Advanced Image Processing Algorithms for Breast Cancer Decision Support and Information Management System

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Abstract This paper reviews image analysis approaches developed within the DESIREE European project for the implementation of a decision support system (DSS) for breast cancer. These include robust algorithms for image segmentation, classification and imaging biomarker extraction, as well as a solution for the simulation of surgery outcomes, including a breast reconstruction module and a mechanical and healing model. These algorithms are integrated into the DSS to assist clinicians dealing with the heterogeneous information generated during the course of the disease.

Keywords Breast · Cancer · Segmentation · Radiomics · Modeling

1 Introduction

Breast cancer is the leading cause of cancer-related death among females worldwide (causing 15% of all cancer deaths among women [13]). Breast cancer cases are discussed and managed at Breast Cancer Units (BUs), where different professionals

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(radiologists, doctors, surgeons) gather together to review each case. The Decision Support and Information Management System for Breast Cancer (DESIREE) project aims at improving the management of breast cancer patients by providing BUs with a platform that integrates data and knowledge bases, decision support on the available therapy options and analysis and modeling tools.

Routine imaging examinations provide valuable information for the diagnosis and prognosis of a breast cancer patient. Thus, advanced image processing algorithms for automatized image analysis and quantitative information extraction are highly valuable. Furthermore, the integration of these tools in a web-based interactive image viewer within the Decision Support System (DSS) allows comparing different patients and leveraging the data accumulated from retrospective cases with known outcomes.

Hereby we present the main results achieved in the medical image analysis context of the project, which include: (1) automatic segmentation of breast and tissues, (2) automatic classification of images according to the breast density (BD) ratio, an important biomarker related to the risk of developing cancer, and (3) a biomechanical and healing model of the breast.

2 Image System Overview

One important part of the DESIREE project consists on a web-based magnetic resonance (MRI) and mammogram image analysis module, which includes an image uploader and a viewer. All the image analysis algorithms detailed in the following subsections have been integrated into this module, allowing radiologist to easily interact with the images by providing tools to semi-automatically segment lesions, measure regions or create annotations, as well as to evaluate the results of the multiple automated analyses. A screenshot of the web-based image system is shown in Fig. 1.

Fig. 1 Screenshots of the image analysis module integrated in the breast cancer decision support system: **a** Image viewer, with the tool for manual annotation, **b** Image viewer displaying the 3D breast reconstruction and the tumor segmentation

Some of the analysis are performed automatically after the radiologist uploads images into the system. For mammographic images, the breast is segmented and the BD ratio is calculated. For multi-parametric MRI images, the apparent diffusion coefficient map is generated from diffusion weighted images (DWI), and kinetic parameters are extracted from dynamic contrast enhanced (DCE) images. The breast and its tissues are segmented automatically, using the anatomical images to quantify BD. Breast tissue segmentation is used to generate a 3D breast model, which allows a better visualization of the breast anatomy and tumor location (as shown in Fig. 1). Furthermore, it can be used for the generation of the biomechanical healing model of the breast to predict surgery outcomes.

For tumor segmentation, radiologists can manually annotate a region of interest (ROI), or use a seeded region growing. Several experimental biomarkers (which have been correlated with cancer presence in the literature [4, 14, 26]) are calculated from both DWI and DCE images, which are displayed alongside the images and stored in the DSS.

3 Breast Segmentation and Characterization

3.1 *Breast Segmentation*

The main pre-processing technique in Computer-Aided Diagnosis (CAD) systems is to define the proper region of interest that should be then analysed. Segmentation of the breast from the rest of the body is a challenging task, especially due to the poor contrast between tissues and the diffuse line between the breast and the chest muscle. Obtaining a good segmentation is essential to correctly evaluate BD or to find suspicious masses and calcifications within the breast [6].

