

Implications for the Establishment of Accelerated Fatigue Test Protocols for Prosthetic Heart Valves

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Abstract: The goal of this research is to establish a reliable methodology for accelerated fatigue tests of prosthetic heart valves. A polymer valve was the subject, and the influence of various drive parameters on durability was investigated in three different machines. Valve lifetime was notably shortened by increasing the cyclic rate or stroke even though the maximum pressure difference at valve closure was maintained at 120 mm Hg. These results demonstrate that adjustment of the maximum transvalvular pressure is not sufficient to ensure tests are conducted

under the same conditions and indicate that measurement of the dynamic load would be more efficacious. Moreover, the locations of tears sustained in the accelerated tests differed from those encountered in an animal experiment although in both cases the locations were entirely consistent with the areas of strain concentration revealed by finite element analysis. These findings should be discussed during a revision of ISO 5840. **Key Words:** Accelerated fatigue test—Durability—Fracture—ISO 5840—Polymer valve—Jellyfish valve.

Accurate estimation of durability in a timely manner is one of the most important unresolved issues in the basic research of artificial organs. ISO 5840 (Cardiovascular Implants) prescribes guidelines for accelerated fatigue test methods applied to heart valves (1), the assessment of durability by accelerated cycling having been widely accepted as an essential component in the developmental stage of prosthetic heart valves. However, in bioprosthetic heart valves especially, investigators have reported varying degrees of success in obtaining a correlation between the tears and perforations observed in clinical cases with those failure modes observed during in vitro accelerated fatigue tests (2–4). Furthermore, in the case of polymer valves that have been developed as alternatives to mechanical and bioprosthetic valves for use in artificial hearts, the optimal protocol for accelerated fatigue tests has yet to be established. The authors are accumulating fundamental data on heart valve durability by means of three different types of accelerated fatigue testers. The ultimate

goal of this research is to establish a reliable methodology for accelerated fatigue testing of prosthetic heart valves. The aim of the current study is to investigate the influence of drive parameters on durability under the test conditions recommended by ISO 5840 and also to compare the fracture patterns of heart valves subjected to in vitro accelerated fatigue tests with an animal model.

MATERIALS AND METHODS

Valves used in this study

A polymer valve known as the *Jellyfish valve*, which has been developed for use in artificial hearts (5–6), was used as the test subject throughout this research. The main reasons why this valve was employed are as follows. First, assessments of durability and the locations of membrane fracture have been obtained in experiments in goats in which Jellyfish valves were incorporated into blood pumps as shown in Fig. 1 (7,8); these results provide benchmarks for the accelerated fatigue tests. Second, the durability of the Jellyfish valve in these goat experiments was 312 days, or approximately 10 months. This lifetime was considered to be more convenient, with regard to the prospective duration of the accelerated fatigue tests, than the lifetime that is typical of currently

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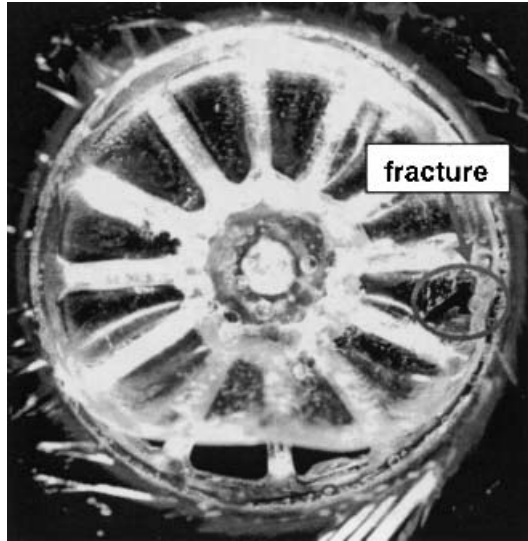


FIG. 1. A membrane fracture in the Jellyfish valve incorporated into a paracorporeal total replacement-type, pneumatically driven blood pump after 312 days of pumping is shown. The valve was explanted from the outlet position of the left-side pump.

available clinical heart valves. Therefore, one experimental plot can be made available within 1 month at a cycling rate of 20 Hz whereas, generally speaking, a valve with an expected clinical durability of 10 years would require about 6 months to yield terminal results under the same accelerated conditions. Third, thanks to well-established fabrication techniques and quality control procedures, these valves can be produced with a high degree of uniformity. Fourth, the polymer leaflet material exhibits viscoelastic behavior that is not unlike that of the tissues used in bioprosthetic leaflets (9); therefore, it is reasonable to assume that data obtained from these polymer valves would be useful for understanding fatigue test results on bioprosthetic heart valves. For these reasons, the Jellyfish valve is seen not only as suitable but ideal in the context of this study.

The Jellyfish valve consists of a flexible membrane and a rigid valve seat, both of which are fabricated by casting techniques. The membrane is made of a copolymer of segmented polyurethane named K-III (Nippon Zeon Co. Ltd., Tokyo, Japan) that possesses excellent blood compatibility. The valve seat is made of a two-component, room-temperature vulcanizing urethane (Quinnate CR330, Ciba Specialty Chemicals K.K., Tokyo, Japan) and then coated with K-III. Finally, the membrane is bonded to the valve seat at a central location, again using K-III. The 20 mm size (which refers to the diameter of the membrane as well as the valve seat) was chosen, this having been used in the animal experiments. In the valves for use in the accelerated fatigue tests, the

outer diameter of the valve seat was widened from 20 mm to 28 mm to provide chuck-area for mounting in the test chambers; however, the flow field of this modified valve is the same as that of the normal (20 mm) valve. The thickness of the Jellyfish valve membrane can be varied by changing the insertion volume of liquid K-III that enters the casting mold. The thickness of the membrane in the Jellyfish valve that was fractured in the animal experiment was around 60 μm . Thus, to ensure correlation between the animal model and the in vitro accelerated fatigue tests, 60 μm membranes were fabricated. And, furthermore, only membranes with a maximum thickness deviation of $\pm 10 \mu\text{m}$ at 24 measuring points (8 points each in the inner, middle, and outer areas of the membrane) were chosen in an effort to eliminate membrane thickness as an independent variable in the durability tests. The typical behavior of the Jellyfish valve in a pulse duplicator under physiological conditions is shown in Fig. 2.

