Dynamic analysis of internal and external mental sweating by optical coherence tomography

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Abstract. Mental sweating is human sweating that is accelerated via the sympathetic nerve by application of mental or physical stress. In the neurosciences, there is keen interest in this type of sweating, because the amount of sweat in response to a stress applied to a volunteer directly reflects activity of the sympathetic nerve. It is therefore of particular value that optical coherence tomography (OCT) can provide clear *in vivo* imaging of the spiral lumen of an eccrin sweat gland in the epidermis with a spatial resolution around 10 μm. We demonstrate dynamic OCT of mental sweating of an eccrin sweat gland on a human fingertip, where the sweating dynamics can be tracked by time-sequential OCT images with a frame spacing of one second. An instantaneous amount of sweat stored in the spiral lumen is evaluated quantitatively in each OCT image, resulting in time variation measurements of excess sweat in response to mental or physical stress. In the dynamic OCT of mental sweating, as demonstrated here, we note for the first time *internal* sweating without ejection of excess sweat from the spiral lumen to the skin surface. *Internal* sweating has not been previously detected without the availability of our dynamic OCT technique. Until now, it has been commonly accepted that sweating is always accompanied with ejection of excess sweat to the skin surface. On the basis of our findings reported here, this type of sweating should now be referred to as *external* sweating. In this study, we demonstrate that *internal* sweating occurs more often in the case where mental stress is applied to a volunteer, and that it is more useful for evaluation of activity of the sympathetic nerve. The dynamic OCT for both *external* and *internal* sweating is demonstrated. © *2009 Society of Photo-Optical Instrumentation Engineers.* [DOI: 10.1117/1.3079808]

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1 Introduction

17 years have passed since the first demonstration of optical coherence tomography (OCT) in 1991.[1] OCT is recognized as a useful technique for *in vivo* tomography, with a resolution around 10 μm underneath the human skin surface. OCT has been developed intensively for its clinical application in ophthalmology, including high-resolution imaging and high-speed data acquisition.[2–6] Very recently, an endoscopic OCT for intravascular imaging has been used for clinical diagnosis of arteriosclerosis.[7,8] In addition to its clinical applications, OCT has proven useful for brain science; for example, Maheswari et al. attained instantaneous A-mode OCT signals of nerve responses to a stimulus in the cerebral cortex of a cat. In this method, OCT is referred to as functional OCT.[9]

Recently, we proposed and demonstrated the use of dynamic OCT, where tomographic images are obtained in a time sequence with a frame spacing of a few seconds or less, for tracking the dynamics of small organs such as eccrin sweat glands and peripheral vessels underneath the human skin surface.[10–12] In particular, our interest is in dynamic OCT analysis of mental sweating, where sweating is accelerated via the sympathetic nerve by mental or physical stress. In OCT of a human fingertip, the eccrin sweat gland in the stratum corneum of the epidermis is clearly recognizable as a spiral duct with a high reflection light intensity, because there is a large refractive-index difference on the wall of a spiral lumen between sweat and keratinous epidermal tissue. In response to a stress, the spiral lumen in the epidermis expands rapidly to take up excess sweat from a sweat coil in the dermis. Quantitative evaluation of this excess sweat is made by summation of the reflection light intensity of all the pixels that constitute the spiral lumen in OCT, as is presented in this work.

In our experiment, it has been found that mental sweating is not always accompanied with ejection of excess sweat from the spiral lumen through a sweat pore on the hill of a fingerprint. In the case where mental stress only slightly stimulates

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the sympathetic nerve, excess sweat stored in the spiral lumen is not ejected to the skin surface, but rather, the sweat returns to the dermis after the sympathetic nerve calms down. This sort of mental sweating is called *internal* sweating, which, it should be emphasized, was not demonstrated prior to the use of dynamic OCT by the authors. Until now, it has been commonly accepted that sweating is always accompanied with ejection of excess sweat through the sweat pore from the spiral lumen, and that sweat droplets always appear on the skin surface; in other words, that *external* sweating occurs.

