

# Automatic quantification of mammary glands on non-contrast X-ray CT by using a novel segmentation approach

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## ABSTRACT

This paper describes a brand new automatic segmentation method for quantifying volume and density of mammary gland regions on non-contrast CT images. The proposed method uses two processing steps: (1) breast region localization, and (2) breast region decomposition to accomplish a robust mammary gland segmentation task on CT images. The first step detects two minimum bounding boxes of left and right breast regions, respectively, based on a machine-learning approach that adapts to a large variance of the breast appearances on different age levels. The second step divides the whole breast region in each side into mammary gland, fat tissue, and other regions by using spectral clustering technique that focuses on intra-region similarities of each patient and aims to overcome the image variance caused by different scan-parameters. The whole approach is designed as a simple structure with very minimum number of parameters to gain a superior robustness and computational efficiency for real clinical setting. We applied this approach to a dataset of 300 CT scans, which are sampled with the equal number from 30 to 50 years-old-women. Comparing to human annotations, the proposed approach can measure volume and quantify distributions of the CT numbers of mammary gland regions successfully. The experimental results demonstrated that the proposed approach achieves results consistent with manual annotations. Through our proposed framework, an efficient and effective low cost clinical screening scheme may be easily implemented to predict breast cancer risk, especially on those already acquired scans.

**Keywords:** 3D CT images, mammary gland regions, density quantification, segmentation, localization.

## 1. INTRODUCTION

The woman's breast density has long been suggested to be the efficient and effective prediction of breast cancer risk on mammography [1]. This risk factor can be easily and more sufficiently measured from 3D CT images [2], which are widely used for chest cancer screening and many other diagnostic purposes. In order to enable the volume and density quantifications for predicting breast cancer risk, robust and accurate mammary gland region segmentation on CT images is necessary and expected by clinical screening scheme. However, automated mammary glands segmentation is very challenging in the non-contrast CT due to low CT image contrast between internal soft tissues of breast regions, irregular shapes of mammary glands, large variance of volumes at different patients and age groups.

A scheme for mammary glands segmentation on high-resolution CT images has been reported in our previous work [3]. Our previous method intended to recognize and strip off the tissues (such as skin, muscle, fat, and ribs) around the mammary glands firstly, and then regard the rest regions as the mammary glands. Recently, Liu et al. presented a similar approach to segment the breast region on low-dose CT images [4]. This work also used the same consideration to recognize and remove major anatomical structures for leaving breast regions in the final processing stage. Although this

approach based on elimination process demonstrated the possibility to segment breast and mammary gland regions on CT images, it still lacked (1) weak robustness due to the stringent condition that requires the successes of all related tissue segmentations, (2) poor efficiency that most segmentation results such as muscle, lung, ribs were useless for predicting breast cancer risk, and (3) large burden and low efficiency on development and maintenance costed by a number of ad-hoc functional-overlapped algorithms that designed specifically for segmenting those related organs. A straightforward approach that can accomplish a robust segmentation of mammary gland regions on CT images is strongly desired but still under development.

In this paper, we propose a novel method to automatically segment and measure intensity and volume of mammary gland regions on non-contrast CT images. Comparing to previous works, the proposed method is (1) a straightforward approach that directly segments mammary gland regions without using any pre-segmentation results of the other tissues, (2) a simple architecture that has two processing steps with distinct functions (global breast region localization, local pixel clustering, and labels classification) that reduces overlap of the total algorithms, (3) mainly based on machine learning approach to learn optimal parameters from the data to gain a superior robustness and computational efficiency. Few of additional domain knowledge of the breast anatomy were used in the last step to adapt to the high-level judgments and special requirements from users. The details of the proposed method are described in the following sections.

## 2. METHODS

### 2.1 Outline

The process flow of the proposed method is shown in Fig.1. As described in the previous section, we achieved the automatic mammary gland region via two steps: (1) “breast region localization” and (2) “breast region decomposition”, with “a high-level label classification” in a style of “from global & coarse to local & fine”. The algorithm was designed separately based on a data-driven, machine-learning approach, and executed sequentially during the segmentation process. In step 1, we used an object detection technique based on supervised learning approach to detect the 3D bounding box of the left and right breast regions on CT images, respectively. In step 2, we used a group-wised, spectral clustering technique based on unsupervised learning approach to decompose the region inside of bounding box (breast) into a number of segments according to the homogeneity of CT intensities. The domain knowledge of anatomy such as spatial relationship between different tissues of breast was used in final stage of step 2 to classify and label the segments for distinguishing the mammary gland regions with the other tissues. The details of each part are described in the following sub-sections.

