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Detection of Basal Cell Carcinoma Using Electrical Impedance and Neural Networks

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***Abstract*—Variations in electrical impedance over frequency might be used to distinguish basal cell carcinoma (BCC) from benign skin lesions, although the patterns that separate the two are nonobvious. Artificial neural networks (ANNs) may be good pattern classifiers for this application. A preliminary study to show the potential of neural networks to distinguish benign from malignant skin lesions using electrical impedance is presented. Electrical impedance was measured in vivo from 1 kHz to 1 MHz at five virtual depths on 18 BCC and 16 benign or premalignant lesions. A feed-forward neural network was trained using back propagation to classify these lesions. Two methods of preprocessing were used to account for the impedance of normal skin and the size of the lesion, one based on estimating the impedance of the lesion relative to adjacent normal skin and one based on estimating the impedance of the lesion independent of size or surrounding normal skin. Neural networks were able to classify measurements in a test set with 100% accuracy for the first preprocessing technique and 85% accuracy for the second. These results indicate electrical impedance may be a promising clinical diagnostic tool for basal cell carcinoma or other forms of skin cancer.**

***Index Terms*—Basal cell carcinoma, bioimpedance, frequency, resistivity, tissue characterization.**

I. Introduction

BASAL CELL carcinoma (BCC) is the most common form of cancer. If detected early, it can be treated and cured without serious side effects. Visual inspection of a lesion, followed by biopsy and appropriate treatment, is the conventional clinical response. Biopsy is very accurate, but many malignant lesions escape biopsy due to errors in visual inspection. In some cases the patient, or even the physician, prefers to delay biopsy if there is not a high degree of certainty that the lesion is malignant. Undetected, the cancer may cause significant local destruction.

Bioimpedance may be a promising tool for detecting skin cancer. Impedance can be measured quickly and easily in the clinic, the instruments needed to measure impedance can be manufactured inexpensively, and the procedure is noninvasive. Bioimpedance varies from one tissue type to another, depending on tissue structure and composition [1]. *Ex vivo* studies have shown abnormal patterns in the impedance of breast cancer and squamous cell carcinoma [2], [3]. *In vivo* studies of the skin have shown abnormal patterns in impedance as a result of irritation or allergic reaction [4], [5]. Clinical studies of basal cell carcinoma have also shown significant differences between the impedance of BCC and normal skin and benign lesions, but a reliable method to identify BCC using impedance is not yet available [6]–[9].

Many studies of the electrical impedance of skin have attempted to use a single measure or index, developed heuristically, to quantify differences between tissue types or conditions. These indices are often based on only one or two features of the measured impedance [4]–[7], [10], potentially ignoring important information necessary for accurate classification [8], [11], and do not consider the impedance of surrounding normal skin. For *in vivo* tests, the impedance of normal skin adjacent to the test site might be used to improve classification of the lesion by accounting for the variation of skin impedance that is normally seen among individuals or among different anatomic locations [10]. It may also help account for the large amount of normal skin that is typically included in a measurement of a suspect lesion. Here, we use neural networks to classify lesions using impedance at 31 frequencies and use impedance of surrounding normal skin to preprocess data.

II. Experimental Methods

Electrical impedance was measured on 26 human subjects using the Impedance Spectrometer (SciBase AB, Huddinge, Sweden) [12]. The impedance spectrometer utilizes a hand-held probe with circular concentric electrodes as shown in Fig. 1. The outermost electrode (D) is approximately 10 mm in diameter. The two outer electrodes [(C) and (D)] are source electrodes. The innermost electrode (A) is a current sink. The electrode (B) surrounding the innermost electrode is a guard electrode, which reduces surface currents. A small time-varying current is sent through the electrodes, and the resulting voltage is measured to calculate the impedance of the skin at 31 logarithmically distributed frequencies from 1 kHz to 1 MHz. Impedance is measured at five skin depths by controlling the distribution of source current between the outer source electrodes, creating a "virtual" electrode between the two source electrodes. Distance between the sink electrode and virtual source determine depth (approximately half the distance). While depth varies with frequency and the structure of the skin, it typically ranges from about 0.1 to 2 mm. Both magnitude and phase are measured, though only magnitude was used in this analysis.