The mechanism and morphology of sweating are described briefly in Sec. 2 to help the reader understand significance of this work, where mental sweating is classified into *external* and *internal* sweating. In Secs. 3 and 4, dynamic analysis of mental sweating is described in detail, including time-sequential OCT images for tracking dynamics of sweating on human fingertips and quantitative evaluation of sweating in each OCT image of the spiral lumen of an eccrin sweat gland. Typical analytical results for dynamic OCT of *external* and *internal* mental sweating are presented in Secs. 5 and 6, respectively.

2 Mechanism, Morphology, and Classification of Mental Sweating

In human perspiration (or sweating), there are two types of sweating, thermal and mental sweating. Thermal sweating is stimulated by external heat, while mental sweating occurs in response to mental or physical stress.[13,14] In thermal sweating, a temperature increase of the skin surface is detected by a temperature-control nerve center in the hypothalamus. This is followed by enhancement of sweating on the whole skin surface except for the palms of the hands and the soles of the feet. A large amount of sweat is also secreted for rapid cooling of the skin surface. It is rather difficult to control thermal sweating in a laboratory.

On the other hand, sweating stimulated by mental or physical stress, or mental sweating, occurs at room temperature and only on the palms of the hands and the soles of the feet. Compared to thermal sweating, in mental sweating only a relatively small amount of sweat is secreted in response to the stress stimulus. The nerve center for detection of the stress is closely connected with the premotor area of the cerebral cortex, the limbic cortex, and the hypothalamus. Excess sweat due to stress is controlled via the cholinergic sympathetic nerve by impulses from the nerve center. The amount of excess sweat, therefore, directly reflects activity of the sympathetic nerve (ASN). Our major interest is in the dynamic analysis of mental sweating as a means of evaluating the functioning of the ASN.

A more detailed description is necessary to understand the morphology of eccrin sweat glands. In the human fingertip, in a part of the dermis over 5 mm deep underneath the skin surface, an eccrin sweat gland coils itself to absorb sweat from the surrounding peripheral vessels and tissues.[15,16] Sweat is exchanged between the coil and the surrounding vessels so that a proper amount of absorbed sweat is always stored in the coil. The coil connects to a straight lumen (or sweat duct) in the dermis, followed by a spiral lumen in the epidermis. In mental sweating, the lumen expands to take up excess sweat from the coil in response to mental stress. The amount of

excess sweat increases in proportion to the strength and duration of the mental stress. In the case where the sweat taken up overflows the expanding spiral lumen, an excess of sweat is ejected to the skin surface through a sweat pore. This can be referred to as *external* mental sweating, because sweat droplets are ejected out of eccrin sweat glands. External sweating can be detected by an existing sweating recorder, which enables us to continuously monitor water vapor of droplets inside an airtight capsule placed on the palm or fingertip of a volunteer that covers several hundred sweat glands.[17] This method basically allows macroscopic detection of sweating without providing any understanding of the sweating dynamics of each individual eccrin sweat gland.

On the other hand, in the case where the sweat taken up does not overflow the spiral lumen in the epidermis, no sweat droplet appears on the skin surface. The entire amount of sweat instead returns slowly to the coil in the dermis through a straight lumen, as the sympathetic nerve quiets down, giving rise to a phenomenon called *internal* mental sweating. For evaluation of activity of the sympathetic nerve, sound stress is very often used in our experiments to moderately stimulate the sympathetic nerve. Sound stress, therefore, gives rise to internal, as opposed to external, mental sweating in most cases, and this internal sweating can be detected only by dynamic OCT, as is presented in Sec. 5.

3 Time-Sequential Optical Coherence Tomography Images of Mental Sweating

Physical stress is applied to a volunteer by a firm grip on a bar with the right hand during a period of 10 sec. In response to the firm hand grip, sweating of the left hand is accelerated through the sympathetic nerve as the volunteer attempts to prevent slip of the bar. In this experiment, sweating dynamics are tracked by time-domain OCT (TD-OCT), where a 1.3-μm superluminescent diode (SLD), with a coherence length of 17 μm, is used as the light source. Two fiber optic PZT modulators, placed on both reference and signal arms of a single-mode-fiber Mach-Zehnder interferometer,[18,19] are driven in the push-pull operation for efficient optical delay line scanning. The scanning speed for the optical delay line is set at up to 2000 scans/sec at the modulation frequency of 1 kHz of the applied voltage, corresponding to 5 to 10 frames/sec. To obtain stable OCT imaging over several minutes, the left hand of the volunteer is fixed with a cast of rubber clay. The skin surface is not covered with any jelly or fluid, so that ejection of excess sweat from eccrin sweat glands is not disturbed. The imaging is then made in noncontact mode with the skin surface. A 10$\times$ objective with an effective NA of 0.08 provides a lateral resolution of 15 μm with a focal depth of 270 μm.

