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In Vivo Maturity Evaluation of Tissue-Engineered Vascular Wall Based on Ultrasonic Measurement of Viscoelasticity

超音波を用いた粘弾性計測に基づく再生血管の生体内成熟度評価

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1. Introduction

Quantitative elasticity measurement of tissue-engineered (TE) vascular wall is expected to be useful for in vivo maturity evaluation because the elasticity of biodegradable material (scaffold) in tissue engineering is related with the biocompatibility and structural intensity, and changes with the maturiry process. Therefore, we have presented in vivo measurement for TE vascular wall elasticity[1,2]. On the other hand, in order to improve the accuracy in maturity evaluation of TE vascular wall, its viscoelasticity should also be considered. Therefore, in this study, we present a method for in vivo maturity evaluation of TE vascular wall based on the viscoelasticity measurement. Moreover, a regeneration score for in vivo maturity evaluation is also presented. The effectiveness of this method was investigated by in vivo experiment.

2. Methods

A measurement system of TE vascular wall viscoelasticity is shown in **Fig.1**. Two thin catheters are inserted into the vessel lumen. One is the intravascular ultrasound catheter with a center frequency of 40 MHz and a diameter of 2.4 Fr for the measurement of circumferential strain of the TE vascular wall due to pulsation, and the other is the pressure sensor catheter with a diameter of 2 Fr and high frequency response (> 10 kHz) for the measurement of intraluminal pressure. The position of these catheters is determined by using the X-ray fluoroscope image. The time-series ultrasonic rf frames and pressure data are recorded by using a high-speed A/D converter with dual channels at a rate of 200 MHz and 14 bits during 4 second. The circumferential strain is obtained by differentiating the temporal set of a circumferential length of circle with the area equivalent to the lumen area calculated by automatically counting pixels of lumen region in the adaptively-binarized ultrasound image, which is constructed by the rf frame data. The quantitative viscoelasticity is measured as the complex modulus, by using pressure-strain loops formed by time profiles of pressure and strain.

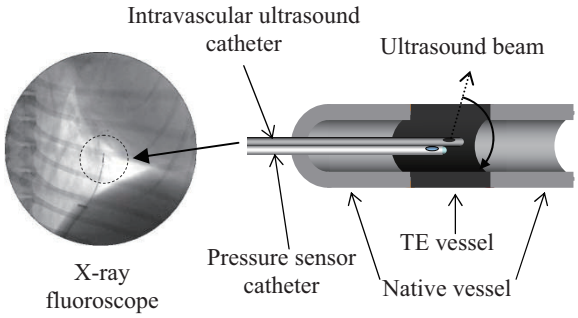

Fig.1 A measurement system of TE vascular wall viscoelasticity.

3. In Vivo Experiments

In order to verify the feasibility of this method, in vivo measurement and tension (mechanical) test for the same native vein of canine (inferior vena cava, IVC) were conducted. As shown in **Fig.2**(a), the pressure-strain loops with significant gradient and area were observed because the IVC is directly connected to the right atrium and minute pulsation exists. As shown in **Fig.2**(b), 9.7±4.2 kPa for in vivo measurement (n=5) and 10.0±2.1 kPa for tension test were obtained as the complex modulus under same pressure levels. Therefore, the feasibility of this method for quantitative complex modulus measurement was verified.

Next, the temporal changes of the complex modulus of TE vascular wall in the canine were followed up for six months. In this experiment, a piece of biodegradable polymer was implanted in the canine IVC as the TE vascular wall, as shown in the ultrasound image of **Fig.3**(a). The catheter position is determined by using the X-ray

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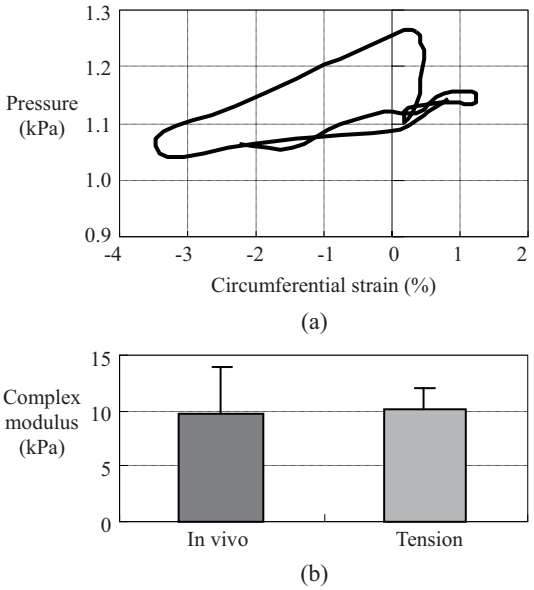

