INTERVIEWEE: Dr. Robert Jones
INTERVIEWER: Jessica Roseberry
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JONES INTERVIEW NO. 1

JESSICA ROSEBERRY: This is Jessica Roseberry. I'm here with Dr. Robert Jones, and he is the Mary and Deryl Hart Professor of Cardiothoracic Surgery. It's April 26, 2007 and we're here in his office in the North Pavilion and I want to thank you Dr. Jones for agreeing to be interviewed today.

ROBERT JONES: Well, thank you. It's my pleasure Jessica.

ROSEBERRY: I wonder if I might start by asking you just a little bit about your background just kind of how you came into the field that you are in. What led you in that direction at that time?

JONES: Well, at age fourteen I had learned I was interested in biology, and we had a career fair at our high school in the evening. You could go to three sessions where an individual would describe what they did. I chose to go to hear an educator, a minister and a doctor speak, and I went home and sat down that night and thought with all of the interest I had in biology and remembering that the first open-heart operation had been done a year before in 1953, and this was 1954, that I thought I might want to be a doctor, and I figured if I were a doctor I could minister to folks all I wanted and could teach folks, and so I left high school a year early and decided at fourteen to be a heart surgeon and never looked back. So that's how I got to Duke from working with Dr. [David]

Sabiston when we were at Hopkins together, and he was strongly interested in physiologic measurements and being very quantitative as a surgeon, and so that's how I got interested in doing research. A lot of the early what's now called nuclear cardiology research, which produces a large amount of data that starts with images but then only makes sense if you match it with clinical data, and so that's kind of the roots of my interest in the cardiovascular database.

ROSEBERRY: So can you talk a little bit more about the measurement and the research that you were working on?

JONES: Yes. Actually I had worked with Dr. Sabiston as a medical student. I actually had the first of what would be three seizures during my medical career, which kind of made me consider whether I should go into surgery or not, but I kind of held fast with that commitment, and during that period of time actually I failed physiology, and so I decided to repeat that because I had no choice if I was going to stay in medical school, but I went to the chair of the department, Dr. Philip Bard and said I'd like to work with you in the laboratory. And to his credit with a failing student—and he was very renowned physiologist—he said, "Certainly, you can work through the summer, and then during the time when you repeat the physiology course—" and so I worked on making brain lesions and looking for the fever center. But that was a milieu where I just suddenly turned my interest towards research, and I asked Dr. Bard who I should work with and he said well the physiologically oriented surgeon here at Hopkins that probably will be the next chair is Dr. David Sabiston, and I would suggest that you should work with him. So I went to talk to him. He was working on pulmonary embolism. Making a model in a dog and then trying to look at the mismatch of perfusion and blood flow when

these clots hit the lung, and so I was very excited because that was the surgical thing to do and it had a lot of physiology, and a week after I started with him he called me in and he said, "I'm sorry, but I'm going to go to Duke." (*laughter*) But he did send me to Dr. Henry Wagner, and he and Dr. Wagner had used some of the first lung scanning which he used a little aggregated particles of albumin labeled with a radionuclide and imaged the lung, and they were looking at the distribution of blood flow in the lung and the various circumstances, and so I got really deep into these physiologic tests of nuclear studies and got because of my seizures in medical school—which frankly after coming to Duke I never had another seizure. (*laughs*) But after those, the government would not take me voluntarily so I could go the Berry Plan with the NIH. So I ended up having to be drafted like every other physician who graduated in 1965 for the Vietnam Conflict. But the government didn't want me right away so I had a little bit of time to do research, and I went to Dr. Sabiston and said, "What do you want me to do? He said, "Well, why don't you go back to doing the lung research you were doing with Dr. Wagner?" And this had required a lot of hand work, and so I went checking around, and there was actually an instrument that was being shown at a regional medical center here in Durham that had computerized the gamma camera which was the first real gamma camera that is now widely used for nuclear imaging and gave actual counts, and so we started injecting this material into dogs, and we could take counts about every half a second, and we could see this material move through the heart and could even see the pulses of the heart. So we started then expanding that observation by getting instruments that would count faster and making prettier images, and so by the early 1970s, we were able to accurately measure cardiac ejection fraction and volumes noninvasively which was not being done

