Near-infrared structural and functional imaging of the human breast

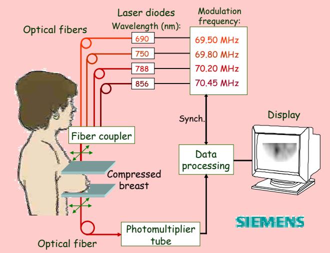
S. Fantini[1], E. L. Heffer[1], V. E. Pera[1], S. Heywang-Köbrunner[2], L. Götz[2], A. Heinig[2], O. Schütz[3], and H. Siebold[3]

[1] Bioengineering Center, Department of Electrical Engineering and Computer Science, Tufts University, Medford, MA, USA ;
[2] Martin Luther Universitaet Halle/Wittenberg, Institut für Diagnostische Radiologie und CT, Halle, Germany; [3] Siemens AG, Medical Engineering, Erlangen, Germany.

Abstract: We present a second-derivative scheme of image processing to enhance the detection of regions of higher absorbance in optical mammograms. The second-derivative images identify regions of interest for a spectral analysis aimed at measuring the oxygenation level of breast lesions. The oxygenation measurement is based on a novel approach that identifies two optimal near-infrared wavelengths. The proposed combination of structural and functional information in optical mammograms shows promise to enhance the sensitivity and specificity of this imaging modality.

I. Instrumentation, and correction for edge-effects (N-images)

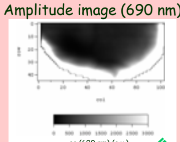
Frequency-domain instrument for optical mammography



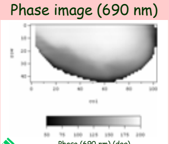
Schematic diagram of the frequency-domain research prototype developed by Siemens Medical Engineering, Erlangen, Germany, for optical mammography [1,2]. The instrument consists of four laser diodes emitting at 690, 750, 788, and 856 nm, respectively, which are intensity-modulated at a frequency of ~70 MHz. The illumination and collection optical fibers are located on opposite sides of the breast, which is slightly compressed between two parallel glass plates. The optical fibers are scanned in tandem across the breast to yield two-dimensional projection images of the phase and amplitude of the intensity-modulated light. Two projections of each breast are typically acquired: craniocaudal (the geometry illustrated in the above figure) and oblique, obtained by rotating the glass plates by 45 degrees.

Using the phase to correct for the edge effects: the *N*-parameter

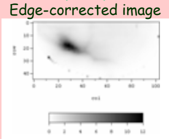
Amplitude image (690 nm)



Phase image (690 nm)



Edge-corrected image



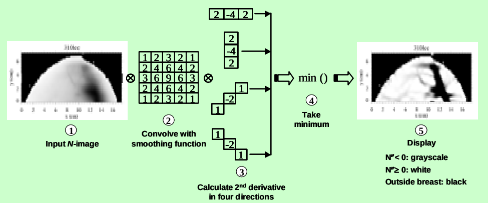
$$N(x,y) = \frac{r_0 \, ac_0}{r(x,y) \, ac(x,y)}$$

$r(x,y)$: breast thickness at pixel (x,y) [from phase measurements];
r_0: separation between glass plates;
$ac(x,y)$: amplitude at pixel (x,y);
ac_0: amplitude at reference pixel.

The amplitude and phase images at each wavelength are combined into edge-corrected (*N*) images that improve the detectability of tumors. This correction of edge effects (which are mostly due to boundary effects and reduced tissue thickness by the breast edge) is based on a normalization of the amplitude according to the tissue thickness estimated with the phase data [3].

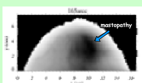
II. 2nd-derivative image processing (structural imaging)

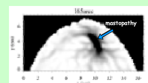
The five steps of this image-processing approach [4]



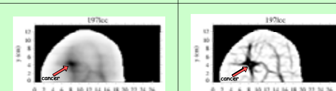
N-images (690 nm)	2nd-derivative images (690 nm)

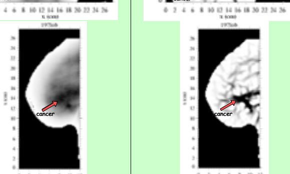
Patient No.: 165
Age: 52 y
Diagnosis: Benign mastopathy in right breast



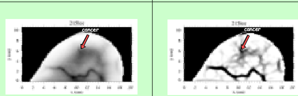


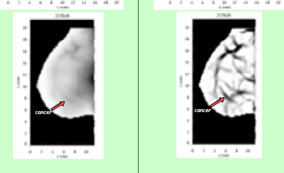
Patient No.: 197
Age: 72 y
Diagnosis: Invasive ductal carcinoma in left breast
Cancer size: 2.5 cm





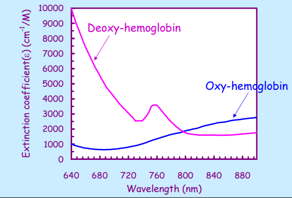
Patient No.: 215
Age: 53 y
Diagnosis: Invasive ductal carcinoma in left breast
Cancer size: 3.0 cm



