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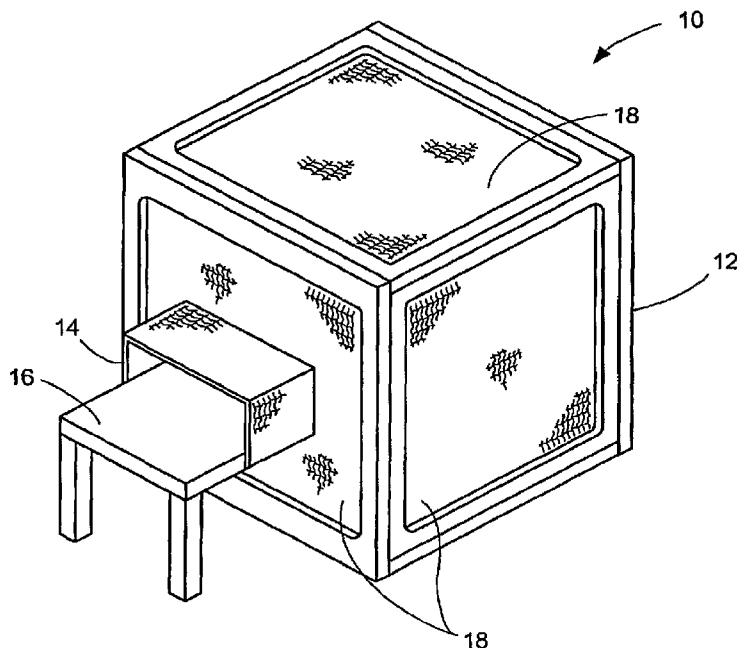
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(54) Title: PORTABLE DEVICE FOR ULTRA-LOW FIELD MAGNETIC RESONANCE IMAGING (ULF-MRI)



(57) Abstract: A portable device for ultra-low field magnetic resonance imaging (ULF-MRI). This portable ULF-MRI device has applications for emergency care, surgery, battlefield care and other trauma applications. The portable ULF-MRI device includes multiple receiver channels, imaging coils and times, and provides enhanced contrast behavior of ultra low field imaging and pulse sequence optimization. Using the additional spatial information that derives from the use of multiple receiver coil, the invention discloses a novel means of MRI signal spatial encoding.

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PORTABLE DEVICE FOR ULTRA LOW FIELD  
MAGNETIC RESONANCE IMAGING (ULF-MRI)

CROSS-REFERENCE TO RELATED APPLICATIONS

5           This application claims priority under 35 U.S.C. §119(e) to co-pending  
and commonly-assigned Provisional Application Serial No. 60/807,147,  
entitled "PORTABLE DEVICE FOR ULTRA LOW FIELD MAGNETIC  
RESONANCE IMAGING (ULF-MRI)," filed on July 12, 2006, by Mark S.  
Cohen, attorney's docket number 30435.183-US-P1 (2006-331-1), which  
10       application is incorporated by reference herein.

          This application is related to the following co-pending and commonly-  
assigned applications:

          U.S. Utility Application Serial No. 10/344,776, filed February 18, 2003, by  
Mark S. Cohen, entitled "METHOD AND APPARATUS FOR REDUCING  
15       CONTAMINATION OF AN ELECTRICAL SIGNAL," attorneys' docket number  
30435.103-US-WO (2000-490-2), U.S. Patent Publication No. 2004/0097802 A1,  
published May 20, 2004, which application claims priority to PCT International  
Application Serial No. WO02/13689, filed August 15, 2001, by Mark S. Cohen,  
entitled "METHOD AND APPARATUS FOR REDUCING CONTAMINATION OF  
20       AN ELECTRICAL SIGNAL," attorneys' docket number 30435.103-WO-U2 (2000-  
490-2), which application claims priority to U.S. Provisional Application Serial No.  
60/267,337, filed February 7, 2001, by Mark S. Cohen, entitled "METHOD AND  
APPARATUS FOR REDUCING CONTAMINATION OF AN ELECTRICAL  
SIGNAL," attorneys' docket number 30435.103-WO-U2 (2000-490-1), and U.S.  
25       Provisional Application Serial No. 60/225,389, filed August 15, 2000, by Mark S.  
Cohen, entitled "METHOD AND APPARATUS FOR REDUCING  
CONTAMINATION OF AN ELECTRICAL SIGNAL," attorneys' docket number  
30435.103-WO-U2 (2000-490-1);

          all of which applications are incorporated by reference herein.

## BACKGROUND OF THE INVENTION

### 1. Field of the Invention.

This invention is related to a portable device for Ultra Low-Field Magnetic  
5 Resonance Imaging (ULF-MRI).

### 2. Description of the Related Art.

(Note: This application references a number of different publications as  
indicated throughout the specification by reference numbers enclosed in brackets, e.g.,  
10 [x]. A list of these different publications ordered according to these reference  
numbers can be found below in the section entitled "References." Each of these  
publications is incorporated by reference herein.)

Magnetic Resonance Imaging (MRI) is considered widely to be the most  
sensitive, most accurate and safest modality available for use in studying the internal  
15 soft tissues of the human body. Unfortunately, practical devices are very large, very  
complicated and very expensive. These costs are attributable primarily to the large  
magnet required for this application and to its secondary consequences including  
powerful imaging gradient fields for spatial encoding, powerful radio transmitters,  
large magnetic field exclusion zone and safety monitoring challenges that arise from  
20 exposure to the radio frequency (RF) and gradient subsystems. Generally, the  
primary magnet is the largest single cost item in the system.

The very strong magnets used for clinical MRI result in serious device  
limitations as well, because the attractive strength of the magnet makes the immediate  
environment unsafe, as the instrument can readily propel very large projectiles toward  
25 the imaging system. The literature reports the deaths of a few people each year,  
resulting from objects as large as fork lift loaders being pulled into the instruments.  
Even at a substantial distance, the MRI device presents a safety hazard, as certain  
implanted bioelectrical devices – most prominently pacemakers – may be adversely  
affected by the stray magnetic field. The imagers thus require a strict exclusion zone

within which pacemakers and other neuroelectrical devices are not allowed. Obviously, this is a health care restriction for individuals who must depend on such devices for life support, as they may not safely be imaged in today's conventional devices.

5           While MRI is based on the production of coherent magnetic fields, the detection of the signal depends in current instruments on the magnetic induction of electrical fields in radio antennas. The sensitivity of such experiments depends crucially on the strength of the imaging magnet for two reasons: the first is that the strength of the magnetic signal itself grows linearly with that of the imaging magnet.  
10          The second is that the strength of the induced electrical field is proportional to the frequency of the magnetic resonance signal, which also depends on the magnet strength. This results in a quadratic overall dependence and pushes the discipline towards the development of ever larger instruments.

