The Mayo Clinic Cardiac Catheterization Laboratory

History, Research, and Innovations

David R. Holmes Jr.
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Preface

We decided to write a history of the Mayo Clinic Cardiac Catheterization Laboratory because it is a fascinating topic and many younger colleagues have asked about its origins. To tell the story, we chose to first focus on origins of the lab and explore the fascinating contributions of Dr. Earl Wood, who set the stage in developing technology to monitor human circulation while studying G forces to protect dive bomber pilots during World War II.

We then approached past and current participants in the cardiac cath lab to share their perspective on how the laboratory developed in specific areas of interest such as congenital heart disease, the introduction of coronary angiography with videometry and videodensitometry, hemodynamics, physiologic studies of coronary reactivity, valvular heart disease, coronary and valvular intervention, and heart failure. Electrophysiology, which also has been a part of the cardiac cath lab from the earliest days, is also a topic of great interest and represents a large component of the current activity in the lab. We also devote several chapters to specific time periods to give a perspective of how the practice evolved. Thus, this is not a single narrative in strict chronological order.

This has been a humbling endeavor as one reflects on how it all began and the extraordinary advances in knowledge and interventions to enhance care of patients with cardiovascular disease. The historic record given in the following chapters provides confirmation of one of Dr. William J. Mayo's famous quotes: "The glory of medicine is that it is constantly moving forward, that there is always more to learn." We have focused on contributions and events at Mayo Clinic but wish to acknowledge the contributions of many institutions and individuals to the progress we all share as a profession in providing care for our patients with cardiovascular disease.

One might question how all of these activities were supported, which is also a part of the historic record. Until the late 1950s, Mayo Clinic did not accept outside funds but relied on funds from the practice to support education and research. But the world changes. Donations and competing for funds are both now essential to support research and education responsibilities. We thus wish to recognize the donor who provided funds to endow the Mayo Clinic Cardiac Catheterization Laboratory as the Dr. Earl Wood Cardiac Catheterization Laboratory.

We have been supported and learned much from the people who helped put this all together. Many thanks to all the contributors, and we also wish to recognize Linda Lee Stelley and the staff of Scientific Publications, without whom this would not have actually happened.

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Acknowledgments

Histories are always built on a foundation of multiple layers beginning from the ground floor, and the concepts and the ideals which constitute that ground floor, and, as importantly, the people who put into place the things that become the underpinnings of the history, the foundation for the future. The ground floors of this Mayo Clinic Cardiac Catherization Laboratory History are based on the ideals of Mayo Clinic wherein projects are developed, then designed to address the clinical needs and questions of the people who we are privileged to serve.

In addition to the patient components who formed the basis for all of this, the "people components" were Mayo Clinic employees, as a rule, from all walks of life, many from this area of the country, some of who had been born and raised here, and they, in aggregate, formed the base upon which this history was fashioned. Most importantly, the people who came to be treated, the technical people, the infrastructure people, the technicians, the patient care advocates, the nursing staff, the research associates (often from around the world), the fellows, all of the other professional staff, the administrators, the inventors, all of whom are too numerous to name individually. To all of these individuals and groups, we owe a debt of gratitude because without them and from where they had come, this history, would never have been made, would never have been fashioned and grown now to be celebrated in this book of our collaborative history. To all of these unstoried but essential people, we owe our incredible debt of gratitude to them as we tell their and, now, our story.

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Chapter 1
1950–1970s: Where We Came From

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The precursor Mayo Clinic Cardiac Catheterization Laboratory opened in 1951 on the first floor of the Medical Sciences building (Fig. 1.1). The initial conference room (Medical Sciences 2-154) was of particular importance, as it was surrounded by the offices of a unique collection of multidisciplinary physiology talent, which included the early pioneers Drs. Earl Wood, Charles Code, Ed Lambert, John Shepherd, David Donald, James Bassingthwaighte, Reg Bickford, and Ward Fowler as well as clinicians and engineers (Section of Engineering located in the same building) among others. It was this close geographic association on an everyday basis that contributed importantly to the success of the early cardiac cath lab. Beyond this rectangular arrangement of offices around the conference room 2-154, on the rest of the Medical Sciences floor was the office of Dr. Jesse Edwards, the world's iconic and most experienced cardiac pathologist, with an extensive collection of anatomic material that formed the basis of formulating strategies of care both for diagnostic imaging in the cath lab and for surgical planning. These multiple disciplines were available for formal and informal discussions and speculations from which came a steady stream of new approaches, new technology, and new scientific insights. This unique environment was the think tank of the future.

