the perspectives of the ranchers and farmers when proposing new systems. "We think of farmers as firms," says Garrett. "But farmers are also consumers, they're households, they're us."

Cows and Trees

Garrett believes that a solution for Brazil—or at least part of it—lies in an approach called "integrated crop, livestock, and forestry": growing crops, cattle, and trees in rotation, or in unison, in a way that decreases the need for fertilizer and pesticides, and increases profit. "That's one potential solution for these ranchers," says Garrett. "We're not going to get rid of ranching. Being a cowboy is so well respected. Having cattle gives you social status. Even *eating* beef is associated with status. It's so socially embedded. So how do we make ranching better?"

Garrett saw some striking success stories when she visited Brazil last summer. One example was a beef cattle rancher who switched to more profitable dairy cows, planted eucalyptus trees to shade the animals, and rotated crops to renew the soil.

"The cattle graze in the shade. That makes the cattle more comfortable, makes them produce more milk," says Garrett. (She notes that some dairy products, such as powdered milk, don't require the same careful handling and refrigeration as fruits and vegetables for long-distance transport.) The cattle eat crop residues and their manure fertilizes crops and trees. The rancher eventually harvests the trees and sells the wood for fuel. It's easy to see the benefits: the rancher keeps ranching and makes more money, and the soils are improved.

Garrett thinks systems like this can become more widespread in Brazil when one high-status person buys in and others follow. "It's actually worked well among a small subset of the population that are leaders, and then it spreads out to other people," she says. According to the Brazilian Agricultural Research Corporation, farmers used integrated systems on about 5,800 square miles of land in 2010. That number rose more than sevenfold by 2016. "Status counts," she says. "Somebody needs to prove that it works."

PHOTOGRAPH BY JACKIE RICCIARDI

Sargent, ENG profs collaborate to prevent strokes that cause dementia / BY DAVID LEVIN

Delivering Drugs by Microbubbles

Memory loss in old age starts small, with misplaced keys or wallets. In some people dementia eventually sets in, robbing them of the memories of faces, names, and important events.

It's devastating for both patients and family members—and it's distressingly common. According to the World Health Organization, more than 47 million people suffer from dementia worldwide.

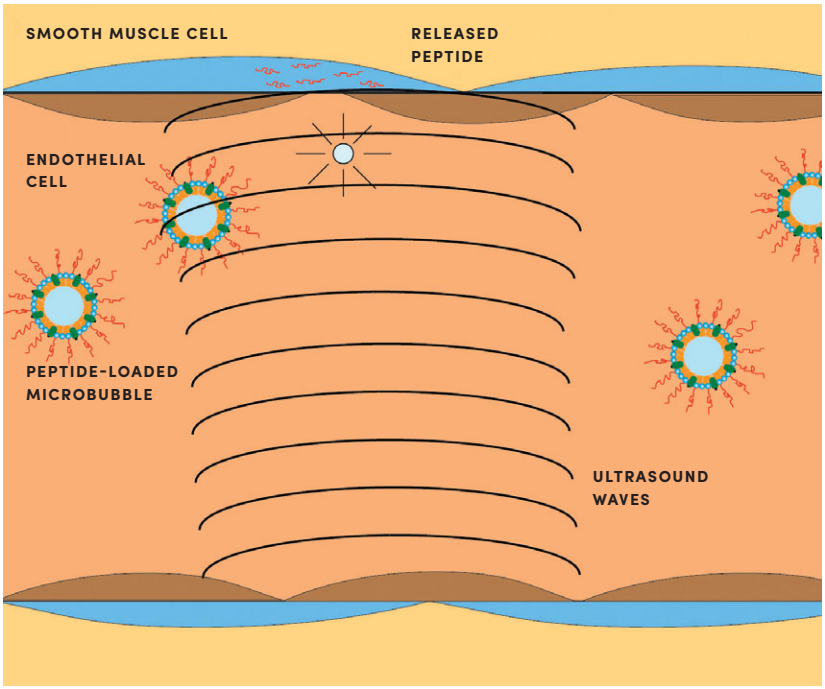
While Alzheimer's disease is probably the most well-known form, dementia also comes in other varieties. Vascular dementia, for example, is the result of tiny blood vessels bursting in the brain and leading to microstrokes and minute bleeds. The condition is closely linked with other age-related memory disorders.

