Comparison of Lesion Size Using Area and Volume in Full Field Digital Mammograms

Jelena Bozek[1], Michiel Kallenberg[2], Mislav Grgic[1], and Nico Karssemeijer[2]

[1] University of Zagreb, Faculty of Electrical Engineering and Computing, Unska 3, HR-10000 Zagreb, Croatia
[2] Radboud University Nijmegen Medical Centre, Department of Radiology, Geert Grooteplein Zuid 18, 6525 GA Nijmegen, The Netherlands
jelena.bozek@fer.hr

Abstract. The size of a lesion is a feature often used in computer-aided detection systems for classification between benign and malignant lesions. However, size of a lesion presented by its area might not be as reliable as volume of a lesion. Volume is more independent of the view (CC or MLO) since it represents three dimensional information, whereas area refers only to the projection of a lesion on a two dimensional plane. Furthermore, volume might be better than area for comparing lesion size in two consecutive exams and for evaluating temporal change to distinguish benign and malignant lesions. We have used volumetric breast density estimation in digital mammograms to obtain thickness of dense tissue in regions of interest in order to compute volume of lesions. The dataset consisted of 382 mammogram pairs in CC and MLO views and 120 mammogram pairs for temporal analysis. The obtained correlation coefficients between the lesion size in the CC and MLO views were 0.70 (0.64-0.76) and 0.83 (0.79-0.86) for area and volume, respectively. Two-tailed z-test showed a significant difference between two correlation coefficients (p=0.0001). The usage of area and volume in temporal analysis of mammograms has been evaluated using ROC analysis. The obtained values of the area under the curve (AUC) were 0.73 and 0.75 for area and volume, respectively. Although a higher AUC value for volume was found, this difference was not significant (p=0.16).

Keywords: digital mammography, temporal change, lesion classification, CAD, breast density

1 Introduction

In developed computer-aided detection (CAD) systems one of the features that has been used for the classification between benign and malignant lesions is the size computed as the area of a lesion [1]. However, since the mammogram is a two dimensional projection of a three dimensional breast, the area of a lesion visible in two mammographic views, namely craniocaudal (CC) and mediolateral oblique (MLO), might differ. To overcome this issue one could calculate volume

of a lesion, as the volume might be a more reliable feature that should remain the same in both views and might be better for use in CAD systems than the area of a lesion. In addition, volume might give reliable information about the lesion seen in two consecutive exams, i.e. for evaluating temporal change in the size of a lesion. Since benign lesions have tendency to stay the same over time and malignant lesions tend to grow, volume might be a useful feature for distinguishing between benign and malignant lesions in temporal comparison of digital mammograms.

Volume of dense tissue in digital mammograms can be computed using the method developed by van Engeland et al. [2]. In this study we investigated the use of volume as a measure of lesion size compared to area. We were interested in the area and volume of a lesion in CC and MLO views. We hypothesized that the effective radius of a lesion obtained from volume is more similar in the two views than the one obtained from area. Additionally, we analysed the effective radius obtained from area and volume in the temporal mammogram pairs. In particular, we explored the possibility of volume as a feature to distinguish benign and malignant lesions in temporal comparison of mammograms.

2 Method

2.1 Dataset

Digital mammograms for this study were collected from the screening-institution Preventicon, Utrecht, the Netherlands, where they were acquired with a Hologic Selenia FFDM system. All mammograms used in the study have a visible lesion that has been biopsy proven as benign or malignant. In this study under the term lesion we consider masses, architectural distortion and bilateral asymmetry. We have included only lesions that are projected within the breast area, i.e. not overlapping with the pectoral muscle.

The dataset for the analysis of area and volume performance for CC and MLO views consisted of 382 digital mammogram pairs with lesion visible in both views, of which 164 were benign and 218 malignant lesions. For the temporal analysis the dataset comprised 120 mammogram pairs, of which 74 benign and 46 malignant lesions that were visible in both prior and current mammogram. All FFDM mammograms were downsampled to a resolution of 200 microns using bilinear interpolation.

2.2 Area and Volume Computation

The center location of each region that contained a lesion was annotated by a radiologist and was used as a seed point for automated segmentation. The segmentation method is based on the region boundary information and grey level distribution of a region of interest around the lesion. The best contour is selected using an optimisation technique known as dynamic programming. The method is explained in detail in [3].