          Even so, the gains are not as strong as one might hope. The larger operational  
15          frequency of the instrument, for example, for a variety of reasons demands an increase in bandwidth, i.e., the range of frequencies used in detection, and this results in an increase in noise. Much more insidiously, the human body tissues are not completely transparent to electrical signals in the tens to hundreds of megahertz used for MRI, and the signal is degraded both spatially and temporally by the transmission  
20          through body tissue. In fact, the problems of electrical resistance of body tissues themselves create a safety concern for high field MRI, as they result in body heating that is also frequency-dependent, and therefore greater power becomes necessary to induce the MRI signal. It is well known that the power required for to induce the MRI signal proportional to the square of the magnetic field strength. At the most  
25          commonly used field strengths of 1.0 Tesla and higher, this power dependence on field strength has resulted in the imposition of legal maximum power deposition that in turn creates use and protocol limitations that degrade the net efficiency of MRI devices to collect patient data. The limitations may be very substantial at the common commercial field strength of 3.0 Tesla and severely compromise the range of imaging

protocols that may be considered safe at the 7.0 Tesla operating point currently being sold to installations worldwide.

It is possible, however, to detect the magnetic signal directly through the use of superconducting quantum interference detectors, or SQUIDS. For example, consider the description found in U.S. Patent Publication No. 20040027125, published February 12, 2004, by John Clarke et al., entitled "SQUID DETECTED NMR AND MRI AT ULTRA LOW FIELDS," which publication is incorporated by reference herein.

With a SQUID detector, the need for a large, expensive, superconducting magnet is eliminated altogether as the imaging is performed at very low magnetic fields. The need for extensive magnetic shielding can be eliminated through the use of SQUID gradiometers that are sensitive to only the local change in magnetic field rather than the overall field, which tends to be quite uniform in most environments. The electrical shielding, needed for the conventional devices, is only a minimal requirement with SQUID detection, and can be made small (comparable to the size of the object being imaged) and lightweight, consisting only of copper screen material. The efficiency of the magnetic pickup is independent of the frequency up to a few tens of kilohertz. Operation at low field requires little radio frequency power. In practice, this means that the device is without safety concerns for human use.

Notably, the applications and methods described herein are not limited to detection by SQUID devices per se. Recent work by Savukov and Romalis described in U.S. Patent No. 7,038,450, issued May 2, 2006, to Romalis et al., entitled "HIGH SENSITIVITY ATOMIC MAGNETOMETER AND METHODS FOR USING SAME", which patent is incorporated by reference herein, has resulted in the development of an atomic magnetometer with sensitivity potentially greater than that of SQUIDS in this NMR application [1]. While there are currently many practical problems with atomic magnetometers as detector elements, they ultimately may be incorporated into ULF-MRI devices as conceived here and share most of the advantages described herein.

Notwithstanding the many innovations noted, however, it is apparent that further improvements are necessary in the use of MRI instruments. Specifically, there is a need in the art for portable MRI instruments, for instruments in which surgery and trauma applications are practical, and for imaging systems that can be deployed in circumstances where a high field unit is not impractical. These include, but are not limited to, regions where high power is not available, where the weight of the conventional instrument is not sustainable and a need for technical innovations that can make ULF-MRI possible. The present invention satisfies these needs.

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#### SUMMARY OF THE INVENTION

To overcome the limitations in the prior art described above, and to overcome other limitations that will become apparent upon reading and understanding the present specification, the present invention discloses a portable device for ultra low field magnetic resonance imaging (ULF-MRI). This portable ULF-MRI device has applications for emergency care, surgery, battlefield care and other trauma applications. The portable ULF-MRI device includes multiple receiver channels and imaging times, and provides enhanced contrast behavior of ultra low field imaging and pulse sequence optimization. Using the additional spatial information that derives from the use of multiple receiver coils, the invention discloses a novel means of MRI signal spatial encoding. The invention may be used in combination with the concepts disclosed in U.S. Utility Application Serial No. 10/344,776, filed February 18, 2003, by Mark S. Cohen, entitled "METHOD AND APPARATUS FOR REDUCING CONTAMINATION OF AN ELECTRICAL SIGNAL," which application is incorporated by reference herein, to create tomographically resolved images of bioelectrical activity.

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#### BRIEF DESCRIPTION OF THE DRAWINGS

Referring now to the drawings in which like reference numbers represent corresponding parts throughout:

FIGS. 1, 2 and 3 are diagrams that illustrate a portable device for ultra low field magnetic resonance imaging (ULF-MRI) according to the preferred embodiment of the present invention;

FIGS. 4 and 5 illustrate an array of SQUID detectors arranged about a patient's head according to one embodiment of the present invention; and

FIG. 6 illustrates a pair of polarization coils arranged on either side of a patient's head for generating a polarization magnetic field.

#### DETAILED DESCRIPTION OF THE INVENTION

In the following description of the preferred embodiment, reference is made to the accompanying drawings which form a part hereof, and in which is shown by way of illustration a specific embodiment in which the invention may be practiced. It is to be understood that other embodiments may be utilized and structural changes may be made without departing from the scope of the present invention.

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##### Overview

FIGS. 1, 2 and 3 are diagrams that illustrate a portable Ultra Low Field-Magnetic Resonance Imaging (ULF-MRI) device (10) according to the preferred embodiment of the present invention. In one embodiment, the portable ULF-MRI device (10) is contained within a collapsible Faraday cage (12).

The Faraday cage (12) includes a waveguide (14), as well as a collapsible patient bed (16) that is inserted into the Faraday cage (12) for imaging, wherein the collapsible patient bed (16) is substantially contained inside the Faraday cage (12). The Faraday cage (12) may be collapsible as well. The use of the waveguide (14) eliminates the need to make the Faraday cage (12) larger and thus is an optional component, although the Faraday cage (12) can be made large enough to contain the collapsible patient bed (16) in its entirety.

25

The portable ULF-MRI device (10) generates a magnetic field using pairs of electromagnet coils (18) integrated on the surface of the Faraday cage (12), wherein

each pair of electromagnet coils (18) is orthogonal to two other pairs of coils (18), and the coils (18) in each pair are positioned opposite each other on the Faraday cage (12) (because of the perspective view in FIG. 1, only three of the coils (18) are visible, and their respective paired coils (18) are on the opposite sides of the Faraday cage (12)).

5 These coils (18) are used to generate the magnetic field in each of three orthogonal directions.

The magnetic field is detected using one or more magnetic field detectors that are typically positioned within the Faraday cage (12) (and thus are not shown in FIGS. 1-3), wherein the detected magnetic field is transformed into an imaging field  
10 by ULF-MRI device (10). Typically, an array of magnetic field detectors are used, wherein the magnetic field detectors are placed in such a manner that they are distributed across the patient, although the array may be placed to localize imaging on a specific portion of the patient, as described in more detail below.

