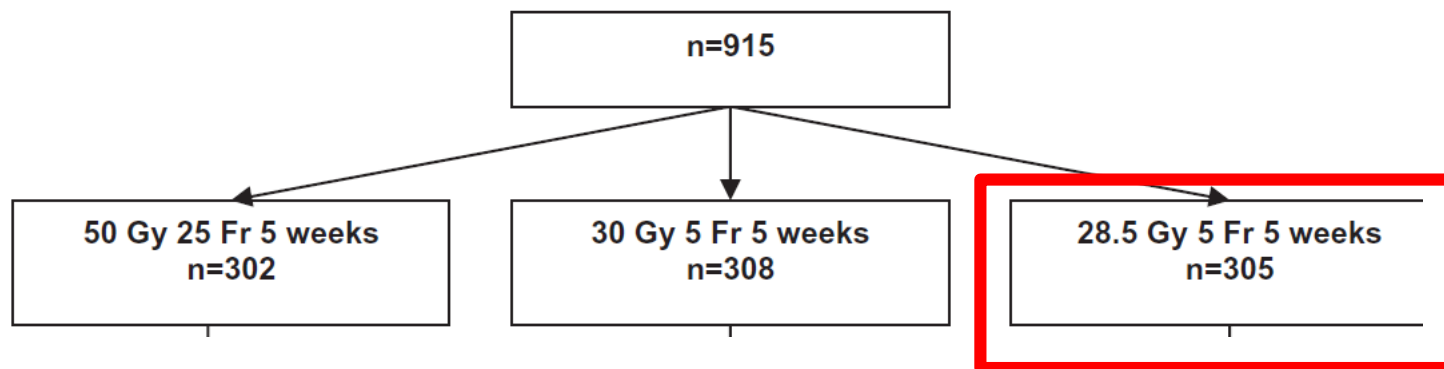
FAST-LIKE



Phase III randomised trial

First results of the randomised UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer (CRUKE/04/015)

The FAST Trialists group¹



Int. J. Radiation Oncology Biol. Phys., Vol. 61, No. 1, pp. 154-162, 2005
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0360-3016/05/\$ - see front matter
doi:10.1016/j.ijrobp.2004.04.059

CLINICAL INVESTIGATION

Breast

LONG-TERM RESULTS OF ADJUVANT HYPOFRACTIONATED RADIOTHERAPY FOR BREAST CANCER IN ELDERLY PATIENTS

CÉCILE ORTHOLAN, M.D.,* JEAN-MICHEL HANNOUN-LÉVY, M.D.,* JEAN-MARC FERRERO, M.D.,†
RÉMY LARGILLIER, M.D.,‡ AND ADEL COURDI, M.D.*

Departments of *Radiotherapy and †Medical Oncology, Centre Antoine-Lacassagne, Nice, France



doi:10.1016/j.ijrobp.2008.11.005

CLINICAL INVESTIGATION

Breast

BREAST-CONSERVING TREATMENT IN THE ELDERLY: LONG-TERM RESULTS OF ADJUVANT HYPOFRACTIONATED AND NORMOFRACTIONATED RADIOTHERAPY

YOULIA M. KIROVA, M.D.,* FRANCOIS CAMPANA, M.D.,* ALEXIA SAVIGNONI, M.D.,† FATIMA LAKI, M.D.,‡
MARIUS MURESAN, M.D.,* REMI DENDALE, M.D.,* MARC A. BOLLET, M.D.,* REMY J. SALMON, M.D.,†
AND ALAIN FOURQUET, M.D.,* FOR THE INSTITUT CURIE BREAST CANCER STUDY GROUP

Departments of *Radiotherapy, †Statistics, and ‡Surgery, Institut Curie, Paris, France

Int. J. Radiation Oncology Biol. Phys., Vol. 75, No. 1, pp. 76-81, 2009
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0360-3016/09/\$ - see front matter

International Journal of
Radiation Oncology
biology • physics

www.redjournal.org

Original Study

Once-Weekly Hypofractionated Whole-Breast Radiotherapy After Breast-Conserving Surgery in Older Patients: A Potential Alternative Treatment Schedule to Daily 3-Week Hypofractionation

Paolo Rovea,¹ Alessandra Fozza,¹ Pierfrancesco Franco,² Chiara De Colle,²
Alessandra Cannizzaro,² Anna Di Dio,³ Francesca De Monte,³ Claudia Rosmino,¹
Andrea Riccardo Filippi,² Riccardo Ragona,² Umberto Ricardi²

Investigation: Breast Cancer

Phase 2 Trial of Once-Weekly Hypofractionated Breast Radiation: First Report of Acute Toxicity, Feasibility, and Patient Satisfaction

Anthony E. Dragan, MD,* Amy R. Quillo, MD,† Elizabeth C. Riley, MD,†
Teresa L. Roberts, RN,* Allison M. Hunter, BA,* Shesh N. Rai, PhD,§
Glenda G. Callender, MD,† Dharamvir Jain, MD,† Kelly M. McMasters, MD, PhD,†
and William J. Spanos, MD*

Departments of *Radiation Oncology, †Surgical Oncology, ‡Medical Oncology, and §Biostatistics and Epidemiology,
University of Louisville School of Medicine, James Graham Brown Cancer Center, Louisville, Kentucky

Phase III randomised trial

First results of the randomised UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer (CRUKE/04/015)

Primary endpoint:
change in photographic breast appearance

Number
randomised

Allocated
fractionation
schedule

α/β :
2.6 Gy

Higher fractionation
sensitivity

n=915
2004-2007

50 Gy 25 Fr 5 weeks
n=302

30 Gy 5 Fr 5 weeks
n=308

**≥ 50 years, BCS, invasive,
 $T < 3$ cm, N0, any breast size (~ 10% large)**

TAM:75%

28.5 Gy 5 Fr 5 weeks
n=305

Test arms equivalent for α/β 4 or 3

56 Gy

51.4 Gy

Change in photographic breast appearance at 2 years by fractionation schedule.

	Fractionation schedule			Total, N = 729 (%)	Risk ratio for 30 Gy vs 50 Gy (95% CI), p-value for trend	Risk ratio for 28.5 Gy vs 50 Gy (95% CI), p-value for trend	Risk ratio for 30 Gy vs 28.5 Gy (95% CI), p-value for trend
	50 Gy, N = 239 (%)	30 Gy, N = 248 (%)	28.5 Gy, N = 242 (%)				
No change	189 (79.1)	160 (64.5)	184 (76.0)	533 (73.1)	1, $p < 0.001$	1, $p = 0.26$	1, $p = 0.002$
Mild change	46 (19.2)	65 (26.2)	49 (20.2)	160 (22.0)	1.48 (1.06–2.05)	1.07 (0.75–1.54)	1.37 (1.00–1.90)
Marked change	4 (1.7)	23 (9.3)	9 (3.7)	36 (4.9)	6.06 (2.14–17.20)	2.25 (0.70–7.18)	2.70 (1.28–5.67)

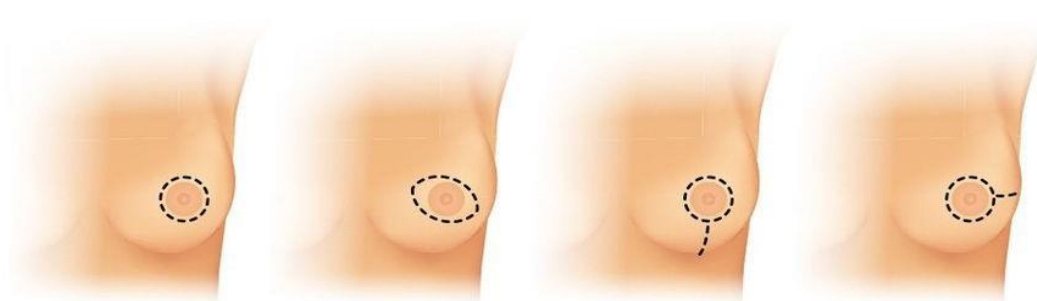
Mild+
marked 9.5% 17.3% 11.1%

Chirurgia Oncoplastica

Approccio multidisciplinare



NIPPLE SPARING MASTECTOMY



Mastectomia Conservativa in IEO

- SOPRAVVIVENZA GLOBALE -

93.5%



Mastectomia Conservativa

Skin-sparing mastectomy (SSM)

- Durante la skin-sparing il chirurgo risparmia la maggior parte della pelle del seno per creare una tasca che viene riempita con la protesi mammaria o con tessuto della paziente

Toth BA et al. Plast Reconstr Surg 1991

Nipple-sparing mastectomy (NSM)

