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Impedance Changes According to the Degree of Atopi Dermatitis in Mice

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***Abstract*—Variations in electrical impedance over frequency might be used to distinguish the degree of atopic dermatitis (AD), even if the mechanisms of the skin barrier impairment due to AD are still unknown. We observed the skin bioimpedance of normal mice and of abnormal mice having atopic with instrument measuring electrical impedance. Electrical impedance was measured from 20Hz to 1MHz at many frequencies and normalized with several indices such as IMP, PIX, IMIX, RIX, and et al. to reduce variation in subjects. The results showed the high relationship between subjective score and indices, especially, the capacitance change and impedance ratio, abs(Z_{1kHz})/abs(Z_{10kHz}). These results indicate electrical impedance may be a promising clinical diagnostic tool to monitor prognosis of skin care for atopic dermatitis. Using developed software application we easily acquired complex impedance data from the instrument and got the analysis results for very kinds of frequency. This may be useful in various bioimpedance studies such as skin cancer assessment or body composition analysis, or etc.**

I. Introduction

ATOPIC dermatitis is an inflammatory skin disease, typically with a chronic relapsing course and a defective skin barrier function. It is a disease that afflicts 15 - 30 % of all children and 2 – 10% of all adults in the industrialised world, with an increase during the last decades [1].

Various studies have been performed to determine the nature of the barrier impairment in atopic dermatitis (AD) skin, in particular compared with healthy skin. Abnormalities in the basic composition of the stratum corneum (SC) have been detected by noninvasive methods and showed an impairment in skin barrier function (an increase in transepidermal water loss, TEWL) [2] and reduction in skin hydration (assessed by capacitance measurements) [3]. With electrical impedance, pathophysiological changes in a tissue are reflected as changes in the electrical current flow of the tissue being studied. Because bioimpedance varies from one tissue type to another, depending on tissue structure and composition [4], the instrument for measuring electrical impedance may assess the barrier function of the SC, which depends on hydration, amount of lipids and several cellular properties [5].

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 [6]. In this study, the aim was to measure the bioimpedance values of the skin of healthy mice and that of mice with AD, and observe the relationship between the subjective score and these two groups.

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II. Materials and Methods

A. Mouse model of atopic dermatitis

Six Nc/NgaTndCrlj male mice (15-23 g each and 5-weeks old) were purchased from Charles River Japan (Yokohama, Japan). The animals were housed in a room maintained at a temperature of 20-25 ℃ with a 12-hour light-dark cycle. They were maintained on commercial food pellets and allowed free access to water. They were divided into two groups. The experimental group induced atopic dermatitis-like skin lesion was topically applied with 1% of 2, 4-dinitrochlorobenzene (DNCB) dissolved in acetone/olive oil (1:3) to the hair-removed back of mice three times per week for 4 weeks. The control group was treated with the vehicle. Each group consisted of three mice [7].

The severity of dermatitis was assessed by scoring the clinical signs and symptoms. The total clinical severity score was defined as the sum of scores grade as none(0), mild(1), moderate(2) and severe(3) for each three aspects: erythema, keratinization and bleeding. The clinical signs and symptoms were measured by taking pictures. Body weight was also measured twice a week before DNCB application.

B. Impedance Measurement

When mice were measured impedance, mice were put into a small cage to prevent movement as shown in Fig. 1. The upper part of the cage was open in order to attach electrodes to the outer side of the atopic lesion.

Impedance was measured with a LCR meter (HP4284A, Agilent, USA). HP4284A is an impedance auto balancing bridge that enables measurement at frequencies between 20Hz and 1MHz. It recorded magnitude and phase spectra of impedance between 20Hz and 1MHz in a defined volume below the probe. We acquired complex impedance data from the instrument such as magnitude, phase, R, X, Cp, and Rp values using manual sweep with 41 frequency points (20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 400, 600, 800, 1k, 2k, 3k, 4k, 5k, 6k, 7k, 8k, 9k, 10k, 20k, 30k, 40k, 50k, 60k, 70k, 80k, 90k, 100k, 200k, 300k, 400k, 500k, 600k, 700k, 800k, 900k, 1MHz). The values were measured repeatedly 7 times at each frequency and averaged. Because it is impossible to read huge data manually, we have built the system around a PC, connected through USB/GPIB interface (NI GPIB-USB-HS, National Instruments, USA) to the LCR impedance meter. The interface provides a direct connection from a USB port on a laptop or desktop PC to GPIB instruments [8]. The control of the instrument is accomplished by the computer application, which we have developed using the LabVIEW v8.2 (National Instrumentations, USA) as shown in Fig. 2. The software application controls the instrument parameters and performs measurements through a defined measurement protocol.

