Diffuse optical spectroscopic imaging of the human lactating breast

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Abstract: Breastfeeding plays a crucial role in public health, but relatively few imaging and sensing technologies are employed to study human lactation physiology. As a consequence, many breastfeeding problems are not well understood. We hypothesize that diffuse optical spectroscopic imaging (DOSI) can potentially reveal important physiological parameters that help to define milk synthesis and secretion: glandular tissue content, hemodynamics and milk ejection. The aim of this study is to investigate the sensitivity of DOSI to these physiological parameters in (i) a case study (1 subject) on mammary involution of the lactating breast to its pre-pregnant state and (ii) a pilot study during milk extraction with a breast pump (4 lactating subjects, 5 non-lactating subjects). For the case study, the measured changes in the DOSI parameters (water, lipid, hemoglobin concentration) were consistent with the gradual replacement of fibro-glandular tissue by adipose tissue and vascular regression during mammary involution. For the pilot study, the measured changes in the DOSI parameters correlated with the extracted milk volume and occurrence of the milk ejection reflex. In conclusion, DOSI is sensitive to human lactation physiology, which can potentially aid to obtaining an in-depth understanding on the origin and treatment of breastfeeding problems.

1. Introduction

Breastfeeding plays a crucial role in public health, as it protects the short and long term health outcomes of both mother and infant[1,2]. Yet, breastfeeding rates are lagging behind. In 2019, only 41% of infants worldwide were exclusively breastfed in the first 6 months of life[3]. According to the Global Nutrition Targets of the World Health Organisation (WHO) and the United Nations Children's Fund (UNICEF)[3], this number should be 70% in 2030. Lactation insufficiency (suboptimal milk supply) contributes significantly to suboptimal breastfeeding rates: 40-50% of breastfeeding mothers stops due to a perception of insufficient milk supply[4], of whom an estimated 10-15% actually fails to produce enough milk[5]. An in-depth understanding of the role of mammary physiology in milk synthesis and secretion is essential in solving this problem[5], but dedicated techniques are lacking to fill this knowledge gap. We hypothesize that diffuse optical spectroscopic imaging (DOSI) can potentially reveal the most important physiological parameters that together define milk synthesis and secretion. Water and lipid concentrations relate to mammary tissue composition[6] and milk content, whereas changes in hemoglobin concentrations relate to mammary hemodynamics, as well as occurrence of the milk ejection reflex[7]. The latter is defined as the active ejection of milk through the nipple upon a temporary increase in oxytocin, a vasodilator[8]. The aim of this study was to investigate the sensitivity of DOSI to these physiological parameters on human lactating subjects in (i) a case study on mammary involution of the lactating breast to its pre-pregnant state and (ii) a pilot study during milk extraction with a breast pump.

2. Methods

2.1 DOSI system and signal processing

Full details on the DOSI system and signal processing can be found in reference [9]. In brief, broadband near-infrared spectroscopy (NIRS) and frequency domain photon migration spectroscopy at four wavelengths (FDPM, modulated at 50-500 MHz) were combined into a handheld, fiber-coupled probe. This enabled diffusion model based estimates of tissue optical properties (absorption μ_a, and reduced scattering μ_s' coefficient spectra, λ = 650–1000 nm) at a single source-detector separation of 28 mm. The individual DOSI parameters ([water], [lipid], oxyhemoglobin [HbO2], deoxyhemoglobin [Hb] concentration) were obtained by fitting their known molar extinction coefficient spectra to the acquired tissue absorption coefficient spectrum. Total hemoglobin and oxygen saturation are calculated using $[tHb] = [HbO_2] + [Hb]$ and $StO_2 = [HbO_2]/[tHb]$. Optical scattering was characterized

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by parameterizing the reduced scattering spectrum as $\mu_s' = a(\lambda/500)^{-b}$, where a is a scattering prefactor that indicates the reduced scattering coefficient at λ=500 nm and b is the scattering power which describes the wavelength dependence of scattering. DOSI 2D-breast scans were obtained from sequential measurements in a grid pattern (10 mm spacing) on the breast. A second fiber-optic monitoring probe was developed to measure DOSI signal changes during milk extraction. This probe was attached to the breast and connected to the NIRS and FDPM modules of the DOSI hardware, resulting in a time dependent measurement at a single breast location (sampling frequency ~0.3Hz).

