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A Telemetric Multichannel Computer-Based System for Monitoring Urodynamic Parameters in Awake Rhesus Monkeys

[Investigative Urology]

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Outline

Graphics

ABSTRACT

For comprehensive telemetric monitoring of bladder function in monkeys, transducers were implanted in the bladder wall and abdominal cavity. The EMG lead was buried in the external sphincter. All wires terminated in a subcutaneous transmitter. Conventional urodynamics were performed for comparison. Excellent reproducibility with conventional urodynamics was found. Implantation caused detrusor instability, which subsided in 6 to 8 weeks.

Real-time computer-based multichannel telemetric studies of voiding are feasible and reliable. Telemetric studies monitor for long periods without stress or anesthesia and provide an excellent model for lower urinary tract studies.

Key Words: telemetry, urodynamics, multichannel, monkeys

In recent years there has been growing dissatisfaction with conventional urodynamics, especially in basic research. Conventional experimental urodynamic studies utilize catheters and wires to detect urinary responses in which non-physiologic conditions (e.g., anesthesia and filling) prevail. [1] The task of explaining how the lower urinary tract functions in an unanesthetized, unrestrained, intact animal is formidable. Telemetric systems should be developed to achieve this goal.

Telemetry can be defined quantitative measurement at a distance. Modern telemetry transmits signals using radio waves to a decoder makes the data readable. While other medical disciplines have applied telemetry successfully in their research to advance the understanding and the treatment of different diseases, there have been only few trials in urology. Most of these trials were plagued by technical difficulties and were abandoned. [2,3] In the early 1960's and 1970's, several groups experimented with using telemetry to measure pressures from within the body. [11-13] Several of these early studies employed a small capsule to measure temperature, pressure, or pH. In urology, this was first applied to measure intravesical pressure. Gleason and associates used a small capsule which was introduced into the bladder of several patients. The telemetered signal was then received on a donut-shaped antenna around the patient's waist and bladder pressure was registered on a strip chart recorder. The study was plagued by many technical artifacts that prevented its subsequent use. Later telemetric studies used catheters and electrodes connected to a transmitter box that was worn on the belt of the subject. [14,15] While these studies met with some success, this is not a suitable method of data acquisition in animals because they will try to remove any foreign objects that are attached to them. Also, most of these techniques are not real-time and none of them made use of a computer-based data acquisition system.

There are certain advantages of telemetry in basic research. It reduces stress to the animal, since there is no handling, restraining or tethering to recording machines, no anesthesia, and no invasive techniques during monitoring. It provides meaningful physiological data performed in a natural setting over a long period of time. The data are accurate, with fewer artifacts than in conventional monitoring techniques, and the system allows for watching the progression or regression of a pathological condition. [4-7] Computer-based monitoring is accurate, easy to use, and allows complicated mathematical analysis. Most importantly, it reduces the number of animals needed to carry out a study.

Clinical applications of telemetry would provide certain advantages in problems of voiding dysfunction by simulation of several daily activities without the patient's being tethered to a laboratory equipment, lowered psychogenic stress because the patient would be left undisturbed and could urinate in a normal position, and prolonged monitoring of bladder and sphincter activities. [8]

Telemetry is indicated for those cases in which conventional urodynamics fail to provide a diagnosis, such as urge syndrome, uncertain cases of bladder outlet obstruction, enuresis, augmentation cystoplasties, bladder replacements, neurogenic bladder (alone or combined with upper tract malfunction), and certain psychogenic and habitual dysfunctions. [9]

Recent advances in computer technology have allowed us to develop a system that is totally implantable and remotely controlled. The purpose of this work is to develop a comprehensive telemetric system that is practical, feasible, reliable, and capable of monitoring multiple functions for long durations and acquiring data for storage and analysis.

MATERIALS AND METHODS

The system has four components: the telemetric implants, the modified metabolic cage for housing the animal, the uroflow system, and the data acquisition system housed in a PC Figure 1.