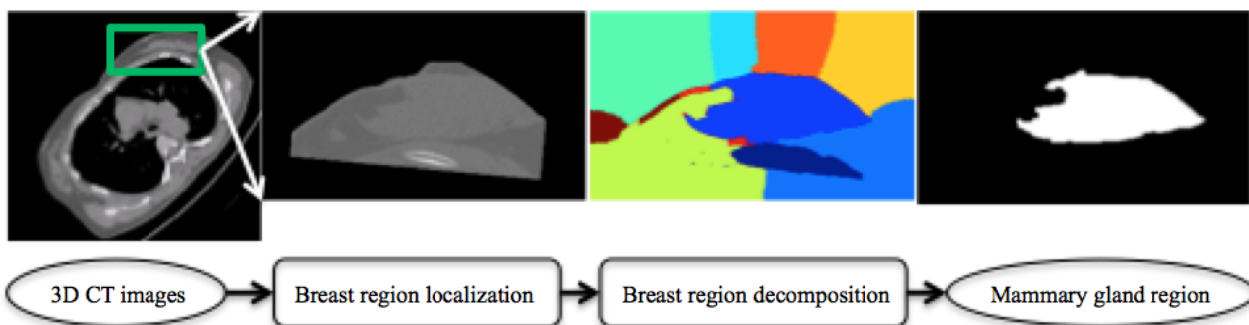


Fig.1. Processing flow of the proposed method for segmenting mammary gland region on 3D CT images.

### 2.2 Breast region localization

The location of a breast region was regarded as a 3D minimum-bounding rectangle (MBR) that includes all the voxels of breast region and a number of voxels of the other tissues as little as possible. A 3D MBR was presented by six coordinates of two corner points and two angles that show orientation of the rectangle in a 3D image space. The automatic localization was to decide those parameters on CT images automatically. We have proposed a universal framework to localization different organs in CT images in previous work [5,6]. This method used a window sliding and matching to scan all the positions on a CT image and find out the MBR of a target organ. The pattern matching was

proceeded in an ad-hoc feature space that is optimized for specifically distinguishing the left and right breast region from the other tissues on 3D CT images based on a machine learning method [7]. In our approach, we first built a feature space that is spanned by a redundant set of Haar-like features [8, 9] and local binary patterns [10, 11], and then our learning method was applied to find a subspace that gives the minimal classification error between breast and other tissue. This classification is trained by a number of training CT images, on which the locations (MBR) of breast regions were indicated manually by human operators. The classification is accomplished in a trial and error style.

Instead of doing the breast localization directly on a 3D image space, the proposed method proceeds with multiple independent localizations on a series of consecutive 2D slices along different image orientations, so that all detected 2D-MBRs are accumulated and stacked up in the 3D space to construct a final 3D-MBR. The advantage of this approach is (1) ease of training a useful detector under the limitation that only a small number of CT cases were available. The reason was that a 3D CT images can be decomposed to thousands of 2D slices and larger number of training samples generally derives a better performance; (2) higher accuracy of the decision in 3D that benefits from the mutual consent of multiple independent 2D detections; (3) better robustness for unknown abnormal CT cases (may appear a large distortion from 3D view) due to this approach try to catch local and partial 2D information of a 3D image redundantly.

After breast localization step, we obtained two 3D MBRs that tightly enveloped left and right breast regions from a 3D CT image. Our approach normalized 3D MBRs on CT images from different patients to a standard space within the same orientation, scale, and center position by using an affine transformation. Those normalized MBRs were passed to the next step for segmentation process.

### 2.3 Mammary gland segmentation by using breast region decomposition

The mammary gland region segmentations were realized through a spectral clustering of breast regions from a group of CT images. The aim of our approach was to automatically obtain the information of general anatomical structures of breast region, and to perform mammary gland segmentation by using unsupervised learning from the inputted CT images. The new contributions of our method can be concluded as (1) using a group-wised segmentation approach instead of individual segmentation for each CT image independently; (2) using the pair-wised relationships between any two-pixels within CT images instead of local information from neighborhood pixels. The details of the processing flow for segmentation are described as the following steps:

- (1) For an input dataset ( $n$  3D images cropped from CT images based on MBRs of breast regions), we extracted one central sections (2D slices) in sagittal and axial body directions respectively and generated a dataset includes  $2n$  images that shown majority of appearances of mammary gland regions on the inputted dataset.
- (2) We grouped those  $2n$  images and proceed a spectral clustering by an algorithm that proposed in [12]. At first, we accomplished a spectral decomposition to get a set of spectral bases for each 2D image individually according to the pixel-wised similarity. Those spectral bases can represent the patterns of pixel-wise similarity of original 2D image. Because the breast regions of different CT images shared a similar intensity appearance, the pixel-wise similarity patterns of each image should also be similar. We therefore shuffled and recombined the spectral bases of each image in the group, generating a set of synchronized spectral bases that can be used to represent the joint appearances (general anatomy of breast) in  $2n$  images. A clustering (k-means) on the synchronized spectral bases separated those joint appearances and divided each image into a number of massive regions (segments). The detailed algorithms can be referred in [12].
- (3) The segments on each image were labeled as mammary gland region, fat, and background by using a two-step image processing procedure based on hand draft algorithms. Firstly, the lines of skin and pectoral muscle were extracted automatically by using the Euclidean distances to the air region (with CT number about 0 H.U.) inside and outside of human body. We then classify the segments that enveloped by the lines skin and pectoral muscle using a linear classifier based on features of density distribution within each segment.

The segments that labeled as mammary gland regions on each 2D image were outputted as the final results. For each CT image, our approach detected two MBRs that indicate the location of right and left breast regions, and outputted the mammary gland regions on two crossed 2D sections for each MBR respectively. The volume and CT number distributions of the mammary gland regions were measured and outputted for estimating the risk factor of breast cancer on CT images.

### 3. EXPERIMENT AND RESULTS

We applied this approach to segment mammary gland regions in left and right breast for predicting the risk of breast cancer on CT images. A dataset that includes 300 torso CT scans sampling with the equal numbers from 30 to 50 year-old-women was used for performance evaluation. Those CT scans were collected in Gifu University Hospital by two kinds of multi-slice CT scanners (LightSpeed Ultra16 of GE Healthcare and Brilliance 64 of Philips Medical Systems). Each CT scan used a common protocol (120 kV/Auto mA) and covered the entire human torso region. Each 3D CT scan has approximately 800-1200 axial CT slices by an isotropic spatial resolution of approximately 0.6-0.7 mm and a density (CT number) resolution of 12 bits. All of these CT images were taken for the patients with certain real or suspicious abnormalities.

We manually annotated MBRs of the breast regions on all the CT images for evaluation. A medical specialist for breast cancer interpretation manually annotated left and right mammary gland regions on randomly selected 10 CT cases as ground truth (GS). The Jaccard index between GS and segmented mammary glands was used for evaluating the volume of segmented mammary gland regions. Because the dense of mammary glands was used as the major measure for cancer risk prediction, the CT number histograms within segmented mammary gland regions were also compared with the histograms measured from GS based on Bhattacharyya distance.

Examples of the segmentation results on 3D CT images are shown in Fig.2. We selected four CT images that were classified to Breast Composition Categories *a-d* defined by BI-RADS 5th edition [13] as examples and shown the results of each processing step for each example from left to right column. For each example, one slice of 3D CT image, localized bounding box for breast region, spectral clustering results, region enveloped by the lines skin and pectoral muscle, segmentation results, ground truth, and CT number histograms of mammary gland regions of each example are shown from the top to bottom lines respectively.

### 4. DISCUSSION AND CONCLUSION

In our test, the breast location detected if the majority parts (two thirds of the volume) of detected 3D rectangle and the ground-truth MBR overlap with each other. Our evaluation based on 300 test CT cases showed that the overlap rate (Jaccard index) between the MBR to the GS for left and right breast regions were larger than 85% and error (distance) of the center positions were smaller than 5.3 (mm). We confirmed that the breast region localization for the normal women breast appearances were closed enough to the GS. The deterioration on accuracy was occurred in the extremely small breast or abnormal lung textures (pneumonia) cases that were not included in training samples. This deterioration should be improved by using more abnormal CT images during the training stage.

The average values of Jaccard indices for segmentation results of breast region were distributed from 0.23 to 0.96 with the average of 0.68. The low Jaccard indices have been confirmed on the CT cases that only had few mammary glands. In such cases, the mammary gland regions looked like a number of lines instead of massive pattern that cannot be evaluated properly by using Jaccard indices. We confirmed the segmentations on the cases in which the mammary glands has a massive appearance (maybe higher risk in breast cancer) were successful from the preliminary experimental results. Because the purpose of the segmentation was risk predicting of breast cancer that was based on density distribution of the mammary gland regions, we compared CT number histograms measured from segmented mammary gland regions and GSs. Bhattacharyya distance between those two histograms was used as similarity measure. The evaluation results showed that Bhattacharyya distances were distributed from 0 to 0.16 even for the case with a poor value of Jaccard indices. Those results showed the density distributions on segmented mammary gland region and GS were quit similar to each other and may led to the same result for predicting the breast cancer risk.

