Development of a novel, compact, and transportable multispectral imaging device for wound healing monitoring

Marta Marradi*[a,b], Luca Giannoni[a,b], Marco Marchetti[c], Domenico Alfieri[c], Lorenzo Targetti[d], Stefano Gasperini[d], Francesco Saverio Pavone[a,b,e]

[a] Department of Physics and Astronomy, University of Florence, Florence, Italy;
[b] European Laboratory for Non-Linear Spectroscopy, Sesto Fiorentino, Italy;
[c] Light4Tech S.r.l., Sesto Fiorentino, Italy;
[d] EmoLED S.r.l., Sesto Fiorentino, Italy;
[e] National Institute of Optics, National Research Council, Sesto Fiorentino, Italy.

ABSTRACT

Multispectral imaging (MSI) devices are optical diagnostic tools that can be used for the non-invasive monitoring and characterization of various kinds of pathologies, including skin conditions such as wounds and ulcers, due to the capability of such technology to track alterations of structural and physiological parameters (e.g., oxygenation and haemodynamics) from changes in the optical properties of the investigated tissue across a large number of spectral bands. In this work, a novel, compact and transportable MSI device based on spectral scanning and diffuse reflectance imaging is going to be presented. The apparatus is composed of light emitting diodes (LEDs) as light sources and a CMOS camera, making it a very compact, manageable, user-friendly, and cost-effective system. The wavelengths of the LED sources, that are located in the visible-NIR portion of the spectrum, have been specifically selected to target and monitor alterations of oxygenation and haemodynamics that can provide biomarkers of monitoring wound healing in chronic ulcers. The calibration of the MSI system is going to be illustrated, discussing the calibration procedure and results obtained with (1) Monte Carlo-based, digital phantoms and (2) liquid optical phantoms. Both types of phantoms mimic the properties of biological tissues and allow to introduce variations in a controlled manner. The proposed MSI system is also going to be tested on patients affected by chronic skin ulcers in order to assess its efficacy and accuracy.

Keywords: Multispectral imaging, diffuse reflectance imaging, wound healing monitoring, chronic ulcers, skin pathologies, oxygenation, haemodynamics, optical phantoms.

1. INTRODUCTION

Chronic skin ulcers are defined as lesions that show no tendency to heal after three or more months, with symptoms that can include pain, swelling, foul odor, bleeding, discharging and reduced mobility, leading to significant emotional and physical distress of the patient. In the most severe cases, chronic non-healing wounds may lead to serious events such as limb amputation and premature death[1]. Considering the increasing percentage of elderly and the prevalence of diseases such as obesity and diabetes, the burden of chronic ulcers is destined to become higher in the next future. For this reason, new preventive and monitoring technologies are needed, but the innovation in new therapies and diagnostic tools is impaired due to the lack of knowledge regarding the biological processes of wound healing and to the uncoordinated approach by medical staff[2]. For an early detection of the tissue health status and successful treatment guidance, a solution may be the design of an innovative, non-invasive healing monitoring system, based on multispectral imaging (MSI). MSI is an emerging imaging technology that uses light in the visible and near-infrared (NIR) portion of the spectrum. When biological tissues are invested by light, the latter undergoes multiple scattering and is absorbed for the most part by haemoglobin, water, fat, and melanin, thanks to which quantitative/qualitative information regarding the tissue pathology can be extracted and inferred[3].

*Corresponding author: Marta Marradi; marradi@lens.unifi.it

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In MSI, a limited number of wavelength bands are sampled (typically up to ten). This number is lower than the one used for hyperspectral imaging (HSI), giving the advantage of a less complex and more cost-effective instrumentation. The output of MSI techniques is a three-dimensional dataset (x, y, n), where n is the number of wavelengths that are used[3]. MSI may be used as a diagnostic tool in biomedical imaging thanks to its monitoring capabilities for chromophores contained in the blood, including oxyhemoglobin and deoxyhemoglobin. These important chromophores provide information about the local degree of oxygenation, perfusion, and the microcirculatory status of the analyzed tissue region[3]. Currently, there are other existing methods used for the evaluation of these characteristic parameters in the wound: ankle-brachial index (ABI), Doppler ultrasound, and transcutaneous oxygen partial pressure ($TcPO_2$). Unfortunately, these techniques are not applicable for all kinds of patients and present some limitations. For example, ABI is not indicated for patients with diabetes, renal failure, and advanced age; in addition to this, it provides indirect information on arterial dysfunction and is unable to localize the disease[4]. Doppler ultrasound is an old-fashioned technique, no longer routinely used in modern clinics and that should be combined with other imaging tools[4]. Lastly, the reliability of $TcPO_2$ is strongly debated and studies have shown low reproducibility and accuracy[5].

