

Are medial breast cancers without
axillary node involvement really node-
negative?

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for the

International Breast Cancer Study Group



IBCSG

Zucali R, Mariani L, Marubini E, Kenda R, Lozza L, Rilke F, Veronesi U. Early breast cancer: evaluation of the prognostic role of the site of the primary tumor.
J Clin Oncol. 1998;16:1363-6

- 2,396 patients treated from 1973 to 1989 with QuaRT
- 1,002 node negative
- 1,619 lateral and 777 internal/central
- Median follow up of 147 months

Results of Multivariate Cox model:

<u>End Point</u>	<u>Hazard Ratio</u>	<u>95% CI</u>	<u>P-value</u>
Distant metastases	1.29	1.07-1.55	0.006
Survival	1.19	1.01-1.41	0.03



Lohrisch C, Jackson J, Jones A, Mates D, Olivotto IA.
 Relationship between tumor location and relapse in 6,781
 women with early invasive breast cancer.
 J Clin Oncol 2000;18 :2828-35

- 6,781 patients referred to the database of the BCCA
- 4,187 node negative
- 1,511 medial and 3,848 lateral
- Median follow up of 3.9 years

	<u>Low Risk</u>			<u>High Risk</u>		
<u>Systemic Therapy</u>	Medial	Lateral	P-value	Medial	Lateral	P-value
5-yr DFS(%)	89	85	0.6	66	74	0.003
<u>No Systemic Therapy</u>	Medial	Lateral	P-value	Medial	Lateral	P-value
5-yr DFS(%)	90	93	0.1	75	76	0.4



IBCSG Research Project

- Information on predominant site of primary tumor on patients in Trials I – VII

6765 patients

- The predominant site was classified as central, medial, lateral, or *other*



Characteristics of IBCSG Trials I- VII

<u>Trial</u>	<u>Population</u>	<u>Years Accrual</u>	<u>Eligible Patients</u>	<u>Median Years F-U</u>
I	Pre 1-3 N+	1978-81	491	20
II	Pre 4+ N+	1978-81	327	20
III	Post Age <65	1978-81	463	20
IV	Post Age 66-80	1978-81	320	20
V	Pre/Post N-	1981-85	1275	16
V	Pre/Post N+	1981-85	1229	16
VI	Pre	1986-93	1475	10
VII	Post	1986-93	1212	10



Materials and Methods

- Endpoints: Overall and Disease-free survival
- Examined 8 other factors: “nodal” group, menopausal status, estrogen receptor status, vessel invasion, tumor grade, tumor size, and treatment regimen



Site Distribution

<u>Predominant Site</u>	<u>Percent of Categories</u>
Medial	18.1%
Lateral	61.4%
Central	18.2%
Other	2.3%



Site Distribution and Nodal Status

Nodal Group	Medial	Lateral/Central/Other
	<u>N (%)</u>	<u>N (%)</u>
0	308 (25)	966 (17)
1 – 3	618 (51)	2724 (49)
4 +	297 (24)	1852 (33)
Total	1223	5542



Disease Free Survival

Predominant Site of <u>Primary Tumor</u>	<u>N</u>	<u>HR</u>	<u>95% CI</u>	<u>P-Value</u>
Medial vs. Lateral/Central/Other	6765	1.26	1.17 – 1.36	< 0.01
Medial vs. Lateral	5375	1.30	1.20 – 1.41	< 0.01

Overall Survival

Predominant Site of <u>Primary Tumor</u>	<u>N</u>	<u>HR</u>	<u>95% CI</u>	<u>P-Value</u>
Medial vs. Lateral/Central/Other	6765	1.29	1.18 – 1.41	< 0.01
Medial vs. Lateral	5375	1.33	1.21 – 1.45	< 0.01