In one embodiment, the Faraday cage (12) has width, height and length  
15 dimensions that are each less than 2 meters, with an aperture for the patient's extremities. In another preferred embodiment, the Faraday cage is made large enough to accommodate the entire body of the patient and therefore each dimension is approximately 1 meter longer (i.e., the width, height and length dimensions are each less than 3 meters).

20 The Faraday cage (12) may also include an earth field cancellation coil set (18) integrated into the walls of the Faraday cage (12), the purpose of which is to correct for magnetic field inhomogeneities introduced into the imaging field created by the magnetic field of the earth and its interaction with the instrument and neighboring magnetizable objects.

25 Moreover, the Faraday cage (12) not only encases the electronics of the device (10), but includes support for the coils (18). The Faraday cage (12) serves to shield the sensitive electronics contained within it from the power sources and other instrumentation needed to support the imaging system.

This portable ULF-MRI device (10) has applications for emergency care, surgery, battlefield care and other trauma applications. The portable ULF-MRI device (10) includes multiple receiver channels and imaging coils, and provides enhanced contrast behavior of ultra low field imaging and pulse sequence optimization.

FIG. 4 illustrates an embodiment where an array of magnetic field detectors (20), which may comprise, but are not limited to, SQUID devices and atomic magnetometers, are arranged about a patient's head (22) in order to implement ULF-MRI. In an alternative embodiment, as noted above, the array of magnetic field detectors (20) may be placed in such a manner that they are distributed across the patient as a whole.

FIG. 5 illustrates an embodiment where polarization coils (24) are placed on either side of the patient's head (22) generate a polarization magnetic field (26). This is required because the strength of the magnetic resonance signal is proportional to the spin polarization. As noted in U.S. Patent Publication No. 20040027125, published February 12, 2004, by John Clarke et al., entitled "SQUID DETECTED NMR AND MRI AT ULTRA LOW FIELDS," which publication is incorporated by reference herein, the requirements on this component for field uniformity are minimal which results in dramatic cost savings.

FIG. 6 further illustrates the positioning of polarization coils (24) on either side of a patient (22) to generate the polarization field.

#### Surgical Applications

Operation at an ultra low field means that surgical instruments can be brought into the imaging suite without risk. Not only are the attractive forces insignificant, but the distortions they create in the images, which are directly proportional to the magnetic field strength, are of no concern, as long as the devices are not already magnetized. Thus, virtually any surgical device may be operated under the guidance of direct MRI visualization. Surgical guidance is a new and important application,

and this invention considers specifically the development of an instrument for this application.

#### ULF-MRI

5           While it has been noted that SQUID-based ULF-MRI could be made portable, there have been no specific disclosures regarding how to do so, and no claims to this effect. The present invention considers this in detail and is concerned with the solution of several attendant practical problems.

10           Imaging at ultra low fields is different in several respects from imaging with the traditional instruments. In particular, the ULF-MRI device: (a) exploits different contrast mechanisms and (b) has different instrument timing constraints to take advantage of the temporal characteristics of the signal. Moreover, this specification discusses specific “pulse sequences” that are advantageous.

15           U.S. Patent Publication No. 20040027125, published February 12, 2004, by John Clarke et al., entitled “SQUID DETECTED NMR AND MRI AT ULTRA LOW FIELDS,” which publication is incorporated by reference herein, describes very specifically the use of a single detector element.

20           However, the use of multiple detector arrays has been demonstrated for conventional MRI and is substantially more important in SQUID detection. This is due to the fact that the sensitive volume of traditional SQUIDs is limited. The detectors themselves are necessarily small, because of the means in which they must be fabricated. The magnetic signals are typically coupled to the SQUID detectors somewhat indirectly through another set of magnetic coils and a superconducting flux transformer. The latter is needed to compensate for a substantial impedance  
25           mismatch as the sizes of the loop coils is varied. Even so, the entire apparatus must be cooled to superconducting temperatures. Unfortunately, the size of the inductive pickup affects its sensitivity profile; smaller coils are sensitive over shorter distances. Yet, the human imagers must detect signals tens of centimeters away. The work of Savukov and Romalis [1] also envisions a multiple detector system and recognizes

some of its advantages for use in ULF- MRI. However, the array conceived therein is inherently planar, which precludes it from being closely conformal to the body of the patient. As the sensitivity of the detector falls very rapidly with distance from the patient, the planar array may not be an effective solution to biological MRI.

5           As noted above, FIGS. 4 and 5 both illustrate an array of SQUID detectors (20) arranged about a patient's head (22). It has been well demonstrated that in "phased array" configurations, a group of detectors arranged around an object can be used to make a virtual large detector with some special advantageous characteristics. Specifically, while the sensitivity at the center of the array is essentially equivalent to  
10           that of a single large detector, the sensitivity near to the individual array elements may be many times better, as much as an order of magnitude. The use of arrayed detectors (20) in this device (10) is a non-obvious solution to a problem specific to SQUID detection, even though it has proven and established advantage in conventional imaging.

15           The traditional means of detected the magnetic resonance signal, through electrical induction, is not three-dimensionally symmetrical. The sensitivity of the radio antenna depends on its orientation with respect to the magnetic field used for imaging. In conventional instruments, this orientation is necessarily fixed along a single axis of the instrument, because it is created either by passing a large current  
20           through miles of superconducting wire wound around a tube-shaped former (in which the patient lies) or through the creation of a static magnetic field in permanent magnets, such as iron, that are immovable.

          In ULF-MRI, however, because it is small, the imaging magnetic field can be created using very simple electromagnets (18) that pass a few amperes of current.  
25           Because of this, it is a comparatively simple matter to electrically "steer" the magnetic field orientation. In practice, this means that the sensitivity of the detectors (20) can be made independent of orientation. Depending on the body location, this might be expected to add something on the order of a square root of 2 improvement in overall sensitivity.

An “imaging field” is created by a set of three coil (18) pairs, as shown in FIG. 1, which are mutually orthogonal. With them, an imaging field of arbitrary orientation may be created. The MR imaging programs (the pulse sequence) can be designed to collect the signal in all three orthogonal magnetization planes, or to orient the magnetization along a particular axis of peak sensitivity with respect to the magnetic detector coils.

SQUIDs, incorporated into magneto-encephalography and magneto-cardiography instruments, are an important means of detecting bioelectrical signals indirectly through their induced magnetic fields. This strength of the technology is of mixed impact on SQUID-based MRI, however. On the one hand, it has been demonstrated that it is possible to combine the detection of the MRI and bioelectrical data, which is of potentially large value (similar ideas on combined EEG and MRI are described in the cross-referenced applications set forth above). On the other hand, the groups working in these areas do not seem to have considered the extent to which the bioelectrical signals might be potential MRI noise sources nor do they address means to mitigate this problem, as discussed herein.

#### Switching the Amplitude of the Magnetic Polarization Field

The present invention also proposes a specific time course for switching the amplitude of the magnetic polarization field, chosen to minimize the possibility of producing uncomfortable physical sensations in the patient.