really by echo at that time or really any other technique. And this became a kind of exciting thing for all the young cardiologists here at Duke and everybody came up with different kinds of physiologic questions as well as clinical questions, but also we began to provide to patients who were willing to undergo the study clinical information to their doctors of ejection fraction and even as early as 1975 function during exercise. So we walk people around the hall and look at their function, and that became an exciting prognostic test, and that's how we particularly were wedded with the database, because we merged into the SCOR grant that was ongoing and needed to have a good repository for the clinical information. So very early as we were doing these studies that we were doing up to a rate of ten or twenty a day, both on normal subjects: Duke medical students who would be paid to take a certain drug or to do various things like strenuous exercise and so forth, but also clinical patients that Drs. Floyd, Whalan or Morris—the three real clinical cardiologists at Duke at that time—would refer or those that came to cath lab where there'd be—Jess Peter would have done the cath and would let us image these patients if the patients agreed so we could make sure our techniques were accurate and so forth. So this was basically a kind of a bit of a Duke phenomena that I was kind of pleasured to sit in the middle of and have a lot of fun with. It was Phil Harris who was a young fellow then who's now in Sydney, Australia, a very distinguished cardiologist there. But he was the first one that put any imaging data into the cardiovascular database and actually built the physiologic data that was put in there, and early on statisticians began to work with some of the young people, particularly with Rob Califf and others, to look at the prognostic information. David Pryor was one who wrote one of the very first papers and then Kerry Lee, other papers, Karen Pieper was on those papers, so this has

been a great marriage of anatomic information, physiologic information, and clinical outcomes. It's really been the source of a lot of very important publications and specifically publications on prognosis. So that's a long-winded answer, Jessica, to kind of some of the history that kind of brought this about. But I think it's interesting to reflect on those things, because a whole lot of unplanned events that just kind of came together as we were just having fun and asking questions—and often you kind of think you're going in one direction looking to pulmonary embolism a dog and before long you've done some fun things, and you've taken opportunities, and now you're actually do some of the first physiologic tests that are being done in patients under stress or with a variety of other conditions. And that's the way kind of medical research goes forward. You just kind of enjoy asking questions and answering them, and in those days the Duke environment had no walls. There weren't the silos or the rigorous kind of things. You'd go talk to someone, and they'd get excited about your idea, or they would bring their idea to you, and you'd get excited, and it was very collegial. And I didn't mention it, but we interacted with Pediatric Cardiology, because in those days cathing a child was a very awesome event, and there weren't too many ways other than with radionuclides to try to find out if this murmur was really from a shunt or how bad the shunt was, and so we also interacted a lot with Pediatric Cardiology, and that was another whole segment as well. But hopefully Duke will, as we continue to grow and refine and specialize in both research and clinical care, have mechanisms to maintain and increase these bridges and cross collaborations, because that's where really a lot of the forward progress comes. It's not any one single person that just goes down a straight path. Very often these are these

zigzags where the real true fun and maybe meaningful—we hope meaningful—for our patients research projects originate and then cascade forward.

ROSEBERRY: Now, you mentioned the SCOR grants, and I'm wondering if you could maybe kind of outline some of the language that that was, that you were?

JONES: Right.

ROSEBERRY: —working into.

JONES: Right. The SCOR was Specialized Centers of Research, and they had SCORs. The one we had was for, I believe it was for atheroscolosis. It was, anyway atherosclerotic cardiovascular disease in some way but it was to be a melding of clinical and basic work together that would kind of foster this kind of kind of cross collaboration, and it really served to do that. There were other kinds of SCORs for other kinds of things as I recall: the pulmonary SCOR and so forth later. But these were something like twelve centers the NIH gave a grant and each center could kind of do its own thing, but there was also expected to be cross collaboration among centers where you would get together and share some of the findings and even build multi-institutional collaboration. That SCOR process started as I recall in the early seventies, but it had been preceded by what was called the MIRU which was the Myocardial Infarction Research Units, and that came out of the spread of what we now call acute care units where heart attack patients who previously had just been put out in a quiet dark place and kept without a rectal exam and then kept on their back for seven days and that kind of thing were now moved into situations where it was more high intensity. I remember when one room I think on what was called Drake Ward at that time that had a big giant monitor that would be laughable by today's standards of microprocessing but that these patients would get hooked to, and

