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DEVELOPMENT AND TESTING OF A MANUALLY ACTUATED HYDRAULIC SPHINCTER FOR THE CONTROL OF URINARY INCONTINENCE

This article covers the development and testing (*in vitro* and *in vivo*) of an implanted artificial sphincter for the control of urinary incontinence. The implant includes a cuff to be implanted around the urethra, and an actuator unit to activate and deactivate the cuff and to control the cuff pressure. The design overcomes some of the limitations of other such implants by providing easy adjustment of the nominal cuff pressure, an increase in cuff pressure in response to transient increases in peritoneal pressure, and an easier way for the patient to pressurize and depressurize the cuff. The original design concept is evaluated, and the evolution of the design as a result of *in vivo* testing in dogs is described, along with details on the value and difficulties of such testing.

INTRODUCTION

When the Manually Actuated Hydraulic Sphincter (MAHS) Program was started in late 1982, the primary problem with the then most widely used artificial sphincter was erosion of the cuff through the urethra.¹⁻⁴ The cause of this erosion was believed to be the cuff pressure.²⁻⁴ The physician had to choose a single pressure and hope that it would provide the needed closure of the urethra but not be so great as to cause necrosis and/or erosion of the cuff through the urethra. Another problem was that the control mechanism for deactivating the cuff to allow voiding of the bladder was awkward for the patient to use. The task therefore was to design an implant that would overcome the limitations of the earlier devices.

The design approach was based on a concept of Robert E. Fischell at APL. The initial system concept (Fig. 1) consisted of an inflatable cuff implanted around the urethra, an actuator unit implanted subcutaneously in the abdominal area, and a pressure-sensing bulb implanted in the bladder wall. The initial concept of the actuator unit (Fig. 2) was a three-chamber device, with access to each chamber provided by septums on the centerline. Each chamber could be accessed using Whitacre-type hypodermic needles (Fig. 3). The hole in the needle was located such that it was in one of the three chambers when the needle was inserted until the tip touched the inner surface of the actuator's lower shell. Thus, the fluid quantity and pressure in each chamber and the cuff and sensor bulb could be adjusted after implantation was completed and healing had taken place. Finger pressure exerted on the outer diaphragm through the skin moved

the inner diaphragm, expanding the sphincter-fluid chamber and thereby withdrawing fluid from the cuff to allow the patient's bladder to void. When the finger pressure was removed, the spring force of the inner diaphragm returned the fluid to the cuff.

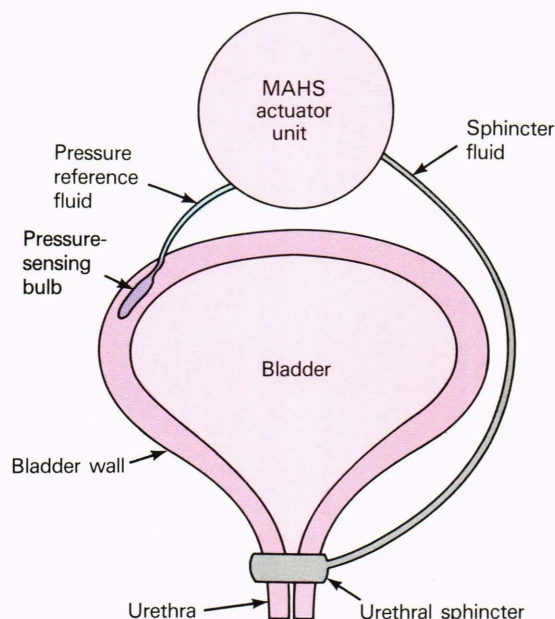


Figure 1—The MAHS initial system concept.

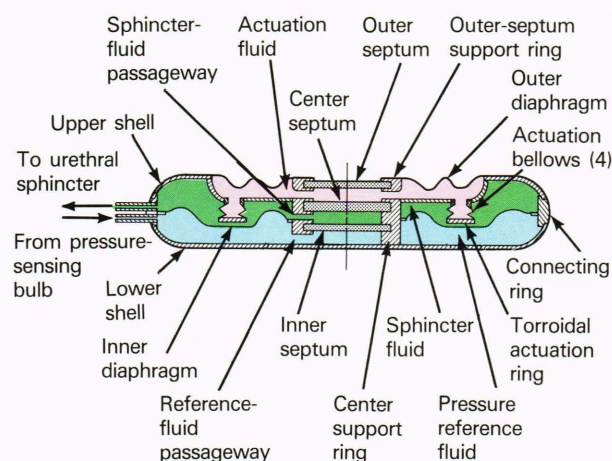


Figure 2—A cross section of the initial concept of the MAHS actuator.

