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(54) Title: MAGNETIC RESONANCE IMAGING OF BONE TISSUE

(57) Abstract: A medical apparatus includes a magnetic resonance imaging system for acquiring magnetic resonance data from an imaging volume, a processor for controlling the medical apparatus, and a memory containing machine executable instructions and a pulse sequence. The magnetic resonance data acquired using the pulse sequence comprises free induction decay data and multiple gradient echo data. Execution of the instructions causes the processor to acquire the magnetic resonance data using the magnetic resonance imaging system in accordance with the pulse sequence, and reconstruct an in-phase image, a fat-saturated image, a water-saturated image, and an ultra-short echo time image from the magnetic resonance data, wherein the ultra-short echo time image comprises bone image data.



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Magnetic resonance imaging of bone tissue

FIELD

The invention relates to magnetic resonance imaging, in particular to the use of magnetic resonance imaging for radiation therapy planning.

5 BACKGROUND

Magnetic Resonance (MR) images that can separate tissue, bone, and air are beneficial for all applications where MR is used in combination with irradiating imaging techniques, such as Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT), and with planning for irradiating therapy techniques, such as Magnetic Resonance - Radio Therapy simulation. Unlike Hounsfield units used in CT, there is no simple relation between the MR image intensity and tissue density. For instance, using conventional MR sequences, cortical bone and air filled cavities both show no signal intensity whereas their densities are substantially different. Ultimately the ability to reliably identify additional tissue types in an MR image while the MR-acquisition time should be kept at a minimum would be beneficial.

SUMMARY

Embodiments of the invention may provide for a means of identifying different tissue types within a subject using magnetic resonance imaging. Embodiments may achieve this by using a pulse sequence which comprises commands to acquire free induction decay data and multiple gradient echoes. The free induction decay data is acquired on a timescale of several milliseconds. This enables the acquisition of free induction decay data from bone tissue. Data from multiple gradient echoes is also acquired. The commendation of acquiring the free induction decay data and the multiple gradient echo data allows a variety of images to be constructed: an in-phase image, a fat-such saturated image, a water-saturated image, and an ultra-short echo time image. Using a pulse sequence which may be used to reconstruct such different images may be beneficial because all of the image data necessary for radiation therapy planning and/or reconstructing images from radio-isotope imaging

systems is provided. Using such a pulse sequence may also be beneficial because it may reduce the time necessary to acquire the images.

An embodiment of the invention may provide for a pulse sequence for magnetic resonance imaging which combines the features of an ultra-short echo time (UTE) pulse sequence with a DIXON acquisition. For example the pulse sequence may be a UTE triple-echo (UTILE) MR-sequence combining the UTE and DIXON acquisition in a single acquisition. This example may be implemented using a pulse sequence that samples fast induced decay (FID) at short echo times, at time TE1, followed by two gradient echoes, at times TE2 and TE3. The echo times TE2 and TE3 may be optionally adjusted to where water and fat are almost opposed- and in-phase, respectively.

Cortical bone may be segmented from the calculated relative difference between the magnitude information of echo one (M1) and echo three (M3) by an empirically determined global threshold after masking out air areas, potentially by thresholding. Soft tissue and adipose tissue decomposition may be achieved by applying a three point Dixon signal modeling technique using the magnitude and the unwrapped phase information of all three echoes. This single acquisition may provide up to 5 sets of images:

1. images of bone
2. water-only images (i.e., fat-saturated images)
3. fat-only images (i.e., water-saturated images)
4. in-phase images
5. opposed-phase images

A 'computer-readable storage medium' as used herein encompasses any tangible storage medium which may store instructions which are executable by a processor of a computing device. The computer-readable storage medium may be referred to as a computer-readable non-transitory storage medium. The computer-readable storage medium may also be referred to as a tangible computer-readable medium. In some embodiments, a computer-readable storage medium may also be able to store data which is able to be accessed by the processor of the computing device. Examples of computer-readable storage media include, but are not limited to: a floppy disk, a magnetic hard disk drive, a solid state hard disk, flash memory, a USB thumb drive, Random Access Memory (RAM), Read Only Memory (ROM), an optical disk, a magneto-optical disk, and the register file of the processor. Examples of optical disks include Compact Disks (CD) and Digital Versatile Disks (DVD), for example CD-ROM, CD-RW, CD-R, DVD-ROM, DVD-RW, or DVD-R disks. The term computer readable-storage medium also refers to various types of recording

media capable of being accessed by the computer device via a network or communication link. For example a data may be retrieved over a modem, over the internet, or over a local area network. References to a computer-readable storage medium should be interpreted as possibly being multiple computer-readable storage mediums. Various executable components of a program or programs may be stored in different locations. The computer-readable storage medium may for instance be multiple computer-readable storage medium within the same computer system. The computer-readable storage medium may also be computer-readable storage medium distributed amongst multiple computer systems or computing devices.

‘Computer memory’ or ‘memory’ is an example of a computer-readable storage medium. Computer memory is any memory which is directly accessible to a processor. Examples of computer memory include, but are not limited to: RAM memory, registers, and register files. References to ‘computer memory’ or ‘memory’ should be interpreted as possibly being multiple memories. The memory may for instance be multiple memories within the same computer system. The memory may also be multiple memories distributed amongst multiple computer systems or computing devices.

‘Computer storage’ or ‘storage’ is an example of a computer-readable storage medium. Computer storage is any non-volatile computer-readable storage medium. Examples of computer storage include, but are not limited to: a hard disk drive, a USB thumb drive, a floppy drive, a smart card, a DVD, a CD-ROM, and a solid state hard drive. In some embodiments computer storage may also be computer memory or vice versa. References to ‘computer storage’ or ‘storage’ should be interpreted as possibly being multiple storage. The storage may for instance be multiple storage devices within the same computer system or computing device. The storage may also be multiple storages distributed amongst multiple computer systems or computing devices.

A ‘processor’ as used herein encompasses an electronic component which is able to execute a program or machine executable instruction. References to the computing device comprising “a processor” should be interpreted as possibly containing more than one processor or processing core. The processor may for instance be a multi-core processor. A processor may also refer to a collection of processors within a single computer system or distributed amongst multiple computer systems. The term computing device should also be interpreted to possibly refer to a collection or network of computing devices each comprising a processor or processors. Many programs have their instructions performed by multiple

processors that may be within the same computing device or which may even be distributed across multiple computing devices.

A 'user interface' as used herein is an interface which allows a user or operator to interact with a computer or computer system. A 'user interface' may also be referred to as a 'human interface device.' A user interface may provide information or data to the operator and/or receive information or data from the operator. A user interface may enable input from an operator to be received by the computer and may provide output to the user from the computer. In other words, the user interface may allow an operator to control or manipulate a computer and the interface may allow the computer indicate the effects of the operator's control or manipulation. The display of data or information on a display or a graphical user interface is an example of providing information to an operator. The receiving of data through a keyboard, mouse, trackball, touchpad, pointing stick, graphics tablet, joystick, gamepad, webcam, headset, gear sticks, steering wheel, pedals, wired glove, dance pad, remote control, and accelerometer are all examples of user interface components which enable the receiving of information or data from an operator.

A 'hardware interface' as used herein encompasses a interface which enables the processor of a computer system to interact with and/or control an external computing device and/or apparatus. A hardware interface may allow a processor to send control signals or instructions to an external computing device and/or apparatus. A hardware interface may also enable a processor to exchange data with an external computing device and/or apparatus. Examples of a hardware interface include, but are not limited to: a universal serial bus, IEEE 1394 port, parallel port, IEEE 1284 port, serial port, RS-232 port, IEEE-488 port, Bluetooth connection, Wireless local area network connection, TCP/IP connection, Ethernet connection, control voltage interface, MIDI interface, analog input interface, and digital input interface.

A 'display' or 'display device' as used herein encompasses an output device or a user interface adapted for displaying images or data. A display may output visual, audio, and or tactile data. Examples of a display include, but are not limited to: a computer monitor, a television screen, a touch screen, tactile electronic display, Braille screen, Cathode ray tube (CRT), Storage tube, Bistable display, Electronic paper, Vector display, Flat panel display, Vacuum fluorescent display (VF), Light-emitting diode (LED) displays, Electroluminescent display (ELD), Plasma display panels (PDP), Liquid crystal display (LCD), Organic light-emitting diode displays (OLED), a projector, and Head-mounted display.

Radio-isotope imaging data is defined herein as two or three dimensional data that has been acquired using a medical imaging scanner that is configured to detect the radioactive decay of radioisotopes. A radio-isotope imaging system is defined herein as an apparatus adapted for acquiring information about the physical structure of a patient and
5 construct sets of two dimensional or three dimensional medical image data by detecting radiation emitted by radioactive markers or traces within the patient. Radio-isotope imaging data can be used to construct visualizations which are useful for diagnosis by a physician. This visualization can be performed using a computer.

Magnetic Resonance (MR) data is defined herein as being the recorded
10 measurements of radio frequency signals emitted by atomic spins by the antenna of a Magnetic resonance apparatus during a magnetic resonance imaging scan. A Magnetic Resonance Imaging (MRI) image is defined herein as being the reconstructed two or three dimensional visualization of anatomic data contained within the magnetic resonance imaging data. This visualization can be performed using a computer.

15 In one aspect the invention provides for a medical apparatus comprising a magnetic resonance imaging system for acquiring magnetic resonance data from an imaging volume. The medical apparatus further comprises a processor for controlling the medical apparatus. The processor may be replaced by a controller or a control system. The medical apparatus further comprises a memory containing machine executable instructions and a
20 pulse sequence. The machine executable instructions may cause the processor to control the magnetic resonance imaging system. A pulse sequence as used herein is encompassed by a set of instructions or operations performed as a function of time which together may be used to control or to generate commands for controlling the magnetic resonance imaging system to acquire the magnetic resonance data. The pulse sequence may be in a machine executable
25 form or it may be in a graphical form which is adapted for manipulation or change by a human operator on a graphical user interface. If in graphical form the pulse sequence may be converted into a machine executable form by a suitable program or program module.

The magnetic resonance data acquired using the pulse sequence comprises free induction decay data and multiple gradient echo data. Free induction decay data as used
30 herein encompasses a measurement of the free induction decay curve measured during the acquisition of the magnetic resonance data. The free induction decay data may for instance be free induction decay which decays in a characteristic time constant T_2 or T_2^* . An echo signal is a signal which is generated from a free induction decay using a bipolar switched magnetic gradient. There is an echo which is produced when the magnetic field gradient is reversed.

