Electrical Impedance Spectroscopy in Skin Cancer Diagnosis

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KEYWORDS

• Melanoma • Basal cell carcinoma • Skin cancer • Squamous cell carcinoma • Nevus • Electrical impedance • Diagnosis

KEY POINTS

- Electrical impedance spectroscopy (EIS) is a noninvasive method of diagnosing skin cancer based on differences in electrical impendence between normal and abnormal skin.
- EIS is best performed by physicians who are trained to clinically detect seborrheic keratoses because these lesions are frequently inaccurately classified as malignant by EIS.
- EIS is safe with a high sensitivity in melanoma detection for lesions that are deemed suspicious on clinical and dermoscopic examination.

INTRODUCTION

Electrical impedance spectroscopy (EIS) is a noninvasive method that aims to help diagnose skin cancer. It is based on measuring electrical impedance in normal (banal) and abnormal (skin cancer) skin and using these measurements to differentiate nevi from melanoma.[1] EIS has been studied since the 1980s and the technique available is now commercially in some countries. Normal and abnormal tissues differ with respect to cell size, shape, orientation, compactness, and structure of cell membranes. These different properties on a cellular level influence the ability of the cells to conduct and store electricity, which is reflected in differences in EIS measurements.

TECHNOLOGICAL EQUIPMENT

The EIS device consists of a handheld probe equipped with a disposable electrode that is applied directly on the skin (**Fig. 1**). This probe is connected to a small electrical device that is connected to a touch screen monitor via a cable (**Fig. 2**). The latest generation of the EIS device permits integration of dermoscopy images into the patient chart together with the EIS measurements data. This feature permits the clinician to integrate the clinical, dermoscopic, and EIS information to augment the cognition of the operator in his or her decision making.

Electrode

The "microinvasive" electrode of the EIS machine only penetrates to the depth of the stratum corneum (**Fig. 3**). The surface of each electrode is furnished with small gold covered microinvasive pins. These pins have a triangular shape and approximately 150 μm high with a 170-μm triangular base. These spicules penetrate into the stratum corneum and have a sand paperlike feel; the application of the electrode is painless. The electrode can obtain several measurements and can be

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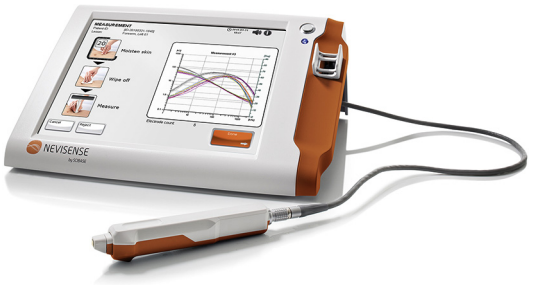

Fig. 1. Nevisense device including hand piece and touch screen monitor. (*Courtesy of* SciBase, Stockholm, Sweden; with permission.)

used on multiple lesions per patient. Because the electrode does penetrate the stratum corneum, it must be discarded after each patient.

Frequencies

The EIS system measures bioimpedance of the skin at 35 different frequencies, logarithmically distributed between 1.0 and 2.5 MHz, at 4 different depths using 10 permutations. The depth selectivity is measured by using different bars of electrodes (**Fig. 4**). The spatial localization of the sense pin and depth pin determines the 4 depths of penetration calculations used in EIS measurements. In general, impedance at low frequencies is related to the resistive properties of the extracellular environment and impedance at high frequencies is related to the resistive properties of the intracellular and extracellular environment and the capacitive properties (reactance) of the cell membranes. The applied voltage and resulting current is limited to 150 mV and 75 μA, respectively. The electrical current cannot be perceived by the patient and a complete electrical impedance measurement study takes less than 10 seconds to perform.

Fig. 2. Electrode of the Nevisense electrical impedance spectroscopy device. (*Courtesy of* SciBase, Stockholm, Sweden; with permission.)

Measurements

The measurement outcome of an EIS measurement is magnitude and phase shift at each frequency included in the spectrum. The measurements are displayed as curves of magnitude and phase shift at 4 different depths (different colors), and 10 permutations at various frequencies (*x* axis). Before the application of the electrode and before any measurements are taken, the skin site of interest be moistened with 0.9% saline solution for at least 30 seconds. For each lesion being investigated, the EIS measurements must be performed twice. The first measurement is called the reference measurement and this is obtained on healthy "normal" skin located at least 2 to 3 cm away from the lesion of interest. This reference measurement can even be obtained on the contralateral side. The measurements from the healthy adjacent or similar contralateral skin provides an intraindividual reference measurement that takes into account individual variability of the skin owing to both intrinsic and extrinsic factors. The second EIS measurement is obtained from lesional skin.

Studies

The EIS diagnostic algorithm was developed based on the EIS measurement results acquired on 751 lesions from 681 patients. All lesions were subsequently excised and the diagnosis histopathologically verified. In this initial trial 2 different algorithms were created and tested.[2] For the first algorithm, data from 40% of the lesions were used for training and 60% for testing. The sensitivity for melanoma was calculated to be 98.1%, for nonmelanoma skin cancer it was 100%, and for dysplastic nevi with severe atypia it was 86.2%. The overall calculated specificity for this first algorithm was 23.6%.

For the second classification algorithm, approximately 55% of the data was used for training and 45% for testing. The observed sensitivity for melanoma was 99.4%, for nonmelanoma skin cancer 98.0%, and dysplastic nevi with severe atypia was 93.8%. The overall observed specificity was 24.5%.[2] The observed sensitivity of the local pathologist (as compared with the dermatopathology panel as gold standard) for melanoma was 86.1%, nonmelanoma skin