AJNR

Point: CFD––Computational Fluid Dynamics or Confounding Factor Dissemination

D.F. Kallmes

AJNR Am J Neuroradiol 2012, 33 (3) 395-396
doi: https://doi.org/10.3174/ajnr.A2993
http://www.ajnr.org/content/33/3/395

4. A history of transhumanist thought. www.nickbostrom.com/papers/history.pdf. Accessed April 1, 2011
5. Transhumanism: the world's most dangerous idea? http://www.nickbostrom.com/papers/dangerous.html. Accessed April 1, 2011
6. The Singularity Is Near. Wikipedia. http://en.wikipedia.org/wiki/The_Singularity_Is_Near. Accessed April 1, 2011
7. Ray Kurzweil. Wikipedia. http://en.wikipedia.org/wiki/Ray_Kurzweil. Accessed April 1, 2011
8. Kurzweil Technologies. http://www.kurzweiltech.com/ktiflash.html. Accessed April 1, 2011
9. 1965–"Moore's Law" predicts the future of integrated circuits. Computer history museum. http://www.computerhistory.org/semiconductor/timeline/1965-Moore.html. Accessed April 1, 2011
10. Singularity Institute. http://singinst.org. Accessed April 1, 2011
11. **Merely Human? That's So Yesterday.** *New York Times.* Business Day. June 12, 2010. http://www.nytimes.com/2010/06/13/business/13sing.html?pagewanted=2&sq=singularity%20university&st=cse&scp=1. Accessed April 1, 2011
12. Are you ready for the future? Singularity University. http://singularityu.org/programs/graduate-studies-program/#admissions. Accessed April 1, 2011
13. Future studies and forecasting. Singularity University. http://singularityu.org/programs/graduate-studies-program/curriculum. Accessed April 1, 2011

M. Castillo
Editor-in-Chief

http://dx.doi.org/10.3174/ajnr.A2664

EDITORIAL

Point: CFD—Computational Fluid Dynamics or Confounding Factor Dissemination

Stimulated by our ongoing uncertainty about which unruptured cerebral aneurysms to treat brought about by a near-complete lack of meaningful clinical trial data, facilitated by substantial increases in computing power, and promulgated by scientists and engineers facile in generating massive amounts of data on estimated flow in virtual tubes, computational fluid dynamics (CFD) now holds a prominent position in the endovascular research community. Physicians see color displays generated by CFD and hope that we are starting to gain insight into why some aneurysms rupture and others do not. Journal editors have welcomed the field of CFD because of its captivating color schemes perfect for cover material, prompting some observers to propose that "Color For Doctors" represents the true meaning of CFD in the clinical realm.[1] I, on the other hand, propose a different perspective on the emerging field of CFD: confounding factor dissemination.

By way of full disclosure, I am not a professional computational scientist. However, I did learn in college how to calculate a Reynold's number. By way of a little investigating, I also know the following: 1) that most published CFD articles apply boundary conditions on the basis of idealized flows from articles published in the late 1980s (rather than individualized patient flows), 2) that the walls of the vessels are assumed to be rigid, and 3) that estimated numeric outputs can vary as much as 50% on the basis of whether geometries used CTA or 3D rotational angiography.[2] Finally, I know that the simple mathematic definition of wall shear stress (WSS) is simply the slope of the line from a curve plotting velocity as a function of distance from the vessel wall.

I have been told by computational scientists that we clinicians do not really need to know all of the gory details anyway, just as we do not really need to know all of the details about how the x-ray equipment works to perform angiography. I beg to differ. For example, many or most computational articles at least mention WSS, and in numerous articles, WSS represents the prime focus and the potentially "bad actor" in aneurysm rupture. However, there are as many, or more, definitions of "WSS" as there are types of intracranial aneurysms. WSS can be averaged with time ("time averaged" WSS) or over an area (the inlet zone, outlet zone, or dome) or can be maximal (typically at peak systole) or minimal (at end diastole). It can be oscillatory (oscillatory shear index), can be normalized to the parent artery flow or not, or can be a difference of 2 WSSs (WSS gradient). Thus, to say that WSS is correlated with a specific phenotype may mean a lot of different things to different people, and it is no wonder that, in turn, both elevated and diminished WSS has been associated with rupture in various studies.[3,4] Moreover, of course, correlation does not always equate to causation.

Unfortunately, defining WSS is just the beginning of the confusion. Each new computational article seems to introduce a new index or 2. We now need to learn, in addition to WSS, terms related to kinetic energy, vorticity, impact zone size, aneurysm-size ratio, aspect ratio, nonsphericity index, relative residence time, energy loss, and gradient oscillatory number[5]—and the list goes on and likely will continue to get longer. Given the rapid expansion of the number of potential CFD "outcomes," it is highly likely that many new "correlations" between these outcomes and rupture will be found—that is, the more comparisons you do, the more likely you are to find a spurious difference.

Perhaps a key problem with CFD research is that it is generally performed by isolated groups analyzing data from a very small number of cases. Relatively small studies provide substantial value in screening potential indices but, in my opinion, are as likely as not to identify confounding variables rather than the true agents of harm. Moreover, this is even assuming that aneurysm rupture is hemodynamic rather than biologic, which remains unclear to say the least. To really figure out what, if any, clinical utility CFD has, we need collaboration across specialties, including but not limited to statisticians, endovascular therapists, and clinical trialists. Performing statistical correlations between dozens (now) and hundreds (soon) of computational indices with aneurysm phenotype (typically ruptured versus unruptured) likely will require extremely large clinical datasets and sophisticated tools such as machine learning.

