Dipartimento di Radiologia Diagnostica
Ospedale “Sacro Cuore – Don Calabria” Negrar (VR)
Direttore: Dott. Giovanni Carbognin

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

FOLLOW-UP

Dott. ssa Anna RUSSO
Dott. Federico ZAMBONI

BRCA 1, BRCA2 E NEOPLASIA MAMMARIA

- Più del 90% dei casi di neoplasie mammarie ereditarie sono associate a mutazioni del gene BRCA1 e BRCA2.

- Rischio di sviluppare tumore mammario con BRCA1 mutato è pari al 60%,con età media d'incidenza pari a 43 anni.

- Rischio di sviluppare tumore mammario con BRCA2 mutato è pari al 55%, con età media d'incidenza pari a 47 anni .

Linee Guida AIOM, Ed. 2016

Collegio Italiano Senologi – Linee guida 2016

PROTOCOLLO DI FOLLOW-UP

- Età d'insorgenza spesso nelle fasce più giovani della popolazione, (al di fuori dal range d'età coperto dallo screening)

- Neoplasie BRCA correlate sono istologicamente caratterizzate da elevata velocità di proliferazione cellulare ed alto grado di indifferenziamento cellulare

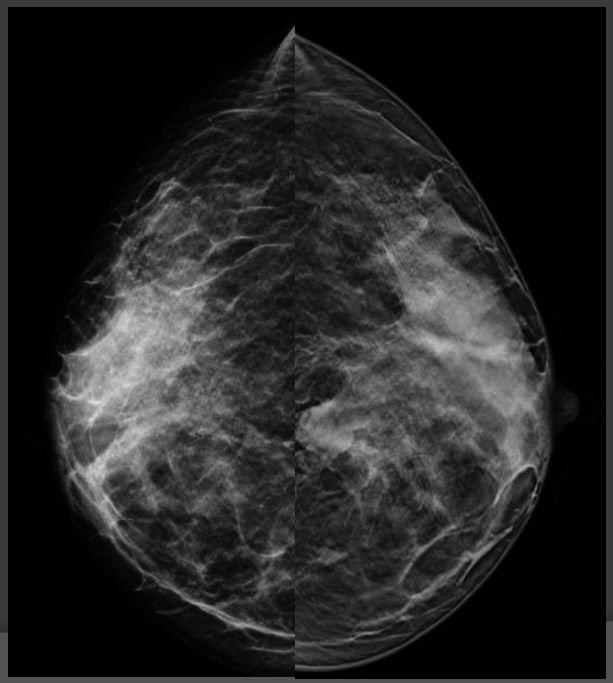
- Protocollo sorveglianza intensivo
- Procedure diagnostiche ad alta sensibilità
- Utilizzo esami diagnostici costosi in termini economici

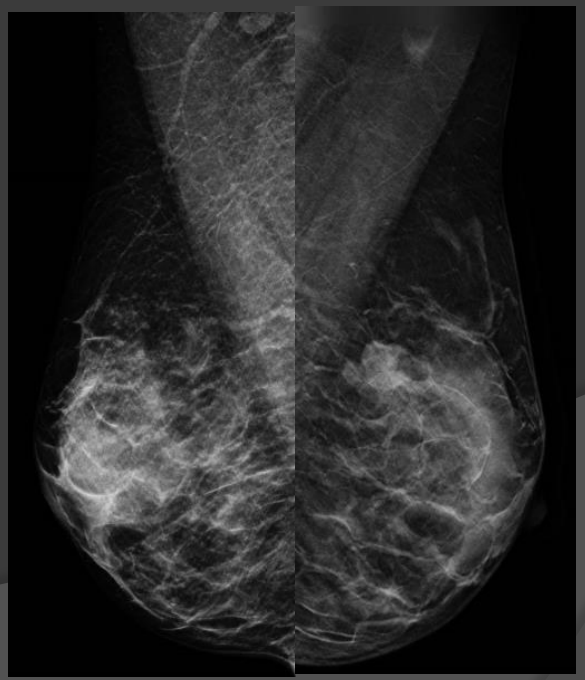
Collegio Italiano Senologi – Linee guida 2016

MAMMOGRAFIA

- Costi ridotti.
- Rapidità d'esecuzione.
- Standardizzazione dell'esame.
- Non richiede somministrazione di mdc ev.
- Alta sensibilità per microcalcificazioni (DCIS di piccole dimensioni).
- Guida a procedure bioptiche.

