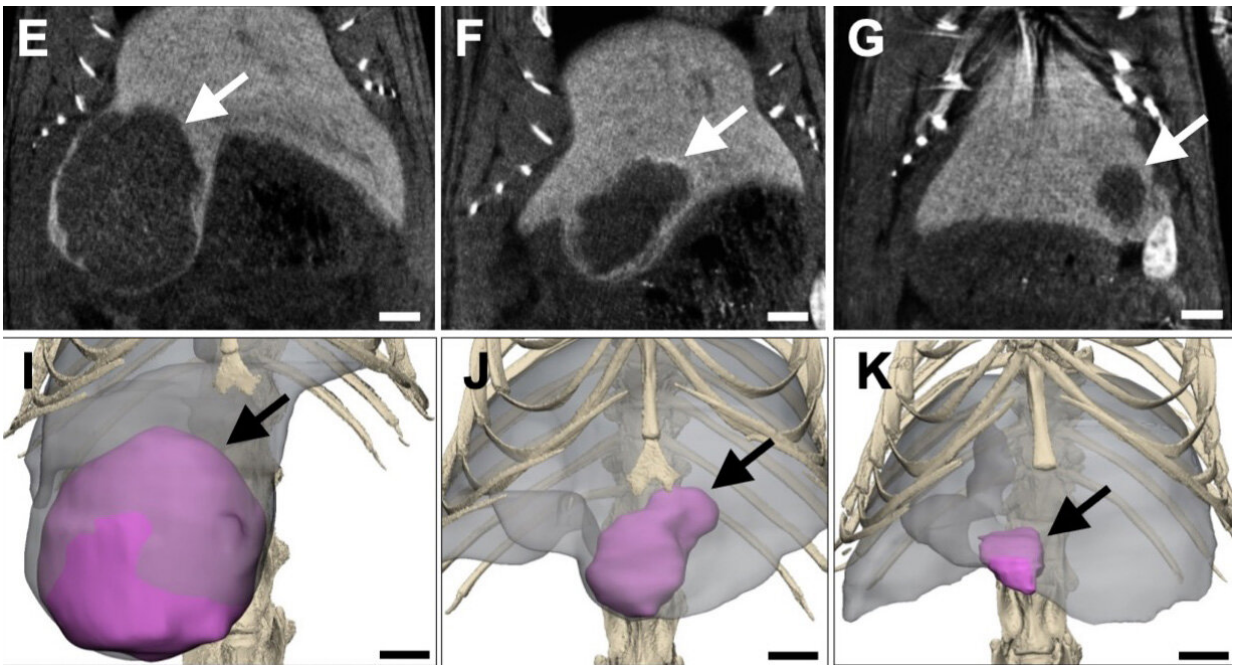
Ionic liquid formulation uniformly delivers chemotherapy to tumors while destroying cancerous tissue

February 11 2021, by Julie Janovsky-Mason



MicroCT images and 3D renderings of tumors in the livers of rats two weeks after receiving either saline (left), ethanol (middle), or LATTE (right). Credit: H. Albadawi et al., Science Translational Medicine (2021)

A Mayo Clinic team, led by Rahmi Oklu, M.D., Ph.D., a vascular and interventional radiologist at Mayo Clinic, in collaboration with Samir Mitragotri, Ph.D., of Harvard University, report the development of a

new ionic liquid formulation that killed cancer cells and allowed uniform distribution of a chemotherapy drug into liver tumors and other solid tumors in the lab. This discovery could solve a problem that has long plagued drug delivery to tumors and provide new hope to patients with liver cancer awaiting a liver transplant. The preclinical study results are published in *Science Translational Medicine*.

Dr. Oklu, study author and director of Mayo Clinic's Minimally Invasive Therapeutics Laboratory, says uniform drug delivery to tumors is often riddled with challenges. It's an issue he and the research team are aiming to solve, particularly for patients with liver cancer who are awaiting a transplant.

Dr. Oklu says higher drug doses are often used to encourage drug delivery into the tumor, and these higher doses could lead to significant toxicity. "If the drug cannot penetrate the tumor and remain there, then it cannot do its job," he says.