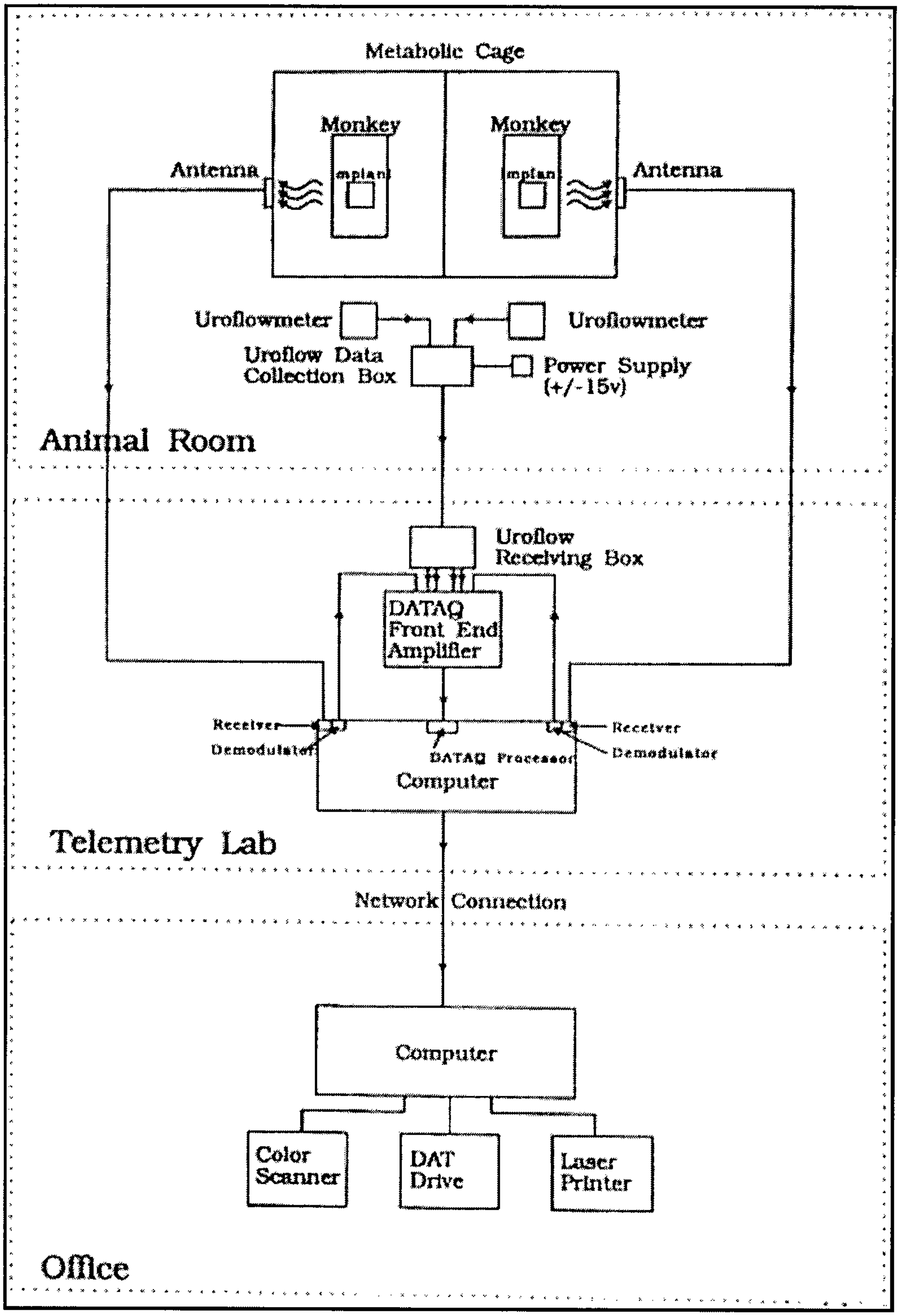

Figure 1. Block diagram showing four components of the telemetry system as well as three physical stations.

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1. Telemetry implants.

A set of two pressure transducers, 6.5 mm. in diameter, with EMG leads connected to a transmitter powered by a battery (Konigsberg Instruments, Inc., Pasadena, CA) was connected to a remotely controlled switcher Figure 2. The transmitter/mainframe had a size of 5.6 x 2.7 x 1.01 cm. and a weight of 17 grams. The mainframe was capable of a sampling rate of 600 Hz with a frequency response from DC to 200 Hz. The signal to noise ratio of the system was around 40 dB. The transmitter generated pulse interval modulated signals transmitted in the AM mode, but transmitted on the FM band with a range of 87 to 109 MHz. This method of modulation was used for power considerations and resulted in a transmit duty cycle of 2%. This range of transmitted frequencies was used because it radiates well from the tissue of the research subjects. Since this is the range of commercial radio broadcasts, care had to be taken to insure that the frequencies chosen for the implants did not conflict with local radio stations. The transmission range was rated for 3 meters in air but below that range when implanted. The battery option chosen for this project was a heavy duty battery with a life of 9000 hours. The battery measured 1.9 cm. in diameter by 6.35 cm. long and weighed 50 grams. Included with the battery option was a remotely operated RF switch allowing the implants to be turned off when not in use to conserve the battery. This was accomplished with the use of a hand-held transmitter which was placed over the region where the switch is located. The switch was 3.3 cm. in diameter by 1.1 cm. thick and weighed 12 grams.

