Direzione Radiodiagnostica
Fondazione del Piemonte per l'Oncologia
Istituto di Candiolo IRCCS - Istituto di Ricovero e Cura a Carattere Scientifico
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Chemioterapia Primaria

L. Martincich

Argomenti

- Valutare il ruolo della RM nel monitorare la risposta tumorale a NCT;
- Illustrare le problematiche aperte;
- Valutare il potenziale ruolo della RM come Imaging biomarker;
- Illustrare come valutare un esame RM e cosa riportare nel referto quando l'indicazione e' il monitoraggio della risposta tumorale (casi clinici).

Eusoma reccomendations (EJC, 2010)

Indicazione al trattamento neoadiuvante definita da team multidisciplinare;

1. Baseline MRI: large potentially operable breast cancer, prima dell'inizio della PCT (LoE-1; DoR-A)
2. Post PCT MRI: dopo 2 settimane da ultimo ciclo e entro due settimane dalla chirurgia (EPO);

   -In caso di non risposta clinica o all'Imaging convenzionale la RM non e' mandatoria

In entrambe le condizioni i tempi di programmazione ed il management dei risultati della RM (additional lesions) non devono determinare posticipazioni del trattamento terapeutico.

Protocollo tecnico: T2 e DCE-MRI

Ruolo della RM nel monitorare la risposta tumorale a NCT

DOI:10.1093/jnci/djs528
Advance Access publication January 7, 2013

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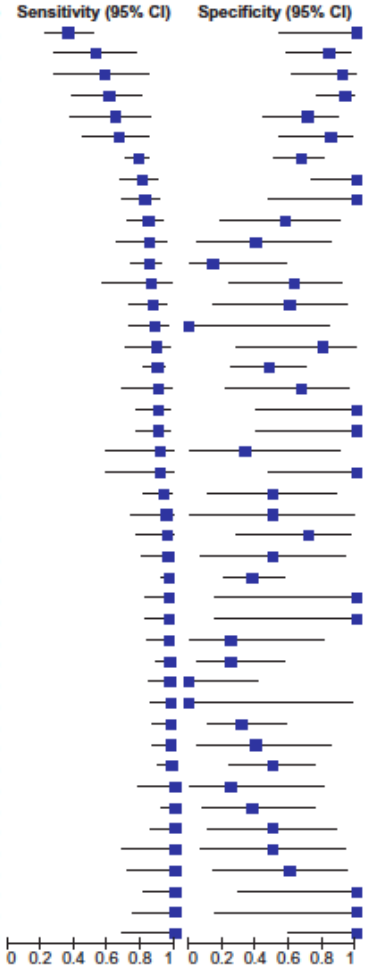
REVIEW

Meta-Analysis of Magnetic Resonance Imaging in Detecting Residual Breast Cancer After Neoadjuvant Therapy

Michael L. Marinovich, Nehmat Houssami, Petra Macaskill, Francesco Sardanelli, Les Irwig, Eleftherios P. Mamounas, Gunter von Minckwitz, Meagan E. Brennan, Stefano Ciatto†

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Park 2010(21)	17	0	30	6	0.36 (0.23 to 0.51)	1.00 (0.54 to 1.00)
Hsiang 2007(22)	9	3	8	15	0.53 (0.28 to 0.77)	0.83 (0.59 to 0.96)
Chen 2008(23)	7	1	5	11	0.58 (0.28 to 0.85)	0.92 (0.62 to 1.00)
Chen 2008(24)	14	2	9	26	0.61 (0.39 to 0.80)	0.93 (0.76 to 0.99)
Baek 2009(25)	11	5	6	12	0.65 (0.38 to 0.86)	0.71 (0.44 to 0.90)
Bahri 2009(26)	16	2	8	11	0.67 (0.45 to 0.84)	0.85 (0.55 to 0.98)
Straver 2010(27)	130	14	36	28	0.78 (0.71 to 0.84)	0.67 (0.50 to 0.80)
Warren 2004(28)	46	0	11	12	0.81 (0.68 to 0.90)	1.00 (0.74 to 1.00)
Balu-Maestro 2002(29)	45	0	10	5	0.82 (0.69 to 0.91)	1.00 (0.48 to 1.00)
Rieber 2002(30)	43	3	8	4	0.84 (0.71 to 0.93)	0.57 (0.18 to 0.90)
Yeh 2005(31)	22	3	4	2	0.85 (0.65 to 0.96)	0.40 (0.05 to 0.85)
Bodini 2004(32)	56	6	10	1	0.85 (0.74 to 0.92)	0.14 (0.00 to 0.58)
Fangberget 2011(33)	12	3	2	5	0.86 (0.57 to 0.98)	0.63 (0.24 to 0.91)
von Minckwitz 2005(34)	39	2	6	3	0.87 (0.73 to 0.95)	0.60 (0.15 to 0.95)
Murata 2010(35)	30	2	4	0	0.88 (0.73 to 0.97)	0.00 (0.00 to 0.84)
Bhattacharyya 2008(36)	24	1	3	4	0.89 (0.71 to 0.98)	0.80 (0.28 to 0.99)
Nakamura 2007(37)	84	11	10	10	0.89 (0.81 to 0.95)	0.48 (0.26 to 0.70)
Nicoletto 2008(38)	18	2	2	4	0.90 (0.68 to 0.99)	0.67 (0.22 to 0.96)
Belli 2002(39)	37	0	4	4	0.90 (0.77 to 0.97)	1.00 (0.40 to 1.00)
Belli 2006(40)	37	0	4	4	0.90 (0.77 to 0.97)	1.00 (0.40 to 1.00)
Delille 2003(41)	10	2	1	1	0.91 (0.59 to 1.00)	0.33 (0.01 to 0.91)
Corcioni 2008(42)	10	0	1	5	0.91 (0.59 to 1.00)	1.00 (0.48 to 1.00)
Wright 2010(43)	41	3	3	3	0.93 (0.81 to 0.99)	0.50 (0.12 to 0.88)
Rosen 2003(44)	18	1	1	1	0.95 (0.74 to 1.00)	0.50 (0.01 to 0.99)
Choi 2010(45)	21	2	1	5	0.95 (0.77 to 1.00)	0.71 (0.29 to 0.96)
Trecate 1999(46)	25	2	1	2	0.96 (0.80 to 1.00)	0.50 (0.07 to 0.93)
Moon 2009(47)	160	18	6	11	0.96 (0.92 to 0.99)	0.38 (0.21 to 0.58)
Wasser 2003(48)	28	0	1	2	0.97 (0.82 to 1.00)	1.00 (0.16 to 1.00)
Abraham 1996(49)	28	0	1	2	0.97 (0.82 to 1.00)	1.00 (0.16 to 1.00)
Schott 2005(50)	30	3	1	1	0.97 (0.83 to 1.00)	0.25 (0.01 to 0.81)
Garimella 2007(51)	62	9	2	3	0.97 (0.89 to 1.00)	0.25 (0.05 to 0.57)
Cocquyt 2002(52)	34	7	1	0	0.97 (0.85 to 1.00)	0.00 (0.00 to 0.41)
Akazawa 2006(53)	36	1	1	0	0.97 (0.86 to 1.00)	0.00 (0.00 to 0.97)
Bollet 2007(54)	39	11	1	5	0.97 (0.87 to 1.00)	0.31 (0.11 to 0.59)
Dose-Schwarz 2010(55)	40	3	1	2	0.98 (0.87 to 1.00)	0.40 (0.05 to 0.85)
Woodhams 2010(56)	53	8	1	8	0.98 (0.90 to 1.00)	0.50 (0.25 to 0.75)
Tozaki 2004(57)	15	3	0	1	1.00 (0.78 to 1.00)	0.25 (0.01 to 0.81)
Partridge 2002(58)	44	5	0	3	1.00 (0.92 to 1.00)	0.38 (0.09 to 0.76)
Martincich 2004(59)	24	3	0	3	1.00 (0.86 to 1.00)	0.50 (0.12 to 0.88)
Armitage 2005(60)	10	2	0	2	1.00 (0.69 to 1.00)	0.50 (0.07 to 0.93)
Kwong 2006(61)	11	2	0	3	1.00 (0.72 to 1.00)	0.60 (0.15 to 0.95)
Montemurro 2005(62)	18	0	0	3	1.00 (0.81 to 1.00)	1.00 (0.29 to 1.00)
Londero 2004(63)	13	0	0	2	1.00 (0.75 to 1.00)	1.00 (0.16 to 1.00)
Drew 2001(64)	10	0	0	7	1.00 (0.69 to 1.00)	1.00 (0.59 to 1.00)



pCR and DCE-MRI

Mean Accuracy 88%

44 studies
2,949 patients

Mean pCR rate 16%
(2.6%-54.9%)

Ruolo della RM nel monitorare la risposta tumorale a NCT

Insights Imaging
DOI 10.1007/s13244-013-0219-y

ORIGINAL ARTICLE

The role of magnetic resonance imaging in assessing residual disease and pathologic complete response in breast cancer patients receiving neoadjuvant chemotherapy: a systematic review

M. B. I. Lobbes · R. Prevos · M. Smidt · V. C. G. Tjan-Heijnen · M. van Goethem · R. Schipper · R. G. Beets-Tan · J. E. Wildberger

Table 3 Correlation coefficients of MRI and histopathological tumour measurements

Author	Correlation coefficient	P-value
Partridge et al.	0.89	<0.001
Cheung et al.	0.982	<0.001
Martincich et al.	0.72	<0.001
Segara et al.	0.749	<0.0001
Kim et al.	0.645	<0.001
Moon et al.	0.584	NA
Wright et al.	0.49	NA
Park et al.	0.667	NA
Nakahara et al.	0.21	NS
Wang et al.	0.866	<0.01
Dongfeng et al.	0.698	<0.001
Fangberget et al.	0.87	<0.001
Guarneri et al.	0.53	NS
Shin et al.[a]	0.97	NA
Chen et al.	0.30	0.03
Kim et al.	0.619	<0.0001
Shin et al.[b]	0.781	NA

NA not available, *NS* not significant

[a] 2011 paper, [b] 2012 paper

Residual disease and DCE-MRI

3,119 citations
35 selected papers;
2,359 patients

Extent of residual disease
DCE-MRI vs Pathology
Correlation Coefficient
0.698 (range 0.21–0.982)

Ruolo della RM nel monitorare la risposta tumorale a NCT

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ORIGINAL ARTICLE

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M. B. I. Lobbes · R.
V. C. G. Tjan-
R. G. Beets

Residual disease and DCE-MRI

In tutti i soggetti candidabili a PCT secondo i criteri appena visti ed indipendentemente dal tipo di intervento pianificabile post PCT

Multicentricita': Chemo-sensitivity

Kim et al.	0.619	<0.0001
Shin et al.[b]	0.781	NA

NA not available, *NS* not significant
[a] 2011 paper, [b] 2012 paper

? Multicentricita’ + PCT?

