Mechanical Analysis of Pulsation Behavior of Human iPSC-Derived Cardiomyocytes

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Introduction. Regenerative medicine has been attracting attention as a treatment for heart disease, which is the most common cause of death in the world. Recently, tissue engineered cell sheets prepared from human iPSC cell-derived cardiomyocytes (hiPS-CM) has also been studied in order to use them in the cardiac regenerative medicine. It is therefore important to accumulate the basic knowledge about hiPS-CM from biological and biomechanical points of view. In this study, the beating behavior of a hiPS-CM sheet was quantitatively examined and furthermore, the dynamic behavior was analyzed using the dynamic finite element method with use of a biomechanical model of cardiac tissue.

Experimental and Analysis. hiPS-CM (Carmy A, Myoridge Co.) were pre-incubated for 3 days and then seeded by 1.0×10⁶ cells/well on a 24-well thermoresponsive flat bottom plate (UpCell, CellSeed Co.). It was then placed in an incubator at 37°C, 100% humidity and 5% CO₂-95% air atmosphere. A spheroid was also formed by seeding 1.6×10⁴ hiPS-CM per well on a non-adhesive 96 well-U bottom plate, which allowed the cells to aggregate in a floating state. The beating behavior of the sheet and the spheroid was observed by a laser microscope equipped with a high-speed camera. The beating behavior was evaluated quantitatively by analyzing the variation of luminance in the images. G-CAMP was also used as a calcium probe, and the transformation of Ca²⁺ was analyzed from the variational behavior of luminance. The dynamic deformation behavior was also analyzed using the image correlation method to evaluate the displacement and strain variation.

Beating behavior of the cardiac tissue was analyzed by the dynamic finite element method with cardiac muscle model¹(²). Commercial FEM code LS-DYNA was utilized for the simulation study. The contractive deformation of the FE model was then compared with the experimental result.

Results and Discussion. Variational behavior of luminance corresponding to the flow of Ca²⁺ within the spheroid is shown in Fig.1. It is clearly seen that the Ca²⁺ flow coincides with the beating behavior. Displacement and strain fields on the surface of the sheet are shown in Fig.2. These deformation fields are seen not to be uniformly distributed. The normalized strain of the spheroid is shown with the FEM result in Fig.3(a). The spheroid exhibited a typical contraction-relaxation behavior of heart tissue. The time interval was about 1.2 second for the behavior. From the FE analysis, although the contraction behavior was obtained, the time to the peak was much faster than the experimental and there was no relaxation behavior was obtained. Experimental and FEM results of the normalized strain of the sheet are also shown in Fig.3(b). The cell sheet exhibited the contraction-relaxation behavior. The FEM result also showed the contraction behavior, however, the time to the peak was much slower than the experimental.

Fig.1 Variational behavior of Ca²⁺

Fig.2 Displacement and strain fields on sheet (a) Spheroid (b) Sheet

Fig. 3 Strain variation

References.