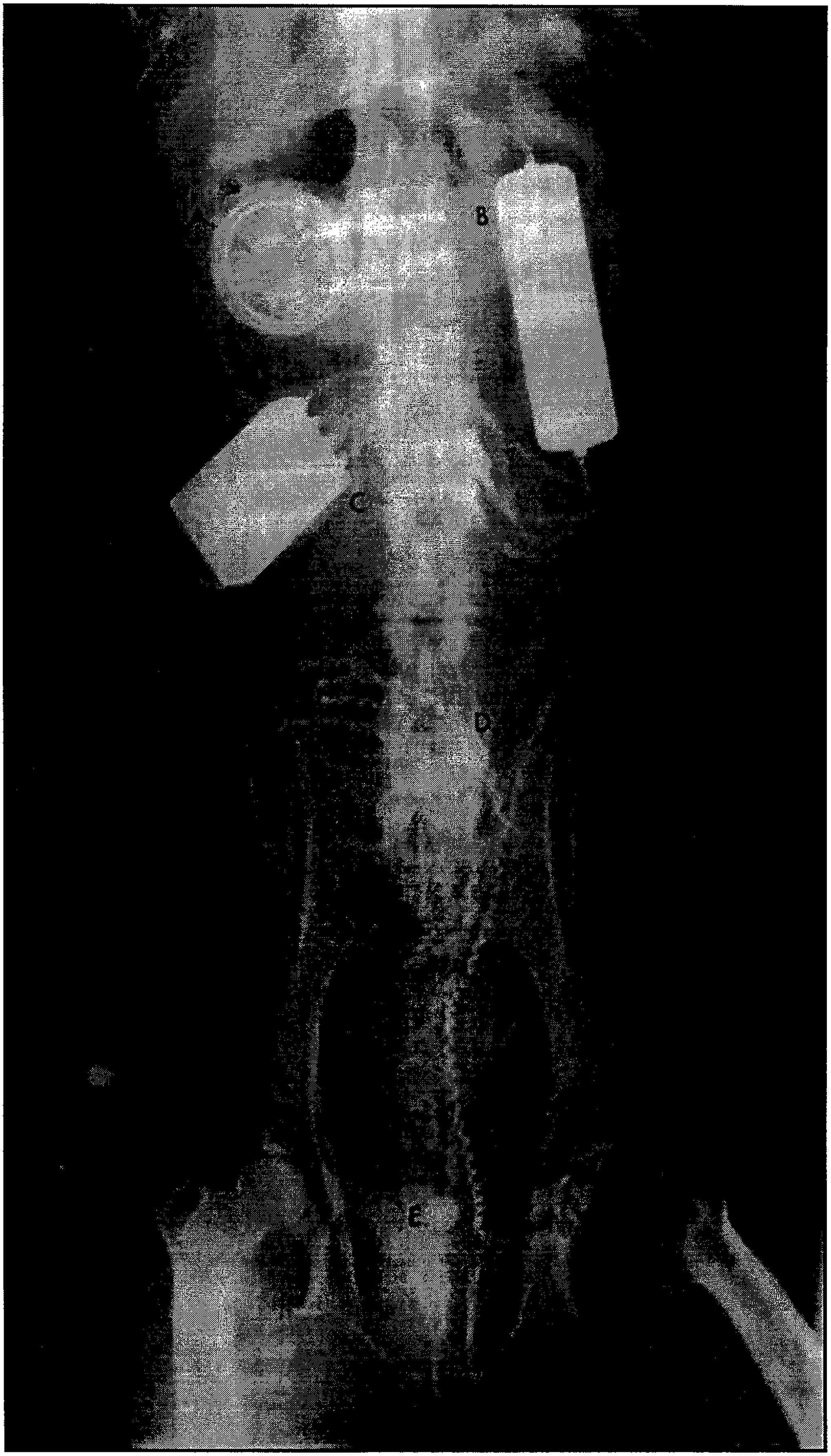

Figure 2. X-ray showing positions of implants: switch (A), battery (B), transmitter (C), abdominal transducer (D), bladder transducer (E), and EMG electrode (F).

The signals from the implants were picked up by two antennas, one on each side of the cage. The cables from the antennas were run to the telemetry lab where they were connected to the receivers and demodulators housed in the computer. The receiver was a PC bus-controlled radio receiver tuned to the specific frequency of each implant and plugged into a free slot in the computer. Also present on the receiver was a video output. This allowed a view of the raw un-demodulated signal on an oscilloscope to aid in tuning. From the receiver, the signal was passed to the demodulator. The demodulator's function was to convert the pulse interval modulated (PIM) signal and the pulse width modulated (PWM) signal to its appropriate analog outputs for bladder pressure, abdominal pressure, and EMG (electromyography) of the external urethral sphincter. The demodulator also provided for zero gain and filtering, which were all controlled by the provided software package. There were two sets of receivers and demodulators, allowing the simultaneous tuning and receiving of two sets of signals.

2. Metabolic cage.

The animal was housed in a specially modified metabolic cage (Lab Products, Inc., Maywood, NJ). This cage had a series of screens on the bottom to filter out fecal matter and food. Below the screens was a funnel which directed the flow of urine into a beaker. The front of the cage was covered with plexiglass to keep the animal from urinating outside the cage. The water system was completely outside the cage to prevent water from leaking into the cage causing an error in the uroflow data. The sides of the cage had plexiglass windows and rails for mounting the telemetry antennas. It was necessary to use two antennas per cage to have enough coverage overlap to pick up a clear signal in most regions of the cage.

3. Uroflow system.

Urine passed through the screens on the metabolic cage into a funnel under which was a uroflowmeter (R. L. Medical, Williston, VT) with a beaker. [10] The uroflowmeter had two analog outputs corresponding to volume and flow rate (d volume/dt). Both of the uroflowmeters were connected to a uroflow data collection box (produced in-house) which also provided power via a connected power supply. The outputs from the data collection box ran to the telemetry lab where they were connected to the data acquisition system.