#### Surgical Applications

The use application to surgery does not require a great deal of detailed explanation. The physical factors of most concern are the physical access to the patient, which must be guaranteed by the form factor of the scanner. FIGS. 1-5 indicate specifically a configuration that will enable this use. The operation of the low field imager generally requires the use of a “pre-polarization” field of several hundred Gauss, comparable to that of hobbyist bar magnets. In general, the stainless

steel used for surgical devices is only very weakly magnetic. The experience of the inventor, and the opinions of MRI safety experts, suggests that the overwhelming majority of surgical tools, such as retractors, forceps, scalpels, trephines, etc., can be used without modification.

5

### Portability

The potential for portability of this technology derives from the essential simplicity of the instrument. However, a portable unit must nevertheless involve special design concerns, including ease of field set up, weight, vibration isolation, power considerations and so on. The diagrams of FIGS. 1-3 include a design concept that addresses these issues directly.

For example, the device (10) is designed to be highly compact, and to fit, in collapsed form, into a small vehicle, such as a truck, SUV, van or jeep. The cryogen pumping system, needed for the SQUID detectors (20), is driven either electrically (cryo-pumps may be made with power demands of less than 200W, or by direct mechanical connection to the automobile engine.) The Faraday cage (12), used to reduce the possibility of electrical noise interference, may be folded flat using hinged joints. The earth field cancellation coil set (18) is made integral with the Faraday cage (12). Because of the relatively large separation distance between the shield elements and the patient, the need for precise alignment is reduced greatly. Similarly, the imaging gradient set may be separately mounted on a folding frame.

All of the devices placed within the Faraday cage (12), and importantly the structural members used to support the instrument (10), are made of non-magnetic and non-conductive materials, such as G10 fiberglass or laminated woods, that offer a good combination of low weight, structural rigidity and machinability. It is reasonable to assume that such a device (10) could be made fully operational within tens of minutes of delivery to a remote location. This opens up exceedingly important potential applications in trauma, both civilian and battlefield.

MRI is seldom used in trauma for several reasons: the instruments are essentially all based in fixed locations, requiring that the patient be transported to the device. For trauma requiring that the patients not be moved, or where the situation is too urgent to allow the time for transportation, conventional x-ray or ultrasound are used instead, but their diagnostic power is much less than that of MRI, particularly for soft tissue damage or intra-cranial (brain) injuries. When hospital transport is possible, the trauma victim usually receives an x-ray computed tomography (CT), rather than an MRI, because of the possibility of the possibility that foreign bodies may be lodged in the patient, and produce a substantial safety risk. Finally, MRI devices are 2 to 5 times as expensive as CT instruments. In practice, this means that there is seldom MRI scan time available on an urgent basis.

Beyond the collapsible configuration suggested here, the instruments can certainly be made lightweight and small enough to place onto small transport vehicles, such as trucks, SUVs, vans or jeeps. Moreover, the required Faraday cage (12) may supplied by or integrated with the transport vehicle itself. That is, the rear part of a vehicle, in this case, is constructed entirely of conductive materials and electrically isolated from the rest of the vehicle. The shield is connected to a single point "earth" ground, either through the supply of grounded power to the equipment, or through a literal earth probe that can be placed on site into the ground.

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#### Imaging Strategy

The use of so-called gradient coils has been noted above. These are used in conventional Nuclear Magnetic Resonance (NMR) instruments, as described by Paul C. Lauterbur [2], in order to make the spin precessional velocity a function of spatial position, thereby creating a basis for spatial encoding. This strategy is the basis of virtually all present day image reconstructions for MRI. It is well known, however, that the magnetic dipole fields from sources inside the body also produce localizing information by virtue of their 3 dimensional distributions as recorded externally. This is the basis by which both "Magnetoencephalography" (MEG) and certain forms of

“Electroencephalography” (EEG) are used to form tomographic images. Although it is of comparatively coarse resolution, the positional signal from field sources inside the body can be derived by comparing the magnetic field distribution as detected by the multiple receivers that are included in our ULF-MRI device. When SQUID  
5 detection is used, for example, the image reconstruction means used in MEG may be used, in this case, for reconstruction of the spatial distribution of the magnetic resonance signal. This is significant because the dipole field is independent of the alternative gradient-based imaging localization. As a result, the localizing information from both methods (MEG and ULF-MRI) may be combined in order to  
10 reduce overall imaging times.

#### MRI Pulse Sequence

MRI is based on the ability to detect small variations in the so-called magnetic relaxation rates, T1 and T2. Roughly, these are effectively the rates at which a  
15 substance magnetizes and the rate at which the magnetic resonance (MR) signal decays. At high fields, it is known that the T1 times become longer, which introduces severe pressure on the minimum time required to make an images, and that the T1 rates of various body tissues become more similar, reducing the available contrast. The observed T2 is the product of many factors. In general, however, as the magnetic  
20 field strength is reduced, T2 increases and in the limit approaches T1. As T2 determines the total amount of time available to collect the MR signal, the longer T2 is, the easier it is to create an image and the better the final signal to noise ratio. T2 may be ten times longer at low field than at the high fields used for current generation clinical MRI instruments. T2 is an extremely important contrast parameter in MRI, as  
25 it seems to reflect pathological processes (at high field) much more sensitively than T1. However, at very low field it has been reported that the range of T2’s becomes reduced as compared to high field studies. Some components of the T2 contrast disappear altogether at low field. These include, for example, the strong T2 (actually

called T2\*) effect created by accumulations of blood in clots and the important T2-related effects exploited in functional MRI.

It is well known that the application of a so-called “inversion” RF pulse that rotates the sample magnetization by 180° effectively doubles the useable T1 contrast in the images. This is known as an inversion recovery (IR) sequence. Despite the high contrast, IR is seldom used in high field scanners, because the recovery of the magnetization, which occurs at the T1 rate, takes a prohibitively long time. The T1 of body tissue in ULF-MRI is as much as an order of magnitude shorter, making IR imaging highly practical. Further, the nature of the so-called inversion recovery sequence incorporates the inversion pulses as a setup process prior to actual data collection. In conventional imaging, this is often dead-time.

However, in a ULF-MRI context, the initial magnetization is created in a pre-polarization step. The present invention proposes to incorporate the inversion pulses in that interval (during the pre-polarization step), where the pulses do not burden the signal collection phase. Specifically, the present invention comprises a method, performed by the device (10) in FIGS. 1-3, of improving contrast in ULF-MRI, by performing an initial magnetization step over a time interval, thereby exposing a sample to fields of order 10 milli-Tesla, and then applying at least one inversion pulse to rotate the sample’s magnetization during the time interval, wherein the inversion pulse is adiabatic.