you could monitor the ECG particularly for arrhythmias, and you could stand in there and give xylocaine and watch the arrhythmias go away. Of course we've learned now that it's what you need to do, but in those days it was very exciting to do that, and you could even with a little bit of effort get cardiac outputs with indicator collusion curves off these big giant things. But to fund this kind of thing you had the MIRU grant, and by my memory those started in the late sixties, maybe 1967, '68. The times where I was a resident and some of our cardiac surgical patients we would use some of this technology, too, as a spin off. Dr. Newland Oldham was the surgical representative as I recall on the MIRU project and continued as it went into the SCOR kind of with more of the clinical side of things. And I was kind of the resident that was more involved with the research and remember very much frequently going into what later became the database office that had been kind of constructed, appended onto (*chuckles*) the old Duke Hospital in a little center where it wouldn't be seen by the architectural policemen that wanted everything to have Duke stone and was kind of a very temporary rooftop unit but had the giant computers with by today's standards laughable power. But it had also keypunch cards that we'd enter data on and, but it had in there Frank Starmer and Galen Wagner was there frequently and Bob Rosati and later people like Bill Stead. But of course Gene Stead would come in very often and get excited about the computer being such a great tool to make a living textbook of medicine, as he was known to call this whole project. Actually I remember on one of the SCOR renewals or maybe even the initial proposal when I was there in attendance in the boardroom, as was everybody else that could know anything about kind of heart (*chuckles*) physiology—I mean, we kind of rolled out everybody at Duke who had done much of any research at all which was pretty well a

room full; nothing like today of course but things weren't going too well. Andy Wallace had taken over the leadership of the project, and he was fairly inexperienced at that time and was doing really a good job, but he was kind of missing the concerns of the reviewers. And all of us began to get pretty nervous that he was kind of becoming more defensive. Instead of saying, Well, you make a good point but had you ever considered this he was kind of coming back like we young folks do sometimes. We're combative and even argue them down, which is not a good way to get their favor and get a high SCOR. And all of a sudden Gene Stead, who'd been quiet through this whole thing and tried to kind of sit on the edge got up and started saying "Well, now, you know, we need to step back and think of this in the broadest sense. And let me tell you what we're really trying to do for the folks that we're taking care of." And he went ahead with his kind of southern talk for about three minutes, and he just kind of totally turned the whole discussion around. So all of a sudden people got kind of excited about his vision, and Gene had such a special way of being able to communicate to people very quickly with just very few words but powerful words, concepts that really came from a heart that was full of a mission, and he was a very special person for that reason.

ROSEBERRY: So what kinds of information—you talked about the imaging information or data being entered into the databank, and I wonder if you could break that down for me and kind of outline what kinds of information went into the databank from your perspective?

JONES: Right. For my laboratory we pretty well standardized all the information to be some index of the amount of exercise the patient had done. We started with bicycle exercise so the chest wouldn't move that much but we evolved the technology to be able

to use a treadmill and actually to, as the instruments improved over the years, to trace the motion as patients would walk with a second isotope and it'd correct for motion so we could actually use a treadmill. But we would then look at the workload and physiologic things that you would get off of either the treadmill or the bicycle and how much EKG ischemia one saw. But then with this single bolis transit, the standard things that we would measure of course would then be at the peak heart rate, but at that heart rate the left ventricular function and filling parameters, regional function, we would measure pulmonary blood flow, and we were fairly certain we could accurately measure right heart function as well, although we didn't at that time have anything much to calibrate that against, but the left heart function we did. So we ended up with volumetric cardiac outputs at rest and at different levels of exercise and so forth, and additionally we would look at all sorts of regional pictures and quantizations of functions, so that these were kind of three-dimensional count profiles that you then could really turn into some fun kinds of images that showed not only that a certain wall would not move in that much, but the timing of the rate so that it would be also slow to start *(chuckles)* and not move as far or whatever else. So we saw a lot of things that we didn't have time to report that have been discovered later. Things like the effect of bundle branch block on ventricular dyssynchrony and so forth that we observed very frequently. I mean, at those times we were observing so many things that you couldn't even report them. We were some of the first to observe—for example a young lady came with a horrible tachycardia and very low ejection fraction. As I recall she was sixteen or yeah, it was something like fourteen. In those days Dr. [Will] Sealy was doing a lot of the arrhythmia surgery and he ablated the focus of this very rapid heart rate that she had, and we studied this girl about a week

