India makes her own heart valve prosthesis

A. V. Ramani

The article by M. S. Valiathan (see page 77) gives an overview of India's need for artificial heart valves and the excellent solution arrived at at his institute. The achievement of the Chitra Tirunal Institute in developing a clinical model of a mechanical heart valve can rank alongside any major scientific or technological development in India. The article is unduly modest, hiding as it were the light of the institute under a bushel and sidestepping the leadership he himself gave to the large group working on this development. It was a massive, painstaking, and often frustrating multidisciplinary effort spanning more than a decade.

A little-realized fact in technological development is worth a mention. A study in the USA revealed that even in a technology-driven, fast-paced industry like electronics where a new product gets launched every 90 days the actual effort spans many years, usually ten to fifteen. It is much longer for implantable biomedical devices. It is, therefore, a remarkable feat that the Sree Chitra Tirunal Institute could come out with a successful clinical model of a mechanical heart valve, fully conforming to applicable international standards in just 10 years from conception to clinical trials passing through three fully developed models on the way.

Why an Indian heart valve?

Is the magnitude of the problem in India large enough to justify such an effort? Rheumatic heart disease, which leads to damaged heart valves needing prosthetic replacement, affects the poor at a young age. It is likely that there exists now a population of about one million young people who need a valve at a young age. It is likely that there exists now a population of about one million young people who need a valve replacement. To this must be added about 20,000 new patients every year. Considering that less than 4000 valves are implanted every year in the country, one can realize the staggering backlog of cases. One fervently wishes that rheumatic heart disease is wiped out from India by a proper primary health effort in schools, as has been done in the advanced countries. Till then India will have to depend on palliatives like the artificial heart valve to clear up the depredation rheumatic heart disease leaves behind. The cheapest imported valve, which is not necessarily the best, costs about Rs 10,000 each. This means that about Rs 40 million a year is being spent on foreign exchange on this account alone. The cost of the valve is a significant part of the total expenses associated with the valve replacement operation.

Sree Chitra Tirunal Institute decided that it did indeed make eminent sense to take up the development of an indigenous artificial heart valve.

What kind of valve?

The next question to be resolved was what type of valve suited India best. The biggest cause for valve replacement in India is the rheumatic heart disease. This is mostly a childhood condition caused by repeated throat infections which were neglected. By far the largest fraction of patients needing heart valve replacement are below 25 years of age with a whole productive lifetime ahead of them. This means that the prosthetic replacement should last a minimum of 25 years and more. Artificial heart valves would be (i) homograft valves procured from human cadavers soon after death, (ii) xenograft valves which are obtained from pigs and denatured, (iii) tissue valves made from other animal tissues like the bovine pericardium, and (iv) mechanical valves. The heart valve opens to allow blood to flow with minimum pressure drop in the forward direction and closes when the pressure reverses. The problem with implanting a minimum pressure drop in the forward direction and closes when the pressure reverses. The problem with implanting a foreign substance in the blood stream is the tendency for blood to deposit proteins on such surfaces which can grow into large clots, leading to valve failure or embolization. This means that a person with an artifical heart valve has to be on some form of *monitored* anticoagulation therapy. The best modern tissue valves do not need such careful anticoagulation. But they all have a tendency to calcify quickly. So far they have a poor mechanical life and are very expensive. They are best suited for the elderly patient who cannot be easily on an anticoagulant.

The mechanical heart valves *do* need anticoagulation. But the problem can be mitigated by a proper choice of materials, ensuring a high degree of surface finish, and a tightly controlled manufacturing programme. A well-made mechanical valve, using a proper combination of materials, can easily have a mechanical life of 25 to 50 years. The mechanical valve is also the lowest in cost.

Mechanical valves usually consist of three parts viz. (i) an occluder which moves and allows the blood to flow in one direction and occludes the orifice on pressure reversal, (ii) a cage made of a metal or carbon to house the occluder, to allow it to function freely, yet prevent it from working loose, and (iii) a sewing ring made of a fabric which permits attachment of the device to the heart muscle. Mechanical valves can be divided into two large classes—the caged ball type, and the tilting disc or hinged leaflet type. The latter type has better haemodynamic properties and a low profile. In the Indian context, the functioning of a high-profile-ball valve can get affected by the surrounding tissue pressing in on it.

Considering the age of the patient, cost of the device and haemodynamics a decision was taken to develop a tilting disc valve.

Materials of construction

Materials of construction

Materials toxicology

A *sine qua non* for any candidate material for biomedical devices is its biocompatibility for the intended application. In the case of artificial heart valves not only should the materials qualify for long-term implantation but

also should meet the demands of continuous service in the flowing blood stream. The toxicology and pathophysiology groups of the institute have done yeoman service throughout the development, screening and clearing of all the materials used in the study prior to fabrication.

