Intra-operative Tumor Margin Evaluation in Breast-Conserving Surgery with Deep Learning

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***Abstract*—Breast-Conserving Therapy (BCT) followed by irradiation is the treatment of choice for early-stage breast cancer. A positive margin may result in an increased risk of local recurrences after BCT for any malignant tumor. In order to reduce the number of positive margins would offer surgeon real-time intra-operative information on the presence of positive resection margins. This study proposed an intra-operative tumor margin evaluation in breast-conserving surgery. The proposed method utilized image segmentation and deep learning techniques to segment the cancerous tissue and then to evaluate the margin width of normal tissues surrounding it. With this work, surgeons might have more information to get clean margins when performing breast conserving surgeries.**

***Index Terms*—intra-operative margin evaluation, breast-conserving therapy, specimen mammography, deep learning, image segmentation**

I. Introduction

Breast cancer is the most commonly diagnosed cancer in women. Fortunately, early detection and treatment can prevent the disease from worsening and reduce patient's mortality significantly. Surgery is one of the most important treatments for breast cancer. There are two kinds of surgery, one is mastectomy, which occurs when the tumor is too large (particularly in a small breast) or more than one area of cancer in the breast. The other one is Breast-Conserving Therapy (BCT), in which only cancerous tissue plus a rim of normal tissue can be cleaned without removing the breast. BCT is the best choice for the treatment of early stage invasive breast cancer. This surgery can not only remove the tumor but also preserve the shape of the breast.

A positive margin may result in an increased risk of local recurrences after BCT for any malignant tumor. Until now, the definition of a positive margin has been the subject of frequent debate [1]. In reality, surgeon removes the tumor is done by rough estimation of the boundary. Surgeon could not accurately determine the margin width until the pathologist makes a microscopic assessment. Pathologist’s report might require a week or more to completed. If it shows the margins are not wide enough, the patient must undergo a second operation to remove the remaining malignant tissue. It is second physical and mental injury to patient.

For removing the tumor while minimizing the risk of leaving residual disease, many intra-operative methods have been proposed for breast tumor margin assessment, such as Optical Coherence Tomography (OCT) [2], spectroscopy [3], MarginProbe system and molecular fluorescence imaging [4]. However, these methods require special equipment to estimate the margin or a contrast medium injection for patient few days before the BCT. These would bring the burden to the hospital and patients. In order to reduce the number of positive margins would offer surgeon real-time intra-operative information on the presence of positive resection margins. This study proposed computer-aided margin estimation methods by using the specimen mammography during BCT.

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II. Material and Methods

A. Data Acquisition

Two Full Field Digital Mammography (FFDM) systems were included in the study: GE Senographe Essential and Hologic Selenia Dimentions system. After wide excision of the tumor, location stiches were made on 12 (0^o), 3(90^o), 6 (180^o) and 9 (270^o) o'clock direction and clipped on the stiches in order to be easily identified on specimen mammogram. There were 1, 2, 3 and 4 clips on each stich. This study included 24 patients who received BCT. Each specimen mammogram has a corresponding ground truth image which is manually annotated by experienced surgeons. All obtained images were stored on the hard disk and transferred to a personal computer using a DICOM connection for image analysis.

B. Flow-Chart of the Proposed Method

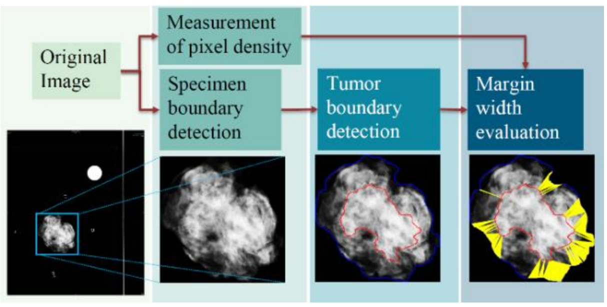

Figure 1. Flow chart of the proposed method.

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At first, the proposed method measured the pixel density and extracted the ROI by detecting the specimen boundary. Then the tumor boundary was detected by the proposed contouring methods on the ROI. Distance evaluation was applied in a final stage. Flow chart of the proposed method is shown in Fig. 1.

