

Clinicopathologic Characteristics of Breast Cancers Detected by Ultrasound

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Background

- Supplemental US screening in addition to mammography (MG) has increased cancer detection compared to MG alone.
- However, little is known about the clinicopathologic characteristics of US-detected breast cancers.



Berg WA *JAMA* 2008
Crystal P *AJR* 2003



Purpose

To evaluate the clinical, imaging, and pathologic characteristics of US-detected cancers compared to cancers detected by screening MG.



Study Group

6837 consecutive women who underwent breast cancer surgery between Sep 2003 and Apr 2010



1047 asymptomatic women with nonpalpable cancer



254 women with US-detected cancer



793 women with MG-detected cancer



2 bilateral cancers
254 women / 256 cancers



14 bilateral cancers
793 women / 807 cancers

Data Collection

- **Clinical:** age, menopausal status, family Hx, personal Hx, prior benign biopsy
- **Imaging:** mammographic breast density
final assessment BIRADS category
- **Pathologic:** type of surgery, tumor histology, tumor grade, multifocality, axillary LN metastasis, molecular markers (ER PR HER2 Ki67 p53 Bcl2)



Immunohistochemically Defined Breast Cancer Subtype

Luminal A	ER+ PR+ HER2-
Luminal B	ER+ PR+ HER2+
HER2+	ER- PR- HER2+
Basal-like	ER- PR- HER2- and cytokeratin (CK) 5/6+ and/or EGFR+
Unclassified	ER- PR- HER2- CK5/6- EGFR-



Statistical Analysis

- **Univariate analysis**
 - Chi-square or Fisher's exact test
 - Student's *t*-test
- **Multivariate logistic regression analysis**
 - Odds ratios
 - 95% confidence intervals



GBCC 2011

Results



Clinical Features

Characteristics	US-detected (N=254)	MG-detected (N=793)	P-value
Age			< 0.0001
Mean \pm SD	48 \pm 7	52 \pm 9	
30-39	23 (9.1)	62 (7.8)	
40-49	122 (48)	267 (33.7)	
50-59	90 (35.4)	295 (37.2)	
\geq 60	19 (7.5)	169 (21.3)	
Menopausal status			< 0.0001
Premenopausal	152 (59.8)	311 (39.2)	
Peri- or Post-	102 (40.2)	482 (60.8)	
Family history	9 (3.5)	16 (2)	< 0.0001
Personal history	7 (2.8)	10 (1.3)	< 0.0001
Prior benign biopsy	*14 (5.5)	14 (1.8)	< 0.0001

* This group includes one case of atypical ductal hyperplasia



Imaging Features

Characteristics	US-detected (N=254)	MG-detected (N=793)	P-value
Breast density (BIRADS)			< 0.0001
1	2 (0.8)	79 (10)	
2	25 (9.8)	199 (25.1)	
3	145 (56.3)	428 (54)	
4	84 (33.1)	87 (10.9)	
Final BI-RADS assessment			< 0.0001
3	2 (0.8)	0 (0)	
4	187 (73.6)	313 (39.5)	
4a	79 (31.1)	28 (3.5)	
4b	68 (26.8)	142 (17.9)	
4c	40 (15.7)	143 (18)	
5	65 (25.6)	480 (60.5)	

Pathologic Features (I)

Characteristics	US detected (N=256)	MG detected (N=807)	P-value
Type of surgery			< 0.0001
Breast-conserving surgery	216 (84.4)	552 (68.4)	
Mastectomy	40 (15.6)	255 (31.6)	
Lymph node metastasis			< 0.0001
None	235 (91.8)	679 (84.1)	
1-3	17 (6.6)	96 (11.9)	
4-10	3 (1.2)	24 (3)	
>10	1 (0.4)	8 (1)	

Pathologic Features (II)

Characteristics	US-detected (N=256)	MG-detected (N=807)	P-value
Tumor histology			< 0.0001
DCIS	48 (18.8)	214 (26.5)	
Invasive	208 (81.2)	593 (73.5)	
invasive ductal	190 (74.2)	560 (69.5)	
invasive lobular	12 (4.7)	23 (2.8)	
mixed	6 (2.3)	10 (1.2)	
Invasive tumor size (cm)			
Mean ± SD	1.32 ± 0.67	1.70 ± 1.05	< 0.0001
≤ 1.0	85 (41.5)	191 (32.2)	0.008
1.1-2.0	100 (48.3)	265 (44.7)	0.162
2.1-5.0	21 (10.1)	130 (21.9)	0.285
5.1-10.0	0 (0)	7 (1.2)	



Pathologic Features (III)

Characteristics	US-detected (N=256)	MG-detected (N=807)	p-value
Histologic grade			0.008
I	44 (22.6)	94 (17.4)	
II	117 (60.0)	288 (53.3)	
III	34 (17.4)	158 (29.3)	
Unknown	13	53	
Nuclear grade			0.018
1	41 (16.7)	113 (14.2)	
2	137 (56)	342 (43.1)	
3	67 (27.3)	339 (42.7)	
Unknown	11	13	



Pathologic Features (IV)

	US detected (N=256)	MG detected (N=807)	P-value		US detected (N=256)	MG detected (N=807)	P-value
ER			0.015	Ki-67			0.423
Negative	47 (18.7)	202 (25.7)		< 20%	247 (97.6)	753 (96.3)	
Positive	204 (81.3)	584 (74.3)		≥ 20%	6 (2.4)	29 (3.7)	
Unknown	5	21		Unknown	3	25	
PR			< 0.0001	p53			0.117
Negative	67 (26.3)	342 (43.5)		Negative	68 (27.3)	257 (32.9)	
Positive	183 (73.7)	444 (56.5)		Positive	181 (72.7)	525 (67.1)	
Unknown	6	21		Unknown	7	25	
HER2			<0.0001	Bcl-2			0.033
Negative	191 (75)	497 (62.6)		Negative	41 (16.2)	176 (22.5)	
Positive	64 (25)	124 (37.4)		Positive	212 (83.8)	605 (77.5)	
Unknown	1	13		Unknown	3	26	



Breast Cancer Subtype

Subtype	US detected	MG detected	<i>P</i> -value
Luminal A	167 (66.5)	393 (49.6)	<0.0001
Luminal B	52 (20.9)	211 (26.6)	0.067
HER2+	12 (4.8)	81 (10.2)	0.009
Basal-like	6 (2.4)	8 (1.0)	0.097
Unclassified	14 (5.6)	100 (12.6)	0.002
Unknown	5	14	

Multivariate Analysis

Significant Independent Variables were...

Mammographic breast density

Final BIRADS category

PR, HER2

Breast cancer subtype

Tumor size



Characteristics	aOR (95% CI)	P-value
Mammo density Non-dense (1, 2) Dense (3, 4)	Ref 3.71 (2.33-5.91)	<0.01
BIRADS 4 5	Ref 0.24 (0.17-0.33)	<0.01
PR Negative Positive	Ref 2.00 (1.29-3.09)	<0.01
HER2 Negative Positive	Ref 0.55 (0.38-0.78)	<0.01
Breast cancer subtype Luminal A Luminal B	Ref 0.52 (0.35-0.77)	<0.01
Tumor size (cm) >2 1-2 <1	Ref 2.25 (1.19-4.24) 2.21 (1.13-4.31)	 0.01 0.02



Conclusions

- Most tumors discovered by US screening were small-sized invasive cancers with lower levels of suspicion of malignancy at US.
- These cancers were more likely associated with the luminal A compared to luminal B.
- US-detected cancer can therefore benefit from early detection, which would allow breast conservation and the use of less toxic therapy.

