Communicating Research to the General Public

At the March 5, 2010 UW-Madison Chemistry Department Colloquium, Prof. Bassam Z. Shakhashiri, the director of the Wisconsin Initiative for Science Literacy (WISL), encouraged all UW-Madison chemistry Ph.D. candidates to include a chapter in their Ph.D. thesis communicating their research to non-specialists. The goal is to explain the candidate's scholarly research and its significance to a wider audience that includes family members, friends, civic groups, newspaper reporters, program officers at appropriate funding agencies, state legislators, and members of the U.S. Congress.

Over 50 Ph.D. degree recipients have successfully completed their theses and included such a chapter.

WISL encourages the inclusion of such chapters in all Ph.D. theses everywhere through the cooperation of Ph.D. candidates and their mentors. WISL is now offering additional awards of $250 for UW-Madison chemistry Ph.D. candidates.

Wisconsin Initiative for Science Literacy

The dual mission of the Wisconsin Initiative for Science Literacy is to promote literacy in science, mathematics and technology among the general public and to attract future generations to careers in research, teaching and public service.

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Quantitative Ultrasound Imaging Parameters for Evaluation of Carotid Atherosclerotic Plaque

By

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A Preface for Everyone

Dear Reader,[1] I'd like to tell you a story about family, inspiration, and science.

It was late December 2003, and I was eleven years old. We (my parents and I) were spending that awkward, dazed time in between Christmas and New Year's anxiously waiting in the scratchy upholstered seats of a hospital waiting room.

It was either that or sitting in teal-colored chairs that made ripping noises whenever you moved and looked like they could be cleaned with a Clorox wipe.

The sprightly garland and cheerful red ribbons that hung around the room bore a stark contrast to the members of my family, many of whom were pacing nervously. Conversation circled around the hospital and its doctors, my grandpa (my dad's dad), and if he would recover.

About a week and a half before, my grandpa had a stroke while he was working in his toolshed. One of the blood vessels in his brain had burst, causing him to collapse. He wasn't found for nearly six hours, by which point he was irreversibly paralyzed.

Nearly two decades later, stroke remains a major cause of death and disability in the United States and around the world. Stroke affects hundreds of thousands of families just like mine: every 40 seconds, someone suffers from a stroke.

My grandpa survived his stroke, but he has limited mobility. It is these events, in part, that influenced my decision to perform research on a condition related to stroke: atherosclerosis.

In college, I dabbled in everything from psychology and archaeology to general relativity and medical physics. When I decided to go to graduate school, I gravitated towards researching stroke. I also knew I wanted to study it from a medical imaging perspective (think: CT, MRI, X-ray, ultrasound). I was inspired by the possibilities of applying the principles of physics and engineering to unsolved problems in medicine and health.

When I entered the medical physics department at the University of Wisconsin–Madison in 2015, I joined the ranks of hundreds of researchers and clinicians at the university who are studying new medications, lifestyle changes, and interventions that can help improve a person's quality of life after they have a stroke and lower someone's risk of having a stroke in the first place. In my research group in the Department of Medical Physics, we try to literally *see* inside our carotid arteries to learn about what's there…but shouldn't be…and ultimately, one day, try to prevent stroke.

Let's back up and break that all down, shall we?

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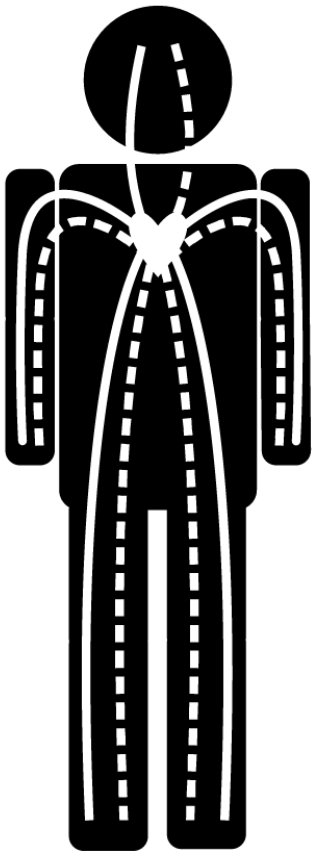
[1] This chapter written as part of the Wisconsin Initiative for Science Literacy (WISL) Award for Communicating PhD Research to the Public program. To learn more about this program, visit http://scifun.org/Thesis_Awards/thesis_awards.html.



Where we begin: The carotid arteries

The carotid arteries are like rivers. They carry all sorts of valuable resources from throughout the body to their destination – the brain.

