

# Evaluation of Effects of HRT on Breast Density

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**Abstract.** Breast density segmentation and classification methods are combined to enable the automatic and quantitative comparison of temporal mammograms of women using Hormone Replacement Therapy (HRT). The results are based on registration and density quantification, so that potentially the clinician may be informed about substantial localised breast density changes. The measures use texture based density segmentation as well as a normalized representation of mammograms.

## 1 Introduction

Hormone Replacement Therapy (HRT) replaces the hormones a woman's body ceases to produce after the menopause. However, the use of HRT in post-menopausal women has created controversy, not least, because its effects are difficult to characterise and quantify. According to the Million Women Study in the UK [1], HRT use is associated with increased incidence and risk of breast cancer mortality, especially so for combined oestrogen-progesterone therapy. The risk increases with the duration of use and decreases after cessation. It seems that this may be due to *localised* increases in breast density, a known risk factor for breast cancer [2].

The response to HRT is specific to the individual. The changes due to HRT are neither necessarily homogeneous nor global, rather, they depend on the hormonal receptivity of the epithelial elements. Therefore, HRT use may result in density increases both locally, or in the breast pattern, globally. The changes can be characterised as:

- Tissue regeneration: increase in breast density over time.
- No change: no obvious change in breast density.
- Involution: decrease in breast density over time.

The type and degree of change depends on the receptivity of the hormones by the individual, and on the combination of hormones used. Localised tissue changes visible in a mammogram may signal the development of a new cancer, especially if breast cell proliferation occurs in high risk areas such as the Upper Outer Quadrant of the breast. For all of these reasons, there is broad consensus that women taking HRT should be monitored more carefully and more frequently

for breast cancer. Density segmentation, mammogram registration and local tissue density quantification can be incorporated into a clinical framework to assess the general effects of exogenous factors such as HRT.

The Standard Mammogram Form (SMF) representation of interesting tissue introduced by Highnam and Brady [3] is a method to normalise mammograms by calculating anatomical information from the mammogram image. In the resulting SMF image, each pixel represents the thickness of ‘interesting’ (non-fat) tissue of the compressed breast above that pixel. This effectively provides objective quantitative information about the breast anatomy. Changes of fatty to glandular tissue are precisely changes in non-fatty *i.e.* ‘interesting’ tissue. This information, combined with the information obtained using the texture-based approaches, can potentially provide both local and global quantitative information about density changes.

This paper describes how texture-based breast parenchymal density classification [4] and SMF may be combined with breast registration to enable automatic and quantitative comparison of temporal mammograms of women using HRT.

## 2 Method

Initially, the method needs to evaluate whether tissue density has changed due to use of HRT. To this end, two measures, one based on a texture-based segmented representation, the other based on the SMF representation are computed. For the texture based representation each pixel in the mammogram is replaced by the texton (texture primitive element) in the texton dictionary which lies closest to it in the texture feature space [5]. The texton value is achieved following texture classification as presented in [6]. The texton dictionary is obtained by clustering mammogram filter responses with the MR8 filter bank [6] using the following procedure: all filtered responses are aggregated over all the randomly selected training images and the k-means algorithm [7] is used to compute  $n$  cluster centres. The training test included mammograms of women using HRT and women who were not using HRT. As usual, the cases of mammograms in this training set were excluded from the test set of mammograms for which the results are presented. The measure using breast density analysis, *mean texture based difference*,

$$\Delta T_\mu = T_\mu(\text{current}) - T_\mu(\text{previous})$$

is based on evaluating the difference between the mean texton values  $T_\mu$  representing the breast area in each of the temporal mammograms. The different density classes are assigned numbers/labels  $T_l$  from 1 to  $n$ , the total number of textons used to segment the mammograms, according to the energy of the texton they represent. The mean texture based density value is given by:

$$T_\mu = \frac{1}{N_b} \sum_{i=1}^{N_b} T_l(i) \quad (1)$$

where  $N_b$  is the total number of pixels in the breast area. The second measure, *difference sum of interesting tissue*,