One advantage of the ULF-MRI is that the spatial homogeneity of the pre-polarization field does not need to be high. However, in most cases, the production of the MRI signal itself, depends critically on the field homogeneity, as the phenomenon depends on an exact match of the frequency of the excitation radio pulse and the frequency of precession of the nuclear spins - which is itself proportional to the magnetic field. Specifically, the present invention proposes the use so-called “adiabatic” pulses that allow a uniform inversion even in a non-uniform field, specifically during the pre-polarization window.

Inversion during polarization offers an interesting advantage, in that for the ULF-MRI experiment, the polarization field must be removed prior to data collection. The polarization field is itself created by an electromagnet that must be energized and de-energized to create and remove the field. The energy storage in the device is not trivial, and takes some time to remove. Further, it has been established that exposure of humans to rapidly varying magnetic fields may result in the induction of electrical currents in the body that produce uncomfortable sensations in the patient, known as “magneto stimulation.” This effectively limits the rate at which the field can be changed. In today’s prototype designs, at least a hundred milliseconds is needed between the polarization and imaging phase for the field ramp down to occur. This otherwise dead time is an ideal moment for the recovery phase of the inversion recovery sequence.

Heretofore, only the most basic spatial encoding schemes have been contemplated, in which the images are formed using what is known as a spin-warp encoding scheme, that forms the images from the signals collected after a series of excitations. While this has been demonstrated as being effective, it is more efficient to utilize what is known as “echo-planar imaging” (EPI). Specifically, the present invention comprises a method of providing ULF-MRI by utilizing an echo planar imaging technique in the ULF-MRI device (10) to improve contrast.

EPI has a decided advantage in this context, because the final spatial resolution depends very sensitively on the T2 of the sample. The fact that T2 is so much increased at ultra-low fields enables EPI scanning to be performed without some of the problems that it suffers at high field, notably spatial blurring from the short tissue T2s, shape distortions in the images that are known to be proportional to magnetic field and signal losses that relate to signal dropouts that are created by accelerated dephasing in the neighborhood of tissues that vary in magnetization, an effect that too dependent on field strength and is negligible at fields less than a few hundred Gauss. Specifically, the present invention comprises a method of providing ULF-MRI by generating a magnetic field using the ULF-MRI device (10), and then

scanning the magnetic field in a range 1-500 micro-Tesla using the ULF-MRI device (10).

The T1 of tissue is known to have a very strong dependence on fields in the low field range from 1 to 500 micro-Tesla used in the SQUID MRI system. This suggests an additional contrast mechanism beyond the set used in high field MRI. Namely, that in the ULF-MRI device (10), it is possible to vary the imaging field over orders of magnitude, from micro-Tesla to milli-Tesla, simply by controlling the current in the relevant windings.

The present invention therefore proposes to do so in the context of an MRI pulse sequence. One instantiation of which is to collect a series of echo-planar images, each with a different imaging field, resulting in a spread of T1 contrasts that should be useful in medical diagnosis in exposing differences in tissue properties not visible at a fixed field.

#### Arrayed Detector Elements

Arrayed detector elements are an established concept in conventional MRI. Essentially, each detector is set up to act independently to sample the MRI signal adjacent tissue. The signals from these various elements are combined to make an image with an overall increased field of view.

The physical manufacture of SQUID devices produces limitations on the detector size. This arises from the fact that the detector coil must couple its signal to the SQUID itself through an inductive flux transformer. This process is optimized when the electrical inductance of the detector coil is matched to the SQUID. Unfortunately, the inductance is a strong function of the coil size, and it is difficult to make large detector coils as a result.

Thus, it is believed that the advantages of detector arrays address as well a special limitation in ULF-MRI and the present invention proposes the construction of so-called phased array detector coils into a configuration that places active detector

(20) elements as uniformly as possible over the subject's head (22), as shown in FIGS. 4-5.

As noted above, the potassium magnetometer device described by Savukov and Romalis [1] is highly amenable to the construction of detector arrays. In particular, they note that there is no inductive coupling between the detector elements, a feature that greatly simplifies the design and fabrication of arrayed units.

A problem of arrayed detectors in conventional MRI systems is that the orientation of the detector coil with respect to the magnetization determines the sensitivity of the detector. If the overall sample magnetization is oriented along, for example, the z-axis, the MR signal is created by the precession of nuclear spins in the X-Y plane. This signal is detected by coils whose planar axes are rotations within the Z axis. Coils in the X-Y plane will pick up no signal. The array coil devices therefore, have notable limitations in the top of the head in high field MRI devices, for example, where a simple circular coil configuration has near zero sensitivity.

A unique solution to this problem becomes possible with the ULF-MRI device (10). Namely, that the polarization field and the imaging field are created separately. By setting up pairs of electromagnets (18) to create the imaging field in each of three orthogonal planes, for example, the cardinal X, Y and Z planes, it is possible to create arbitrary net orientations for the imaging field. Thus, the plane of nuclear precession can be steered to the sensitivity of the relevant coil array. This results in a theoretical signal to noise ratio (SNR) gain up to 41% (the square root of 2) overall, and much more for specific body regions. The re-orientation of the magnetization from the polarizing axis to the imaging axis must be performed adiabatically, which places minor constraints on the sequence timing, but is part of the published art for ULF-MRI.

#### Local Coil Examinations

The steerable field is also enabling for certain types of local coil examinations. For example, in an array coil study of the brain, the limitation that all of the elements

be outside of the head leaves an area in the center of the head, and therefore the base of the brain, with much reduced SNR. It also means that the sensitivity of the signal is very inhomogeneous, some parts of the brain having SNR five times that of others, which may cause substantial problems in certain types of studies.

5           It has been recognized for some time that placing a coil in the subject's mouth would be an ideal solution to this, as this would bring the receiver into close proximity of the base of the brain. Unfortunately, with a high field MRI device, there is no known reasonable shape for this coil that would allow it to pick up the MRI signal from this location, because of the axis of spin precession. On the other hand, if  
10 the spin axis is varied by 90°, a simple planar coil can be used with optimal sensitivity, and good comfort for the subject.

Consequently, the present invention comprises a method of providing ULF-MRI by generating a magnetic field using the ULF-MRI device (10), and placing an imaging coil inside a patient's mouth to image inside the patient's brain using the  
15 magnetic field of the ULF-MRI device (10).

Magneto-encephalography (MEG) is a means of detecting brain electrical activity through the tiny magnetic potentials created by electrical currents. The magnetic potentials are so small that they can be detected only with SQUID devices. Typically, they carry signal energy in the range of 1 Hz or so to a few kilohertz. The  
20 images that have been displayed using ULF-MRI were created at imaging field strengths that bring the resonance signal into the kilohertz range. Thus, the MEG signal is a potentially significant source of imaging noise. It is apparent that this has not been recognized fully.