Accelerated fatigue testers for heart valves

Three different types of accelerated fatigue testers were employed in this study as described below. A Helmholtz-type accelerated fatigue tester (Helmholtz-Institute for Biomedical Engineering, Aachen, Germany) (10) is shown in Fig. 3. In this tester, transvalvular flow is produced by the combination of a rotary pump, located below, and a rotating disk

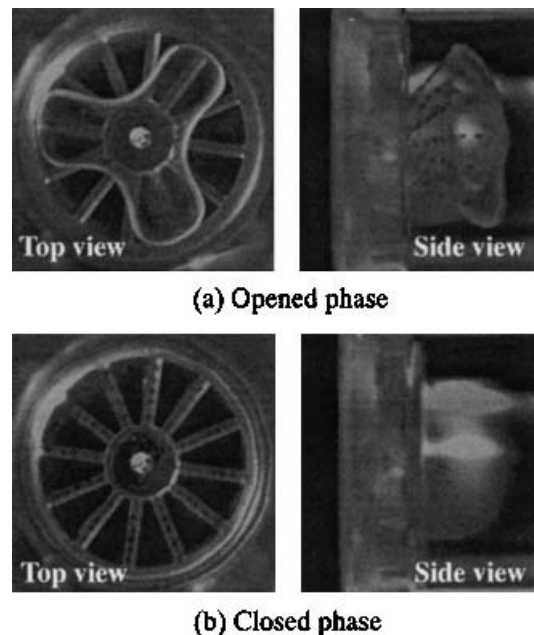


FIG. 2. Typical behavior of the Jellyfish valve membrane in the outlet position of a pulse duplicator is shown. Mean transvalvular flow rate was adjusted to 5 L/min against a mean aortic pressure of 100 mm Hg.

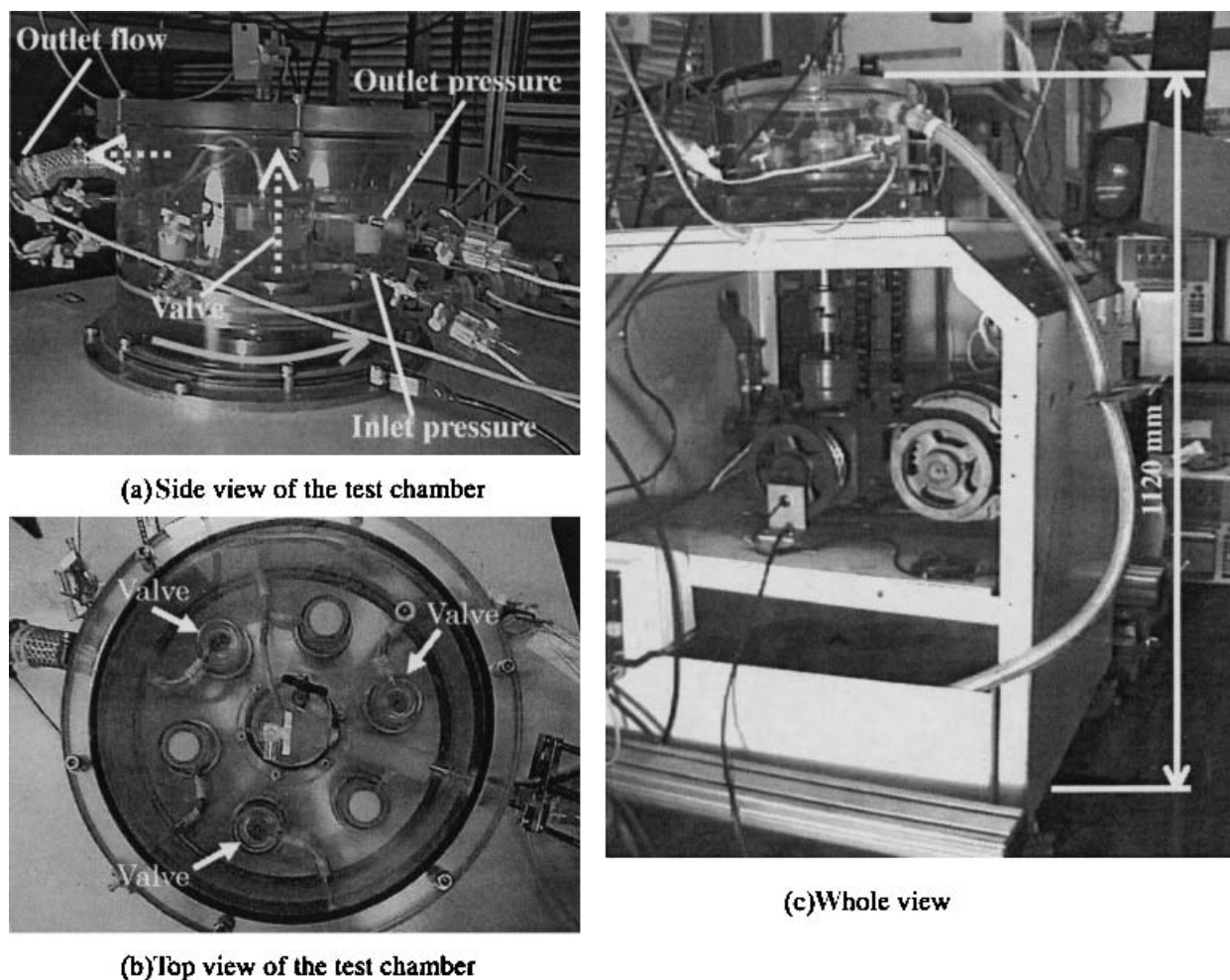


FIG. 3. A Helmholtz Institute-type accelerated fatigue tester for prosthetic heart valves is shown.

