Skin Acetone | Biochip | Health Management

Technology Reports

Wearable Skin Acetone Analyzer and its Applications in Health Management

NTT DOCOMO is progressing toward realizing the "biochip mobile phone"– a device that will enable advanced health management and diagnosis by biochemical analysis of biological samples that are simple to collect. Among the health management issues worthy of attention, obesity is one issue that is known to cause a wide range of diseases, and hence there are demands for technologies that can measure fat burning automatically, and thus relieve users from the need to perform any operations. To meet these demands, we developed an easy-to-wear skin acetone analyzer to enable "visualization" of fat burning in daily life. To prevent and rectify obesity, this analyzer makes it possible to provide health advice tailored to the individual based on the individual's pattern of fat burning throughout the day.

Research Laboratories
Yuki Yamada
Satoshi Hiyama
Tsuguyoshi Toyooka

1. Introduction

In the burgeoning cost of national healthcare, the medical expenses of the late elderly have become particularly high. In 2012, the late elderly medical expenditures*1 were 39.2 trillion yen and are projected to reach 52.3 trillion by 2025 [1] [2]. Thus, urgent measures are needed to bring down these costs. To bring down these costs, it is crucial that the period that people can live independently and healthily without being bed-ridden or requiring nursing care, i.e. healthy life-span, should be extended as long as possible. The keys to achieve this are improving lifestyle habits and preventive care*2 to prevent diseases before they take hold and retard the advance of existing ailments.

For preventive care to succeed, ideally, analyzers that are easy to use and that can be used every day to examine and confirm the state of the user's health in detail so that suitable advice can be provided to the user are important. Here, because smartphones and mobile phones are now in wide use by 94.5% of the population [2], powerful healthcare tools can be enabled by including these analyzers in smartphones or wearable devices that can connect to smartphones and deploying preventive care services linked to these technologies.

NTT DOCOMO is leading the world with its ongoing R&D of its world first concept of a "biochip mobile phone" that will enable advanced preventive care and diagnostic services tailored to individuals by biochemical analysis of biological samples*3 such as the breath or skin gases*4 that are easy to collect and analyze on biochips*5 connected to smartphones [3]-[5].

One of these technologies enables

*1 **Late elderly medical expenditure:** The cost of healthcare for those over 75 or those over 65 with certain disabilities.

*2 **Preventive care:** Medical actions and services that serve to prevent illnesses before they happen.

measurement of the acetone[*6] emitted from the skin (skin acetone), which is a chemical marker of body fat burning. We have developed the world's first compact and lightweight wearable skin acetone analyzer, which we exhibited at CEATEC JAPAN[*7] 2014 [6]. This article provides an overview of the analyzer and introduces examples of its practical applications in healthcare (**Figure 1**).

2. Significance and Challenges of Skin Acetone Measurement

Skin gas contains a range of constituents that relate to the state of the body (**Table 1**) [7]-[9]. Skin acetone is a metabolite emitted from the surface of the skin produced in the blood during exercise or hunger when body fat is broken down. For this reason, it is a useful indicator of the dynamic state of fat metabolism. Because obesity is said to cause a range of diseases and thus raises the risk of contracting a lifestyle-related illness, measuring the amount of acetone emitted from the skin to monitor the state of fat burning can play a pivotal role in daily health management. Acetone is constantly and unnoticeably emitted from the skin. Thus, measuring it with an easy-to-wear device such as a watch or innerwear-type device would make preventive care services more easily available to users. Conventionally, large analyzers (gas chromatography apparatus) were normally used to measure skin acetone emissions because the amount of acetone emitted from the skin is extremely low (normally between 10-200 pg/cm^2·min[*8]). This meant that wearable, compact and lightweight skin acetone analyzers were not commercialized.

NTT DOCOMO planned a new gas analysis device to concentrate and measure skin acetone (**Figure 2**) [10], and developed the world's first analyzer small and light enough to wear.

Figure 1 CEATEC JAPAN 2014 reference exhibit

Table 1 Examples of skin gas constituents and their body condition markers

Skin gas constituent	Body condition
Acetone	Fat burning
Ethanol	Alcohol intoxication
Acetaldehyde	Hangover
Methane	Changes in intestinal environment, constipation
Nonenal	Progress of aging
Formaldehyde	Onset/progress of cancer

3. Overview of Device Development

For this development, a compact, high-sensitivity, low-cost, long-life and maintenance-free semiconductor-based gas sensor[*9] is preferable as the gas sensor to be implemented in the wearable device. However, measuring the low skin acetone emission is difficult even with

*3 **Biological sample:** A sample derived from a living organism for analytical purposes.

