

Combination of various methods or modalities with diffuse optical tomography (DOT) for breast cancer imaging

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Introduction

Within the optical mammography project in Philips Research, various DOT methods are investigated. The goal is to enhance the results of DOT for breast tissue analysis and eventually to increase the sensitivity and specificity of optical mammography for breast cancer imaging.

Optical mammography: improved sensitivity by combined absorption and fluorescence analysis

The Philips optical tomography system is used in combination with a fluorescent contrast agent to enhance tumor detectability in breasts. During a measurement, transmission data at 4 wavelengths and fluorescence data for excitation at 1 wavelength are collected after injection of an optical contrast agent. The data are reconstructed into 3D images of the absorption and fluorescence distributions. Combining those images, a statistical method is investigated to enhance the sensitivity of the Philips DOT system. The linear discriminant analysis tool is employed for this purpose: at first to combine all the data in order to get more information out of the combination, then to validate the statistically suspicious regions. Here, we investigate the relevance of our method in phantom experiments.

Instrumentation

A description of the Philips scanner is presented in [1]. This scanner combines a DOT system and a fluorescent contrast agent. During a phantom measurement, the phantom is illuminated sequentially from all sides via 253 optical fibers that are mounted on the surface of the measurement cup. Another 254 fibers are used for parallel probing of the light emanating from the breast for each illumination position. The system uses near-infrared light of continuous wave solid-state lasers to illuminate the breast at four different wavelengths (690, 730, 780, and 850 nm). A complete measurement involves five scans: transmission data are collected for the four wavelengths, and fluorescence data for excitation at one wavelength. The excitation light is filtered from the fluorescent light emitted by the contrast agent. At last, the detected signals are reconstructed into three-dimensional absorption images –one image per wavelength, and into a three-dimensional image of the fluorescence emission.

The fluorescent contrast agent used in that study is called omocianine. Its absorption and emission wavelengths ranges are in the near-infrared. The third wavelength of the Philips mammography system, i.e. 730 nm, is used as excitation wavelength for the omocianine.

This study investigates 2 phantom measurements: they are performed with 2 hollow Delrin objects double-cone shaped as phantom-lesions. They are named lesion L (large) and M (medium), and have a diameter of 20 and 15 mm respectively which corresponds to volumes of 2.1 and 0.9 ml respectively. A phantom measurement is done with the cup filled with a combination of the fluorescent dye and of a fluid matching the optical properties of average breast. A phantom-lesion filled with the optical matching fluid, mixed with the same dye at a different concentration is suspended by a thin thread in the cup. This measurement situation, a lesion in a background, imitates the case of a diseased homogeneous breast with a size fitting the measurement cup. Each of the phantom-lesions is scanned with the Philips optical mammography system. To mimic the specific extravasation of the dye in the

tumor, the phantom-lesion is filled with a solution of 25 nM concentration of dye, while the concentration in the background is 5 nM.

Data classification - Proof of principle

Data classification is a statistical tool to help categorizing data [1]. The data classification is done with the Linear Discriminant Analysis (LDA) [1]. Here, the LDA classifies the voxels into one of the two groups, “lesion” and “non-lesion”, based on a set of features that describe the objects, i.e. fluorescence and absorption values of each voxel.

The voxels of a training dataset, here dataset obtained for lesion M, are labeled as “lesion” and “non-lesion”. The LDA finds a set of 5 weight factors that when applied to the absorption data at the four wavelengths and the fluorescence intensity of the training dataset, the classes “lesion” and “non-lesion” are best separated. These weight factors can then be tested on the other dataset obtained for lesion L, the test dataset. In other words, the linear combination of the test dataset lesion L and of the weight factors is calculated. This calculation returns the predictions: the voxels are predicted in the “lesion” or “non-lesion” groups. Comparing the voxels predicted as lesion and the real lesion-voxels, it is found that all the voxels in the lesion have been correctly predicted as lesion. The sensitivity of this prediction is thus 100%. The classification is able to validate the presence of the phantom-lesion.

The image resulting from the linear combination of the weight factors and the test dataset is investigated. This image will be called “combined image”. The Contrast to Noise-Ratio (CNR) of the lesion is calculated and compared to the CNR of the lesion in the absorption and fluorescence images in Table 1. The CNR is determined here by the subtraction of the average intensities in the lesion and in the background, divided by the standard deviation of the intensity in the background.

