Intracoronary Brachytherapy
Time to Sell Short?

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The introduction of innovative new devices and drugs has been a major influence in the dissemination of catheter-based coronary revascularization procedures into clinical practice. Systematic appraisals of effectiveness have typically come only after regulatory approval and widespread clinical acceptance. Consideration of the potential economic implications of these technologies, if performed at all, has taken place even later. Because percutaneous coronary intervention (PCI) is now not only a central part of modern cardiovascular therapeutics but is also “big business,” any significant change in the technology or its use may have an important impact on national healthcare costs and health outcomes. For this reason alone, a more proactive approach utilizing large randomized trials with clinically relevant end points and prospective economic analyses is crucial to allow for an informed debate on new advances.

See p 691

Although early visionaries predicted that percutaneous technology would create a less invasive (and less expensive) alternative to coronary bypass surgery, surgery volume actually increased during the exponential growth period of PCI. Currently, >1 million PCI procedures are performed in the United States each year, with >80% involving the use of a coronary stent. For the most part, these are not procedures that have replaced expensive surgeries. Instead, they have “replaced” medical therapy and added billions of dollars each year to the US healthcare budget. Although each major improvement in PCI technology tends to rekindle hopes for a viable percutaneous alternative to bypass surgery, the result has often been to extend the reach of PCI more to medical than surgical patients. In addition, although some PCIs provide better patient outcomes than the alternative medical therapies, numerous procedures are done on low-risk patients and have no discernible effect on either prognosis or quality of life. This phenomenon of spending more and more money to buy ever-shrinking benefits is termed “flat of the curve” medicine.

If the US healthcare system had an unlimited budget, then the uncoupling of considerations of value from those of therapeutic decision-making would be much less of a problem than it is. However, the healthcare budget is constrained in several important ways: Taxpayers do not wish to pay more taxes to increase Medicare funding but also do not wish to divert funds from education and defense to pay for healthcare; employers do not wish to pay more for the healthcare insurance benefit of their employees; and the public does not wish to pay more healthcare costs out of pocket. Physicians often assume that, in a nation that spends $2.6 billion on potato chips each year, these constraints on medical care spending can be overcome. Yet, unless the payers can be persuaded to pay more, new advances will have to be funded by savings elsewhere in the healthcare system. There is no historical precedent to suggest that physicians will voluntarily give up marginally effective medical care that has become accepted standard practice to enable the use of newer, expensive technologies that might provide a better return on investment. Given the recent reacceleration of growth in health spending, this Gordian knot is likely to get much tighter before policy makers become sufficiently motivated to develop workable solutions. In the meantime, new technologies will get much harsher scrutiny than old ones, and costs will tend to be more important than value. In this environment, any new therapy that can rigorously demonstrate its value for money spent deserves special recognition.

One unintended consequence of the dramatic growth in the use of PCI has been the creation of a new iatrogenic disease, restenosis. Often described as the Achilles heel of angioplasty, restenosis currently is understood to consist of at least 2 main subtypes: recoil and remodeling of the vessel wall after dilation, and neointimal proliferation. Coronary stenting produced a significant reduction in the former type of restenosis. Economic analysis has demonstrated that the reduction in restenosis associated with stenting relative to balloon angioplasty produces a partial offset of the extra costs associated with the use of coronary stents. However, the introduction of coronary stents into interventional practice also created in-stent restenosis, a particularly refractory form of restenosis secondary to progressive neointimal proliferation.

The demonstration that brachytherapy nearly halves the incidence of in-stent restenosis has been regarded as a major advance in interventional cardiology. As is typical of effective new cardiovascular therapies, brachytherapy also adds significantly to the cost of restenosis treatment. In this issue of Circulation, Cohen and colleagues provide the first rigorous analysis of the costs of brachytherapy. Several findings from their work are particularly noteworthy. First, brachytherapy, as reflected in the procedures used in the Gamma-1 trial, costs about $4100 more than conventional therapy for...
restenosis. Importantly, this figure includes an equipment cost of $2500 per procedure as well as amortization of the initial laboratory set-up costs for brachytherapy ($25 000) over 5 years. Second, the reduction in re-restenosis from brachytherapy in Gamma-1 was associated with a $2300 cost offset over the subsequent year. Finally, the authors project that with modern post-Gamma-1 practice (avoidance of repeat stenting at the time of brachytherapy, elimination of routine use of intravascular ultrasound, and extended anti-platelet therapy with aspirin and a thienopyridine), the long-term benefits of brachytherapy would likely fully offset the initial $4100 cost of the procedure.