*4 **Skin gas:** A gas emitted from the surface of the skin.

*5 **Biochip:** A chip which has a built-in mechanism to detect or analyze biological samples.

*6 **Acetone:** A highly volatile organic compound - chemical formula C_3H_6O.

*7 **CEATEC JAPAN:** The largest international imaging, information and communications technology exhibition in Asia.

*8 **pg/cm^2·min:** The amount of acetone emitted from 1 cm^2 of skin per minute. 1 pg is 1 trillionth of 1 g.

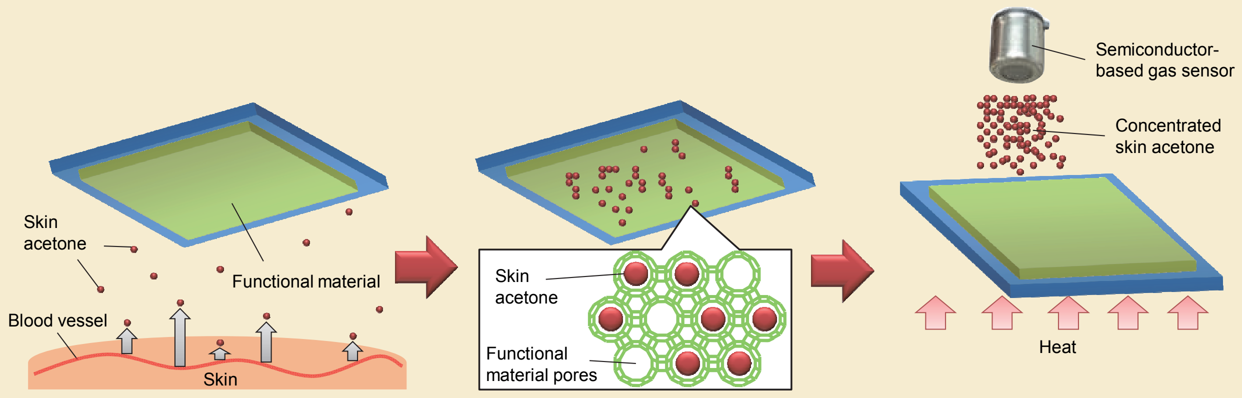

Figure 2 Concentration measurement mechanism

the world's most sensitive semiconductor-based gas sensors [5], which means, for example, a method to concentrate the skin acetone so that it can be measured is required [10]. Thus, the device in this development consists of a semiconductor-based gas sensor and a functional material*10 with pores slightly larger than the molecular size of acetone. The acetone molecules naturally emitted from the skin surface are collected for a certain amount of time by using the functional material to adsorb the skin acetone. Then, by flash heating the functional material, the adsorbed acetone is released from the functional material all at once, which temporarily concentrates it so that it can be measured by the semiconductor-based gas sensor (fig. 2). For the semiconductor-based gas sensor, we selected a tungsten oxide sensor for its particularly high sensitivity to acetone.

The device weighs 54 g, is 40 × 78 mm in size - smaller around than a credit card - and at 13 mm thick can easily fit into a breast pocket. We have successfully prototyped a compact and lightweight device roughly 1/120 of the weight of the conventional apparatus and 1/380 of its volume. The results of skin acetone measurement can be sent by radio to a paired smartphone or tablet by Bluetooth®*11. To respond to the skin acetone measurements, we also developed an application to visualize and display the user's current state of fat burning and healthy diet advice on the Graphical User Interface (GUI)*12 of the paired smartphone or tablet that receives the data from the device (**Figure 3**).

4. Performance Testing

To verify the principle of this developmental skin gas measurement mechanism, we tested the performance of the device. Because skin acetone is a constituent of biological gas that originates in the blood and can therefore be measured from various parts of the body as well as the arms, we measured skin acetone from the palms of multiple subjects and compared measurements taken with the device with measurements taken using conventional large-sized measuring equipment (gas chromatography apparatus). This test showed that the measurements taken by the device we developed had a strong positive correlation with those of the large-size apparatus (correlation coefficient*13 $R = 0.96$) (**Figure 4**). This level of accuracy means that this device could make it easy users to know their fat burning trends and targets. The performance of this prototype remains close to conventional large size apparatus, but we have succeeded in drastically reducing size and weight.