In this work, the use of a novel MSI device is proposed to address the above-mentioned problems and for a more accurate monitoring and early diagnosis, with the aim of reducing amputation rates and achieving successful healing outcomes. The portable MSI device has been designed to be used in a quick, non-invasive manner, with simple and easy-friendly functionality, at a cost-effective value. The first step towards an extraction of quantitative data is the calibration of the system. For this task, liquid optical phantoms composed of known concentrations of water, intralipid (IL) and dyes have been used. Liquid optical phantoms are widely used for the calibration procedures of novel spectroscopic systems thanks to their easy fabrication, availability of materials, and their ability to mimic the properties of biological tissues[6]. Data obtained from the analysis of the optical phantoms are then compared with Monte Carlo-based digital phantoms, which are modelled to replicate the spectroscopic response of the device, knowing the concentrations and optical characteristics of the analyzed substances.

2. METHODS AND MATERIALS

2.1 Portable Multispectral Imaging System

The MSI device uses LEDs as light sources, with wavelengths located in the visible-NIR portion of the spectrum. LED technology offers several advantages, such as high energy efficiency, long durability, cost-effectiveness[7], and no warm-up period in required. The system can be classified as monochrome CMOS camera based, with a generated FOV of about 15 cm x 15 cm. With monochrome camera-based devices, each LED is illuminated in a sequence, and the camera captures the reflectance image generated by each single LED. The result is the creation of n-band multispectral images (where n is the number LEDs used)[7]. In the case of the presented MSI device, the number of LEDs is seven and have been specifically selected to target and monitor alterations of oxygenation and haemodynamics, providing biomarkers for wound healing monitoring in chronic ulcers. In general, the use of LEDs combined with a CMOS camera makes the device very compact, transportable, user-friendly, non-invasive and guarantees a fast and efficient acquisition of images. A picture of the system is shown in Figure 1.

Figure 1. MSI imaging device used in the present work. The CMOS monochrome camera is positioned at the center, meanwhile the LEDs are mounted around it. The LEDs are covered by polarizing film to exclude specular reflection from the diffuse reflectance images.

2.2 Preparation of liquid optical phantoms

For the calibration procedure of spectroscopic systems, the use of liquid optical phantoms has been proved to be one of the best options due to their ability to mimic the properties of biological tissues and for their easy fabrication[6]. For this work, liquid optical phantoms based on water, Intralipid-20% (IL), and dyes have been used. The aim is to design a tissue-like phantom composed of a purely absorbing medium (dye) with known characteristics and concentration and of a highly scattering agent (IL). It is assumed that dyes act as pure absorbers, thus their addition to the phantom is expected to have a negligible effect on scattering[8,9].

One of the dyes used in this work is green food dye. It is diluted with deionized water and analyzed with a commercial spectrophotometer (PerkinElmer LAMBDA 950) for a spectral characterization and to decide the best range of concentration to use. Five concentrations have been chosen and reported in volume fraction (0,0190 µl/µl, 0.0286 µl/µl, 0.0381 µl/µl, 0.0476 µl/µl, 0.0570 µl/µl), which give an absorption coefficient (μ_a) close to the corresponding values reported for human dermis. The volume concentration of IL used is equal to 6,67% and the final volume of the phantom is equal to 300 ml. The liquid phantoms composed of water, IL and the selected concentrations of dye are kept constantly agitated via magnetic stirring inside a black box (10 cm x 10 cm x 5 cm) and are kept at room temperature during the image acquisition. Below in Figure 2 is reported a picture of a green dye phantom and of the experimental setup using the MSI device:

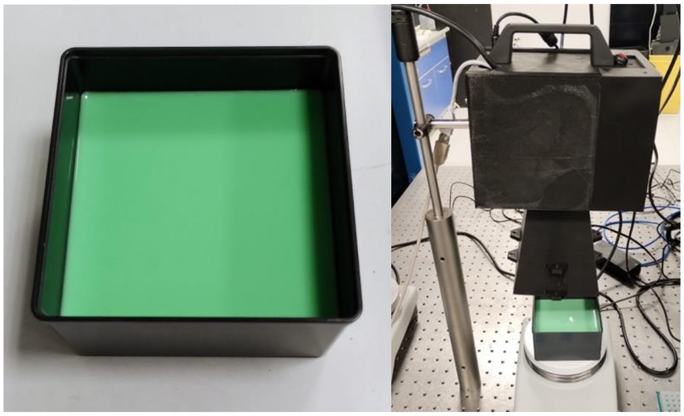


Figure 2. Example of a liquid green dye optical phantom (left) fabricated for the calibration procedure of the novel MSI device and of the experimental setup (right).