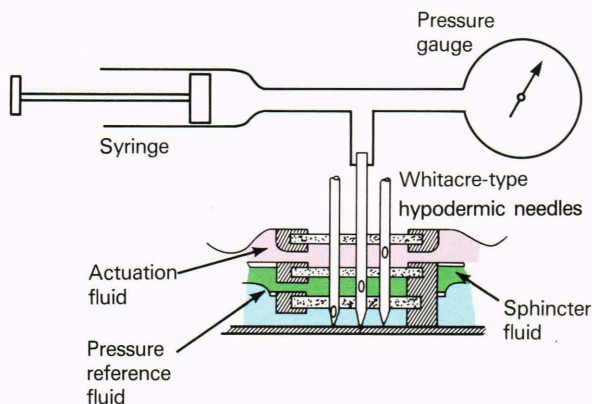


Figure 3—Whitacre-type hypodermic needles used with the MAHS actuator.

DISCUSSION

The program to refine the design and to build and test the MAHS implant was funded by a grant from the Public Welfare Foundation, by funds from the JHU/APL Development Fund, and by matching funds from CR Bard, Inc., which also provided personnel and facilities. Under a licensing agreement, CR Bard agreed to build and market the device when successful development was completed. Robert D. Jeffs, Professor of Pediatric Urology and Director of the Division of Pediatric Urology at the James Buchanan Brady Urological Institute of the Johns Hopkins Hospital, was the primary medical collaborator on the program and assisted with the animal trials carried out at Johns Hopkins Hospital.

Design of the MAHS Sphincter

The initial hardware development effort consisted of reviewing and refining the initial conceptual design. On Dr. Jeffs' recommendation, the idea of locating the sensor bulb in the bladder wall was changed to simply plac-

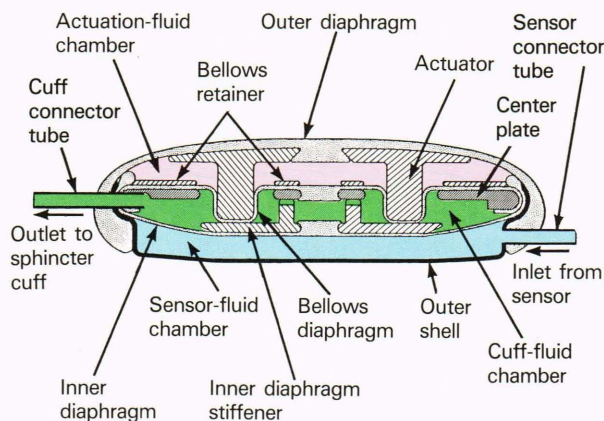


Figure 4—A cross section of the actuator used in the first animal trials.

ing it in the peritoneal cavity, preferably near the bladder.

Several modifications to the basic actuator were designed and tested, resulting in a number of significant changes until the design shown in Fig. 4 evolved; this was the design used in the initial animal trials. With this configuration, force on the outer diaphragm is transmitted by a direct mechanical linkage to the inner diaphragm, which, in turn, moves to expand the volume of the cuff-fluid chamber and thereby withdraw fluid from the cuff. At the same time, the volume in the sensor-fluid chamber is reduced. This reduction in volume is accommodated by fluid moving from the sensor-fluid chamber into the sensor bulb, which can expand to accommodate the extra fluid while at the same time creating little or no increase in back pressure.

