# Computational Modeling and Flow Diverters: A Teaching Moment

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spending at the level of overall price inflation; the other, at the gross domestic product plus a small percentage. If one used data from recent years, both of these metrics would only slow the growth of health spending relative to the size of the economy as a whole.

We do not expect that Baumol's hypothesis[2] will be proved false, but one may reasonably hope that the previously inexorable expansion of the fraction of our national effort that is devoted to health care may proceed more slowly than it has since the Medicare program began in the 1960s. Perhaps, when observing from some future vantage point, we will attribute a large part of our social progress to medical improvements and see a society in which health care has not consumed all of the increases in wealth that our ingenuity has created. Perhaps when health care spending has increased as Baumol's hypothesis predicts, at least we will see that the money has been allocated as effectively as possible.

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**EDITORIAL**

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Less than a decade ago *AJNR* published some of the first case studies of cerebral aneurysm hemodynamics using the then-novel combination of computational fluid dynamics (CFD) and 3D medical imaging. *AJNR* has since become the pre-eminent venue for such "image-based" or "patient-specific" CFD models, which have provided important clues about the roles that hemodynamic forces may play in the natural history and management of cerebral aneurysms. It is perhaps no surprise, then, that *AJNR* now plays host to what is arguably this young field's first real controversy, by virtue of its potential for immediate clinical and economic impacts.

In last month's issue of *AJNR*, Fiorella et al[1] took exception to conclusions drawn by a paper published earlier this year by Cebral et al,[2] which had used image-based CFD models to show that "flow-diversion devices can cause intra-aneurysmal pressure increases, which can potentially lead to rupture, especially for giant aneurysms." Fiorella et al expressed grave concerns about the accuracy of the CFD models and the design of the study, and cautioned against any rush to judgment about the safety of these devices for certain patient populations. In their reply, Putman et al[3] vehemently defended their results and study design, and took exception to what they perceived as an attack on their scientific integrity.

What is the reader to make of this heated and often highly technical exchange between 2 of the most expert groups in aneurysm hemodynamics and flow diverters? As it turns out, both sides raise valid and important points that reflect issues at the heart of computational modeling and its use in clinical research. And so, in the parlance of contemporary American political discourse, this presents an opportune "teaching moment."

### *In theory there is no difference between theory and practice. In practice there is. – Attributed to Yogi Berra*

On the face of it, Cebral et al's study was straightforward: 1) take 3 cases of aneurysms that had ruptured during or soon after treatment with flow diverters; 2) perform image-based CFD analysis of each aneurysm before and after virtual deployment of the device(s); and 3) identify any hemodynamic factors that might have differed between the 2 simulations. In cases 1 and 3, strong pressure drops proximal to the aneurysm, arising from a stenosis or area reduction, were resolved following recanalization of the parent artery, exposing the CFD model aneurysms to 20–25 mm Hg higher peak systolic pressures posttreatment. For case 2, the virtual deployment of the flow diverter resulted in an increase in flow resistance that required a 25-mm Hg–pressure increase to maintain the same flow rate.

Referring to cases 1 and 3, Fiorella et al argue that the pretreatment pressure drops (and hence the posttreatment aneurysmal pressure rises) predicted by CFD are as much as an order of magnitude greater than those calculated via "the principles of conventional fluid mechanics," which are in turn shown to be consistent with classic in vitro and animal experiments. Putman et al's reply is essentially to point out that those principles and experiments are based on idealized or simple vascular geometries, whereas CFD implicitly accounts for the anatomically realistic geometries in the Cebral et al study.

