Original Investigation

Optical Mammography in Patients with Breast Cancer Undergoing Neoadjuvant Chemotherapy: Individual Clinical Response Index

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Abbreviations and Acronyms

[Hb] concentration of deoxyhemoglobin

[HbO_2] concentration of oxyhemoglobin

[HbT] concentration of total hemoglobin

CRI cumulative response index

Hgb hemoglobin concentration in blood

MRI magnetic resonance imaging

NAC neoadjuvant chemotherapy

NACP neoadjuvant chemotherapy patient

NR nonresponders

pCR pathologic complete response

PET/CT positron emission tomography-computed tomography

Rationale and Objectives: We present an optical mammography study that aims to develop quantitative measures of pathologic response to neoadjuvant chemotherapy (NAC) in patients with breast cancer. Such quantitative measures are based on the concentrations of oxyhemoglobin ([HbO_2]), deoxyhemoglobin ([Hb]), total hemoglobin ([HbT]), and hemoglobin saturation (SO_2) in breast tissue at the tumor location and at sequential time points during chemotherapy.

Materials and Methods: Continuous-wave, spectrally resolved optical mammography was performed in transmission and parallel-plate geometry on 10 patients before treatment initiation and at each NAC administration (mean number of optical mammography sessions: 12, range: 7–18). Data on two patients were discarded for technical reasons. The patients were categorized as responders (R, >50% decrease in tumor size), or nonresponders (NR, <50% decrease in tumor size) based on imaging and histopathology results.

Results: At 50% completion of the NAC regimen (therapy midpoint), R (6/8) demonstrated significant decreases in SO_2 (–27% ± 4%) and [HbT] (–35 ± 4 μM) at the tumor location with respect to baseline values. By contrast, NR (2/8) showed nonsignificant changes in SO_2 and [HbT] at therapy midpoint. We introduce a cumulative response index as a quantitative measure of the individual patient's response to therapy. At therapy midpoint, the SO_2-based cumulative response index had a sensitivity of 100% and a specificity of 100% for the identification of R.

Conclusions: These results show that optical mammography is a promising tool to assess individual response to NAC at therapy midpoint to guide further decision making for neoadjuvant therapy.

Key Words: Optical mammography; near-infrared spectroscopy; breast cancer; neoadjuvant therapy.

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PR1
partial response 1

R
responders

ROI
region of interest

SO_2
hemoglobin saturation

TNBC
triple-negative breast cancer

INTRODUCTION

Neoadjuvant Chemotherapy (NAC)

NAC is administered to patients before surgery in an effort to reduce the primary tumor size, whereas adjuvant chemotherapy is administered following surgery in an effort to reduce the risk of residual disease and cancer recurrence. A patient's response to NAC may be assessed by physical examination or breast imaging (clinical response), or by histology post surgery (pathologic response) (1,2). Assessing response to neoadjuvant treatment is crucial, as a pathologic complete response (pCR), defined as having no residual carcinoma in the resected breast tissue and in axillary lymph nodes, has been associated with improved survival (2–5). Strictly defined, pCR requires the absence of invasive tumor in the resected specimen, although some clinicians use the more restrictive requirement of no residual invasive or in situ disease (3). Because of the better outcome associated with pCR, finding tools that can define the individual clinical response during the course of therapy and accurately predicting pathologic response would be of great benefit. This is also true in patients with poor response to treatment, as early identification of this problem may allow the physician to alter the chemotherapy regimen to avoid disease progression and to identify a more effective chemotherapy option.

Imaging Modalities Under Investigation to Monitor Therapy Response

Imaging methods sensitive to functional tissue changes are being investigated for monitoring breast cancer patients' response to NAC. Functional tumor changes are of particular interest because of the limitations of structural assessment of tumor response based on physical examination, ultrasound imaging, or mammography (6). Current imaging methods used to assess clinical response are via a decrease in the standard uptake value of 18-fluorodeoxyglucose by positron emission tomography-computed tomography (PET/CT) (7,8), or a decrease in tumor size by contrast-enhanced magnetic resonance imaging (MRI) (7,8). Both of these methods, however, are expensive and invasive, as PET/CT requires an injection of a radiopharmaceutical, and MRI requires an injection of a gadolinium-based contrast agent. Furthermore, the appropriate timing and frequency for assessing clinical response have not been established, and studies thus far have typically imaged at a single time point during therapy (7,8).

Optical mammography utilizes light in the wavelength range of 650–1000 nm to sense the absorption and scattering properties of breast tissue. Diffuse optical imaging techniques have intrinsically low spatial resolution (on the order of 1 cm); however, this is not a limiting factor in a study on patients undergoing NAC, as they often have large palpable tumors that are several centimeters in size. Functional tissue information can be obtained by recovering the concentrations of oxyhemoglobin, deoxyhemoglobin, water, and lipids (denoted in the text as [HbO_2], [Hb], [H_2O], and [lipid], respectively) based on the wavelength-dependent absorption of light in breast tissue (9). Scattering amplitude and scattering power can also be measured, which relate to the size and density of the scattering centers in tissue (9). Optical breast imaging approaches have been developed using a handheld probe for diffuse reflectance measurements (10–17), a circular arrangement of optical fibers around the pendulous breast (18–21), or a parallel-plate, planar geometry for transmission measurements on the mildly compressed breast (22–29). Quantification of breast tissue optical properties may be performed using homogeneous models (10,12,14,15,17,24), which yield average measurements over the interrogated tissue volume, or perturbation approaches (23,29) and tomographic reconstructions (11,13,16,20–22,25–28), which yield spatially resolved measurements. Homogeneous models are not able to accurately recover the localized tumor properties because they provide the overall optical properties of the probed breast volume, which may be composed of both cancerous and healthy tissues. However, the approach based on homogeneous models benefits from being robust against measurement errors and able to provide fewer, but more reproducible, parameters; these are two important features for a longitudinal study where patients are imaged at multiple time points during NAC.

Following initial case studies that first demonstrated the optical approach (17,30,31), several groups have investigated optical methods to assess response to treatment in patients with breast cancer undergoing neoadjuvant therapy. Studies aiming to predict therapeutic response early in the treatment have shown significant differences between responders