Role of New Technology in Balloon Angioplasty

Spencer B. King III, MD

It is difficult to think of balloon angioplasty as a mature technique with which new devices must now be compared. It seems as if it were only yesterday that Gruentzig demonstrated a new and radical approach to myocardial revascularization. As success rates have leveled off at 90% or higher, half or more of current patients have complex or multivessel disease, bail-out methods and surgical backup systems have been tested and refined, and clinical trials are now well under way to compare percutaneous transluminal coronary angioplasty (PTCA) with modern bypass surgery (the Emory Angioplasty Versus Surgery Trial [EAST] results will be available in summer 1993), the method has indeed entered a mature phase. Maturity, of course, in no way implies perfection. There are technical problems with angioplasty that fall into one of three categories: 1) lesions that cannot be opened (usually chronic total occlusions), 2) abrupt closure at the time of PTCA that causes complications, and 3) restenosis of the lesion in the months following the procedure that leads to recurrent ischemia. Because problems exist, other methods for opening arteries should be considered.

I once gave a presentation to my son’s third-grade class. After describing the problems of blocked arteries, I asked each child to draw a solution to the problem, hoping they would recognize the usefulness of coronary bypass surgery (the only method then available). To my surprise, they drew a wide collection of “roto-rooters” and other interventional devices, but none drew the balloon. This is not to imply that the new devices are created from third-grade mentality but rather that some of these ideas approach the obvious. On a somewhat more sophisticated level, if one looks at the pathology that occurs after balloon angioplasty, it is not surprising that new ways for opening arteries are sought. The flaps and cracks have a frightening appearance, and one continues to be amazed that balloon angioplasty works at all. In theory, any number of new devices should produce a better initial result than balloon angio-

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With its forward-facing cutting blades and aspiration feature, the transluminal extraction catheter may be best suited to diffusely diseased vein grafts, thereby reducing the likelihood of distal embolization.\(^6\) Observational studies regarding this issue have leaned heavily toward use in diffusely diseased vein grafts. Extensive use of the device involves aspiration of not only the minced plaque material but also much blood.

The rotoblator, a high-speed rotating burr with attached microscopic diamond chips, is designed to file down hard, unyielding tissue and allows the fine debris to be flushed distally.\(^7\) This device's major successes have been in lesions so firm that the balloon could not dilate, even at high pressure.\(^8\) Expectations that the highly polished surface that is left behind would be advantageous for long-term patency have yet to be confirmed. Because the burr must fit through a guiding catheter, it is usually limited to a size smaller than the coronary artery being treated. In some cases, balloon angioplasty is added to complete the opening of the vessel to the desired size. This device appears to produce significant but reversible coronary spasm in some cases.\(^9\)

Multifiber laser catheters with over-the-wire guidance are designed to core out tissue without lateral stretching.\(^10\,11\) In some long lesions, these may offer a debulking effect, which alone or combined with balloon angioplasty may leave a more satisfactory lumen than would have been achieved with balloon angioplasty alone. Ostial aortic lesions treated with the laser may have an improved initial result compared with those treated with balloon angioplasty. So far, for safety reasons, these laser catheters are limited to sizes well within the margin of the artery. In addition to the laser, subsequent balloon angioplasty has been required in approximately half of the cases. Perforation of the artery, although rare, is more likely with highly eccentric lesions, especially if they are located in bends.\(^12\)

Lasers for opening total occlusions have been a dream that so far has had limited success. Laser balloon angioplasty or other low-intensity thermal catheters were designed to "weld together" separated plaque and arterial wall layers.\(^13\) Success has been achieved in a number of dissected arteries, but in some of our cases early reclosure has demonstrated that the weld may not always be firm enough or that subsequent thrombosis may be a complicating feature.

Because of their scaffolding nature, stents are best designed to repair the dissected and occluded coronary artery. Early trials of stents have shown that they have the ability to restore the occluded post-PTCA artery to a near-normal geometry by pushing the plaque material and flaps aside.\(^14\,15\) The major limitation has been the potential for thrombosis on the stainless steel foreign body and resultant threat of acute closure necessitating vigorous antithrombotic regimens. Recent multicenter experience in Europe with the Medinvent stent indicated a post-placement thrombotic closure rate close to 20%,\(^16\) although the largest single experience reported a significantly lower rate.\(^17\) Thrombosis has been experienced with other stent designs after stenting but to a much smaller degree when adequate anticoagulation is applied.

### Potential for Reducing Restenosis

Manufacturers of these devices would naturally like their inventions to receive more widespread use, and all have postulated that the devices may also reduce the restenosis rate in certain kinds of lesions. In Table 2, the potential mechanisms by which rese-
^6^11 Thrombosis could be altered by mechanical devices are listed.