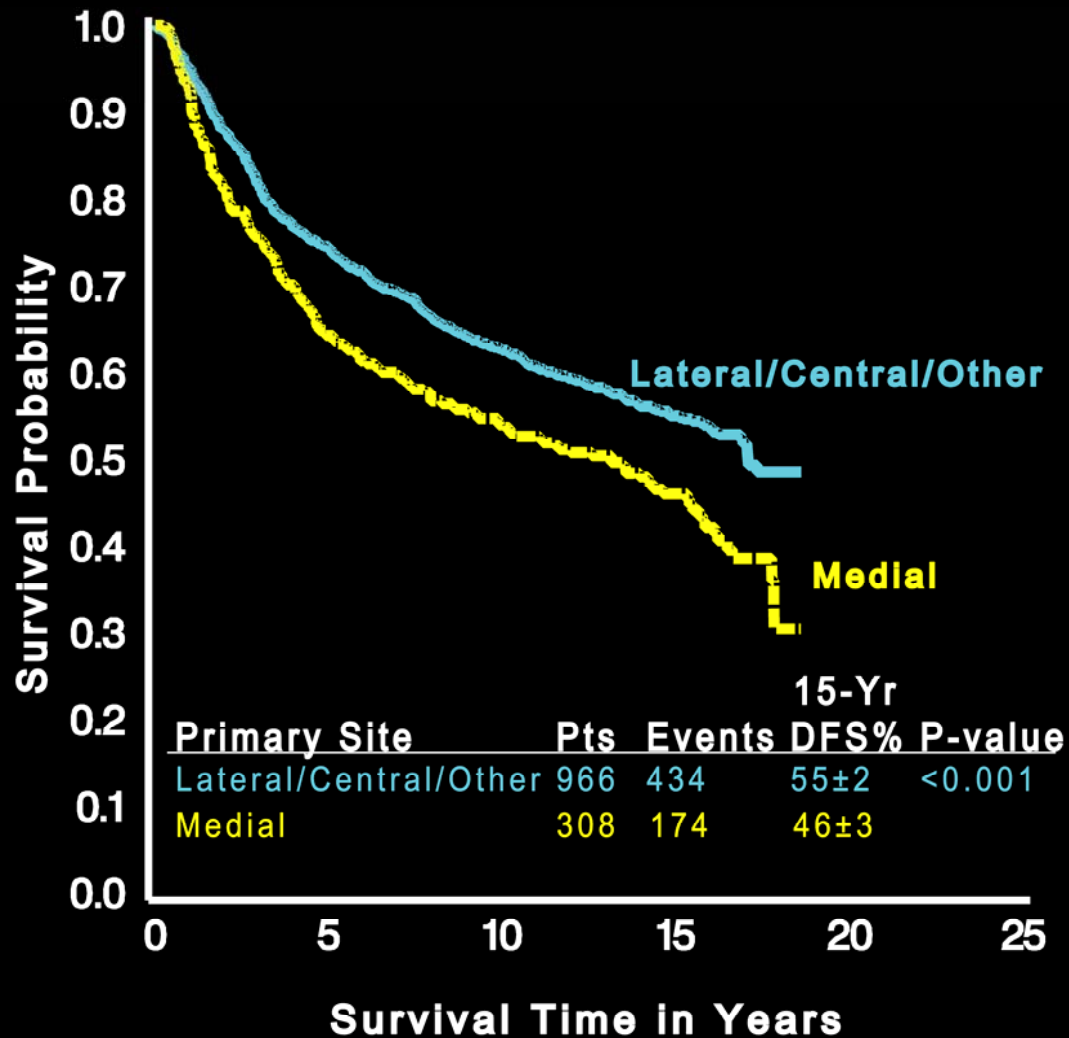


Disease Free Survival according to Nodal Status

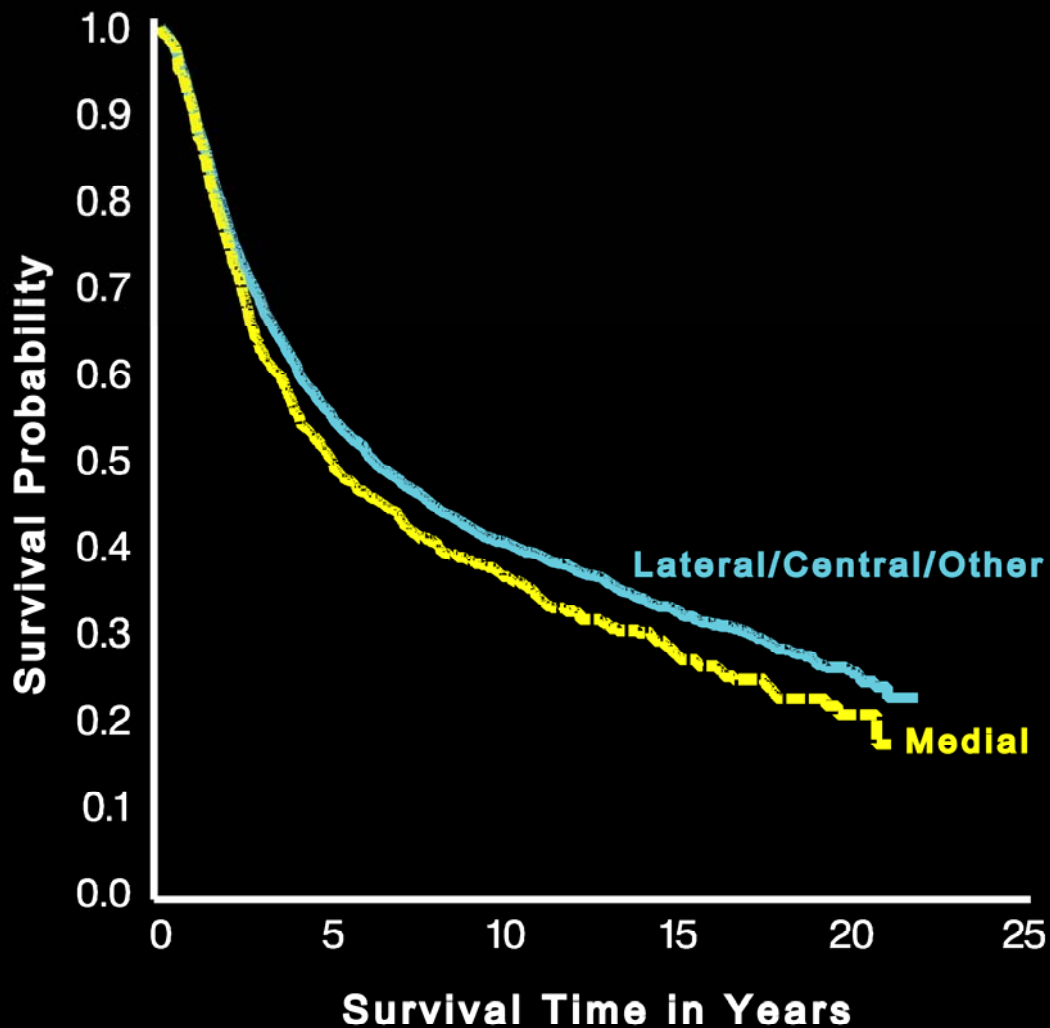
<u>Nodal Group</u>	<u>Group</u>	<u>N</u>	<u>15-yr DFS %</u>	<u>HR</u>	<u>95% CI</u>	<u>P-Value</u>
0	Medial	308	46 ± 3	1.37	1.15 – 1.64	< 0.01
	Lateral/Central/Other	966	55 ± 2			
1 – 3	Medial	618	33 ± 2	1.28	1.14 – 1.43	< 0.01
	Lateral/Central/Other	2724	42 ± 1			
4 +	Medial	297	15 ± 2	1.11	0.97 – 1.28	0.12
	Lateral/Central/Other	1852	18 ± 1			



Disease Free Survival Node Negative



Disease Free Survival Node Positive



Primary Site	Pts	Events	15-Yr DFS%	P-value
Lateral/Central/Other	4576	2913	32±1	0.003
Medial	915	624	27±2	



Percentage distribution of medial tumors and the tumors in the external quadrants of the breast according to the site of first failure

<u>Site</u>	<u>Medial</u>	<u>Lateral/Central/Other</u>	<u>Lateral</u>
Local	10.4	9.2	8.7
Contralateral	3.8	3.9	3.8
Soft tissue	2.6	1.9	1.8
Bone	15.7	13.4	13.2
Viscera	19.0	16.8	16.4

