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Initial Clinical Experience with AView—A Clinical Computational Platform for Intracranial Aneurysm Morphology, Hemodynamics, and Treatment Management

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Abstract

Background—Intracranial aneurysm (IA) management is challenging. Clinicians often rely on varied and intuitively disparate ways of evaluating rupture risk that may only partially take into account complex hemodynamic and morphologic factors. We developed a prototype of a clinically-oriented, streamlined, computational platform, AView, for rapid assessment of hemodynamics and morphometrics in clinical settings. To show the potential clinical utility of AView, we report our initial multicenter experience highlighting the possible advantages of morphologic and hemodynamic analysis of IAs.

Methods—AView software was deployed across 8 medical centers (6 US, 2 Japan). Eight clinicians were trained and used the AView software between September 2012 and January 2013.

Results—We present 12 illustrative cases that show the potential clinical utility of AView. For all, morphology and hemodynamics, flow visualization, and rupture resemblance score (a surrogate for rupture risk) were provided. In 3 cases, AView could confirm the clinicians' decision to treat; in 3 cases, it could suggest which aneurysms may be at higher risk among multiple aneurysms; in 5 cases, AView could provide additional information for use during treatment decisions for ambiguous situations. In one stent-assisted coiling case, flow visualization predicted that the

intuitive choice for stent placement could have resulted in sacrifice of an anterior cerebral artery due to blockage by coils and led clinicians to reconsider treatment plans.

Conclusions—AView has the potential to confirm decisions to treat IAs, suggest which among multiple aneurysms to treat, and guide treatment decisions. Furthermore, the flow visualization it affords can inform aneurysm treatment planning and potentially avoid poor outcomes.

Keywords

Clinical tool; Computational fluid dynamics; Decision-making; Hemodynamics; Intracranial aneurysm; Morphometrics; Rupture Resemblance Score

Introduction

Intracranial aneurysms (IAs) are potentially devastating lesions that are estimated to impact 5–8% of the population.^{1, 2} Aneurysmal rupture is responsible for the most devastating type of hemorrhagic stroke, with high fatality rates (45% overall during the first year),² high disability rates (50% of survivors have major disabilities and 64% never recover their previous quality of life), and high health care costs.^{3, 4} The management of IAs is problematic because although rupture can be catastrophic, rupture rates are low and the risk of treatment complications is significant.^{2, 5} The American Heart Association/Stroke Association guidelines for IA management suggest that clinicians “consider morphological and hemodynamic characteristics of the aneurysm when discussing the risk of aneurysm rupture.”⁶ However, morphometrics and hemodynamics require extensive engineering expertise to calculate. Currently, there is no such tool in clinical practice to obtain these parameters in a reliable and timely fashion.

We created such a tool through collaboration among neurointerventionists, engineering researchers, and software engineers. We developed a prototype for a clinical software platform, “AView,” for rapid assessment of patient-specific IA hemodynamics and morphometrics in the clinical setting.⁷ We then deployed this prototype at 8 clinical centers to test its technical feasibility. All participating clinicians embraced this innovative clinical tool, and all of them underscored the urgent need for such a tool to be integrated into the day-to-day clinical workflow for IA management.

In this paper, we briefly introduce this tool, AView, and describe the clinical experience associated with this tool by sharing 12 aneurysm cases from the AView clinical pilot study.

Material and Methods

Development of AView Software

AView was designed to be used by clinicians as a tool in the routine management of aneurysms. During the design phase, we initially identified features that would be desirable to clinicians. We then conducted a survey of 50 potential clinical end-users with a broad range of understanding of computational fluid dynamics (CFD), including neurosurgeons, neuroradiologists, and neurointerventionists to formalize user requirements. The survey sought to ascertain the desired features in terms of data input, data output, levels of

interaction between the user and the tool, acceptable time frames for user interaction, as well as timeframes for obtaining flow simulation results, modalities of visualization, and integration of the system within the clinical workflow.