The initial grounding for the development of the tools needed for a modern-day cath lab resulted from Earl Wood's work after he was hired in 1942 to use the Mayo Clinic human centrifuge to investigate and establish the cause of acceleration-induced loss of consciousness (G-LOC) and then develop a strategy to mitigate it (Fig. 1.2). This resulted in the G-suit (Fig. 1.3a, b), which had a dramatic safety

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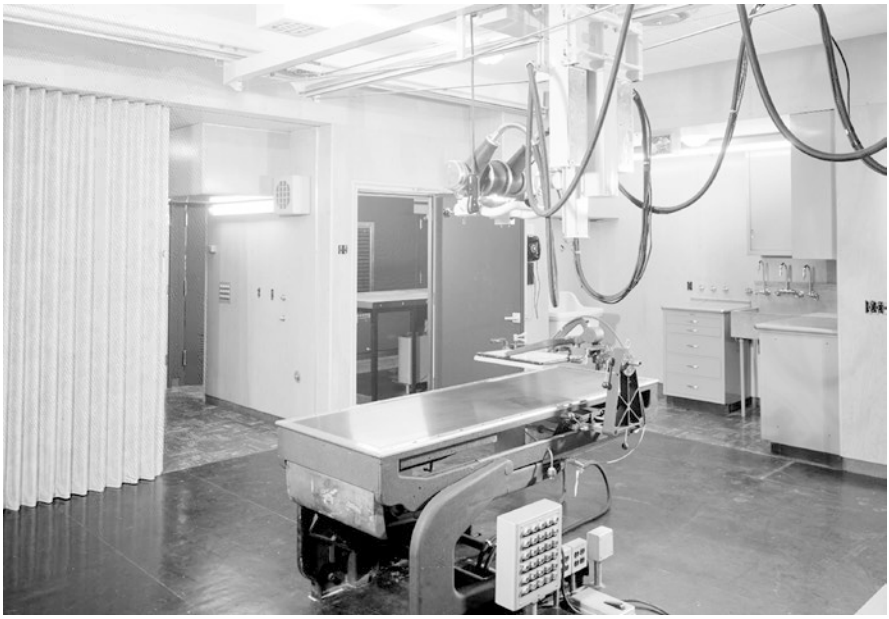

Fig. 1.1 The catheterization laboratory included a single plane angiographic system, with multiple input and output circuits seen under the base of the table used for recording and analysis and data accumulated during extensive physiologic studies. (Used with permission of Mayo Foundation)

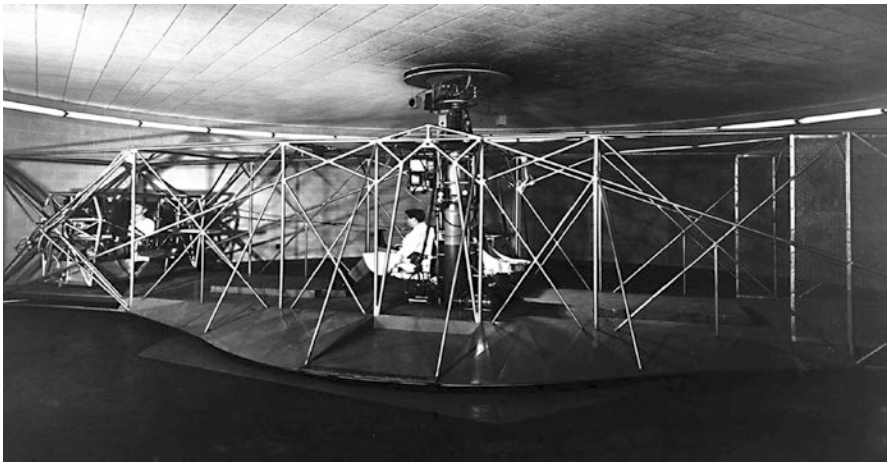

Fig. 1.2 An early focus of Wood's career involved the construction and implementation of a human centrifuge designed to investigate the cause of acceleration-induced loss of consciousness and resulted in the development of the G-suit. In this picture, Wood serves as the monitor for the experiment and the "volunteer" is seen on the left. (Used with permission of Mayo Foundation)