with a flow passage comprising one-third of the total cyclic area and located in the casing. When the rotating flow passage encounters the test chamber, flow rapidly opens the valve membrane, and it closes as soon as the flow passage rotates beyond the test chamber. Accordingly, the effective systolic fraction is approximately 33%. The maximum pressure gradient following valve closure was adjusted to 120 mm Hg as recommended by ISO 5840 (1). In addition to this condition, the mean outlet pressure of the valve was adjusted to 115 mm Hg because this fatigue tester allowed a variety of dynamic conditions to be obtained under a given maximum pressure drop. Moreover, the mean transvalvular flow rate was adjusted to 5.0 L/min to ensure that the opening behavior of the membrane was similar to that at physiological cycle rates. The temperature of the working fluid was maintained at 37°C throughout the study. Typical pressure waveforms in this machine are shown in Fig. 4. In this tester, durability tests were conducted under the cycle rates of 400, 500, and 600

bpm. Thus, the influence of cyclic rate on durability, for a fixed maximum pressure difference at valve closure, was examined.

Figure 5 shows a modified version of the commercially available Rowan Ash accelerated fatigue tester (Rowan Ash Ltd., Sheffield, England). The original tester was designed without a compliance element. The upper casing was flat, thus failing to model the elastic effects of the aorta. The preliminary experimental study indicated that this limitation resulted in an insufficient opening motion of the Jellyfish valve membrane. Therefore, the upper casing of the tester was modified to incorporate an air compliance chamber as shown in Fig. 5. Changes in pressure waveforms as a function of air volume under the same maximum pressure difference of 120 mm Hg at valve closure are shown in Fig. 6. In order to keep the same maximum pressure difference of 120 mm Hg, the amplitude of the sinusoidal stroke was controlled as shown in Fig. 7. The drive amplitude had to be increased after the inclusion of the air compli-

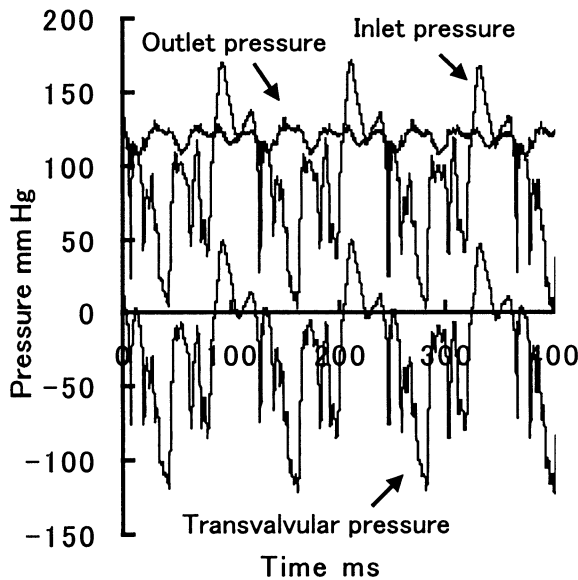


FIG. 4. Simultaneous pressure waveforms are shown in the Helmholtz-type accelerated fatigue tester under a cycle rate of 500 rpm. The maximum pressure difference at valve closure was adjusted to 120 mm Hg under a mean flow of 5.0 L/min. Mean outlet pressure was adjusted to 115 mm Hg.

ance element. Movement of the membrane is induced by the inertia of the fluid as the valves are sinusoidal displaced, on hollow pistons, by the stroke of a linear motor. The temperature of the test fluid did not need to be controlled because it was in a closed circuit and remained at room temperature (around 20°C). The cycle rate was adjusted to 1,200 bpm, and the maximum pressure gradient at valve closure was maintained at 120 mm Hg. Then, the influence of air compliance on durability was investigated.

The Tsinghua-type accelerated fatigue tester (Tsinghua University, Beijing, China) is shown in Fig. 8. The motion of the valve membrane is ensured by the sinusoidal stroke of the linear motor located on the upper side of the test chamber. The valve is mounted in a holder and connected to the axially vibrating rod. The Tsinghua University machine has an open loop (the working fluid in the inflow side of the valve is open to atmosphere) unlike the Rowan Ash system. The Tsinghua University machine has the important advantage that the dynamic load acting on the valve can be measured by installing a load cell into the oscillating rods. The authors have been conducting preliminary experiments to investigate the influence of dynamic load on durability, the details of which will be discussed elsewhere. In this paper, the maximum pressure difference at valve closure was adjusted to 120 mm Hg to maintain equivalence among the three different accelerated test systems. The temperature of the circulating water was