5. Service Examples

1) Dietary Support

This system could be used to offer services to users who are concerned about

*9 **Semiconductor-based gas sensor:** Using metallic oxide semiconductors as sensor elements, these sensors enable gas concentrations to be measured from the changes in electrical resistance in the sensor element that occur due to oxidation-reduction reactions with gas constituents in gaseous mixtures.

*10 **Functional material:** A material whose functions can be controlled externally. In this case, these materials selectively adsorb molecules which are then released by external stimulus such as heat.

*11 **Bluetooth®:** A standardized short-range wireless communication (IEEE 802.15.1) that operates in the 2.4 GHz band, and does not require registration or licensing for use. Bluetooth and the Bluetooth logo are registered trademarks of Bluetooth SIG, Inc. in the United States.

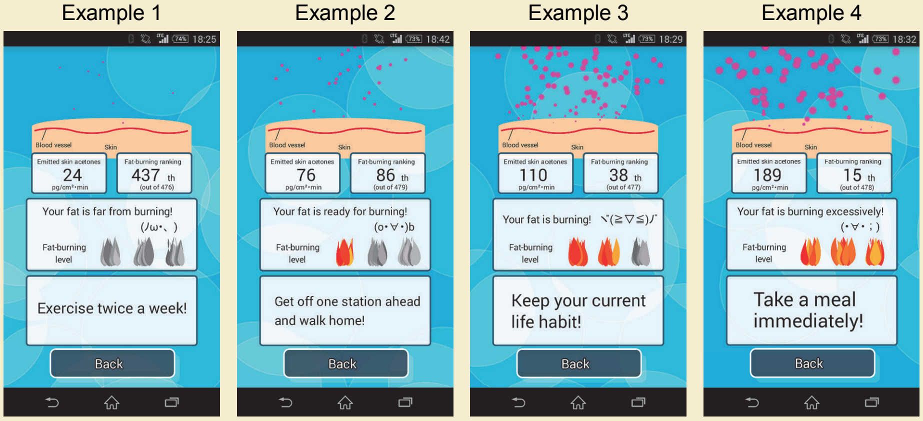

Figure 3 Examples of results displayed from measurement by the skin acetone analyzer

their diet or users who are troubled by metabolic syndromes, and could be used at work and at home on a daily basis. Specifically, this opens the potential to provide dietary support programs that include appropriate timing for meals and exercise, recommendations for menus and the size of meals, and exercise amount and load tailored to the characteristics of the user's metabolism (**Figure 5**). **Figure 6** shows the results of measurement taken by the device being worn for one day. In fig. 6, it's clear that the amount of emitted acetone from the skin changes throughout the day. For example, when the amount of emitted skin acetone is low before lunch, body fat is not being burnt much, which suggests that there is a high amount of sugar remaining in the body. In this case, because eating can lead to weight gain at this time, the user is advised to eat only a light snack and avoid large amounts of carbohydrates. In contrast, when the amount of emitted skin acetone is markedly high, the user

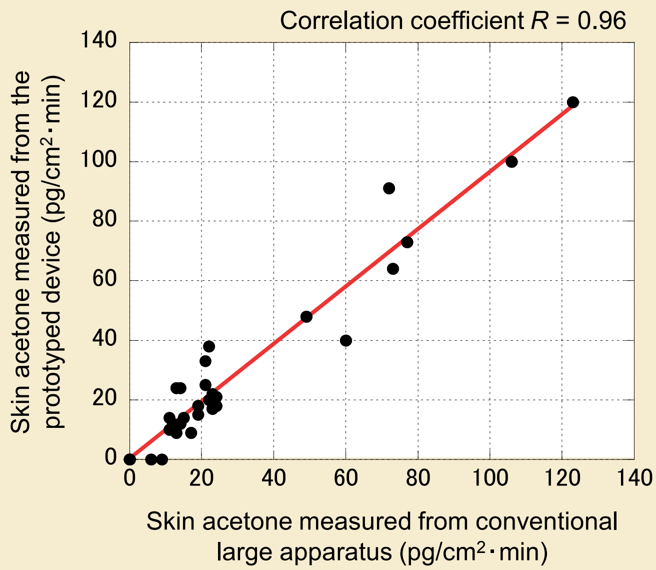

Figure 4 Comparison of skin acetone measurements

is advised to beware of potentially excessive dieting with unreasonable dietary restriction. In a different usage scenario, the user can compare the amount of emitted skin acetone before and after exercise to determine whether the exercise burnt fat effectively. Fig. 6 shows a successful exercise session, however, if there is not a marked change in the amount of emitted skin acetone before and after exercising, either the load was too low or the session was too short. Thus, advice can be given to adjust the amount of time and load for exercise in stages.