On the basis of the pre-design survey results, we designed the AView workflow, consisting of 6 modules: clinical data, segmentation, morphology analysis, flow simulation, flow visualization, and report (Figure 1). The details of each module were described previously.⁷ Briefly, in the clinical data module, clinical demographic data (including age, sex, family or previous history of IAs, smoking habits, hypertension) are collected in an anonymous form. In the segmentation module, three-dimensional (3D) models of the aneurysm and adjacent vascular structures are generated from 3D images, including rotational catheter angiography, computed tomographic angiography (CTA), and magnetic resonance angiography (MRA). To define the vascular structures, the user can interactively place spheres of varying radii on vessels in individual image slices, or use a threshold-based segmentation method. For sphere placement, after the spheres are placed they are connected to form tubes that are merged and refined to form the vessel surface. The user can then clean the geometry using a pre-processing module, where the geometry can be smoothed, and the inlets and outlets can be trimmed. In the previously validated morphology analysis module,⁸ the final surface geometry is used to interactively perform morphometric calculations by asking the user to trace a line across the aneurysm neck (for non-fusiform lesions) or region of dilatation (for fusiform aneurysms) on a projection view of the 3D IA geometry and to select the main inlet parent vessel. The segmented IA surface geometry is loaded into the flow simulation module for model pre-processing and mesh generation. Then, the user specifies boundary conditions at inlets and outlets. The inlet waveform can be defined as the generalized patient waveform used in previous studies,^{9, 10} or the user can import a patient-specific waveform. The user can also define blood viscosity and density values. Blood flow simulations are exported to an open-source parallel incompressible flow-simulation solver, GnuId,¹¹ and simulation data are automatically imported back to AView for postprocessing.

The hemodynamics of bulk blood flow can be visualized as pathlines, streaklines, flow jets, and velocity vectors. Wall hemodynamics can be shown as maps of wall shear stress (WSS) magnitude and oscillatory shear index (OSI) distribution. Figure 2 shows an example of the flow pattern (pathlines) and WSS distribution. Synthetic hemodynamics indices for the aneurysm sac are automatically computed and reported to the user.⁷ Finally, a report with a summary of clinical data, computed morphologic and hemodynamic quantities, and rupture risk assessment is provided to the user (Figure 1). The statistical models from Xiang et al.⁹ have been adopted to calculate the rupture resemblance score (RRS). In the retrospective study by Xiang et al. of 119 IAs, morphologic and hemodynamic characteristics were identified that discriminated ruptured from unruptured IAs using multivariate logistic regression. The resulting classification model identified high size ratio (SR), low WSS, and high OSI as the only independently significant factors associated with IA rupture status. The predictive model was subsequently reinterpreted as RRS, where a score of 100% represented an aneurysm with the most resemblance to previously known rupture components. RRS can act as a surrogate marker for identifying potentially dangerous unruptured aneurysms that highly resemble the hemodynamic and/or morphological parameters of ruptured aneurysms.¹²

The current implementation of AView is a Mac-based platform for research purposes. Simulations can be run locally on a user-specified number of cores, or the user can manually submit simulation files to remote computing centers. Typical simulation time using a coarse volumetric mesh is 3 hours with 4 cores (or 12 computing-hours) and with a fine volumetric mesh can be up to 10 hours with 24 cores (or 240 computing-hours).

Clinical Pilot Study of AView

To test the technical feasibility of AView for use in the clinical setting, we conducted a pilot study among clinicians. Six clinical centers from the US, including our own, and two from Japan participated in a trial of the use of AView, launched in September 2012. Clinicians from each participating center were trained to use AView either in person or via a video conference. Between September 2012 and January 2013, clinicians retrospectively analyzed cases with AView after treatment decisions were made. Institutional review board approval for this study was initially obtained at the University at Buffalo and subsequently at each of the participating centers.

AView was used to analyze morphology and hemodynamics and provide clinicians with the aforementioned various outputs (Figure 2), including flow visualization, morphometrics, and hemodynamics. On the basis of these parameters, AView calculated an RRS that related the parameters for the aneurysm of interest to those of a database of previously studied ruptured and unruptured lesions. Clinician treatment decisions were compared to AView-derived RSS to evaluate how recommendations might have impacted treatment decisions. From 10 patients, we present 12 aneurysm cases from the multicenter trial that illustrate the potential impact of AView. These cases demonstrated the potential clinical utility of AView with respect to aneurysm treatment decision-making and treatment planning.