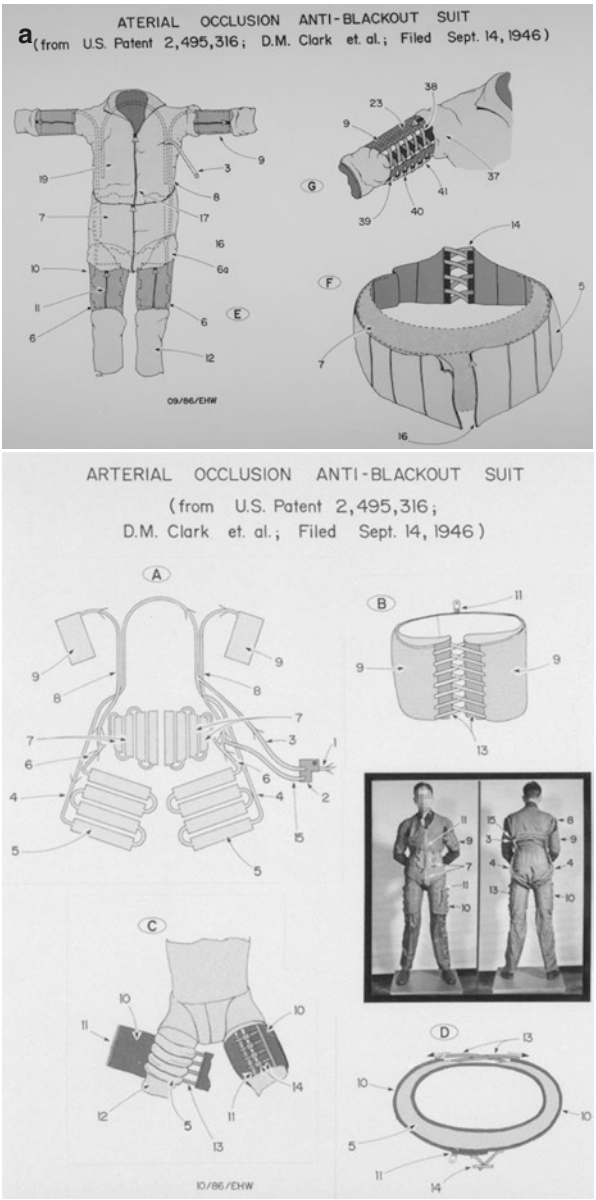

Fig. 1.3 (**a**) Patent application (2,495,316) filed on September 14, 1946, which resulted in the development of the G-suit with inflatable bladders on the calves, thighs, and abdomen. As the g-forces increased, bladder inflation resulted in peripheral arterial compression so that blood pressure increased sufficiently to maintain blood flow to the brain. (**b**) Physiology staff Ralph Sturm in G-suit. (Used with permission of Mayo Foundation)

Fig. 1.3 (continued)

benefit for pilots. The basis of this work and his incredible scientific and intellectual heritage has been highlighted in the most recent biography of Earl Wood by Ritman [1]. Elements in that project had immediate and direct implications for the entire field of cardiac catheterization. Two novel instruments of particularly early importance were developed. Pressure-measuring transducers were fabricated (Fig. 1.4) and made suitable for use with a fluid-filled intravascular catheter [2]. They were used to measure blood pressure (BP) at the level of the heart and simultaneously at head level by holding one catheterized radial artery in the wrist at heart level and the other wrist held at head level, respectively [3]. The other instrument that was developed was an earpiece device that measured the blood content of tissue by using infrared transmission (Fig. 1.5) [4]. Both were incorporated rapidly for investigational studies and then applied widely in clinical practice.