Gradient echo data as used herein encompasses the measurement recording of such an echo signal. Multiple gradient echo data as used herein encompasses the recording of multiple echo signals.

Execution of the instructions causes the processor to acquire the magnetic resonance data using the magnetic resonance imaging system in accordance with the pulse sequence. This is to say that the pulse sequence commands or control sequences were used to control the magnetic resonance imaging system to acquire the magnetic resonance data. Execution of the instructions cause the processor to reconstruct an in-phase image, a fat-saturated image, a water-saturated image, and an ultra-short echo time image from the magnetic resonance data. The ultra-short echo time image comprises bone image data. An in-phase image as used herein encompasses an image reconstructed from magnetic resonance data that comprises the T1 and regular proton weighted image.

A fat-saturated image as used herein encompasses an image where the fat protons were saturated prior to image acquisition so that only a small nuclear magnetic resonance signal results from the fat protons. A fat-saturated image is typically used to show the concentration or location of water protons with the fat protons removed. Likewise a water-saturated image as used herein encompasses an image reconstructed from magnetic resonance data where water protons were saturated prior to the acquisition of data such that the water protons or hydrogen protons produces a small nuclear magnetic resonance signal. A water-saturated image is typically used for showing the location of fat or adipose tissue. An ultra-short echo time image as used herein encompasses an image reconstructed from a free induction decay data where the free induction decay occurred on an extremely short timescale. The free induction decay may have a time constant on the order of several milliseconds. The ultra-short echo time enables the imaging of tissue with extremely small free induction decay values such as tendons or bone. Bone image data as used herein encompasses magnetic resonance data which contains free induction decay data which is descriptive of the position and location of bone within the subject.

This embodiment may have the advantage that the in-phase image, the fat-saturated image, the water-saturated image, and the ultra-short echo time image were acquired using a single pulse sequence. This may mean that all of these images have the same positional relationship and are able to be used for more accurately reconstructing the geometric structure or internal anatomy of a subject. Further since all these images are acquired at the same time the acquisition time is reduced.

The reconstruction of the in-phase image, the fat-saturated image, the water-saturated image and the ultra-short echo time image may for instance be reconstructed using a Dixon method. For instance the images may be reconstructed using a two-point Dixon method.

5 In another embodiment execution of the instructions further cause the processor to construct a medullary bone image from the water-saturated image. In some embodiments fat that is imaged in the water-saturated image may be removed from the medullary bone image by a suitable anatomical model. For instance a deformable shape model may be fit to the medullary bone identified in the medullary bone image and used to
10 remove fat or adipose tissue. Execution of the instructions further causes the processor to construct a cortical bone image by subtracting the in-phase image from the ultra-short echo time image. Medullary bone as used herein refers to an image showing the location of medullary bone. Medullary bone is synonymous with trabecular or cancellous bone. Cortical bone is the hard outer layer of a bone and may also be referred to as compact bone tissue.
15 Execution of the instructions further causes the processor to construct a complete bone image by adding the medullary bone image to the cortical bone image. This embodiment of the invention may have the advantage that the magnetic resonance imaging system was used for constructing an image of the bone tissue within a subject. This may be used for studying the bone tissue or it may be used in therapy planning.

20 In another embodiment execution of the instructions cause the processor to calculate a spatially dependent radiation attenuation coefficient using the complete bone image, the fat-saturated image, the in-phase image, and the ultra-short echo time image. For instance the ultra-short echo time image may be used to identify the location of bone and air pockets, for instance the ultra-short echo time phase may be used to identify the location of
25 air pockets such as the sinuses of a subject. The complete bone image may contain information about varying bone density. The cortical and medullary bone have different densities. Using the information about the varying bone density in the calculation of the spatially dependent radiation attenuation coefficient may allow the spatially dependent radiation attenuation coefficient to be determined more accurately.

30 This embodiment may also have the advantage that the various types of images which are acquired or constructed may be used to accurately calculate a spatially dependent radiation attenuation coefficient. The spatially dependent radiation attenuation coefficient may for instance be used for either radiation therapy planning or in diagnostic radiology where the absorption of radiation needs to be accurately predicted for imaging such

as positron emission tomography. These images allow the identification of different types of tissues or regions within the body. This anatomical information may be used to accurately model the absorption of radiation by different portions of the subject. In particular the in-phase image may be used for fitting segmentation models to the images. This may be extremely beneficial in further refining the calculation of the spatially dependent radiation attenuation coefficient.

In another embodiment the ultra-short echo time image is used for differentiating bone and air. The in-phase image is used for image segmentation. The fat-saturated image is also used for image segmentation.

Execution of the instructions further causes the processor to display the fat-saturated image, the in-phase image, the complete bone image, and the ultra-short echo time image on a graphical user interface. Execution of the instructions further causes the processor to receive radiation therapy planning data from the graphical user interface. In some embodiments the spatially dependent radiation coefficient is used along with input from the graphical user interface to calculate the radiation therapy planning data. This embodiment may be particularly beneficial because the data necessary for an operator or a physician to plan a radiation session or therapy is displayed on the graphical user interface. The user or operator may study the images and then use a mouse or other human input device to manipulate shapes and controls on the graphical user interface. The user's entry may then be translated into the radiation therapy planning data. This embodiment may be particularly beneficial because the data necessary for performing the radiation therapy has been presented and acquired all at the same time. This may result in an increase in the speed in which radiation therapy planning can be performed.

In another embodiment execution of the instructions further causes the processor to generate radiation therapy planning data using the fat-saturated image, the in-phase image, and the ultra-short echo time image, the complete bone image, the spatially dependent radiation coefficient, and a treatment plan using a radiation therapy planning program module. A treatment plan as used herein encompasses a data file descriptive of a plan for performing a radiation therapy. For instance the treatment plan may contain anatomical data descriptive of the patient or subject in conjunction with regions of the subject to be treated. The radiation therapy planning program module may contain executable code which is able to interpret the treatment plan and register it to at least one of the fat-saturated image, the in-phase image, and the ultra-short echo time image. This embodiment may have

the advantage that the medical apparatus is able to acquire the magnetic resonance data and then proceed with planning and executing a radiation therapy on the patient or subject.

In another embodiment the medical apparatus further comprises a radiation therapy system. Execution of the instructions further causes the processor to generate radiation therapy control commands using the radiation therapy planning data. Execution of the instructions further causes the processor to treat the subject with the radiation therapy system by executing the radiation therapy control commands. The radiation therapy control commands as used herein encompass machine executable commands which control a radiation therapy system.

In another embodiment the radiation therapy system is a linear accelerator.

In another embodiment the radiation therapy system is a gamma knife.

In another embodiment the radiation therapy system is a charged particle therapy system. A charged particle therapy system as used herein is a system which is adapted for shooting charged particles such as charged nuclei or molecules at a target region of the subject. For example carbon nuclei or protons may be directed at a target zone of the subject.

In another embodiment the radiation therapy system is a proton therapy system. A proton therapy system as used herein is a therapy system which is adapted for shooting proton such as hydrogen nuclei at a target zone of the subject.

In another embodiment the radiation therapy system is an x-ray therapy system. An x-ray therapy system as used herein encompasses a system for directing x-rays in a target zone of a subject for performing radiation therapy.

In another embodiment the radiation therapy system is an external beam radiation system. An external beam radiation system as used herein encompasses a radiation therapy system for directing an external radiation beam at a target zone of a subject.

In another embodiment the radiation therapy system is a brachytherapy system.

In another embodiment execution of the instructions further causes the processor to receive radio-isotope imaging data. Radio-isotope imaging data as used herein encompasses data generated by the detection of radioactive decay of an isotope. The radio-isotope imaging data is generated in diagnostic imaging of a subject or patient.

Execution of the instructions further causes the processor to calculate a medical image using the radio-isotope image data and the spatially dependent radiation attenuation coefficient. The radio-isotope imaging data is generated by recording the detected

radio-isotope decays within a subject. Knowing the spatially dependent radiation attenuation coefficient allows a more accurate determination of the location of the radio-isotope. The attenuation of the detected radiation can be better predicted by using knowledge of how this radiation is attenuated within the subject.

5 In another embodiment the medical apparatus further comprises a radio-isotope imaging system for acquiring the radio-isotope imaging data.

In another embodiment execution of the instructions further causes the processor to acquire the radio-isotope imaging data using the radio-isotope imaging system.

10 In another embodiment the radio-isotope imaging system is a positron emission tomography system.

In another embodiment the radio-isotope imaging system is a single photon emission computer tomography system.

15 In another embodiment execution of the instructions further causes the processor to reconstruct an opposed phase image from the magnetic resonance data. An opposed phase image as used herein encompasses an image with a signal from two distinct components such as fat and water signals are 180 degrees out of phase which causes the destructive interference of the nuclear magnetic resonance signal within a particular voxel. This embodiment may be beneficial when performing radiation therapy planning on particular types of tissue. For instance it may be beneficial in identifying lesions in the liver
20 or the adrenal glands. It may also be beneficial for identifying the various pathological regions in the brain. The opposed phase image may for instance be displayed on the graphical user interface during the radiation therapy planning or it may for instance be used as an input for the radiation therapy planning program module.

25 In another embodiment execution of the instructions further causes the processor to reconstruct multiple echo images. An echo image is an image reconstructed from the recorded magnetic resonance data of a gradient echo. Multiple echo images are multiple images each reconstructed from the magnetic resonance data of multiple gradient echoes. the in-phase image, the fat-saturated image, the water-saturated image, and the ultra-short echo time image are constructed from the magnetic resonance data using a Dixon signal model.
30 For instance the Dixon signal model may be a two-point Dixon signal model, a three-point Dixon signal model, or a four-point Dixon signal model. This embodiment may be advantageous because this provides for an effective and accurate means of constructing these images. The three-point Dixon signal model may be used in some embodiments to

reconstruct the opposed phase image from the magnetic resonance data at the same time that the other images are also reconstructed.

In another aspect the invention provides for a method of operating a medical apparatus. The medical apparatus comprises a magnetic resonance imaging system for acquiring magnetic resonance data from an imaging volume. The method comprises the step of acquiring the magnetic resonance data using the magnetic resonance imaging system. The magnetic resonance data acquired comprises free induction decay data and multiple gradient echo data. The method further comprises the step of reconstructing an in-phase image, a fat-saturated image, a water-saturated image and an ultra-short echo time image from the magnetic resonance data. The ultra-short echo time image comprises bone image data.

