

ROBERT ARZBAECHER

An Interview Conducted by

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Interview: Robert Arzbaecher
Interviewer: Frederik Nebeker
Date: 14 October 1999
Place: Atlanta, Georgia

Nebeker: When and where you were born?

Arzbaecher: I was born in Chicago in 1931, one of four children.

Nebeker: What did your father do for a living?

Arzbaecher: My father drove a bread truck. That was during the Depression. My mother was a public school teacher. In addition to her Teacher's College certificate my mother had a university degree, which was unusual for a woman in those days. She spent forty years in the Chicago public school system. I was raised on the south side of Chicago, where I am living presently. I was born a twin, my wife is a twin, my wife and I have twins, and my twin sister has twins. It's surprising that I became a biomedical engineer instead of a Mendelian geneticist.

Nebeker: Do you know if that's an inherited trait?

Arzbaecher: I don't know much about it. Classical wisdom that says twins run in families, and that seems to be true. I think some of those secrets will be unraveled soon.

Nebeker: Yes, with the human genome project. Is your brother a biomedical engineer?

Arzbaecher: No, both of my brothers are retired, one living in Florida and the other in Seattle. One was president of a company in the Mead Paper group. They haven't been able to stay in the Chicago area. I've been lucky. I was educated in the parochial school system in Chicago, and then went to college and became an electrical engineer at a small school which existed eight or nine years before going out of business.

Nebeker: What was the name of that college?

Arzbaecher: The Fournier Institute of Technology. When they closed down I decided I had better get a graduate degree from another university, so I went to the University of Illinois at Urbana. My graduate studies were interrupted by a couple of years in the Army in 1955-56. Unfortunately the GI Bill died a month before I got drafted. I got married while I was in the Army. We were used to being poor in the military service, so when I got out of the Army we decided to go to graduate school. We went back to Urbana and I got a Ph.D. in Electrical Engineering in 1960.

Nebeker: What was your thesis work?

Arzbaecher: My thesis was a force reflecting servomechanism. That was in the control systems area, which was my expertise. During the period from 1953 to 1960, which includes my two-year stint in the Army, I spent five years at Argonne National Laboratory working in nuclear reactor control and instrumentation. When I got drafted into the Army I ended up in Washington at the Army Reactors Branch of what was then the Atomic Energy Commission, so I spent most of my time in the Army under reasonably pleasant, though poor, conditions.

Nebeker: The last years of Von Neumann's life were at the Atomic Energy Commission.

Arzbaecher: The peaceful use of atomic energy, mostly for power, was making its ascent when I was in Washington. We worked one floor below Admiral Hyman Rickover, who was in the Navy Reactors Branch. The Army was building reactors for electrical power generating plants powering field installations and the Navy was building reactors for submarine propulsion. Working in the same building, we had a close relationship between the two groups.

Nebeker: Did that Army program lead to something that was actually used?

Arzbaecher: Yes. The Army package power reactor became the prototype for pressurized water reactors which is now pretty much the standard in America. The American nuclear power industry didn't go very far because of public concern, although Western Europe and other countries are 50 percent nuclear powered.

Nebeker: Your work had to do with control systems. Is that how you got into that field?

Arzbaecher: Yes, and I focused my graduate work on that. When I finished my degree in 1960 and left Urbana I took a teaching position at the Christian Brothers College in Memphis, Tennessee. Christian Brothers College had a good undergraduate engineering school, particularly in the electrical area. They graduated forty electrical engineers every year. It was not a small school, but not much was going on in the area of control. Certainly not much in the area of reactor control was going on in Memphis. I taught electrical engineering but was not able to continue my research. It was in that context that my conversion from electrical to biomedical engineering began.

For a year I looked for a challenging research opportunity in Memphis to go with my teaching. Then I met Daniel Brody at a cocktail party. He was a cardiologist from the University of Tennessee College of Medicine in Memphis. Unknown to me at the time, he was a very well known cardiac theoretician. Brody's undergraduate training was in physics. Before the war, because he couldn't get a job as a physicist, he went to medical school. He said to me, "So you're an electrical engineer. You know, the heart is electrical." I said, "Bullshit," and he said, "No, really. The heart is electric. There are currents flowing in and around

the heart that produce a potential distribution on the body which satisfies Laplace's Equation.” Standing there talking to a cardiologist about Laplace's Equation I thought, “Hey, this is really great. I can't believe this guy.” When I found out more about his background, it was the beginning of a wonderful relationship. I spent the next seven years working with Brody in his laboratory every chance I could get, on Saturday, Tuesday and Thursday afternoons to the extent I could arrange my teaching schedule. We worked in what is now called theoretical electrocardiography, which is the physical and mathematical basis for interpretation of the human electrocardiogram in health and disease. Brody and I wrote a lot of papers together. That's how I became a biomedical engineer.

Nebeker: Was this mainly theoretical work?

