be sacrificed as part of the process.[65] FDG is a substrate for the glucose transporter, so it is rapidly absorbed by cells, and it is also a substrate for hexokinase, the enzyme responsible for the first step in glucose metabolism. Hexokinase phosphorylates FDG, producing FDG-6-phosphate, but the absence of a hydroxyl group in the 2-position of this compound blocks further metabolism via the glycolysis pathway. As a result, FDG-6-phosphate accumulated in the cells.

Of course, all cells use glucose, so if all other things were equal, then the distribution of FDG-6-phosphate would be uniform across the body and PET imaging using this radioligand would not be very useful. There are, however, important differences between normal cells and malignant cells that provide an opportunity for PET imaging of several types of cancers. In many cases, the significantly greater energy demand of malignant cells is supported by upregulation of both glucose transporters (e.g., GLUT-1) and hexokinase.[66] This increases the uptake of FDG by certain types of malignancies relative to normal cells. The low levels of FDG-6-phosphate produced in normal tissues serves as a background for the higher levels of FDG-6-phosphate produced in cancerous tissues. These differences can be visualized using PET imaging techniques, providing a method of diagnosing and staging a number of different malignancies. This technique has been successfully applied to colorectal cancer, melanoma, lymphoma, and non-small-cell lung cancer.

It should also be clear that PET imaging agents such as FDG and other compounds that are selectively absorbed by malignant cells can be a very effective tool in the identification of new therapeutic agents. Tumor size and disease progression could be tracked over time in an appropriate animal model using a PET ligand. At the same time, animals can be treated with a candidate compound while monitoring for changes in tumor size and disease progression using the same PET ligand. If the candidate compound produces no change in the PET scan images when comparing treated versus untreated animals, then the candidate compound is not effective and should be discontinued for this particular indication. On the other hand, if tumor size decreases or disease progression is slowed/stopped, then further investigation of the candidate compound is reasonable. PET imaging methods can be applied at the *in vivo* animal model stage or in human clinical trials. In both cases, PET imaging techniques may provide insight into the utility of candidate compound well ahead of the traditional survival end points. Although these biomarkers are not sufficiently well-defined at this time to qualify as surrogate end points, the information derived from these experiments can be used to make educated decision on whether or not to continue pursuing a candidate compound and minimize patient risks associated with exposure to candidate compounds with limited safety profiles.