2.2 Case study on mammary involution

We studied the longitudinal changes in tissue composition in the left breast of a subject (age 37) upon ceasing breastfeeding after a lactation period of 14 months. A total of 9 DOSI scans were made over a period of 237 days (8 months). The subject did not breastfeed or extract any milk during this period. Ethical approval was obtained from the IRB of the University of California, Irvine (#1995-563) and the participant gave written informed consent.

2.3 Pilot study during milk extraction

In 4 lactating subjects, we made a DOSI scan of one breast directly before and after milk extraction. During milk extraction, we recorded the DOS (diffuse optical spectroscopic) signal at a single location. Cumulative weight of the extracted milk was recorded with a digital scale. The same measurements were repeated on a control group of 5 non-lactating subjects (no milk extraction), to assess reproducibility. Ethical approval was obtained from the CMO Arnhem-Nijmegen (#2019-5610) and all participants gave written informed consent.

3. Results and discussion

3.1 Case study on mammary involution

Results for the case study on mammary involution are shown in Figure 1. Significant changes were observed for all DOSI parameters over time (non-parametric statistical analysis, $p < 0.05$). The relative changes in mammary water content (-50%) and lipid content (+59%) between day 0 and 237 are consistent with the gradual replacement of glandular tissue by adipose tissue during the involution process. The relative change in THb content (-48%) implies a decrease in mammary blood volume, which can be ascribed to vascular regression during mammary involution. The more modest 11% difference in StO_2 is supported by similar StO_2 levels between fibroglandular and adipose tissue in the breast[9].

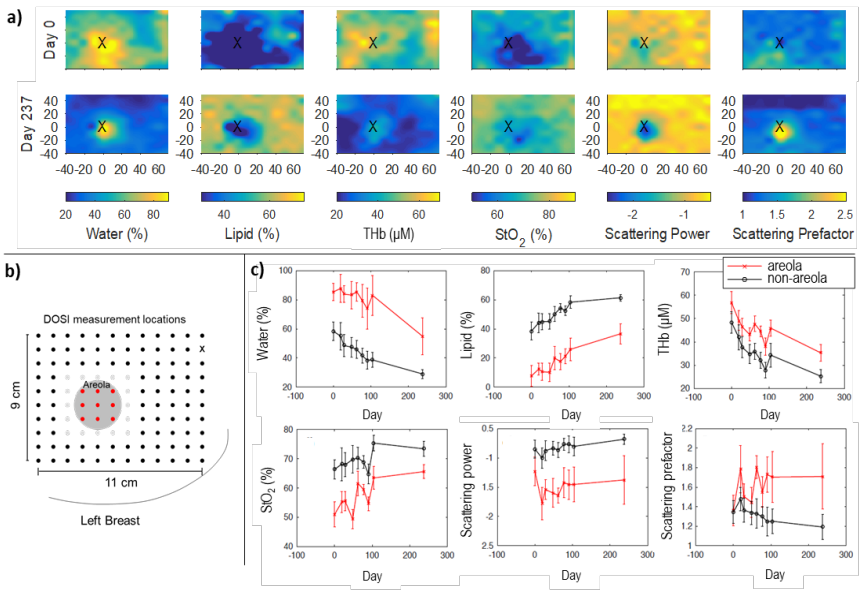

Figure 1. Spatiotemporal changes in DOSI parameters during mammary involution. a) 2D maps for the spatial distribution of all DOSI parameters at day 0 and day 237 (days in between not shown). X marks the position of the nipple. b) Schematic of the measurement grid on the breast. c) Median DOSI parameters versus time for the areolar and non-areola region.

