ESE 589

Non-Invasive monitoring of Cerebral Blood Flow (CBF) and Oxygen Metabolism in Stroke Patients for Detection of Ischemic Stroke using Hybrid PACT-DCS

Investigators:
Jonathan Ko
Xuhan Li
Lleyton Martin
Emily Zeiberg

SPECIFIC AIMS

About 795,000 people per year have a stroke in the US, 87% of which are ischemic strokes [1]. Ischemic strokes occur when a blood vessel in the brain is blocked because of a blood clot or buildup of fatty plaque, interrupting the delivery of oxygen to brain tissue. After a stroke, this damaged tissue causes long-term effects, such as speech challenges, reduced coordination, and muscle weakness. Reflecting the significant burden of these outcomes, strokes cost the U.S. approximately $56.2 billion in diagnosis, treatment, and rehabilitation expenses between 2019 and 2020 [1].

A major factor that determines the outcome of a stroke is the amount of time it takes for the patient to receive treatment. The treatments for ischemic strokes include performing a thrombectomy or administering tissue plasminogen activator (tPA) drugs [2]. However, before either of these treatments are performed, doctors must confirm that the patient is having a stroke and determine which type of stroke it is. These decisions are primarily guided by imaging the patient's brain, primarily using CT or MRI, which typically takes 20 minutes to an hour to perform [3]. These scans are timely, expensive, and can pose additional health risks to patients.

We propose creating an imaging modality that combines photoacoustic computed tomography (PACT) and diffuse correlation spectroscopy (DCS) to improve ischemic stroke outcomes. PACT utilizes the photoacoustic effect to image blood vessels and has been shown to offer high-resolution images of structures a couple of centimeters below the skin's surface [4]. DCS measures the scattering of light from blood cells, providing information about the blood flow rate [5]. Since PACT offers information about the anatomical structure of blood vessels and DCS provides information about blood flow, combining these modalities gives doctors a fast, non-invasive way to see if and where a blood clot has occurred.

The Specific Aims of the application are as follows:

1. **Develop and validate a computational model of PACT+DCS imaging**

We hypothesize that combining PACT and DCS in MATLAB will demonstrate improvements in spatial resolution and hemodynamic contrast compared to either modality alone.

2. **Construct and test a bench PACT+DCS system using tissue-like phantoms**

We hypothesize that physical integration of a pulsed laser, single-photon detectors, and ultrasound transducers will yield measurable improvements in depth-resolved hemodynamic imaging.

3. **Evaluate system performance in small animal models**

We hypothesize that in vivo testing will reveal clinically relevant biomarkers of ischemia while identifying unmodeled scattering and absorption effects in biological tissue.

Each of these aims will take about a year to complete, allowing us to finish this study in three years. After successful completion, we will have a new imaging modality that can be used to detect ischemic strokes in a safe, efficient, and inexpensive manner, which will help improve the outcome of patients experiencing an ischemic stroke.

RESEARCH STRATEGY

A. SIGNIFICANCE

Stroke remains a leading cause of serious long-term disability and death in the United States, affecting approximately 795,000 people annually, with ischemic strokes accounting for 87% of all cases [1]. Current clinical management of strokes is constrained by the need for rapid, accurate diagnosis to distinguish between ischemic and hemorrhagic events. The currently popular diagnostic tools are computed tomography (CT) and magnetic resonance imaging (MRI) [3]. However, CT and MRI have several limitations. Firstly, CT and MRI are time-consuming and usually take 20 to 60 minutes to complete. Also, CT and MRI instruments are costly and may not be immediately accessible in all clinical settings, such as in an ambulance. Furthermore, delays in imaging directly impact the timely administration of life-saving interventions such as thrombectomy or tissue plasminogen activator (tPA) therapy, worsening patient outcomes, and contributing to the $56.2 billion stroke-associated healthcare costs reported between 2019 and 2020 [1].

This project addresses a critical problem in stroke care: the urgent need for a safe, portable, fast, and cost-effective imaging modality capable of rapidly detecting ischemic events at the point of care. By developing a hybrid photoacoustic computed tomography (PACT) and diffuse correlation spectroscopy (DCS) imaging system, this project offers a new approach to stroke diagnosis. PACT provides high-resolution anatomical imaging of blood vessels based on laser-induced acoustic signals, while DCS measures cerebral blood flow by detecting light scattering from moving red blood cells [4][5]. Together, these modalities can offer both structural and functional information about cerebral vasculature without relying on ionizing radiation or complex hospital-based scanners.

