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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.

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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

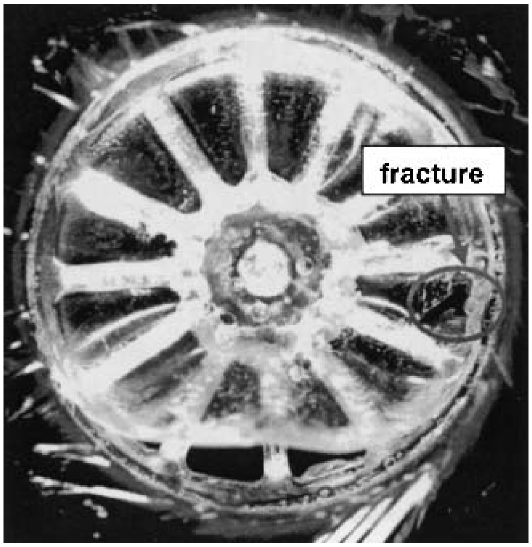

FIG. 1. A membrane fracture in the Jellyfish valve incorporated into a paracoporeal total replacement-type, pneumatically driven blood pump after 312 days of pumping is shown. The valve was explanted from the outlet position of the left-side pump.

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 ±10 μm 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

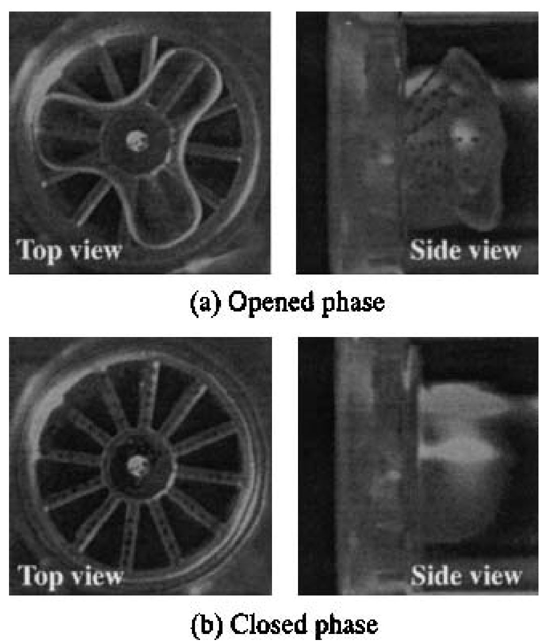

FIG. 2. Typical behavior of the Jellyfish valve membrane in the outlet position of a pulse duplicator is shown. Mean transvalvular flow rate was adjusted to 5 L/min against a mean aortic pressure of 100 mm Hg.

