Tomosynthesis-based Tomography for Intraoperative Evaluation of Breast Tumor Margin

A Simulation Study

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***Abstract*—Breast conserving surgery involves an excision procedure to achieve clear margins. This goal is usually achieved by performing intraoperative margin assessment with specimen imaging and immediate excision of any margins thought to be close or positive. However, routine two-dimensional specimen radiography cannot clearly discern residual disease at the margins. Quasi-three-dimensional digital breast tomosynthesis potentially increases sensitivity but still cannot sufficiently meet the need, due to the limitation of its cross-sectional in-plane images. We propose a novel tomographic technique that uses limited-angle tomosynthesis projections to reconstruct 3D transverse images. A simulation study was performed based on the geometry of a commercial DBT system to demonstrate the feasibility. The proposed tomographic technique will have the potential to more effectively guide surgeons to precisely remove the tumor with a clear margin and better cosmetic result, significantly reducing the need for a return to the operating room**

Keywords—breast conserving surgery, excision, 3D imaging, image reconstruction, tomosynthesis, digital breast tomosynthesis, specimen

I. INTRODUCTION

In the United States, there are over 300,000 people diagnosed with invasive or in situ breast cancer each year. The majority of these cases are amendable to being treated with breast conservation [1]. Achieving negative margins during the surgical procedure is critical as it is an important prognostic factor. Positive margins are associated with a nearly two-fold risk of local recurrence and mandate a return to the operating room for a re-excision [2].

In routine practice, standard two-dimensional (2D) specimen radiography is used to guide intraoperative excision of margins in patients undergoing breast conserving surgery. However, 2D specimen radiography is only reliable at determining whether the target lesion has been removed. It cannot reliably define margins of the specimen [3]. This is primarily due to the limitation of using 2D mammography to characterize a three-dimensional (3D) specimen where the tumor boundary is poorly defined. Fig. 1 shows such an example from our routine clinical practice.

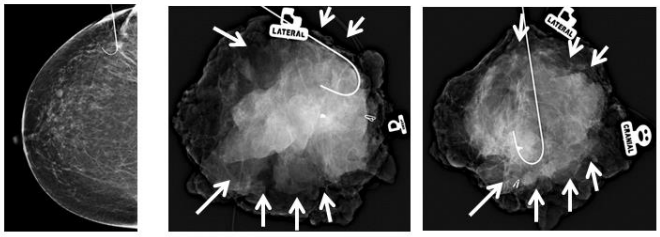

Fig. 1 An example of intraoperative specimen radiographic images with positive margins (indicated by arrows) from a 61 year-old patient with breast cancer. The left image shows pre-surgical needle localization; the middle and the right radiographic images show two orthogonal views of the specimen. Due to limitations of the 2D images, the patient underwent a second surgery for positive margins 20 days later.

There is no consensus regarding the radiological size of the specimen to obtain a histologically clear margin. More breast tissue than cancer is often removed due to lack of accurate references to the margin. However, wide surgical excision will often cause poor cosmetic defects in the breast. Precise removal of all the cancer and maintaining good cosmetic results are important.

Recent studies show that 3D specimen imaging such as digital breast tomosynthesis (DBT) has a potential to reduce the rate of re-excisions compared to routine 2D radiography (e.g., full field digital mammography, FFDM)[4, 5]. However, our routine practice indicates DBT is still not satisfactory in defining the specimen margin. A new full 3D intraoperative breast specimen imaging with more accurate representation of the real specimen is needed.

In this work, we propose a novel tomographic technique which uses limited angle tomosynthesis projections to reconstruct Computer Tomography (CT) images. A simulation study based on the geometry of a commercial DBT system is performed to demonstrate the design feasibility. The proposed 3D imaging will have the potential to more effectively guide surgeons to excise a comfortable size of specimen in the

operation room to achieve negative margins and better cosmetic results, significantly reducing re-excision rates.