Given successful completion of our specific aims, the proposed PACT+DCS system will significantly advance scientific knowledge and technical capability in non-invasive neuroimaging. Specifically, a successful computational model will demonstrate the synergistic benefits of combining optical and acoustic techniques, offering improved spatial resolution and hemodynamic contrast beyond what either modality can achieve alone. Building and validating a prototype using tissue-like phantoms will set the stage for real-world applications, while preclinical testing in small animal models will establish the system's ability to detect clinically relevant biomarkers of ischemia under physiologic conditions. Also, preclinical testing in animals with larger brains, such as pigs, will demonstrate the efficiency of the proposed system under more human-like conditions.

Successful completion of this work will change the way ischemic stroke is diagnosed and managed. Clinically, it will allow for bedside, real-time assessment of stroke, enabling faster initiation of treatment and thereby improving neurological outcomes. Conceptually, it will advance the integration of multimodal imaging techniques, paving the way for future technologies that combine anatomical and functional imaging in compact, accessible platforms. Methodologically, it will foster new approaches to modeling and combining light-based and sound-based imaging systems. From a healthcare services perspective, earlier stroke detection

and treatment could dramatically reduce the economic burden associated with long-term rehabilitation and care.

Ultimately, the PACT+DCS system will offer a safer, more efficient alternative to current imaging methods. By doing so, it supports broader public health goals of reducing disability, mortality, and healthcare costs, while empowering clinicians with more effective diagnostic tools at the point of care.

B. INNOVATION

Our project introduces a new approach to stroke diagnosis by combining PACT and DCS into a single, portable imaging platform. Our proposed system does not rely on large, resource-intensive imaging modalities like CT and MRI. By combining structural and functional imaging into a compact, bedside system, we aim to shift how ischemic strokes are detected and managed, making diagnosis faster, safer, and more accessible.

Shifting the Current Paradigm

Today, stroke diagnosis typically depends on hospital-based CT or MRI scans, which, while effective, are slow, expensive, and sometimes out of reach. These delays can have irreversible damage to the patient's brain by slowing down critical decisions like whether to administer clot-busting drugs or proceed with a thrombectomy. Our project proposes a new workflow by developing an imaging system that comes to the patient, not the other way around. By offering real-time, bedside visualization of blood vessels and blood flow, the PACT+DCS system has the potential to change how and where stroke care begins, making it faster, more efficient, and available to more people.

Conceptual and Methodological Innovation

While PACT and DCS have each shown promise individually, bringing them together for stroke detection is a novel idea. PACT offers detailed images of blood vessels using ultrasound signals generated by laser pulses, while DCS measures how light scatters from moving red blood cells to assess blood flow. Combining them gives doctors a two-part view of the brain: where the vessels are and how well blood is moving through them. No single technology currently offers both pieces of information at the bedside. Also, our system can provide real-time information on the blood flow of the patient. This capability is particularly valuable, not only for initial diagnosis, but also for post-intervention monitoring. For example, after treatments such as thrombectomy or administration of tPA drugs, continuous assessment of blood flow can help doctors evaluate the effectiveness of the treatment, detect early signs of re-occlusion, and guide future treatment decisions.

Beyond the idea itself, we’re introducing new ways to make it practical. We will develop an integrated computational model in MATLAB that uses Monte Carlo simulations to predict how PACT and DCS signals behave together in tissue. By modeling photon transport and acoustic wave propagation through realistic brain-like media, we can explore different system designs virtually, optimizing parameters such as spatial resolution, penetration depth, and

acquisition speed before we actually build the hardware. The system itself will capture optical and acoustic data in real time, using a pulsed laser, single-photon detectors, and ultrasound transducers. To further bridge the gap between simulation and experimental validation, we will also use tissue phantoms that closely mimic the optical and acoustic properties of the brain, providing a realistic and controlled environment to fine-tune our system before proceeding to animal testing. Because imaging deeper brain areas can challenge both light and sound signals, we plan to develop adaptive focusing strategies and real-time signal processing algorithms in future phases of this project. These approaches will be aimed at boosting image contrast and minimizing motion artifacts, particularly in complex in vivo environments. Although these refinements are not part of our initial system build, they represent important future steps toward making the PACT+DCS platform clinically viable and not just a laboratory demonstration.

Broad Applicability Across Fields

Although our immediate goal is to improve stroke diagnosis, the potential applications of a portable, real-time PACT+DCS system extend well beyond stroke care. This technology could be adapted for rapid neurotrauma assessments in emergency rooms, monitoring of vascular dementia progression, or critical care hemodynamic monitoring in intensive care units [6][7]. The ability to image both vascular structure and function at the bedside has broad relevance across neurology, emergency medicine, and critical care.

