32nd IFSCC Congress
London 19–22 September 2022

Poster ID:203

Novel image analysis technique decodes the physiological information engraved on stratum corneum

Takeshi Tohgasaki[1*]; *Saki Aihara*[1]; *Mariko Ikeda*[1]; *Minako Takahashi*[1]; *Shioji Ishiwatari*[1]; *Masaya Eto*[2]; *Riki Kudo*[2]; *Hiroshi Taira*[2]; *Ai Kido*[2]; *Shinya Kondo*[1]; *Tetsuhito Sakurai*[1]

[1] *FANCL Research Institute, FANCL Corporation, Yokohama, Kanagawa, Japan*

[2] *Software and AI Technology Center, Toshiba Digital Solutions Corporation, Kawasaki, Kanagawa, JAPAN*

Introduction:

We aimed to develop a method for comprehensively decoding the physiological information contained in the stratum corneum (SC) cells of the skin. As SC cells are formed through the process of keratinization after division of basement membrane cells in the skin, they are imprinted with congenital and acquired physiological information. Although the relationship between SC cell shape and skin physiology has been studied for a long time, there is still room for analysis. Furthermore, there are few techniques for estimating skin conditions using a large number of indices such as the shape of stratum corneum cells and biomarkers. Toward this end, we established a novel image analysis technique based on artificial intelligence (AI) and multivariate analysis to estimate the skin condition.

Materials & Methods:

■***Establishment of machine learning for analysis of SC cells***

SC cells from 996 women* were used to construct two machine learning models. The collected SC cells were imaged using Dino-lite (AnMo Electronics Corp., Taiwan). To construct an automatic recognition model of individual SC cell regions, each SC cell in images were annotated using Labelme (MIT, MA, USA) (Figure 1). An instance segmentation model pre-learned with ImageNet was used. To construct a biomarker, estimation model was trained based on the levels of nine biomarkers measured by **enzyme-linked** immunosorbent assay (ELISA) using a convolutional neural network (CNN).

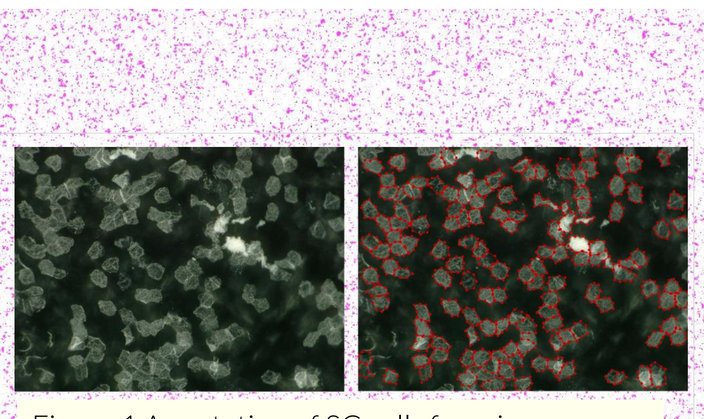

Figure 1 Annotation of SC cells from images
Raw image (left) and annotated data (right). Annotated region (Red frame).

■ ***Establishment of mathematical model to estimate skin physiological indicators***

SC cell sampling, skin physiological assessment, and questionnaires were conducted on 516 women*. The SC cell regions were labeled using Otsu's method and a constructed AI model, and the morphological parameters were quantified. Nine biomarkers [heat shock protein 27 (HSP27), macrophage migration inhibitory factor (MIF), interleukin 1 receptor antagonist (IL-1Ra), DJ-1, galectin-7 (GAL-7), arginase-1 (ARG1), neutrophil gelatinase-associated lipocalin (NGAL), epidermal fatty acid binding protein (FABP5), and enolase-1 (ENO-1)] levels were estimated using the constructed AI model. Tewameter VapoMeter (Keystone Scientific, Japan), SKICON 200EX skin conductance meter (Yayoi Co., Ltd., Japan), MPA580 Cutometer® (Courage + Khazaka Electronic GmbH, Germany) and VISIA evolution system (Canfield Scientific, NY, USA) were used.

■***Statistical analysis***

In this study, correlation analysis, multiple regression analysis, and discriminant analysis were performed using JMP® 16.2.0 (SAS Institute Inc., Cary, NC, USA). Results were considered significant when $P < 0.05$.