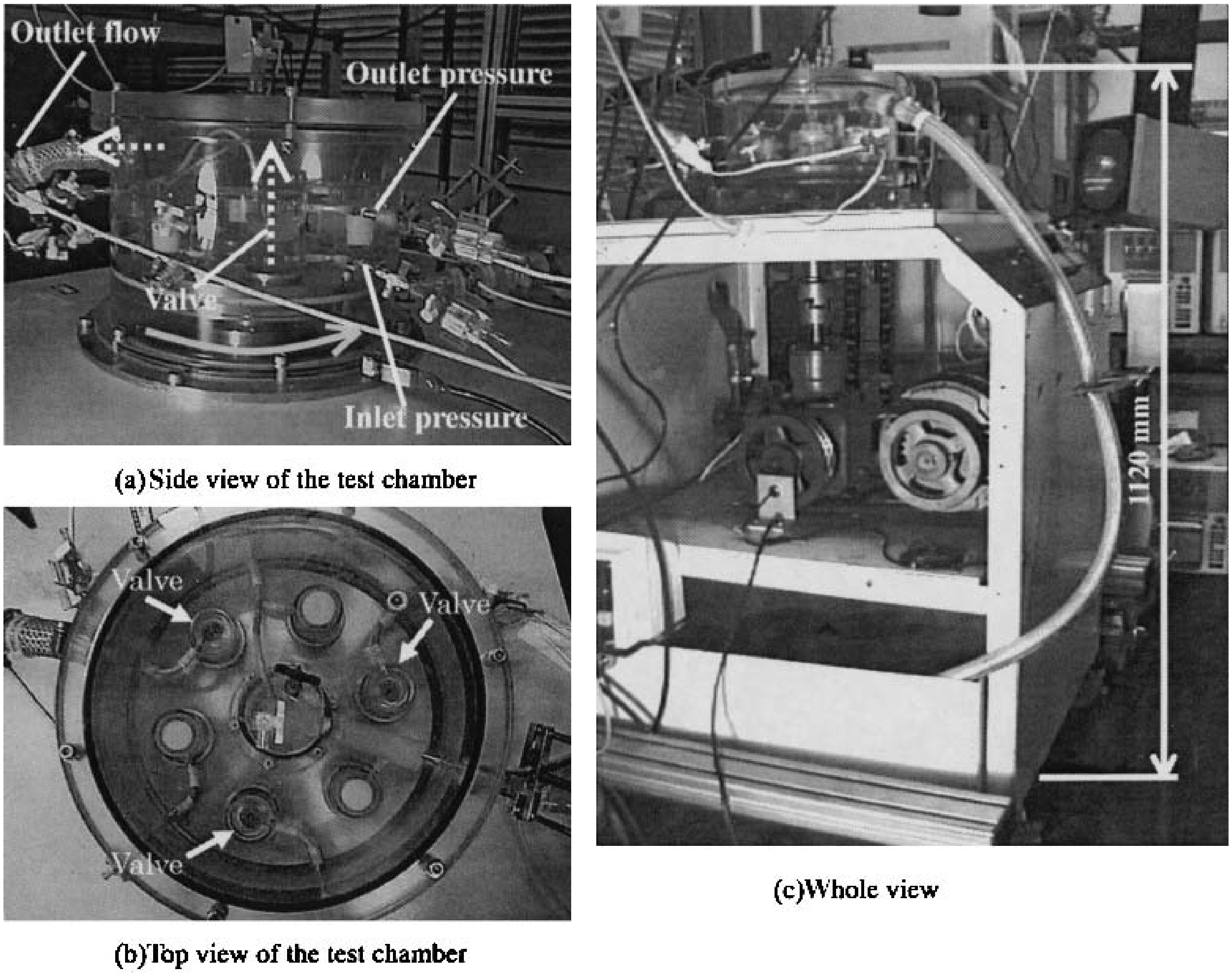

FIG. 3. A Helmholtz Institute-type accelerated fatigue tester for prosthetic heart valves is shown.

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-

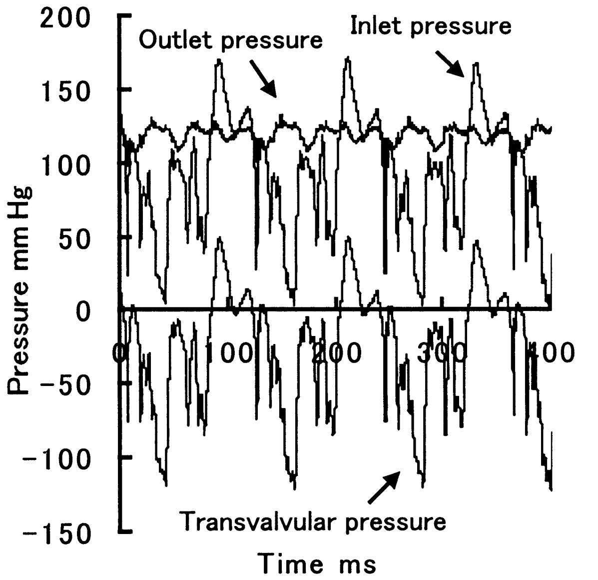

FIG. 4. Simultaneous pressure waveforms are shown in the Helmholtz-type accelerated fatigue tester under a cycle rate of 500 rpm. The maximum pressure difference at valve closure was adjusted to 120 mm Hg under a mean flow of 5.0 L/min. Mean outlet pressure was adjusted to 115 mm Hg.

