

Development of the Micro-electrode Device for Electrical Diagnosis and Cure for Skin Function

Yuina Abe¹, Kuniaki Nagamine¹, Mayu Nakabayashi¹, Takeshi Yamauchi²,
Kenshi Yamasaki² and Matsuhiko Nishizawa¹

¹ Tohoku Univ.

Department of Finemechanics, Graduate School of Engineering
6-6-01 Aramaki Aza Aoba, Aoba-ku, Sendai 980-8579, Japan
Phone: +81-22-795-3586 E-mail: abe@biomems.mech.tohoku.ac.jp

² Tohoku Univ.

Department of Dermatology, Graduate School of Medicine
1-1 Seiryō-cho, Aoba-ku, Sendai, 980-8574, Japan

Abstract

Skin has important functions to protect inner organs sensing outer environment. In this study, those functions are evaluated by an electrical measurement system. The electrical potential generated across the epidermis in the skin, transepidermal potential (TEP), has been suggested to be related to skin barrier health. This measurement system could measure local TEP in minimally-invasive way and may be a personal diagnostic and therapeutic tool in the fields of medicine and cosmetics in future.

1. Introduction

The skin works as a multi-functional interface to maintain homeostasis of living body separating internal organs from external environment[1]. The epidermis, the outermost layer of the skin, is at the forefront of the protection providing cornified layer to keep the inner skin from drying and infection. The cells in the epidermis such as keratinocytes are actively transport ions in the tissue, generating ion localization and potential difference across the layer[2], [3]. This potential difference is called transepidermal potential (TEP). TEP has been suggested to be related to wound healing, skin barrier function, etc. and supposed to be a quantitative index of the skin functions[4]–[6].

Measurement of TEP requires vertical alignment of a pair of electrodes, where an inner electrode is set under the epidermis while outer electrode is set on the surface of it. Conventionally, the inner electrode was connected through surgically created wound on the skin[2], [5], [6]. As non-invasive alternate, sublingual area was used as a site of the inner electrode[4], [7]. For the measurement of absolute TEP, two electrodes desired to be juxtaposed to suppress noises.

In this study, minimally invasive TEP measurement system was developed. The inner electrode using fine microneedle (0.18 mm in outer diameter) was slightly cut into the skin and worked as a salt bridge. This electrode enabled convenient local TEP evaluation.

2. Material and Methods

Microneedle-based Salt Bridge

A painless syringe needle (Nanopass 34G, Terumo) was

hydrophilized by ozone oxidation treatment for 10 min (SSP17-110, SenLights Corporation). 2wt% of agarose in Ringer's solution was filled and gelation was followed. The conventional tubular salt bridge was connected on the side-wall and silicone elastomer ring was equipped around the shaft of the needle to control the insertion depth into the skin. For the stable measurement, the tip of the needle was desired to be kept within the dermis, the layer under the epidermis, and keeping from subcutaneous tissue, the layer under the dermis and rich in fat.

TEP Measurement of Porcine Skin Sample

The Ag/AgCl reference electrodes were fabricated as previously reported[8]. Two Ag/AgCl electrodes were measured prior to experiment using a voltmeter (ALS760C, BAS Inc., operated in the voltmeter mode, 10MΩ of input impedance).

Porcine skin sample was cut into a 50 x 50 mm piece and kept in room temperature. The surface of the skin sample was connected to the Ag/AgCl electrode by conventional tubular salt bridge and the subepidermal area was connected by microneedle-based salt bridge. Then the potential difference generated across the epidermis was measured by the voltmeter.

Fabrication of the TEP Measurement Probe

A painless syringe needle was attached at an end of a silicone tube (inner diameter: 3 mm, outer diameter: 5 mm, length: 20 mm) with a silicone elastomer ring. This tube assembled within a thicker probe tube (inner diameter: 7.9 mm, outer diameter: 11.2 mm, length: 30 mm) and those tubes were filled with 2wt% agarose gel containing Ringer's solution. Two narrow Ag/AgCl electrodes were attached to the end of the tubes.

Using the probe, local TEP measurement of porcine skin sample was conducted. For the comparison, skin barrier was locally disrupted in two different ways. One was tape-stripped to remove the cornified layer and another was treated with acetone-soaked cotton to remove the lipid of the cornified layer (disrupted area: 10 x 10 mm).

In some experiment, surgically created wound was used as a site of the inner tubular salt bridge instead of inserting needle salt bridge.

3. Results and Discussions

Fig. 1(a) is a schematic diagram of the entire TEP measurement system using microneedle-based salt bridge. The subepidermal region was electrically connected less-invasively via fine needle shown in Fig. 1(b). Fig. 1(c) shows the TEP of a piece of porcine skin measured by this system. Stable potential was obtained regardless of the insertion point of needle electrode (20, 10 and 2 mm). Importantly, the quick and stable response of the measured potential was only obtained with the silicone spacer and the hydrophilic treatment of the needle.