Until now, neurointerventionalists have marveled at the aesthetically pleasing color images that CFD provides, hoping that someday soon they would lead to clinical application. Clinicians would love to have a CFD button to push that provides a "treat/do not treat" decision for a given patient, but that is probably not going to happen soon. To help define what, if any, flow-related parameters really matter clinically, CFD researchers will need to do a lot more work to close the gaps in information and address the conflicting information and confounding variables.

References

1. Steinman DA. **Computational modeling and flow diverters: a teaching moment.** *AJNR Am J Neuroradiol* 2011;32:981–83
2. Geers AJ, Larrabide I, Radaelli AG, et al. **Patient-specific computational hemodynamics of intracranial aneurysms from 3D rotational angiography and CT angiography: an in vivo reproducibility study.** *AJNR Am J Neuroradiol* 2011;32:581–86
3. Sforza DM, Putman CM, Scrivano E, et al. **Blood-flow characteristics in a terminal basilar tip aneurysm prior to its fatal rupture.** *AJNR Am J Neuroradiol* 2010;31:1127–31
4. Shojima M, Oshima M, Takagi K, et al. **Magnitude and role of wall shear stress on cerebral aneurysm: computational fluid dynamic study of 20 middle cerebral artery aneurysms.** *Stroke* 2004;35:2500–05
5. Shimogonya Y, Ishikawa T, Imai Y, et al. **Can temporal fluctuation in spatial wall shear stress gradient initiate a cerebral aneurysm? A proposed novel hemodynamic index, the gradient oscillatory number (GON).** *J Biomech* 2009;11;42:550–54. Epub 2009 Feb 4

D.F. Kallmes
Mayo Clinic
Rochester, Minnesota

http://dx.doi.org/10.3174/ajnr.A2993

EDITORIAL

Counterpoint: Realizing the Clinical Utility of Computational Fluid Dynamics—Closing the Gap

With great interest, we read the stimulating editorial by Dr Kallmes, who raises important questions regarding the potential utility of computational fluid dynamics (CFD) in guiding neurointerventional and neurosurgical treatment of cerebral aneurysms. We believe that Dr Kallmes' opinion is representative of that of most avant-garde clinicians who have collaborated with computational scientists or engineering researchers. These clinicians not only appreciate the aesthetic and intuitive aspects of CFD simulations but also recognize their enormous potential for providing objective, quantitative, and mechanism-based parameters to stratify aneurysm rupture risk and help aneurysm management. Recently clinical journals such as the *American Journal of Neuroradiology* have seen an increasing number of articles about CFD. It is sobering to reflect on where we are and where we should be heading.

Dr Kallmes' main points are the following: 1) CFD involves assumptions that might make results questionable; 2) a large number of hemodynamic parameters have surfaced in recent publications, which are confusing and confounding; 3) to change the current situation of isolated groups working on a small number of cases, cross-disciplinary collaboration on a large amount of clinical data is required to realize the clinical utility of CFD; and 4) CFD researchers need to close the gaps in information and address the conflicting information and confounding variables. These are excellent points (despite a few minor misconceptions), with which we emphatically agree.

We wish to express our thoughts in response to Dr Kallmes' points. CFD holds great promise for revealing aneurysm pathophysiology and for becoming a tool that the neurointerventionalists could expect to use routinely someday to assess patients' aneurysm rupture risk and to guide treatment. However, an aneurysm is a complex problem. To make CFD work for clinical practice, computational scientists/engineers and clinicians have to work much closer together. We are fully on board with Dr Kallmes in his call for multidisciplinary collaboration to build a large clinical data base for CFD and to realize its clinical utility.

How Much Detail Should Clinicians Know about CFD and Its Assumptions?

Dr Kallmes raises an important question about whether clinicians need to know the details of CFD computations. We are of the opinion that though clinicians do not need to understand all the details of how CFD calculations are performed, just as they do not know all the details about the medical imaging equipment they use, it is very important that they at least understand the approximations, assumptions, and limitations of these techniques, just as they do with medical imaging systems.

Dr Kallmes mentions some typical approximations made in most CFD studies, apparently implying that because of these, the CFD methodology is inaccurate and unreliable. CFD has played an indispensible role in almost every aspect of technology that we enjoy in modern life, including aircraft design, food processing, and weather forecasting. Its technology is sound and its efficiency is increasing. To make the computational problem tractable, approximations and assumptions are inevitable. In fact, approximation is the way of modeling, whether it is numeric or physical. Some of these mentioned assumptions and approximations are not exclusive to CFD modeling. For instance, experimental in vitro flow models have similar limitations regarding flow conditions and geometry reconstruction, while animal models and in vivo flow measurements introduce a whole universe of other assumptions and limitations.

The decision of whether to accept certain approximations and simplifications is a trade-off between accuracy and cost and sometimes feasibility. What is important in our opinion is to understand the effects of these approximations and to understand what to expect from the computational, experimental, or animal models. These effects can be and some have been studied through sensitivity analyses to understand their relative importance. For instance, vascular wall motion can be considered a second-order effect compared with the variability of the physiologic flow conditions.[1] Computational models are particularly well-suited to perform this kind of analysis because they allow us to explore the effect of different factors independently.

Why There Are a Large Number of Parameters Published

Dr Kallmes expressed his concern over the growing number of hemodynamic factors being proposed as potential indicators of aneurysm rupture risk, leading him to wonder if CFD is "confounding factor dissemination." We understand that this situation is frustrating for clinicians, who, being initially excited by CFD as the aesthetically pleasing "color for doctors," are led to hope that this powerful simulation tool will soon help save patients' lives.

We think that the growing number of proposed parameters principally stems from the complexity of aneurysm rupture mechanisms and the scarce knowledge we have about them. Furthermore, the growing number of proposed parameters and conflicting results indicate that we are still in an exploration phase. Some divergence during this phase in the search for understand-