Now, in order to function, our brains use up a lot of resources, especially oxygen. Because of this, the carotid arteries, which are located in our necks, are vital to our survival. Approximately 0.3 inches in diameter, or about half the size of an aspirin tablet, the carotid arteries pump around 600-700 milliliters of blood to the brain *every minute of every day*. To put this in perspective, that would be like downing 2-3 mugs full of your beverage of choice…*every minute of every day*.

That is, unless the supply chain to the brain gets interrupted, or if something bad enters the supply chain. That's when the type of stroke that I study – ischemic stroke – can happen. But I'm getting ahead of myself. What can interrupt the supply chain?

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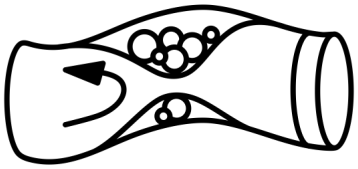
Have you ever heard of atherosclerosis?

The protagonist in this story is atherosclerosis. Atherosclerosis is a buildup of nasty substances like cholesterol along the walls of the major arteries in your body. Scientists think that atherosclerosis begins when the wall of the artery gets injured somehow.

Many people develop some amount of atherosclerosis over their lifetimes, but for some people, it can become a problem. When atherosclerosis begins to restrict blood flow, it's called plaque.



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Right now, you may be fighting the formation of plaque without even *knowing* it by eating healthy, getting exercise, or managing diabetes and other conditions.

But once certain plaques have been around long enough, what's in them – their composition – starts to change. Plaques that are bad enough have been growing and changing for decades and look nothing like they did when they first started. In these so-called complex plaques, you can find cholesterol, calcium, and inflammation, as well as areas of hemorrhage and ulceration from where areas of plaque filled with blood and ruptured. All of these things may put someone at risk of having an ischemic stroke.

Some people have to have beneficial medical procedures performed to remove the plaques blocking their carotid arteries and prevent an ischemic stroke from happening. Doctors may ask you to have a device called a stent put in to open up your artery. Other times, your carotid artery plaque may be removed by a surgeon during a surgical procedure called carotid endarterectomy.

As part of our research (more on that later), we keep surgically removed plaques to do more studies on them, and our surgeons and pathologists take note of what components are in plaque so that we have something we can compare our results to.

It unroofs, folks!

So plaque definitely interrupts the flow of blood through the carotid arteries and can mess with that supply chain to the brain. But something else can happen, too, and it's a common cause of ischemic stroke.

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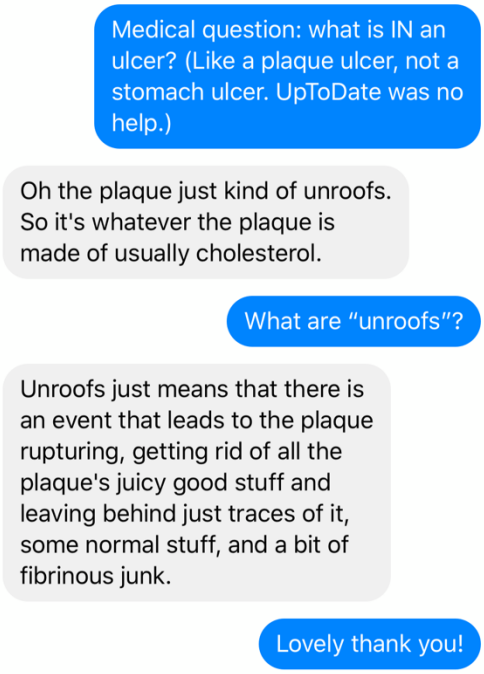
Pieces of a plaque can *break off* and cruise up to the brain. As those pieces travel, they see a narrowing tunnel: they have to squeeze through smaller and smaller blood vessels to reach their destination. When one of them gets stuck, that's the second path to ischemic stroke.

What can cause this breakage? Well, that's a matter of debate among clinicians and researchers. One of my friends coined a quippy way of putting it, though. One day we were texting about my research, and she said the plaque "unroofs."



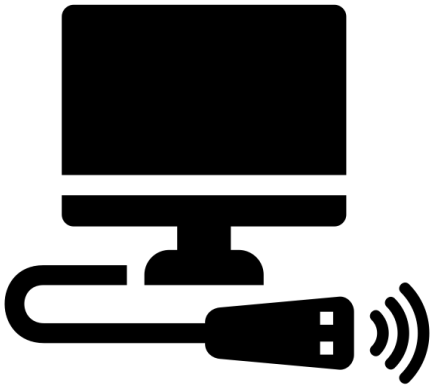
What lovely imagery, eh? Some unknown precipitating event can cause a plaque to burst open and release all its "juicy" goodness to the arteries, leaving behind the rest of the plaque and traces of the "junk tissue" that was once there.