2) Monitoring Support for the Elderly

This system could be used for care

*12 **GUI:** A superior type of interface that offers visibility and intuitive operability by expressing operations and objects visually on a screen.

*13 **Correlation coefficient:** An index used in statistics to indicate the degree of similarity between two variables. The closer to 1 this value is, the more similar the variables, while the closer to 0, the more dissimilar.

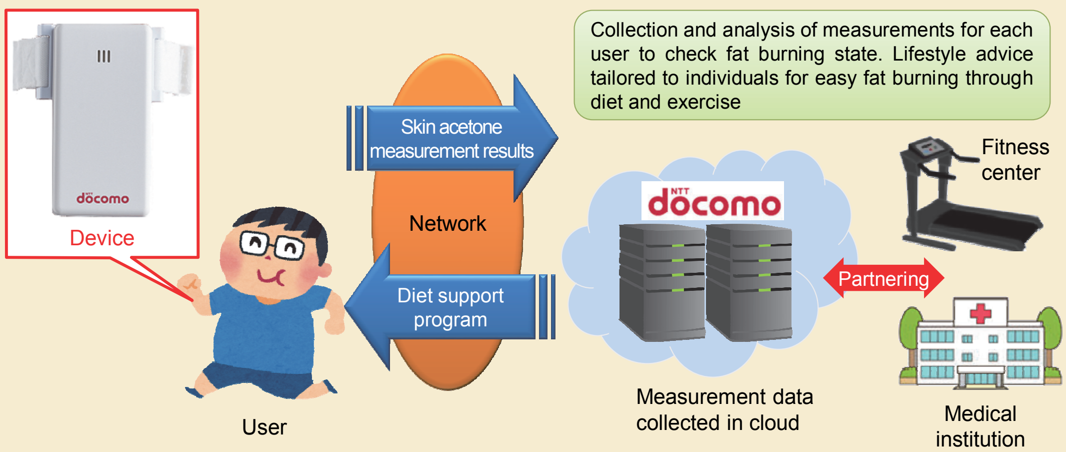

Figure 5 Service example with the wearable skin acetone analyzer

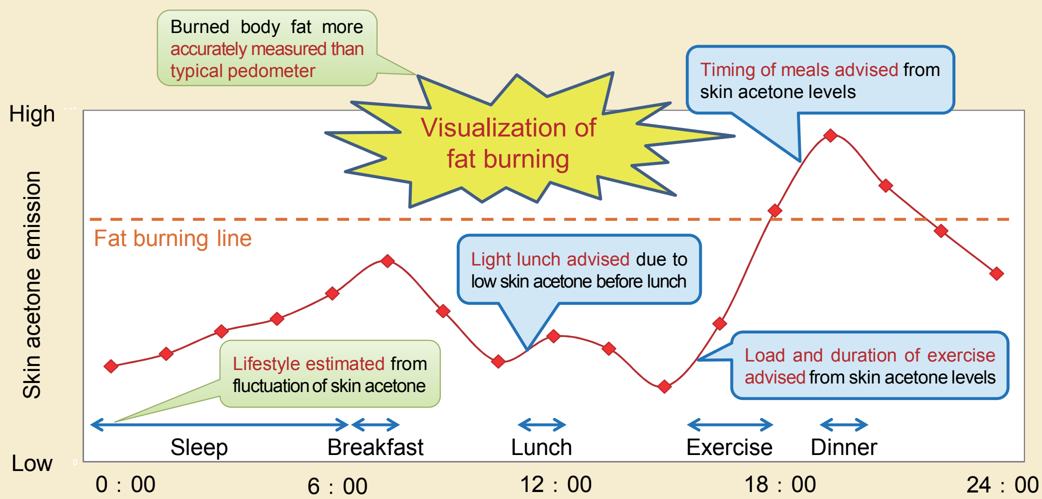

Figure 6 Measuring skin acetone emissions and advising improvement to lifestyle

and dietary management for the elderly. When an elderly person dramatically reduces the amount of food they consume or forgets to eat they can unwittingly fall into a state of malnutrition. In such a case, the skin acetone levels will be very high. Thus, whether the elderly person is eating properly can be determined objectively by measuring the skin acetone level regularly and sharing the data with families and carers to contribute to maintaining the safety and security of the elderly.