Arzbaecher: At that time, yes. After six years of theoretical mathematical modeling work I had an urge to get closer to clinical electrocardiography. I had an opportunity to go to Europe for a year on a National Science Foundation fellowship, and Dan Brody set up an opportunity for me to work in the laboratory of Dirk Durrer at the University of Amsterdam. That experience was of major significance in my career. Durrer had a concept for removing the human heart soon after clinical death and keeping the heart alive long enough to map its electrical activation. This had been done with the hearts of animals, and Durrer was poised to do the same thing with the human heart. The instrumentation requirements of that task were significant. With the isolated heart on a perfusion stand, needle electrodes were placed all over the heart to record on a multi-channel basis. This was in the mid-'60s, when that was not an easy thing to do. My time in Amsterdam was

fortuitous for him and for me. I got involved at the highest level of experimental cardiology, and he got a trained electrical engineer to help him with instrumentation problems. During that year we did the first isolated human heart mapping experiment and published in *Circulation*.

Nebeker: Were the results different from what was expected?

Arzbaecher: The results confirmed some of the activation data that had come from the animal laboratories and confirmed guesses of brilliant electrocardiographers who figured out from body surface measurements the pattern and sequence of activation of the human heart. It was a wonderful opportunity for me. We put our children into a Dutch school and they became fluent in Dutch. It was a great sabbatical year, and confirmed me into biomedical engineering. It added a brand new and much larger dimension to the mathematical and theoretical work I had done with Brody, which is the dimension of clinical and experimental cardiac electrophysiology.

Nebeker: Did this experience with gathering and obtaining those data change your way of proceeding theoretically?

Arzbaecher: Not really. Following my year in Amsterdam I returned to Memphis and resumed my work with Dan Brody. When I was offered a position in Chicago at the then new University of Illinois at Chicago I left Memphis to return to the town we call home. As a result of that move, I shifted my focus of research mostly into the clinical and experimental areas and moved further away from mathematical electrocardiography.

Nebeker: Was the mathematical work that you were doing in the '60s computer modeling?

Arzbaecher: Yes, primarily.

Nebeker: To what computer did you have access?

Arzbaecher: In Dan Brody's lab we had an IBM 1620. We had bought a DEC PDP-8 and a PDP-15, so we were involved in the revolution from the mainframe to the minicomputer. Soon after arriving at my laboratory in Chicago I acquired a PDP-11. Much of my work has been based on mini- and microcomputer technology applied to signal processing from the heart.

Nebeker: What was the impact of the minicomputer on electrocardiography and similar areas?

Arzbaecher: There were two impacts. First, it made it possible for many laboratories without major computer resources to acquire significant computing resources. Secondly, it led to digital signal processing, which is now standard, and also online real time signal processing. Without the smaller computer and its capabilities for online acquisition, analog-to-digital conversion and processing in the digital domain, that wouldn't have happened so quickly. My experience before then had been with punch card machines, batch processing and number crunching.

Nebeker: Brody had his own machine even before that.

Arzbaecher: Brody had his own 1620, but that was because we were doing a lot of heavy mathematics in the theoretical area. Batch processing with a number crunching machine was appropriate. Later as we began to do more signal processing and real time analysis, the minicomputer made a major impact.

Nebeker: Was the all work you did with Durrer analog recording?

Arzbaecher: Yes, recording on a fourteen-channel magnetic tape. If that work had been done five years later it would have taken on a completely different look.

Nebeker: When did you get into digital techniques on the data acquisition side of things?

Arzbaecher: I began with that in the early '70s in my laboratory at the University of Illinois at Chicago. We had a significant research grant that was supporting seven or eight students and acquired a large PDP-11 operating under RSX-11M, an operating system which allowed real time acquisition of data. With that system we first began digitizing tape-recorded data.

Nebeker: Was this electrocardiogram data?

Arzbaecher: Yes. Later we began digitizing live data in real time.

Nebeker: Was that a difficult job at the time?

Arzbaecher: It was not easy. We needed a multitasking environment in which an A to D converter could be processing while we worked with the data on an interrupt driven basis. We were getting a thousand samples a second. There would be an interrupt that would allow A to D conversion of the next number, and in between samples at the one millisecond level we would do our FORTRAN number crunching waiting for the next A to D converter interrupt to occur. That was a lot of hard work.

Nebeker: Was that in the early '70s?

Arzbaecher: Yes. There wasn't much software available for that in the early '70s.

Nebeker: Did you write your own programs?

Arzbaecher: Gosh, Rik, not I. Some very bright graduate students of mine wrote programs.

Nebeker: What about the A to D converter itself? Was that something you could buy off the shelf at that time?

Arzbaecher: Yes. A to D converters had recently become available, and it was packaged in fact as part of the hardware on the PDP-11M we bought.

Nebeker: Did you succeed in getting this data from the heart in real time?

Arzbaecher: Yes.

Nebeker: What difference did that make?

Arzbaecher: One thing was that we no longer had to deal with the mess of tape recording. That was a minor concern however compared to my major goal, which was to deliver anti-arrhythmic drugs to coronary care patients with life-threatening arrhythmias. That's a closed loop control system environment where the computer is monitoring the patient online in real time and running a pump.

Nebeker: Was delivering the drug automatically your objective?

Arzbaecher: Yes. That was my dream. It has been a long time in bearing fruit.

Nebeker: It sounds very ambitious for the '70s.

Arzbaecher: Yes, it was. Support came from the pharmaceutical company G.D. Searle. They were particularly interested in finding out whether their drug Norpace was effective in treating atrial arrhythmias. Necessity being the mother of invention, I invented the esophageal electrode for recording the electrocardiogram from the esophagus. It's a small electrode at the end of a pair of very thin and flexible wires. The electrode is encapsulated in an ordinary pharmaceutical capsule. The patient swallows the capsule with water in the usual way and just ignores the little wires.

