

Andreas R. Gruentzig, MD (1939–1985)

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Andreas Gruentzig may rightfully be called the father of modern cardiology. This is entirely accurate if we consider what is meant by the words “modern cardiology.” Gruentzig alone created the field of interventional cardiology, and this new field opened the way to everything else that has happened in the modern era. Beginning with balloon dilatation angioplasty to treat atherosclerotic obstructions in arteries by reducing the degree of obstruction and restoring blood flow back to more normal values, the interventional techniques pioneered by Gruentzig evolved rapidly to include bare metal stents, drug-eluting stents, bioresorbable vascular scaffolds, structural heart procedures like transcatheter aortic and mitral valve replacement, and mitral valve clipping for mitral regurgitation, as well as atrial and ventricular septal defect closures, left atrial appendage occlusion, and a whole host of others. All of these procedures will continue to be refined and improved, and no doubt some will come and go just as they have in the past. Prior to Andreas Gruentzig, cardiology was a diagnostic specialty focused on measuring, counting, and interpreting. After Gruentzig, it became a therapeutic specialty too. Development of these powerful therapeutic treatments, which in many cases can be corrective or sometimes even curative, indeed marks the advent of “modern cardiology.”

Andreas Roland Gruentzig was born in Dresden, Germany, in June 1939, approximately 10 weeks before Adolph Hitler launched the invasion of Poland that began

World War II. Andreas had an older brother, Johannes, who was 18 months his senior. With the war firmly underway, the Gruentzig family left Dresden for the nearby smaller and presumably quieter and safer city of Rochlitz. Gruentzig’s father, Wilmar Gruentzig, was a secondary school science teacher with a PhD in chemistry. As part of the war effort, he was conscripted into the meteorological service of the Luftwaffe. Wilmar apparently died in 1945 in the devastation surrounding the fall of Berlin, for he never returned home and there was no further word of him. Gruentzig’s mother, Charlotta, who taught piano and singing, supported the family in the post-war years by giving private music lessons.

In the late 1940s, there were enormous tensions in Germany, mostly due to the continued partition of the country into the Western and Eastern sections. In 1950, Charlotta and the 2 young boys moved to Argentina with the help of an uncle. However, it quickly became apparent that Johannes and Andreas would be able to obtain better educations back in Germany. In 1952, the small family returned home. They went to Leipzig and Charlotta’s mother’s house, where Charlotta and her sister could help care for their mother and the 2 boys could continue their schooling. Both boys were highly intelligent and studious. They both entered the St. Thomas School (Thomas-

Dr. Anderson was a research fellow with Dr. Gruentzig in 1983–1985.

schule) in Leipzig, founded in 1212 by the Augustinians under the patronage of the Margrave Dietrich von Meissen, and one of the oldest and most prestigious secondary schools in the world. Notable graduates of the St. Thomas School include Gottfried Wilhelm Leibniz and Richard Wagner. Johann Sebastian Bach was the musical director (Thomaskantor) of the St. Thomas School from 1723 until his death in 1750. Andreas Gruentzig graduated with highest honors from the St. Thomas School in 1957.

It was in 1956 that the elder brother, Johannes, permanently fled across the border into West Germany, where he entered Heidelberg University in the medical curriculum. One year later, after his graduation from the St. Thomas School, Andreas followed his brother permanently across the border to the west. They joined up once again, for in the fall of 1958 Andreas too enrolled at Heidelberg University in the medical curriculum, graduating in 1964.

Between 1964 and 1968, Andreas completed a number of clinical rotations in various specialties, including one at the Max Ratschow Clinic in Darmstadt, where he learned angiology, the study of blood vessels, which included angiography. This prestigious clinic was founded in 1963 as a specialized research center for angiology. It was here that Gruentzig had his first direct experiences making images of atherosclerotic disease in the peripheral arteries of the legs and examining the correlations between the amount and severity of vascular disease and the sometimes devastating clinical progression to ulceration and limb destruction that could develop. It is illustrative of the seriousness of this clinical problem that the name for the disease at that time was arteriosclerosis obliterans. After finishing these clinical assignments in 1968, Andreas then completed additional training in statistics and epidemiology in London.

