Multispectral reflectance enhancement for breast cancer visualization in the operating room

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ABSTRACT

A color enhancement method to optimize the visualization of breast tumors in cancer pathology is proposed. Light scattering measurements are minimally invasive, and allow the estimation of tissue morphology and composition to guide the surgeon in resection surgeries. The usability of scatter and absorption signatures acquired with a micro-sampling reflectance spectral imaging system was improved employing an empirical approximation to the Mie theory to estimate the scattering power on a per-pixel basis. The proposed methodology generates a new image with blended color and diagnostic purposes coming from the emphasis or highlighting of specific wavelengths or features. These features can be the specific absorbent tissue components (oxygenated and deoxygenated hemoglobin, etc.), additional parameters as scattering power or amplitude or even the combination of both. The goal is to obtain an improved and inherent tissue contrast working only with the local reflectance of tissue. To this aim, it is provided a visual interpretation of what is considered non-malignant (normal epithelia and stroma, benign epithelia and stroma, inflammation), malignant (DCIS, IDC, ILC) and adipose tissue. Consequently, a fast visualization map of the intracavity area can be offered to the surgeon providing relevant diagnostic information. No labeling or extrinsic indicators are required for proposed methodology and therefore the possibility of transferring absorption and scattering features simultaneously into visualization, fusing their effects into a single image, can guide surgeons efficiently.

Keywords: breast tumor; localized backscattering; multispectral enhancement; principal component analysis; hemoglobin absorption; inherent tissue contrast

1. INTRODUCTION

Identification of tumor margin in breast conserving surgery is still an issue in the intraoperative context. Breast Conserving Therapy (BCT) continues as one of the regular therapies for patients with early invasive breast cancers [1]. However, its major limitation is the current inability to accurately assess tumor margins. Margin assessment is routinely conducted post-operatively by standard histology, but an intraoperative alternative lacks standardization. Any effort in this sense could avoid recurrent tumors that reduce the patient's prognosis and increase the psychological effects of mastectomy and/or repeated surgery, as well as the risk and costs of reappearance of the disease.

Here, scatter-imaging signatures and enhancement of spectral absorption features with physiological meaning have been used to improve tumor contrast. The idea is to provide a tumor contrast tool based solely on the multispectral data acquired with a quasi-confocal fiber optic system. No additional labeling, exogenous particles or numerical classification algorithms are required to enhance the tissue contrast. Only reflectance data is employed for the visualization of tumor tissue. The multispectral enhancement procedure has been applied before [2] to data from a 16-band multispectral camera for different applications: enhancement of a skin image, automatic grading of hematoxylin and eosin staining images and the analysis of rice paddy images. Here, the method is applied to a dense spectral data set of localized reflectance from breast tissue.

The ultimate goal of this work is to provide a map to guide tumor resection. This image has to be as simple as possible to be usable by oncological surgeons. The map will be obtained from the intrinsic enhancement of the reflectance spectral data. Combination of absorption and scattering events will play a role in tumor delineation. This way, the initial enhancement procedure has been modified in this work to incorporate also scattering features.

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2. MATERIALS AND METHODS

2.1 Localized reflectance and scattering model

Surgical breast tissue specimens were imaged with a custom-built micro-sampling reflectance system [3] consisting of a quasi-confocal spectroscopic set-up (510:785 nm, 1 nm resolution) and a raster-scanning sampling system. The system constrains the overlapping illumination and detection spot sizes within approximately one scattering distance in tissue (~100 μm in the visible). Tissue samples were hydrated with a phosphate buffer solution during the measurement procedure. The background response, $R_{bkgrd}(\lambda)$, is subtracted from the measured spectra, $R_{acquired}(\lambda)$, and the data is normalized, $R(\lambda)$, with respect to a diffuse reflectance standard (Spectralon, Labsphere, Inc., North Sutton, New Hampshire) to allow comparison between tissue specimens.

An empirical approximation to Mie theory and a Beer's Law attenuation factor is applied to describe the reflectance, $R(\lambda)$ [4], as shown on (Eq.1).

$$R(\lambda) = A\lambda^{-b} \exp^{-\Gamma*[HbT]\{StO_2*\varepsilon_{HbO_2}(\lambda)+(1-StO_2)*\varepsilon_{Hb}(\lambda)\}} \quad (1)$$

where Γ refers to the mean optical pathlength (dependent on the illumination and detection geometry), $[HbT]$ is the total hemoglobin concentration, StO_2 is the oxygen saturation factor (ratio of oxygenated to total hemoglobin), ε_{HbO_2} and ε_{Hb} refer to the molar extinction coefficients of these two chromophores, respectively (Oregon Medical Laser Center Database, [5]); A and b are the scattering amplitude and the scattering power and both depend on the size and number density of scattering centers in the tissue. According to previous studies [6], the scattering power parameter, b, provides the best tissue discrimination capability.