C. Measurement of Pixel Density

In the dataset, different image operators lead to different image sizes. In order to accurately measure the distance between the tumor and the tissue, a standard one-dollar coin (20mm diameter) was placed in the specimen mammogram as a measuring scale. Pixel resolution was converted to millimeter by according the radius of the coin.

D. Specimen Boundary Detection and ROI Extraction

Image pre-processing is very important in order to remove the noise, and to enhance the quality of the image. The major problem with the precise segmentation of the specimen boundary is the existence of such noises, which may affect the detection results. In order to suppress the noise in the background, automatic thresholding method was first applied to the specimen mammogram. However, the images also contain artifacts in the form of labels, wedges, markers, and some patient information in the background region. The connected component algorithm was utilized to extract the largest component (specimen), which means artifacts were discarded. Morphological operators [5], i.e. fill-hole, opening, closing and erosion, were used to smooth the boundary. The obtained specimen boundary was utilized as extract ROI for tumor boundary detection.

E. Tumor Boundary Detection

The varying quality of specimen mammography makes tumor detection become a difficult task. In order to overcome the conditions where specimen mammography has varied contrast, this study performed five contouring methods: grey level transformation, K-means clustering, region-growing, U-net and SegNet to sketch tumor boundary.

1) Grey level transformation

Generally, the grey-scale image has pixel intensities from 0 to 255, and a specimen mammogram contains at least three regions, i.e. background, normal tissue, and cancerous tissue. Therefore, this study set the initial number of classes *NC* as three and divided the pixel intensities range into three parts with two predefined thresholds. In grey level transformation, pixel intensities ranged [0, 85] was denoted as level 1, [86, 170] was denoted as level 2, [171, 255] was denoted as level 3, respectively. The pixels were combined into homogenous regions according to the intensity levels of the regions. Then the *NC* was increased one each time. When the segmented region with the highest intensity level becoming steady stable, the *NC* - 1 is chosen as the final number of classes. Region with the highest intensity level was identified as the tumor area. The morphological operators opening and closing were utilized to exclude undesired regions and extract the region of tumor.

2) K-means clustering

Clustering is a method to divide a set of data into a specific number of groups. K-means clustering, one of the popular clustering techniques, is an iterative algorithm that minimizes the sum of the distance of each object to its cluster centroid [6]. The method consists of two separate phases, first, it calculates the k centroids, second, it takes each point to the cluster which has nearest centroid from the respective data point.

The drawback of k-means clustering is initial centroid usually selected randomly with global cluster, on the other words, different initial centroid can result in different final clusters. To overcome this obstacle, we using the local boundary to generate initial centroids. For example, we set the number of classes is three which divided the pixel intensities into three parts, then randomly select initial centroids in three parts respectively. The pixels are combined into homogenous regions according to the centroids. The default setting was 20 iterations. As the same as the proposed grey level transformation, the morphological operators were performed to extract the region of tumor.

3) Region growing

Region growing [7], one of simple region-based methods, established from a seed point, the region would grow by appending to each seed those neighboring pixels that similar to the seed. Here this study used 8-connected neighborhood to grow from the seed point. The growing procedure will iterate until the criterion is satisfied. Pixel intensity were utilized as growing condition.

However, most of the region growing methods require manually selecting the initial seed point. Considering the stability of the segmentation, the proposed method select the initial seed point automatically. The K-means clustering algorithm is used to find the cluster with the highest intensity level, and then the center of mass is calculated as the seed point for region growing procedure.

4) U-net

U-net [8] is a convolutional networks for fast and precise image segmentation. The model has won two challenge at the ISBI 2015 and also has outstanding performance in biomedical image segmentation. U-net is an improved version of the of Full Convolutional Neural network (FCN), which means using convolution instead of the fully connected layer. This strategy allows input any size of images, and the output is also a picture, in the other words, it is an end-to-end network. The U-Net owes its name to its symmetric shape, and the architecture composes three parts: contracting path, bottleneck, and expansive path.