For an experiment on mental sweating, a sweat gland of the fingertip of the left hand of volunteer 1 (a 23-year-old male) is observed by the TD-OCT, as described earlier. To select an appropriate active sweat gland, one has to see if the reflection light intensity of the spiral lumen is changed substantially by a firm hand grip, indicating an active sweat gland. Once an active sweat gland is selected and prior to the application of the physical stress, the volunteer is confirmed to be in the resting state, as the reflection light intensity from the spiral lumen in the epidermis is small enough to indicate
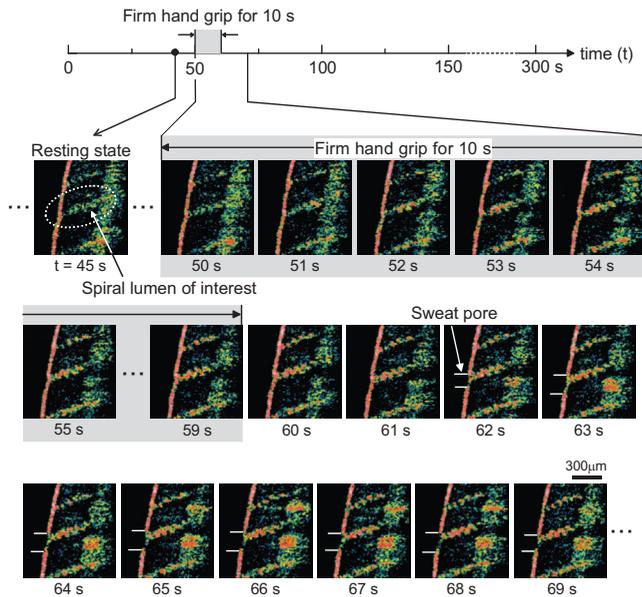
Fig. 1 Time-sequential OCT images of mental sweating on a fingertip of the left hand of volunteer 1 (23-year-old male), where physical stress is applied to the volunteer by firm grip of a bar with the right hand for 10 sec. OCT images were obtained in a time sequence with frame spacing of 1 sec by the TD-OCT. The white-dot circle indicates a spiral lumen of interest.

Fig. 2 Observation of a sweat droplet ejected from the spiral lumen in volunteer 2 (a 23-year-old male). This OCT image was obtained 8 sec after application of the stress.
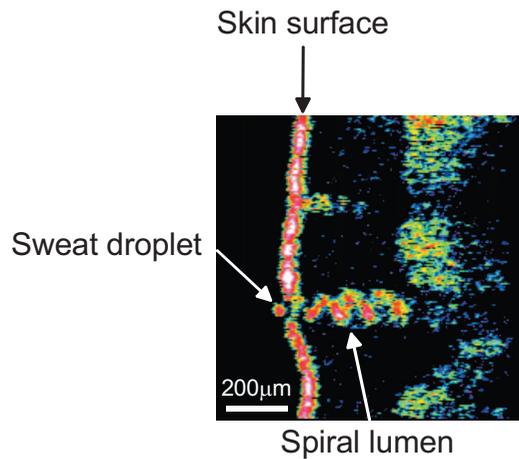
less sweating. Time-sequential OCT images of the fingertip of the left hand of volunteer 1 are shown in Fig. 1, where the frame spacing is 1 sec. Immediately after the firm hand grip on a bar, the lumen expands rapidly to store excess sweat; as a result, the reflection light intensity of the spiral lumen increases substantially, as shown in Fig. 1.

