A history of collaboration between electrophysiologists and arrhythmia surgeons

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Abstract

Introduction: The notion that medically-refractory arrhythmias might one day be amenable to interventional therapy slowly began to appear in the early 1960's. At that time, there were no "interventional electrophysiologists" or "arrhythmia surgeons" and there was little appreciation of the relationship between anatomy and electrophysiology outside the heart's specialized conduction system.

Methods: In this review, we describe the evolution of collaboration between electrophysiologists and surgeons.

Results: Although accessory atrio-ventricular (AV) connections were first identified in 1893 and the Wolff-Parkinson-White (WPW) syndrome was described 37 years later (1930), it was another 37 years (1967) before those anatomic AV connections were proven to be responsible for the clinical syndrome. The success of the subsequent surgical procedures for the WPW syndrome, AV node reentry tachycardia, automatic atrial tachycardias, ischemic and non-ischemic ventricular tachycardias and atrial fibrillation over the next two decades depended on a close, sometimes daily, collaboration between electrophysiologists and surgeons. In the past two decades, that tight collaboration was largely abandoned until the recent introduction of "hybrid procedures" for the treatment of atrial fibrillation.

Conclusions: A retrospective assessment of the 50 years of interventional therapy for arrhythmias clearly demonstrates the clinical benefits of a close collaboration between electrophysiologists and arrhythmia surgeons, regardless of which one is actually performing the intervention.

KEYWORDS
atrial fibrillation, atrial fibrillation surgery, electrophysiology, multidisciplinary collaboration
INTRODUCTION

This article is a summary of the closing lecture at the Catheter Ablation and Surgical Therapies for Atrial Fibrillation (CAST-AF) conference held in Chicago, Illinois on August 27–28, 2021. The annual CAST-AF conference is structured around the objective of bringing interventional electrophysiologists (EP) and arrhythmia surgeons together to exchange knowledge across specialties to enhance both group's understanding of the interventional treatment of atrial fibrillation. This article is not meant to be a definitive historical account of the evolution of interventional arrhythmia therapy. Rather, it is meant to be an account of the most successful examples of collaboration between surgeons and cardiologists that impacted the current state of arrhythmia therapy. The main criterion used to select the events discussed in this article was that the contribution had to come from an EP/surgeon team, not from an individual EP or an individual surgeon. An exception to that restriction was Haissaguerre's identification of pulmonary vein triggers which opened the way for catheter ablation. That contribution was too important to go unmentioned, though there was no apparent surgical involvement in the event. Restricting the selected events to only those generated by a collaborative EP/surgeon team automatically excluded a number of important historical events that were critical to the understanding and evolution of the interventional therapy for arrhythmias.

IDENTIFICATION OF THE SITE-OF-ORIGIN OF ISCHEMIC VENTRICULAR TACHYCARDIA (VT)

From the late 1960s to the late 1990s, the collaboration between cardiologists and surgeons in developing interventional therapy for refractory cardiac arrhythmias was sustained and intense. In 1964, Cox (an aspiring surgeon) began working as a freshman medical student in the basic science electrophysiology laboratory of Dr. Nancy Flowers (electrophysiologist) and Dr. Leo Horan (electrophysiologist). Flowers and Horan were both friends with John Boineau, a young pediatric cardiologist/electrophysiologist at Duke University who had spent 1963–1964 working in the laboratory of the man who eventually became known as the "Father of Electro-physiology," Prof Dirk Durrer of Amsterdam (Figure 1). Flowers introduced Cox to Boineau at the American Heart Association meeting in New York City in November 1966.

