

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
8 September 2006 (08.09.2006)

PCT

(10) International Publication Number
WO 2006/093804 A2

(51) International Patent Classification: Not classified

(21) International Application Number:
PCT/US2006/006459

(22) International Filing Date:
24 February 2006 (24.02.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
11/067,325 25 February 2005 (25.02.2005) US

(71) Applicant (for all designated States except US):
NANOSET LLC [US/US]; 349 West Commercial
Street Suite 2490, East Rochester, NY 14445 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **WANG, Xingwu**
[US/US]; 1886 East Drive, Wellsville, NY 14895 (US).
GREENWALD, Howard J. [US/US]; 111 Hickory Ridge
Road, Rochester, NY 14625 (US).

(74) Agents: **CURATOLO, Joseph G.** et al.; 24500 Center
Ridge Road, Suite 280, Cleveland, OH 44145 (US).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US,
UZ, VC, VN, YU, ZA, ZM, ZW.

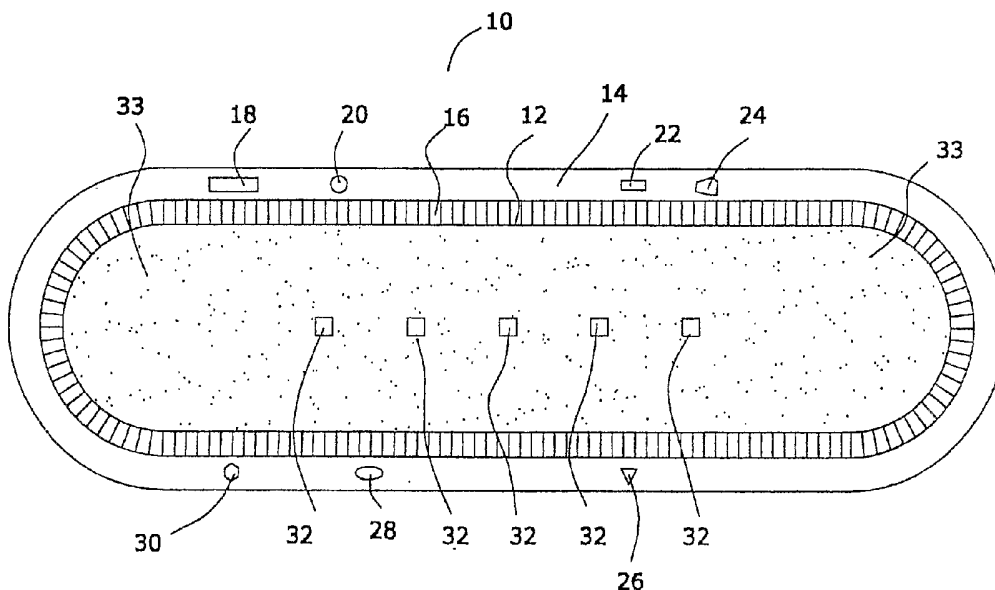
(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT,
RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished
upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: COATED SUBSTRATE ASSEMBLY



(57) Abstract: A coated assembly comprised of a coating that has a relative magnetic permeability of at least 1.1 over the range of frequencies of from about 10 megahertz to about 200 megahertz, an increase of such relative magnetic permeability over such range of from about 1×10^{-14} to about 1×10^{-6} per hertz, and a magnetization, when measured at a direct current magnetic field of 2 Tesla, of from about 0.1 to about 10 electromagnetic units per cubic centimeter.

WO 2006/093804 A2

COATED SUBSTRATE ASSEMBLYField of the invention

A coated assembly comprised of a coating that has a relative magnetic permeability of at least 1.1 over the range of frequencies of from about 10 megahertz to about 200 megahertz, an increase of such relative magnetic permeability over such range of from about 1×10^{-14} to about 1×10^{-6} per hertz, and a magnetization, when measured at a direct current magnetic field of 2 Tesla, of from about 0.1 to about 10 electromagnetic units per cubic centimeter.

Background of the invention

Published United States patent application US 2004/0093075 discloses that, although magnetic resonance imaging (MRI) is widely used, there is a difficulty in using MRI with prior art stents because such stents distort the magnetic resonance images of blood vessels. As is disclosed in column 2 of this published U.S. patent application, "In the medical field, magnetic resonance imaging (MRI) is used to non-invasively produce medical information....While researching heart problems, it was found that all the currently used metal stents distorted the magnetic resonance images of blood vessels. As a result, it was impossible to study the blood flow in the stents and the area directly around the stents for determining tissue response to different stents in the heart region. A solution, which would allow the development of a heart valve which could be inserted with the patients only slightly sedated, locally anesthetized, and released from the hospital quickly (within a day) after a procedure and would allow the in situ magnetic resonance imaging of stents, has long been sought but yet equally as long eluded those skilled in the art" (see paragraphs 0008, 0009, and 0010).

