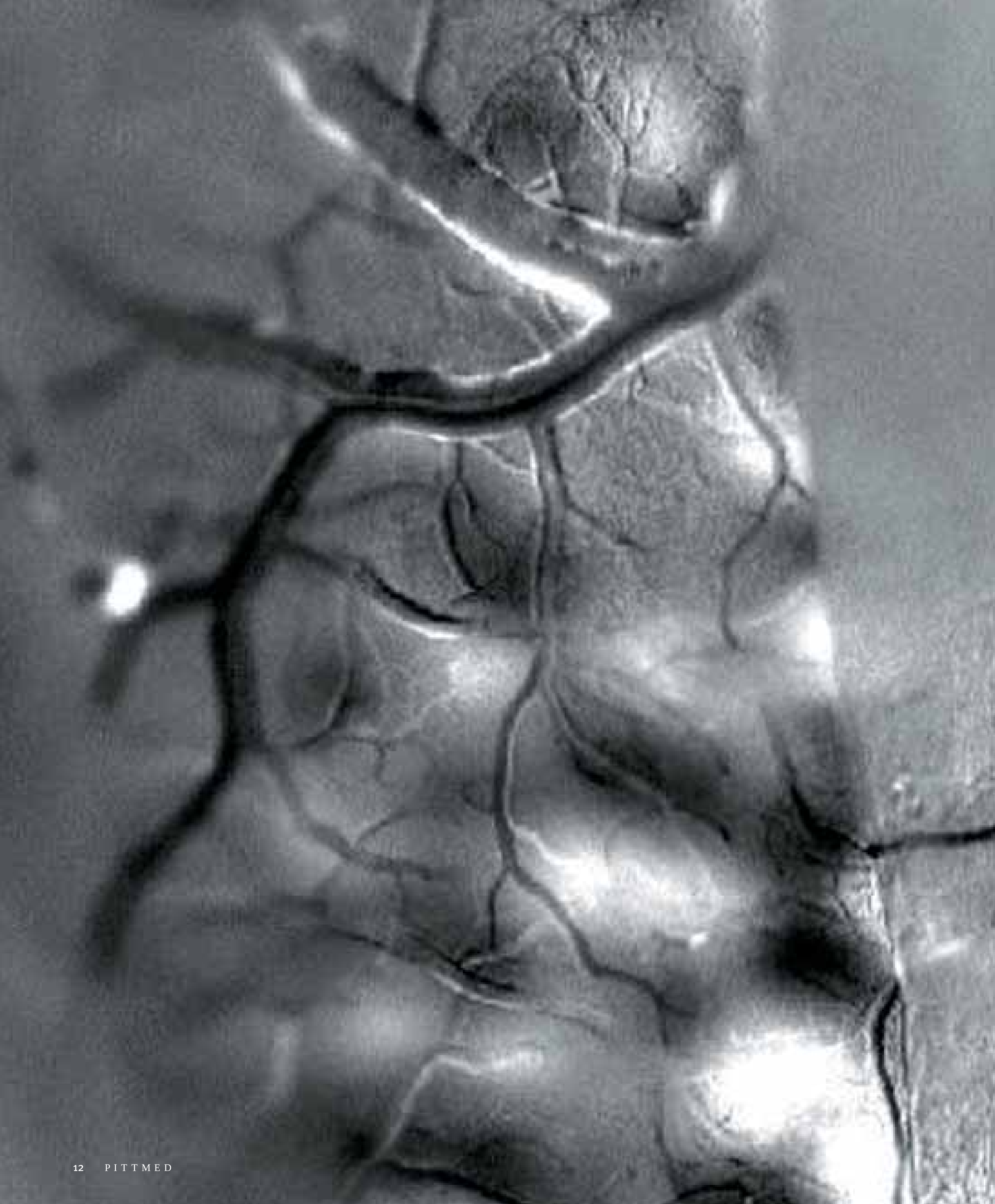


DOES IMAGING TECHNOLOGY TELL DOCTORS WHAT THEY THINK IT TELLS THEM?

