Origins of Medical Innovation
The Case of Coronary Artery Stents

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Background—Innovative medical devices make major contributions to patient welfare, and coronary stents have been among the most important device developments of recent decades. However, the origins of such breakthrough medical technologies remain poorly understood.

Methods and Results—Using a comprehensive database of patents, we identified all individuals and institutions that developed intellectual property related to stent technology early in its development process. The patents were categorized and described using a predetermined qualitative coding strategy. We found 245 granted patents related to bare metal coronary artery stents from 1984 (when the first patent issued in this field) to 1994 (after the first stents were approved). Each year showed an increase in the number of patent filings: from 1 in 1984 to 97 in 1994. The largest fraction of patents was issued to private entities (44.9% of the total). Public companies, individual inventors, and nonprofit institutions represented 31.4%, 18.0%, and 5.7%, respectively. The top 10 most-cited patents in the field were dominated by 2 private entities, Expandable Grafts Partnership and Cook Inc, organizations created by or dependent on the work of independent academic physician-inventors.

Conclusions—Coronary artery stent technology first arose from individual physician-inventors within academic medical centers and their associated private companies. After these initial innovations were in place, the field became dominated by large public companies. This history suggests that policies aimed at encouraging transformative medical device development would have their greatest effect if focused on individual inventors and scientists performing the early stages of technology development. (Circ Cardiovasc Qual Outcomes. 2012;5:743-749.)

Key Words: stents ■ device innovation ■ patents

Millions of patients depend on a widening array of medical devices to support the diagnosis of disease and management of their health. The US medical device industry has surpassed $200 billion in annual revenue, including a steady 9% growth rate during the past few years. Yet, despite this growth, there is a great deal of uncertainty about the future clinical and financial success of the medical device sector. Some commentators have argued that onerous regulatory requirements have stifled new medical device development and have raised concern about how constraints on healthcare reimbursement in the United States might affect investments in the medical device pipeline by leading companies.

These issues raise the question of how innovation occurs in the medical device industry. Some studies point to the public sector’s key role in basic science leading to drug development, but it is widely believed that medical technology development occurs primarily in the private sector. In contrast to pharmaceuticals, medical devices often have more incremental improvements and shorter product life cycles. Case studies and other reviews of medical device development support these perspectives, focusing on the central role of medical device companies in bringing devices to market. However, the process of developing medical technologies remains poorly understood. Although there is clear evidence that innovation in medical technologies happens at the public/private interface, there is little research on the relative roles of contributors from different market sectors in the inception and development of these radical technologies.

One way to assess medical device innovation process is through an analysis of the record of patents related to the development of a given product. Because patents are also published, their review can provide evidence of the timing and nature of a participant’s contribution to the field. When submitting a patent application to the United States Patent and Trademark Office, inventors are required by law to cite previous patents relevant to their work. As a result, patents can provide a useful research tool for identifying and connecting various contributors to the innovative process. For example, Trajtenberg collected patent and citation records related to computed tomography (CT)
scanner technology, and his analysis of the results found that subsequent citations accurately reflect patent importance. Examining patent literature is a viable way of assessing the origins of transformative technology because information can appear earlier in patents than in scientific journals and because patents may include information that does not appear in medical literature.\textsuperscript{17–19}

Given the need for a better understanding of the first origins of device development, and its implications for policies to foster such innovation, we sought to collect the full universe of patents addressing a particular innovative medical device, but with a different goal: to understand the sources contributing to the discovery of that device.\textsuperscript{20} We chose the case example of bare metal stents for treatment of coronary artery disease,\textsuperscript{21,22} a transformative device\textsuperscript{23} that spawned the modern era of interventional cardiology\textsuperscript{24,25} and became a multibillion-dollar industry,\textsuperscript{26} despite ongoing controversy over who deserved credit for their development.\textsuperscript{27} We used a comprehensive database of patents and patent citations to identify all patents related to coronary artery stents. We then categorized the patents on the basis of the business or clinical environment from which they arose, and assessed how the characteristics of those patents changed from the first patents until the approval of the first bare metal stent. Our goal was to evaluate the contribution of these different sectors to the innovation that led to this transformative device.