Nebeker: The wires are so tiny that they won't cause gagging?

Arzbaecher: Oh yes, they're very flexible. They're like sewing thread. The patient swallows the electrode, and when the electrode gets down to a measured distance the wire is taped to the face so that it doesn't continue to descend. Then the gelatin capsule dissolves and the electrode is positioned immediately posterior to the left atrium in the esophagus.

Nebeker: Was this your invention?

Arzbaecher: Yes. Thirty years earlier the patient was anesthetized and the electrocardiogram measured from the esophagus with a nasogastric tube. As you can imagine, it was an unpleasant experience. Reports from the mid-1930s were very promising, but because the technique was so difficult for both patient and cardiologist it never went anywhere. The pill electrode was a simple and easy answer to that. It was interesting how I discovered it. Are you interested in hearing about that?

Nebeker: Yes, absolutely.

Arzbaecher: In the lab, I had a graduate student of mine push a catheter electrode down my nose and into my throat and esophagus. I was able to measure a beautiful p-wave, which was an atrial recording in the electrocardiogram.

Nebeker: Did you get a much clearer signal that way?

Arzbaecher: The p-wave obtained is three to four times bigger than QRS. Compared to routine electrocardiography on the body surface, the esophagus gives a beautiful p-wave from the atrium. The recording we made was clear, but it hurt. That night I could still feel the irritation in my throat that had been caused by the catheter.

Nebeker: You're in the class of people who experiment on themselves.

Arzbaecher: That was in the days before we were so careful about human investigation. My throat and sinuses hurt, I realized that the problem was that big old stiff catheter. All I really wanted were the two rings at the end of the catheter. The next morning I went into the lab, took a pair of diagonal cutters and stripped away the polyethylene coating until I was left with the tip of the catheter and the pair of wires. Then I buried the catheter tip in a spoonful of ice cream and swallowed it. My students laugh about this. One doesn't chew ice cream, so the bipolar pair of electrodes caused no problem. I just swallowed it, and down went the pill. That was the first pill electrode. That was the business end of a catheter electrode with a bipolar pair and a pair of wires holding it up. Within a week or two I discovered a source of very thin and flexible stranded stainless steel wire with Teflon insulation.

Nebeker: I would think the wires would make you gag.

Arzbaecher: No, there is very little gagging. Few patients have trouble with that. Peristalsis holds it down pretty well, and you have tape on the wire that keeps it from going too far down. I've had the electrode in place for twenty-four hours and done Holter recording from the esophagus. When you're done with the recording the patient just pulls the wires and the electrode comes out. It's a very simple procedure.

Nebeker: That's amazing.

Arzbaecher: After you've had it in place for a while and remove it, then you feel the wires again. It's the same phenomena as an after image on the retina. One usually becomes unaware of the wires within five minutes after swallowing. When they

have been down for a length of time one becomes aware of them again when removing the electrodes. That's the famous Arzbaecher pill electrode for esophageal electrocardiography.

Nebeker: How widely is that used today?

Arzbaecher: To my regret, not very widely. I would like to come back to the pill electrode story a little later.

Nebeker: Please.

Arzbaecher: In my lab in Chicago in the early '70s the other half of this problem was running a pump. The esophageal electrode gave us the signal with which atrial arrhythmias could be instantly recognized. Atrial arrhythmias are not easy to recognize on the body's surface.

Nebeker: Is this a recognition that comes visually with knowledge or is it an algorithmic cognition?

Arzbaecher: It's computer recognition. The algorithm looks at the esophageal signal, analyzes it and comes up with a rhythm diagnosis in real time. The whole spectrum of cardiac arrhythmia can be detected, including atrial fibrillation, atrial flutter, atrial tachycardia, premature atrial beats and ventricular arrhythmias.

Nebeker: Had that been worked on previously?

Arzbaecher: No, this was the first time. We got the ventricular activity directly from a typical surface lead. There was nothing unique about that, but until that time computer interpretation of the electrocardiogram from the viewpoint of rhythm analysis was always done from surface electrocardiograms. Surface electrocardiograms fail dismally in analyzing atrial arrhythmias. Our interest was in treating atrial

arrhythmias with a Searle drug. I had the first half of that problem solved, which was how to automatically recognize the onset of an atrial arrhythmia in a coronary care patient.

Nebeker: Did you write programs to analyze the p-wave?

Arzbaecher: Yes, my students and I wrote them. A student who helped with that was Janice Jenkins. She is now a professor at the University of Michigan and on leave from Michigan serving as the program director of bioengineering at NSF. She took the esophageal signal and wrote the program to analyze the arrhythmia. It was the first dual chamber arrhythmia analysis program ever written. Her thesis was published in the American Heart Association's *Circulation*, which was certainly the premier cardiology journal of the time.

Nebeker: That must be very unusual for a thesis.

Arzbaecher: Yes. She is the only student I've ever had whose thesis was published in *Circulation*.

Nebeker: That's amazing.

