

## Thermal-driven biomarkers for breast cancer screening using dynamic infrared imaging modality

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### Abstract

In this study, we delve into the applications of infrared based diagnostic system for early diagnosis of breast cancer or symptomatic patients. We used low-rank sparse Non-negative matrix factorization (NMF) to select the main bases of the thermal images to determine the subsurface thermal heterogeneous patterns in these sets. For that, 55 participants for infrared breast screening selected from Database for Mastology Research (DMR) dataset with symptomatic and healthy participants. We calculate five derived properties of the breast area (contrast, correlation, dissimilarity, homogeneous, and energy) using thermal level co-occurrence matrices (TLCMs) and train a logistic regression to stratify between healthy and symptomatic patients.

We compared the ability of sparse-NMF to the state-of-the-art thermographic approaches such as principal component analysis/thermography (PCT), candid covariance-free incremental principal component thermography (CCIPCT), Sparse PCT, non-negative matrix factorization (NMF). Results indicate significant performance for Sparse-NMF (DMR: 74.1%). The results indicate considerable performance sparse-NMF, which conclusively indicates promising performance in terms of the accuracy and the robustness as a confirmation for the outlined properties.

**Keywords:** Breast cancer screening, infrared imaging modality, computer-aided diagnosis (CAD), Sparse non-negative matrix factorization.

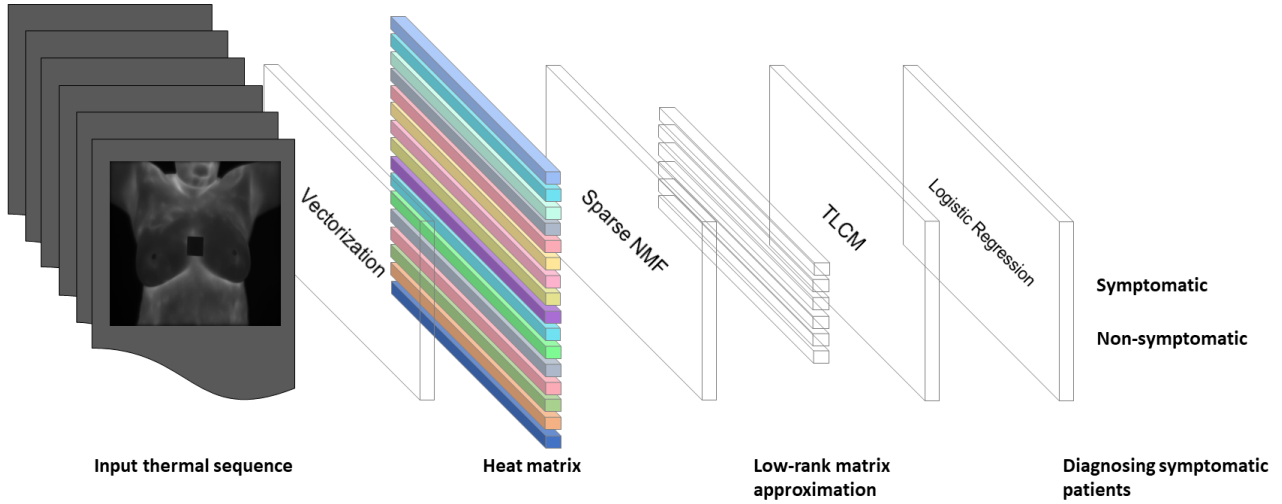
### 1. Introduction

According to the world health organization (WHO), cancer is a foremost cause of death worldwide, accounting for an overall estimation of 9.6 million deaths in 2018, where breast cancer considers being the most common cancer with lung cancer having 2.09 million cases, which leads to 627,000 deaths [1,2]. Despite a far better survival rate versus lung cancer, early detection of breast abnormality creates a tremendous effect on prognosis and course of treatment. Breast screening usually performs by mammography (which in X-ray (ionized imaging modality)) [3,4] or magnetic resonance imaging (MRI), and relatively expensive. With current developments in infrared thermography, breast screening using dynamic thermography seemingly a great alternative imaging modality for early diagnosis of breast abnormality [5,6]. Thermal images captured using dynamic protocol after air stream cooling the breasts, 20 sequential thermal images were taken within the intervals of 15 seconds during returning the patient's body to the environment (or body) equilibrium temperature. Then, several other images were taken from different angle orientations [5,6].