Actuators for this configuration were fabricated and subjected to extensive *in vitro* testing. Typical curves of cuff pressure versus force on the actuator and cuff pressure versus sensor pressure are shown in Figs. 5 and 6, respectively. The reaction time between a change in sensor pressure and a subsequent change in cuff pressure was on the order of 0.05 s and was considered satisfactory. Life testing was started using a specially designed and fabricated computer-controlled test setup to repeatedly apply and release pressure on the outer diaphragm of several control modules and to record the cuff pressures. For those tests, the actuators were submerged in water, and water was used as the working fluid in the modules to preclude the osmosis of fluid through the silicone rubber diaphragms. (In the actual implant, the normal saline solution used as the working fluid will have the same saline content as body fluids, and thus there should be no osmosis of fluid through the silicone rubber parts.) Each control module was subjected to 40,000 cycles, which is equivalent to the maximum number of cycles that might be expected over 10 to 15 years of use.

The control module was analyzed for failure. Fortunately, all failures resulting in leaks in the unit also resulted in a drop in cuff pressure and thus fell into a "fail-safe" category for the patient.

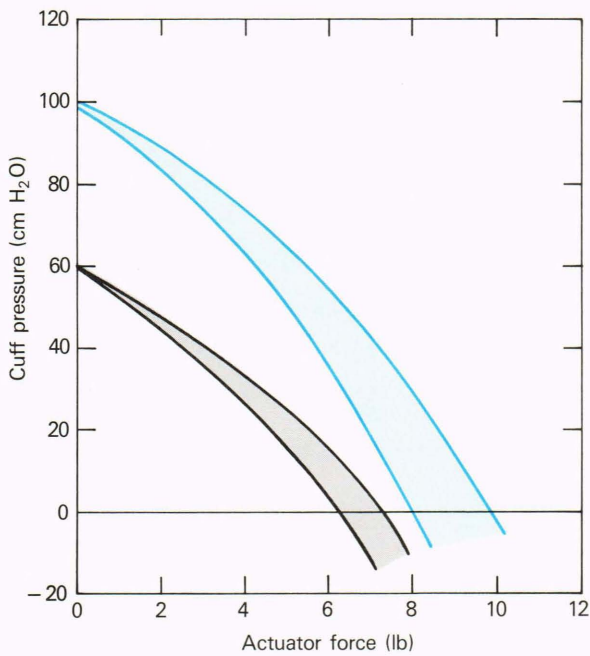


Figure 5—Cuff pressure versus force on the actuator, for four units.

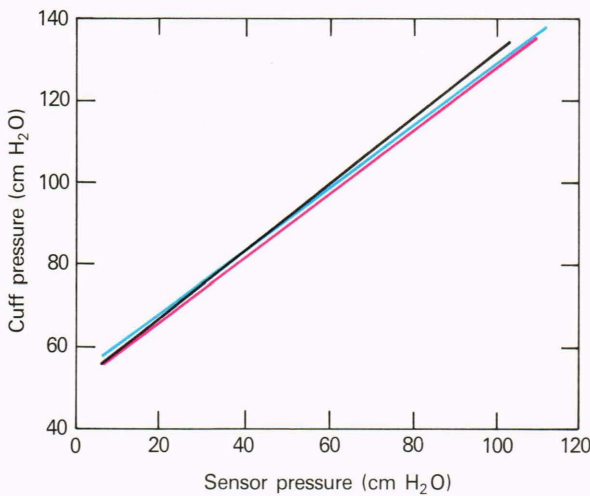


Figure 6—Cuff pressure versus sensor pressure, for four units.

Although there was some concern about possible inconsistency of performance of the control modules resulting from assembly procedures and fabrication of the silicone rubber parts, *in vitro* testing showed that all the units were quite uniform and well within the tolerances needed for satisfactory functioning.

The cuff and sensor bulb (Fig. 7) were developed concurrently with the control module. They are fabricated from silicone rubber, and the primary development effort was carried out by CR Bard, which has considerable background in the development and fabrication of silicone rubber devices for medical use. Several evolutions in the cuff design resulted in one that was expected to reduce the potential for local “pinching” of the urethra compared with other sphincter cuff designs. The sensor bulb also evolved after a series of designs. The main criterion was that it should be able to receive fluid from the sensor-fluid chamber when the actuator is depressed, with a minimum resulting increase in pressure in the sensor-fluid chamber.