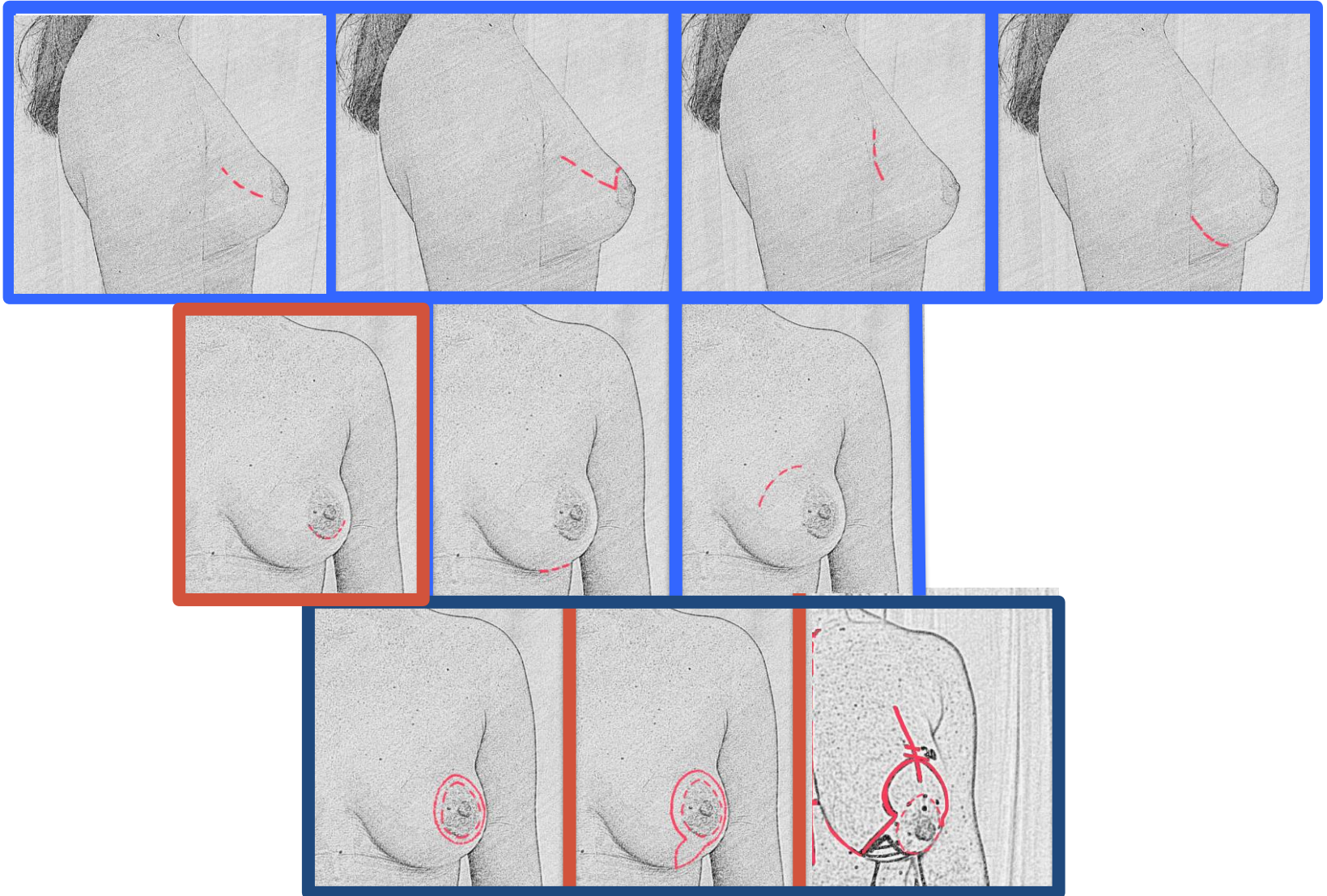
- Nipple-sparing mastectomy è simile alla SSM, ma la vera innovazione conservativa è che viene conservato il complesso areola-capezzolo

Freeman BS et al. Plast Reconstr Surg Transplant Bull 1962

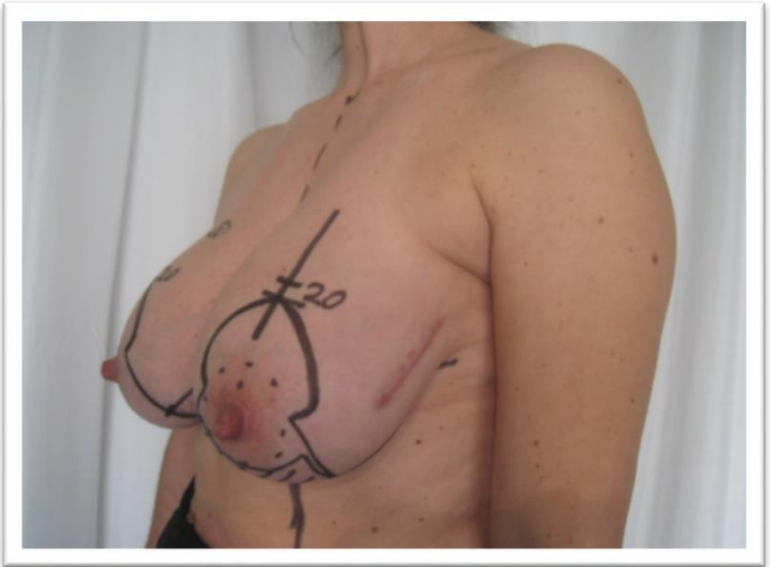
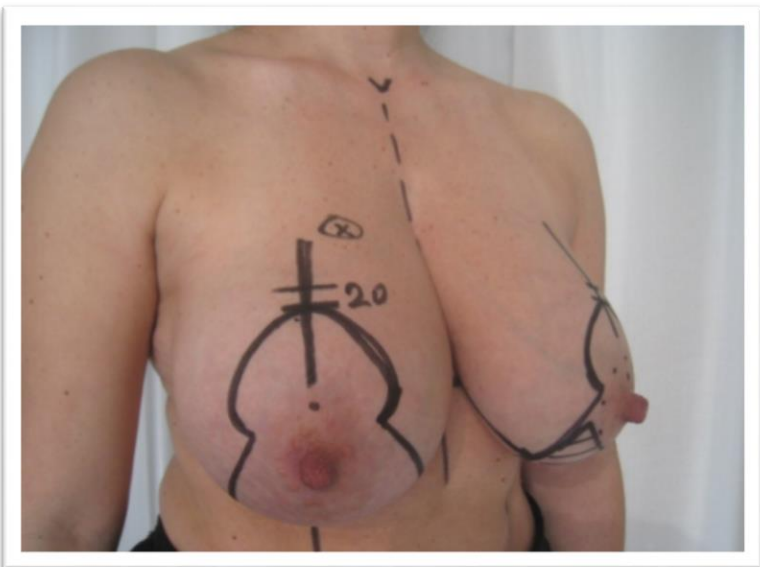
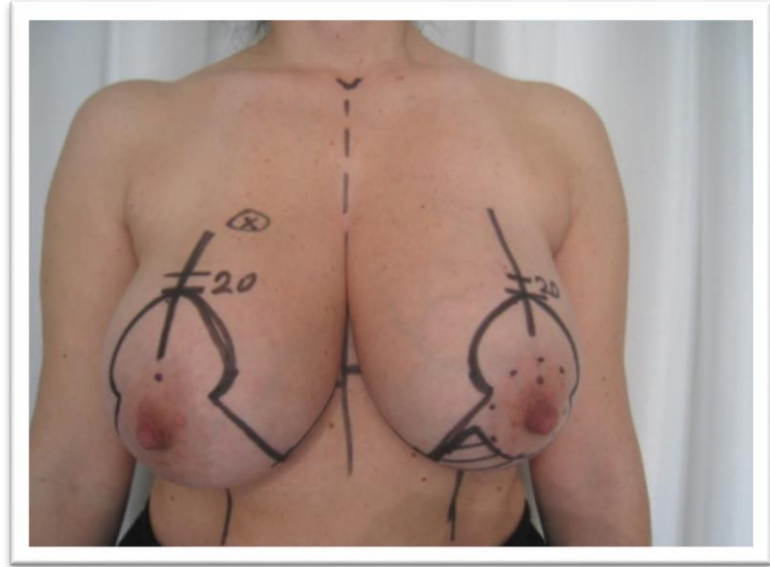
Kissin MW et al. J Surg 1987