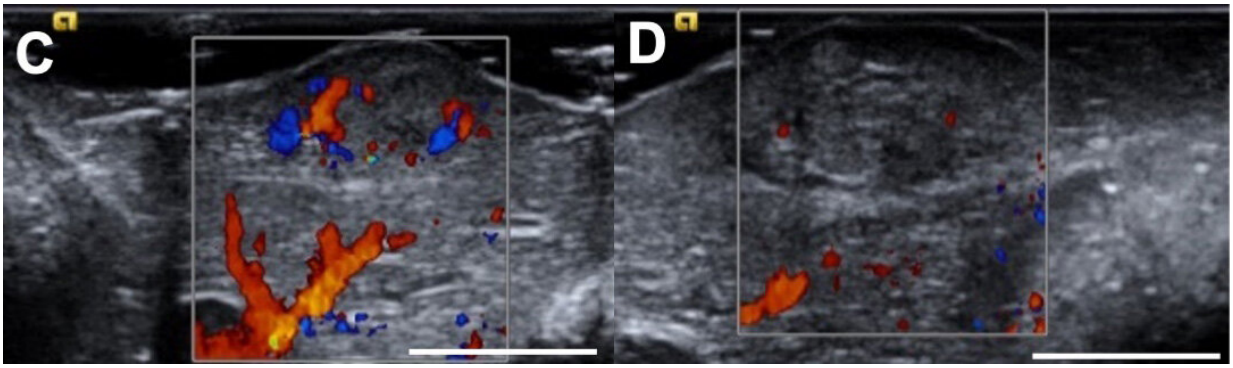
Current treatment involves ablation, which involves heating or cooling the tumor or infusing radioactive particles into the arteries of the tumor to destroy the cancer cells and keep patients within the criteria for a transplant. "You could do a microwave ablation and basically burn the tumor, but that is often not an option if the tumor is close to the heart or other important structures. And sometimes it is hard to find the blood supply of the tumor to infuse the radioactive particles," Dr. Oklu adds.

Dr. Oklu and his colleagues developed an ionic liquid—essentially salt in a liquid state—as an alternative way to deliver drugs into tumors through an ultrasound-guided needle injection. Once injected, the authors say the ionic liquid deposited the chemotherapy drugs uniformly, killing the cancer cells as the liquid engulfed the tumors.

The researchers reported this approach was successful in preclinical

studies using freshly resected human tumors in the lab and liver tumors in animal models. In addition, the authors report that the chemotherapy remained in the targeted zone for the length of the 28-day trial.

Whereas drugs often wash away quickly from direct injection into tumors or from standard IV delivery of chemotherapy through the veins of the arm, the ionic liquid, which the authors call a "locally active agent for tumor treatment and eradication," or LATTE, also encouraged immune cell infiltration in the microenvironment of the tumor. This may play a role in achieving immunotherapy in solid tumors. The researchers say this could solve current challenges, especially in hepatocellular carcinoma — the most common form of liver cancer — where liver transplant can be curative.



Before (C) and after (D) images of a liver tumor in a rabbit treated with an injection of the ionic liquid LATTE. Credit: H. Albadawi et al., Science Translational Medicine (2021)

"Ionic liquids are an exceptionally versatile group of materials. In our lab, we have already demonstrated that they have the ability to overcome a variety of biological barriers within the body for delivering drugs. In

this study, we demonstrate a novel application of ionic liquids to deliver chemotherapeutic drugs in the liver tumor, says Dr. Mitragotri.

The authors suggest that LATTE may work via diverse methods, and future studies are planned to expand on these preclinical findings. Future efforts might examine additional chemotherapy drugs, effects of immunotherapy agents and effects on overall survival, and involve a detailed analysis of local and bodywide immune implications of this experimental intervention.

More information: Hassan Albadawi et al. Percutaneous liquid ablation agent for tumor treatment and drug delivery, *Science Translational Medicine* (2021). DOI: 10.1126/scitranslmed.abe3889

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