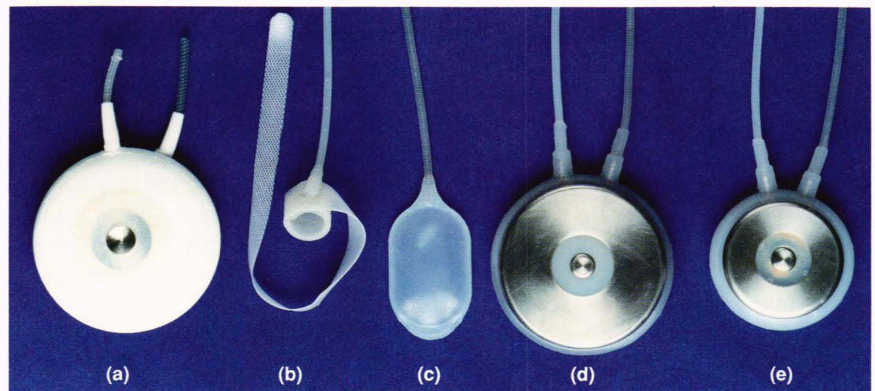
Of primary concern for all the implant elements was reliability, most particularly for the cuff, because of the surgical problems of installation or replacement. Simplicity of design and ease of manufacture were therefore very important. At this point in the program, the designs were considered suitable to meet the reliability needs, and units were manufactured for use in animal trials. All system components for the animal trials were the same as those planned for use by humans, except the cuff, which was of the same configuration but sized smaller to be suitable for the animal selected.

Animal Testing

Animal testing was considered necessary to verify that the device would function properly *in vivo* and ultimately to be able to apply for FDA approval for initial clinical trials in humans. Of particular concern was verification that the actuator could be depressed by force on the skin over the actuator, that the chambers in the actuator unit could be accessed after implantation, that the desired cuff pressures could be set and would be sustained, and that the cuff was effective.

All animal models present problems for such testing, but dogs were preferred because considerable handling

Figure 7—The MAHS actuator cuffs and sensors. (a) Silicone rubber actuator used in animal trials. (b) Cuff. (c) Sensor. (d) Titanium actuator used in animal trials. (e) Smaller actuator for use in humans.



of the animal would be required after the implant operation and having a docile animal was important. For anatomical reasons, male dogs are unsuitable models; but the urethra in a 50- to 60-pound female dog is suitable if a smaller cuff is used, and such an animal is large enough to be appropriate for the rest of the system implant. One difficulty with any animal model is that there is no known suitable means to make the animal incontinent in a way that would allow its further use in the planned testing. Also, there were serious questions about whether the dog would void its bladder when someone was applying force on the control module. Thus, there was a possibility that the dog would retain urine until its bladder became distended. Other investigators⁵ had used continent female dogs and cuff pressures low enough so that the cuff did not prevent the dog from voiding. We decided to use cuff pressures that applied some restriction to the urethra but not enough to prevent the dog from voluntarily voiding. Thus, the cuff pressure to be used became a somewhat subjective decision.

At this point in the program, an implant that had undergone extensive *in vitro* performance testing was available, and it was anticipated that the animal testing would be routine and completed on the proposed schedule. As it turned out, this would not be so. An important lesson learned was that animal testing is likely to present unforeseen problems and require significantly more time than anticipated.

Before the first implant of the MAHS system in a living animal, a trial implant in the cadaver of a 50-pound bitch verified that the urethra was suitable for installation of a cuff and that the inflated cuff could stop the flow of urine. In addition, procedures for the implant operation were confirmed to be suitable.

The first MAHS animal implants were made in September 1984. Three implants were made using the actuator configuration shown in Fig. 4. Tests revealed that, although the units appeared to function as predicted over short periods of time, there apparently were leaks of cuff fluid. The units were removed in January 1985 and examined. We found a leak in the outer diaphragm of one unit—evidently the result of a needle puncture. An internal leak in the other unit resulted from our depending on a compression seal. A septum that had been punctured many times with a hypodermic needle was examined with an electron microscope. The punctures in any area under compression sealed well, but those in an area under tension did not seal. We determined that punctures should be avoided near the outer edges of the septum.