In the expansive path, each time the upsampling is performed, it combines the result and the feature map from downsampling path, so it can finally obtain a general information combining context and location information. The architecture of U-Net is shown in Fig. 2. This study utilized U-Net to segment specimen mammography.

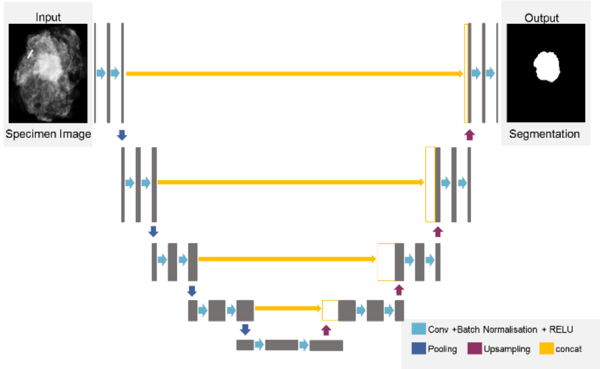


Figure 2. U-net architecture.

5) SegNet

SegNet [9] is a deep convolutional network proposed by Cambridge University to address image semantic segmentation for autonomous driving or intelligent robots. The model is designed based on FCN. SegNet is composed of a symmetry network: the encoder (left) and the decoder (right). The architecture of SegNet is shown in Fig. 3.

The structure of Encoder is similar to VGG-16, it composed of three kinds of network: Convolution, Batch Normalization and Pooling. Convolution layers are used to extract local features, Batch normalization layers are used to expedite learning, and Pooling layers are utilized to down sampling feature map.

Decoder aims to map the low-resolution feature maps from the encoder to obtain the same resolution as the input image feature map for pixel-level classification. The highlight of SegNet is that decoder utilized max-pooling indices from the corresponding encoder stage to upsample, this gives reasonably good performance and is space efficient, this is also why we choose SegNet as one of the methods in this work.

This study performed U-net and SegNet to contour the tumor in specimen mammography. Due to the number of image dataset is small, data augment was used to create new images. In this work, 20 new images were generated from the each case. Combination of flipping, rotation, distortion and zoom transformations were performed randomly. In order to maintain a fair measure of the performance of the convolutional networks, the leave-one-out cross validation was applied on U-net and SegNet segmentation. Finally, the morphological operator erosion was used to figure the obtained tumor boundaries.

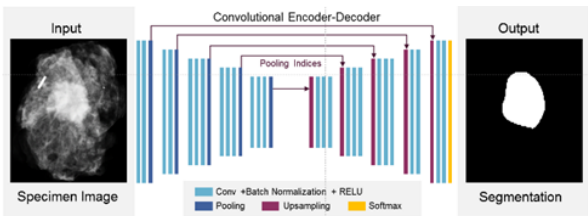


Figure 3. SegNet architecture

F. Margin Width Evaluation

The distance between specimen boundary and tumor boundary was estimated as margin width. This study evaluated the margin width by the Euclidean distance. In an image coordinate plane, the distance between two points is usually given by the Euclidean distance (2-norm distance). The distance from a point to a line is the shortest distance from a fixed point to any point on a fixed line in Euclidean geometry. In this study, the safety margin width is recommended as 10mm. When the margin width is less than 10mm, the system will display the area in yellow. Fig. 4 illustrates the segmentation result and estimation result.

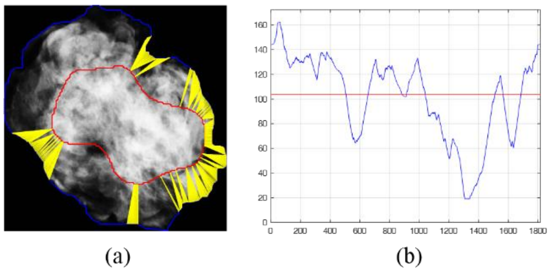


Figure 4. (a) Segmentation result (extracted specimen boundary (blue), tumor boundary (red) and the region less than margin width (yellow)) and (b) evaluated margin width.

