HPCI magazine Vol.16

HPCI magazine
富岳百景
FUGAKU HYAKKEI

Digital Twin of Cerebral Blood Circulation Provides Optimal Medical Care for Individuals

Satoshi Ii
Professor, Department of Mechanical Engineering, School of Engineering, Tokyo Institute of Technology

Cerebral infarction and subarachnoid hemorrhage are serious and scary conditions related to abnormalities in the circulation of blood within the brain. Imaging tests such as CT (computed tomography) and MRI (magnetic resonance imaging) are used to diagnose these diseases, but they do not provide detailed information on blood flow. Some brain diseases are also related to the circulation of cerebrospinal fluid and cerebral interstitial fluid. Therefore, Prof. Satoshi Ii and his colleagues are conducting research to create a “brain circulation digital twin” that reproduces the cerebral circulation of an individual patient in cyberspace, so that clinicians can predict the risk of disease at the point of care.

Simulating Blood Flow throughout the Brain

Until fiscal year 2022, Prof. Ii was a member of the research project of the Program for Promoting Research on the Supercomputer Fugaku led by Prof. Shigeo Wada of Osaka University. “When it comes to the brain, neural activity tends to attract attention, but blood circulation that carries oxygen and nutrients supports neural activity. Furthermore, abnormalities in blood circulation can lead to illness, so detailed information on circulation could be used to help with diagnosis in clinical settings. That’s why Prof. Wada thought about simulating blood circulation throughout the brain,” Ii said, explaining how his research began.

To simulate blood circulation, we must first create a model of the entire vascular network of the brain. Prof. Ii undertook this task. “In the brain, the thick carotid arteries branch into thinner vessels that spread throughout various parts of the brain and then reconverge into the thick jugular veins. While the shapes of the thick vessels can be determined from CT or MRI images, the arrangement of the thinner vessels cannot be seen. Therefore, we established mathematical rules to create the network of thin vessels,” he explained.

The brain vascular network model constructed in this manner (Fig. 1) closely replicated the actual vascular network. Furthermore, in this project, other members created a “physical model” that modeled the flow of blood according to the physical laws. This enabled a successful simulation of blood flow through the vascular network model that Prof. Ii had built (Fig. 2). This has made it viable to analyze cerebral blood flow in detail and examine its relationship with brain diseases.

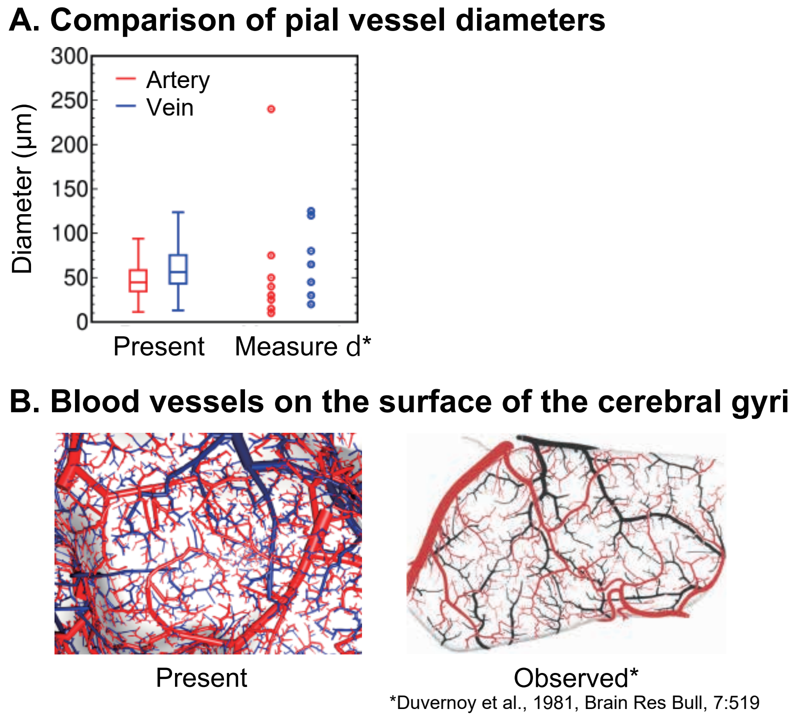

Fig. 1: Comparison of the brain vascular network model and the actual brain vascular network

Rules such as “blood flow at the terminal is proportional to the brain region size” and “minimize the total volume of the entire pathway” were presupposed to create the thin vessels and construct a model of the vascular network across the entire brain surface. The distribution of the diameters of the model’s vessels closely matches the distribution of the diameters of actual vessels (A), and the shape of the vascular network is also very similar to observed results (B).