Flowers and Horan suspected that VT associated with myocardial infarctions most likely originated in an undefined zone of myocardium located outside the actual infarction that was neither normal myocardium nor dead myocardium. However, no such intermediate zone had ever been identified histologically, so Cox was given the task as a medical student of finding it if it existed. Experimental myocardial infarctions were created in dogs and following sacrifice several weeks later, a commercial meat slicer was used to slice the infarcted hearts serially into cross-sectional 1 cm slabs from apex to base. Each 1 cm cross-sectional heart slab was then divided into individual segments and each segment was quick-frozen with liquid nitrogen. Multiple 8 micron-thick endocardial-to-epicardial slices of each frozen segment were harvested with a cryotome and stained for succinic dehydrogenase with nitro blue tetrazolium for histological examination. After numerous failures, the pH of the staining solution was inadvertently adjusted incorrectly 1 day and to everyone's surprise, three separate "zones" of the myocardium could actually be seen on the microscopic slides with the naked eye. The pH of the stain was adjusted accordingly for subsequent experiments and it soon became apparent that myocardial infarctions were characterized by a central zone of necrosis that was separated from normal myocardium by an intervening zone of viable but damaged myocardium. This study was the first to document the presence of an anatomic "ischemic border zone" surrounding acute myocardial infarction and it served as the basis for numerous subsequent efforts to decrease the ultimate size of myocardial infarctions over the ensuing two decades.
At that time, the WPW syndrome was recognized as a potential godsend to those who were interested in developing interventional arrhythmia therapy for arrhythmias because of the simplicity of the underlying anatomic-electrophysiologic abnormality. However, despite the WPW syndrome having been described first in 1931, there was still surprisingly vigorous debate among authorities regarding the underlying electrophysiology of the syndrome in the late 1960s. Many believed that the reciprocating tachycardia (RT) associated with the WPW syndrome was the result of longitudinal dissociation within the Bundle of His while others believed that it was due to conduction across an anatomic accessory atrio-ventricular (AV) connection first described by Stanley Kent in 1893. These abnormal AV connections were often called “Kent Bundles” but until 1967, no anatomic Kent Bundle had ever been documented to conduct electrical activity.

In 1967, Boineau mapped the epicardium in a dog with the WPW syndrome brought to him by E. Neil Moore, MD, DVM an electrophysiologist at the University of Pennsylvania Veterinary School. Boineau and Moore mapped the dog extensively and were able to identify the precise site of ventricular pre-excitation during normal sinus rhythm and the earliest site of atrial activation during induced RT. The animals’ heart was then submitted for histological examination to Dr. Donald Hackel, a cardiac pathologist at Duke, who was purposely kept unaware of Boineau’s suspected location of the accessory AV connection. The AV grooves of both the right and left sides of the heart were serially sectioned by Hackel in search of an anatomic accessory AV connection and one was found (Figure 2) at the exact site that the mapping had predicted. This confirmed that the single, large, and macro-reentrant circuit that could be mapped during the RT in WPW patients was dependent on the ability to conduct electrical activity across an abnormal AV connection. This observation was not published in a peer-reviewed journal until 1970, but it was well known within the small community of cardiologists and surgeons working in the field in 1967.

In early, 1968, Dr. Howard Burchell (electrophysiologist) and Dr. Dwight Magoon (surgeon) at the Mayo Clinic had a patient with the WPW syndrome who needed her secundum atrial septal defect closed. At surgery, Burchell electrically mapped the heart and located the site of ventricular pre-excitation in the right ventricular free-wall (Figure 3). Based on Boineau’s recent documentation of the now indisputable anatomic-electrophysiologic basis of the WPW syndrome, Magoon injected lidocaine into the AV groove at the site of the suspected AV connection and the pre-excitation disappeared immediately. Electrical conduction across the accessory AV connection resumed shortly after surgery but the temporary lidocaine block
Successful Surgical Interruption of the Bundle of Kent in a Patient with Wolff-Parkinson-White Syndrome

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in conduction across the accessory AV connection further confirmed the pathophysiology underlying the WPW syndrome. Three months later, on May 2, 1968, Drs. John Boineau and Andrew Wallace (electrophysiologist) mapped a patient with the WPW syndrome and Dr. Will Sealy (surgeon) performed the first surgical transection of an accessory AV connection (Figure 4). In doing so, they initiated the era of interventional therapy for the treatment of cardiac arrhythmias. The patient, a fisherman from the Outer Banks of North Carolina, lived another 33 years and never had another episode of tachycardia.