In 1969, Gruentzig joined the faculty of the Department of Radiology at the University of Zurich in Switzerland. His interests quickly led him into the orbit of Alfred Bollinger, a prominent specialist in vascular medicine and physiology, who had just been asked to develop a clinical and research laboratory focused on vascular medicine and angiology. Bollinger was one of the early pioneers in using Doppler ultrasound combined with plethysmography and angiography to study atherosclerotic arterial disease of the lower extremities. In a highly prescient work published in 1971, Bollinger and Gruentzig, along with their colleague Felix Mahler [1], reported their initial studies correlating Doppler-derived flow indices, ankle-brachial pressure differences, and angiography. It was just these combined techniques that Andreas carried

forward to his work in the coronary arteries. Later, he would demonstrate that stenosis reduction in the coronaries (measured angiographically) was accompanied by lower transstenotic or translesional pressure gradients, improved myocardial perfusion, and less or no angina, thereby laying the foundation for what is now known as coronary physiology.

It was also in 1971 that Andreas attended a lecture given by Eberhardt Zeitler, another angiologist and radiologist, where Zeitler described Charles Dotter's [2] method for treating atherosclerotic lesions in peripheral arteries. Dotter had developed a set of concentric telescoping catheters that could be passed in sequence, smaller to larger, through an obstructing lesion, pushing aside or compressing the atherosclerotic plaque material and reducing the degree of stenosis. The resulting increased blood flow due to lessened obstruction in many cases permitted healing of chronic foot and ankle ulcers and in some serious cases even helped avoid amputation. Nevertheless, the Dotter technique was neither risk free nor ideal. The relatively rigid, large-bore catheters could only be used in large, straight arteries, and the longitudinal shear forces created by catheter passage occasionally fractured the plaque and created large distal emboli. Gruentzig was immediately struck by the Dotter method. He perceived the logic behind the physics involved and the potential clinical value of the treatment technique, but he also recognized the challenges presented by the need to improve it. This became his life work.

In December of that year, 1971, Eberhardt Zeitler visited Andreas in Zurich and together they performed the first angioplasty there using the Dotter technique. Andreas afterward continued using this technique in his practice in Zurich, supported by his mentor Bollinger, and as true angiologists they carefully documented the pre-procedure and post-procedure findings [3]. Andreas also set about intensively studying how the Dotter method could be improved.

Charles Dotter himself had stated that the action of passing the rigid, telescoping catheters through an atherosclerotic obstruction caused radial, outward-directed force to be applied, thereby "dilating" the channel (lumen) to a larger diameter. It was the longitudinal shear force along the axis of the artery that created the problems. It would be better if all the force could be directed radially outward, with only very minimal or no longitudinal shear force at all. These concepts led immediately to the idea of a balloon. A balloon attached to the tip of a very thin, flexible catheter could be introduced into the vessel via a small puncture hole, could be maneuvered

around curves and bends, could be passed through an obstruction with minimal shear force, and once placed into position could be inflated to a larger size, applying only radial pressure outward and dilating the channel.

Balloon-tipped catheters were not new to medicine. The Foley bladder catheter (introduced in 1935), the Fogarty embolectomy catheter (1961), and the Swan-Ganz pulmonary artery catheter (1970) are all examples of balloon-tipped catheter devices. However, the soft latex material used in the balloons of these catheters is not adequate for dilating atherosclerotic lesions. Some “constraining” element was needed to keep the soft balloons from just enlarging under pressure until they burst. At the moment when Gruentzig was beginning to think about improving on Dotter’s technique, a prominent German radiologist, Werner Porstmann, was working on the balloon approach and conceived the idea of a caged or “corseted” balloon that might achieve the right combination of pressure and size, but his solution also turned out to be bulky and unworkable [4]. Andreas himself tried using a fine silk mesh for constraining the balloon, until he finally realized a plain, uncaged, uncovered balloon composed of a plastic material with appropriate physical characteristics was required. He sought out Heinrich Hopff, a Professor of Polymer Chemistry at the Swiss Federal Polytechnic Institute, not far from his office at Zurich University, and began having detailed discussions with him. Hopff suggested polyvinyl chloride and further suggested ways to form it into appropriately shaped and sized balloons. Ultimately, this approach was successful [5, 6].