"I suspect that vascular dementia and Alzheimer's are really just two different angles on the same disease," says Kathleen Morgan, a Sargent College of Health & Rehabilitation Sciences professor of health sciences. "There are plaques in the brain tissue of Alzheimer's patients that are visible at autopsy, but we know that if you have them, you'll probably see evidence of microbleeds as well."

If burst blood vessels are implicated in early-stage dementia, Morgan says, it may be possible to stop that damage before it starts. With help from a $2.5 million grant from the National Institute on Aging (NIA), she is examining a synthetic prototype drug that could prevent microbleeds in mouse brains. Morgan has joined forces with Tyrone Porter, a College of Engineering associate professor of mechanical engineering, to develop a new delivery system for the drug. Their solution uses microbubbles—tiny bubbles of inert gas smaller than capillaries—along with a focused ultrasound beam to help push the drug into a specific part of the body: the large blood vessels next to the heart.

Most brain bleeds, Morgan says, start in the aorta, the body's largest artery, which connects directly to the heart. With each beat, the heart exerts enormous amounts of pressure straight onto that conduit, which is made of smooth muscle cells that expand and contract like a rubber hose as blood flows past them. "Those smooth muscle cells are very important for controlling the pressure of your vascular system on a beat-to-beat basis," she says.

In younger bodies—both mouse and human—smooth muscle in the aorta expands with each beat, acting as a sort of shock absorber for the pressure coming out of the heart. In older bodies, though, the aorta becomes less elastic; if it becomes stiff enough, blood can surge at high pressure straight into tiny, sensitive blood vessels in the brain, which may burst under the strain.



TYRONE PORTER

▲ In their drug-delivery system, the scientists attach the drug to microbubbles smaller than capillaries and use a focused ultrasound beam to guide the bubbles and then burst them, delivering the drug directly into smooth muscle cells. They hope their system can be used to deliver drugs to the large blood vessels next to the heart.

▼ Kathleen Morgan holds a vial containing a mouse brain. Removed from an aged mouse, it is comparable to the brain of a 75-year-old human. Morgan and Tyrone Porter are using mice to test a prototype drug that could prevent stroke-causing microbleeds.

Morgan is developing new ways to reverse the stiffening of arteries. If she can restore some of the aorta's elasticity, she reasons, it may be possible to prevent new microbleeds.

To test this idea, she's concocted a new peptide—a small chain of amino acids—that allows the smooth muscles to remain supple. The challenge is delivering those molecules directly to the smooth muscle inside a living aorta. Unlike other drugs, releasing this one system-wide—or even artery-wide—could be disastrous. "Smooth muscle tissue isn't just in the aorta. It's in your vascular system, urinary tract, uterus, lung tissue, and digestive system," she notes. "If the peptides got into those tissues, it could cause incontinence, premature labor, all sorts of awful things."

To get the drug exactly where it's needed, you first have to dig into the artery itself.

"The cells we need to target don't come in contact with flowing blood," says Porter. "They're behind a layer or two of other cells and connective tissue in the blood vessel walls." To break through those layers and deliver the drug to smooth muscle cells, Porter attaches Morgan's peptides to the outside of each microbubble. Focused ultrasound can be used to push the microbubbles toward the aortic wall and pop them to release the peptide. The popping process also disrupts the lining of the aorta, making the blood vessel wall temporarily permeable. "Once that happens, the peptide can flow into the spaces that open up in the vessel wall and go straight into the smooth muscle tissue," he says.

Until now, Morgan has been able to test her peptide and its new delivery system only on smooth muscle cells in a petri dish. With the NIA grant, she and her collaborators are looking to scale up their research, and they will use their approach for the first time on a living animal.