or two after that and the ejection fraction go back to normal and we thought we had made a mistake. I mean, to go from ejection of probably about twenty back to sixty. Clearly it's known since that you can deplete the ATP energy stores of the heart, and you can induce heart failure by pacing dogs. In fact we went ahead and confirmed that and subsequently many people noted this that a lot of times that what appears to be dysfunction is just clearly a temporary, very reversible sort of thing if you get rid of some of these very frequent tachyarrhythmias. So a lot of these kind of observations just kind of—you know, we didn't have time to publish all of these as individual cases and so forth. And we did a large series of things that never got published unfortunately. Things that would have been fun to do but there was just so much going on we kept waiting for the series to get larger and larger. We, in those days, often had patients come for valve replacement that had been kind of in the North Carolina mountains and just came in with horrible, horrible, big hearts. I mean football-sized hearts. End-systolic volumes in excess of four or five hundred milliliters. And as the patients would come back to clinic as they often would want to do at Duke, and we'd see them yearly for a few years and do these measurements with their consent, we were surprised that not only did the rest ejection fraction normalize but the exercise ejection fraction would normalize, too, and they would come back to normal size hearts, and a lot of people still frankly don't even know how much the heart can— now it's called reverse remodel, *(chuckles)* and we would try to get a series of about twelve of those and show it and we'd just, again, we ended up with ten or so. We never did get out and publish the physiology, and it's kind of known that's happened. I think most people don't really understand how much reserve the heart can have particularly in an area of regurgitation, and it's just amazing some of

the physiology that we see. Some of the most fun things we did were in the Duke athletes or in the medical students. All medical students were ready to do about anything for a hundred dollars or something like that (*chuckles*). So one of the best things we did with medical students was, with their consent, we gave them high doses of beta blockers and did a rest and then an exercise study of just the maximum workload they could get to and the beta blockers lowered the heart rate, but we did a measurement there. And then we let the beta blocker clear and then a week or two later they came back, and we did a rest. Of course off the betablocker their heart rate was a little higher. But then we took them to the heart rate that they got on the first study, the maximum heart rate they could get on the beta blocker which was something around a hundred or something like that, and then we did a study there, and then we exercised them to the maximum workload they could do again. And then of course their heart rate now where at maximum it had been maybe a hundred goes up now to a hundred and sixty or something like that. *(chuckles)* And the very interesting thing in every measurement LV [left ventricular] function, the ejection fraction, the volumes, everything, at that intermediate heart rate, one which was off, the other which was on beta blocker, was exactly the same. And we reported that. In fact it was published and so forth, but a lot of people still did not understand that. There was such a fear that beta blockers really would have some much depression of intrinsic contractility that you ought to be very careful of using them in many, many situations. Well, I mean, that showed that yes there is a slight depression, when you've got a strip of muscle, but there's so many compensatory mechanisms as the heart tries to seek the very best position on the Starling curve where it can work most favorably that the heart's just very, very, the normal heart is just extremely resilient, and that there's not that much