Andreas spent countless hours in his kitchen over the next few years making both balloons and the catheters to carry them. At first, it was single-lumen balloon catheters, which he used for the first time in 1974, but once these were perfected, he quickly started on making double-lumen catheters too, which he was able to fabricate and use for the first time in 1975 (Fig. 1). The concept behind the double-lumen catheter was straightforward – he needed one lumen to inflate and deflate the balloon, and he needed a second, central lumen for passing a guidewire, obtaining pressure measurements in the artery, and providing perfusion distally while the balloon was inflated.

Andreas Gruentzig had stated, and in later years I myself heard him say this on several occasions, that it was his intention from the very beginning to prove his technique in the peripheral arteries and then move on to the coronary arteries. The proof for this is that Andreas, already a fully trained radiologist and full-time faculty member, began training in cardiology in the fall of 1973, before he

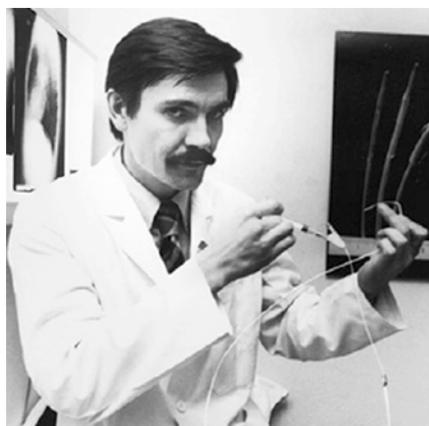


Fig. 1. Andreas Gruentzig and his double-lumen balloon catheter for coronary angioplasty. (Photo courtesy of Maria Schlumpf and Bernhard Meier).

had perfected his single-lumen balloon catheter and well before he had either developed or miniaturized his double-lumen catheter.

The years 1973–1977 were astonishingly creative and productive for Gruentzig. He continued using the Dotter technique in peripheral arteries until he perfected his balloon-tipped catheters, which he then employed in place of the Dotter method. He miniaturized his double-lumen catheter to a size appropriate for coronary artery work. Importantly, he developed a partnership with Hugo Schneider, a businessman with a small medical equipment company in Zurich. Schneider began the commercial manufacture of Andreas’s balloon catheters, which were assembled by hand using jeweler’s instruments and required difficult and painstaking handiwork.

By 1976, Andreas had his double-lumen catheter system ready for coronary artery atherosclerotic lesions. First, however, he had to test its feasibility. He worked with a cardiac surgeon named Marko Turina in order to create a suitable experimental model. In a series of dogs, the surgeon created a partial stenosis of a coronary by placing a silk ligature around it, not tight enough to occlude the artery but tight enough to partially obstruct it. Andreas then performed standard cardiac catheterization, maneuvered his balloon-tipped catheter into position in the stenosis, and “popped open” the ligature. It worked [7, 8].

Once it was clear that the balloon-tipped catheter method was feasible in the coronaries using a percutaneous approach, it was then necessary to get it into humans. This was first accomplished by attempting it using a direct approach during coronary bypass surgery [9]. These

attempts were “successful” in the sense that the balloon catheters were able to be maneuvered into the lesions and dilatations performed. But aside from a sense of satisfaction, this artificial construct did not contribute much if anything at all to understanding the technique.

Gruentzig had to wait a long while for his opportunity. Inevitably, there was the issue of obtaining permission to attempt the new procedure in the hospital cath lab. Even more inevitably, there was the issue of obtaining agreement from the cardiac surgeons to permit this new treatment for coronary disease to be used as an alternative to bypass surgery. The surgeons would have to be on standby to operate if a complication occurred. I once heard it said that Andreas’s second greatest personal achievement was in his convincing the cardiac surgeons to let him try an angioplasty. Using supreme diplomacy and tact, skills which he possessed in abundance, he obtained the needed permissions. Andreas also realized that despite his eagerness to apply the device he had created, he needed to wait until he had an almost ideal patient. Many months elapsed until finally in September of 1977 one of his students, Bernhard (Bernie) Meier, brought him the angiogram of a patient who in fact was an ideal candidate. There was a single, short, discrete lesion in the proximal left anterior descending coronary artery. This was it. On September 16, 1977, the first human coronary angioplasty was performed in the cath lab at Zurich University Hospital. Of course, tension was high in the room. Yet, the procedure was smooth and uncomplicated. Those who were present, including Andreas himself, later described how undramatic and almost anticlimactic it was [10].