Arzbaecher: It was a two-channel scheme for taking the atrial electrogram from the esophagus and the ventricular electrogram from the body surface and then with that data constructing the entire taxonomy of cardiac arrhythmias. This was done online in real time using a PDP-11 operating system.

Nebeker: Was this digitized signal data?

Arzbaecher: Right. That was important. The task that then remained was how to put a pump on it so that after the arrhythmia was recognized a protocol for running an IV pump would automatically follow. That was another task to which we dedicated

ourselves in my laboratory. We got involved in the pharmacokinetics of most anti-arrhythmic drugs and how they should be delivered. We came up with optimal schemes for delivering drugs that would result in quick arrival with accurate maintenance of therapeutic levels. We never did much with that clinically. At the present time, twenty-five years after the original concept, I think I have the clinical situation where all of this will finally come together. I will tell you about that in a minute, but to keep it chronological I want to go back to the '70s.

In 1976 the University of Iowa offered me the position of Chairman of the Department of Electrical and Computer Engineering as well as an appointment as Professor of Medicine in Cardiology and I spent the next five years at the University of Iowa. I perfected the pill electrode during that time. I sent pill electrodes to friend and colleagues all over the world, including Dirk Durrer in Amsterdam. There was a significant awakening of interest in esophageal electrocardiography as a result of this simple procedure. I found myself spending too much time making pill electrodes and sending them to friends. My wife talked me into going into business, and I went to the University of Illinois where the invention was first conceived and asked them if they were interested in getting a patent and promoting it as intellectual property. The University of Illinois took the concept to the patent committee and made the decision the clinical market was not big enough to be worth their while and turned the rights over to me as the inventor.

I began to think about how to get this new medical device on the market. From the medical device amendments I found in a copy of the Food, Drug and Cosmetic Act as amended in 1976 and 1978 I learned what was necessary to manufacture and sell a product. The FDA told me I could use the 510K route, which is not a full pre-market approval but rather an approval based on the substantial equivalence of a device with an earlier device already approved by the FDA. I did that, and argued that the pill electrode was substantially equivalent to a nasogastric esophageal electrode that had been on the market in the '40s. The difference was that mine was easier for the patient to swallow and less painful. The FDA agreed, and I got permission to market the pill electrode.

My family set up the business. My wife was the business manager and two of my children were the only employees. I wasn't an employee because I was busy doing research in my laboratory at the University of Iowa. My family put together an advertising brochure which they sent to every hospital in the country with more than 150 beds. Then we just waited for orders. That was done from the basement of our home in Iowa City from the late '70s until the early '80s when it became too big a burden. I had to decide whether I wanted to be an academic or a business man.

Nebeker: Did you get quite a few orders?

Arzbaecher: We did. One day in my laboratory in Iowa City I disconnected the pill electrode from the electrocardiograph, connected it to an external stimulator and discovered I could pace my heart. That generated additional sales.

Nebeker: More experiments on yourself.

Arzbaecher: By connecting the electrode located immediately behind the left atrium to an external pacemaker I was able to capture the heart and run it at any rate I wanted.

Nebeker: Why did you try that?

Arzbaecher: I knew a lot about cardiac pacing because of my experiments in the engineering approaches to cardiac rhythm management and similar experiments. I knew the heart could be paced from the esophagus and I had seen in the literature that it had been done once or twice. The esophagus was also used as a site for defibrillation in classic experiments by Paul Zoll. I knew the esophagus was close enough to the heart to pace from it, but didn't know much more. After obtaining some data on esophageal pacing, I recognized that this was a really hot item. Instead of merely recording from the pill electrode, I also could pace from it.

I worked on a small business proposal to the NIH for the next several years to support the clinical testing of this technique for esophageal pacing. I got Phase I and Phase II SBIR grants for my small company, Arzco Medical Systems. With those grants I was able to recruit 140 patients to do clinical studies in five different centers. We proved that esophageal pacing was both safe and effective and got pre-market approval. No longer a substantial equivalence thing, this required the full FDA pre-market route. It was necessary to perform experiments and prove there would be no damage to the esophagus. It also had to be proved that this device was effective in pacing the heart. Following all those studies we appeared before the FDA Cardiology Advisory Board at the end of 1986 and got the PMA approved. I developed a small battery-operated electronic external

pacemaker to which the pill electrode could be connected. That was it. It could pace the heart.

This created an opportunity to do a number of things that couldn't be done before. For example, a lot of patients can't exercise due to age, infirmity, obesity, and other reasons. Cardiac stress testing can be done by pacing the heart rather than by exercising the patient. That was an important development. Imaging studies such as echocardiograms could also be done. Temporary esophageal pacing could be used to convert arrhythmias. Atrial flutter, especially in children, is easily converted by over-drive pacing. A short ten-second burst of temporary pacing from the esophagus could convert the arrhythmia to normal rhythm.

Nebeker: Would the electrode have to be there all the time in that situation?

Arzbaecher: No. It is only necessary to convert the arrhythmia. Then the patient stays in normal rhythm.

Nebeker: I see. It is for when they go into that state.