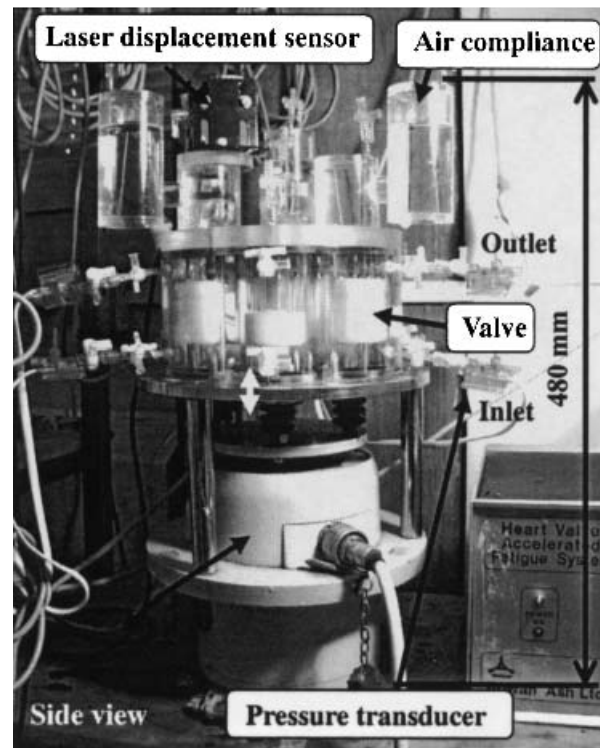
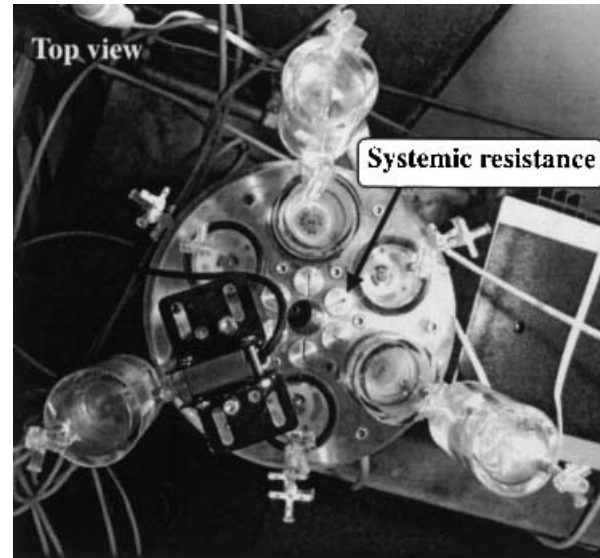


FIG. 5. A modified version of the Rowan Ash accelerated fatigue tester for prosthetic heart valves is shown. A compliance element was added to the original system.

maintained at 37°C by a heater. The test was conducted under a drive rate of 1,200 bpm. Simultaneous pressure waveforms are shown in Fig. 9.

RESULTS

Influence of drive parameters on lifetime

Accelerated fatigue tests were conducted by three different machines under the same maximum pres-

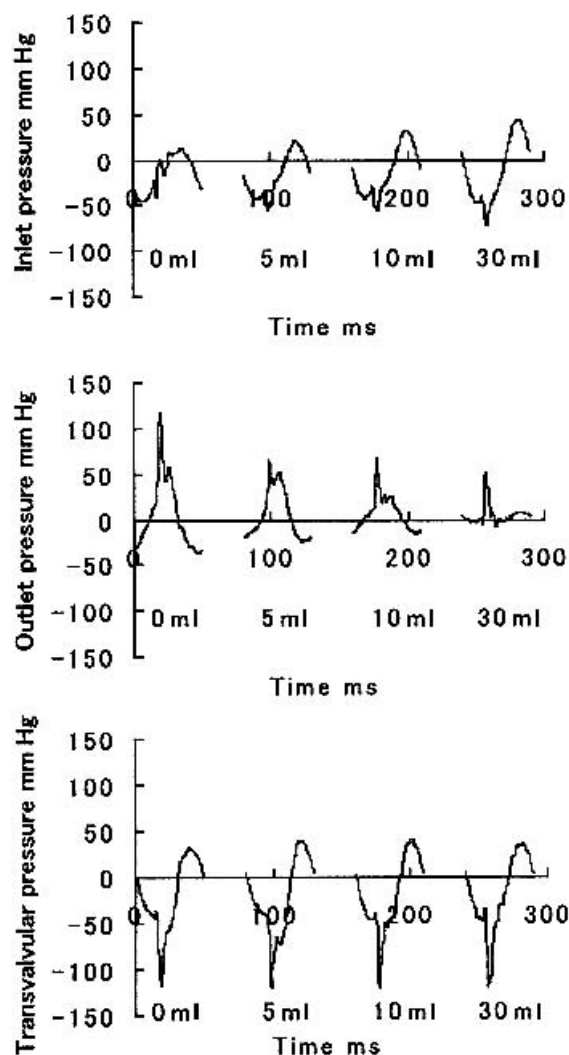


FIG. 6. Changes in pressure waveforms are shown as a function of air-compliance volume at the outlet position of the valve. The maximum pressure difference at valve closure was maintained at 120 mm Hg under a drive rate of 1,200 bpm. Inclusion of the air-compliance element increased the pulse pressure in the inlet position and also decreased that in the outlet position.

sure difference (120 mm Hg) at valve closure. In addition, in the Helmholtz tester, the influence of cyclic rate on lifetime was investigated while, in the Rowan Ash tester, the influence of drive amplitude on lifetime was investigated. The results in the Helmholtz tester are shown in Fig. 10. The repetition numbers to fracture were 7.3×10^6 cycles, 7.9×10^6 cycles, and 13.8×10^6 cycles under cycle rates of 600 rpm, 500 rpm, and 400 rpm, respectively. These results indicate that increased cycle rate shortens valve lifetime. Figure 11 shows the results in the Rowan Ash tester. The repetition numbers to fracture were 8.3×10^6 cycles and 3.1×10^6 cycles under drive amplitudes of 0.4 mm (without air compliance) and 0.9 mm (with air compliance), respectively. In-