In another embodiment the method further comprises the step of constructing a medullary bone image from the water-saturated image. The method further comprises the step of constructing a cortical bone image by subtracting the in-phase image from the ultra-short echo time image. The method further comprises the step of constructing a complete bone image by adding the medullary bone image to the cortical bone image.

In another embodiment the method further comprises the step of calculating a spatially dependent radiation attenuation coefficient using the complete bone image, the fat-saturated image, the in-phase image, and the ultra-short echo time image.

In another embodiment the ultra-short echo time image is used for differentiating bone and air. The in-phase image is used for image segmentation. The fat-saturated image is also used for image segmentation.

In another aspect the invention provides for a tangible computer-readable storage medium containing machine readable instructions for execution by a processor controlling a medical apparatus. The medical apparatus comprises a magnetic resonance imaging system for acquiring magnetic resonance data from an imaging volume. The computer-readable storage medium further contains a pulse sequence for controlling the magnetic resonance imaging system. The magnetic resonance data acquired using the pulse sequence comprises free induction decay data and multiple gradient echo data. Execution of the instructions causes the processor to acquire the magnetic resonance data using the magnetic resonance imaging system. Execution of the instructions further causes the processor to reconstruct an in-phase image, a fat-saturated image, a water-saturated image and an ultra-short echo time image from the magnetic resonance data. The ultra-short echo time image comprises bone image data.

In another embodiment execution of the instructions further causes the processor to construct a medullary bone image from the water-saturated image. Execution of the instructions further causes the processor to construct a cortical bone image by subtracting the in-phase image from the ultra-short echo time image. Execution of the instructions further causes the processor to construct a complete bone image by adding the medullary bone image to the cortical bone image.

In another aspect the invention provides for a controller for a medical apparatus. A controller as used herein encompasses an electronic apparatus adapted for controlling other systems or apparatuses. Since a processor or microcontroller are two non-limiting examples of a controller. The medical apparatus comprises a magnetic resonance imaging system for acquiring magnetic resonance data from an imaging volume. The controller is arranged to acquire the magnetic resonance data using the magnetic resonance imaging system. The controller is arranged to use a pulse sequence to control the operation of the magnetic resonance imaging system during acquisition of the magnetic resonance data. The magnetic resonance data acquired using the pulse sequence comprises free induction decay data and multiple gradient echo data. The controller is further arranged to reconstruct an in-phase image, a fat-saturated image, a water-saturated image, and an ultra-short echo time image from the magnetic resonance data. The ultra-short echo time image comprises bone image data.

In another embodiment the controller is further arranged to construct a medullary bone image from the water-saturated image. The controller is further arranged to construct a cortical bone image by subtracting the in-phase image from the ultra-short echo time image. The controller is further arranged to construct a complete bone image by adding the medullary bone image to the cortical bone image.

BRIEF DESCRIPTION OF THE DRAWINGS

In the following preferred embodiments of the invention will be described, by way of example only, and with reference to the drawings in which:

Fig. 1 shows flow chart which illustrates a method according to an embodiment of the invention,

Fig. 2 shows flow chart which illustrates a method according to a further embodiment of the invention,

Fig. 3 illustrates a pulse sequence according to an embodiment of the invention in the form of a timing diagram,

Fig. 4 shows a cortical bone image,

Fig. 5 shows a medullary bone image,

Fig. 6 shows a complete bone image,

Fig. 7 shows a fat-saturated image,

5 Fig. 8 shows an in-phase image,

Fig. 9 shows the ultra-short echo time phase image,

Fig. 10 shows a block diagram which illustrates a medical apparatus according to an embodiment of the invention,

10 Fig. 11 shows a block diagram which illustrates a medical apparatus according to a further embodiment of the invention, and

Fig. 12 shows a block diagram which illustrates a medical apparatus according to a further embodiment of the invention.

Fig. 13 shows images for four subjects which include Digital Reconstructed Radiographs (DRRs).

15

DETAILED DESCRIPTION

Like numbered elements in these figures are either equivalent elements or perform the same function. Elements which have been discussed previously will not necessarily be discussed in later figures if the function is equivalent.

20 Fig. 1 shows a flow diagram which illustrates a method according to an embodiment of the invention. In step 100 magnetic resonance data is acquired using an MRI system and a pulse sequence. The pulse sequence may for instance be a pulse sequence as is demonstrated in Fig. 3. Next in step 102 an in-phase image, a fat-saturated image, a water-saturated image, and an ultra-short echo time image may be reconstructed from the magnetic resonance data.

25 The ultra-short echo time image comprises bone image data.

Fig. 2 shows a block diagram which illustrates a further embodiment of the method. In step 200 magnetic resonance data is acquired using the MRI system and a pulse sequence. In step 202 an in-phase image, a fat-saturated image, a water-saturated image, and an ultra-short echo time image are reconstructed from the magnetic resonance imaging data.

30 The ultra-short echo time image comprises bone image data. A bone image data is image data which is descriptive of the anatomy of bone tissue within a patient or a subject. In step 204 a medullary bone image is constructed from the water-saturated image. In some embodiments this step may consist of removing information from the image using a model, for instance removing adipose tissue from the image. Next in step 206 a cortical bone image is

constructed by subtracting the in-phase image from the ultra-short echo time image. Next in step 208 a complete bone image is constructed by adding the medullary bone image to the cortical bone image. Finally in step 210 a spatially dependent radiation attenuation coefficient is calculated. In step 210 this may include using the complete bone image, the fat-saturated image, the in-phase image, and/or the ultra-short echo time image.

Fig. 3 illustrates a pulse sequence 300 in the form of a timing diagram. In this pulse sequence 300 there are four timelines, there is timeline 302 which illustrates when radio frequency energy is applied. Timeline 304 illustrates the readout gradient. Timeline 306 illustrates a gate for data acquisition. Timeline 308 illustrates the nuclear magnetic resonance signal. On timeline 302 a radio frequency pulse 310 is applied during time Trf. On timeline 308 a free induction decay 314, a first gradient echo 316 and a second gradient echo 318 are shown. On timeline 308 there are three gradient pulses. Timeline 304 shows when a first gradient pulse 320, a second gradient pulse 322, and a third gradient pulse 324 are applied. The first gradient pulse 320 is applied during the free induction decay 314. The second gradient pulse 322 causes the first gradient echo 316. The third gradient pulse 324 causes the second gradient echo 318. The characteristic time rate at which the free induction decay 314 decays such as the T1, the T2, or T2* time constant is indicated as TE1 326. The first gradient echo 316 has a maximum at TE2 328. The second gradient echo 318 has a maximum at TE3 330.

Timeline 306 shows when magnetic resonance data is acquired. The free induction decay data is acquired during time interval Taq1 332. The first gradient echo data is acquired during time interval 334. The second gradient echo data is acquired during time interval 336. The pulse sequence illustrated in Fig. 3 is representative. Changes in the pulse sequence may be made. For instance the time when the free induction decay data is acquired may be delayed until the time marked 338.

In the example shown in Fig. 3, the echo times are chosen such that the echo times are acquired at in-phase and opposed-phase times. However, they do not need to be in-phase or opposed-phase echo times. An appropriate Dixon model may be used such that the gradient echoes may be acquired at non-specific echo time. For instance, various Dixon models will work for 2, 3, or 4 non-specific echo times.

Fig. 4 shows an example of a cortical bone image 400. In this image 400 cortical bone 402 is shown. The cortical bone image 400 was constructed by subtracting the in-phase image from the ultra-short echo time image.

Fig. 5 shows a medullary bone image. Medullary bone 502 is clearly shown in the medullary bone image 500.

Fig. 6 shows a complete bone image 600 that was constructed by adding images 400 and 500. In region 602 cortical plus medullary bone is shown.

5 Fig. 7 shows a fat-saturated image 700.

Fig. 8 shows an in-phase image 800.

Fig. 9 shows the ultra-short echo time image 900 for phase. An air cavity 902 is visible in this image.

Fig. 10 shows a block diagram which illustrates a medical apparatus 1000
10 according to an embodiment of the invention. The medical apparatus 1000 comprises a magnetic resonance imaging system 1002. The magnetic resonance imaging system 1002 is shown as comprising a magnet 1004. The magnet 1004 shown in Fig. 10 is a cylindrical type superconducting magnet. The magnet 1004 has a liquid helium cooled cryostat with superconducting coils. It is also possible to use permanent or resistive magnets. The use of
15 different types of magnets is also possible for instance it is also possible to use both a split cylindrical magnet and a so called open magnet. A split cylindrical magnet is similar to a standard cylindrical magnet, except that the cryostat has been split into two sections to allow access to the iso-plane of the magnet, such magnets may for instance be used in conjunction with charged particle beam therapy. An open magnet has two magnet sections, one above the
20 other with a space in-between that is large enough to receive a subject: the arrangement of the two sections area similar to that of a Helmholtz coil. Open magnets are popular, because the subject is less confined. Inside the cryostat of the cylindrical magnet there is a collection of superconducting coils. Within the bore 1006 of the cylindrical magnet 1004 there is an imaging zone 1008 where the magnetic field is strong and uniform enough to perform
25 magnetic resonance imaging.

Within the bore 1006 of the magnet 1004 there is also a magnetic field gradient coil 1010 which is used for acquisition of magnetic resonance data to spatially encode magnetic spins within the imaging zone 1008 of the magnet 1004. The magnetic field gradient coil 1010 is connected to a magnetic field gradient coil power supply 1012. The
30 magnetic field gradient coil 1010 is intended to be representative. Typically magnetic field gradient coils 1010 contain three separate sets of coils for spatially encoding in three orthogonal spatial directions. A magnetic field gradient power supply supplies current to the magnetic field gradient coils. The current supplied to the magnetic field coils is controlled as a function of time and may be ramped or pulsed.

Adjacent to the imaging zone 1008 is a radio frequency coil 1014 for manipulating the orientations of magnetic spins within the imaging zone 1008 and for receiving radio transmissions from spins also within the imaging zone 1008. The radio frequency coil may contain multiple coil elements. The radio frequency coil or each of any multiple coil elements may also be referred to as a channel. The radio frequency coil may also be referred to as an antenna. The radio frequency coil 1014 is connected to a radio frequency transceiver 1016. The radio frequency coil 1014 and radio frequency transceiver 1016 may be replaced by separate transmit and receive coils and a separate transmitter and receiver. It is understood that the radio frequency coil 1014 and the radio frequency transceiver 1016 are representative. The radio frequency coil 1014 is intended to also represent a dedicated transmit antenna and a dedicated receive antenna. Likewise the transceiver 1016 may also represent a separate transmitter and receivers.

