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Characterizing Breast Lesions Using Functional Optical Imaging Guided by an Independent X-Ray Mammogram

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Motivation

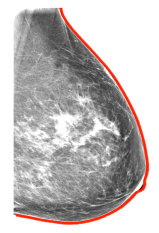
Functional breast imaging technique, such as tomographic optical breast imaging (TOBI), reveals valuable tissue metabolic information indicated by total hemoglobin concentration (HbT), oxygen saturation (SO_2), and reduced scattering coefficient (μ'). Multi-modal breast imaging techniques fuse these physiologically relevant information with anatomical structure depicted by mammographic images to facilitate more specific diagnosis of breast cancer. Despite the success of our integrated three dimensional (3D) digital breast tomosynthesis (DBT)/TOBI system in earlier clinical studies, its commercial promotion is restrained by a very limited market presence of DBT. Given over 9,000 existing two-dimensional (2D) digital mammography machines installed in the US alone, an efficient implementation and rapid clinical adoption could be achieved by using TOBI as a stand-alone optical imaging device in conjunction with an existing 2D mammography system.

Goals

1) Can we post-register separately acquired functional optical images with 2D digital mammograms for joint diagnosis?
2) Are the optical properties obtained from a 2D-guided reconstruction similar to those from a DBT/TOBI analysis?
3) Are the findings differentiating malignant from benign lesions of DBT/TOBI approach, shown in our previous publications, still valid?

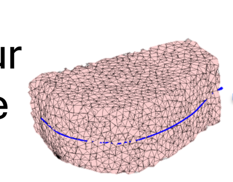
Step I: Image Registration

Step 1: Identify breast contour from 2D mammogram.



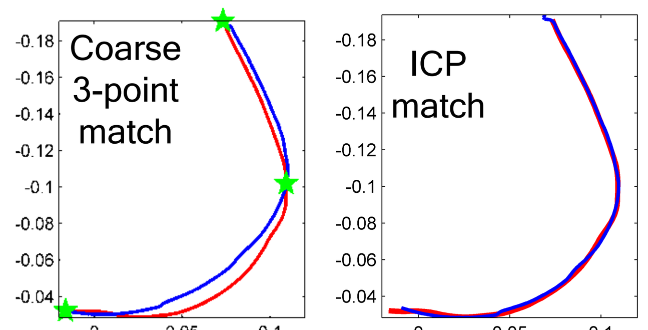
Breast contour found through adaptive thresholding method

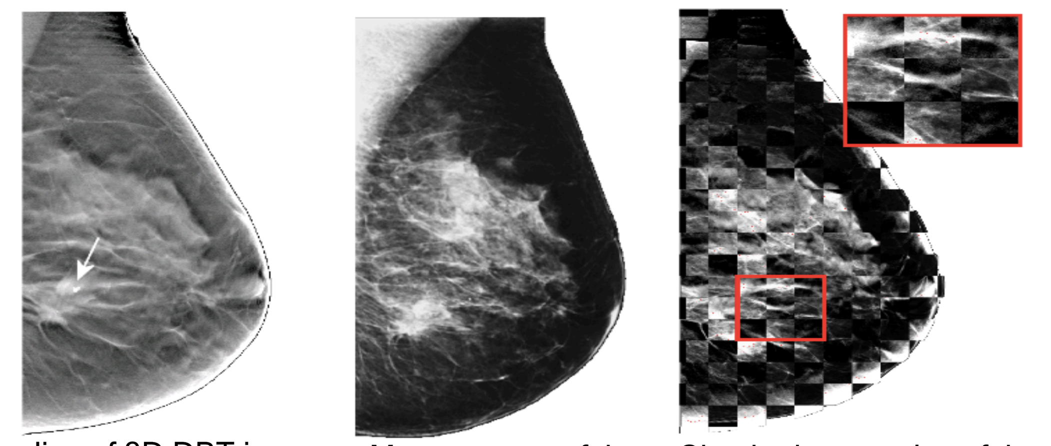
Step 2: Identify breast contour from 3D breast shape model.



take the lesion/center slice and trace outer polygon cut

Step 3: Contour based affine registration to translate mammogram coordinates to mesh coordinates.





