

June 2022 Shiseido Company, Limited

Shiseido Becomes World's First to Quantify Age-Dependent Changes in Superficial Musculoaponeurotic System

~A unique solution for facial sagging by targeting SMAS, the deepest layer of the skin~

Shiseido Company, Limited ("Shiseido") has succeeded in quantitatively measuring age-dependent morphological changes in the superficial musculoaponeurotic system (SMAS)*¹, which lies at the deepest layer of the facial skin, for the first time in the world through joint research with Dr. Daiki Tamada, Assistant Professor at the University of Yamanashi, Department of Radiology. By applying advanced MRI*², which is used to diagnose brain and liver diseases, to estimate the quality of the SMAS*³ using its water content as an indicator, we quantified the age-dependent morphological changes of the SMAS in a non-invasive way. Even when age and BMI, the key factors for the development of sagging, are comparable, the group with the aged SMAS showed more sagging and less firmness of the skin than the group with the younger SMAS. These results indicate that not only are aging of the dermis and subcutaneous fat involved in facial sagging, which we had previously reported, but morphological changes in the SMAS are also a contributing factor to facial sagging. In addition, we have developed a beauty solution that combines a massage technique and base formulation for facial sagging by targeting the SMAS and we showed, using our accurate sagging measurement method, the efficacy of eight-week application of the beauty solution.

We at Shiseido are promoting this research with the Inside/Outside approach from our unique R&D philosophy "DYNAMIC HARMONY". We will leverage cutting-edge technology that takes a threedimensional approach on facial appearance to unravel the potential of the deep part of the skin and create innovative solutions to facial aging.

*¹ Abbreviation for superficial musculoaponeurotic system. It is a sponge-like anatomical structure composed of muscle cells, collagen fibers, and elastin fibers, and lies at the deepest part of the facial skin (Figure 1).

*² Magnetic resonance imaging. It utilizes magnetic properties to create an image of the inside of an object in a non-invasive way. In addition to its general purpose of imaging, the MRI used in this study simultaneously utilizes an advanced technology that calculates the water content in tissues based on signal intensity from hydrogen atoms of water molecules.

*3 Thinning from the original state of the skin, which is caused by the loss of skin's innate properties due to aging, etc.

Research background

We have been conducting research and development focusing on "facial sagging" since 2000 ahead of other companies. Facial sagging is an aging phenomenon in which the skin is drooped down by gravity, and one of the most common skin concerns that become more noticeable with aging. To date, we have actively created new values for these skin concerns not only by taking dermatological approaches, such as our previous discoveries of dermal anchoring structures that supports skin shape and the mechanism of subcutaneous fat infiltration into the dermal layer of aged skin, but also by developing the accurate sagging measurement method.



Figure 1. SMAS lies at the deepest part of the skin. (BLUE: collagen, RED: muscle fibers, etc.)

The SMAS, a structure unique to the facial skin, is known in an aesthetic surgical procedure of "lift-up" to reduce sagging severity and anatomical direct observation has suggested that the SMAS thinning occurs with aging. At the same time, because the SMAS lies in the deepest layer of the skin, it has been difficult for us to conduct non-invasive observation, hindering us from fully understanding whether the SMAS thinning is a cause of sagging or a correlated phenomenon of aging. Thus, in order to quantitatively clarify the relationship between age-dependent SMAS morphological changes and the sagging severity, we developed a non-invasive method using the advanced MRI. In addition, we developed a beauty solution that is considered to be effective on sagging caused by morphological changes in the SMAS and verified the effectiveness of application of the beauty solution for eight weeks.

Advanced MRI technology reveals age-dependent SMAS morphological changes

The SMAS is a sponge-like tissue filled with interstitial fluid. However, as the SMAS thins with aging, it loses the interstitial fluid, resulting in an increased fiber ratio. In collaboration with the University of Yamanashi, Department of Radiology, we applied advanced MRI to the face and visualized the water molecule signals in the SMAS. Consequently, we succeeded in quantitatively measuring the age-dependent morphological changes of the SMAS for the first time in the world. The results revealed that the water signals of the SMAS were strong in MRI images of the subjects in their 20s, whereas the water signals of the SMAS were weak with subjects in their 60s (Figure 2). The relationship between the SMAS water content, which indicates the degree of thinning, and the subject's age showed that it is possible to quantitatively measure the SMAS morphological changes (Figure 3). When we compared a group with high SMAS water content (Group A where SMAS is less aged) and a group with low SMAS water content (Group B where SMAS is aged), both being comparable in age and BMI, the group B showed more sagging and less firmness of the skin than the group A. These results suggest that sagging is caused not only by the dermis and subcutaneous fat, but also by the SMAS, which lies in the deepest layer of the skin.



Figure 2. MR images of the face in supine position, sliced through the nose and cheek areas. (The dermis and SMAS appear bright with high water content, while the subcutaneous fat in between appears dark with low water content.)



Figure 3: Relationship between signal intensity of SMAS water content and age.



Figure 4: Comparison in the degree of sagging between groups with younger SMAS (A) and with aged SMAS (B), both are comparable in age and BMI.

