

Prediction of Local Recurrence on Preoperative Breast MRI

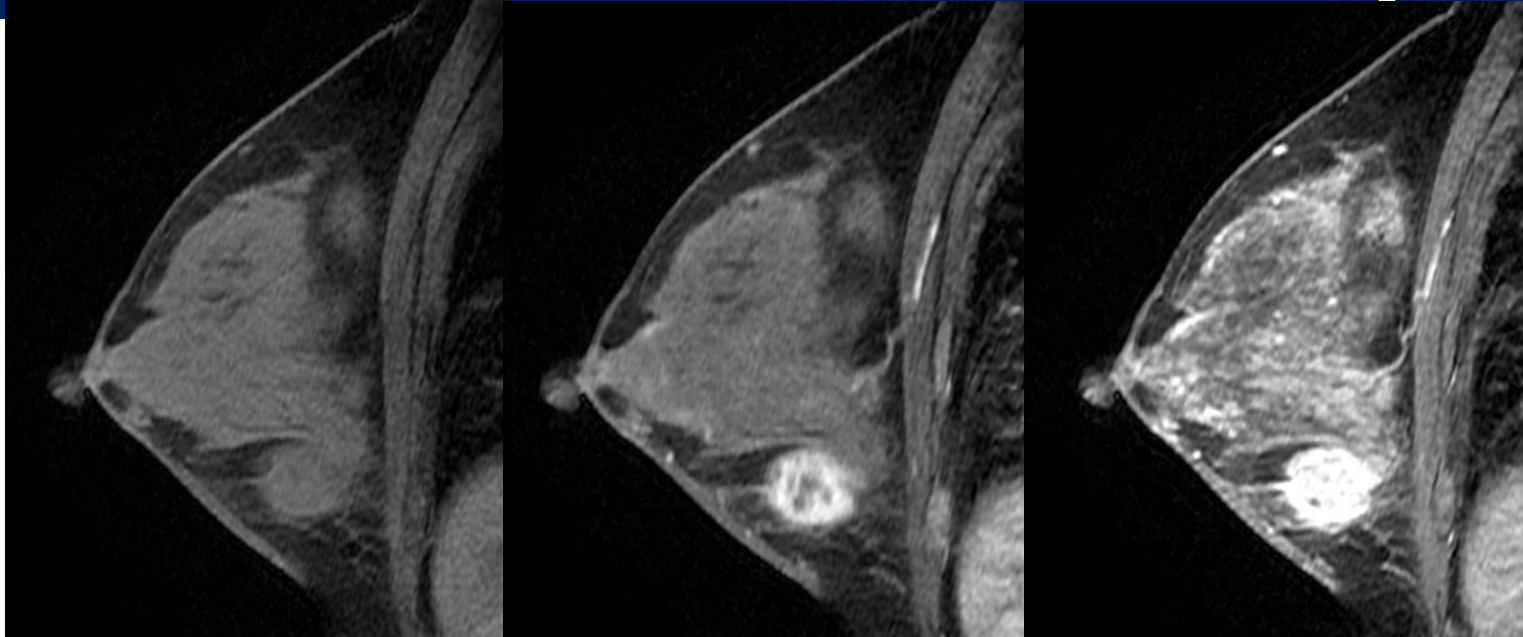
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Which Patient Would Develop IBTR?



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Criteria **First Case**

Age:

Tumor Size:

Tumor Grade:

Margin Status:

Lymphovascular Invasion:

Chemotherapy:

Tamoxifen/Aromatase Inhibitor:

HG3, NG3, Triple Negative

10-Year Risk of Ipsilateral Breast Tumor Recurrence

With Radiation Therapy:	6.9%
Without Radiation Therapy:	23.0%

Criteria **Second Case**

Age:

Tumor Size:

Tumor Grade:

Margin Status:

Lymphovascular Invasion:

Chemotherapy:

Tamoxifen/Aromatase Inhibitor:

HG3, NG 3, HER-2 (+)

10-Year Risk of Ipsilateral Breast Tumor Recurrence

With Radiation Therapy:	10.8%
Without Radiation Therapy:	36.0%

Purpose



- **If preoperative MRI could help predict subsequent IBTR?**
- **Which imaging factor has the most predictive power?**
- **How important are imaging factors compared to clinicopathologic variables?**

Which imaging factors?