Results

Of the 12 aneurysm cases presented here, AView could confirm the clinicians' decisions to treat IAs in 3 cases, suggest which aneurysm to treat among multiple aneurysms in 3 cases, recommend critical treatment guidance for ambiguous situations in 5 cases, and provide direction regarding potential stent placement in one case. A summary of the 12 cases is presented in Table 1.

Example Cases Demonstrating Potential Impact of AView on Aneurysm Treatment and Decision-Making

1. Confirmation of decision to treat

Case 1: This 73-year-old woman was admitted with a history of dizziness and nausea for several months. Catheter angiography revealed an 8mm right posterior inferior cerebellar artery aneurysm. The aneurysm was slightly larger than the conventional threshold for treatment of 7mm¹³ and had a high two-dimensional (2D) aneurysm-to-parent vessel SR,^{14, 15} thus, the clinicians decided to treat the aneurysm. Using AView, we calculated the aneurysm's 3D morphological and hemodynamic parameters (Figure 3). Its high SR (9.6; mean ratios were 3.14 for ruptured and 1.58 for unruptured IAs from our previous cohort of 119 IAs),⁹ extremely low normalized WSS (0.1; mean normalized WSS values of 0.33 for

ruptured and 0.68 for unruptured IAs),⁹ and very high OSI (0.0179, mean OSI of 0.016 for ruptured and 0.0035 for unruptured IAs)⁹ yielded high RRSs of 100% and 94% from the morphological and hemodynamic models, respectively. These scores indicated high risk and were consistent with the clinician's intuitive choice that the unruptured IA should be treated.

Case 2: This 50-year-old woman presented with the sudden onset of the worst headache of her life, dizziness, and left-sided weakness. A CT scan demonstrated subarachnoid hemorrhage in the basal cisterns. Catheter angiography demonstrated an 11.7mm paraclinoid internal carotid artery (ICA) aneurysm with irregular contours. Treatment of the aneurysm was planned and carried out. The images were imported into AView for geometry calculation and flow simulation to confirm the decision-making. The flow visualization module revealed complex flow within the aneurysm sac and a complicated WSS distribution structure, resulting in high OSI distributions on the aneurysm surface (Figure 3). These features led to high RRSs of 70% and 75% for the morphological and hemodynamic models, respectively. AView calculations confirmed high rupture risk for this aneurysm; and thus, the decision for aneurysm treatment.

Case 3: This patient presented with worsening headaches. CTA revealed a 9mm posterior cerebral artery aneurysm. The clinician decided to treat this aneurysm with stent-assisted coiling due to its large size, high 2D SR, and irregular shape. AView calculations yielded a high SR (4.79), extremely low normalized WSS (0.18,) and relative high OSI (0.0097) (Figure 3). The resulting RRSs were high: 92% from the morphological model and 74% from the hemodynamic model. AView risk prediction was consistent with the intuitive clinical decision to treat this large, irregularly-shaped aneurysm.

2. Ambiguous cases in which the lesion does not meet customary (size) treatment thresholds—AView could assist aneurysm treatment decisions in cases where the lesion does not meet customary treatment thresholds, such as excessive dependence on size <7mm alone.¹³ The following cases demonstrate utility in such situations.

Case 4: A patient presented with a 5.5mm posterior communicating artery aneurysm observed during routine CT angiography. Due to low procedural risk and the location, the aneurysm was treated. AView flow visualization revealed flow impingement and diversion at the aneurysm dome (Figure 3). Although calculations demonstrated an aneurysmal WSS value close to the parent vessel (normalized WSS=0.79), an extremely high OSI (0.032) was found. The RRS from the hemodynamic model was high at 95%, whereas the morphological model yielded a more moderate RRS of 32%. Despite the aneurysm's smaller size, the high RRS from the hemodynamic model was consistent with the clinical decision for treatment.

Case 5: A 63-year-old woman had hyperlipidemia and carotid ultrasound imaging showed mild intima-media thickness. Subsequent MRA revealed an unruptured 6mm middle cerebral artery (MCA) aneurysm. The aneurysm was treated by clipping. AView calculations showed a high SR of 4.31, strong flow impingement at the aneurysm tip, a low WSS of 0.26, and an extremely high OSI of 0.031 (Figure 3). These values generated high RRSs of 84% and 99% for the morphological and hemodynamic models, respectively. Despite the

aneurysm's smaller size, the high RRS from the hemodynamic model was consistent with the clinical decision for treatment.