Additionally, by eliminating the need for ionizing radiation and reducing imaging costs and infrastructure needs, this platform could help generalize access to advanced neurovascular imaging. Clinics, ambulances, and field hospitals could benefit from technology that is not confined to specialized imaging centers.

Advancing the Field Through New Applications

This project goes beyond improving existing technologies, and it applies known physical principles in a new way to solve a major clinical challenge. By combining light absorption and scattering-based measurements into a single diagnostic tool, we move beyond what either PACT or DCS could achieve alone. This project lays the groundwork for future platforms that could combine structural, functional, and even metabolic brain imaging in compact, accessible systems.

C. APPROACH

SPECIFIC AIM 1: Develop and validate a computational model of PACT+DCS imaging

Rationale

The integration of PACT and DCS for stroke diagnosis requires advanced computational modeling to account for the complex properties of ischemic brain tissue. A unified computational framework will enable optimization of system parameters before costly

hardware implementations and provide benchmarks for interpreting combined PACT+DCS data in clinical applications.

Task 1: Model Development

The computational model will be developed using Monte Carlo methods implemented in MATLAB and C. The PACT and DCS systems will be modeled separately to verify performance, and then the simulations will be combined to model the joint system. The bases of our individual models follow methodologies introduced in previously published research papers on PACT and DCS [4][5].

PACT System

The PACT model uses the k-wave toolbox to simulate how the waves produced from the photoacoustic effect will propagate. A 5cm x 5cm head phantom, shown in Figure 1, was created to conduct this simulation on. The acoustic attenuation coefficients, density, Gruissen parameters, and speed of sound were defined for each tissue type [4][8]. Once the phantom was created, it was used to generate the input parameters for the Monte Carlo simulation using C [9]. A 532 nm wavelength was used as the source to distribute about 2.7 million photons during the 10-minute simulation. The Monte Carlo simulation produced a file that provided the fluence at each voxel, shown in Figure 2.

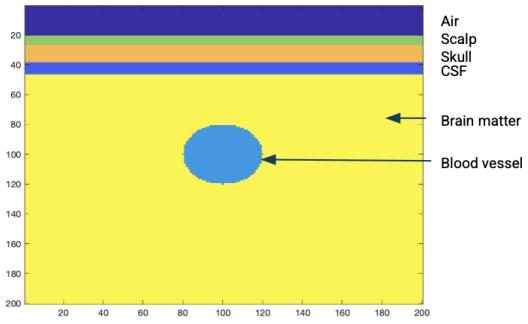

Figure 1: Tissue phantom used for simulation

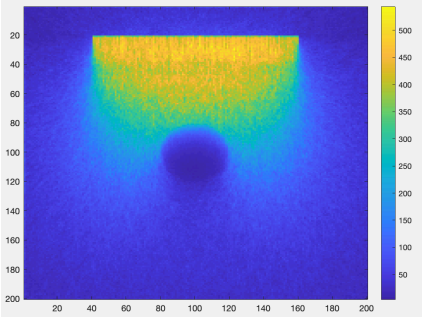

Figure 2: Relative fluence in each voxel obtained using Monte Carlo simulation. The values indicate the number of photons per square millimeter.

The fluence file was then used in MATLAB to generate the initial pressure distribution for the k-wave simulation. The initial pressure distribution is computed using the following equation:

$$P_0 = \Gamma \times \mu_a \times \phi$$

where Γ is the Gruissen parameter, μ_a is the acoustic attenuation coefficient in $dB/(MHz \cdot cm)$, and ϕ is the fluence in J/cm^2 at each voxel. The sound waves produced from this pressure distribution were measured with an arc-shaped transducer, using the `'kspaceFirstOrder2D'` function. This function models how the sound waves propagate through the tissue based on the density and speed of sound. The waves that end up at the transducer are recorded and then reversed to determine the initial location of these waves. By using the reconstructed pressure distribution, an image of the tissue is produced, as shown in Figure 3.