Table 1 shows the distribution of the Regions of Interest (ROIs) imaged over tissue [4] where 42 different ROIs, corresponding to 3 different diagnosis categories, were diagnosed: non-malignant (normal epithelia and stroma, benign epithelia and stroma, inflammation), malignant (DCIS, IDC, ILC) and adipose.

Table 1. Distribution of the analyzed categories of breast tissue.

Tissue type	No of ROIs
Non-Malignant	19
Malignant	12
Adipose	11
Total ROI	**42**

2.2 Image recovery from the localized reflectance

Towards the goal of providing a usable guide to surgeons, a digital color reproduction of the spectroscopic breast tissue information (510:785 nm) is generated. The alternative color representation of breast data is created by using a color-matching function (CMF) such us CIE 1931 2º XYZ CMF [7], an illumination spectrum such as D65 [7] and a matrix for XYZ to RGB transformation. To this end, a color stimulus is created as a function of tissue reflectance $R(\lambda)$ and it is converted into tristimulus values XYZ through the color matching functions$(\bar{x},\bar{y},\bar{z})$. At the final step, XYZ coordinates were transformed into RGB coordinates for a standard digital color reproduction.

2.3 Multispectral enhancement method

The proposed method works with the multispectral, almost hyperspectral, tissue reflectance data enhancing specific spectral features. These features are translated into a user-defined color representation and superimposed to the color image generated from tissue reflectance. The method is based on Hashimoto's work [2] whose process is displayed in Fig.1. In an initial step, the original breast data is approximated by the *m*-KL vectors, also known as principal components, to obtain a description of tissue as a function of its highest spectral variance. An adaptive threshold method [8] has been selected for vector selection.

After that, the estimated dataset is subtracted from the original one and the difference is enhanced. The key issue of the enhancement process is the so-called weighting factor matrix **W**. This matrix allows intensifying by a factor *k* a specific wavelength of the data set to observe its impact over the whole tissue color representation. In this work, the selected features are those related with the tumor-associated angiogenesis: oxygenated and de-oxygenated hemoglobin presence at 542, 576 and 556 nm [5]. Once the feature is enhanced, it is combined with the original data set and a final digital color representation is again generated.

Different color strategies can be used to enhance a specific wavelength: the corresponding color in the spectral range or a color specified by the user through its RGB coordinates.

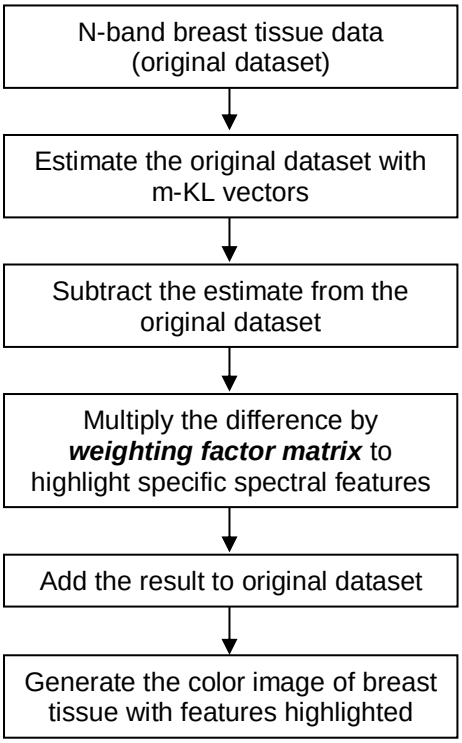

Figure 1. Color enhancement process [2] applied to breast tissue data.

2.4 Scattering embedded enhancement method

The proposed modification consists in the incorporation of the estimated scattering parameters (*b*, power and *A*, amplitude) into the breast tissue multispectral data set. These scattering parameters are considered now as "virtual" or "fictitious" wavelengths located far away from the measurement spectral range (510:785 nm). The scattering power becomes located at 430 nm and the scattering amplitude at 460 nm. In this sense, the data set appears enlarged, but the general procedure of enhancement becomes maintained. The main advantage of this modification is the ability of combining both absorption and scattering enhancement over the same tissue sample in order to get a better contrast in the identification of tumor.