- **Tumor environment might mediate resistance to treatment**
 - correlated with the prognosis*
- **Imaging biomarkers which can reflect tumor environment in breasts**
 - Mammographic density
 - Background parenchymal enhancement
 - Background parenchymal signal enhancement ratio

* Magdalena A . J Mammary Gland Biol Neoplasia (2010)
15:389–397



Two Studies in SNUH

- Patient with IDC: 133 pts (1:6 control, 19 recur and 114 control, case-control, presence of IBTR)*
- Patients with DCIS: 215 consecutive pts (15 recur and 200 control, IBTR-free survival)**

*Kim MY and Cho N. Acta Radiologica 2013

** Kim SA and Cho N. Radiology 2013 In Press

Patient Selection



**From Jan '04 ~ Dec '09, Pure DCIS pts
w/ preop MRI & surgery (n=320)**

No available 2 year f/u data (n=3)

Previous hx of breast cancer (n=2)

Underwent total mastectomy (n=88)

MRI taken at outside facility (n=12)

Included patients (n=215)

Variables



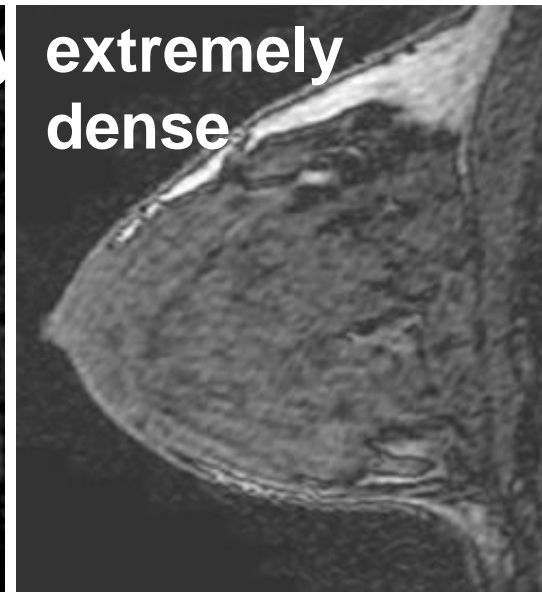
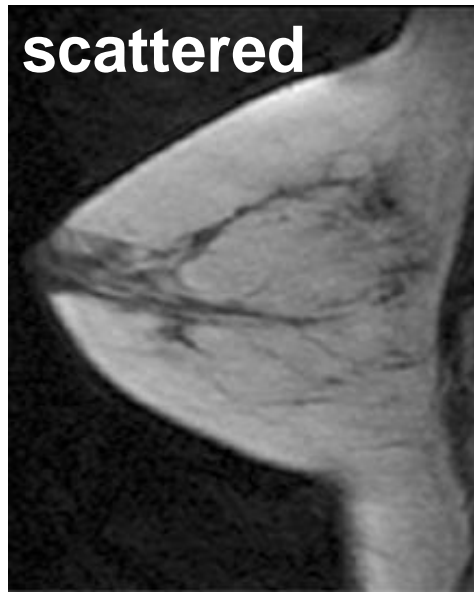
- ▶ **Clinicopathologic features**
 - **Age, menopausal status, adjuvant therapy (RT,HT),**
 - **ER, PR, HER2 status, nuclear grade, margin status**

- ▶ **MRI features: by two radiologists in consensus**
 - **Lesion size, Lesion type (Mass vs. NMLE)**
 - **Tumor kinetics type**
 - **BPE: minimal, mild, moderate, or marked**
 - **Fibroglandular density: fatty, scattered, heterogeneously dense, or extremely dense**
 - **Background parenchymal signal enhancement ratio (SER)**