Other elements in the field facilitated the application of open-heart surgery, which was made possible by the development of the heart-lung bypass machine, as well as antibiotics. Unfortunately, the early success rate was very poor, in large

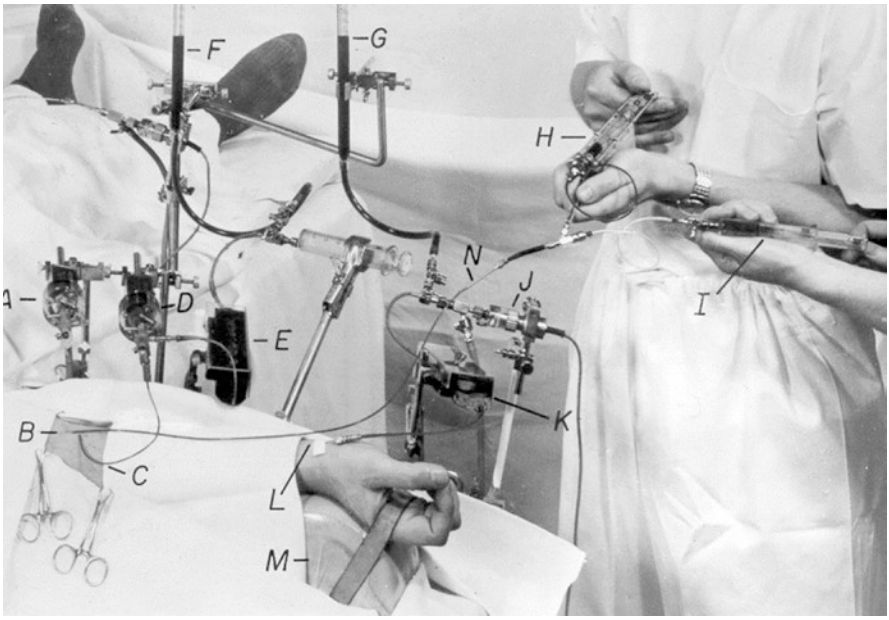

Fig. 1.4 Pressure transducers, blood oxygen content, and indocyanine dilution measurements were an integral part of physiologic experiments and procedures. They allowed measurement in a variety of clinical settings such as supine bicycling and measuring simultaneous pressures in different vascular beds. (Used with permission of Mayo Foundation)

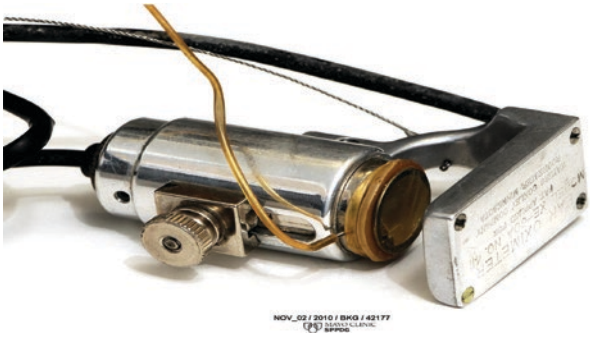

Fig. 1.5 The development of an earpiece oximeter in Dr. Earl Wood's laboratory at Mayo Clinic used light source and plunger in fully retracted position, with air tube to support inflation of rubber membrane against the pinna. This allowed rapid measurement of the blood content of tissue. The sensor could also provide a signal proportional to the oxygen saturation. (Used with permission of Mayo Foundation)

measure, because of inaccurate diagnosis of the anatomic problem [5]. Subsequent to the initial experiences and addressing lessons learned from Dr. John Gibbon working in Philadelphia, work continued at Mayo Clinic's Department of Physiology

Fig. 1.6 The initial Mayo-Gibbon heart-lung machine developed by Mayo Clinic in combination with Dr. John Gibbon was used in experimental procedures and then, in 1955, was used in an operation to close a large ventricular septal defect. (Used with permission of Mayo Foundation)

and the Section of Engineering and resulted in the Mayo-Gibbon heart-lung machine (Fig. 1.6), which was first used on March 22, 1955, by Kirklin in a 5-year-old girl with a large ventricular septal defect. In other patients with congenital heart disease and right-to-left shunts, there was mixing of non-oxygenated blood with oxygenated blood; the oxygen content of blood was therefore decreased, resulting in the clinical condition of "blue" babies [6].