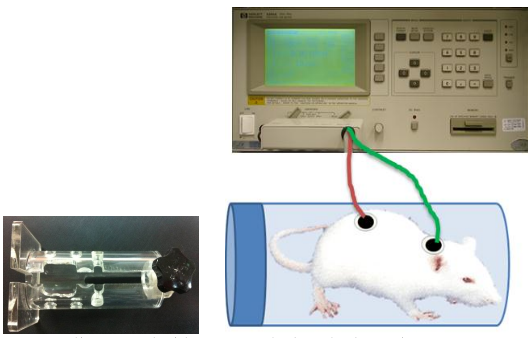

Fig. 1. Small cage to hold a mouse during the impedance measurement (left) and connection diagram of probes (right).

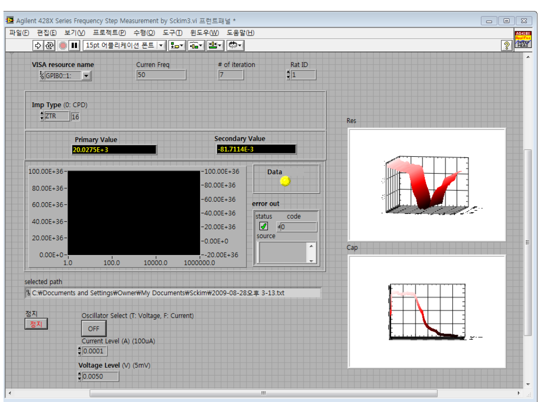

Fig. 2. Main screen of the impedance measurement program to conveniently measure impedance value.

Because impedance value also depends on the subject, the previous researchers used some indices such as MIX, PIX, RIX, IMIX to reduce the individual variance. The four indices are defined as follows [9]:

- Magnitude index, MIX: $abs(Z_{freq1}) / abs(Z_{freq2})$
- Phase index, PIX: $arg(Z_{freq1}) - arg(Z_{freq2})$
- Real part index, RIX: $Re(Z_{freq1}) / abs(Z_{freq2})$
- Imaginary part index, IMIX: $Im(Z_{freq1})/abs(Z_{freq2})$.

Where abs is the magnitude, arg is the phase angle in degree, Re and Im are the real and imaginary parts of the impedance Z at the frequencies indicated, and freq1 and freq2 are 20kHz and 500kHz, respectively. Because we had data at 41 frequencies, there are a lot of combinations (41*40=1640).

Because the data were not stable at low frequencies less than 100Hz and there were not big difference in the adjacent frequency bands, we neglected data in the low frequency and used only 8 different frequencies such as 100Hz, 1kHz, 10kHz, 20kHz, 40kHz, 100kHz, 500kHz, and 1MHz. The combinations are only 56 (8*7=56).

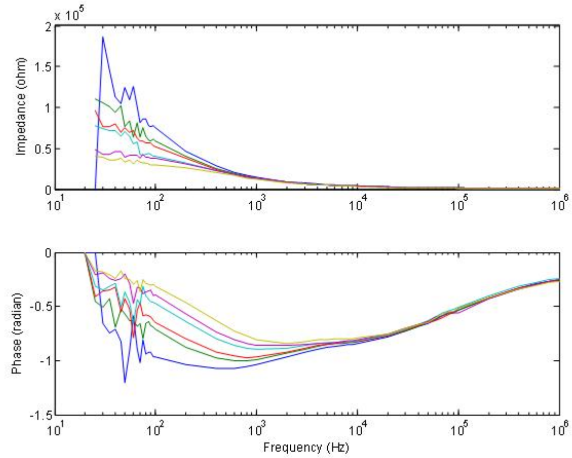

Fig. 3. Example of measured impedance and phase information from 10Hz to 1MHz.

C. *Statistics analysis*

The significance of differences between patients with AD and healthy subjects before treatment were tested using the Mann–Whitney nonparametric test. The effects of the treatment were analyzed using a two-way ANOVA with repeated measures of two factors.

III. Results & Discussion

Fig. 4 showed the skin of a mouse induced by the mouse model of atopic dermatitis from days 1 to days 28 and Fig. 5 showed the weight change. The mouse weight in two groups was the same before the treatment on day 1. The weight was significantly less in AD mice than in healthy mice during DNCB treatment.

