If you wonder why a small start-up company is represented at IAGS, I would like to remind you that about three quarters of all medical device industry players have 100 employees, or less. It is also well recognized that over the years many of the true innovations have originated in small, less structured and less risk averse environments. I would like to thank Dr. Myler for recognizing that dynamic and for giving me the opportunity to participate in this open forum.

Whether change is evolutionary or revolutionary, it is the driving force of progress. Without change innovation is by definition unachievable (Figure 1). It is an unpopular thought — and you may choose to acknowledge it or not — but, the days when you as a physician could have the clinical benefit of patients as your sole consideration are waning. In the future, the healthcare system itself will become an equivalent component of the medical progress formula. In this new model (Figure 2), technique and technology will continue to drive clinical progress, but costs, outcomes and regulation will determine the pace of the convoy. Since any convoy advances at the speed of its slowest vehicle, you can expect regulatory pressures to add greatly to your frustration in the USA, both in terms of reduced scientific study opportunities and in terms of product non-availability.

I wouldn’t be an entrepreneur if I didn’t spend most of my time on the clinical change components — for that is where the real excitement and satisfaction is for all of us — but, I will give healthcare delivery change its due by letting it dominate my conclusion.

Another way to present Dr. Myler’s phenomenal interventional growth slides, is to project the

---

From InterVentional Technologies Inc., San Diego, California.
Address reprint requests to: Rob Michiels, President & C.O.O., InterVentional Technologies, Inc., 3574 Ruffin Road, San Diego, CA 92123.

Figure 1

Figure 2
advancement of technique and technology in terms of increasing complexity of performed procedures since the early days less than two decades ago (Figure 3). The main clinical significance of technique and technology lies in the fact that in spite of rapidly growing complexity of lesions treated, the acute success rates and in–hospital complication rates have remained pretty much constant (Figure 4). To gain regulatory and/or market acceptance, the resulting acute gold standard must be met by any new technology right out of the starting gate.

Throughout this evolution, the third criterion on our minds — restenosis — also didn’t change its incidence much, and actually became the all consuming challenge for the interventional cardiology community and for industry. In spite of the infinite complexity of this phenomenon — if we as engineers are to design and craft devices that address the issue — we must try to break it down into small, understandable bits of mechanisms to which we can apply laws of physics, chemistry, etc … in order to bring about a change. During the last few years, many have focused on vascular recoil/remodeling and on intimal hyperplasia (wound healing) as the two major mountains to climb in dealing with “restenosis” (Table 1).

The mechanical solution to dealing with vascular recoil and remodeling has two extremes. One can try to support the vasculature in such a way that it is prevented from moving in on itself, or one can try to alter the structural integrity of the vasculature in such a way that it does not have the desire or ability to do so on its own. The technologies involved are stents in the case of scaffolding, and every indication is that this approach has brought us closer to a solution, at least in larger size vessels. Future improvements are likely to focus on the optimization of structural geometries and the application of superior materials. However, the stent cost paid is leaving behind a foreign object in the body with all resulting unanswered questions. The alternative technology is microsurgical dilatation, where stress fracture mechanics may alter the vessel’s mechanical properties enough by scoring through the intima and into the media, so that the arterial contractility is compromised and thus mitigating a large portion of the recoil/remodeling effect.

Similarly, the mechanical solution to dealing with intimal hyperplasia has extremes. One can either eliminate or reduce the trauma imparted, or one can stop cold the reaction provoked by the trauma necessarily induced. Reducing trauma can be accomplished mechanically by reducing inflation pressures, inflation times, and number of inflations. An attempt to combine all of the above in one again translates into microsurgical dilatation and is accomplished by localizing the dilatation forces in small sections of the treatment area and applying fracture mechanics to obtain a cleaner and gentler dilatation. Stopping cell proliferation in damaged areas falls outside purely mechanical approaches and will probably be a race between chemical and radiation technologies.