Arzbaecher: It's for treating paroxysms. Two of the clinical trials were related to the termination of super ventricular tachycardias by temporary esophageal pacing. In another of the clinical trials echocardiographs were done during stress testing. This was pacing stress rather than stress from exercise. After FDA approval it was on the market. This new device attracted interest from the investment community and sales took off. In the first quarter of 1987 we sold about \$150,000 worth of product. That was not bad for a guy with a full-time academic job, but my family was becoming overly stressed with the responsibilities of the business. The children had grown and could no longer make electrodes after school. They now

had real jobs and decided to leave the family enterprise. At the end of 1987 we sold the company. That's my story as an entrepreneur with the Arzbaecher magic pill electrodes.

Nebeker: Does the device continue to be used?

Arzbaecher: The device is still on the market and manufactured by a company called Cardiac Control in Tampa, Florida. They have the patent now. I have no direct contact with the company, so I don't know how well they are doing. It's still a small operation.

Nebeker: When you had this idea and showed that it was effective, why didn't you go to some big company in the field to get them to do the testing, development and marketing?

Arzbaecher: I did do that. First I tried to get them interested in distribution. Manufacturing the pills was not a problem. The problem with our business was that we didn't know how to market the product. I spoke with several medical device manufacturers. At one point Marquette Electronics, a major manufacturer of electrocardiographs, was interested to the point they were willing to put an advertising page in their catalog. However it never became a very hot item. That's when I realized I had to market it myself. After demonstrating that pacing was possible it became much easier to sell the company. That's the end of that story.

I want to go back now to the other half of the business. What we're talking about is closed loop treatment of arrhythmia where a patient with a paroxysm of atrial arrhythmia can be automatically treated by a drug delivery system in the form of a motorized pump. There are not many examples of closed loop control in the

clinical environment. This one, which has been my concept for twenty-five years, remains a bit elusive. I have identified the implant scenario as the circumstance where it is probably most appropriate. It is an implantable drug pump with a microprocessor and a catheter through which the drug is delivered, and the catheter also has electrodes for measuring the atrial electrocardiogram. It's an ordinary atrial pacemaker electrode. The original concept of control of drug infusion in the intensive care unit is revived here in terms of automatic treatment of atrial fibrillation in the ambulatory patient. That has been exciting.

Nebeker: Do ambulatory patients use drugs when there are crises?

Arzbaecher: With the exception of the diabetic patient who does self-injection, they do not. It's a revolutionary concept, and the advantages are profound. Chronic oral drug therapy to prevent recurring attacks of atrial fibrillation does not work very well. No matter what drug is prescribed prophylactically to prevent the onset of atrial fibrillation, 50 percent of patients will have a recurrence within a year. This is roughly speaking over a large spectrum of patients.

Nebeker: Oral drug therapy does not prevent attacks of atrial fibrillation over long periods of time?

Arzbaecher: Right. Secondly, the drugs have serious side effects. The toxicity of the drugs becomes a problem, especially when taken on a long term basis. Long term oral therapy in general has these disadvantages. My idea was that atrial fibrillation should be treated acutely rather than preventively, at least until preventive drugs are better. Acute treatment is a different story. It is well known that atrial fibrillation is easily treated by intravenous infusion when within a few minutes of

onset. An episode of atrial fibrillation is not life-threatening in itself. It is symptomatic and can be treated. This is like a pacemaker, with an atrial electrode in place. It has a programmed microprocessor.

Atrial fibrillation is an interesting disease. For a long time atrial fibrillation was not regarded as serious because it does not bear anywhere near the mortality and morbidity of ventricular arrhythmia. In addition, no one knew how to treat it.

Often, atrial fibrillation is symptomatic and doesn't go away. The present method of treatment when a patient has an episode of atrial fibrillation is that paddles are placed on the patient's chest in a hospital emergency room and the patient is shocked just as in the treatment for ventricular fibrillation. The patient with atrial fibrillation is awake and conscious. That shock is a painful thing and the patient has to be anesthetized.

Nebeker: Aren't there drugs that could be used in those situations?

Arzbaecher: Yes, that's an alternative. A new drug, ibutilide, was approved by the FDA two years ago, attempts to convert atrial fibrillation with an intravenous injection. However it is not as effective as shock, especially if the patient has been in atrial fibrillation for several hours. When these episodes recur on a monthly basis, which is the case with a large patient population, the trip to the emergency room, undergoing anesthesia and electrical shock and then going back home becomes a difficult experience to revisit. There is a nuisance value. More importantly, in the last few years it has become clear that atrial fibrillation has very serious long term consequences, especially due to an enormous risk of stroke which increases with age. In the sixth and seventh decades of life, the incidence of atrial fibrillation

begins to rise to the 3 to 5 percent level. The risk of stroke in the population of those with atrial fibrillation can be as much as ten times that of the normal population. By the time people are in their seventies and eighties, the prevalence of atrial fibrillation can reach 10 percent, so there is a huge population at risk. It is well known that atrial fibrillation is a cause of stroke. It is perhaps the major cause of stroke in the elderly. It is a problem of the fibrillating atria not vigorously contracting so that there is a stasis, a pooling and stagnation of blood, especially in the out pouching of the left atrium. Then coagulation can occur and thrombosis can develop which can then embolize up to the brain and cause a stroke. More and more it is being recognized that atrial fibrillation should be treated. For these reasons my concept for automatic drug delivery for treating arrhythmias has focused on the problem of atrial fibrillation.

