

Magnetic Resonance Contrast Agents for Medical and Molecular Imaging

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1. INTRODUCTION	2
1.1. Magnetic Resonance Imaging	2
1.2. Classes of Contrast Agents	3
2. CONTRAST AGENTS FOR DIAGNOSIS	5
2.1. Cancer	5
2.1.1. Gd(III) DTPA and Its Derivatives	6
2.1.2. Mn(II) and Fe ₂ O ₃ Agents	7
2.2. Non-Cancer Diseases	9
2.2.1. Blood Pool Related Diseases	9
2.2.2. Diseases of the Gastrointestinal Tract	10
2.2.3. Skeletal System Diagnosis	10
2.2.4. Other Diseases	11
3. TARGETED DELIVERY OF CONTRAST AGENTS	11
3.1. Contrast Agent Delivery	12

3.1.1. Gd(III) Containing Agents	12
3.1.2. Iron Oxide Agents	12
3.2. Penetrating the Blood Brain Barrier	13
4. IMAGING BIOCHEMICAL EVENTS	14
4.1. Enzymatically Activated Contrast Agents	14
4.2. Contrast Agents to Detect Biologically Significant Molecules	17
4.3. pH Sensitive Agents	22
5. CONCLUSIONS AND OUTLOOK	26
ACKNOWLEDGMENTS	26
ABBREVIATIONS	26
REFERENCES	28

1. INTRODUCTION

This chapter focuses on the wide range of chemical and biological applications that exist for magnetic resonance imaging (MRI) contrast agents. We begin with a brief introduction of how MRI and contrast agents function followed by a review of both clinical and experimental uses for MRI contrast agents. We proceed with a description of the targeted delivery of contrast agents including how they bind to and accumulate in specific biological tissues. Finally, we describe the new class of bio-activatable MR contrast agents. These agents respond to a biological phenomenon by altering the intensity of the observed signal in a conditional fashion.

1.1. Magnetic Resonance Imaging

MRI has become an extremely important tool for clinical diagnosis of disease and as a noninvasive method of acquiring threedimensional images of opaque experimental animals. MRI is based on the same principles as nuclear magnetic resonance (NMR) spectroscopy. Briefly, samples are placed in a large magnetic field and exposed to radiofrequency (rf) pulses. The relaxation times of the excited nuclei (usually protons from water)

are then detected. Water protons are typically weighted using T_2 (spin-spin relaxation time) contrast and inhomogeneous (e.g. water) gradients. In order to create an image, the spatial information is encoded into the magnetic field gradients that alter the magnetic field of spatial positions to frequencies. This is then formed to produce images from the data.

Since the development of MRI, advances have led to increases in both the strength of conducting magnets have made possible higher image resolutions than were previously possible. Modern computers and software have improved image quality and decreased scan times. Images can now be obtained in minutes (single slice) compared to hours as X-ray computed tomography. Where higher fields (>10 T) are used, smaller cells (~10 μm) have been resolved. This is the primary imaging mode for MRI. This source for a complete description of the *Chemistry of Contrast Agents* is edited by Merbach and Tóth, *Contrast Agents and Their Interrelations*.

1.2. Classes of Contrast Agents

MRI can distinguish between different tissues based on differences in water concentration. The use of contrast agents improve image contrast. Optical dyes such as fluorescent dyes provide contrast as a result of their interaction with magnetic molecules, because they are not MRI contrast agents. They interact with nearby proton spins, thus enhancing the signal in the image. The mechanism of