PET imaging of the EGRF is accomplished by using a new technique called [18F]f-DOPA. Radioisotope-labeled dopamine blocks activation of the EGRF, and potentially blocks the growth of tumor cells with mutation of the EGRF. EGRF mutations are found in multiple cancers and occur in many forms. Those with truncating mutations, which abrogate the receptor’s activity, are the Yale team’s current focus. The radiolabeled form of dopamine was planned and synthesized by a member of the team, radiochemist Yiyan Henry 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 [18F]f-DOPA into mice with lung cancer tumors harboring EGRF mutations. Erin Morris, PhD, Associate Professor of Radiology and Biomedical Imaging, Procter, and Biomedical Engineering and Co-Director of the PET Imaging Section, modeled the radiotracer’s distribution and the team 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 EGRF activity. Their结论 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 at every site in the body. If tumors are not targeted by [18F]f-DOPA, radiolabeled PET, doctors can consider using another protein kinase inhibitor or irradiating the skin missed by the drug. The technique can also reveal when patients are developing resistance to a drug, either generally or at certain sites, and hence could 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 Yaler 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 decision-making for patients with EGFR mutations,” said Dr. Contessa. The team believes this technique can be used for other types of cancer. “There are other tumors that have specific mutations, and we might be able to develop radiotracers 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.”