These events represent the first examples of EP and surgeons working together to treat cardiac arrhythmias successfully by direct intervention. Hundreds of patients in the United State, Europe, Asia, and Australia subsequently underwent surgery for the WPW syndrome over the ensuing decade with results that were quite good, although multiple separate operations were often required to attain final success.

In the summer of 1969 Cox (Duke surgical resident) spent 1 year working full-time in Boineau’s basic electrophysiology laboratory at Duke University (Figure 5). Together, they performed extensive mapping of infarcted canine ventricles and showed that just as Flowers and Horan had suspected earlier, ischemic VT was induced by premature ventricular beats that were initiated by micro-reentry in the damaged but viable ischemic zone surrounding acute myocardial infarctions.

Dr. John Gallagher (electrophysiologist) led the clinical electrophysiology team at Duke beginning in 1971 and with Dr. Sealy as the...
arrhythmia surgeon, they were successful in ablating 61% of WPW syndromes with a single surgical procedure and 87% with single or multiple surgical procedures over the next decade. In 1978, Cox gradually assumed Dr. Sealy’s role in arrhythmia surgery at Duke and in 1980, modified the surgical technique for performing WPW surgery with the full support of Drs. John Gallagher, Larry German, Ed Pritchett, and Woodrow Benson, all clinical EP. Thereafter, the success rate for WPW surgery at Duke, and later at Washington University in St. Louis, was 100% with the initial single surgical procedure.8

4 | SURGERY FOR ISCHEMIC VT

In the late 1970s, the clinical focus in arrhythmia surgery shifted to VT. In the fall of 1976, three arrhythmia surgeons (Sealy, Cox, and Girard Giraudon of Paris) and one electrophysiologist (Gallagher) had a memorable dinner in Durham, NC during which numerous table napkins were cut into pieces late into the evening while trying to visualize a surgical procedure that might be successful for the treatment of ischemic VT. By 1978, Guiraudon and his EP, Guy Fontaine and Robert Frank in Paris, had developed just such a direct surgical approach to ischemic VT therapy called the Encircling Endocardial Ventrilulotomy.9–13 Virtually simultaneously, Drs. Mark Josephson (electrophysiologist) and Alden Harken (arrhythmia surgeon) developed the Subendocardial Resection procedure for ischemic VT at the University of Pennsylvania9 to which Cox and Gallagher at Duke added endocardial cryoablation (Figure 6). The latter procedures were based on multiple analog mapping systems that were specifically developed with a team of arrhythmia surgeons, EP, biomedical engineers, and technicians. (Figure 7).15