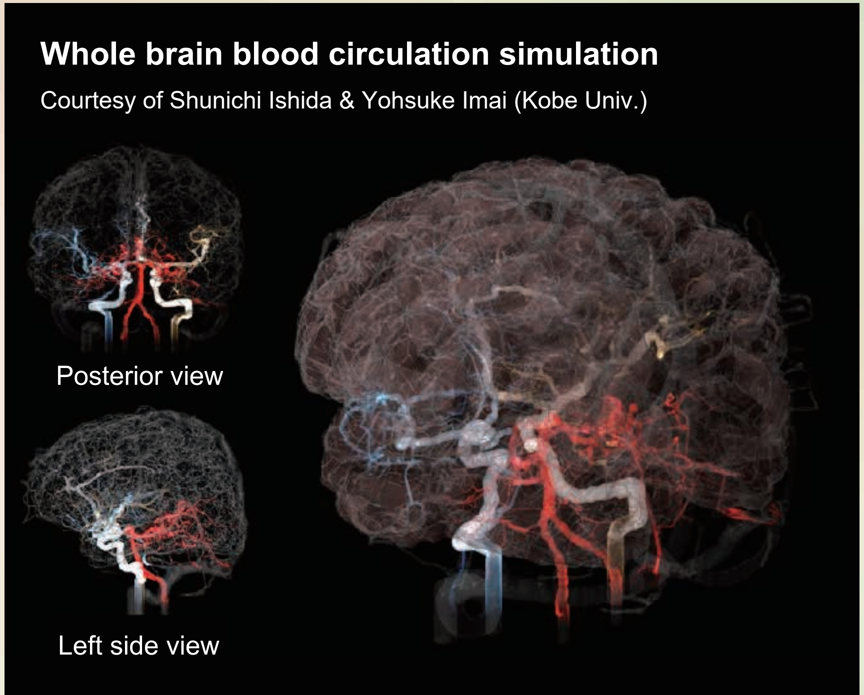

Fig. 2: Whole brain (surface) blood circulation simulation

A scene from a video showing blood entering from the carotid artery, circulating through the brain surface, and flowing out to the jugular vein. The peripheral blood vessels (microcirculation) extending from the brain's surface toward the center have not yet been calculated. However, this simulation required the full power of the K computer.

Cerebral Aneurysms: Difficulties in Assessing Risks between Surgery and Observation

Since fiscal year 2023, Prof. Ii has been working on a new research project as the principal investigator. "In this project, the goal is to extend the results of Prof. Wada's work to other aspects of brain circulation beyond blood, as well as to develop tools that can be immediately used by doctors in clinical settings," he said. Let's illustrate how this research is progressing, using a cerebral aneurysm as an example.

A cerebral aneurysm is a bulging, weakened area in the wall of a blood vessel in the brain (Fig. 3). The rupture of this bulge leads to subarachnoid hemorrhage, which can be fatal in many cases. There are two main treatments for cerebral aneurysms. One involves performing a craniotomy to clip the base of the aneurysm, preventing blood flow to it. The other involves using a catheter to deliver metal coils into the aneurysm through the blood vessel, filling it internally. Both treatments carry significant risks and are challenging procedures.