4. Data acquisition system/computer.

The analog signals corresponding to bladder pressure, abdominal pressure, EMG activity and voided volume were plugged into the data acquisition system (DATAQ Instruments, Inc., Akron, OH) front end module. This system was capable of acquiring 16 single-ended channels of data, 8 differential inputs, or 8 digital input and output channels, and 1 digital to analog converter output channel. This system allowed data to be viewed in real time during acquisition as well as during playback. Sampling rates can be chosen up to 50 KHz, but for our purposes 25 samples/sec/channel were sufficient to keep the file manageable. The data displayed on the screen can be calibrated into cm. H_2O, micro v, ml., and ml./s. This is more accurate than reading values from conventional strip chart recorders. A high degree of flexibility was incorporated into the system allowing for many different ways to view, compress, and print the displayed data. Advanced mathematical functions allowed the user to calculate the channels from acquired channels. For example, a channel for detrusor pressure can be calculated by subtracting the abdominal pressure channel from the bladder pressure channel. the advanced mathematical functions supported were differentiation, integration, moving average, peak and valley capture, waveform rectification and arithmetic operations. This allowed enough flexibility to calculate almost any parameter imaginable. There were no limitations on the file size except for the available space on the hard drive. Data for one animal for 22 hour period yielded a file size of approximately 14-15 megabytes. For this reason it was necessary to have some type of mass media storage device. A streaming 4 mm. DAT drive (Archive Corporation) with a 1.3 gigabyte capacity was used to archive the data files.

The computer chosen for this project was an 80486 processor running at 33 MHz. All components of it were FCC Class B Certified. An important consideration when choosing a computer was that it possess Class B certified components because these emit much lower levels of radio frequency interference which could interfere with the telemetry signal. Due to the enormous amount of data collected, one major consideration for the computer was hard drive space (500 megabyte). Another important consideration was the available space and the expandability of the computer. The telemetry equipment requires 4 slots on the bus for the two receivers and the two demodulators. The data acquisition system requires another slot for its board. This took up most of the available slots in the computer, leaving room for a network card, a video card, and one open slot. A computer identical to the data acquisition computer existed in an office with a network connection running between them. This allows data to be downloaded from the data acquisition computer to the office computer for analysis. Also, because the two computers were identical, they shared most of the same components, which allowed sharing of parts should one computer develop a hardware failure.

Surgical procedure.

Implantation of the telemetry implants was carried out under general anesthesia initially with the animal in the prone position. A midline incision was made in the interscapular region and the skin on both sides was undermined in order to make a space for the transmitter, battery, and switch. They were secured to the fascia covering the back muscles on each side of the spinal column. A strain relief suture was fixed on each of the cables near the connections to the various components. After the transmitter, battery, and switch were in place, a subcutaneous tunnel around to the front of the animal was established using a long hemostat. A piece of Tygon tubing (3/8" inner diameter, 3/32" wall thickness, 20 cm. length) was routed under the skin to allow the passage of the transducers and EMG leads without damaging them. The animal was then turned to a supine position and a midline suprapubic incision was made. The tubing was pulled through the anterior incision and the back incision was closed. The bladder was then filled with normal saline and the transducer was implanted submucosally in the anterior wall of the bladder. The transducer was secured in place by a purse-string suture around its neck. One of the EMG leads was buried in the pelvic floor musculature near the external urethral sphincter, and the other one (ground) was implanted in the subcutaneous fat. The abdominal transducer was left free in the peritoneal cavity. All layers were closed, and the animal was transferred back to its metabolic cage. Intravenous injection of 250 mg. of cefonobid was given one hour pre-operatively and a similar dose was given next day. Trimethoprim/Sulfa pediatric syrup (5 ml. p.o., b.i.d.) was given for one week post-operatively.

Telemetry protocol. To begin a study, the metabolic cage was moved into the animal room. The antennas were then mounted on the windows of the cage and the appropriate connections to the lab were made. Next, a shot of ketamine (10 mg./kg. body weight) was administered to the animal. Then the telemetry software was run to tune and set filter for the implants. The approximate frequency of the particular set of implants was selected on the computer and a low pass filter (cutoff frequency = 31.25 Hz) was set. The oscilloscope was also turned on and connected to the video output of the receiver board. The animal was moved to the metabolic cage and the implants turned on with the external transmitter and implanted RF switch. The exact frequency could then be tuned in. This was done by watching the center tune bar of the telemetry software and by actually watching the signal as it appeared on the oscilloscope. When tuned in correctly, the signal was rectangular and relatively free from noise. The implants were tuned in at this point and the telemetry software was exited from. The uroflow equipment was set up next. The uroflowmeter with the beaker was placed under the funnel part of the cage. The connections were made to the wire-handling box and the cable to the lab. Next, the data acquisition software was run. At the end of the monitoring period, the data acquisition software was exited and the data file sent across the network to the office computer. Since the equipment was still in place and the implants were still tuned in, a new data file could be acquired. When the animal was no longer needed for data, it was again administered a shot of ketamine. When the animal was anesthetized, the implants were turned off, the animal was returned to its normal cage, and the metabolic cage was sent for cleaning. This same process can be carried out for two animals if it is necessary to monitor both of them at once.

