COMPOSITION AND METHOD FOR DELIVERING ACTIVE AGENTS

CROSS REFERENCE TO RELATED APPLICATION

This is a continuation of U.S. Ser. No. 07/685,211, filed Apr. 12, 1991, now U.S. Pat. No. 5,496,535.

FIELD OF THE INVENTION

The present invention relates to radiological imaging systems, and more particularly to use of a contrast enhancing agent in magnetic resonance imaging (MRI), computed tomography (CT), or conventional radiography (X-ray). In particular, this invention relates to improved fluorocarbon-based contrast agents with enhanced contrast effects in the gastrointestinal (GI) tract, which agents may require a lesser amount of fluorocarbon to be effective, thereby reducing costs and increasing patient compliance. This invention also relates to an improved fluorocarbon composition having improved palatability, and to fluorocarbon compositions for delivering active agents, including pharmacological and bioactive agents. The invention further relates to methods for producing such preparations.

BACKGROUND OF THE INVENTION

Contrast agents are useful adjuncts in radiological imaging because they make it possible to determine the location, size and conformation of organs or other structures of the body in the context of their surrounding tissues. Cells which make up the tissues of soft non-bony body parts are comprised primarily of water, even among parts that differ markedly in shape and structure such as the liver, pancreas and intestine. Radiography procedures of CT and MRI operate on the basis of distinct physical principles, and each detects and maps variances in the composition of a target object. These imaging techniques can therefore be used to differentiate between normal tissue and tumors, lesions, or blockages. Small tumors and overlapping tissues, however, are difficult to distinguish. In the diagnosis of disorders of the GI tract, for example, blockage or abnormalities in the conformation of loops of intestine lying one on the other are difficult to identify unless the section of the GI tract is filled with a contrast agent which enables definition of volumes and delineation of boundaries.

In the conventional radiographic procedure, a beam of X-rays passes through a target object and exposes an underlying photographic film. The developed film then provides an image of the radiodensity pattern of the object. Less radiodense areas produce a greater blackening of the film; more radiodense, bony tissues produce a lighter image. Effective contrast agents for X-ray may be either less radiodense than body tissues or more radiodense. The less radiodense agents include air and other gases; an example of a more radiodense contrast material is a barium sulfate suspension.

Computed tomography (CT) is superior to conventional radiography in its ability to image, with extremely high resolution, a succession of thin sections of an object at specific points, lines or planes along the X, Y, or Z axis of the target object. However, because this procedure is also based on the detection of differences in radiodensity, requirements for contrast agents in CT are essentially identical with those for conventional radiography.

Magnetic resonance imaging (MRI) systems for body imaging operate on a different physical principle. Literature describing the theoretical and practical use of MRI systems is available from manufacturers such as General Electric & Co., which markets commercial systems. In general, advantage is taken of the fact that some atomic nuclei, e.g., hydrogen nuclei, have both nuclear spin and nuclear magnetic moment, and therefore can be manipulated by applied magnetic fields. In the conventional type of MRI system, a magnetic field is established across a body to align the spin axes of the nuclei of a particular chemical element, usually hydrogen, with the direction of the magnetic field. The aligned, spinning nuclei execute precessional motions around the aligning direction of the magnetic field. For the aligned, spinning nuclei, the frequency at which they precess around the direction of the magnetic field is a function of the particular nucleus which is involved and the magnetic field strength. The selectivity of this precessional frequency with respect to the strength of the applied magnetic field is very sharp, and this precessional frequency is considered a resonant frequency.

In a customary MRI system, after alignment or polarization of the selected nuclei, a burst of radio frequency energy at the resonant frequency is radiated at the target body to produce a coherent deflection of the spin alignment of the selected nuclei. When the deflecting radio energy is terminated, the deflected or disturbed spin axes are reoriented or realigned, and in this process radiate a characteristic radio frequency signal which can be detected by an external coil and then discriminated in the MRI system to establish image contrast between different types of tissues in the body. MRI systems have a variety of different excitation and discrimination modes available, which are known in the art.

Contrast agents for MRI must possess a substantially different concentration of the nuclei used as a basis for scanning. In a hydrogen scanning system, an agent substantially lacking hydrogen can be used; in an MRI system which scans for a physiologically minor nucleus, e.g., fluorine nuclei, a substance with a high concentration of that nucleus would provide appropriate contrast.

Contrast agents may be introduced into the body space in various ways, depending on the imaging requirement. In this application, emphasis is placed on oral administration, albeit other modes may also be appropriate. A suitable contrast agent must be biocompatible, that is, non-toxic and chemically stable, not absorbed by the body or reactive within the tissue, and eliminated from the body within a short time. Efforts to enhance imaging have also included the use of CO_2 gas, which is known to have an enhancing effect, particularly in the GI tract. Few satisfactory agents have been developed for MRI, although many have been tried. For example, GI imaging has been enhanced with mineral oil.

It is known to use fluorocarbons, including brominated perfluorocarbons, as a contrast enhancement medium in radiological imaging as shown in U.S. Pat. No. 3,975,512 to Long. Brominated and other fluorocarbons are known to be safe and biocompatible when used in the body. It is also known to use these agents in the context of the MRI procedure to contrast more clearly and more distinctly in MRI-produced images the several body parts which normally have substantially higher water content and which are close or overlaid one on the other, as in the GI tract.

Previous investigations into the effectiveness of radiological examination of the GI tract have revealed that conventional contrast media, such as barium or clay-based media taken by the patient prior to such examination, do not enable small lesions, such as shallow ulcers, and flat or surface