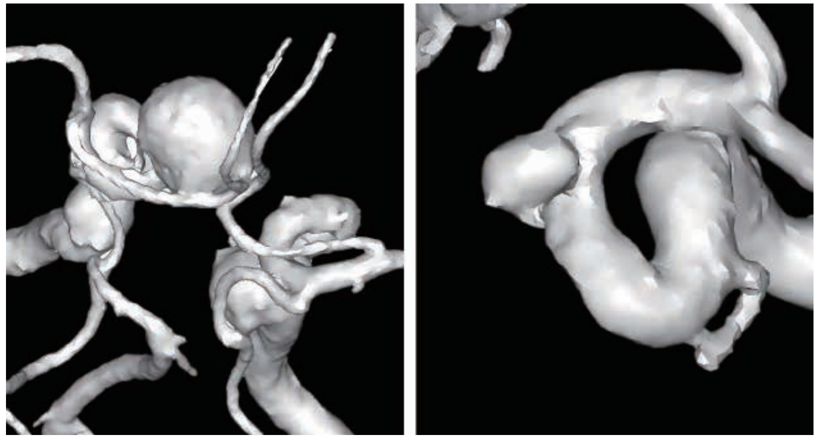

Fig. 3: Three-dimensional shape of cerebral aneurysm constructed from MRI Images

Cerebral aneurysms can form at a branching point (left) or on the side (right) of cerebral arteries.

For physicians, whether to adopt a treatment is a dilemma, since many individuals with cerebral aneurysms live their entire lives without experiencing a rupture. Assessing whether the risk of the aneurysm growing and rupturing is greater than the risk of treatment is difficult. This has led to a growing demand for predicting the rupture risk of specific aneurysms in specific patients.

Blood Flow Simulation of Cerebral Aneurysm

Cerebral aneurysm growth and rupture are thought to be influenced by the pressure of blood flowing through the aneurysm and the wall shear stress (shear forces exerted on the blood vessel wall). Therefore, Prof. Ii utilized insights gained from the previous project led by Prof. Wada to simulate the blood flow near the aneurysm.

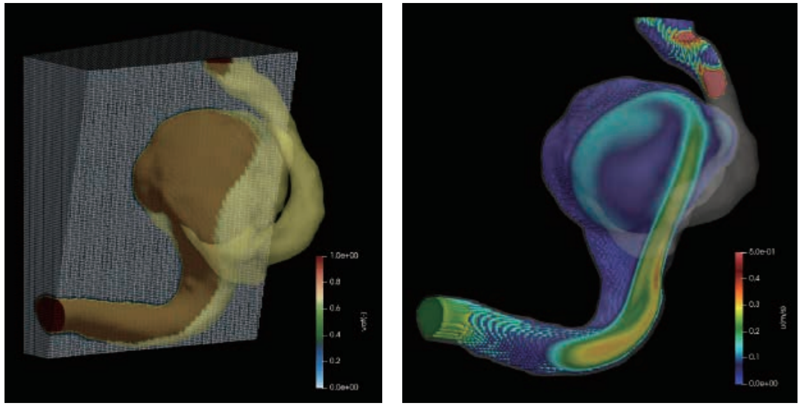

Fig. 4: Blood flow simulation near cerebral aneurysm

Blood vessels near the cerebral aneurysm (in this case, with a diameter of approximately 14mm for the aneurysm, and overall approximately 20mm) segmented into orthogonal grids for simulating blood flow.

Specifically, Prof. Ii segmented the blood vessels near the cerebral aneurysm into an orthogonal grid, and conducted simulations using a physical model (Fig. 4). Since each patient's blood vessel shapes vary, using an orthogonal grid approach avoids the complexity of generating calculation grids that align with the vessel shapes each time. One reason for choosing orthogonal grids is their suitability for large-scale parallel computing, at which Fugaku excels.

A significant feature of this research is the incorporation of "data assimilation," which is used in applications such as meteorological simulations. Data assimilation involves integrating observational data into