- Esposizione radiazioni ionizzanti.
- Bassa sensibilità nelle mammelle dense.





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	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive Predictive Value % (95% CI)	Negative Predictive Value % (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
Overall (1592 rounds)						
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Mammography	25/50 50.0 (35.5–64.5)	1035/1045 99.0 (98.2–99.5)	25/35 71.4 (53.7–85.4)	1035/1060 97.6 (96.5–98.5)	52.3 (23.8–114.7)	0.50 (0.31–0.82)
Ultrasonography	26/50 52.0 (37.4–66.3)	1000/1016 98.4 (97.5–99.1)	26/42 61.9 (45.6–76.4)	1000/1024 97.7 (96.5–98.5)	33.0 (16.7–65.5)	0.49 (0.30–0.80)
MRI	42/46 91.3 (79.2–97.6)	966/999 96.7 (95.4–97.7)	42/75 56.0 (44.1–67.5)	966/970 99.6 (98.9–99.9)	27.6 (16.1–47.6)	0.09 (0.03–0.25)
Mammography + ultrasonography	30/48 62.5 (47.4–76.0)	975/999 97.6 (96.4–98.5)	30/54 55.6 (41.4–69.1)	975/993 98.2 (97.2–98.9)	26.0 (14.1–47.9)	0.38 (0.22–0.67)
MRI + mammography	41/44 93.2 (81.3–98.6)	944/980 96.3 (95.0–97.4)	41/77 53.2 (41.5–64.7)	944/947 99.7 (99.1–99.9)	25.4 (14.8–43.5)	0.07 (0.02–0.23)
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Ultrasonography	9/21 42.9 (21.8–66.0)	620/630 98.4 (97.1–99.2)	9/19 47.4 (24.4–71.1)	620/632 98.1 (96.7–99.0)	27.0 (9.9–73.4)	0.58 (0.28–1.19)
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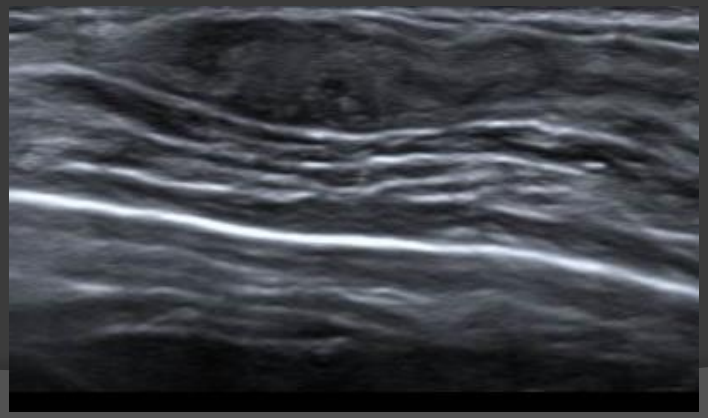
Ultrasonography	17/29 58.6 (38.9–76.5)	380/386 98.4 (96.6–99.4)	17/23 73.9 (51.6–89.8)	380/392 96.9 (94.7–98.4)	37.7 (13.8–103.0)	0.42 (0.21–0.84)
MRI	26/28 92.9 (76.5–99.1)	371/383 96.9 (94.6–98.4)	26/38 68.4 (51.3–82.5)	371/373 99.5 (98.1–99.9)	29.6 (13.5–64.9)	0.07 (0.02–0.31)

