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Intracranial Aneurysms, Cancer, X-Rays, and Computational Fluid Dynamics

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uity probably due to the fact that teratomas (which may have fetal-like components) arise, not uncommonly, from it.

To give a balanced view of this man, I asked several individuals who were his residents what they thought of him. Many answered that he loved teaching and was very concerned about them as people and that he was very keen on patient care and became emotional when things were not correctly done. To me, this last observation is not surprising. Individuals who set a high bar for themselves and who deeply care for their patients are often this way. To understand how deeply he cared about patients, I offer the last part of my anecdote:

Once we made it back to the hospital lobby, I told Dr. Shapiro that maybe it was better to return to the reading room and catch up with work. He returned a look as if I had gone crazy. We then took the elevator up to the top floor, talked to the patient, and listened to his lungs. All was going well until he handed me the electrocardiogram strip and asked me to interpret it. When a dumb look crept into my face, he snatched it from me, told me that this time he would excuse my ignorance, and proceeded to give me a lecture on the basics of its interpretation. Dr. Shapiro was the only neuroradiologist whom I have known to be able to do this.

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EDITORIAL

Intracranial Aneurysms, Cancer, X-Rays, and Computational Fluid Dynamics

Recent editorials by Kallmes, Cebral, and Meng, along with a current commentary by Robertson and Watton, have addressed the limitations, capabilities, and potentials of using computational techniques as aids to better understanding both the natural history and the impact of endovascular interventions as they relate to intracranial aneurysms (IAs). We would like to add to this discussion the perspective of 2 colleagues, one an engineer and computational scientist and the other a clinician and interventional neuroradiologist, who have worked together using and developing these techniques over the last 6 years.

Intracranial Aneurysm: A Single Disease?

As recently as the mid-1970s, it was common for physicians deeply involved in oncology research to speak and write about

finding both a “cause and a cure for cancer.” Today, such a notion is archaic. We now find ourselves speaking and writing about IAs using almost identical jargon. Why is it that IAs are considered a single disease and not a spectrum or continuum of a disease, or even multiple diseases having, as their common target, the arterial wall of intracranial arteries? Perhaps it is because, until recently, clinicians have largely thought of the arteries from which aneurysms arise as being “pipes” and of aneurysms as representing a weak spot on an arterial wall, similar to a weak spot on a balloon or inner tube, that is, unable to remodel or repair itself. Only 15 years ago, a review paper in the *New England Journal of Medicine* considered vascular remodeling to be an “emerging concept,”¹ and only in the last several years has the dynamic and rapid responsiveness of vascular remodeling and arterial homeostasis become generally apparent. Perhaps another reason is that, on angiograms, IAs look remarkably similar, hence the moniker “berry aneurysms.” Further contributing to this lack of insight is that the infrequency of patients having serial angiograms has severely limited the ability of practitioners to observe this phenomenon in their patients. Finally, the near absence of naturally occurring IAs in creatures other than humans and the difficulties associated with obtaining suitable tissue at the time of necropsy or surgery have served to severely restrict the study of the sequential biologic changes that occur as IAs form, grow, and rupture.

Computational Fluid Dynamics (CFD): A Virtual Instrument After All

Simply put, CFD produces results of mathematic models (ie, Navier-Stokes equations) that researchers postulate capture the basic laws governing the physics of fluid flows. Only in the late 1950s and early 1960s did it become possible to perform realistic simulations related to air flow over a blunt object, such as a space capsule heat shield, and only in the mid-1990s did it become realistic to perform simulations of blood flow using computational resources, then available only at a limited number of facilities. In the last 5–10 years, research has shown that we can be successful at simulating/predicting how blood flows in and around IAs. In other words, CFD is capable of providing new data with information about the in vivo patterns of blood flow in IAs; these are difficult or even impossible to investigate with imaging modalities. With further experience and dissemination, it seems probable that insights from CFD will, over time, ascend the DIKW (data, information, knowledge, wisdom) ladder. Still, no matter how sophisticated the applications or the knowledge (or even wisdom) that should be derived from these applications, the results will inescapably provide only one, albeit significant, element of the information required to elucidate the natural history of IAs.

Too Many CFD Parameters: Growing Pains or Is There Something Else Predictive of the Natural History of IAs?