3) Support for Diabetics and Potential Diabetics

Users who suffer from diabetes and potential diabetics could also use this system. The first attempt to treat diabetes often involves dietary changes. However, if symptoms do not improve, treatments include oral medication or insulin injections. In any case, if treatments are not effectively controlling symptoms, the emitted skin acetone tends to rise and could therefore be used as an indicator in diabetes diagnosis and follow-up. In particular, this system could be used to take measurements in situations that have conventionally been problematic such as in the homes of outpatients or at the bedside of hospital inpatients.

6. Conclusion

As an example of development towards the realization of the "biochip mobile phone," this article has introduced an easy-to-wear skin acetone analyzer that enables visualization of body fat burning patterns. As a world first, this device features an independent concentration measurement mechanism with performance close to that of a conventional large-size device but much more compact and lightweight. Able to be worn like a watch or innerwear, or be incorporated into a range of other wearable devices, this device could be used to provide customized dietary support programs that are easy to follow.

We will continue our research and development into the "biochip mobile phone" and aim to develop analyzers that can comprehensively measure other gas constituents as well as acetone. These developments will contribute to the creation of new value in the healthcare and medical fields by enabling preventive care services and thus help deal with the social issue of increasing cost of national health services.

References

[1] Ministry of Health, Labour and Welfare: "FY 2012 Overview of National Medical Expenditure," (in Japanese).
http: //www. mhlw. go. jp/toukei/saikin/hw/k-iryohi/12/

[2] Ministry of Internal Affairs and Communications: "2013 White Paper on Information and Communications in Japan."
http://www.soumu.go.jp/johotsusintokei/whitepaper/eng/WP2013/2013-index.html

[3] S. Hiyama et al.: "Molecular Transport System in Molecular Communication," NTT DOCOMO Technical Journal, Vol.10, No.3, pp.49-53, Dec. 2008.

[4] Y. Yamada et al.: "Breath Acetone Analyzer to Achieve "Biochip Mobile Terminal," NTT DOCOMO Technical Journal, Vol.14, No.1, pp.51-57, Jul. 2012.

[5] T. Toyooka, S. Hiyama and Y. Yamada: "A Prototype Portable Breath Acetone Analyzer for Monitoring Fat Loss," J. Breath Res., Vol.7, No.3, 036005, 2013.

[6] NTT DOCOMO Press Release: "DOCOMO to Showcase Latest Technologies at CEATEC JAPAN 2014," Sep. 2014.
http://www.nttdocomo.co.jp/english/info/media_center/pr/2014/0918_00.html

[7] T. Tsuda, T. Ohkuwa and H. Itoh: "Findings of Skin Gases and Their Possibilities in Healthcare Monitoring," Gas Biology Research in Clinical Practice. Baserl, Karger, pp.125-132, 2011.

[8] Y. Sekine, S. Toyooka and S. Watts: "Determination of Acetaldehyde and Acetone Emanating from Human Skin Using a Passive Flux Sampler - HPLC System," J. Chromatography B, Vol.859, No.2, pp.201-207, 2007.

[9] C. Turner, B. Parekh, C. Walton, P. Spanel, D. Smith and M. Evans: "An Exploratory Comparative Study of Volatile Compounds in Exhaled Breath and Emitted by Skin Using Selected Ion Flow Tube Mass Spectrometry," Rapid Commun. Mass Spectrom., Vol.22, No.4, pp.526-532, 2008.

[10] Y. Yamada, S. Hiyama, T. Toyooka, S. Takeuchi, K. Itabashi, T. Okubo and H. Tabata: "Ultratrace Measurement of Acetone from Skin Using Zeolite: Toward Development of a Wearable Monitor of Fat Metabolism," Analytical Chemistry, Vol.87, Issue 15, pp.7588-7594, 2015.