IMAGES | SEONG-GI KIM
TEXT | JOE MIKSCH

WHERE THOUGHTS HAPPEN

Before we head over to the South Side of Pittsburgh and Seong-Gi Kim's lab, a brief visit to England is in order. In 1890, a pair of Charleses—Charles Roy and Charles Sherrington—proposed that neural activity could be correlated with increased blood flow to the active part of the brain. The harder nerve cells work, Roy and Sherrington's research suggested, the greater their need for oxygen and, therefore, the greater the need for blood at the site of increased neural activity.

This discovery, coupled with technological advances made over the course of the next century, has given the scientific community a powerful tool with which to see what's going on in the brain without cracking the skull: functional magnetic resonance imaging (fMRI). Essentially, fMRI uses powerful magnetic fields to monitor vacillations in blood flow. Hemoglobin, the iron-containing oxygen transporter in mammalian red blood cells, repels magnetic fields when oxygenated and is attracted when deoxygenated. The resulting three-dimensional images give a snapshot of a brain at work.

Or do they?

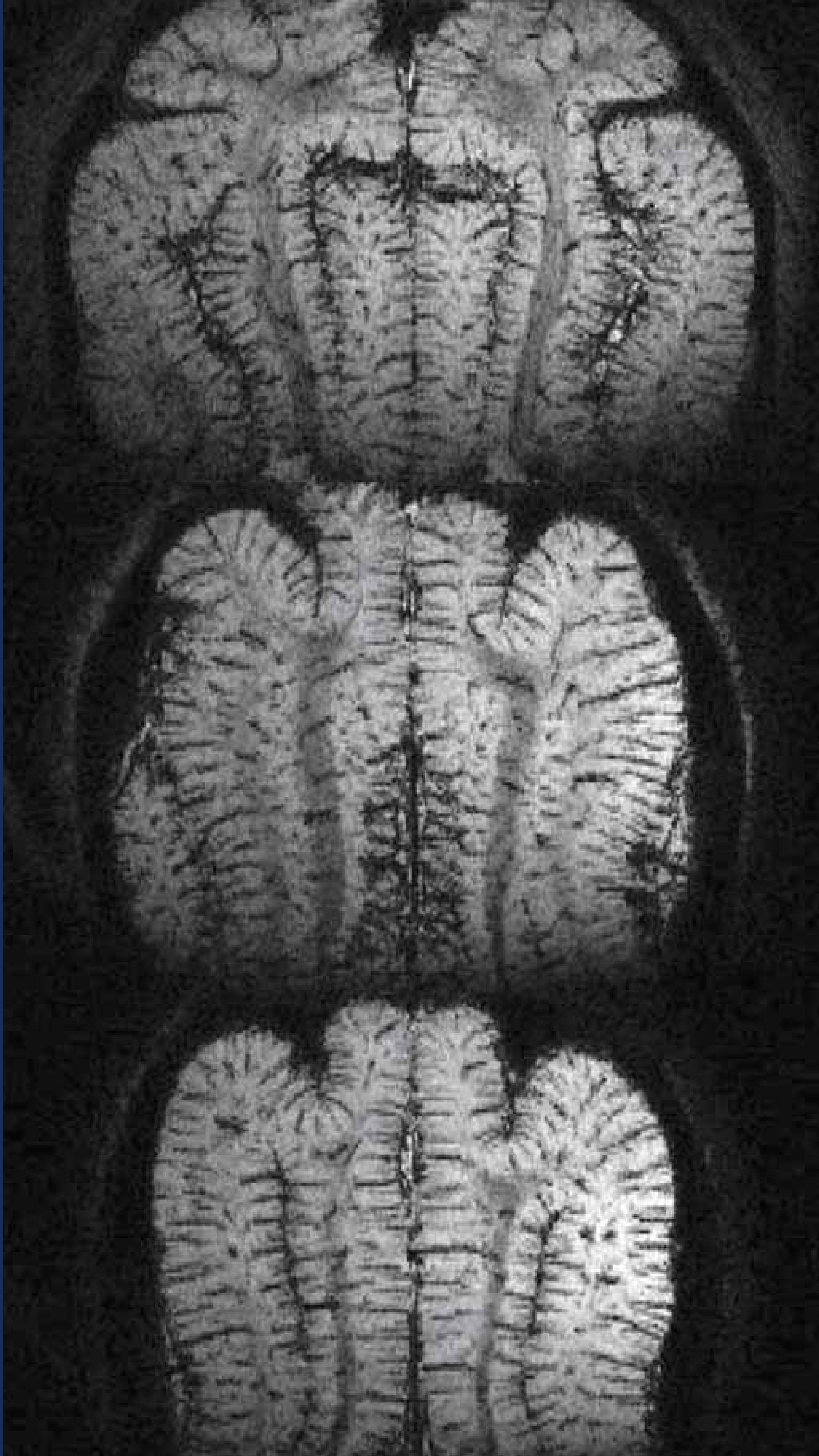
The answer to that question passes judgment on the accuracy of thousands of research programs attempting to understand how we think and what is happening when our brains don't behave in healthy ways.