WHAT IS KNOWN

• Medical device innovation is essential for improving patient care.
• Medical device innovation occurs in both the public and private sectors and can generate substantial economic benefits. However, how best to incentivize innovation is unknown.
• Coronary artery stents are one of the most transformative new medical devices in the past 25 years, form the basis of a multibillion-dollar industry, and can serve as a model for defining whether the key innovations in the field have occurred within industry or academia.

WHAT THE STUDY ADDS

• By closely studying the patent records for coronary artery stents, it is clear that physician-innovators and their small private companies were instrumental in the discovery and early stages of development.
• Larger public companies made their contributions to this innovation at a relatively late stage, after significant product development and testing had already occurred.
• New policies aimed at encouraging transformative innovation should focus on providing the necessary tools and support to physician-innovators.

Methods

Stent Timeline

To determine the time period for the patent search, we first performed a Medline search in English to identify reports of the major clinical events in the development of coronary artery stents. Our search terms were (history or development) and (stent or coronary stent or bare metal stent). From this, we identified more recent review articles describing the history of the bare metal coronary stents as well as the earliest clinical validation studies. We also searched the Food and Drug Administration (FDA) online database for premarket approval applications to identify the major regulatory approvals in this field. On the basis of a review of major events in the early progression of the technology, we focused on the period before the publication of the first pivotal studies on the effectiveness of the technology in 1994 and corresponding FDA approval.

Patent Searching

To identify patents of interest, we used the Thomson Innovation comprehensive patent database of US patent applications and granted patents.\textsuperscript{28} This tool, updated biweekly, includes indexes content from the Derwent World Patents Index and the European Patent Office’s International Patent Documentation Center database. Overall, these records encompass 90 countries with full-text documents from 7 authorities—the United States, Canada, European Patent Office, Patent Cooperation Treaty, France, Germany, and the United Kingdom, and English translations of abstracts from Japanese and Korean applications and granted patents. We focused on patents granted in the United States, which has been the most lucrative single medical device market worldwide. Given the size and importance of the US market, we predicted that medical device companies would prioritize patent protection in the United States. Patents in this database are searchable by terms of interest within the patent, including the title, assignee (the person or company that owns the inventor’s legal patent rights), abstract (short description), claims (list of items on which the applicant is seeking exclusive rights), description (a longer explanation of the elements of the invention and its function), and the classification code (internationally agreed upon hierarchical system of language independent symbols for the classification of patents).\textsuperscript{29}

We used the World Intellectual Property Organization’s natural language search engine (TACSY version 2.1.1) to locate the appropriate International Patent Classification designation used by patent reviewers for classification of applications related to stents (A61F). Within this patent classification section, we identified A61F2/82 to A61F2/94 as the group subclasses encompassing coronary artery stents (Table 1). Thomson Reuter’s innovation platform was then used to identify all patents filed under these patent classification subclasses until 1994. We found a total of 532 relevant patents that met these criteria. Two of the authors (S.X., A.S.K.) then manually reviewed each patent and excluded those that covered the following: vascular grafts, delivery systems for stents, catheters, stent removal or expansion devices, and stents designed for use outside of the vasculature (eg, urological applications). Patents that covered combination catheter and stent systems were included along with novel methods to manufacturer stents. Our final sample comprised 245 patents.

Data Extraction

From each patent record, one of the authors (S.X.) extracted the date of application, date of approval, name of the inventor, name of the assignee (if any), and characteristics of the claims covered by the patent. An assignee is the person or company that owns the inventor’s legal patent rights. To determine the rate of patent citations, our sample of patents were manually inputted by their application number to an electronic database of patents compiled by the National Bureau of Economic Research.\textsuperscript{30} The National Bureau of Economic Research database comprises detailed information on
Table 1. Search Strategy Used to Identify Coronary Artery Stent Patents