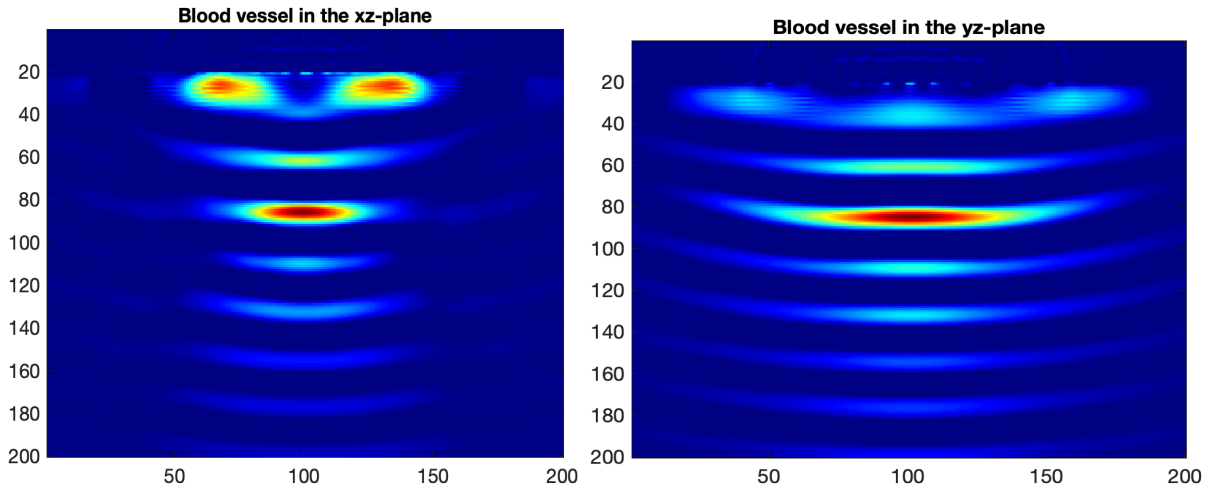

Figure 3: Reconstructed PACT image viewed in two planes. The xz-plane shows a cross-section of the vessel, and the yz-plane shows the longitudinal view of the vessel.

The top of the blood vessel was accurately reconstructed, as indicated by the red region in the center of the image. The two red regions near the top of the xz-plane image are where the concave transducer made contact with the skin, so the signal was more focused on these regions. In the yz-plane image, a linear transducer was used, so the sensitivity regions were spread out along the surface. In both of the images, only the top of the vessel is visible, which is a result of the shadow artifacts that often arise when performing optical imaging. This is because as light travels deeper, it is scattered and absorbed by the tissue, so less energy is delivered to deeper layers, causing the photoacoustic effect to be weaker in these areas. As clearly shown in the fluence map in Figure 2, this causes the energy to be more focused at the top of the vessel, resulting in a stronger signal.

DCS System

To simulate the DCS system, a blood flow index (BFi) map was created, defining the blood flow in each region of the phantom. Since DCS measures the dynamic scattering induced by moving blood cells and the degree of photon interactions is directly influenced by the local optical flux, we used the fluence from the Monte Carlo simulation to calculate the flux and generate the BFi map. This was sufficient for our preliminary studies, but in our next steps, we will update the Monte Carlo simulation from the PACT system so that the information for DCS is also tracked, and the true BFi map will be used instead of an estimated one.

After obtaining the BFi map, we then used the Siegert relation to estimate the intensity autocorrelation function $g_2(\tau)$ using the following equation:

$$g_2(\tau) = 1 + \beta e^{-2k_0^2 \times BFi \times \tau}$$

where β is the spectral contrast parameter, k is the optical wavenumber, τ is the decay time, and $e^{-2k_0^2 \times BFi \times \tau}$ is the decay function, commonly denoted as $g_1(\tau)$ [10]. $g_2(\tau)$ is what the detector would measure, so these values were used for image reconstruction. The Siegert relation was rearranged so that $g_1(\tau)$ was solved for and the slope of $g_1(\tau)$ was calculated at each voxel to reconstruct the BFi map.

For simulating stroke conditions, the optical and dynamical parameters were adjusted to reflect physiological changes observed during ischemic events. The absorption coefficient (μ_a - 0.11 mm^{-1}) was slightly decreased compared to the healthy case, accounting for possible reductions in hemoglobin oxygenation. The reduced scattering coefficient (μ'_s = 1.2 mm^{-1}) was lowered to represent tissue edema and structural degradation, which are known to reduce scattering. The source-detector separation (ϱ = 2.5 mm) was chosen with reasonable testing and measuring distances. Critically, the Brownian diffusion coefficient ($D_b = 200*10^{-9}$ mm^2/s) was slightly reduced to model the slower decorrelation rates associated with decreased blood flow during stroke. These parameter adjustments allowed for a more realistic simulation of DCS signals.

These parameters were used to create a temporal point spread function output. This was then used as the path length distribution for the $g_1(\tau)$ and $g_2(\tau)$ equations. The output of our simulation is shown below in Figure 4.