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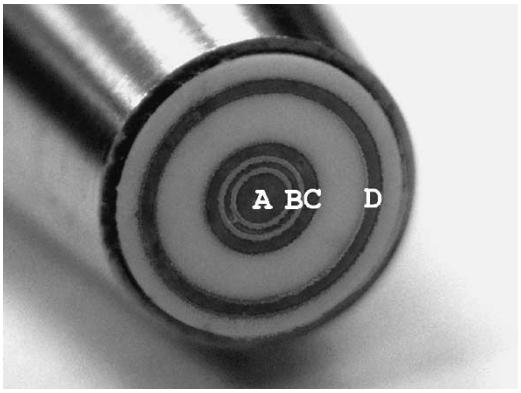

Fig. 1. Probe tip of impedance spectrometer. The probe tip consists of four electrodes, an outer source electrode (D), an inner source electrode (C), a guard electrode (B), and a sink electrode (A). The outer source electrode is approximately 10 mm in diameter.

Measurements of electrical impedance were made on 18 BCC and 16 benign or premalignant lesions. Lesions ranged in size from 2 to 15 mm. Subjects ranged from 28 to 85 years old. Benign and premalignant lesions included two actinic keratoses, two compound nevi, four intradermal nevi, one chromoblastomycosis, one cutaneous polyp, and six seborrheic keratoses. These diagnoses were encountered along with the basal cell carcinomas in the clinic. The benign and premalignant set is very heterogeneous. Results might be improved by using a more homogeneous set to compare with BCC, but we believe that the heterogeneous set better reflects the heterogeneity of BCC mimics and is a more valid test of our methods.

When possible, impedance was measured at five locations for each lesion: once with the probe centered over the lesion, twice with the lesion centered between the outer source and sink electrodes (once each on opposite sides of the lesion), and twice over normal skin adjacent to the lesion site (on opposite sides of the lesion). In some cases five measurements were not possible because of time constraints or placement of the lesion. Before making a measurement, the skin was soaked for two minutes in a 0.9% saline solution to reduce the high impedance of the stratum corneum that would otherwise prevent accurate measurement of the living skin layers. The skin was also soaked for one minute between subsequent measurements. After impedance was measured, a shave biopsy was obtained for histopathology determination of the diagnosis. Additional information on the data and methods is available in [6] and [13].

III. Neural Network Analysis

Before analysis, data were checked for obvious errors (change in sign of phase, abrupt and abnormal changes in magnitude, zero impedance, etc) [13]. Erroneous data were discarded, approximately 5% of the total. Data measured at depth 5, the "deepest" measurement, were not used, in order to reduce the size of the data set. Because depth 5 uses only the outer source electrode and most lesions were much smaller than the size of this electrode, this measurement may conceivably be most affected by the normal skin surrounding the lesion. In a previous study of BCC, benign lesions and normal skin using impedance, we found that differences were more significant at depths 1–4 than at depth 5 [6].

