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# Evaluation of contraction characteristics of cardiac cells by continuous exchange of culture media

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## Abstract

In this study, an automatic culture medium change system was manufactured to analyze changes in cardiac contraction characteristics according to the state of the cell culture medium. A thermoelectric device-based temperature maintenance device was designed and manufactured to stably store cell cultures for a long time, and the characteristic evaluation showed that the temperature was maintained at  $5$  to  $8$  °C and pH  $7.39 \pm 0.15$ . Cell culture media was continuously exchanged at a flow rate of  $1.38 \mu\text{l}/\text{min}$  during the growth of cardiomyocytes using an interlocking pump. After evaluating the basic characteristics of the proposed system, SU-8 cantilever was produced using MEMS process technology, and cardiomyocytes was cultured. It was found that cardiomyocytes grown in a system that automatically exchanges cell culture media had a uniform heart rate compared to heart cells that were manually replaced every three days and generated greater contraction power in the contraction and relaxation cycles of heart cells. The proposed SU-8 cantilever-based automatic replacement system shows uniform heartbeat and contraction, which is expected to improve high reliability in cardiac toxicity evaluation by drugs.

**Keywords:** Perfusion, Cardiomyocytes, Maturation, Contraction force, Beat rate

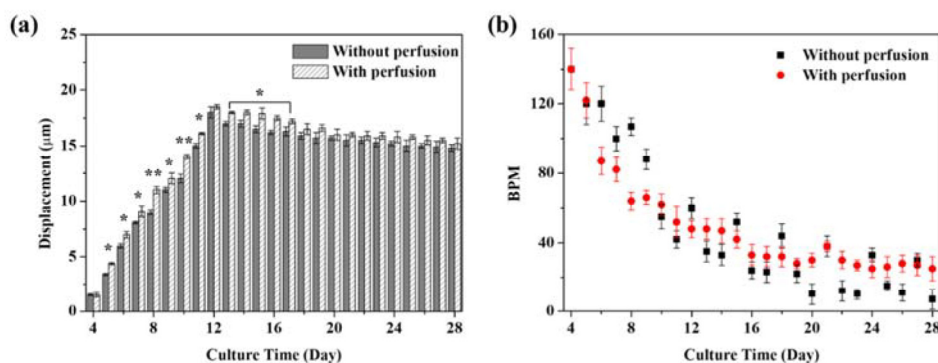


Figure 1. 심장세포 성장날짜에 따른 SU-8 캔틸레버 변위 및 심장 박동수 변화; (a) 캔틸레버의 변위 변화, (b) 심장 박동수 변화. The bars and error bars indicate the mean  $\pm$  s.d., ( $n = 8$ ). \* $P < 0.05$ , \*\* $P < 0.01$ .

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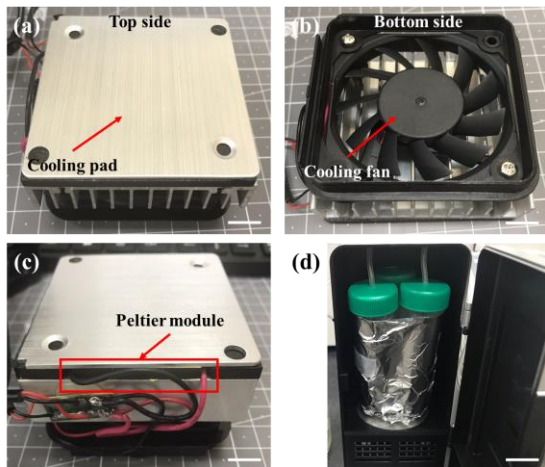
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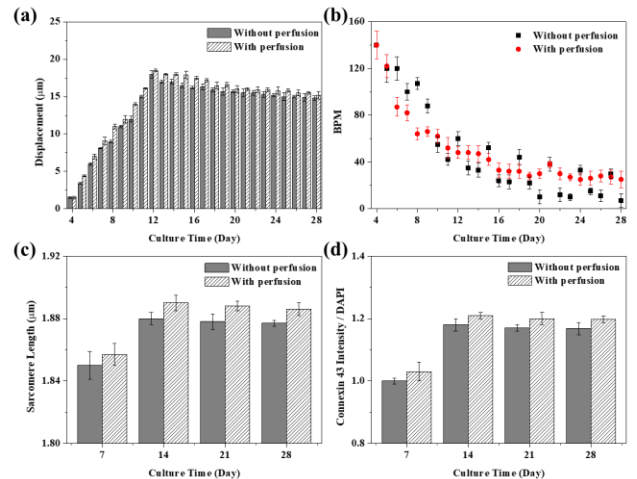
## Abstract