One slice of 3D DBT image with malignant lesion | Mammogram of the same breast | Checkerbox overlay of the registered DBT/mammogram

Step II: Compositional Priors

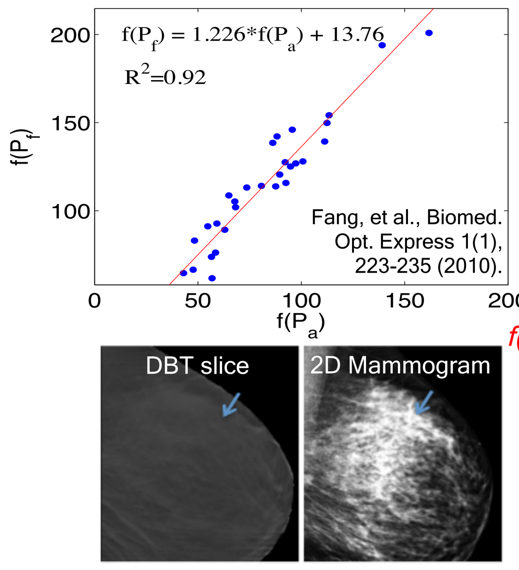
To jointly consider the structural information, compositional priors derived from mammograms were used to guide optical image reconstructions.

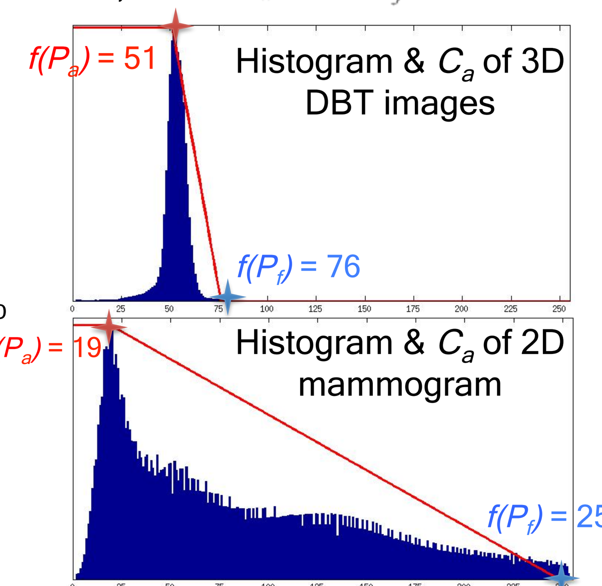
- A finite number of independent components, namely, adipose, fibroglandular, and lesion (if applicable).
- Image intensity of each pixel in the structural image is a linear combination of the separate contrast from each of its components, which is proportional to its concentration.

$$I_s(r) = \sum_i C_i(r) f(P_i)$$

to be specific,

$$C_f = I_s - f(P_a) / [f(P_f) - f(P_a)] \text{, and } C_a = 1 - C_f$$





- Tumor prior was determined by a Gaussian-sphere profile at lesion centroid with maximum of 1 and FWHM of 2 cm.

Clinical Study

- Conducted under a HIPAA compliant protocol approved by Massachusetts General Hospital IRB.
- Sample size: a total of 34 cases.
  - Malignant: 10 cases.
  - Solid Benign: 7 cases.
  - Healthy: 17 cases.
- Bilateral study: among these cases, 8 pairs of bilateral breasts from 8 patients, one side malignant and the other healthy, were used in the bilateral comparison study.

Statistical Tests

a. Paired two-tailed *t*-tests between various tissue types (A: adipose; F: fibroglandular; T: tumor) of the same breast, grouped by lesion types.

(a) Within the same breast			
HbT	A vs. F	A vs. T	F vs. T
Malignant (10)	**0.0347**	**0.0022**	**0.0026**
Solid Benign (7)	**0.0433**	0.4024	0.4550
Healthy (17)	0.3984	--	--
SO_2			
Malignant (10)	0.4465	0.9074	0.6581
Solid Benign (7)	0.5125	0.9721	0.9121
Healthy (17)	0.3694	--	--
μ_s' at 830 nm			
Malignant (10)	0.0963	**0.0059**	**0.0075**
Solid Benign (7)	**0.0342**	0.3358	0.3448
Healthy (17)	0.1509	--	--

b. Two-sample two-tailed *t*-tests of normalized optical properties (by those of adipose) between lesion types.

