Long-Term Monitoring of Skin Recovery by Micromachined Microwave Near-Field Probe

Fritzi Töpfer, *Student Member, IEEE*, Lennart Emtestam, and Joachim Oberhammer, *Senior Member, IEEE*

Abstract—The water content in the epidermis correlates with different pathologic states of the skin; thus its assessment can aid the diagnosis and monitoring of conditions such as inflammation, edema, burns, and skin cancer. A micromachined microwave near-field probe, operating from 90 to 106 GHz, which, in contrast to earlier used microwave probes, has a minimized sensing area of $0.6 \text{ mm} \times 0.5 \text{ mm}$ and an optimized sensing depth of $400 \text{ }\mu\text{m}$ in tissue, has been developed and technically characterized by the authors earlier. This letter reports on the long-term monitoring of sodium lauryl sulfate (SLS)-induced skin irritations with the micromachined microwave probe. Aqueous solutions with 1%, 2%, 5%, and 10% SLS were applied to the forearm of a volunteer for 24 h and microwave reflection measurements were taken before and during 11 days after the SLS application. For all SLS-treated spots the microwave absorption reached the highest levels of 4 to 7 days after SLS application and afterward converged toward baseline levels again. The observed biphasic progression of the microwave reflection signal agrees well with trends from the literature for capacitance measurements and for epidermal thickness and signal attenuation in optical coherence tomography after SLS exposure. The measurements indicate that the microwave probe is very suitable to determine changes in the water content in the epidermis and can aid in the diagnosis of pathologic conditions including skin cancer.

Index Terms—Medical application, micromachining, monitoring, near-field probe, skin cancer, sodium lauryl sulfate (SLS).

I. INTRODUCTION

THE content of free and bound water in the epidermis correlates with different pathologic states of the skin, such as inflammation, edema, burns, and skin cancer, and thus its assessment can aid the diagnosis of these conditions [1], [2]. The assessment of the epidermis hydration does not necessarily need to be of absolute nature, relevant information can be derived from the difference to surrounding tissue or the relative hydration change over time. Different techniques for *in vivo* skin hydration measurement have been introduced in the past. Infrared spectroscopy, and capacitive and conductive measurements are capable of determining the hydration of the stratum corneum, the outermost, up to $100 \text{ }\mu\text{m}$ thick layer of the skin, but fail to provide information about the state

Fig. 1. (a) Micromachined microwave probe used for the measurements on skin with a minimized sensing area of $0.6 \text{ mm} \times 0.5 \text{ mm}$ and an optimized sensing depth of $400 \text{ }\mu\text{m}$ [12]. (b) Photograph of the probe.

of the viable epidermis and the dermis [3]. Confocal Raman spectroscopy and magnetic resonance imaging are capable of quantifying the epidermis hydration, but require expensive and large instrumentation and are limited by long measurement times [4], [5]. The measurement of the transepidermal water loss (TEWL), also used in this letter for reference measurements, provides information about the skin water barrier function, but not about the water content of the skin tissue [6]. An alternative, as reported in this letter, is microwave reflection measurements. The complex permittivity of tissue depends on its water content [7]; and microwave near-field probes have been shown to be very sensitive to the water content of tissue [8]–[10] and to be suitable for the diagnosis of skin tumors including malignant melanoma [11]. For such measurements standard open-ended waveguide probes have been used in research, which measure the average properties of a tissue volume of several cubic millimeters and therefore cannot resolve early stage skin tumors or small inhomogeneities in tumors [10]. Therefore, a micromachined microwave near-field probe, operating from 90 to 106 GHz in a one-port reflection measurement setup, has been developed and technically characterized by the authors, including responsivity, repeatability, and resolution [12] (see Fig. 1). The probe has a substantially minimized sensing area of $0.6 \text{ mm} \times 0.5 \text{ mm}$, which is only 9% of the area of a conventional W-band open-ended waveguide probe ($2.56 \text{ mm} \times 1.27 \text{ mm}$), which results in high lateral resolution for assessing tumor inhomogeneities, which is an important diagnosis criterion. Furthermore, the size and frequency choice results in an optimum sensing depth

Final manuscript. (Corresponding author: Fritzi Töpfer.)

F. Töpfer and J. Oberhammer are with the Department of Micro and Nanosystems, School of Electrical Engineering, KTH Royal Institute of Technology, 114 28 Stockholm, Sweden (e-mail: fritzi@kth.se).

L. Emtestam is with the Section of Infectious Diseases and Dermatology, Department of Medicine Huddinge, Karolinska Institutet, Stockholm, Sweden.