Case 6: This asymptomatic, neurologically intact 52-year-old woman had a primary family history of aneurysmal subarachnoid hemorrhage and so underwent screening MRA. This noninvasive imaging demonstrated a 4.6mm right MCA aneurysm that was subsequently confirmed by catheter angiography. Also found in that study was a left parietal arteriovenous malformation that was remote from the aneurysm. The patient was treated with clip ligation of the aneurysm. AView analysis found this aneurysm to bear rupture characteristics of high size ratio, low normalized WSS, and high OSI (Figure 4). The calculated RRSs were 31% and 80% from morphological and hemodynamic models, respectively. Despite the aneurysm's smaller size, the high RRS from the hemodynamic model was consistent with the clinical decision for treatment.

Case 7: A 52 year-old woman had a family history of IAs and was found on screening noninvasive imaging to harbor an unruptured 6.6mm right ICA aneurysm. On the basis of traditional size thresholds, this small aneurysm may be considered low risk and be observed with serial imaging. However, as a preventative measure, the aneurysm was treated with clip ligation. Using AView, we calculated the morphological ($SR=2.15$) and hemodynamic metrics ($WSS=0.18$, $OSI=0.012$) (Figure 4). According to these metrics, the calculated RRSs were 54% and 30% from the morphological and hemodynamic models, respectively. Providing such insight to an ambiguous case may aid in treatment decision.

Case 8: This 64-year-old man with a history of laryngeal carcinoma, status-post resection, adjunctive chemotherapy, and radiation therapy, was found on surveillance imaging to have an incidental 7mm left supraclinoid ICA aneurysm. The decision of whether to treat this 7mm aneurysm was difficult for the clinicians. However, the clinicians decided to treat this aneurysm because of the low procedural risk at this location. AView flow visualization demonstrated that the flow was rather regular, with inflow through the aneurysm distal neck, forming a stable, large vortex, and ultimately exiting the aneurysm at the proximal neck region (Figure 4). This type of flow generated normal levels of WSS and OSI. AView calculations generated moderate RRSs of 32% and 39% for the morphological and hemodynamic models, respectively. The model predictions suggested low to moderate rupture risk.

3. Which aneurysm to treat among multiple aneurysms

Case 9, 10, 11: Aneurysm cases 9, 10, and 11 are from the same patient. This patient (a 67-year-old woman) presented with right hand and foot numbness. Diagnostic catheter angiography revealed 3 aneurysms located at the left ICA (Case 9, 10mm), the left MCA (Case 10, 3mm), and the basilar apex (Case 11, 7mm). The clinical team initially decided to treat the left ICA aneurysm due to the patient's symptoms. AView calculated the SR, WSS, and OSI for all 3 aneurysms to evaluate the RRSs (Figure 4). The RRSs of the left ICA aneurysm were 53% (morphological model) and 28% (hemodynamics model). Despite its smaller size, the basilar tip aneurysm had higher RRSs of 82% (morphological) and 55% (hemodynamics), whereas the RRSs of the left MCA aneurysm were less than 20% for both

models. The clinical team decided to treat the basilar tip and left ICA aneurysms but not the MCA aneurysm. AView prediction was consistent with clinical decisions.

4. Direction as to stent placement

Case 12: AView could aid treatment planning by visualizing flow directions, impingement, and flow jet locations. Figure 5 shows a 6.6mm wide-necked proximal anterior cerebral artery (ACA) aneurysm just distal to the ICA terminus. Given that it incorporated the origin of the ACA with circumferential involvement, treatment options for this aneurysm included flow diversion from ICA-MCA and stent-coiling from ICA-ACA. Flow diversion from ICA to MCA would have been technically far easier than stent-coiling given the acute angle from ICA to ACA. However, stent-coiling from the ICA to the ACA was chosen to avoid potential ACA sacrifice as it was assumed based vessel size that less blood flow may be entering the ACA. AView analysis of some flow pathlines showed an unexpected flow pattern with flow to the ACA traveling from the ICA through the aneurysm dome and with flow within the distal ACA primarily coming from the anterior communicating artery (AComMA). With significant AComMA flow, flow diversion of the aneurysm from ICA-MCA may not result in obliteration. Given this visualization, an informed decision could be made to place the stent from the ICA to the ACA.