In tutti i soggetti candidabili a PCT secondo i criteri appena visti ed indipendentemente dal tipo di intervento pianificabile post PCT

Performance diagnostica RM e caratteristiche biologiche della neoplasia

Original Research

Breast magnetic resonance imaging use in patients undergoing neoadjuvant chemotherapy is associated with less mastectomies in large ductal cancers but not in lobular cancers☆

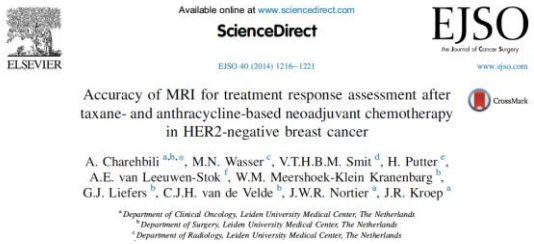
European Journal of Cancer 81 (2017) 74–80

"Variables associated with breast MRI use on performing mastectomy after neoadjuvant chemotherapy per histologic subtype"

Variables	Margin involvement for breast conserving surgery as first surgical procedure			Mastectomy as final surgery			Contralateral breast cancer		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
MRI									
No	1 (Ref)			1 (Ref)			1 (Ref)		
Yes	0.60	0.32–1.10	0.10	0.89	0.73–1.09	0.27	0.84	0.50–1.40	0.51
Year of incidence									
2011	1 (Ref)			1 (Ref)			1 (Ref)		
2012	1.53	0.83–2.83	0.17	1.09	0.89–1.33	0.40	1.16	0.67–2.01	0.59
2013	1.37	0.76–2.44	0.29	0.86	0.72–1.03	0.11	1.21	0.73–2.01	0.46
Age group (years)									
50–69	1 (Ref)			1 (Ref)			1 (Ref)		
<50	1.12	0.71–1.77	0.63	1.66	1.43–1.94	<0.001	0.83	0.55–1.24	0.36
Clinical tumour stage									
cT1–2	1 (Ref)			1 (Ref)			1 (Ref)		
cT3	2.66	1.49–4.72	<0.001	5.64	4.60–6.92	<0.001	0.37	0.19–0.72	0.00
Clinical nodal stage									
cN0	1 (Ref)			1 (Ref)			1 (Ref)		
cN1–3	1.34	0.83–2.15	0.23	1.17	1.00–1.37	0.05	0.34	0.22–0.51	<0.001
Histology									
Ductal	1 (Ref)			1 (Ref)			1 (Ref)		
Lobular	4.53	2.67–7.67	<0.001	2.16	1.67–2.79	<0.001	1.20	0.68–2.12	0.53
Other	1.13	0.25–5.06	0.87	1.48	0.92–2.37	0.11	1.43	0.50–4.07	0.51
Tumour grade									
Good	1 (Ref)			1 (Ref)			1 (Ref)		
Intermediate	2.36	0.67–8.33	0.18	1.07	0.70–1.63	0.77	0.84	0.30–2.34	0.73
Poor	1.29	0.31–5.44	0.73	1.59	1.03–2.46	0.04	0.93	0.31–2.84	0.90
Unknown	1.12	0.33–3.82	0.86	1.25	0.84–1.85	0.28	1.12	0.44–2.87	0.82
ER, PR and HER2 status									
ER+ or PR+, and HER2−	1 (Ref)			1 (Ref)			1 (Ref)		
ER+ or PR+, and HER2+	0.41	0.18–0.92	0.03	0.99	0.79–1.24	0.92	0.49	0.24–1.00	0.05
ER− and PR-, and HER2−	0.14	0.04–0.44	<0.001	0.91	0.74–1.12	0.36	0.33	0.16–0.66	0.00
ER− and PR−, and HER2+	0.36	0.12–1.02	0.05	1.00	0.77–1.31	0.98	0.26	0.08–0.82	0.02
Multifocality									
No	1 (Ref)			1 (Ref)			1 (Ref)		
Yes	0.96	0.55–1.67	0.88	2.93	2.46–3.49	<0.001	0.84	0.52–1.35	0.48

MRI, magnetic resonance imaging; ER, oestrogen receptor; PR, progesterone receptor; HER2, HER2-receptor.

Performance diagnostica RM e caratteristiche biologiche della neoplasia



Available online at www.sciencedirect.com
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EJSO
the Journal of Cancer Surgery
EJSO 40 (2014) 1216–1221
www.ejso.com

Accuracy of MRI for treatment response assessment after taxane- and anthracycline-based neoadjuvant chemotherapy in HER2-negative breast cancer

A. Charehbili [a,b,*], M.N. Wasser [c], V.T.H.B.M. Smit [d], H. Putter [e], A.E. van Leeuwen-Stok [f], W.M. Meershoek-Klein Kranenbarg [b], G.J. Liefers [b], C.J.H. van de Velde [b], J.W.R. Nortier [a], J.R. Kroep [a]

[a] Department of Clinical Oncology, Leiden University Medical Center, The Netherlands
[b] Department of Surgery, Leiden University Medical Center, The Netherlands
[c] Department of Radiology, Leiden University Medical Center, The Netherlands

194 patients with HER2-negative breast cancer.
82.5% of the cases were ER-positive

MRI before and after NCT

Radiologic response determined on RECIST 1.1. criteria

Table 2
Concordance between pCR and complete response as measured with DCE-MRI.

Pathological response	MRI
Measurement after 6 cycles	$N = 194$
CR concordance	15/41
Accuracy for pCR	76%
Sensitivity for pCR	43%
Specificity for pCR	84%
Positive predictive value for pCR	37%
Negative predictive value for pCR	87%

AUC value

MRI and pCR	0.63 (95% C.I. 0.52-0.74)
ER-negative	0.75 (95% C.I. 0.57-0.94)
ER-positive	0.57 (95% C.I. 0.44-0.70)

Correlation coefficient for the residual tumour size

MRI and pathology	0.46 (P < 0.001)
ER-negative breast tumours	0.76 (P < 0.001)
ER-positive tumours	0.40 (P < 0.001)

Performance diagnostica RM e caratteristiche biologiche della neoplasia

VOLUME 29 · NUMBER 6 · FEBRUARY 20 2011
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Magnetic Resonance Imaging Response Monitoring of Breast Cancer During Neoadjuvant Chemotherapy: Relevance of Breast Cancer Subtype

Claudette E. Loo, Marieke E. Straver, Sjoerd Rodenhuis, Sara H. Muller, Jelle Wesseling, Marie-Jeanne T.F.D. Vrancken Peeters, and Kenneth G.A. Gilhuijs

188 patients

"All HER2-positive tumours were treated with a trastuzumab-based regimen."

Conclusion

MRI during NAC to monitor response is effective in triple-negative or HER2-positive disease but is inaccurate in ER-positive/HER2-negative breast cancer.

Table 3. Lesion Morphology and Pattern of Reduction at MRI Stratified by Breast Cancer Subtype

	Triple Negative (n = 47)				HER2 Positive (n = 38)				ER Positive/HER2 Negative (n = 103)			
	Prevalence		PPV		Prevalence		PPV		Prevalence		PPV	
Variable	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Pathology												
Residual tumor	31	66			23	61			96	93		
Lesion morphology at baseline MRI												
Mass unifocal	27	57	18	67	7	18	6	86	34	33	31	91
Mass multifocal	15	32	11	73	20	53	9	45	31	30	28	90
Diffuse	5	11	2	40	11	29	8	73	38	37	37	97
Pattern of reduction*												
Shrinking mass	26	55	19	73	11	29	7	64	43	42	41	95
Diffuse decrease	3	6	1	33	6	16	4	67	36	35	35	97
Small foci	6	13	1	17	4	11	3	75	7	7	5	71
No enhancement	5	11	3	60	12	32	4	33	5	5	4	80
No change	7	15	7	100	5	13	5	100	12	12	11	92

NOTE. Total No. of patients = 188.
Abbreviations: MRI, magnetic resonance imaging; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PPV, positive predictive value for residual tumor.
*Pattern of reduction from baseline MRI to MRI during neoadjuvant chemotherapy.