III. Result

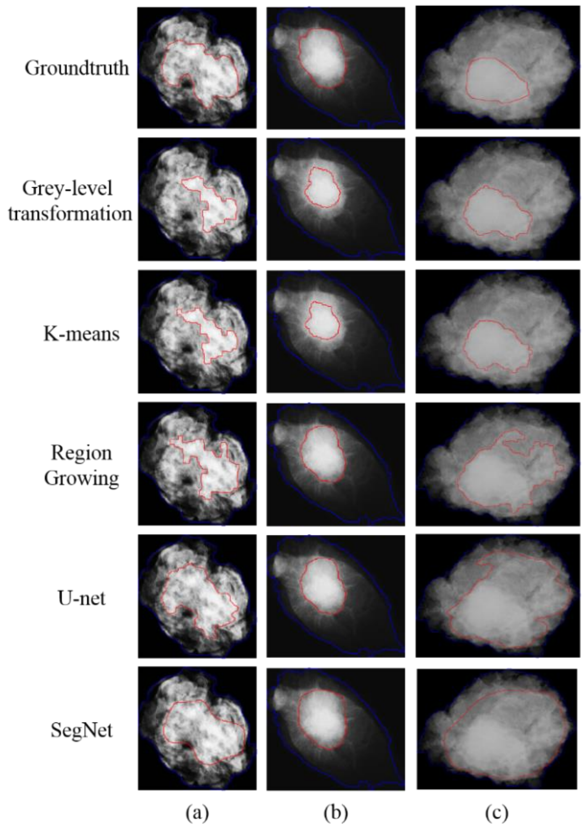


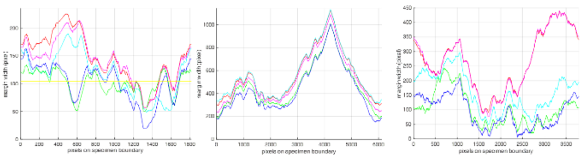
Figure 5. Final Segmentation result of specimen boundary (blue) and tumor boundary (red).

This study totally experimented 24 cases with manual sketched boundaries to test the accuracy of the proposed method. This study proposed five contouring approach to obtain the tumor boundaries. Fig. 5 demonstrates three examples by using the proposed methods. The experimental results revealed that the U-net and SegNet extracted tumor region more precisely under normal condition. Deep convolutional networks might find many contrasting features that are highly complex and difficult to describe in words from medical images. Although the segmentation result of traditional image processing (grey-level transformation, K-means clustering, region-growing) is not as good as U-net and SegNet, in a few special cases (low contrast), traditional approaches could obtain the better tumor region.

In terms of efficiency, the execution time of traditional approaches are shorter, and deep learning approaches take longer. That is because U-net and SegNet must take long time for training procedure. Even so, all of them could be done in 25 mins, which means the proposed system is suitable for intra-operative tumor margin evaluation. The comparison of efficiency is shown in Table I. After obtaining the specimen boundary and tumor boundary, the margin width with Euclidean distance was estimated. Fig. 6 shows the evaluation results (in pixel) using proposed five methods.

TABLE I. COMPARISON OF EFFICIENCY

Method	Execution time (sec)
Grey-level transformation	5.2
K-means clustering	6.0
Region growing	6.5
U-net	1338.0
SegNet	372.0



(a) (b) (c)

Figure 6. Evaluated margin between specimen boundary and tumor boundary.

IV. CONCLUSION

This study proposed effective computer-aided methods for detecting tumor boundaries and estimating margin width. Measurement of pixel density was first applied by estimating coin size. Adaptive thresholding was utilized to eliminate artifacts and obtain rough specimen region. Five contouring approaches were proposed to generate the tumor regions individually. Morphological operators were used to obtain desired specimen and tumor boundary. Evaluated the margin width by the Euclidean distance. Although the experimental results revealed that the traditional image processing obtained tumor boundary, deep-learning techniques can sketch boundary more reasonably, that is due to deep-learning has the opportunity to automatically find new features without human intervention. With the aid of deep learning techniques, the proposed scheme would be a potential intra-operative measurement system.

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