<table>
<thead>
<tr>
<th>International Classification</th>
<th>Category Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A61F2/82</td>
<td>Devices providing patency to, or preventing collapsing of, tubular structures of the body</td>
</tr>
<tr>
<td>A61F2/84</td>
<td>Instruments specially adapted for their placement or removal</td>
</tr>
<tr>
<td>A61F2/86</td>
<td>Stents formed from wire-like elements</td>
</tr>
<tr>
<td>A61F2/88</td>
<td>Formed as helical or spiral coils (nets formed from intersecting coils)</td>
</tr>
<tr>
<td>A61F2/90</td>
<td>The wire-like elements forming a net structure</td>
</tr>
<tr>
<td>A61F2/92</td>
<td>Stents in the form a rolled-up sheet expanding after insertion into the vessel</td>
</tr>
<tr>
<td>A61F2/94</td>
<td>Stents retaining their form after locating in the predetermined place</td>
</tr>
</tbody>
</table>

≈3 million US patents granted between 1963 and 1999, which spans beyond the time period of our study, and displays the number of times each patent was cited by another patent (citations received). Citation count is a surrogate measure of the value of a patent and has been linked to patent value and importance in previous economic analyses.

Next, using a methodology from our prior research, we categorized each assignee as belonging to 1 of 3 groups: publicly traded, privately held, or not for profit at the time of patent application. To determine the status of assignees, we used Hoover’s database (Hoover’s Inc, Austin, TX). Hoover’s includes records of 65 million companies searchable by name, location, or industry. The profiles include overviews, history, financial records, and IPO information starting from 1948. Subsidiaries of public companies were categorized as public companies. Assignees without records in the Hoover’s database were researched with supplemental Google, Bloomberg, and Elsevier business intelligence searches. The authors assumed the company to be privately held for 20 entities without available data. Patents not assigned to a particular entity are legally the property of the named individual inventor(s).

Finally, we identified patents that had been abandoned because of delinquent fees or penalized for late upkeep fees required by the Patent and Trademark Office. By definition, delinquent patents are more likely to be of minimal value and not contribute meaningfully to a marketable product.

Results

Accounts of coronary artery stent development date back to the late 1970s, although the first clinical report did not appear until 1985 (Table 2). Until 1994, there were a number of key preclinical, clinical, and regulatory steps leading to the approval of bare metal stents for use in coronary arteries, which quickly became widely used after that point. In an analysis of 12 US hospitals, stent use as a percentage of percutaneous transcatheter angiography procedures increased from 5.4% in 1994 to 69% by 1997.

Overall Patent Data

We identified 245 patents relating to coronary artery stents during the years 1984 through 1994 that involved 107 unique assignees. Private companies were assigned the most patents (110, 44.9%), followed by public companies (77, 31.4%), individual inventors (44, 18.0%), and nonprofit entities (14, 5.7%) (Table 3). Twenty entities that were not identified within our database searches were designated as private. Public companies had the greatest ratio of patents filed to assignees (4.3) among all the different assignee subtypes, suggesting that public companies were the most likely to seek multiple patents in this area. Average citation count was similar across

Table 2. Timeline of Major Preclinical, Clinical, and Regulatory Events in the Early Development of Coronary Artery Stents