*All studies were conducted with the approval of the ethical committee of FANCL Co., Ltd. and as per the principles of the Declaration of Helsinki. Written informed consent was obtained from all the subjects.

Results & Discussion:

Figure 2. shows the study strategy. First, we developed two machine learning models: one that automatically recognizes individual SC cell regions in an image and another that estimates nine biomarker levels of SC cells (reportedly associated with skin) from images. The skin physiological indicators were estimated by multivariate analysis using the morphological parameters and biomarker levels from constructed machine learning model.

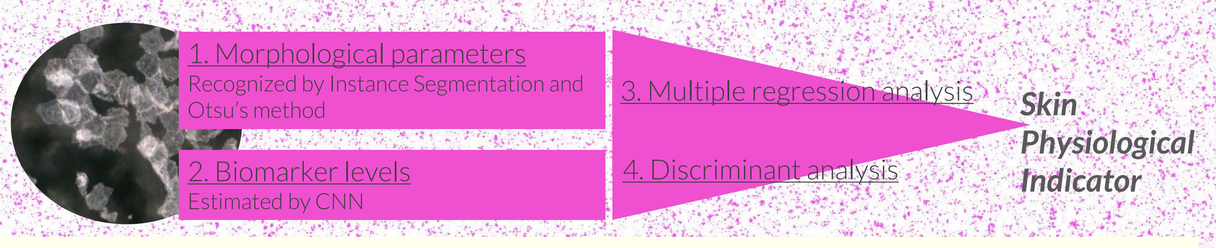

Figure 2 Scheme for estimating skin physiological indicators from SC cell images

■*Establishment of two machine learning model for SC cells analysis*

1. Machine learning model automatically recognizes individual SC cell regions

The number of cells recognized by the model was lower than that annotated. The estimated cell region coincided approximately with the annotated region (Figure 3). The intersection over union (IoU), recall, precision, and F-measure was 0.613, 0.953, 0.640, and 0.766, respectively.

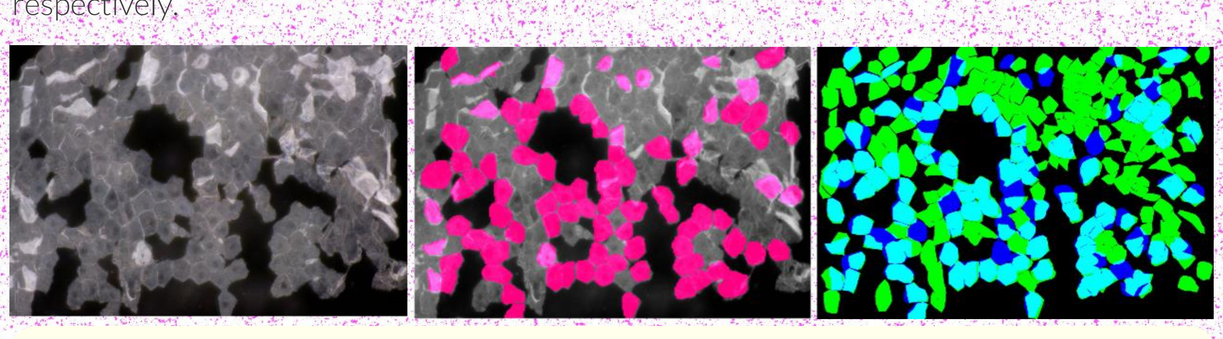

Figure 3. Evaluation of predicted and annotated regions
Raw image (left). Regions predicted by the machine-learning model (center); the pink area indicates the predicted region. Merged image (right); green: annotated area (false negative), blue: predicted area (false positive), cyan: true positive.

2. Machine learning model estimates approximate biomarker levels.

Correlation analysis was performed between the measured and estimated values. The estimated values of the nine biomarkers significantly correlated with the measured values (Figure 4). The predicted values of all markers were lower than the measured values and the distribution ranges were narrower.