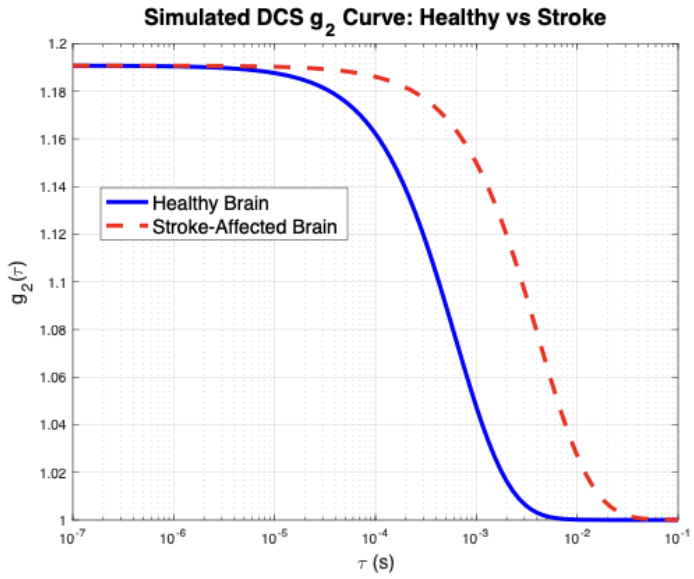

Figure 4: Simulated DCS $g_2(\tau)$ outputs of a healthy and a stroke-affected brain

The DCS simulation uses the $g_2(\tau)$ curve and the normalized intensity autocorrelation function, which reflects how the intensity of scattered light at a detector changes over time due to the motion of scatterers, such as red blood cells. The rate of decay in the curve indicates the speed of these moving scatterers. In the figure above, the faster decay of the Healthy Brain curve suggests quicker motion of scatterers, corresponding to higher blood flow. Conversely, the slower decay observed in the Stroke-Affected Brain curve reflects reduced scatterer motion, indicating lower blood flow, a key characteristic of stroke.

PACT+DCS System

The joint system uses the PACT simulation to identify the key anatomical structures. The measurements are normalized to be between 0 and 1, and any voxel that has a value greater than 0.5 is considered a structure of interest. The values of the BFi map at these voxels were extracted, so that only relevant measurements were displayed in the image. The PACT image is displayed as a grayscale image, and the DCS image is displayed as a colored image, as shown in Figure 5.

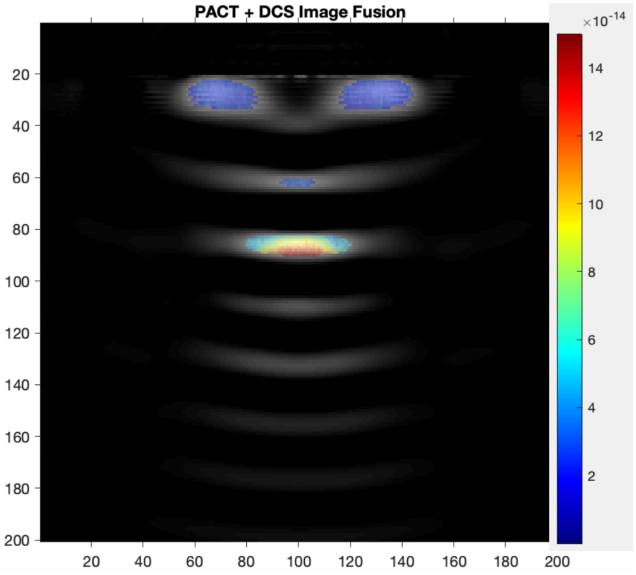

Figure 5: Reconstructed image using PACT+DCS simulation. The colorbar has units cm²/s.

Again, the two circles at the top of the image show where the concave detector made contact with the skin. In the joint image, it is clear that these structures are not important since the BFi is very low. The circle in the middle of the image is the top of the blood vessel, and this has a much stronger DCS measurement. The signal gets stronger closer to the center of the blood vessel, which is expected since this region has better blood flow. As mentioned before, the numerical values are not accurate for measuring the exact blood flow, but they are accurate for representing regions with faster vs. slower blood flows. After we implement the updated Monte Carlo simulation for DCS, these measurements will reflect the true blood flow.

Task 2: Validation

Validation will proceed in two phases. First, we will compare simulations to experimental data from phantoms with normal and decreased blood flow. Based on our simulated $g_2(\tau)$ curve that compares healthy vs. stroke-affected vessels, the DCS measurements using the low blood-flow phantom will be weaker than the measurements from the healthy phantom. When used to reconstruct the PACT+DCS image, these weaker measurements will correspond to a different color, allowing the viewer to easily identify which image presents a stroke.

