A Brief History of Interventional Cardiology

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In the past few decades there has been increased development and demand for minimally invasive procedures in orthopedic and soft tissue surgery. Cardiology is no exception to this trend, but it is interesting to see where interventional cardiology began. Interventional cardiology procedures originated in diagnostics, and several decades passed before therapeutic techniques were developed. Most of the developments in interventional cardiology were a result of the resourcefulness of doctors and engineers, their ability to risk patients’ health, and their interest in improve patients' health. Veterinary and human cardiology have been interdependent since their inception.

As primitive cardiology techniques were developed more information was learned about the heart and how it functions. In the early 1700s, Stephen Hales measured the blood pressure of multiple animals including horses and dogs using a glass cylinder. He attached the glass cylinder to the carotid artery using a goose trachea\(^5\). This method is similar to how central venous pressure is currently measured. Hales also exsanguinated a horse and filled the ventricle with wax to calculate the stroke volume and cardiac output of the horse. Over a century later J.B. Auguste Chauveau and Etienne Marey made catheterization records in 1860 which allowed them to determine that the apex beat happened in conjunction with systole\(^5\). Together Marey and Chauveau recorded transvascular cardiac pressures using homemade balloon catheters in the right side of the heart and over the intercostal muscles. Alongside the discovery of information regarding the heart’s function such as blood pressure, stroke volume, and cardiac output, invasive techniques were developed to assess the heart and the cardiovascular system.

Cardiac catheterization, as Bernard Cournand said, was “the key in the lock” for interventional cardiology, opening the door for the development of much more advanced techniques such as pacemaker implantation, percutaneous PDA occlusion and balloon valvuloplasty. In cardiac catheterization procedures a catheter is passed through a peripheral blood vessel, often the femoral vein or artery, into a chamber of the heart. Cardiac catheterization did not appear until Bernard described it when describing his successful attempt in a horse. Williams and Dunlop, the authors of *Veterinary Medicine: An Illustrated History*, named Bernard as the pioneer of cardiac catheterization for completing the first cardiac catheterization on a horse in 1844\(^8,9\). Bernard entered the right and left ventricles using a retrograde approach from the jugular vein and carotid artery, and discovered that the blood’s temperature in the right side of the heart exceeded the left proving the lungs were not the source of the body’s heat generation as previously thought\(^5\). The left heart was possibly first catheterized in 1831 by Dieffenbach, a Prussian surgeon\(^7\). But this was really an attempt to perform a better therapeutic phlebotomy in a patient dying of cholera. There is some doubt of course about this attempt because there is little to no documentation, and so traditionally the credit of the first successful human cardiac catheterization has gone to Dr. Werner Forssmann.
who performed it on himself in 1929. He hoped to be able to administer medications and contrast material directly into the right atrium for cardiac resuscitation. Despite losing his job over the self-experiment, Forssmann was awarded the Nobel Prize in Medicine in 1956 along with Dr. Andre Courmand and Dr. Dickinson Richards10. Louis Desliens was able to use cardiac catheterization to study cardiac diseases in horses and cattle, as well as develop a carotid artery injection method and a new way of recording cardiovascular information called blood throw. His method for detecting blood pressure was called hemodynamometrie. Diagnostic uses of cardiac catheterization were just the first step in its development.