To help makes sense of this disagreement, consider that the Navier-Stokes equations, which govern fluid flow, comprise 4 competing terms, which account for pressure, shear, momentum, and inertia. Under certain simplifying assumptions (eg, long straight tube, unidirectional flow, etc), these equations can be simplified greatly, such that the effects on pressure of shear, momentum, and inertia can each be separated and solved by hand, namely the Poiseuille, Bernoulli, and Newton laws employed by Fiorella et al. As long as those simplifying assumptions hold approximately, these laws can be used individually or together with confidence. Such is likely the case for the experiments cited by Fiorella et al to back up their calculations, which involved the use of relatively straight tubes or arteries, shallow ($<1°$) tapers, and/or ideal stenosis geometries. It is debatable, however, whether they hold for the complex, irregular, and tortuous geometries considered by Cebral et al.

Having said this, Fiorella et al's back-of-the-envelope calculations are an essential part of any engineering analysis, because such large discrepancies with theory can indeed point to problems in an experiment or simulation; however, they may simply reflect factors that cannot be captured by simple calculations. The former is the position of Fiorella et al, the latter that of Putman et al. Without further evidence it is difficult to know who is right, but as is often the case, the truth probably lies somewhere in between. To their credit, Putman et

al have offered their geometries to allow others to verify that they are indeed solving the Navier-Stokes equations correctly.

### *Solving the equations right [versus] solving the right equations.– PJ Roache*[4]

Fiorella et al's more serious and contentious accusation is that Cebral et al invoke autoregulatory mechanisms to align the negative findings of case 2 with their hypothesis. In their sharply worded reply, Putman et al deny any such bias, and attribute this to "an incomplete understanding of the handling of patient 2." In fact, it appears those authors invoked autoregulatory mechanisms in a well-intended but incomplete attempt to rationalize assumptions they were forced to make about the flow rates through their models.

Before continuing, it is important to note that Cebral et al did not have access to any information about patient-specific flow rates either before or after treatment, as they readily concede. Instead, as is done in many computational hemodynamics studies, they prescribed their model flow rates by combining a characteristic flow waveform shape with a mean flow rate estimated from a scaling law. Specifically, they assumed a mean inlet wall shear stress (WSS) of 15 dyn/cm$^2$ for all cases, which allowed the mean flow rate to be calculated, via Poiseuille's law, from the model's inlet diameter raised to a power of 3. This so-called cube law dates back to the Murray principle of minimum cardiovascular work,[5] and the "normal" WSS level of 15 dyn/cm$^2$ was popularized by the influential review article of Malek et al.[6] Physically, these scaling arguments are consistent with observations that arteries tend to adjust their caliber to changes in flow to maintain WSS.[7] As stated in their Methods, Cebral et al based each case's flow rate on the model's parent artery inlet dimensions, and "identical boundary conditions and model parameters were used in the pre- and poststent placement models."

For case 2, their posttreatment simulations predicted an increase in vascular resistance across the model domain, which would require a 25 mm Hg increase in peak systolic pressure to maintain the same flow rate before and after treatment, and hence an increase in aneurysmal pressure consistent with that predicted for the other 2 cases. However, Cebral et al seemed to recognize that an increase in vascular resistance after treatment could also lead to a redistribution of flow through lower-resistance collateral pathways. Using a simple electrical analog model, they predicted a 20% reduction in flow and, consequently, a negligible intra-aneurysmal pressure rise of only 2 mm Hg. On the other hand, they argued that it was possible that autoregulation might serve, at least in part, to justify their assumption of the same flow rate before and after treatment, and thus the possibility of a ~25 mm Hg posttreatment aneurysmal pressure rise.

In their reply, Putman et al concede that a reduction in flow rate posttreatment, and thus a negligible pressure rise for case 2, is probably the more likely scenario, owing to the circle of Willis. They reiterate, however, that their assumption of a fixed flow rate is plausible for patients who might have inadequate collateral pathways, and thus a marked increase in aneurysmal pressure posttreatment is possible in this case. This is not unreasonable, but it remains that Cebral et al did not appear to consider, or at least did not discuss, the implications of possible flow redistributions for the other cases, and this may be what troubles Fiorella et al.