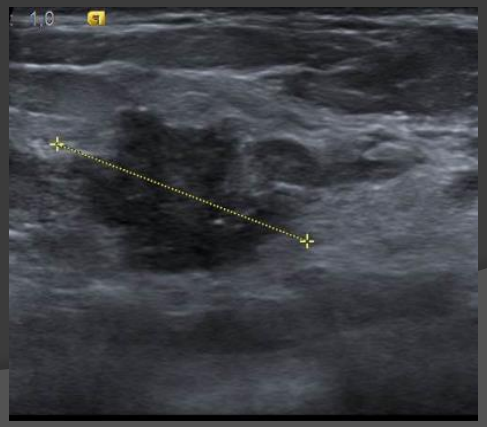
Multicenter Surveillance of Women at High Breast Cancer Risk, Sardanelli et al. 2011

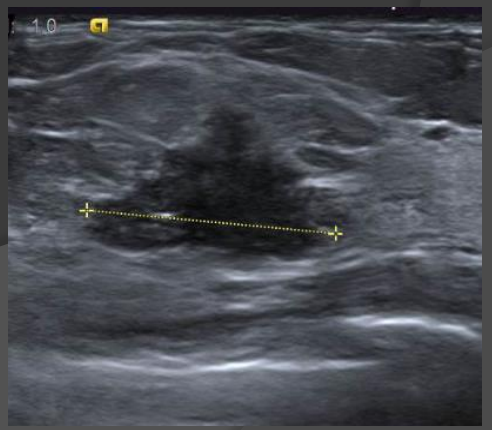
ECOGRAFIA

- Costi ridotti.
- No radiazioni ionizzanti.
- Non richiede somministrazione di mdc ev.
- Guida a procedure bioptiche.

- Esame operatore-dipendente.
- Difficile standardizzazione dell'esame.
- Lunghi tempi d'esecuzione.
- Alto tasso di falsi positivi.
- Sono identificate neoplasie in fase più avanzata (infiltranti).
- Non esistono studi che dimostrino riduzione mortalità.







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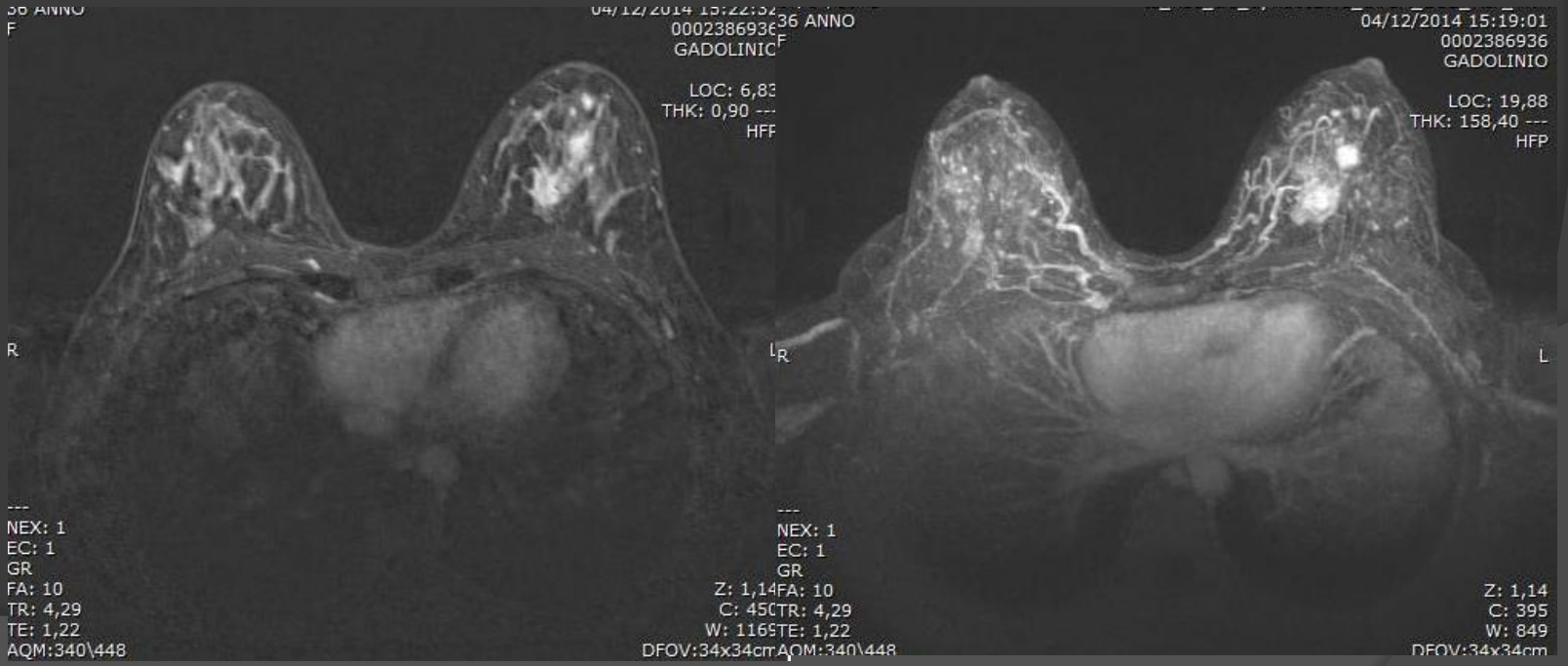
RISONANZA MAGNETICA