Methods



▶ Fibroglandular Tissue Density

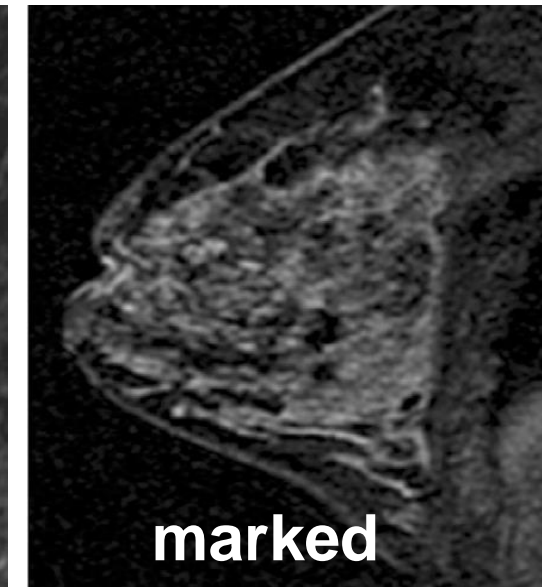
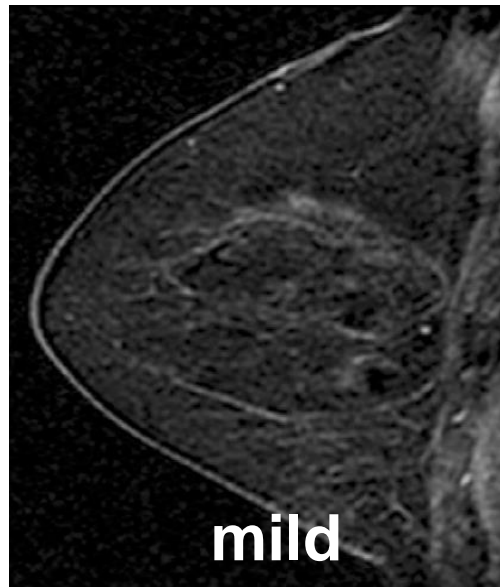
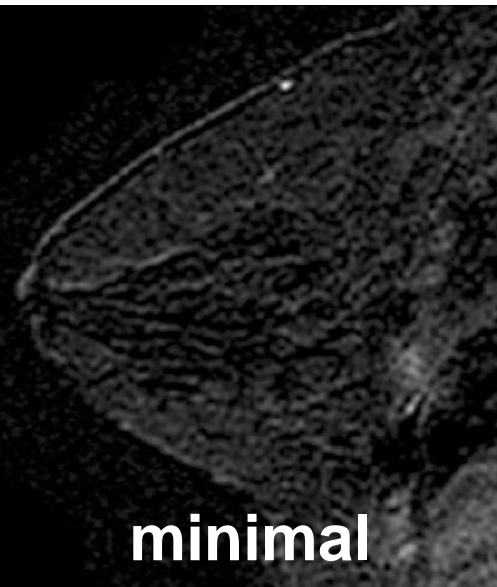


- Visually assessed using T2WI and FS T1WI
- Any non-fatty, non-cystic breast parenchyma

Methods



▶ BPE (background parenchymal enhancement)