In this study, an automatic culture medium change system was manufactured to analyze changes in cardiac contraction characteristics according to the state of the cell culture medium. A thermoelectric device-based temperature maintenance device was designed and manufactured to stably store cell cultures for a long time, and the characteristic evaluation showed that the temperature was maintained at  $5$  to  $8$  °C and pH  $7.39 \pm 0.15$ . Cell culture media was continuously exchanged at a flow rate of  $1.38 \mu\text{L}/\text{min}$  during the growth of cardiomyocytes using an interlocking pump. After evaluating the basic characteristics of the proposed system, SU-8 cantilever was produced using MEMS process technology, and cardiomyocytes was cultured. It was found that cardiomyocytes grown in a system that automatically exchanges cell culture media had a uniform heart rate compared to heart cells that were manually replaced every three days and generated greater contraction power in the contraction and relaxation cycles of heart cells. The proposed SU-8 cantilever-based automatic replacement system shows uniform heartbeat and contraction, which is expected to improve high reliability in cardiac toxicity evaluation by drugs.

## Materials and methods

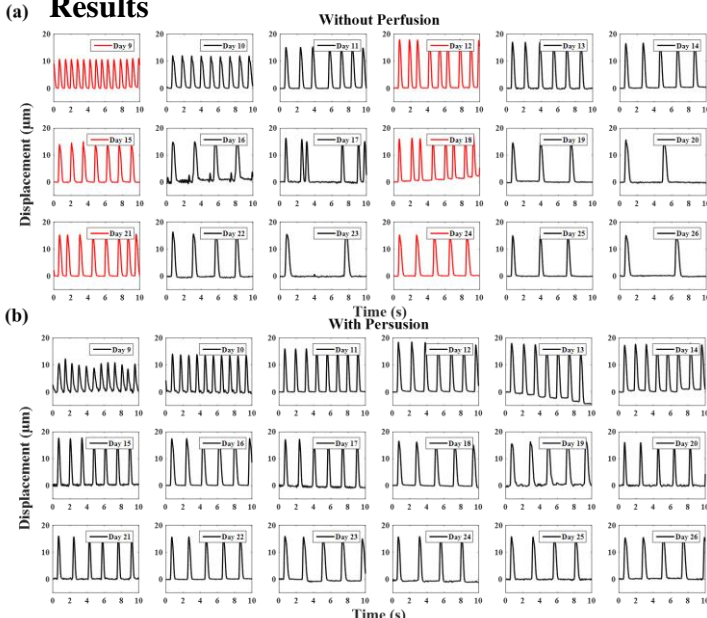


제작된 USB type 펠티어 냉장고; (a) 상부 냉각 판, (b) 하부 쿨링팬, (c) 펠티어 소자 및 5 V usb 서킷, (d) 펠티어 냉장고 케이스 (Scale: 1 cm)



With and without perfusion의 날짜에 따른 심근세포의 특성변화; (a) 캔틸레버의 변위 변화, (b) 심장 박동수 변화, (c) sarcomere 길이 변화, (d) 배양 날짜에 따른 Cx43 intensity 변화

## (a) Results



배양액 교체에 따른 심근세포의 수축 특성 변화 변화 (a) without perfusion (red-배양액 교체), (b) with perfusion

## Conclusion

본 연구에서는 세포 배양액 상태에 따른 심장 수축 특성 변화를 분석하였다. 세포 배양액의 pH는 보관 온도 및  $\text{CO}_2$  농도에 따라 변화하였고 열전소자 기반 온도 유지장치를 제작하여 pH  $7.41 \pm 0.4$ 를 유지하였다. 연동 펌프를 사용하여  $1.38 \mu\text{L}/\text{min}$ 의 속도로 culture media perfusion을 진행하였고 심근세포의 심장박동수가 유지됨을 확인하였다. 3일 주기로 교체하는 심근세포는 세포 활동에 따라 pH가 변화하였고 7.1 이하에서 불규칙한 심장박동이 발생하였다. 세포 배양 후 지속적으로 배양액을 교체 및 공급하는 perfusion 세포는 균일한 심장박동을 유지하였으며 without perfusion 세포에 비해 더 큰 수축력 및 생물학적 성숙을 측정하였다. 제안된 culture media perfusion 시스템을 통해 배양된 심근세포는 규칙적인 심장박동과 세포 성숙을 통해 약물 반응성 평가의 신뢰성 향상을 보일 것으로 판단한다.

## Acknowledgement

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