We will also validate our results by measuring the resolution of each system. The PACT system will be evaluated based on the number of voxels a structure has to occupy to appear in the reconstruction. This structure will have the same properties as our simulated blood vessel and will be placed in our phantom consisting of the brain, skull, etc. to ensure that the same obstructions appear as in a real-imaging scenario. The size that the structure needs to be in order to appear in the image is also depth-dependent, so this test will be repeated at various depths in our phantom. Additionally, this will allow us to determine the

maximum imaging depth of our PACT system. The DCS system will be evaluated using the signal-to-noise ratio. To calculate this, we will image a blood vessel and compare the measurements to the true blood flow index map.

Task 3: Identification of Potential Problems and Alternative Strategies

Our system has already demonstrated shadowing artifacts that cause some features to not be visible in the reconstructed image, and we plan to remove these using machine-learning models designed for optical and acoustic shadows [11][12]. Our simulation may also have excessive computational demands, which we will mitigate using reduced-order modeling techniques.

SPECIFIC AIM 2: Construct and test a bench PACT-DCS system using tissue-like phantoms

Rationale

Following the development of a computational model in Aim 1, the next critical step is to construct and validate a bench-top system that integrates PACT and DCS. This system will allow us to address the practical challenges of combining optical and acoustic modalities into a unified imaging platform. Testing on tissue-like phantoms, which replicate the optical scattering and acoustic properties of the brain, will allow us to evaluate imaging performance. Through this process, we can optimize system design, verify resolution and flow sensitivity, and troubleshoot technical issues before moving to animal studies.

Task 1: System Design and Assembly

Task 1 will involve the design and assembly of the bench-top PACT+DCS system, as outlined in Figure 6. The PACT configuration contains a pulsed laser and an ultrasound transducer to measure the resulting sound waves. These two modules will be attached using an adjustable arm so that the user has an easier time controlling both units. The DCS system requires a continuous-wave laser and a single-photon detector that measures the light after it is scattered. These units should be placed about 3 cm away from each other so that the light can penetrate deeper tissue. Since PACT and DCS require different light sources, time-gating will be used to prevent cross-talk. The PACT laser will use a 10 nanosecond pulse at a frequency of 20 hertz. The DCS laser will always be on, but it will use a longer wavelength, and the photodetectors will not record measurements during a PACT pulse. Also, the DCS setup is slightly offset relative to the PACT system, so the two sources will have less interference when they are both on.

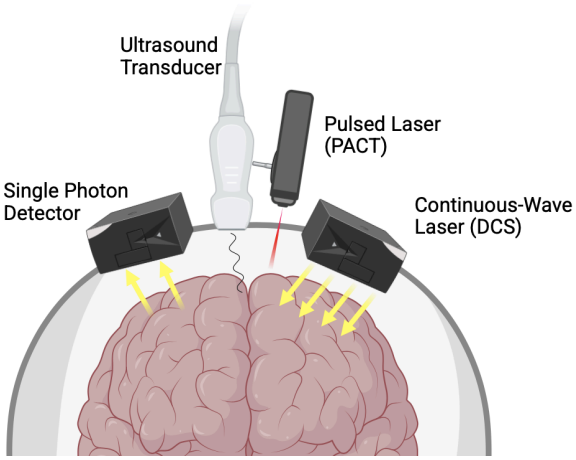

Figure 6: Diagram of PACT+DCS system hardware

Task 2: Phantom Fabrication

We will create phantoms with tunable optical scattering and absorption properties, embedding vessel-like structures filled with dynamic flow using syringe pumps to simulate physiological conditions. Phantom compositions will be tailored to replicate the optical and acoustic properties of brain tissue.

Task 3: Imaging Performance Evaluation:

We will conduct various imaging experiments to evaluate system performance. Spatial resolution, signal-to-noise ratio (SNR), flow sensitivity, and depth of penetration will be measured across a range of phantom conditions. Acquisition parameters such as laser fluence, detector positioning, and synchronization timing will be iteratively optimized based on imaging results to achieve better performance.

Task 4: System Calibration and Validation

After optimizing imaging parameters, we will perform calibration studies and final validation to confirm the repeatability and accuracy of both anatomical and functional imaging metrics across multiple phantom tests. This final validation will ensure that the system meets the necessary performance threshold for transition to in vivo studies.

Success Criteria

The successful completion of this aim will be demonstrated by the PACT+DCS system's ability to resolve vessel-mimicking structures up to 3 cm deep with sub-millimeter spatial resolution and to measure flow rates within 10% of the ground truth values. Meeting these benchmarks will indicate that the system is ready for preclinical animal testing.