Performance diagnostica RM e caratteristiche biologiche della neoplasia

TABLE 3 Agreement between the tumor size by MRI and by pathology according to clinicopathologic and radiologic factors

	N	Size discrepancy, mean (±SD)	*P* value
Total	166	12.6 (±17.6)	
Age (year)			0.388
<30	6	6.7 (±8.8)	
30–39	47	11.5 (±17)	
40–49	72	15.5 (±19.8)	
50–59	34	8.9 (±12.7)	
≥60	7	12.9 (±23.2)	
Initial MRI size (mm)		44.3 (±8.4)	0.066
<50	59	6.1 (±7.5)	
50–80	66	13.1 (±14.1)	
≥80	41	7.6 (±9.4)	
Breast cancer subtype			0.005
Triple-negative	43	8.0 (±12.9)	
HER2-positive	50	10.1 (±16)	
ER-positive	73	17.2 (±21.1)	
EIC[a]			0.479
Absent	94	12.2 (±16.8)	
Present	32	17.1 (±20.9)	
Nuclear grade[a]			0.007
1	17	28.5 (±29.8)	
2	31	9.3 (±14.7)	
3	78	11.8 (±14.1)	
Lymphovascular invasion[b]			0.575
Absent	69	14.7 (±18.1)	
Present	71	13.9 (±18.6)	
Initial MR pattern			0.001
Single circumscribed mass	65	7.2 (±8.5)	
Multiple mass	29	9.1 (±11.6)	
Diffuse non-mass–like enhancement	59	22.0 (±24.2)	
Focal non-mass–like enhancement	13	4.7 (±7.2)	
Regimen			
AC	62	12.8 (±17.1)	0.305
AT	15	16.9 (±22.8)	
AC-T	42	15.0 (±20.9)	
HER2/Neu monoclonal antibody based chemotherapy	47	8.8 (±12.4)	

Regimens of chemotherapy: *A* adriamycin, *C* cyclophosphamide, *T* docetaxel

EIC extensive intraductal component

[a] Limited to patients with invasive carcinoma ($n = 126$)

[b] Limited to patients with viable invasive or in situ tumor ($n = 140$)

TABLE 3 Agreement between the tumor size by MRI and by pathology according to clinicopathologic and radiologic factors

	N	Size discrepancy, mean (±SD)	*P* value
Breast cancer subtype			0.005
Triple-negative	43	8.0 (±12.9)	
HER2-positive	50	10.1 (±16)	
ER-positive	73	17.2 (±21.1)	
Nuclear grade[a]			0.007
1	17	28.5 (±29.8)	
2	31	9.3 (±14.7)	
3	78	11.8 (±14.1)	
Initial MR pattern			0.001
Single circumscribed mass	65	7.2 (±8.5)	
Multiple mass	29	9.1 (±11.6)	
Diffuse non-mass–like enhancement	59	22.0 (±24.2)	
Focal non-mass–like enhancement	13	4.7 (±7.2)	

dicting residual lesion size for these cancers. In our study, a diffuse non-mass–like enhancement pattern on initial MRI showed the biggest size discrepancy ($P = 0.001$). In con-

Ko ES, Ann Surg Oncol 2013

Problematiche aperte

? Multicentricita' ?

? CLI multicentrici ?

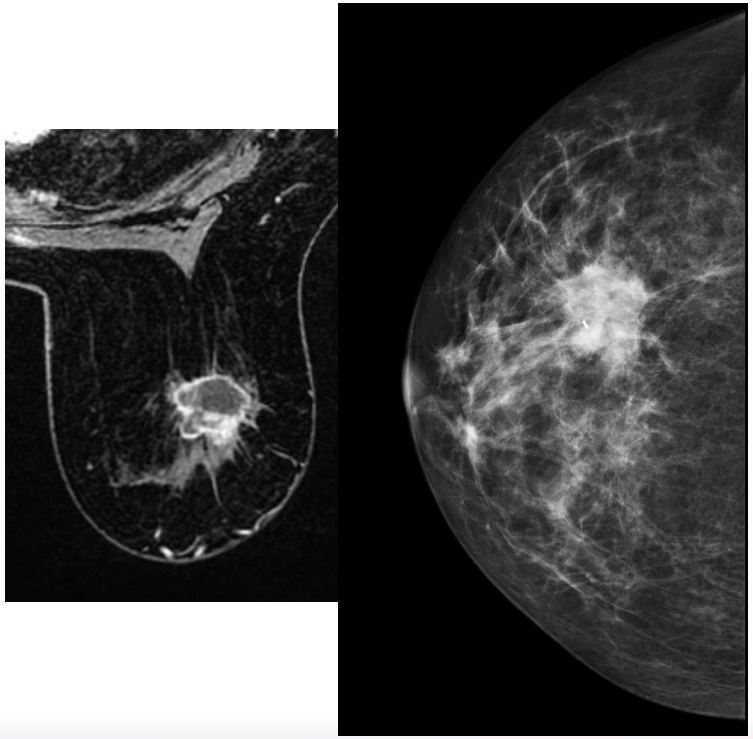
? Neoplasie luminali ?

? Lesioni non mass a distribuzione diffusa?

In ~~tutti~~ i soggetti candidabili a PCT secondo i criteri appena visti ed indipendentemente dal tipo di intervento pianificabile post PCT

Reperimento pre-trattamento

- E’ raccomandato in quanto il downstaging chemioindotto potrebbe rendere non più identificabile la sede della pregressa neoplasia al termine della NAC.
  - Neoplasia unifocale e multifocale (pCR e BCS probabile post NAC)
  - Centrolesionale
  - Clips amagnetiche radiopache/ecovisibili o marcate con tracciante radioattivo.



ypTo;No
No residual invasive cells.
Grade of response 5/5 (pCR)

Eusoma reccomendations (EJC, 2010)

Come valutare e cosa riportare nel referto se l'indicazione della RM e' monitoraggio PCT

- Concomitante valutazione delle variazione dei reperti RM fra pre e post PCT
  - Anche alla luce dell'Imaging Convenzionale (microcalcificazioni associate)
- Nel post PCT, l'enhancement residuo nella sede della pregressa neoplasia deve essere considerata come segno di rimanenza di malattia.
- Misurazione del residuo di malattia dopo PCT, secondo criteri RECIST or WHO;
  - Se multifocalita' o multicentricita' somma del diametro massimo delle lesioni.

Performance diagnostica RM e classificazione della risposta (rCR)…

DOI:10.1093/jnci/djs528
Advance Access publication January 7, 2013
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REVIEW

Meta-Analysis of Magnetic Resonance Imaging in Detecting Residual Breast Cancer After Neoadjuvant Therapy

Michael L. Marinovich, Nehmat Houssami, Petra Macaskill, Francesco Sardanelli, Les Irwig, Eleftherios P. Mamounas, Gunter von Minckwitz, Meagan E. Brennan, Stefano Ciatto†

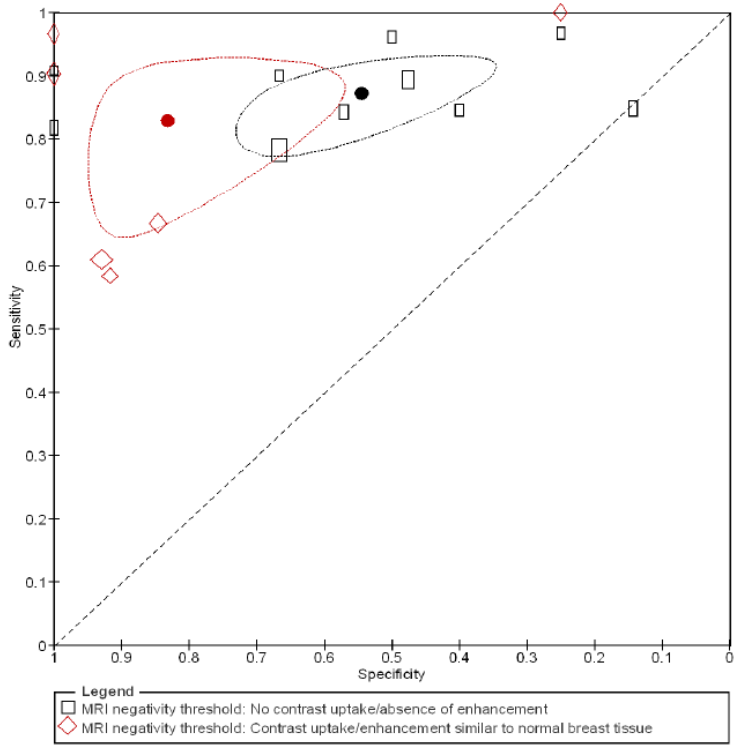
44 papers; 2,949 patients
pCR mean rate 16% (2.6%-54.9%)

MRI accuracy differed according to the definition of radiologic Complete Response (P = .01)

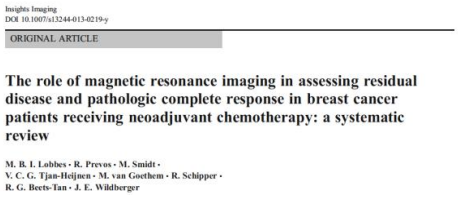
Complete absence of MRI enhancement (threshold 1)
Sensitivity 87% (80-92)
Specificity 54% (39-69)

Contrast enhancement equal to/less than normal breast tissue (threshold 2)
Sensitivity 83% (69-91)
Specificity 83% (64 -93)

Appendix I: Summary sensitivity and specificity for MRI positivity/negativity thresholds



…pur considerando le implicazioni



Insights Imaging
DOI 10.1007/s13244-013-0219-y

ORIGINAL ARTICLE

The role of magnetic resonance imaging in assessing residual disease and pathologic complete response in breast cancer patients receiving neoadjuvant chemotherapy: a systematic review

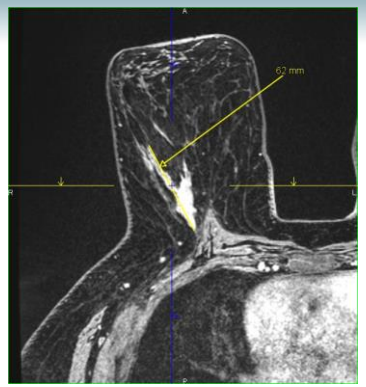
M. B. I. Lobbes · R. Prevos · M. Smidt · V. C. G. Tjan-Heijnen · M. van Goethem · R. Schipper · R. G. Beets-Tan · J. E. Wildberger

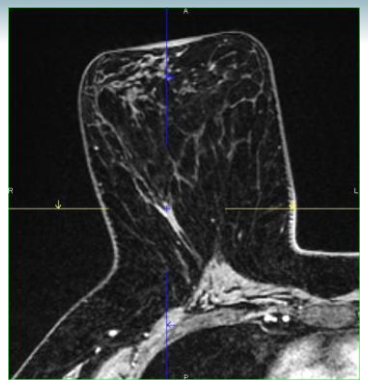
- *"Factors in overestimating tumour size might be:*
  - *reactive inflammation caused by tumour response and healing,*
  - *surrounding sclerosis and necrosis,*
  - *multiple scattered lesions and presence of accompanying ductal carcinoma in situ*

- *Underestimation was also observed in the NAC setting. Causes might be:*
  - *antivascular effects of docetaxel (resulting in less tumour enhancement),*
  - *lack of inflammatory response surrounding the tumour in docetaxel patients,*
  - *more extensive ductal carcinoma in situ components*
  - *partial volume effects in very small foci of residual disease"*

Similar with 3T equipment

Chen, Radiology, 2011





MICROFOCOLAIO RESIDUO (diametro < 0,5 mm) DI CARCINOMA DUTTALE *IN SITU* DI ALTO GRADO NUCLEARE (c.d. DIN3 sec. WHO 2003) IN PARENCHIMA MAMMARIO CON ESITI DI TERAPIA NEOADIUVANTE (fibrosclerosi, microcalcificazioni distrofiche, focolai di flogosi cronica).