Sewing ring. Of the three parts of a mechanical valve, the sewing ring is a passive part made of a fabric of polytetrafluroethylene (PTFE) or polyester. Since India did not have any PTFE fabric production and polyester was available in plenty, a polyester sewing ring was chosen. Even though the material was available it took three to four years of study to qualify the material and the cleaning procedures. K. N. Seshan and the South India Textile Research Association, Coimbatore, produced the fabrics in various knitted and woven forms of different porosities. During implantation trials, it was found that there was a tendency for the fabric to encourage thick tissue growths on the surface which could cause obstruction to flow. This was traced to the presence of low-molecular-weight oligomers of the polyester on the surface of the fabric. A new regimen of cleaning and solvent extraction eliminated this problem. Since then this material has been in use unchanged for all the models of heart valves developed, including for the final clinical model that is expected to be commercialized.

The cage. The human heart beats about one billion (10^9) times in 25 years. A valve is called upon to function for this length of time without any kind of servicing. Since the cage is sitting in the blood stream it has to have a slim profile in the flow direction to minimize pressure drops. All passages should ideally be streamlined to reduce clotting. The cage material should be capable of taking a high polish. It goes without saying that the material should be implantable and blood compatible.

It is no wonder that only high performance aerospace materials make the grade. Titanium and its alloys, chrome-cobalt alloys, and pyrolytic graphite are the materials of choice.

Because of its availability in India, titanium was first chosen as the cage material. Valiathan's article discusses the reasons for veering away from titanium to chrome cobalt for the final model.

The occluder. Since there is no way of replacing worn out parts and the need for a life of 10^9 cycles, the choice for the occluder becomes very limited. Added to this is the problem of blood compatibility. Beyond all, there is the prime consideration of the tribological behaviour of the cage–occluder combination. Some of these are covered in Valiathan's article. The final choice was a disc made from ultra-high-molecular-weight high-density polyethylene (UHMWHDPE).

Materials science in heart valve development

The entire course of development of the Chitra heart valve was a fascinating study of all aspects of materials science. The design of the cage and the occluder, and the arduous testing of the combination involved basic materials science, mechanical design, fatigue testing, tribology, and biocompatibility evaluation. Unconventional fabrication methods, post-fabrication finishing and special assembly procedures had to be evolved.

G. S. Bhuvaneshwar and his team in the artificial internal organs division in the Biomedical Technology Wing (BMT Wing) of Sree Chitra Tirunal Institute bore the brunt of the often frustrating work. Much is owed to this group's tenacity in the face of severe odds for the successful culmination of a clinical model.

During the course of development, electron beam welding, 3-D pantographic milling, electric discharge machining, electrochemical machining, thermal polishing and cryomachining were all tried; some to be retained—many to fall by the wayside. Special-purpose machines like pulse duplicators and accelerated-durability testers had to be built based on very sketchy information available in the literature. O. S. N. Nair and his band of workers of the tool room of the Institute did a marvellous job of tackling all these machining and fabrication problems.

While it would be fascinating to take a trip through the entire developmental activities spanning more than a decade, space constraints makes one to look at just the highlights and milestones.

Some of the early problems were due to the lack of knowledge in the behaviour of materials in unfamiliar environments. One example: in the early days of accelerated-durability testing a curious phenomenon was noticed. The test consisted of subjecting the valves under test to an oscillating liquid column at about 12 Hz for a total of about 400 million cycles. The liquid used was a blood analogue consisting of a 35% w/v solution of glycerine in water. The cage was of titanium and the occluder of polyacetal. It was found that the struts supporting the disc at closure wore away fast. This inexplicable behaviour of a soft plastic wearing away a metal was explained by one of the visiting professors of the Institute (Prof. S. Ramaseshan) as possibly due to very fine, difficult to see iron oxide particles liberated by the circulating system getting embedded in the soft plastic scouring the metal. Use of antirust compounds, noncorrosive plumbing and pump, and an on-line fine filter solved this problem.

The first model valve had a cage made of titanium with two struts of bent titanium wire electron beam welded to the housing. This model had a poor mechanical life, strut failure being the cause. Studies made by the failure analysis group at the National Aeronautical Laboratory, Bangalore, showed brittle fracture probably caused by residual gases in the electron beam welding chamber.

This was the start of a totally new approach to fabrication. The idea of the monolithic cage was born then. A solid disc of titanium was machined by spark erosion to have an integral major strut—the one that used to break—while the minor strut on which the disc pivoted was welded. This model successfully crossed 400 million cycles of accelerated test. That the model failed on account of the polyacetal disc is now history and described in Valiathan's article.