In this case, three eccrin sweat glands are observed in the same OCT. These glands, however, are out of alignment with each other along the scanning direction of the optical beam. In the experiment, the beam position was adjusted so that the central spiral lumen was observed clearly for quantitative evaluation of sweating. The reflection light intensity of the spiral lumen increases rapidly after the firm hand grip. Nearly 10 sec after the start of the firm hand grip, the sweat pore opens to be as large as 150 μm in diameter to eject an excess of sweat from the spiral lumen, although a sweat droplet does not appear in OCT images. The sweat pore opens continuously for 40 sec after the firm hand grip. The mental sweating described here is obviously external because of existence of the sweat pore, although sweat droplets are not observed in OCT images of Fig. 1, because a sweat droplet does not exist on the same cross section as the OCT images of the spiral duct in most cases.

Occasionally, a sweat droplet is observed as well as a sweat pore, as shown in Fig. 2. A droplet is ejected to the skin surface within 10 sec of the onset of the physical stress, and then it disappears gradually due to water evaporation.
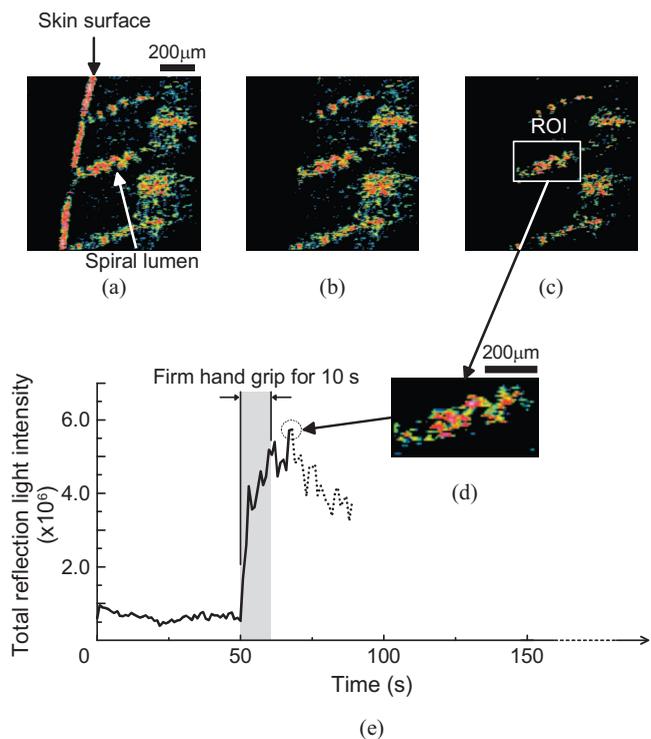
4 Quantitative Evaluation of Mental Sweating

In the discussion described before, it is pointed out that the spiral lumen suddenly expands to take up excess sweat from the coil in the dermis in response to physical stress. This

function of the eccrin sweat gland is recognized by the abrupt increase in the reflection light intensity of the spiral lumen in the resulting OCT of Fig. 1. This fact suggests that an instantaneous amount of sweat stored in the spiral lumen can be evaluated quantitatively by summation of the reflection light intensity of all pixels included in the spiral lumen. The simple image processing for quantitative evaluation of sweat stored in the spiral lumen is shown in Fig. 3. First, the bright line

