ALTO RISCHIO: QUALI PROTOCOLLI DI SORVEGLIANZA SONO EVIDENCE BASED?

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Interval breast cancers: Absolute and proportional incidence and blinded review in a community mammographic screening program

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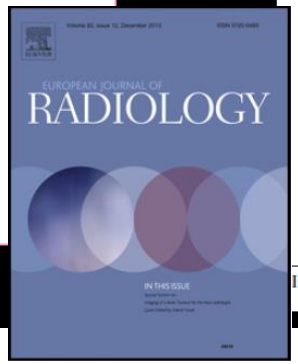


Table 1
Interval cancers, number of screening examinations, and interval cancers absolute incidence per 10,000 examinations during the time period 2001–2006.

Years	ICs	Number of screening examinations	ICs absolute incidence per 10,000 examinations
2001	12	7,897	15 (10–30)
2002	26	13,557	19 (10–30)
2003	28	14,629	19 (10–30)
2004	26	15,101	17 (10–30)
2005	27	17,269	16 (10–20)
2006	26	17,823	15 (10–20)
2001–2006	145	86,276	17 (10–20)

IC, interval cancer. 95% confidence intervals are shown in brackets.

Table 2
Expected breast cancers, observed invasive interval cancers, and interval cancer proportional incidence during the time period 2001–2006.

Year	Expected cancers per year	First year IC	First year IC proportional incidence	Second year IC	Second year IC proportional incidence	Two-year period expected cancers	Two-year period interval cancers	Two-year period proportional incidence
2001	23	4	18% (5–39%)	6	26% (10–49%)	46	10	22% (11–37%)
2002	37	8	22% (10–38%)	17	46% (30–63%)	74	25	34% (23–46%)
2003	38	8	21% (9–37%)	16	42% (26–59%)	77	24	31% (21–43%)
2004	42	7	17% (7–31%)	18	43% (28–60%)	84	25	30% (20–41%)
2005	45	9	20% (10–34%)	17	38% (24–53%)	91	26	29% (20–39%)
2006	49	8	16% (7–30%)	17	35% (22–50%)	97	25	26% (17–37%)
2001–2006	234	44	19% (14–24%)	91	39% (33–45%)	468	135	29% (25–33%)

IC, interval cancer. 95% confidence intervals are shown in brackets. IC proportional incidence was calculated as the ratio between observed ICs and expected breast cancers.

Quale evidenza per i test diagnostici?

Il caso della RM per lo screening nell'alto rischio

Performance diagnostica?

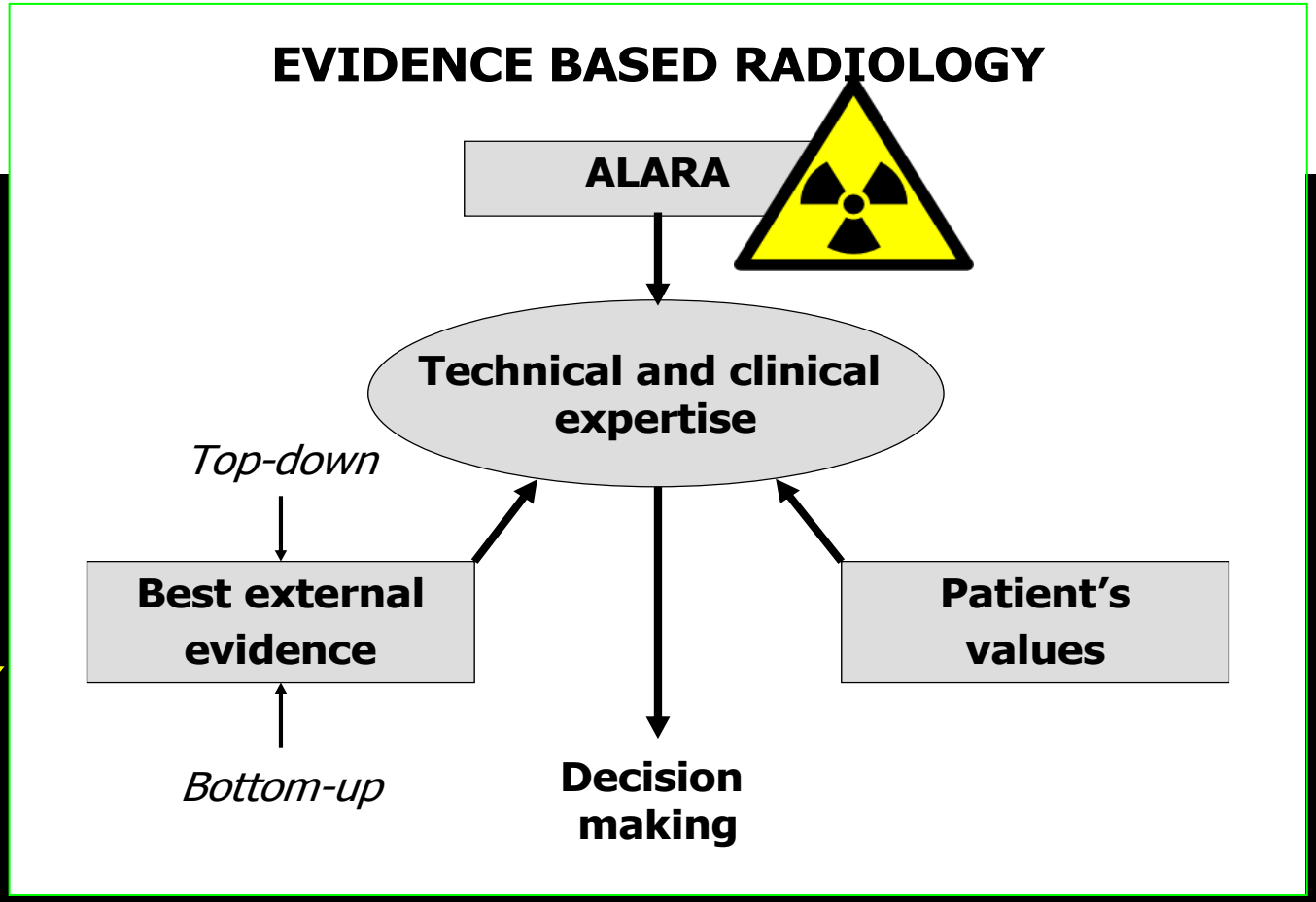
<u>Patient outcome?</u>

Eur Radiol (2010) 20: 1–15
DOI 10.1007/s00330-009-1574-4

HEALTH ECONOMY

Francesco Sardanelli
Myriam G. Hunink
Fiona J. Gilbert
Giovanni Di Leo
Gabriel P. Krestin

Evidence-based radiology: why and how?

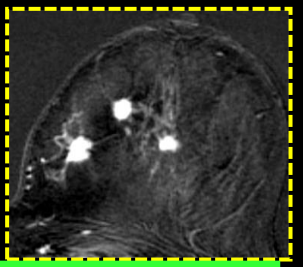


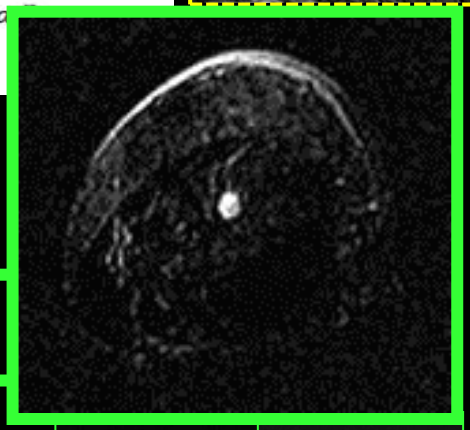
ALARA = "as low as reasonably achievable" ionizing radiation exposure

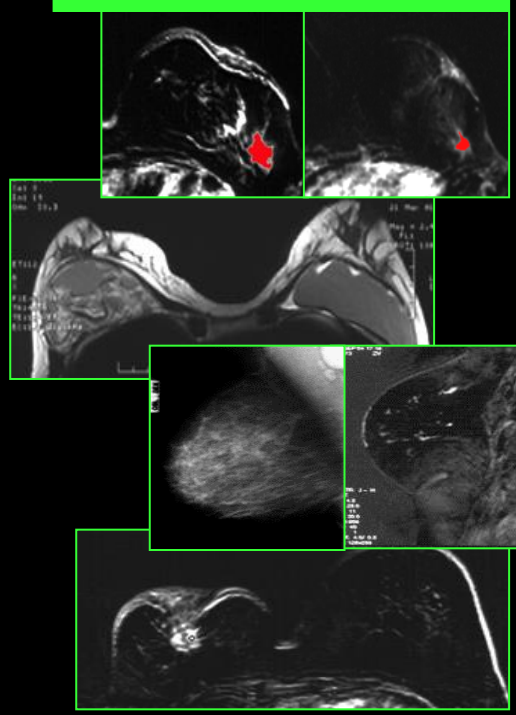
Position Paper

Magnetic resonance imaging of the breast: Recommendations from the EUSOMA working group

Francesco Sardanelli [a,*], Carla Boetes [b], Bettina Borisch [c], Thomas Decker [d], Massimo Federico [e], Fiona J. Gilbert [f], Thomas Helbich [g], Sylvia H. Heywang-Köbrunner [h], Werner A. Kaiser [i], Michael J. Kerin [j], Robert E. Mansel [k], Lorenza Marotti [l], Laura Martincich [m], Louis Mauriac [n], Hanne Meijers-Heijboer [o], Roberto Orecchia [p], Pietro Panizza [q], Antonio Ponti [r], Arnie D. Purushotham [s], Peter Regitnig [t], Marco Rosselli Del Turco [l], Fabienne Thibault [u], Robin Wilson [v]



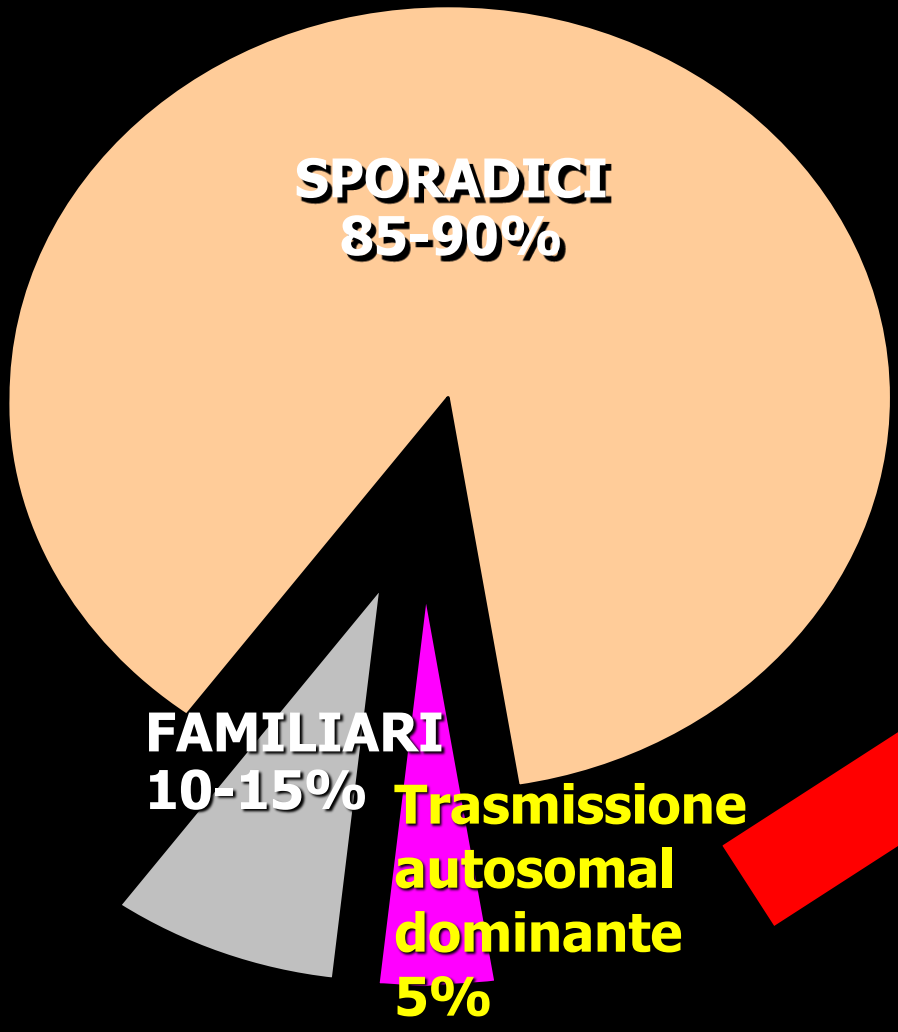


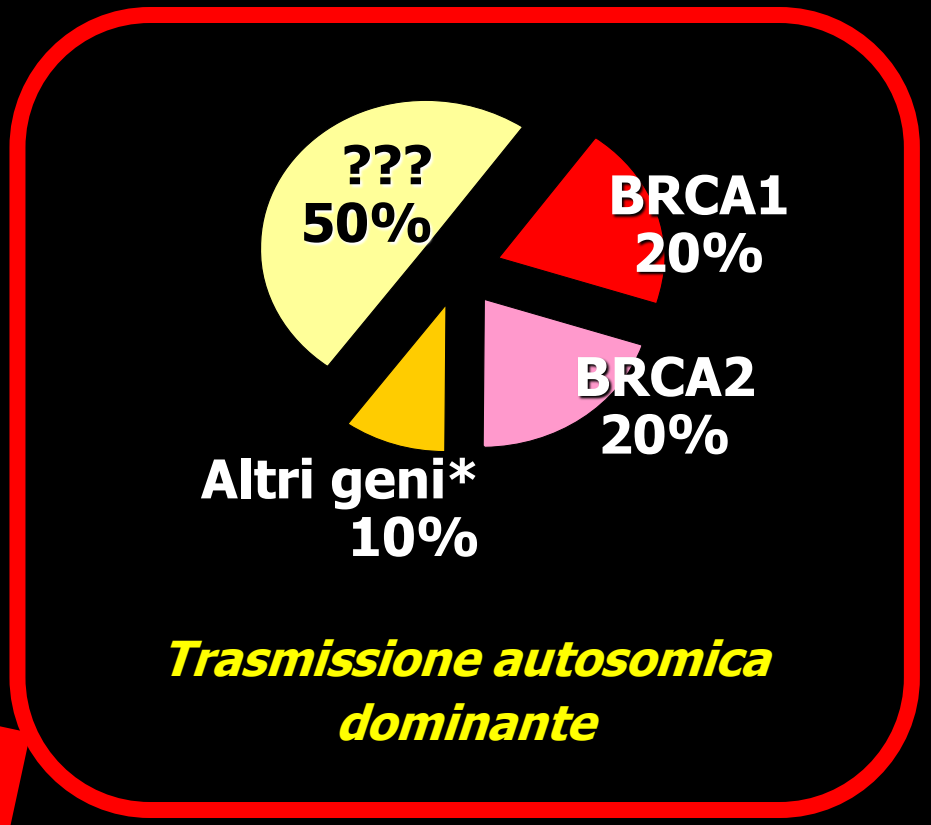


Indicazione	MdC?	Consenso
1. **Staging (RM preoperatoria)**	**MdC**	**Limitato[1]**
2. Screening rischio elevato	**MdC**	**SI**
3. **Valutazione risposta alla NAC**	**MdC**	**SI**
4. **Protesi** (*sospetta rottura*)	**No MdC**	**SI**
5. **TMM primitivo occulto**	**MdC**	**SI**
6. **Sospetta recidiva locale**	**MdC**	**SI**
7. **Equivocal findings at mammo/US**	**MdC**	**Limitato[2]**
8. **Mammella secernente**	**MdC**	**NO (?)**
9. **Tumore infiammatorio**	**MdC**	**NO**
10. **Mammella maschile**	**MdC/no MdC**	**NO**

