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# Rat Mammary Gland Analysis in T1 Weighted MR Images

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## Abstract

*In studying the relationship between risk factors and breast cancer, growth patterns of the fat pads and glandular tissues are important features. The goal of this small animal study is to measure the size of mammary pads over the time and to quantify the development of glandular structures. To achieve this goal, we propose a hierarchical approach to segmenting out rat body, mammary fat pads and glandular tissues in T1 weighted magnetic resonance (T1W-MR) images. Particularly, we have developed a new approach combining watershed transform and region competition for improved fat pad segmentation. An efficient strategy, termed as competition propagation, is developed to propagate the region competition result from one slice to next slice, resulting in a fast convergence in region competition algorithm otherwise computationally costly. The glandular tissues, the fine structures within the fat pads, are then located and segmented out by analyzing the isolable-contour map. The method has been applied to 18 volumetric sets of T1W-MR images acquired from this study. The experimental results showed the great utility of this approach as it can provide accurate measurements to assess novel risk factors for breast cancer.*

## 1. Introduction

Breast cancer is the most frequently diagnosed cancer and the second leading cause of cancer related death in US women [1]. Knowing that almost all instances of breast cancer originate in the lobules or ducts of the mammary glands, researchers have special interest in using noninvasive imaging techniques to study mammary glands in search for novel risk factors. Among all dietary factors, alcohol is most consistently associated with an increased breast cancer risk, evidenced by its association with high frequency of mammary cancer in rodent models. To assess the risk of alcohol for breast cancer, we believe that the growth patterns of the mammary fat pads and glandular tissues are important features. In this study, we evaluate these important features with T1 weighted magnetic resonance (T1W-MR) rat images in conjunction with whole mount histology for studies of gland development and glandular tissue density.

However, it is time consuming and tedious to manually delineate the mammary fat pads and glandular tissues in T1W MR images for calculating the measurements. Segmentation techniques are needed for this task to extract fat pads and glandular tissues. Moreover, accurate segmentation is the basis of convincing measurements of the tissues in a rat image. Although there are many segmentation methods in the literature, few can fulfill the requirement of this small animal study. For example, watershed transform is a popular segmentation method [3], but, its well-known drawbacks, over-segmentation and sensitivity to noise, prevent direct use of the results as meaningful segmentation. Region merging is a common post-processing technique to deal with the over-segmentation problem [2]. But, during such process, once a region has been merged to another, their combination will be preserved to the end. In fact, region merging can be viewed as a kind of optimization process, but it is likely to be trapped in local optima due to its sequential and non-reversible strategy.

In this paper, we present a new approach for segmentation of mammary fat pads and glandular tissues in rat T1W-MR images. Segmentation is carried out in a hierarchical way – segmenting out the body, the mammary fat pads and the glandular tissues sequentially. Body segmentation is accomplished through analyzing the radial gradient. Within the body area, an efficient method, competition propagation that integrates watershed transform and region competition, has been developed to segment the fat pads. With a strategy in propagating the region competition result from one slice to next slice, a fast convergence can be obtained in region competition for optimizing the segmentation result. The glandular tissues, which are the fine structures in the gland, are then located and extracted by an analysis of the isolable-contour map. The proposed method has been applied to 18 volumetric sets of T1-W MR images (acquired from 6 rats, each with 3 scans). The experimental results are presented to demonstrate its ability to provide accurate measurements of fat pad size and glandular tissue density.

## 2. Rat Mammary Gland Analysis

In normal conditions, the mammary apparatus is formed by six pairs of fat pads. Three pairs are situated in the thoracic and the others in the abdominal-inguinal region. When completely developed, the fat pads are quite extensive and occupy nearly all the subcutaneous region, except for some areas of the back. In T1W-MR images, the fat pads are mostly connected to each other, and the precise transition from one fat pad to another is hard to define. In this section, we will present a sophisticated approach for mammary gland analysis, which essentially consists of three sequential segmentation steps: rat body delineation, fat pad segmentation and glandular tissue extraction. In the following sections, we will give a detailed description of the techniques involved in each segmentation step.

### 2.1. Rat body delineation

This step is to segment out the rat body from background. Generally, the body covers only less than half of the whole image area, which means that computational cost for fat pad segmentation could be greatly reduced if confining the subsequent analysis within the body. In this paper, a radial gradient-based method is used for rat body segmentation.