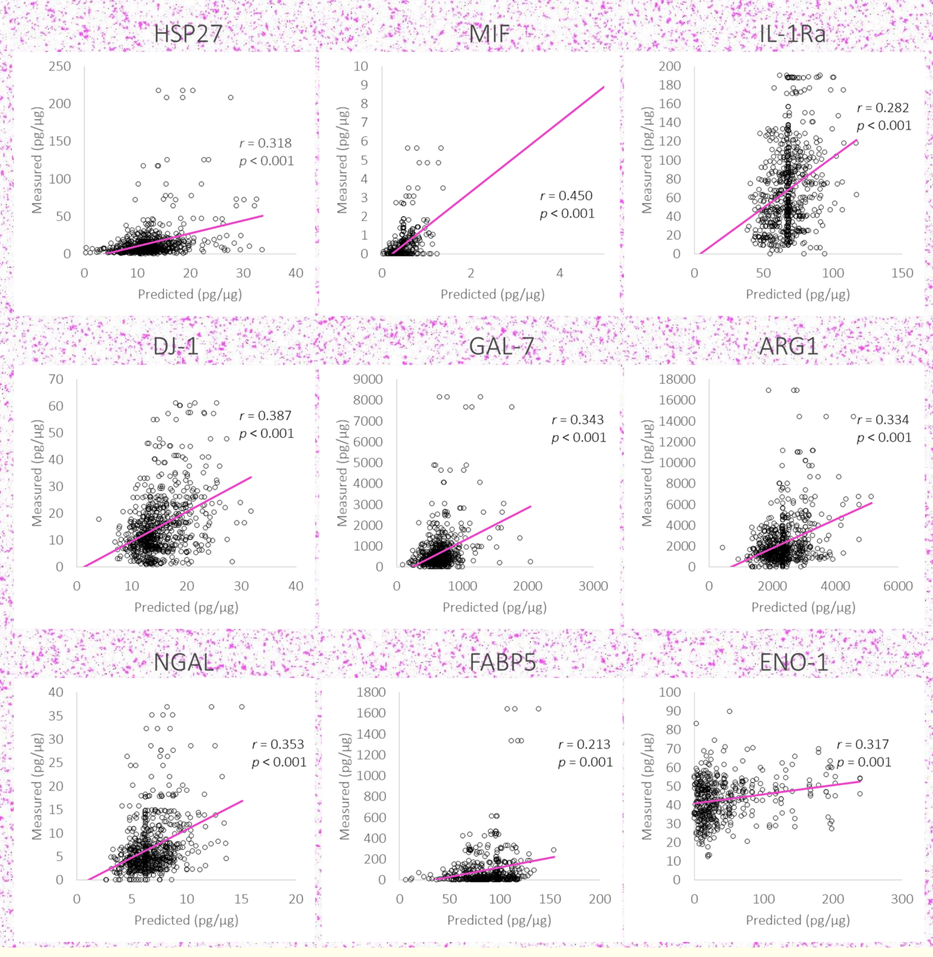

Figure 4 Correlation plots of predicted values determined by the machine-learning model and the values measured by ELISA for nine biomarkers in SC cells.

■*Estimating skin physiological indicators from SC images*

3. Multiple regression analysis could estimate skin physiological indicators

The estimated values of skin physiological indicators by multiple regression analysis using morphological values and biomarker levels of SC cells output from the constructed models significantly correlated with the measured values (Figure 5).

