Sharper imaging would promote earlier diagnosis of malignancies

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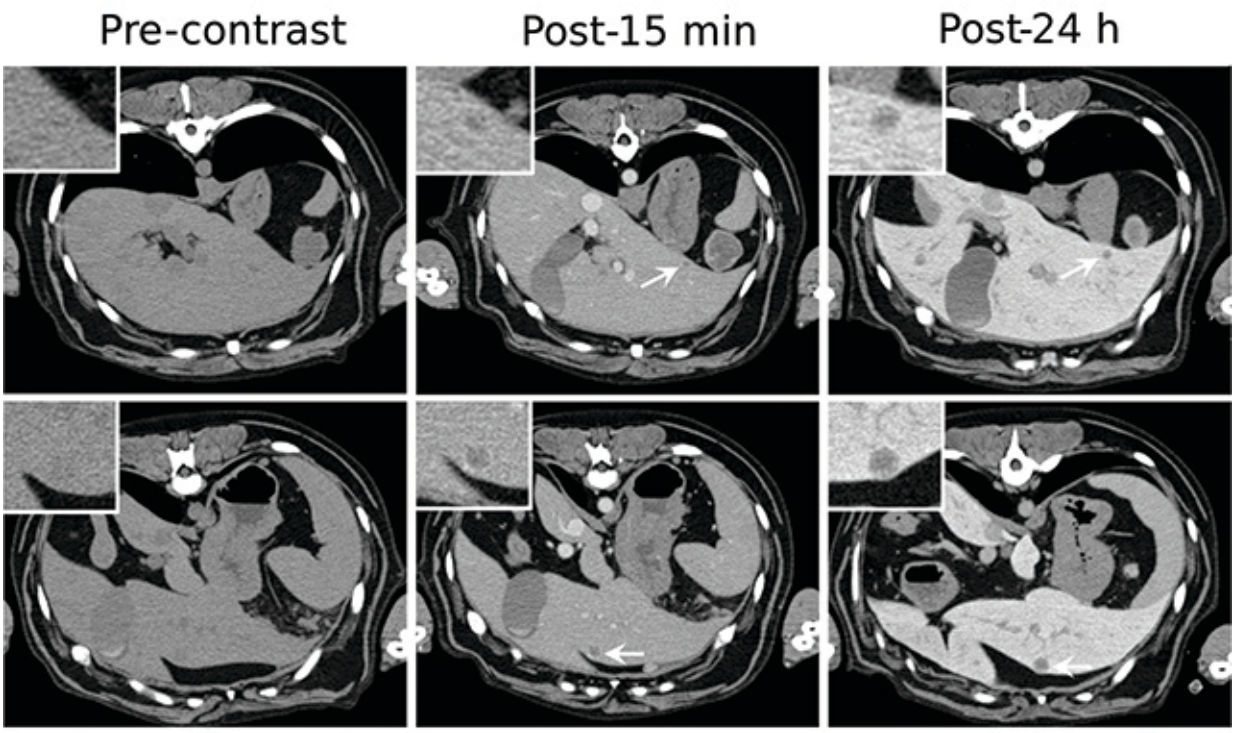

A tiny suspicious lesion in the liver, shown in the top right image, appeared quite visible 24 hours after the new contrast agent was injected. The top left image was taken before the injection. Credit: *PLOS One*

A common chemical element embedded in a tiny bubble of fat has the potential to advance cancer imaging. In a study of pet dogs that were

biopsied for cancer, a new contrast agent used in CT imaging allowed veterinarians to more easily pinpoint suspicious masses and detect typically elusive tumors in the liver. The finding could lead to better cancer diagnosis in human patients.

The new material—an iodine-infused bubble that's at least 50 times smaller than a red blood cell—was tested in CT scans of 13 dogs suspected of having cancer to determine whether it would pick up naturally occurring tumors similar to those that physicians diagnose in human medicine.

In the dogs, the contrast agent made suspected lesions visible for much longer periods, which could improve the ability to catch metastasizing cancer early on, says Amy Sato, a veterinary radiologist at Cummings School who evaluated the new contrast agent with colleagues from Texas Children's Hospital and the University of Wisconsin-Madison School of Veterinary Medicine.

In both human and veterinary patients, conventional contrast agents, which typically contain the chemical elements iodine or barium, enhance pictures of organs, blood vessels and tissues by changing the way that CT scans and other imaging tools interact with the body. When injected or swallowed, these agents block or reduce the ability of X-rays to pass through the body and allow doctors to better distinguish abnormalities from normal surrounding tissue.

Cancer that has spread to the liver, where some types of human and animal tumors commonly metastasize, often can't be seen if the contrast agent isn't visible on the scan, says Sato. Existing agents provide fleeting opportunities for clinicians to identify potential problems.

"You start to lose the ability to see the contrast on CT within three minutes," she says. "So if you do see a lesion and want to check if it's

cancer, you may have to give several doses of the contrast material" to get enough images to pinpoint where to place a biopsy needle.

Because the conventional iodine-based agent is encased in a fat globule known as a liposome, it is cleared from the body via the spleen and the liver. As a result, the agent highlights tumors in both organs for 24 hours and even longer.

"The liver and spleen actually became brighter over time because cells in these organs had internalized the agent," says Sato, who worked with Cummings Veterinary Medical Center surgeon John Berg to assess the effectiveness of the new agent. "It appears that you may actually be able to see liver lesions better after 24 hours," especially those smaller than 1 centimeter (about the width of a fingernail), than you would initially.

The new contrast agent also may be safer to use in human and animal patients with poor kidney function, says Sato. With existing contrast agents, the kidneys excrete the iodine solution, which is mildly toxic. "It's usually not a problem for most people or pets," she says, "but if an older person or cancer patient has known renal disease, you certainly don't want to insult their kidneys any further."

Dogs treated at Tufts and the University of Wisconsin-Madison underwent CT scans before they were injected with the iodine bubbles. The scans were repeated 15 minutes and 24 hours afterward; then the pets underwent needle or surgical biopsy to check any suspicious lesions.

The study was published in the nonprofit, open-access journal *PLOS ONE* in March 2016. Its lead author, Ketan Ghaghada, an assistant professor of pediatric radiology at Texas Children's Hospital and an expert on contrast agents, says the researchers want to conduct more studies to assess the agent's sensitivity and specificity in detecting different types of naturally occurring canine tumors.

"Companion dogs develop many types of spontaneous cancers that share strong similarities with human cancers," Ghaghada says, "including tumors' size and growth pattern, which can be seen with the same imaging hardware used in humans. As a result, preclinical imaging studies conducted in companion dogs… can help build the case for bringing new technologies for diagnosing and treating those diseases to the market, where they could help both people and pets."

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