Discussion

AView is a clinician-oriented, integrated, image-based computational tool for assessment of aneurysm morphology, hemodynamics, flow visualization, and RRSs.⁷ In this paper, we report 12 aneurysm cases from the AView pilot study to test the feasibility of this technology. We demonstrate that AView has the potential to help clinicians in both aneurysm treatment decision-making and treatment planning. AView predictions could confirm decisions to treat or not, inform treatment decisions in ambiguous cases, and inform clinicians of potential for varied risk in cases of multiple IAs. Furthermore, we demonstrate that AView could potentially influence aneurysm treatment planning, as shown in Case 12, wherein detailed visualization of flow pathlines guided stent placement in a case of stent-assisted coiling.

Over the past decade, in conjunction with advancements in 3D medical imaging, CFD has become increasingly prevalent for vascular flow simulation. Diagnosis and management of vascular diseases using simulation tools have now become reality. As one example, HeartFlow[®] was approved by the Food and Drug Administration (FDA) in November 2015 for determination of the necessity for coronary stenting based on hemodynamics calculation of noninvasive fractional flow reserve derived from standard acquired coronary CTA datasets (FFR_{CT}).¹⁶ FFR_{CT} was validated in four clinical trials.^{16–19} The calculation of FFR_{CT} by HeartFlow has the potential to become an integral part of care for patients who are at risk for coronary artery disease because of its potential to improve clinical outcomes, improve the patient experience by avoiding invasive tests, and reduce the cost of care. At the same time, the FDA's initiative pathway encourages computational simulations to take a more substantial role in submissions made for medical device approval (regarding the simulation tool itself [e.g., HeartFlow or AView] as a device).

Image-based CFD, such as AView, can provide important clues about the role of hemodynamics throughout the natural history of an IA.^{20, 21} Three recent CFD challenges, in 2012,²² 2013,²³ and 2015 (<http://cfdchallenge2015.c.ooco.jp/index2.html>), have pushed the frontiers of image-based CFD for IAs. In the 2015 CFD challenge, 28 groups of CFD researchers were asked to predict the rupture status for 5 ruptured MCA aneurysms through hemodynamics calculation. More than 200 clinicians were also asked to predict the rupture status on the basis of visual inspection of aneurysmal anatomy. Whereas 83% of experienced CFD researchers predicted the aneurysm ruptures correctly, only 67% of neurointerventionists correctly predicted ruptures (unpublished results, American Society of Medical Engineers [ASME] Summer Biomechanics, Bioengineering, and Biotransport Conference 2015 [SB³C 2015]). Demonstrations such as these hint at the potential for image-based CFD to improve clinical IA management.

Our research group was able to robustly predict rupture possibility in these challenges, based on years of work in assessing characteristics of aneurysm rupture.^{9, 10, 12, 24, 25} We calculated the hemodynamics for more than 200 patient-specific aneurysms and developed robust regression models to quantify the resemblance of aneurysms to a ruptured cohort using a parameter, termed RRS.^{9, 12} Our hemodynamics RRS model was validated in another 85 aneurysms by our Buffalo-based research group.¹² Furthermore, this model was able to correctly distinguish ruptured MCA aneurysms from unruptured MCA aneurysms and also predicted the rupture region for the ruptured MCA aneurysms in the 2013 CFD challenge;²³ in addition, our hemodynamics RRS model was able to accurately predict the two ruptured MCA aneurysms from the three unruptured MCA aneurysms with similar size and shape in the 2015 CFD challenge (Varble N, Meng H: unpublished data, February 2015). Although RRS can potentially detect a high similarity of new IAs to already ruptured IAs in our cohort, future longitudinal studies should investigate the ability of RRS to predict eventual rupture.

