Title: Assessment of Breast Density Using Unsupervised Variational Autoencoders

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Abstract

About 1 in 8 U.S. women will develop breast cancer in their lifetime. Breast density is a strong indicator for breast cancer. Women with extremely dense breasts have a sixfold greater risk of developing breast cancer. This study is about the assessment of breast density by using unsupervised deep learning algorithms. I trained a variational autoencoder algorithm on 6,987 patient mammograms without any manual annotations of the dense regions of the breast. With the use of the encoder model, I was able to predict the breast density as the ratio of the fibro glandular tissue to the whole breast accurately.

Introduction

About 12% of women in the U.S. will develop invasive breast cancer over the course of their lifetime (Breastcancer.org, 2021). Breast density is about the ratio of fibroglandular tissue (FGT) in a breast, and it’s a strong indicator for breast cancer. Women with extremely dense breasts have a sixfold greater risk of developing breast cancer (Mandelson, 2000). There are currently 4 categories of breast density ranging from almost all fatty tissue to extremely dense tissue with very little fat (Mayo Clinic Staff, 2020).

Diagnostic accuracy could be improved by calculating the breast density as a ratio of the fibro glandular tissue to the whole breast. Speed of diagnosis could be improved by using a deep learning algorithm rather than waiting for a radiologist to review the mammograms. Cost of diagnosis could be minimized by avoiding the need for additional and expensive procedures such as MRI and ultrasound for less dense breasts.

Background Research

There are similar medical applications such as supervised convolutional neural networks to assess breast density from mammograms. However, they’re either doing binary classifications such as dense or not dense (Lehman, 2018), or multi-class classification such as fatty, scattered, heterogeneous, or dense (Mohamed, 2018). Those solutions don’t offer accurate information for breast density such as a specific ratio of the dense portion to the area of the breast. They also require annotations of images by radiologists to train their supervised learning algorithms.

Current proposed study will be a regression algorithm to make a solid prediction about the density of a breast in terms of a ratio of dense regions to the whole breast. Hypothesis of this study is that an unsupervised variational autoencoder (VAE) algorithm (Jordan, 2018) trained on mammograms without any annotation of breast or dense regions can generate accurate results for breast density.

Materials and Methods

In this study, 734 3D MRIs and 6,987 2D mammograms of 734 unique UCI patients were selected from 2014 to 2019. For each MRI, mammograms of the same patient from the closest possible date have been used. These MRIs and mammograms were anywhere from 1 week to 3 years apart.

The ground-truth breast density was calculated by using the segmentations of FGT in the patient's MRI. The segmentation was done by a U-Net (Ronneberger, 2015) that was trained on 238 MRIs. The breast MRIs have been resampled to a fixed 5mm slice thickness and 128x256x256 voxels. The breast mammograms have been resampled to 512x512. Both types of images were normalized by subtracting the mean and divided by the standard deviation of its respective image.

As part of image preprocessing, a separate U-Net segmentation algorithm was trained to mask the pectoralis section of breast on mediolateral oblique (MLO) images. This mask was later used to remove the armpit portion shown on breast mammograms.

Development environment included Python 3.6, TensorFlow 2.1.0, and Keras 1.0.8. The model was trained on 10 GeForce RTX Titan servers at the UCI lab.

The overall process can be summarized as:

* Train the VAE models on all mammograms
* Run encoder model prediction on each 512x512 input image
* Generate a 16x16 latent feature matrix for a patch shape of 32x32
* Clean up latent feature matrix by applying a mask from preprocessing
* Collapse masked latent matrix into a single value such as mean, median, 25th, or 75th percentile
* Correlate them with the FGT/breast ratios from U-Net on MRIs

Analysis and Results

Pearson correlation between the mean of masked latent and the original FGT/breast ratio was calculated as 0.68. Linear regression showed a mean absolute error of 0.05. The breast density (FGT/breast ratio) shown as the output y can be calculated by using the formula below, where the input *x* stands for the mean of masked latent: y = 0.23x + 0.38

Even though decoder predictions show more clear distinction between FGT and breast in lower number of features, somehow higher latent dimensions result in higher correlation. The model must be learning more about contrast in those additional features.

The data supports my hypothesis that an unsupervised deep learning algorithm such as VAE can be used to predict breast density. Even though supervised algorithms such as regular CNN and U-Net models still provide higher accuracy, radiologists need to spend a long time to annotate MRIs, CT scans, and mammograms manually. Unsupervised techniques will be the next breakthrough in the use of AI in medical diagnosis as there will be no need to annotate images anymore. This study proves that new unsupervised techniques can be used to address some of the current medical diagnosis needs.

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