2.3 Image acquisition and processing

Images have been acquired before adding dyes (water and IL only) and for each concentration of the dye-based phantom. Images of a white calibration standard (Labsphere Spectralon® 5") have also been acquired. The phantom images are then normalized with the white standard reference images, after dark counts subtraction. The reflectance (R) images are also converted to attenuation (scattering + absorbance) (A) values using the equation A = -log(R) to compare the obtained results with the data acquired using the commercial spectrophotometer.

2.4 Monte Carlo-based digital phantoms

The composition of the liquid optical phantoms has been then reproduced using a Monte Carlo (MC) light transport model to create digital optical phantoms, and to computationally simulate the reflectance datasets obtained using the MSI system. The aim is to determine a potential calibration factor which should take into account the instrumentation and geometry factors of the MSI device and that can then be applied to calibrate the images and to correlate its outcomes to know quantitative information from controlled settings.

The MC model is based on the software Mesh-based Monte Carlo (MMC)[10,11] and uses a computational HSI framework developed by Giannoni et al.[12]. For the modelling of the liquid phantoms, a semi-infinite, meshed domain is constructed having homogeneous optical properties (absorption and scattering) based on the same volumetric contents and concentrations of water, intralipid and dye of the mixture of the real phantoms (Figure 3). A 2D divergent source and planar detector (both of size equal to 1 mm^2) are also added to the model, to simulate illumination at the selected wavelengths of the MSI device and corresponding diffuse reflectance at the top surface of the digital phantom. Examples of simulated light diffusion and absorbance within the phantom volume at different cross-sections have also been reconstructed and reported in Figure 3b.

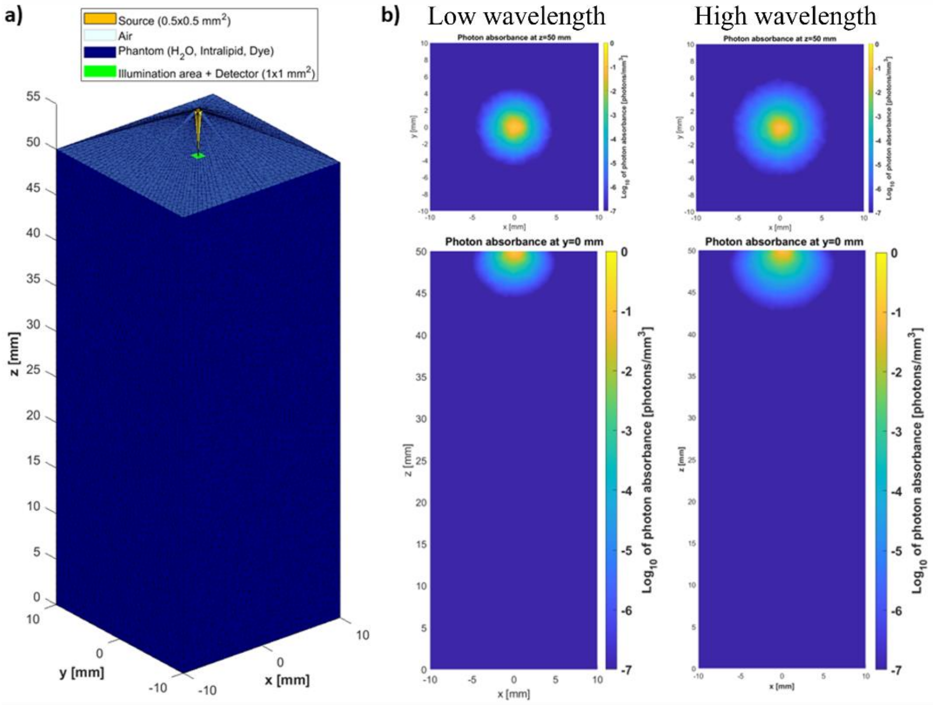


Figure 3. a) The MC model geometry and composition, simulating the liquid optical phantom composed of water, intralipid and dye, as well as the 2D illumination and detection at multiple wavelengths; b) Examples of MC-simulated light transport, diffusion and absorbance throughout the digital phantom volume, for XY and XZ cross-section, at a low and a high wavelength.