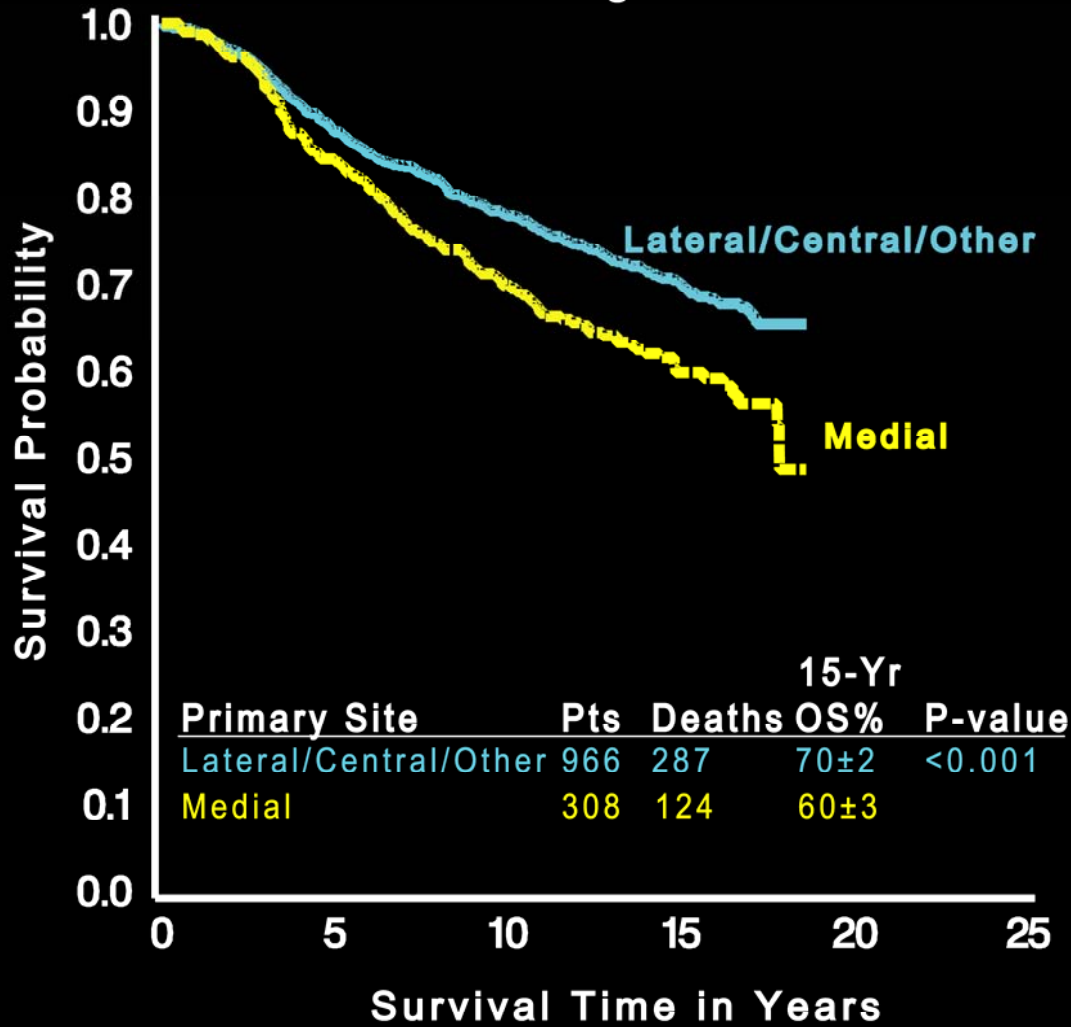


Overall Survival according to Nodal Status

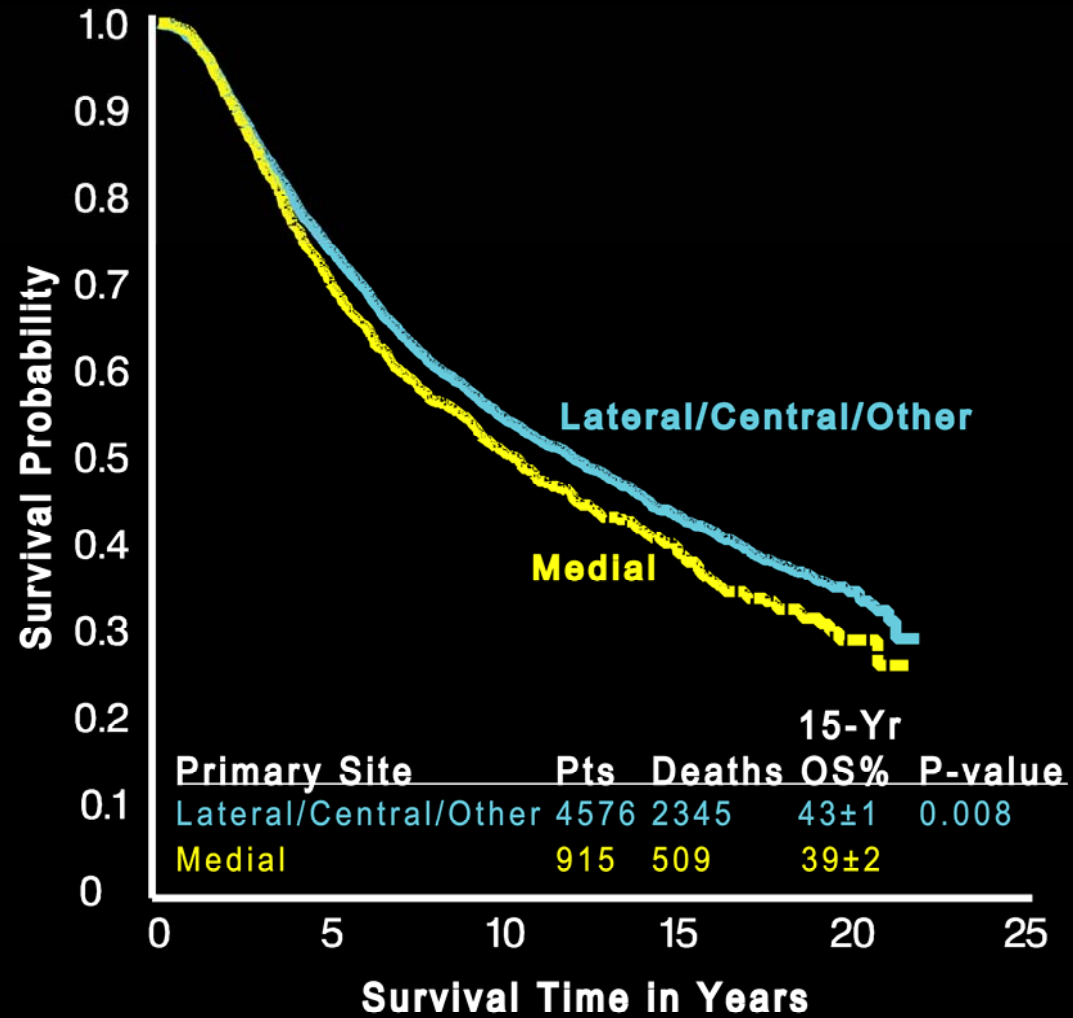
<u>Nodal Group</u>	<u>Group</u>	<u>N</u>	<u>15-yr OS %</u>	<u>HR</u>	<u>95% CI</u>	<u>P-Value</u>
0	Medial	308	60 ± 3	1.42	1.15 – 1.76	< 0.01
	Lateral/Central/Other	966	70 ± 2			
1 – 3	Medial	618	48 ± 2	1.24	1.09 – 1.41	< 0.01
	Lateral/Central/Other	2724	54 ± 1			
4 +	Medial	297	21 ± 3	1.19	1.03 – 1.37	0.02
	Lateral/Central/Other	1852	28 ± 1			



Overall Survival Node Negative



Overall Survival Node Positive



Conclusions

- Site of disease is a powerful prognostic feature especially in node negative patients
- New staging procedures including biopsy of the sentinel internal mammary node should be further studied in patients with medial tumors





International Cooperation

Thanks to patients,
investigators, nurses,
data managers and
all other members of
the IBCSG for
allowing us to
understand and move
forward....