Optimizing patient selection criteria and outcome was, in large part, dependent on the instruments Wood and his team developed for monitoring cardiovascular parameters for use during physiologic studies with the centrifuge and then applied in the clinical arena to increase diagnostic accuracy. Of special note is the incidental observation that the earpiece device (Fig. 1.5) for monitoring tissue blood content showed a change in signal due to the passage of a bolus of intravascular saline injected to flush the needle in the radial artery. This formed the basis for utilizing the shape and time distribution of indicator dilution curves to demonstrate the presence of intracardiac anatomic short circuit shunts.

Indicator dilution curve studies played a central role. However, a saline injection resulted in a small signal, so a dye was used to enhance the signal. For this, the indicator dye is injected into the arterial vascular bed or chamber under study. After rapidly injecting a known quality of the dye, there is mixing with flowing blood. After injection, the blood is then withdrawn at a constant speed downstream from the injection site through a device calibrated to detect the dye concentration. Flow can be calculated by the formula of the amount of dye injected, the mean

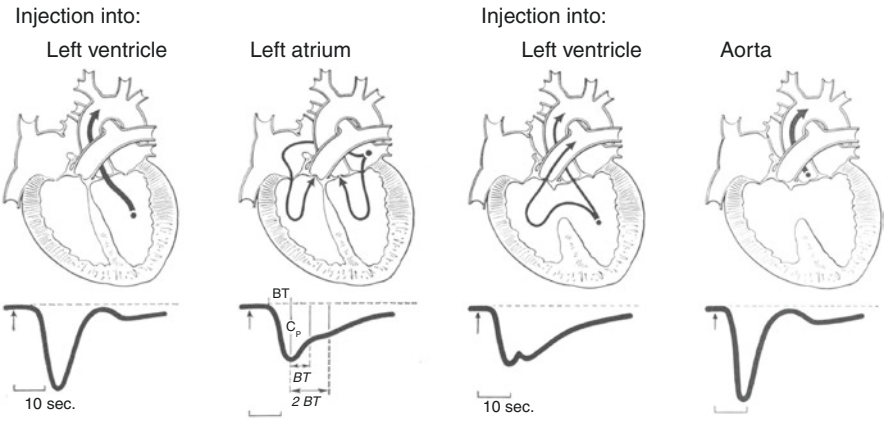

Fig. 1.7 Application of indicator dilution techniques in congenital heart disease. With injection into the left ventricle and sampling downstream, cardiac flow can be measured. An important component is complete mixing of the indicator, in this case in the left ventricle. The shape of the indicator dilution curve could provide information about intracardiac anatomic defects, as illustrated in this cartoon. (From Wood [7]; used with permission)

concentration of the dye, and the time of the concentration curve to the downstream detector, so as to provide the quantitative data needed to solve the Henriques-Hamilton principle [6] and determine flow. This method can be used for calculations of cardiac output as well as detection of intracardiac shunts in which there is recirculation of the dye (Fig. 1.7).

At that time, Evans blue dye was commonly used as the indicator for generating the dye curve rather than saline, as it generated a much more obvious dilution curve than did saline. The problem though was that in congenital heart disease, the blood is often poorly oxygenated (blue babies), and hence even the Evans blue curve would have reduced specificity and accuracy.