3. RESULTS AND DISCUSSION

One of the main goals of this proposal is to validate the contrast ability of the color representation of a multispectral reflectance data set. Fig.2 shows one of the breast tissue samples when a conventional color image obtained from a digital camera (Fig.2a) is compared with the color image recovered from the reflectance data (Fig.2b). On the reflectance image, the cyan circle delimits adipose tissue whereas the grey circle demarcates the presence of ILC tumor tissue. In the reflectance image (Fig.2b) more contrast is obtained around the tumor area being able to see hidden structures in tissue.

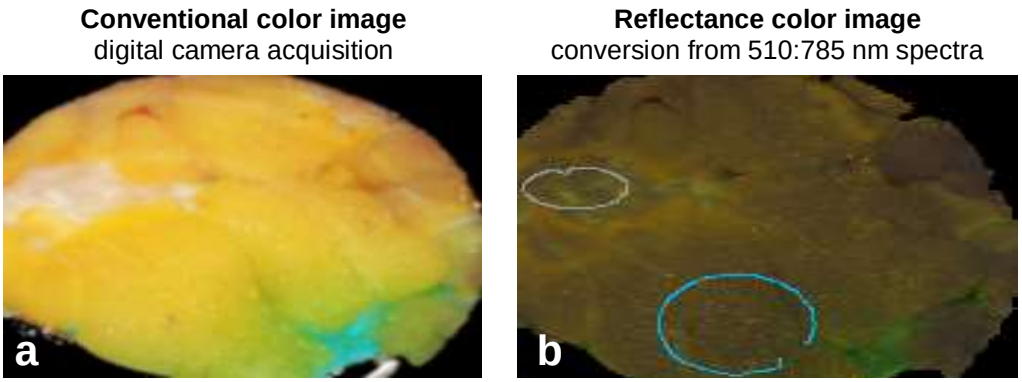

Figure 2. Breast tissue sample with ILC (grey circle) and adipose tissue (cyan circle): (a) color image from a digital camera; (b) color image recovered from the multispectral reflectance data (510:785 nm).

When absorption features related with the angiogenesis process are considered, Fig. 3, the contrast between adipose and ILC tissue becomes more evident than in Fig.2b. Few differences could be observed between the deoxygenated and the oxygenated hemoglobin intensification. However, in both cases tumor tissue appears with a greener shade due to the selection of green for the enhancement visualization improving the contrast when compared with the reference reflectance color image (Fig.2b). The presence of hemoglobin seems to be distributed within the inner area of tumor, whereas there is no presence of hemoglobin in the adipose tissue area.

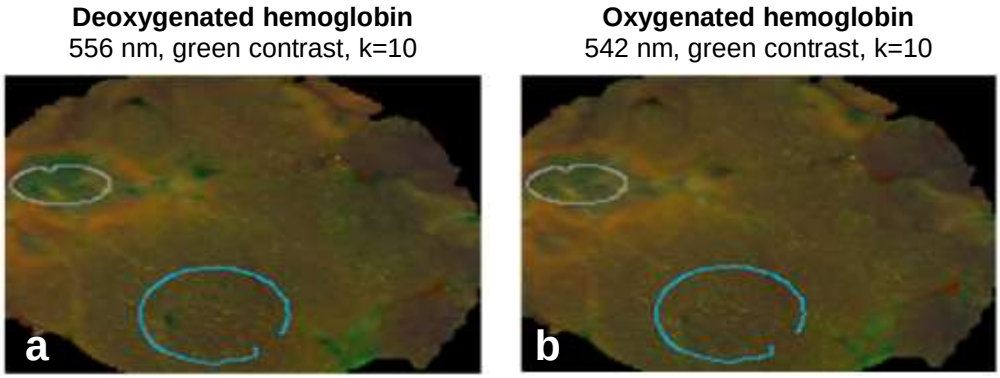

Figure 3. Hemoglobin enhancement on breast tissue sample: (a) deoxygenated hemoglobin at 556 nm, k=10; (b) oxygenated hemoglobin at 542nm, k=10.