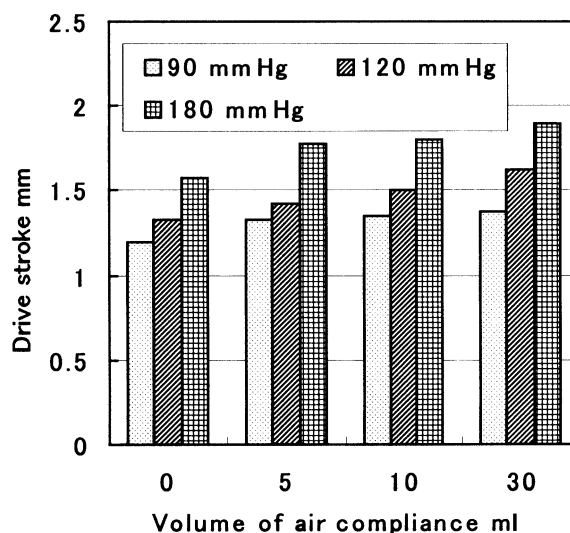


FIG. 7. Influence of inclusion of the air-compliance element on drive amplitude under three typical transvalvular pressures at closure are shown. In order to maintain the specified pressure drop, the drive amplitude was increased.

creased stroke amplitude shortened valve lifetime despite inclusion of the compliance element in the outflow section which should have approached a more realistic simulation of normal valve motion. In

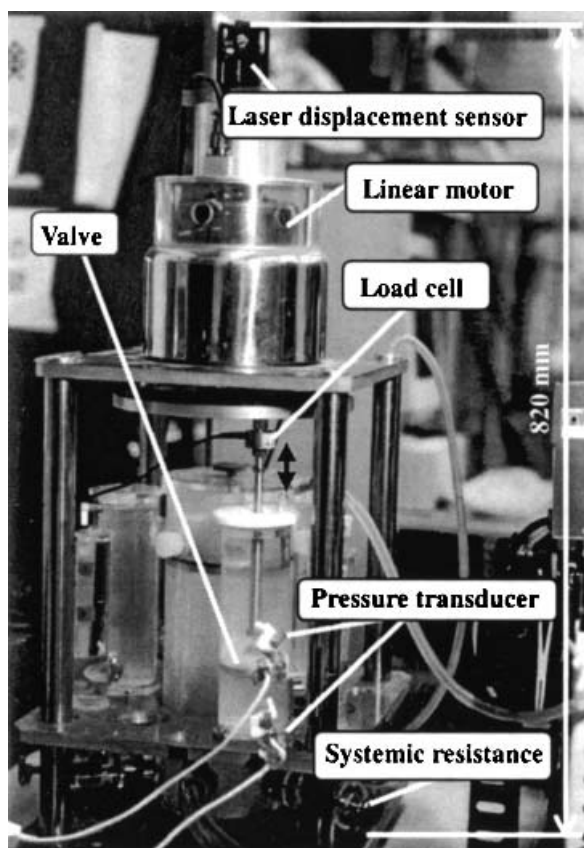


FIG. 8. A Tsinghua University type accelerated fatigue tester for prosthetic heart valves is shown.

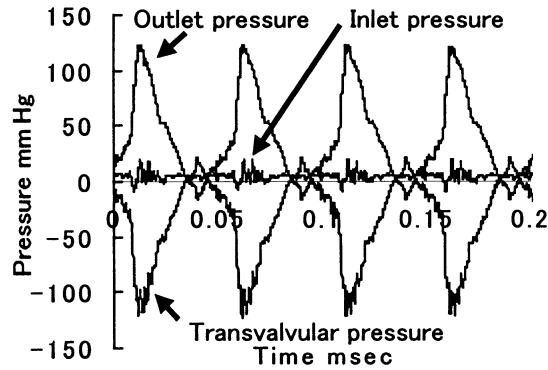


FIG. 9. Simultaneous pressure waveforms are shown in the Tsinghua-type accelerated fatigue tester under the drive rate of 1,200 bpm. Sampling time was 100 μ s.

the Tsinghua University tester, the repetition number to fracture was 8.7×10^6 cycles.

Membrane fractures in accelerated fatigue tests

A typical fracture pattern in the accelerated fatigue tests is shown in Fig. 12. Tears always occurred alongside the edge of the spoke in the three types of accelerated fatigue testers. Figure 13 shows the fracture surface at the locations of A, B, and C in Fig. 12 as observed by a scanning electron microscope. The fracture surface indicated that the crack initiated in location A in the outer area of the membrane.

The fracture locations in the accelerated fatigue tests did not coincide with those in the animal experiment.

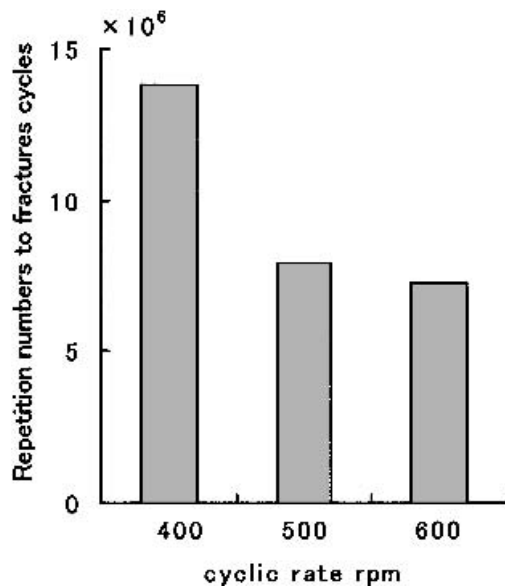


FIG. 10. Influence of cycle rates on durability under the specified maximum pressure difference of 120 mm Hg in the Helmholtz-type accelerated fatigue tester is shown.