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

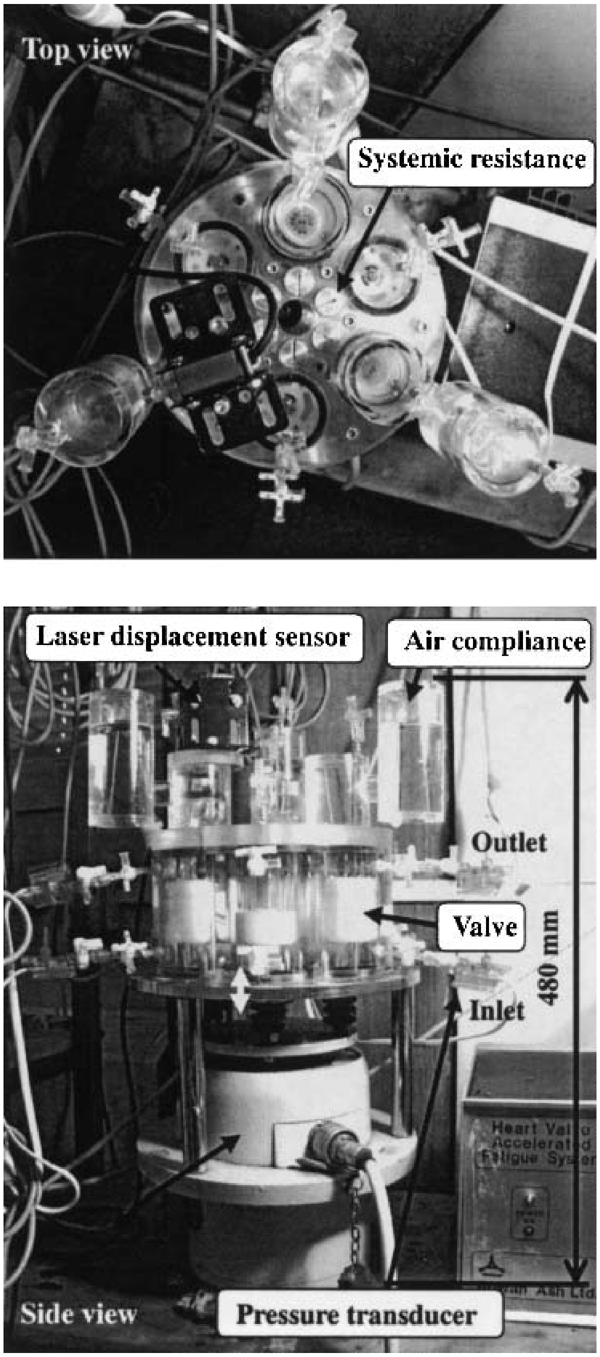

FIG. 5. A modified version of the Rowan Ash accelerated fatigue tester for prosthetic heart valves is shown. A compliance element was added to the original system.