Fig. 2. (a) Volar forearm of healthy volunteer with the five test sites exposed to different concentrations of SLS and pure water (control) for 24 h using a patch test system. (b)–(f) Microwave reflection S_{11} at 96 GHz measured before and after SLS exposure and TEWL measured after SLS exposure on the different spots exposed to 10% SLS, 5% SLS, 2% SLS, 1% SLS, and pure water (control), respectively. Mean and standard deviation for $n = 3$. The baseline was calculated as linear regression of the control site measurements. The standard deviation for all measurements on the control side is 0.32 dB or 7.2%.

of 400 μm in tissue, which guarantees that the probe interacts mainly with the epidermis and the upper part of the dermis and not with deeper tissue layers, which is a requirement for high sensitivity to early-stage skin tumors. To demonstrate the probe's capability of evaluating the water content of the epidermis, a sodium lauryl sulfate (SLS) exposure test was conducted. Application of SLS at low concentrations on the skin induces (among other reactions) spongiosis, i.e., an increase in tissue water content [13]. The change of the microwave signal directly after a single SLS application, which caused a weak reaction to the skin of a volunteer, has been measured and presented in [14]. Here, the results from using the microwave probe for monitoring the long-term skin reaction to SLS application of different concentrations over a time course of 11 days after application are presented for the first time.

II. MATERIAL AND METHODS

Sodium lauryl sulfate (SLS) solutions in distilled water with concentrations of 1%, 2%, 5%, and 10% SLS by weight

were applied to the forearm of a volunteer for 24 h using a standard Van-der-Bend closed patch test system with five square (1 cm $\times$ 1 cm) chambers containing filter paper. Chambers 1–4 were filled with 80 μl of 1%, 2%, 5%, and 10% SLS solution, respectively, and chamber 5 was filled with pure distilled water as reference. Microwave reflection measurements with the microwave probe were taken on two random positions within each spot (1–5) before application of the SLS (day 0) and 3 h after the removal of the patches (day 1) and in the subsequent days 2–5, 7, 9, and 11 using the micromachined microwave probe.

Additionally, TEWL was measured on all spots using the Tewameter TM 300 (Courage+Khazaka electronic GmbH, Cologne, Germany) subsequent to the microwave measurements on days 1–5, 7, 9, and 11; two measurements series on all spots were taken each day. TEWL is commonly used to quantify the water barrier function of the skin, which is known to be diminished after SLS exposure [13]. Thus, an increased TEWL is a sign of a skin reaction to SLS exposure. TEWL provides no direct information about the skin water content

Fig. 3. Robustness of the measurement against variations in contact pressure: Placing the probe against the skin and controlling that the probe tip indents the skin by at least 0.5 mm ensures a trustworthy measurement. Microwave signal (at 96 GHz) measured while the probe was lowered stepwise onto the skin and beyond skin contact, temporarily indenting the skin slightly. (a) Above soft tissue. (b) Above muscle tissue.

and therefore not on skin tumors either, but can serve as an estimate for the skin response to the SLS exposure and thus as reference for the experiments in this letter.

III. RESULTS AND DISCUSSION

The measured microwave reflection S_{11} at 96 GHz is displayed in Fig. 2. The measurements on the SLS-treated spots show a clear change in the signal following the SLS exposure: the microwave absorption reached the highest level 4–7 days after patch removal. An increased absorption indicates spongiosis, i.e., an increase in the water content, of the viable epidermis, which is known to develop after SLS exposure [13]. Thereafter, absorption levels converged toward baseline levels again. The values measured at the control spot show only a small signal fluctuation assumed to be caused by random factors such as temperature, air humidity, and circulation. Long-term monitoring of the water content of the viable epidermis after SLS exposure has, to the best of our knowledge, not been published before this letter. Other skin response parameters following SLS exposure, such as capacitive measurements [15] and optical coherence tomography [16], have confirmed the biphasic progression behavior with the maximum effect of 4–7 days after SLS exposure, which are for the first time reported in this letter for water content assessment of the viable epidermis by microwave measurements. Also, the progression of the TEWL levels in this letter, used for reference, is similar to the ones observed by [15] and by [16]: TEWL levels were the highest directly (day 1 or 2) after the SLS exposure and subsequently converged to a level corresponding to skin that had not been exposed to SLS (Fig. 2).

Furthermore, this letter has confirmed that the probe–skin contact pressure has no significant influence on the microwave signal. Robust measurements are easily achieved by gently pressing the probe against the skin so that the probe tip indents the skin by at least 0.5 mm (Fig. 3).