[1] CLI, alto rischio, discrepanza dimensionale mammo/eco >1 cm, partial breast irradiation
[2] Quando l'agobiopsia non può essere eseguita

TUMORI MAMMARI MALIGNI (TMM)





BRCA1-2 = 2-3%
di tutti i TMM

* TP53, STK11, PTEN, NF1, CHEK2, ATM, BRIP1, PALB2

Sardanelli et al, Syllabus Sezione RM SIRM, 2010

RISCHIO GENETICO

BRCA-1 e BRCA-2 (disponibili test genetici)

50% dei TMM ereditari; 80% dei TMM nelle donne giovani

Lifetime risk 60-85%

30-60%: TMM controlaterale o k ovarico entro 5 anni

BRCA-1

Sede 17q21; associazione con k ovarico

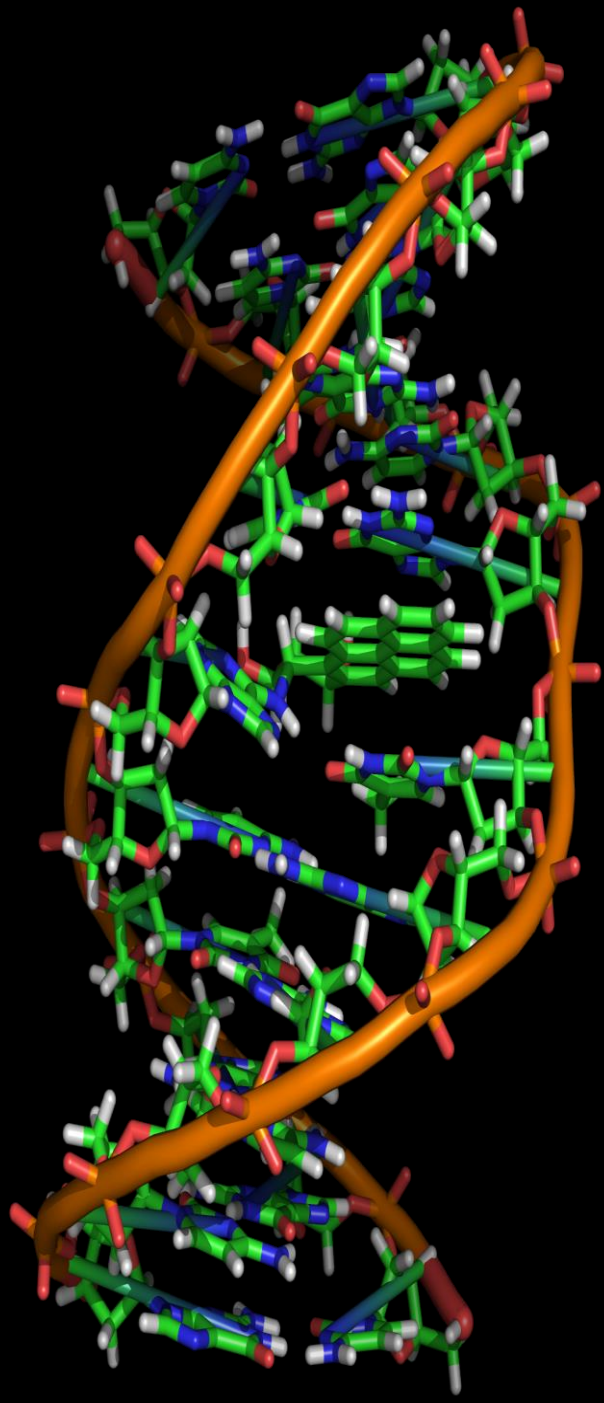
BRCA-2

Sede 13q12-13; TMM maschile

Profilo di rischio in età più avanzata rispetto a BRCA1

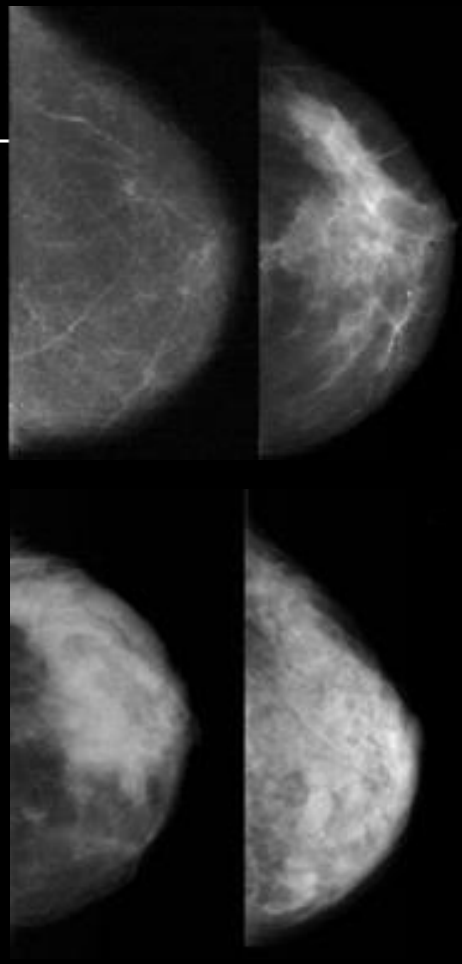
? **BRCA X** = importante storia familiare, mancato rilevo di mutazioni deleterie BRCA1/2

? Importante storia familiare, test genetico non eseguito



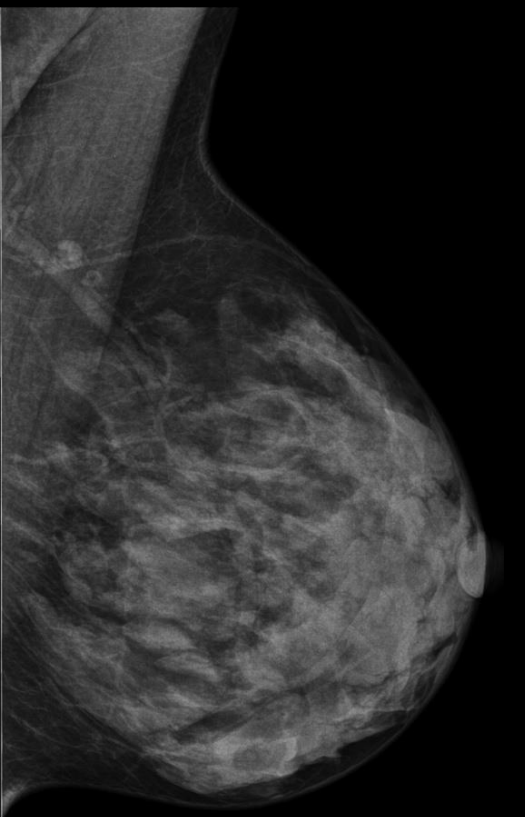
SCREENING MAMMOGRAFICO?

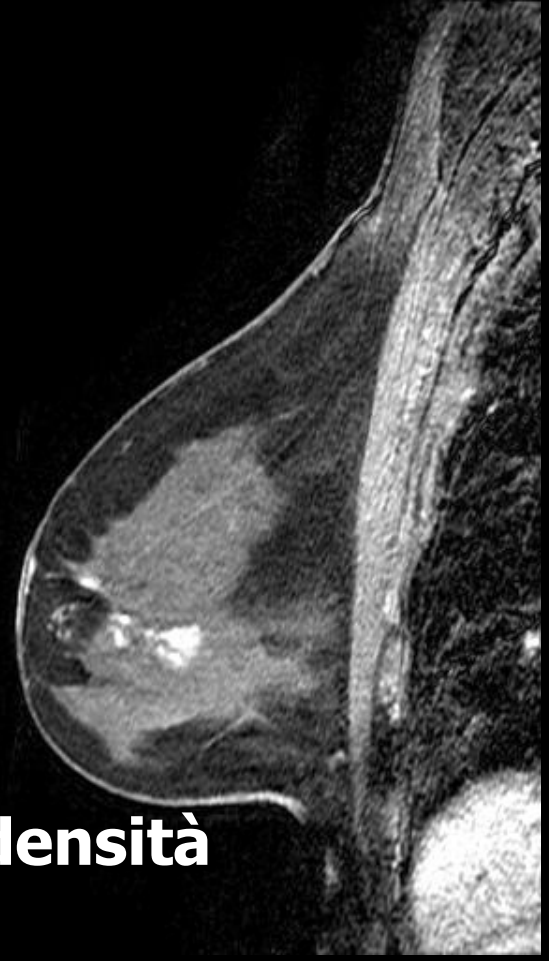
	Popol. femm. generale (> 50 anni)	Alto rischio familiare (dai 25 anni)
Studi	**Randomizzati**	**Non-randomizzati [2]**
Sensibilità [1,2]	**~ 80%**	**29-50%**
Cancri d'intervallo	**20-25%**	**35-50%**
Diametro >10 mm [2]	**65%**	**40-78%**
Metastasi linfonodali [2]	**22%**	**20-56%**
Riduzione mortalità specifica		
Globale [3-6]	**15-31%**	**???**
Donne partecipanti [7,8]	**45-48%**	**???**



1 Feig SA 2005; 2 Dent R and Warner E 2007; 3 Humphrey LL et al 2002; 4 de Koenig HJ et al 2003; 5 Harris R 2006; 6Gotzsche PC and Nielsen 2006; 7 Puliti D et al 2008; 8 Allgood PC et al 2008

SCREENING
NEL RISCHIO ELEVATO





Inzio precoce

Controlli ravvicinati

Indipendenza dalla densità

Non esposizione a radiazioni

BRCA1/2 interagiscono con Rad51 (riparo DNA). Soggetti BRCA1/2+ sono più sensibili alle radiazioni ionizzanti, come già dimostrato per modelli animali (Sharan et al, Nature 1997) e più recentemente su colture celluylari umane (Colin et al, IJRB 2011)

SCREENING RM IN DONNE A RISCHIO ELEVATO
EVIDENZA DA OTTO STUDI PROSPETTICI

Donne	5299
% di BRCA mutate	8% - 100%
Eventi di screening	14110
Età media all'arruolamento	40 - 47 yrs
Intervallo età	18 - 80 yrs
Round per donna	1.7 - 3.4
Tasso di detezione	1.0% - 4.8%
Cancri d'intervallo	2% - 9%
Dimensioni ≤ 1 cm	33% - 59%
Casi N0 / tumori invasivi	67% - 89%

Netherlands (Kriege, 2004); Canada (Warner, 2004); UK (Leach, 2005); Germany (Kuhl, 2005); Norway (Hagen, 2007); Austria (Riedl, 2007); Germany (Kuhl, 2010); Italy (Sardanelli, 2007, 2011)

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BREAST

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Franca Podo

Breast MR imaging in women at high-risk of breast cancer. Is something changing in early breast cancer detection?

Una nuova prospettiva...

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Abstract In the last few years, several papers have addressed the introduction of contrast-enhanced MR imaging for screening women at high risk for breast cancer. Taking in consideration five prospective studies, on 3,571 screened women with hereditary predisposition to the disease and 9,652 rounds, we found that 168 patients were diagnosed with breast cancer (155 screen-detected, eight interval, and five cancers excluded from analysis) with a detection rate per year of 1.7%. These cancers were small (49% equal to or less than 10 mm in diameter) but aggressive, 82% being invasive and 49% with histologic grade 3; however, only 19% of these invasive cancers were associated with nodal involvement. The pooled sensitivity was 16% for clinical breast examination, 40% for mammography, 43% for ultrasound, and 81% for MR. The positive predictive value (calculated on the basis of the number of invasive diagnostic procedures due to false positives) was 33%, 47%, 18%, and 53%, respectively. Aim of the present article is to present the historical development of MR imaging of breast tumors that made this application theoretically and technically possible, to explain what strategic problems we face in the presence of a hereditary predisposition to the disease, to review the main results of the published studies, and to outline open problems and future perspectives.

Keywords Breast neoplasms · MR · Cancer screening · Genes and genetics

American Cancer Society Guidelines for Breast Screening with MRI as an Adjunct to Mammography

2007

CA Cancer J Clin 2007;57:75–89

Debbie Saslow, PhD; Carla Boetes, MD, PhD; Wylie Burke, MD, PhD; Steven Harms, MD; Martin O. Leach, PhD; Constance D. Lehman, MD, PhD; Elizabeth Morris, MD; Etta Pisano, MD; Mitchell Schnall, MD, PhD; Stephen Sener, MD; Robert A. Smith, PhD; Ellen Warner, MD; Martin Yaffe, PhD; Kimberly S. Andrews; Christy A. Russell, MD (for the American Cancer Society Breast Cancer Advisory Group)

ABSTRACT New evidence on breast Magnetic Resonance Imaging (MRI) screening has become available since the American Cancer Society (ACS) last issued guidelines for the early detection of breast cancer in 2003. A guideline panel has reviewed this evidence and developed new recommendations for women at different defined levels of risk. Screening MRI is recommended for women with an approximately 20–25% or greater lifetime risk of breast cancer, including women with a strong family history of breast or ovarian cancer and women who were treated for Hodgkin disease. There are several risk subgroups for which the available data are insufficient to recommend for or against screening, including women with a personal history of breast cancer, carcinoma in situ, atypical hyperplasia, and extremely dense breasts on mammography. Diagnostic uses of MRI were not considered to be within the scope of this review. *(CA Cancer J Clin 2007;57:75–89.)*

ORIGINAL RESEARCH ■ BREAST IMAGING

2007

Multicenter Comparative Multimodality Surveillance of Women at Genetic-Familial High Risk for Breast Cancer (HIBCRIT Study): Interim Results[1]

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Purpose: To prospectively compare clinical breast examination (CBE), mammography, ultrasonography (US), and contrast material–enhanced magnetic resonance (MR) imaging for screening women at genetic-familial high risk for breast cancer and report interim results, with pathologic findings as standard.