Gruentzig went on to perform more coronary angioplasty procedures, building up his case material and examining the clinical parameters of the procedures as well as the short- and long-term outcomes [11, 12]. He also initiated what turned out to be another fantastic innovation of his, the teaching course, or as he liked to call them, demonstration course. These courses began in 1978 in Zurich and were composed of live angioplasty cases conducted in the cath lab at Zurich University Hospital and transmitted by closed circuit television to a nearby hospital auditorium. The cases were interspersed with discussion sessions where all aspects of the new procedure were debated, often hotly. At first, only a handful of interested practitioners attended, some of them very skeptical of the procedure, but very quickly the attendance grew. When the first publication on coronary angioplasty appeared in a major medical journal in 1979, the world was ready and waiting [13].

In an odd twist of circumstance, Andreas Gruentzig and his new treatment for coronary artery disease were not all that well regarded in Zurich. The place and time were just not right for that. After working with multiple limitations and constraints placed on him, Andreas decided to leave Zurich. He had perceived that attitudes toward coronary angiography and nonsurgical interventions were more favorable in the USA, and so he was interested when several centers approached him. In late 1980, he moved from Zurich to Emory University in Atlanta, GA, USA. Emory had a large and active cardiovascular program, including a busy cath lab under the leadership of Spencer King, and furthermore it was one of the leading centers in the world for coronary bypass operations. It is likely that the size and success of the cardiac program at Emory created a level of confidence and comfort there that allowed the cardiologists and most especially the surgeons to welcome and embrace Andreas and his new procedure.

During the 5 years that Andreas worked at Emory, he built a world-class clinical and research department. After his tragic death in 1985, the department was renamed The Andreas Gruentzig Cardiovascular Center in his honor. From its very beginning under Gruentzig, it was the world leader in coronary angioplasty. It was Andreas who introduced the steerable coronary guidewire, which for the first time made all regions of the coronary system potentially reachable with angioplasty equipment [14–16]. He developed new balloons and catheters [16, 17]. He experimented with lasers and other devices [18]. He defined the “intermediate” coronary lesion and demonstrated that intervention may not be the most appropriate choice [19]. He conducted the first randomized trial ever done in coronary angioplasty [20]. Interestingly, it was a trial comparing coumadin versus aspirin for prevention of restenosis – and it was “negative,” that is, no difference. The volume of cases and the breadth and depth of the clinical research at Emory were astounding. In the spring of 1985, just a few months before his untimely death, a retired radiologist named Cesare Gianturco came to Andreas with a prototype of a vascular stent appropriate in size for coronary arteries. Andreas passed it to the senior fellow, Gary Roubin, and asked Roubin to begin studies as soon as possible in animal models. This story of the world’s first balloon expandable coronary stent is fascinating in itself and well worth reading [21]. Of course, every stent used today depends on Andreas’ balloon for its placement.

Andreas Gruentzig died in an airplane crash in October 1985, aged 46. He was flying his twin-engine airplane

back to Atlanta from his vacation home on the Georgia coast. Characteristically, he was hurrying back to Atlanta in bad weather in order to check on a patient who had developed complications from the angioplasty Andreas had performed 2 days earlier. His wife Margaret Anne was with him and died in the crash too. It was a tragic end to one of the most brilliant lives in history. Yet, appropriately, the legacy of Andreas lives on, in the work he produced, the people he trained, and the creativity he fostered. All of us but especially all the patients are the beneficiaries. In 1990, the International Andreas Gruentzig Society (IAGS) was founded, under the leadership of Gary Roubin and Eberhardt Zeitler, to preserve and maintain the pioneering vision of Andreas for future gen-

erations of cardiologists, radiologists, surgeons, and basic scientists [22]. Although he himself departed from it far too soon, the father of modern cardiology bequeathed to the world a dynamic, courageous, and fitting patrimony.

Conflict of Interest Statement

The author has no conflicts of interest to declare.

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