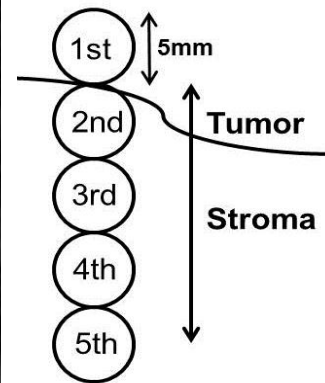
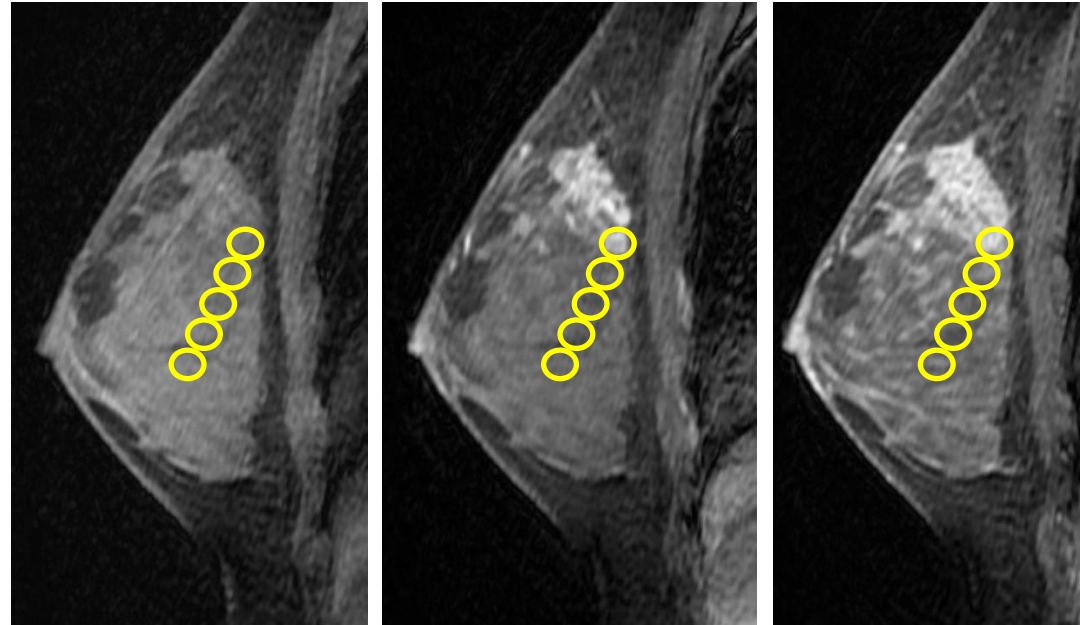
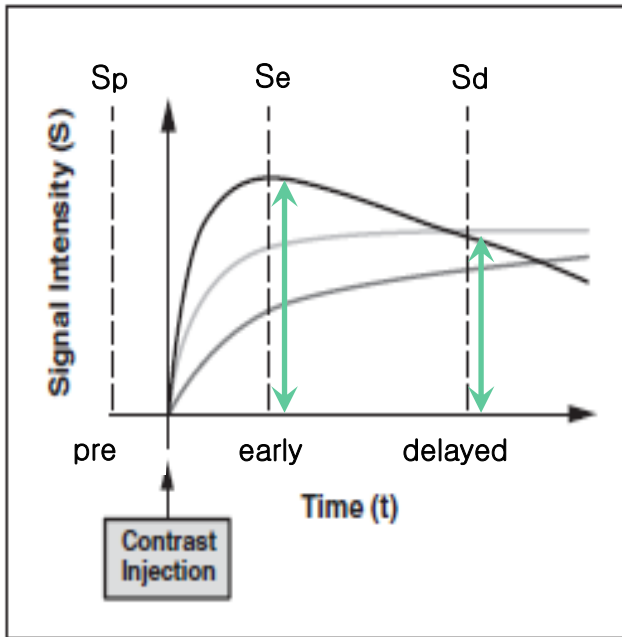


- Assessed using pre- and early enhanced FS T1WI and subtraction images

Methods



▶ BP SER (Signal Enhancement Ratio)



$$\text{SER} = (\text{Se} - \text{Sp}) / (\text{Sd} - \text{Sp})$$

$$\text{SER}(\text{ROI}^{2\text{nd}}) = \{\text{Se}(\text{ROI}^{2\text{nd}}) - \text{Sp}(\text{ROI}^{2\text{nd}})\} / \{\text{Sd}(\text{ROI}^{2\text{nd}}) - \text{Sp}(\text{ROI}^{2\text{nd}})\} = (416 - 315) / (435 - 315) = 0.84$$
$$\text{Mean SER} = \{\text{SER}(\text{ROI}^{2\text{nd}}) + \text{SER}(\text{ROI}^{3\text{rd}}) + \text{SER}(\text{ROI}^{4\text{th}}) + \text{SER}(\text{ROI}^{5\text{th}})\} / 4 = (0.84 + 0.63 + 0.56 + 0.66) / 4 = 0.67$$