Non e' una problematica sulla pianificazione chirugica

se pianificato BCS

ma potrebbe essere un limite ora che si sta iniziando a parlare di omissione chirugica nelle pCR

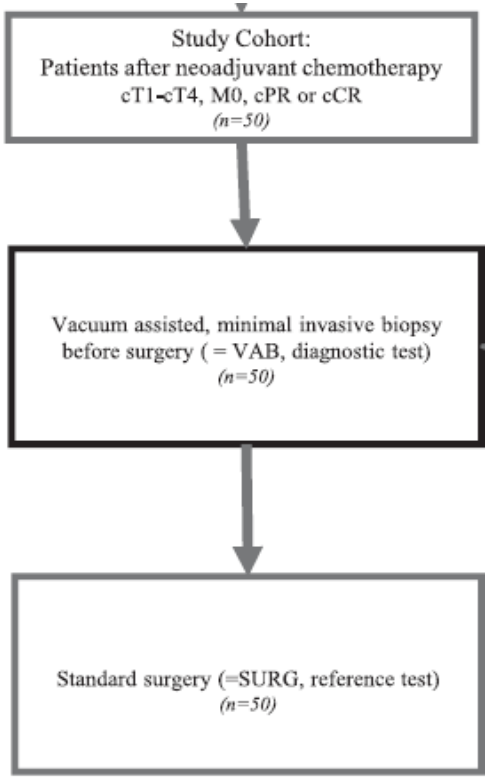
Problematiche aperte

Can a pathological complete response of breast cancer after neoadjuvant chemotherapy be diagnosed by minimal invasive biopsy?

European Journal of Cancer 69 (2016) 142–150

Omissione chirurgia

pCR= no in situ ed invasive



Rationale

Recent studies have demonstrated that shrinking tumours need less surgical treatment. Extrapolating this to the extreme, patients with a pCR would potentially not require surgery at all.

Prospective

The radiological complete response (cCR= cCR+nearcCR) was diagnosed integrating all findings of the imaging available by our internal standard operating procedures (MRI > ultrasound > mammography).

Problematiche aperte

Can a pathological complete response of breast cancer after neoadjuvant chemotherapy be diagnosed by minimal invasive biopsy?

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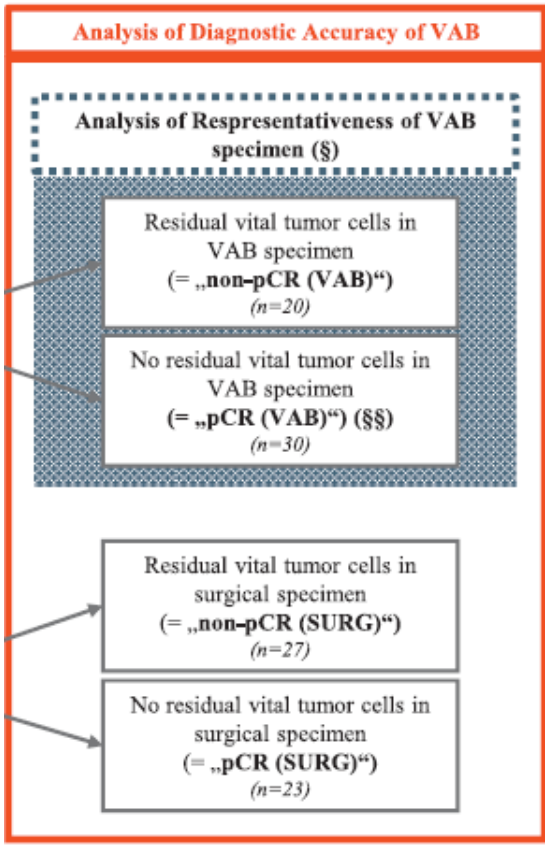

Omissione chirurgia

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Rationale

Recent studies have demonstrated that shrinking tumours need less surgical treatment. Extrapolating this to the extreme, patients with a pCR would potentially not require surgery at all.

Prospective

The radiological complete response (cCR) was diagnosed integrating all findings of the imaging available by our internal standard operating procedures (MRI > ultrasound > mammography).

NPV	76.7%	(95% CI 65.0-88.4)
FNR	25.9%	(95% CI 13.8-38.0)

A confirmative, multicenter, diagnostic trial to validate these results is warranted

Risposta a livello ascellare

Problematiche aperte
Valutazione della risposta ascellare

Original article

Using ultrasound and palpation for predicting axillary lymph node status following neoadjuvant chemotherapy – Results from the multi-center SENTINA trial

The Breast 31 (2017) 202–207

1240 breast cancer patients undergoing NCT

Arm C/D pathologic nodal status vs. palpation results of cN status.

	cN after NST by palpation									
	Missing				Negative				Positive	
	N		%		N		%		N	%
pN										
Negative	2		28.6		307		46.6		17	34.7
Positive	5		71.4		352		53.4		32	65.3

Predictive test	True negative	False negative	True positive	False positive	Sensitivity, %	False negative rate, %	Specificity, %	False positive rate, %	Positive predictive value, %	Negative predictive value, %
cN after NACT by palpation	307	352	32	17	8.3	91.7	94.8	5.2	65.3	46.6

Table 3
Arm C/D pathologic nodal status vs. axillary ultrasound interpretation of cN status.

	cN after NST by ultrasound			
	Negative		Positive	
	N	%	N	%
pN				
Negative	299	50.3	27	22.5
Positive	296	49.7	93	77.5

Predictive test	True negative	False negative	True positive	False positive	Sensitivity, %	False negative rate, %	Specificity, %	False positive rate, %	Positive predictive value, %	Negative predictive value, %
cN after NACT by US	299	296	93	27	23.9	76.1	91.7	8.3	77.5	50.3

"Demonstrating that the diagnostic performance of axillary ultrasound might be influenced by NST.
Single-center data demonstrates that implementation of further imaging techniques like MRI or PET can improve the accuracy but data from prospective multi-center trials are not available.
Improving the accuracy in predicting axillary lymph node status will need a more comprehensive approach".

Problematiche aperte

Valutazione della risposta ascellare

Ann Surg Oncol (2013) 20:3199–3204
DOI 10.1245/s10434-013-3118-z

Annals of SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Imaging Response and Residual Metastatic Axillary Lymph Node Disease after Neoadjuvant Chemotherapy for Primary Breast Cancer

Tina J. Hieken, MD[1], Judy C. Boughey, MD[1], Katie N. Jones, MD[2], Sejal S. Shah, MD[3], and Katrina N. Glazebrook, MD[2]

[1]Department of Surgery, Mayo Clinic, Rochester, MN; [2]Department of Radiology, Mayo Clinic, Rochester, MN; [3]Department of Pathology, Mayo Clinic, Rochester, MN

272 Patients

US, MRI e CT-PET before and after NCT

TABLE 2 Performance characteristics of post-NAC axillary imaging modalities in detecting persistent nodal metastatic disease in cN1 patients

Imaging modality	Sensitivity, % (95 % CI)	Specificity, % (95 % CI)	Negative predictive value, % (95 % CI)	Positive predictive value, % (95 % CI)	Accuracy, %
Ultrasound	69.8 (56.8–80.4)	58.1 (42.2–72.6)	56.8 (41.1–71.3)	71.0 (57.8–81.4)	65.1
MRI	61.0 (47.4–73.1)	58.6 (39.1–75.9)	42.5 (27.4–59.0)	75.0 (60.1–85.9)	60.2
PET-CT	63.2 (38.6–82.8)	84.6 (53.7–97.3)	61.1 (36.1–81.7)	85.7 (56.2–97.5)	71.9

NAC neoadjuvant chemotherapy, *CI* confidence interval, *MRI* magnetic resonance imaging, *PET-CT* positron emission tomography-computed tomography

"Performance characteristics of US, MRI, and PET-CT, while informative, were inadequate to preclude surgical axillary staging of in breast cancer patients after NAC"

Problematiche aperte

Valutazione della risposta ascella

MRI and Prediction of Pathologic Complete Response in the Breast and Axilla after Neoadjuvant Chemotherapy for Breast Cancer

http://dx.doi.org/10.1016/j.jamcollsurg.2017.08.027

SLNB — 74 pazienti

25 successiva DA

DA — in 30 pazienti

Table 4. Correlation of Pre- and Post-Neoadjuvant Chemotherapy Axillary Nodal Status on MRI with Final Pathology Finding for Entire Population (n =129)

	Final pathology of axillary nodes			
	No metastasis (n = 80)		Metastasis (n = 49)	
Axillary nodal status on MRI	n	%	n	%
Normal pre- and post-NAC (n = 32)	26	81.2	6	18.8
Abnormal pre-NAC, normal post-NAC (n = 50)	34	68	16	32
Abnormal pre- and post-NAC (n = 47)	20	42.6	27	57.4

NAC, neoadjuvant chemotherapy.

