

Microwave and pulsatile circulation decellularization treatment on bovine arteries

QUAN Meixuan, IMAI Shinya, NAKAMURA Tokio, UCHIYAMA Koudai, HATANAKA Atsushi,
IWASAKI Kiyotaka*, *Member IEEE

Abstract— To produce a decellularized small-caliber aortic vascular graft utilizing microwave and pulsatile circulation decellularization treatment, and to evaluate residual DNA and mechanical properties of the decellularized bovine arteries.

Clinical Relevance— This research may solve the shortage of autologous sources of vascular transplantation.

I. INTRODUCTION

Coronary artery bypass surgery improves the ischemic state of myocardium by using autologous blood vessels. However, nearly 30% of the patients cannot find suitable autologous blood vessels¹⁾. Moreover, the patency rate of the small-caliber ($\leq 6\text{mm}$) artificial blood vessels is only 39%²⁾. Decellularized small-diameter arteries from animal sources have the potential to be used for coronary artery bypass. In this study, using a microwave and pulsatile circulation decellularization method³⁾, we investigated residual DNA and mechanical properties of decellularized bovine arteries.

II. METHODS

Residual amount of DNA of luminal and adventitial sides of small-diameter artery tissues were assessed after the decellularization treatment. PicoGreen DNA assay kit was used. The amount of DNA was quantified by measuring the fluorescence intensity of labeled G-C bases (guanine-cytosine) in double-stranded DNA. Mechanical compliance of the decellularized small-diameter grafts were investigated and compared with the non-treated grafts. Changes in vessel diameter in response to luminal pressure increase were measured, and stiffness parameter β by formula (1) were obtained with the pressure of 100 mmHg (range: 80 ~ 120 mmHg).

$$\beta = \frac{\ln\left(\frac{P}{P_s}\right)}{\left(\frac{D}{D_s} - 1\right)} \quad (1)$$

Parameter of the formula above are P : Pressure, D : Vessel diameter, P_s : 100 mmHg, D_s : Vessel diameter at the pressure of 100 mmHg.

III. RESULTS

The DNA residue was 9 ng/mg, and reduction rate of DNA in comparison with the native non-treated artery was 97.7% (Fig. 1). The amount of residual DNA was less than 50ng/mg⁴⁾,

considered as a borderline in terms of safety. The stiffness parameter β of the decellularized artery were comparable to that of the untreated artery (Fig. 2). This data indicates that our decellularization method does not cause damage on the artery.

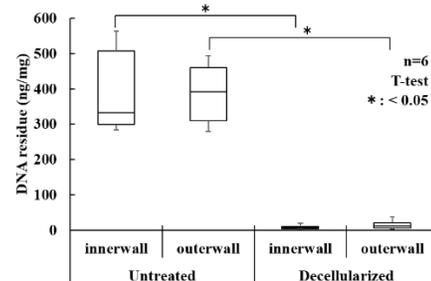


Figure 1. Residual amount of DNA after the decellularization

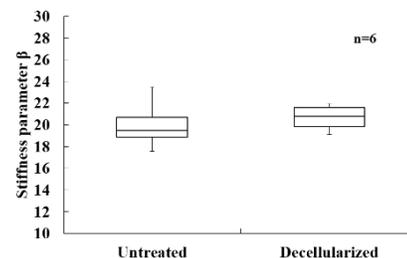


Figure 2. Comparison of stiffness parameter β

IV. DISCUSSION & CONCLUSION

The decellularized small-diameter artery with equivalent mechanical stiffness to the untreated artery were successfully developed utilizing our decellularization method.

REFERENCES

- [1] Lin, P.H., Chen, C., Bush, R.L., 2004, Small-caliber heparin-coated ePTFE grafts reduce platelet deposition and neointimal hyperplasia in a baboon model, *Journal of Vascular Surgery*, vol. 39, no. 6, 1322-1328.
- [2] Klinkert, P., Post, P., Breslau, P. & Van Bockel, J. 2004, "Saphenous vein versus PTFE for above-knee femoropopliteal bypass. A review of the literature", *European Journal of Vascular and Endovascular Surgery*, vol. 27, no. 4, 357-362.
- [3] Iwasaki K, Ozaki S, Kawai T, Yamaguchi S, Eto M, Ohba Y, Umezu M, Innovative bioreactor technologies produced a completely decellularized and pre-endothelialized functional aortic valve, *Proceedings of the 12th International Conference on Biomedical Engineering*, 2005.
- [4] Crapo, P.M., Gilbert, T.W. & Badyal, S.F. 2011, "An overview of tissue and whole organ decellularization processes", *Biomaterials*, vol. 32, no. 12, 3233-3243.

*Research supported by JSPS KAKENHI Grant number JP21H03016.
M. Q., S. I., T. N., K. U., A. H., and K. I. Authors are with Waseda University
TWINs, 03C-204 JP (K. I. Corresponding author: iwasaki@waseda.jp)