- Alta sensibilità.
- Possibile standardizzazione dell'esame.
- Guida a procedure bioptiche.

- Costi elevati.
- Lunghi tempi d'esecuzione.
- Necessaria somministrazione di mdc ev.
- Bassa specificità.



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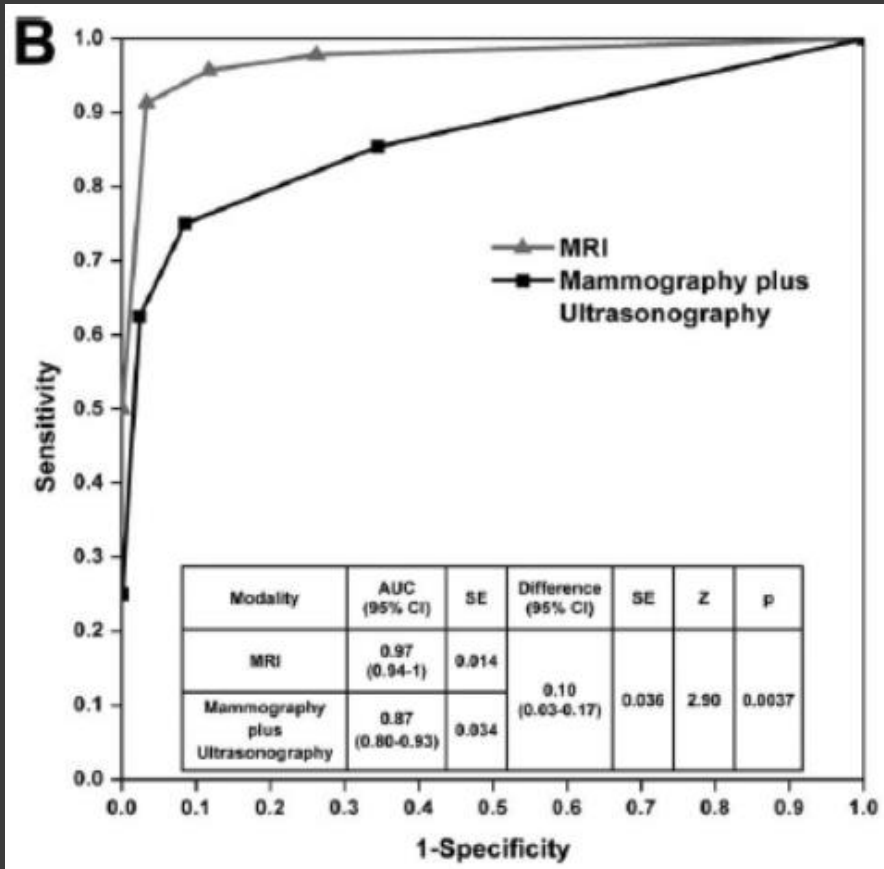
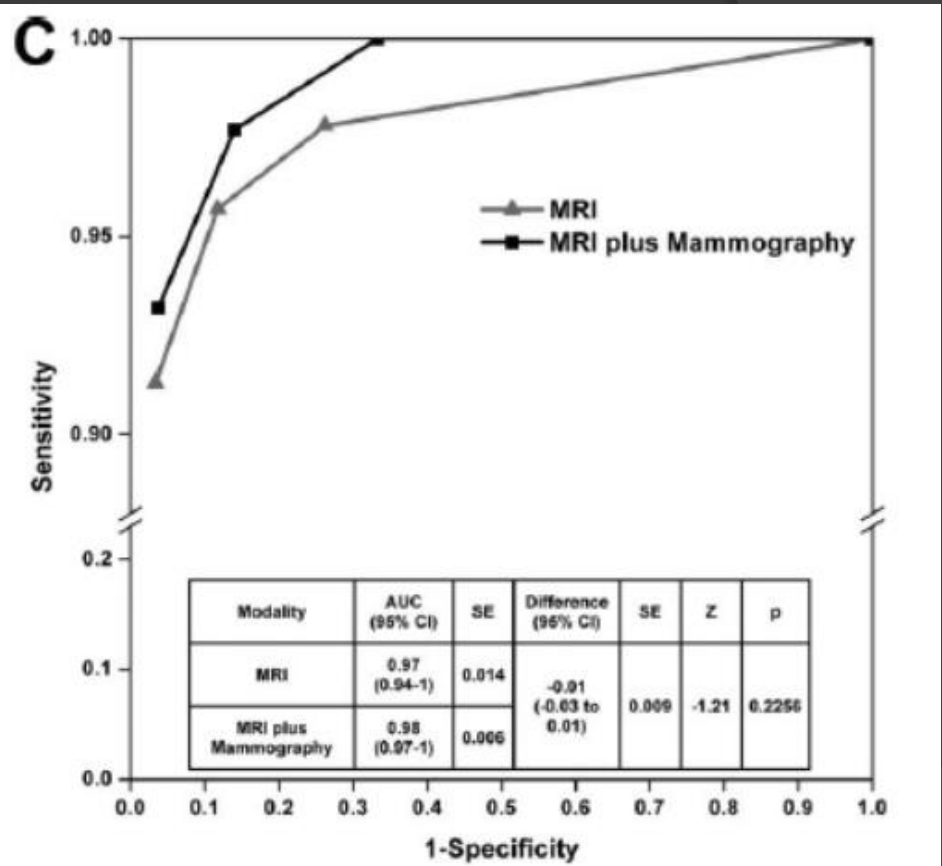


