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A Review On Absorption Spectroscopy and Laser Speckle Techniques for Wound Healing Assessment

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ABSTRACT

A comprehensive understanding of the histological changes involved during different stages of healing would provide a better insight on the studies of wound healing assessment. The conventional method of assessing wound healing progress via visual inspection, although convenient, has certain limitations in terms of reliability and accuracy in its diagnosis. A more accurate approach previously employed to document wound recovery progress is based on changes in skin microcirculatory activities namely tissue oxygenation and blood perfusion level at different stages of wound healing. In this paper, the use of spectroscopy and laser speckle techniques is summarized for an effective wound healing management and to discover potential fields for future laboratory and clinical research. It is expected that the development in this research could provide an efficacious solution for clinical practitioners to come up with proper diagnosis with respect to different prescribed treatment.

Key words : Blood flow rate, Laser speckle, Spectroscopy, Tissue oxygenation, Wound healing.

1. INTRODUCTION

A specific definition of wound would be a disruption of the anatomic structure and functionality of the skin tissue caused by an injury inflicted on the skin barrier. Wounds are commonly categorized into either acute or chronic wound, taking into account several contexts such as the distinctive appearance and severity of the wound, and the recovery rate of which the anatomical structure of the wounded tissue is eventually restored [1]. An injury or abrasion that only affected the superficial skin surface and known to heal within a timely and orderly period is described as an acute wound. Contrary to this, the healing rate of chronic wound is unpredictable. The causes of a chronic wound are due to a more complex pathology, hence the inability to establish full recovery of the anatomic and functional integrity of tissue. Wounds are healed after going through the fundamental healing stages following injury. The various stages of wound healing can be defined as an overlapping process that occurs concurrently within a specific time length immediately after the skin barrier is disrupted. Tissue perfusion and local oxygenation parameters change with the stages of wound healing namely inflammatory, proliferative stage that includes reepithelialization of tissue granulation and tissue remodeling [2]. The inflammatory stage involved aggregation of platelets to initiate coagulation following injury, proliferative phase stimulates microangiogenesis that promote development of new vessels while tissue remodeling stage involves differentiation of fibroblasts. Failure of the wound to heal is often caused by impairment of tissue oxygenation or blood perfusion, or both. This would result in amputation of the affected body part or in worse cases, may bring fatal consequences if the condition deteriorated.

Visual inspection of wound physical appearance is one of the commonly practiced ways of evaluating wound [3]. Assessments were made based on the width and depth of the wound but did not take into account the underlying histological aspects. A more objective approach of wound healing assessment, however, is via means of an invasive method, which required biopsies of tissue samples [4]. Throughout the years, researchers had came up with different approaches for a more reliable and accurate wound diagnosis. These techniques include the raman spectroscopy [5], investigation of angiopoietin-like 4 (ANGPTL4) as determinant [6] and optical thermography [7]. Hence, a thorough understanding of various processes involved during wound healing progression is crucial in order to distinguish clinical parameters suitably used as guides for proper clinical diagnosis and therapeutic measures. Furthermore, a non-invasive diagnosis tool which could provide accurate *in-vivo* information of the cutaneous skin tissue would be a preferable alternative to the standard clinical routine using surgical punch biopsy technique. This paper is organized as follows. In Section 2, the parameters used to indicate wound healing progress are described. A comparison between the absorption spectroscopy and laser speckle technique for wound healing assessment used in previous studies is presented in Section 3. This is followed by a summary of this paper in the final section.

2. WOUND HEALING INDICATOR

2.1. Wound Tissue Oxygenation Status

To date, mean blood oxygen saturation, SO_2, is the most commonly used indicator for quantitative analysis of wound healing status. Scientific studies revealed a strong correlation between local oxygen consumption and tissue oxygen saturation during post-operative assessment of skin graft [8]. The imperative role of oxygen has been duly acknowledged in the multifaceted stages of healing for optimal repair of new tissue cells and production of collagen by fibroblast. In addition to this, oxygen is also essential to build up body's immune system against bacteria via neutrophils production. Poor oxygenation in wound has been identified as one of the factors leading to the formation of necrotic tissue and eschar on the wound bed [9]. Under ischemic condition, the delivery of oxygen to tissues is limited, therefore, hindering collagen distribution and consequently promoting bacterial proliferation. These factors have also been listed as the major pathologies associated with the rising prevalence of diabetes foot ulcer (DFU) among diabetes patients [10]. Previous works focused on investigating wound healing mechanism by attempting to monitor the fluctuation in transcutaneous oxygen saturation (S_tO_2) during different healing phases as wound healing progressed [11].