All of this sounds terrible. Tell me something *positive*, Catherine!

Now we're getting to my research.

People who agree to enroll in our (my research group's and our collaborators') research studies as participants have plaques that are bad enough to require surgical removal by carotid endarterectomy. While they're in the hospital getting some pre-operative tests done, we perform some additional medical tests and imaging sessions to evaluate their health and their plaque.

One of those imaging sessions is focused on ultrasound imaging.



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Ultrasound is a harmless and noninvasive way we can see inside the body. This is why its most famous application is keeping tabs on a fetus' growth inside a womb. It can also be used to look at carotid arteries and plaque. With ultrasound, we send sound waves at frequencies far above what we can hear into plaque using a wand-like device called a transducer. When the sound waves hit the plaque, they can be absorbed or reflected back to the transducer, where they are then collected. Then, the ultrasound system creates an image of plaque that appears on a screen, and we download the raw signals collected by the transducer for more analysis later.

From these ultrasound images and raw signals, we can assess a plaque's properties, including its tissue composition and how it deforms as blood flows around it. Quantitative, numerical information we extract from these assessments, in turn, may help us determine which plaques are likely to "unroof" and cause an ischemic stroke, ideally before that happens.

During our ultrasound imaging sessions with our research participants, we collect images and data from plaque on three separate ultrasound systems. I used the data and images from one of these systems during my time as a graduate student. Because our raw signal processing codes haven't been integrated into clinical practice yet, we need to perform some additional steps to get our data from the ultrasound system, compute our parameters, and form images.

For that, we connect a laptop computer to the ultrasound system and run computer codes on the laptop that tell our ultrasound system which raw data it should collect and save. Each code takes about two minutes to run, so our sonographer (the person who collects the ultrasound images and raw data) needs to hold their hand steady to collect motion-free data that will form good images.

Once the imaging session is over and our research participant leaves, we download all this raw data, upload it to more powerful computers, and run additional codes to compute some parameters. Then, we form some images using these parameters and analyze what our parameters mean relative to information about the plaque's composition that we get from our surgeons and pathologists.

What have I learned about plaque during my time as a graduate student?

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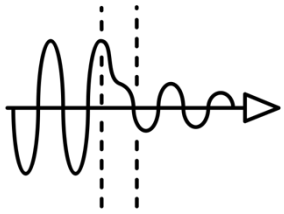
Using the images from the ultrasound system, we can see that each plaque is like a snowflake, albeit not beautiful but unique in its size, shape, and composition. This uniqueness presents a challenging and technical problem for us to solve. For instance, the computer algorithms used by the ultrasound systems and the images they produce couldn't give us the quantitative information we needed at the resolution we needed it!

For my work as a graduate student, we would need to tease out information about plaque composition from raw signals rather than from the images an ultrasound system displays.

We had our work cut out for us. Fortunately, some of my former co-workers had spent *their* time in graduate school developing new computer algorithms that might achieve exactly what we needed.

These new algorithms were great for processing raw ultrasound signals collected from small and complex plaques, computing parameters, and turning these parameters into colorized images showing variations in the parameters throughout each plaque. For example, we look at a parameter called attenuation – basically, how much tissues in the human body cause the ultrasound waves to decrease in intensity as the waves pass through – and we could potentially relate that to plaque composition.



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But we couldn't take anyone's word for it that the new algorithms would perform *well* in plaque just because they had performed better in computer simulations (basically, trying to mimic real-world scenarios but with computers and numbers) and in phantoms (blocks of well-characterized materials that we use to test the performance of ultrasound systems and processing algorithms). We had to compare these new algorithms to some tried-and-true algorithms used for decades by other scientists who were trying to learn about the composition of different parts of the human body in a noninvasive way.