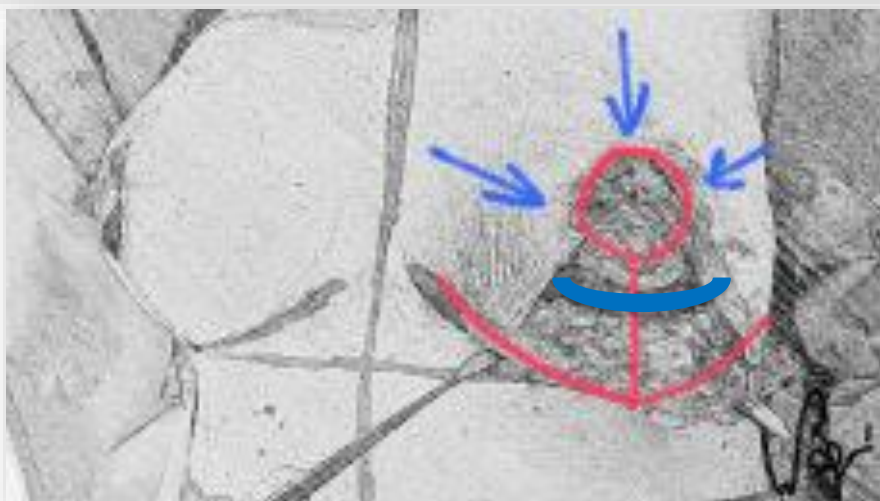
Entrambe le tecniche sono associate a migliori risultati estetici ed a una maggiore soddisfazione delle pazienti

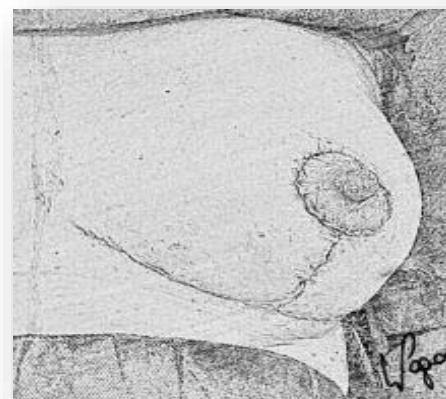
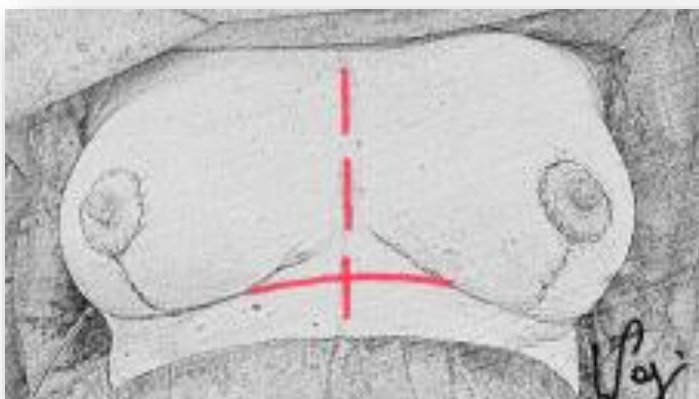
Skin incisions for NSM



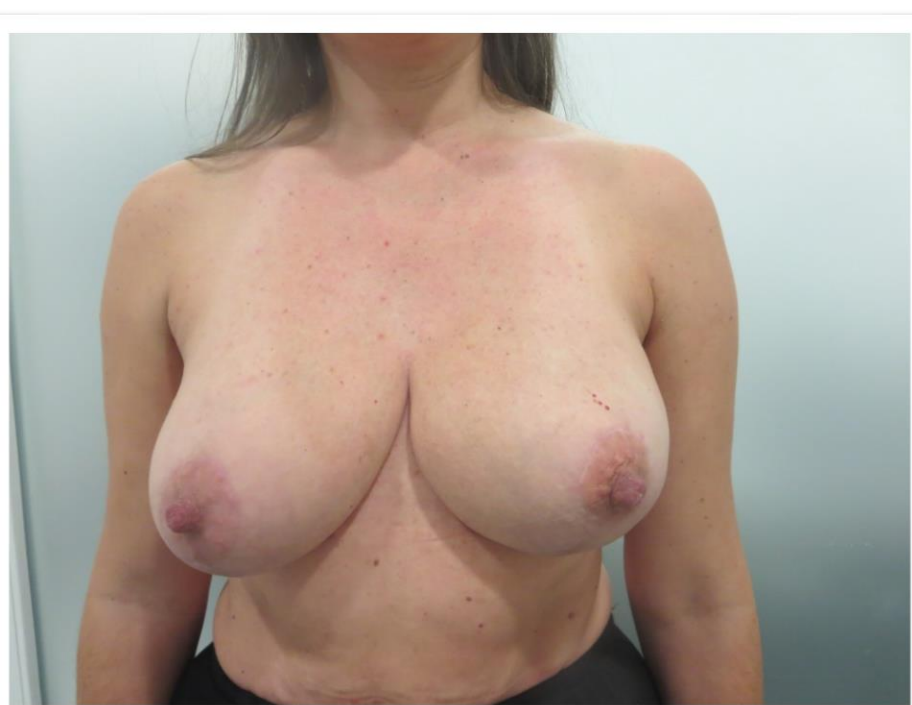
WISE PATTERN







Result after 12 months



Nipple-sparing mastectomies at IEO

From January 2003 to December 2016

4,801 patients



A diagram showing the distribution of 4,801 patients. Two red arrows originate from the text '4,801 patients' and point to two separate blue boxes below. The left box contains '4,109 Invasive cancers' and the right box contains '692 In situ cancers'.

4,109

Invasive cancers

692

In situ cancers

Nipple-sparing mastectomies at IEO

Follow-up: 2003 through 2011

1,989 patients

```
graph TD; A["1,989 patients"] --> B["1,711*  
Invasive cancers"]; A --> C["278  
in situ cancers"];
```

*1,711**

Invasive cancers

278

in situ cancers

*140 (8,2%) neoadjuvant treatment

1,711 invasive cancers (Jan 2003 - Dec 2011)

Events

Event	N (%)
Local recurrence	91 (5.3)
Axillary recurrence	27 (1.6)
Regional lymph node recurrence	28 (1.6)
Simultaneous local and regional	6 (0.4)
Distant metastasis	197 (11.5)
Other primary tumor	90 (5.3)
Total events	439 (25.6)

Median follow-up 94 months, IQR 70-117

1,711 invasive cancers (Jan 2003 - Dec 2011)

NAC removal

Cause	n. (%)
Invasive local recurrence	18 (1.0)
Non-invasive local recurrence	9(0.3)
Necrosis	60 (3.5)
Total	87 (5.1)

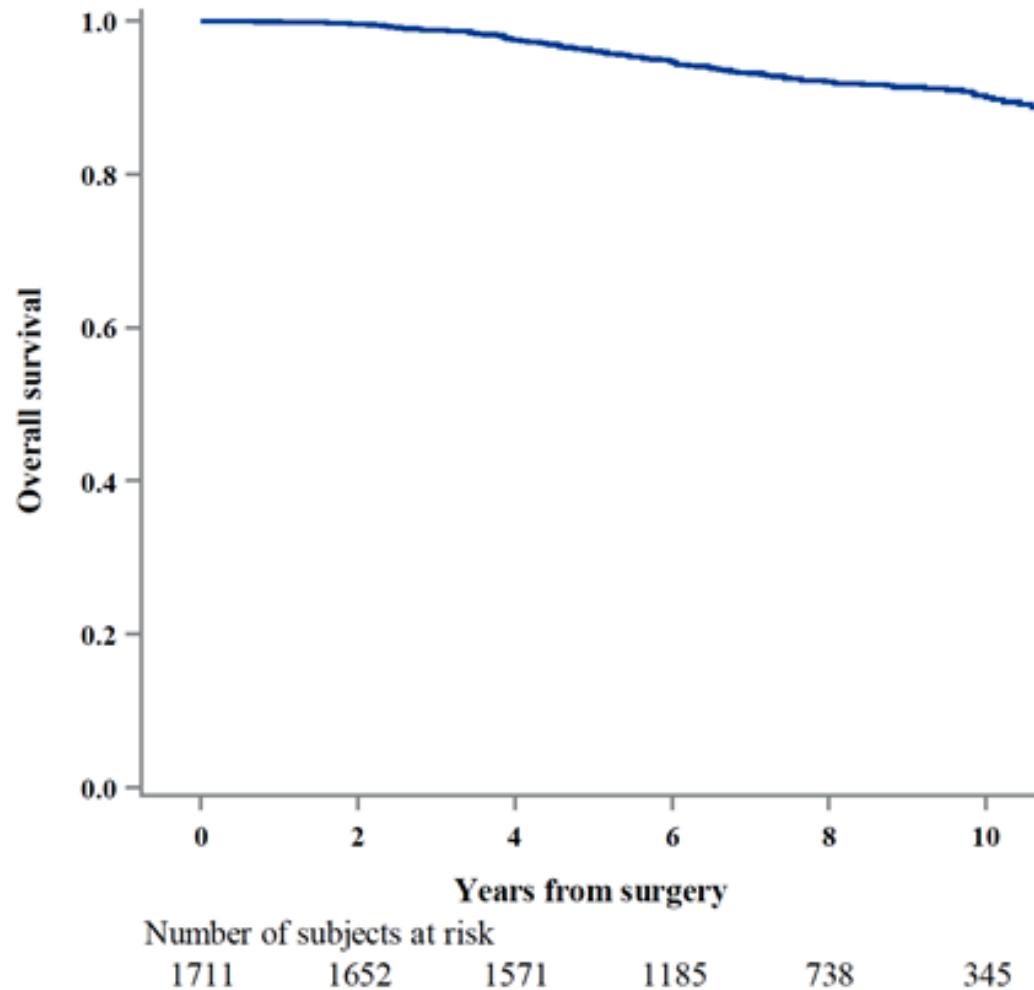
1,711 invasive cancers (Jan 2003 - Dec 2011)