Modality	AUC (95% CI)	SE	Difference (95% CI)	SE	Z	p
MRI	0.97 (0.94-1)	0.014	0.10 (0.03-0.17)	0.036	2.90	0.0037
Mammography plus Ultrasonography	0.87 (0.80-0.93)	0.034				



Modality	AUC (95% CI)	SE	Difference (95% CI)	SE	Z	p
MRI	0.97 (0.94-1)	0.014	-0.01 (-0.03 to 0.01)	0.009	-1.21	0.2256
MRI plus Mammography	0.98 (0.97-1)	0.006				

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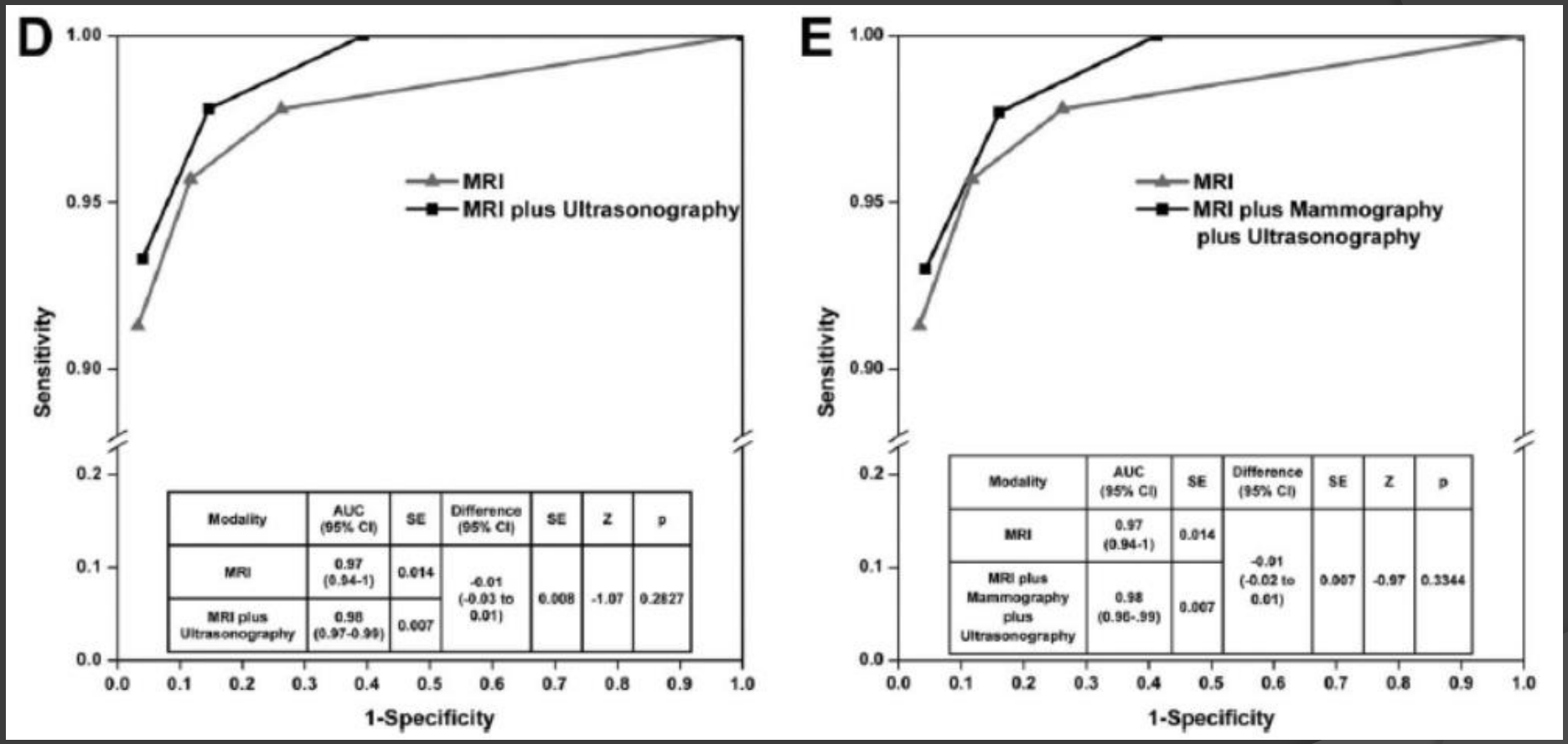

Modality	AUC (95% CI)	SE	Difference (95% CI)	SE	Z	p
MRI	0.97 (0.94-1)	0.014	-0.01 (-0.03 to 0.01)	0.008	-1.07	0.2827
MRI plus Ultrasonography	0.98 (0.97-0.99)	0.007				

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MRI plus Mammography plus Ultrasonography	0.98 (0.96-.99)	0.007				

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RISONANZA MAGNETICA

- ✓ Limiti attuali dell'uso di RM come sorveglianza della popolazione:

  a. costi elevati
  b. limitata disponibilità

- ✓ Il protocollo correntemente utilizzato in RM di screening è identico al protocollo usato per la RM diagnostica

- ✓ ridurre tempo di acquisizione/aumentare il numero di esami
- ✓ ridurre il tempo di lettura
- ✓ disporre di Radiologi esperti di imaging mammario per leggere le immagini

RISONANZA MAGNETICA
Protocollo “FAST”

- ✓ Pre gado FS T1W AX
- ✓ Post gado FS T1W AX
- ✓ Immagini di sottrazione
- ✓ MIP COR e AX