For case 3 there was no change in total vascular resistance across the model posttreatment, and so there would be no reason to invoke collateral pathways or autoregulation. For case 1, however, Cebral et al reported a reduction in total vascular resistance across the model posttreatment, opposite to the situation for case 2. Consequently, it is plausible, and perhaps even likely, that flow rates were lower before versus after treatment, and consequently the 25-mm Hg pressure drop across the proximal stenosis, which accounts for the posttreatment aneurysmal pressure rise in case 1, might also have been negligible. (Confusingly, Cebral et al noted in their discussion of cases 1 and 3 that "Reduction in this proximal resistance led to increased flow into the aneurysm segment and a subsequent increase in intra-aneurysmal pressure," which seems at odds with the assumption of fixed flow rates inferred from their Methods.) In other words, for 2 of the 3 cases the glass may be half empty or half full depending on what you believe about the prescribed flow rates and assumptions made.

Cebral et al, among others, have been proactive in stress-testing image-based CFD models to uncertainties about flow rates and other assumptions, and these models have undoubtedly proved their worth by providing valuable insights into intra-aneurysmal velocity and WSS patterns. Until now, less attention has been paid to pressure or the impact of virtual interventions on the prevailing flow conditions, and this reflects a well-appreciated challenge of modeling the outcome of an intervention via CFD, namely the need for "prediction, not prescription, of flow distribution".[8] In other words, as Fiorella et al imply and Putman et al admit, solving the Navier-Stokes equations correctly is a necessary but not sufficient condition for proving that they, or at least their boundary conditions, are correct from a physiologic or clinical point of view.

### *There's something happening here. What it is ain't exactly clear. – Buffalo Springfield*

It is undeniable that questions are emerging about potential complications associated with the use of flow diverters. Cebral et al have not used CFD to identify a new problem—the 3 cases in question did rupture during or soon after treatment by flow diverters—nor did they insist on any immediate change in the design and use of flow diverters based on their admittedly preliminary findings. Rather, as Putman et al clarify in their reply, they have used CFD as proof-of-principle of a novel and plausible hypothesis that might explain the poor outcome for these and other cases. True, their CFD-predicted pressures may be overestimated, and their assumptions about flow rates are necessarily primitive—and untested, as they readily admit. Their study is based on only 3 cases, all giant internal carotid artery aneurysms, and only crudely controlled by 4 other cases. Nevertheless, and notwithstanding any systematic errors, they are right to point out that such forensic CFD analyses are ideal for highlighting potential differences that deserve further investigation.

So what is to be done? First, these CFD simulations have undoubtedly highlighted possible high-resistance anatomic features (eg, stenoses, sharp bends, strong tapers) that can be identified and documented retrospectively for cases of periprocedural rupture. As Putman et al point out, their hypothesis should "provide the incentive to measure systemic blood pressure or intra-arterial pressures" where possible and ethical. More broadly, there is a pressing need to acquire not just anatomic but functional information, at least in some cases, in order for image-based CFD models to be confidently validated as patient-specific. Dynamic angiographic data can certainly help in this regard,[9] and Doppler sonography measurements, though subject to various artifacts and assumptions, would provide an important reality check on pre- versus postprocedural differences in flow rates or flow patterns. Recent advances in phase-contrast MR imaging may ultimately allow for a more thorough validation of image-based CFD models,[10] or replace them altogether, even for estimation of pressures.[11]

In the end, Cebral et al probably could have been more circumspect about the broad conclusions spelled out in the abstract of their paper. For this reason alone Fiorella et al were right to highlight the real

possibility that the results of this study could be misinterpreted by careless readers or misused by those with a hidden agenda, with the potential for real consequences to the health of patients, and perhaps that of medical device companies. Any real or perceived inferences of unscientific or unethical behavior are groundless, and indeed, both groups agree that further investigations are required before these findings should make their way into clinical decision-making. On the bright side, that the results of this study could be considered to have an acute enough impact on patient care and the medical device industry to warrant such strongly worded correspondence is a sure and healthy sign that image-based CFD has matured into something more than "Color For Doctors."

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