In conclusion, we proposed a novel approach to segment the mammary gland regions of left and right breast regions on 3D CT images automatically. This approach has a simple architecture and is mainly based on both supervised and unsupervised machine learning methods. The experimental results on real clinical CT images showed that our approach could segment the mammary gland regions successfully and provide very similar appearance on CT number distribution of mammary glands comparing to the manual extraction results from the doctor. Our proposed framework, an efficient and effective low cost clinical screening scheme may be easily implemented to predict breast cancer risk, especially on those already acquired scans.

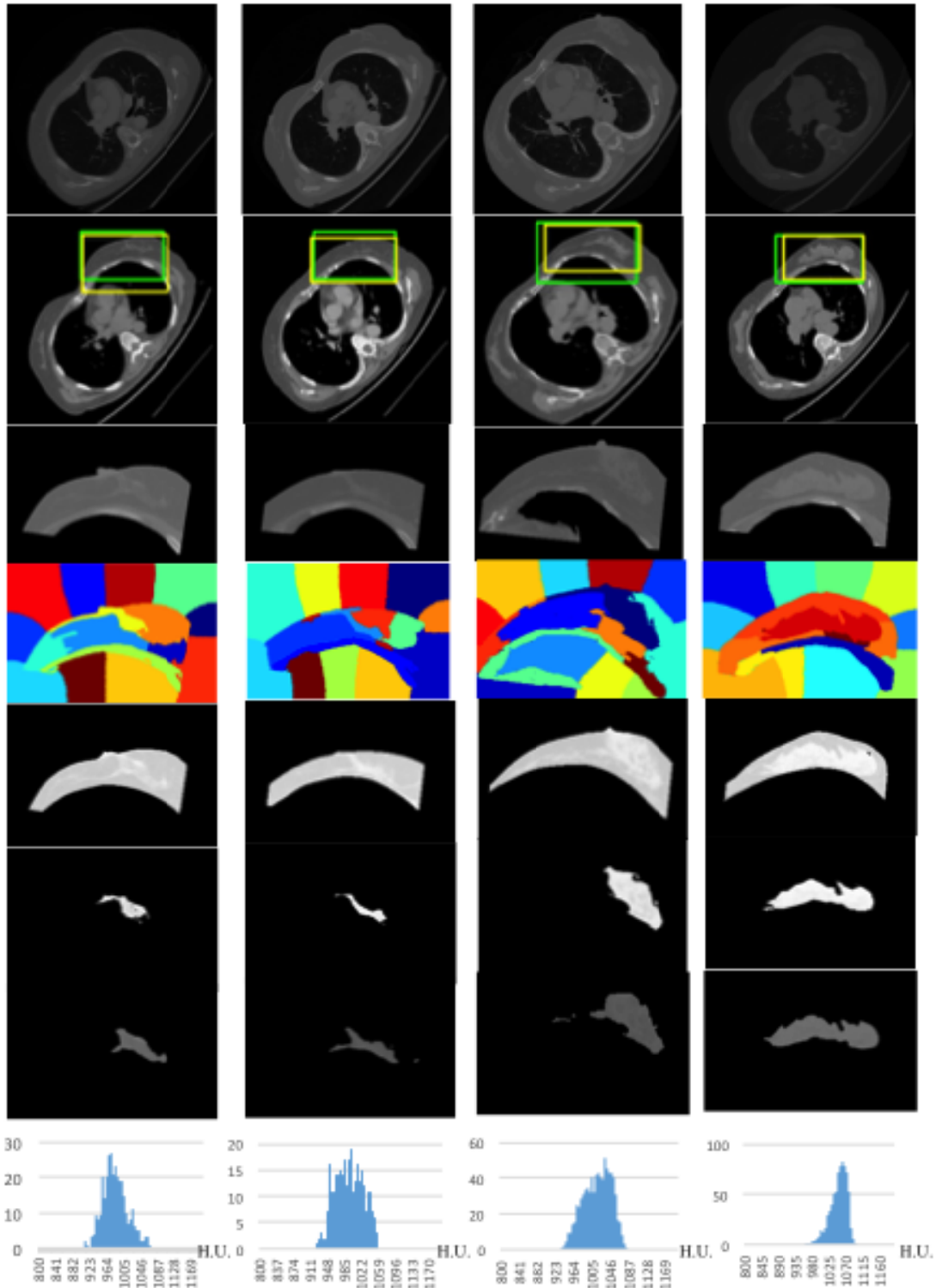


Fig.2. Results of mammary gland region segmentations from four CT cases from left to right column. (From top to bottom line: one slice of a 3D CT image, detected bounding box (yellow) with the ground truth (green)), breast region for segmentation, spectral clustering result, enveloped region by the contours of skin and muscle, segmentation results of mammary gland regions, ground truth from a doctor, and CT number histograms of mammary gland regions)

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