Seong-Gi Kim photographed this surface-level image of a cat's cortex to examine it alongside an fMRI image of what's thought to be the same area.

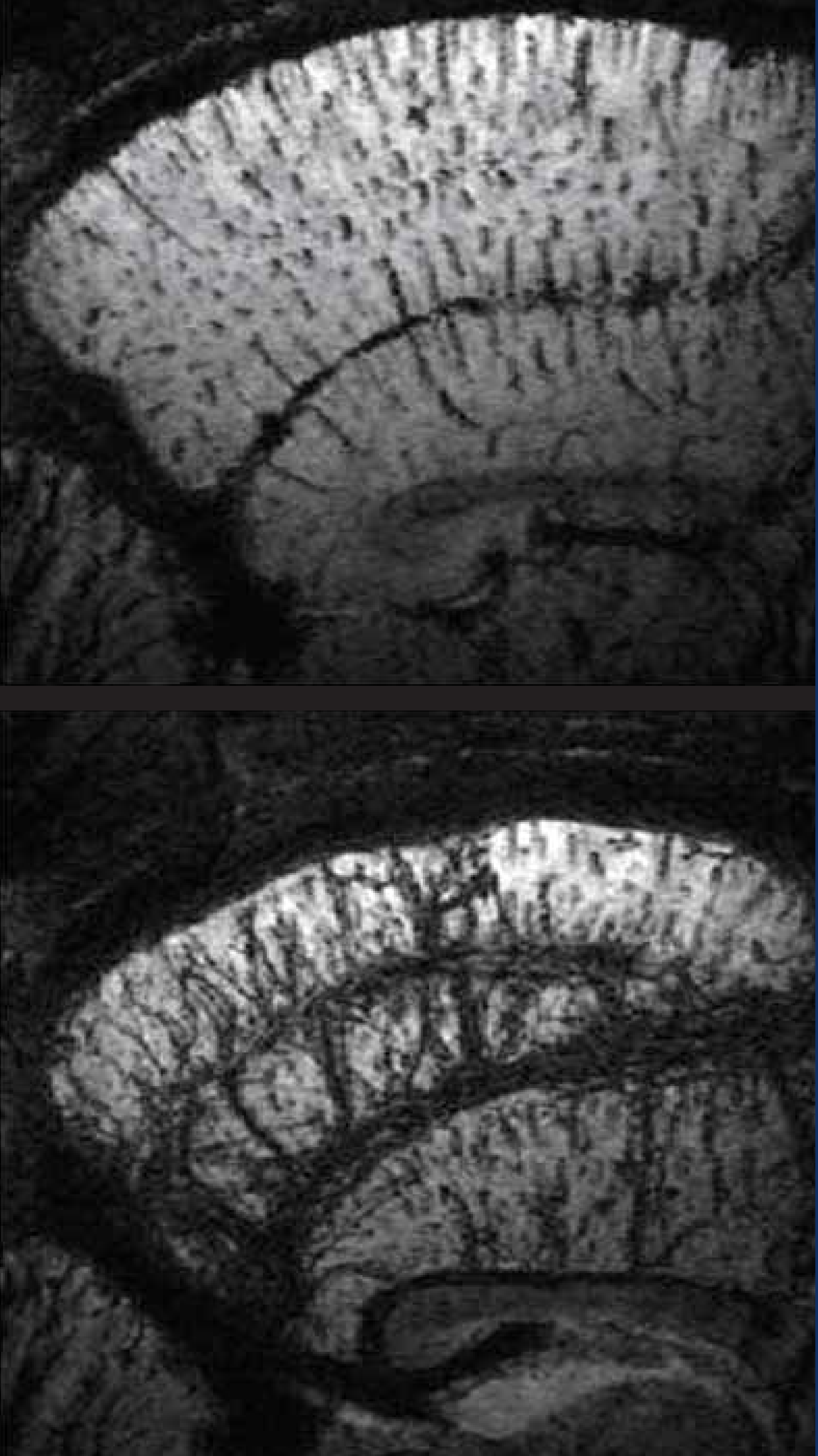
Since the early 1990s, when the first fMRI machines were built, there's been some controversy over whether the technical capabilities of the device and the techniques doctors use to interpret fMRI results truly measure what they are thought to measure. It's true that fMRI doesn't measure neural activity directly, so maybe there's some chance that an apples-and-oranges thing is going on here. It's also possible that different areas of the brain oxygenate and deoxygenate differently, skewing comparisons. And though the most powerful fMRI machines can measure activity in a physical space smaller than a millimeter, even with the latest technology, images aren't captured often enough to plot neural activity in real time. Neural activity takes place on a submillisecond timescale.