Deaths

Cause	N (%)
Breast cancer	108 (5.5)
Other cancer	3 (0.2)
Cardiovascular disease	1 (0.1)
Unknown	16 (0.9)
Total	128 (7.5)

Median follow-up 94 months, IQR 70-117

Overall survival in the invasive group



278 in situ cancers (Jan 2003 - Dec 2011)

Events

Event	N (%)
Local recurrence	11 (4.0)
Axillary recurrence	-
Regional lymph node recurrence	-
Simultaneous local and regional	3 (1.1)
Distant metastasis	2 (0.7)
Other cancer	17 (6.1)
Total events	33 (11.9)

Median follow-up 94 months, IQR 70-117

278 in situ cancers (Jan 2003 - Dec 2011)

NAC removal

Cause	n. (%)
Invasive local recurrence	18 (1.0)
Non-invasive local recurrence	5 (1.8)
Necrosis	6 (2.2)
Total	29 (5.0)

278 in situ cancers (Jan 2003 - Dec 2011)

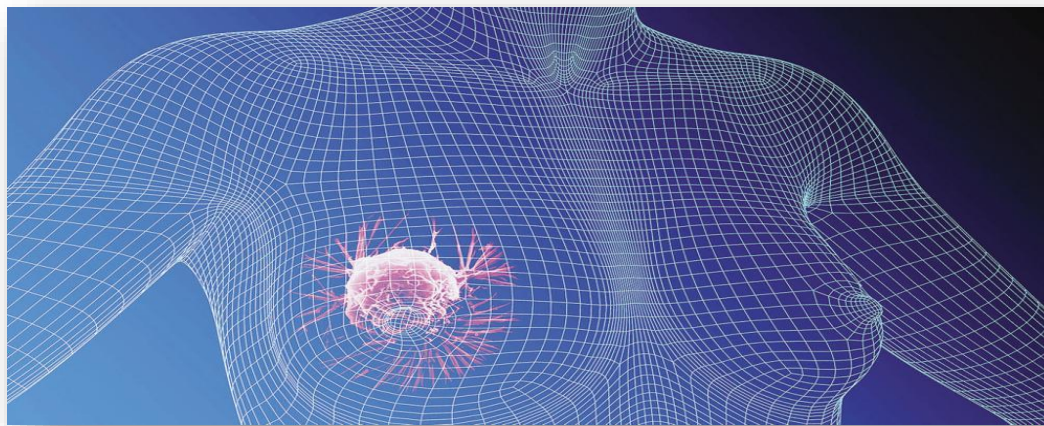
Deaths

Cause	N (%)
Breast cancer	1 (0.4)
Other cancer	1 (0.4)
Unknown	1 (0.4)
Total	3 (1.1)

Median follow-up 94 months, IQR 70-117

TRATTAMENTO CHIRURGICO

- Chirurgia conservativa e ricostruttiva
- Conservazione linfonodi ascellari



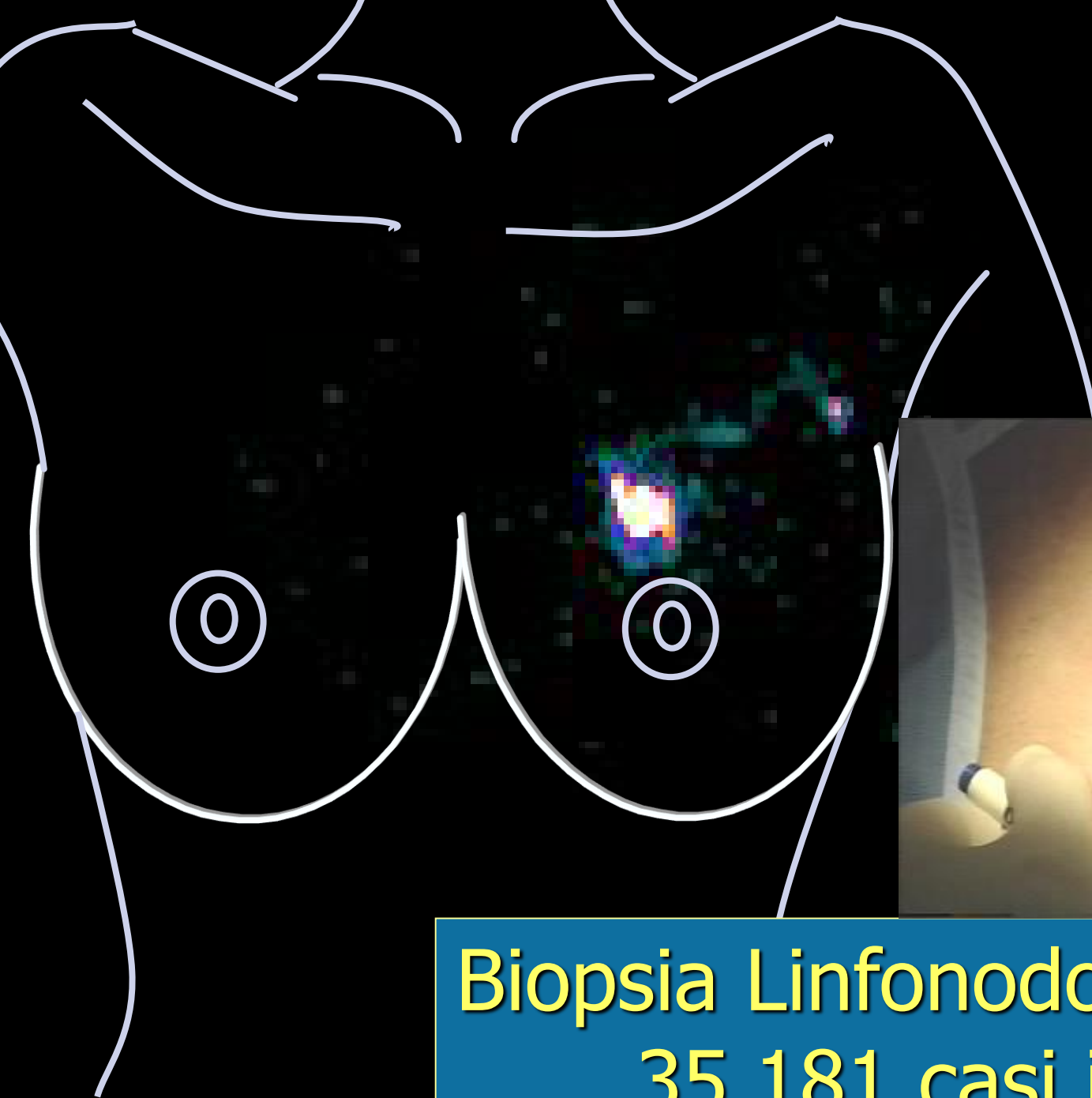
Vecchio Paradigma:



“La dissezione ascellare è
una componente necessaria
del trattamento del tumore
al seno”

Changelling

- La diagnosi sempre più precoce ha portato a percentuali ancora più basse di pazienti con ascella positiva
- L'importanza dell'AD come procedura di stadiazione è diminuita
- Così l'urgenza è stata quella di trovare un approccio più conservativo per il cavo ascellare
- Questo è accaduto negli anni '90 con lo sviluppo della BLS