In each slice image, as the first step, the horizontal and vertical ranges of the body region is determined through an analysis of horizontal and vertical intensity profiles of the image. Once the ranges are available, a bounding rectangle for the body region is obtained. A common rectangle for all images is specified as the union of the rectangles for each individual image. The center point of the common rectangle is regarded as the center point of the body. Polar rays are formed starting from the center point, and gradients in the polar direction along the rays are calculated. The edge point on a ray is chosen as the outermost point of gradient value above a predefined threshold. Inevitably, there exist outliers that are not situated at the true edge of the body, which are adjusted by smoothing the edge curve with a one-dimensional median filter.

When all single images have been processed, a mesh enclosing the body surface is obtained. Considering the smoothness of the object, two-dimensional median filtering is carried out on the mesh to smooth the body surface. The body region is readily obtained through filling the volume enclosed by the smoothed mesh.

### 3.2. Fat pad segmentation

**Preprocessing.** In T1W-MR images, the fat pads appear as bright areas located below the epidermis and are extended through the subcutaneous region. The intensity transition between epidermis and fat pads is not so clear, thus operation is required to remove the epidermis for future processing. Since it is shown as a strip region of uniform thickness around the body, the epidermis can be removed through shrinking the body region with a predefined size, which is implemented with a morphological erosion operator.

Due to the imaging noise and detailed structures within them, the intensity distribution in fat pads is not necessary homogeneous. As watershed transform is sensitive to noise, in order to reduce the over-segmentation, a filter should be applied to preprocess the image. In this paper, bilateral filtering [6], a simple, non-iterative but effective scheme for edge-preserving smoothing, is considered to fulfill the task.

**Competition propagation.** Since simple segmentation methods like region growing and watershed transform often result in over-segmented regions, we propose to combine watershed transform with region competition for fat pad segmentation. Region competition was proposed in [8], which combines the geometrical features of deformable models and the statistical nature of region growing. In the original pixel based setup of this model, in order to reduce the sensitivity of the statistics force to noise, a circular window around each boundary point is selected and its probability is replaced by the joint probability of the points in the window. However, it is not easy to select a proper window size for a particular application.

Instead of performing competition on single pixels, the watershed transform can be incorporated to form a region-based competition scheme. Watershed always produces a complete division of the image. Though the image is over-segmented, each of the generated minute regions is homogeneous. Further, when applied to image gradient, the watershed lines are actually formed by the points of locally maximal gradient. Consequently, statistics estimation on such small regions will be more accurate than that on single pixels, and selection of a proper local window is not necessary any longer.

This region-based competition method can be readily extended to three-dimensional volume data. However, it is inefficient and also not necessary to handle the whole volume at one time. As known, during the competition process, only those unit regions along the partition boundary are moved back and forth. And, most physical objects represented in the image data possess kind of smoothness, that is, their properties, such as shape, intensity distribution and inter-object relationship, will not be changed abruptly.

In this paper, we propose a strategy to efficiently propagate the competition result from one slice to next slice for volume segmentation. We call this approach as *competition propagation* method. For the T1W-MR rat images, since the segmentation result of the previous image is considered as a close guess for that of the current image, from which much less effort will be required to reach the final segmentation. The competition propagation method is detailed as follows:

1) Choose a start slice and perform an initial segmentation using adaptive thresholding [5]. The image is thus partitioned into a set of regions $R_i$, $i=1,\ldots, N$, each of which is regarded as an object.
2) Apply the watershed transform to divide the image into a set of small unit regions, $r_j, j=1,\ldots,n$.
3) Categorize the unit regions according to the initial partition. The updated partition of the image can be represented as.
$$R_i = \left\{r_{i1}, r_{i2}, \cdots, r_{in_i}\right\} \text{ and }$$
$$\bigcup_{i=1}^{N} R_i = \left\{r_1, r_2, \cdots, r_n\right\}$$
where each $r_{ij}$ is fully or mostly covered by $R_i$.
4) Locate the set of unit regions situated along the boundary of the current partition, that is, each of these regions connecting at least two objects. Denote this unit region set as $\{r_{b1}, r_{b2}, \ldots, r_{bm}\}$.
5) Locate the $R$-$r$ pair with the largest force, where $r \in \left\{r_{b1}, r_{b2}, \cdots, r_{bm}\right\}$ being connected to $R$ but $r \notin R$ in current partition. The force for competition is formulated as:
$$F = \alpha \cdot F_h + \beta \cdot \left(F_g + F_l\right)$$
As shown in Figure 1, the force is composed of three components:

$$F_h = \frac{1}{\sqrt{2\pi}\sigma_R}\exp\left\{-\frac{(m_r - m_R)^2}{2\sigma_R^2}\right\}$$

$$F_g = \frac{\bar{g}_{b2}}{\bar{g}_{b1}} \quad \text{and} \quad F_l = \frac{l_{b1}}{l_{b2}}$$

where $F_h$ is the homogeneity component, $m_r$ is the intensity mean of $r$, and $m_R$ and $\sigma_R^2$ the intensity mean and variance for the object $R$; $F_g$ and $F_l$ are the forces imposed by the boundary of $r$, $\bar{g}_{b1}$ and $l_{b1}$ are the mean gradient on and length of the common boundary segment $b_1$, and $\bar{g}_{b2}$ and $l_{b2}$ that of the non-common segment $b_2$.

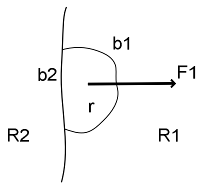


Figure 1. The force for competition

6) If the $R$-$r$ pair in step 5) exists, then change the belonging of $r$ to $R$, and update the partition of the image accordingly, go to step 4) to repeat the competition process; otherwise, stop the competition process and finalize the partition for the current image, and activate the segmentation on the next image and set the segmentation on the current image as the initial partition, go to step 2).
7) Repeat the above steps until all the images in the volume data have been processed, and the final segmentation of the whole volume data is obtained.

**Segmentation by competition propagation.** After computing the gradient of the image, the watershed transform is carried out, and the image is divided into a set of small homogeneous regions. Among the several implementations of the watershed transform available in [3], the first-in-first-out (FIFO) queue based one described in [7] is considered in this paper. The regions are categorized according to the objects covering them and the competition process as described above is activated to segment the image. From the center slice, two sequential processes are invoked to segment the volume data. The first process is forward and segmenting the images slice by slice from the center slice to the first one; another is backward from the center to the last slice.

When all the images have been segmented, the volume data are partitioned into sub-volumes corresponding to different structures, among which the fat pads will be selected. Considering the anatomy of the model animal, the largest component situated attaching to the skin is selected and regarded as the fat pad volume. Some post-processing, such as morphological smoothing of the gland surface and filling holes in the volume, is to be carried out before the final fat pad volume segmentation is determined.

### 3.3. Glandular tissue extraction

As mentioned before, glandular tissues are shown as small darker often discontinuous areas distributed within the mammary glands, of irregular shapes, varying sizes and intensity levels. In order to effectively segment glandular tissues, single thresholding is not appropriate since the fat pad is not of uniform intensity. Since the glandular tissues are of low contrast compared with surrounding gland area and the relatively low resolution of the images, deformable model based methods, such as snakes, also tend to fail. In this paper, an isolable-contour map based method is developed for glandular tissue segmentation. Multilevel thresholding is carried out on the image where pixels within the same intensity range defined by each pair of consecutive threshold values are given a distinct label [4]. The resulting image is composed of connected sets with uniform labels, and pixels the lie on the boundary of a set form an isolable-contour. The union of all such isolable-contours forms the corresponding isolable-contour map of the input image.

To help detect this type of minute structures, a bilinear interpolation is first performed on the images to obtain a better resolution. Upon the resized image, multilevel thresholding is applied. In order to effectively treat glandular tissues of varying contrast to their surroundings, non-uniformed thresholding intervals are considered. Specifically, fifteen levels are used in the proposed method, where the distribution of the levels within the higher intensity range is denser than that in the lower part.

With the isolable map obtained, connected sets of locally minimum labels are determined and considered as initial regions for glandular tissues. The segmentation of a single glandular tissue object is fulfilled through an analysis of the evolving pattern of the isolable-contours surrounding its initial region. The change of the features of the area enclosed by the consecutive isolable-contours from the initial contour to the outward is explored. The isolable contour at which the features begin to change precipitously is chosen as the actual boundary of the tissue object. Finally, an area filtering is applied to exclude objects of size larger than a given threshold.