Published United States patent application US 2004/0093075 does not provide a solution to the MRI imaging of stents that it broadly applicable to many prior art stents, and to other assemblies. Although the applicant of this patent application claims that the stents depicted in his Figures 11, 12, 13, and 14 have improved imageability, there is no claim made of a process for rendering other stents (and assemblies) with different configurations more imageable; furthermore, it is not clear whether the process of this published patent application provides good resolution. It is an object of this invention to provide such a process, and such an improved stent.

Summary

There is provided a coated assembly comprised of a coating that has a relative magnetic permeability of at least 1.1 over the range of frequencies of from about 10 megahertz to about 200 megahertz, an increase of such relative magnetic permeability over such range of from about 1×10^{-14} to about 1×10^{-6} per hertz, and a magnetization, when measured at a direct current magnetic field of 2 Tesla, of from about 0.1 to about 10 electromagnetic units per cubic centimeter.

Brief description of the drawings

The above noted and other features of the invention will be better understood from the following drawings, and the accompanying description of them in the specification, wherein like numerals refer to like elements, and wherein:

Figure 1 is a schematic diagram of one preferred seed assembly of the invention;

5 Figure 1A is a schematic diagram of another preferred seed assembly of the invention;

Figure 2 is a schematic illustration of one process of the invention that may be used to make nanomagnetic material;

Figure 2A is a schematic illustration of a process that may be used to make and collect nanomagnetic particles;

10 Figure 3 is a flow diagram of another process that may be used to make the nanomagnetic compositions of this invention;

Figure 3A is a graph of the magnetic order of a nanomagnetic material plotted versus its temperature;

15 Figure 4 is a phase diagram showing the phases in various nanomagnetic materials comprised of moieties A, B, and C;

Figures 4A and 4B illustrate how the magnetic order of the nanomagnetic particles of this invention is destroyed at a temperature in excess of the phase transition temperature;

Figure 5 is a schematic representation of what occurs when an electromagnetic field is contacted with a nanomagnetic material;

20 Figure 5A illustrates the coherence length of the nanomagnetic particles of this invention;

Figure 6 is a schematic sectional view of a shielded conductor assembly that is comprised of a conductor and, disposed around such conductor, a film of nanomagnetic material;

Figures 7A through 7E are schematic representations of other shielded conductor assemblies that are similar to the assembly of Figure 6;

25 Figure 8 is a schematic representation of a deposition system for the preparation of aluminum nitride materials;

Figure 9 is a schematic, partial sectional illustration of a coated substrate that, in the preferred embodiment illustrated, is comprised of a coating disposed upon a stent;

30 Figure 9A is a schematic illustration of a coated substrate that is similar to the coated substrate of Figure 9 but differs therefrom in that it contains two layers of dielectric material;

Figure 10 is a schematic view of a typical stent that is comprised of wire mesh constructed in such a manner as to define a multiplicity of openings;

Figure 11 is a graph of the magnetization of an object (such as an uncoated stent, or a coated stent) when subjected to an electromagnetic field, such as an MRI field;

35 Figure 11A is a graph of the magnetization of a composition comprised of species with different magnetic susceptibilities when subjected to an electromagnetic field, such as an MRI field;

Figure 12 is a graph of the reactance of an object (such as an uncoated stent, or a coated stent) when subjected to an electromagnetic field, such as an MRI field;

Figure 13 is a graph of the image clarity of an object (such as an uncoated stent, or a coated stent) when subjected to an electromagnetic field, such as an MRI field;

5 Figure 14 is a phase diagram of a material that is comprised of moieties A, B, and C;

Figure 15 is a schematic view of a coated substrate comprised of a substrate and a multiplicity of nanoelectrical particles;

Figures 16A and 16B illustrate the morphological density and the surface roughness of a coating on a substrate;

10 Figure 17A is a schematic representation of a stent comprised of plaque disposed inside the inside wall;

Figure 17B illustrates three images produced from the imaging of the stent of Figure 17A, depending upon the orientation of such stent in relation to the MRI imaging apparatus reference line;

15 Figure 17C illustrates three images obtained from the imaging of the stent of Figure 17A when the stent has the nanomagnetic coating of this invention disposed about it;