Table 5. Correlation of Pre- and Post-Neoadjuvant Chemotherapy Axillary Nodal Status on MRI with Pathologic Complete Response in Patients with Biopsy-Proven Node-Positive Disease (n = 65)

	Final pathology of axillary nodes			
	Nodal pCR† (n = 33)		No nodal pCR† (n = 32)	
Axillary nodal status on MRI*	n	%	n	%
Abnormal pre-NAC, normal post-NAC (n = 33)	22‡	66.7	11	33.3
Abnormal pre- and post-NAC (n = 32)	11	34.4	21§	65.6

*Patients with pre-NAC biopsy-proven malignancy, but who had normal nodes on MRI pre- and post-NAC were not included in the tables.
†pCR defined as no residual disease in the axillary nodes.
‡Post-neoadjuvant chemotherapy MRI negative predictive value.
§Post-neoadjuvant chemotherapy MRI positive predictive value.
NAC, neoadjuvant chemotherapy; pCR, pathologic complete response.

Problematiche aperte
Valutazione della risposta ascella

Diagnostic performance of breast ultrasonography and MRI in the prediction of lymph node status after neoadjuvant chemotherapy for breast cancer

Acta radiologica 2017

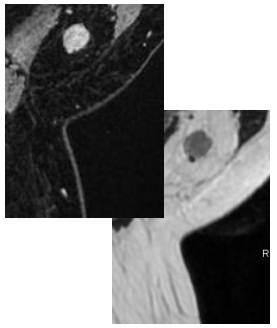
157 patients
both initial and follow-up US and MRI
Ax pCR achieved in 20–42% of patients.

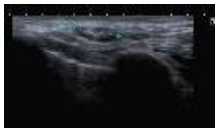
Nodal metastasis at US:

loss of fatty hilum,
cortical thickening more than 3 mm,
round or irregular shape,
increased extrahilar vascularity

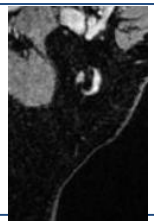
Nodal metastasis at MRI:

Contrast enhancement,
irregular nodal contour,
nodal size >5 mm
Absence of fatty hilum





rCR ascellare =
normalità in termini di dimensioni e caratteristiche radiologiche.



Problematiche aperte
Valutazione della risposta ascella

Diagnostic performance of breast ultrasonography and MRI in the prediction of lymph node status after neoadjuvant chemotherapy for breast cancer

Acta radiologica 2017

157 patients
both initial and follow-up US and MRI
Ax pCR achieved in 20–42% of patients.

ER positivity was related to discordant diagnoses on ultrasonography, MRI, and combined imaging

Table 1. Nodal metastasis detection in pre-NAC and post-NAC axillary imaging modalities.

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
Pre-NAC					
US	118/118 (100)	15/39 (38.46)	118/142 (83.1)	15/15 (100)	133/157 (84.71)
MRI	115/118 (97.46)	11/39 (28.21)	115/143 (80.99)	11/14 (78.57)	126/157 (80.25)
US or MRI	118/118 (100)	10/39 (25.64)	118/127 (80.27)	10/10 (100)	128/157 (81.53)
Post-NAC					
US	45/75 (60.00)	26/43 (60.47)	45/67 (72.58))	26/56 (46.43)	71/118 (60.17)
MRI	43/75 (57.33)	31/43 (72.09)	43/55 (78.18)	31/63 (49.21)	74/118 (62.71)
US or MRI	49/75 (65.33)	26/43 (60.47)	49/66 (74.24)	26/52 (50.00)	75/118 (63.56)

118 patients pre-NAC positive metastatic lymph nodes on fine-needle aspiration,

POST NAC
75 (64%) had positive lymph nodes
43 (36%) showed conversion to negative axillary lymph node status on final surgical pathology

Problematiche aperte

Valutazione della risposta ascella

Ann Surg Oncol. 2017 March ; 24(3): 645–651. doi:10.1245/s10434-017-5765-y.

Is Routine Axillary Imaging Necessary in Clinically Node-Negative Patients Undergoing Neoadjuvant Chemotherapy?

Andrea V. Barrio, MD[1,*], Anita Mamtani, MD[1,*], Anne Eaton, MS[2], Sandra Brennan, MD[3], Michelle Stempel, MPH[1], and Monica Morrow, MD[1]

402 cN0 patients. Median tumor size was 4cm.
38% were ER+/HER2-, 30% HER2+, and 32% triple negative.

All had pre-NAC mammograms, 40% axillary ultrasound, 83% MRI, and 51% PET.
Abnormal nodes on imaging were seen in 208 patients (52%)
128 had pre-NAC node biopsy, and 75 were positive.

Overall, 28% (n=111) of patients were ypN+ after NAC

Synopsis

The benefit of axillary imaging in cN0 breast cancer patients selected for NAC is uncertain. Here we find that pre-treatment axillary imaging does not predict nodal metastases post-NAC with sufficient accuracy to be clinically useful in this patient population.

Problematiche aperte

JAMA Surgery | Original Investigation

Identification of Patients With Documented Pathologic Complete Response in the Breast After Neoadjuvant Chemotherapy for Omission of Axillary Surgery

JAMA Surgery Published online April 19, 2017

Omissione chirurgia

BpCR= no in situ ed invasive

527 consecutive patients with TN and *HER2+*
237 N1 290 No
251 BCS 276 mastectomy
Final nodal surgery consisted of sentinel node biopsy in 302 patients and axillary lymph node dissection in 225.
(36.6%) achieved a breast pCR

Table 2. Pathologic Axillary Status in 527 Patients With and Without a Breast pCR After NCT

Breast Cancer Subtype	No. of Nodes With Positive Histologic Finding, No. (%) of Patients				
	0	1	2	≥3	All
HER2+ and TN					
T1N0	18 (100)	0	0	0	18 (100)
T2N0	98 (100)	0	0	0	98 (100)
T1N1	16 (84.2)	2 (10.5)	1 (5.3)	0	19 (100)
T2N1	53 (91.4)	3 (5.2)	0	2 (3.4)	58 (100)
HER2+ and TN					
T1N0	14 (93.3)	1 (6.7)	0	0	15 (100)
T2N0	150 (94.3)	9 (5.7)	0	0	159 (100)
T1N1	13 (56.5)	1 (4.3)	4 (17.4)	5 (21.7)	23 (100)
T2N1	55 (40.1)	11 (8.0)	32 (23.4)	39 (28.5)	137 (100)

BpCR

No BpCR

Problematiche aperte

JAMA Surgery | Original Investigation

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527 consecutive patients with TN and *HER2+*
237 N1 290 N0
251 BCS 276 mastectomy
Final nodal surgery consisted of sentinel node biopsy in 302 patients and axillary lymph node dissection in 225.
(36.6%) achieved a breast pCR

Table 3. Relative Risk for Residual Axillary Nodal Metastases After NCT in Patients Without vs With Breast pCR

Subgroup	RR (95% CI)	*P* Value
N0	14.0 (0.8-237.0)	.07
N1	5.3 (2.7-10.3)	<.001
HER2+	4.9 (2.0-11.9)	<.001
TN	11.6 (3.7-36.0)	<.001
All	7.4 (3.7-14.8)	<.001

Abbreviations: NCT, neoadjuvant chemotherapy; pCR, pathologic complete response; RR, relative risk; TN, triple-negative; +, positive.

"Patients without a pCR had a relative risk for positive final nodal pathologic findings of 7.4 (95% CI, 3.7-14.8; P < .001) compared with patients with a pCR"

"The greatest increase in relative risk was seen in patients who presented with N0 disease and who did not have a breast pCR (14.0; 95%CI, 0.8-237.0)"

Ruolo della RM come Imaging biomarker

Eusoma reccomendations (EJC, 2010)

Research issues

Value of non-conventional MR techniques such as contrast-enhanced perfusion studies for kinetic evaluation, diffusion-weighted imaging, and proton MR spectroscopy (single-voxel or 2D/3D chemical shift imaging).

Pianificazione chirurgica e prediction

Value of CAD systems for automated tumor volume determination.

Usefulness of additional MR examinations during the NAC aimed at evaluating early and intermediate tumor response.

Clinical value of NAC switching on the basis of MRI data (welcome RCTs)

3) Problematiche aperte

- 70 locally advanced breast cancer in 69 patients
- Imaging: before and after PCT
- Standard of Reference: pathology (pCR vs size of residual disease)

DWI

Table 3

Agreement of Residual Disease Classification between DW Imaging and Pathologic Findings

	DW Imaging			
Pathologic Finding	Category 1	Category 2	Category 3	Category 4
Category 1 ($n = 9$)	8	1	0	0
Category 2 ($n = 19$)	2	16	1	0
Category 3 ($n = 24$)	0	1	23	0
Category 4 ($n = 18$)	0	0	1	17

Note.—Data are numbers of lesions. Category 1, no residual disease; category 2, single residual disease limited to one quadrant; category 3, multiple residual diseases including extensive intraductal component limited to one quadrant; and category 4, multiple residual diseases in two or more quadrants.

Sensitivity 97%
Specificity 89%
Accuracy 96%

Table 4

Agreement of Residual Disease Classification between Contrast-enhanced MR Imaging and Pathologic Findings

	Contrast-enhanced MR Imaging			
Pathologic Finding	Category 1	Category 2	Category 3	Category 4
Category 1 ($n = 9$)	5	4	0	0
Category 2 ($n = 19$)	4	15	0	0
Category 3 ($n = 24$)	0	2	22	0
Category 4 ($n = 18$)	0	0	1	17

Note.—Data are numbers of lesions. Category 1, no residual disease; category 2, single residual disease limited to one quadrant; category 3, multiple residual diseases including extensive intraductal component limited to one quadrant; and category 4, multiple residual diseases in two or more quadrants.