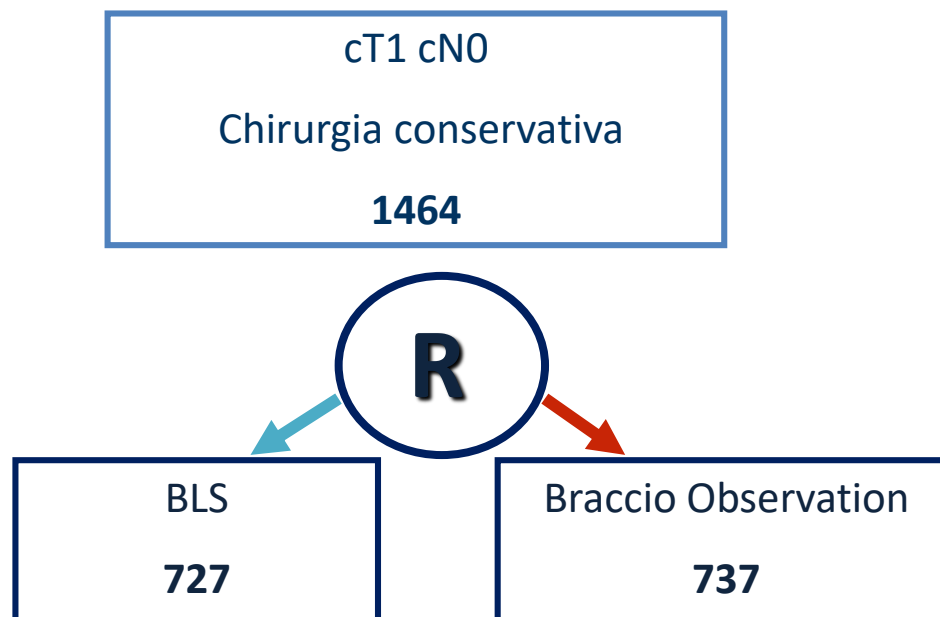
Biopsia Linfonodo Sentinella
35.181 casi in IEO



TRIAL IEO S637/311 SOUND

2012-2017 · 1464 casi cT1 cN0 · randomizzati

- Inizio arruolamento:
26/01/2012
- Chiusura arruolamento:
30/06/2017



CENTRO	N paz randomizzati	Data attivazione
0001 - IEO	685	Gennaio 2012
0002 - MANTOVA	41	Dicembre 2012
0003 - INT MILANO	146	Febbraio 2013
0004 - BRESCIA	25	Aprile 2013
0005 - COMO	45	Giugno 2013
0006 - HUMANITAS	4	Giugno 2013
0007 - TORINO	191	Giugno 2013
0009 - BOLZANO	24	Luglio 2013
0010 – PIACENZA	68	Novembre 2013
0011 – NAPOLI FEDERICO II	60	Dicembre 2013
0012 – CAGLIARI	35	Marzo 2014
0013 – NAPOLI INT	10	Marzo 2014
0014 – VALENCIA	20	Ottobre 2014
0015 – BERNA	8	Settembre 2015
0016 – CASTELLANZA	3	Aprile 2015
0017 – SANTIAGO DEL CILE	3	Giugno 2015
0018 – ROMA	0	Luglio 2015
0019 – PAVIA	58	Gennaio 2016
0020 – MILANO SAN RAFFAELE	38	Aprile 2016
TOTALE	1464	



Dettaglio linfonodi sentinella positivi Pazienti braccio BLS

	N	%
pN1mi	36	5.10
pN1a	53	7.51
<i>Nessun ulteriore Inn positivo</i>	39	5.52
<i>Un ulteriore Inn positivo</i>	12	1.70
<i>Due Inn positivi</i>	2	0.28
pN2	4	0.57
TOTALE	93	13.17