Once cardiac catheterization was developed other techniques and products would soon follow, and one of the next logical steps was coronary arteriography. Before both cardiac catheterization and coronary arteriography were developed, angiography was first performed by physicist Eduard Haschek and Dr. Otto Lindenthal in 189610. Angiography is the “radiographic technique which enables the blood-flow to and from an organ to be visualised after injection of a contrast medium11”. Haschek and Lindenthal used the hand of a corpse, injected an iodine solution into the arteries, and applied X-rays producing the first angiogram10. This then progressed to the first angiogram of peripheral arteries done by Dr. Barney Brooks in 192410. The use of angiography specifically in the coronary arteries is called coronary arteriography. Coronary arteriography was first performed by Dr. Mason Sones in 195812, and led to the discovery of coronary artery disease. However, a coronary arteriogram was not the primary purpose of Sones’ procedure. It began as an aortic root aortography, but the catheter entered the right coronary artery. Before the catheter could be relocated contrast was administered, producing the first coronary arteriogram13. Dr. Sones realized what occurred and its possible applications. Dr. Sven-Ivar Seldinger developed the percutaneous approach for coronary revascularization in 1953 which is more commonly used today over the previous “cut down” method in which soft tissue was dissected until the artery or vein was visualized2. Using the Seldinger technique (Figure 3) the vessel is located using the arterial pulse, and a catheter is entered into the vein through the skin and subcutaneous tissues. Dr. Melvin Judkins began making the materials specific to coronary artery arteriography in the 1960s, and developed the percutaneous transfemoral technique for selective coronary arteriography14. As early as 1968 Judkins’ catheters were being commercially manufactured. Dr. Judkins’ wife talked about his view of the technique:

“Although a properly shaped catheter was the key to success, he always emphasized that his technique was not confined to the use of his catheters. The Judkins technique embraced a combination of professional skill in transfemoral access and manipulation of unique preshaped catheters, proper patient position for filming, and high-quality radiographic hardware to produce and record optimum information while protecting patient and laboratory team from unnecessary radiation exposure14.”

Throughout his career Dr. Judkins never made any attempts to patent or monetize the production of his devices. He cited his reason for this as “he wanted to make safe coronary arteriography available to as many patients14.”
One type of product made possible by cardiac catheterization, and also utilized to treat coronary artery disease is a coronary stent. As is often the case, stents were first explored in animals. In 1912 Alexis Carrel described his attempt at permanent intubation of the aorta in a dog. Carrel said: “The permanent intubation of a large vessel is a simple operation. It may become practical, if the shape and the nature of the tube be modified as to avoid lacerations…. The question of the application of this method to human surgery may then, possibly, be considered.” Coronary angioplasty, the surgical unblocking of the coronary artery, was originally theorized in 1964 by Dr. Charles Dotter and Dr. Melvin Judkins, but it wasn’t performed until 1977 by Andreas Gruntzig. Later that year Gruntzig would perform the same procedure in an awake patient. Dotter and Gruntzig received a nomination for the Nobel Prize in Physiology and Medicine in 1978 for the use of balloon angioplasty as a therapeutic procedure for atherosclerotic vascular disease. Angioplasty without stent placement is termed plain old balloon angioplasty (POBA). Since its introduction balloon angioplasty has become one of the most frequently used therapies for vascular emergencies in the heart and peripheral circulation of the body.

Coronary stents started to be produced beginning in the mid-1980s. Coronary stents were devised mainly to combat many of the complications associated with POBA including dissection or elastic recoil, vascular remodeling and neointimal proliferation. Stents began with Dr. Julio Palmaz who attended a lecture by Gruntzig in 1978 and theorized “the problem that doctor Gruntzig had with his balloon could be avoided by inserting some sort of a scaffold at the time of dilatation.” In Palmaz’s design the wire was wound around a pencil, and was soldered so the mesh could keep its shape. Unfortunately his design was too rigid and companies refused to produce it. At the end of the 1980s Dotter tried a different method, inserting plastic tubes and collapsible stainless-steel prostheses instead of dense metallic devices, into the femoral or popliteal arteries of dogs. In 1986 another leap in interventional cardiology was made when Sigwart and Paul implanted the first stent in a human coronary artery. This first stent called a Wallstent was a self-expanding structure made from stainless steel wire mesh. The Wallstent had limited clinical applications and was removed from production just five years after its introduction. The FDA first approved a stent in 1987, produced by Schatz and his colleagues. This version was a balloon-expandable, slotted tube device made of stainless steel and was commonly used in the 1990s. The high density metal of the Schatz’s stent resulted in higher reports of stent thrombosis and failure of deployment due to its complex nature.