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Event Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976</td>
<td>Earliest description of balloon angioplasty for use in the coronary arteries by Gruentzig</td>
<td>Preclinical</td>
</tr>
<tr>
<td>1978</td>
<td>Gruentzig presents his angioplasty technique at the 1978 Society of Interventional Radiology Meeting in New Orleans, and concern about restenosis. Palmaz is in attendance</td>
<td>Clinical</td>
</tr>
<tr>
<td>1985</td>
<td>Gruentzig initiates a collaboration with Gianturco to develop a stent to reduce restenosis</td>
<td>Preclinical</td>
</tr>
<tr>
<td>1985</td>
<td>Palmaz and Schatz describe the use of balloon-mounted slotted-tube stent in the peripheral arteries</td>
<td>Clinical</td>
</tr>
<tr>
<td>Mar 1987</td>
<td>First experimental coronary stent implantation in human patients by Sigwart using WallStent design</td>
<td>Preclinical</td>
</tr>
<tr>
<td>May 1987</td>
<td>Strecker describes a new flexible intravascular stent at the Cardiovascular and Interventional Radiological Society of Europe and the Society of Cardiovascular and Interventional Radiology</td>
<td>Preclinical</td>
</tr>
<tr>
<td>Feb 1991</td>
<td>FDA approval of Palmaz-Schatz balloon-expandable stent (Expandable Grafts Partnership, Johnson &amp; Johnson) for the biliary system</td>
<td>Regulatory</td>
</tr>
<tr>
<td>1992</td>
<td>Studies report efficacy and use of Gianturco-Roubin (Cook Inc) stent to prevent emergency bypass surgery after angioplasty</td>
<td>Clinical</td>
</tr>
<tr>
<td>May 1993</td>
<td>FDA approval of Gianturco-Roubin stent for coronary procedures, specifically emergency management of coronary closures during angiography</td>
<td>Regulatory</td>
</tr>
<tr>
<td>1994</td>
<td>BENESTENT study demonstrating efficacy of Palmaz-Schatz stent in patients with new coronary lesions in the main coronary arteries (n=520) published</td>
<td>Clinical</td>
</tr>
<tr>
<td>1994</td>
<td>STRESS study demonstrating efficacy of Palmaz-Schatz stent (n=410) published</td>
<td>Clinical</td>
</tr>
<tr>
<td>Aug 1994</td>
<td>FDA approval of Palmaz-Schatz stent for elective coronary artery stenting</td>
<td>Regulatory</td>
</tr>
<tr>
<td>1997</td>
<td>Stent use found in 69% of angioplasty procedures</td>
<td>Clinical</td>
</tr>
<tr>
<td>1998</td>
<td>Restenosis Stent Study Group reported a major benefit of stenting for patients who experienced restenosis of a coronary vessel after balloon angioplasty</td>
<td>Clinical</td>
</tr>
</tbody>
</table>
individual inventors, nonprofits, private companies, or public companies. Individual inventors (19, 43%) and nonprofit entities (5, 36%) were more likely to be associated with patents that were delinquent in fees or expired because of lack of payment. This was expected, because individual inventors and nonprofit entities have less funding for the purposes of filing and maintaining a patent. Removing these patents from the database did not substantially change the average patent citation count for any of the assignee subtypes.

**Most Influential Patents**

To identify the key sources of intellectual property contributed to coronary artery stent development, we then focused on the most highly-cited patents and found that the share of patents belonging to privately-held companies increased compared with the overall sample. Among the top 25% of the most highly-cited patents, privately-held companies contributed 31 (51%), publicly-traded companies contributed 16 (26%), individuals contributed 12 (20%), and nonprofit entities contributed 2 (3%).

The top 10 cited patents in our sample are even further skewed toward privately-held companies (Table 4). Expandable Grafts Partnership, a private company started by the physician coinventors of the Palmaz-Schatz stent, owned the most highly-cited patent (1857 subsequent cites), as well as 4 of the top 10. Cook Incorporated, another privately-owned company that commercialized the Gianturco-Roubin stent, owned the third-most highly-cited patent (1017 subsequent cites) and fifth-most highly-cited patent (966 subsequent cites). The Gianturco-Roubin stent and Palmaz-Schatz stent were the first 2 stents approved in the US market, in 1993 and 1994, respectively (Table 2). Medtronic, a public company, owned the second-most highly-cited stent (1039 subsequent cites), although its Wiktor stent was relatively

