specific radio frequency in the presence of an oscillating magnetic field. The various tissues, organs, fluids, and other components of the body each have their own unique resonance frequency, which creates contrast between the various body components when an MRI image is generated. As with PET, SPECT, and X-ray CT, the data collected in this process can be used to generate three-dimensional images of the subject.

It is also possible to use contrast agents in MRI studies. Unlike PET and SPECT radioligands, however, the incorporation of radioisotopes is not necessary. MRI contrast agents, also referred to as shift reagents, contain paramagnetic atoms that can impact the resonance frequencies of nearby atoms. This creates an observable change in the MRI signals and can be especially useful if the contrast agent is differentially absorbed in the body. Dotarem® (Gadoteric meglumine, Figure 10.6), for example, is a Gadolinium chelating

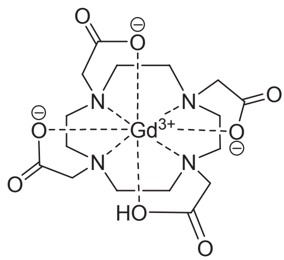

FIGURE 10.6 Dotarem® (Gadoteric meglumine).

agent that has been used to study cerebral pathologies, medullar pathologies, and vascular disease.[37] MRI has also been successfully applied to the study of Alzheimer's disease,[38] cardiovascular disease,[39] and multiple sclerosis.[40]

Functional magnetic resonance imaging (fMRI) is a variation on MRI technology that has provided substantial insight into brain function. This technique takes advantage of changes in cerebral blood flow that occur in concert with changes in neuronal activity. Blood-oxygen-level dependent (BOLD) contrast is the most commonly used fMRI procedure. In this method, differences in blood oxygenation are detected based on the magnetic properties of the iron atom in hemoglobin. Oxygenated hemoglobin (oxygen-rich blood) contains a diamagnetic iron atom, whereas the iron of deoxygenated hemoglobin (oxygen-poor blood) is paramagnetic. The two magnetic states of iron are distinct in their impact on MRI signals, and this difference can be exploited to create heat maps that describe amounts of oxygenated versus deoxygenated blood. Increased neuronal activity is associated with an increase in oxygen-rich blood. As a result, the aforementioned heat maps provide not only an indication of the oxygenation levels of blood in various areas of the brain, they also provide a heat map of brain activity across the various regions of the brain.[41] fMRI has been successfully applied in the study of depression,[42] pain,[43] as well as a wide range of CNS disorders.[44]