II. Methods

A. Digital Breast Tomosynthesis (DBT)

Digital breast tomosynthesis (DBT) is an emerging technology that generates quasi-3D images by performing a series of low-dose radiographic exposures [6]. Specifically, the x-ray tube moves in an arc overhead, generating a series of projection images at preset angles, as shown in Fig. 2. The projection images can then be reconstructed into sections as thin as 1 mm in the plane parallel to the detector. DBT allows 3D estimation of tissue distribution, reduces the summation of overlapping breast tissue, and improves details of noncalcified mammographic findings.

Differing from CT, DBT reconstruct cross-sectional in-plane images in standard mammographic views.

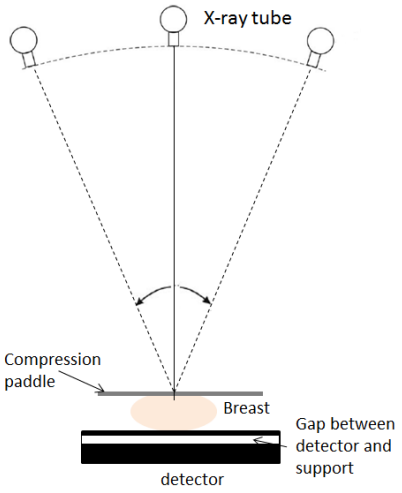

Fig. 2 Schematic diagram showing the principle of digital breast tomosynthesis system.

B. Geometric Parameters

For a Hologic DBT system (Hologic Inc., Bedford, MA, USA), the source-to-imaging detector distance (SID) is 70 cm. The x-ray tube rotation angles ranges from -7.5 degrees to 7.5 degrees. The detector size used for tomosynthesis is 18 x 29 cm, with detector element of 70 μm. No antiscatter grid is used, and a 2x2 pixel binning of the digital detector array (140 μm sampling) is used to acquire projection images. The location of the reconstructed plane depends on the reconstruction algorithm. The number of reconstructed images depends on the compressed breast's thickness.

The proposed simulation study is performed based on above parameters. The source-to-object distance (SOD) for the simulation is 65 cm, which can be adjusted according to the specimen size.

C. Reconstruction Technique

The projection data collected in the proposed geometry is incomplete. Thus, the traditional filtered back-projection (FBP) method cannot be directly applied to reconstruct an object. To use an iterative algorithm instead, we calculated the intersection length between each x-ray beam and every image pixel, and constructed a system matrix. Then, the projection data can be modeled as $b = Af$, where A is the system matrix, f is a vector representing the underlying image, and b is the projection data. Using a typical compressed sensing technique [7-9], we can include a total variation (*TV*) measure and minimize the following objective function for limited-view dual-angular-range tomography:

$$\min_x \|b - Af\|_2 + TV(f) \tag{1}$$

where *TV* is expressed as

$$TV(f) = \sum_m \sum_n \sqrt{(f_{m+1,n} - f_{m,n})^2 + f_{m,n+1} - f_{m,n})^2 + \varepsilon^2} \tag{2}$$

where ε is a small constant to avoid singularity when computing TV's gradient by

$$\begin{aligned} d_{m,n} &= \frac{\partial TV(f)}{\partial f_{m,n}} \\ &= \frac{2f_{m,n} - f_{m+1,n} - f_{m,n+1}}{\sqrt{(f_{m+1,n} - f_{m,n})^2 + f_{m,n+1} - f_{m,n})^2 + \varepsilon^2}} \\ &+ \frac{f_{m,n} - f_{m-1,n}}{\sqrt{(f_{m,n} - f_{m-1,n})^2 + f_{m-1,n+1} - f_{m-1,n})^2 + \varepsilon^2}} \\ &+ \frac{f_{m,n} - f_{m,N-1}}{\sqrt{(f_{m+1,n} - f_{m,n-1})^2 + f_{m,n} - f_{m,n-1})^2 + \varepsilon^2}} \end{aligned} \tag{3}$$

We follow the same procedure to optimize Eq. (1) as in reference [7] and its pseudo-code is shown in Table 1.