Just as we search for and expand the parameters used for measurement of brain perfusion, hoping for better and more reproducible results, we should likewise explore and expand the search for hemodynamic parameters that may correlate with the origin, growth, and rupture of IAs. Our study of the hemodynamic changes in IAs, which are associated with changes in heart rate, is one example of what we view as a potentially

significant parameter that has yet to be fully evaluated.² New technologies develop and evolve so as to both optimize their capabilities and expand the applications to which they may be applied. Such it was with x-rays, and such it is with CFD. New technologies are most often overvalued when first described; then, as they become disseminated, they sink below their true value, finally reaching a state of realistic value only when they have been widely tested and optimized. Potential applications of CFD have not been fully explored, optimization of computational techniques for assessing blood flow in and around IAs is ongoing, and the definition of the most meaningful output parameters are not at a stage where there can be any broad consensus. Thus, in our opinion, it is not realistic to make a value judgment regarding the ultimate value of CFDs, either as a means for investigating basic hemodynamic phenomena or as a tool that may be useful in a clinical environment.

Next Step and Closing Remarks

To us, it seems implausible to expect that, in isolation, CFD studies may reveal singular keys to important questions about a biologic process such as the initiation, growth, and rupture of IAs. It does, however, seem quite plausible that the results from CFD studies on large populations could provide great help in categorizing aneurysms according any number of hemodynamic parameters. Perhaps, then, these categories, when correlated with other factors known to be important in vascular health—such as collagen mutations, smoking, family history, and so on—and then if further combined with information specific to individual patients—such as age, sex, and perianeurysmal environment—could give insights that might prove useful in predicting the risk of aneurysm rupture. We fully realize that correlations do not represent causation; however, in our experiences, as well as in those of others, they sometimes offer very significant hints.^{3,4} As the ability to perform CFD in clinical environments on large numbers of patients increases, as more insight is gained into the regulation of arterial health (homeostasis) and remodeling, as more understanding is gained about the mechanics of the vascular wall, as the ability to image not only the vascular lumen but also the arterial wall increases, this additional information may send computational scientists back to broaden and refine their mathematic models, thereby leading to methods that would allow investigation and integration of other important and potentially clinically relevant parameters, such as collagen turnover, cross-linking, and so on (eg, fluid-structure-growth modeling).

Believing in the great potential for the integration of observations and measurements made by clinicians with simulations, calculations, and models made by scientists, we feel that this is a time to be optimistic and proactive in collaborations that unite and optimize our ability to define just what value CFD adds to the ability to mitigate the death and misery currently associated with IAs.

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EDITORIAL

Computational Fluid Dynamics in Aneurysm Research: Critical Reflections, Future Directions

Dr Kallmes’ provocative editorial “Point: CFD—Computational Fluid Dynamics or Confounding Factor Dissemination” raises a number of important questions about the status of aneurysm research.¹ It has served to initiate a public discourse between engineers and clinicians on the contributions of computational fluid dynamics (CFD) to this research field.² We would like to add to what we hope is an ongoing, informative, and productive dialogue.

The first article applying CFD to the field of aneurysm research appears to be that of Gonzalez et al in 1992.³ Despite the conclusion in this seminal article that “computer modeling can further our understanding of factors that determine the origin and progression of intracranial aneurysms,” it was more than 10 years before CFD took off as a tool for studying cerebral aneurysms. Indeed, in an advanced title search (TS) on the Web of Science for articles matching TS = (aneurysm AND [cerebral OR (cranial)]) AND TS = ([computational and fluid] OR [CFD]) came up with only 12 articles through 2004, increasing to 10 in 2006 alone, 19 in 2008, and 55 in 2011, with a total of 195 articles through 2011. In fact, the number of publications has grown nearly exponentially since 2002. Hence, it is certainly an appropriate time to step back as a community to reflect on where we are now and to consider where we would like to go.

In this Editorial, we focus on some of the questions raised by Dr Kallmes and comment on what we perceive as the most serious barriers to progress. While this complex and important subject clearly cannot be comprehensively addressed in a handful of editorials, we hope this initial dialogue will instigate a deeper analysis that will identify the most important technical limitations and highest priority avenues for future research.

Why Are There So Many Idealizations in CFD Studies?

While Dr Kallmes’ comments were directed specifically at CFD researchers, most of his questions are actually equally relevant to investigators using other tools to study aneurysms. For instance, if we ran the same hemodynamic studies in an experimental system, we would similarly need to question whether blood should be modeled as a single-phase liquid with constant viscosity, whether we have suitable inflow and out-