Calibration of the telemetry data using conventional urodynamics presented several problems. Pressure calibration was performed under ketalar sedation using a standard 7 Fr three channel catheter for bladder pressure and a rectal balloon catheter for abdominal pressure. Telemetry data was also acquired at the same time on the computer. Corresponding pressures were measured simultaneously on a polygraph and on the data acquisition system during cystometry and manual abdominal compression Figure 3, A & B. The figures show calibrated pressures (top tracing) from the polygraph compared to raw voltage acquired from the telemetry data (bottom tracing). From this calibration study it was possible to calculate a relationship between voltage and cm. H_2O which can be applied to actual studies. This relationship is calculated using the following:

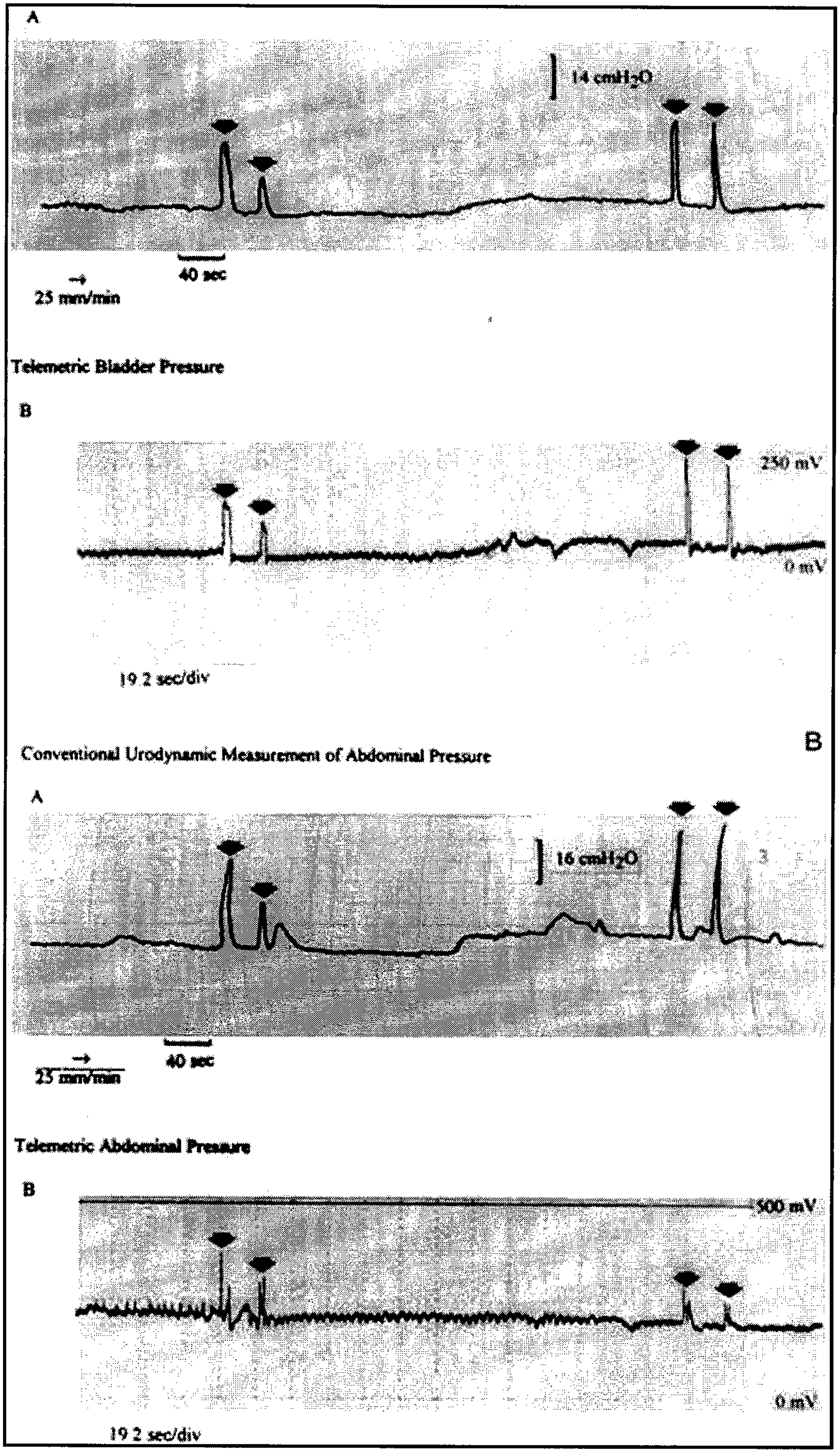

Figure 3. A, Calibration of bladder pressure. Conventional measurement via catheter (A) and implanted transducer (B). Top tracing is in cm. H_2O and bottom tracing is in volts. B, Calibration of abdominal pressure. Conventional measurement via catheter (A) and implanted transducer (B). Top tracing is in cm. H_2O and bottom

tracing is in volts.

$(V_{end} - V_{beg})/(P_{end} - P_{beg})$volts = 1 cm. H_2O where, V_{end} = end point voltage (volts) from telemetry V_{beg} = beginning point voltage (volts) from telemetry P_{end} = end point pressure (cm. H_2O) from polygraph P_{beg} = beginning point pressure (cm. H sub 2 O) from polygraph.

Previous tests using the same types of transducers showed that the implanted bladder pressure transducer correlated well with pressures measured by the catheters. However, the baseline for the abdominal transducer shifted every few weeks. This was attributed to the movement of the transducer throughout the abdominal cavity and growth of tissue over the diaphragm of the transducer. This problem was overcome by calibration every month and securing the abdominal pressure transducer during the implantation.