Fig. 3 Image processing for quantitative evaluation of sweating. (a) The original image at t=69 sec in Fig. 1. (b) The bright line along the skin surface is removed. (c) Elimination of background noise under the threshold value. (d) Summation of all the pixels along the spiral lumen in the region of interest (ROI). (e) Variation of the total reflection light intensity of the ROI with time.
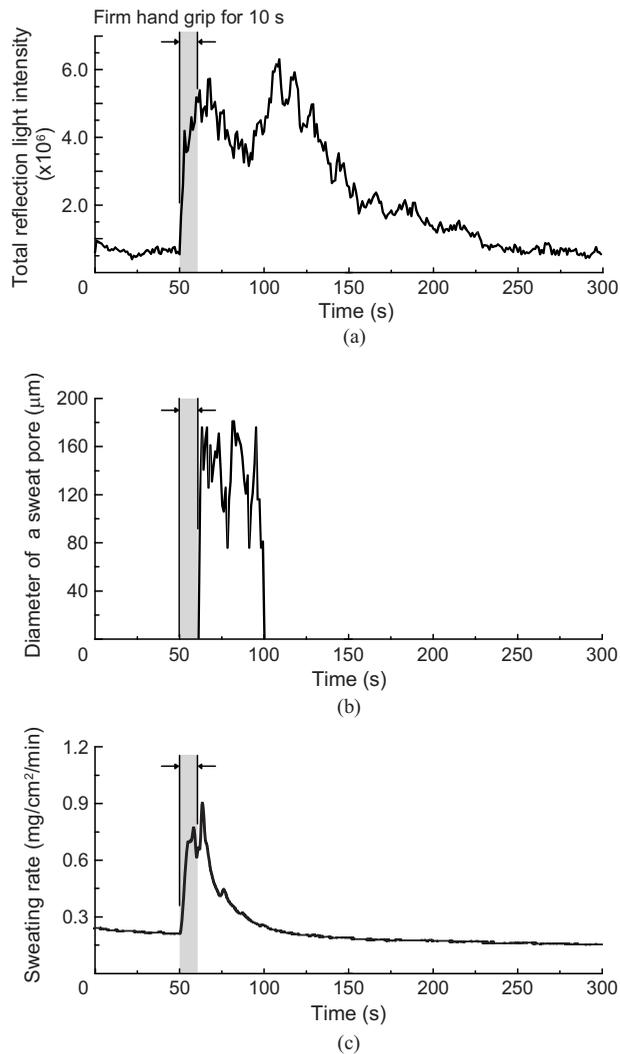
Fig. 4 Analytical results of *external* mental sweating stimulated by application of a firm hand grip to volunteer 1. (a) Time variation of the total reflection light intensity along the spiral lumen corresponding to the instantaneous amount of sweat stored in the spiral lumen. (b) Time variation of the diameter of a sweat pore. (c) Detected signal by the existing sweating recorder.

showing the skin surface is removed from an original image, as shown in Fig. 3(b). The intensity level is then set to zero in all the pixels having an intensity level below the threshold value, defined as the maximum intensity level of background noise in the pixels, resulting in Fig. 3(c). Subsequently, the spiral lumen is framed with the region of interest (ROI), followed by summing up the reflection light intensity of all the pixels in the ROI. The total intensity of the ROI is recognized as the instantaneous amount of sweat stored in the spiral lumen.

The total intensity (or the amount of sweat) is counted for each image in the time-sequential OCT images of Fig. 1, with the result that one can find variation of the instantaneous amount of sweat stored in the spiral lumen over time, as shown in Fig. 4(a). The active sweat gland makes a quick response to a firm hand grip within 10 sec. The sweat-pore

diameter also varies with time in response to the stress, as shown in Fig. 4(b).
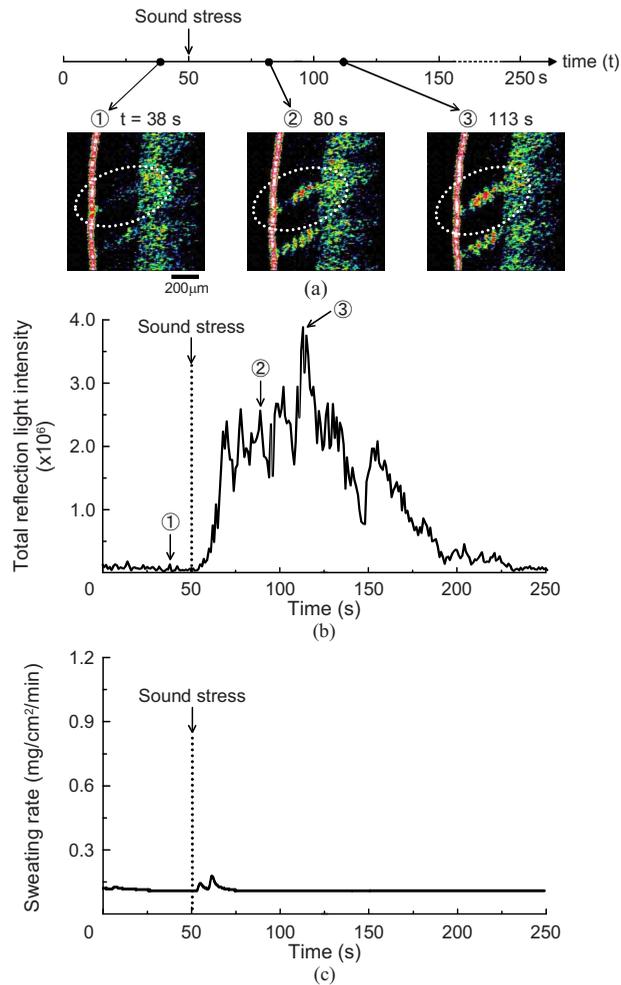
5 External Sweating