Matrix factorization techniques are known to be very effective in detection of subsurface heterogeneous thermal patterns in sequence of thermal images [7-15]. Some well-known matrix factorization methods such as principal component analysis/thermography (PCA/PCT) [10], and non-negative matrix factorization (NMF) [7] have been used for past several years in different applications.

This paper describes an application of sparse non-negative matrix factorization (Sparse NMF) to compress thermal sequence images and thermal-driven biomarkers for infrared based breast cancer screening to determine the patients with breast cancer symptoms. Moreover, clinical information and demographics for 55 patients also gathered for each patient. The original assessment for these patients took place using mammographic imaging modality with an experience radiologist that used as gold standard for our analyses.

In the next section, the methodology of the approach will be briefly described by applying Sparse-NMF analysis for thermography. The study population and the experimental and computational results are then presented in Sections 3 and 4, respectively. Finally, the conclusions are presented in Section 5.



**Fig. 1. Workflow.** An application of low-rank matrix approximation using sparse NMF and thermal feature extraction to determine the breast abnormality within the cohort.

## 2. Sparse NMF for an infrared system

Let  $I$  is a sequence of thermal images where each image has spatial dimension of  $N \times M$ . The  $X$  is the input data constructed by appending a set of vectorized images,  $X = \{x_1, x_2, x_3, \dots, x_t\}$ .

The PCT [10], using singular value decomposition (SVD), decomposes the input data,  $X$ , to  $U\Sigma V^T$ , where  $U$  and  $\Sigma$  represent the eigenvector (basis) and eigenvalue (coefficient) matrices sorted on descent order. The low rank matrix approximation of the input thermal sequence obtains by selecting the higher eigenvectors, which represent the defective patterns in the data. We select  $k$  first initial bases and reshape them back to make eigen-images. In the sparse PCT [11,12,13], these bases are optimized by penalty terms to have sparse matrix as its outcome (bases select from the basis matrix  $U$ ). Like PCT, the NMF algorithm can be presented by a linear combination of  $k$  basis vectors to reconstruct the data,  $X$ . NMF is comparable to the PCA decomposition yet the PCA's basis vectors can be negative.

Denoting an observation matrix, input data  $X$ , having  $t$ -dimension has basis vector of  $B = \{\beta_1, \beta_2, \beta_3, \dots, \beta_k\}$ , and  $A$  is called the linear combination coefficient, and the entire elements of data ( $X$ ) can be presented by the following matrix approximation:

$$X = BA \quad \text{s.t.} \quad A \geq 0, B \geq 0 \quad (1)$$

where  $X \in \mathbb{R}_{MN \times t}^+$ ,  $A \in \mathbb{R}_{k \times t}^+$ , and  $B \in \mathbb{R}_{MN \times k}^+$  or with  $\ell_2$  equation that provides Euclidean distance [16,17]:

$$\min_{B,A} f(B,A) = \|X - BA\|^2 \quad \text{s.t.} \quad A \geq 0, B \geq 0 \quad (2)$$

NMF assumes that matrices  $X$ ,  $B$ , and  $A$  are not negative, but when the data matrix is unconstrained (*i.e.* there will be a chance of mixed signs exist among the matrices) The aforementioned minimization problem does not have concurrent convex property for both matrices,  $A$ ,  $B$ , whereas the problem is convex for each matrix discretely. Many researches have proposed ways and optimization solution such as: GD algorithm and NNLS by Paatero and Tapper [18], multiplicative algorithm by Lee and Seung [16], a computational improved GD algorithm, and modified alternating non-negative least squares (ANNLS). To compensate the uniqueness of the decomposition and enforcing a representation of basis sparseness constraints are proposed for NMF [19]. A  $\ell_1$  norm penalty term has been introduced by implementing the following equation:

$$C_{\text{SparseNMF}} = \frac{1}{2} \|X - BA\|_F^2 + \lambda \|B\|_1 \quad (3)$$

Let  $\|B\|_p$  is the  $\ell_p$ -norm of  $B$  given by  $L_p = \left( \sum_{d,m} \|B_{d,m}\|^p \right)^{1/p}$  similar to usual  $\ell_1$  penalty term to imitate the  $\ell_0$  behavior [20] to calculate  $B$  for convex  $A$ . It is the unconstrained least squares minimization with  $\ell_1$ -norm constraint, also referred as least absolute shrinkage and selection operator (LASSO) [21]. The solution for all values of  $\lambda$  achieves through applications of the least angle regression and selection algorithm (LARS) [22]. Similar to Sparse PCT, low rank sparse NMF is obtained by selecting  $k$  bases correspond to highest coefficients. Having  $k$  highest bases, we manually select the best representative of thermal sequence.