RESULTS

The correlation between conventional and telemetric urodynamics was excellent. There was a similar rise of pressure during bladder filling and during manual compression of the suprapubic area. The effect of the implants on micturition as tested in another two monkeys is shown in Table 1. Detrusor instability Figure 4 was noticed immediately after implantation but returned to normal 6-8 weeks after implantation.

Parameter	Pre-implantation	1–2 Weeks	6–8 Weeks
Frequency/24 hr.	8.45	13.9	8.44
Detrusor instability	N/A	0.86	5.4
Voided volume (ml.)	43.7 ± 10.6	33.6 ± 12.1	46 ± 3.4
Qmax (ml./sec.)	5.5 ± 0.9	2.9 ± 0.5	3.4 ± 0.6
Pdet, max (cm. H_2O)	N/A	29 ± 15.3	29.4 ± 18.4

Table 1. Comparison between pre and post-implantation urodynamic parameters

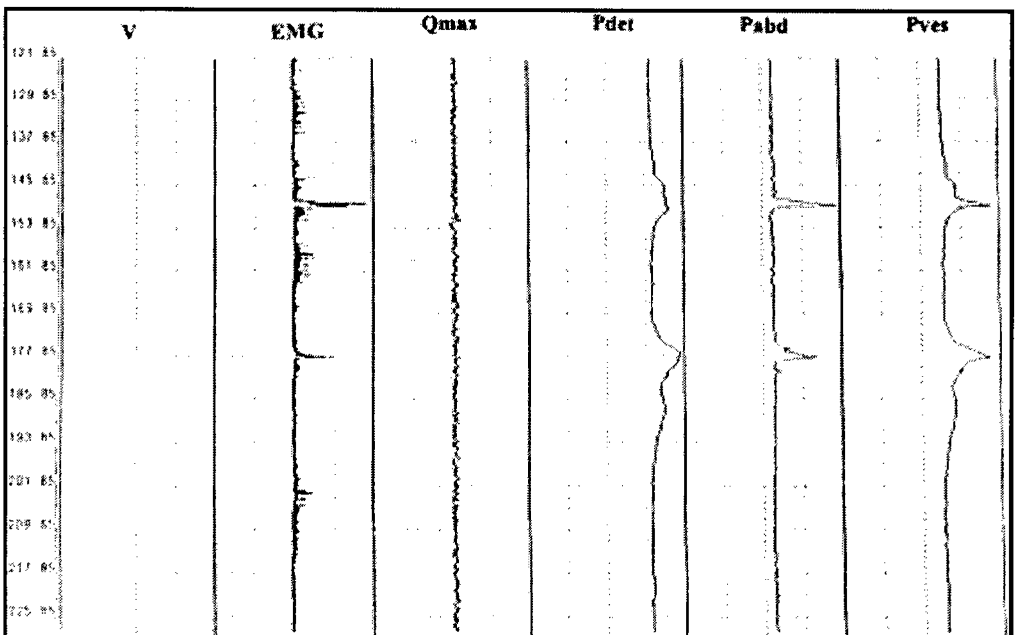

Figure 4. Printout of actual telemetry file one week after surgery. Occurrence of bladder instability (increased EMG activity and vesical pressure with no flow) was high.

Problems.

Several problems were encountered during this study. The first of these problems was a weak signals to the data acquisition front end module. This was caused by the long cable run from the animal room to the telemetry lab. This was solved by placing a 10 dB booster amp on the line. There was also a problem with the signal breaking up when the animal was in certain locations within the cage. This was due to the fact that there was initially only one antenna on each cage. One antenna did not provide enough coverage inside the cage for all positions of the animal. This was solved by cutting another window in the cage on the opposite side and at a different level, thereby providing some overlap of the coverage area.

Another problem encountered was erosion of the bladder transducer through the mucosa of the bladder. When this occurred, there was a significant shift in the baseline of the bladder pressure channel. Subsequent x-rays and examinations showed that the transducer was in fact in the bladder. Corrective surgery was performed to remove the transducer from the bladder, re-implant it, and place stay sutures around the wire to the transducer to keep it out of the bladder should it erode again. This is now part of the implantation surgery protocol.

A few studies yielded extremely large urine volumes at the end of 22 hours. Some of these studies overflowed a 1 liter beaker. Specific gravity tests of the fluid in the beaker confirmed that the bulk of the fluid was water. It was later determined that the animal was playing with the water system and dumping water inside the cage. Total volumes for each study were calculated by summing the individual voids separately, not by reading the final value for volume. This way, we were able to screen out artifacts induced by water leaking or being placed inside the cage.

DISCUSSION

An early system was developed for monitoring left ventricular diameter and pressure in dogs by telemetry in 1974. [16] This system allowed the animals to be monitored while unrestrained, but it still recorded on a conventional strip chart recorder. Another drawback is that it was not totally implantable and required the animal to carry the modulator and battery back externally in a package that weighed 3.5 pounds. The battery for this system only allowed for continuous monitoring for periods not longer than eight hours. This system suffered from a short battery life and was only able to measure one parameter. Most of these systems required the subject to be very near an antenna which not only picked up the signal, but in some instances provided the power for the capsule by inductively charging the passive capsule. Recording techniques used for these studies also employed strip chart recorders which are not practical for very large amounts of data.