2.2. Cutaneous Wound Blood Flow Measurement

While it is important to maintain tissue oxygenation during healing, this is also subject to smooth and continuous blood flow perfusion. This is necessary to guarantee consistent delivery of oxygen and nutrients to the wounded skin sites. Blood flow perfusion is listed as one of the reliable biomarkers to map microcirculatory changes and to identify abnormal hispathological changes in the body [12]. This was demonstrated in a recent work conducted on a group of subjects diagnosed with chronic leg ulcers and sickle cell anemia [13]. Clinical evidences revealed anomalous blood flow at the ulcer bed and compared this with that at different skin regions. High blood flow was reported at the ulcerated skin and the authors discussed extensively reasons for this occurrence such as cutaneous vasodilatation and severe inflammation. This suggested that the wound healing status is directly related to blood flow levels within the microcirculatory system.

3. METHODS OF WOUND HEALING ASSESSMENT

3.1. Absorption Spectroscopy

3.1.1. Visible Light Reflectance Spectroscopy

Spectroscopic imaging is a unique technology that enables detection of light intensity across the spatial and spectrum directions at chromatic resolution not visible to the naked human eyes [14]. The basis of the visible reflectance spectroscopy technique depends on a priori knowledge of absorbing constituents in epidermal and dermal layers. The optical properties of a scattering and absorbing medium can be deduced from the spectroscopic data using a look-up table or a forward model. The Lambert-Beer law has been vastly used as a foundation in the present analytical models to quantify absorption properties of a medium [15, 16]. As a matter of fact, this concept is applied in major researches of skin oximetry, taking into account the nonlinear change in the light intensity depending on the absorptivities of two major hemoglobin derivatives present they are namely deoxyhemoglobin (Hb) and oxyhemoglobin (HbO_2). The SO_2 is defined as the blood oxygen saturation value or fractional concentration of oxyhemoglobin with respect to the total hemoglobin concentration. The latter is given by the summation of concentration of Hb and HbO_2. Duling and Pittman described invariant changes in the medium's scattering properties with the wavelength of the illuminating light, and signals measured at any wavelength have the same light path length and attenuation offset [17, 18]. The absorption properties of these absorbers can be illustrated in Figure 1. The information on absorption and scattering properties of a multilayered skin tissue can be deduced from light signals reflected from the particular skin site. Many of the workers employed light of visible range, which penetration depth is up to two to three millimeters below the skin surface [14, 19], for the investigation work. One such example is the Extended Modified Lambert Beer (EMLB) model by Huong and Ngu [16], wherein the workers related the changes in light attenuation with light scattering and absorption properties of the medium in the wavelength range of 520 – 600 nm. The selection of this wavelength range is also considering the distinguished changes in the absorption of hemoglobin derivatives within the specified wavelength range as indicated by the red box in Figure 1.

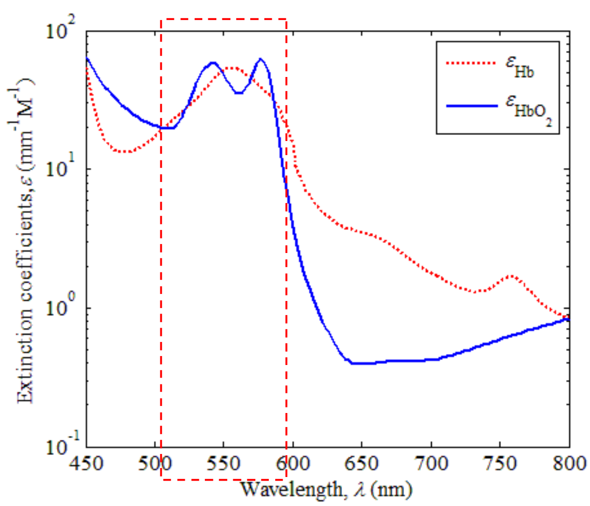

Figure 1: The extinction coefficients of Hb and HbO_2 compiled by Zijlstra *et al.* [20].

3.1.2. Hyperspectral Imaging Technique

Spatially dependent measurement of light intensity reflected from an imaged skin site can be conducted via the use of a constant light source and the detection of light intensity is by using either a complementary metal oxide semiconductor (CMOS) or a charge coupled detector (CCD). The hyperspectral camera is a favorable choice for spectroscopy imaging owing to the ability of the device to capture images across a series of wavelengths with fast scanning rates, thus, allowing a large quantity of intensity data to be measured over a short amount of time. In comparison to its counterparts namely frequency-domain and time-domain measurement techniques, this technique is relatively simpler. This system is often integrated with polarizer system to reduce scattering effects in the detected light [21].