The last result shows the performance of the scattering power enhancement for tissue contrast evaluation. Fig.4 shows another breast tissue fragment where IDC tumor tissue (purple circle) and inflammation (green circle) appear together on the same sample. The reflectance image (Fig.4b) correlates with the digital camera one (Fig.4a) but low contrast is achieved for this sample. As told in the third part of this proposal, the scattering power was included in the breast multispectral dataset as a "fictitious" wavelength located at 430 nm. The intensification of this wavelength provides a purple contrast on the reflectance image (Fig.4c) that identifies areas where IDC tumor tissue is present. Moreover, the inflammation area is not affected by the intensification of the scattering power parameter showing again that the scattering power provides interesting discrimination abilities as discussed before [6].

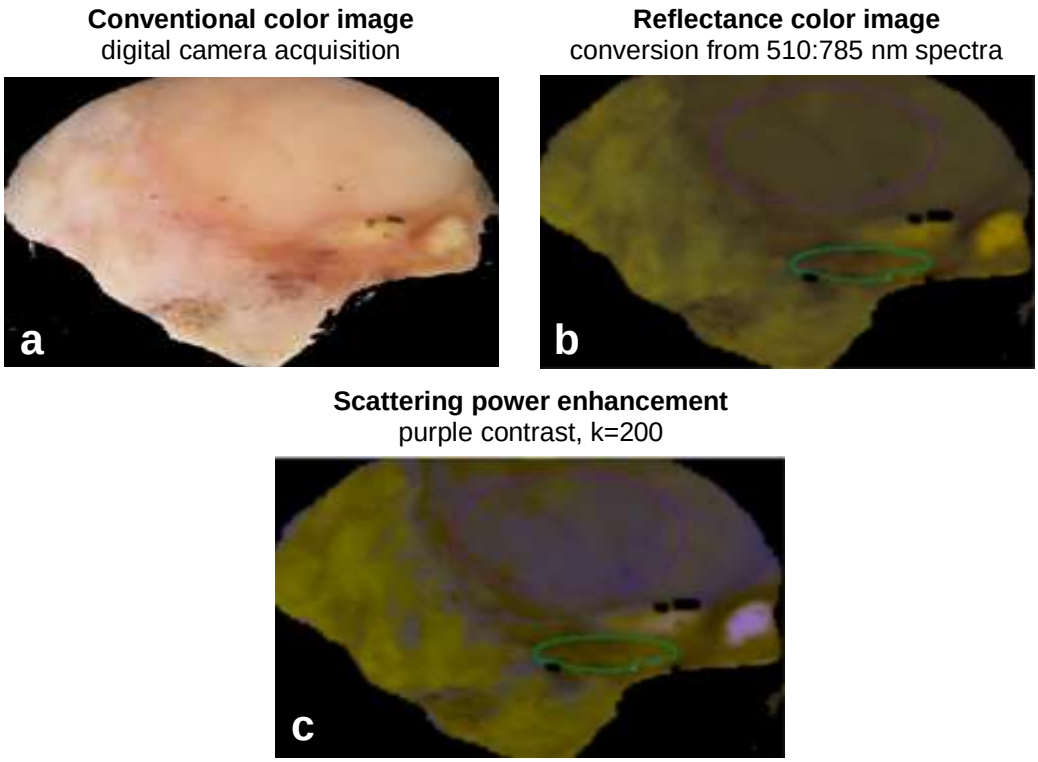

Figure 4. Breast tissue sample with IDC (purple circle) and inflammation tissue (green circle): (a) color image from a digital camera; (b) color image recovered from the multispectral reflectance data (510:785 nm); (c) scattering power enhancement, k=200.

4. CONCLUSIONS

A new method for contrast enhancement related with tumor delineation has been presented. The goal is to explore all the possibilities of the spectral data from a micro-sampling localized reflectance measurement set-up. In a first approach, the color representation of the measured reflectance has shown interesting contrast abilities when compared with conventional photographs from visible silicon cameras. On the other hand, an enhancement procedure has been implemented to highlight the absorption and scattering events present in the spectral reflectance data. Once the user selects the parameters (amplification factor, wavelength and color for the enhancement) the process generates an image where all the effects are summed up and overlaid over the reflectance image. The scattering power has delimited tumor areas whereas the intensification of oxygenated and deoxygenated hemoglobin has marked the inner limits of tumor proliferation. An optimization procedure is being investigated to select the best magnification factor to improve the differentiation of tissues.

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