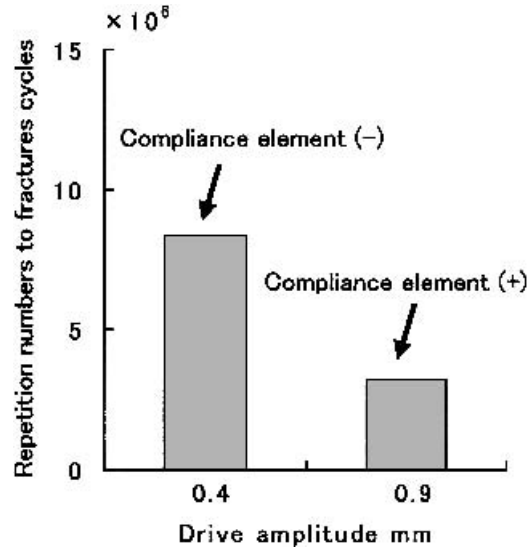


FIG. 11. Influence of drive amplitude on durability under the specified maximum pressure difference of 120 mm Hg in the Rowan Ash accelerated fatigue tester is shown.

DISCUSSION

Differences in durability under pressure condition recommended by ISO

The durability of polymer valves of consistent quality was compared under the same maximum pressure difference at valve closure as recommended by ISO 5840. The durability tests conducted using the Helmholtz-type tester indicated that an increase in drive rate shortens the lifetime of the valve. In the

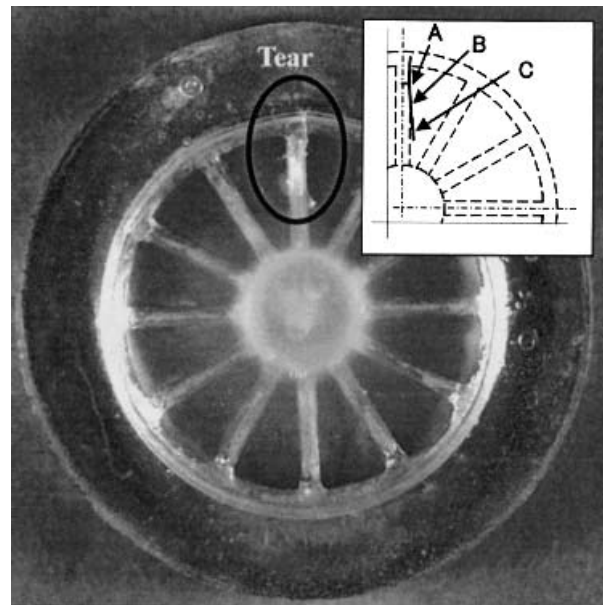


FIG. 12. Shown is a typical fracture pattern in the accelerated fatigue testers. Tears always occurred alongside the edge of the spoke.

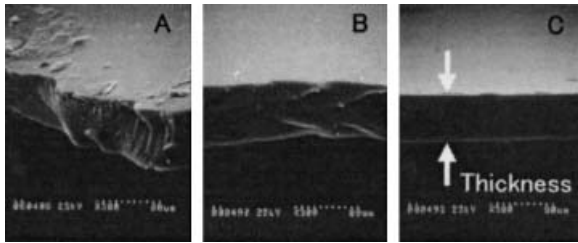


FIG. 13. Scanning electron microscope views of the fracture surfaces are shown. The crack initiated at location **A** and propagated toward locations **B** and **C**.

Rowan Ash tester, it was shown that the increasing of the drive amplitude of the axially oscillating rod also shortens the lifetime. Figure 14 shows changes in maximum velocity during the closing phase of the Jellyfish valve membrane as a function of drive rate in the Helmholtz tester. The motion of the membrane was captured by a laser displacement sensor (LB-01, LB-60, Keyence Corporation, Osaka, Japan). The maximal velocity during the closing phase was increased by increasing the drive rate. Figure 15 shows a comparison of membrane surfaces along the spoke edge between two different test conditions in the Rowan Ash tester. Distinctly deeper abrasion was observed in the membrane surface that was tested under the drive amplitude of 0.9 mm (with compliance element) as compared with the surface that was tested under the drive amplitude of 0.4 mm (without compliance element). This difference could be explained by the fact that the maximal velocity of the rod under the drive amplitude of 0.9 mm was 9.3 m/s which is 2.2 times faster than that under the

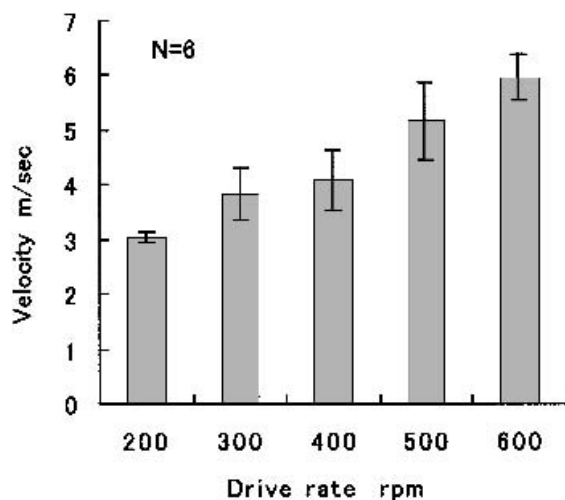


FIG. 14. The graph shows changes in maximum velocity of the Jellyfish valve membrane during the closing phase as a function of drive rate in the Helmholtz-type accelerated fatigue tester. The maximum pressure difference at valve closure was maintained at 120 mm Hg.

