Closomer MRI and CT Contrast Agents

Magnetic Resonance Imaging (MRI) is an extraordinarily useful method for diagnostic imaging and it is noted for the high spatial resolution

The development of known MRI contrast agents (CAs) largely based upon Gd(III) chelates has progressed to the extent that they are employed in the clinical imaging of cancer and other diseases and at the frontiers of medical research exemplified by molecular imaging and “smart” CAs. Commercially available agents include relatively simple, low molecular weight species and dozens of contrast agents of the $T_1$ type have been synthesized and evaluated. The structures of these CAs are largely based upon the paramagnetic Gd(III) ion complexed by a rapidly exchangeable H$_2$O molecule and a robustly bound multiligand organic chelate system comprised of common coordinating groups (-COO$^-$, -NR$_3$, -O$^-$, -OPO$_2$R and others). The discovery of new chelation systems has evolved into a large library of useful complexes from which candidate structures may be selected for a wide variety of experimental purposes. However, an ongoing need exists for the design, synthesis and evaluation of Gd(III)-based CAs which present improved properties such as higher $T_1$ relaxivity per Gd(III) center and multinuclear structures as well as the selective targeting of large amounts of Gd(III) for molecular imaging.

Overview of Closomer-based Contrast Agents

A closomer based novel contrast enhancement agent will have maximal water exchange while creating a higher relaxivity. This is accomplished using a closomer scaffold, upon which twelve Gd(III) are substituted. The ligands are synthesized as part of a radial armature tethered to the closomer core through a suitable linker.

Space filling models of $B_{12}H_{12}$, $B_{12}(OH)_{12}$, and $B_{12}$-DOTA-Gd twelvefold conjugate dianion
Tissue Specific Targeting and Imaging

Through a unique synthetic differentiation strategy developed in our laboratory, it is now possible to reserve one of the twelve boron vertices for targeting purposes. This methodology now allows for a bioligand, such as an antibody, to be attached to the nanoprobe via suitable linkage to this unique position. As the remaining vertices are charged with Gd(III) chelates, a potent combination of enhancement and directivity ensues. The result is that the targeted tissue will appear with intensity many times that of the surrounding tissue on the MRI output.