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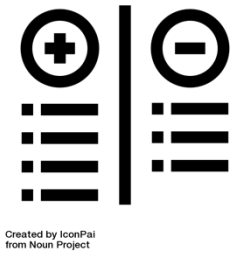
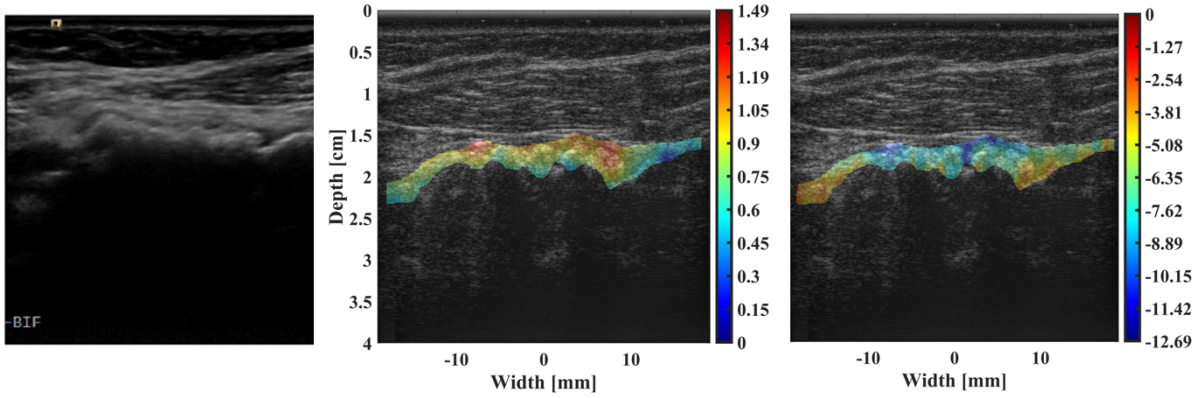
To test our hypothesis that our new algorithm would give us better results, we ran raw data we collected from over 50 peoples' plaques through two algorithms (one new, one old), created what we call parametric images, which display the variation in our attenuation parameters throughout plaque, and compared the performance of the two algorithms. We found that the new algorithm gave us fewer nonphysical (basically, results that are less than zero, which are not possible) attenuation results than the old one!



An added bonus of the new algorithm is that it's more resistant to change, which, paradoxically, is a good thing for us. We can pick smaller blocks of data to run through our new algorithm and still get results that make sense. Because our old algorithm wasn't nearly as good in that way, that *also* meant that the parametric images we created with the old algorithm were not as high-resolution as those created with the new algorithm! Getting images with high resolution was important to us because it helps us visualize with detailed images rather than numerical data how our parameters change throughout plaque, and images are likely to be what clinicians use if and when our methods are implemented in hospitals and other clinical practices.

These results were exactly what we needed for looking at plaque composition using ultrasound. With the old algorithm, we kept getting negative values of attenuation in plaque. As the smallest amount of attenuation that a tissue can have is zero, negative values just aren't possible. The new algorithm performed better on this essential metric. With fewer negative attenuation results in plaque, we could go on to compute different descriptive attenuation parameters, such as the middle, or median, attenuation value in plaque. We could also compute other parameters that might relate to the acoustic properties of plaque, such as the integrated backscatter, the amount of signal that returns to the transducer after being reflected off of tissue!

"Well," we said, "Why not actually 'do' instead of saying 'could' and 'should'?" So, we did.



We found that our attenuation parameters and integrated backscatter parameters are related to plaque components, including cholesterol, hemorrhage, and inflammation, that previous research says may put a plaque at risk of "unroofing" and causing an ischemic stroke. We also believe that, even at this early stage of the research, the parametric images that we create using these parameters also give us more quantitative information than the images produced by the ultrasound system would have (for an example, see the images above, from left to right – one type of ultrasound system-created image, called a brightness-mode image; our attenuation parametric map; our integrated backscatter parametric map).

But what if our attenuation parameters weren't properly accounting for the attenuation of ultrasound through tissues above the plaques, meaning that we weren't even really measuring the attenuation of plaque itself? To test this, we imaged plaques after they were removed during surgery. Results for some of our parameters were consistent, while for attenuation, the parameter we started with, we saw no relationship to plaque composition at all. To see if these relationships hold, we need to have more research participants join our research study and look at more plaques. After further study, we'll know which parameters are most useful for looking at plaque composition, and we'll have confirmed that, under some assumptions, parameters computed using raw ultrasound data could be related to plaque composition both inside *and* outside the body.

There's much more we can discover

In science, there's always more experiments you can run, and there's no such thing as the perfect study. Now that my PhD is coming to an end, there are *so many things* I wish I could go back and do differently, including helping to lead the design of an experiment that wasn't nearly as great as we thought it was (check out Chapter 7 if you're interested).

In the end, though, it's all about how you look at things. My dissertation research used new computer algorithms to learn more about plaques we think might cause ischemic stroke. One day, the parameters I computed may be used in real-time ultrasound imaging or maybe even to help people like my grandpa avoid having a stroke. So I would say that all in all, my time as a graduate student was fruitful, even if I was looking at "junk tissue" most of the time. 😉

Thanks for reading,
Catherine

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P.S. I would like to thank all of our research participants, our research study coordinators, our nurses, our surgeons, our pathologists, our sonographers, our engineers, and everyone else involved in this research for their willing participation and engagement. I would also like to thank the Wisconsin Initiative for Science Literacy for supporting doctoral candidates' efforts to communicate and engage with non-scientists and non-experts about scientific research.