For each pixel in the segmented region we have determined the thickness of dense tissue based on a physical model of image acquisition. The model proposed by van Engeland et al. [2] assumes that the breast is composed of two types of tissue, dense glandular tissue and fatty tissue. The attenuation of a mixture of dense and fatty tissue at a given location is given by

$$\frac{I}{I_0} = \int_{E=0}^{\infty} p(E) e^{-\mu_f(E)h_f - \mu_d(E)h_d} dE \tag{1}$$

where I is the X-ray exposure, $p(E)$ is the normalized photon energy spectrum, μ_d and μ_f are linear attenuation coefficients for dense and fatty tissue, respectively, and h_d and h_f are thicknesses of dense and fatty tissue, respectively.

Since in an unprocessed full field digital mammograms pixel values are proportional to the total exposure $I(\mathbf{r})$, the image model is obtained from (1) by replacing exposure value (I) with pixel value (g)

$$\begin{aligned} \frac{g(\mathbf{r})}{g_0} &= \int_{E=0}^{\infty} p(E) e^{-\mu_f(E)h_f(\mathbf{r}) - \mu_d(E)h_d(\mathbf{r})} dE \\ &= \int_{E=0}^{\infty} p(E) e^{-\mu_f(E)h(\mathbf{r}) - (\mu_d(E) - \mu_f(E))h_d(\mathbf{r})} dE. \end{aligned} \tag{2}$$

In this equation the normalized photon energy spectrum $p(E)$ and the attenuation coefficients $\mu_f(E)$ and $\mu_d(E)$ are known from the empirical data. Computation of the dense breast tissue thickness $h_d(\mathbf{r})$ would be straightforward if it would be possible to determine breast thickness $h(\mathbf{r})$ and the pixel value associated with the incident X-ray beam g_0. Unfortunately, it is not easy to accurately obtain estimates of these parameters in practice.

Hence, van Engeland et al. [2] applied thickness correction transform on the mammogram in which a layer of adipose tissue with attenuation coefficients $\mu_f(E)$ and thickness $H - h(\mathbf{r})$ was added to the breast. In the obtained image the following relation holds

$$\frac{\bar{g}(\mathbf{r})}{g_0} = \int_{E=0}^{\infty} p(E) e^{-\mu_f(E)H - (\mu_d(E) - \mu_f(E))h_d(\mathbf{r})} dE \tag{3}$$

In this image pixel values only vary with dense tissue thickness. By setting $h_d(\mathbf{r})$=0 in (3) image model for purely fatty tissue is obtained as

$$\frac{\bar{g}_f}{g_0} = \int_{E=0}^{\infty} p(E) e^{-\mu_f(E)H} dE. \tag{4}$$

By substituting the pixel value of fatty tissue $\bar{g}_f$ in (3) we obtain

$$\frac{\bar{g}(\mathbf{r})}{\bar{g}_f} = \frac{\int_{E=0}^{\infty} p(E) e^{-\mu_f(E)H - (\mu_d(E) - \mu_f(E))h_d(\mathbf{r})} dE}{\int_{E=0}^{\infty} p(E) e^{-\mu_f(E)H} dE} \tag{5}$$

In principle, $h_d(\mathbf{r})$ can be solved from this equation if H is known. However, due to the internal calibration with a fatty tissue pixel value, the value of H is not critical anymore.

To simplify the computations, van Engeland et al. [2] computed effective attenuation coefficients for fatty and dense tissue. The effective attenuation coefficients depend on acquisition parameters and are computed as a function of the anode and filter material, tube voltage and breast thickness H. For typical spectra used in mammographic imaging this attenuation can very well be approximated by an exponential function. As such, we obtain the logarithm of attenuation written as

$$\begin{aligned} \ln \frac{I}{I_0} &\approx -\mu_{f,\text{eff}} h_f - \mu_{d,\text{eff}} h_d \\ &= -\mu_{f,\text{eff}} (H - h_d) - \mu_{d,\text{eff}} h_d \end{aligned} \tag{6}$$

where H is breast thickness, and $\mu_{f,\text{eff}}$ and $\mu_{d,\text{eff}}$ are effective attenuation coefficients for fatty and dense tissue, respectively. By applying the exponential approximation (6) and rewriting (5) with the effective attenuation coefficients $\mu_{f,\text{eff}}$ and $\mu_{d,\text{eff}}$ the explicit dependency of H dissapears. The thickness of dense tissue at a location $\mathbf{r}$ is obtained by the following relation

$$h_d(\mathbf{r}) = -\frac{1}{\mu_{d,\text{eff}} - \mu_{f,\text{eff}}} \ln \frac{\bar{g}(\mathbf{r})}{\bar{g}_f}. \tag{7}$$

From the obtained thickness and area of the lesion we have computed its volume. For the comparative analysis of the performance of area and volume as a measure of lesion size we have computed effective radiuses as follows:

$$r_{\text{eff,area}} = \sqrt{\frac{A}{\pi}} \tag{8}$$

$$r_{\text{eff,volume}} = \sqrt[3]{\frac{3V}{4\pi}} \tag{9}$$

where A is area and V volume of the segmented region.