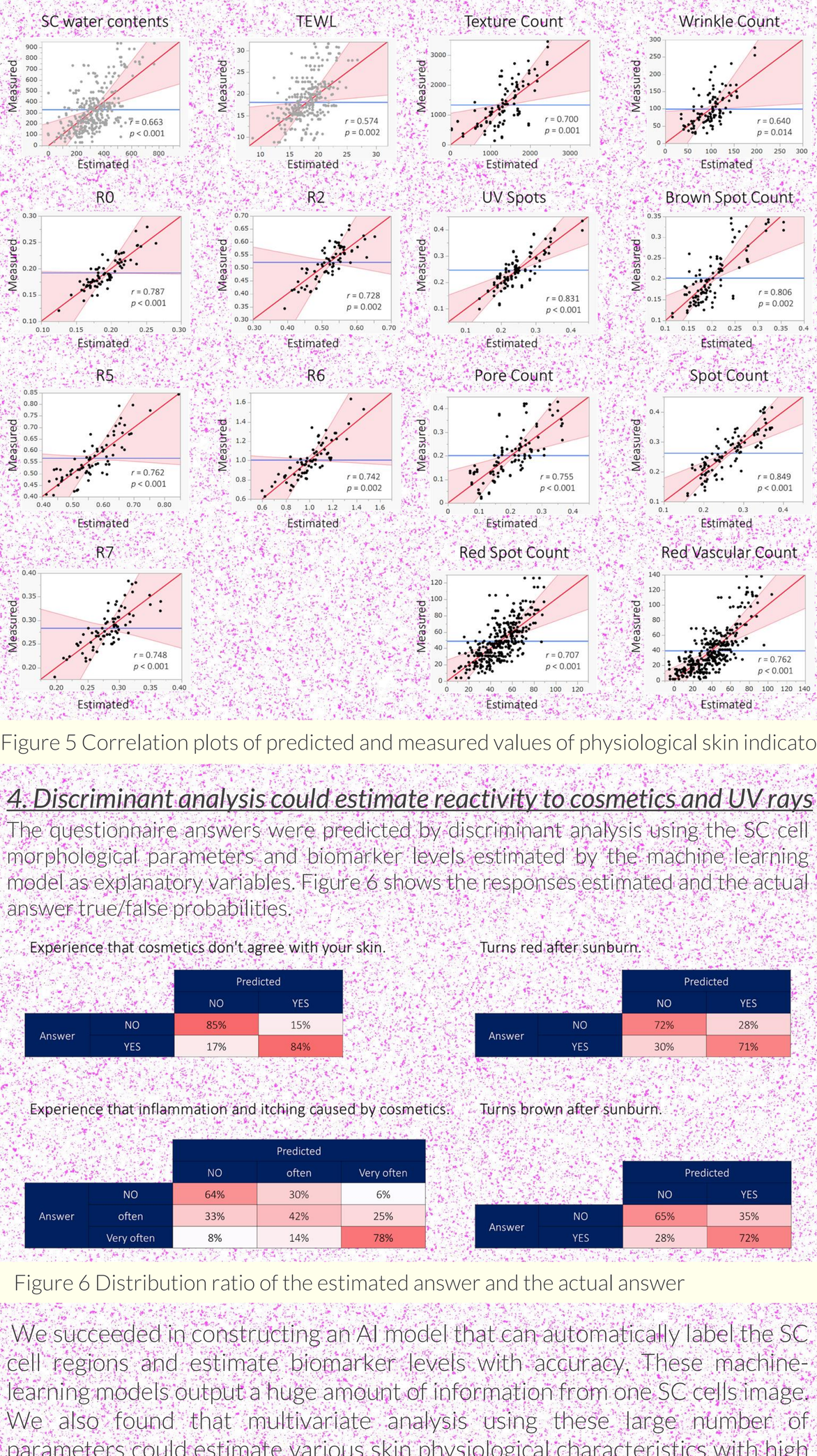

Figure 5 Correlation plots of predicted and measured values of physiological skin indicator

4. Discriminant analysis could estimate reactivity to cosmetics and UV rays

The questionnaire answers were predicted by discriminant analysis using the SC cell morphological parameters and biomarker levels estimated by the machine learning model as explanatory variables. Figure 6 shows the responses estimated and the actual answer true/false probabilities.

Experience that cosmetics don't agree with your skin.

		Predicted	
		NO	YES
Answer	NO	85%	15%
	YES	17%	84%

Turns red after sunburn.

		Predicted	
		NO	YES
Answer	NO	72%	28%
	YES	30%	71%

Experience that inflammation and itching caused by cosmetics.

		Predicted		
		NO	often	Very often
Answer	NO	64%	30%	6%
	often	33%	42%	25%
	Very often	8%	14%	78%

Turns brown after sunburn.

		Predicted	
		NO	YES
Answer	NO	65%	35%
	YES	28%	72%

Figure 6 Distribution ratio of the estimated answer and the actual answer

We succeeded in constructing an AI model that can automatically label the SC cell regions and estimate biomarker levels with accuracy. These machine-learning models output a huge amount of information from one SC cells image. We also found that multivariate analysis using these large number of parameters could estimate various skin physiological characteristics with high accuracy. Moreover, this technique can generate output in seconds without extensive time, money, or equipment, and no limitation for sample volume.
However, this research is only the beginning of the application of machine learning to dermatology, and further research is needed. The accuracy of the AI model can be improved by adding data and optimizing machine learning curriculum, etc. Many more types of biomarkers and physiological indices could be estimated.

Conclusion: AI improves comprehensive analysis of SC cells and skin physiological evaluation!