Fig.2 Feasibility study using native IVC of canine. (a) obtained pressure-strain loop and (b) comparison of results of in vivo measurement and tension test.

fluoroscope image, shown in **Fig.3**(b). As a result, the pressure-strain loops in native and TE vascular walls were obtained as shown in **Fig.3**(c). Although the biodegradable polymer immediately after implanting is stiffer than the adjacent native vessel, the polymer degrades with the maturity. Therefore, based on the vessel construction as shown in **Fig.1**, as an explicit index for in vivo maturity evaluation, the regeneration score was defined by using the difference between the complex modulus of TE and adjacent native (AN) vascular walls, so that the maturity of TE vessel wall can be evaluated by percentage. That is, the regeneration score exhibits 0 % for initial state immediately after implanting and 100 % for no difference between the complex modulus of TE and AN vascular walls and complete regeneration. Calculated results of regeneration score are shown in **Fig.4**. As these results, scores of 59 % after one month, 82 % after three months and 96 % after six months were obtained in consistency with histopathological findings. These results revealed the effectiveness of this method for TE vascular wall maturity evaluation.

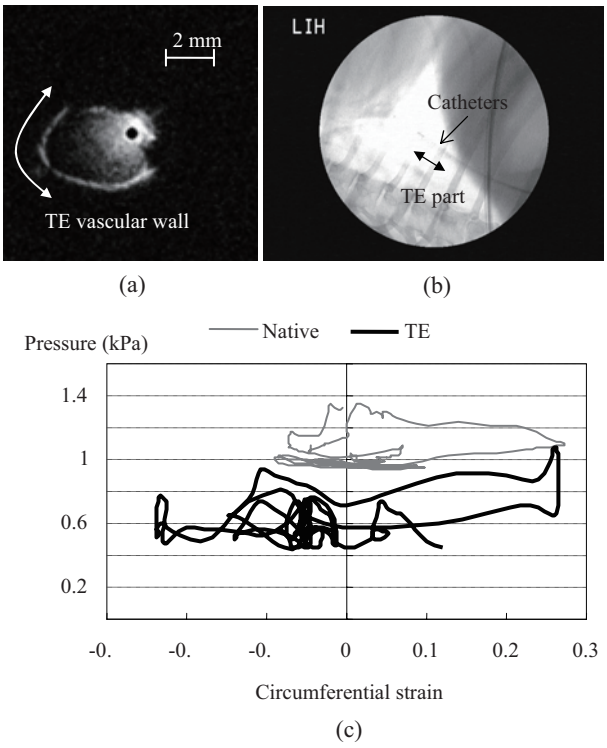

Fig.3 In vivo measurement results of native vessel and implanted TE vascular wall. (a) intravascular ultrasound image, (b) X-ray fluoroscope image, and (c) pressure-strain loops of native and TE vessels after six months..

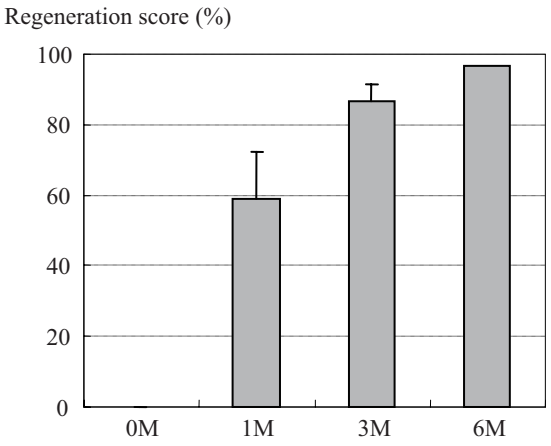

Fig.4 Regeneration scores of implanted TE vascular wall. (n=3)

4. Conclusions

In this study, a method for evaluating the maturity of TE vascular wall was presented. This method uses the intravascular ultrasound and pressure catheters, and evaluates the viscoelasticity of TE vascular wall. In vivo experiments revealed that the regeneration score calculated by using the complex modulus was highly-correlated with the polymer degradation.

In future work, we are going to conduct many experiments and ensure the effectiveness of this method.

References

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