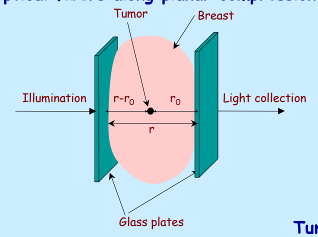


III. Spectral oximetry of detected lesions (functional imaging)

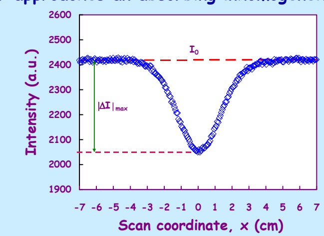
The near-infrared absorption spectrum of hemoglobin is strongly dependent on its oxygen saturation



Collinear scan of the illumination and collection optical fibers along planar compression plates



The detected intensity decreases as the optical scanner approaches an absorbing inhomogeneity (tumor)



Tumor oxygenation [5]

On the basis of the measured relative change in the intensity at two wavelengths λ_1 and λ_2, we calculate the tumor oxygenation (SO_2) from:

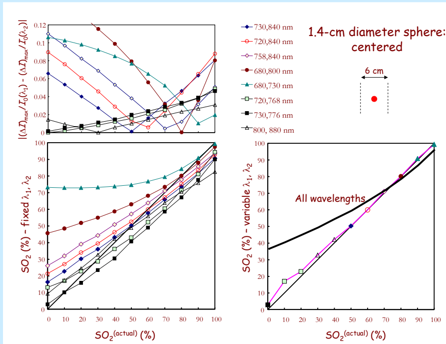
$$SO_2 = \frac{\varepsilon_{Hb}(\lambda_2) - \varepsilon_{Hb}(\lambda_1) \dfrac{\mu'_{s0}(\lambda_1)}{\mu'_{s0}(\lambda_2)} \dfrac{\Delta I/I_0|_{max}^{(\lambda_2)}}{\Delta I/I_0|_{max}^{(\lambda_1)}}}{\left[\varepsilon_{Hb}(\lambda_2) - \varepsilon_{HbO_2}(\lambda_2)\right] + \left[\varepsilon_{HbO_2}(\lambda_1) - \varepsilon_{Hb}(\lambda_1)\right] \dfrac{\mu'_{s0}(\lambda_1)}{\mu'_{s0}(\lambda_2)} \dfrac{\Delta I/I_0|_{max}^{(\lambda_2)}}{\Delta I/I_0|_{max}^{(\lambda_1)}}}$$

where ε is the molar extinction coefficient, μ'_{s0} is the reduced scattering coefficient of breast tissue, and λ_1 and λ_2 are two optimal wavelengths that:

$$\text{minimize} \left| \frac{\Delta I}{I_0}\bigg|_{max}^{(\lambda_1)} - \frac{\Delta I}{I_0}\bigg|_{max}^{(\lambda_2)} \right|$$

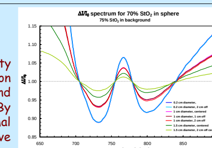
A theoretical test of the proposed approach to tumor oximetry

We tested our proposed approach to tumor oximetry in the case of a spherical inhomogeneity (tumor) embedded in a uniform turbid medium (breast tissue) using an analytical solution to the diffusion equation for this case [6], and software developed by D. Boas *et al.* [7]. We considered typical optical properties of breast tissue and a hemoglobin concentration at the tumor 60μM higher than in the background.



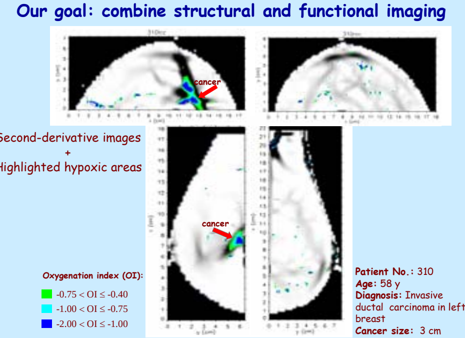
Two-wavelength oximetry vs. multi-wavelength oximetry

The spectral shape of the measured intensity depends on the tumor oxygenation but also on geometrical parameters (size, shape, and location of tumor) that are unknown. By contrast, the values of the two optimal wavelengths λ_1 and λ_2 are strongly insensitive to geometrical parameters.



Our goal: combine structural and functional imaging

Second-derivative images + Highlighted hypoxic areas



Patient No.: 310
Age: 58 y
Diagnosis: Invasive ductal carcinoma in left breast
Cancer size: 3 cm

Conclusions

- **2nd-derivative optical images provide structural imaging of the breast for:**
  - Enhanced detection of breast lesions and vasculature;
  - Identification of regions of interest to be further analyzed to assess their oxygenation.
- **Spectral data is used to identify two optimal wavelengths (λ_1 and λ_2) for tumor oximetry:**
  - The intensity perturbation associated with the tumor is the same at λ_1 and λ_2;
  - λ_1 and λ_2 depend on the tumor oxygenation but not on its geometrical parameters.
- **Combining structural and functional (oximetry) information into optical mammograms may improve the sensitivity and specificity of this imaging modality**

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