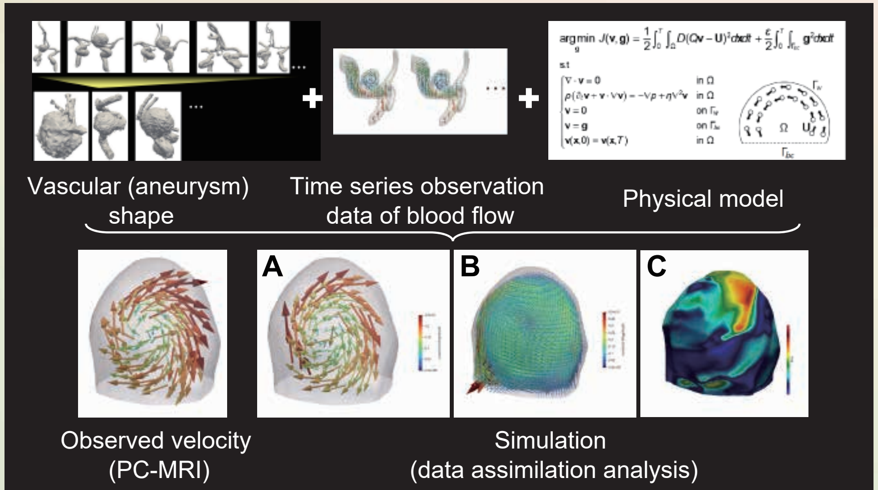

Fig. 5: Blood flow simulation using data assimilation

Time-series data of the blood flow velocity measured by PC-MRI was incorporated into the simulation. With PC-MRI it is possible to observe the blood flow velocity at various points inside the blood vessels, though the level of granularity is low as shown in the lower left. By assimilating this data into the simulation, it becomes viable to calculate the blood flow velocity (B) and shear stress on the vessel wall (C) at each point with high resolution. Image A was prepared by decimating the high-resolution blood flow velocity distribution data obtained from the simulation (B) to reproduce the observed velocity.

simulations to ensure that simulations do not deviate from the reality. "In this case, we are simulating a portion of the brain's blood vessels, so we need to define boundary conditions such as the flow velocity entering that area. Using average values alone would not replicate the individual conditions of each patient," explained Prof. Ii. Therefore, he enabled specific simulations to each patient by assimilating the flow velocities at various points inside the blood vessels measured using PC-MRI*1 (Fig. 5).

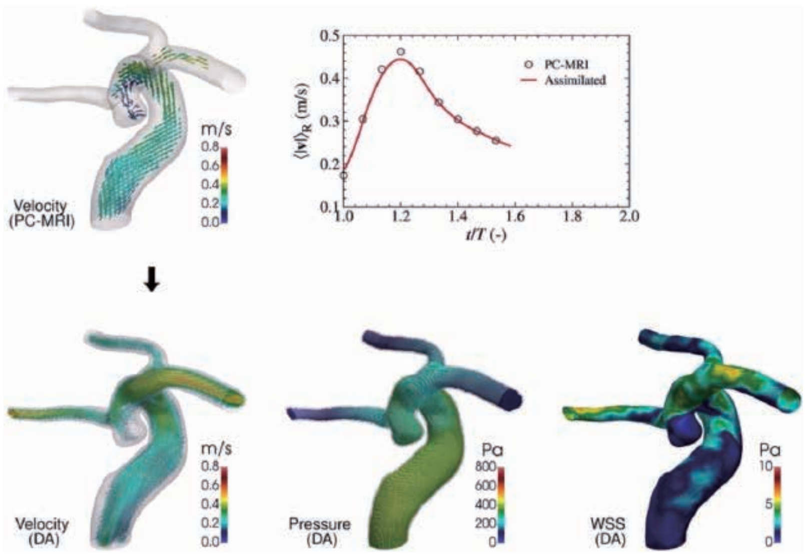

Fig. 6: Scene from a simulation video of one cardiac cycle of a cerebral aneurysm

From left to right in the lower section: Blood flow velocity, pressure exerted on the vessel wall, and wall shear stress are shown. The intensity increases from blue to red. The upper left section shows observational results from PC-MRI. The circles (〇) on the right graph represent blood flow velocity measured by PC-MRI. The solid red line represents the blood flow velocity obtained from the simulation. The measured and simulated values closely match.

In this way, it is now possible to perform blood flow simulations for individual cerebral aneurysms (Fig. 6). Preparations have finally been completed to gather data on wall shear stress and local pressure, which cannot be known with imaging devices. "The risk factors for the growth of cerebral aneurysms are still not clearly understood. There are reports suggesting that strong wall shear stress contributes to growth, while others indicate that significant changes lead to growth, creating divided opinions on what exactly constitutes a risk factor. To clarify these risk factors, it is crucial to accumulate numerical data obtained through simulations and analyze them quantitatively," Prof. Ii explained, emphasizing the significance of this approach.

Aiming to Develop Applications That Can Be Used in Clinical Settings

"However, even if the risk factors are identified, it is impractical for physicians to conduct patient-specific simulations to predict the growth or rupture risks of cerebral aneurysms in clinical settings. Considering the busyness of clinical environments and computing resources, a simpler predictive model is needed. Therefore, we are focusing on developing machine learning models," Prof. Ii continued.