### Table 4. Top 10 Cited Patents Related to Coronary Artery Stents (1984–1994)

<table>
<thead>
<tr>
<th>Patent</th>
<th>Assignee</th>
<th>Assignee Type</th>
<th>Filing Date</th>
<th>Title</th>
<th>Patent Cite Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>US4733665A</td>
<td>Expandable Grafts Partnership</td>
<td>Private company</td>
<td>11/7/1985</td>
<td>Expandable intraluminal vascular graft has tube formed of thin rectangular section bars which expand to fit lumen</td>
<td>1857</td>
</tr>
<tr>
<td>US4886062A</td>
<td>Medtronic Inc</td>
<td>Public company</td>
<td>10/19/1987</td>
<td>Intravascular radially extendable stent comprises zigzag wire wound into helix and made of low memory metal</td>
<td>1039</td>
</tr>
<tr>
<td>US4800882A</td>
<td>Cook Incorporated</td>
<td>Private company</td>
<td>3/13/1987</td>
<td>Endovascular stent for delivery system comprises wire formed into serpentine shape with alternating loops and bent into cylinder</td>
<td>1017</td>
</tr>
<tr>
<td>US4776337A</td>
<td>Expandable Grafts Partnership</td>
<td>Private company</td>
<td>6/26/1986</td>
<td>Expandable intraluminal vascular graft using angioplasty balloon associated with catheter to dilate and expand lumen of blood vessel</td>
<td>986</td>
</tr>
<tr>
<td>US4580568A</td>
<td>Cook Incorporated</td>
<td>Private company</td>
<td>11/13/1984</td>
<td>Percutaneous endovascular stent has zigzag stainless steel wire which is compressed for insertion</td>
<td>966</td>
</tr>
<tr>
<td>US4739762A</td>
<td>Expandable Grafts Partnership</td>
<td>Private company</td>
<td>12/12/1985</td>
<td>Expandable intraluminal graft has thin walled tube with slots parallel to longitudinal axis</td>
<td>919</td>
</tr>
<tr>
<td>US5064435A</td>
<td>Schneider Inc</td>
<td>Public company</td>
<td>6/20/1990</td>
<td>Self-expanding prosthesis having stable axial length has slidable connected stent segments of open weave constructions which are elastically deformable to reduce radius dia</td>
<td>848</td>
</tr>
<tr>
<td>US4994071A</td>
<td>Cordis Corporation</td>
<td>Private company</td>
<td>5/22/1989</td>
<td>Bifurcating stent device has balloon-deflatable for withdrawal from vessel and used to expand stent</td>
<td>838</td>
</tr>
<tr>
<td>US4856516A</td>
<td>Cordis Corporation</td>
<td>Private company</td>
<td>1/9/1989</td>
<td>Endovascular stent structure has cylindrical form expandable by applying radially outward force</td>
<td>736</td>
</tr>
<tr>
<td>US5102417A</td>
<td>Expandable Grafts Partnership</td>
<td>Private company</td>
<td>3/28/1988</td>
<td>Implanting expandable vascular graft involves number of expandable and deformable grafts expanded within blood vessel</td>
<td>688</td>
</tr>
</tbody>
</table>
late to the US market and was not approved by the FDA until June 1997.

Temporal Trends in Patenting

Starting in 1984, the total number of stent-related patents filed per year steadily increased (Figure). The largest percentage increases in patent counts were in 1992 (68%) and 1994 (97%). Privately-held companies dominated patenting early in the study period, contributing the majority of patents in every year from 1984 through 1989. Publicly-traded companies did not control a majority of patents until the final 2 years (1993 and 1994), although the increase in public company patenting rose substantially during the last 5 years of the sample. Rates of patents owned by individuals and nonprofit entities stayed generally constant throughout the time period studied.

Discussion

This study of patents and patent citations focused on the years preceding the clinical introduction of coronary artery stents, a key transformative medical device that has since helped countless patents and turned into a multibillion-dollar industry. Our results show that smaller private-held companies—created by, or based around, the work of individual physician-inventors—contributed the most patents as well as the most high-impact patents, suggesting that these entities were the main source of innovation during that time. Despite the current dominance of large publicly-traded companies in the coronary artery stent market, such corporations did not contribute substantially to early-stage intellectual property creation, although their patent contributions rose sharply in the period leading up to the approval of the device.