Table 1. Pseudo-code for the SART-TV algorithm

1.	Set $k := 0, f^{(0)} = 0, \omega := -1$
2.	Set $\alpha := 0.00005, \alpha_s = 0.997, P_{TV} := 5$
3.	Repeat Steps 4-12 until a stopping criterion is satisfied
4.	$f^{(k+1)} = f^{(k)} + \frac{\omega}{\sum_{i=1}^{M} A_{ij}} \sum_{i=1}^{M} \frac{A_{ij}}{\sum_{j=1}^{N} A_{ij}} (b_i - [Af]_i)$
5.	For $P_{TV} = 1$ to P_{TV} do
6.	Compute the gradient of *TV*, $d_{m,n}$
9.	$\beta := \max(\lvert f^{(k+1)} \rvert) / \max(\lvert d_{m,n} \rvert)$
10.	$f^{(k)} = f^{(k)} - \alpha \times \beta \times d$
11.	$\alpha = \alpha \times \alpha_s$
12.	End for loop P_{TV}

III. Simulation Result

A 2D numerical phantom created to mimic a breast tumor was used to evaluate the proposed system and reconstruction algorithm. The phantom shown in Fig. 3 was defined on a 350x350 grid and was of size 5x5cm. Thus, the pixel size of the image was 143 μm. The geometric parameters were the same as in the previous section. 15 projections were acquired from -7.5 degrees to 7.5 degrees.

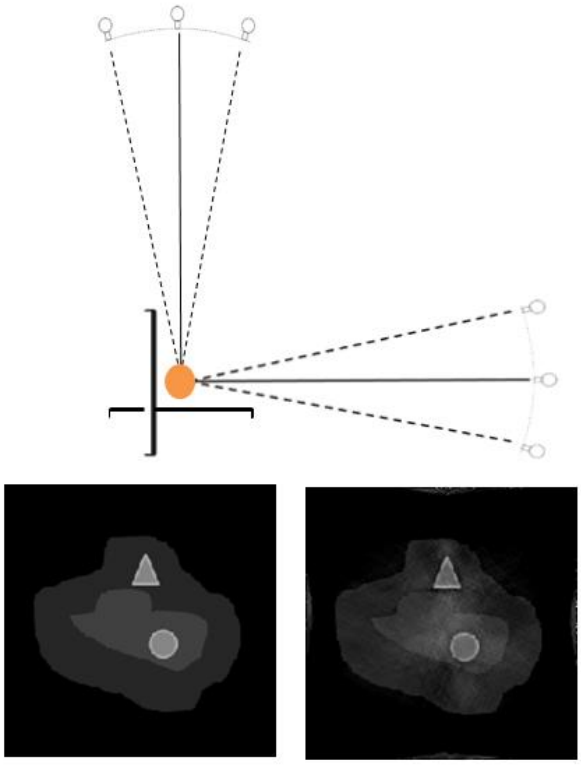

Fig. 3 Two-view limited-angle reconstruction. The scanning scheme is on the top; the original 2D image created randomly to mimic abreast tumor is on the lower left; and the reconstruction image in the bottom right.

Two image acquisition configurations were proposed to acquire projection data. The first configuration used two-view angles, 0 and 90 degrees; while the second one used three-view angles, -60, 0, and 60 degrees. The proposed two configurations can easily be implemented in a DBT system. For each view a series of projection images were acquired, following a routine tomosynthesis acquisition, as described in Fig. 2. Figs. 3 and 4 show the acquisition configuration, original phantom and the reconstructed images, respectively.

IV. Discussions and Future Work

In this study, we proposed a novel method to reconstruct 3D images of specimens from limited-angle tomosynthesis projections. The acquisition protocols including the limited projection angular ranges were addressed for 3D image reconstruction. The preliminary results clearly support the feasibility of the proposed tomographic imaging scheme.