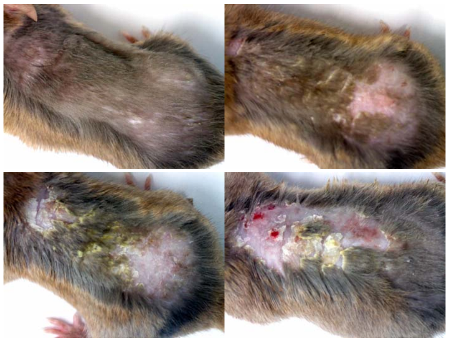

Fig. 4. Photos of the dorsal skin of a rat according to the degree of atopic dermatitis (Left top: none, right top: mild, left bottom: moderate, right bottom: severe).

The skin of AD mice in this study was compared with healthy skin without treatment. We compared weight-change trend between normal and control groups. The mice weight in control groups was less than that in normal groups when there was induced atopic dermatitis, but that was recovered when there was without treatments as shown in Fig. 5.

We found no statistically significant change in the IMIX, PIX, RIX indices in this study, but the MIX index of AD mice in the experiment group tended to be decreased and increased during treatment as shown in Fig. 6. The MIX values in normal mice were rather constant. This trend was consistent with the subjective score. The status of AD was recovered slowly according to the score and it was also shown in MIX index. We think that the mice in the experimental group were adapted to DNCB. Dry atopic skin showed lower capacitance and changes in certain impedance indices in a few other studies [10].

We calculated just capacitance change according to time, it was not ratio. It showed interesting results that capacitance was increased proportional to the degree of AD at 100Hz even if it was subjectively scored as shown in Fig. 7. The same results were not showed at the other frequency.

This may indicate a higher water content of the stratum corneum in healthy than in AD skin. The electrical characteristics of the skin affected by large variations in factors, such as hydration, lipid content, number of cell layers in the stratum corneum, size of the corneocytes and some properties of deeper skin layers, which may affect the complex nature of skin barrier.

IV. Conclusion

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. In this paper we have built the system around a PC, connected through USB/GPIB interface to the LCR impedance meter. Accurate measurements from 20Hz to 1 MHz could be obtained by HP4284A precision LCR meter. HP4284A is based on the auto-balancing bridge method which offers high accuracy over wide impedance range and relatively wide frequency coverage. User friendly control of the instrument is accomplished by the computer application. Using developed software application we easily acquired complex impedance data through a defined measurement protocol from the instrument and got the analysis results for very kinds of frequency.

We found the high relationship between subjective score and impedance ratio, $abs(Z_{1kHz})/abs(Z_{10kHz})$, and that certain impedance indices (capacitance at 100Hz), which depend to some extent on capacitance, were lower in atopic skin. We will confirm this study with more data in the future because the number of samples in this study was not enough data.

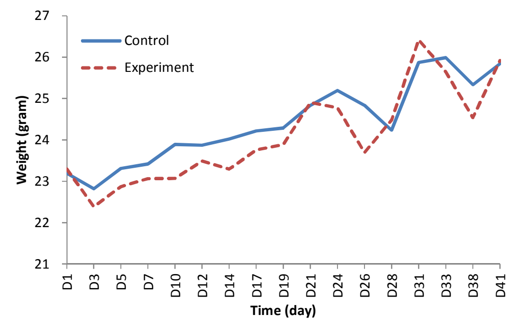

Fig. 5. Comparison of weight-change trend between control and experimental groups.

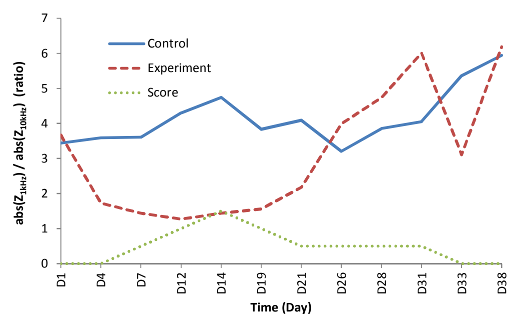

Fig. 6. Impedance ratio (MIX) between control and experimental groups when freq1 and freq2 is 1kHz and 10kHz, respectively.

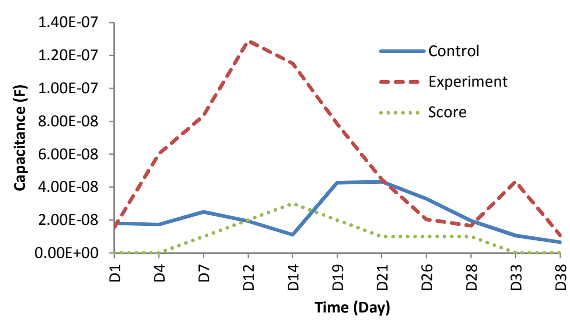

Fig. 7. Comparison of capacitance between control and experimental groups at 100Hz frequency.

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