Figures 18A and 18B illustrate a hydrophobic coating and a hydrophilic coating, respectively, that may be produced by the process of this invention;

Figure 19 illustrates a coating disposed on a substrate in which the particles in their coating have diffused into the substrate to form an interfacial diffusion layer;

20 Figure 20 is a sectional schematic view of a coated substrate comprised of a substrate and, bonded thereto, a layer of nano-sized particles;

Figure 20A is a partial sectional view of an indentation within a coating that, in turn, is coated with a multiplicity of receptors;

25 Figure 20B is a schematic of an electromagnetic coil set aligned to an axis and which in combination create a magnetic standing wave;

Figure 20C is a three-dimensional schematic showing the use of three sets of magnetic coils arranged orthogonally;

Figure 21 is a schematic illustration of one process for preparing a coating with morphological indentations;

30 Figure 22 is a schematic illustration of a drug molecule disposed inside of an indentation;

Figure 23 is a schematic illustration of one preferred process for administering a drug into the arm of a patient near a stent via an injector;

Figure 24 is a schematic illustration of a preferred binding process of the invention;

Figure 25 is a schematic view of a preferred coated stent of the invention;

35 Figure 26 is a graph of a typical response of a magnetic drug particle to an applied electromagnetic field;

Figures 27A and 27B illustrate the effect of applied fields upon a nanomagnetic and upon magnetic drug particles;

Figure 28 is graph of a preferred nanomagnetic material and its response to an applied electromagnetic field, in which the applied field is applied against the magnetic moment of the nanomagnetic material;

Figure 29 illustrates the forces acting upon a magnetic drug particle as it approaches nanomagnetic material;

Figure 30 illustrates the situation that occurs after the drug particles have migrated into the layer of polymeric material and when one desires to release such drug particles;

Figure 31 illustrates the situation that occurs after the drug particles have migrated into the layer of polymeric material but when no external electromagnetic field is imposed;

Figure 32 is a partial view of a coated container over which is disposed a layer of material which changes its dimensions in response to an applied magnetic field;

Figure 33 is a partial view of magnetostrictive material prior to the time an orifice has been created in it;

Figure 34 is a schematic illustration of a magnetostrictive material bounded by nanomagnetic material;

Figure 35 is a schematic illustration of a preferred implantable device of this invention with improved MRI imageability;

Figure 36 is a sectional view of a component of a preferred stent assembly;

Figure 37 is a graph of the relative permeability of a coating of nanomagnetic material, and a coating of ferrite material, over the range from 0 hertz to greater than 1 gigahertz;

Figure 38 is a schematic illustration of the effects on the deposition of iron onto a substrate of a magnetron, illustrating how the concentration of iron decreases as the coated film thickness increases;

Figure 39 is a graph of the concentration of iron in the coating depicted in Figure 38 versus the thickness of the coating;

Figure 40 is a schematic of a preferred process for imaging a coated stent; and

Figure 41 is a schematic illustration of the resolution obtained with applicants' coated stent and, in particular, of the resolution obtained by MRI imaging of objects disposed within such coated stent;

Figure 42 is a flow diagram of a preferred phase imaging process;

Figure 43 is a schematic illustration of the phase shift obtained with applicants' coated stent; and

Figure 44 is a schematic illustration of one preferred coated stent assembly.

Description

In the first part of this specification, a preferred seed assembly will be described. Thereafter, other embodiments of the invention will be described.

Figure 1 is a schematic diagram of a preferred seed assembly 10 of this invention. Referring to Figure 1, and to the preferred embodiment depicted therein, it will be seen that assembly 10 is comprised of a sealed container 12 comprised of a multiplicity of radioactive particles 33.

In one preferred embodiment, and referring to Figure 1A, the assembly 10 is preferably comprised of a shield 35 that is adapted to prevent radiation from escaping from assembly 10 when such shield is in a first position, and to allow radiation to escape from assembly 10 when such shield is in a second position. It should be recognized that the depiction in Figure 1A is merely a schematic one that does not necessarily accurately illustrate the size, scale, shape, or functioning of the shield 35.

One may use prior art radiation shields as shield 35 to effectuate such a selective delivery of radiation from radioactive material 33. Some of these shields are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

Referring again to Figures 1 and 1A, and to the preferred embodiment depicted therein, the seed assembly 10 is preferably comprised of a polymeric material 14 disposed above the sealed container 12. In the embodiment depicted in Figure 1, the polymeric material 14 is contiguous with a layer 16 of magnetic material. In another embodiment, not shown in Figure 1, the polymeric material 14 is contiguous with the sealed container 12.