The technology is there. Implantable drug pumps are on the market. They are used for treating intractable pain in terminally ill cancer patients where a morphine drip is continually maintained. Implanted pumps have also been used in delivering a chemotherapeutic agent directly to the liver where a cancer may reside. There have been efforts made to develop suitable hardware and it's an area that needs a lot more development.

The dream of the drug pump people is the treatment of diabetes. A drug pump with insulin to automatically treat the diabetic patient would be a marvelous technology. Billions of dollars have been spent to develop that technology, and several companies are involved. They have been stymied largely by the absence of a good glucose sensor. The pump can deliver insulin, but no way has been

found to close the loop. Insulin is not an easy drug to store and deliver in an implanted pump, but the biggest problem is the measuring of glucose levels to trigger the pump. That technology is still being developed. I believe implantable pumps will become more commonplace, and maybe with time the particular notion of an implantable pump for the treatment of atrial fibrillation will become more attractive.

Nebeker: Is the control system developed? Would it be easy to program and process that?

Arzbaecher: Yes. For my own lab I have published protocols for running a pump. The implantable pumps that are available do not have motors in them. They have valves. There is a pressurized reservoir of drug with a valve. When you open the valve, drug squirts into a catheter and then moves into a central vein. That device is pretty reliable. There are not many moving parts and it is easy to control. All that has to be controlled is the rate at which the valve is operating.

Nebeker: Are these valve controlled electromagnetically?

Arzbaecher: Yes. I have a concept I have tested on animals in which I programmed an implantable drug pump with a valve to deliver pharmacokinetically designed exponentially tapered infusions, which are known to give and maintain a good therapeutic response. Control of the pump is not difficult, and the problem of recognition of atrial fibrillation is well in hand in my laboratory as well as in other places.

Nebeker: How would this work in terms of hardware? Would it still be a sensor in the esophagus?

Arzbaecher: No, there would be no need for the esophagus in this case. The pump would look like a pacemaker. It would be implanted under the skin in the pectoral region. The pump would have two catheters. It would have an electrode catheter introduced into a vein using the standard pacemaker technology and would be advanced under fluoroscopic control into the atrium. That's the catheter for sensing, and also pacing if you wish. That would be directly into the atrium. The other is a drug delivery catheter that could be introduced into any vein, but presumably into the same vein. An attractive design would be an electrode catheter with a hole down the middle through which the drug is delivered. Then there would be a single catheter advanced into the atrium. That's a procedure that would be very similar to the implanting of a pacemaker. That's a one-hour procedure that is done under local anesthetic and the patient goes home. It is not a very difficult thing to do. If the hardware could be made small enough it would be very much like pacemaker implantation.

What are the problems? You brought up one problem already, Rik. We don't have experience with intravenous infusion in ambulatory patients. Whether the medical community is ready to have intravenous drug delivery taking place outside of the closely monitored hospital environment is another question. There are major problems here, and it is true that some of the drugs effective in treating atrial fibrillation of recent onset, such as procainamide, may cause a fall in blood pressure when delivered rapidly. Apparently ibutilide will not have that effect. There may be other effects about which we don't know. Ibutilide is suspect because in 1 to 2 percent of patients it can produce a ventricular arrhythmia while

converting atrial fibrillation, which is a much more serious problem. These are problems still to be solved.

From the engineering standpoint the problems or tasks are (1) achieving very reliable recognition of the onset of the arrhythmia so that the drug is released only when at the right time; (2) optimal operation of the pump from a pharmacokinetic sense, and (3) making the implant small enough to be acceptable to patients. I think they are well in hand. The problems that need to be addressed now are the clinical problems. Studies need to be done in which rapid drug delivery is done in the lab under controlled circumstances with patients who have atrial fibrillation. The safety and efficacy of this kind of thing must be well demonstrated long before we can start implanting patients.

Nebeker: Are you working on some of these problems at your lab at IIT?

Arzbaecher: Indirectly. The idea of an implanted drug pump for the treatment of atrial fibrillation is a concept that has developed in my laboratory at IIT, so the intellectual property belongs to IIT. IIT has been trying to license the patent to an appropriate company in order to move on to the next stages of development. Three years ago IIT licensed to a startup company in Minneapolis, but after a couple of years of very good work in developing the hardware and refining and getting additional patent protection the company went bankrupt. IIT has revoked the license and is now looking for another company with which it can continue this work. When we find the licensing company that will carry this technology to the next stage work will probably continue to be done at IIT. Certainly that was the case with this startup in Minneapolis. I was actively involved in my laboratory

with animal studies, design and pharmacokinetic work to support the overall effort. However most of the effort needs now to be done by a company with significant resources.

Nebeker: What was your position at IIT, the Pritzker Institute of Medical Engineering?

Arzbaecher: When I was Chairman of Electrical and Computer Engineering at Iowa City I received an offer from IIT to become the first director of a newly endowed research institute. The Pritzker family of Chicago gave IIT five million dollars to create a research institute for biomedical engineering called The Pritzker Institute of Medical Engineering. The lure of Chicago was a strong one. I was happy, my family had done well, the children had all graduated from the University of Iowa. Everyone was happy, but I had a yen to be back in Chicago. The prospect of being the founding director of a new research institute also appealed to me, so I came back to Chicago and started up the Pritzker Institute of Medical Engineering. I also have an appointment as Professor of Electrical Engineering, and an appointment at the University of Chicago, which is where I have done most of the clinical and some of the animal experiments associated with this research we have been talking about. That is my academic status at the moment.