The transceiver 1016 and the magnetic field gradient coil power supply 1012 are connected to a hardware interface 1024 of a computer system 1022. The computer system 1022 further comprises a processor 1026. The processor is connected to the hardware interface 1024 which enables the processor 1026 to control the operation and function of the medical apparatus 1000. The processor 1026 is further connected to user interface 1028. The processor 1026 is also connected to computer storage 1030 and computer memory 1032.

The computer storage 1030 is shown as containing a pulse sequence 1034. The pulse sequence 1034 may be used for controlling the magnetic resonance imaging system 1002. The computer storage 1030 is shown as further containing magnetic resonance data 1036 that was acquired from the magnetic resonance imaging system 1002 using the pulse sequence 1034. The computer storage 1030 is further shown as containing an in-phase image 1038, a fat-saturated image 1040, a water-saturated image 1042 and an ultra-short echo time image 1044 that was reconstructed from the magnetic resonance data 1036. The computer storage 1030 is also shown as containing an opposed phase image 1046 that was reconstructed from the magnetic resonance data 1036. The opposed phase image 1046 is not calculated or reconstructed in all embodiments.

The computer storage 1030 is further shown as containing a medullary bone image reconstructed from the water-saturated image 1042. The computer storage 1030 is further shown as containing a cortical bone image 1050 reconstructed by subtracting the in-phase image 1038 from the ultra-short echo time image 1044. The computer storage 1030 is shown as further containing a complete bone image 1052 which is constructed by adding the medullary bone image 1048 to the cortical bone image 1050. The computer storage 1030 is

shown as containing a spatially dependent radiation attenuation coefficient 1054 which is not present in all embodiments. The computer storage 1030 is further shown as containing a radiation therapy planning data 1056. The radiation therapy planning data 1056 is optional and is not present in all embodiments. The computer storage 1030 is further shown as
5 containing a treatment plan 1058 which is optional also.

The computer memory 1032 contains computer executable instructions for controlling the operation and functioning of the medical apparatus 1000. The computer memory 1032 is shown as containing a control module 1060. The control module 1060 contains computer executable code which allows the processor 1026 to control the operation
10 and function of the medical apparatus 1000. The computer storage 1032 is further shown as containing an image reconstruction module 1062. The image reconstruction module 1062 contains computer executable code for reconstructing the images 1038, 1040, 1042, 1044, 1046 contained within the computer storage 1030. The computer memory 1032 further contains an image manipulation module 1064 which allows the processor 1026 to manipulate
15 such as adding and subtracting images.

The computer memory 1032 is shown as optionally containing a three-point Dixon signal model which may be used by the image reconstruction module 1062. The computer memory 1032 is further shown as containing an image segmentation module 1068. In some embodiments the image segmentation module may be used to segment any of the
20 images contained within the computer storage 1030. The computer memory 1032 is further shown as containing the radiation attenuation coefficient calculation module 1070. The radiation attenuation coefficient calculation module 1070 may in some embodiments be used to calculate the spatially dependent radiation attenuation coefficient 1054 from the complete bone image 1052, the fat-saturated image 1040, the in-phase image 1038, and the ultra-short
25 echo time image 1044.

In some embodiments there may be a radiation therapy planning data generation module 1072 present in the computer memory 1032. The radiation therapy planning generation module 1072 is adapted for automatically generating the radiation therapy planning data 1056 using the treatment plan 1058 and the spatially dependent
30 radiation attenuation coefficient 1054. Some embodiments may also have a graphical user interface control module 1074 present in the computer memory 1032 for controlling the operation and function of a graphical user interface 1076. The optional graphical user interface 1076 is shown as displaying a complete bone image 600, a fat-saturated image 700, an in-phase image 800, and an ultra-short echo time image 900. The graphical user interface

1076 further contains a radiation therapy planning interface 1078 where an operator or physician may enter radiation therapy planning data 1056.

Fig. 11 shows an embodiment similar to that shown in Fig. 10. The medical apparatus shown in Fig. 11 includes a radiation therapy system 1122. The magnet 1004 is a superconducting magnet and includes a cryostat 1124 with several superconducting coils 1126. There is also a compensation coil 1128 which creates an area of reduced magnetic field 1130 which surrounds the magnet 1004. The radiation therapy system 1122 in this embodiment is intended to be representative of radiation therapy systems in general. The components shown here are typical for LINAC and x-ray therapy systems. However with minor modifications such as using a split magnet charged particles or beta particle radiation therapy systems can also be illustrated using this diagram. There is a gantry 1132 which is used to rotate a radiotherapy source 1134 about the magnet 1004. The gantry 1132 is rotated about the axis of rotation 1133 by a rotation actuator 1135. There is a radiation therapy source 1134 which is rotated by the gantry 1132. The radiotherapy source 1134 generates a radiation beam 1138 which passes through collimator 1136. In the Fig. a target zone labeled 1142 which is irradiated by the radiation beam 1138 is shown. As the radiation source 1134 rotates about the axis of rotation 1133 the target zone 1142 is irradiated. There is also a support positioning system 1140 for positioning the support 1020 to optimize the location of the target zone 1142 relative to the radiation therapy system 1122.

The hardware interface 1024 is shown as being connected to the transceiver 1016, the power supply 1012, the rotation actuator 1135, and the support positioning system 1140. The hardware interface 1024 allows the processor 1026 to send and receive control signals to all of these components 1012, 1016, 1135, 1140.

The computer storage 1030 is shown as containing radiation therapy control commands 1150. The radiation therapy control commands 1150 comprise instructions that when executed by the radiation therapy system 1122 cause the radiation therapy system 1122 to treat the target zone 1142. The computer memory 1032 is shown as containing a radiation therapy control command generation module 1152. The radiation therapy control command generation module 1152 contains instructions which allow the processor 1026 to generate the radiation therapy control commands 1150 from the radiation therapy planning data 1056.

Fig. 12 illustrates a medical apparatus 1200 similar to that shown in Fig. 10. In this embodiment a radio isotope imaging system 1202 has been integrated into the medical apparatus 1200. The radio-isotope imaging system 1202 comprises a scintillator ring 1204 adapted for detecting ionizing radiation. The individual scintillators which make up the

scintillator ring may be connected to a set of light pipes 1206 or fiber optics which are led out of the magnet 1004 to a series of light detectors 1208. Within the subject 1018 is shown a concentration of radio-isotope 1210. Ionizing radiation is emitted 1212 and is absorbed in the scintillator ring 1204. Within the computer storage 1030 is shown the radio-isotope imaging data 1220. The radio-isotope imaging data 1220 is the recorded data acquired by the light detectors 1208. The computer storage 1030 is further shown as containing a medical image 1222. The medical image is an image, reconstruction, or rendering of the radio-isotope imaging data which is descriptive of the location of radio-isotope 1210 within the subject.

The medical image 1222 was reconstructed from the radio-isotope imaging data 1220. The radio-isotope imaging system 1202 may for instance be a positron emission tomography system or a single photon emission computer tomography system. The computer memory 1032 is shown as containing a medical image reconstruction module 1230. The medical image reconstruction module 1230 contains computer executable code which the processor 1026 may use to reconstruct the medical image 1222 from the radio-isotope imaging data 1220. The computers 1022 shown in the embodiments of Figs. 10, 11, and 12 are equivalent as is the software and data stored within the computer memory 1032 and computer storage 1030 respectively.

Fig. 13 shows images for four subjects. Each row includes images for one subject generated by the single imaging sequence. The columns of images from left to right include bone-enhanced images **400**, water-only images **700**, in-phase images **800**, opposed-phase images **1046**, fat-only images **500**, and digital reconstructed radiographs (DRRs) **1240**. The bone enhanced images **400** contrast cortical bone corresponding to Fig. 4 and are constructed by subtracting the in-phase image **800** from the ultra-short echo time image corresponding to Fig. 9. The difference between the images of Fig. 4 and the column of bone enhanced images includes a weighting of the in-phase image which reduces the presence of the brain. The water-only images **700** are T1w images with fat-saturation corresponding to Fig. 7. The in-phase images **800** correspond to Fig. 8. The fat-only images **500** correspond to Fig. 5 and include medullary bone. The last column includes the DRRs **1240**. The DRR is constructed as a 2-dimensional projection of the 3-dimensional volume of the bone-enhance image **400**. Alternatively, the DRR is constructed as a 2-dimensional projection of the weighted in-phase image subtracted from the ultra-short echo time image. The projections are shown as sagittal perspectives. The DRRs are of sufficient quality to be used in 2-dimensional patient matching. Patient matching is used to position the subject **1018** in

radiation therapy. Adjustments to the subject **1018** position are done by the support positioning system **1140**. The DRR images can replace conventional CT images.

In another embodiment, the bone enhanced image or cortical bone image are used to register the images with other images including other imaging modalities such as PET, SPECT, CT, etc. The images generated from the pulse sequence **300** are inherently registered. The bone-enhanced images provide both registration and density information for attenuation. Furthermore, the generated MR images from the pulse sequence include soft-tissue images which further enhance attenuation.

While the invention has been illustrated and described in detail in the drawings and foregoing description, such illustration and description are to be considered illustrative or exemplary and not restrictive; the invention is not limited to the disclosed embodiments.

Other variations to the disclosed embodiments can be understood and effected by those skilled in the art in practicing the claimed invention, from a study of the drawings, the disclosure, and the appended claims. In the claims, the word "comprising" does not exclude other elements or steps, and the indefinite article "a" or "an" does not exclude a plurality. A single processor or other unit may fulfill the functions of several items recited in the claims. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage. A computer program may be stored/distributed on a suitable medium, such as an optical storage medium or a solid-state medium supplied together with or as part of other hardware, but may also be distributed in other forms, such as via the Internet or other wired or wireless telecommunication systems. Any reference signs in the claims should not be construed as limiting the scope.