The photograph and the schematic diagram of the compact probe integrating those electrodes were in Fig. 2(a). The distance between needle and the neighbor salt bridge was ca. 2 mm. The local TEP measurement was conducted as shown in Fig. 2(b). Although skin barrier disruption by tape or acetone caused slight difference in the appearance, the value of local TEP was considerably decreased in the treated areas (B) compared to the adjacent areas (A, C). Local TEP could be an index of skin barrier health which is easily measured by compact device.

3. Conclusions

In this study, we demonstrated minimally-invasive TEP measurement system using microneedle as possible evaluator of skin barrier health. Microneedle salt bridge can be applied for living skin and the system may extend the applicability of TEP as the index of skin health.

Furthermore, skin barrier function has been suggested to be regulated by electrical stimulation[9]. The present TEP measurement system can also be applied to the electrical cure as a transepidermal stimulation system and its effect of the stimulation on TEP is currently being studied. In addition, TEP could be related with other skin functions. Therefore, TEP system developed here may emerge new aspects of skin.

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References

- [1] E. Proksch, J. M. Brandner, and J. M. Jensen, *Exp. Dermatol.* **17** (2008) 1063.
- [2] A. T. Barker, L. F. Jaffe, and J. W. Venable Jr., *Am. J. Physiol.* **242** (1982) R358.
- [3] M. Denda, Y. Ashida, K. Inoue, and N. Kumazawa, *Biochem. Biophys. Res. Commun.* **284** (2001) 112.
- [4] E. Kawai, J. Nakanishi, N. Kumazawa, K. Ozawa, and M. Denda, *Exp. Dermatol.* **17** (2008) 688.

- [5] J. Dubé *et al.*, *Tissue Eng. Part A* **16** (2010) 3055.
- [6] V. J. Moulin *et al.*, *Adv. wound care* **1** (2012) 81.
- [7] E. Kawai, N. Kumazawa, K. Ozawa, and M. Denda, *Exp. Dermatol.* **20** (2011) 757.
- [8] G. A. East and M. A. del Valle, *J. Chem. Educ.* **77** (2000) 97.
- [9] J. Kumamoto *et al.*, *Exp. Dermatol.* **22** (2013) 421.

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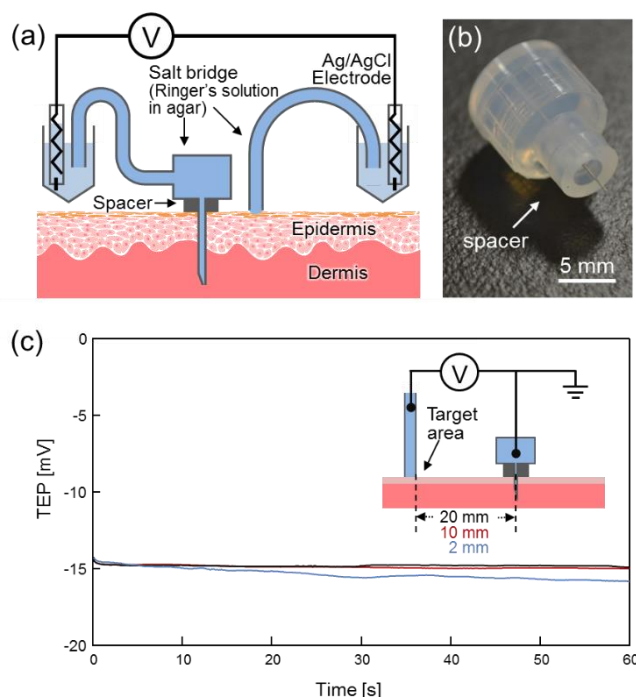


Fig. 1. TEP measurement using microneedle salt bridge.

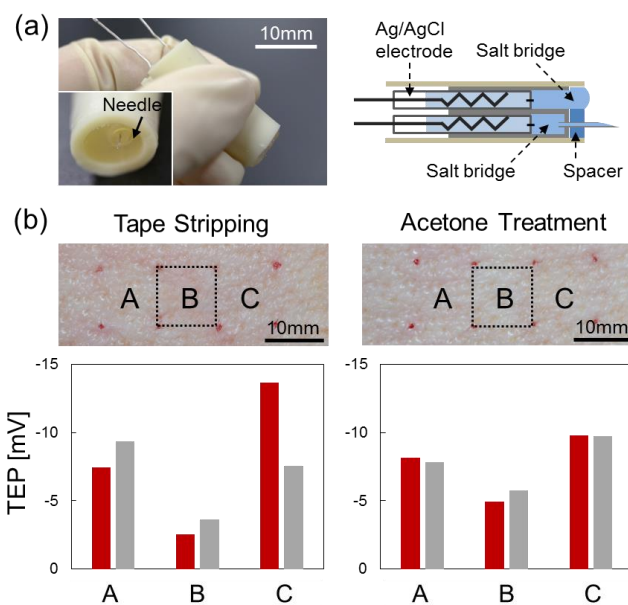


Fig. 2. Local TEP measurement by an integrated probe.