Breast and pectoral muscle segmentation in mammograms While defining the breast-air interface is straightforward using simple image processing algorithms such as thresholding, finding the boundary between the breast and the pectoral muscle is challenging due to: (1) the similar intensity between the muscle and dense tissues, which can overlap and obscure the pectoral boundary; (2) the presence of the axillary fold that can be confused with the boundary; and (3) the varying shape of the boundary. Traditionally, thresholding and contrast enhancement algorithms, techniques based on the curvature or the edge, Hough transform, graph-cut methods, region growing, wavelet-based segmentation techniques and active contour models have been employed to separate the breast from the muscle [6, 15, 18, 24, 39]. Many of these methods rely on the contrast between both regions or on finding a straight boundary line, which is not always the case, and are usually designed only for digital or digitised mammography images. More recently, deep learning-based approaches have also been proposed [28, 34], whose main drawback refers to the lack of large and diverse image databases.

Fig. 2 Pipeline for breast and pectoral muscle segmentation using canny edge detection and active contours: **a** Segmentation process, which consists in finding the pectoral contour (left) and finding the breast-air interface (right), **b** Example of the results obtained for breast segmentation applying this method on two patients (DBT images from Eresa Grupo Medico)

Table 1 Quantitative results for pectoral muscle segmentation obtained for MIAS, InBreast, BCDR and CBIS-DDSM databases. All metrics are presented as percentages with standard deviation

Database	Jaccard index	Dice coefficient	Accuracy	Sensitivity	Specificity
MIAS	94.6 $\pm$ 9.8	97.5 $\pm$ 7.5	99.3 $\pm$ 1.4	98.2 $\pm$ 7.6	99.5 $\pm$ 1.2
InBreast	92.6 $\pm$ 10.6	95.6 $\pm$ 8.4	99.6 $\pm$ 2.2	95.2 $\pm$ 8.6	99.8 $\pm$ 1.8
BCDR	96.9 $\pm$ 4.1	98.8 $\pm$ 2.2	99.9 $\pm$ 1.1	99.6 $\pm$ 1.4	99.9 $\pm$ 1.0
CBIS-DDSM	95.1 $\pm$ 9.4	98.1 $\pm$ 7.1	99.5 $\pm$ 1.3	98.3 $\pm$ 7.6	99.6 $\pm$ 1.4

Within this project, two different approaches to pectoral muscle segmentation have been developed. The first method [33], depicted in Fig. 2, applies a Canny edge detector and computes edge features (e.g. length, eccentricity, orientation, intensity and extent) to select initial edge candidates. A majority voting approach is then used to choose the best edge as the initial boundary, which is subsequently refined based on intensity. Finally, the breast and muscle are segmented from the background using thresholding and active contours.

The second approach finds the pectoral boundary using a convolutional neural network designed for detecting contours [23]. From the network boundary generated probability maps, a post-processing step is applied to obtain the segmentation of the whole pectoral muscle region. This method, which yields the best results, has been evaluated on four different databases, i.e. MIAS [41], InBreast [22], BCDR [11] and CBIS-DDSM [16], and is the largest validation study to date. Results are presented in Table 1.

Breast and pectoral muscle segmentation in MRI MR images show strong contrast between soft tissues and provide three-dimensional coverage of the entire breast. There are different approaches to automatically locate the breast-chest wall line: atlas-based methods [10, 17], body landmark-based methods, [20] and methods mainly based on intensity differences and edge detection [9, 43].

Fig. 3 Representative results of MRI segmentation on MRI images from ERESA Grupo Médico: **a** pectoral segmentation **b** tissue segmentation using convolutional neural network

In contrast to previous methods, our approach only relies on prior anatomical knowledge during the process of constructing a simple mathematical model of the breast; no knowledge is required during the segmentation process. In a first step, the algorithm estimates the breast-background boundary based on the best edge features using a combination of Otsu's thresholding and Canny's edge detection. Then, the pectoral-breast boundary is estimated using the breast model in conjunction with active contour models. Figure 3 presents an example of the results.

3.2 Breast Characterization

Breast Density (BD) is a risk factor associated with the development of cancer [40], and it is usually assessed by visual examination of the mammograms and classified using the BI-RADS, (American College of Radiology's Breast Imaging Reporting and Data System), which can be subjective and lead to intraobserver variability [12]. Therefore, many CAD systems aim at developing fully automatic systems to provide an objective and quantitative assessment of BD and cancer risk scoring. Since a mammogram is a projection image, differences in body position, level of compression or x-ray intensity can lead to an inaccurate measure of BD, specially in very dense breasts that have a higher cancer risk. Thus, recent studies aim at quantifying BD using magnetic resonance images (MRI) [5, 29], which provide strong contrast between tissues and three-dimensional coverage of the entire breast.