The polymeric material 14 is preferably comprised of one or more therapeutic agents 18, 20, 22, 24, 26, 28, and/or 30 that are adapted to be released from the polymeric material 14 when the assembly 10 is disposed within a biological organism. The polymeric material 14 may be, e.g., any of the drug eluting polymers known to those skilled in the art. These drug eluting polymers, and other polymeric materials, are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

Referring again to Figure 1, the release rate(s) of therapeutic agents 18 and/or 20 and/or 22 and/or 24 and/or 26 and/or 28 and/or 30 may be varied in, e.g., the manner suggested in column 6 of United States patent 5,194,581.

Referring again to Figure 1, the polymeric material 14 may comprise a reservoir for the therapeutic agent(s) 18 and/or 20 and/or 22 and/or 24 and/or 26 and/or 28 and/or 30. Such a reservoir may be constructed in accordance with the procedure described in United States patent 5,447,724. United States patent 5,447,724 also discloses the preparation of the "reservoir" in e.g., in columns 8 and 9 of the patent.

Referring again to Figure 1, the therapeutic agent(s) 18 and/or 20 and/or 22 and/or 24 and/or 26 and/or 28 and/or 30 may, e.g., be any one or more of the therapeutic agents disclosed in column 5 of United States patent 5,464,650.

Referring again to Figure 1A, the polymeric material 14 may be bound to the therapeutic agent(s) 18 and/or 20 and/or 22 and/or 24 and/or 26 and/or 28 by a linker, such as a photosensitive linker 37; although only one such photosensitive linker 37 is depicted in Figure 1A, it will be apparent

to those skilled in the art that many such photosensitive linkers are preferably bound to polymeric material 14.

In another embodiment, depicted in Figure 1A, the photosensitive linker 37 is bound to layer 16 comprised of nanomagnetic material. In yet another embodiment, the

photosensitive linker 37 is bound to the surface of container 12. Combinations of these bound linkers, and/or different therapeutic agents, may be used. This process of preparing and binding these photosensitive linkers is described in columns 8-9 of United States patent 5,470,307.

Referring again to Figure 1, one may use any of the therapeutic agents disclosed at columns 3 and 4 of United States patent 5,605,696 as agents 18 and/or 20 and/or 22 and/or 24 and/or 26 and/or 28 and/or 30.

Referring again to Figure 1, and to the preferred embodiment depicted therein, the therapeutic agents 18 and/or 20 and/or 22 and/or 24 and/or 26 and/or 28 and/or 30 may be one or more of the drugs disclosed in United States patent 6,624,138.

Delivery of anti-microtubule agent

In one embodiment, referring again to Figure 1, and referring to United States patent 6,689,803 (the entire disclosure of which is hereby incorporated by reference into this specification), one or more of the therapeutic agents 18 and/or 20 and/or 22 and/or 24 and/or 26 and/or 28 and/or 30 may be an anti-microtubule agent.

The term "anti-microtubule," as used in this specification (and in the specification of United States patent 6,689,803), refers to any "...protein, peptide, chemical, or other molecule which impairs the function of microtubules, for example, through the prevention or stabilization of polymerization.

Nanomagnetic particles 32

Referring again to Figures 1 and 1A, and to the preferred embodiment depicted therein, the sealed container 12 is preferably comprised of one or more nanomagnetic particles 32. Furthermore, in the preferred embodiment depicted in Figures 1 and 1A, a film 16 is disposed around sealed container 12, and this film is also preferably comprised of nanomagnetic particles 32 (not shown for the sake of simplicity of representation).

These nanomagnetic particles are described in "case XW-672," filed on March 24, 2004 by Xingwu Wang and Howard J. Greenwald as United States patent application U.S.S.N. 10/808,618.

In the remainder of this section of the patent application, reference will be had to some of the disclosure of U.S.S.N. 10/808,618 to help describe the nanomagnetic particles 32.

In one embodiment of the invention depicted in Figure 1, and disposed within sealed container 12, there is collection of nanomagnetic particles 32 with an average particle size of less than about 100 nanometers. The average coherence length between adjacent nanomagnetic particles is preferably less than about 100 nanometers. The nanomagnetic particles 32 preferably have a saturation magnetization of from about 2 to about 3000 electromagnetic units per cubic centimeter, and a phase transition temperature of from about 40 to about 200 degrees Celsius.