After the dynamic OCT, as described earlier, macroscopic detection of mental sweating stimulated by the firm hand grip was made by a sweating recorder,[17] where the sensing head with a hole of 1 cm^2 was placed on the same middle finger tip of volunteer 1, that included the active sweat gland of interest observed by the dynamic OCT. There are several hundred eccrin sweat glands on average on a human fingertip covered by the sweating recorder. In the case of mental sweating due to the firm hand grip, the sweating recorder exhibits a sharp response, as shown in Fig. 4(c), indicating that water vapor of sweat droplets ejected from at least a few hundred eccrin sweat glands is detected. The detected sweating is certainly external. The macroscopic detection time for mental sweating is as short as 30 sec, which is in agreement with the opening time of the sweat pore, as shown in Fig. 4(b).

In addition, the dynamic OCT for the upper and lower sweat glands in time-sequential OCT images of Fig. 1 is obtained by shift of 15 to 30 μm of the beam scanning position. It is found that quantitative evaluation of mental sweating is different in the response time and the amount of excess sweat, even for adjacent active sweat glands. This fact apparently shows disorder of eccrin sweat glands, in agreement with a very recent study that confirmed this disorder using a quasi 3-D OCT image constructed by maximum-intensity-projection (MIP) imaging, where several eccrin sweat glands adjacent to each other were tracked simultaneously.[20] However, it is reasonable to conclude that this sort of disorder is necessary to control precisely the amount of excess sweat in response to the strength of mental stress, because we believe there is no waste in human physiological functions.

6 Internal Sweating

In the case where stress is applied by a firm hand grip, as described before, ejection of excess sweat to the skin surface is required to prevent slipping of the bar. Some moisture of the skin surface is necessary to prevent slipping of the bar.[14] The mental sweating stimulated by the firm hand grip, therefore, is usually accompanied with ejection of excess sweat from the spiral lumen through the sweat pore on the hill of the fingerprint, as shown in Fig. 1. The firm hand grip is thus a rather strong stress. However, the whole amount of sweat stored in the spiral lumen is not always ejected to the skin surface. In the case where strong stress is applied to a volunteer, most excess sweat in the spiral lumen is ejected, while the remaining returns to the coil in the dermis.
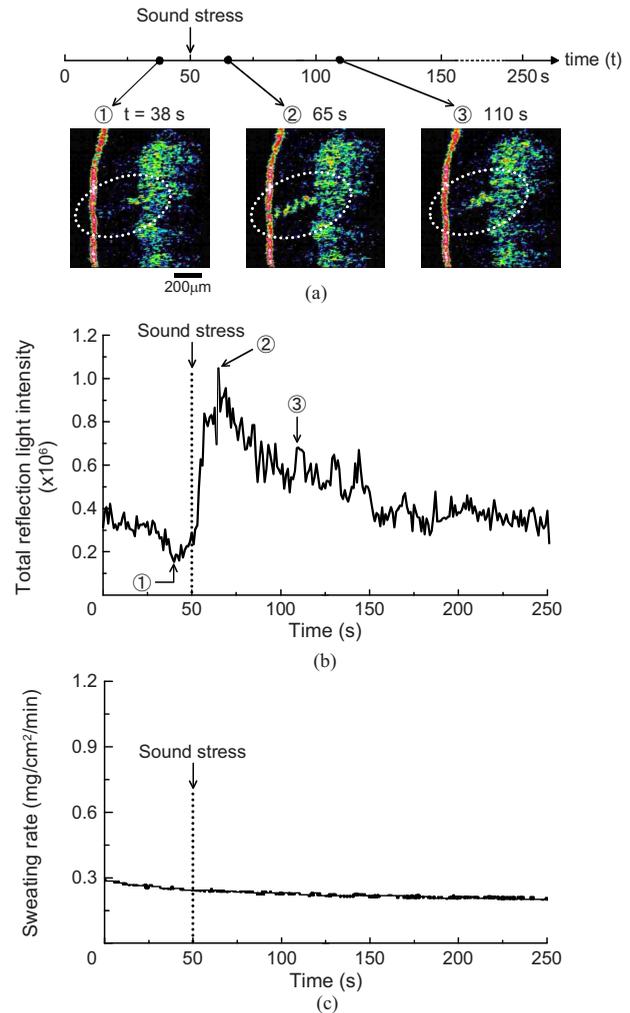
On the other hand, mental sweating is not accompanied with ejection of excess sweat in the case where an applied stress does not stimulate the sympathetic nerve to as great a degree. For instance, mental sweating stimulated by an unpleasant sound is not detected very often by the use of the existing sweating recorder, because excess sweat is often not ejected from the spiral lumen. In this case, however, dynamic OCT indicates that the amount of sweat stored in the spiral lumen increases rapidly in response to the sound stress, but the stored sweat disappears slowly without ejection of sweat. Typical examples of mental sweating stimulated by unpleas-