Materials and Methods: Institutional review board of each center approved the research; informed written consent was obtained. CBE, mammography, US, and MR imaging were performed for yearly screening of *BRCA* first-degree relatives of *BI* ers, or women enrolled b of breast or ovarian cance or second-degree relativ cluded b ovarian any age)

Radiology

HIBCRIT-1 (2000-2008)

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UNIVERSITÀ DEGLI STUDI DI TRIESTE

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QUID EST HOMO

Università Vita-Salute San Raffaele

ORIGINAL ARTICLE

Multicenter Surveillance of Women at High Genetic Breast Cancer Risk Using Mammography, Ultrasonography, and Contrast-Enhanced Magnetic Resonance Imaging (the High Breast Cancer Risk Italian 1 Study)

Final Results

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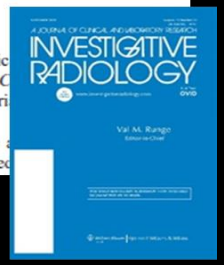
Objectives: To prospectively compare clinical breast examination, mammography, ultrasonography, and contrast-enhanced magnetic resonance imaging (MRI) in a multicenter surveillance of high-risk women.

Materials and Methods: We enrolled asymptomatic *BRCA* mutation carriers; first-degree relatives of *BRC* and women with strong family history of breast/ovari those with previous personal breast cancer.

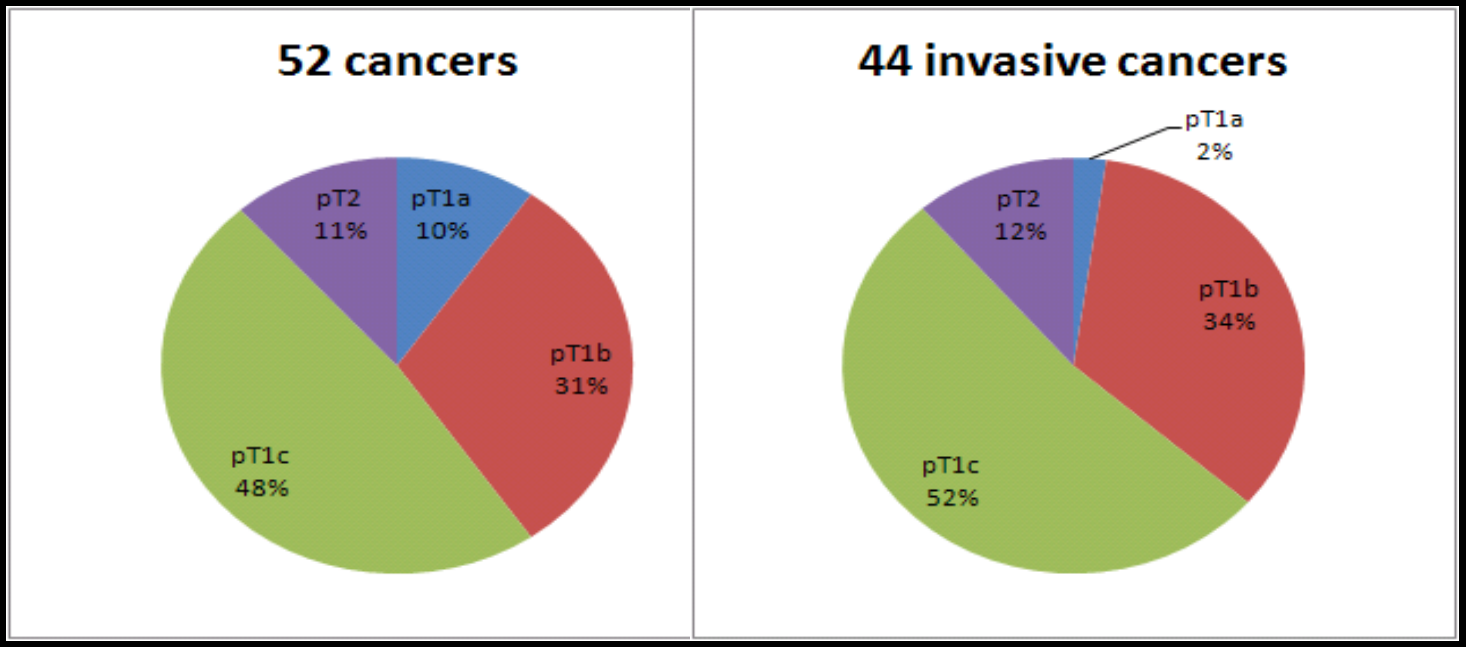
Results: A total of 18 centers enrolled 501 women rounds (3.2 rounds/woman). Forty-nine screen-detecte



Invest Radiol. 2011

HIBCRIT-1: Risultati finali

Invasivi	44
IDC	31
IDC+DCIS	6
ILC	2
IDC+ILC	2
ILC+DCIS	2
Medullary	1
In situ	8
DCIS	6
DCIS+LIN	2



Stadio pT		
pTis	8	
PT1a	2	
pT1b	15	*92%*
pT1c	23	
pT2	4	
>pT2	0	

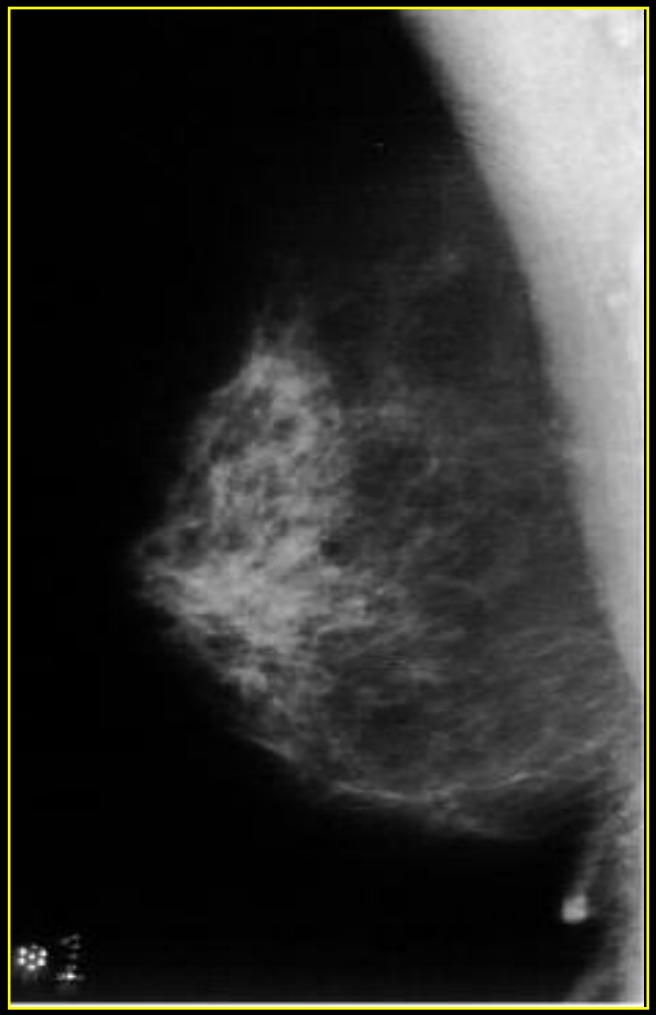
Cancri d'intervallo= 3/52 (5.8%)

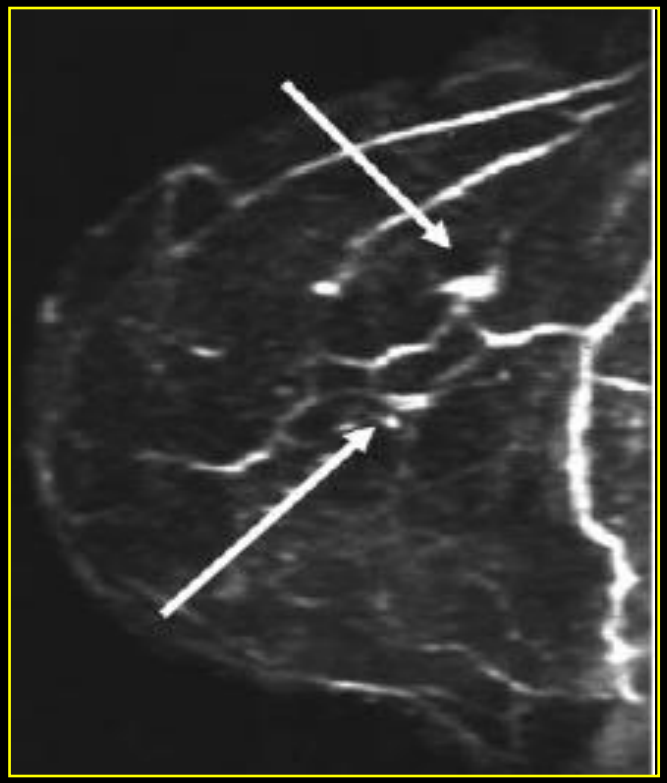
(2 IDCs; 1 IDC+DCIS:
12-18 mm, G3, N-; 2 diagnosticati ecograficamente sette mesi dopo un round negativo, uno alla visita senologica tre mesi dopo un round negativo)

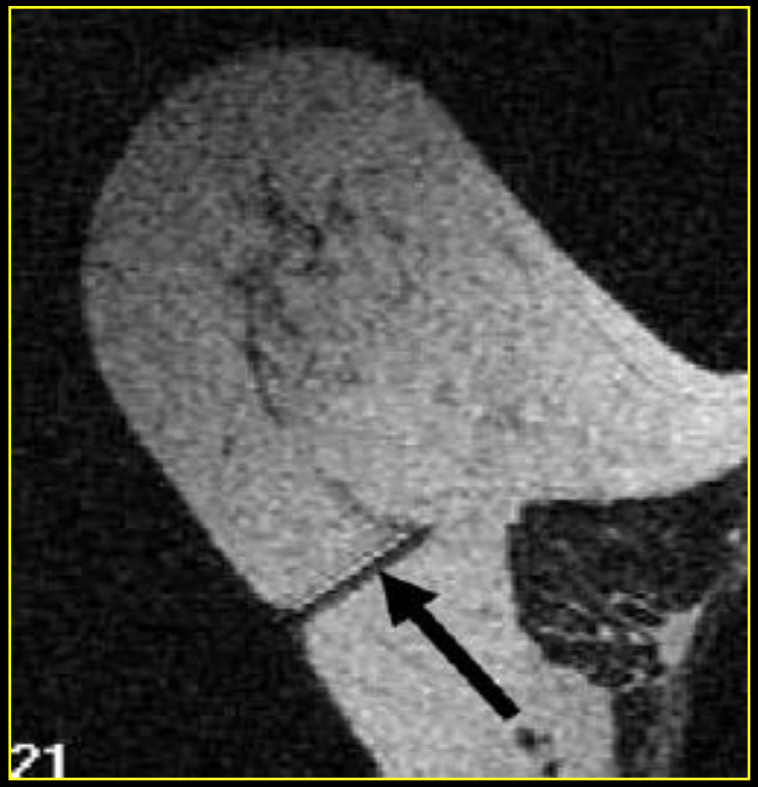
G3
32/52 = 62%

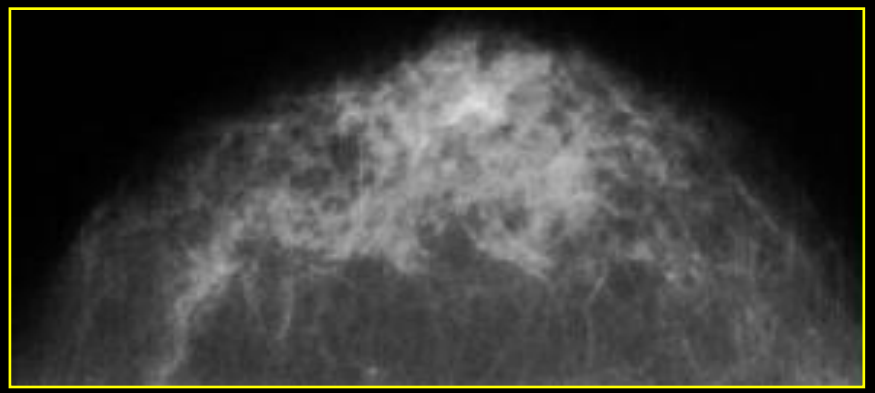
N0
28/39 = 72%

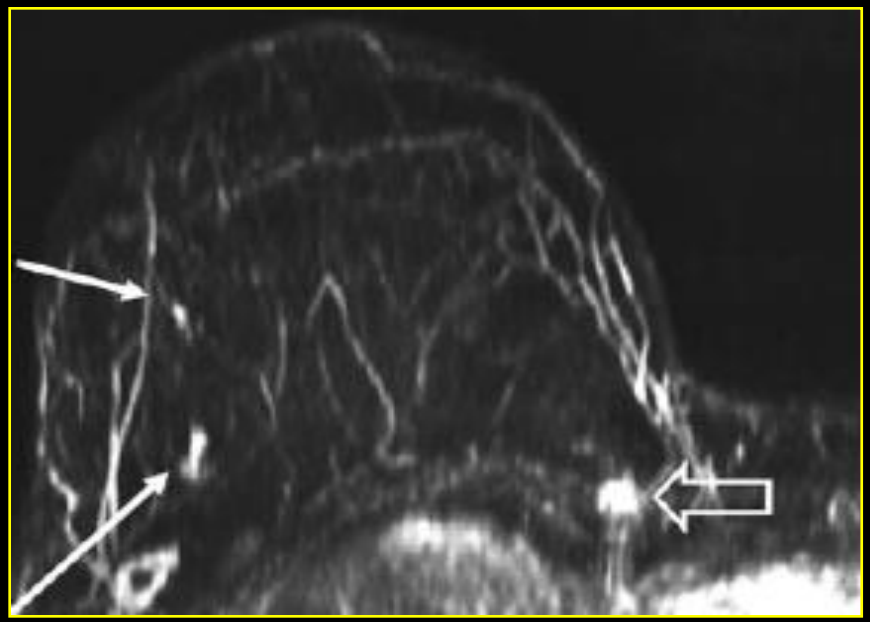
Diagnosi solo RM =16/52 = 31%
Oltre 50 anni = 8/21 = (38%)
≥50 anni= 8/31 (26%)
P=n.s.