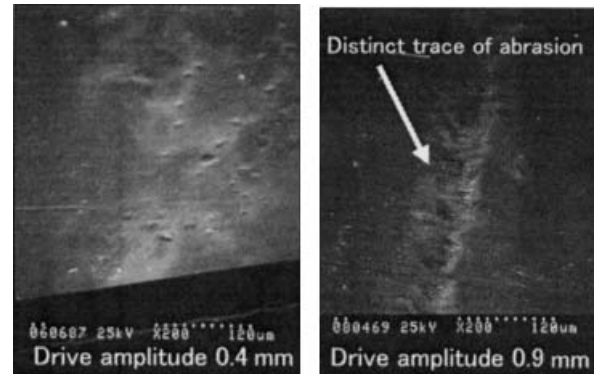


FIG. 15. Comparison of membrane surfaces of the Jellyfish valve under the two different drive amplitudes in the Rowan Ash accelerated fatigue tester are shown. The right side represents a drive amplitude of 0.4 mm while the left side represents 0.9 mm. The maximum pressure difference at valve closure was maintained at 120 mm Hg.

drive amplitude of 0.4 mm. Apparently, the actual dynamic load conditions were different even though the pressure difference at valve closure was adjusted to the same value. This implies that different durability results can be obtained by variation of drive conditions within the guidelines of ISO 5840. In other words, specification of only the maximum pressure difference drop at valve closure is not sufficient to ensure that tests are conducted under equivalent conditions. The results indicate that measurement of the dynamic load acting on heart valves would be of importance for the establishment of a reliable, standard test methodology. To this end, the authors have developed a technique for measuring dynamic loads in the Tsinghua tester (11), and the influence of dynamic load on durability is now under investigation.

Comparison of fracture locations between the accelerated fatigue tests and animal experiment

If in vitro accelerated fatigue testing could reliably predict in vivo failure patterns, it would indeed be a very powerful tool. In this study, the fracture locations of Jellyfish valves obtained in three different accelerated fatigue-tests machines were compared with those observed in an animal experiment. All the membrane fractures occurred along the spoke edge in the accelerated fatigue tests while the membrane was fractured in the region between adjacent spokes in the animal experiment. The results showed that the fracture locations in the accelerated fatigue tests were not consistent with those in the animal model. In this study, the question of reproducibility of the single animal experimental result is of much importance. However, accumulation of long-term animal experimental data (over 300 days, for example) is

extremely difficult. Therefore, in order to predict possible fracture sites in the Jellyfish valve from mechanical considerations, the distributions of strain, deflection, and stress in the membrane were analyzed using the finite element method. The analysis was performed on the closed phase of the Jellyfish valve. Because the membrane of the Jellyfish valve is not restrained during the opening and opened phases except at the central attachment to the valve seat, as shown in Fig. 2, the mechanical restraint of the membrane by the supporting valve seat was assumed to be the major factor for inducing the membrane fracture. Taking advantage of the axial symmetry of the valve, the analysis was performed on only one of the twelve radial segments of the Jellyfish valve. Figure 16 shows the analytical model with the applied boundary conditions. The model radial segment of the valve seat is contained within the area surrounded by bold lines. As indices of prediction of possible fracture sites in the Jellyfish valve, the distribution of equivalent elastic strain (ϵ_e), deflection, and equivalent Von Mises stress (σ_e) were analyzed by the following equations:

$$\epsilon_e = \left[\frac{4}{9} (\epsilon_x^2 + \epsilon_y^2 + \epsilon_z^2 - \epsilon_x \epsilon_y - \epsilon_y \epsilon_x - \epsilon_z \epsilon_x) + \frac{1}{3} (\gamma_{xy}^2 + \gamma_{yz}^2 + \gamma_{zx}^2) \right]^{\frac{1}{2}} \quad (1)$$

$$\sigma_e = \frac{\sqrt{2}}{2} [(\sigma_x - \sigma_y)^2 + (\sigma_y - \sigma_z)^2 + (\sigma_z - \sigma_x)^2 + 6(\tau_{xy}^2 + \tau_{yz}^2 + \tau_{zx}^2)]^{\frac{1}{2}} \quad (2)$$

where ϵ is tensile strain, γ is shear strain, σ is tensile stress, and τ is shear stress. The results are shown in Fig. 17. Strain concentrations were observed in two distinct areas of the membrane: midway between adjacent spokes and adjacent to the spoke edges. The maximum strain occurred in the former region, corresponding to the location of maximum deflection. The latter region was consistent with that of maximum stress concentration.

The fracture location in the animal experiment was clearly coincident with that of maximum strain concentration caused by the deep deflection of the membrane at valve closure. Therefore, it was confirmed that the fracture location observed in the animal experiment was predictable from a mechanical point of view. Furthermore, the fracture locations in the accelerated fatigue tests were consistent with the regions associated with stress concentration. Although the positions of fracture were different between the accelerated fatigue tests and the animal experiment, they were, in both situations, entirely consistent with the regions of high strain concentration. The difference in fracture locations could have been the result of changes in the viscoelastic properties of the membrane in the physiological environ-

