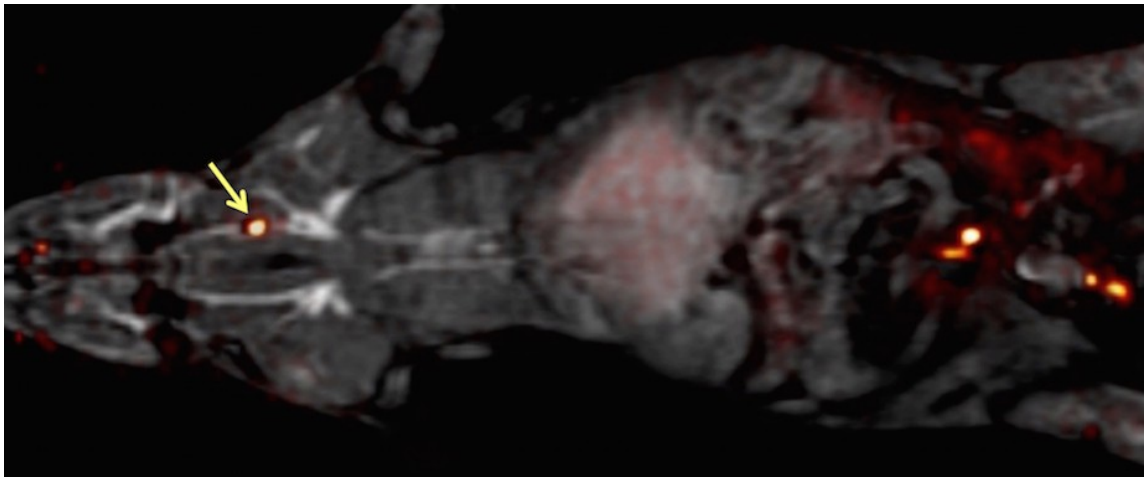
One scan to detect clots could replace many



A blood clot in the body can set off life-threatening conditions such as a heart attack, a stroke, or deep vein thrombosis, to name a few. And current imaging techniques are not always equal to the task of pinning down the clot's location fast enough to prevent further complications.

Why is it important to have a technique to scan the entire body for clots at one go? In the case of a stroke, for instance, a blood clot breaks off and travels to the brain. If some portion of the clot is still at the point of origin, there is a risk of secondary stroke. Physicians also use the location and size of the clot to determine whether to use drugs or surgery to treat the clots.

Researchers at Massachusetts General Hospital have invented a molecular probe which, "upon injection into a vein, will travel through the body and find blood clots wherever they occur, be that in the venous system, in the arteries, in the chambers of the heart or in the lungs," said Peter Caravan, director of the Institute for Innovation in Imaging at MGH.

Caravan presented his team's findings at the 250th National Meeting & Exposition of the American Chemical Society, which wrapped up in Boston Wednesday.

To detect the precise location of a blood clot, a physician now relies on a combination of methods: ultrasound to check legs and the carotid arteries that supply the head and neck, magnetic resonance imaging for the heart, and computed tomography, or CT, for the lungs. The researchers wanted a method that could detect blood clots anywhere in the body with a single whole-body scan.

In 2011, Caravan and his team at the Martinos Center for Biomedical Imaging at MGH reported the discovery of a peptide that binds specifically to fibrin, a protein found in blood clots. They attached a radioisotope, a chemically unstable form of an element, to their binding peptide.

Positron emission tomography, or PET, is an established technique to track radioisotopes anywhere in the body, so their probe could potentially pinpoint the location of any clot. It could also give an indication about the size of the clot.

The researchers used different combinations of radioisotopes, peptides, and linkers to identify which probe would give the brightest PET signal from blood clots. They analyzed how each of their candidates bonded with fibrin in a test tube. Inside the body of a rat, metabolic processes made short work of some of the probes. Their best performer was

metabolic processes made short work of some of the probes. Their best performer was the fibrin binding probe 8, or FBP8 for short, with copper-64 as the radioisotope.

In work published last week in the online edition of the journal of Arteriosclerosis, Thrombosis and Vascular Biology, the researchers demonstrated that their method simultaneously detects all the clots in the body of a rodent model. Also, they found that the newer the clot, the better the probe binds to fibrin, a fact that could allow physicians to decide which clot to go after first.

This approach is not suitable for diagnosis of clots in the emergency department, where immediate care is vital. It may be most beneficial when the life-threatening culprit is under control, but the source of the clot is still unknown, and the risk of recurrence is high, the researchers wrote. Caravan said they will test the probe in humans later this year, or early next year, at MGH.

This novel method addresses a huge unmet need, said Dr. Zahi Fayad, who is the director of cardiovascular imaging research at Mount Sinai Medical Center. A third or more of stroke patients in the US are given a diagnosis of "cryptogenic stroke," meaning no one knows the source of the stroke. Consequently, they are not given proper treatment. Since the underlying technology of the radioisotope is familiar is to hospitals all over the country, it could be adopted easily.

Each individual scan could cost more than the $350 Medicare cost for a typical scan, Caravan said. Still, because of the high sensitivity of PET, physicians will use only micrograms of the radioisotope, compared with the grams of material needed for MRI, thus reducing potential of chemical toxicity to the patient.

But the real value of this test could be that a single, convenient scan can encompass the whole body and replace multiple tests, Caravan said, and help prevent strokes. "If you are going to prevent a stroke, you are going to save the health care system a tremendous amount of money," he said. According to the American Journal of Managed Care, stroke is the third-leading cause of death in the US, accounting for more than $65 billion in direct and indirect costs annually.