<u>Tempi di refertazione</u>

Tempo lettura immagini MIP: 3 secondi

Tempo lettura immagini di sottrazione: 28 secondi ± 23 secondi

KULH CK, et Al. Abbreviated Breast Magnetic Resonance Imaging (MRI): First Postcontrast Subtracted Images and Maximum-Intensity Projection—A Novel Approach to Breast Cancer Screening With MRI J Clin Oncol 2014; 32:2304–2310

FOLLOW-UP

SCREENING DELLE DONNE AD ALTO RISCHIO

Nelle donne ad alto rischio per importante storia familiare di carcinoma mammario o perché portatrici di mutazione di BRCA1 e/o BRCA-2 i controlli mammografici dovrebbero essere iniziati all'età di 25 anni o 10 anni prima dell'età di insorgenza del tumore nel familiare più giovane, nonostante la bassa sensibilità della mammografia in questa popolazione.

La risonanza magnetica con cadenza annuale come metodica di screening in aggiunta alla mammografia e all'esame clinico, trova indicazione[52] nelle donne ad alto rischio definite come segue:

- Mutazione BRCA1 o BRCA2;
- Lifetime risk del 20 – 25% secondo i comuni modelli di predizione del rischio;
- Anamnesi di radioterapia a carico della parete toracica all'età di 10-30 anni;
- Diagnosi di sindrome di Li-Fraumeni, Cowden o Bannayan-Riley-Ruvalcaba.

Linee guida neoplasia mammella AIOM edizione 2016

FOLLOW-UP

18-25 ANNI	**• Autoesame ogni 3-4 mesi + Visita senologica**
25-30 ANNI	• Visita clinica semestrale • Ecografia mammaria semestrale • RM mammaria annuale
30-35 ANNI	• Visita clinica semestrale • Ecografia mammaria semestrale • RM annuale • Mammografia annuale (Solo proiezioni oblique)
35-50 ANNI	• Visita clinica semestrale •Mammografia annuale standard • Ecografia mammaria semestrale • RM annuale
> 50 ANNI	• Visita clinica semestrale • Mammografia annuale standard • Ecografia mammaria (a giudizio del Radiologo) • RM annuale