Breast density assessment in mammograms Traditional approaches relied on the intensity differences between bright fibro-glandular (FG) tissue and fat tissue; thresholding [19], clustering methods [27], and texture analysis [21, 30] have been the most widely used techniques. Recently, deep learning approaches have been proposed [28].

Within DESIREE, a SVM model was trained to classify mammography images in four classes, according to BI-RADS scores. After applying the breast segmentation method previously explained, a disk area of FG tissue was extracted from the breast and Local Quinary Patterns were used to capture local texture patterns at different resolutions. Histograms obtained from different resolutions were concatenated and

Fig. 4 An overview of the feature extraction for BD classification using multiresolution LQP operators. From [32]

Table 2 Quantitative results for tissue segmentation on MRI datasets provided by ERESA Grupo Medico using UNET for 3 class classification

Tissue	Total overlap	Jaccard index	Dice coefficient	False negative	False positive
Fat tissue	0.918747	0.788398	0.877872	0.081253	0.157543
FG tissue	0.669296	0.574157	0.724251	0.330704	0.202799

used as features to train the SVM model [31, 33], which yielded a classification accuracy over 86%. Figure 4 summarizes this process.

Breast density quantification on MRI Identification of FG tissue in MR images can be difficult due to intensity inhomogeneities in the images and because it appears as very thin fibers, especially in mostly fatty breasts (low density). Some fully automatic methods for tissue segmentation have been proposed, using clustering methods as fuzzy C-mean [25], intensity differences between multi-parametric MRI sequences [42], machine learning with hand-crafted features [44] and deep-learning [3].

In this project a convolutional neural network was designed and trained to segment breast tissues from T2 MRI [8]. 2D slices extracted from MRI volumes from 34 different patients provided by ERESA Grupo Medico were employed for training and validating the net. Images were annotated by a radiologist and a trained expert to evaluate inter observer variability.

For the segmentation of the tissues, two network architectures were proposed: (1) a modified holistically-nested edge detection network (HED) [45] and (2) a 3 class U-NET architecture [35]. BD was obtained as the ratio between the voxels of each class and the assigned BI-RADS class was correct on all test cases. Examples of the qualitative results are shown in Fig. 3, and quantitative results for the U-NET, which performed better, are summarized in Table 2.

4 Predictive Modelling

Advances in breast cancer diagnosis have improved early detection rates and thus, the development of Breast Conserving Therapy (BCT) that combines lumpectomy with radiation and adjuvant therapy. BCT has been shown to improve the quality of

Fig. 5 Flowchart of the multiscale model of BCT ([37])

life and cosmetic outcome of patients. Even if several studies have been published in the field of breast tissue modeling [1, 2], they are not specific to BCT interventions. In DESIREE we have developed a predictive multi-scale modeling solution, which allows the simulation of the breast before and after surgery and validated with data from a clinical trial in the Houston Methodist Hospital [7, 38]. Its goal is to aid surgeons better predicting the breast shape after lumpectomy and to support their dialogue with the patient, by showing them the prospective cosmetic outcome of their surgery.

The model incorporates a mechanical model of the breast, including different tissues, a biological model of healing, and radiotherapy and adjuvant therapy models [36, 37], as depicted in Fig. 5. Finite element modeling is used to simulate and predict the effects of the surgery.

5 Conclusion

This paper summarizes the image analysis algorithms developed within the framework of the DESIREE European project for the development of a breast cancer decision support system.

These algorithms include methods for the fully automatic assessment of the BD, both from mammograms and T2 MRI sequences, with results comparable to the radiologists' performance. A fully automatic pectoral muscle segmentation method from mammograms has also been proposed, which yields high accuracy results across different datasets in the largest validation study to date.

Furthermore, an advanced novel mechanical and biological model of the breast to predict breast conservative therapy outcomes has been introduced. This model assist patients and surgeons during the treatment decision making.

All these methods have been integrated into a web-based intuitive software platform, that together with a knowledge-based decision support system, improves the personalized, collaborative and multidisciplinary management of primary breast cancer patients at breast units.

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