All of those analog mapping systems were supplanted by the first multipoint computerized mapping system developed by Drs. Frank Witskowski (cardiologist/engineer) and Peter Corr (electrophysiologist/pharmacologist) at Washington University in St. Louis in the early 1980s. In 1983, Cox joined Witkowski and Corr, as well as the clinical EP at Barnes Hospital/Washington University, Drs. Michael Cain and Bruce Lindsay. Eighteen months later, Drs. John Boineau and Richard Schuessler (biomedical engineer) were recruited to direct the Cardiac Surgery Research Laboratories at Washington University. They quickly established a basic electrophysiology unit that supported the clinical electrophysiology/arrhythmia surgery team. The first patients who were mapped using this new computerized mapping system had either the WPW syndrome or ischemic VT. Dr. Jeffrey Kramer (surgical resident at Wash U) and Dr. Peter Corr developed the “band electrode” that greatly simplified and shortened the mapping of WPW patients.
In 1979, Cox performed several regional surgical isolation procedures for the treatment of both idiopathic nonischemic VT and arrhythmogenic right ventricular dysplasia (ARVD) based on preoperative and intraoperative mapping by Gallagher (Figure 8, upper panel). In 1982, Guiraudon combined our two regional RV isolation procedures into a single procedure for isolating the majority of the free wall of the RV from the rest of the heart for ARVD, a rare condition that had originally been described by his EP, Fontaine and Frank. Based on preoperative and intraoperative mapping performed by Gallagher and Dr. Larry German (electrophysiologist), Cox successfully performed two Right Ventricular Disconnection Procedures in 1982 in which the entire RV free wall was separated from the rest of the heart (Figure 8, lower panel). One of these patients was a 16 year-old male who had previously received full cardio-pulmonary resuscitation (CPR) for ventricular fibrillation over 250 times due to ARVD. Drs. Levi Watkins (arrhythmia surgeon) and Phil Reed (electrophysiologist) at Johns Hopkins University had previously implanted one of the first automatic defibrillators in the patient and while effective, it did not entirely ameliorate the problem of repeated episodes of cardiac arrest requiring CPR. At surgery, the defibrillator was removed and a Right Ventricular Disconnection Procedure was performed. The patient never had another episode of VT and actually became an accomplished weight lifter. He was finally lost to follow-up in 1999, 17 years after surgery.

5 | SURGERY FOR NON-ISCHEMIC VT

In 1980, we reported the surgical technique for the Left Atrial Isolation Procedure that was developed experimentally by Cox and Williams (Duke surgical resident) over the previous 2 years in our Surgical Electrophysiology Laboratory. Based on preoperative and intraoperative mapping performed by Gallagher and Dr. Larry German (electrophysiologist), Cox successfully performed two Right Ventricular Disconnection Procedures in 1982 in which the entire RV free wall was separated from the rest of the heart (Figure 8, lower panel). One of these patients was a 16 year-old male who had previously received full cardio-pulmonary resuscitation (CPR) for ventricular fibrillation over 250 times due to ARVD. Drs. Levi Watkins (arrhythmia surgeon) and Phil Reed (electrophysiologist) at Johns Hopkins University had previously implanted one of the first automatic defibrillators in the patient and while effective, it did not entirely ameliorate the problem of repeated episodes of cardiac arrest requiring CPR. At surgery, the defibrillator was removed and a Right Ventricular Disconnection Procedure was performed. The patient never had another episode of VT and actually became an accomplished weight lifter. He was finally lost to follow-up in 1999, 17 years after surgery.

6 | DEVELOPMENT OF SURGICAL PROCEDURES FOR OTHER CARDIAC ARRHYTHMIAS 1978–1983

In 1980, we reported the surgical technique for the Left Atrial Isolation Procedure that was developed experimentally by Cox and Williams (Duke surgical resident) over the previous 2 years in our Surgical Electrophysiology Laboratory. Not only was this procedure successful for its intended purpose, but the conduction of electrical activity by the coronary sinus was first documented during the development of this procedure. Years later, this observation became critical to the success of the Maze procedure for atrial fibrillation. After intraoperative mapping by Gallagher and German, the Left Atrial Isolation Procedure was first applied clinically in December 1982 by Cox on a patient of Dr. Michael Cain, an electrophysiologist from St. Louis (an initial surgeon/electrophysiologist collaboration that was destined to become much closer in the near future). After nearly 2 years of intensive experimental work in our laboratory by
Holman, Masatoshi Ikeshita (visiting surgeon from Japan), and Cox on AV node reentry tachycardia (AVNRT). Cox and Gallagher performed the first clinical Discrete Cryosurgical Procedure for AVNRT in June 1982 in a 37-year-old female who remained free of AVNRT thereafter. One year later, both Gallagher (cardiologist) and Cox (surgeon) left Duke University for the Sanger Clinic in Charlotte and Barnes Hospital/Washington University in St. Louis, respectively.