It is believed to be a significant realization that this problem will be an SNR  
25 limiting step in the suggested instrument configurations. To date, there have been no published ULF-MRI images from living samples, so this problem probably has not been recognized. The present invention therefore proposes that the device should be designed with this specifically in mind. In practice, this means that the MRI signal

should be detected in imaging fields of 500 milli-Gauss or more, where it is above the frequency range where such contamination will be problematic.

This is another area in which the array coil concept has special relevance. An advantage of the MEG device is that it is possible, under reasonable assumptions, to independently localize the electrical dipoles that create the detected magnetic flux. Solving for these apparent dipoles can be a means to exclude the MEG signal from the imaging signal, as the signal components in the detected signal that make up these dipoles might be subtracted from the signal used in imaging.

Consequently, the present invention provides a method of mathematically combining magnetoencephalography (MEG) and magnetic resonance imaging (MRI) signals, comprising generating MEG signals and MRI signals in the ULF-MRI device (10), and then detecting dipole fields from the MEG signals to identify approximate locations of sources of internally generated signals for a sample placed within the ULF-MRI device (10), wherein the sources of internally generated signals are excluded from the MRI signals' reconstruction in order to both improve an overall signal-to-noise ratio and to associate locations of the MRI and MEG signals.

#### Ramp Up and Ramp Down Curves for Polarization Coils

As noted above, exposure to time varying magnetic fields, as occur when the polarization coil is switched, may result in uncomfortable magneto-stimulation. It has been shown that the threshold for such stimulation is proportional to both the time rate of change of the fields, and to the absolute field strength [3,4]. This suggests that the ramp up and ramp down curves for the polarization coils should be adjusted such that the field rate of change be made roughly inversely proportional to the present field strength - an exponential time course for ramp up where, B, the magnetic field is described as:

$$B(t) = B_{\max} (1 - e^{-\frac{t}{\tau}})$$

and a ramp down, where:

$$B(t) = B_{\max} \times e^{-\frac{t}{\tau}} B$$

5            This consideration will allow the use of the maximum possible polarization fields without magneto-stimulation of the patient.

            Consequently, the present invention provides a method of ULF-MRI, comprising generating a magnetic field using the ULF-MRI device (10), and then adjusting the magnetic field's rate of change using the ULF-MRI device (10), so that  
10          it is inversely proportional to the magnetic field's strength. The adjusting step comprises the step of ramping the magnetic field exponentially as a function of time. Preferably, the magnetic field used in ULF-MRI is greater than 500 milli-Gauss.

#### References

15            The following publications are incorporated by reference herein:

[1] Savukov, M and Romalis, Physical Review Letters, 94 (12), p. 12300 (2005).

[2] Lauterbur, P.C., "Image formation by induced local interactions: Examples employing nuclear magnetic resonance," Nature, 242, p. 190-191 (1973).

20            [3] Cohen, M.S., Weisskoff, R.M., Rzedzian, R.R., and Kantor, H.L., "Sensory stimulation by time-varying magnetic fields," Magnetic Resonance in Medicine, 14(2): p. 409-14 (1990).

[4] Harvey, P.R., and P Mansfield, P., "Avoiding peripheral nerve stimulation: gradient waveform criteria for optimum resolution in echo-planar imaging," Magnetic  
25          Resonance in Medicine, 32 (2): p. 236-41 (1994)

#### Conclusion

            This concludes the description of the preferred embodiment of the present invention. The foregoing description of one or more embodiments of the invention

has been presented for the purposes of illustration and description. It is not intended to be exhaustive or to limit the invention to the precise form disclosed. Many modifications and variations are possible in light of the above teaching. It is intended that the scope of the invention be limited not by this detailed description, but rather by

5 the claims appended hereto.

## WHAT IS CLAIMED IS:

1. An apparatus for Ultra Low Field Magnetic Resonance Imaging, comprising:  
a portable Ultra Low Field-Magnetic Resonance Imaging (ULF-MRI) device,  
5 contained in a Faraday cage, for generating a magnetic field that is detected using one or more magnetic field detectors for use as an imaging field, wherein the magnetic field is generated using pairs of electromagnet coils, each pair of electromagnet coils is orthogonal to two other pairs of electromagnet coils, and the electromagnet coils in each pair are positioned opposite each other on the Faraday cage's surface.  
10
2. The apparatus of claim 1, wherein the magnetic field detectors are superconducting quantum interference devices (SQUIDs).
3. The apparatus of claim 1, wherein the magnetic field detectors are  
15 based on an atomic magnetometer.
4. The apparatus of claim 1, wherein the Faraday cage is collapsible.
5. The apparatus of claim 1, wherein the Faraday cage has width, height  
20 and length dimensions less than 2 meters.
6. The apparatus of claim 1, further comprising an earth field cancellation coil set integrated into the Faraday cage's walls.
7. The apparatus of claim 6, wherein the Faraday cage provides support  
25 for the electromagnet coils.
8. The apparatus of claim 1, further comprising a collapsible patient bed substantially contained inside the Faraday cage.

9. A method of Ultra Low Field Magnetic Resonance Imaging,  
5 comprising:  
generating a magnetic field using a Ultra Low Field-Magnetic Resonance  
Imaging device; and  
adjusting the magnetic field's rate of change, so that it is inversely  
proportional to the magnetic field's strength.
- 10
10. The method of claim 9, wherein the adjusting step comprises the step  
of ramping the magnetic field exponentially as a function of time.
11. The method of claim 9, wherein the magnetic field is greater than 500  
15 milli-Gauss.
12. A method of performing Ultra Low Field Magnetic Resonance  
Imaging, comprising:  
generating a magnetic field using a Ultra Low Field-Magnetic Resonance  
20 Imaging device; and  
placing arrays of magnetic field detectors distributed across a patient to detect  
the magnetic field.
13. The method of claim 12, wherein the magnetic field detectors are  
25 superconducting quantum interference devices (SQUIDs).
14. The method of claim 12, wherein the magnetic field detectors are  
atomic magnetometers.

15. The method of claim 12, comprising setting up pairs of electromagnets to generate the magnetic field in each of three orthogonal directions.

5 16. The method of claim 15, comprising steering the magnetic field using the electromagnets.

17. A method of improving contrast in Ultra Low Field Magnetic Resonance Imaging (ULF-MRI), comprising:

10 (a) performing an initial magnetization step for a Ultra Low Field-Magnetic Resonance Imaging device over a time interval, thereby exposing a sample within the device to magnetic fields of order 10 milli-Tesla; and

(b) applying at least one inversion pulse to rotate the sample's magnetization during the time interval.

15 18. The method of claim 17, wherein the inversion pulse is adiabatic.

19. A method of Ultra Low Field Magnetic Resonance Imaging (ULF-MRI), comprising:

20 generating a magnetic field using a Ultra Low Field-Magnetic Resonance Imaging device; and

utilizing an echo planar imaging technique for the magnetic field to improve contrast.

