Interventional Treatment of Coronary Heart Disease and Peripheral Vascular Disease

Spencer B. King III, MD; Bernhard Meier, MD

In 1950, the ground for catheter-based interventions in peripheral or coronary arteries was laid (Table), but no activity had started.1

Diagnostic Catheter Procedures
In 1958, Mason Sones and his colleagues developed selective coronary angiography and published it as an abstract in Circulation.2 As a cardiologist at the Cleveland Clinic, he performed angiography of the aortic root in a patient with valvular heart disease. Looking directly into the x-ray beam, as was customary in the era before image intensifiers coupled to television systems (Figure 1), Sones recognized that the catheter had inadvertently slipped into the right coronary artery. The patient had transient asystole but no ventricular fibrillation. The high-quality picture of the right coronary artery obtained ushered in the era of selective coronary angiography, Sones subsequently refined this technique for routine use through a cut-down of the brachial artery. In parallel, Kurt Amplatz3 and Melvin Judkins4 further developed the technique using a femoral approach made possible by the Seldinger technique, introduced in 1953.5

Precoronary Therapeutic Catheter Interventions
The turn from purely diagnostic procedures to therapeutic interventions was launched in 1964 by Charles Dotter.6 In collaboration with Judkins at the University of Oregon in Portland, the vascular radiologist Dotter used coaxial catheters of increasing diameters to “bougie” narrowed leg arteries in patients with peripheral artery disease, analogous to the Benique technique for the urethra of 1846. In parallel, Kurt Amplatz7 and Melvin Judkins4 further developed the technique using a femoral approach made possible by the Seldinger technique, introduced in 1953.8

Precoronary Balloon Angioplasty
In 1974, Andreas R. Gruentzig introduced the concept of balloon dilatation of arterial stenoses into clinical medicine. Dismayed with the limited potential of the Dotter method, he sought a solution to dilate arteries through a tiny entry hole. The balloon had been the solution on hand for Reybard to dilate the urethra in 1855. It was also the solution on hand for Gruentzig. The material used for the balloon turned out to be the key for success. Porstmann had just failed with a latex balloon. To contain the expansion of the balloon, he had caged it in a plastic catheter sliced longitudinally. Gruentzig had the splendid idea to walk across the street from his place of work, the University Hospital of Zurich, to the Technical University. There, a plastics expert suggested using polyvinyl chloride (PVC). The PVC balloon catheter Gruentzig manufactured with help from his wife and friends had a sausage shape and remained fairly form-constant once it reached its predesigned outer diameter. The Gruentzig balloon catheter was born,9 and 26 years later, in the year 2000, it was improved but unchanged in its basic characteristics.

Coronary Balloon Angioplasty
In 1977, the breakthrough for catheter-based arterial therapeutic interventions came with the first coronary angioplasty procedure, performed by Gruentzig at the University Hospital of Zurich on September 16. A 38-year-old businessman had been hospitalized for a first bout of unstable angina. The symptoms subsided, and he underwent an exercise test, which showed anterior ST-segment elevation and ventricular ectopy accompanied by angina at peak exercise. A coronary angiogram performed on September 14, 1977, revealed a discrete but tight proximal stenosis of the left anterior descending coronary artery just before the takeoff of the first diagonal branch. One of the authors (B.M.), who was taking care of the patient at that time (as ever since), introduced him to Gruentzig, who offered him the option to have a balloon angioplasty attempted instead of the otherwise unavoidable bypass operation. The patient granted consent without hesitation, as he stated later, immediate faith both in the

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(Circulation. 2000;102:IV-81–IV-86.)

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Circulation is available at http://www.circulationaha.org

IV-81
method and even more so in the person of Andreas Gruentzig. He was not to regret it. The procedure was a full success. It engraved itself into the memories of the few persons present (including B.M.) and is still reminisced about at countless meetings dedicated to the method. The patient has remained absolutely symptom-free up to the year 2000. He underwent a coronary control angiography on the exact 10th anniversary of the intervention, performed by one of the authors of this article (S.B.K.). At almost 23 years of follow-up, he had an episode of atypical chest pain at rest. This prompted an additional coronary angiogram by the other author (B.M.), which showed that the dilated site was pristine (Figure 2).10,11 The first American publication about this method was an abstract published in Circulation and presented as a poster at the American Heart Association meeting in Miami, Fla, in November 1976 (Figure 3).12 The first few cases were published in the Lancet,13 and the first series in the New England Journal of Medicine.14 Thousands of subsequent articles, reviews, editorials, book chapters, books, videos, CDs, and internet publications have appeared subsequently on the topic, among them the first guidelines issued by a joint task force of the American Heart Association and the American College of Cardiology15 and a comprehensive review by one of the authors (S.B.K.),11 both published in Circulation.