Sagging improvement effect of a unique beauty solution inspired by SMAS study findings

Although the SMAS is a structure unique to the facial skin, fascia itself exists throughout the body, and it is already known that myofascial adhesion causes stiff shoulders and lower back pain. One of solutions to myofascial adhesion is suctioning (temporarily and physically peeling apart), which is performed at osteopathic clinics, etc. This procedure has the effect of releasing adhesions and improving stiff shoulders and lower back pain. Inspired by this procedure, we developed a new beauty treatment that combines a unique massage technique and base formula^{*4}. The technique lifts up the cheeks resulting from the stimulating the skin by pinching and pulling up the deeper part of the skin with fingers as if physically peeling apart the aged SMAS, and the base formula helps this technique to be performed more effectively. After eight weeks of continuous application of this treatment, the sagging factor^{*5} significantly decreased (Figure 5), indicating that the newly developed beauty solution is effective in improving facial sagging (Figure 6).

*⁴ Base agent designed to spread smoothly over the entire face and help the technique deliver its effects deep into the skin without the hands getting too slippery on the skin surface during performing the technique.

*⁵ Converted score of the volume difference calculated based on the shape of the face in sitting and supine positions. With the factor, "sagging" can be objectively and quantitatively evaluated as the factor correlates very well with the sagging score (visual evaluation score).



Figure 5: Change in sagging factor with the application of the beauty solution

Figure 6. Sagging improved by the beauty solution. (Sagging images from a 45-degree angle on both sides)

Future prospects

Sagging is a phenomenon in which the face shape noticeably alters by gravity, and its impact to facial appearance is significant, making it a major concern for our customers. It is said that due to the COVID-19 outbreak, people wear masks on a daily basis, and a growing number of people feel their faces stiffened as they rarely change their facial expressions. In this study, we revealed that sagging is an extremely complex phenomenon that involves the SMAS in the deeper part of the skin and that sagging can be improved by stimulating the SMAS and eliminating "facial stiffness".

In the cross-sectional research on aging, we have pioneered the field of facial sagging, which was thought to be outside the scope of skin care, by unraveling the age-related phenomena that occur within the skin one by one. We will further accelerate research and development to meet the expectations of people who suffer from skin aging by leveraging our research, like the ones that won the highest award at four consecutive IFSCC Congresses (International Federation of Societies of Cosmetic Chemists) by Shiseido's Fellow, Tomonobu Ezure.

[Related news releases]

Shiseido Develops An Accurate Sagging Measurement Method (2021) <u>https://corp.shiseido.com/jp/news/detail.html?n=0000000003235</u> (Japanese only)

Shiseido's R&D philosophy "DYNAMIC HARMONY"

Shiseido Formulates its Unique R&D philosophy "DYNAMIC HARMONY" (2021) https://corp.shiseido.com/en/news/detail.html?n=0000000003252

The DYNAMIC HARMONY special website:

https://corp.shiseido.com/en/rd/dynamicharmony/

<Reference>

Researchers' challenge

Targeting age-related changes in the internal structure of the face

Dr. Takai, who is in charge of this study, studied at the Massachusetts General Hospital, Cutaneous Biology Research Center (CBRC*) in Boston, Massachusetts, USA, for eighteen months since 2016. CBRC conducts research on the skin from various aspects including immunity, nerves, blood vessels, and skin morphology by using cutting-edge molecular biological techniques, and he was engaged in research on epidermal homeostasis and its mechanisms therein. After returning to Japan, he started to elucidate the mechanism of age-related morphological changes in the deepest layer of facial skin by combining his knowledge and skills in engineering, which he acquired before going to CBRC, with the experience of studying in US. As a result, he successfully found that the SMAS morphology significantly changes with age.



Researcher, Eisuke Takai, Ph.D.

* Cutaneous Biology Research Center: A general research institute for advanced research and development in the field of dermatology established by Harvard Medical School and Massachusetts General Hospital with support from Shiseido in 1989. Shiseido dispatches researchers to the center to conduct joint research with world-class researchers.

Ideas based on his own experience and joint research with the University of Yamanashi, Department of Radiology

Since 2018, we have been conducting joint research with Dr. Daiki Tamada, an assistant professor at the University of Yamanashi, Department of Radiology, who has expertise in MRI. It took two years for us to find the most appropriate conditions to apply the MRI technology to the face because the anatomical structure of the face is extremely complex. In addition to that, several months were needed to obtain data from more than 50 women because we were able to examine the skin of only two people per day since the experiments had to be conducted after usual daily clinical examinations were finished at the University of Yamanashi Hospital. Dr. Takai commuted to the University Hospital every week during the experiment.

In verifying how to approach the SMAS, which lies at the deepest part of the skin, Dr. Takai got a hint from the "myofascial release" treatment, which he personally received at a chiropractic clinic for the back pain he had been suffering for many years. Based on the sensation of myofascial adhesions being peeled apart during the treatment and its dramatic effects, he thought about proposing a new concept of "myofascial release for the face", and he applied it to the development of a beauty treatment in this study.

Curiosity about facial aging as a universal phenomenon

In addition to the previous achievement of the accurate sagging measurement method, Dr. Takai and his collaborator succeeded non-invasive observation of the SMAS by using MRI, with an attitude of curiosity to elucidate age-related changes in the deeper layer of the skin that have not yet been clarified. Going forward, he will continue to conduct comprehensive research and development to understand age-related changes in the complex structure of the face by investigating the skin's internal structure and to create solutions to improve these changes. The face is a unique body part which readily grabs our attention, and apparently, we can even estimate one's age and health conditions such as fatigue level just by looking at their face. We will also focus on the conscious and unconscious psychological aspects of human perception of the face and will continue our research to develop solutions that can be beneficial for all our customer.