Fig. 5 Dynamic OCT of *internal* mental sweating, where an unpleasant sound was applied to volunteer 3 (a 21-year-old male). (a) A portion of time-sequential OCT images. (b) Time variation of the total reflection light intensity along the spiral lumen. (c) Detected signal by the existing sweating recorder.
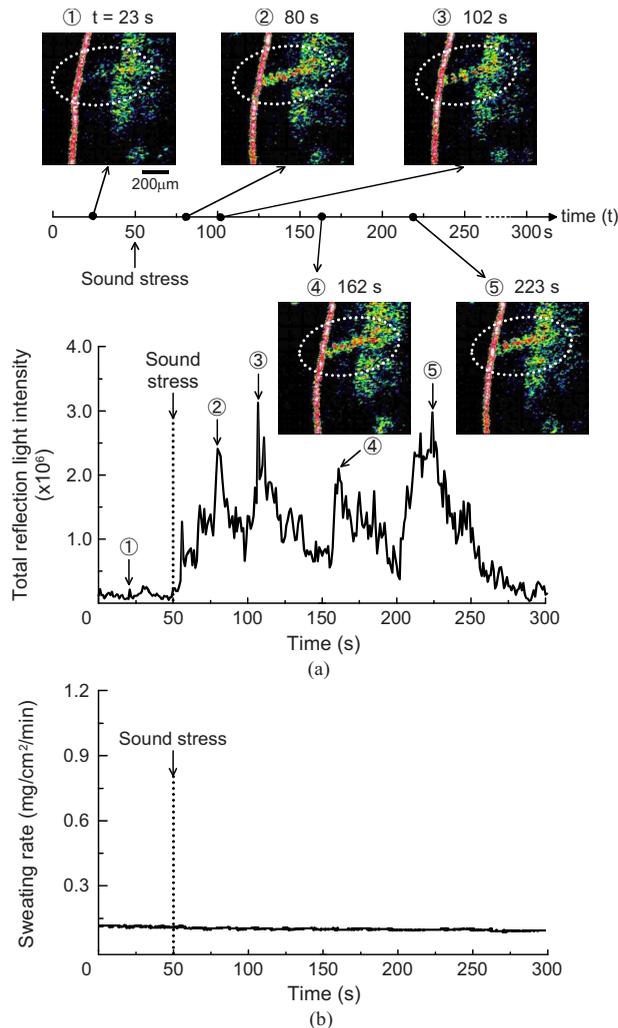

Fig. 6 Dynamic OCT of *internal* mental sweating for volunteer 4 (a 22-year-old female). (a) A portion of time-sequential OCT images. (b) Time variation of the total reflection light intensity along the spiral lumen. (c) Detected signal by the existing sweating recorder.

ant sound for volunteers 3 and 4 (21-year-old male and 22-year-old female) are shown in Figs. 5 and 6, respectively, where the mental stress is the sound of breaking glass for 0.5 sec at a sound level of 90 dB. It can be seen in the experimental results that the sweat pore does not open, even though the stored sweat in the spiral lumen becomes maximal. This sweating, without ejection of excess sweat to the skin surface, is referred to as *internal* sweating. The instantaneous amount of sweat in the spiral lumen increases rapidly in response to the sound stress, and the excess sweat is stored in the spiral lumen for 150 to 200 sec, as shown in Figs. 5(b) and 6(b). The signals detected by the sweating recorder are quite low, as shown in Figs. 5(c) and 6(c), in comparison with the result of Fig. 4(c) in the case of the firm hand grip. Even in the case of the sound stress, only a few tens of sweat glands may exhibit external sweating among the several hundred glands in the detected area on a human fingertip.