Directional atherectomy by actually removing tissue and leaving a larger lumen might produce less turbulence and less elastic recoil. Restenosis rates, however, have not been reduced overall, although the ostial left anterior descending coronary artery lesions that our group reported as having a 60% restenosis rate in 1984^18^ appear to have a restenosis rate of more than 30% but less than 40% with directional atherectomy.^

The transluminal extraction catheter and rotablator have not been studied as extensively, but restenosis remains a significant problem with these as well. The rotablator has been associated with a restenosis rate in restenotic lesions similar to that in undilated lesions.^

It has been hoped that by debulking and avoiding stretch injury to the vessel wall, lasers would be associated with a lower restenosis rate. This has not been the case so far; there are two possible reasons.^

If the laser alone is used, thereby avoiding or minimizing the stretch injury, then a degree of stenosis that is moderate to significant is left behind. On the other hand, if the artery is to be opened completely, this usually requires the addition of balloon angioplasty, perhaps negating the beneficial effect of the debulking process. Laser balloons were expected to leave a more desirable lumen by reattaching flaps, sealing cracks, and reducing elastic recoil. Initial trials have not shown any reduction in restenosis and, at higher energy levels, may have actually increased the restenosis rate.^

Intracoronary stents are being evaluated as a means to reduce restenosis with the hypothesis that if the artery can be opened widely with the stent, then even if intimal proliferation occurs, it will take a great deal more hyperplasia to significantly narrow the lumen than if PTCA alone were used. This has been demonstrated in animal models in short-term experiments.^

The self-expanding Medinvent stent, which has been tested in Europe, appeared to achieve this reduced restenosis rate, although at the cost of a very high thrombosis rate early after placement.^

In a multicenter US trial, under rigorous optimization of both the procedural result and the postprocedure management, the Palmaz-Schatz stent produced restenosis rates in some subsets that may be less than would be found with balloon angioplasty alone. The rates in the US trials are higher in restenotic lesions than in de novo lesions.^

However, in one large center's experience in France, a similarly low recurrence rate has been found in both primary and restenotic lesions.^

Placement of multiple stents in the same artery, however, has led to significantly increased rates of restenosis. The initial enthusiasm for a dramatically reduced restenosis rate has been modified somewhat with the analysis of the results by a core laboratory using a definition of 50% diameter stenosis at follow-up. This question of the effect on restenosis will be answered in newly begun randomized trials that will compare the Palmaz-Schatz stent with balloon angioplasty in both native arteries and vein grafts. Other stents such as the Gianturco-Roubin, Wiktor, and Cordis stents have not yet undergone large restenosis trials. Because of the potential for subacute thrombotic complications after stent placement, trial design must take into account a compulsive anticoagulant program, which is necessary in the stented group, and careful surveillance of acute and subacute complications in the days after stent placement to ensure that ischemic events are not significantly increased. Early thrombotic closure would more than offset any advantage of reduced restenosis rates.

Other new diagnostic and therapeutic technologies have been developed, and some, such as intravascular ultrasound and Doppler flow devices, are being studied in clinical trials. The images obtained with ultrasound are improving; however, the clinical usefulness of this information has not been demonstrated. Other technologies with potential include local drug delivery devices and coated or polymeric stents as well as hemostatic devices for use at arterial puncture sites. All of these devices are in the preclinical phase. In the future, angioplasty followed by placement of stents carrying compounds that are antithrombotic and/or modify the healing process.

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**TABLE 2. Potential Mechanisms for Reducing Restenosis**

<table>
<thead>
<tr>
<th>Method</th>
<th>Improved surface</th>
<th>Atheroma mass</th>
<th>Larger lumen than balloon percentual transluminal coronary angioplasty</th>
<th>Stretch injury</th>
<th>Destroy smooth muscle cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atherectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Directional</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Extraction</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Rotational abrasive</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Lasers</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Over-the-wire ablative</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Thermal balloon</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Stents</td>
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</table>
may be routine, but there remains a long distance between bench research and clinical application.

How Should New Devices Be Investigated?

New devices are not developed in the same way as new drugs. Once a drug is developed for testing, it can be subjected to safety evaluation and then clinical trials in a blinded manner. In this way, drugs can be given to impartial investigators who are independent of the developer.

Devices, on the other hand, seldom reach their final form before testing on humans. The vagaries of the morphology and composition of plaques or the tortuosity of proximal segments of coronary arteries in clinical situations often suggest improvements to the device while it is undergoing clinical testing. The inventor of the device is usually the most knowledgeable and motivated to make these improvements. To bar the inventor from early clinical testing and close supervision is neither practical nor desirable. Any claims by the inventor, however, should be viewed with healthy skepticism. As soon as a device has reached a form that can be safely used by others, it should be selectively disseminated for more objective clinical testing.

Even in the hands of clinical investigators, it is difficult to eliminate undue enthusiasm for new devices. It is therefore very important that the results of their research be subjected to the objective rigor of an independent core laboratory for analysis of acute angiographic results as well as angiographic and clinical follow-up results.

If evaluation of restenosis is to be done, it must be measured directly with angiographic means. Some at the FDA have insisted on clinical follow-up, claiming that the angiographic follow-up is only a surrogate. Ultimately, an improved clinical outcome must be the final objective; however, I contend that if the goal of specific therapy is to prevent restenosis, then restenosis must be measured directly and clinical parameters are insufficient surrogates. The vagaries and inconsistencies of clinical follow-up mean that a great many patients must be evaluated to determine meaningful clinical end points, thereby requiring very expensive large trials and potentially subjecting many patients to increased risk. Smaller studies can be revealing if we look directly at what we intend to alter, namely, the degree of narrowing of the treated segment at follow-up. By this method, ineffective approaches can be abandoned early, reducing the cost and subjecting fewer patients to procedures that do not work. Finally, the scientific community will not accept “clinical” restenosis as a surrogate for angiographic follow-up.