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-

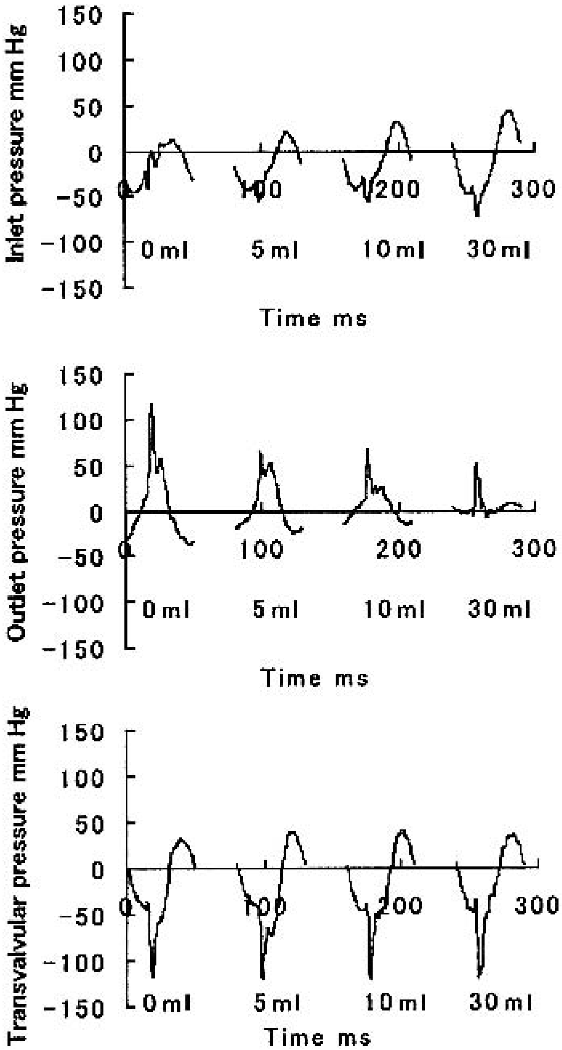

FIG. 6. Changes in pressure waveforms are shown as a function of air-compliance volume at the outlet position of the valve. The maximum pressure difference at valve closure was maintained at 120 mm Hg under a drive rate of 1,200 bpm. Inclusion of the air-compliance element increased the pulse pressure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

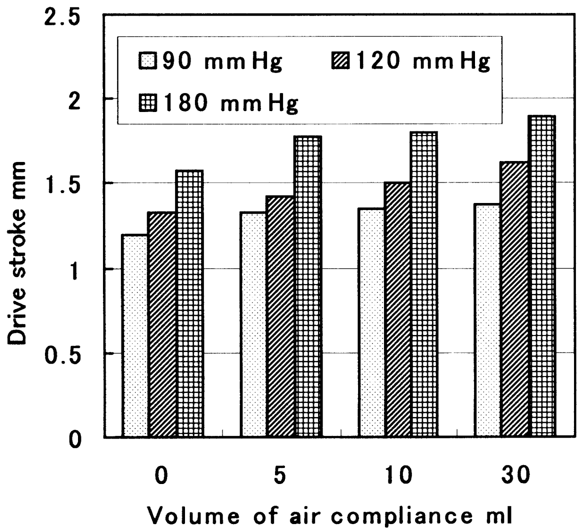

FIG. 7. Influence of inclusion of the air-compliance element on drive amplitude under three typical transvalvular pressures at closure are shown. In order to maintain the specified pressure drop, the drive amplitude was increased.

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

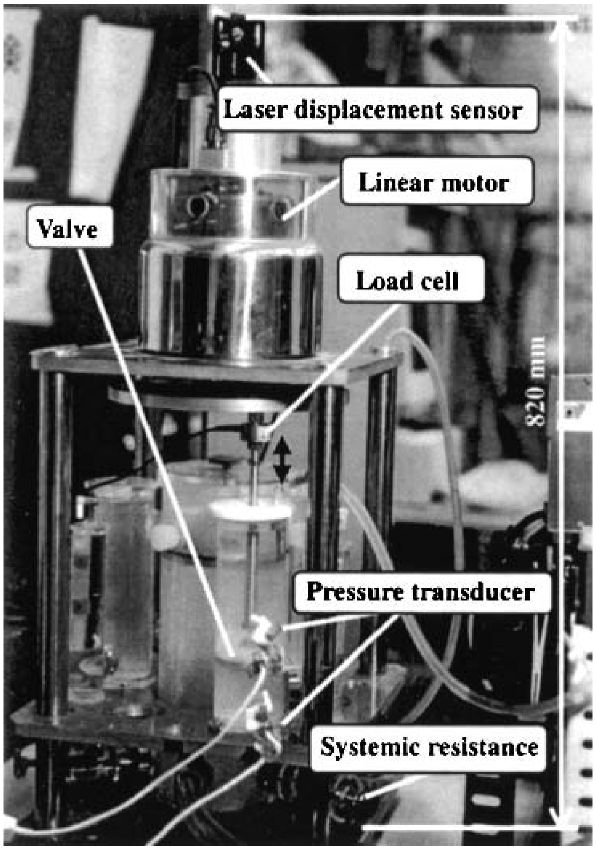

FIG. 8. A Tsinghua University type accelerated fatigue tester for prosthetic heart valves is shown.

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