Another typical example of internal mental sweating is shown in Fig. 7, where volunteer 5 is a 21-year-old female. This type of mental sweating is characterized by a wave response in time variation of the instantaneous amount of sweat

stored in the spiral lumen. Actually, there are several peaks in excess sweat, showing echo responses of the sympathetic nerve to mental stress. This type of echo response is found very often for those volunteers who have their first experience of the mental sweating test, because they are so sensitive to mental stress; in other words, it seems that the echo response indicates a certain high degree of excitement of the sympathetic nerve. The sweat pore does not open, even for several peaks of excess sweat, as shown in Fig. 7(a), and the sweating recorder does not detect the echo response. Consequently, *internal* sweating is tracked only by the dynamic OCT, as demonstrated here.

7 Conclusion

We demonstrate the dynamic analysis of mental sweating by time-sequential OCT imaging of eccrine sweat glands on human fingertips. Dynamic OCT shows that, in response to mental or physical stress, the spiral lumen in the epidermis expands rapidly to take up excess sweat from a coil of the sweat gland in the dermis. The instantaneous amount of sweat stored

Fig. 7 Echo response to the sound stress in *internal* mental sweating for volunteer 5 (a 21-year-old female). (a) Time variation of the total reflection light intensity along the spiral lumen as well as a portion of time-sequential OCT images. (b) Detected signal by the sweating recorder.

in the spiral lumen is evaluated quantitatively by summation of the reflection light intensity of all the pixels along the spiral lumen. It can only show changes in the OCT signal due to these phenomena that can be evaluated over time in a quantitative way. In particular, we describe for the first time *internal* sweating without ejection of excess sweat from the spiral lumen to the skin surface. *Internal* sweating occurs very often in the case where an unpleasant sound is applied to a volunteer, because the sound stress does not stimulate the sympathetic nerve as much as other stresses. It is emphasized that *internal* sweating can be detected only by the dynamic OCT. Thus, dynamic OCT proves to be much more sensitive to mental sweating when compared with the sweating recorder that now exists, and which measures only *external* sweating, as it depends on ejection of excess sweat to the skin surface. The dynamic OCT, however, has a current disadvantage against the sweating recorder that measurement of excess sweat is limited to a few sweat glands. Very recently, we reported MIP OCT imaging, which makes it possible to track

simultaneously mental sweating dynamics for five sweat glands.[20] It has been confirmed in our experiment that the sweat glands behave nonuniformly, although these five sweat glands are adjacent to each other. Accordingly, if an eccrin sweat gland is picked up at random, there is a higher sampling error for evaluation of mental sweating dynamics. The sampling error can be overcome, as described in the following. Fortunately, all eccrin sweat glands lie along a ridge of fingerprints on human fingertips. The position of a sweat gland of interest, therefore, can be identified according to the pattern of fingerprints of a volunteer, using an enface image derived from the 3-D OCT constructed by volume rendering of B-mode OCT images of the human fingertip. In fact, one can select easily the identical sweat gland of interest in this manner described whenever the activity of the sympathetic-nerve activity is evaluated based on mental sweating. Very recently, time variation of the sympathetic nerve activity for on taking a meal has been evaluated by measurement of mental sweating of the identical sweat gland just before lunch and every one hour after lunch. This interesting result will appear soon elsewhere.

Our major interest in using dynamic OCT to measure mental sweating is as an evaluation method for the activity of the sympathetic nerve (ASN). A key point for the quantitative evaluation of ASN is that mental stress such as unpleasant sound or mental arithmetic is moderate enough that excess sweat does not saturate in the spiral lumen in epidermis; in other words, the quantitative evaluation of ASN is not possible unless *internal* sweating is detected by the dynamic OCT. The detailed description of the evaluation of ASN will appear elsewhere.

Acknowledgments

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