Companies sponsoring new devices would be wise to provide such independent evaluation as soon as possible in the development of new products to avoid fooling themselves, to point out areas of weaknesses that can be improved, and to make important financial decisions regarding allocation of resources. An important addition to industry data bases is the development of the New Approaches to Coronary Interventions Registry sponsored by the National Heart, Lung, and Blood Institute. Directional coronary atherectomy, the Palmaz-Schatz and Gianturco-Roubin stents, the AIS excimer, and the Spectranetics excimer laser have already been included in this registry, and other device sponsors are expected to join soon. By tracking the uses of new devices and the results, this independent registry can provide important guidance for the medical community.

Independent observational studies may provide the answers in some situations but fall short in others. If a device for reliably solving acute occlusive dissection is invented, then clinical studies should be centered on determining the success rate and any complications in an objective manner. No comparative trial against ineffective methods is necessary or appropriate.

On the other hand, some questions cannot be answered by even the most objective observational study. These questions require prospective, randomized trials. If the possibility exists that directional atherectomy can provide a lower restenosis rate than balloon angioplasty in certain situations or that excimer laser can open long segments of occlusion better than balloons, then these approaches should be subjected to randomized trials by unbiased investigators. In randomized trials such as these, investigators with a direct interest in the new devices should refrain from participation in trial design. If individuals with vested interests perform as participants in randomized trials, their results should be compared with those of others because blinding is impossible and any bias toward the best approach may alter the outcome. Strict monitoring of protocols and independent core laboratories are essential to obtain believable data.

Testing of these new devices, however, will never be as “clean” as testing of new drugs. After all, given the task of evaluating the use of an axe or a saw for dividing wood, one would need to consider the characteristics of the wood, the direction of the grain, and the desired final form of the wood before selecting a tool. With this information, the selection might be obvious and may not require a trial. An example would be a totally eccentric plaque in a large vessel that cannot be altered significantly with a balloon but might be excised with directional atherectomy. Another would be a hard, undilatable lesion that does not yield even to very high balloon pressure but might be opened with the rotablator device.

What Do You Do If You Do Not Have These New Devices?

In the meantime, what is the disadvantage to a patient whose physician does not possess a host of new technologies? The vast number of patients who are currently suitable for angioplasty are best treated with balloon angioplasty. It is true that some high-risk patients can be approached with an increased sense of safety in centers with stent availability for
bailout application and that certain ostial lesions that do not respond well to balloon angioplasty might be better approached with laser therapy or atherectomy, but the referral of such patients to other centers would produce little change in current practice patterns. In 1990, of 1,863 interventional procedures performed at Emory University Hospital (by Dr. John Douglas, Dr. Nicholas Lembo, and Dr. Spencer King), 88% were handled with balloon angioplasty alone (Figure 1). Only 223 of these patients (12%) were treated with an investigational device; of these 223, 81 were treated with directional atherectomy (36%), 63 with excimer laser (28%), 36 with stents (16%), 19 with laser balloon angioplasty (9%), and 13 with a combination of these devices (6%) (Figure 2). These new devices may have been more appropriate in this population than in the general population because a significant number of patients were referred specifically for such interventions because of unique anatomic situations. Therefore, currently, the vast majority of patients are not being significantly disadvantaged by the seemingly slow deliberations of the FDA in releasing these new devices.

Many patients and some physicians have expectations for new technologies that are not yet fulfilled. There is a tendency when considering restenosis after balloon angioplasty to assume that a new technology might have a better chance of success. There are, in most cases, no better options available for the patient than at least one repeat angioplasty. As has been shown many times, redilatation results in lasting success in most patients.

Despite all of the reservations expressed about the new technologies and their current roles as niche devices, it is crucial that research and development continue. Although balloon technology is the de facto gold standard in interventional cardiology, it will not always be so. Defects in new technology cry out for improvements, and many innovations will follow. Significant questions remain regarding the dissemination of new technology. Should devices designed to address problems with balloon angioplasty be subjected to randomized trials, or should they be released early to fill a niche that cannot be served by current balloon technology? How will the practitioner of interventional cardiology become trained to use the new devices that fill only the occasional niche? Will patients be best served by regionalization to centers with experienced personnel, or should we insist that new technology development become so fail-safe that it can also be used safely by the inexperienced, occasional user? Who should bear the cost of new technology testing? How extensive should clinical testing be?

Finally, the value of new technology will not be established by the zealot who invented it, by those who attempt to bash it, or by those who call for testing. Those developing new technologies should bear in mind that the success of their venture depends in the long run not only on approval by the FDA but also on convincing the practitioner, sometimes through compelling observational studies, sometimes through results of believable randomized trials, and ultimately through widely held consensus, that this technology will be of significant benefit to the patient.

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