The multidisciplinary applications of hyperspectral imaging system range from agricultural and food processing [22], remote sensing to pharmaceutical and medical image processing [23, 24]. Recent advancement in the biomedical field demonstrated the application of hyperspectral imaging to monitor changes in wound healing progression. Over the years, the development of a noninvasive medical diagnostic tool has been a topic of interest among researchers. Novel medical findings revealed the use of hyperspectral imaging tool by Fontaine *et al.* [25] to investigate HbO_2 level of infected foot among the patients with DFU following medical surgery for removal of soft tissue and bone debridement. This technique has also proven successful to study the severity of peripheral vascular disease (PVD) through the distinguished changes in the S_tO_2 map [26]. The results reported correlative changes between oxygen saturation and the severity of the disease.

3.1.3. Multispectral Imaging Technique

A multispectral imaging system, although similar to the hyperspectral imaging system, differs in terms of sampling number of data. This technology captures image at a relatively narrow and discrete band of not more than 20 bands in each pixel as compared to the latter approach which deals with up to hundreds and thousands of spectral bands [27]. Taking this into consideration, a shorter computational time is often required for the analysis of multispectral data sets. Figure 2 shows an example of a simple spectroscopy system used to measure the spectral response of a selected experimental subject via light diffraction from a diffraction optic [28].

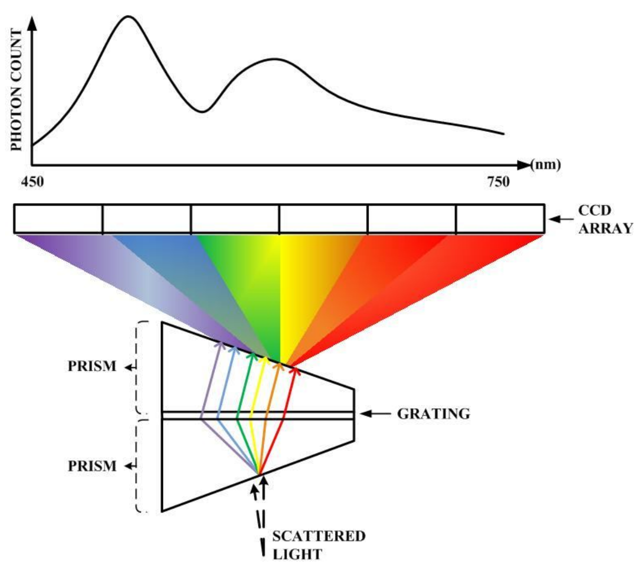

Figure 2: Formation of intensity spectrum.

Some of the notable achievements of this technique include tumor detection [29], burn wound assessment [30] and in a profound study of the brain of Alzheimer's disease patients [31]. King *et al.* recently attempted to study the severity of burn wound tissue using porcine burn model which resembled the human skin [30]. The authors employed specific wavelengths to classify burn thickness by depth (i.e. healthy, superficial partial, and deep partial) and proposed an appropriate wavelength for guiding the surgical wound debridement. Although the corresponding work was conducted on animal model, the results revealed promising information that could prove beneficial among clinical burn patients. In a separate work, Huong *et al.* conducted a clinical investigation among injured human subjects with superficial wounds at different skin locations using S_tO_2 as a marker to predict wound recovery status [9]. These results were presented in the form of color map and the difference between the normal skin region (control site) and wounded skin were compared using a line profiler. The workers concluded that a high S_tO_2 of approximately 60% is necessary to ensure positive and timely healing.

3.2. Laser Speckle Technique

Laser Doppler flowmeter is a state of the art device clinically adopted to measure cutaneous blood flow [32]. Meanwhile, laser speckle imaging is a technique that has advanced over recent years and it is widely applied in medical researches such as cerebral blood flow imaging [33], post-operative diagnosis tool for oral surgery [34] and clinical evaluation of superficial burn wound [35]. It is understood that the resulting laser contrast images functioned as a biomarker to identify changes in superficial skin blood flow.

The primary foundation of the laser speckle technique relies on the interference pattern of reflected and scattered light from an illuminating surface [36]. The resulting granular effect is then known as a speckle pattern. Previous observations on the speckled pattern of the emitted light showed correlation between displacement of an object and the pattern, which prompted the idea of relating the speckled pattern with changes in blood flow velocity. This is in such a way that the speckle contrast can be translated into blood flow, wherein a reduced contrast is to be found in regions of high blood flow and a more enhanced contrast when blood flow is restricted. This phenomenon is then explained to be a result of using the measurement of standard deviation in relative to the mean intensity.

4. CONCLUSION

From this review, it can be summarized that the development of a multimodal wound imaging system, which integrates laser speckle approach and optical microangiography technique, would prove beneficial to both patients and medical practitioners. Early identification of factors impeding chronic non-healing wounds such as that related to extreme-anoxic hypoxia would allow appropriate medical decisions to be made. With the aid of a laser speckle integrated spectroscopy imaging system, clinicians might have a better comprehension of the healing mechanism and hemodynamic response in wounded skin tissue following injury, and this is also to ease wound care management.

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