### Coronary Stenting

On March 28, 1986 (just 5 months after October 27, 1985, when Gruentzig tragically perished in a plane crash piloting his twin-engine plane back from a weekend retreat, accompanied by his second wife and his dogs), Jacques Puel implanted the first coronary stent in a patient in Toulouse, France.16 The first clinical series on coronary and peripheral stenting were published jointly from Toulouse, France, and Lausanne, Switzerland.17 In Atlanta, Ga, the group of one of the authors (S.B.K.) was at that time on the brink of

#### Milestones for Human Cardiovascular Catheterizations up to 1950

<table>
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<tr>
<th>Year</th>
<th>Method</th>
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<td>Blood vessel access</td>
<td>Mayor</td>
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<tr>
<td>1846</td>
<td>Dilatation of urethra with increasing catheter diameters</td>
<td>Benique</td>
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<tr>
<td>1855</td>
<td>Balloon dilatation of urethra</td>
<td>Reybard</td>
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<tr>
<td>1895</td>
<td>X-ray</td>
<td>Roentgen</td>
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<td>1898</td>
<td>Contrast medium</td>
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<td>1912</td>
<td>X-ray plates for documentation</td>
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<td>1924</td>
<td>Arteriography with contrast medium</td>
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<td>1937</td>
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<td>1939</td>
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<td>1945</td>
<td>Visualization of coronary arteries</td>
<td>Radner</td>
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![Figure 1](image1.png)

**Figure 1.** F. Mason Sones (1919–1985) in the catheterization laboratory in Cleveland.

![Figure 2](image2.png)

**Figure 2.** Stenosis before (a), immediately after (b), 10 years after (c), and 23 years after (d) the world’s first coronary balloon angioplasty, performed by Andreas R. Gruentzig in Zurich, Switzerland, on September 16, 1977. The functional long-term success is documented by normal stress tolerance and normal exercise ECG (e) of the now 61-year-old patient, who was an age-mate of Gruentzig when he underwent the intervention at the age of 38 years.
introducing coronary stenting to the United States, using a device pioneered by Cesare Gianturco, one of the most gifted inventors in the field. At the same time, a group in La Jolla, Calif, was working with a stent made by another great pioneer of catheter interventions, Julio Palmaz. Both of their seminal reports appeared in Circulation.18,19 It is noteworthy that stenting of peripheral arteries had already been experimented with in the 1960s by Dotter, who already envisioned the use of stents in the coronary vasculature in his article at that time.20

Although not recognized by everyone right away, the stent was the only prodigy among the many so-called new devices popping up to assist or replace the balloon in the late 1980s.21 Although some found niche applications, none of the other devices (atherectomy of the directional, rotational, or excrational kind or laser) designed for removing plaque tissue have stood the test of randomized trials. The stent, on the other hand, which simply shoves the tissue out of the way and scaffolds the occasionally occurring obstructive dissection, proved to be superior to balloon angioplasty in a large number of randomized trials, albeit only for reduction of restenosis and the need for reintervention. As a conceptually preventive tool against acute or subacute coronary closure, it proved salutary when used as a bail-out device but ineffective, if not deleterious, when used indiscriminately. This is mainly because of late occlusions, which are germane with stents but exceedingly rare with balloon angioplasty. The risk of such occlusions with stents initially prompted operators to use prolonged and intensified anticoagulation protocols. These and the lengthy approval process for implantable devices by the regulatory agency in the United States caused a somewhat sluggish acceptance of the stent in this country. Improved antiplatelet regimens that avoided oral anticoagulation22 and the easy availability of a variety of second- and third-generation stents finally induced a lively increase in coronary stenting among angioplasty procedures in the late 1990s. Interventional cardiology virtually turned into “interventional” cardiology. Currently, the stenting rate in most institutions ranges from 70% to 90% of cases and 60% to 70% of lesions. The use of a stent-armed balloon as first instrument (direct stenting) in all suitable cases seems to be unstoppable and just around the corner, although certain conditions, ie, long lesions, small vessels, and bifurcation lesions, have not been solved by stenting. The British government issued a recommendation in May 2000 that all coronary lesions undergoing angioplasty be stented for safety and cost reasons, if at all feasible.23

Figure 3. Andreas R. Gruentzig (1939–1985) explaining a poster describing percutaneous dilatation of coronary artery stenosis to a flabbergasted crowd at the American Heart Association meeting in Miami, Fla, in November 1976.

Randomized Studies With Medical Treatment or Surgery

Gruentzig used to say: “If in doubt, randomize.” The first randomized study comparing angioplasty with bypass surgery was indeed conceived by Gruentzig himself and conducted by one of the authors (S.B.K.). It started in 1987 and was published in 1994.24 Similar trials were published simultaneously.25,26 They showed that in selected patients with multivessel disease, the outcome was not significantly different between the 2 treatment modalities in terms of mortality and subsequent infarction. However, angioplasty had a markedly higher need for subsequent reinterventions, prompted, among other things, by more persisting or recurrent symptoms.

