2021 43rd Annual International Conference of the
IEEE Engineering in Medicine & Biology Society (EMBC)
Oct 31 - Nov 4, 2021. Virtual Conference

Analysis of Echocardiography Images of Diseased Mice to Evaluate the Effect of Hypoxia Inducible Factor-1 Alpha on Cardiomyocytes

Kento Fujino[1], Tatsuyuki Sato[2], Innocentio A. Loe[3], Masato Sugino[3], Norihiko Takeda[2], Yasuhiko Jimbo[3] and Kiyoshi Kotani[4]

***Abstract*— Hypoxia Inducible Factor-1α (HIF-1α) is thought to be a critical factor associated with heart failure, but its function remains unclear. In this study, we developed a machine learning approach to evaluate the effect of HIF-1α in cardiomyocytes of HIF-1α knockout mice under heart failure. Our model suggests that HIF-1α affects the contraction of cardiomyocytes when heart failure occurs.**

***Clinical relevance*— This study shows a machine learning approach to evaluate the effect of HIF-1α in cardiomyocytes under heart failure from echocardiography images.**

I. INTRODUCTION

Hypoxia Inducible Factor-1α (HIF-1α) is an important factor in elucidating the mechanism of heart failure. It is a protein that is up-regulated in hypoxia and regulates the expression. Although there are several studies on HIF-1α in cardiomyocytes under heart failure, the effects of HIF-1α have been unclear[1][2]. In particular, it is not clear how HIF-1α affects the contraction of cardiomyocytes. Currently, there is no standard method to evaluate it. In this study, we developed a machine learning approach to evaluate the effect of HIF-1α in cardiomyocytes of HIF-1α knockout (KO) mice under heart failure.

II. METHODS

First, the region inside the ventricle was extracted from the M-mode images, and we defined the phase and distance from the boundary of a certain pixel in the anterior wall. The phase is set to 0 rad at the end of diastole and the distance is set to 0 mm at the boundary. Second, we extracted SURF (Speeded-Up Robust Features) from the anterior wall of the image, created a histogram by BoF (Bag of Features), and made a model to discriminate the features of KO mice by SVM (Support Vector Machine). The hyperparameters are the threshold of SURF (ranging from 50 to 500) and the number of clusters (ranging from 1 to 50) for clustering by BoF. We calculated the combination of hyperparameters with high leave-one-out accuracy, model accuracy with all images, and clustering robustness. Third, from the weights of each cluster in the model, we identified the most important cluster. We then calculated the phase and distance distribution of the ratio of feature points belonging to the most important cluster with respect to all feature points on each image.

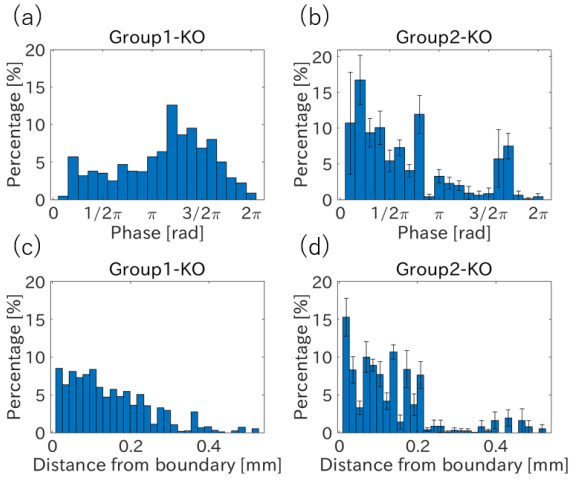

Fig. 1. Phase and Distance distribution of KO mice
(a) Phase distribution in Group1 (b) Phase distribution in Group2
(c) Distance distribution in Group1 (d) Distance distribution in Group2

III. RESULTS & DISCUSSIONS

Several combinations of hyperparameters with good results were obtained, which were divided into two groups based on the SURF threshold. The combinations using smaller threshold values was defined as "Group1" (n=1) and the higher one as "Group2" (n=7). The distributions of the phase and distance for Group1 and Group2 are shown in Fig.1. For the phase distribution, large percentage of the phase values within π to 3/2π rad (early in systole) was found for Group1, and within 0 to 1/2π rad (early in diastole) for Group2. For the distance distribution, large percentage of the distance values within 0 to 0.3 mm was found for Group1, and within 0 to 0.2 mm for Group2. The results from our study suggests that HIF-1α affects the contraction of cardiomyocytes when heart failure occurs.

REFERENCES

[1] J. Krishnan, M. Suter, R. Windak, T. Krebs, A. Felley, C. Montessuit, et al., "Activation of a HIF1α-PPARγ Axis Underlies the Integration of Glycolytic and Lipid Anabolic Pathways in Pathologic Cardiac Hypertrophy," *Cell Metabolish*, Vol. 9, No. 6, 2009, pp. 512-524.

[2] M. Sano, T. Minamino, H. Toko, H. Miyauchi, M Orimo, Y. Qin, et al., "p53-induced inhibition of Hif-1 causes cardiac dysfunction during pressure overload," *Nature* , Vol. 446, 2007, pp. 444-448.

*This study was supported by KAKENHI (18H04122). [1]K. Fujino is with The University of Toyko, Tokyo, 153-8904 Japan, phone: +81-3-5452-5183(55183); e-mail: fujino@neuron.t.u-toyko.ac.jp [2]Center for Molecular Medicine, Jichi Medical University, Shimotuke, Tochigi, 329-0998, Japan. [3]Graduate School of Engineering, The University of Tokyo, Tokyo 113-8656, Japan. [4]Research Center for Advanced Science and Technology, The University of Tokyo, Tokyo 153-8904, Japan.