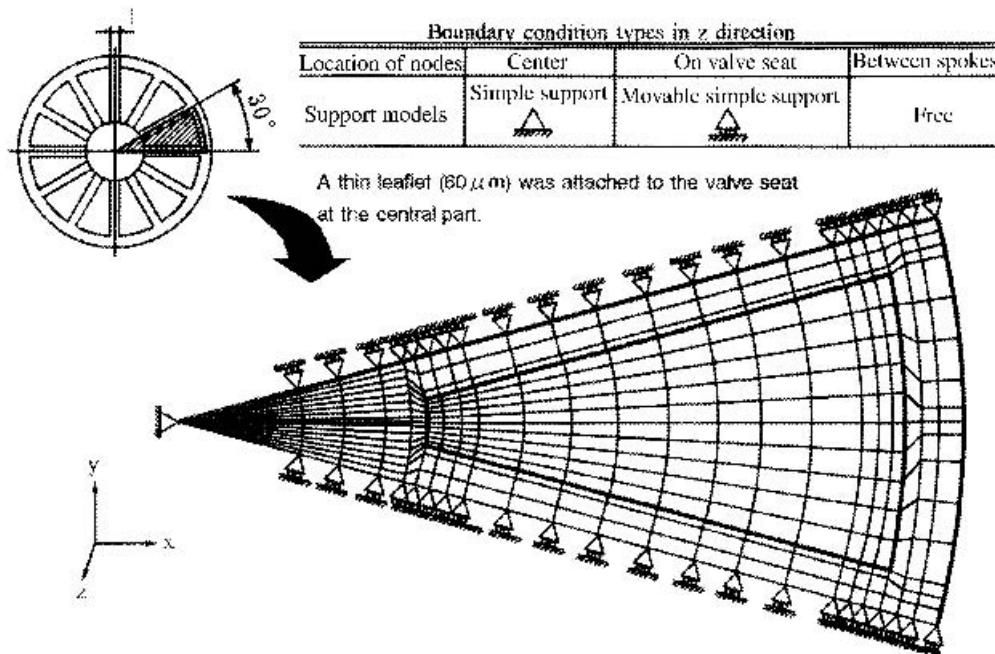
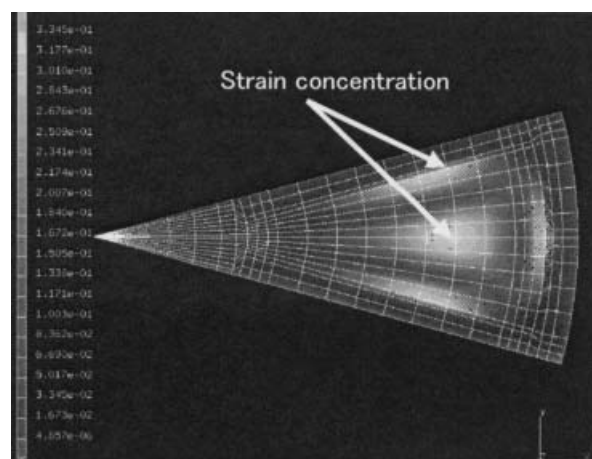
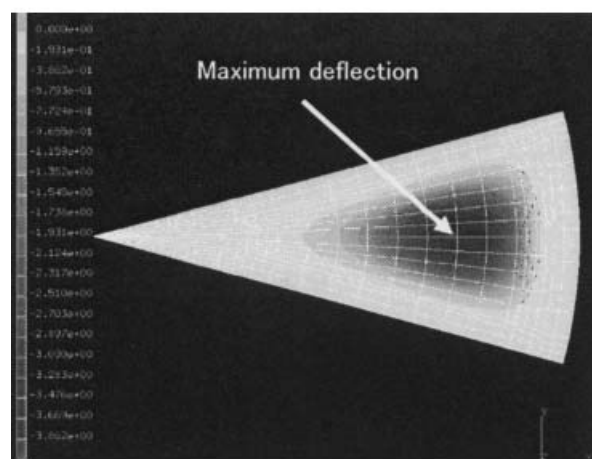


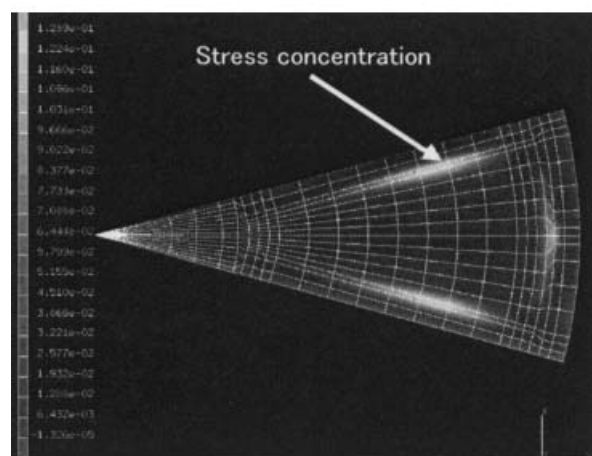
FIG. 16. The analysis model and boundary conditions for finite element analysis of the Jellyfish valve membrane are shown. Only one of twelve radial segments was treated, taking advantage of the axially symmetric shape.



(a) Strain distribution



(b) Deflection distribution



(c) Stress distribution

FIG. 17. Distribution of the equivalent elastic strain, equivalent Von Mises stress, and deflection of the Jellyfish valve membrane under a pressure load of 90 mm Hg are shown.

ment. In vitro reproduction of the in vivo fracture locations is indispensable for the establishment of a reliable protocol for accelerated fatigue tests. Therefore, a method for compensating for the hypothesized difference in viscoelastic performance of the polymeric material in the accelerated fatigue tests could be one of the essential steps in the reproduction of in vivo fracture modes. Whereas this study dealt with the durability of a polymer valve in the accelerated fatigue environment, the similarity in viscoelastic behavior of clinical bioprosthetic heart valves begs that further research should be conducted to extend the current protocol to bioprosthetic valves.

CONCLUSIONS

The durability of a polymer valve was significantly altered by employing different drive conditions in accelerated fatigue tests even though all of these tests complied with the recommendations of ISO 5840 (Cardiovascular Implants). Moreover, fracture locations between the accelerated fatigue tests and the animal experiment were not coincident although, in all cases, the fracture locations were consistent with the areas of high strain concentration as computed by finite element method. Further research should be conducted into the influence of the dynamic load acting on valves and the differences in viscoelastic behavior between the physiological and accelerated-rate environments, especially for polymer and bioprosthetic heart valves. Discussion of these basic data would be useful in a revision of the durability test protocol prescribed by ISO 5840.

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