At the University of Pittsburgh's McGowan Institute for Regenerative Medicine on East Carson Street, Kim is in the midst of a decade-plus-long effort to refine fMRI technology. The essentials of the professor of radiology and neurobiology's lab consist of an fMRI machine and a cadre of cats. With these tools, Kim seeks to find out whether fMRI indeed depicts with precision specific areas of neural activity. In short, do the places that light up on a scan truly show where a given thought happens?

Kim is mapping bunches of neurons called cortical columns to find out. To perform his cortical-column mapping, Kim, a PhD, sedates the felines to calm them, though they remain conscious. Images of black-and-white bars within circles projected in front of the cats elicit neuronal activity, sort of a kitty kaleidoscope. Before fMRI, scientists first mapped cortical columns in live animals by using voltage-sensitive



dyes and a video camera. That was around 1986. Later, the preferred technique was to measure the light-absorbing properties of hemoglobin. These approaches limited research conclusions, considering the scientists could see only the uppermost layers of the exposed animal cortex.



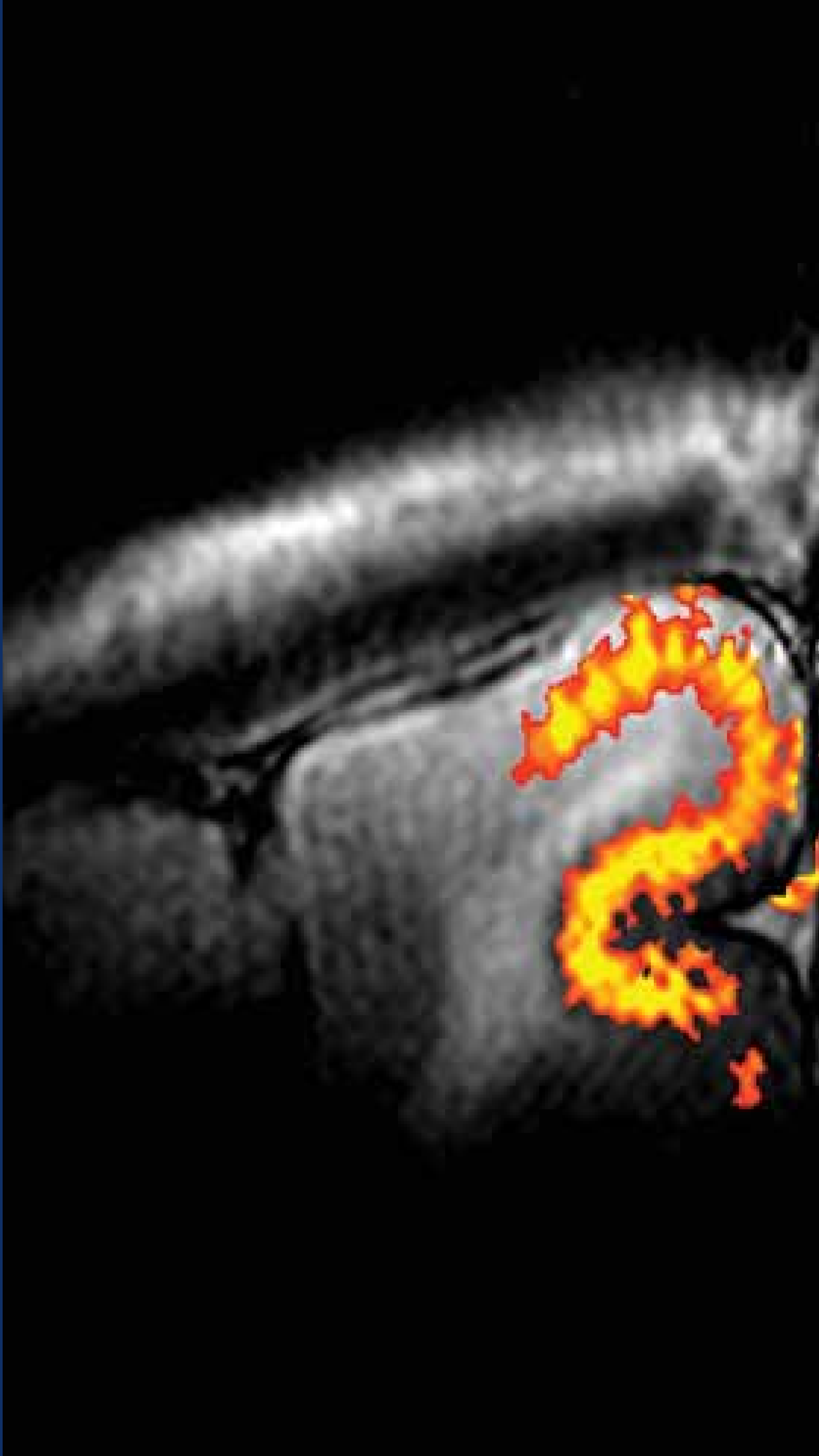
LEFT: Thin horizontal slices of a cat's cortex are depicted via fMRI to a resolution of 78 microns. The dark areas, both spots and lines, are veins. The vertically oriented slices on the far left provide a detailed map of a very small portion of an active cat cortex. Kim's lab can capture such high-resolution images by using an experimental 9.4 Tesla fMRI scanner—most commercially available scanners operate at 7 Tesla or less—which enables the machine to detect blood oxygenation changes in extremely small vessels. Kim's scanner's magnetic field strength is about 188,000 times stronger than the Earth's.