This machine learning model infers the pressure on blood vessel walls and wall shear stress from imaging data. Since inference is feasible even with the computational power available in clinical settings, this model could enable PC applications where, for example, clicking on an aneurysm's wall in an MRI image displays the pressure and wall shear stress there. Physicians could use this information to assess the risk.

However, to create this machine learning model, it is necessary to train it on a large teaching dataset pairing imaging examination data (vascular shape and velocity field) and data calculated from simulations, including the pressure on the blood vessel wall and the wall shear stress. Gathering these data by conducting PC-MRI examinations on a large number of patients in clinical settings is not feasible. Therefore, Prof. Ii and his team plan to generate teaching data using simulations. While individual simulations are not computationally intensive, they intend to leverage the computational power of Fugaku to quickly obtain simulation results for tens of thousands of different scenarios.

To obtain teaching data, they will create a large amount of pseudo-image test data from single image test data by slightly changing the shape of blood vessels, blood viscosity, etc., and perform a blood flow simulation for each. Using the simulation results as teaching data has the advantage of creating a machine learning model with better performance than using noisy image test data as is.

Predicting Disease Progression with Digital Twins

In Prof. Ii's project, Prof. Marie Oshima from the University of Tokyo, another participant, aims to construct a different type of machine learning model focusing on severe internal carotid artery stenosis. Instead of directly simulating, the model aims to infer simulation-equivalent results using parameters such as the length of the vessel and the degree of narrowing or derive risk factors (such as changes in blood flow velocity in this case) by transforming outcomes.

Furthermore, in this project, they are expanding the scope of simulations and machine learning to include not only blood-related fluids relevant to conditions like stroke and cerebral aneurysm, but also cerebrospinal fluid related to hydrocephalus and brain interstitial fluid associated with Alzheimer's disease.

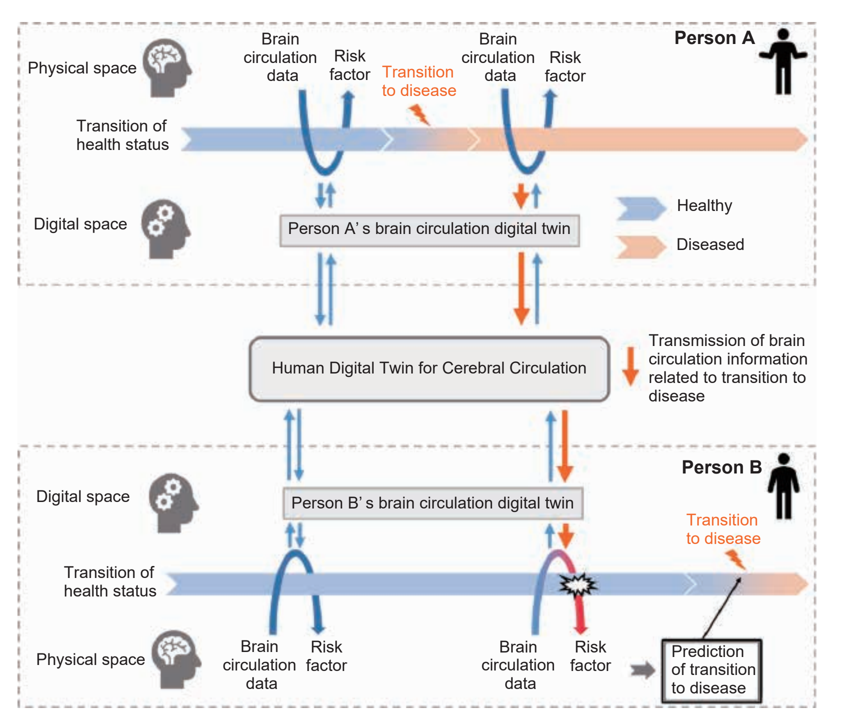

Fig. 7: Predicting disease progression using "Human Digital Twin for Cerebral Circulation"

Using the digital twin of brain circulation for an individual (Person A), the values of risk factors can be determined from their brain circulation data. Each examination provides the values of risk factors, which are then sent to the "Human Digital Twin for Cerebral Circulation" along with clinical information representing the disease state. By implementing this for many individuals and accumulating data, a "Human Digital Twin for Cerebral Circulation" is created that depicts the relationship between the longitudinal changes in risk factors and the progression of disease. Using this, it becomes possible to predict the progression of disease for another person (Person B). In other words, by analyzing the longitudinal changes in risk factors and health status obtained from Person B's brain circulation digital twin with the "Human Digital Twin for Cerebral Circulation," physicians will be able to predict the progression of Person B's disease. This figure illustrates an example of predicting the transition to disease before the onset of illness.

