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An accomplished inventor and investigator discusses how to bring a concept to market and the future of interventional radiology and CAS in the US.

As a physician experienced in developing inventions, how would you describe the process of bringing a device from concept to reality? In the early stages, how do you determine the need for a product? First there has to be a need for a product. Attempting to create a need for product is frequently difficult and invariably unsuccessful. For these reasons, after there is an established need for the product, and with some basic due diligence to confirm that observation, it has been our practice to develop a prototype. The prototype device is ordinarily funded by the developer from the prototype and the basic engineering model, we ordinarily proceed to animal work. From the animal work, we establish the criteria for a clinical feasibility study. Ordinarily this is done overseas. This, however, frequently requires a round of financing, which is obviously preceded by incorporating and establishing filing for appropriate patents so that intellectual property that had previously been evaluated is now established. Assuming the feasibility study goes well, one can then decide on additional financing to do a US clinical trial or integrate these development activities with a corporate partner. The Series A financing is ordinarily done among other physician friends or interested parties with a commonality of interest in medical devices. Series B financing is ordinarily done with the assistance of venture capital funding. One thing we have learned from previous entrepreneurial start-ups is that if you are convinced there is a demanding need for the product, then it requires overwhelming patience and obviously additional funding to achieve success.

How will the practice of endovascular therapies evolve over the next 10 years? In what ways will interventional radiology evolve? There is absolutely no question that endovascular therapies are replacing many of the previously described surgical procedures and that most of the specialties presently involved in endovascular management will show some degree of integration in a team approach. It is certainly encouraging to see the younger generation of interventional radiologists now clearly seeing the definition of this model, and slowly separating themselves from totally unrelated imaging procedures (ie, gastrointestinal radiology, pulmonary, etc). There is absolutely no correlation between diagnostic mammography, obstetrical ultrasound, and cardiovascular radiology. Hopefully the American Board of Radiology will allow, as an early decision process in the training program, the option of a clinical year in cardiology or vascular surgery and eliminate those subspecialty programs that are of no interest to the interventionalist.

I also see an expansion in the overall, minimally invasive potential for a variety of procedures of which I would include endovascular aneurysmal repair. As the profiles move into the 14-F range and lower, I believe cardiologists, interventional radiologists, and certainly the vascular surgeons will all participate in aneurysmal management. Obviously, what is happening in the neurosciences and in the endovascular method for managing intracranial aneurysmal disease, as well as interventional management of stroke, has a huge potential.

Having been a principal investigator in both ARCHeR and SAPPHIRE, two crucial, highly scrutinized trials of carotid artery stenting (CAS), what are your perspectives on the procedure and its associated technologies? Few procedures in the history of medicine have met such resistance as endovascular carotid stenting as an alternative to endarterectomy. Certainly some of this is quite reasonable considering that endarterectomy has been the gold standard and has been a reimbursed procedure since 1976. The NASCET trial further confirmed that surgical management of carotid artery occlusive disease was preferable to best medical management. The data from the registries, and certainly the landmark SAPPHIRE trial suggested that in a well-defined high-risk subset of patients, carotid stenting might be preferable to endarterectomy.

The primary endpoint at 360 days in the randomized treated patients in the SAPPHIRE study had a major adverse event rate of 11.9% in the stenting arm, but 19.9% in the endarterectomy arm with 2.5% Q-wave and non-Q-

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wave MI in the stenting arm versus 7.9% in the surgical arm. Interestingly, major ipsilateral stroke was 0% in the stenting arm versus 3.3% in the surgical arm. Minor ipsilateral stroke, however, had a 3.8% incidence in the stenting versus 2% for the surgical group. Deaths in the stenting arm were 6.9% versus 12.6% in the endarterectomy arm and this included a significant number of nonneurologic deaths in the group. The diabetic subgroup within the randomized trial was even more impressive, with 2.4% periprocedural stroke in the stenting arm versus 6.8% in the surgical arm at 30 days with no additional strokes at 1 year, still maintaining the 2.4% incidence and 11.4% strokes in the surgical arm at 1 year. Major adverse events without nonneurologic deaths demonstrated in this diabetic subset 4.8% versus 25% in the endarterectomy arm. The diabetic subset included 86 patients with 42 patients in the stenting arm and 44 patients in the endarterectomy arm. Based on the data from the two landmark trials—SAPPHIRE and ARCHeR—it would appear that endovascular carotid stenting has a fairly well established position especially in the high-risk subset population.

Do you foresee CAS expanding beyond high-risk patients? I believe the final answer is not yet in. The data from single-institution studies (where these reports are occurring), however, and certainly the European data suggest that endovascular stenting can be done, and hopefully with a periprocedural event rate less than 3%. This would then be quite competitive with ACAS and certainly better than NASCET. What we may look for in this country is a trial to include a low-to-moderate risk group that could be either randomized or done as a significant-sized registry with a parallel surgical group or historical controls.

What is the ideal CAS physician team, and what training do you think each operator should have? Obviously, the ideal CAS physician team is in fact a team utilizing the talents of both the interventional radiologist as well as the vascular surgeons and/or cardiologists with adequate training in both the extra- and intracranial circulation. There should be a sincere interest in providing the training essentials for those physicians who have an interest in endovascular carotid programs. Major industry is now in the process of establishing regional educational centers to provide the necessary training; these programs will include an intensive on-line didactic program as well as both taped case discussions and live cases with performance by the training team. This will also result in proctoring of the physicians as they move through the training course. Those physicians entering the training program will be screened before being accepted and obviously experience in diagnostic arteriography of the extra and intracranial circulation may be necessary before initiating the training.

What role do you see Medical Simulation having in CAS training? Medical simulation programs will be integrated with the training course and will have a significant impact on expediting the ability for understanding the extra and intracranial circulation as well as developing the catheter skills necessary for complex carotid procedures.

Of which invention are you most proud and why? Although I have been involved in several inventions and several successful as well as unsuccessful entrepreneurial start-ups, the one that has probably been the most outstanding and certainly required a significant amount of time and effort is as a cofounder of Medrad Inc., which distributes the Mark series flow-rate-controlled angiographic injection systems. This was the first flow-rate-controlled angiographic injector and now has a dominant position in the world market for angiographic injection systems. I had just returned from my fellowship when Steven Heilman, the original founder, asked what devices are the highest priority and most necessary when the angiographic market was just evolving. A small, select group, which included Dr. Heilman, Rudy Kranys, and myself, put in endless years before we fashioned a functioning flow-rate-controlled injector that now dominates the market.

Which project commands most of your energies today? A considerable amount of my energy today is spent in new device development, and a few are still quite confidential, but one that certainly seems to be evolving is a nonpolymeric nanoporous surface coating for balloon-expanding and self-expanding stents. The porous surface will allow variability in architecture and this will allow not only a choice of drugs, but also variation in the timing elution.

The endovascular field has become a family affair for the Wholeys, with one son an interventional radiologist, another in medical device sales, and a wife who is a coding specialist and has her own physician reimbursement corporation. Does endovascular therapy play a dominant role in your family discussions? It is true that quite a few members of the family have a major commitment in vascular therapy and certainly device development, and innovative ideas are a priority topic during most of our free-time discussions. Rarely a day goes by that we are not considering alternative ideas in terms of device development. ■