Sensitivity 93%
Specificity 56%
Accuracy 89%

Woodhams, Radiology 2010

3) Problematiche aperte
Valutazione della risposta ascella

European Review for Medical and Pharmacological Sciences 2017; 21: 695-705

Role of DWI assessing nodal involvement and response to neoadjuvant chemotherapy in advanced breast cancer

P. BELLI[1], E. BUFI[1], C. BUCCHERI[1], P. RINALDI[1], M. GIULIANI[1], M. ROMANI[1], G. FABRIZI[1], A. D'ANGELO[1], C. BRUNELLI[2], A. MULE'[2], G. FRANCESCHINI[3], C. COLOSIMO[1]

49 Pazienti con metastasi ascellare (FNAB) pre NAC.
RM pre e post
Trattamento Chirurgia mammaria e DA.

Table II. Number (N) of lymph nodes and mean ADC values compared between baseline (t0) and after chemotherapy (t1) in pathologic axilla (PA), healthy axilla (HA), "non responders" (NR), "responders" (R), "macrometastasis" (MA) and "micrometastasis" (Mi). All ADC values are expressed as × 10^{-3} mm^2/sec.

	t0	t1	*p*
N PA	4 (±2)	3 (±3)	0.153
N HA	3 (±3)	3 (±2.75)	0.952
PA	0.92 ± 0.07	0.97 ± 0.06	0.284
HA	0.89 ± 0.06	0.92 ± 0.06	0.403
NR	0.90 ± 0.09	0.97 ± 0.07	0.085
R	0.95 ± 0.11	0.95 ± 0.14	0.954
MA	**0.86 ± 0.10**	**0.99 ± 0.09**	**0.055**
Mi	0.99 ± 0.23	0.95 ± 0.15	0.667

«DWI is not useful in assessing nodal status in advanced breast cancer… An increase of mean ADC which is close to statistical significance has been observed after neoadjuvant chemotherapy in lymph nodes with residual macrometastases».

Eusoma reccomendations (EJC, 2010)

Research issues

Value of non-conventional MR techniques such as contrast-enhanced perfusion studies for kinetic evaluation, diffusion-weighted imaging, and proton MR spectroscopy (single-voxel or 2D/3D chemical shift imaging).

Pianificazione chirurgica e prediction

Value of CAD systems for automated tumor volume determination.

Usefulness of additional MR examinations during the NAC aimed at evaluating early and intermediate tumor response.

Clinical value of NAC switching on the basis of MRI data (welcome RCTs)

DCE-MRI

Outcome a breve termine: Identificazione precoce della risposta

Contents lists available at SciVerse ScienceDirect
The Breast
journal homepage: www.elsevier.com/brst

Original article

Early prediction of pathologic response to neoadjuvant therapy in breast cancer: Systematic review of the accuracy of MRI

M.L. Marinovich [a,*], F. Sardanelli [b], S. Ciatto [c], E. Mamounas [d], M. Brennan [a], P. Macaskill [a], L. Irwig [a], G. von Minckwitz [e], N. Houssami [a]

- 9 studi: criterio uni o bidimensionale
- 3 studi: 3D volume
- 4 studi: criteri funzionali (Ktrans, kep, contrast uptake)
- 1 studio: patterns di shrinkage

classificazione della pCR

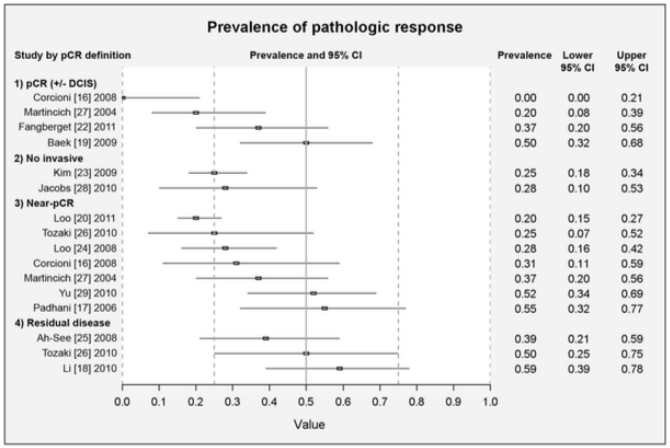

Fig. 1. Study-specific rates of pathologic response by response definition.

Marinovich L, The Breast 2013

Volume DCE-MRI

Outcome a breve termine: Identificazione precoce della risposta

Contents lists available at SciVerse ScienceDirect

The Breast

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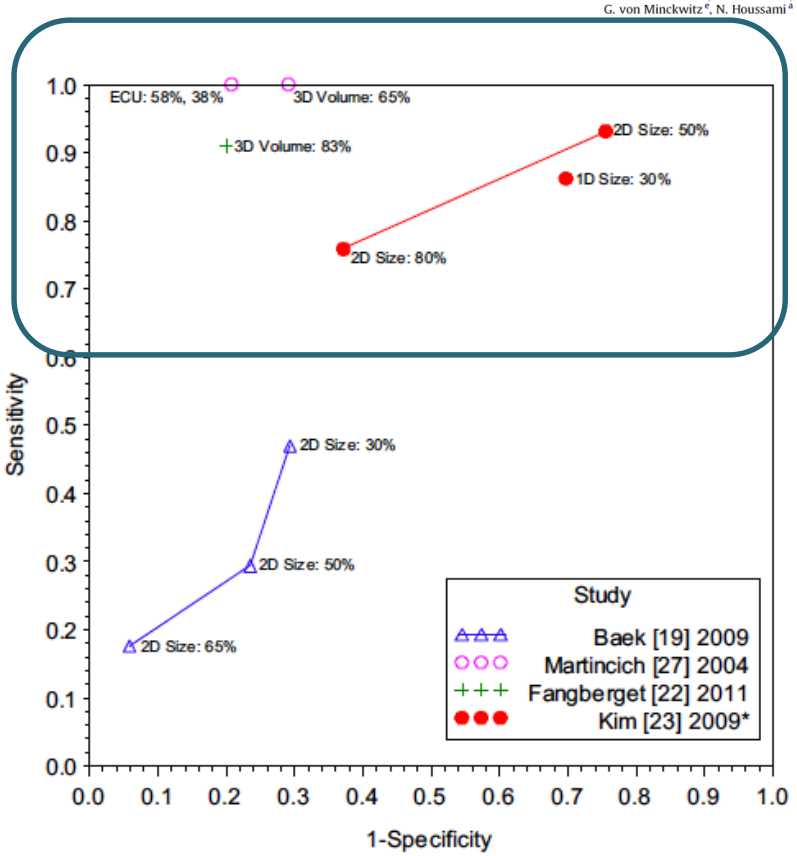


* pCR defined as no residual invasive disease (with no reference to DCIS) in breast *and* axilla.

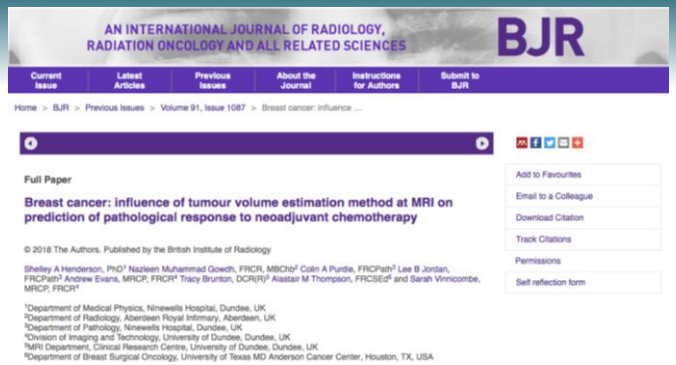
Pathologic Complete Response (pCR)

Breast and Axillary Level

Modificazioni durante PCT vs Baseline

1) volume tumorale >65%

Marinovich L, The Breast 2013



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Home > BJR > Previous Issues > Volume 91, Issue 1087 > Breast cancer: influence ...

Full Paper

Breast cancer: influence of tumour volume estimation method at MRI on prediction of pathological response to neoadjuvant chemotherapy

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[3]Department of Pathology, Ninewells Hospital, Dundee, UK
[4]Division of Imaging and Technology, University of Dundee, Dundee, UK
[5]MRI Department, Clinical Research Centre, University of Dundee, Dundee, UK
[6]Department of Breast Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX, USA

109 lesioni mass; 27 non mass

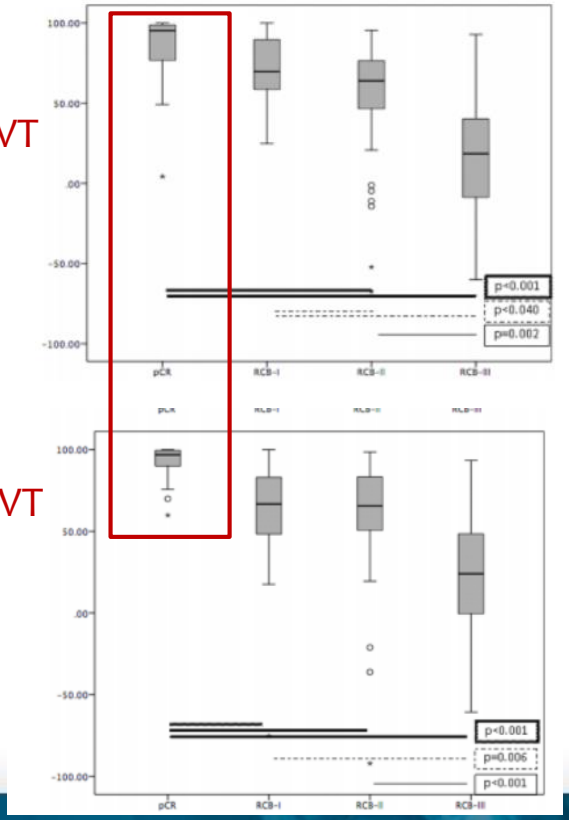
Baseline e meta' trattamento

pCR (24) vs RCB (112)

Functional tumour volumes (FTVs), automatically derived using vendor software
Enhancing tumour volumes (ETVs), using a semi-automated thresholding technique

FVT

EVT



	FTV	ETV
	Optimal threshold: 75.6%	Optimal threshold: 89.8%
Sensitivity	80.0%	81.0%
Specificity	76.8%	91.8%
Accuracy	77.4%	89.8%
PPV	42.1%	68.0%
NPV	77.4%	95.7%

ETV, enhancing tumour volume; FTV, functionaltumour volume; NPV, positive-predictive value; PPV, negative-predictive value.