The next model to be tried was the sapphire disc–titanium cage valve. This disc was made of a single-crystal sapphire. In durability testing the cage wore to an unacceptable extent. The cage was nitrided *in situ*, which helped to a limited extent. When the coating wore out the wear reverted to the initial high values. The final solution for this

model was a titanium nitride-coated chrome-cobalt monolithic cage machined from a block of the alloy.

The accelerated durability test was conducted in glycerine–water mixture as prescribed in international standards for heart valves. The valve performed well and was implanted in sheep. The death of a few animals caused by disc fracture showed up the deficiencies in the engineering evaluation even if applicable standards were followed. It was finally found that the blood analogue used was tribologically incompatible with the cage–disc combination under trial. The Chitra Tirunal Institute was the first one to use this single-crystal ceramic in the blood stream. Although this has been given up here in favour of other materials for the occluder it is interesting that elsewhere others have taken up this material for detailed study.

Large-animal evaluation

A small digression is relevant here. The literature does not reveal details of the surgical procedures for valve replacement in animals. The applicable standards only indicate that the intended clinical model needs to be tested in a suitable animal. It required three years, many failures, and the combined skills of the cardiac surgical team led by Valiathan, augmented by the animal expertise of the vivarium headed by the veterinary surgeon G. A. V. Lal to standardize an ovine-animal model for *in vivo* testing of heart valves. But for the invaluable contributions of this group, progress towards a clinical model would not have been possible.

Search for new materials and methods

So, it was back to the drawing board for Sree Chitra Tirunal Institute and all prospects seemed bleak. This was when the development had already seen eight years of work and it was hoped to start clinical trials. Concerned by the many setbacks, Valiathan constituted a small committee to review thoroughly the whole issue of the heart valve development, its materials, engineering evaluation, and fabrication methods with the instruction that a solution must be found. It is gratifying to note that a satisfactory solution was found. After detailed discussions, S. Ramaseshan and the author of this paper, who was then heading the BMT Wing of the Chitra Tirunal Institute, decided that development of the valve had to be divided into three parts: (i) the selection of candidate materials subject to known constraints, (ii) the evolving of simple but crucial test procedures for *quick screening* of cage–disc combinations, and (iii) identifying fabrication techniques.

The following recommendations came out of these discussions:

Candidate materials

Based on the need for low wear, high-fatigue resistance, high toughness and known biocompatibility, the choice of disc materials was headed by UHMWHDPE which is one of the toughest materials in use today. Lower in the list came super-tough Delrin, PTFE–DELRIN, and EKONOL (a composite of high-temperature polyester and PTFE). UHMWHDPE is no stranger to biomedical devices. Since its introduction it has been in continuous use in orthopaedic devices. Yet there was a certain reluctance in using this material as an occluder in a critical application like the heart valve. It was amusing that what almost amounted to surreptitious testing had to be resorted to, for convincing every single participant about the preeminent performance of this material.

Screening methods

Since abrasion resistance of the disc material and adhesive wear between the disc and the cage were the most important criteria, a sand–slurry test for the former and a pin-on-wheel test for the latter were decided upon.

Fabrication methods

The cage fabrication methods were generally under control. However, it was felt that computer numerical control (CNC) wire cutting methods would be the answer to bulk production. Once this was decided upon, K. G. Krishnadas Nair of Hindustan Aeronautics Limited and his competent team worked out a method of CNC–EDM wire cutting for the basic profile of the cage, followed by an EDM die sinking operation to shape the struts in the flow direction. The process was transferred to the Government Toolroom and Training Centre (GT&TC), Bangalore, which is currently fabricating batch quantities of the cages. In the case of UHMWHDPE the large molecular weight (4 to 6 million) prevents injection moulding. Either powder metallurgical techniques or thermal polishing after conventional machining were suggested to give the desired surface finish. The possibility of laser glazing was indicated.

After initial screening by sand-slurry and pin-on-wheel tests (Figures 1 and 2), UHMWHDPE disc and Haynes 25 cage were chosen as the valve materials