Nebeker: How has the Pritzker Institute developed over the last decade or so?

Arzbaecher: We have used the interest on the endowment as seed money to develop various areas of research, one of which is the one we are talking about in drug therapy.

Nebeker: Do other faculty full time positions there?

Arzbaecher: Most of the faculty are associated. They have their principal appointments in the other academic departments.

Nebeker: Do they get funding through Pritzker for certain research work?

Arzbaecher: They get funding through Pritzker Institute and are given laboratory space and time. That is the way we have operated for the past seventeen or eighteen years. We have research activities involving faculty of the university departments as well as Pritzker Institute faculty. There are two full time faculty lines in the Pritzker Institute. In one of those we have done a lot of work over the years in the area of rehabilitation engineering.

Nebeker: Have you been involved in that yourself?

Arzbaecher: No, I have not. That is the work of Bob Jaeger, who is now at the National Institute for Disability Research and Rehabilitation. A second faculty member, Phil Troyk, has been developing microelectronics and encapsulation techniques that will allow neural stimulation from very tiny implants. He has support from the National Institute of Health and is developing some of the forerunner multi-electrode stimulating technology for the visual prosthesis. That's another story. There are different areas of research interest in the Pritzker Institute and in other places at IIT. Happily, this last year we have all gotten together and put together a Ph.D. program. Now IIT offers the Ph.D. degree in Biomedical Engineering through the Pritzker Institute, enjoying the cooperation of lots of faculty.

Nebeker: Does that include the University of Chicago faculty?

Arzbaecher: That's the big one. How did you know that?

Nebeker: You said you were affiliated with the University of Chicago.

Arzbaecher: Okay. Yes, the University of Chicago has gotten together with IIT, and we now have a cooperative program in which students can take courses at both

universities. We enjoy the participation of faculty from both universities in teaching and advising students, and there are many clinical research opportunities at the University of Chicago which have now opened up to IIT graduate students and vice versa. We are looking forward to having University of Chicago graduate students in the life sciences, in medicine and physiology studying some engineering at IIT.

Nebeker: Has the University of Chicago had a biomedical engineering school?

Arzbaecher: No, the University of Chicago has no engineering school. The reason this cooperation is so attractive is because IIT has no medical school and the University of Chicago has no engineering school. This is a brand new relationship I am very excited about. We have a proposal in to the Whitaker Foundation to support this new effort, and hopefully that will come through. We will hear about that in a month or so.

Nebeker: Would you tell me a little bit about the rehabilitative engineering? It's a field of biomedical engineering I know nothing about. What sorts of things have been worked on in that field?

Arzbaecher: In our lab we began in the mid- to late '80s looking at electrical stimulation of paralyzed muscle. When electrodes are put on the upper thighs of a paraplegic patient and deliver enough current, the underlying muscles contract. These are muscles that have been denervated by spinal cord injury. This electrical stimulation causes the patient no pain, and the muscles can be made to contract. If done correctly, a patient in a wheelchair can turn on electrical stimulation of the upper legs and get the quadriceps to contract as he pushes himself out of the chair.

He can then arrive at a standing position, get his knees locked with the contraction of the quadriceps and stand for significant lengths of time. That may seem a small thing, but it has great advantages psychologically. For example, it allows a patient who is confined to a chair to stand up and work in the kitchen, reach into the cabinets and have access to kitchen and bathroom sinks. Also, this stimulation may offer a benefit to atrophied muscles. That was one project.

We studied a dozen or so patients in our laboratory looking at complicated problems such as how to maintain balance and anteroposterior sway under circumstances of standing erect. Some questions are, “When a patient has no sense from the feet and no feeling for ground reaction vectors, how can the proper stance be maintained? What kinds of railings or balance aids need to be incorporated?” Sensing and control of stimulation can also be provided in other ways. That has been an exciting area. Pulmonary problems are a serious source of morbidity, particularly in quadriplegic patients. We’ve thought of ways of enabling them to cough and clear their lungs of secretions. We discovered that electrical stimulation of the abdominal muscles, which can be done from the skin, create a productive cough through vigorous and sudden contraction of the abdominal muscles. That’s an area in which Bob Jaeger is actively working. Some have been interested in going further and allowing walking. It’s been demonstrated in a small group of patients that by exciting the quadriceps in an alternating fashion a kind of a walk can be produced in which the patient sequentially contracts and relaxes the leg muscles while swinging forward.

Nebeker: Is a walker used with that procedure?

Arzbaecher: Yes, a walker or parallel bars. There have been some laboratory reports of walking without a full walker, but in most cases a walker is used. Much depends on the personal motivation of the patient, because this procedure is very tiring and requires a lot of training and practice. We are not pursuing that now, but these are some of the goals of other laboratories. We are working in the micro-stimulation area looking at arrays of electrodes that can be used to stimulate auditory and visual centers in the brain. That's an exciting area, and we've had pretty good support for doing that work from NIH.

Nebeker: You mentioned signal processing of the electrocardiogram signals. How has the development of that field, beginning in the 1960s, impacted other areas of biomedical engineering? Has there been much transfer of technology from techniques developed elsewhere by seismologists or speech people to any of the problems in biomedical engineering?

