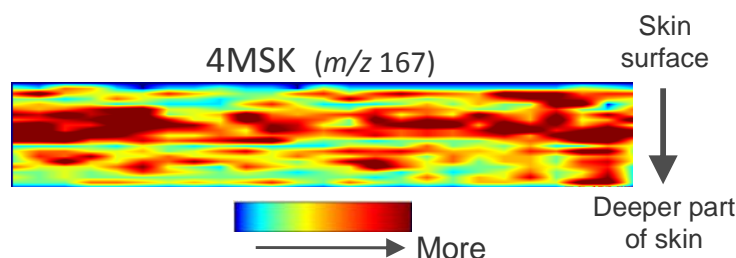


Shiseido the World's First to Succeed in Displaying Clear Visual of Cosmetic Ingredients Permeating the Skin ^{*1}

-Realizing Quantitative Display in terms of Depth Direction, Which Has Been Difficult to Achieve-

Shiseido succeeded for the first time in the world in developing a new technology of simple, quantitative and clear visualization for displaying the state of permeation of cosmetic ingredients through the skin ^{*1} after applying cosmetics to the skin in terms of depth direction, which has been quite difficult to achieve up until now. This technology has been applied to evaluate the state of permeation into the skin of "4MSK", an effective whitening ingredient originally developed by Shiseido. Going forward, Shiseido aims to apply this technology in cosmetics development, including developing cosmetic products with even stronger permeation strength, as well as research on the route and amount of active ingredients permeating into the skin, which has been difficult up until now. (Figure 1)

^{*1} The term "skin" here refers to the stratum corneum

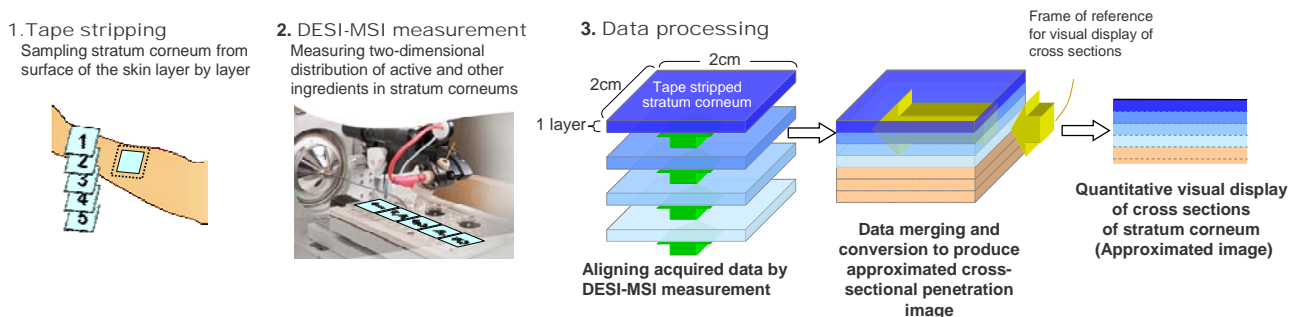


(Figure 1) Measurement Example of Permeation of 4MSK into the Stratum Corneum
(changed color to emphasize the state of permeation)

Shiseido has applied for a patent regarding this new technology, which was made possible by the following:

1. "Tape stripping," which entails taking a 2-square-centimeter sample of the stratum corneum (multiple sampling from the same place [surface → deep part]) using special adhesive tape
2. Acquiring two-dimensional distribution (surface) data of target ingredients of each sampled stratum corneum utilizing the newly developed "DESI-MSI" (Desorption Electrospray Ionization - Mass Spectrometry Imaging) ^{*2} method, which detects target ingredients according to their molecular weights [size of molecule].
(Shiseido established its own optimum conditions to measure the amount of cosmetic ingredients in the stratum corneum.)
3. Devising a data processing method to convert two-dimensional distribution (planar) data to an approximate quantitative and clear visual image of depth direction permeation and distribution states of target ingredients.

This achievement dramatically improves simple, quantitative and clear visualization of the state of permeation of active ingredients into the stratum corneum across cross-sectional surfaces compared with existing methods. (Figure 2)



(Figure 2) Measurement Flow of Newly Developed Technology Enabling Approximate, Quantitative and Clear Visual Display

*2 DESI-MSI (Desorption Electrospray Ionization - Mass Spectrometry Imaging)

An analysis method that allows for visual display of two-dimensional quantitative distribution (flat surface) of target ingredients by quantitative detection of the molecular weight (size of molecule) on and beneath the surface of planar samples.

Measurement is conducted by spraying positive or negative electrically charged liquid droplets in a fine mist on the surface of the sample under atmospheric pressure, simultaneously extracting and ionizing substances from near the surface of the sample and detecting target molecules after inserting into a high-vacuum mass spectrometer. Two-dimensional quantitative distribution (flat surface) data is obtained by moving the spray position at a constant speed on the flat surface, whereby the data can be visualized and displayed as an image. This method is relatively new and was reported by Dr. G Cooks (U.S.) for the first time in 2004 in the world-renowned U.S. science magazine *Science*.

Current Status of Technology for Visualizing the State of Permeation of Active Ingredients into the Stratum Corneum

Up until now, the most common method of visualizing the permeation state has been to permeate active ingredients on a part of the skin which can be surgically removed and observe cross sections using a fluorescence microscope^{*3}. In recent years, methods such as using a confocal laser microscope^{*4} to measure active ingredients on living subjects have been developed. However, all of those devices are cumbersome and time-consuming to operate and are only able to obtain unclear visual images. Furthermore, that fact that these devices are able to target only ingredients that emit fluorescence has posed a problem.

Therefore, Shiseido started developing an analysis method for customers to visually understand the permeation state of active ingredients and as a means for Shiseido to advance research related to the permeation of active ingredients by enabling simple, quantitative and clear visual display including the depth direction of the state of permeation regarding cosmetic ingredients or skin constituents.

*3 Fluorescence microscope: Microscope to observe substances that emit fluorescence or fluorescent-stained substances.

*4 Confocal laser microscope: Microscope with a laser as a light source for observing substances that emit fluorescence or fluorescent-stained substances. The microscope is able to obtain two-dimensional images of specific flat surfaces of thick impermeable substances via variable focal points. Also, the microscope is able to create three-dimensional images by overlaying two-dimensional images.

Newly Developed Visual Display Technology of Cross Sections of Stratum Corneum

Firstly, Shiseido focused on “tape stripping,” which has been a common evaluation analysis method that has previously been established, and DESI-MSI, a recently developed mass spectrometry method that is able to

quantitatively measure two-dimensional distribution of a number of ingredients simultaneously. Shiseido also succeeded in developing a technology for quantitative and clear visual display in terms of depth direction by using multiple two-dimensional distribution data collected via DESI-MSI using a newly devised patent-pending data processing method. However, this cross-sectional visual display developed at this time provides approximated images via data processing that combines planar images.

A significant feature of the newly developed measuring method (DESI-MSI) is that it can analyze multiple ingredients at the same time in a single measurement process. Therefore, for research on the permeation state of cosmetics ingredients in the skin, this makes it possible to simultaneously analyze aspects that include other formulated ingredients and the relationship with constituents in the skin. By utilizing this feature, there is the potential of broader applications, including new cosmetics development with even stronger permeation strength and in-depth research on the elucidation of the state of permeation into the skin, which has been difficult up until now.

This technology has been applied as a method to evaluate the permeation strength of “4MSK”, an effective whitening ingredient in SHISEIDO WHITE LUCENT POWER BRIGHTENING MASK (to be released from February 1, 2013 onward).