Statistical Analysis

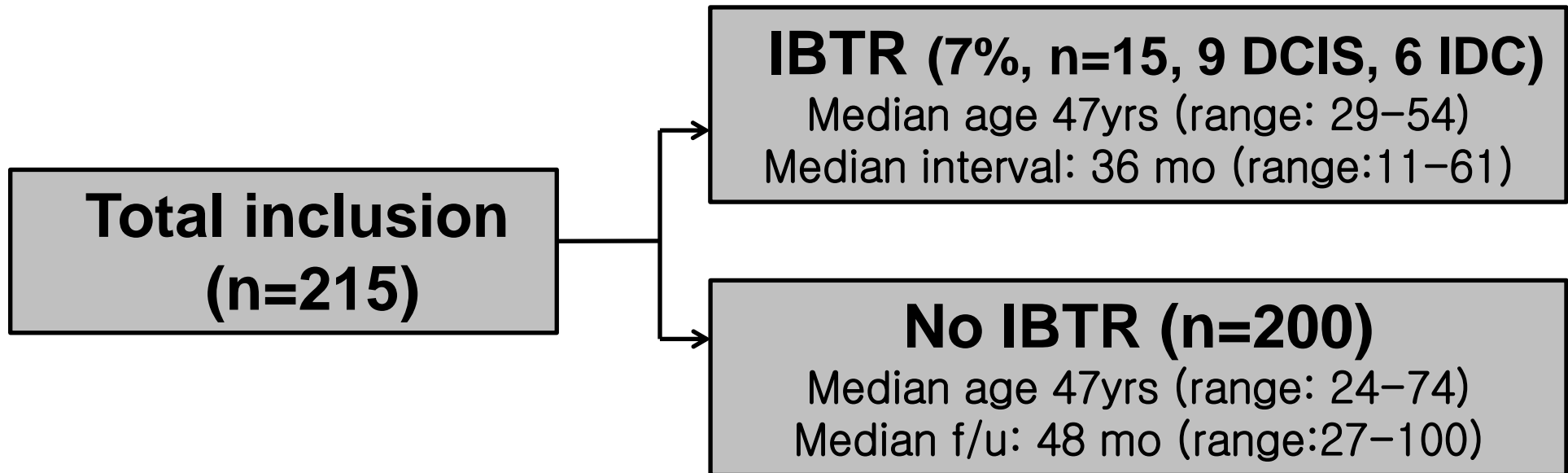
- ▶ **Recurrence free survival (RFS): Kaplan-Meier method**
- ▶ **Univariate comparison: Log-rank test**
- ▶ **Multivariate Cox proportional hazards model: association between RFS and MRI variables, adjusting for clinicopathologic variables**
- ▶ **ICC: reproducibility of SER measurements**



Results



Rate of IBTR



Patient Characteristics



Characteristic		IBTR (n=15)	No IBTR (n=200)	<i>P</i>
Age at surgery	< 45	7 (46.7)	69 (34.5)	.404
	> 45	8 (53.3)	131 (65.5)	
Menopausal status	Pre/peri	13 (86.7)	136 (68.0)	.157
	Post	2 (13.3)	64 (32)	
Clinical presentation	Radiologic	9 (60.0)	153 (76.5)	.210
	Clinical	6 (40.0)	47 (23.5)	
Radiation therapy	Yes	11 (73.3)	183 (91.5)	.045
	No	4 (26.7)	17 (8.5)	
Endocrine therapy	Yes	7 (46.7)	152 (76.0)	.018
	No	8 (53.3)	48 (24.0)	

Histopathologic Characteristics



Characteristic	IBTR (n=15)	No IBTR (n=200)	P-value
Nuclear grade			
Low	8 (53.3)	87 (43.5)	.592
Intermed/high	7 (46.7)	113 (56.5)	
Molecular subtype			
Luminal	12 (80.0)	157 (78.5)	.838
HER2	1 (6.7)	22 (11.0)	
TPN	2 (13.3)	21 (10.5)	
Margin			
Negative	10 (66.7)	166 (83.0)	.156
Close	5 (33.3)	34 (17.0)	



SER: Reproducibility & Performance in Prediction of IBTR

- ▶ **ICC between repeated measurements for SER**
 - **0.889 (95% CI: 0.857, 0.914; P < .001)**
→ **Excellent agreement**
- ▶ **ROC analysis: best cut-off of 0.51, Sensitivity 80%, Specificity 88%**
- ▶ **Az 0.885 (95% CI 0.817-0.952), P < .001**

Univariate Analysis: Clinicopathologic Variables & RFS

characteristics	Total (n=215)	IBTR (n=15)	HR	95% CI	P
Age (<45)	76(35.3)	7 (46.7)	1.652	0.598,4.563	.328
Pre/perimenopause	149(69.3)	13(86.7)	2.964	0.669,13.138	.133
Clinical presentation	53(24.7)	6 (40.0)	2.271	0.806, 6.399	.121
No RT	21(9.8)	4 (26.7)	3.455	1.092,10.938	.025
No HT	56 (26.0)	8 (53.3)	3.730	1.347,10.327	.007
Intermediate/high gr.	120(55.8)	7 (46.7)	0.734	0.266, 2.027	.549
Close/positive margin	39(18.1)	5 (33.3)	2.204	0.753, 6.451	.139
ER status (-)	59(27.4)	4 (26.7)	1.064	0.338, 3.351	.915
Molecular subtype					
luminal	169(78.6)	12(80.0)	1		.830
HER2	23(10.7)	1(6.7)	0.650	0.085, 5.005	
TPN	23(10.7)	2 (13.3)	1.356	0.301, 6.104	
Histologic tumor size (cm)	2.90 ± 1.99	3.91 ± 2.13	1.270	1.016,1.589	.036