The ultimate goal of these studies, as pursued by Prof. Ii and his team, is to construct a "Human Digital Twin for Cerebral Circulation" (Fig. 7). "Up to this point, our aim has been to create individual digital twins of brain circulation in cyberspace, enabling to determine values of risk factors such as wall shear stress and use them for risk prediction," Prof. Ii explained. "The 'Human Digital Twin for Cerebral Circulation' aggregates these digital twins from numerous individuals, akin to a databank that combines values of risk factors derived from individual brain circulation data with information on disease progression. Referencing an individual's digital twin against the 'Human Digital Twins for Cerebral Circulation' will allow us to make predictions of disease progression beyond what an individual digital twin alone can achieve."

However, achieving such research goals is not achievable with engineering researchers alone. Therefore, Prof. Ii's project involves collaboration with medical researchers, including Lecturer Shigeki Yamada from Nagoya City University and Prof. Yoshiyuki Watanabe from Shiga University of Medical Science. Together with medical researchers, they are advancing the collection of clinical data and striving to understand the relationship between diseases and brain circulation.

Prof. Ii started his tenure at the Tokyo Institute of Technology in April 2024. Around the same time, "TSUBAME 4.0" began operations at the Tokyo Institute of Technology (Photo 1). "TSUBAME 4.0" is equipped with high-performance GPUs (a type of computing device) suitable for machine learning. In his research on brain circulation digital twins, Prof. Ii is eager to use "TSUBAME 4.0." While it requires a different approach from the Fugaku CPU, leveraging the strengths of each, he aims to advance his research. The day may soon come when hospitals will ask us, "Could you provide data to the 'Human Digital Twins for Cerebral Circulation'?"

Photo 1: "TSUBAME 4.0"
The theoretical computing performance in the computing mode used for machine learning, etc. (16-bit, half precision), has achieved 952 petaflops. As of June 2024, it ranks second among supercomputers at domestic research/educational institutions, following Fugaku. It can also be utilized as one of the computing resources in the HPCI (High Performance Computing Infrastructure) system.

※1 Phase contrast (PC) MRI is one of the imaging methods used in MRI. It provides images that reflect blood flow velocity.

About the
Researcher

Prof. Ii is an active simulation specialist. Surprisingly, he hardly opened the PC he bought when he enrolled until his third year of university, and wrote almost all of his reports by hand. When choosing a laboratory, he learned about a study simulating the flight of insects and was impressed that “simulation can reveal so much about the flow of invisible things.” He entered the world of simulation research, and after a period of research on the simulation technique itself, he wanted to create a simulation that would be useful in some way, so he followed the path of biological simulation.

Looking back on that time, he said he was impressed by the fact that an approach that combines simulation with physics such as fluid mechanics can elucidate complex biological phenomena.

To relax on his days off, Prof. Ii tries his hand at cutting-edge programming. When he gets a headache, he can’t help but think of various diseases and the state of their circulatory fluids.

Associated Research Project: Development of personalized medical support technology based on simulation data science of whole brain blood circulation (hp220161)
Principal Investigator: Shigeo Wada, Osaka University
Associated Research Project: Development of human digital twins for cerebral circulation using Fugaku (hp230208)
Principal Investigator: Satoshi Ii, Tokyo Institute of Technology
Tokyo Institute of Technology and Tokyo Medical and Dental University will merge in October 2024, becoming Institute of Science Tokyo.

HPCI magazine
富岳百景
FUGAKU HYAKKEI

Registered Institution for Facilities Use Promotion /
The Representative for HPCI Operation
Research Organization for Information Science and Technology
1-5-2, Minatojimaminami-machi, Chuo-ku, Kobe, Hyogo, 650-0047 JAPAN
Tel: +81-78-599-9511

HPCI Portal site https://www.hpci-office.jp/en
HPCI PR site https://fugaku100kei.jp/en

Issued: August 2024