As a result of this experience, the actuator units were modified. Silicone rubber adhesive was used to improve the seal between the outer edges of the diaphragm. Barbs were added to the sensor and cuff outlet tubes to provide better mechanical connection. The bellows retainer was modified to provide a smaller hole over the center of the outer diaphragm. A titanium needle guide, 1½ inches in diameter, was added to provide a small hole to access the septum at its center; the guide also protected the outer diaphragm from punctures during at-

tempts to access the septum when the needle was improperly centered over the actuator.

Life tests with the modified actuators were conducted to verify that the modifications corrected the leakage problems. Between May 1985 and September 1985, seven modified units were implanted in dogs.

The principal conclusions of the dog trials at that point were as follows:

1. Infection was a problem and was aggravated by the need to access the actuator frequently (something that would not be necessary in normal human use), in spite of care taken to keep the procedure sterile.

2. It was difficult to determine the cuff pressure that would put some force on the cuff but not prevent the dog from urinating. The ideal pressure varies from dog to dog because, to some degree, it is a function of the size of the urethra.

3. The unit functioned *in vivo* as expected, except for one critical item: obtaining the desired stable cuff pressure took too long, if it was achieved at all. The reason was probably the increased force on the outer diaphragm, resulting from encapsulation of the actuator. The surface area is large; as encapsulation increases, it causes increased force on the actuator, which, in turn, causes the inner diaphragm to be depressed slowly over time, thereby reducing the cuff pressure slowly over time.

4. It was difficult to access the septums because of the small size of the target, even though it was at the center of the actuator.

5. There was no apparent need to access the sensor fluid chamber after the actuator was implanted.

Design and Testing of the Second-Generation Sphincter

At this stage in the program, the design, fabrication, and testing of the second-generation actuator (MKII) had progressed to where the planned *in vitro* testing was nearly complete. A decision was made to abandon the earlier configuration (Fig. 4) and continue with the MKII configuration.

The MKII design of the MAHS actuator (Fig. 8) contains features that we believed would correct the prima-

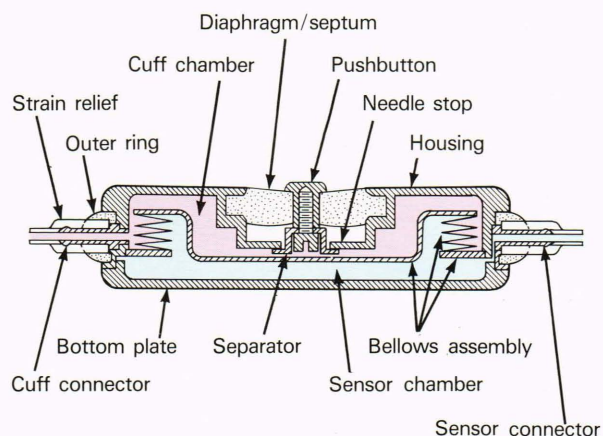


Figure 8—A cross section of the MKII actuator.

ry difficulties noted in the dog trials with the earlier designs. In particular, the septum presented a significantly larger target, and no damage would result to the unit if insertion of a needle was attempted outside the septum area, since that area was covered by the titanium housing. The outer surface where the septum and pushbutton are located is essentially flat, and the area that can be pushed to move the bellows is relatively small; therefore, pressure on the unit resulting from encapsulation was not expected to be a factor. The inner diaphragm has been replaced by a metal bellows. The spring tension in the bellows folds returns the bellows to its nominal position and repressurizes the cuff when force is released from the pushbutton and septum. To keep complexity and costs down, the inner diaphragm (bellows) septum was eliminated. Typical performance curves for the MKII actuator are shown in Figs. 9 and 10.

Starting in March 1986, the MAHS with the MKII actuator was implanted in seven dogs. Three dogs remained in the program long enough to meet the protocol requirements; one remained for 16 months, the other two for 8 months.

At this point, the satisfactory functioning of the MKII actuator had been well demonstrated, but the question remained whether the cuff pressures had been truly representative. Cystoscopic examinations and urethral pressure profiles had shown that the cuff indeed squeezed the urethra. But our desire to determine the effects on urethral tissue over an extended period of sustained high cuff pressures (high enough to stop the flow of urine completely) had not been satisfied. Also, a review of the available data indicated that there was no evidence of cuff erosion of the urethra, but more conclusive tests were needed.