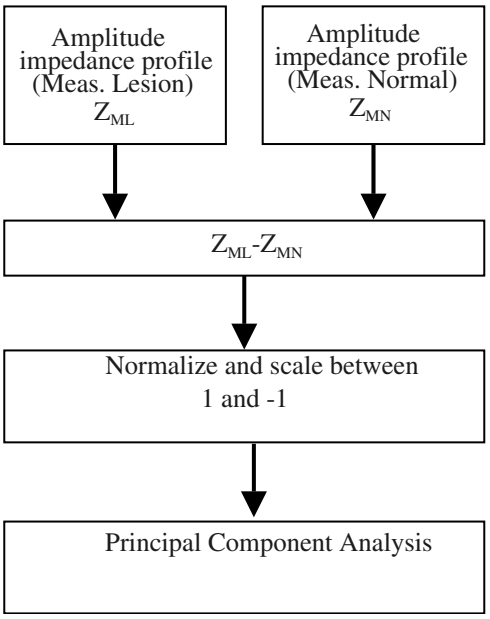

Fig. 2. Preprocessing of data profiles for method 1. Impedance measured on normal skin is subtracted from impedance measured over the lesion and then normalized. Data reduction is achieved using PCA.

Two types of preprocessing were employed to account for the impedance of the normal skin of each subject. The first technique relies on a subtraction of impedance measured over normal skin from the impedance measured over the lesion. The second technique attempts to "remove" the lesion from the surrounding normal skin to estimate the impedance of the lesion alone. After preprocessing, data were normalized and reduced using principal component analysis (PCA) [14]. The resulting profiles were processed benign and cancer profiles. Neural networks were trained to classify benign and malignant lesions using these profiles. Configurations for the neural networks were chosen according to the configuration that performed best for each set of processed data.

A. Method 1: Subtraction of Impedances

1) Preprocessing: More than one study has shown differences in the impedance among normal tissue and malignant and benign tumors [2], [3], [6], [7]. Differences in skin impedance may result because benign lesions tend to be drier and more highly keratinized than normal skin and BCC tends to be more highly vascularized and better hydrated than normal skin. These differences will vary over frequency, which is important to consider when attempting to classify lesions based on measured impedance [2], [3]. The following technique explores the possibility that the relative difference in impedance over the lesion and over adjacent normal skin may be used to identify lesion type.

Fig. 2 graphically depicts the preprocessing technique employed. First, the magnitude of impedance of normal skin (measured at a site adjacent to the suspect lesion) is subtracted from