Recent advances in computer technology have allowed us to develop a system that is totally computer-controlled and employs fully implantable sets of implants. This means that the animals do not have anything coming out of them or attached to them. The computer system that controls the implants also serves to acquire the data much as a strip chart recorder does but with the added computational capabilities of a PC computer. The system is capable of being operated nearly 24 hours a day while recording real-time data to the hard drive. The original specifications for this system called for a method to monitor bladder pressure, abdominal pressure, EMG activity of the external urethral sphincter, voided volume and urine flow rates in a manner that would not require restraint or tethering of the animal and would allow for long periods of monitoring and computer analysis. The previous phase in the development of this system made use of implantable pressure transducers (Konigsberg, Inc., Pasadena, CA) with a cable that was run under the skin to the back. When it was necessary to perform a study on the animal, it was restrained in a special chair and a small incision was made in the back to expose the ends of the cables so they could be connected to a conventional polygraph. These preliminary studies were important for testing the feasibility of using these types of transducers and EMG leads.

The value of telemetry in monitoring physiological parameters has been demonstrated effectively in humans and animals. In an animal model, the greatest benefits are the ability to monitor parameters without physical or mental stress. Also, it is possible to acquire data for long periods while the animal is in its natural state. In addition, studying the effects of drugs and different pathological conditions conceivably will be more reliable and free of artifacts.

The ideal telemetry system should monitor over a long period of time, the subject should be kept in its regular environment, the bladder should be filled at a physiological rate and the data should be acquired without inserting catheters or needles. The ideal telemetry transmitter should posses an adequate signal-noise ratio in order to ensure accurate data. Transmission range, operating life, and transmitter size should be adjusted according to the specific application. An on-line display can ensure proper operation of the system, allow for troubleshooting problems, and aid in reducing artifacts. The data-acquisition system must allow for manipulation of different parameters, environmental or pharmacological, and detect these reactions immediately. The entire system, especially the transducers, should be resistant to infection, erosion and encrustations.

CONCLUSIONS

This system is comprehensive, reliable and capable of monitoring, acquiring and processing many urodynamic parameters in real time. Its downside are that it is time consuming, difficult and expensive.

An important goal of this area of biomedical investigations is to refine the telemetry techniques and adapt them to studies of the human genitourinary system. With a broad base of accurate data, the generation of computer models will be possible, further minimizing and in some situations, eliminating the use of animals.

In the future, telemetry may be used as a feedback system for acquiring data which will control unwanted events or produce a specific reaction in the urogynecological patient.

REFERENCES

1. Torren, M.: Urodynamics. In: The Physiology of the Lower Urinary Tract Function. Edited by M. Torrens and J. F. B. Morrison. Berlin: Springer-Verlag, pp. 277-307, 1987. [Context Link]

2. Warrell, D. W., Watson, B. W. and Shelley, T.: Intravesical pressure measurement in women during movement using a radiopill and air-probe. J. Obest. Gynec. Brit. Commonw., 70: 959, 1963. [Context Link]

3. Thuroff, J. W., Jonas, U., Petri, E. and Frohneberg, D.: Telemetric urodynamic investigations in female incontinence. Prog. Clin. Biol. Res., 78:211, 1981. [Context Link]

4. Griffiths, C. J., Assi, M. S., Styles, R. A. and Neal, D. E.: Ambulatory long-term monitoring of bladder and detrusor pressure. Neurourol. Urodynam., 6: 161, 1987. [Context Link]

5. Griffiths, C. J., Assi, M. S., Styles, R. A., Ramsden, P. D. and Neal, D. E.: Ambulatory monitoring of bladder and detrusor pressure during natural filling. J. Urol., 142: 780, 1989. **Bibliographic Links** [Context Link]

6. Webb, R. J., Griffiths, C. J., Ramsden, P. D. and Neal, D. E.: Measurement of voiding pressures on ambulatory monitoring: comparison with conventional cystometry. Brit. J. Urol., 65: 152, 1990. **Bibliographic Links** [Context Link]

7. Webb, R. J., Griffiths, C. J., Zachahiah, K. K. and Neal, D. E.: Filling and voiding pressures measured by ambulatory monitoring and conventional studies during natural and artificial bladder filling. J. Urol., 146: 815, 1991. **Bibliographic Links** [Context Link]

8. Neal, D. E., Ramsden, P. D., Sharples, L., Smith, A., Powell, P. H., Styles, R. A. and Webb, R. J.: Outcome of elective prostatectomy. Brit. Med. J., 229: 762, 1989. [Context Link]

9. Styles, R. A., Neal, D. E., Griffiths, C. J. and Ramsden, P. D.: Long-term monitoring of bladder pressure in chronic retention of urine: the relationship between detrusor activity and upper tract dilatation. J. Urol., 140: 330, 1988. **Bibliographic Links** [Context Link]

10. Ghoniem, G. M., Shoukry, M. S., Walker, C. F. and Kaack, M. B.: Continuous monitoring of micturition pattern in non-human primates: technique. Neurourol. Urodynam., 11: 131, 1992. **Bibliographic Links** [Context Link]

11. Gleason, D. M.: A study of micturition with electronic measuring devices. Ann. NY. Acad. Sci., 17: 118, 1964. [Context Link]