LIST OF REFERENCE NUMERALS

	300	pulse sequence
	302	RF
	304	read out gradient
5	306	data acquisition gate
	308	nuclear magnetic resonance signal
	310	radio frequency pulse
	312	time T_{RF}
	314	free induction decay
10	316	first gradient echo
	318	second gradient echo
	320	first gradient pulse
	322	second gradient pulse
	324	third gradient pulse
15	326	TE_1
	328	TE_2
	330	TE_3
	332	TAQ1
	334	TAQ2
20	336	TAQ3
	400	cortical bone image
	402	cortical bone
	500	medullary bone image
	502	medullary bone
25	600	complete bone image
	602	cortical plus medullary bone
	700	fat-saturated image
	800	in-phase image
	900	ultra-short echo time image (phase)
30	902	air
	1000	medical apparatus
	1002	magnetic resonance imaging system
	1004	magnet
	1006	bore of magnet

	1008	imaging zone
	1010	magnetic field gradient coil
	1012	magnetic field gradient coil power supply
	1014	radio frequency coil
5	1016	transceiver
	1018	subject
	1020	subject support
	1022	computer
	1024	hardware interface
10	1026	processor
	1028	user interface
	1030	computer storage
	1032	computer memory
	1034	pulse sequence
15	1036	magnetic resonance data
	1038	in-phase image
	1040	fat-saturated image
	1042	water-saturated image
	1044	ultra-short echo time image
20	1046	opposed phase image
	1048	medullary bone image
	1050	cortical bone image
	1052	complete bone image
	1054	spatially dependent radiation attenuation coefficient
25	1056	radiation therapy planning data
	1058	treatment plan
	1060	control module
	1062	image reconstruction module
	1064	image manipulation module
30	1066	three-point Dixon signal model
	1068	image segmentation module
	1070	radiation attenuation coefficient calculation module
	1072	radiation therapy planning data generation module
	1074	graphical user interface control module

	1076	graphical user interface
	1078	radiation therapy planning interface
	1122	radiation therapy system
	1124	cryostat
5	1126	superconducting coil
	1128	compensation coil
	1130	reduced magnetic field region
	1132	gantry
	1133	axis of rotation
10	1134	radiotherapy source
	1135	rotational actuator
	1138	radiation beam
	1140	support positioning system
	1142	target zone
15	1150	radiation therapy control commands
	1152	radiation therapy control command generation module
	1200	medical apparatus
	1202	radio-isotope imaging system
	1204	scintillator ring
20	1206	light pipes
	1208	light detectors
	1210	concentration of radio isotope
	1212	radiation
	1220	radio-isotope imaging data
25	1222	medical image
	1230	medical image reconstruction module
	1240	digital reconstructed radiograph (DRR)

CLAIMS:

1. A medical apparatus comprising:

a magnetic resonance imaging system which acquires magnetic resonance data from an imaging volume;

a processor for controlling the medical apparatus; and

5 a memory containing machine executable instructions and a pulse sequence, wherein the magnetic resonance data acquired using the pulse sequence comprises free induction decay data and multiple gradient echo data, wherein execution of the instructions causes the processor to:

10 acquire the magnetic resonance data using the magnetic resonance imaging system in accordance with the pulse sequence; and

reconstruct an in-phase image, a fat-saturated image, a water-saturated image, and an ultra-short echo time image from the magnetic resonance data, wherein the ultra-short echo time image comprises bone image data.

15 2. The medical apparatus of claim 1, wherein execution of the instructions further causes the processor to:

construct a medullary bone image from the water-saturated image;

20 construct a cortical bone image by subtracting the in-phase image from the ultra-short echo time image; and

construct a complete bone image by adding the medullary bone image to the cortical bone image.

25 3. The medical apparatus of claim 2, wherein execution of the instructions causes the processor to calculate a spatially dependent radiation attenuation coefficient using the complete bone image, the fat-saturated image, the in-phase image, and the ultra-short echo time image.

4. The medical apparatus of claim 3, wherein the ultra-short echo time image is used for differentiating bone and air, wherein the in-phase image is used for image segmentation, and wherein the fat saturated image is used for image segmentation.

5 5. The medical apparatus of claim 3, wherein further execution of the instructions causes the processor to:

display the fat-saturated image, the in-phase image, the complete bone image and the ultra-short echo time image on a graphical user interface; and

receive radiation therapy planning data from the graphical user interface.

10

6. The medical apparatus of claim 3, wherein execution of the instructions further causes the processor to generate radiation therapy planning data using the fat-saturated image, the in-phase image, the ultra-short echo time image, the complete bone image, the spatially dependent radiation attenuation coefficient, and a treatment plan with a radiation therapy
15 planning program module.

7. The medical apparatus of claim 6, wherein the medical apparatus further comprises a radiation therapy system, wherein the execution of the instructions further causes the processor to:

20 generate radiation therapy control commands using the radiation therapy planning data; and

treat the subject with the radiation therapy system by executing the radiation therapy control commands.

25 8. The medical apparatus of claim 7, wherein the radiation therapy system is any one of the following: a linear accelerator, a gamma knife, a charged particle therapy system, a proton therapy system, an x-ray therapy system, external beam radiation system, and a brachytherapy system.

30 9. The medical apparatus of claim 3, wherein execution of the instructions further causes the processor to:

receive radio-isotope imaging data, and

calculate a medical image using the radio-isotope image data and the spatially dependent radiation attenuation coefficient.

10. The medical apparatus of claim 9, wherein the medical apparatus further comprises a radio-isotope imaging system for acquiring the radio-isotope imaging data, wherein the radio-isotope imaging system is any one of the following: a positron emission tomography system and a single photon emission computed tomography system, and wherein execution of the instructions further causes the processor to acquire the radio-isotope imaging data using the radio-isotope imaging system.

11. The medical apparatus of claim 1, wherein execution of the instructions further causes the processor to reconstruct an opposed phase image from the magnetic resonance data.

12. The medical apparatus of claim 1, wherein execution of the instructions further causes the processor to reconstruct multiple echo images, wherein the in-phase image, the fat-saturated image, the water-saturated image, and the ultra-short echo time image are reconstructed from the multiple echo images using a Dixon signal model.

13. The medical apparatus of claim 2, wherein execution of the instructions further causes the processor to construct a digital reconstructed radiograph image based on the cortical bone image.

14. The medical apparatus of claim 13, wherein the digital reconstructed radiograph image is used for 2-dimensional patient matching with a support positioning system.

15. A method of operating a medical apparatus, wherein the medical apparatus comprises a magnetic resonance imaging system for acquiring magnetic resonance data from an imaging volume, wherein the method comprises the steps of:

acquiring the magnetic resonance data using the magnetic resonance imaging system, wherein the magnetic resonance data acquired comprises free induction decay data and multiple gradient echo data; and

reconstructing an in-phase image, a fat-saturated image, a water-saturated image, and an ultra-short echo time image from the magnetic resonance data, wherein the ultra-short echo time image comprises bone image data.

16. The method according to claim 15, further including:

constructing a digital reconstructed radiograph image based on a 2-dimensional projection of the ultra-short echo time image.

17. The method according to claim 16, further including:

5 matching a patient position with a support positioning system in a radiation therapy system in 2-dimensions based on the digital reconstructed radiograph image.

18. The method according to claim 15, further including:

 constructing a cortical bone image by subtracting the in-phase image from the
10 ultra-short echo time; and
 wherein the cortical bone image is used to register the images.

19. A non-transitory computer-readable storage medium containing machine
readable instructions for execution by a processor controlling a medical apparatus, wherein
15 the medical apparatus comprises a magnetic resonance imaging system for acquiring
magnetic resonance data from an imaging volume, wherein the computer-readable storage
medium further contains a pulse sequence for controlling the magnetic resonance imaging
system, wherein the magnetic resonance data acquired using the pulse sequence comprises
free induction decay data and multiple gradient echo data, wherein execution of the
20 instructions causes the processor to:

 acquire the magnetic resonance data using the magnetic resonance imaging
system; and

 reconstruct an in-phase image, a fat-saturated image, a water-saturated image,
and an ultra-short echo time image from the magnetic resonance data, wherein the ultra-short
25 echo time image comprises bone image data.

20. A controller for a medical apparatus, wherein the medical apparatus comprises
a magnetic resonance imaging system for acquiring magnetic resonance data from an
imaging volume; wherein the controller is configured to:

30 acquire the magnetic resonance data using the magnetic resonance imaging
system, wherein the controller is arranged to use a pulse sequence to control the operating of
the magnetic resonance imaging system during acquisition of the magnetic resonance data,
wherein the magnetic resonance data acquired using the pulse sequence comprises free
induction decay data and multiple gradient echo data; and

reconstruct an in-phase image, a fat-saturated image, a water-saturated image, and an ultra-short echo time image from the magnetic resonance data, wherein the ultra-short echo time image comprises bone image data.

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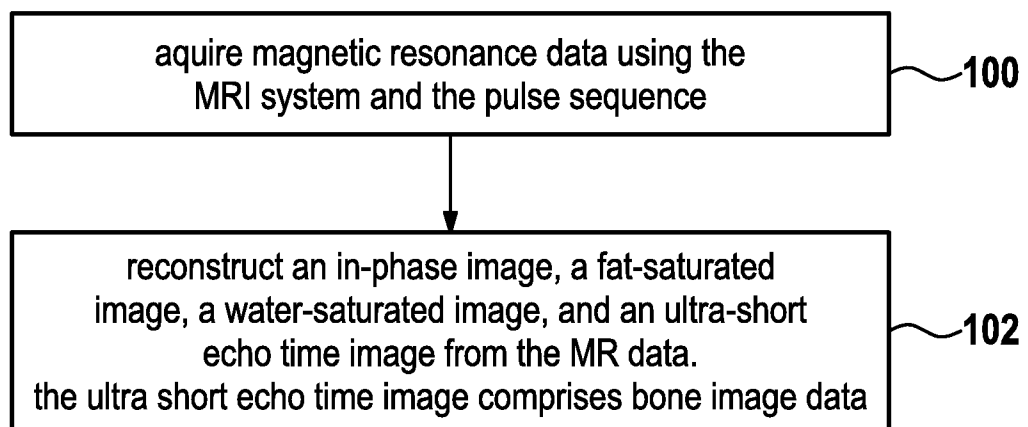