## 3. Experimental Results

The proposed segmentation approach has been applied to 18 T1W-MR volumetric images acquired from 6 rats; each with 3 scans. An example of the experimental results is presented in Figure 2. One original image of the slices is shown in Fig. 2(a), and the segmentation for the previous slice image is shown in Fig. 2(b). Fig. 2(c) shows the watershed map for the image in Fig. 2(a). As we can see, due to the use of a bilateral filter, the over-segmentation is indeed alleviated. Fig. 2(d) shows the initial partition after categorizing the watershed regions according to the previous segmentation result in Fig. 2(b). Based on the initial partition, the region competition process gives us the final segmentation result as shown in Fig. 2(e). An overlay of the fat pad area after skin removal on the original image is given in Fig. 2(f). Finally, the glandular tissues are detected within the fat pads, as shown in Fig. 2(g).

As we can see from Fig. 2(d) and Fig. 2(e), there is only little difference (mainly near the border area) between the initial partition and the result by region competition. Therefore, the competition tends to converge very fast. In average, it requires less than 15 iterations for the competition to stop. Consequently, the proposed method is

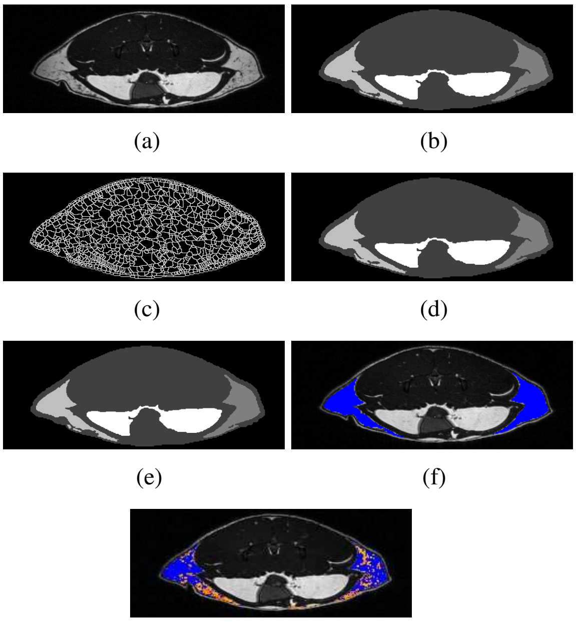
(a) (b) (c) (d) (e) (f) (g)

Figure 2. The method on an image

computationally very efficient for volume data segmentation.

In Figure 3, the method for fat pad volume segmentation is compared to that by region growing. The original image is shown in Fig. 3(a), and Fig. 3(b) is the segmentation result by region growing. As can be seen, region growing failed to handle weak edges and leaked to non-desirable structure at the side. The result by the proposed competition propagation method described in Section 2 is given in Fig. 3(c), where the unwanted "interfering" structure has been successfully excluded from the fat pad region.

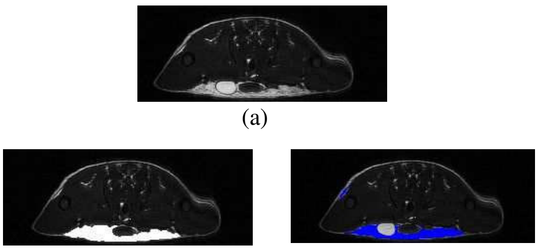
(a) (b) (c)

Figure 3. Comparison with region growing

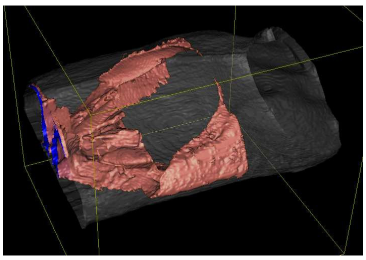

Figure 4. The rendered volume

The surface rendering of the segmented volume is shown in Figure 4, where the outer grey shell is the surface of the animal body, and the brick red volume within the body is the segmented fat pad volume.

## 4. Conclusion

In this paper, we have presented a complete approach for mammary gland analysis in T1W-MR images. In particular, methods for segmentation of mammary fat pads and glandular tissues have been developed to quantify the growth pattern of mammary gland in rodents. We have incorporated the knowledge regarding the anatomy of the animal model and corresponding representation in T1W-MR images into our segmentation method. For fad pad segmentation, we have developed a novel approach combining watershed and region competition, in that a competition propagation strategy is developed to greatly speed up the convergence of the region competition algorithm. The experimental results have demonstrated the utility of this approach for studying novel risk factors for breast cancer.

The small animal study presented in this paper is an on-going effort. Measurements regarding the growth patterns for fat pads and glandular tissues are important features and of special interest to this study. We are undertaking the improvement of the method for accurate quantification of these features. It is expected that this image analysis tool will facilitate the study of risk factors associated with breast cancer.

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