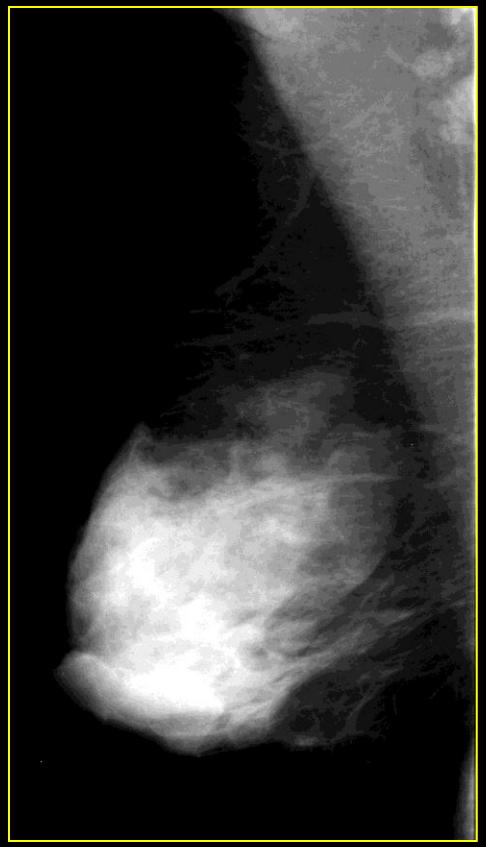
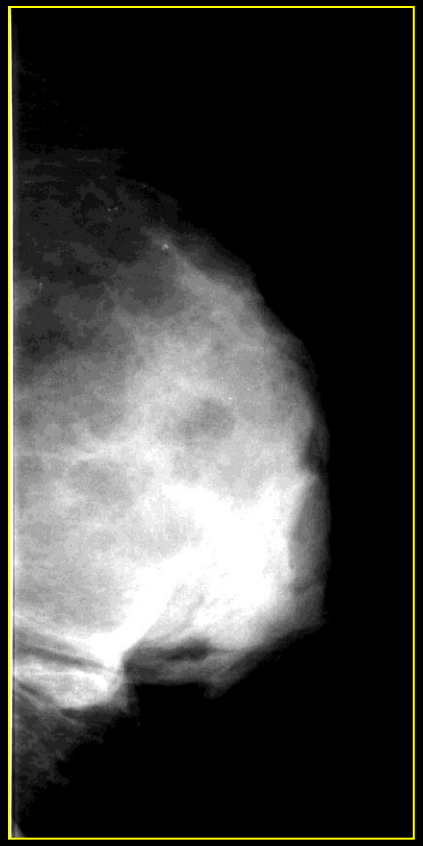
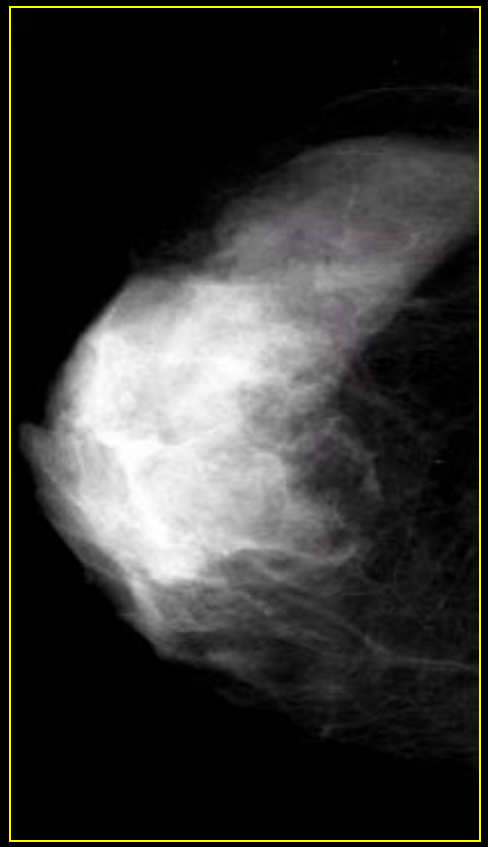
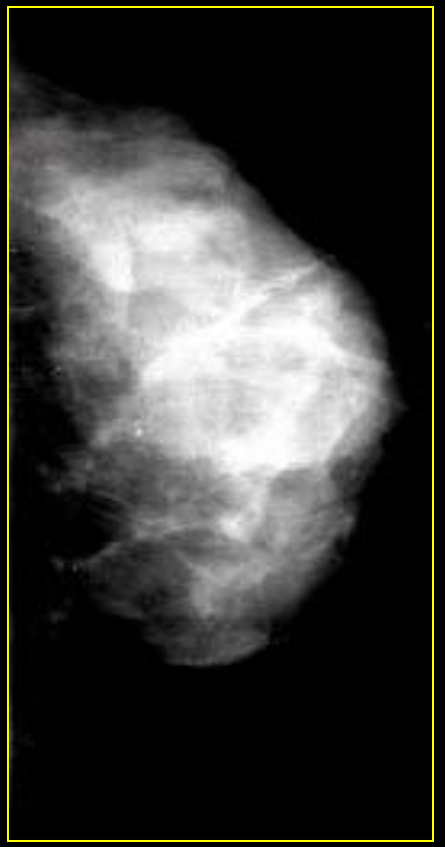






Asintomatica, 69 anni, BRCA1+, precedente mastectomia per IDC; visita, mammo ed ecografia negative.

Istologia: due foci di DCIS (3 mm).

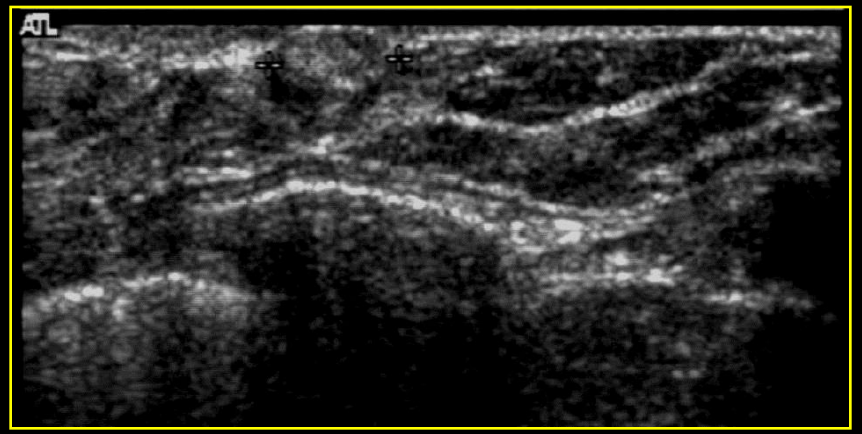
61 anni

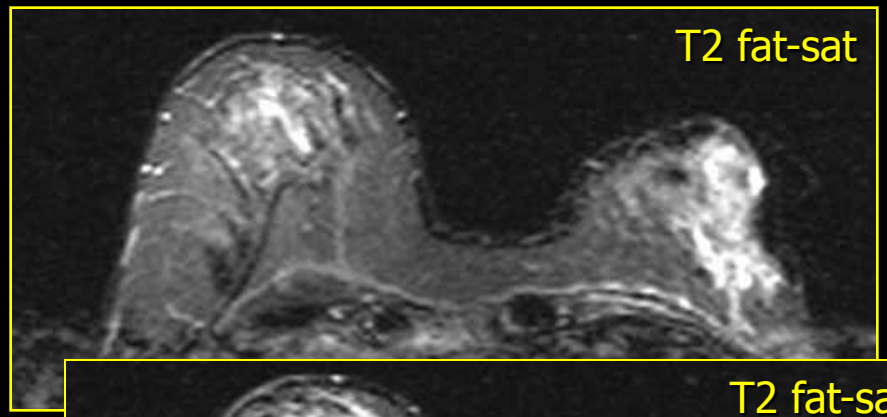
Precedente ILC a sinistra

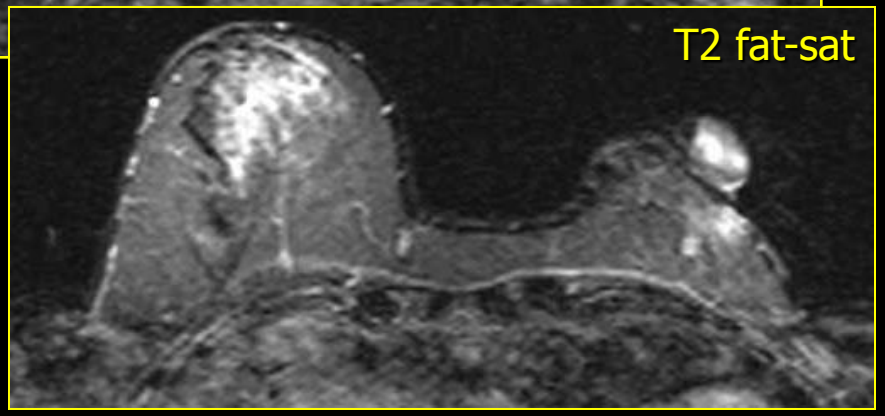
Arruolamento per storia familiare

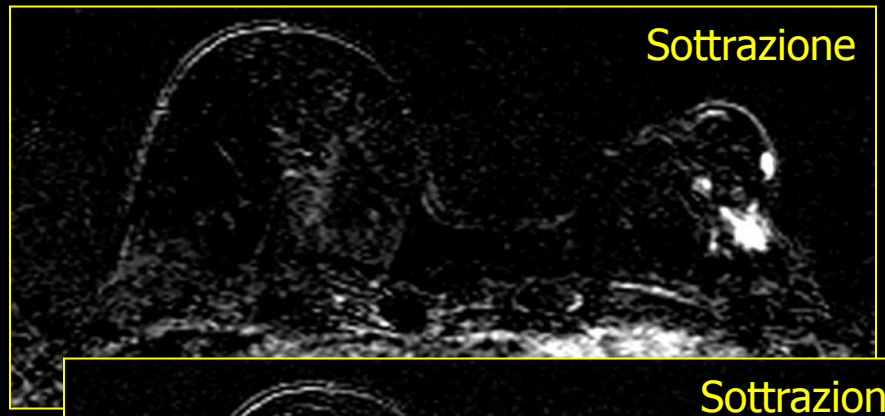
Mammografia ed ecografia negative

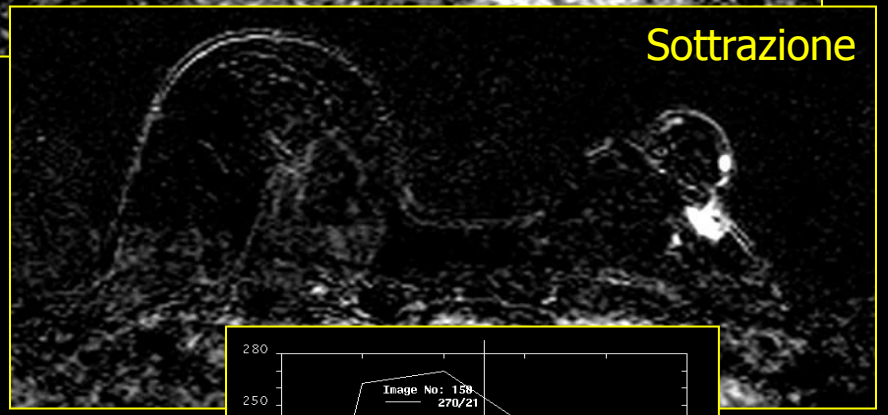
a destra, inconclusive a sinistra (esiti)