7 | 3-DIMENSIONAL (3-D) MAPPING DURING ATRIAL FIBRILLATION

In the early 1980s, Dr. Michael Vanier, a radiology colleague in the Mallinkrodt Institute of Radiology at Washington University, developed a technique of “stacking” magnetic resonance imaging (MRI) brain scans to create 3-D reconstructions of the anatomy of the brain and cranium. In 1986, we asked him if he could do the same with the heart and he responded by developing “gated MRI scanning” that could be synchronized with the patient’s electrocardiography to allow reconstruction of the specific 3-D anatomy of that subject’s heart. By 1985, Boineau, Schuessler, and computer programmer Barry Branham, had developed computerized methods in our surgical electrophysiology laboratory for mapping atrial electrical activity from multiple sites in the atria simultaneously. They developed silastic molds of dog atria and embedded 256 bipolar “target” electrodes on the surfaces of the endocardial molds (Figure 9, left panel). By superimposing the specific 3-D electrophysiology maps in each animal on the 3-D anatomic image of the atria in that specific animal, it was possible for the first time to construct anatomically-accurate 3-D maps of experimental atrial fibrillation (Figure 9, right panel). Boineau and Schuessler then constructed thin silastic sheets that form-fit onto the exposed epicardial surfaces of both atria in humans and they then embedded an array of 156 bipolar electrodes on the surface of those silastic sheets (Figure 10, left panel). This made it possible to create 2-D global maps of atrial fibrillation for the first time in humans (Figure 10, right panel).

8 | SURGERY FOR ATRIAL FIBRILLATION

The development of an experimental animal model of AF that was more relevant to clinical AF by Cox and Dr. Peter Smith (Duke surgical resident) in 1980 served as the cornerstone for the experimental mapping studies of AF for the next decade. The details of that model have been described previously. We also had the availability of mapping human atrial fibrillation during clinical surgery.
FIGURE 9  Electrode arrays for Computerized Mapping of experimental atrial fibrillation. Left panel: 3-dimensional (3-D) silastic mold electrode arrays that made it possible to perform 3-D mapping of atrial fibrillation in dogs for the first time. Right panel: Images taken from a video of experimental atrial fibrillation in which the 3-D electrode array data were superimposed on the reconstructed 3-D image of the animal's atria from gated magnetic resonance imaging scans. This particular map was recorded in 1987.

FIGURE 10  Mapping of human atrial fibrillation, c. 1987. Left panel: Electrode arrays with a total of 156 bipolar electrodes in three separate silastic sheets. They are shaped to cover (A) the anterior-superior epicardial surfaces of both atria, (B) the posterior-inferior epicardial surfaces of both atria, and (C) the right atrial free-wall epicardial surface. Septal electrode arrays were added later. Right panel: The first ever multipoint, global computerized map of human atrial fibrillation. For purposes of illustrating 3-dimensional data in a 2-dimensional format, imagine that a sagittal section across both atria has been made and you are viewing the atria from the posterior view with the anterior half of the atria "flipped" up so that the electrical events there can be seen. Note that there are two macro-reentrant circuits present, one in the left atrial isthmus and a larger one utilizing the right atrial free-wall and atrial septum. LAA, left atrial appendage; M, mitral valve orifice; PV, pulmonary veins; RAA, right atrial appendage; SVC, superior vena cava; T, tricuspid valve orifice.
because of the large number of patients referred to us for the surgical treatment of the WPW syndrome, 30% of whom also had AF. An understanding of AF commensurate with the development of a surgical procedure to ablate AF depended on having the multipoint electrode arrays for both animals and humans developed by Boineau and Schuessler and the correct interpretation of the AF maps that we could now obtain. Once the electrophysiology of AF was understood, it was possible to conceive of an operation that would ablate it.
This vast collaborative effort between surgeons and nonsurgeons culminated in the first clinical Maze procedure being performed on September 25, 1987. Several modifications of the procedure have evolved since that time to make today's procedure safer, quicker, and less invasive.