3. RESULTS AND DISCUSSION

For a preliminary and qualitative evaluation of the results obtained with the MSI device, the latter are compared with the absorption coefficient spectra acquired using the commercial spectrophotometer. The results obtained for the green dye-based phantom are illustrated in Figure 4:

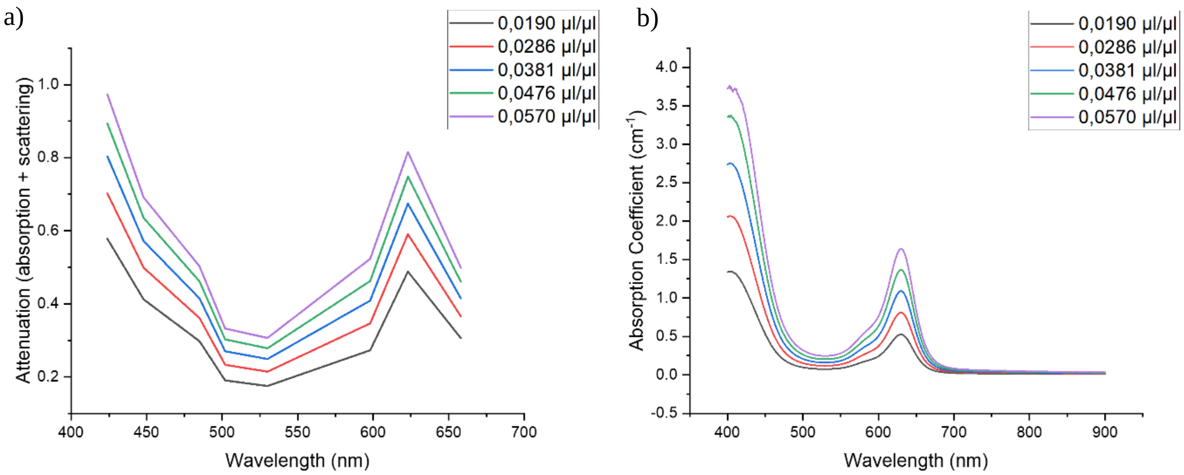
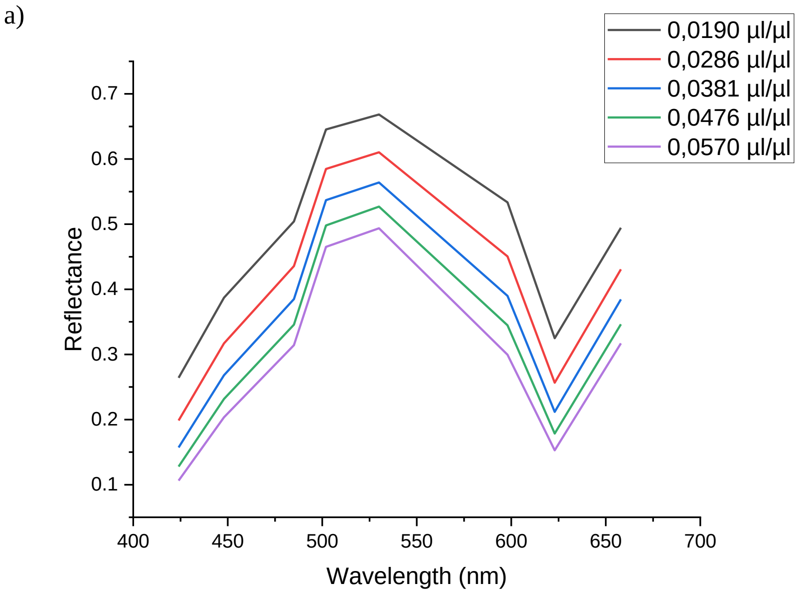


Figure 4. a) Attenuation (absorption + scattering) data for each dye concentration (reported in volume fraction, µl/µl) acquired with the MSI system. b) Comparison with the absorption coefficient spectra collected using the commercial spectrophotometer, at the same dye concentrations used for the optical phantoms.

The absorption coefficient spectra collected using the spectrophotometer (Figure 4b) are reproduced with good accordance by the MSI device (Figure 4a), using only seven wavelengths. For a deeper analysis, the reflectance data acquired with the MSI system have been compared to the reflectance data extracted from the MC simulations, reported in Figure 5:



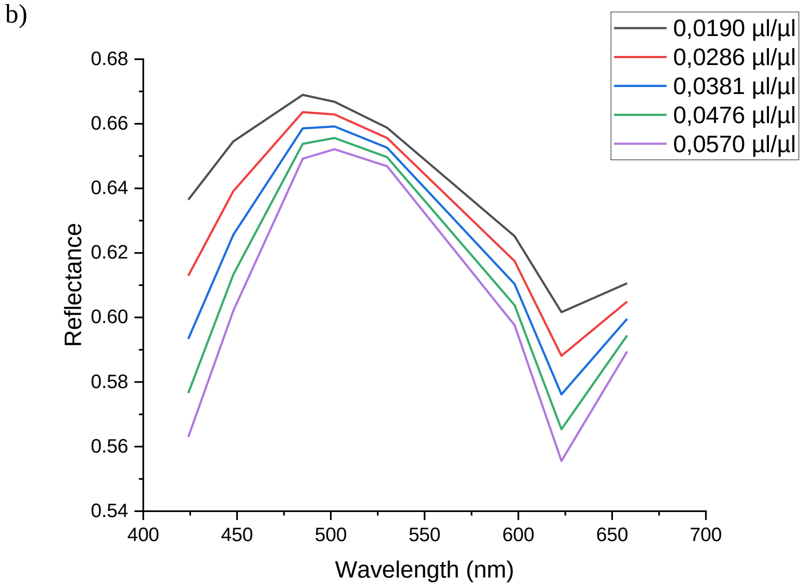


Figure 5. a) Reflectance data for each dye concentration (reported in volume fraction, µl/µl) acquired with the MSI system. b) Comparison with the MC-simulated reflectance spectra, at the same concentrations used for the optical phantoms.

The comparison between experimental and simulated data shows qualitatively the same trend and similar reflectance values, especially for lower concentrations. For additional testing, the MSI system has been used to monitor qualitatively the healing progress of chronic wounds, before and after therapy and treatment. The wavelengths of the LEDs have been combined in an algorithm designed to extract an index proportional to the saturation level of the tissues. Preliminary qualitative data acquired from a patient affected by a chronic foot ulcer is shown below in Figure 6:

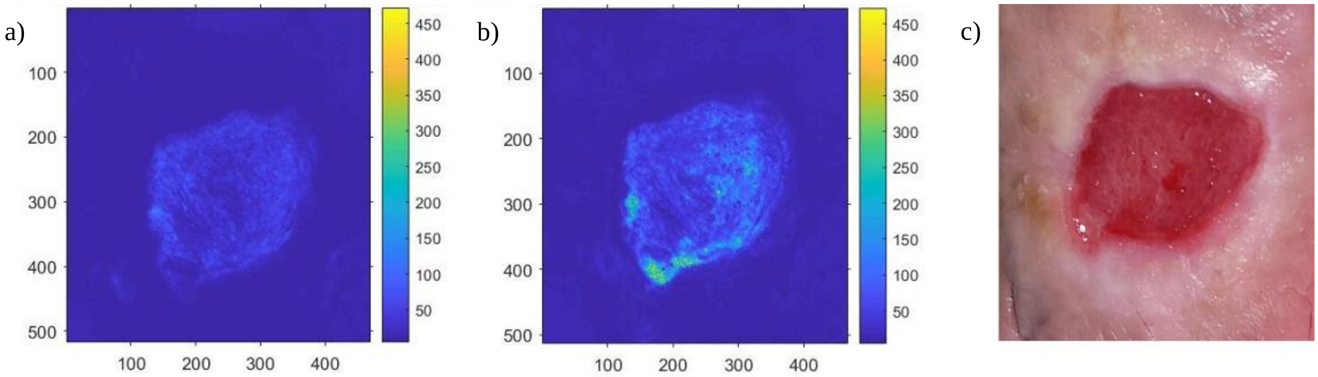


Figure 6. a) Saturation index color map of the chronic ulcer before treatment. Yellow in the color map corresponds to high levels of saturation, meanwhile blue indicates low levels. b) Saturation index map of the chronic ulcer after treatment. c) RGB image of the chronic foot ulcer.

Figure 6b shows that there has been an activation of the ulcer tissue due to treatment and therapy, resulting in a higher degree of saturation.

4. CONCLUSIONS

The qualitative data acquired with the novel MSI device presented in this work demonstrates that diffuse reflectance imaging systems are capable of monitoring the healing progression of chronic skin ulcers and of monitoring the efficacy of treatments, in a non-invasive modality. This can be of particular importance not only to assess the degree of healing in general, but also for the personalization of therapies and for the amplification of their efficacy. LED-based MSI systems have also the advantage of being cost-effective, compact, user-friendly, and can be used in a fast and efficient manner. Further work is going to be needed for the extraction of robust quantitative indexes. The comparison between experimental data using dye-based phantoms acquired with the MSI device, the spectrophotometric data and the results obtained with the MC simulations shows a good preliminary accordance, but improvement is still needed to obtain absolute correspondence.

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