A vagino-vesicle anastomosis procedure suggested by Peter Schlegel was tried on two dogs, without making a MAHS implant, to develop the surgical procedures and ascertain the viability of the operation. The anastomosis proved successful, and MAHS implants using the MKII actuator were made in eight dogs starting in April 1987. A vagino-vesicle anastomosis was performed on

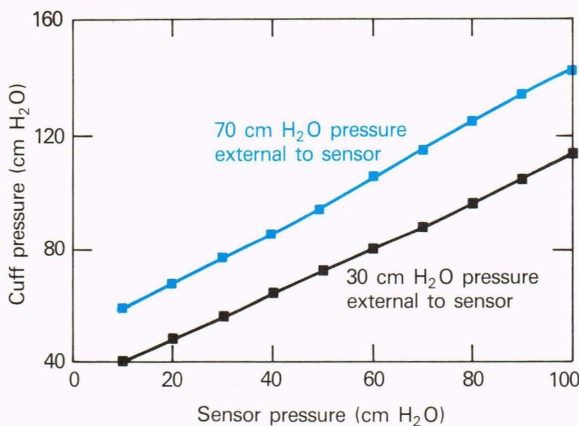


Figure 9—Cuff pressure versus sensor pressure for two pressures external to the sensor, with the MAHS MKII actuator.

all of those dogs as part of the implant operations. This provided an alternative path for the flow of urine and, therefore, continuous high cuff pressures could be used without causing distention of the bladder.

Of the dogs completing the program, one had cuff pressures sustained in the 80 cm H₂O range, one in the 70 cm H₂O range, and one in the 60 cm H₂O range. The cuffs in the last two were pressurized in the 50 to 60 cm H₂O range. (Centimeters of water [cm H₂O] is the standard unit of pressure used in this field.)

Urethral pressure profiles were performed on all dogs in the final phase of the animal trials. They were repeated at several cuff pressures to yield plots of urethral pressure versus cuff pressure. A typical result is shown in Fig. 11. Before sacrifice, the dog's own natural sphincter dominates, and intraurethral pressure does not fol-

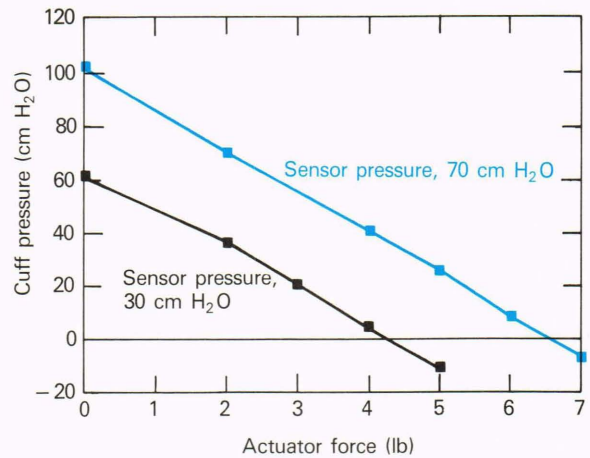


Figure 10—Cuff pressure versus actuator force for two sensor pressures, with the MAHS MKII actuator.

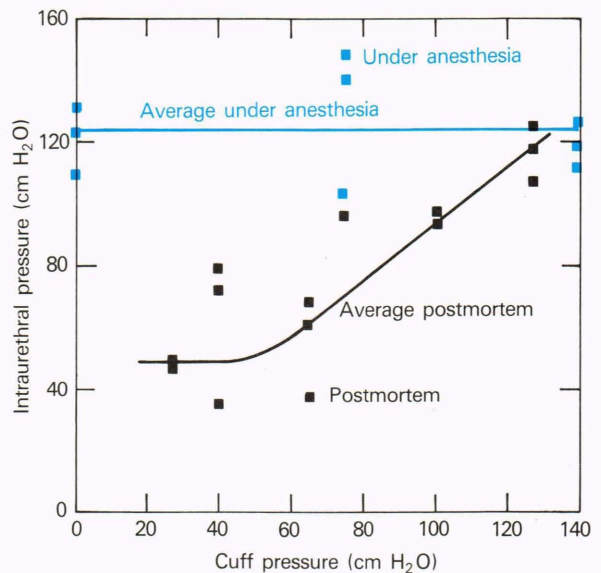


Figure 11—Typical pre-mortem and post-mortem urethral pressure profiles.

low cuff pressure. A postmortem investigation showed that there is a one-to-one relationship between urethral and cuff pressures after an offset cuff pressure is reached (about 50 cm H₂O in Fig. 11).