Overall stents were so successful that before the turn of the century 85% of percutaneous coronary intervention procedures included stenting. After many permutations, the current standard of care in humans consists of balloon angioplasty and drug eluting stents. The drug-eluting stent (DES) was first used by Eduardo Sousa in 1999, and has been important in preventing restenosis (one of the major complications of stents). DES devices contain two parts: a polymer which coats it and a drug which is delivered to the vessel wall. As with most medical products, stents have undergone many changes in materials. Originally they were stainless steel which is biologically inert but they were later altered to cobalt-chromium which can be thinner. Currently stents are being developed in different polymers and drug-eluting stents with.

Figure 4: Depiction of early coronary stents, including the Wallstent
different coatings. While coronary angioplasty is not performed in veterinary medicine, it has become a mainstay in human medicine thanks to the first attempts done in animals.

Another interventional technique, balloon valvuloplasty, is the treatment of choice for pulmonic stenosis, a common congenital cardiac disease, in both humans and dogs. Balloon valvuloplasty can also be used for dogs with clinical signs related to severe aortic or subaortic stenosis, though this use is far less common than that of pulmonic stenosis. Balloon valvuloplasty was first tested in dogs at Johns Hopkins University, where the review board approved it for use in humans once the safety in dogs was established. The first patient at Johns Hopkins was a 5-month old English Bulldog who underwent balloon valvuloplasty on October 7th, 1980. Unfortunately this dog died due to the coronary artery anomalies, but this did not stop the development of the balloon valvuloplasty procedure which is now used daily to treat humans with pulmonic stenosis. Use of balloon dilatation to treat a stenotic valve was concerning from its inception because the technique would result in a sudden increase in right ventricular pressure and an interruption in circulation. However in the case of this first Bulldog, his death was likely due to the coronary anomalies associated with the English Bulldog breed; a study of balloon valvuloplasty in 35 dogs where two dogs died, both English Bulldogs, confirms this correlation and likely causation. Balloon valvuloplasty was first performed in humans for the treatment of pulmonic stenosis in 1982 when it was first utilized on a child, followed soon after by an adult.

A third condition that is consistently treated using an interventional method is patent ductus arteriosus (PDA), one of the most common congenital heart defects in canines, and caused by the failure of the ductus arteriosus muscle to constrict after birth. The treatment of PDAs began as a standard surgical procedure, first performed in a human by Gross and Hubbard in 1939 and in a dog by Dr. Willis Potts in the 1950s. But today this is commonly corrected using minimally invasive techniques, including thorascopic ligation and intravascular coils or other occluding devices such as duct occluders or vascular plugs. These interventional techniques have been so successful thus far that traditional surgical and thorascopic ligation is becoming less common. Interventional techniques have a combined morbidity and mortality rate of 1% compared to 2-8% associated with surgical ligation. Portsmann was the first to attempt the transcatheter PDA closure in 1967. Almost thirty years later in 1994 the percutaneous transvascular PDA closure was completed in a dog. Interventional closure of PDAs has become so common place that traditional surgical closures are being taught in fewer and fewer programs, and the condition itself is so common that specific devices have been developed for its occlusion making the need for surgical closure more and more obsolete.

Another common interventional cardiology procedure is the implantation of cardiac pacemakers to treat a variety of cardiac conditions. Dr. Paul Zoll developed an external pacemaker in 1951 that was utilized to effectively treat heart block. Zoll’s design included an electrocardiograph (ECG) to monitor the heart’s rhythm and an electric pulse generator used to pace the heart periodically. A year after its development, Zoll used his external pacemaker to treat two people with prolonged ventricular standstill. The first “wearable” pacemaker was developed in 1957 by Earl E. Bakken, an electrical engineer and TV repairman. Bakken’s device was the first battery operated device, but despite this development Bakken said “We never made any serious money on that early custom-building activity, rarely even recouping the cost of the prototype….everything we did, we lost money on!” In the late 1950s a cardiac surgeon at the University of Minnesota, Dr. C. Walton Lillehei, produced the myocardial wire which was implanted into the myocardium and connected to an exterior stimulator. With the new