really depression of contractility. Most of what happens is just mediated through the change in heart rate, quite frankly. The athlete studies were quite interesting where we'd get a group of physical therapy students and looked at two hour exercise and then saw how if you say, Well, this person just exercised long and they're just tired, they're at the end of a marathon if you will, and you say, Okay, go as hard as you can and we would compare at that happens at that last thing and really what people could do is squeeze out just a little bit more heart rate and it makes their cardiac output go up. We also looked at the effects of exercise training on LV function and Dr. Steve Rerych did that who had been himself a gold medal winner in the Mexico Olympics at swimming, and he encouraged the swim coach at North Carolina State to encourage a group of their male and female teams to cooperate. My memory is we had about fifteen that were willing to come in right at the beginning of the season and let us do a rest exercise study and then right after their final swim meet when they should have been in their very best condition and do another study. And the thing that we found was that what happens is that the heart with training learns how to work at a little bit higher end-diastolic volume or a little bit further out on the Starling curve. So all of that extra blood that the heart fills with, at end systole gets converted to forward stroke volume so the heart rate doesn't go up, the ejection fraction actually doesn't go up, but because the end diastolic volume is bigger, the stroke volume goes up, and you increase the cardiac output about 20 percent actually with exercise condition. So that's kind of the physiology of conditioning. And during that there was a very large also Olympic swimmer that had been in the Montreal swimming meet but also bicycled for hobby, and we would test him on a bicycle. He was a very tall guy, and he was recorded to have a 53.6 if I'm remembering exactly cardiac

output, (*chuckles*) which of course was for only the period of a few seconds that the tracer bolus went through his heart. It might not have been sustained for a long period of time like a minute or two that you need if you're using indocyanine green cardiac output. But we measured the world's largest cardiac output that had been reported at that time or I think ever has been since. Prior to that a Swedish one we found was reported. Also this was a marathon runner of 42.3 or something like that. So the American took the cardiac output gold medal as well, I guess, so. But there was a lot of fun things like that that kind of went on with that, and we kept all of that physiologic data but we also were at the same time doing clinical studies on as many of ten or twenty patients a day without any charge, but then we would also report that clinically after, you know, this was a pretty mature test and eventually became a charge study and was used pretty widely. And that's what led into the prognosis because we started getting almost every cath patient who would consent, and so we would have the cath, the physiologic information, and we could find then that actually the exercise ejection fraction was the single most prognostic information in the cardiovascular database more so than coronary anatomy or anything. It did not interact with treatment, so actually we still wanted to know the coronary anatomy to make the decision about whether you should treat the patient medically or surgically, but if you speak about just predicting mortality after five years or so the exercise ejection fractions are a very, very powerful prognostic tool and particularly was very useful and still very useful. If you have a normal ejection fraction, if during exercise you have the ejection fraction that's about 50, then thinking about going to surgery probably doesn't make any sense because the mortality is so low. Once it begins to get lower and lower then it's probably worth cathing that person, looking at the anatomy and

going forward so. So that's where the database came to such power to be able to go in there and pick out the 751 medically treated patients and know all the clinical variables that were important, do that model, and then add in this other variable. And the fact is you look back at the imaging literature I think some of that was the first to really do things as right as could be done where you, instead of saying well this test is positive in these people and it's negative in those and it's so valuable that you forget all the other clinical information that's so easy to get—and you add a test like a treadmill and so forth and you attribute all the power to the treadmill that you have of how much angina the patient had and a bunch of other types of things so obviously to be able to do a multivariable test and of course that's the way everybody now does it that does it properly, and I don't mean that we were the only ones that were doing that, but we were among the first to present that kind of quality of data where it was done prospectively. There couldn't be any question. You had a consecutive series that you predefined your methodology and standardized, and we knew the variability in it and all those sorts of things. So some of that for the time was some leading edge kinds of things. It's now kind of old, (*chuckles*) if we look at it.

ROSEBERRY: Well, what is the ejection fraction? Tell me (*unintelligible*)—

JONES: That's the fraction of blood that squeezes out of the heart with each beat, and it's so important because it basically is what we call the stroke volume that is how many milliliters of blood go out each time the heart beats divided by how much was there to start with, and it's those two parameters that are these components if you will of the Starling curve, because the heart has a way that the more it fills, the more you stretch it and unless you stretch it so much you disrupt it and pull it apart, but whether you're

talking a leg muscle or a heart muscle, the more you stretch it and then you stimulate it the more powerful the contraction will be. It's a beautiful physiologic mechanism that we've been blessed with to kind of help us perform when we need to as best we can, and the heart has that really amazingly. So you can use that Starling mechanism, and we often do to overcome such things as some blockage of the coronary arteries where we lose the squeeze in one region of the heart, but the rest can very often make up for it. That's why people live through heart attacks. That's one of the many mechanisms the heart has to adjust.