FIG. 1

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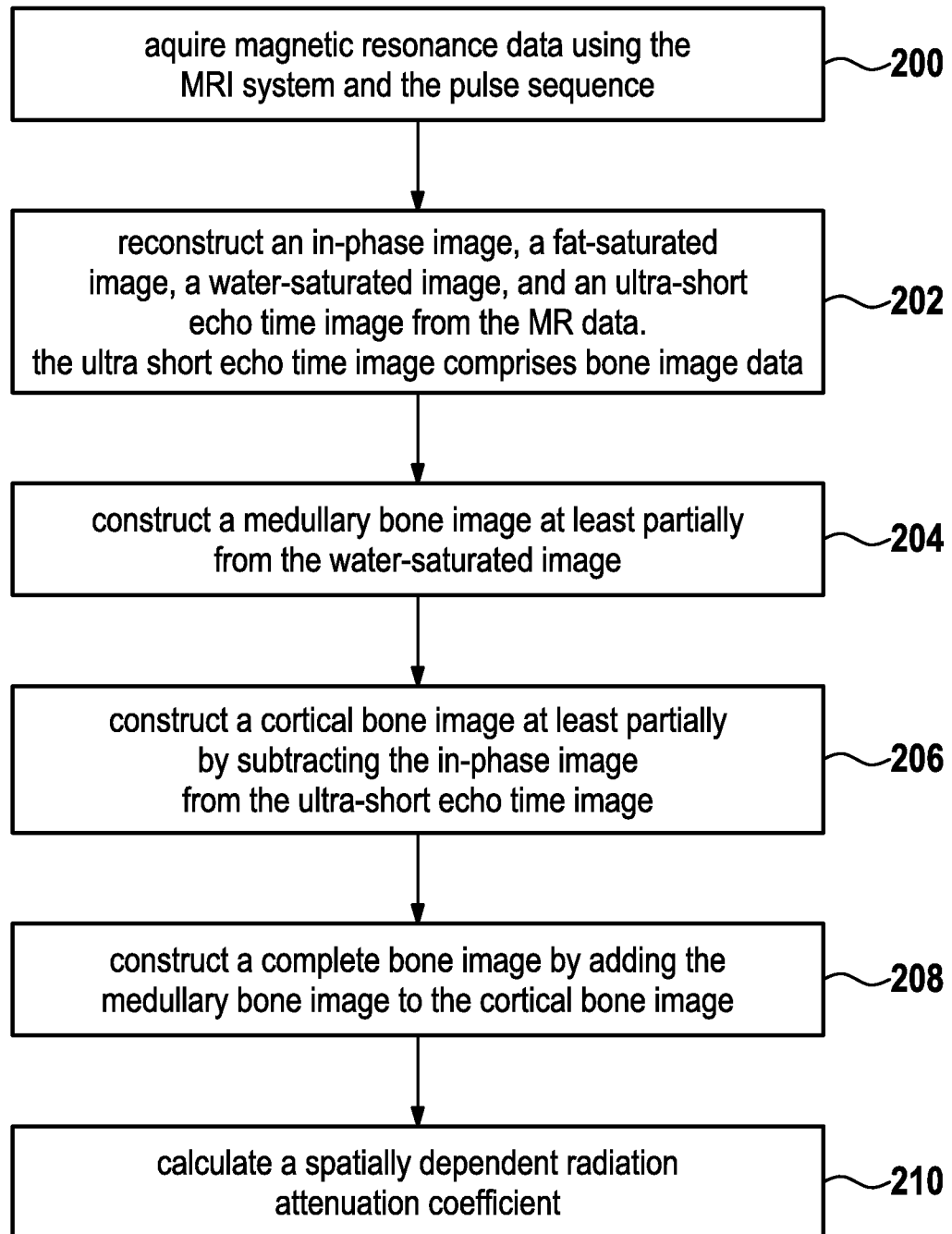


FIG. 2

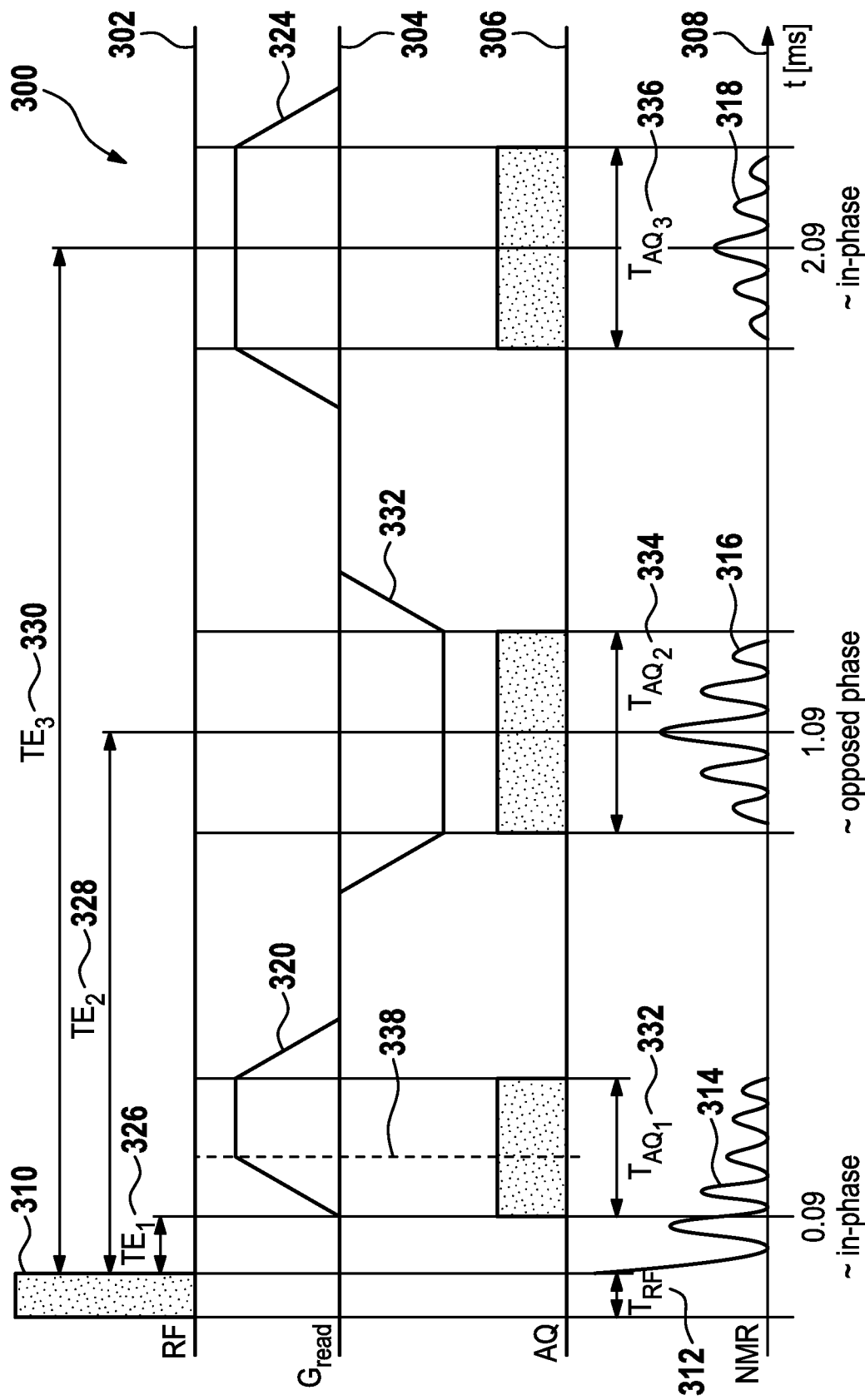


FIG. 3

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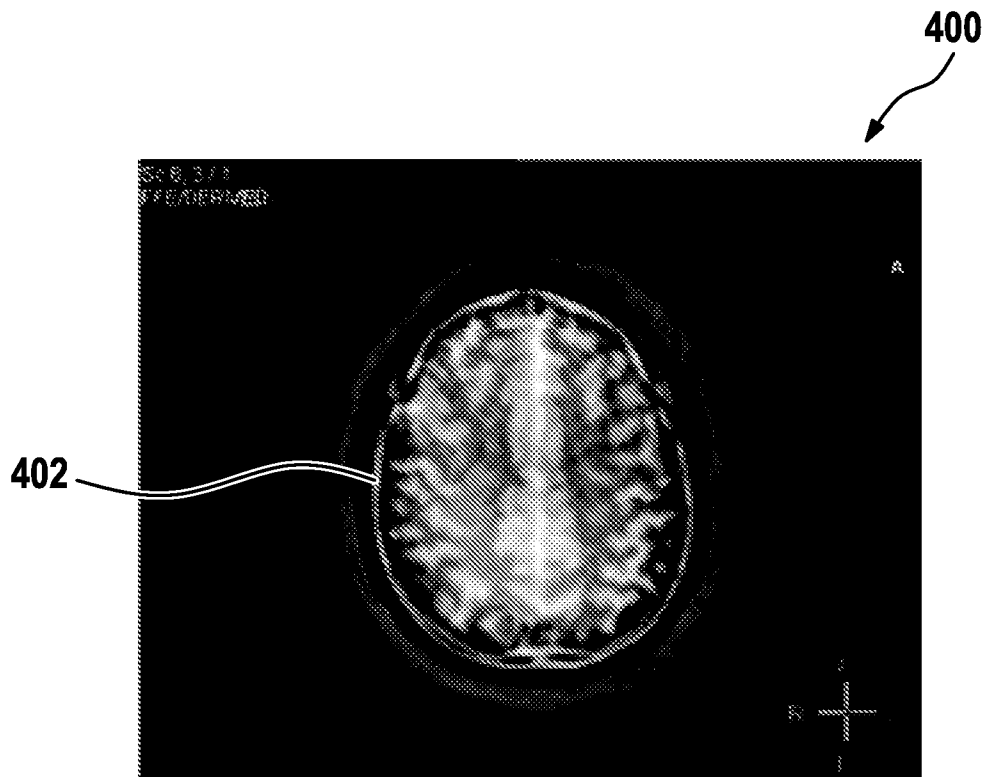