A 50-year time-line from 1970 through 2020 documents that highly successful surgical procedures for all of the major clinical arrhythmias preceded the development of catheter ablation for those same arrhythmias by several years (Figure 11). For example, cardiac arrhythmia surgery began in 1968 with the successful surgical treatment of the WPW syndrome but it was over 20 years before the WPW syndrome could be treated by catheter ablation. Similar delays occurred between the initial surgical procedures and subsequent catheter procedures for elective His bundle ablation, ischemic and nonischemic VT, AVNRT, and atrial fibrillation. While the critical developments in the surgical treatment of cardiac arrhythmias over the past half-century resulted from a close collaboration between EP and cardiac arrhythmia surgeons, the development of catheter ablation procedures largely excluded the collaboration of surgeons. As a result, many of the mistakes made by interventional EP during the initial years of catheter ablation could have been avoided if they had taken advantage of the vast surgical experience that had preceded the development of catheter ablation.

A summary of the evolution of interventional therapy for cardiac arrhythmias demonstrates the impact of certain critical events (Figure 12). Interventional therapy for cardiac arrhythmias began in 1968 with the first surgical cure of the WPW syndrome. We think of the period from 1968 until roughly 1990 when RF catheter ablation became possible as the "Open-Heart Surgery" period that lasted for 22 years. During that period, WPW surgery was perfected and new surgical procedures were developed for AVNRT, nonischemic VT, ischemic VT, and atrial fibrillation. However, all of those procedures
required cardiopulmonary bypass so there was always a stimulus to make the interventions less invasive. Within a few months after RF catheter ablation became available around 1990, the interventional treatment of all of the cardiac arrhythmias except atrial fibrillation shifted from surgery to catheter ablation. AF continued to be treated surgically, but the arrhythmia surgeon was always surrounded by collaborating EP [Figure 13].

In 1998, Haissaguerre published a seminal article that was the first to identify pulmonary vein triggers as the primary basis for the induction of AF. This was a major milestone that led to the widespread use of catheter ablation for AF, but it also led to a virtual end of the collaboration between EP and arrhythmia surgeons. EP performed pulmonary vein isolation for paroxysmal AF with satisfactory results, but their results in patients with persistent and especially long-standing persistent AF remained suboptimal. Surgeons focused on developing minimally invasive surgical techniques to treat AF but all of those procedures remained far more invasive than catheter ablation and not much more effective. This period of electrophysiologist/arrhythmia non-collaboration lasted for approximately 12 years and remains the most stagnant period in the evolution of interventional treatment for cardiac arrhythmias. The consistently poor results of catheter ablation for long-standing persistent atrial fibrillation (LspAF), and the development of thoroscopic surgical techniques led to a return of collaboration of EP and arrhythmia surgeons starting around 2010 in the form of so-called “hybrid” procedures that take advantage of the capabilities of both groups. Since that time, hybrid procedures for recalcitrant AF, especially LspAF, have attained a success rates approximately midway between less invasive, less effective catheter ablation alone and more invasive, more effective open-heart surgical procedures.

10 | THE LESSON OF COLLABORATION

The evolution of mapping techniques, surgical therapy, and catheter ablation for cardiac arrhythmias has been spectacular over the past half century. A critical look at that evolution reveals the central lesson that hopefully, we have all learned to appreciate the importance of collaboration between EP and cardiac arrhythmia surgeons. The lesson is that when collaboration is the rule, great progress is made, but when collaboration is abandoned, progress slows dramatically. Surgeons will never know as much electrophysiology as EP, but EP will never have the 3-D picture of anatomy that surgeons must possess to be successful and innovative, so it is critical to take advantage of the special talents and knowledge of both. Perhaps the best way of putting it from a surgeon’s standpoint, is a statement that the first author has repeated hundreds of times over the past several decades: “An arrhythmia surgeon is only as good as his/her electrophysiologist.” That remains as true today as it was 50 years ago.

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