	Fluo.	Abs.690nm	Abs.730nm	Abs.780nm	Abs.850nm	“combined image”
CNR _{lesion} (+/- SD)	4.6 (+/-0.2)	2.6 (+/-0.3)	5.5 (+/-0.2)	6.8 (+/-0.2)	5.9 (+/-0.2)	-6.9 (+/-0.1)

Table 1: CNR (and its standard deviation (SD)) of the lesion in the fluorescence and absorption images of the dataset lesion L and in the “combined image” of the test dataset lesion L (classifier trained with dataset lesion M)

Table 1 shows that the CNR of the lesion calculated in the combined image is in the same range as the CNR of the lesion calculated in the absorption at 780 nm image, the best CNR calculated in the fluorescence or absorption images.

These results show that the classification of the dataset lesion L is possible using the training dataset obtained for lesion M.

The investigation of the opposite situation (training dataset obtained for lesion L, test dataset obtained for lesion M) shows that the classifier cannot predict the lesion: the sensitivity is only 3%. Therefore, this classification method needs improvement.

Optimization of the data classification

The improvement consists of optimizing the method by training several times the training dataset using the results of the prediction as label for the next training. This process is repeated 6 times. The six classifiers resulting from the six training steps were applied on the test dataset obtained for lesion M. The results of the six predictions are shown in Fig. 1.

Fig. 1 shows an important increase of the sensitivity of the classification at each iteration of the training; the sensitivity reaches quickly 100% at the third iteration. This increase in sensitivity is unfortunately coupled with a decrease in specificity, i.e. an increase in number of FP. But fortunately, after the fifth iteration, the specificity converges to a point where the training has no more influence on the classification.

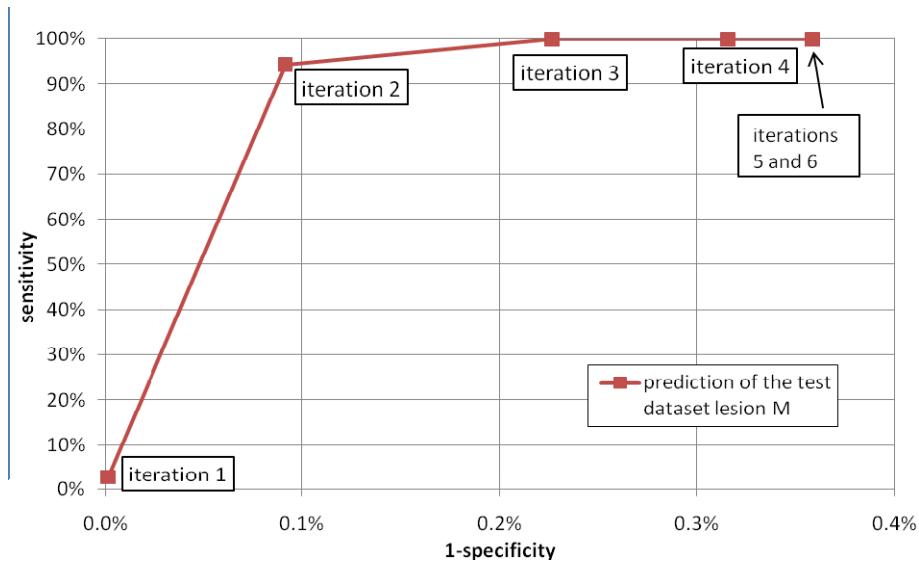


Fig. 1: “ROC curve” (sensitivity versus (1-specificity)) of the classifier trained six times.

Then, table 2 shows that the CNR of the lesion in the “combined image” (at iteration 4) is higher in absolute value than the CNR of the lesion in the absorption and fluorescence images.

	Fluo.	Abs.690nm	Abs.730nm	Abs.780nm	Abs.850nm	“combined image” Iteration 4
CNR _{lesion} (+/- SD)	2.3 (+/-0.2)	1.5 (+/-0.3)	3.5 (+/-0.2)	4.4 (+/-0.2)	3.4 (+/-0.2)	-5.0 (+/-0.1)

Table 2: CNR (and its standard deviation (SD)) of the lesion in the fluorescence and absorption images of the dataset lesion M and in the “combined image” of the test dataset lesion M (classifier trained with dataset lesion L)

As a conclusion, this optimization of the training of the classifier significantly improves the sensitivity of the classification.

Conclusion

The LDA, with specific optimizations, can validate the presence of phantom-lesions. Besides, the linear combination of the absorptions and fluorescence data using the LDA coefficients enhances the CNR of the lesion, enhancing the sensitivity of the system. The next step is to try this statistical tool in patient measurements. Ideally, the goal is to have a classifier per lesion type. It would indeed probably permit the discrimination between benign and malignant lesions by comparing the predictions of the different classifiers on the suspicious area. This could be done training various classifiers with appropriate patient datasets with different lesion types.

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References

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