12. Gleason, D. M., Lattimer, J. K. and Bauxbaum, C.: Bladder pressure telemetry. J. Urol., 94: 252, 1965. **Bibliographic Links** [Context Link]

13. Timm, G. W., List, J. S., Bradley, W. E. and Scott, F. B.: Frequency stability of an implantable pressure telemetry capsule. IEEE. Trans. Biomed. Eng., 22: 250, 1975. [Context Link]

14. Bahatia, N. N., Bradley, W. E., Haldeman, S. and Johnson, B.: Continuous monitoring of bladder and urethral pressure: new technique. Urology, 18: 207, 1981. **Bibliographic Links** [Context Link]

15. O'Donnell, P. and Hanish, H. M.: Telemetric electromyographic monitoring in elderly incontinent men. Neurourol. Urodynam., 11: 115, 1992. **Bibliographic Links** [Context Link]

16. Patrick, T. A., Vatner, S. F., Kemper, W. S. and Franklin, D.: Telemetry of left ventricular diameter and pressure measurements from unrestrained animals. J. Appl. Physiol., 37: 276, 1974. [Context Link]

Accession Number: 00005392-199702000-00092

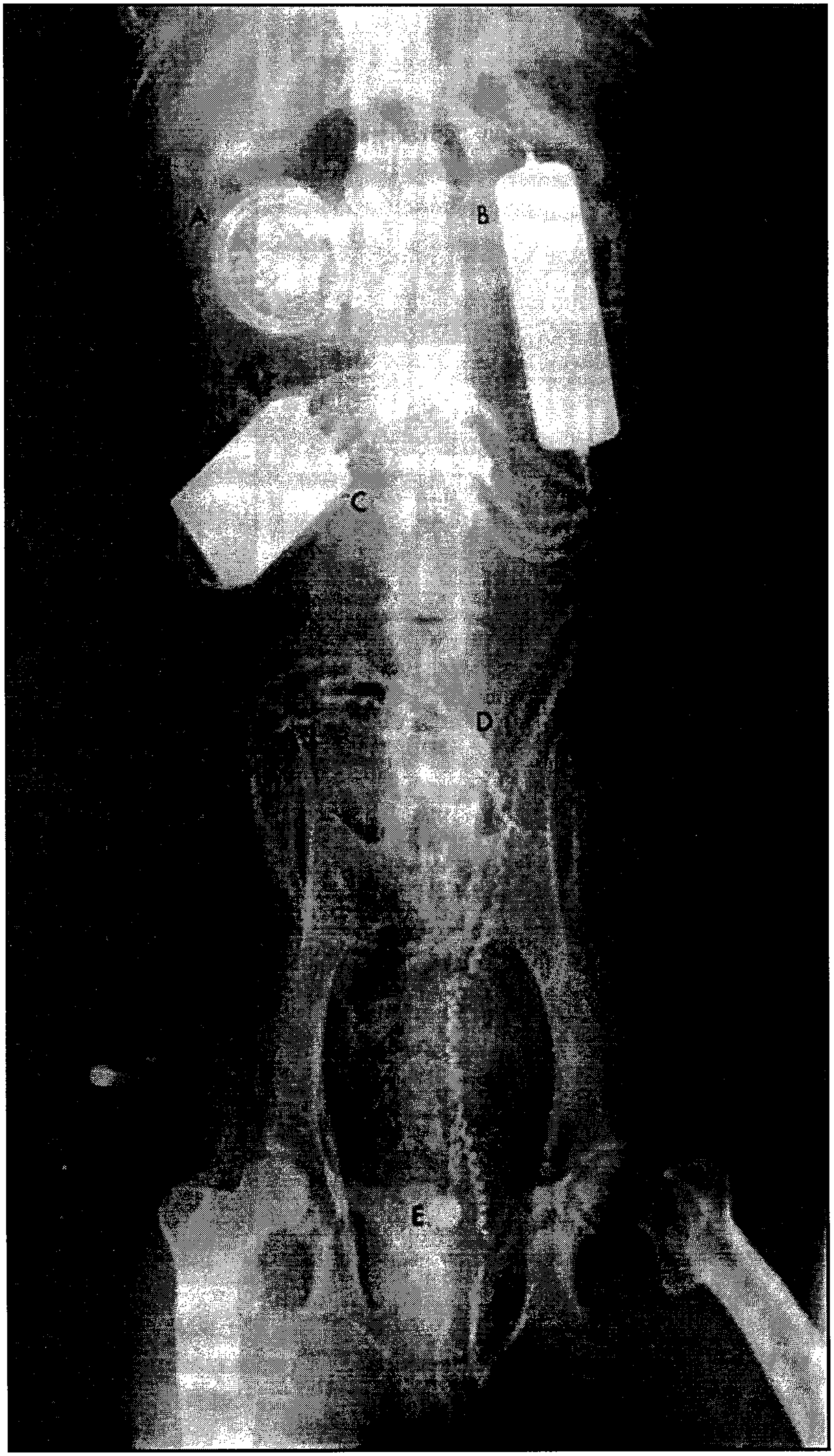

Figure 2. X-ray showing positions of implants: switch (A), battery (B), transmitter (C), abdominal transducer (D), bladder transducer (E), and EMG electrode (F).