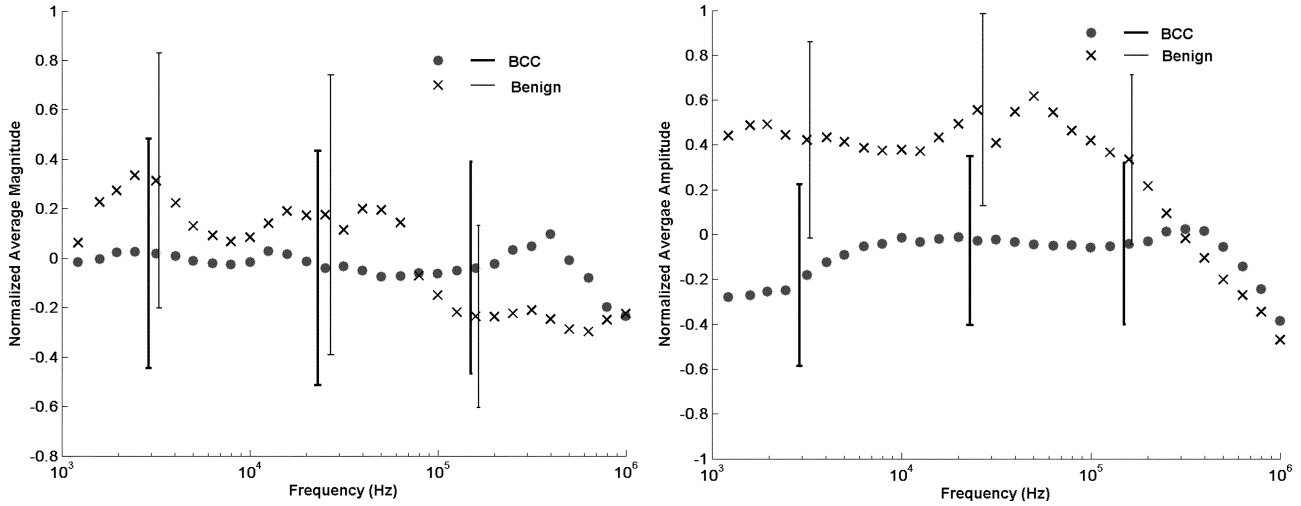

Fig. 3. Preprocessed data for (a) method 1 and (b) method 2. Plots show the average value of data among lesions after preprocessing and normalization, but before PCA. Data are shown only for depth 1. A complete profile consisted of depths 1–4. Whiskers show the standard deviation of data about the mean at 3.2, 25, and 159 kHz. A bold whisker is used to show variance for BCC and a thin whisker for benign lesions.

the magnitude of impedance of the (malignant or benign) lesion, giving a measure of the difference in impedance between the two. The resulting profile contains 124 data points—the difference in magnitude at 31 frequencies for each of four depths. A total of 167 profiles were generated using this process. Out of these, 87 profiles were of malignant lesions and 80 were of benign lesions. PCA was then performed on the profiles to remove data redundancy [14].

The original vectors were normalized using an algorithm available in MATLAB. This algorithm scales the values between -1 and 1 by normalizing the mean and standard deviation of the vector. Normalization is a prerequirement for the MATLAB PCA procedure. The PCA algorithm has three effects: it orthogonalizes the components of the input vectors to make the resultant vectors uncorrelated, it orders the resulting orthogonal components so that those with largest variation come first; and it eliminates those components that contribute the least to the variation in the data set. The resulting vector had four components. A plot of the average normalized values of impedance at depth 1, before PCA, are shown in Fig. 3.

2) Neural Network Architecture and Training: A 4, 20, 10, 5, 1 artificial neural network (ANN) was used for training and simulating the data [15]. An output of "1" was chosen to signify a malignant lesion and "-1" to signify a benign lesion. The network was trained and simulated using the MATLAB neural network toolbox [14]. The tan-sigmoid transfer function (TANSIG) was used for all four layers. The entire data set was divided randomly into a training set (the first 147 vectors) and a test set (the remaining 20 vectors) giving a train/test ratio of approximately 7:1, a common ratio used for small data sets. The training set included data from 76 malignant and 71 benign profiles and the test set data from 11 malignant and 9 benign profiles. The profiles in the test set were generated from different lesions than profiles in the training set. The conjugate gradient method [16] was used to train the network to a mean square error of 1.0×10^{-5}.

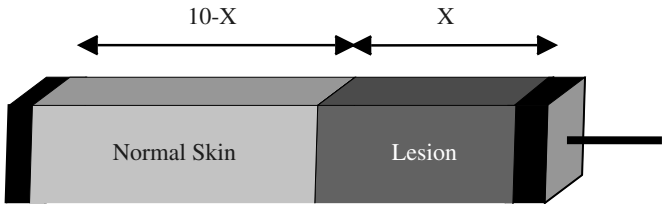

Fig. 4. Impedance measurements of a lesion with normal skin might be approximated as resulting from a series combination of an impedance composed of normal skin and an impedance composed of tissue from the lesion. These impedances could be assumed to have the same cross-sectional area but different length. In this case, the lesion has a length x(in millimeters) and the normal skin a length $10 - x$.

B. Method 2: Estimation of Lesion Impedances

1) Preprocessing: When the probe makes a measurement, it measures both normal skin and the lesion. The measured impedance results from a complex interaction among the major variables: impedance of the tissues and the size and location of the lesion within the skin. However, it might be possible to model this interaction approximately as the result of two impedances in series (Fig. 4), where one impedance is set by the impedance of normal skin and the other impedance is set by the lesion. This approximation is appropriate for a hypothetical case where the center electrode of our probe is placed directly over the center of a cylindrical lesion. If one assumes the cross-sectional area for both lesion and normal skin is the same, then the resulting impedance is a direct function of the length of the current path through the lesion and through the normal skin included in the measurement, as shown in Fig. 4. The length of the lesion would be proportional to the lesion diameter, x, and the length of the normal skin proportional to the amount of tissue remaining under the probe, or proportional to $10 - x$ for a 10-mm probe. In this case, the measured impedance would be given by

