Editor’s Perspective

First-in-Man

Primacy and the Nexus of Innovation in Interventional Cardiology

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I have long been intrigued by the fashion for attributing originality by naming a procedure, complex, or clinical sign after the first person to describe it, and by the perseverance with which such eponyms persist. Blalock-Taussig, Norwood, Glenn, Fontan—marks of honor bestowed by the community in a frontier culture—remain prevalent monikers of operations performed for congenital heart disease, decades after introduction, despite the rationalizing simplifications they represent, and in defiance of the many departures that have transformed their original iterations. That historical field brings to mind a surgeon I encountered many years ago who cataloged his personal, if not eponymous, procedural innovations; notches in a belt, akin to a compendium of patents received or invited lectures given. As I began to explore the literature in that field, aiming to develop a better understanding of how technical progress is chronicled in the medical record, it became clear that, just as the fidelity of certain procedural eponyms may be suspect, the novelty and provenance of purported innovations can be ambiguous, and that, more generally, claims of primacy are inherently fraught. Years later, I came to appreciate the implications of that list, similar to but more acquisitive than the historical stream of eponymous procedures in its insinuation that technical innovations are uniquely forged by a single person, that procedural primacy is the embodiment of innovation in interventional medicine.

Innovation, however, is much more complex, almost inevitably occurring within and evolving from an array of inputs and influences, both successes and failures, emanating from the individual him- or herself, as well as countless predecessors and contemporaries. This observation should go without saying, but it is worth a reminder in the current era, in which innovation has become uniquely esteemed. Accounting for all the influences contributing to the execution of any new procedure, to acknowledge all the contributions to a novel effort, no matter how incremental, is impossible. But when it comes to credit for innovation, one thing is certain: rarely does it reside alone with the first person to perform a procedure in a human.

Almost all procedures are the natural extension of another, and nearly all innovations are tightly coupled to antecedent innovations and indirectly based on many others. Illustrations of this truth abound.

One of the most anticipated and irrefutable innovations in cardiac medicine was culminated on December 3, 1967, when Christian Barnard performed the first human heart transplant. He is and will forever be famous for crossing that transformational threshold, much more so than the runner up, Adrian Kantrowitz, who equaled the task only 3 days later. Perhaps the most instrumental figure in the development of cardiac transplantation surgery and science, Norman Shumway, was a distant third, an entire month later. Barnard’s milestone was far from his or his team’s achievement alone. He trained with Lillehei in Minnesota along with Shumway, where both drew from the vast experience of the team there. And it was only because of work by Shumway and others, not to mention sociocultural conditions where the 3 surgeons were practicing, that Barnard had the opportunity to perform his pioneering innovation. Human heart transplantation was inevitable—someone needed to be first, and Barnard was the person who did it. But the same groundbreaking event would have been performed in short order if the stars had not aligned over Cape Town that day. A similar inevitability hovers over most clinical innovations.

A more recent and proximate example of the nexus within which even profound innovations occurs is the ever-expanding realm of transcatheter heart valve therapy, the most prolific focus of change in interventional cardiology during the past several years. New devices, novel solutions, and creative applications are introduced regularly—on the whole, the technology has been game changing, even disruptive. Once technical feasibility and commercial viability were established after the first human pulmonary and aortic valve implants early this century,1,2 the dam broke and the field has accumulated momentum since, driven by relentless and manifold inputs. Looking forward now, in the early days of 2015, it is not difficult to imagine a long preoccupation with extending and improving this armamentarium. Like transplantation 3 decades earlier, the first human transcatheter valve implant was clearly a monumental innovation, but as the inventor of the first approved percutaneous valve routinely acknowledges in recounting the incubation and hatching of his achievement, that journey and those eventuating in the various other devices that are now revolutionizing therapy for valve disease, were indebted to numerous investigators working from the 1960s up until the current era.3–10

In my editorial capacity, I have the opportunity to review and process many manuscripts, and as a practicing interventionalist, I keep abreast of the broader literature. In doing so, I
run across the terms first-in-man or first-in-human frequently. In some instances, the term and the claim it underlies are fitting—the first human implant of a novel transcatheter valve prosthesis—but in others, the claim is pinned on incremental permutations of a fresh and rapidly evolving technology. These terms, which came into regular use early this century as synonyms for phase I study, were later stretched to indicate not simply a trial, but a discrete step in the device development-regulatory approval-commercialization process. At some point, devices in preclinical development become clinical, and the first-in-man application that marks that transition has clear meaning, if variable significance. But the terms have since morphed into much broader application as signifiers of validity for a purportedly novel modification or use of an existing device. It is a curious, if understandable, instance of lexical creep, in which a term imbued with credibility through its original indication of a clear investigative process has been appropriated to denote and substantiate more incremental and less certain firsts.