Potential Problems and Alternative Strategies

One anticipated challenge is that the optical scattering or absorption within the phantoms may limit imaging depth and degrade signal quality. If this occurs, we will adjust

the concentrations of optical absorbers and scatterers to more closely mimic brain tissue properties and explore longer excitation wavelengths to improve light penetration. Signal interference between PACT and DCS measurements may also arise due to cross-talk between acquisition pathways, even with the time-gating precautions we have in place. In response, we will redesign the acquisition sequence to perform sequential rather than simultaneous data collection. Through iterative optimization, we are confident that we will achieve a robust, high-performance bench-top system.

SPECIFIC AIM 3: Evaluate system performance in small animal models

Rationale

While phantom studies enable precise control over optical and acoustic properties, they cannot fully capture the complexity of biological tissue, including dynamic blood flow regulation, metabolic changes, and structural heterogeneity. Pigs can provide a valuable animal model with brain dimensions, cortical folding, and neurovascular characteristics similar to humans, making them ideal for translation imaging studies [13]. Testing the integrated PACT-DCS system in vivo is critical to assess its ability to detect and quantify ischemic changes under physiologically relevant conditions.

Task 1: Animal Protocol Development and Ethics Approval

We will develop the animal protocol and obtain all necessary ethics approvals. This includes securing approval for porcine imaging procedures involving functional stimulation, monitoring, and humane endpoints. We will select appropriate pigs to match the brain size and physiology of a typical human brain. Research personnel will be trained in handling and imaging procedures specific to pigs.

Task 2: System Calibration and Baseline Imaging

We will perform system calibration and baseline imaging. Under anesthesia and physiological monitoring, pigs will be positioned in the imaging setup. We will acquire baseline data capturing cortical structure, cerebral blood flow, and oxygenation prior to any induced stroke. Imaging parameters such as optical source power, detector gain, and ultrasound pulse sequences will be optimized to maximize penetration depth and signal quality in large tissue volumes while ensuring safe imaging conditions.

Task 3: Induced Stroke and Real-Time Imaging

Strokes will be induced using a well-established middle cerebral artery occlusion (MCAO) method adapted for pigs, either by surgical ligation or intravascular filament insertion [14]. Following occlusion, we will continuously acquire real-time PACT and DCS data to monitor dynamic changes in CBF, oxygen saturation, and vascular integrity during the stroke event and any reperfusion phase.

Task 4: Quantitative Analysis, Biomarker Extraction, and Safety Assessment

Spatiotemporal changes in hemodynamic and metabolic biomarkers will be analyzed to characterize ischemic progression. Key metrics, including CBF reduction, oxygenation drop, and vascular disruption, will be extracted from imaging data. These biomarkers will be correlated with infarct size, histological findings, and clinical outcomes to evaluate the sensitivity, specificity, and translational potential of the PACT+DCS system. Safety and feasibility of the imaging approach will also be assessed by monitoring for tissue damage or adverse events.

Success Criteria

For this study to be successful, our small animal study must accomplish three goals. First, the system must produce high-resolution images so that anatomical features can easily be identified, and the reconstructed BFi maps must present plausible measurements. This will ensure that there are key differences between healthy and stroke-affected vessels, so the imaging system can be used to diagnose an ischemic stroke. Second, the results must be consistent between trials. Given that the tests are performed while the animal is under anesthesia, the blood flow measurements should be relatively constant if multiple trials are conducted on the same animal. If the results are different each time, this indicates there is a significant source of noise, and the results cannot be used to accurately measure blood flow. Lastly, the imaging system must be proven to be safe by showing that there is no thermal, mechanical, or biological damage caused by the system. This requires imaging the animals in the same spot on a different day to ensure that the tissue that was shown to be healthy in the first scan is still functioning normally.

Potential Problems and Alternative Strategy

One challenge that may arise is motion artifacts from cardiac activity or breathing. These artifacts can be removed using motion correction algorithms, such as two-stage motion correction [15]. Also, the signal-to-noise ratio may be decreased as a result of noise sources that were unaccounted for or different scalp and skull thickness between animals. This can be prevented by identifying the optimal source frequency for general testing, and we can implement a preliminary test for each scan that identifies the optimal frequency for that animal. Because the lengths of scans and the thickness of attenuating tissue can vary between pigs, we will also implement real-time temperature monitoring that will automatically stop the scan if the equipment or tissue gets too hot.

Timeline

This study is expected to take three years to complete, with each specific aim taking one year to fulfill. The first year will be focused on designing the PACT, DCS, and PACT+DCS simulations and refining the results until all of our validation criteria are met. The second year will be focused on building the hardware, designing the phantom, and testing our software on a physical system. About halfway through the second year, we will also

prepare our application to the IACUC so that we will have the necessary permissions to begin the small animal study by year three. Once the first round of in vivo tests is complete, we will compile data about the efficacy and safety of our system so that we can make and test all improvements by the end of the project timeline.