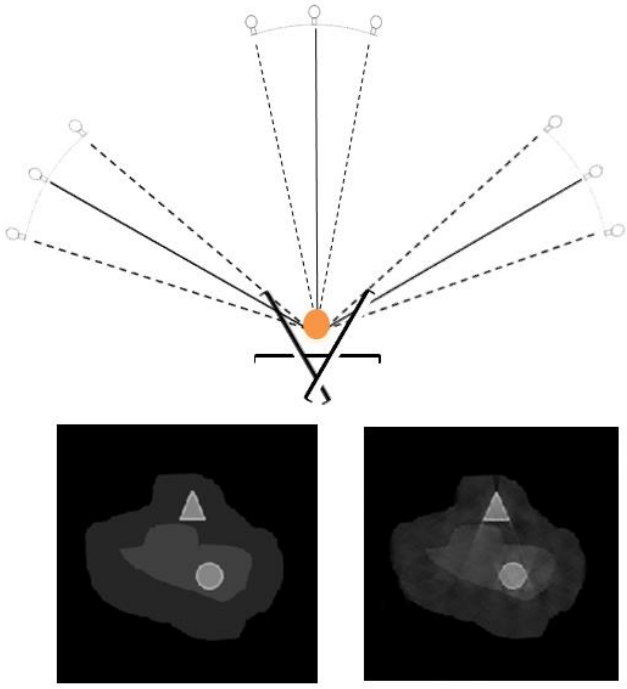

Fig. 4 Three-view limited-angle reconstruction. The scanning scheme is on the top; the original 2D image created randomly to mimic abreast tumor is on the lower left; and the reconstruction result on the bottom right.

Many imaging modalities may be used for the guidance of intraoperative breast conserving treatment. Radiographic imaging, including conventional mammography and/or tomosynthesis, is the most adopted in the current practice, due to its similarity to diagnostic images and cost-effectiveness. Mammography is compromised by the over-lapping of 3D structures. While tomosynthesis may partially overcome this limitation; its image quality suffers from crude depth resolution and associated strong artifacts. Our proposed method offers an innovative solution with a minimum system adaption.

Contrast-enhanced CT may be valuable for diagnosing local breast cancer recurrence after conservative treatment [10]. However, CT has not been used for imaging specimens mainly due to limitations in its image quality, i.e., low contract and spatial resolution. Dedicated breast CT provides better image quality and can be used to image specimens [11-13]. In January 2015, the FDA approved the Koning breast CT system, a dedicated breast imaging system that acquires 3D CT images without compressing the breast, making this technique available for routine practice [14]. However, to this date the dedicated CT system has not been accepted by medical centers. Our proposed imaging technology could be an alternative solution in this context.

Micro-CT is a useful imaging tool for a wide range of biomedical research and preclinical applications. It has potential to image specimens [15, 16]. Micro-CT can produce accurate 3D images of the subject but its cost is a major concern.

The emerging dual-energy CT may be another option to image specimens [17]. Conventional CT relies on density of the object, while dual-energy CT allows material decomposition. Dual-energy tomosynthetic imaging seems to be a good mode for specimen characterization, and will be further evaluated in our future work.

Magnetic Resonance Imaging (MRI) may accurately evaluate surgical specimens [18, 19]. Specimen imaging with high magnetic field MRI provides promising results for improvements in lesion identification and margin localization for invasive ductal carcinoma [19]. However, MRI is expensive, and poses technical challenges in the visualization of ductal carcinoma in situ lesions. Moreover, most breast MRIs are performed with intravenous contrast. It makes the comparison between diagnostic images and specimen images difficult, reducing the clinician's efficiency and confidence in assessing tumor margins.

The proposed 3D imaging technique is unique in providing more detailed tomographic images showing tumor margins than 2D radiographic mammography and quasi-3D tomosynthesis with consecutive image slices of the lumpectomy specimens. Most interestingly, this imaging technique can be readily applied to any DBT system with no requirement for hardware update. In the future, we will work on the system integration, data acquisition strategy and image reconstruction optimization, and translate our technology to surgical suites for healthcare benefits.

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