Attuali indicazioni e raccomandazioni per il trattamento del cavo ascellare

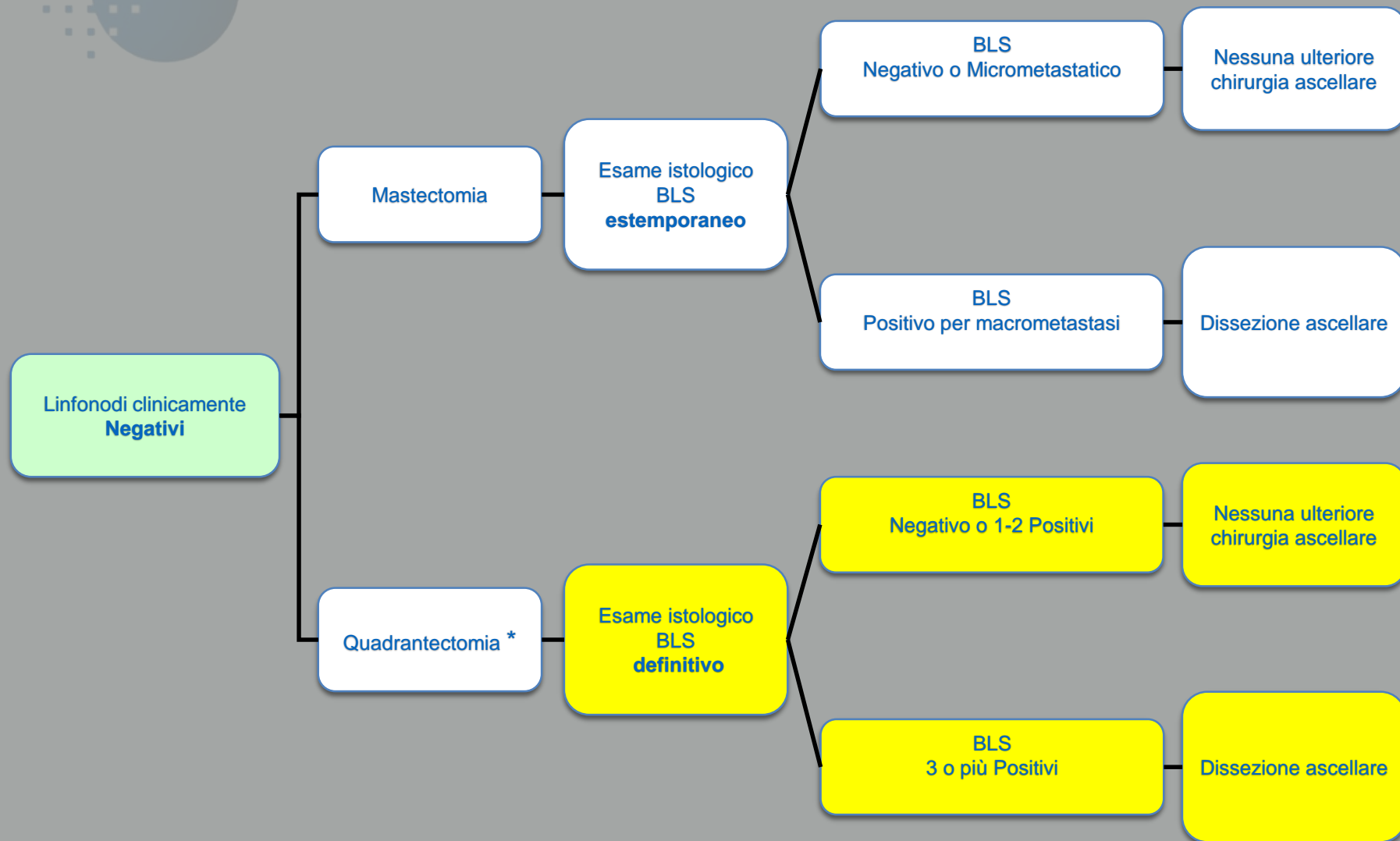


IEO

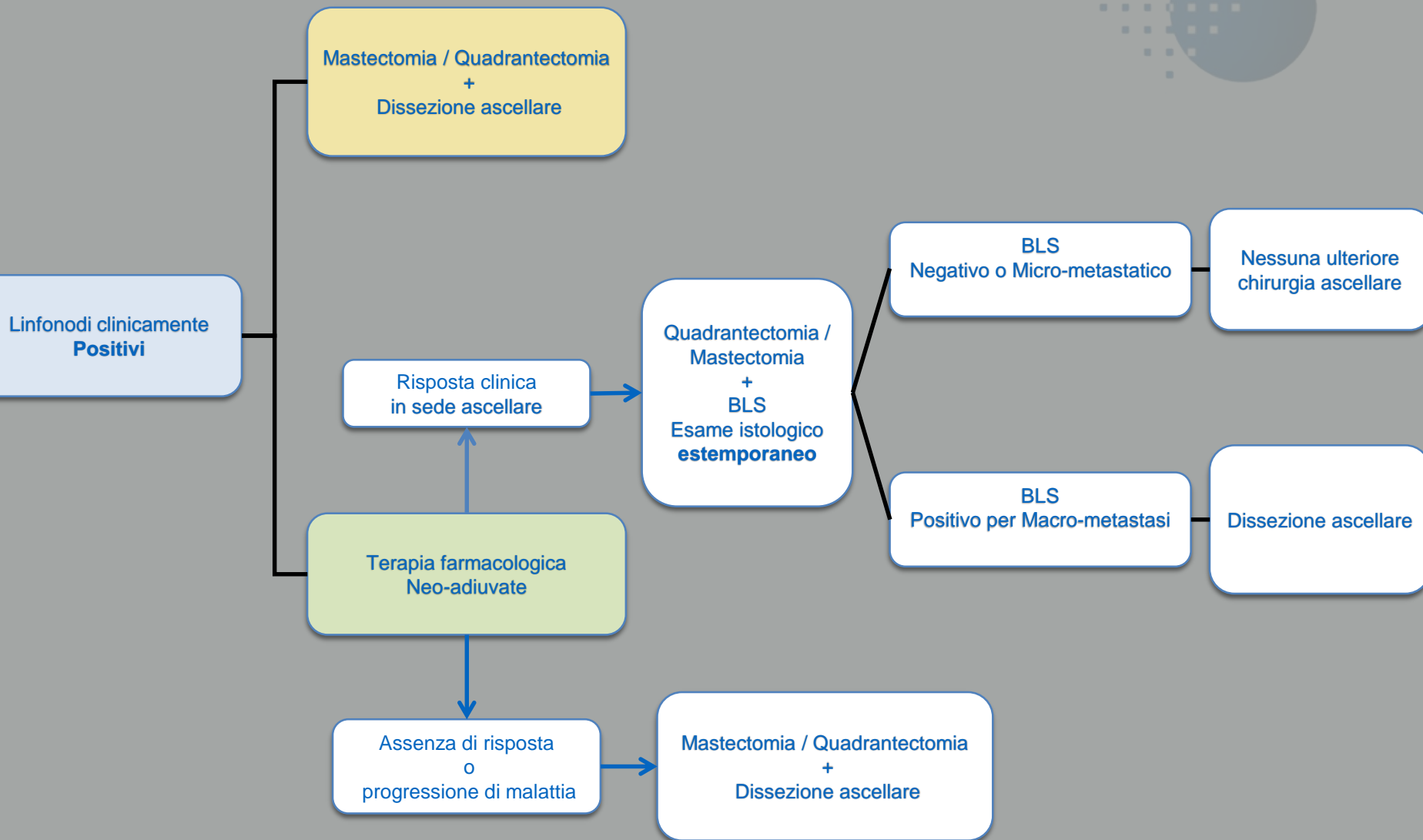
Istituto Europeo di Oncologia



■ Linfonodi clinicamente negativi e tumore mammario infiltrante



■ Linfonodi clinicamente positivi



TRATTAMENTO MEDICO

De-escalating and Escalating Treatments for Early Stage Breast Cancer: The St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer 2017



15th St.Gallen International Breast Cancer Conference 2017
Primary Therapy of Early Breast Cancer – Evidence, Controversies, Consensus
15–18 March 2017

BCC 2017



Information
St.Gallen Oncology Conferences (SONK)
c/o Tumor and Breast Center ZeTuP
Rorschacherstrasse 150
CH-9006 St.Gallen/Switzerland
info@oncoconferences.ch
www.oncoconferences.ch

Welcome dear colleagues, to „St.Gallen-2017“ in Vienna !

Endocrine Therapy: Postmenopausal patients

- Tamoxifen alone is still appropriate for some patients
- An AI should be used at some point during the course of adjuvant therapy
- Factors that favored the use of an AI include N+, high Ki67, high grade, lobular histology, and HER2 positivity
- In women at high risk of recurrence, favored the use of an aromatase inhibitor as initial therapy

Endocrine Therapy

Extended Therapy

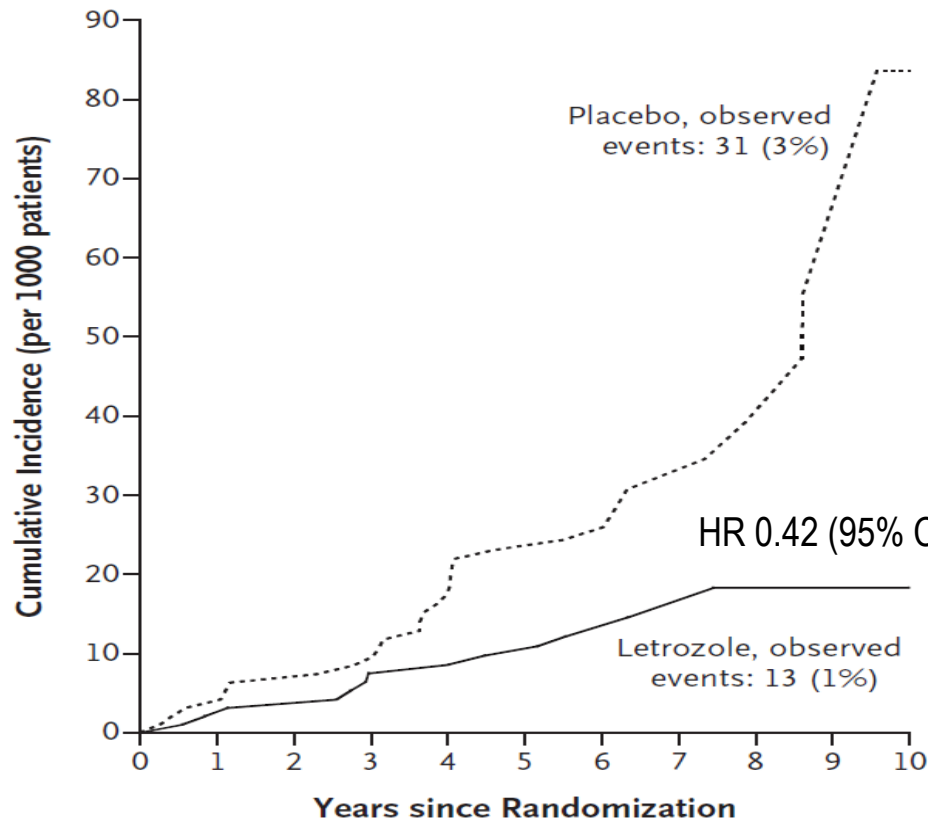
Postmenopausal

- **Options include** extended tamoxifen to 10 years, extended AI therapy to 10 years, or five years of tamoxifen and then switching to an AI
- Importance **of patient preference and tolerability** in this treatment decision
- Extended therapy:
 - associated with ongoing menopausal symptoms and risks to bone health
 - yield only modest benefits in terms of preventing breast cancer recurrence, especially in those who have completed 5 years of AI therapy

Extended adjuvant endocrine therapy – Clinical trials

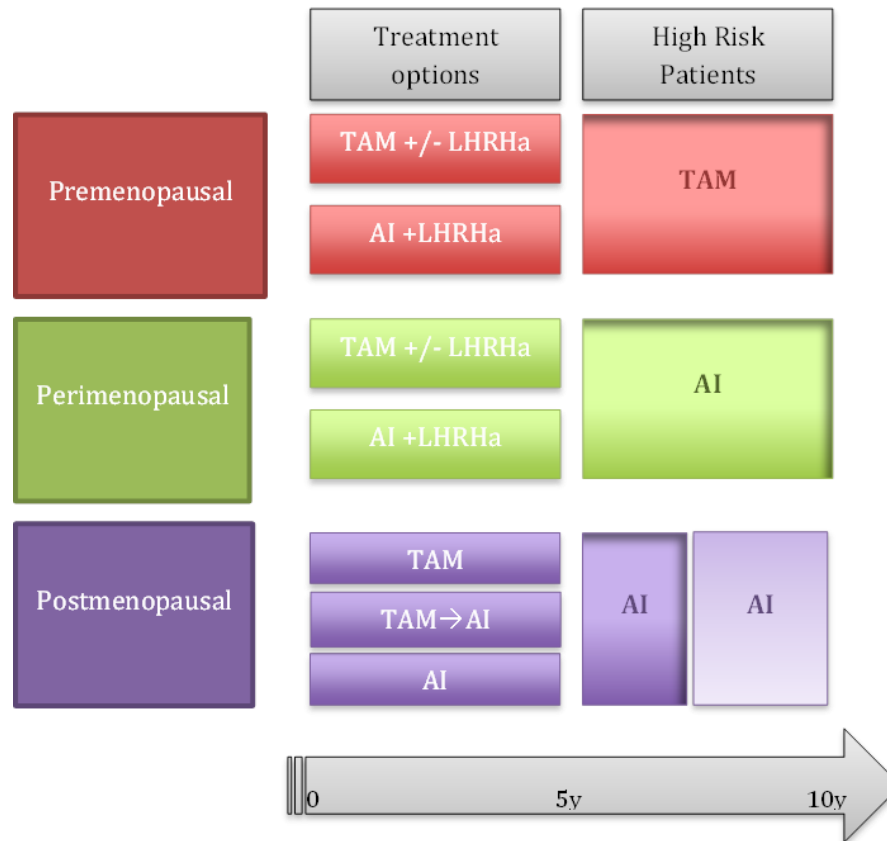
Trial	Population	Menopausal status	FU yrs	Prev. treatment	Extended treatment	HR DFS (p)	HR OS (p)
NSABPB-14	1172 ER+/N-	Pre and post	7	TAM	TAM	1.3 (p=0.03)	NR (p=0.07)
ATLAS	6846 ER+/N any	Pre and post	8	TAM	TAM	0.84 (p=0.002)	0.71 (p=0.01)
aTTom	6953 ER+(39%)/N any	Pre and post	9	TAM	TAM	0.86 (p=0.003)	0.91 (p=ns)
MA.17	5187 ER+/any N	Post	5.4	TAM	LET	0.52 (p<0.001)	0.61 (p<0.001)
ABCSG 6a	586 ER+/any N	Post	5.2	TAM	ANA (3yrs)	0.62 (p=0.031)	0.89
NSABP B-33	1598 ER+/any N	Post	2.5	TAM	EXE	0.68 (p=0.07)	NS
SOLE	4884 ER+/N+	Post	5	Any ET	LET cont. vs int.	1.08 (p=0.31)	0.85 (p=0.16)
DATA	1912 ER+/any N	Post	4.1	TAM 2-3 y	ANA 6vs3	0.79* (p=0.7)	0.91* (p=0.60)
NSABP B-42	3966 ER+/any N	Post	6.9	AI or TAM/AI	LET	0.85 (p=0.048)#	1.15 (p=0.22)
IDEAL	1824 ER+/any N	Post	6.6	Any ET	LET 5vs2.5	0.92 (p=0.49)	1.04 (p=0.79)
ABCSG-16/SALSA	3484 ER+/any N	Post	8.8	Any ET	ANA 2vs5	1.007 (p=0.925)	NS
MA. 17R	1918 ER+/any N	Post	6.3	TAM	LET-LET	0.66 (p=0.01)	0.97 (p=0.83)