Collegio Italiano Senologi – linee guida 2016

Sacro Cuore Don Calabria
Cancer Care Center
Negrar - Verona

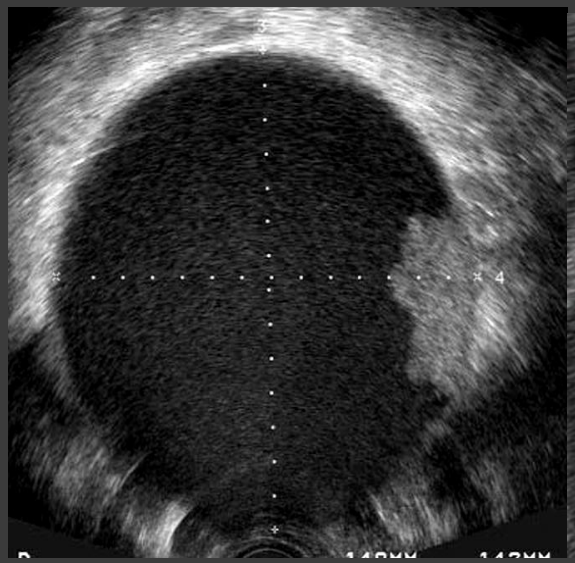
FOLLOW-UP

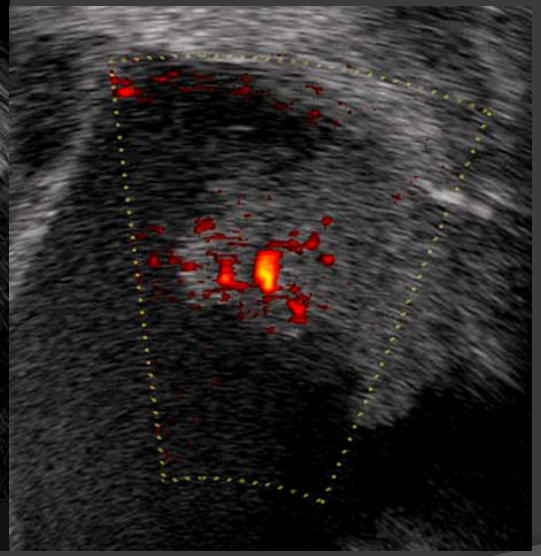
Radiologic Procedure	Rating	Comments	RRL*
Mammography screening	9	Beginning at age 25–30 or 10 years before age of first-degree relative with breast cancer or 8 years after radiation therapy, but not before age of 25. Mammography and MRI are complementary examinations, both should be performed.	☢ ☢
Digital breast tomosynthesis screening	9	Beginning at age 25–30 or 10 years before age of first-degree relative with breast cancer or 8 years after radiation therapy, but not before age of 25. Mammography and MRI are complementary examinations, both should be performed.	☢ ☢
MRI breast without and with IV contrast	9	Mammography and MRI are complementary examinations, both should be performed.	O
US breast	6	If patient cannot have MRI.	O
FDG-PEM	2		☢ ☢ ☢ ☢
Tc-99m sestamibi BSGI	2		☢ ☢ ☢ ☢
MRI breast without IV contrast	1		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

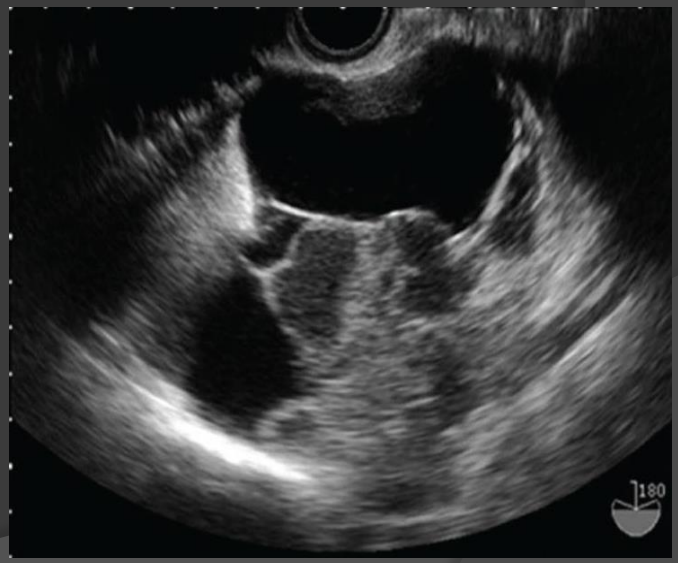
American College of Radiology ACR Appropriateness Criteria® 2016

BRCA 1, BRCA2 E NEOPLASIA OVARICA