3.2 Pilot study during milk extraction

Results for one of the lactating subjects in our pilot study during milk extraction are shown in Figure 2. Fig. 2b demonstrates how two DOSI parameters (water and lipid) vary both spatially over the scanned breast area, as well as in time (before/after milk extraction). The high density of water-rich glandular tissue in the areolar region (Ar), is confirmed by high water, and low lipid concentrations. The decrease in water concentration after milk extraction in the areolar region can be ascribed to milk removal. Fig. 2c shows the time-dependent behaviour of all DOSI parameters (except scattering) for a point measurement at location P (Fig. 2a) during milk extraction. Milk flow rate was acquired simultaneously from the cumulative milk weight. Only the first milk ejection reflex (MER1) was

sensed by the subject and subsequent MER's (magenta lines) were identified by a sharp increase in milk flow rate[10]. These data demonstrate that all DOSI parameters show a higher degree of variation during pumping, than before/after pumping (excluding the movement artifact at t=1 min). Similar to previous near-infrared spectroscopy (NIRS) studies[7], MER's are accompanied by a brief decrease in [tHb], followed by an increase. Furthermore, an increase in milk flow rate is accompanied by an increase in lipid concentration. On a more subtle scale, also water and StO_2 show a correlation with milk flow rate.

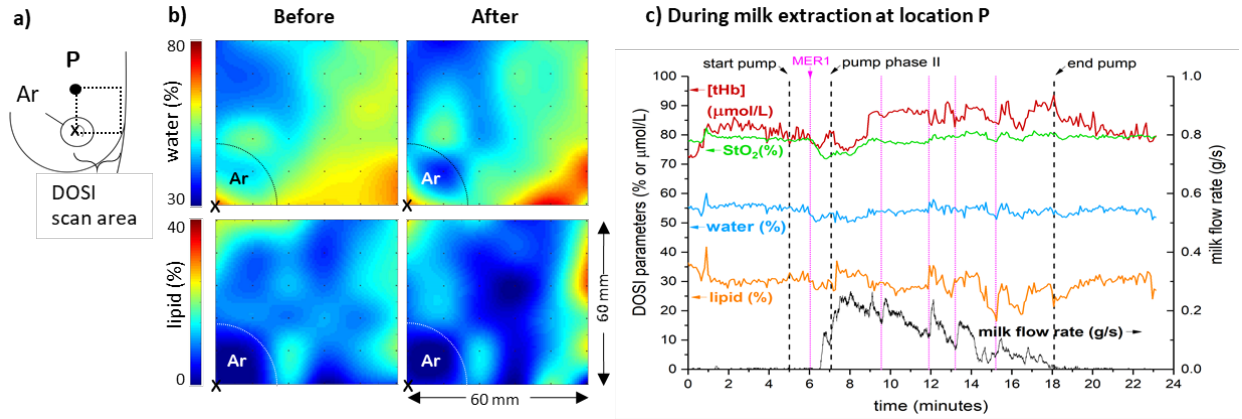

Figure 2. Spatiotemporal changes in DOSI parameters during milk extraction. a) Schematic for data acquisition from the left breast of a lactating subject before, after and during milk extraction. X nipple location, Ar areola, P location for time-dependent DOSI measurement. b) Water and lipid distribution before and after milk extraction. c) Time-dependent DOSI measurement during milk extraction. Pumping was started at t = 5 min with high frequent vacuum changes to evoke the first milk ejection reflex (MER1). Pump phase II less frequent vacuum changes for milk extraction. Pumping was stopped at t = 18 min. Milk flow rate was derived simultaneously from the cumulative extracted milk weight. Subsequent MER's are marked with vertical magenta lines.

4. Conclusion

In conclusion, DOSI is sensitive to a variety of parameters that are relevant in studying human lactation physiology. These parameters include mammary tissue composition (glandular/adipose tissue content, blood content), hemodynamics/milk ejection (changes in blood content) and milk content (changes in water/lipid content). A more elaborate evaluation is needed to assess the full potential of the technology for lactation research. This study introduces a highly relevant new application field for DOSI, as an in-depth understanding of lactation physiology will contribute to better treatment of breastfeeding problems – in particular lactation insufficiency.

5. References

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