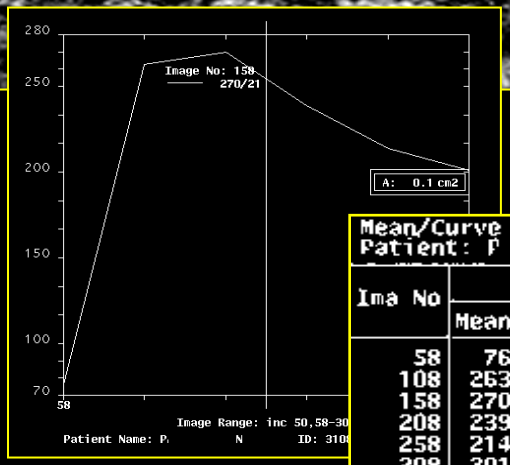






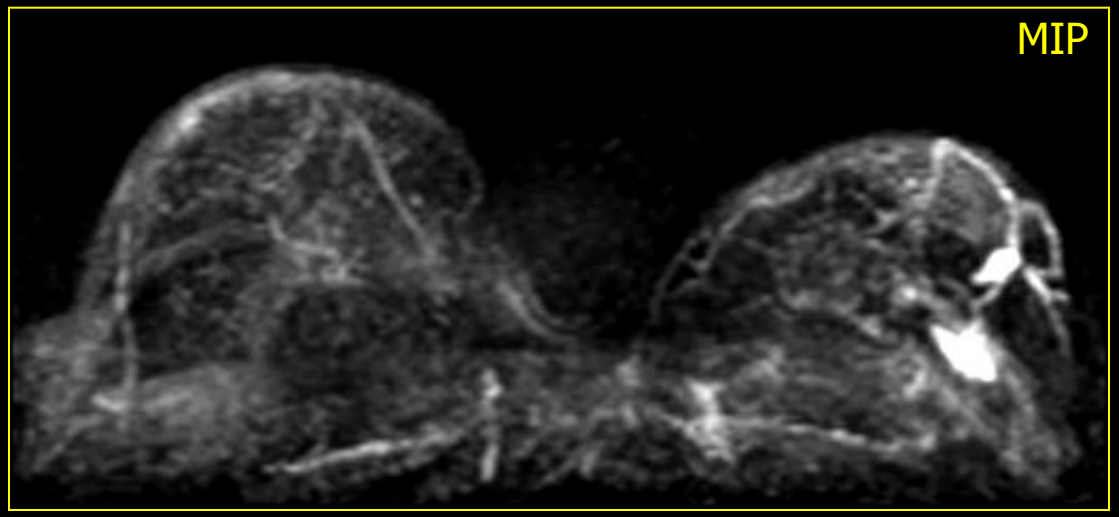




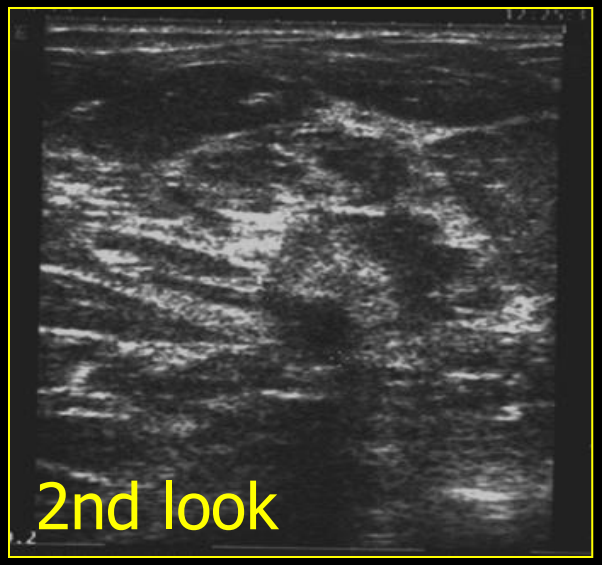


Mean/Curve Calculation
Patient: F N

Ima No	ROI1			
	Mean	StD	Area	Me
58	76	10	0.1	
108	263	10	0.1	
158	270	21	0.1	
208	239	17	0.1	
258	214	16	0.1	
308	201	18	0.1	



Istologia: ILC+IDC

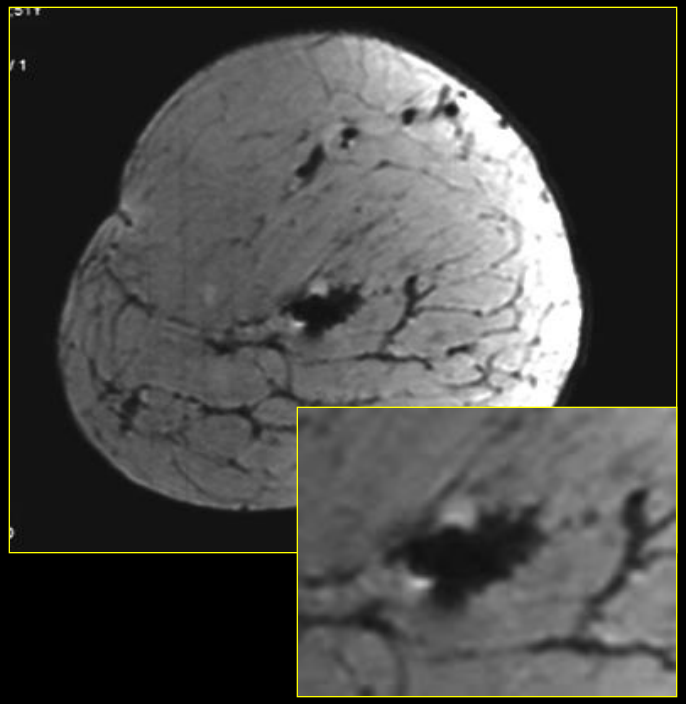


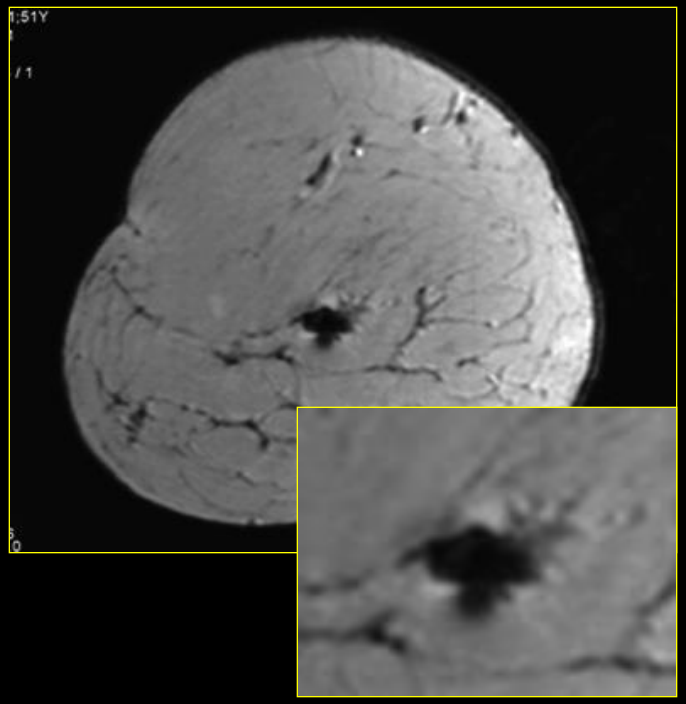
52 anni

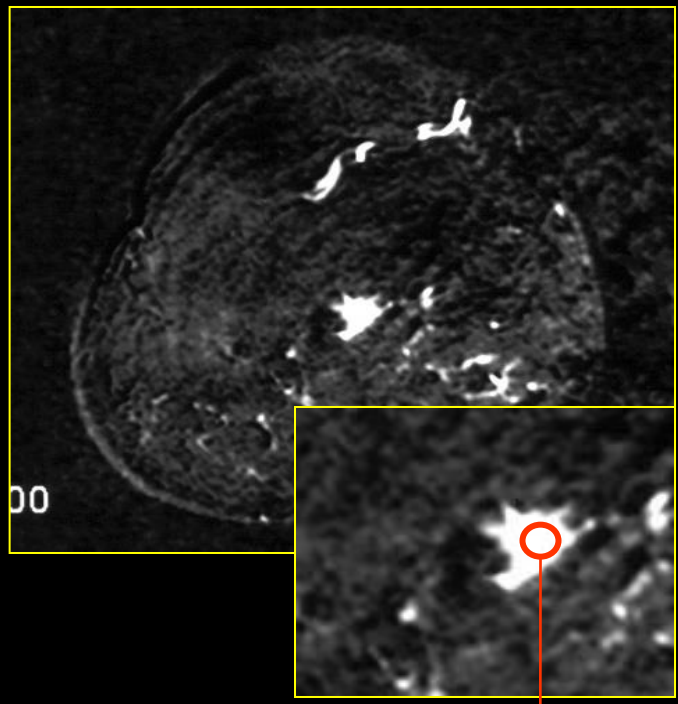
Arruolamento per storia familiare

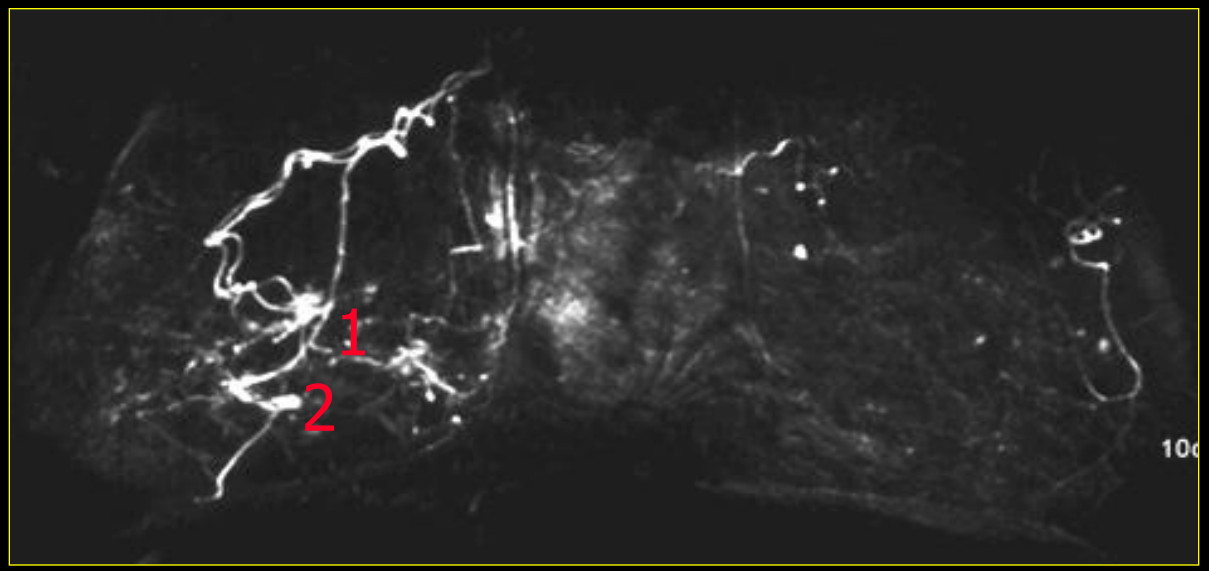
Pregressa QUART a destra per IDC

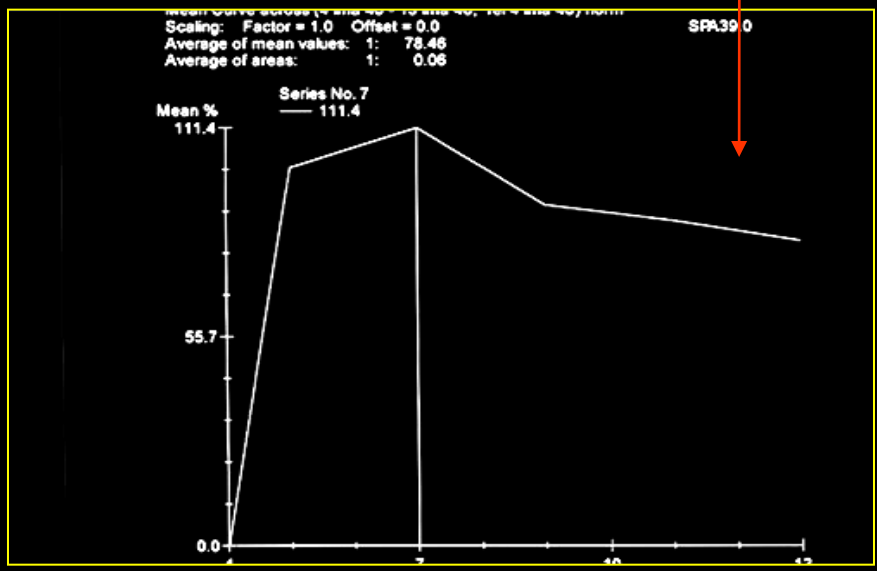
Visita ed ecografia (1st look) negative











Istologia: IDC (10 e 6 mm)

HIGH-RISK SCREENING: HIBCRIT-1

Modality	*Sensitivity %*	*Specificity %*	*PPV2 %*	*NPV %*	*LR+*	*LR-*
CBE	17.6	**99.4**	60.0	96.1	30.9	0.83
Mammography	50.0	**99.1**	73.5	97.6	58.1	0.50
US	52.0	**99.2**	76.5	97.7	66.0	0.48
MRI	**91.3***	**97.4**	**61.8**	**99.6***	**35.1**	**0.09***
Mam + US	62.5	**98.4**	65.2	98.2	39.0	0.38
MRI + Mammo	93.2	**97.0**	58.6	99.7	31.5	0.07
MRI + US	93.3	**97.1**	60.0	99.7	32.0	0.07

** Stat. significance*

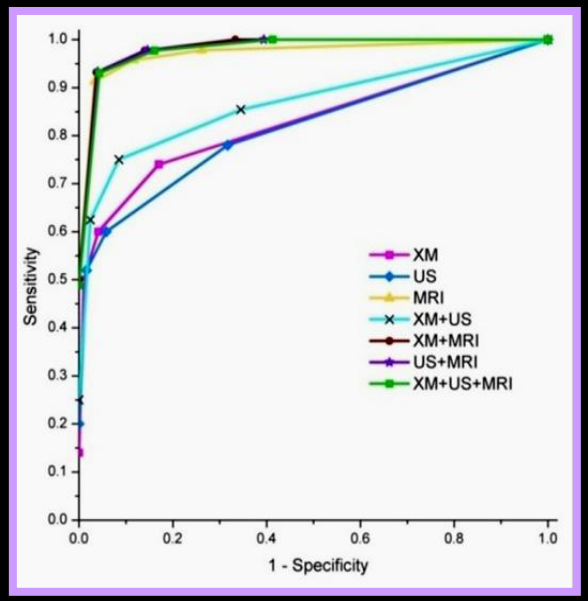
Overall Sensitivity

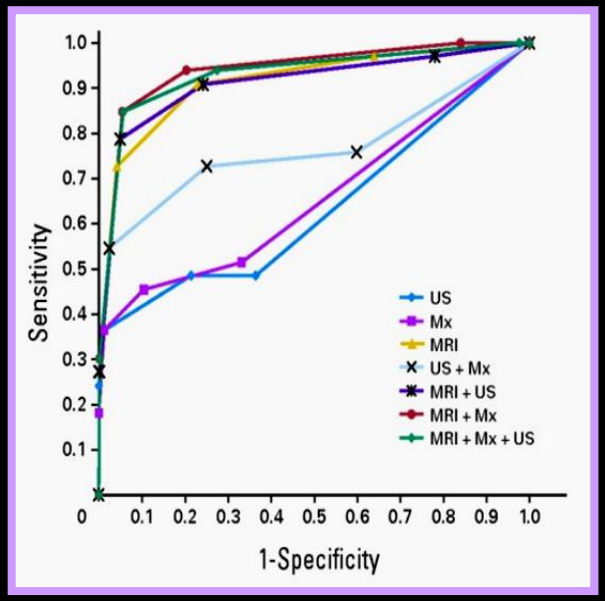
Film-screen	17/31	*55%*
Digital (CR or FFD)	8/19	*42%*

Sensitivity for pT1a-b

Mammo & US	10/20	*50%*
MRI	18/19	*95%*

Sardanelli F et al. Invest Radiol 2011





Kuhl CK et al. JCO 2010 (EVA trial)

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Purpose
We investigated the respective contribution (in terms of cancer yield and stage at diagnosis) of clinical breast examination (CBE), mammography, ultrasound, and quality-assured breast magnetic resonance imaging (MRI), used alone or in different combination, for screening women at elevated risk for breast cancer.

