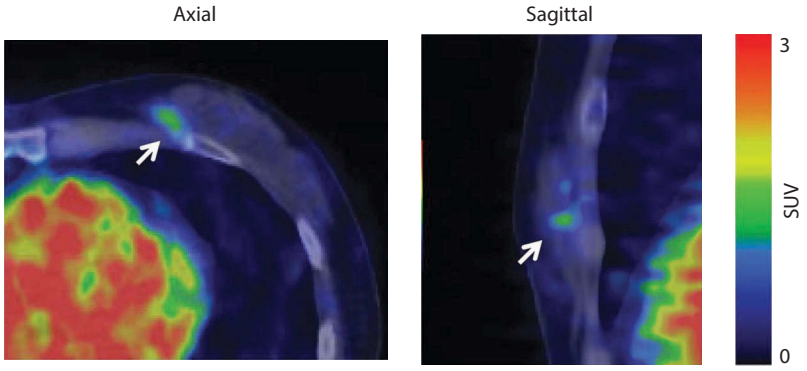

FIGURE 8.10 ^{64}Cu-DOTA-trastuzumab PET images of HER2-positive primary breast tumor. Arrows show primary breast tumor in patient. (Red regions indicate high uptake ^{64}Cu-DOTA-trastuzumab in heart and blood vessels.) This research was originally published in JNM. (From Tamura, K. et al., *J. Nucl. Med.*, 54(11), 1869, 2013. Figure 8.3. Copyright by the Society of Nuclear Medicine and Molecular Imaging, Inc.)

blockade leads to extrapyramidal motor symptoms, whereas lower striatal D_2 blockade diminishes the therapeutic effect drastically.

8.8.5 Companion Diagnostics

Companion diagnostics help tailor treatment schemes to individual patients and monitor the success of the selected treatment. In the drug development, the ability to identify and select patients that will benefit from the treatment enables smaller and more cost-effective clinical trials.

A prominent example for in vivo monoclonal antibodies (mAbs) companion diagnostic imaging is human epidermal growth factor receptor 2 (HER2)-positive breast cancer imaging with ^{64}Cu-labeled Herceptin (trastuzumab). The labeled mAbs can be used for patient selection, characterization of the target binding, and determination of the mAb's fate in vivo. In general, HER2 is a very attractive drug target since an outstanding therapy response rate up to 86% has been observed—unfortunately, only 20%–25% of all breast cancers are HER2-positive (Figure 8.10).

8.9 DETERMINATION OF FUNCTIONAL ACTIVITY RESPONSE

The ability to image a drug's effects on a biological process in vivo provides a direct readout of the efficacy of the potential drug. Molecular imaging of functional responses can validate whether a prospective drug is able to modulate the desired target in vivo or not. The metabolism of glucose, amino acids, and lipids can be imaged with PET. These measurements appear to be superior when assessing tumor response to targeted drugs which predominantly result in no or minor tumor size changes early in a treatment cycle.

8.9.1 [^{18}F]FDG

[^{18}F]FDG (FDG) is the most widely used tracer for PET imaging in oncology. FDG is transported into cells by the glucose transporter, and then phosphorylated by a hexokinase to form FDG-6-phosphate. This phosphorylated product of FDG (in contrast to the phosphorylated product of glucose) is not a substrate for further glycolysis and accumulates in cells that have increased activity of hexokinase and increased glucose transporter levels. Tumor cells typically display such a characteristics (the Warburg effect) and FDG is routinely used in cancer-related investigations.