Breast lesion detection using diffuse optical imaging
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Citation for published version (APA):
Leproux, A. (2012). Breast lesion detection using diffuse optical imaging

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In this thesis the results of a research project on diffuse optical imaging of breasts are presented.

Breast cancer is worldwide the most frequently diagnosed cancer in women and is the second leading cause of cancer death in women. Studies have demonstrated that early detection of breast cancer through mammography greatly improves treatment options and prognosis for recovery. X-ray mammography is currently the main screening tool used to detect breast cancer. However, this technique has several drawbacks. First, it uses ionizing radiation; regular check-up of women who have an increased risk to develop breast cancer is therefore not possible with X-ray mammography. Further, breasts are compressed during examination, which is often experienced as uncomfortable. Another problem is the high number of false positives, resulting in a large number of negative biopsies.

Diffuse optical imaging (DOI) is a non-invasive technique that provides functional information on haemoglobin, bulk lipids and water concentration by measuring near-infrared (NIR) tissue optical properties. As DOI is fast, relatively inexpensive, non-invasive and harmless, it could become an alternative or supporting technique to detect lesions and/or distinguish between malignant and benign lesions.

Philips has developed and built 2 generations diffuse optical tomography (DOT) systems for breast imaging using near infrared light, the Mammoscope and the fDOT (fluorescence diffuse optical tomography) system. Both generations of prototype scanners are in form of a bed with a cup in which a woman can position her breast. The space between the breast and the cup surface is filled with a fluid, which closely matches the average absorption and scattering properties of breasts. During a measurement, the breast is sequentially illuminated from about 250 source positions on all sides. Light emanating from the breast is detected by another set of detectors (about 250) surrounding the breast. Both systems use near-infrared light of continuous wave solid-state lasers to illuminate the breast. The detected signals are reconstructed into three-dimensional absorption images per wavelength. By combining the absorption images, information on functional properties, such as blood volume, water and lipid content, of the breast tissue can be obtained. The fDOT system can be used in combination with a fluorescent contrast agent. The contrast agent is injected intravenously. Because the blood vessels in tumors are leaky, the contrast agent tends to accumulate in tumors. The emitted fluorescence is detected and reconstructed into three-dimensional fluorescence images.
Beckman Laser Institute has developed and built a diffuse optical spectroscopy system (DOS) for breast examination, the LBS (laser breast scanner). It uses a handheld probe that measures the scattering and absorption spectra of a small volume of tissue in front of the probe over a large range of wavelengths (650 to 1000 nm). Using the absorption spectra, blood volume, water and lipid concentration can be quantified. By manually scanning the probe over the breast, maps of these functional properties can be produced.

In the first chapter of this thesis, an introduction on breast cancer and optical imaging is given. The second chapter presents a description of the instruments that have been used to collect the data that have been analyzed in this thesis, i.e. the Mammoscope, fDOT system and LBS. An overview of some of the clinical studies performed with these instruments is presented in the same chapter.

In chapter 3, the average optical properties of breast tissue are investigated in order to give insight into the optical properties of breast tissue. Using the data collected with the Mammoscope, the average attenuation of healthy breasts is compared to demographic information and the average attenuation of healthy and diseased breasts are compared. Statistically significant but weak negative correlations between the average attenuation and subjects’ age and breast volume were observed. The breast tissue optical properties vary highly between women. The results show also no significant difference in average attenuation was found between healthy breasts and breasts with cysts, benign solid lesions or malignancies. This suggests that diseased breasts cannot be distinguished from healthy breasts based on the average optical properties of the whole breast measured with the Mammoscope.

Then, in chapters 4 and 5, 2 techniques to improve lesion detection for the data collected with the fDOT system are investigated. The first described technique uses a statistical method to combine the absorption and fluorescence data from phantom measurements. With an optimized training of the statistical algorithm, voxels of test datasets were classified as healthy or malignant and phantom-lesions were therefore detected. Chapter 6 described a technique to combine absorption and fluorescence data into one graph, the scatterplot. Phantom-lesions that were missed in the fluorescence images were detected in scatterplots. Applied to 6 patients, all lesions were observed in the scatterplots. Other normal structures, such as areola, glandular tissue were identified in the scatterplot. The different rate of uptake and wash out of the contrast agent in the healthy and malignant tissues was also observed in the scatterplot.

In chapter 6, an algorithm for lesion detection was tested with data collected with the LBS. The results show that lesion detection using this algorithm is independent of any type, location and amount of normal breast tissue used for referencing. This suggests that bilateral measurement is not required for lesion detection. This also suggests that lesions can be detected in both fatty and dense breasts. This is an important result as breast lesions are difficult to detect in young and mammographically dense breast women.

The conclusions obtained from this work are summarized in chapter 8. Outlook for DOI in breast cancer research is also given.