Preliminary Evidence of the Efficacy of Time-Resolved Broad-Spectrum Optical Mammography in Monitoring Neoadjuvant Chemotherapy

Giulia Maffeis[1,*], Nikhitha Mule[1,2], Carolina Santangelo[2], Rinaldo Cubeddu[1], Antonio Pifferi[1,3], Pietro Panizza[2] and Paola Taroni[1,3]

[1]Politecnico di Milano, Dipartimento di Fisica, Piazza Leonardo Da Vinci 32, 20133, Milano, Italy;
[2]Scientific Institute (IRCCS) Ospedale San Raffaele, Breast Imaging Unit, Via Olgettina 60, 20132, Milano, Italy;
[3]Consiglio Nazionale delle Ricerche, Istituto di Fotonica e Nanotecnologie, Piazza Leonardo da Vinci 32, 20133, Milano, Italy;
**giulia.maffeis@polimi.it*

Abstract: We present initial results of a clinical trial involving breast cancer patients under neoadjuvant chemotherapy, monitored through our time-resolved optical mammograph. Besides hemoglobin, water and lipids, we assess collagen concentration systematically for the first time.

1. Introduction

NeoAdjuvant Chemotherapy (NAC) is more and more recommended as initial treatment for locally advanced and large breast tumors [1]. Together with a more efficient chirurgical approach due to tumor reduction, NAC allows also for the evaluation of the treatment efficacy through sequential imaging and biopsies. The correlation between clinical monitoring and patient's final response offers the unique opportunity to estimate the predictive potential of the tumor initial features. In the long run, that would enable personalized therapeutic plans.

Optical mammography has already been proposed as a potential tool for NAC monitoring and prediction of therapy outcome, given its capability to assess breast tissue composition non-invasively. In literature, it is reported that the tumor's hemoglobin, water and lipid contents change differently in responders and non-responders. Moreover, the therapy efficacy could depend on the initial breast constituents' concentrations [2].

In this work, we present the initial results of NADOPTIC. It is a clinical trial hold at San Raffaele Hospital (Milan, Italy) involving NAC patients monitored through our time-resolved multi-wavelength optical mammograph, together with conventional imaging. Our aim is to retrospectively evaluate the consistency of the two approaches. Our broad spectral range (635-1060 nm) enables collagen assessment, which has never been systematically studied during NAC so far.

2. Materials and methods

2.1 Clinical protocol

The clinical protocol envisions 6 different measurement sessions throughout the treatment (5/6 months duration): just before the first infusion (*i.e.* baseline), 2/5 days after the first infusion, 6/8 days after, 2 weeks after, approximately at mid-therapy and after the final infusion (just before surgery). Some flexibility is granted to adapt to the patients' needs. At every session, we perform 4 acquisitions: cranio-caudal right and left, oblique right and left.

So far, 5 patients have joined the trial, after signing the informed consent. All of them responded at least partially to NAC: initially the tumor sizes range was 28-70 mm, the final range 0-25 mm.

2.2 Instrument

Our optical mammograph includes 7 picosecond lasers, from 635 to 1060 nm [3]. It operates in time domain and in transmission mode. Light raster scans the mildly compressed breast and then it is collected by a SiPM-based detector (S13360-1350PE, Hamamatsu Photonics, Japan) along the line of sight. A Time-to-Digital Converter (MultiHarp 150 8N, PicoQuant, Germany) takes care of Time-Correlated Single Photon Counting. The measure is run by a PC.

2.3 Data analysis

The extension of the tumors is compatible with the application of a spectrally-constrained homogeneous model of the diffusion equation, under the diffusion approximation, for a slab medium. Average constituent concentrations

have been retrieved over a rectangular region of interest enclosing an approximately homogeneous portion of tumor or healthy tissue in mirror position on the contralateral breast.

3. Results

Fig. 1 summarizes results about variations in breast tissue composition during NAC for all patients. When the therapy is effective, we expect the tumor fibrous tissue to reduce, in favor of adipose tissue. Indeed, we can observe a decreasing trend in the tumor hemoglobin, water and collagen content and an increasing one in lipids for all patients. Trends are less definite and slower for limited nodule shrinkage (*e.g.* patient P3), while variations are stronger for patients with initially larger tumors and wider size contraction (*e.g.* P1, P5). In particular, P5's blood absorption at baseline is so high, that the analytical model underestimates it. Besides, we notice that the healthy tissue behavior is not always stable, but it might exhibit trends as well, which could be due to the systemic nature of NAC.

Results suggest that collagen could play a meaningful role: it reduces almost monotonically of 32-57% from the first to the last session for all patients, which suggests it as a possible biomarker for NAC efficacy.

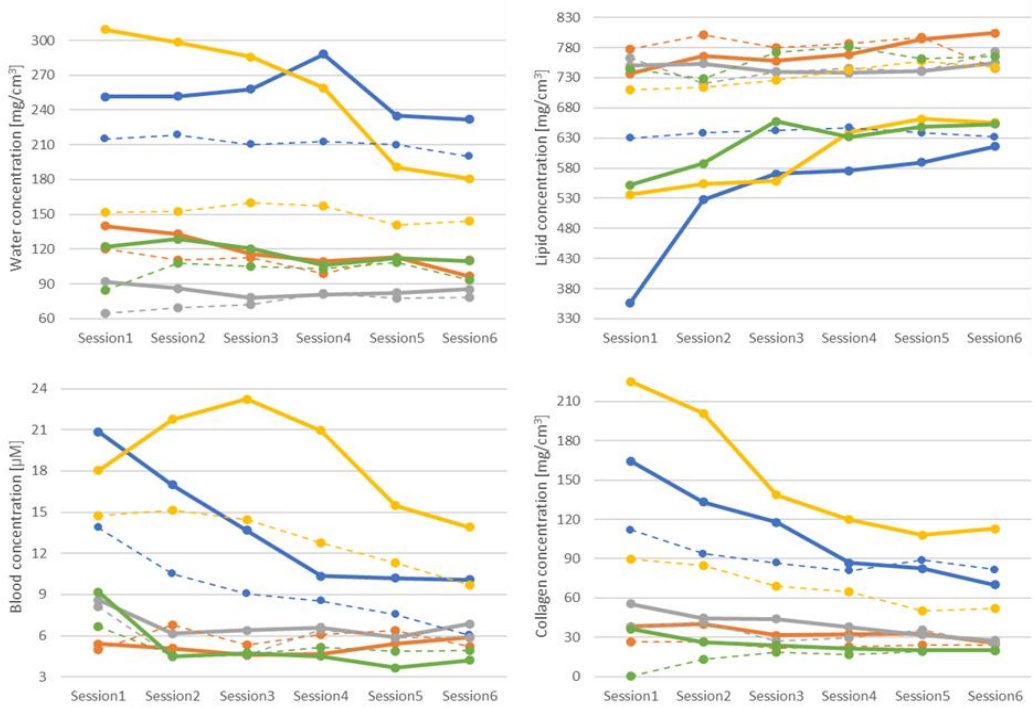

Fig. 1. Water, lipid, hemoglobin and collagen concentrations for cranio-caudal view over sessions for P1 (blue), P2 (green), P3 (orange), P4 (gray), P5 (yellow). Solid lines refer to the tumor composition, dash lines to the healthy tissue on the contralateral breast.

In conclusion, optical results seem to be consistent with medical findings and hint that we should further investigate collagen in upcoming patients.

4. Acknowledgements

The work was partially funded by Fondazione Umberto Veronesi and H2020-MSCA-ITN PHAST (Grant No. 860185).

5. References

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