A New Additive Diagnostic Assay for Breast Cancer Screening: Total Biochemical Infrared Analysis of Immune Cells and Plasma

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Background

Screening for early diagnosis of breast cancer is currently based on imaging of the breast. Screening mammography, the most commonly used imaging modality, carries a sensitivity and specificity of approximately 80%, even less in dense breast tissue.

Fourier transform infrared (FTIR) spectroscopy of peripheral blood mononuclear cells (PBMCs) has been shown in previous studies to differentiate between patients with breast cancer and healthy controls or patients with benign breast disease with a sensitivity of about 90% and specificity of 80%.

AIM

To further study the utility of FITR spectroscopy of PBMCs to detect breast cancer in a larger group of patients and controls.

Patients & Methods

A total of 190 women were studied: 50 patients with breast cancer, 79 who underwent a biopsy for benign breast disease, and 61 with no detectable abnormality. Breast cancer patients included 6 cases of pure DCIS, 42 cases of IDC, 1 case of ILC and 1 case of LCIS.
Ten ml of blood were drawn and separated by Ficoll gradient into PBMCs and plasma. The samples were dried on a zinc selenide window and analyzed by FTIR spectrometer. The spectra were analyzed by the proprietary software TodoSpectra to distinguish between infrared spectra of cancer patients vs. patients with benign findings and healthy controls. The influence of age and breast density on TM-B1^{TM} results were evaluated.

Table 1a: Patient characteristics

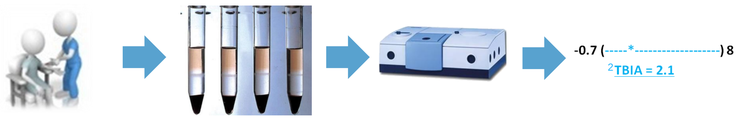
	Healthy N=61	Benign N=79	Cancer N=50
Age ± SD (range)	47±12 [24,70]	46±12 [22,71]	55±14 [31,78]
Breast Density (%)			
A	8 (13%)	6 (8%)	2 (4%)
B	10 (16%)	11 (14%)	12 (24%)
C	21 (34%)	31 (39%)	10 (20%)
D	12 (20%)	18 (23%)	13(26%)
NA	10 (16%)	13 (16%)	13(26%)

Table 1b: Breast Cancer Patient characteristics

Histology	**DCIS**	**LCIS**	**IDC**	**ILC**	
	6 (12%)	1 (2%)	42 (84%)	1 (2%)	
Stage	**0**	**I**	**II**	**III**	**IV**
	7 (14%)	24 (48%)	14 (28%)	3 (6%)	2 (4%)

Technique

Standard Blood Draw with Todos Kit → **Mononuclear Cells & Plasma Separated** → **FTIR[1] Analysis with Todos Algorithm** → **Results Reported to Doctor**



1) Fourier Transform Infra-Red (FTIR) spectroscopic analysis of the immune system's response to cancer
2) TBIA - Total Biochemical Infra-Red Analysis

Results

Table 2a: TM-B1 Performances – Classification

Clinic \ TM-B1	Healthy	Benign	Cancer	Total
Healthy	51 (83.6%)	7 (11.5%)	3 (4.9%)	61 (100%)
Benign	4 (5.1%)	75 (94.9%)	0 (0.0%)	79 (100%)
Cancer	2 (4.0%)	5 (10.0%)	43 (86.0%)	50 (100%)

Table 2b: TM-B1 Performances – Accuracy

Clinic \ TM-B1	Negative	Positive	Accuracy
Control	TN=137	FP=3	SP=97.9%
Cancer	FN=7	TP=43	SN=86.0%
Prevalence	NPV=93.5%	PPV=95.1%	

Figure 1: Representative section of the second derivative of the infra-red spectra of PBMCs for healthy (blue), benign (black) and cancer (red). The mean and standard error are represented by the thickness of the line.

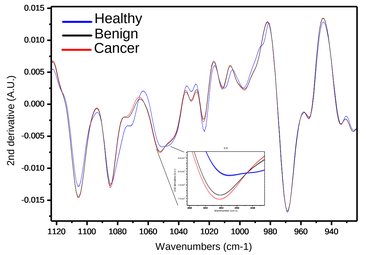
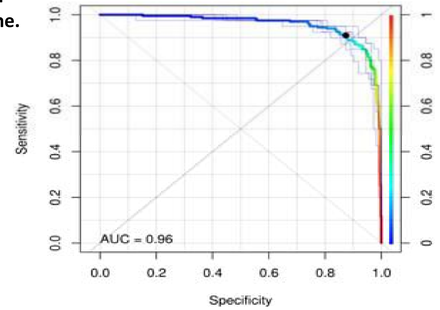


Figure 2: Receiver operating characteristic curve for healthy and benign vs. cancer.



The TM-B1 assay obtained a sensitivity of 86 % and specificity of 98 % for breast cancer detection. The positive predictive value (PPV) was 95.1% and the negative predictive value (NPV) was 93.5%. Dense breast tissue (BIRADS categories C&D) was present in 55 % of the subjects. The specificity and sensitivity for patients with dense breasts was 99 % and 83 % respectively. No major differences in accuracy of TM-B1 were found due to age, stage or histology (including DCIS).

Conclusions

TM-B1 in conjunction with current imaging techniques may contribute to early detection of breast cancer by increasing sensitivity and reducing false positive results and unnecessary biopsies. Further studies with larger numbers are required to establish the utility of adding the TM-B1 assay to current standard screening for breast cancer.

References

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