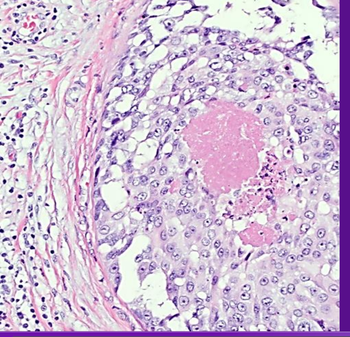

Tumor-Infiltrating Lymphocytes (TILs) in a Cohort of Women with DCIS

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BACKGROUND and PURPOSE

- A major issue in defining ductal carcinoma in situ (DCIS) is whether it is a precursor or a risk factor for the development of invasive breast cancer.
- 50% of DCIS recurs as invasive carcinoma, which is associated with an 18.1 greater likelihood of dying from breast cancer.
- The purpose of this study was to investigate the tumor's immune microenvironment and to investigate the association of TILs in those patients who had DCIS and had a recurrence compared to those who did not recur.

METHODS

- Our institutional database was queried for all patients with pure DCIS from 2010 to 2018.
- TILs were evaluated by the guidelines published by the International Immuno-Oncology Biomarker Working-Group for evaluating TILs in DCIS (Hendry et al. Adv Anat Pathol (2017) 24(5):235–51).
- Percentage of TILs was assessed from the densest focus (hotspot) in one high power field of stroma touching the basement membrane.
- Statistical methods included cluster analyses to define sparse TILs (<45%) vs. dense TILs (≥45%), multivariate logistic regression to compare the clinicopathologic characteristics with TILs and the Kaplan-Meier and Cox regression models were performed to analyze disease-free survival.

RESULTS

Table. Clinicopathologic Factors and TILs Multivariate Analysis

Variable	Total N=69	Sparse TILs (highest %<45) N=47	Dense TILs (highest %≥45) N=22	p-value
Median Age (years)	62.0 (34-88)	65.0 (34-88)	54.5 (35-86)	**0.019**
Race				0.502
Black	6 (9%)	4 (9%)	2 (9%)	
Asian	8 (12%)	3 (6%)	5 (23%)	
Hispanic	3 (4%)	3 (6%)	0 (0%)	
White	51 (74%)	37 (79%)	14 (64%)	
Other	1 (1%)	0 (0%)	1 (5%)	
Tumor Size (cm)	12.0 (0.1-8.0)	1.31 (0.1-5.0)	3.38 (0.8-8.0)	**<0.001**
Multifocal				0.854
Yes	22 (32%)	15 (32%)	7 (32%)	
No	47 (68%)	32 (68%)	15 (68%)	
Nuclear Grade				**0.010**
Low	4 (6%)	4 (9%)	0 (0%)	
Intermediate	26 (38%)	24 (51%)	2 (9%)	
High	39 (56%)	19 (40%)	20 (91%)	
Comedo Histology				**0.033**
Yes	21 (30%)	10 (21%)	11 (50%)	
No	48 (70%)	37 (79%)	11 (50%)	
Necrosis				**0.027**
Yes	48 (70%)	29 (62%)	19 (86%)	
No	21 (30%)	18 (38%)	3 (14%)	
Estrogen Receptor				**0.037**
Positive	56 (81%)	41 (87%)	15 (68%)	
Negative	13 (19%)	6 (13%)	7 (32%)	
Progesterone Receptor				0.081
Positive	52 (75%)	38 (81%)	14 (64%)	
Negative	17 (25%)	9 (19%)	8 (36%)	
Hormone Therapy				0.083
Yes	22 (32%)	18 (38%)	4 (18%)	
No	47 (68%)	29 (62%)	18 (82%)	
Radiation Therapy				0.219
Yes	41 (59%)	26 (55%)	15 (68%)	
No	28 (41%)	21 (45%)	7 (32%)	
Ipsilateral Recurrence				**0.008**
Yes	13 (19%)	4 (9%)	9 (41%)	
No	56 (81%)	43 (91%)	13 (59%)	

Figure 1. Sparse vs. Dense TILs

Sparse TILs (DCIS grade 2) | **Dense TILs (DCIS grade 3)**

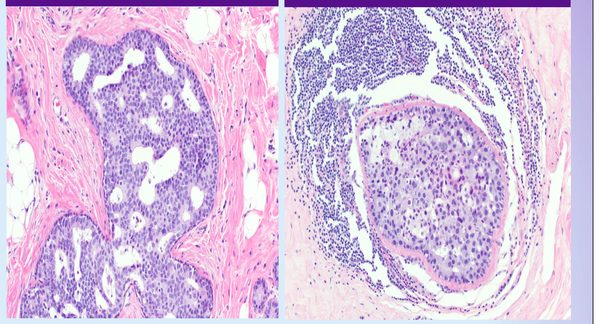
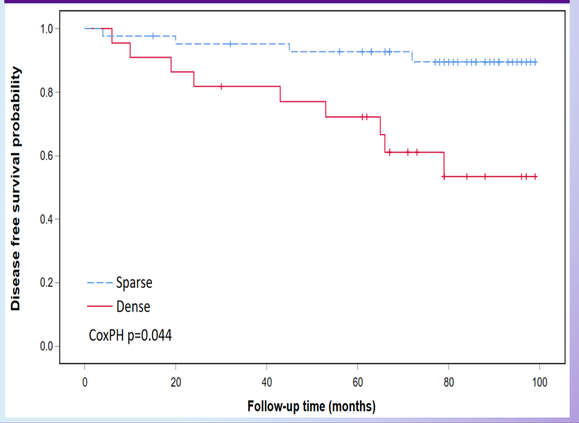


Figure 2. Disease Free Survival Analysis of TILs



RESULTS

- There were 581 (21%) patients with pure DCIS. Of those, sixty-nine patients with pure DCIS were evaluated, of whom 54 (78%) were treated by breast conserving surgery.
- Out of the 69 patients evaluated for TILs, 47 (68%) had sparse TILs and 22 (32%) had dense TILs (Table and Figure 1).
- The median age was 60.2 years and the median follow-up for this cohort was 6.7 years.
- After adjusting for age, dense TILs was associated with younger age (p=0.019), larger tumor size (p< 0.001), high nuclear grade (p=0.010), comedo histology (p=0.033), necrosis (p= 0.027), ER-positivity (0.037) and recurrence (p= 0.008) (Table).
- We found that dense TILs was a significant predictor of recurrence (HR=4.1, 95%CI 1.0-15.9, p=0.044) (Figure 2).

CONCLUSIONS

- In our study, we found that dense TILs is a significant predictor of recurrence in patients with DCIS treated by breast conserving surgery.
- Our study suggests the relevance of the immune microenvironment to further profile those DCIS lesions that may be obligate precursors of invasive breast cancer.
- Further studies are warranted to define the impact of immunologic and molecular profiling for the clinical management of DCIS patients.

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