The first results emerging from trials comparing stenting with bypass surgery drew a similar picture. Yet, the need for subsequent interventions in the stenting arm was lower than it had been with the balloon alone. This appears to make stenting cost-efficient relative to bypass surgery (at least in the 1-year time frame), which prompted the British government to advocate stenting rather than surgery in cases in which both were feasible.23 Diabetic patients with multivessel disease remain a problem for interventional techniques, as shown in the Bypass Angioplasty Revascularization Investigation (BARI) Trial.27 Whether stenting and modern antiplatelet drugs will engender tighter competition for these patients remains to be seen. In parallel to angioplasty results, surgical results are improving as well, thanks to, eg, enhanced use of arterial conduits. The advent of minimally invasive surgery, new potent drugs supporting percutaneous coronary intervention (and surgery for that matter), and the possibility of hybrid procedures warrant further randomized studies.

A comparison of coronary angioplasty with medical treatment was published before the trials comparing with surgery.28 Angioplasty turned out to be beneficial in terms of symptoms and exercise tolerance but not in terms of longevity in the group of patients selected for randomization (primarily single-vessel disease).

In unstable patients, a strategy of immediate catheterization and possibly revascularization was not superior to medical treatment in a randomized trial.29 However, only 11% more patients were revascularized in the revascularization group than in the medical group, and a 12% first-month mortality in the patients revascularized surgically compromised the outcome of the revascularization group, in which there was no mortality with angioplasty. Another randomized study on unstable patients showed the interventional treatment to be superior to the medical treatment at 6 months.30

A recent trial looking at the most common angioplasty patient, namely the one with stable coronary artery disease,
found a high-dose statin regimen to be at least equal, if not superior, to angioplasty over the initial 18 months of follow-up. This points to the beneficial potential of statins in coronary artery disease, which should be fully exploited in the interventional arm as well.

Interventions for Acute Coronary Syndromes
The appropriateness and necessity of performing coronary catheter interventions urgently for myocardial infarction or unstable angina were leading topics of the past years.

In 1982, Meyer advocated, in Circulation, the recanalization by angioplasty of the acutely occluded coronary artery during the initial stage of myocardial infarction in case of failure of intracoronary streptokinase infusion. One year later, Serruys suggested that angioplasty should be used acutely to deal with the underlying stenosis even if intracoronary streptokinase had been successful. In the same year, Hartzler presented the first series in which coronary angioplasty was used as sole emergency therapy for acute myocardial infarction. Although a first randomized study in 1986 showed the superiority of direct angioplasty over intracoronary fibrinolysis for acute infarction, the upsurge of intravenous fibrinolysis with new drug schemes and an apparent inefficacy of associated balloon angioplasty damped the enthusiasm for acute interventions for a while. Acute coronary angioplasty for infarction was declared dead. In fact, as we know now, it had only gone into hibernation. It rose like the phoenix from the ashes as the interventional arm as well.

Randomized studies between angioplasty and intravenous fibrinolysis brought primary angioplasty back into the picture. It rose like the phoenix from the ashes as the acknowledged overall best treatment for acute myocardial infarction. Currently, the combination of primary angioplasty with fibrinolytic agents in conjunction with modern antiplatelet treatment is the focus of attention.

A first publication from Rotterdam, Netherlands, had shown that balloon angioplasty was feasible for unstable angina. As the pathophysiology of unstable angina and non–ST-segment elevation myocardial infarctions has become understood to be thrombus-mediated, the combination of angioplasty and antithrombotic measures applied early has proved efficacious. New drugs have helped to make angioplasty for acute coronary syndromes more reliable and safe.

Help From Drugs and Radiation
Acetylsalicylic acid and heparin were used in the acute phase of coronary angioplasty from the beginning without their role ever being challenged. Many other drugs came and went, such as coumarin, dextran, dipyridamole, or sulfinpyrazone for the acute phase and calcium blockers, fish oil, ACE inhibitors, statins, and others to prevent restenosis. The glycoprotein IIb/IIa receptor antagonist abciximab was the first to clearly show superiority in terms of prevention of acute events.

The only nonmechanical means to reproducibly reduce restenosis appears to be the “sledgehammer” approach in the form of brachytherapy. This method was clinically applied to peripheral arteries by Liermann et al in Cologne, Germany, before it was used in coronary angioplasty and published in Circulation by Condado et al from Caracas, Venezuela. Since then, radiation with both γ- and β-sources has proved efficacious in randomized studies. The method has already been adopted as routine therapy for coronary angioplasty, in particular for in-stent restenosis, in a number of institutions outside the United States. Brachytherapy is expensive, is somewhat cumbersome, and requires the help of a licensed radiotherapist in most countries. Concerns about late occlusions (already observed) and late side effects (hypothetical) persist. Hence, other modes of therapy, eg, local drug delivery, coated stents, or covered stents, continue to be studied and may perhaps compete with or replace brachytherapy for prevention of restenosis.