Conclusion

In this work, we propose the design and validation of an integrated PACT and DCS system to rapidly detect ischemic strokes. To ensure robust system performance, we will first simulate light propagation, acoustic signal generation, and DCS autocorrelation functions to optimize imaging parameters and probe designs. Hardware development will focus on integrating optical and acoustic components to maximize sensitivity, spatial resolution, and measurement speed. We will validate the system using physical phantoms with tissue-like properties to replicate brain tissue under healthy and ischemic conditions. Finally, we will conduct a small-animal study to assess the system's ability to detect and monitor stroke-related hemodynamic changes. The goal of this project is to develop a safe, fast, and effective imaging modality capable of improving the early diagnosis and treatment of ischemic strokes, resulting in reduced time to intervention and improved patient outcomes.

References

[1] "Stroke Facts," *Stroke*, Oct. 24, 2024. https://www.cdc.gov/stroke/data-research/facts-stats/index.html#:~:text=Fast%20facts,2

[2] "Ischemic stroke (Clots)," *American Stroke Association*. https://www.stroke.org/en/about-stroke/types-of-stroke/ischemic-stroke-clots (accessed Apr. 28, 2025).

[3] Northwestern Medicine, "Computed tomography (CT) scan for stroke," *Northwestern Medicine*. https://www.nm.org/conditions-and-care-areas/tests/computed-tomography-ct-scan-for-stroke

[4] F. Zhang *et al.*, "Photoacoustic digital brain and deep-learning-assisted image reconstruction," *Photoacoustics*, vol. 31, p. 100517, May 2023, doi: 10.1016/j.pacs.2023.100517.

[5] M. Mokin *et al.*, "Preliminary experience with diffuse correlation spectroscopy in acute ischemic stroke neurointerventional procedures," *Journal of NeuroInterventional Surgery*, vol. 16, no. 6, pp. 624–631, May 2023, doi: 10.1136/jnis-2023-020407.

[6] S. Stamenkovic, Y. Li, J. Waters, and A. Shih, "Deep imaging to dissect microvascular contributions to white matter degeneration in rodent models of dementia," *Stroke*, vol. 54, no. 5, pp. 1403–1415, Apr. 2023, doi: 10.1161/strokeaha.122.037156.

[7] M. B. Robinson *et al.*, "Portable, high speed blood flow measurements enabled by long wavelength, interferometric diffuse correlation spectroscopy (LW-iDCS)," *Scientific Reports*, vol. 13, no. 1, May 2023, doi: 10.1038/s41598-023-36074-8.

[8] C. M. I. Quarato *et al.*, "A Review on Biological Effects of Ultrasounds: Key Messages for Clinicians," *Diagnostics*, [Online]. Available: https://doi.org/10.3390/diagnostics13050855

[9] "Mcxyz.c." https://omlc.org/software/mc/mcxyz/index.html

[10] D. Ferreira, R. Bachelard, W. Guerin, R. Kaiser, and M. Fouché, "Connecting field and intensity correlations: The Siegert relation and how to test it," *American Journal of Physics*, vol. 88, no. 10, pp. 831–837, doi: 10.1119/10.0001630.

[11] J. Huh, S. Khan, and J. C. Ye, "Unsupervised Learning for Acoustic Shadowing Artifact Removal in Ultrasound Imaging," *2017 IEEE International Ultrasonics Symposium (IUS)*, pp. 1–4, doi: 10.1109/ius52206.2021.9593451.

[12] H. Cheong *et al.*, "DeshadowGAN: A Deep Learning Approach to Remove Shadows from Optical Coherence Tomography Images," *Translational Vision Science & Technology*, vol. 9, no. 2, p. 23, doi: 10.1167/tvst.9.2.23.

[13] C. Betourney, "Pigs help scientists understand human brain," *UGA Today*, Aug. 16, 2019. https://news.uga.edu/pigs-help-scientists-understand-human-brain/

[14] S. R. Platt *et al.*, "Development and characterization of a Yucatan miniature biomedical pig permanent middle cerebral artery occlusion stroke model," *Experimental & Translational Stroke Medicine*, vol. 6, no. 1, Mar. 2014, doi: 10.1186/2040-7378-6-5.

[15] S. Harput *et al.*, “Two-Stage Motion Correction for Super-Resolution Ultrasound Imaging in Human Lower Limb,” *IEEE Transactions on Ultrasonics Ferroelectrics and Frequency Control*, vol. 65, no. 5, pp. 803–814, Apr. 2018, doi: 10.1109/tuffc.2018.2824846.