The focus of early studies evaluated the physiology of cardiac flow and function initially in experimental models and then in volunteers (Fig. 1.8) who were typically "recruited" Mayo Clinic fellows and graduate students interested in the field. Many of these fellows and students subsequently became leading Mayo Clinic staff physicians in cardiology, cardiac surgery, pulmonology, and physiology, while others moved to prestigious medical institutions throughout the world. Given their recruitment for multiple studies during training, it has been said that early cardiologists trained by Earl Wood often had absent radial pulses related to the frequent use of this artery for monitoring blood pressure during studies (a precursor of the now dominant use of percutaneous radial approaches for cardiac catheterization). As previously mentioned, studies involved the validation of an indicator dilution technique to evaluate flow patterns using Evans blue as the indicator for the measurement of flow and to evaluate recirculation patterns for detection of intracardiac shunts [8–10]. This indicator was subsequently discontinued, as it resulted in

Fig. 1.8 Cockpit of Mayo Clinic centrifuge, depicting "Project Mercury" experimental astronaut "couch," human volunteer wearing earpiece oximeter on the right ear, and powered injection syringe for indicator dilution studies of cardiac function. (Used with permission of Mayo Foundation)

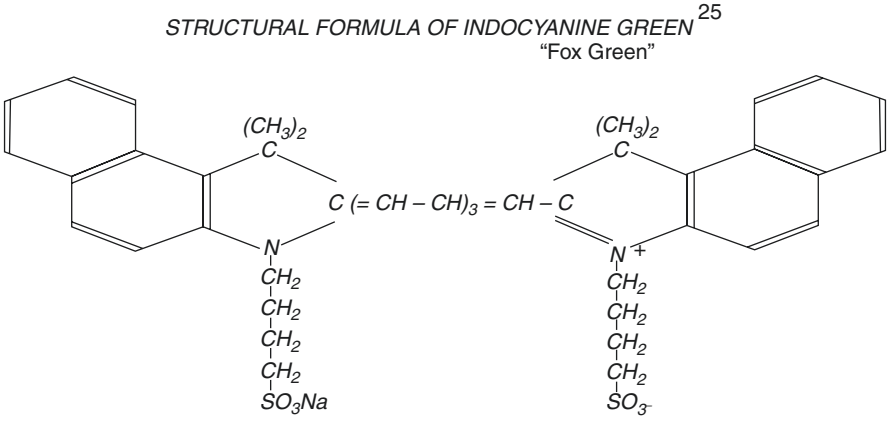

Fig. 1.9 Chemical structure of indocyanine green which became standard for catheterization indicator dilution studies. Its advantage was that its signal was not affected by the oxygen content of the blood

transient bluish coloration of the lips of the volunteers who were then easily identifiable by others as fellows in training.

Subsequent to the use of Evans blue, in 1957, indocyanine green dye (Fig. 1.9) developed by I.J. Fox, then a fellow, working in Earl Wood's laboratory [11, 12], became the standard. This dye subsequently became the worldwide standard for indicator dilution studies and forms the basis for indicator dilution approaches for assessment of cardiac function. Subsequent indicators have been incorporated in

pulmonary arterial catheters (aka Swan-Ganz catheters [10]) using temperature as the indicator or use of microbubbles in ultrasound imaging [11].

During this early time, clinical efforts were focused mainly on two groups of patients – those with congenital heart disease, both children and adolescents who were often cyanotic and patients with rheumatic heart disease, typically rheumatic mitral stenosis. Dramatic advances were being made in the surgical arena focusing, in part, on a Mayo Clinic program for performing open-heart surgery. John Kirklin (cardiovascular surgery) and Earl Wood met with the Mayo Clinic Sciences Committee to discuss the "production and experimental use of a mechanical heart in certain types of cardiac surgery" (p. 208) [13]. The team assembled at this time consisted of a research associate in physiology (Dr. H.J.C. (Jeremy) Swan), the Section of Engineering (Richard Jones), and a veterinary surgeon and physiologist (David Donald). This initiative plus other major collaborating work from pioneers throughout the country led to the field of open cardiac surgery and the initial experience with the Mayo-Gibbon heart-lung machine (Fig. 1.6).

Simultaneously, through this time period, there was the development and introduction of open surgical techniques for the treatment of structural heart disease, including both stenosis and regurgitant lesions of both the aortic and mitral valves, typically the result of rheumatic heart disease.

These advances, taken together, required continued development of techniques to evaluate and diagnose both congenital and valvular heart diseases. Accordingly, the new catheterization laboratory became increasingly busy, focusing predominantly on the application of indicator dilution techniques to accurately diagnose congenital heart disease aimed at evaluating patients for open-heart surgical procedures.