FIG. 4



FIG. 5

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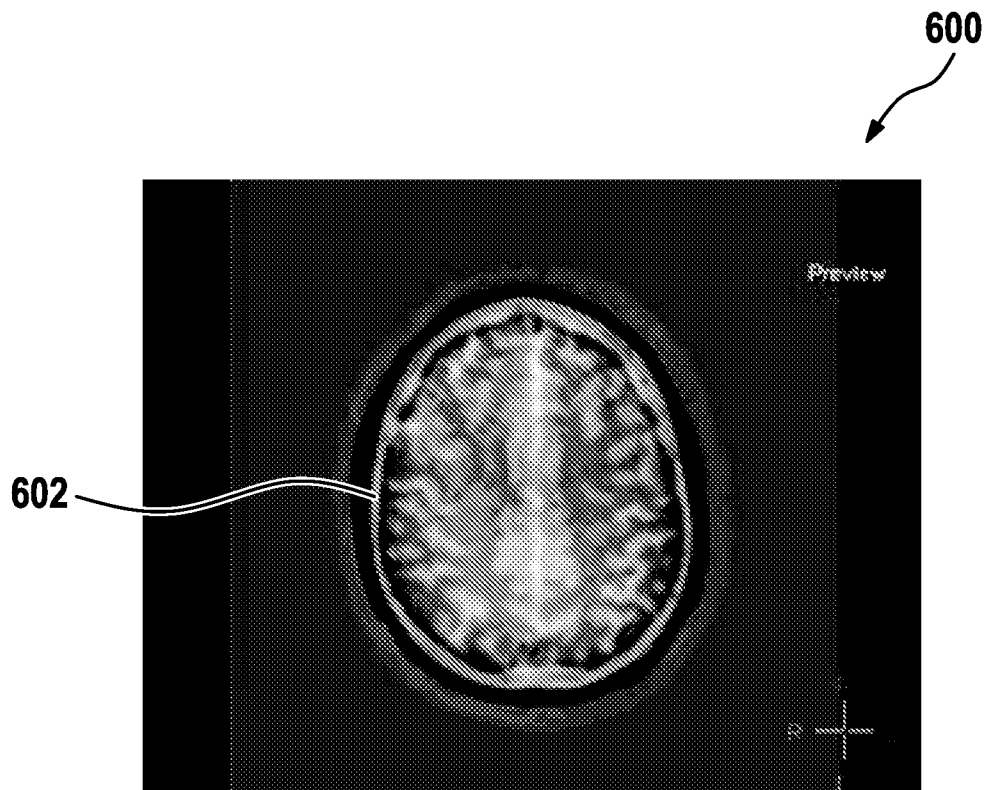


FIG. 6

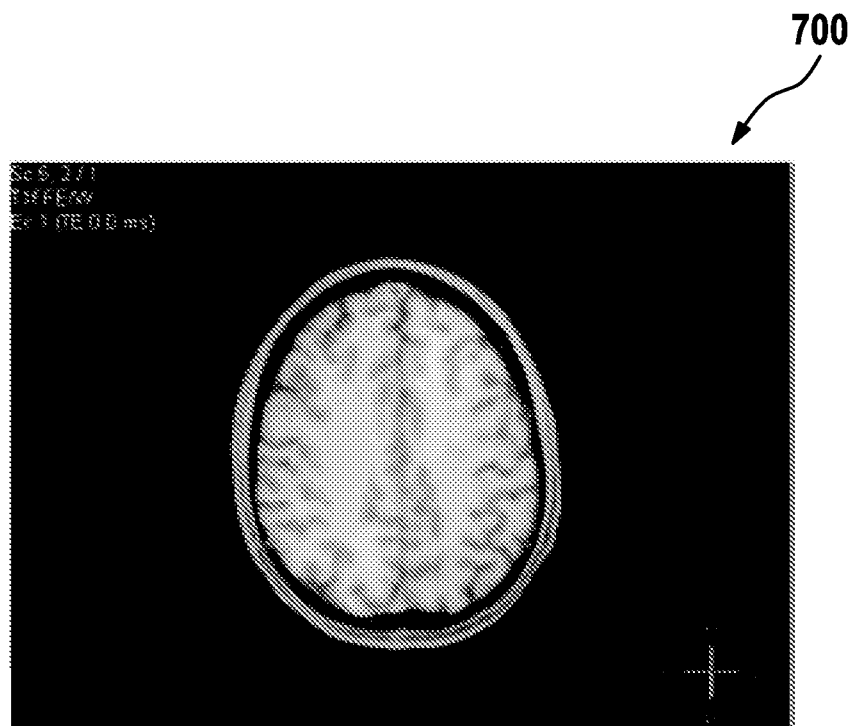


FIG. 7

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FIG. 8

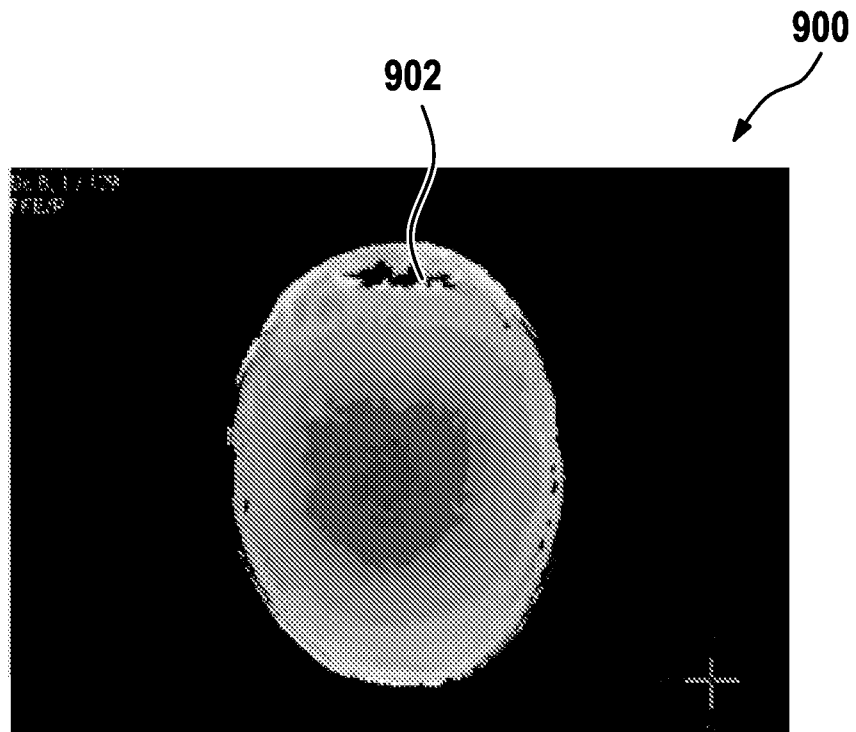
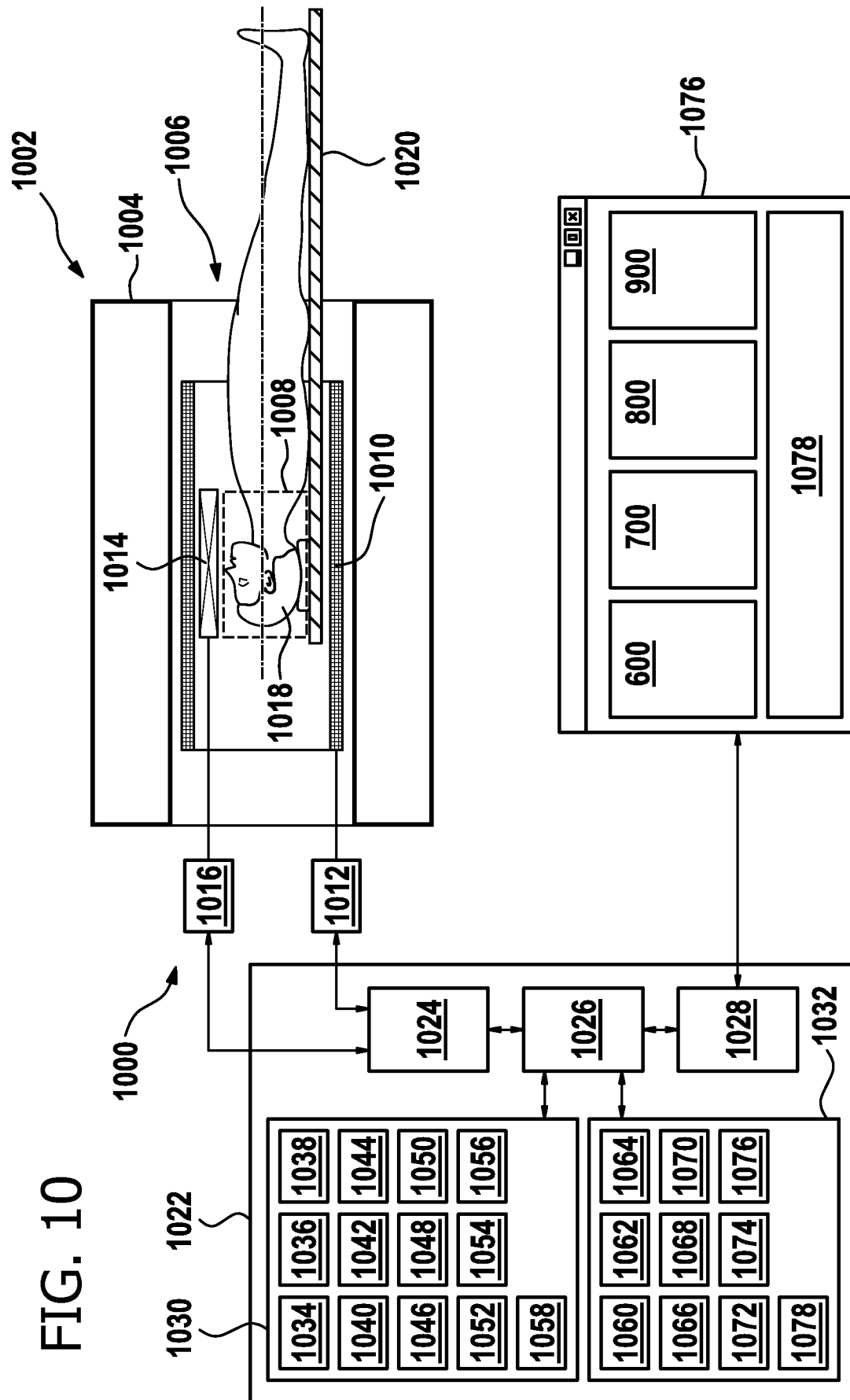
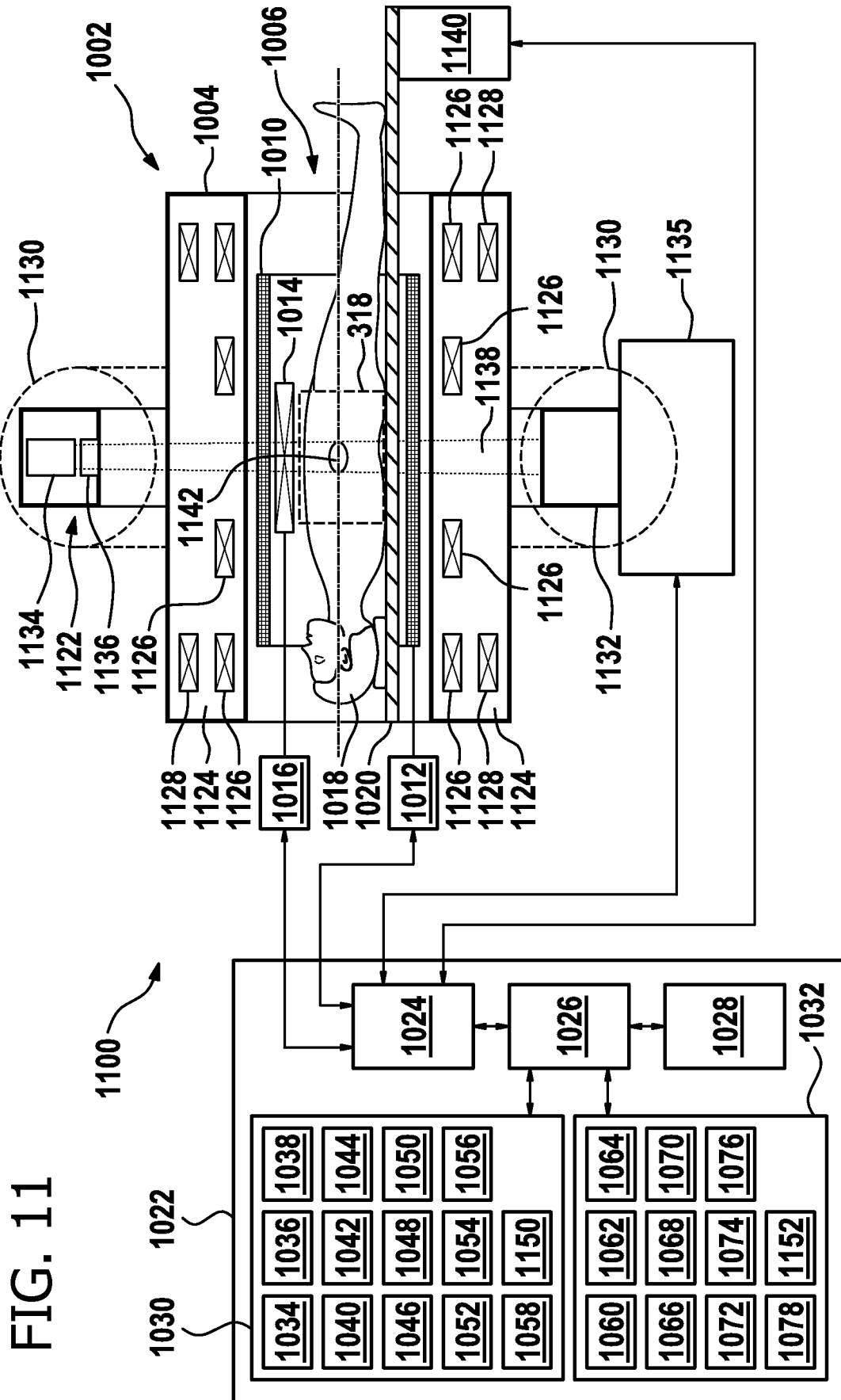