25 20. A method of Ultra Low Field Magnetic Resonance Imaging (ULF-MRI), comprising:

generating a magnetic field using a Ultra Low Field-Magnetic Resonance Imaging device; and

scanning the magnetic field in a range 1-500 micro-Tesla.

21. A method of Ultra Low Field Magnetic Resonance Imaging, comprising:

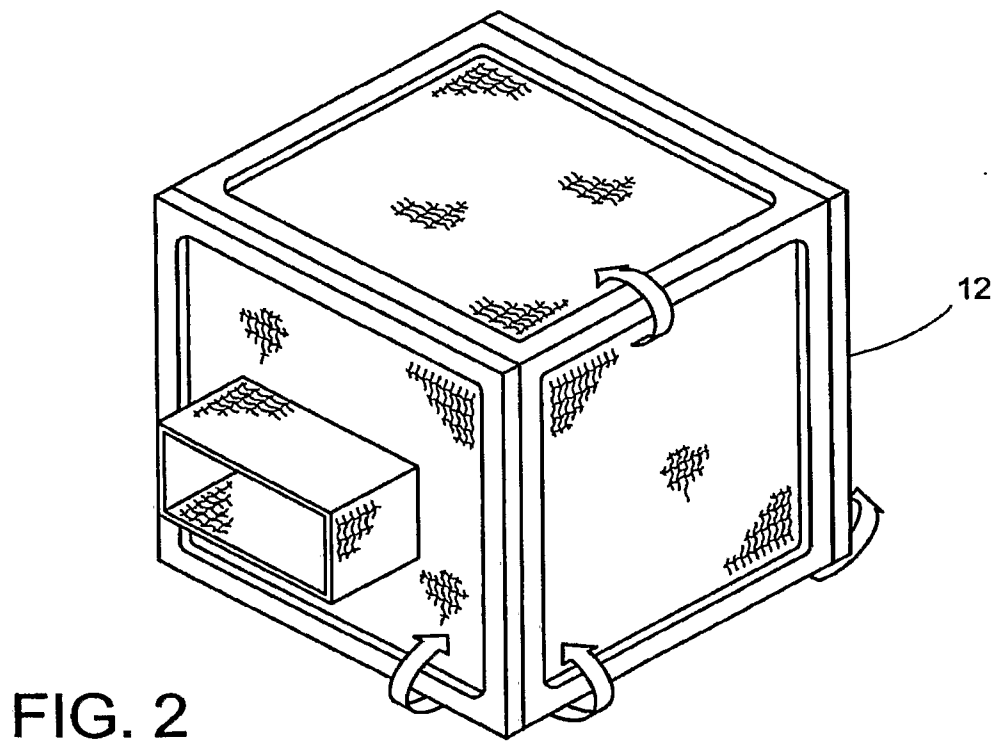
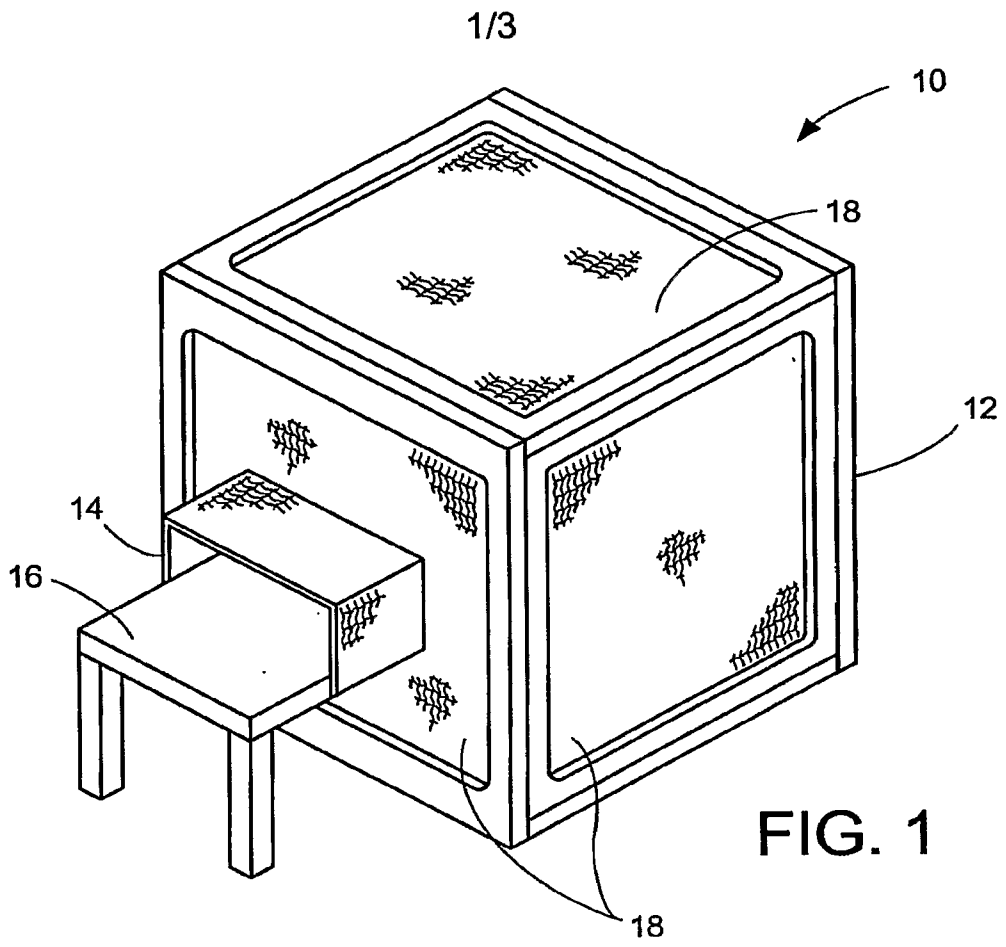
generating a magnetic field using a Ultra Low Field-Magnetic Resonance Imaging device; and

5 placing an imaging coil inside a patient's mouth to image inside the patient's brain using the magnetic field.

22. A method of mathematically combining magnetoencephalography (MEG) and magnetic resonance imaging (MRI) signals, comprising:

10 generating MEG signals and MRI signals in a Ultra Low Field-Magnetic Resonance Imaging device; and

detecting dipole fields from the MEG signals to identify approximate locations of sources of internally generated signals for a sample placed within the Ultra Low Field-Magnetic Resonance Imaging device, wherein the sources of internally  
15 generated signals are excluded from the MRI signals' reconstruction in order to both improve an overall signal-to-noise ratio and to associate locations of the MRI and MEG signals.



