Can Start-Ups Finish Up?

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In this issue of *Circulation: Cardiovascular Quality and Outcomes*, Xu et al present findings from a search of US patents related to bare-metal coronary stents in an effort to gain insight on how medical device innovation starts and how policies in the United States might help to promote more innovation. Of the 245 patents identified by their search strategy for the years 1984 to 1994, the authors report that the most frequently cited stent patents (their measure of patent importance to innovation headlined by the Palmaz and Gianturco patents) were from individual physician inventors working in academic medical centers and their small private companies. They also report a temporal trend that shows, in later years, more patents were granted to public companies. They concluded that policies aimed at supporting these entities might enhance and accelerate innovation because early innovation, in this case, was spurred by individual inventors with their small companies.

It is true that individual practitioners struggling with the challenges of everyday practice are an important source of new-device concepts that can possibly solve an unmet clinical need. However, the journey of successful innovation to maximized impact on public health requires that these early ideas (such as the original stiff, boxcar like tubular stent of Palmaz or the poorly scaffolding clam shell stent of Gianturco) need significant refinement through subsequent innovation (such as the later, industry-based Lau patent of the Multilink stent that enabled broad application to the coronary circulation). Innovation may begin with practicing physicians, but the ultimate benefit of a technology to society depends on continued innovation throughout product development and iterative refinement as contributed by companies with greater financial resources and a larger workforce of engineering and scientific talent.

The hypothesis that the most cited patents may represent the most influential ones (eg, producing the most clinically and commercially successful devices) may not always be the case, as evidenced in the current study by the fact that many of the top 10-cited patents never became a clinical stent. Such a hypothesis would require some technical analysis of the various designs and how they might have contributed to the successful development of clinical science, the treatment of patients, further innovation, and, ultimately, success in the marketplace.

The use of the assignee and its classification according to type in the study is also complex. For example, the nature of the actual inventors, regardless of whether they were physicians, or whether they were independent inventors or closely associated with the assignee (eg, as an employee), is not clear, as well as the distinction between private and public companies and what might properly be inferred from it. Dominik Wiktor, who is the named inventor of the number 2 patent of the top 10-cited patents in Table 4, for example, was a nonphysician, independent inventor who happened to license his patents to a public company. Cordis Corporation, the assignee of numbers 8 and 9 in the top 10, was typed as a private company, yet it was already an established medical device company with sales from $80 million to $443 million during the period of 1984 to 1994. Likewise, Cook Inc (founded in the 1960s and the owner of the Gianturco patent) was an established medical device company with established product lines. These entities are hardly comparable with the 3-person Expandable Grafts Partnership (Palmaz patent) that, in contrast, apparently had no products or sales, but was formed to market an invention to an established company that could then develop it into a product (very successfully).

Despite the challenges of the current study, the results represent an interesting historical case study 3 decades ago and beg the question of why medical device innovation is slowing today in the United States. In the current cardiovascular device arena, there can be no question that the number and complexity of stakeholders in device innovation has increased dramatically.

First, the concerns about safety from the public, lawmakers, and regulatory and reimbursement agencies, as well as intense medical–legal influences, have resulted in a risk-averse environment in the United States. This has led to the requirement for exhaustive bench and preclinical data before any clinical feasibility pilots can begin, and the uncertainty about the level of clinical trial evidence that will result in regulatory approval or, separately, reimbursement. Thus, the risk of ultimately failing to navigate all of these layers in the United States has negatively impacted private-equity investments and resulted in an exodus of small companies to friendlier offshore countries. New efforts, aimed at bringing together all the stakeholders at an early stage of device development to establish how safe is safe enough, will be critical to setting earlier expectations and expediting the approval process.

Efforts by the Centers for Device and Radiologic Health at the Food and Drug Administration (FDA) and the Centers for Medicare and Medicaid Services such as the Critical Path,4 the Innovation Initiative,4 Global Harmonization Task Force,5 risk–benefit analysis,6 and parallel review7 are good beginnings, but
more work is needed. Reforms to the FDA approval process included in the recently enacted FDA Safety and Innovation Act, specifically the requirement that the FDA’s performance be independently assessed, may be key to reducing rhetoric in the debate on how to advance innovation and give policymakers meaningful data on how the FDA can be more effective.\(^8\)

Second, recent studies show clearly that venture capital, the traditional source of early financial support for individual inventors and small companies in the United States, has dramatically exited this space,\(^9\) in large part because of an aversion to the risk of challenging regulatory and reimbursement processes and approvals. And, of course, these approvals, especially reimbursement, represent the ultimate end game defining the success of commercialization of a device and, consequently, access for patients.

Thus, government policy changes such as tax incentives or other programs to support individual inventors and small companies, as suggested by the current authors, may facilitate only one small step in the complex pathway of successful device innovation and, by themselves, not significantly change the landscape in the United States.

To spur innovation, multiple layers of change need to take place across the spectrum of stakeholders to support small- and large-company innovators from concept through product development. The end game of innovation, and clinical and commercial success requires significant financial wherewithal and stamina; without a change in the current environment, the appetite of venture capitalists and even larger company investments for device innovation will continue to wane, and many great innovations for unmet clinical needs may never reach patients. Encouragingly, there has been a significant increase recently in discussions and collaboration among the venture capital community, small- and large-company industry, professional societies, the FDA, and the Centers for Medicare and Medicaid Services with the objective of expediting the regulatory and reimbursement pathways. These changes are welcomed by all stakeholders, and especially by our patients, so that start-ups can finish up and accelerate the number and quality of innovations impacting health care in the United States.

**Disclosures**

Dr Simonton is an employee of Abbott Vascular.

**References**

8. FDA Safety and Innovation Act (FDASIA) P.L. 112–144 was signed into law by President Obama on July 9, 2012.

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