Extending Aromatase-Inhibitor Adjuvant Therapy to 10 Years



N Engl J Med 2016;375:209-19

Optimal duration of ET



Special populations

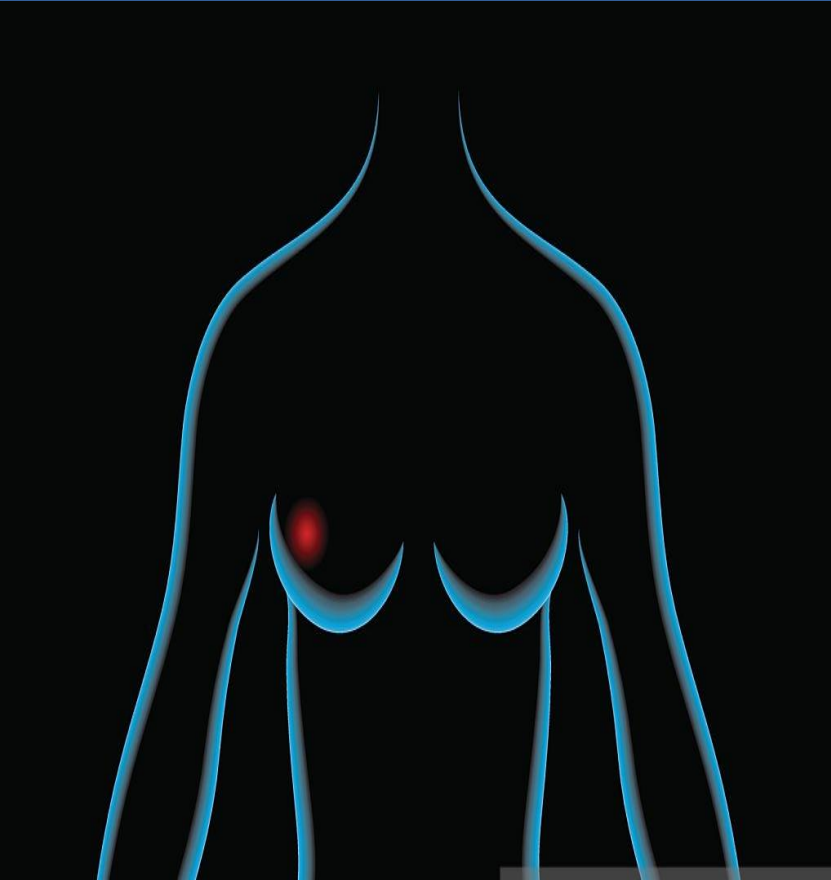
Elderly patients

- No absolute age limit for the use of standard chemotherapy
- The use of such treatments should depend on disease characteristics, co-morbidity, life expectancy and patient preference
- Many older patients with ER positive, HER2 negative, low clinical and/or genomic risk and taking adjuvant endocrine therapy could omit radiation therapy after breast conserving surgery, particularly those with multiple comorbid health conditions.

Migliorare la qualità della vita

- Innovazioni -

1. Mastectomia Robotica
2. Alopecia e chemioterapia



Mastectomia Robotica



Fornire una tecnica alla chirurgia mini-invasiva che potrebbe ridurre sensibilmente gli effetti negativi di una mastectomia profilattica eseguita con tecnica classica

Robotic Nipple Sparing Mastectomy and Immediate Robotic Reconstruction with Implant

LETTER TO THE EDITOR

Robotic Nipple-sparing Mastectomy and Immediate Breast Reconstruction With Implant: First Report of Surgical Technique

To the Editor:

Technical innovations have made it feasible to conduct endoscopic nipple-sparing mastectomy (NSM), which has been reportedly well tolerated and associated with greater patient satisfaction.¹ However, the endoscopic technique (ET) has not had a wide diffusion and many centers have abandoned this technique because of technical challenges.²⁻⁴ In fact, the manual control of a 2-dimensional endoscopic in-line camera produces an inconsistent optical window around the curvature of the breast skin flap. Furthermore, the internal mobility results are limited and the dissection angles inadequate,^{5,6} because rigid tube instruments are working through a single access.

The aim of the present study was to evaluate feasibility, safety, advantages and limitations of robotic surgery to perform NSM and immediate breast reconstruction (IBR) with implant. Our hypothesis is that robotic technology could exceed the technical limits of ET. We describe the surgical technique of the first 3 operations carried out.

To exercise caution with regard to the oncological safety, we selected BRCA mutation carrier patients with a previous history of breast cancer surgery who had decided to receive a delayed contralateral risk-reducing NSM and IBR.

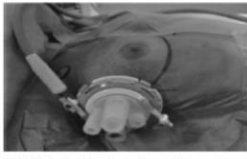


FIGURE 1. Single-port axillary access before robot docking and instrument positioning.

avoid conflicts during dissection. The cavity was observed through a 30° 12-mm-diameter camera (Intuitive Surgical, Denzlingen, Germany). Dissection was carried out with a 5 mm monopolar cautery with spatula tip (Intuitive Surgical, Sunnyvale, CA) used on the right robotic arm. Traction and counter-traction, along with maintaining exposure and stretching out the tissue, was carried out with a 5 mm Maryland Bipolar Forceps (Intuitive Surgical, Sunnyvale, CA) fitted on the left robotic arm. The dissection started from the superficial flaps in all quadrants, then breast tissue was pulled up to create a sufficient posterior working space on the major pectoral fascia and completed dissection. The gland was then removed entirely en bloc through the 2.5 cm axillary skin incision using a "weaving flag technique," moving the slippery and greased gland freely and gently back and forth or up and down (greater size of the gland was 8.5 × 3.5 × 2 cm; areolar flap thickness ranged between 0.3 to 0.5 cm). In the reconstructive phase, as the gas pressure

patients were discharged on the second postoperative day. After a mean follow-up of 8 months, no long-term complications were observed.

Although experience with NSM carried out by robotic-assisted technique is very limited and initial, we clearly noted 2 main advantages:

(1) The use of carbon dioxide enables the reduction of bleeding, offering a better view of the proper surgical dissection plane. The tenfold image magnification, the 3-dimensional view, and the intense lighting increase the difference in contrast of colors of different structures, thus highlighting blood vessels, lymphatics, adipose lobules, the crests of Duret, Cooper's ligaments, the mammary gland itself, and the skin. Sharpness and clarity of the image, associated with a high precision of the instrument movement, stability due to tremor abolition and greater accuracy, permitted a better detachment of the gland by its suspensory ligaments. In addition, the robotic optical window allowed the intercostal perforators to be readily recognized and saved, which contribute significantly to the overall circulation of both the nipple-areola complex (NAC) and the mastectomy flaps.⁷ Furthermore, the robotic instruments have 7° of freedom of motion at the tips which allows negotiation around the curvature of the breast skin cupola. All these features have been reported as being a limitation of ET.⁸