Ruolo della RM come Imaging biomarker

ADC - DWI

Outcome a breve termine: Identificazione precoce della risposta

Role of the Apparent Diffusion Coefficient in the Prediction of Response to Neoadjuvant Chemotherapy in Patients With Locally Advanced Breast Cancer

Enida Bufi,[1] Paolo Belli,[1] Melania Costantini,[1] Antonio Cipriani,[1] Marialuisa Di Matteo,[3] Angelo Bonatesta,[1] Gianluca Franceschini,[2] Daniela Terribile,[2] Antonino Mulé,[3] Luigia Nardone,[4] Lorenzo Bonomo[1]

225 pazienti
DWI pre e post NCT
pCR rate 17.3%

Table 3 Data Concerning Mean ADC Values of Tumors Before NAC

Phenotype	Mean ADC Overall	Mean ADC		*P* Value
		pCR	No pCR	
Total population	1.099 ± 0.19	1.132	1.092	.23
Luminal (n = 143)	1.082 ± 0.17	1.157	1.077	.59
Hybrid (n = 28)	1.064 ± 0.13	1.036	1.079	.53
Triple negative (n = 37)	1.141 ± 0.22	1.034	1.114	.06
HER2$^+$ (n = 17)	1.163 ± 0.34	1.101	1.232	.05

Data presented as mean ± standard deviation.
Abbreviations: ADC = apparent diffusion coefficient; HER2 = human epidermal growth factor receptor 2; NAC = neoadjuvant chemotherapy; pCR = pathologically complete response.

Table 4 ROC Curves for General Population and Different Phenotypes With ADC Cutoff Before NAC Obtained Using the Youden Index Method

Variable	ADC Cutoff Value	ROC Curve	*P* Value
Total population	0.975	0.587	.1
Luminal	0.832	0.588	.380
Hybrid	0.959	0.567	.565
Triple negative	0.995	0.766	.013
HER2$^+$	0.971	0.813	.030

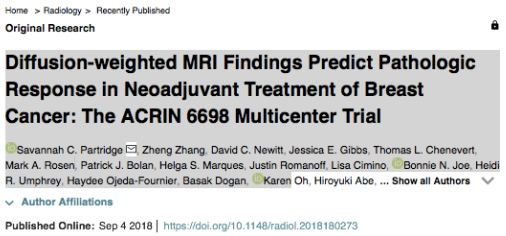
Abbreviations: ADC = apparent diffusion coefficient; HER2 = human epidermal growth factor receptor 2; NAC = neoadjuvant chemotherapy; ROC = receiver operating characteristic.

Bufi E, Clinical Breast Cancer 2015

Ruolo della RM come Imaging biomarker

ADC - DWI

Outcome a breve termine: Identificazione precoce della risposta



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Original Research

Diffusion-weighted MRI Findings Predict Pathologic Response in Neoadjuvant Treatment of Breast Cancer: The ACRIN 6698 Multicenter Trial

Savannah C. Partridge, Zheng Zhang, David C. Newitt, Jessica E. Gibbs, Thomas L. Chenevert, Mark A. Rosen, Patrick J. Bolan, Helga S. Marques, Justin Romanoff, Lisa Cimino, Bonnie N. Joe, Heidi R. Umphrey, Haydee Ojeda-Fournier, Basak Dogan, Karen Oh, Hiroyuki Abe, ... Show all Authors

Author Affiliations

Published Online: Sep 4 2018 | https://doi.org/10.1148/radiol.2018180273

242 pazienti

DWI pre, dopo 3 e 12 settimane e post NCT

pCR (yTois/No) 80/242

Maggiore significativita' statistica per luminali HER2 -

Table 2: Performance of Tumor ΔADC for Predicting pCR at Each Treatment Time Point

	Patients with pCR		Patients without pCR				
Treatment Time Point	No. of Patients	Mean ΔADC ± Standard Deviation (%)	No. of Patients	Mean ΔADC ± Standard Deviation (%)	AUC	95% Confidence Interval	*P* Value
Early treatment/3 weeks	71	18 ± 20	156	16 ± 21	0.53	0.45, 0.61	.48
Midtreatment/12 weeks	70	50 ± 49	140	36 ± 44	0.60	0.52, 0.68	.017*
Posttreatment	63	64 ± 49	123	50 ± 47	0.61	0.52, 0.69	.013*

Note.—AUC = area under the receiver operating characteristic curve, ΔADC = change in tumor apparent diffusion coefficient (from pretreatment value), pCR = pathologic complete response.

* Significant at $P < .05$, but not after multiple-comparison adjustment ($P < .003$).

4) ruolo della RM come Imaging biomarker

ADC - DWI

Outcome a breve termine: Identificazione precoce della risposta

Home > Radiology > Recently Published

Original Research

Diffusion-weighted MRI Findings Predict Pathologic Response in Neoadjuvant Treatment of Breast Cancer: The ACRIN 6698 Multicenter Trial

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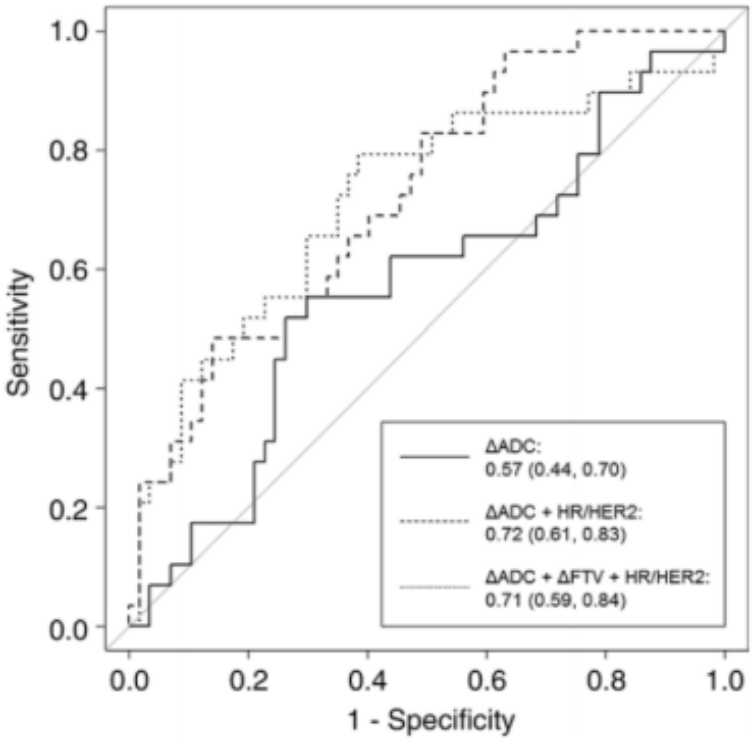


No Associazione ADC e DCE-MRI

Si' ADC changes a 12 settimane

Protocollo standardizzato e verificato mediante utilizzo di fantoccio

Ruolo della RM come Imaging biomarker

Texture

A computer-aided diagnosis (CAD) scheme for pretreatment prediction of pathological response to neoadjuvant therapy using dynamic contrast-enhanced MRI texture features

[1,2]VALENTINA GIANNINI, PhD, [1,2]SIMONE MAZZETTI, PhD, [2]AGNESE MARMO, MSc, [3]FILIPPO MONTEMURRO, MD, [1,2]DANIELE REGGE, MD, Prof and [2]LAURA MARTINCICH, MD

44 pazienti

pCR+ (Smith's Grade = 5) *vs* pCR– (Smith's Grade < 5);

pCRN+ (breast and axylla pCR) *vs* pCRN–.

Variable	AUC	SE	Cut-off	Sensitivity (%)	Specificity (%)
Cluster shade	0.685	0.0842	≤7039	92.3	41.9
Sum variance	0.687	0.0817	>74770	92.3	51.6
LRE	0.712	0.0790	>1.258	84.6	61.3
LRHGE	0.747	0.0731	>24213	100.0	54.8

AUC, area under the ROC curve; SE, standard error;LRE, long run emphasis, LRHGE, low run high grey level emphasis; pCR+ Smith's Grade = 5; pCR–, Smith's Grade < 5; pCRN+, pCR+ plus either complete absence of residual nodal metastases or presence of nodal micrometastasis; pCRN–, Smith's Grade < 5 and any other status of axillary lymph node metastases.

"When considering the prediction of pathological response at both breast and axillary level (pCRN+ vs pCRN–), four parameters were able to discriminate, before the treatment, between patients achieving pCRN+ and subjects obtaining pCRN–, and all of them reached high sensitivity, with poor specificity."