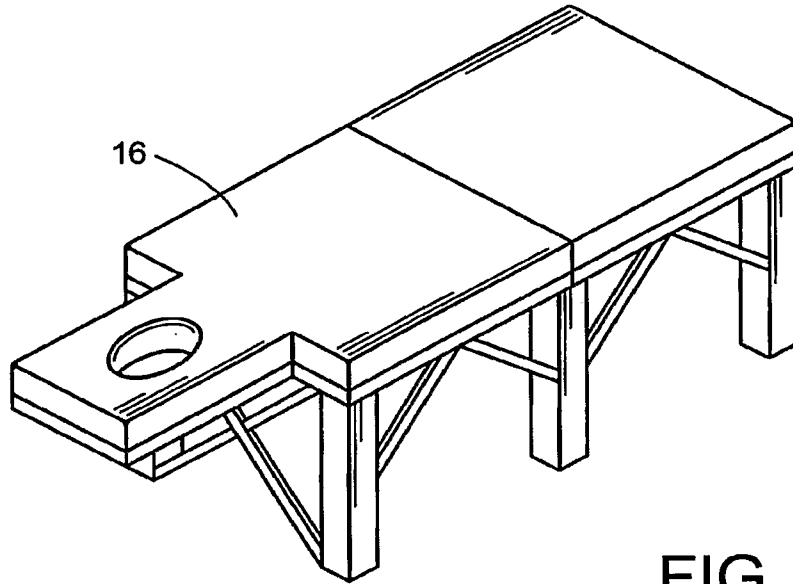


FIG. 3

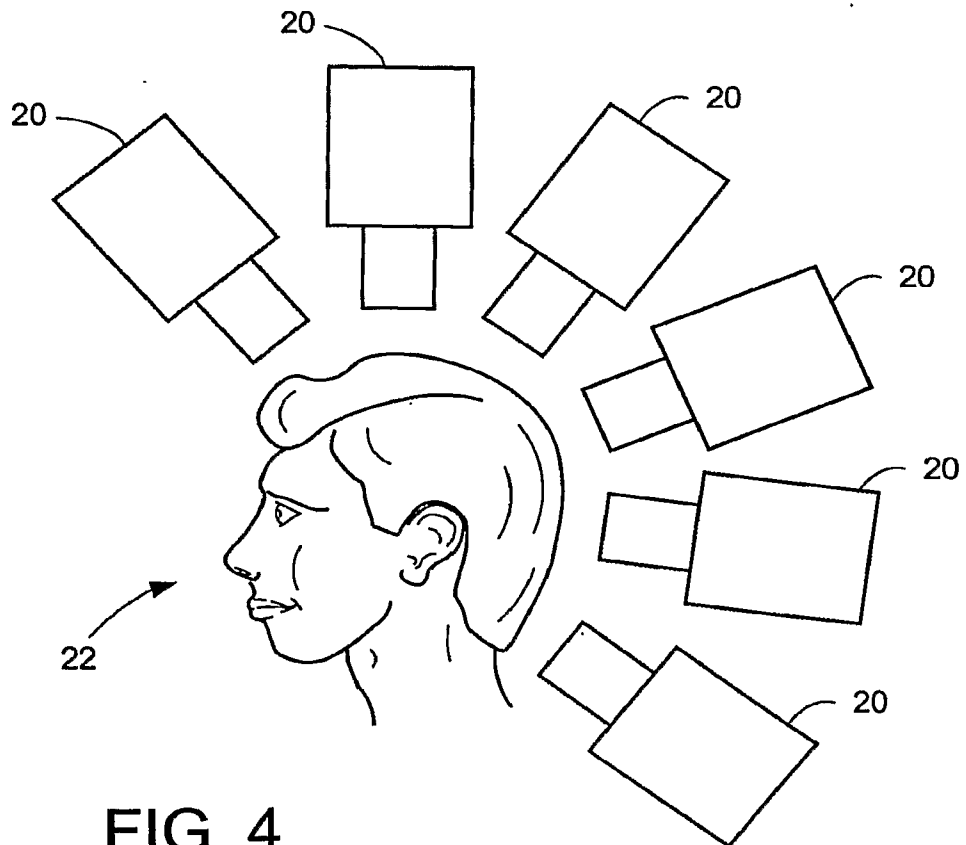


FIG. 4

3/3

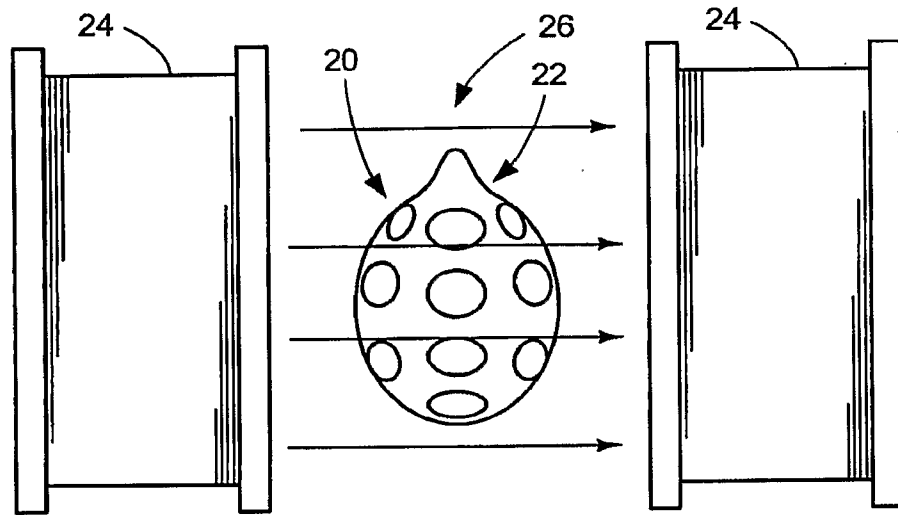


FIG. 5

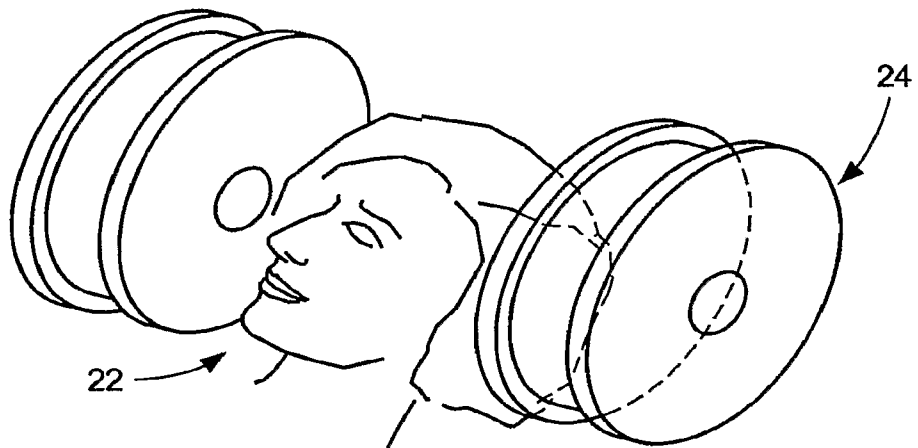


FIG. 6