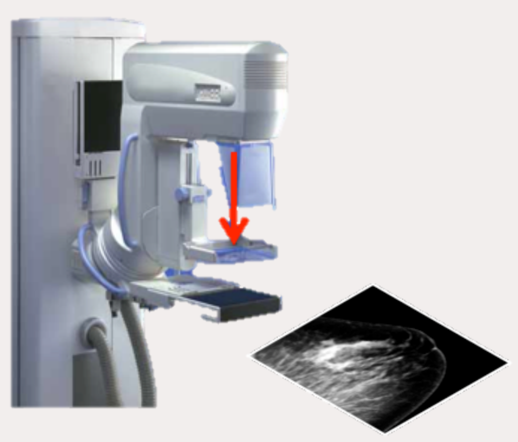
(b) Cross group comparisons	Malignant vs. Solid Benign	Malignant vs. Healthy	Solid Benign vs. Healthy
HbT	**0.0111**	**0.0003**	0.7967
SO_2	0.9314	0.7739	0.6863
μ_s'	0.5268	**0.0019**	0.2664

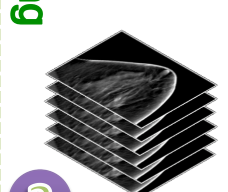
c. Paired two-tailed t-tests of normalized optical properties between bilateral cases.

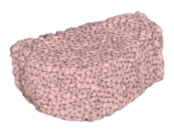
(c) Bilateral comparisons	Fibroglandular	Healthy vs. Malignant
HbT	0.1708	**0.0267**
SO_2	0.2572	0.2101
μ_s'	0.9653	0.0526

Note: p-values shown in tables are based on 2D-guided reconstructions. Significance is determined at 95% confidence level. Colored fonts compare significance differences between 2D- and 3D-guided results: **bold blue** for both significant; **bold green** for only significant in 2D-guided reconstructions.

DBT / TOBI .... Workflow Comparison .... Mammo & TOBI







Step III: Priors Guided Optical Image Reconstructions

To enable a pair-wised analysis between the lesioned and the contralateral healthy breast, the same contour-based registration algorithm was applied to co-register bilateral mammograms, and then the tumor centroid of the lesion side was mirrored to the healthy side as a ***false*** lesion.

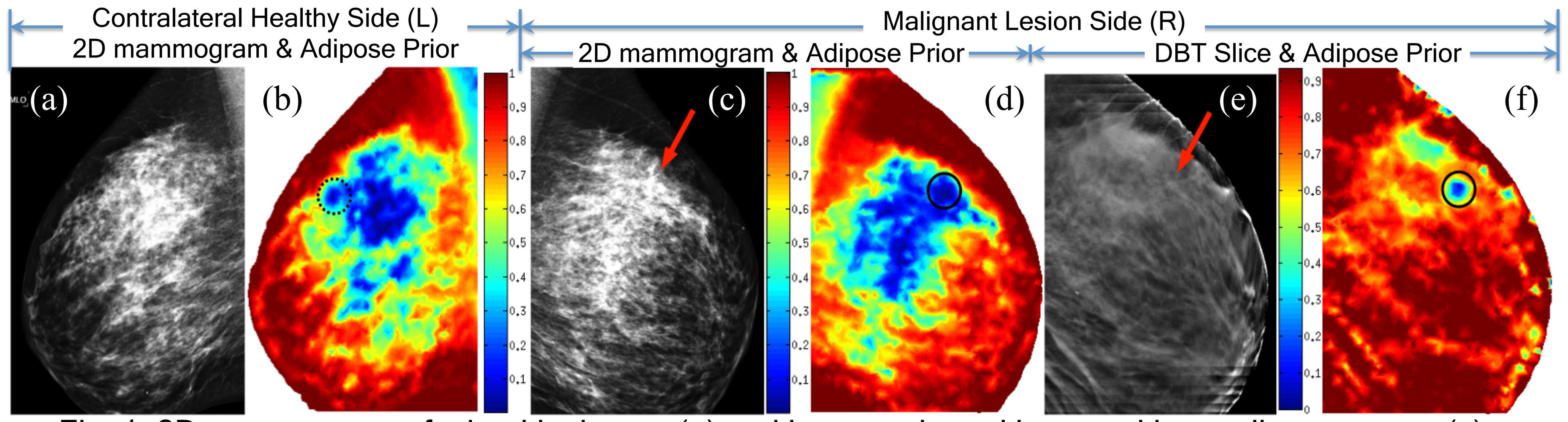


Fig. 1. 2D mammogram of a healthy breast (a) and its contralateral breast with a malignant tumor (c), followed respectively by their 2D-guided priors presented by probabilities of being adipose (b,d). For comparison, a DBT slice of tumor breast (e) and its adipose prior (f) also plotted. Red arrow: tumor centroid; Solid circle: tumor prior centroid; Dotted circle: mirrored centroid.