While most of the medical community is already familiar with stent technology, microsurgical dilatation did not become a practical reality until recently in the form of the Cutting Balloon™ (Figure 5). Since this concept represents a radical departure from conventional thinking — but then so did stents 10 years ago and dilatation 20 years ago — it will have to be proven in a randomized clinical trial against conventional PTCA. Such a study is underway in 30 centers around the world, and at present enrollment rates, the acute phase will be completed by the end of 1996, and final trial results are expected by September 1997 (Table 2). The designed interim analysis revealed favorable cutting balloon target lesion revascularization results, holding promise...
Intramural drug delivery presents an entirely new challenge, not only from the perspective of overcoming the shortcomings of presently available intraluminal delivery devices, but also from the perspective of “what” to put into the wall (Table 3). From factor antagonists to pathway inhibitors, anti–proliferatives and gene therapy, the common requirement is that anti–restenosis drug therapy demands intramural delivery. Indeed, it is postulated that to date many of the pharmaceutical and/or genetic therapy formulations have not fulfilled their restenosis reduction promise post–PTCA simply because they have had to deal with massive amounts of vessel wall injury. Thus, their concentration/time at site has been insufficient to deal effectively with the various underlying mechanisms. Ergo, the design criteria for the delivery technology must resolve the issues of intrawall delivery efficiency, intrawall volume control, and delivery time.

IVT’s third technology platform addresses all these challenges with an intramural injection design that offers 90% plus delivery efficiency in 10 seconds or less delivery time, meaning no more than 30 seconds inflation/occlusion time. In essence the INFILTRATOR™ catheter features micro–miniaturized injector ports on a balloon and proposes a delivery method as simple as standard needle injection (Figure 6). To–date numerous animal experimentations have been completed successfully in support of the following hypotheses:

1. Low profile injector ports on an angioplasty balloon can penetrate through the elastic lamina into the superficial layers of the tunica media with low balloon inflation pressures.
2. Small amounts of fluid delivered slowly with low pressure through the injector ports will be distributed among the tunica media layers without separation, dissection or acute occlusion.
3. The delivered substance will be distributed in the whole circumference and thickness of the treated segment.
4. Low pressure delivery at one to one sizing does not provoke significant proliferation.
5. The device is suitable for primary dilatation thus suitable for one step dilatation/drug delivery/
6. The device will yield high intra–wall uptake with minimal washout, i.e. 90% delivery efficiency.

This research project has progressed very rapidly and a human safety study was completed early 1996. Additional clinical studies are planned or in progress and European regulatory CE Marking is underway. It is estimated this catheter will be available in Europe for investigational human drug trials by 1997.

Having committed IVT to funding the development of such novel technologies brings me full circle to the issue of health care delivery change, or what I call the new industry rules for technology

*Caution: In the USA this device is limited by Federal (USA) Law to investigational use only.
development. In a climate beset by economic and political uncertainty, all segments of the health care industry are rethinking short- and long-term strategies. While health care reform will not be immediate and will be subject to hard-fought political compromise, there is no doubt that by the end of this century American health care systems and practice will have undergone a dramatic transformation. Both industry and physicians will have to contend with a greater deal of change and will each face specific challenges, regardless of whether the government interventionists or the more market based reformers prevail. For companies intent on expanding and sustaining market leadership in medical technology, product innovation, and health care delivery, nothing will be more critical than a solid understanding of the specific implications created by the reform process.

The most compelling driving change in the medical environment is the migration of an increasing number of patient treatments to lower cost settings with known, predictable and acceptable outcomes. As payors adhere closely to the bottom line, cost-reducing productivity-enhancing, outcome-enhancing technologies will be heavily in demand. As a result, technological development will be focused in the specialty area at the detriment of commodities, and the challenge of the specialty devices will be to meet each of the following demanding criteria: \(^{16-19}\)

1. Offer a clear and demonstrable clinical patient outcome better than existing therapy, or address a totally unmet medical need.
2. Offer the new therapy at a demonstrable savings as compared to existing treatment modalities.
3. Avoid creating a totally new cost that will be insurmountable because it is unreimbursable in a capitated system, even though a previously unmet need is at stake.

The first criterion used to be the only important factor, in that clinical benefit to the patient used to be sufficient to provide a reasonable expectation of return on the development investment. However, since criteria two and three have now become *conditio sine qua non*, the inability to recuperate incurred product development cycle and regulatory costs will preclude many potentially beneficial technologies from reaching your clinical practice. Indeed, they virtually eliminate the so-called limited application technologies that were part of most companies’ portfolios in a not so distant past.

Oddly enough, in spite of the current appetite for optimal efficiencies in the delivery of health care, the overall market opportunity will continue to expand with continued worldwide population growth and steady aging of the developed nations’ populations. The demand for life-saving, life-expanding and quality of life enhancing technologies and techniques is virtually unstoppable in an egalitarian society equipped with a never-seen-before access to information about worldwide medical progress.

The disease entity enemy is the same, but the rules of engagement have changed. This is why it is all the more important to forge a better understanding and dialogue between the medical community and industry, so that we jointly may continue to focus as much energy as possible on patients’ needs and clinical progress, in spite of increasing econo-socio-political pressures.
REFERENCES