3 Results

The comparison of area and volume was performed for the corresponding lesions in the CC and MLO views as well as in the temporal mammogram pairs using

the effective radiuses. In order to evaluate volume compared to area in CC and MLO views we computed Pearson's correlation coefficient. The correlation plots for all data, i.e. both benign and malignant lesions, are presented in Fig. 1. The correlation coefficient between CC and MLO views for the area of a lesion is 0.70, with 95% confidence interval 0.64-0.76. The correlation coefficient between CC view and MLO view for the volume of a lesion is 0.82, with 95% confidence interval 0.79-0.86. The significance of the difference between two correlation coefficients was assessed with a two-tailed z-test. The obtained z-score was 4.03 which corresponds to the p-value of 0.0001 and shows that the difference is significant.

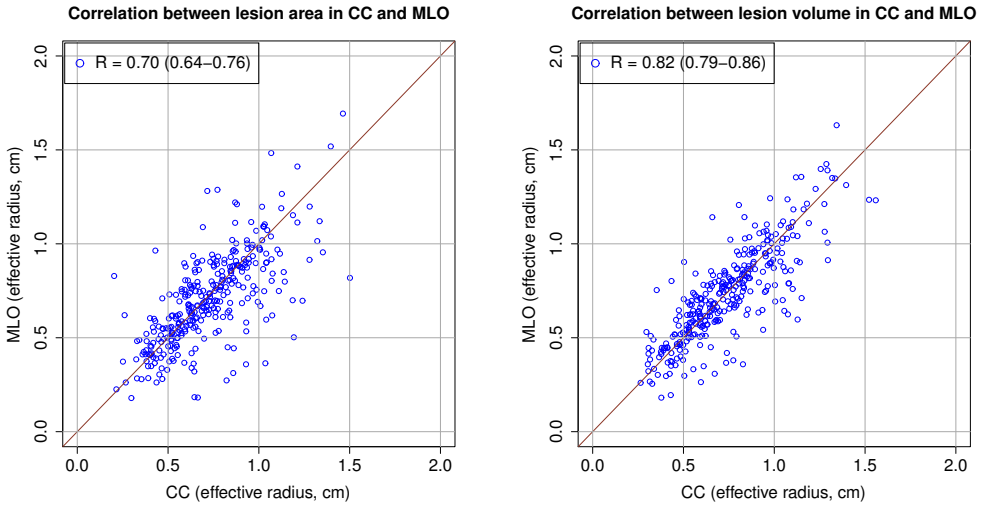

Fig. 1. Correlation for effective radiuses of lesion area and lesion volume between CC and MLO views

For the analysis of temporal mammogram pairs we used Pearson's correlation coefficient between current and prior mammogram for lesion area and volume. Correlation plots for temporal change in area and volume in subsequent screening intervals for benign and malignant lesions are presented in Fig. 2. The correlation coefficient for the area of a lesion is 0.79, with 95% confidence interval 0.68-0.86, for benign lesions and 0.63, with 95% confidence interval 0.38-0.79, for malignant lesions. The correlation coefficient for the volume of a lesion is 0.86, with 95% confidence interval 0.79-0.91, for benign lesions, and 0.69, with 95% confidence interval 0.47-0.83, for malignant lesions.

Assuming that benign lesions are stable and malignant lesions grow, we used change of lesion size as an indicator of malignancy and computed the receiver operating characteristic (ROC) curve using change in lesion size as a single

feature. The feature was computed in two ways, using size of a lesion in the current view and in the prior view obtained by

$$A_{\text{diff}} = A_{\text{current}} - A_{\text{prior}} \tag{10}$$

$$V_{\text{diff}} = V_{\text{current}} - V_{\text{prior}} \tag{11}$$

where A_{current} and A_{prior} are areas of a lesion in the current and prior view, and V_{current} and V_{prior} are volumes of a lesion in the current and prior view. ROC curves for area and volume change were plotted using the ROCR package [4] and are shown in Fig. 3. The obtained values of the area under the curve (AUC) were 0.73, with 95% confidence interval 0.62-0.82, and 0.75, with 95% confidence interval 0.66-0.85, for area and volume, respectively. However, use of volume compared to area did not show significant improvement in distinguishing between benign and malignant lesions as assessed by bootstrapping (p=0.16) using the pROC package [5].