IV. CONCLUSION

This letter indicates that the presented micromachined microwave probe is very suitable to determine changes in the water content of the epidermis. In particular, this letter found that trends in long-term monitoring of skin alterations can be reliably followed, and agree with alternative measurement principles published in the literature. Thus, the presented microwave probe has the potential to aid in the diagnosis of skin cancer and/or other conditions characterized by a change in water content in the epidermis.

ACKNOWLEDGMENT

All procedures involving humans were approved by the Stockholm Regional Board for Research Ethics (ref: 2013/1900-31/4).

REFERENCES

- [1] V. Suntzeff and C. Carruthers, “The water content in the epidermis of mice undergoing carcinogenesis by methylcholanthrene,” *Cancer Res.*, vol. 6, pp. 574–577, Sep. 1946.
- [2] Y. Hayashi, N. Miura, N. Shinyashiki, and S. Yagihara, “Free water content and monitoring of healing processes of skin burns studied by microwave dielectric spectroscopy *in vivo*,” *Phys. Med. Biol.*, vol. 50, no. 4, p. 599, 2005.
- [3] J. Serup, G. B. Jemec, and G. L. Grove, Eds., *Handbook Non-Invasive Methods Skin*, 2nd ed. Boca Raton, FL, USA: CRC Press, 2006.
- [4] P. J. Caspers, G. W. Lucassen, and G. J. Puppels, “Combined *in vivo* confocal Raman spectroscopy and confocal microscopy of human skin,” *Biophys. J.*, vol. 85, no. 1, pp. 572–580, 2003.
- [5] J. K. Barral, N. K. Bangerter, B. S. Hu, and D. G. Nishimura, “*In vivo* high-resolution magnetic resonance skin imaging at 1.5 T and 3 T,” *Magn. Reson. Med.*, vol. 63, no. 3, pp. 790–796, 2010.
- [6] J. Pinnagoda, R. A. Tupke, T. Agner, and J. Serup, “Guidelines for transepidermal water loss (TEWL) measurement,” *Contact Dermatitis*, vol. 22, no. 3, pp. 164–178, 1990.
- [7] K. R. Foster and H. P. Schwan, “Dielectric properties of tissues and biological materials: A critical review,” *Critical Rev. Biomed. Eng.*, vol. 17, no. 1, pp. 25–103, 1989.
- [8] J. Nuutinen, R. Ikäheimo, and T. Lahtinen, “Validation of a new dielectric device to assess changes of tissue water in skin and subcutaneous fat,” *Physiol. Meas.*, vol. 25, no. 2, p. 447, 2004.
- [9] S. I. Alekseev and M. C. Ziskin, “Human skin permittivity determined by millimeter wave reflection measurements,” *Bioelectromagnetics*, vol. 28, no. 5, pp. 331–339, Jul. 2007.
- [10] F. Töpfer and J. Oberhammer, “Millimeter-wave tissue diagnosis: The most promising fields for medical applications,” *IEEE Microw. Mag.*, vol. 16, no. 4, pp. 97–113, May 2015.
- [11] P. Mehta, K. Chand, D. Narayanswamy, D. G. Beetner, R. Zoughi, and W. V. Stoecker, “Microwave reflectometry as a novel diagnostic tool for detection of skin cancers,” *IEEE Trans. Instrum. Meas.*, vol. 55, no. 4, pp. 1309–1316, Aug. 2006.
- [12] F. Töpfer, S. Dudorov, and J. Oberhammer, “Millimeter-wave near-field probe designed for high-resolution skin cancer diagnosis,” *IEEE Trans. Microw. Theory Tech.*, vol. 63, no. 6, pp. 2050–2059, Jun. 2015.
- [13] R. A. Tupker *et al.*, “Guidelines on sodium lauryl sulfate (SLS) exposure tests,” *Contact Dermatitis*, vol. 37, no. 2, pp. 53–69, 1997.
- [14] F. Töpfer, L. Emtestam, and J. Oberhammer, “Dermatological verification of micromachined millimeter-wave skin-cancer probe,” in *IEEE MTT-S Int. Microw. Symp. Dig.*, Jun. 2014, pp. 1–4.
- [15] K.-P. Wilhelm, G. Freitag, and H. H. Wolff, “Surfactant-induced skin irritation and skin repair. Evaluation of the acute human irritation model by noninvasive techniques,” *J. Amer. Acad. Dermatol.*, vol. 30, no. 6, pp. 944–949, Jun. 1994.
- [16] J. Welzel, M. Bruhns, and H. H. Wolff, “Optical coherence tomography in contact dermatitis and psoriasis,” *Arch. Dermatol. Res.*, vol. 295, no. 2, pp. 50–55, 2003.