ROSEBERRY: So were you doing long term follow-up on some of the patients that you were studying?

JONES: Well, the beauty of putting this in the cardiovascular database is all of those were being followed-up anyway, and they'd all be cathed, you see.

ROSEBERRY: Gotcha.

JONES: And we did patients also that were not cathed because we wanted to kind of see how good the test was in a different population that came in, and we've also reported those and for those we had to do our own follow-up because they didn't go in the database initially, but then once Phil Harris began to develop our database, then we could merge those two databases. So we basically used Gene Stead's idea. We had two parallel databases until we could kind of blend them together. It took a little bit longer then we expected to blend them together, *(chuckles)* but again we learned some of the hassles of databasing and computerization of the medical record, all those kinds of things where you have to be careful about definitions and so forth so.

ROSEBERRY: What do you mean that you have to be careful about definitions? Why?

JONES: Well, if you're going to try to merge data, you have to make sure that you're kind of calling an apple an apple and an orange an orange in such things as Did a patient have a heart attack? I mean, we still have many different definitions. In fact a lot of this work led into me being interested in guidelines, because I was trying to get people to use the nuclear test to screen, and people that had the very best heart function during exercise, unless they're having pain you didn't really need to go further in the diagnostic process. And yet people seem to cath people if they just were referred even though they pretty well knew that you probably didn't need to do much. Somehow it just kind of, you know, Well, they were sent to Duke to a cath—but it wasn't just Duke, it was everybody around the country. There was not kind of as much acceptance of risk stratifying and trying to be very frugal in the use of medical resources, and that's why I got interested in guidelines quite frankly to think that, Hey, we need, once we need to get some evidence, we need to get it into practice, and so we began to kind of go in that direction, first in the surgical arena and then later on we got the first contract from what was called the Agency for Health Care Policy Research in those days for being able to really go to the literature, do a full scan on unstable angina literature and come up with a guideline kind of *[de novo.* and in that we were able to put some degree of the cardiac imaging and the risk screening particularly using a treadmill with the Dan Mark score that he had developed at that time also. Dan was one of the early cardiology fellows who came through the nuclear lab too as did many, many other people. Some of them spent all the research time there, but they also got some of their first clinical experience with some of the more advanced imaging, and they of course contributed, because they brought a lot of interest, a lot of new questions and excitement. And so it was again a fun kind of thing where

everybody just kind of contributed. There weren't any walls. It was a collaboration, and the kind of thing that we're trying to reproduce at Duke hopefully. We're getting it in various areas, but it's sometimes hard for us not to try to kind of isolate ourselves a little bit and kind of work in our own sandbox you know, and it's really so much more fun to have a group of people together working, and I think all of us kind of dream of doing that, but somehow just the daily pressures of life we tend to segment ourselves a little bit more then we should.

ROSEBERRY: Were there other surgeons who were taking advantage of the databank as well?

JONES: Yes, thank you for asking that. Yes, Dr. Sabiston was strongly supportive of this, and we always had a number of surgeons, and this continued through the years. In fact we took this technology into the operating room. Dr. David Harpole was very instrumental in that. And several others. Dr. Harpole's still on faculty here and along with Dr. Bashore did a lot of studies in the cath lab actually using this technology, and by that time we actually were putting pressure catheters into the left ventricle so we could measure the best physiologic measurements you could make in an intact patient of heart function which is called the pressure volume loop. So you instaneously measure both of those parameters. It's not really instantaneous for us. It was twenty-five millisecond intervals, but that's pretty instantaneous, and we did a number of studies in the operating room. We looked at how much heart surgery depresses heart function, which is frankly very little. We looked at different ways to protect the heart. We looked at the acute effects of valve replacement. We looked at how much you could volume load in the post-operative period and effectively put the patient on the very best Starlingcurve, how

quickly the edema left the heart and so forth. So there's a lot of information that came from the surgeons who were there and I should have mentioned that earlier, and that was another fun thing. That was about the only meeting place that was pretty consistent between the fellows in cardiac surgery and cardiology that day that would kind of focus around clinical research. So there was a lot of cross collaboration of authors like Ray Gibbons *(chuckles)* who has been the president of the American Heart Association and you know was in the lab and some of the surgeons he would work with who—some who know are also very prominent surgeons, and so that's the other advantage of cross collaborations between disciplines that blend. It breeds long-term not only friendships but kind of professional collaborative source of relationships. People who train together also kind of work together in research so they know both sides, the kind of clinical-care patients together and exploring research questions together so.