Univariate Analysis: MRI Variables & RFS



Characteristics	Total (n=215)	IBTR (n=15)	HR	95% CI	P
MR tumor size	2.80 ±1.75	2.39 ±1.08	.875	0.570, 1.343	.541
BPE					
grade1,2	110 (51.1)	5 (33.3)	1		.254
grade 3,4	105 (48.9)	10 (96.7)	1.855	0.632, 5.447	
FGT					
grade1,2	52 (24.2)	2 (13.3)	1		
grade 3,4	163 (75.8)	13 (86.7)	2.300	0.517, 10.237	
SER (high [>0.51])					
measurement1	41 (19.1)	12(80.0)	15.432	4.305,55.322	<.001
measurement2	34 (15.8)	11(73.3)	13.213	4.160,41.961	<.001
Lesion type (mass)					
mass	21(13.3)	2 (22.2)	1.663	0.344, 8.039	.523
NMLE	137(86.7)	7 (77.8)	1		
Lesion kinetics					
wash-out/plateau	34	5	4.541	1.218, 16.927	.013
persistent	124(78.5)	4(44.4)	1		



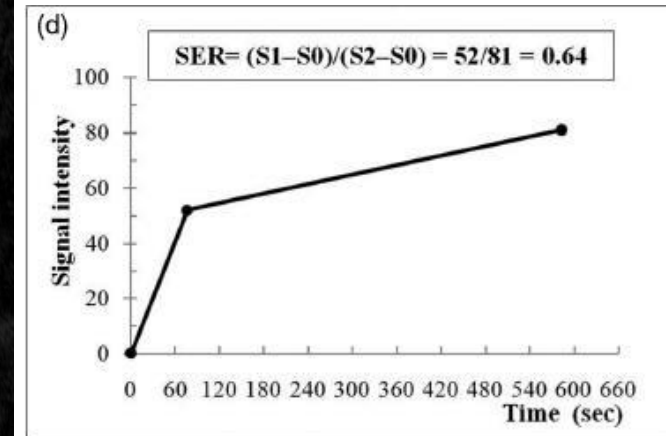
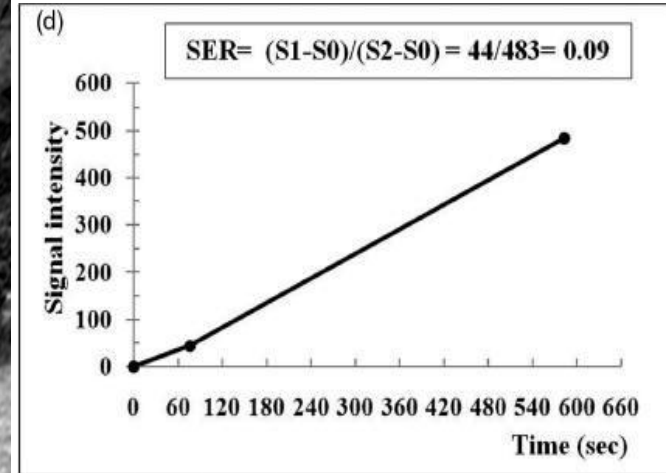
Multivariate Analysis

Characteristics	HR	95% CI	P
Radiation therapy			
No	2.292	0.674, 7.801	.184
Yes	1		
Endocrine therapy			
No	3.554	1.232, 10.251	.007
Yes	1		
Size of tumor at surgical histology	1.311	1.052, 1.634	.016
SER			
>0.51	15.266	4.248, 54.862	<.001
≤0.51	1		

Which Patient Would Develop IBTR?

SER Measurement

46 months later





Take-Home Message

- **Could preoperative MRI help predict subsequent IBTR? → Yes**
- **Which imaging factor has the most predictive power? → Parenchymal SER**
- **How important are imaging factors compared to clinicopathologic variables? --
> ???**



Thank you for your attention !