A clinician's decision making with regards to IAs is complex. Each neurointerventionist, whether endovascular or exovascular, inherently and intuitively computes the potential for rupture for each aneurysm encountered. This includes the clinical demographics, age, comorbidities, smoking, hypertension, and personal or family history of rupture. It also includes the IA shape, location, and, the most widely studied rupture predictor that we focused on in this study, size. These considerations are informed by both personal experience and published literature, which is clouded by a lack of consensus especially when considering the appropriate size threshold that warrants treatment.^{13, 26–28} Then there is consideration of treatment risk. Collectively, these are utilized to come to a treatment decision, we suspect with normal variance. It is this complex task which is performed variably by physicians that can be streamlined by AView, with the expectation that treatment complications could be avoided in low-risk aneurysms whereas rupture complications could be avoided in high-risk aneurysms, ultimately resulting in better care for our patients with IAs and more confident treatment plans by our physicians.

In the future, we would like to assimilate AView into the real-world clinical setting for better aneurysm management. In addition to morphological and hemodynamic factors, AView can incorporate a myriad of clinical and procedural factors for a more comprehensive risk-

assessment model. We envision that this tool could become one of the first clinical decision-making tools for aneurysm management. To reach our goal, we need to (1) make AView more user-friendly, (2) perform a multicenter study to build a larger aneurysm database, and (3) develop treatment planning toolsets, including virtual coiling and stenting, to assess and optimize different treatment strategies. For cases similar to Case 12, larger studies will need to be performed to better understand how specific treatments influence the flow and potentially long-term obliteration, regrowth, or recanalization.

Conclusions

In this study, we introduce AView, an image-based computational tool for IA flow visualization and clinical management and share our clinical experience with its application via the illustration of 12 aneurysm cases. We demonstrate that AView can aid aneurysm rupture risk assessment and treatment planning.

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Abbreviations

2D	two-dimensional
3D	three-dimensional
ACA	anterior cerebral artery
ACommA	anterior communicating artery
CFD	computational fluid dynamics
CT	computed tomography
CTA	computed tomographic angiography
FDA	Food and Drug Administration
FFR_{CT}	noninvasive fractional flow reserve derived from standard acquired coronary computed tomography angiography datasets
IA	intracranial aneurysm
ICA	internal carotid artery
MCA	middle cerebral artery
MRA	magnetic resonance angiography

OSI	oscillatory shear index
RRS	rupture resemblance score
SR	size ratio
WSS	wall shear stress

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Highlights

- A tool for intracranial aneurysm assessment of hemodynamics and morphometrics (AView) is presented
- The potential clinical utility is illustrated in 12 cases derived from 8 centers
- AView has the potential to confirm and guide treatment decisions

Figure 1. Implemented AView workflow consisting of clinical data, segmentation, morphology analysis, flow simulation, flow visualization, and report modules.

Figure 2.
An example of flow visualization of flow patterns (pathlines) and wall shear stress (WSS) with the AView graphical user interface.

Figure 3.
Cases 1–5: Pathlines, WSS, and oscillatory shear index (OSI) distribution

Figure 4.
Cases 6–11: Pathlines, WSS, and OSI distribution

Figure 5.
Case 12: Anterior (left) and posterior (right) visualization of pathlines. MCA, middle cerebral artery; ACA, anterior cerebral artery; ICA, internal carotid artery.

Table 1
Summary of the 12 clinical cases in which AView could aid in clinical decision making or treatment strategy *

Case	Aneurysm Location	Size mm	Morphology	RRS	Hemodynamics	Potential Impact of AView
1	Posterior Inferior Cerebellar Artery	8	100%		94%	Confirmation of decision to treat
2	ICA	11.7	70%		75%	
3	Posterior Cerebral Artery	9.3	92%		74%	
4	Posterior Communicating Artery	5.5	32%		95%	Ambiguous cases in which the lesion does not meet customary treatment thresholds
5	MCA	6.7	84%		99%	
6	MCA	4.6	31%		80%	
7	MCA	6.6	54%		30%	
8	ICA	7.4	32%		39%	
9	ICA	10	53%		28%	Which aneurysm to treat among multiple aneurysms
10	MCA	3	11%		13%	
11	Basilar Tip	7	82%		55%	
12	ICA	8.6	54%		30%	Direction as to stent placement

* Abbreviations: ICA, internal carotid artery; MCA, middle cerebral artery; RRS, rupture resemblance score