Initial catheterization procedures [2, 4, 14] included direct measurements of intravascular pressure, obtaining blood samples for oxygen content, which were used for assessing cardiac and extra-cardiac shunts and flow and for confirmation using indicator dilution studies. The same catheters used for sampling of blood could also be used to deliver radiographic contrast for the new and evolving field of angiocardiography. Earl Wood helped to co-author a 1953 AHA report [15] on the field, which advised that the use of angiocardiography be limited to established laboratories and institutions to obtain the maximum benefit from the clinical studies. An important impediment to the application and wider use of angiocardiography was image quality. Early studies required that the operators use red-tinted goggles (dark adaptor goggles) prior to the procedure to accommodate their eyes to the dim images generated by the X-ray passing through a flat, fluorescent screen (Fig. 1.10). (One of the authors actually used red-tinted glasses for fluoroscopic studies at a remote rural laboratory in Iowa during his moonlighting days in training.) Subsequent to these early dim experiences, in conjunction with biophysicist Ralph Sturm, the laboratory worked to identify X-ray image intensifiers that not only improved image quality but also decreased radiation [14]. Those development efforts, however, were less fruitful at that time (largely because of the inability to record the fluoroscopic image sequences). This resulted in the effect that emphasis remained focused on indicator dilution approaches for evaluating congenital heart disease patients.

Fig. 1.10 Dark adaptor goggles used to allow operators' eyes to adapt to the low-light features of fluoroscopic procedures. These googles implied that the user was close to the fluorescent screen and therefore exposed to the X-ray passing through the fluorescent screen

Fig. 1.11 A panoramic view of the DSR facility in the Medical Sciences building, close to the early cath lab. On the *left* (through the open door), the cath lab preparing the subject prior to the scan. To the *right* of the door is the control desk. Further to the *right* is the entry to the DSR scanner. The patient table advances into the scanner. On the far *right*, through an open door, is a partial view of the multi-X-ray source scanner. (From Ritman et al. [16] used with permission)

While the Mayo Clinic cath lab was located at the Medical Sciences building, the large majority of patients were hospitalized almost 1 mile away at St. Mary's Hospital. Concern arose because of the need for transfer back and forth by ambulance with medical assistance, usually physically, by a cardiology fellow in training with oversight by a staff cardiologist involved in the patient care. This same rather inefficient process was to be repeated some 20 years later, when adult and pediatric patients were transferred by ambulance from St. Mary's Hospital for clinical studies performed in the first fully 3D, cardiac CT scanner – the dynamic spatial reconstructor (DSR) (Fig. 1.11) [16]. One of the first clinical patients evaluated in this way is remembered by Dr. Hugh C. Smith, who had worked in Earl Wood's program and then became focused in clinical cardiology and the catheterization laboratory.

The patient had suffered a large anterior myocardial infarction with a resultant left ventricular aneurysm. Clinical considerations revolved on the ability of cardiovascular (CV) surgery with Dr. Hartzell Schaff to resect the aneurysm and whether that operation would be able to be targeted such that enough viable myocardium remained for patient survival. The DSR images obtained facilitated that discussion and the patient care decision that followed.

During the latter 1950s, those concerns about transfer of patients from St. Mary's Hospital to the "downtown" Medical Sciences building became increasingly more relevant because some of the children were very ill and the catheterization studies with multiple indicator dilution injections were very lengthy. After a very long study, moving into an ambulance for transportation back to the hospital and then returning the patient to their hospital room was fatiguing and a source of concern. These issues formed the basis of robust discussions involving multiple stakeholders – physiologists, cardiologists, cardiovascular surgeons, the Mayo Clinic Sciences Committee, and the Board of Governors. Two main topics were identified relating to somewhat different, although closely related, goals of the cath lab.

1. On the one hand, there were clinical catheterization procedures focused on making or substantiating a clinical diagnosis or used in making decisions as to the therapy or prognosis for the disease or for planning a therapeutic procedure for the specific patient under evaluation.
2. On the other hand, there were catheterization studies more focused for investigative (research) and educational purposes along with diagnostic evaluation as part of graduate school training in cardiovascular physiology [17].