![Figure 5: Bakken's First External Pacemaker](image)
technique of directly stimulating the myocardium a much lower voltage could be used for effective pacing, and the wire could easily be removed if the patient’s heart resumed normal conduction. The first successful use of the Lillehei’s myocardial wire was in a 3-year old girl with heart block on January 30th, 1957. Unfortunately this wire was dependent on the external source powering the stimulator, and limited the portable nature of the device. After the death of a baby on the external stimulator, Lillehei approached Bakken about developing a more portable device. Their first prototype would be tested on a dog; Bakken described it: “without any grandiose expectations for the device, I was moderately optimistic about what it might eventually do for Lillehei’s patients. I drove the device over to the University’s animal lab where it could be tested on a dog. Of course it worked.” Bakken was shocked when he saw the same device on a girl in the hospital the next day; it took only four weeks from initial development to the first implantation in a human. They quickly determined that a similar internal device would be necessary due to the ascending infections associated with the pacing electrodes. In his 1960 paper Lillehei said “the question of how long stimulation can be maintained appears to be related to electrode materials, design and technique of implantation.” Despite all of the developments made by Lillehei and Bakken they would not be the first ones to fashion and implant an internal pacemaker. This honor goes to surgeon Dr. Ake Senning and inventor Dr. Rune Elmqvist who implanted a pacemaker into 43-year old Arne Larsson on October 8th, 1958. For Larsson who suffered from Stokes-Adams attacks, requiring resuscitation multiple times a day, this pacemaker was a desperate measure. The first implanted pacemaker actually failed; Senning said: “Presumably, I had damaged the output transistor or capacitance with the catheter and I did not have the other one which was in the lab. I implanted the other one early the next morning. In the 1950’s we did not have any liability problems. The patient and relatives were happy if the patient survived.” In the end Larsson outlived both Elmqvist and Senning, dying in 2001 at the age of 86, and required 22 pacemakers of 11 different models over the course of his life. In 1958 Wilson Greatbatch, surgeon Dr. William Chardack, and surgeon Dr. Andrew Gage worked together to test a new implantable pacemaker with a much smaller resistor than previously thought possible. On May 7th they tested the device in a dog. Following the first test, the trio conducted two years of experiments in animals, and reported the first successful implantation of the device in a human in 1960. Though pacemakers were developed and tested in animals the first clinical implantation of one did not take place until 1967. This first canine patient was a 10-year old male Basenji who suffered from complete heart block. Over five years later at his pacemaker replacement the dog was still in good health, and his pacemaker was removed easily. Other developments in the following decades would include programming via radio frequencies, dual-chamber pacemakers with the ability to pace and sense both the atria and ventricles, and drug-eluting leads similar to the drug-eluting stents used in to treat coronary artery disease. Though the first pacemakers were not developed in animals, dogs were an important part in the development of the pacemakers we rely on today.

Interventional cardiology is a field that was essentially born less than two centuries ago, and has made the most progress in the last several decades. The area began by developing techniques specifically diagnostic in nature. Now nearly two centuries after the first cardiac catheterization most procedures are for treatment of diseases rather than diagnostics. Many of the procedures done in humans were first attempted in animals, including cardiac catheterization, coronary stents, and internal pacemakers, but were not practiced regularly in animals until a few decades later. Veterinary interventional cardiology is not a recognized subspecialty of veterinary medicine, operating within cardiology services primarily. As
new procedures and equipment are developed, methods beyond treating the three primary procedures, PDA occlusion, balloon pulmonary valvuloplasty, and transvenous pacing are becoming more common. In conjunction with these developments new educational opportunities such as fellowships specific to interventional cardiology are beginning, with the first official program starting in 2016 at Colorado State University. As with most things in medicine, both veterinary and human interventional cardiology is indebted to the animals that were used in the development of procedures and devices.

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