## 2.1 Thermal level co-occurrence features

Statistical analyses were performed to measure the heterogeneity of the breast area using texture analyses. Having thermal measure encoded in the grey level intensity, the grey (thermal) level co-occurrence matrices (TLCMs) of the breast area as our region of interest (ROI) was calculated [23]. For each patch, TLCM with a horizontal offset of 4 (two distances (0,1) and two angles  $[0, \frac{\pi}{2}]$ ) is computed. Then, two properties, dissimilarity and correlation, of the TLCM matrices are computed. Using the TLCM information, many analyses were conducted to measure the level of contrast, dissimilarity, correlation, energy, and homogeneity among the pixels in the ROI using following equations:

Contrast:  $\sum_{i,j=0}^{levels-1} P_{i,j} (i-j)^2$ , Dissimilarity:  $\sum_{i,j=0}^{levels-1} P_{i,j} |i-j|$ , Homogeneity:  $\sum_{i,j=0}^{levels-1} \frac{P_{i,j}}{1+(i-j)^2}$ , ASM:  $\sum_{i,j=0}^{levels-1} P_{i,j}^2$   
Correlation:

$$\sum_{i,j=0}^{levels-1} P_{i,j} \left[ \frac{(i-\mu_i)(j-\mu_j)}{\sqrt{(\sigma_i^2)(\sigma_j^2)}} \right] \quad (4)$$

We stratified the participants based on these properties and compared to ground truth data provided by based on mammography information. A logistic regression model trained and tested on the study population and discriminates symptomatic versus non-symptomatic participants.

## 3. Study population

55 participants for breast screening with healthy (with/without symptoms) and sick (diagnosed by mammographic imaging) conditions were analysed. The median age in our study sample was 61 years, with 28 (51%) Caucasian, 15 African (27.3%), 11 Pardo (20%), 1 Mulatto (1.8%) women, and 18 with history of diabetes in their families (32.7%) and 9 under hormone replacement (16.4%). All patients had IR images obtained by following acquisition protocol: images have spatial resolution of 640 x 480 pixels and were captured by a FLIR thermal camera (model SC620) with sensitivity of less than 0.04°C range and capture standard -40°C to 500°C [5,6]. Table 1 shows the clinical information and demography of the cohort.

**Table 1.** The clinical information and demographics of the database for mastology research is presented.

DMR - Database for Mastology Research		
Age	Median (±IQR)	61 (27,87)
Race	Caucasian	28 (51%)
	African	15 (27.3%)
	Pardo	11 (20%)
	Mulatto	1 (1.8%)
Diagnosis <sup>1</sup>	Healthy <sup>2</sup>	24 (43.6%)
	With symptoms	9 (16.4%)
	Without symptoms	15 (27.3%)
	Sick <sup>3</sup>	28 (51%)
	Unknown	3 (5.4%)
Family history	Diabetes	18 (32.7%)
	Leukemia	1 (1.8%)
Hormone therapy (HT)	None	36 (65.5%)
	Hormone replacement	9 (16.4%)
	None	46 (83.6%)

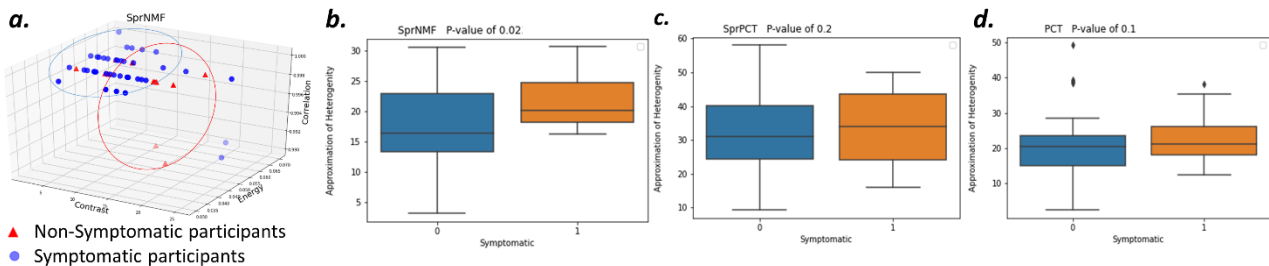
<sup>1</sup> This diagnosis performed with mammography as ground truth in this Dataset.