Methods
Prospective multicenter observational cohort study. Six hundred eighty-seven asymptomatic women at elevated familial risk (≥ 20% lifetime) underwent 1,679 annual screening rounds consisting of CBE, mammography, ultrasound, and MRI, read independently and in different combinations. In a subgroup of 371 women, additional half-yearly ultrasound and CBE was performed more than 869 screening rounds. Mean and median follow-up was 29.18 and 29.09 months.

Results
Twenty-seven women were diagnosed with breast cancer: 11 ductal carcinoma in situ (41%) and 16 invasive cancers (59%). Three (11%) of 27 were node positive. All cancers were detected during annual screening; no interval cancer occurred; no cancer was identified during half-yearly ultrasound. The cancer yield of ultrasound (6.0 of 1,000) and mammography (5.4 of 1,000) was equivalent; it increased nonsignificantly (7.7 of 1,000) if both methods were combined. Cancer yield achieved by MRI alone (14.9 of 1,000) was significantly higher; it was not significantly improved by adding mammography (MRI plus mammography: 16.0 of 1,000) and did not change by adding ultrasound (MRI plus ultrasound: 14.9 of 1,000). Positive predictive value was 39% for mammography, 36% for ultrasound, and 48% for MRI.

Conclusion
In women at elevated familial risk, quality-assured MRI screening shifts the distribution of screen-detected breast cancers toward the preinvasive stage. In women undergoing quality-assured MRI annually, neither mammography, nor annual or half-yearly ultrasound or CBE will add to the cancer yield achieved by MRI alone.

«Management of an Inherited Predisposition to Breast Cancer»

Tre studi prospettici con RM, mammografia ed ecografia nell'alto rischio:

80 TMM in totale

Tre DCIS diagnosticati alla sola mammografia

(e tre tumori invasivi diagnosticati alla sola ecografia)

Rateo di TMM non diagnosticati se non si fosse utilizzata la mammografia

= 3/80 = 4% (solo DCIS)

Nelle donne ad alto rischio genetico-familiare si potrebbe evitare la mammografia e utilizzare solo RM ed ecografia, almeno fino a 35 anni di età

Sardanelli F - Podo F, New Engl J Med 2007 (Letter)

«Estimated risk of radiation-induced breast cancer from mammographic screening for young BRCA mutation carriers»

Lifetime risk di morte da TMM radioindotto da mammografia annuale per 10.000 portatrici di mutazione (stima analoga per BRCA2)

Età esposizione	Mortalità (IC 95%)	Riduzione della mortalità per compensare il rischio (IC 95%)
25-29	26 (14, 49)	51% (27%, 96%)
30-34	20 (11, 39)	12% (6%, 23%)
35-39	13 (7, 23)	4% (2%, 7%)

Assumendo che la riduzione in mortalità dovuta alla mammografia sia 15-25% o meno nelle donne giovani, **se la sola mammografia annuale fosse usata come mezzo di screening** nelle donne BRCA mutate, avremo:

- Danno netto tra i 25 e i 29 anni

- **Nessun effetto o piccolo beneficio tra i 30 e i 34 anni**
- **Beneficio effettivo solo a partire dai 35 anni**

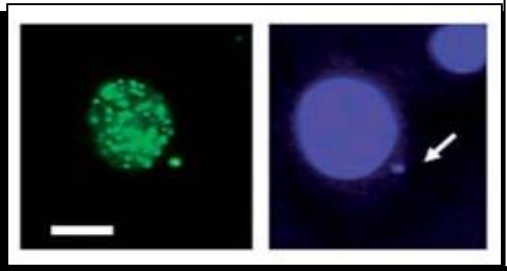
Berrington de Gonzalez et al, J Natl Cancer Inst 2009

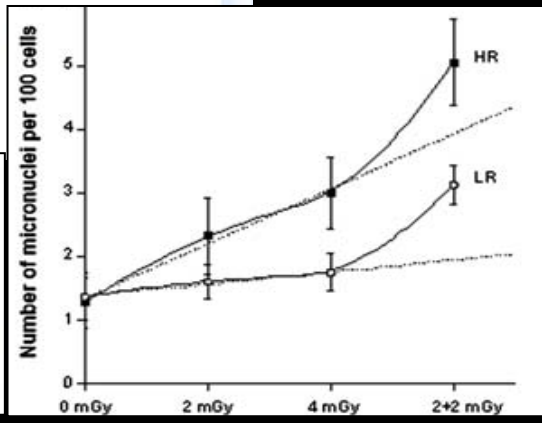
International Journal of Radiation Biology, Early Online: 1–10

DNA double-strand breaks induced by mammographic screening procedures in human mammary epithelial cells

Catherine Colin[1,2], Clément Devic[3], Alain Noël[4], Muriel Rabilloud[5,6], Marie-Thérèse Zabot[7], Sylvie Pinet-Isaac[8], Sophie Giraud[9], Benjamin Riche[5,6], Pierre-Jean Valette[1], Claire Rodriguez-Lafrasse[2,10], & Nicolas Foray[3]

Danno al DNA di cellule ghiandolari mammarie umane dopo esposizione a dosi mammografiche, prelevate a 30 donne a basso rischio (BR) o alto rischio (AR).





Rotture della doppia elica - double-strand breaks (DSB) – quantificate con immunofluorescenza dell'istone H2AX fosforilato (γH2AX) dopo esposizioni mammografiche (2, 4, 2+2 mGy).

Le cellule AR hanno mostrato più DSB spontanei di quelle BR (p=0.014)

Dose-effetto significativo, maggiore in AR (p=0.01)

L'irradiazione ripetuta (2+2 mGy) ha determinato più DSB sponanee e non riparate rispetto all'esposizione a soli 2 mGy o a soli 4 mGy, maggiormente in AR (p=0.006)

«Low-dose effect and LOw and Repeated Dose (LORD) effect»

INIZIALI EVIDENZE SULL'OUTCOME

Comparazione tra due gruppi di portatrici di mutazioni BRCA con diagnosi di TMM (2001-2007):

- Screening RM (n=21), BRCA1+ 74%
- Non screening RM (n=102), BRCA1+ 65%

Assenza di differenze significative per: pN, grado, ER, PR, HER2

	Screening RM	Non screening RM
Dimensione T mediana	6 mm	22 mm
Sentinel node biopsy	57%	28%
Chemioterapia:	43%	86%
Disease-free survival a 3 anni	93%	74%
Overall survival a 3 anni	100%	92%

Differenze non significative (piccolo campione)

Chéreau E, et al. Clin Breast Cancer 2010

VOLUME 28 · NUMBER 36 · DECEMBER 20 2010

JOURNAL OF CLINICAL ONCOLOGY

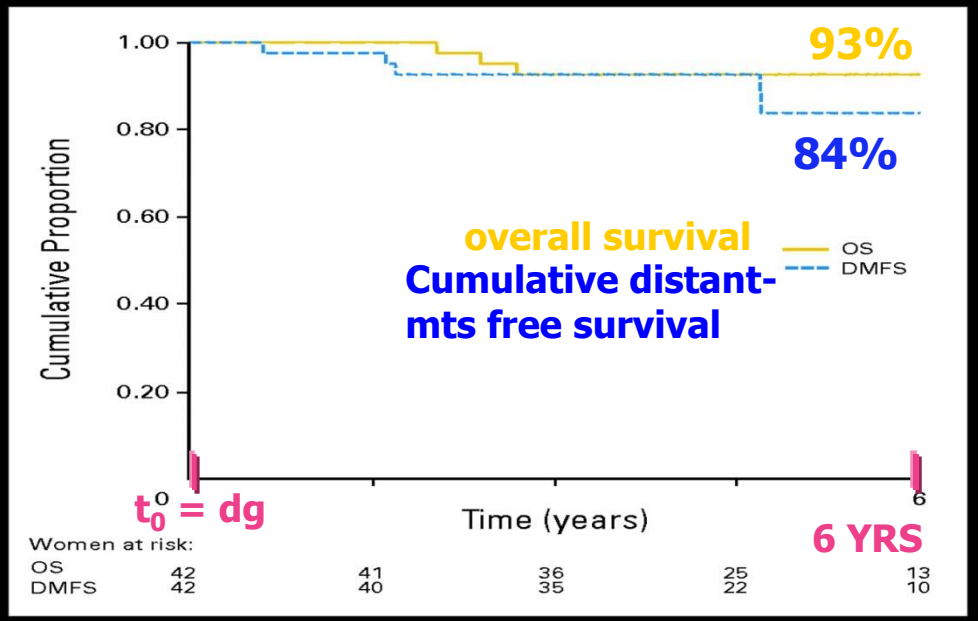
ORIGINAL REPORT

BRCA1-Associated Breast Cancers Present Differently From *BRCA2*-Associated and Familial Cases: Long-Term Follow-Up of the Dutch MRISC Screening Study

La sopravvivenza globale a 5 anni è risultata più alta nella serie con screening RM (93%) rispetto a quella di controlli storici non selezionati della stessa istituzione o quella riportata in 26 serie.

Questi risultati e la **diagnosi di TMM in stadi precoci prognosticamente favorevoli**, particolarmente in donne a rischio intermedio, supportano:

42 BRCA+ women with an invasive breast cancer



1. **Screening RM annuale nelle donne a rischio alto e intermedio**
2. **Modificazione dello screening RM nelle donne BRCA+ (RM ogni sei mesi?)**

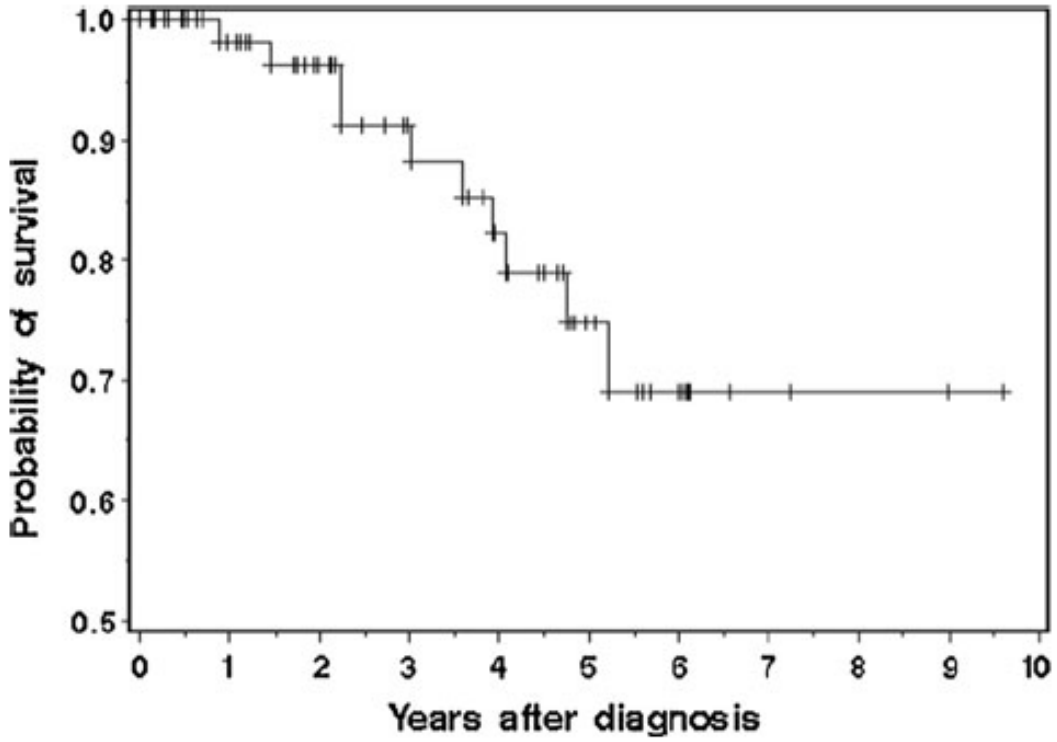
Rijnsburger A J et al. JCO 2010;28:5265-5273

Breast Cancer Res Treat (2013) 139:155–161
DOI 10.1007/s10549-013-2540-z

CLINICAL TRIAL

Survival of patients with *BRCA1*-associated breast cancer diagnosed in an MRI-based surveillance program

Pål Møller · Astrid Stormorken · Christoffer Jonsrud · Marit Muri Holmen · Anne Irene Hagen · Neal Clark · Anita Vabø · Ping Sun · Steven A. Narod · Lovise Mæhle



Abstract We report the 5- and 10-year survival rate of women diagnosed with breast cancer in the context of an annual MRI-based surveillance program. In 2001, as part of a national initiative, women in Norway with a *BRCA1* mutation were offered annual screening with breast MRI in addition to mammography. 802 women with a *BRCA1* mutation were screened one or more times and followed for a mean of 4.2 years. As of December 2011, 68 of 802 women in the screening program were diagnosed with DCIS or invasive breast cancer (8.5 %), including eight prevalent, 50 incident screen-detected and eight interval cancers. Two latent cancers were detected at prophylactic mastectomy. Sixty-three of the cancers were invasive and five were in situ. The mean tumour size was 1.4 cm (range 0.2–4.5 cm), and 85 % of the patients were node-negative. Ten of the 68 patients died of cancer in the follow-up period. The 5-year breast cancer-specific survival for women with cancer was 75 % (95 % CI 56–86 %) and the 10-year survival was 69 % (95 % CI: 48–83 %). The 5-year survival for women with Stage 1 breast cancer was 82 % compared to 98 % in the population. The 5- and 10-year survival of women with a *BRCA1*-associated breast cancer detected in a national MRI-based screening program in *BRCA1* mutation carriers Norway was less than anticipated. The benefit of annual MRI surveillance on reducing breast cancer mortality in *BRCA1* mutation carriers remains to be proven.