$$Z_{ML} = Z_L + Z_N \tag{1}$$

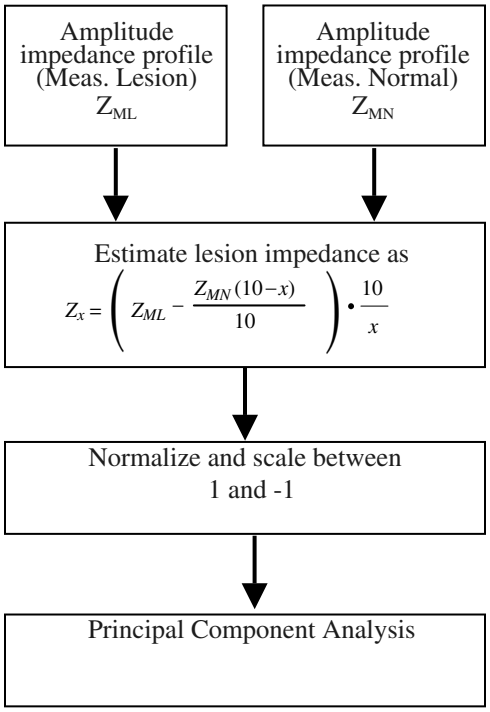

Fig. 5. Preprocessing of data profiles for method 2. Impedance of the lesion by itself—without surrounding normal skin—is estimated from measured impedance and lesion size. Estimated lesion impedance is then normalized. Data reduction is achieved using PCA.

where Z_{ML} is the measured impedance of the lesion (which also contains surrounding normal skin), Z_N is the impedance of the normal skin within the measurement, and Z_L is the impedance of the lesion by itself. The impedance of the lesion would be proportional to the length, x

$$z_L = x\rho_L \tag{2}$$

where ρ_L is the per-unit-length impedance of the lesion. The impedance of the section of normal skin within the measurement, Z_N, would be proportional to the difference of the probe size (10 mm) and lesion size, x

$$z_N = \frac{z_{MN}(10-x)}{10} \tag{3}$$

where Z_{MN} is the measured impedance of normal skin adjacent to the lesion. Using these relationships, one could calculate ρ_L and then use ρ_L to find the impedance that would be measured if the lesion were a full 10 mm in diameter as

$$z_x = \left(z_{ML} - \frac{z_{MN}(10-x)}{10} \right) \bullet \frac{10}{x} \tag{4}$$

where Z_x is the estimated impedance of this 10-mm lesion. At $x = 10$ mm, the lesion would take up the entire space under the probe, giving $Z_x = Z_{ML}$. This estimate would effectively remove the influence of normal skin from the measurement and would normalize the measurement to a single lesion size. In method 2, data were adjusted before application to the neural network using (4), as shown in Fig. 5. If the lesion size was greater than 10 mm, $\mathbf{x}$ was set to 10, because the probe covered the lesion completely (i.e., $Z_x = Z_{ML}$). The data were then normalized and scaled between -1 and 1 as in method 1. Average normalized values are shown in Fig. 3. PCA was also applied to this modified data, resulting in a vector dimension of four.

2) Neural Network Architecture and Training: A 4, 30, 15, 1 ANN was used for training and simulating the data. The network was trained and simulated as with method 1.

IV. Results

Method 1: Every profile in the test set was classified correctly.

Method 2: Of the 20 vectors in the test set, 85% were classified correctly. All nine vectors related to benign lesions were correctly classified (100%). Eight of the 11 vectors related to BCC (73%) were classified correctly.