Peripheral Interventions
It came as no surprise that coronary balloon angioplasty, a derivative of peripheral balloon angioplasty, instigated balloon angioplasty of renal and cerebral arteries as soon as it was shown to be feasible and reasonably safe. The first renal angioplasty was performed in 1978 in Bern, Switzerland, by Mahler, a former colleague of Gruentzig in the Angiology Division in Zurich, where the latter invented peripheral balloon angioplasty. Gruentzig performed a procedure himself a few days later, again on a patient under the care of one of the authors (B.M.), and was the first to publish it. Although the potential of this method to reduce hypertension turned out to be fairly low, there is an additional salutary effect on renal function. Stenting as a complement to balloon angioplasty proved helpful in ostial but not in more peripheral renal artery lesions.

The first angioplasty of a cerebral artery was reported by Sundt and colleagues from Rochester, Minn, in 1980 and pertained to the basilar artery. Balloon angioplasty of the cervical carotid artery followed in 1980, first as an adjunct to surgical endarterectomy and then in 1983 as a stand-alone percutaneous procedure. Carotid stenting was first reported in 1995. Stenting has been rapidly adopted as the exclusive percutaneous treatment of carotid artery stenosis. It was thought that the dreaded risks of peripheral embolism and also restenosis could be further reduced. However, acute local closure and restenosis with balloon angioplasty alone had never been a real problem in light of the comparatively large diameter of these vessels. Because stents did not eliminate the problem of distal embolization (and because no randomized studies exist, they might even increase it), a variety of mechanical protection systems as well as adjunctive drugs are currently under investigation.

Congenital Vascular Interventions
In pediatric cardiology, a flurry of vascular dilatation procedures were described over the last 2 decades. They range from congenital targets, such as stenoses in pulmonary arteries, pulmonary veins, coarctation, and patent or insufficient ductus arteriosus, to postsurgical targets, such as conduit or scar stenoses.

Outlook
There is a remarkable congruence of research interests, disease pathogenesis, disease manifestations, prevention...
strategies, drug therapies, and finally catheter interventions in vascular problems throughout the body. This has led to a mutual fertilization among physicians dealing with these problems.

The cardiologists are the caretakers of the most common vascular problem, ie, coronary artery disease. In addition, they work in fairly small arteries and have to cope with the constant motion of the heart. Consequently, they seem to have developed skills, knacks, and equipment somewhat faster and further than their colleagues dealing with other vessels. Teamimg up with other specialists, on the other hand, has helped the cardiologists to understand noncardiac problems better. Together, cardiovascular catheter specialists are a tremendous asset for modern medicine and offer powerful tools and therapies for patients.

This field of medicine is highly coveted by young cardiologists in training. Research support from industry has been abundant, and so far, reimbursement has been generous. Professional societies, such as the American Heart Association, the American College of Cardiology, and the European Society of Cardiology, have recognized the desirability for practitioners to have extensive experience to ensure optimal outcome. A certifying agency (installed by the American Board of Internal Medicine) has appreciated the extensive fund of knowledge encompassed by the discipline and has instituted a certifying examination to recognize experts in the field.

The ghost of overuse is hovering over this discipline more than over most other medical interventions that are used less frequently. Rigorous quality control instruments have been implemented in a number of countries. They provide a certain guarantee that the catheter interventions for cardiovascular diseases are neither overused nor underused.

Dotter started the discipline of percutaneous vascular interventions in the 1960s. Gruentzig contributed the balloon to make them work in the 1970s. The stent was the outstanding advent in the 1980s. New platelet antagonists, such as the glycoprotein Ib/IIa inhibitors and the thienopyridins, as well as the expanded applications of interventional procedures in acute coronary syndromes and carotid arteries, were prominent in the 1990s.

The first century of the new millennium should see tremendous success in prevention of these diseases, both by conventional risk factor management and by a genetic approach. The interventions will continue to abound for many years to come because of the aging population, who are well informed about treatment options and commonly subscribe to the attitude “because I am worth it.”

In about 50 years, prevention of atherosclerosis will be early, ubiquitous, and uninterrupted, and people will grow very old. Yet, they will no longer suffer from or die of atherosclerosis, currently the most important disease of civilized mankind. By then, the last 50 years of the past millennium will be remembered just like the tale of Atlantis, fascinating but no longer relevant.

References


**KEY WORDS**: angioplasty ■ coronary disease ■ balloon ■ revascularization ■ stents
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Circulation. 2000;102:Iv-81-Iv-86
doi: 10.1161/01.CIR.102.suppl_4.IV-81

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