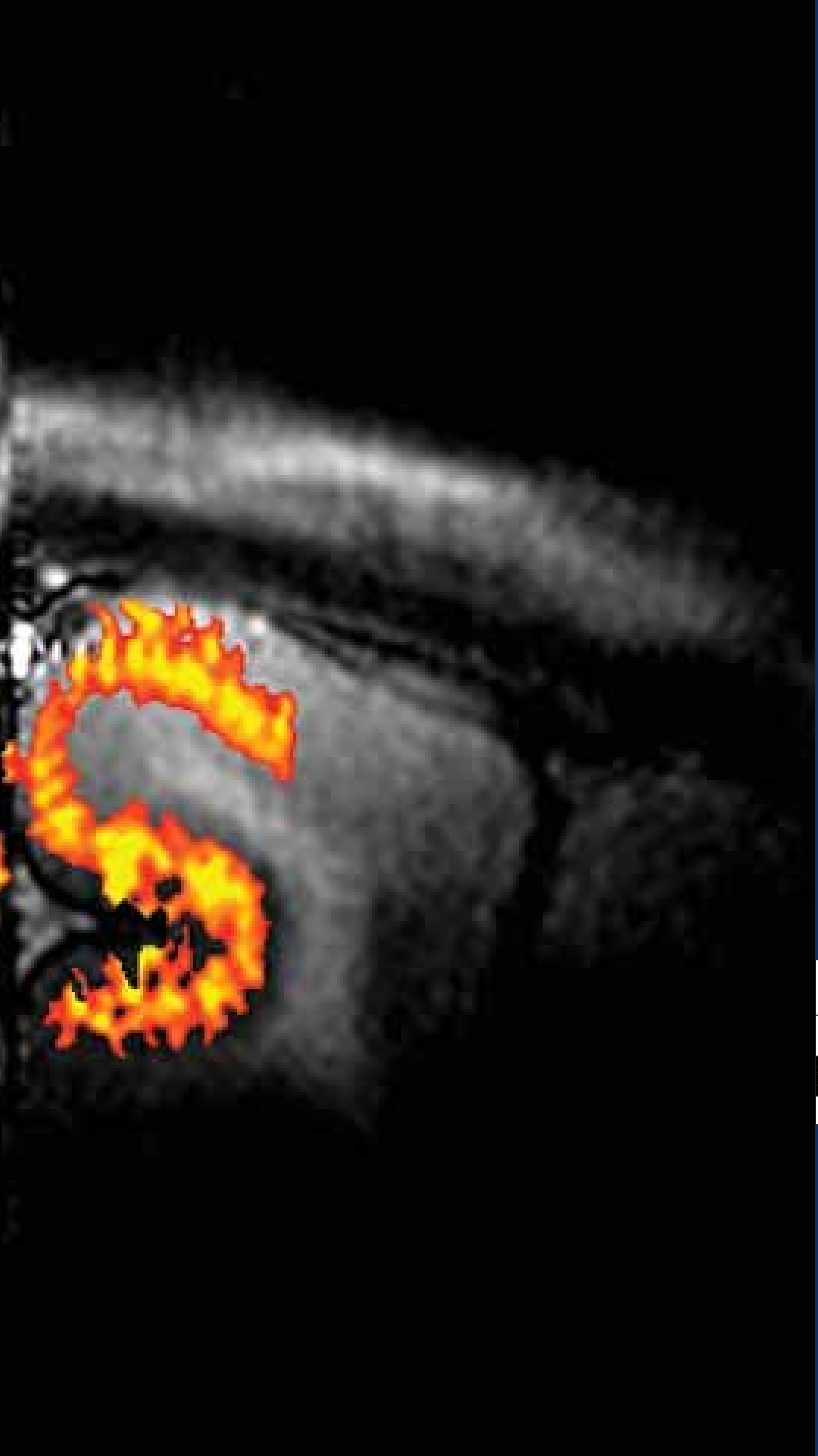
Using fMRI, Kim isn't bound by such constrictions. He can go as deeply into a cortical column as he likes, thanks to the noninvasive nature of the technique. He's eager to learn whether the fMRI signals that have been thought to correlate with neural activity on a large scale (more than a millimeter) are also detectable on a submillimeter scale. In large vessels, there's more blood fueling neural activity and, therefore, more detectable hemoglobin. Capillaries, the focus of smaller scale detection, carry much less blood. Using statistical analyses, Kim can greatly reduce the interference caused by signals from large blood vessels and focus on the little things, which in this case are the big things.

So does fMRI tell doctors and other scientists what they think it does? Right now, science is certainly seeing the neighborhood of neural activity with fMRI, Kim will attest. His work will help researchers get to a precise address.

What's at stake? Science's ability to unravel thought itself.

RIGHT: This is how a cat's brain might behave when it first sees a flicker of a mouse tail out of the corner of its eye. Pictured here is an fMRI-generated functional map—in yellow and orange—atop a composite anatomic image of a visually stimulated cat's brain. The area of the highest neural activity, the colored portion, is where the cat first begins processing visual information. The images of this 1-millimeter-thick slice of cortex were taken more quickly and at a higher resolution than can be obtained from a commercially available fMRI in a hospital. Experiments such as these help confirm scientists' notions about the roles certain areas of the brain perform.





BELOW: The cats Kim studies watch these lined circles. The red arrows indicate the direction in which the images oscillate.