Arzbaecher: That's an interesting question. In cardiology in general, which is the only area with which I am familiar, patient monitoring has benefited from advances in signal processing over the years. All of it is digital now. The electrocardiograph is a digital instrument except for the first stage amplification. The electrocardiograph uses digital processing for all standard filtering, baseline reset operations and diagnostics.

Nebeker: Are hardware and packaged software used by the ADC useful and available?

Arzbaecher: Yes, it is. The biggest change I can point to in my field is that the electrocardiogram is now diagnosed automatically. It's a universal thing. The electrocardiograph is no longer just a recording instrument. It now does a full

diagnosis. It is handled in different ways at different centers. Over reading of the diagnostic report by an electrocardiographer is still common, but the bulk of the work of measurement and first diagnosis is now the work of the computer inside the EKG machine. Signal processing has resulted in inexpensive and extremely valuable technology in that area.

Nebeker: Have you run across impressive figures in biomedical engineering during the course of your career? Did you know Otto Schmitt?

Arzbaecher: I knew him very well. I had the pleasure of serving with Otto on the American Heart Association Committee on Electrocardiography. I gave a eulogy for Otto at the last meeting of the International Society for Computerized Electrocardiography. I am a member of the board of that organization.

Nebeker: He really promoted this new field.

Arzbaecher: Very much. He was trained as a biologist, but Otto was a fellow whose mind would not quit. He was a very accomplished physicist and electronics engineer. He developed the famous Schmitt Trigger, the threshold detecting device, in order to do his biology experiments.

Nebeker: How did he get his electronics training?

Arzbaecher: I don't know. I have always presumed that Otto's was self-training. His attention span was too short and he wouldn't sit still long enough to be trained. He was a wonderful soul, and I counted him as a close friend.

Nebeker: How did you come to know him?

Arzbaecher: In the mid-1970s the American Heart Association decided to update its recommendations for electrocardiographs in view of the newly developed

technology, so a special committee of electrocardiographers and engineers was created. There were eight of us. The engineering people on the committee other than myself were Otto Schmitt, Dave Geselowitz, a notable figure in theoretical electrocardiography, and Alan Bersen. Dave Geselowitz has just recently retired from Penn State. My early work in Dan Brody's lab was in areas in which Dave works, so I knew him very well. Alan Bersen is now at National Heart, Lung and Blood Institute. We laid out requirements for electrocardiographs to be approved by the American Heart Association. The American manufacturers met with us every year, usually at the AHA Scientific Sessions. We would discuss our recommendations with them and they would give their own input and tell us how impossible our demands were in some cases, and how much they appreciated the guidance in other cases. To their credit, companies like Hewlett-Packard, Marquette and other electrocardiograph manufacturers did a fine job in designing and engineering their modern instruments to satisfy the requirements of the American Heart Association. As a result, electrocardiography has reached a fine art in the United States.

Nebeker: How does electrocardiography in the United States compare with Europe?

Arzbaecher: I don't know much about the work done in Europe.

Nebeker: There are some areas where Siemens and other companies are very advanced.

Arzbaecher: There are some differences in the standards between the European electrocardiograph and ours. There is still debate, especially in regard to the amount of 60 cycle current, the so-called leakage current, that can safely flow to

the patient through the electrodes of the electrocardiograph. There is new data indicating that our recommendations are very important.

Nebeker: What about the relationship between engineers and physicians in cardiology? Has that been a good relationship in your career?

Arzbaecher: I have had wonderful relationships with physicians. There are problems. There are cardiologists and other people in medicine whose view of engineering is favorable but limited. They think of engineers as very smart people who can help solve their problems but haven't yet understood that that doesn't happen unless the engineer is deeply involved. The engineer has to participate in the statement of the problem. If the physician knew exactly what the problem was he would probably know the solution or be able to find it. Major progress is made when the engineer is willing to learn enough of cardiology to come up with half of the ideas of a team rather than merely being the instrument for solving the problem. Then the engineer can help identify the problem, help identify what is needed, and work much more effectively. When that happens in cardiology, as it frequently does, beautiful things result.

In cardiology in particular, there has been excellent dialog between physicians and engineers over the years. This has been true in the electrical aspects of cardiology and the electrophysiology of the heart. It has also been true in hemodynamics, ventricular dynamics and in problems of blood flow and materials. The dialog has been excellent and the bioengineer has succeeded, but only because he has been willing to learn. To be effective the bioengineer needs to learn a lot, including the definition and pathogenesis of the disease, the present

standard method of medical management, what is wrong with the present management and what engineering approaches to the problem can add something new to the medical management. All of that requires that you know something about the organ system and the disease.

Nebeker: From the other side, a physician who doesn't understand present technology can't have a full understanding of what's possible or of the significance of the role of the engineer.

Arzbaecher: That's true. It goes both ways. The physician who really enjoys collaboration with an engineer is probably the one who learns a little bit about signal processing, instrumentation, electronics, noise, computers, and other things. The computer has been a wonderful instrument for bringing us together because there are a lot of cardiologists with pretty good computer skills. It's all right.

Nebeker: As we get into doing programming we can be taught very easily.

Arzbaecher: Right.

Nebeker: Thank you very much.