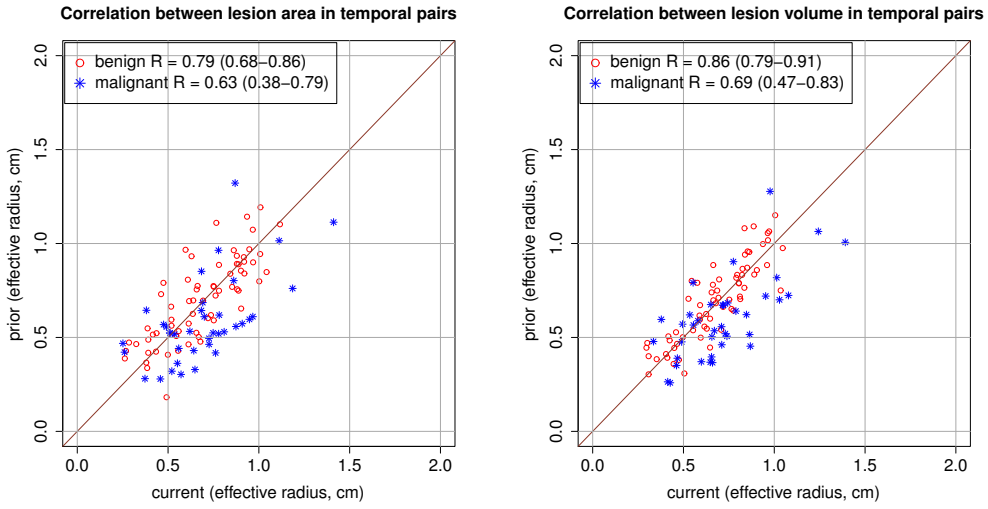

Fig. 2. Correlation for effective radiuses of lesion area and lesion volume between current and prior mammogram

4 Discussion

To the best of our knowledge this is the first paper that validates lesion volume size both in CC and MLO digital mammograms and in temporal mammogram pairs. Results showed that when comparing area and volume of a lesion in the CC and MLO views, area is less consistent between the views than volume, which

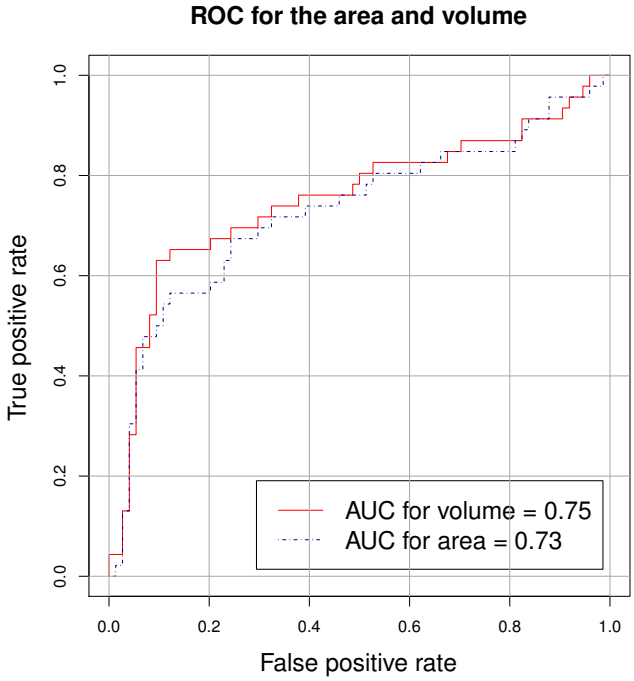

Fig. 3. ROC curves for the area and volume of a lesion

suggests that volume is a more accurate feature for assessing the size of a lesion. These results suggest that volume might be a better feature in CAD systems for measuring size of a lesion than area.

Although in the temporal analysis volume did not significantly outperform area in its performance of distinguishing between benign and malignant lesions, results indicate that it might be a better feature for representing size of a lesion.

Obviously, results depend on the lesion segmentation method that was employed. It is remarked that when lesions are embedded in fatty tissue it will not affect the volume estimates if lesions are oversegmented, as the area outside the lesion will not contribute to its volume due to the fact that in this area dense tissue thickness will be zero. This makes volume a more robust feature.

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