This trend is evident in various domains of interventional cardiology, but I am particularly attuned to its arrival in the structural heart disease arena. For instance, on a recent literature search, I was able to find 12 articles published in 2014 alone claiming first-in-man or first-in-human status for a transcatheter mitral valve repair or replacement technology—most of these were single case applications of an approved device in a new or unusual circumstance. In the same search, I was able to identify previously reported cases—some freestanding, some embedded in larger series—that were substantially similar to other reported firsts, and to unreported cases of which I was aware. Herein lies the major difference in the various uses of the term: first-in-man as applied to secondary applications is really meant to signify a first reported use in a human, but even when that meaning may be accurate, it is not necessarily tantamount to first-in-man, and may not be verified with the same certainty. After all, every procedure that is performed in practice is not submitted for publication—indeed, I suspect that many fewer novel applications and creative modifications of interventional devices are published than not. Not surprisingly, none of the aforementioned claims of primacy were issued for clear technical failures, while many rested purely on the technical innovation, describing little if any follow-up, as though the contribution of a procedural innovation is independent of its clinical effect. In a similarly simplifying act of reification, eponymous attribution of a procedural innovation is tantamount to first-in-man, and may not be verified with the same certainty. After all, every procedure that is performed in practice is not submitted for publication—indeed, I suspect that many fewer novel applications and creative modifications of interventional devices are published than not. Not surprisingly, none of the aforementioned claims of primacy were issued for clear technical failures, while many rested purely on the technical innovation, describing little if any follow-up, as though the contribution of a procedural innovation is independent of its clinical effect. In a similarly simplifying act of reification, eponymous attribution of a procedural innovation freezes in name a precedent that is actually fluid.

With few exceptions, the value of an incremental procedure is just that, incremental, insofar as essentially all innovations build on something that came before. The innovation cascade is an endless and organic unfolding that is punctuated by steps and missteps small and large. Whether incremental or disruptive, the significance of an innovation does not necessarily depend on the magnitude of the leap. For all innovations occur within a context, and in relation to the ramifying nature of technical and clinical progress, the downstream effect of any given step is difficult, if not impossible, to gauge.

In our field, secondary, tertiary, and higher-order innovations inevitably follow the introduction of a new technology or technical departure, as practitioners identify the obvious, and imagine some not so obvious, extensions of the technology or technique. Interventional devices are tools to be enlisted in the solution of problems, and the conceptual applications of these tools are fluid: balloons and stents can be used to enlarge or open obstructions, so it is a natural extension of the concept to apply these devices to new or different types or sites of obstruction. Similarly, occlusion devices can be used to close communications, whether congenital or acquired, and applying such tools to new or unusual defects, or tweaking the shape or function of existing devices, while obviously innovations, depend fundamentally on many antecedent procedures and technologies. Inverting the lens, if one digs deep enough, almost every single procedure performed is a first in at least some particularity.

These observations are not offered in an effort to dampen the innovation pulse. Indeed, in urging restraint in claims of primacy and uniqueness, in suggesting that first-in-man be restored to its original and concrete connotations, my hope is not to dismiss the importance or reality of innovation, but to intercept the trivializing effects of overuse. Similarly, in remotely implying that eponymous attributions diminish the communal process of innovation as much as they honor an individual, my impulse is to resist the mythical notion of progress in medicine as a succession of individual achievements. Creativity is, in many respects, the soul of intervention, and the drive to innovate, to push the boundaries, among the fundamental engines of our discipline. But novelty and departure are woven into a complex fabric and cannot be ends in themselves. Doing something for the first time in a human being, which happens often in our field, is but one of the many critical moments in the stretching web of progress. I am all for broadcasting the novel, but believe that the value of reporting incremental innovations lies not so much in highlighting their first-ness as in establishing their connections within the technical and clinical ecosystems that nurtured them. In other words, the spirit of innovation is more genuinely exemplified by giving credit than by claiming it.

Disclosures

Dr McElhinney is a proctor and consultant for Medtronic.

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