- Rischio di sviluppare tumore ovarico con BRCA1 mutato è pari al 59%.
- Rischio di sviluppare tumore ovarico con BRCA2 mutato è pari al 16%.







PROTOCOLLO DI FOLLOW-UP

- Non vi sono dati sufficienti che provino la riduzione della mortalità per neoplasie ovariche mediante utilizzo di screening.

- Recenti studi hanno dimostrato promettenti risultati mediante screening seriale del Ca 125.

> 30 ANNI	**• Visita ginecologica semestrale.** **• Ecografia trans-vaginale semestrale.** **• Dosaggio marcatore Ca 125 semestrale.**

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CONCLUSIONI

- ✓ I protocolli di sorveglianza per la diagnosi precoce del tumore alla mammella in donne ad alto rischio devono prevedere l'utilizzo combinato di più metodiche diagnostiche, caratterizzate da elevata SE e SP.
- ✓ Ampio consensus per il protocollo di follow-up mediante mammografia ed RM.
- ✓ RM è l'esame di follow-up cardine per l'elevata SE.
- ✓ Protocollo RM "FAST" riduce i costi, il tempo di esecuzione ed il tempo di lettura.
- ✓ Non esiste ampio consensus sulle linee guida di follow-up delle neoplasie ovariche in donne ad alto rischio.
- ✓ Risultati promettenti si stanno ottenendo con Il dosaggio sierico seriale del CA 125

GRAZIE PER L'ATTENZIONE!

Anna.russo@sacrocuore.it