<sup>2</sup> Healthy term is used as non-cancerous patients, but might have symptoms (symptomatic).

<sup>3</sup> We use the term "sick", which includes different types of breast cancer patients diagnosed by mammographic imaging.

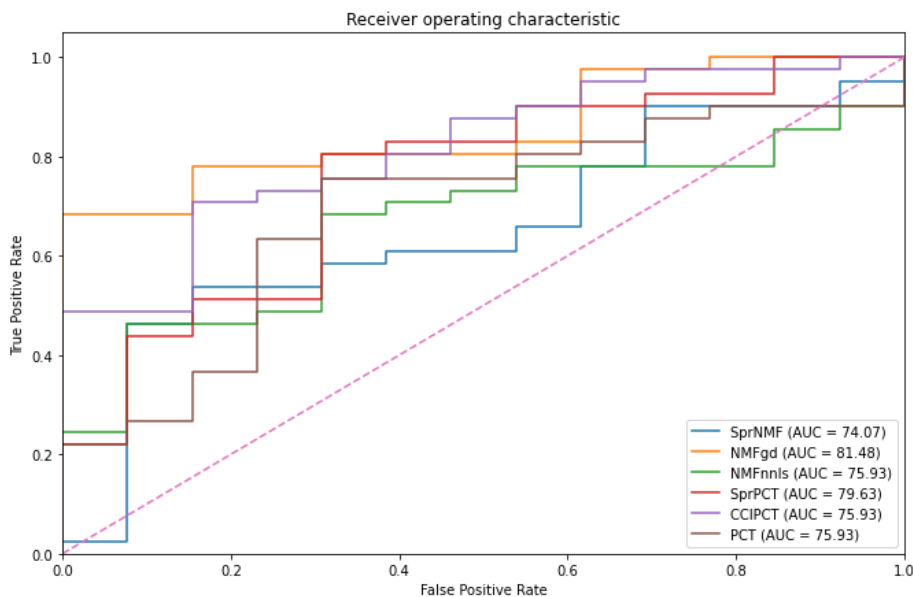
#### 4. Results

The Sparse-NMF were showed statistically significant separation of the two groups of participants ( $p = 0.02$ ) when split on contrast based TLCM (Figure 2) using Kurskal Wallis test. The Sparse-PCT, PCT, CCIPCT, NMF-nnls were not showing strong stratification ability, as they were not significantly discriminated ( $p > 0.1$ ). The NMF-gd showed slight separation strength, although was not significant ( $p = 0.09$ ). Plotting of participants based on TLCM properties also showed potential separability between the groups (Figure 2.a), which followed the results of boxplots for separating participants (Figure 2.b-d).



**Figure 2.** (a.) represents 3D views of grouping using TLCM's properties. The results of stratification among participants into symptomatic and non-symptomatic groups for Sparse NMF, sparse PCT, PCT algorithms are presented by boxplots and Kurskal Wallis test (b-d).

To examine the hypothesis that the thermal heterogeneity can be used as a biomarker to stratify among participant, a logistic regression model fitted for multivariate covariates (contrast, dissimilarity, correlation, homogeneity, and energy), and resulted 74.1% accuracy for Sparse-NMF, respectively. The two highest accuracies were belonged to NMF-gd and Sparse-PCT with 81.5% and 79.6%, respectively. The CCIPCT and PCT were both show 75.9% accuracy. The receiver operating characteristic (ROC) curves using different factorization algorithm are presented in Figure 3.



**Figure 3.** The ROC graph for different matrix factorization approaches are presented for multivariate covariates logistic regression binary classification (abnormal or healthy participants).

#### 5. Conclusions

This study proposed a comparative analyses and new applications of sparse NMF algorithms in infrared diagnostic system. We applied the approaches to measure thermal heterogeneity in breast cancer screening test (DMR). We compared the appropriateness of these approaches to the similar state-of-the-art thermographic methods such as PCT, CCIPCT, Sparse PCT, and standard NMF-gd and NMF-nnls among dissimilar thermal datasets. The results were indicated significant performance of Sparse NMF in preserving thermal heterogeneity to discriminate between symptomatic and healthy participants (accuracy of 74.1%). As future work, some affords should be done to substitute the manual selection of the most efficient basis from the low-rank approximation with an automatic selection. In addition, an expansion of the validation set to a larger infrared imaging cohort can further confirm the strength and pitfalls of these approaches.

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