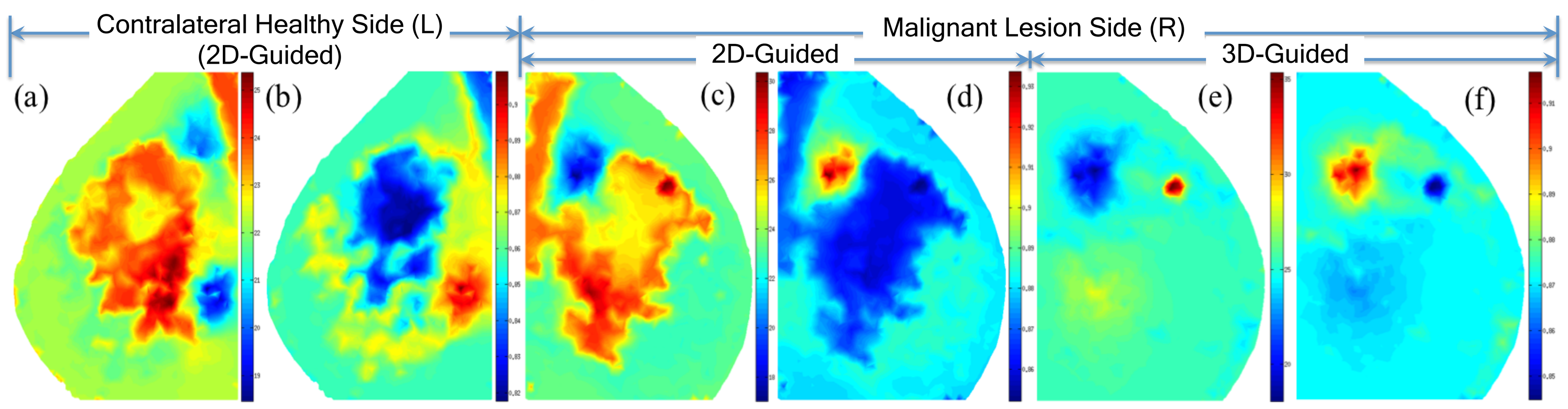


Fig. 2. Reconstructed images of the same set of breasts in Fig. 1: 2D-guided (a) HbT (μM) and (b) SO_2 images of healthy breast; 2D-guided (c,d) and 3D-guided (e,f) images of HbT (μM) (c,e) and SO_2 (d,f), respectively, of contralateral malignant breast.

mean ± std.	HbT (μM) of all cases		HbT Ratio (lesion/adipose) by group		
	Adipose	Fibroglandular	Malignant	Solid Benign	Healthy
	34 cases	34 cases	10 cases	7 cases	17 cases
2D-Guided	29.46 ± 13.67	30.24 ± 13.20	2.19 ± 0.85	1.12 ± 0.58	1.17 ± 0.41
3D-Guided	29.32 ± 13.88	31.73 ± 13.02	2.03 ± 0.11	1.06 ± 0.45	1.29 ± 0.45

✓ The proposed technique is successful in identifying true lesions in bilateral asymmetry.

✓ Optical properties retrieved from 2D mammogram guided reconstruction shows visually and quantitatively similar contrast to 3D DBT guided reconstructions.

Conclusions

In summary, we compared the optical properties recovered based on two different techniques: spatially co-registered 3D DBT-guided reconstruction and a post-registered 2D mammogram guided reconstruction. Results of this pilot clinical study demonstrate that the proposed independent 2D mammogram guided optical image reconstruction technique has comparable capabilities in differentiating lesions of various types to an integrated DBT/TOBI system. This novel approach would allow immediate benefit of physiologically relevant functional information to improve breast cancer diagnosis where thousands of conventional 2D mammographic units are in use, thus suggesting a cost-effective venue for fast implementation of functional breast imaging in the clinical settings.

Acknowledgements

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