In the summer of 1958, after considerable debate, the Mayo Clinic Board of Governors agreed that a new cath lab would be constructed on the grounds of St. Mary's Hospital, focusing more specifically on clinical diagnosis and establishing treatment strategies. However, as part of these considerations, there was an agreement that the facilities at St. Mary's Hospital would be closely associated and aligned with an angiographic (radiology) center, which would include all routine clinical catheterizations. This close association was specifically meant to encourage collaboration between radiologists and cardiologists; however, it had important and long-lasting implications in that radiologists were required to dictate all formal catheterization reports on clinical adult cardiology and pediatric cardiology patients despite the fact that all the procedures were performed by the cardiologists. That "collaborative arrangement" between cardiology and radiology lasted for approximately 15 years, during which time there were often very "frank and open" opinions ventured by cardiology concerning the need for radiology, including George Davis, Owings Kincaid, and Franz Hallerman, among others, to oversee coronary angiographic procedure reports. There were other important issues in the Board of Governors decision that related specifically to catheterization personnel, which also had major implications. A specific recommendation identified that "the best interests of the clinic would not be served in asking members of the Section of Physiology to devote valuable time and effort in the management of diagnostic procedures."

The result of this decision was that the new facility was independent and was formed under the direction and leadership of Swan (p.249) [13], who had been initially a research associate in physiology working under the supervision of Earl Wood. The direction given was that Swan was to confine his research activities to such investigations as "are derived from the clinical work of the laboratory" (p. 249) [13], relinquishing his research interests in other fields of physiology. This former research associate in physiology subsequently became a doyen of clinical cardiology and the President of the American College of Cardiology (1973), among other duties and honors, making fundamental strides and progress in the evaluation and care of patients for the rest of his brilliant career. Throughout that time, Swan influenced generations of physicians and scientists to come. He also continued to blend principles learned in the physiology laboratory under Earl Wood's tutelage, such as indicator dilution techniques with clinical unmet needs, resulting in the development of the ubiquitous "Swan-Ganz" catheter for pulmonary arterial catheterization for measurement of pulmonary flow and pressure in concert with Dr. William (Willie) Ganz in 1970 at the Cedars-Sinai Medical Center of UCLA in Los Angeles [10]. In parallel with that of Swan, Wood's multidisciplinary career as a physiologist continued to flourish and had profound influence on generations of physicians and scientists to come and who became prominent scientists and leaders in their own right. These individuals often maintained close relationships with Earl Wood. Of interest, one prominent biomedical engineer, Peter Osypka, who had trained in a post-doctoral position from 1963–1965 under Earl Wood, became a leading innovator and scientist in Germany. He started his company in the 1970s in Rheinfelden, Germany, after returning home from working in Earl Wood's lab. While in the lab, he developed the first split screen video display of the two biplane, angiographic images, which made Ralph Sturm's videometry feasible [18]. Osypka developed an extensive technological and biomedical engineering facility and large charitable foundation dealing with medical care. His initiatives resulted in a very successful German company, somewhat the equivalent of Medtronics in the United States. In 2002, to honor Earl Wood, Osypka renamed and dedicated the "Earl H Wood Strasse" in Rheinfelden, where the Osypka facility is located (Fig. 1.12). The road was named for Earl Wood as a token of appreciation of Wood giving Osypka his first opportunity to show his capabilities. This is another example of the indirect but significant influence of the cath lab beyond the direct cath lab needs. A notable achievement for Earl Wood was his selection as the tenth scientist who was identified as a "career investigator" of the American Heart Association; he also received the Presidential Certificate of Merit from President Harry Truman in 1947 for his contribution to Operation Paperclip. He would continue and expand his focus on scientific research that would be applied by both clinicians and physiologists in the clinical arena to improve imaging, solve complex physiologic problems, and continue to lead the way for addressing unmet clinical needs in both pediatric and adult patient populations. Both Earl Wood and Swan were the stuff of legends.

- Initially, the cardiac cath lab at St. Mary's Hospital under Swan's leadership remained administratively in the Department of Physiology. Dr. Don Ritter, a