FIG. 9

FIG. 10



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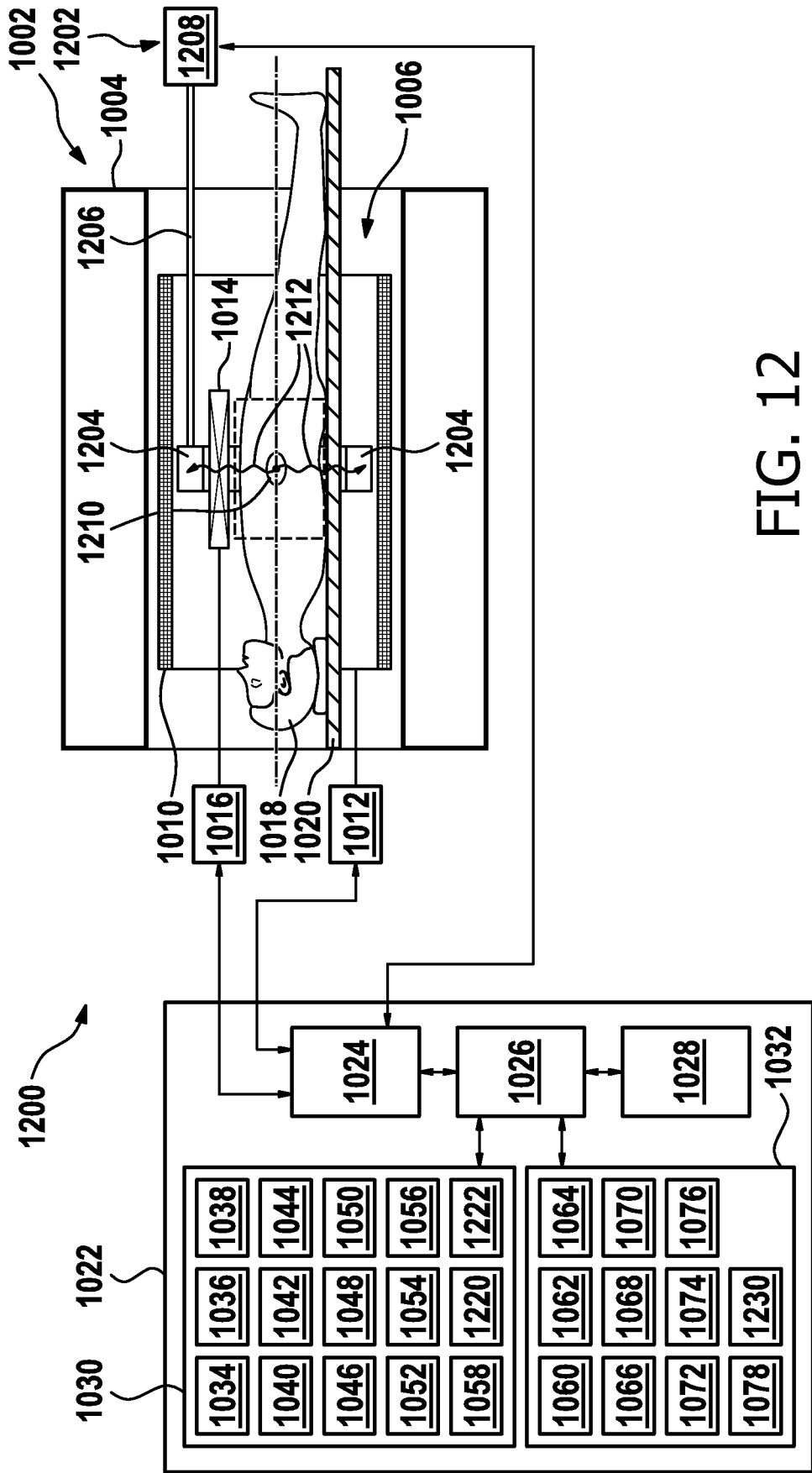


FIG. 12

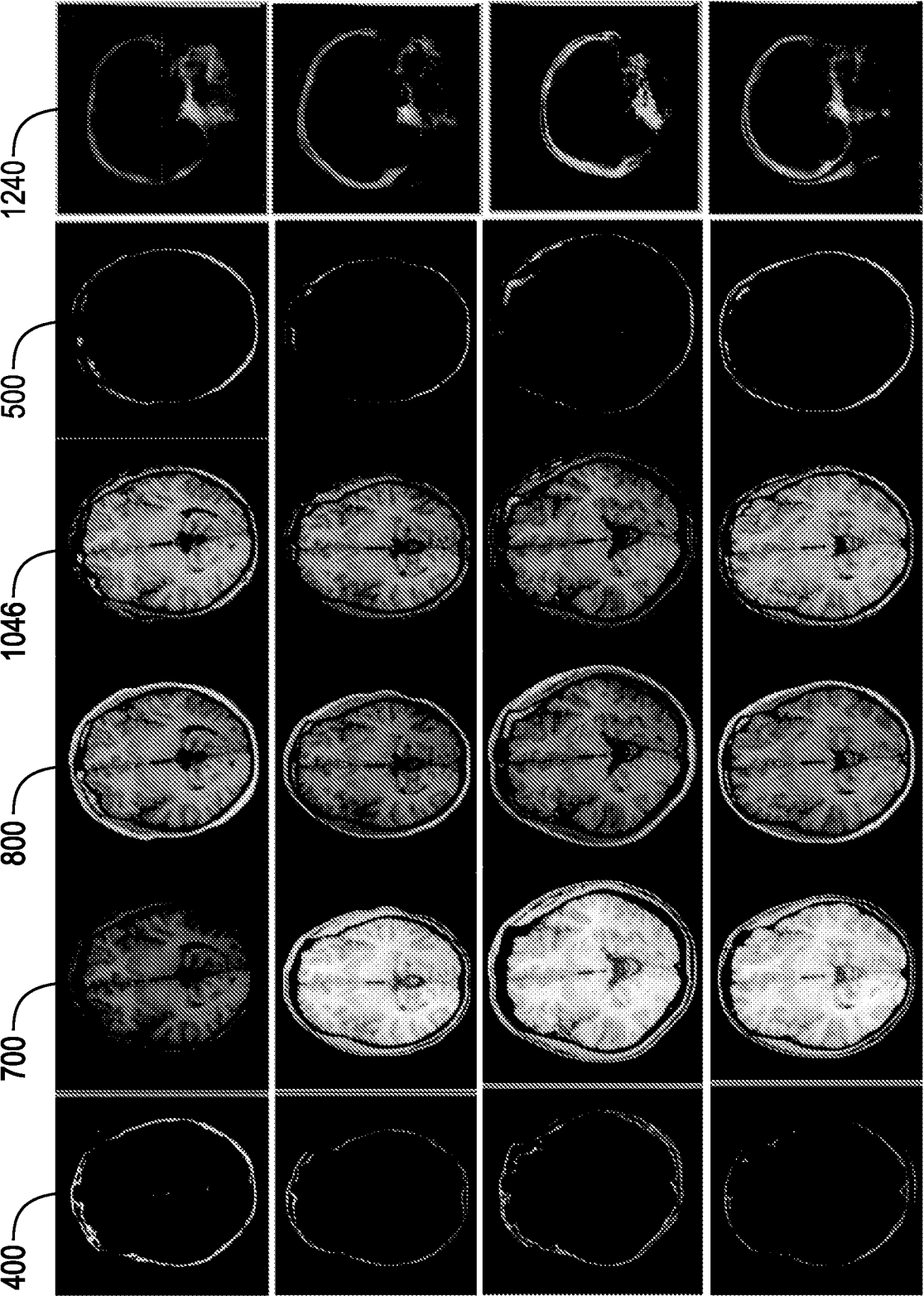


FIG. 13