Ruolo della RM come Imaging biomarker

Prognosis

187 Pz; 38 recidive; follow up medio: 47.4 mesi

Table 2

Univariate Cox Proportional Hazard Analysis of MR Imaging Parameters with Survival Outcomes

		Recurrence-Free Survival			Overall Survival		
MR Imaging Parameter	Mean ± SD	*P* Value	Hazard Ratio	95% CI	*P* Value	Hazard Ratio	95% CI
Pretreatment							
Tumor diameter (cm)	4.9 ± 4.2	.443	1.03	0.96, 1.09	.436	1.04	0.94, 1.17
Tumor volume (mL)	24.3 ± 38.1	.044	1.01	1.00, 1.02	.142	1.01	1.00, 1.02
Peak enhancement	452.7 ± 707.4	.613	1.00	1.00, 1.00	.727	1.00	1.00, 1.00
Persistent component (%)	54.3 ± 23.6	.401	1.01	1.00, 1.03	.256	1.01	0.99, 1.04
Plateau component (%)	21.5 ± 9.9	.468	0.99	0.96, 1.02	.494	1.02	0.96, 1.08
Washout component (%)	24.1 ± 18.9	.053	0.98	0.96, 0.99	.077	0.97	0.93, 1.01
Percent change*							
Tumor diameter (%)	−60.9 ± 55.6	<.001	1.28	1.19, 1.40	<.001	2.65	1.50, 4.69
Tumor volume (%)	−77.2 ± 74.8	<.001	2.62	1.77, 3.88	<.001	1.97	1.34, 2.89
Peak enhancement (%)	−32.4 ± 122.4	.402	1.15	0.98, 1.33	.175	1.16	0.92, 1.47
Persistent component (%)	22.7 ± 125.7	.466	0.90	0.69, 1.19	.765	0.93	0.56, 1.54
Plateau component (%)	−39.1 ± 85.3	.162	1.21	0.93, 1.57	.332	1.24	0.80, 1.91
Washout component (%)	−22.6 ± 210.9	<.001	1.16	1.08, 1.23	.003	1.13	1.03, 1.25

Note.—CI = confidence interval, SD = standard deviation.

* (MR imaging value$_{post}$ − MR imaging value$_{pre}$)/MR imaging value$_{pre}$ × 100], where MR imaging value$_{pre}$ and MR imaging value$_{post}$ are pretreatment and posttreatment values of each MR imaging parameter, respectively.

Smaller tumour volume and contrast uptake reduction → increased recurrence and mortality risk

Yi, Radiology 2013

Ruolo della RM come Imaging biomarker

Prognosis

Hypervascularity Predicts Complete Pathologic Response to Chemotherapy and Late Outcomes in Breast Cancer

Clinical Breast Cancer Month 2016

219 pazienti

Table 2 Tumor Characteristics and Overall Baseline Characteristics of the Study Population According to the AIBV or No-AIBV Status

Characteristics	AIBV (n = 137)	No AIBV (n = 82)	*P* Value
Age, years	47.8 ± 9.9	46.8 ± 10.1	.36
Family history of breast cancer	34.4%	17.3%	**.028**
Post-menopausal state	45.8%	42.3%	.68
Ki67 <40%	44%	67.1%	**.001**
Lesion diameter, mm	53.7 ± 24.1	53.4 ± 30.1	.13
Histology			**.05**
IDC-DCIS	116 (84.7%)	59 (71.9%)	
ILC-DCIS	14 (10.2%)	22 (26.8%)	
Others	7 (5.1%)	1 (1.2%)	
Grading			**<.001**
G1	1 (0.7%)	1 (1.2%)	
G2	49 (35.8%)	54 (65.9%)	
G3	87 (63.5%)	27 (32.9%)	
Phenotype			**.02**
Triple-negative	32 (23.4%)	7 (8.5%)	
Luminal	70 (51.1%)	66 (80.5%)	
$HER2^+$	13 (9.5%)	3 (3.7%)	
Hybrid	22 (16%)	6 (7.3%)	
ADC value	0.0011221	0.0011518	.771

4) ruolo della RM come Imaging biomarker

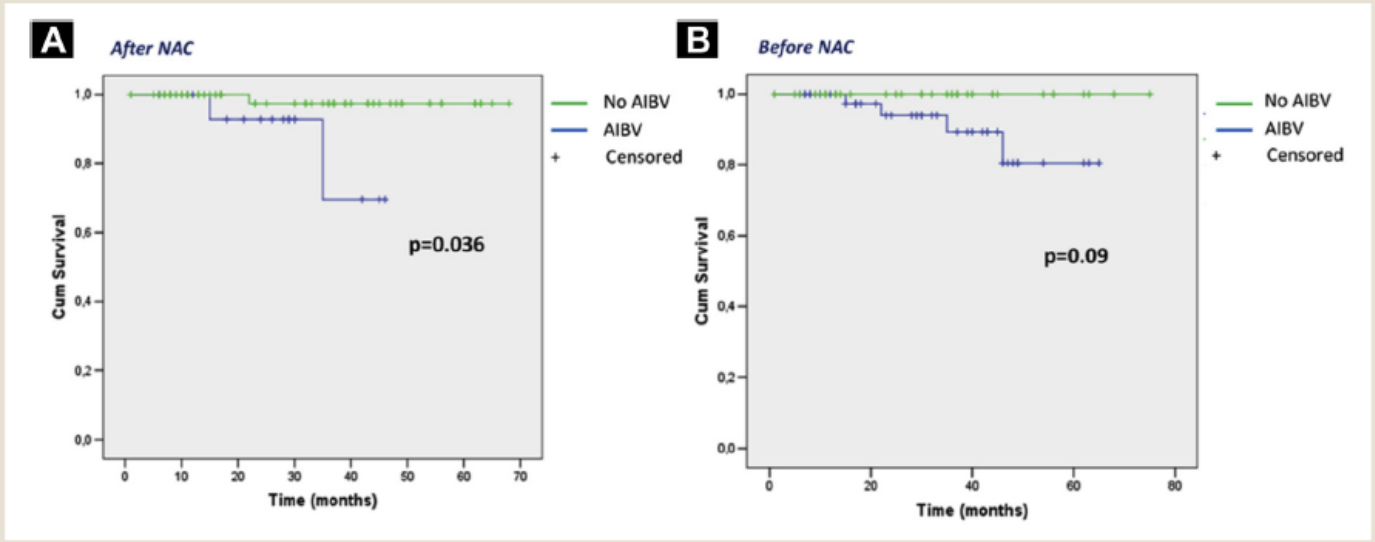
Prognosis

Hypervascularity Predicts Complete Pathologic Response to Chemotherapy and Late Outcomes in Breast Cancer

219 patients

Clinical Breast Cancer Month 2016

Figure 6 Survival at Follow-Up (Kaplan-Meier Analysis) Among Patients Presenting AIBV After (A) and Before NAC (B)



"persistence after NAC should be regarded to as a marker of a particularly aggressive tumor profile".

Eusoma reccomendations (EJC, 2010)

Research issues

Value of non-conventional MR techniques such as contrast-enhanced perfusion studies for kinetic evaluation, diffusion-weighted imaging, and proton MR spectroscopy (single-voxel or 2D/3D chemical shift imaging).

Pianificazione chirurgica e prediction

Value of CAD systems for automated tumor volume determination.

Usefulness of additional MR examinations during the NAC aimed at evaluating early and intermediate tumor response.

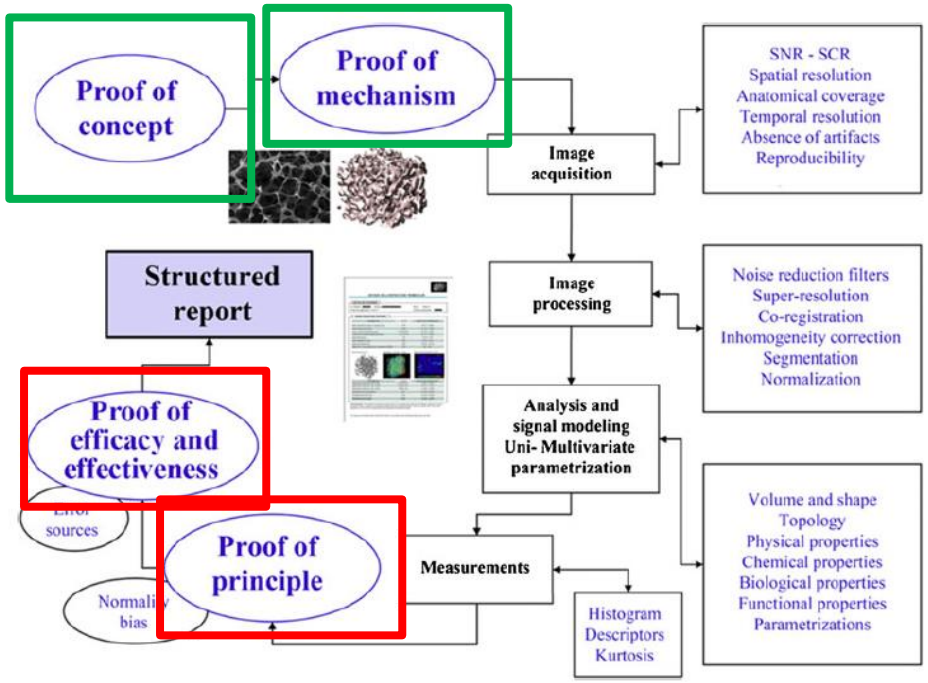
Clinical value of NAC switching on the basis of MRI data (welcome RCTs)

Conclusioni

- RM metodica più accurata (in-breast response)
  - DCI, HER2 type e Triplo Negativi
  - Localizzazione pre NAC
  - DWI probabile futuro
- Risposta ascellare con RM (e Imaging) subottimale
- Presto per parlare di omissione chirugica
- Volume tumorale DCE-MRI e', ad oggi, l'Imaging biomarker maggiormente affidabile e standardizzato
  - Altri Biomarkers: Necessità di standardizzazione

Diagnostic work-up: A possible scheme

- Enhancement residuo nella sede della neoplasia?
- Quale pattern di shrinkage?
- Conspicuita' dell'enhancement residuo?
- Quale dimensione dell'enhancement residuo?



Features relevant to the disease (biological biomarkers) that can be studied using the available imaging and computational techniques (imaging biomarkers).

Relationship between biological and imaging biomarkers

Volume changes during PCT

To do:

Standardization

Evaluation of influence of potential variations related to patient's characteristics and treatment regimens

Design of trials to show the ability of a biomarker to measure the clinical endpoints