Table 3 Hazard ratios associated with prognostic factors, treatments and screening parameters

	Univariate			Multivariate		
	Hazard Ratio	95 % CI	*p* value	Hazard ratio	95 % CI	*p* value
Age						
25–49	1.0			1.0		
50+	0.56	0.15–2.19	0.41	0.59	0.08–0.47	0.61
Size						
0–1 cm	1			1		
1–2 cm	5.09	0.56–45.9	0.15	6.95	0.48–100	0.15
2–5 cm	20.7	0.39–179.8	0.006	32.4	1.93–543	0.02
Nodal status						
Negative	1			1		
Positive	1.01	0.21–4.90	0.99	0.96	0.16–5.79	0.96
Estrogen receptor						
Negative	1			1		
Positive	0.59	0.12–2.82	0.51	1.16	0.05–14.6	0.92
Grade						
I/II	1			1		
III	1.37	0.35–5.33	0.65	0.85	0.05–14.6	0.91
Chemotherapy						
No	1.0			1.0		
Yes	0.88	0.24–3.15	0.84	0.39	0.04–3.38	0.39
Oophorectomy						
No	1.0					
Yes	0.35	0.09–1.41	0.14	0.27	0.04–1.89	0.19
Screen-detected	1					
Interval	5.56	1.28–24.1	0.02	NA	NA	NA

Oophorectomy treated as a time dependent covariate

HIBCRIT-1 database

44 invasive cancers

American Association for Cancer Research

	TNBCs (n=14)	Non-TNBCs (n=30)	p
Median age at diagnosis	49 years (36-62)	53 years (35-72)	n.s.
Pathology	13 IDC, 1 medullary	15 ILC or +DCIS	0.005
Grade 3	11 (79%)	8 (27%)	0.002
Mean T size	16 mm	12 mm	n.s.
Negative nodal status	12 (86%)	16 (53%)	
In: BRCA1+	10 (71%)	9 (30%)	
BRCA2+	2 (14%)	6 (20%)	
BRCA-untested	2 (14%)	15 (50%)	0.028

MRI similarly outperformed CBE, mammography and US in both TNBCs and non-TNBCs

	TNBCs (n=13)	non-TNBCs (n=27)
Follow-up	5.8 years	6.3 years
Mean Dis.-free surv. (range)	7 years (5.8-8.0)	7.2 years (5.2-9.9)
Dis.-free surv. >5 years	8 (62%)	17 (63%)
BC-related deaths	2 (15%)	3 (11%)
Locoregional relapse	1 (8%)	5 (19%)
Distant recurrence	None	2 (7%)

Clinical course/survival of 40 pts (91%)

Podo et al, AACR 2012

PREGRESSA RT PER LINFOMA

Retrospettivo, MMSK, NY

Sung et al, Radiology 2011

Donne (pregresso HL o NHL) = 90 (+1)

Eventi di screening = 247

TMM = 10 (6 DCIS)

- **Solo RM = 4 (3 IDC, 1 mic-DCIS)**
- **Solo mammografia = 3 (con calcif. !) (2 DCIS e 1 mic-DCIS)**
- **RM e mammo = 3 (2 DCIS, 1 IDC+ILC)**

Diagnostic performance

	Sens	Spec	PPV	NPV	Acc
MRI	67%	82%	29%	96%	80%
Mam	67%	93%	55%	96%	90%

Prospettico, DFCI, Boston

Ng et al, JCO 2013

Donne (pregresso HL) = 134

Eventi di screening = 345

TMM = 18 (14 DCIS)

- **Solo RM = 5 (1 IDC, 3 DCIS, 1 Filloide)**
- **Solo mammografia = 6 (con calcif. !) (1 IDC e 5 DCIS)**
- **RM e mammo = 7 (6 DCIS, 1 DCIS)**

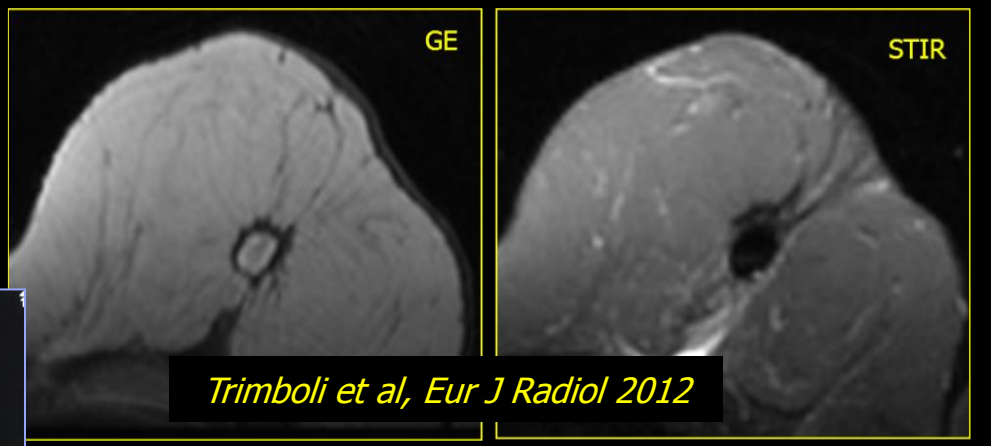
Diagnostic performance

	Sens	Spec	PPV	NPV	Acc
MRI	63%	91%	29%	98%	80%
Mam	68%	92%	34%	98%	91%

MA: Quasi il 50% delle donne tra 25 e 29 anni che hanno eseguito RT toracica per linfoma NON esegue mammografia, il 98% NON esegue RM (Oellinger et al, JAMA 2009)

NON-CONTRAST BREAST MRI

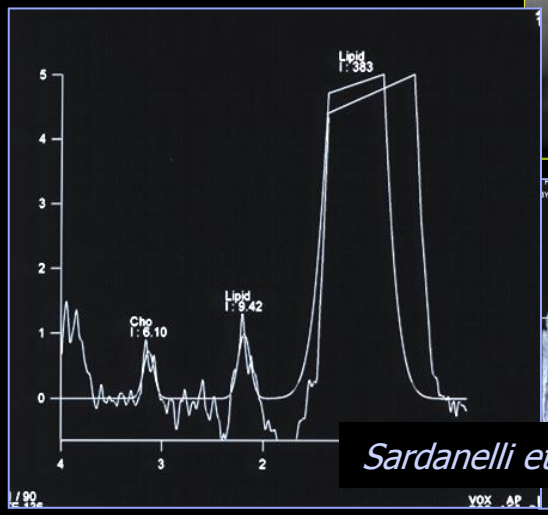
Unenhanced sequences

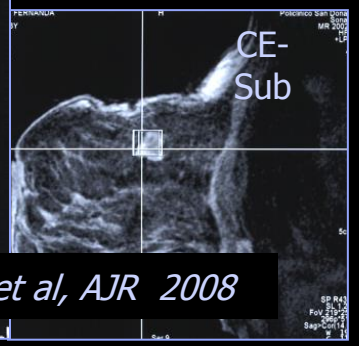


Trimboli et al, Eur J Radiol 2012

Fat necrosis

MRS

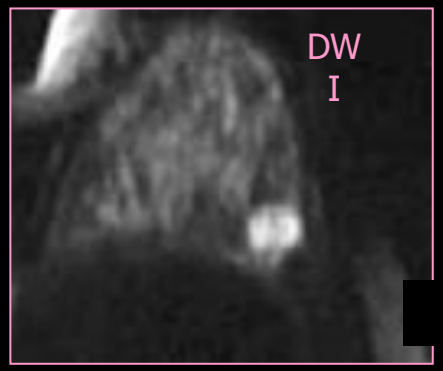


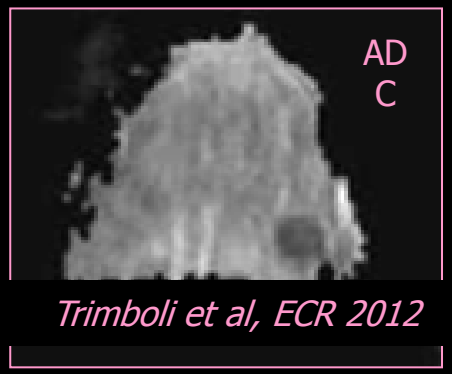


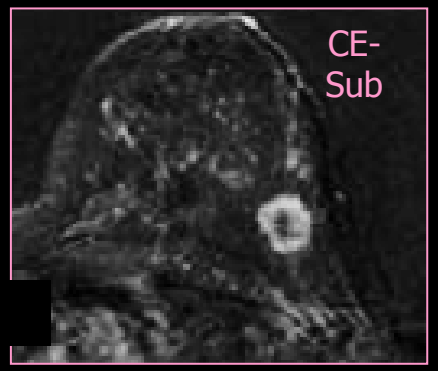
Sardanelli et al, AJR 2008

IDC

DWI







Trimboli et al, ECR 2012

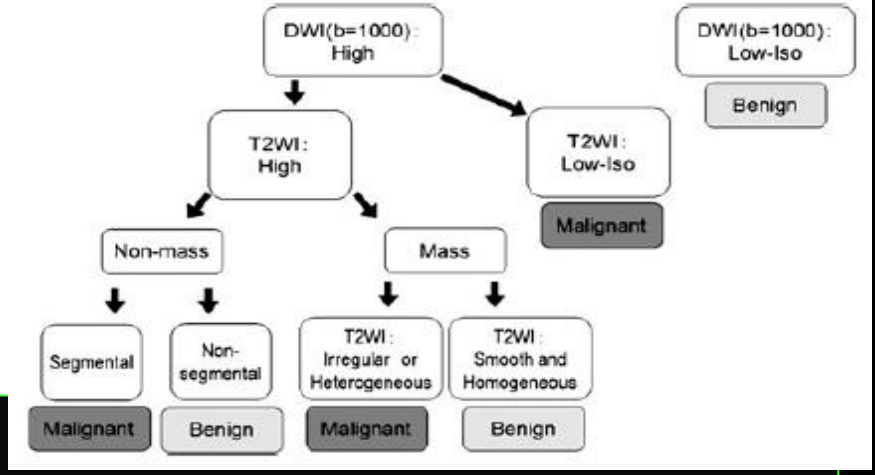
IDC

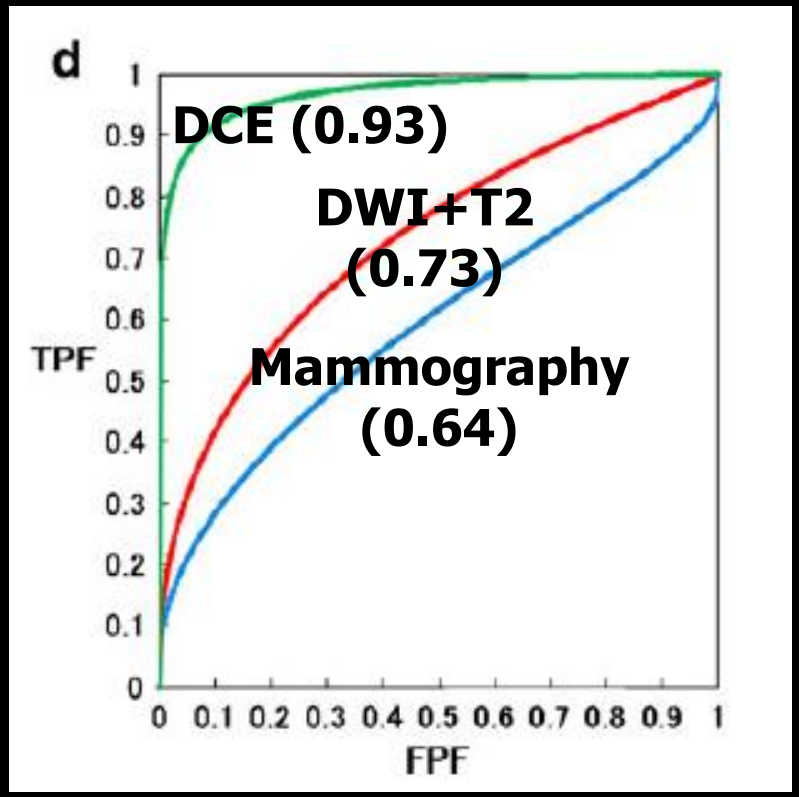
Eur Radiol (2011) 21: 11–17
DOI 10.1007/s00330-010-1890-8

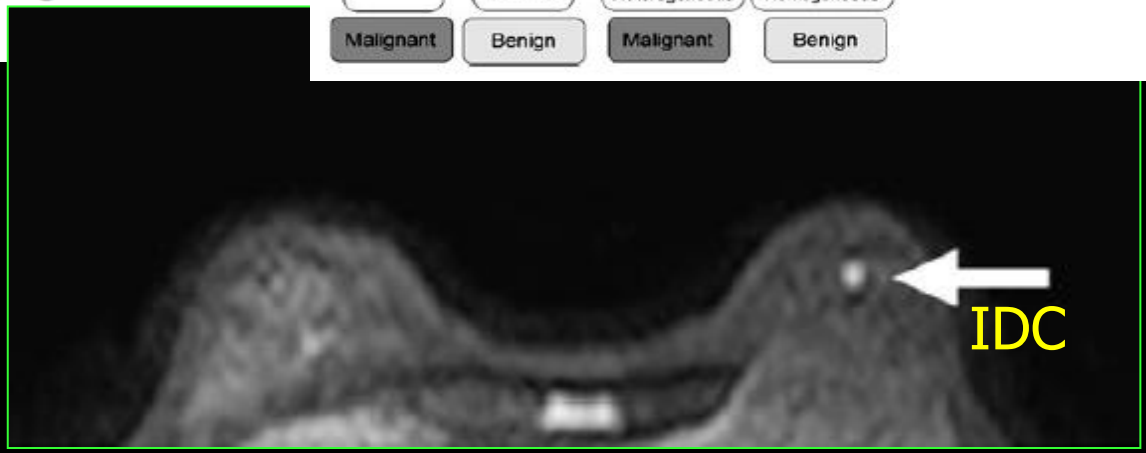
BREAST

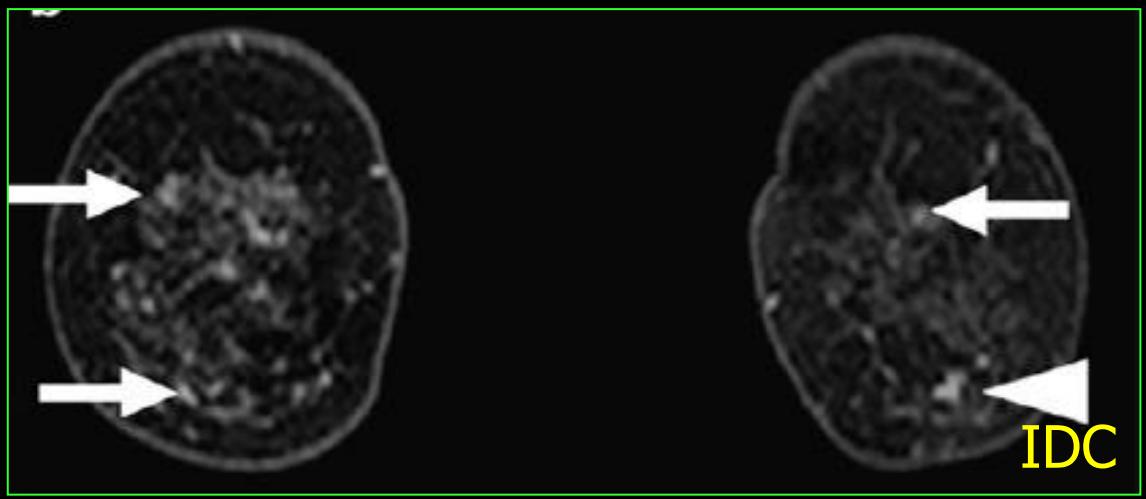
Hidetake Yabuuchi
Yoshio Matsuo
Shunya Sunami
Takeshi Kamitani
Satoshi Kawanami
Taro Setoguchi
Shuji Sakai
Masamitsu Hatakenaka
Makoto Kubo
Eriko Tokunaga
Hidetaka Yamamoto
Hiroshi Honda