ROSEBERRY: Well, let's see, I had a question, but I lost it. I'm sorry. *(laughter)*

JONES: We've gone through a lot here. *(laughter)*

ROSEBERRY: Were there any drawbacks or unrealized potential maybe of the databank that you saw?

JONES: Yes, I think that both the databank and the work that I did in conjunction with the databank just tapped on to a new era of information capture with patients, and there were other—this was being done in other disciplines. It's not like we just invented all, I don't mean to suggest that Duke just invented all of this, but for the cardiovascular arena, this kind of set, I think the database itself or the databank concept, set kind of a standard of thinking about patients that very quickly would lap over actually into the clinical arena, so that you begin to blend your thinking between what was really a research

question and what was a clinical-care question particularly in some of those very unique patients that came in like I was talking about that the young lady with the tachycardia. I mean, that was a very clinical study. You know? I mean, Dr. Sealy in those days would just phenom— I mean, it just changed his, blew his mind to see those two images. I can still remember the very first exercise study that I saw that Steve Rerych and Peter Scholz brought down to my office where they first showed me the exercise study which had an ejection fraction of thirty and I said, "Boy, that's a lot of dysfunction, isn't it?" And then they showed me the next one, and it was sixty. I said, "Well, what are you showing me this other patient for?" They said, No, this is the same patient. I said, "How—you can't do it. I mean, it's impossible. Well, what did you do?" They said, Well, we exercised this guy for two minutes, then we injected him. He had just critical left main and a critical right, and it blew us away, and then we began of course to look at that very prospectively. And then we really began to use that clinically because we were doing so many protocols that normal people could volunteer with. Then we encountered one, in fact one ended up getting a Nobel Prize after we saw his supposedly normal function *(chuckles)* be twenty-five ejection fraction, and with exercise it went down to eighteen. We cathed him. He had a horrible disease. We did surgery, and he lived for many, many years and got the Nobel Prize later. *(chuckles)* So I mean, we had a number of those kinds of events, and in fact it was hard to keep, some of this was covered in national newspapers, and it always came out *new test device removes need for cardiac cath.* And that's because we would say that the proper use of this if you've got very normal function that they need cath less and you could find the people that had a very abnormal function and take them to cath. I mean, that's the message we were trying to get across but of

course newspapers like to make something people will read and make it very flashy. And so we had all these people saying, Well, if you come down and get that imaging thing I won't have to have the cardiac cath. You know? *(chuckle)* And we'd have to say no, no, no it's not that you may not need the cath but we can tell you how much you need the cath and maybe your doctor will decide that you have such low risk and everything else is fairly normal that it doesn't make sense to do a cath now. Maybe we'll watch you and do another study later and so forth. So we had all of these people wanting to come down for this. Of course we were doing it free, because it was paid for by a government grant, and we were trying to get patients in the various protocols and so forth. So it was kind of hard to keep all of this moving in the way that we were extracting all the science we could, because we were also satisfying what people perceived to be a clinical need, and we of course tried to put that first for patients and always put what we would find in a context, and we would be glad to send these studies free to their doctors, the images of the hearts and the measurements that we made and very soon we started doing some courses on this and had a lot of doctors come and begin to adopt this and so forth so.

ROSEBERRY: Well, how has the development of DCRI changed the use of the databank?