The 2 organizations that our data pointed to as central to the origins of coronary artery stent innovation, Expandable Grafts Partnership and Cook Incorporated, were at the time emerging private companies based around the work of individual physician-inventors. Expandable Grafts Partnership was a partnership of 2 clinician-researchers at University of Texas-San Antonio—Julio Palmaz, an interventional radiologist, and Richard Schatz, a cardiologist—and Phillip Romano, a restaurateur and initial funder of Palmaz and Schatz’s coronary stent ideas. Palmaz originally conceived of models for coronary stent technology as far back as 1978 and had developed and tested the idea substantially before forming Expandable Grafts Partnership in 1983 to help further commercialize his and Schatz’s products. Cook Inc was a medical device company whose coronary artery stent work emerged from an established relationship with pioneering interventional radiologist Cesare Gianturco. Gianturco and his colleagues at the University of Texas MD Anderson Hospital developed and tested the first coronary artery stent designs that Cook would go on to commercialize. Gianturco supplied models for coronary artery stents that were further modified and tested by cardiologist Gary Roubin at Emory University. The importance of these inventors in the creation of coronary artery stents is reflected by the fact that their patents are among the earliest filed in this field, and the most highly-cited by subsequent inventors. By the 1980s, Cook had established itself as a leader in interventional cardiology.

This review of the evolution of one of the most important modern medical technologies suggests a useful model of innovation for medical devices. Coronary artery stents had their origins with physician-inventors, some of whom established small private companies. Only later, as these devices came into widespread use, did the patenting related to them expand to large public companies. Current industry leaders either emerged later in the field, as with Boston Scientific, or obtained market power by purchasing intellectual property from the smaller companies that first brought the device to the market, such as was the case when Medtronic purchased Arterial Vascular Engineering in 1998. For example, Johnson & Johnson licensed stent technology from Expandable Grafts Partnership, whereas Schneider Inc, then a subsidiary of Pfizer and now a part of Boston Scientific, purchased MedInvent, a small private Swiss company, in 1986 to gain access to an early stent design pioneered by Ulrich Sigwart, an interventional radiologist working Centre Hospitalier Universitaire Vaudois in Switzerland.

There is much current discussion among policymakers, industry leaders, and physicians on how to best incentivize future medical device innovation. If replicated in other case studies, the experience of coronary artery stents suggests that promoting creativity by individual physician-inventors and development by small device companies is a compelling model for transformative innovation. The interventions that would most directly address these innovators include funding for investigator-directed research and enhanced seed funding by the National Institutes of Health and other sources of venture capital for entrepreneurial investors seeking to develop small private businesses based on their ideas. Similarly, the stent history suggests that policies aimed at encouraging physician-investigators to initiate, or collaborate with, start-up businesses affiliated with their universities could help encourage future transformative innovation. By contrast, policies such as extending patent terms or reducing regulatory fees are more likely to affect established devices and businesses. Our analysis suggests that increasing revenue and reducing cost for larger public companies would be less likely to impact transformative medical device innovation.

These findings are limited by the reach of our search strategy, and we may have missed some patents integral to this field. To reduce this possibility, we used both automated and manual inspection to ensure a complete patent picture for the
technology studied. Still, we may have missed patents if they were only filed outside the United States, or if they were in an entirely unrelated discipline. As a case study, it may not be generalizable. However, our results are consistent with case histories of other transformative medical devices,28 such as coronary balloon catheters29 and bone densitometry scanners.41 Finally, our analysis of the early development of coronary artery stents used patent documents, so if other essential contributions were made and not patented in the United States or if the patent application were rejected by Patent and Trademark Office examiners, we could have missed them. We remain confident in our results, in part because the Patent and Trademark Office ultimately grants patents for 85% of all applications2 and because the 2 private companies that emerged as key to the field through our patent search were also the companies behind the first coronary artery stents approved by the FDA. Still, the role of intellectual contributions not captured by patents in the development of coronary artery stents and other transformative medical devices bears further study.

In summary, we used patent records to build an innovation model of coronary artery stents, one of the most important medical devices in the modern era of cardiology. Our results point to the central role of physician-innovators and their small private companies in helping create this field, with larger public companies making their contributions relatively later in the product development timeline. Although development of future transformative medical devices will depend on all of these contributors, implementing new policies aimed at encouraging innovation should favor actors more likely to be at the vanguard of future transformative medical device discoveries.

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Disclosures
None.

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