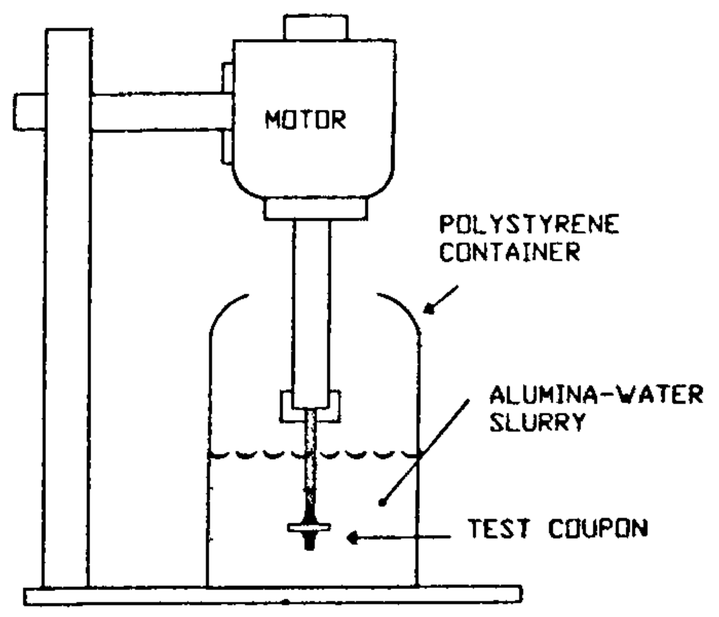

Figure 1. Schematic diagram of sand-slurry set-up.

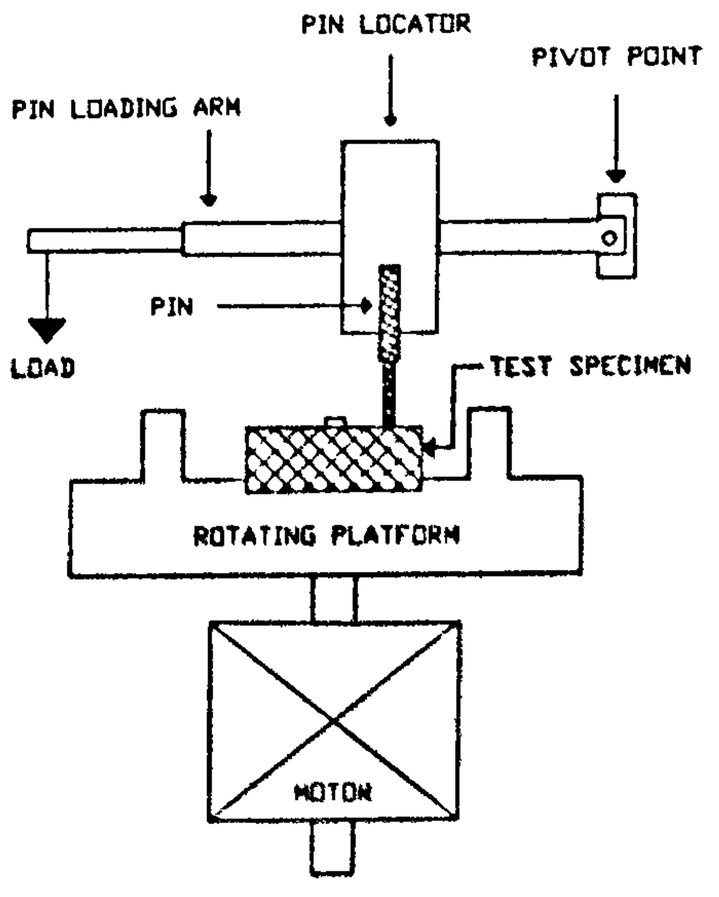

Figure 2. Schematic diagram of pin-on-wheel set up

with the old faithful polyester sewing ring

Success was not yet to be. One last problem related to the finish on the periphery of the disc remained. After machining and thermal polishing, the edge of the disc was carefully trimmed using cryomachining process specifically developed for this purpose.

This is the model currently undergoing clinical trials. As a prelude to commercialization, the Institute has taken up a programme, funded by National Research and Development Council, New Delhi, for a limited production, in three sizes, for further trials at the Chitra Tirunal Institute.

Conclusion

A task that would be daunting to many advanced countries with unlimited resources has been achieved in India though after many setbacks. Only the dedicated work of the team of engineers and scientists under the able stewardship of M. S. Valiathan could see such a job through. Such a development needed the active involvement of a first class cardiac medical centre delivering the best of cardiac health care. It also needed the combined inputs from material science, engineering, toxicology, and animal surgery groups. It was fortunate that all these were integrated together in the Chitra Tirunal Institute.

India now has a low-cost heart valve prosthesis conforming to all applicable international standards. What is more important is that a comprehensive infrastructure has been set up that can tackle the development of any biomedical engineering device.

In spite of the many setbacks the entire development programme was an exciting adventure in materials science and technology in which one was proud to participate.

A. V. Ramani is Director, Peninsula Polymers Limited, Thiruvananthapuram 695 010.

Second Menon Foundation Symposium on Epidemiology in Medicine

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Contact. Dr G. N. Menon
Menon Foundation
14 Raja Ram Mohan Roy Road
Bangalore 560 025