Histology tests were performed on urethral tissue taken from under the cuffs and some distance from the cuffs as a control. The samples were immediately fixed in formalin and were later stained with hematoxylin and eosin stain. Typical cross sections are shown in Figs. 12a and 12b. Under the cuff, the sample shows loss of urothelium (the innermost lining of the urethra) and fibrosis (scarring) of the muscular layer of the urethra (see arrows). The lumen of the urethra was partially or completely obliterated by the scarring. The same results were seen to a lesser degree in the dogs with cuff pressures of 50 and 60 cm H₂O. The loss of urothelium may have been partially due to the urethral pressure profiles that were performed. These pressure profiles had to be obtained at the end of the trials because the procedure carries a significant risk of infection and may have led to some of the observed loss of urothelium. The loss of urothelium and the scarring were worse in the sections of urethra under the cuff, indicating that the results were at least partially due to the pressure applied by the cuff. No sign of necrosis (dead tissue) was seen in any sample. This was the desired histologic result for this trial, and the results were considered satisfactory for demonstrating the suitability of the cuff.

The animal tests were successfully completed in April 1988. Although the animal testing for this implant is believed to have been much more extensive than that carried out for similar devices, in the final analysis it was considered not excessive. The experience pointed up some possibilities that should be considered when planning such trials. The obvious ones are that the trial period is likely to be longer than anticipated and that problems not encountered in *in vitro* testing can be expected. Less obvious is that the trials may require more resources than were initially allocated. Some reasons are discussed below.

Limitations of the Animal Model. Limitations of the animal model may be many and complex. The main limitations of the MAHS implant are as follows:

1. There was no known suitable way to obtain a dog that had urinary incontinence, and testing had to be carried out on female dogs that had functioning sphincters.
2. The physiology of the animal versus that of a human required a smaller cuff for the dog.
3. A dog, even with a full bladder, cannot be depended on to urinate while a handler is applying pressure to the implant.

Unforeseen Events. Many aspects of an animal test program, including scheduling of the operating room and surgeons, are difficult to plan accurately.

Changes in Test Plans. It may be possible to include contingencies in a plan, but they probably will not reflect the need accurately. Animal testing experience with the first MAHS model dictated revisions of the actuator and subsequent *in vivo* testing of the MKII. Ultimately, the desire for more definitive data on the tissue