V. Conclusion and Discussion

Our results are encouraging. In one case, 100% of lesions were classified correctly and in the other case, 85% of lesions were classified correctly. This performance was obtained even though lesions were generally much smaller than the size of the probe. For example, a 2-mm-diameter lesion constitutes only 4% of the area under the probe tip. Preprocessing techniques were devised to look at the relative difference in impedance at the lesion site compared to normal skin and to help account for the normal skin that was measured in addition to the lesion. Best results were obtained using a relative difference, possibly because a relative difference required fewer assumptions about the position and shape of the lesion and because it may account better for variations in impedance among individuals or among different anatomic sites. This result emphasized the possible need to use measures of an individual's normal skin as a reference point when evaluating measures over a lesion.

The fact that benign lesions were identified more accurately than BCC in method 2 may be related to the distribution of BCC and benign data given to the neural network. The neural network was trained to generate the highest classification rate, independent of whether it correctly classified benign lesions or BCC. If BCC and benign data "overlapped" in a sense, so that the neural network was unable to find a weight set that allowed for 100% classification, the training algorithm would find a weight set that minimized misclassification. If a few values of BCC overlapped with many values of benign data, the weight set would misclassify BCC more often than benign lesions. It is likely that another weight set could be found where BCC was classified at a higher rate than benign lesions, but the overall misclassification rate would then be higher too. Another reason method 2 performed more poorly than method 1 may be that the effect of the electrode contact impedance was not considered in the method 2 formulation, which may produce inaccurate estimates of the lesion impedance. For method 1, the effect of contact impedance is largely removed by the subtraction of measurements over normal skin and the lesion if the contact impedance is the same in both cases, which is a reasonable assumption. A concern with method 2 is that it occasionally estimated negative values of impedance, indicating the method was not sophisticated enough to account for all conditions. Method 2 might be improved if it also accounted for depth information, for uncentered lesions, for electrode contact impedance, or for the high impedance of the stratum corneum that may confuse results.

Accurate classification of BCC and benign lesions was most likely due to differences between the lesions and not other differences between the groups, like location of lesions or patient age. In a previous study using the same basic dataset [6], the impedance of normal skin measured next to the lesion on both groups was compared. A high probability of similarity was found between the impedance of normal skin for the two groups while statistically significant differences were found between the impedance of BCC and benign lesions. If differences were caused by age, location, technique, or other factors, differences would also have been found between measures of normal skin next to the lesion site. In addition, because the lesions used in the training set were different than the lesions used in the test set, the neural network could not simply "memorize" the training set to produce good results. The neural network had to find features in the training set that were fundamental to lesion type and could, therefore, also be found in the test set.

As in many applications, preprocessing improved results. Here, PCA reduced each vector, containing magnitude of impedance at 31 frequencies and four depths, to only four components. Because of the data format, it is difficult to relate these components to physical parameters. The data were also manipulated to reflect specific aspects of the impedance measurement. This preprocessing is a significant factor in the quality of results we report. When identification was attempted without preprocessing, results were significantly worse.

A study on a dataset of this size is not conclusive. A much larger study would be desirable, particularly when using machine learning techniques like neural nets. Yet, these preliminary findings are sufficiently promising to argue for additional studies. Future studies might include development of more sophisticated preprocessing techniques, perhaps using statistical methods, analysis of features besides magnitude, like phase or both real and imaginary components, and analysis of other types of lesions including melanoma.

This preliminary study indicates there is sufficient information within electrical impedance measures to distinguish between malignant and benign lesions. Better understanding of the mechanisms behind differences will further improve the utility of these measures. If effective, electrical impedance can form the basis of a safe, inexpensive, and noninvasive method to identify skin malignancies, especially those lesions with atypical clinical appearance.

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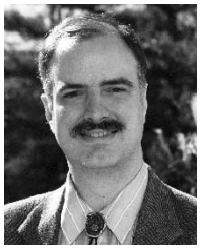

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