Yale scientists have pioneered a new form of positron emission tomography (PET). This new approach to imaging near allows cancer specialists to detect the epidermal growth factor receptor (EGFR), a target for cancer therapy that is expressed on the surface of tumor cells. This new type of PET scan will also monitor drugs that target the EGFR in tumors and could provide a new way to regulate these drugs as treatment options.

The most common form of PET scan is called fluorodeoxyglucose (FDG) PET, in which a cancer patient is given a radioactive sugar that accumulates in the tumor, allowing doctors to view it. The Yale group is using PET technology in a way that hasn’t been done before. Their new technique uses a radioactive drug that specifically binds to the EGFR. The goal is to provide a method for doctors to view the tumor, watch the uptake of the drug, and monitor its effectiveness.

“That’s what we’re really excited about,” said Joseph Contessa, MD, PhD, Associate Professor of Therapeutic Radiology and Pharmacology whose laboratory studies the biology of EGFR. “We have not previously been able to non-invasively monitor the interaction of a cancer drug with its target in patients. With this work we hope to translate our knowledge about the biology of EGFR in a simple and clinically useful PET scan.”

PET imaging of the EGFR is accomplished by using a radioisotope called [11C]achloroetidinium, a drug that blocks activation of the EGFR and potently blocks the growth of tumor cells with mutations of the EGFR. EGFR mutations are found in multiple cancers and come in many forms. These include kinase mutations, which activate the receptor’s activity, or the Yale team’s current focus. The radiolabeled form of achloroetidinium was planned and synthesized by a member of the team, radiopharmacist Yirun Heng Huang, PhD, Professor of Radiology and Biomedical Imaging, and Co-Director of the Yale PET Center. Dr. Huang replaced one of the drug’s carbon atoms with a radioactive carbon, which allows the compound to be traced by PET.

The team tested the technique by injecting [11C]achloroetidinium into mice with lung cancer tumors harboring EGFR mutations. Erron Morris, PhD, Associate Professor of Radiology and Biomedical Imaging, Professor, and Biomedical Engineering, and Co-Director of the PET Imaging Section, modeled the radiotracer’s distribution and the scan was able to watch the drug bind to the tumor. This revealed the presence of the mutation and the effectiveness of the drug in blocking EGFR activity.

“These results could be a big step in the treatment of NSCLC,” explained Dr. Contessa, because a physician can see whether the drug is hitting the target as well as the body. If tumors are not tagged by [11C]achloroetidinium, PET doctors can consider using another prostate kinase inhibitor or radiating the skin mined by the drug. The technique can also reveal when patients are developing resistance to a drug, either generally or at certain sites, and hence would benefit from changing or supplementing their therapies. “We hope this technique will help physicians make these decisions earlier, by giving them more information more quickly,” said Dr. Contessa.

The next step, beginning now, is a Phase I trial with about two dozen patients at Smilow Cancer Hospital. That’s where the fourth member of the team comes in, medical oncologist Sarah Goldberg, MD, MPH, Assistant Professor of Medicine. “Dr. Goldberg is very interested in using this new technique to improve therapeutic decisions—making patients with EGFR mutations,” said Dr. Contessa.

The team believes this technique can be used for other types of cancer. “There are other tumors also with specific mutations, and we might be able to develop radotracers that specifically interact with those mutant proteins to give us a way to image different types of tumors,” said Dr. Contessa. “We think we can start to personalize imaging to find mutations, and use imaging in a way to gauge responses to therapy.”

Imaging the Epidermal Growth Factor Receptor

Photo credit: Carol Fanti, MD and Joseph Contessa, MD, PhD