The relevance of the economic findings of Cohen and colleagues depends heavily upon the relevance of the clinical results of Gamma-1 to contemporary brachytherapy practice. In this regard, it is reassuring that the relative reductions in major adverse cardiac events and repeat revascularization observed in the Gamma-1 trial are similar to more recent randomized trials of both γ- and β-emitting intracoronary brachytherapy. Further, although the increasing use of β-emitting radioisotopes is associated with shorter procedures and potentially less shielding, the overall costs associated with equipment and resource use are unlikely to differ significantly from those associated with the use of γ-emitting radiation. Much has been learned about the methods and treatment of in-stent restenosis with radiation since the completion of Gamma-1, and to the extent that the model-based extrapolations from Gamma-1 described above appear reasonable, brachytherapy can be regarded as an economically dominant therapy, defined as a therapy that improves clinical outcomes at a net equivalent or diminished cost. In addition, from a societal vantage point, although the technology is moderately expensive, these estimates suggest it should not increase the long-term national healthcare bill.

As is typical of most (if not all) medical therapies, the benefits of brachytherapy are not uniformly distributed. In subgroup analyses, Cohen et al. show that patients with clinical and angiographic features that impart a higher risk for repeat restenosis (eg, diabetes, prior restenosis, and longer lesion lengths), and who thus are more likely to benefit clinically from intracoronary radiation, derive even greater economic benefits. Conversely, treatment with brachytherapy of focal lesions identified at low risk for repeat restenosis after conventional therapy alone appears economically unfavorable.

Several important questions about the economics of brachytherapy remain unresolved. Brachytherapy of in-stent restenosis in saphenous vein graft lesions, which are associated with a high likelihood of repeat restenosis and show at least similar clinical benefit with brachytherapy, would be expected to be economically attractive on the basis of extrapolation of Gamma-1 results, but this should be demonstrated with empirical data. In addition, because follow-up data at 5 years suggests some attenuation of the clinical benefit of intracoronary brachytherapy, a longer-term evaluation of the economics of brachytherapy will be important.

Possibly the greatest question about brachytherapy for interventional cardiologists today is whether to invest in intracoronary radiation at all. The newest generation of stents, which act as delivery systems for antiproliferative agents, are positioned as an exciting breakthrough therapy, with restenosis rates approaching zero. Enthusiasm for this latest technology is coupled with predictions that brachytherapy may now be on the road to therapeutic extinction. If drug-eluting stents are adopted as the standard of care within the next 3 to 5 years, and rates of target-lesion repeat revascularization decrease to <5%, then the 5-year amortization of costs assumed by Cohen et al may not be relevant for a hospital currently considering an investment in brachytherapy. Instead, some centers may elect to refer their patients with in-stent restenosis to institutions with existing facilities for intracoronary radiation. However, an average of 1.3 to 1.8 uncoated, conventional stents will be implanted this year in nearly 1 million coronary procedures, and by conservative estimates, 20% will develop restenosis. Furthermore, considering the inconclusive benefits of drug-eluting stents for in-stent restenosis, the need will remain, at least for the next few years, for an effective therapy to treat the large number of uncoated stent patients who will develop restenosis.

Although expected to reduce restenosis to <10% and target-lesion repeat revascularization to <5%, the true effectiveness of drug-eluting stents in the real-world setting of PCI remains to be defined. Adoption of drug-eluting stents (with a cost per stent anticipated to be around $3200) as initial therapy for all PCIs could increase the US health care bill by >$2 billion per year. How much of this incremental cost will be offset by reduced costs due to lowered restenosis rates remains to be defined. What is clearer is that without incremental reimbursement, hospitals with interventional cardiology programs are likely to experience a double negative economic impact from the new stents. First, initial hospitalization costs for PCI will increase because of the higher costs of the new stents, and hospitals may actually lose money on these PCI procedures. Second, because of the reduced restenosis rates, hospitals will have a reduction in the volume of their cases. Whether any of the losses can be offset by “new business” created by the new stents is presently unknown. In economic self-defense, hospitals may be forced to consider significant delays in access to these therapies or selective rationing of drug-coated stents. Some financially disadvantaged programs may be forced to close. Endovascular brachytherapy does not come with such difficult choices. It is clinically effective, has adequate reimbursement, and, combined with newer uncoated stent technologies that may further reduce restenosis (such as thin-strut cobalt-chromium stents), could prove to be an attractive economic and clinical alternative strategy to drug-eluting stents.

Although drug-eluting stents will reduce the need for brachytherapy, predictions of its obsolescence seem premature. Among high-volume programs (eg, ≥1000 PCIs per year) even a 5% target-lesion repeat revascularization rate will produce the 50 in-stent restenosis patients per year assumed in the Gamma-1 economic analysis. Rather than sell brachytherapy short, cautious “shareholders” may accordingly choose not to divest themselves of an already established clinical and economic benefit with intracoronary radiation.
References


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