Detection of non-palpable breast cancer in asymptomatic women by using unenhanced diffusion-weighted and T2-weighted MR imaging: comparison with mammography and dynamic contrast-enhanced MR imaging

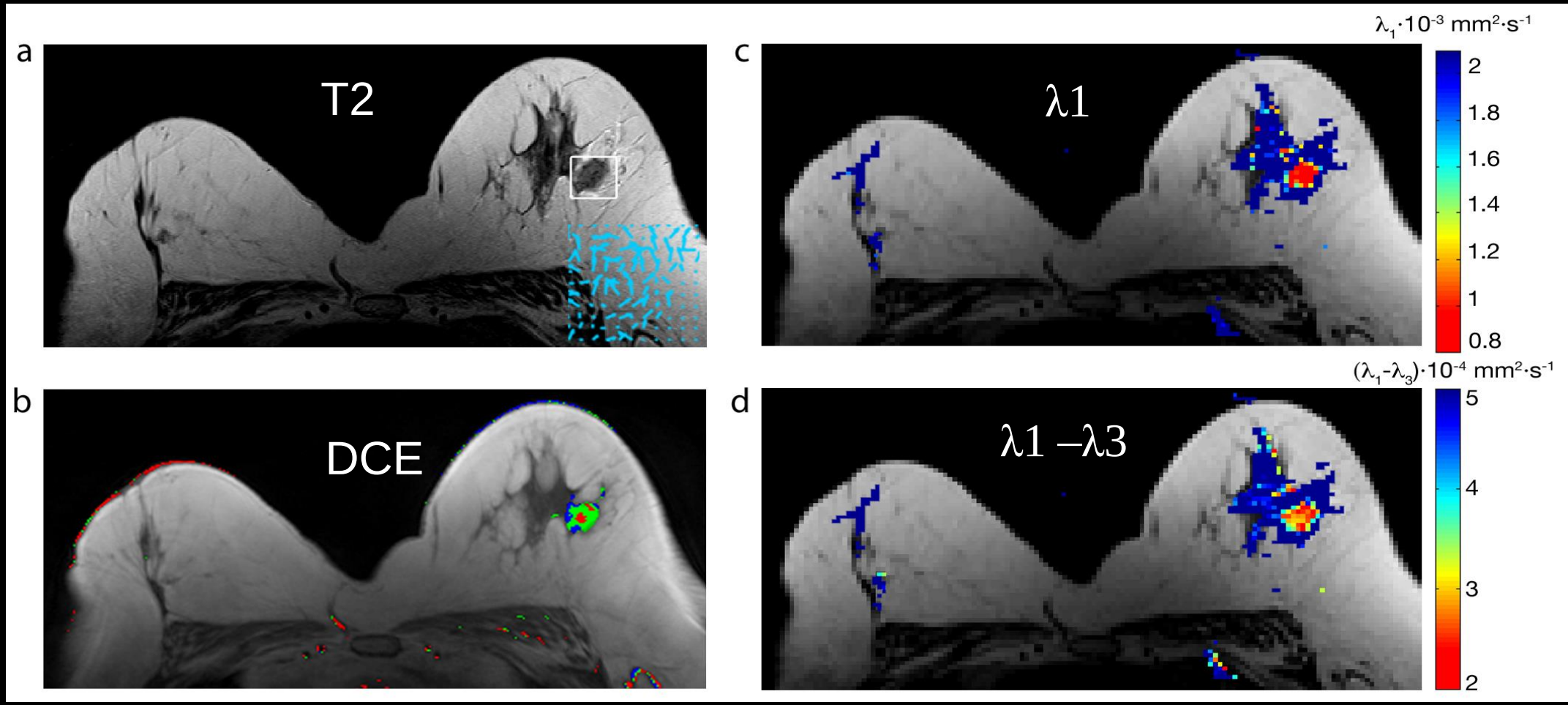








DTI FOR CANCER DETECTION



Courtesy of H. Degani, Rehovot, Israel (Invest Radiol,2012)

Breast Cancer Detection Using Double Reading of Non-contrast MRI (T1, T2-STIR, and DWI): A Proof of Concept Study

Trimboli et al, in press

Retrospective analysis : 67 women, 116 breas
Two blinded readers (R1, R2) independently evaluated non-contrast images using BI-RADS
Ref. standard = pathology or neg. follow-up

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30 IDC (81%) ; 5 DCIS (13%); 2 ILC (6%)
Median size 17 mm

	Sensitivity	Specificity
R1	29/37 (78%)	71/79 (90%)
R2	28/37 (76%)	71/79 (90%)
R1+R2	29/37 (78%)	69/79 (87%)

Almost perfect inter-observer agreement
(κ = 0.873)

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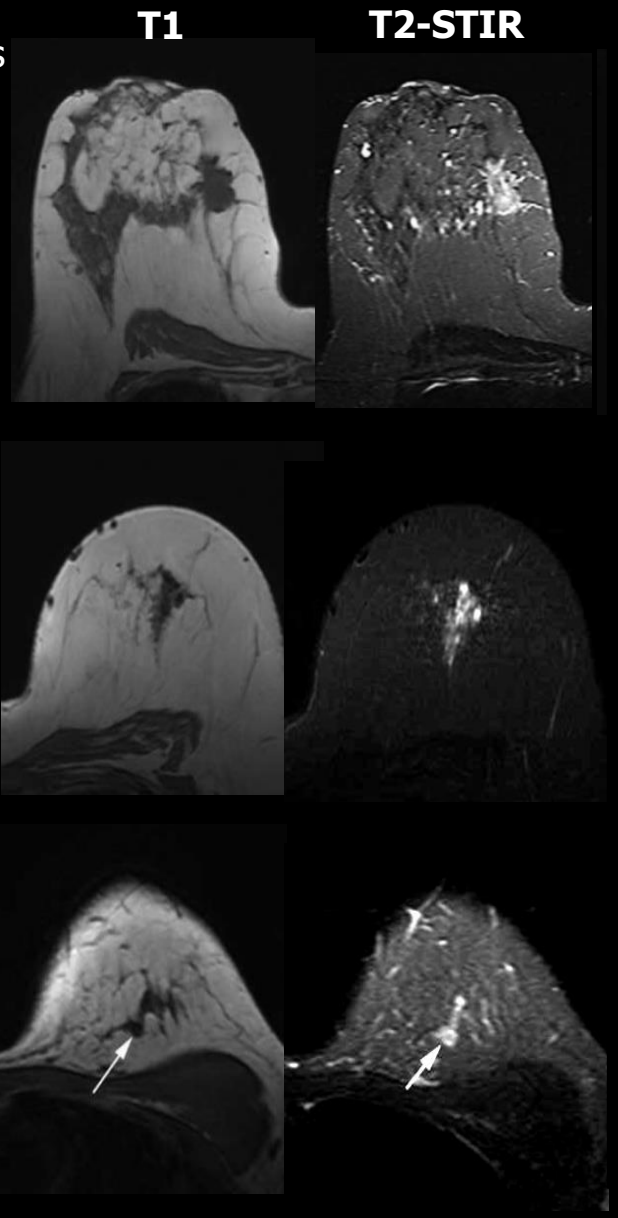

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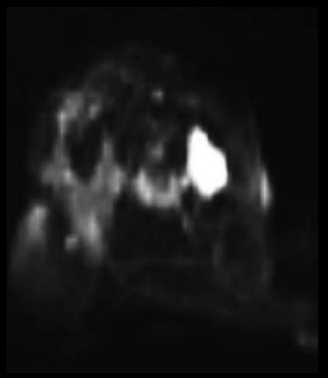
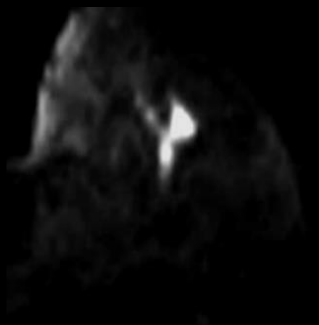
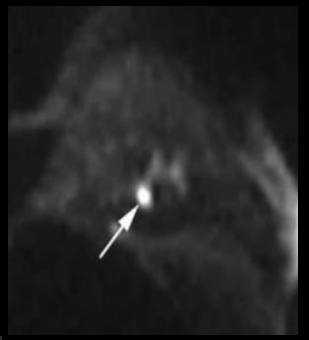
DWI



IDC



DCIS



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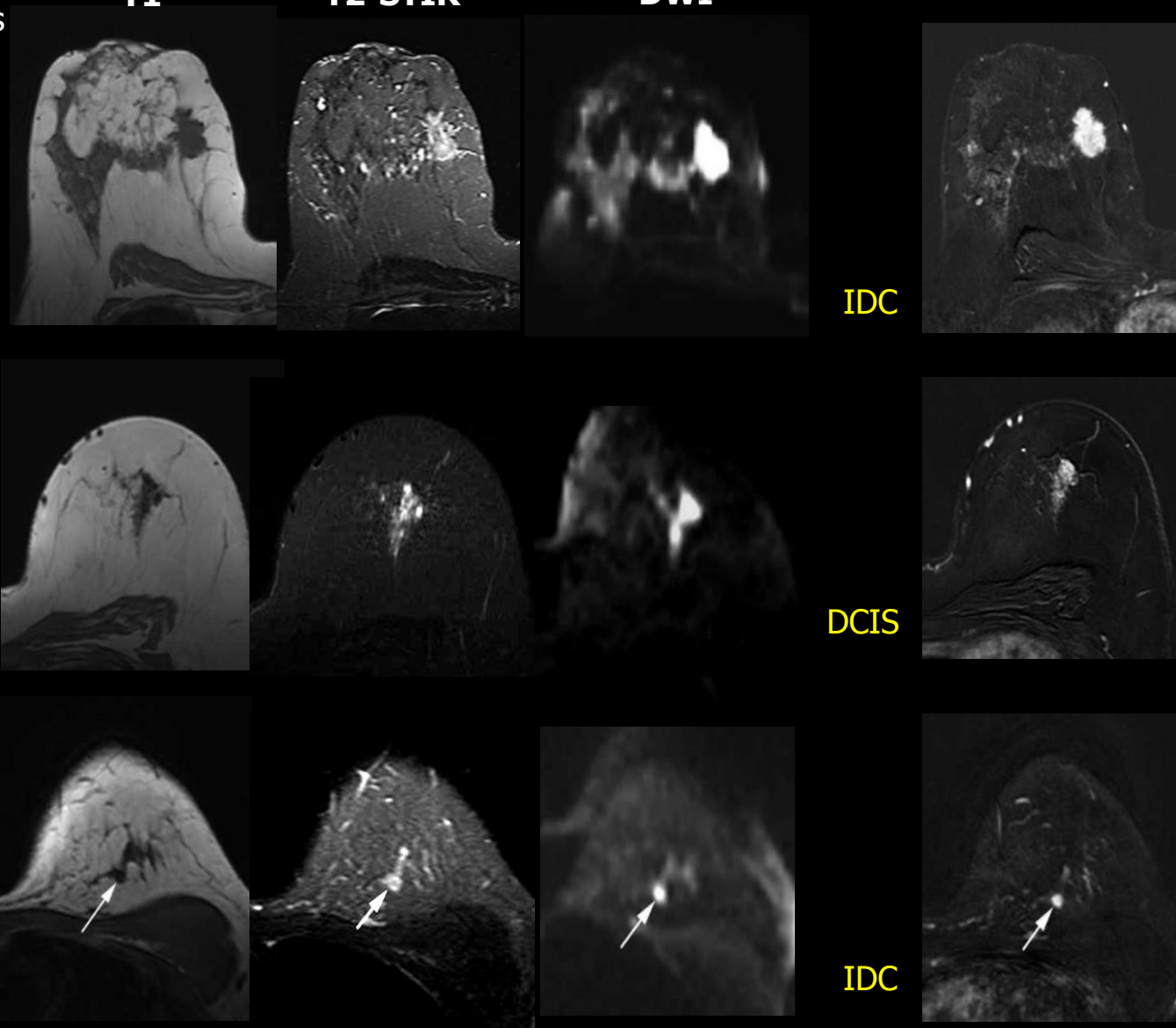

IN BREVE…

1. Identificare le donne ad alto rischio (lifetime risk ≥20%)

- Storia familiare, software IBIS, consulenza genetica, test BRCA
- Pregressa RT toracica per linfoma

2. Alto rischio su base eredo-familiare

- Screening RM dai 25 anni di età
- Se la RM è negativa, la mammografia può essere evitata (ecografia a 6 mesi?)
- Almeno quando un primo BC è diagnosticato in una donna BRCA+ (soprattutto se BRCA1+), l'opzione della mastectomia bilaterale va posta in discussione (elevata probabilità di altri TMM)

3. Pregressa RT toracica per linfoma prima dei 35 anni

- Screening con RM e mammografia a partire da 8 anni dopo la RT ma non prima dei 25 anni di età

Grazie per l'attenzione

francesco.sardanelli@unimi.it