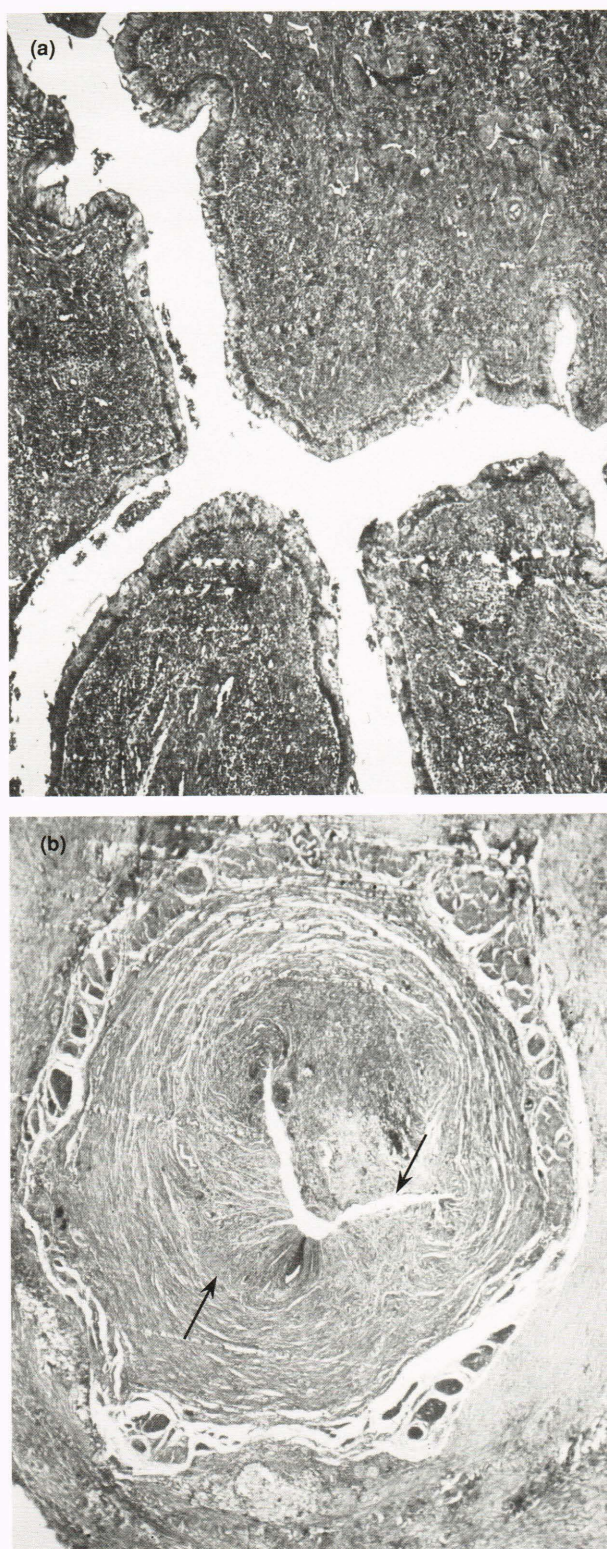


Figure 12—(a) Cross section from a control urethra. (b) Urethral cross section from the area under the cuff.

under the cuff required a greatly modified operation and subsequent additional testing. The result was a significant extension of the test schedule.

Diversity of Priorities. People and organizations may have different priorities, and satisfying all of their priorities may be difficult. Examples of different and sometimes conflicting priorities are research versus accumulation of statistical data, and science versus the need to meet FDA or other regulatory requirements.

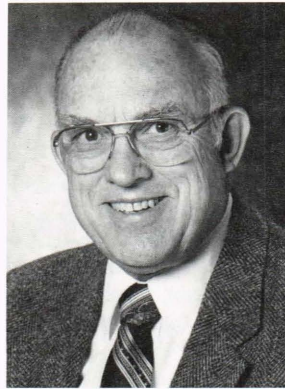
During the final animal trials and before we submitted a request to the FDA to conduct human trials, CR Bard modified the design of the actuator, simply to reduce its diameter. Photographs of the two actuator designs used in the animal tests and the final version planned for human trials are shown in Figs. 7a, d, and e. The functioning and the internal configuration of the final actuator are the same as those of the actuator used in the final dog trials. The animal trials proved to be a vital part of the MAHS testing program, and as a result the human trials are considered to be low risk. When they are completed, the system will be made available to the medical community as a commercial product that we believe will represent a significant advance in such implants.

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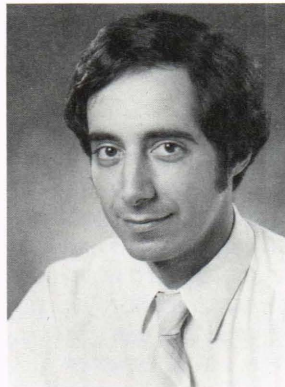
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CHARLES W. MEYRICK was born in Green Bay, Wis., in 1925. He received a B.S. degree from the U.S. Naval Academy in 1949, a B.S. in aeronautical engineering from the U.S. Naval Postgraduate School in 1955, and an M.S. in aeronautical engineering from the Massachusetts Institute of Technology in 1956. While on active duty in the Navy, he was an aviator and an Aeronautical Engineering Duty Officer. He was also program manager for the Navy's TRANSIT navigation satellite program. After retiring from the Navy in 1967, he joined Raytheon Co., where he was program manager for the SPARROW missile. Mr. Meyrick joined APL in 1978. He is a member of APL's Principal Professional Staff and works in the Strategic Systems Department as Group Supervisor of the SATRACK Preprocessing Group, which is responsible for the initial analysis and processing of raw SATRACK data from TRIDENT missile flight tests. Mr. Meyrick has also been involved with various biomedical programs at APL.



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