JONES: Well, fortunately of course all these roots have made many, many beautiful flowers in many places. (*laughs*) So many of the people who have been exposed to Gene Stead and David Sabiston's real kind of ferment that they brought to this institution have gone through multiple generations and nobody can claim any ownership of anything. I'm sure Dr. Sabiston and Dr. Stead would give credit to their mentors and things that went on but of course there's giant amount of talent here. And a lot is in the quantitative kind

of thinking that has come and has now rippled and been refined so that people now are much more sophisticated then we were in those days in the designing the proper order approaches to new information. There's not quite the opportunity to suddenly enter a field that then expands greatly, and in fact now if you look I mean there are about sixteen different non-evasive ways (*chuckles*) to measure left ventricular function. In those days basically, this was some of the first ways that you had to measure, and it was just so fun to begin to measure something that you could measure with a cath, but it was a pretty big deal to do a cath in those days for folks. And we weren't the only, and again I don't mean to suggest that no one had done this before. In fact the first nuclear studies in people were by Blumgart back in the 1920s and he was really trying to do thyroid studies and yet he saw this stuff go through the heart, and he couldn't see the beat-to-beat information but he could do a cardiac output or a transit time and so forth and there had been a few other folks parallel with us that had done some stuff and frankly most of it was kind of discovered independently, and it began to work together. So again I'm not trying to say that we stand alone. I mean, everybody's good idea gets passed from one to another in an ideal research environment, and ideas that Dr. Sabiston and Wagner gave me as a student and then I would cross fertilize back to them and so forth and many, many other people. It really made it so no person could claim some great area. It's just really rare in medicine that you can say, Well, this person did this only *(chuckles)* and that sort of thing and so as you look around, I think there's still that giant cross collaboration in the DCRI, and that has been the great ferment here and hopefully it will continue at Duke. And there's some natural breaking down into working groups. I think, though, still we need to foster this cross collaboration of ideas not only across kind of the

subspecialties but also in level of expertise, and that's why the new center to work on translating this back into practice where you really try to have a whole circle of how you just basically you have a big blur of what is really clinical care and what is clinical research, because you're, there have to be some definitions. Now this is now clinically applicable, and it's not before (*chuckles*) and so forth and clearly I mean, I understand that, but it's not like you're living to kind of go half of your life in clinical care and half of your life in clinical research. As a provider, you use your evolving knowledge and research to begin to try to manage patients as best you can and then you take your patient observations back into the arena where you can build new ways to address issues and that's going on particularly now in the genetic arena of course, and there's still a lot of primitive things there particularly in information capture where people are getting much further ahead in being able to characterize the genome then we are knowing how to take clinical information and figure out what this means for the patient where you can go back then and do something specific. So all of this really comes down to the fact that no one person *(chuckles)* anymore can really make that much difference, but when those one by one join together into a group and each leverage their own strength, then a group can make a major difference, and that's what you see in the DCRI. I mean, if you look at the whole package of the DCRI—Rob Califf of course gets giant credit but he will give credit to many other people going back particularly to Gene Stead. He'll very freely admit that all of, a lot of what I've said he's validated from more of the clinical perspective where he started particularly in the coronary care unit, and I'm sure Galen Wagner will document his feelings from how that's worked in his thinking of electrocardiogram and its position and place and so forth. So the DCRI now will spawn

I'm sure new sets of ideas and thinking and particularly blending now— the key challenge I think is to blend a lot of what we have in the DCRI in information handling in study design with some of the basic kind of genetic and the omics fields if you will, not just genetics but proteomics and so forth where a lot of times the super-sophisticated ways to understand what the cell looks like and is doing and how it's behaving or even the sub cellular membrane and so forth. But you've got a patient sitting there, well, how are you going to translate that over? And most of those folks think, Well, I have this genetic information now, well, I'll go look for some "phenotype," quotes. Well *(chuckle)* phenotypes a very broad thing. Like I say genetic and they say phenotype, and they've got to begin thinking about what kinds of key information do we need and how are we going to collect it, and is it going to be consistent, and what are our definitions and so forth.

ROSEBERRY: Well, Dr. Jones, what did I not ask you today that I should have asked you?

JONES: (l*aughs*) Oh, well, I think you asked great questions. I just talked a lot. I kind of expected we would focus much more on the database, and you got me talking about myself, (Roseberry laughs) so I guess I but hopefully I shared some material that really focuses back on the database. So I thank you, and it's been a pleasure to talk to you.

ROSEBERRY: Thank you, Sir. Thank you.

(*end of interview)*