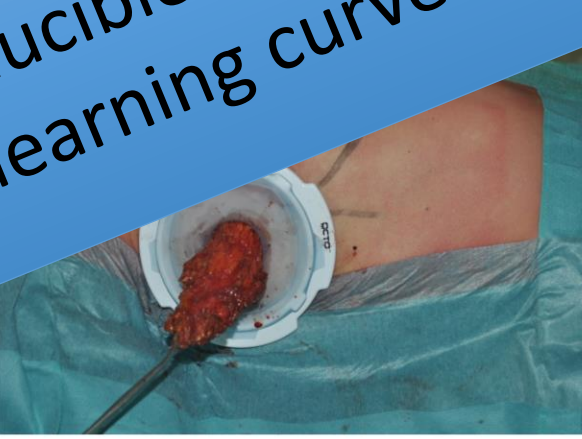
(2) The minimal incision hidden in the axilla and the high respect for anatomical structures lead to high trophism and vitality of the NAC. In our opinion, this minimally invasive approach might reduce changes

THE BREAST

Robotic nipple-sparing mastectomy for the treatment of breast cancer: Feasibility and safety study

Toesca A. ANN SURG 2014

Robotic Nipple Sparing Mastectomy and Immediate Robotic Reconstruction with Implant



This technique is reliable and reproducible with a relative brief learning curve

Preliminary Results

Situation Updated to 24th May 2018

- **42 patients enrolled:**
 - **21 randomized to Arm A (Open NSM)**
(1 drop out)
 - **21 to Arm B (Robotic NSM)**

Data available for 20 patients (9 Arm A and 11 Arm B)

Preliminary Results

Table 2.1 Peri-operative data

	Open N=9	Robotic N=11
Mastectomy procedure time (min)		
Mean	55.40	138
Median (range)	60 (20-135)	134 (75-255)
Reconstruction procedure time (min)		
Mean	48.13	54
Median (range)	48 (14-72)	55 (19-73)
Robotic cases converted to open , N %	n/a	0
Immediate Reconstruction with Implant	6	11
Reconstruction with Expander	3	0
Median postoperative pain evaluated with Numerical Analog Scale (NAS)		
NAS0	3	4
NAS1	1	4
NAS2	3	2
NAS3	2	1
Length of hospital stay- admission to discharge (days)		
Mean	2.2	2.1
Median (range)	2 (2-3)	2(1-5)



Alopecia e chemioterapia nel carcinoma mammario



Il progetto DigniLife in IEO: Background and Rationale

- I capelli fanno parte della nostra identità e per molte pazienti sono un **simbolo importante** per una buona **qualità della vita**.
- La possibilità di preservarli può essere di enorme supporto durante il percorso terapeutico.
- Il sistema DigniLife® è stato sviluppato specificatamente per **prevenire l'alopecia indotta dalla chemioterapia**



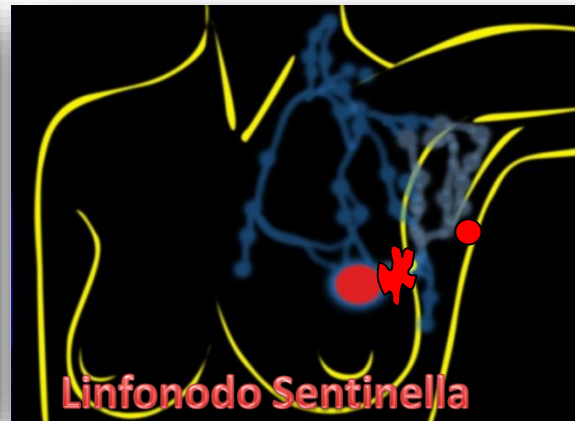
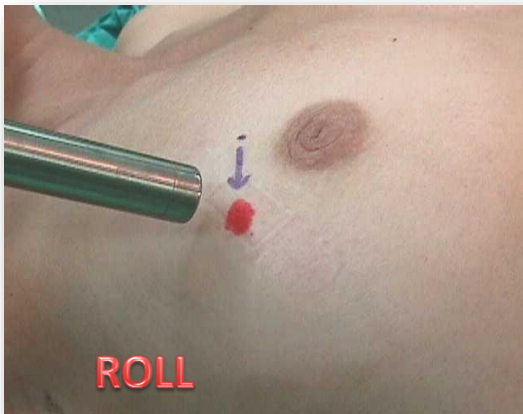
IL TRATTAMENTO COMPLETO IN OTTO ORE

- **Quadrantectomia**
- **Linfonodo Sentinella**
- **Radioterapia intraoperatoria**



IEO 2 DAY CENTER, maggio 2010

- Molti interventi al seno possono essere eseguiti sia in anestesia generale che in anestesia locale più MAC (monitored anesthesia care) in totale comfort per la paziente permettendo la dimissione lo stesso giorno dell'intervento.

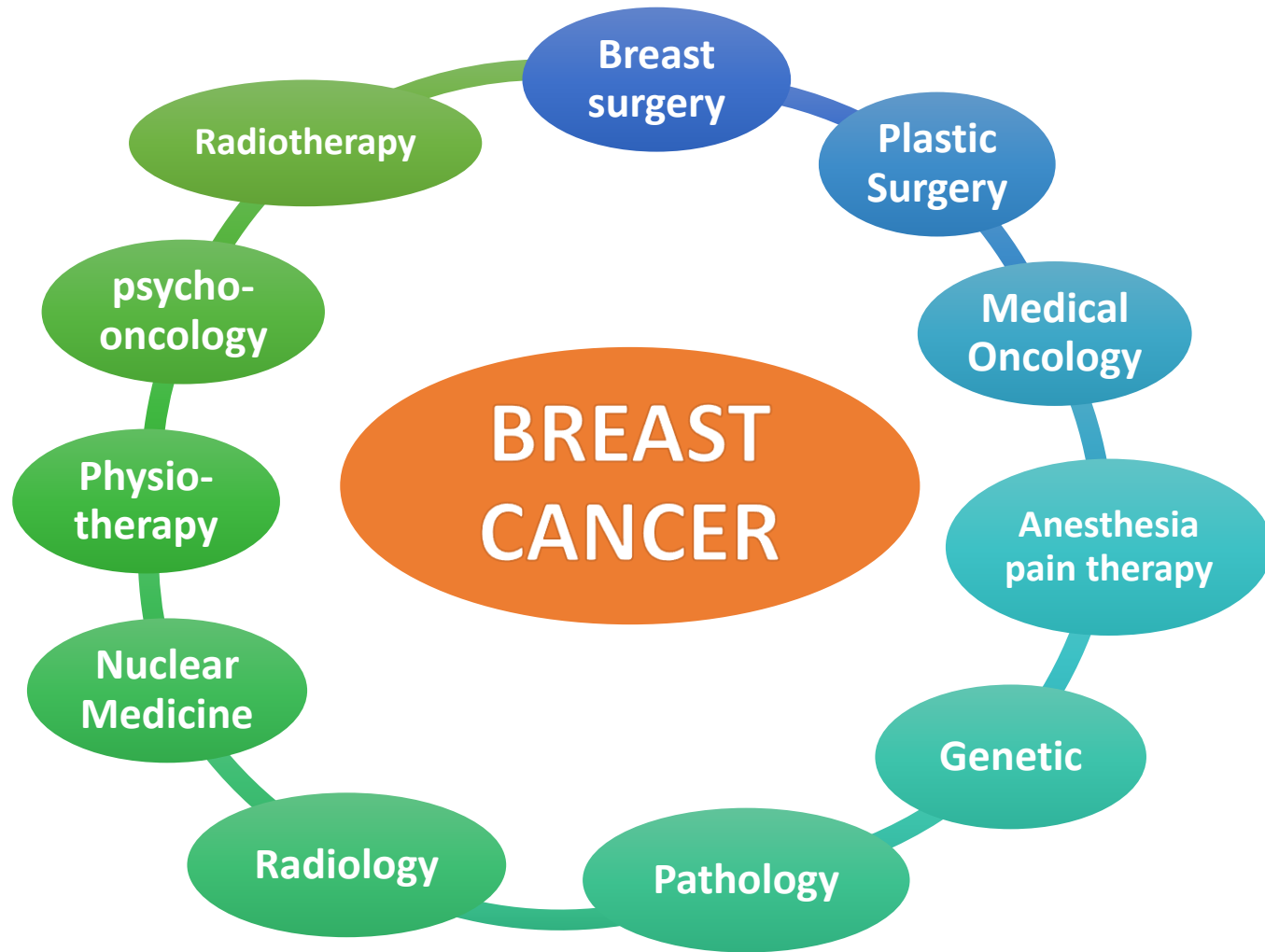


Interventi eseguiti in Day Surgery

dal 2001 al 2017

	2010	2011	2012	2013	2014	2015	2016	2017
Total	3324	3484	3407	3446	3440	3578	3628	3752
Day surgery	342 (10.2%)	644 (18.4%)	862 (25.3%)	1138 (33.0%)	1146 (33.3%)	1214 (33.9%)	1576 (43.4%)	1714 (45.7)

Programma Senologia



Il Programma di Senologia IEO vuole riunire le eccellenze multidisciplinari in ambito clinico, chirurgico e di ricerca per ottenere il massimo dell'efficacia al servizio delle pazienti

Grazie!

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