Some similar nanomagnetic particles are disclosed in applicants' United States patent 6,502,972, which describes and claims a magnetically shielded conductor assembly comprised of a first conductor disposed within an insulating matrix, and a layer comprised of nanomagnetic material disposed around said first conductor, provided that such nanomagnetic material is not contiguous with said first conductor. In this assembly, the first conductor has a resistivity at 20 degrees Centigrade of from about 1 to about 100 micro ohm-centimeters, the insulating matrix is comprised of nano-sized particles wherein at least about 90 weight percent of said particles have a maximum dimension of from about 10 to about 100 nanometers, the insulating matrix has a resistivity of from about 1,000,000,000 to about 10,000,000,000,000 ohm-centimeter, the nanomagnetic material has an average particle size of less than about 100 nanometers, the layer of nanomagnetic material has a saturation magnetization of from about 200 to about 26,000 Gauss and a thickness of less than about 2 microns, and the magnetically shielded conductor assembly is flexible, having a bend radius of less than 2 centimeters.

The nanomagnetic film disclosed in United States patent 6,506,972 may be used to shield medical devices (such as the sealed container 12 of Figure 1) from external electromagnetic fields; and, when so used, it provides a certain degree of shielding. The medical devices so shielded may be coated with one or more drug formulations, as described elsewhere in this specification.

Figure 2 is a schematic illustration of one process of the invention that may be used to make nanomagnetic material. This Figure 2 is similar in many respects to the Figure 1 of United States patent 5,213,851.

Referring to Figure 2, and in the preferred embodiment depicted therein, it is preferred that the reagents charged into misting chamber 11 will be sufficient to form a nano-sized ferrite in the process. The term ferrite, as used in this specification, is refers to a material that exhibits ferromagnetism. Ferrites are extensively described in United States patent 5,213,851.

As will be apparent to those skilled in the art, in addition to making nano-sized ferrites by the process depicted in Figure 2, one may also make other nano-sized materials such as, e.g., nano-sized nitrides and/or nano-sized oxides containing moieties A, B, and C, as is described elsewhere in this specification. For the sake of simplicity of description, and with regard to Figure 2, a discussion will be had regarding the preparation of ferrites, it being understood that, e.g., other materials may also be made by such process.

Referring again to Figure 2, and to the production of ferrites by such process, in one embodiment, the ferromagnetic material contains Fe_2O_3 . See, for example, United States patent 3,576,672 of Harris et al. As will be apparent, the corresponding nitrides also may be made.

In yet another embodiment, the ferromagnetic material contains one or more of the moieties A, B, and C disclosed in the phase diagram disclosed elsewhere in this specification and discussed elsewhere in this specification.

Referring again to Figure 2, and in the preferred embodiment depicted therein, it will be appreciated that the solution 9 will preferably comprise reagents necessary to form the required

magnetic material. For example, in one embodiment, in order to form the spinel nickel ferrite of the formula NiFe_2O_4 , the solution should contain nickel and iron, which may be present in the form of nickel nitrate and iron nitrate. By way of further example, one may use nickel chloride and iron chloride to form the same spinel. By way of further example, one may use nickel sulfate and iron sulfate.

5 It will be apparent to skilled chemists that many other combinations of reagents, both stoichiometric and nonstoichiometric, may be used in applicants' process to make many different magnetic materials.

In one preferred embodiment, the solution 9 contains the reagent needed to produce a desired ferrite in stoichiometric ratio. Thus, to make the NiFe_2O_4 ferrite in this embodiment, one mole of nickel
10 nitrate may be charged with every two moles of iron nitrate.

In one embodiment, the starting materials are powders with purities exceeding 99 percent.

In one embodiment, compounds of iron and the other desired ions are present in the solution in the stoichiometric ratio.

The ions described above are preferably available in solution 9 in water-soluble form, such as,
15 e.g., in the form of water-soluble salts. Thus, e.g., one may use the nitrates or the chlorides or the sulfates or the phosphates of the cations. Other anions which form soluble salts with the cation(s) also may be used.

Alternatively, one may use salts soluble in solvents other than water. Some of these other solvents which may be used to prepare the material include nitric acid, hydrochloric acid, phosphoric
20 acid, sulfuric acid, and the like. As is well known to those skilled in the art, many other suitable solvents may be used; see, e.g., J. A. Riddick et al., "Organic Solvents, Techniques of Chemistry," Volume II, 3rd edition (Wiley-Interscience, New York, N.Y., 1970).

In one preferred embodiment, where a solvent other than water is used, each of the cations is present in the form of one or more of its oxides. For example, one may dissolve iron oxide in nitric
25 acid, thereby forming a nitrate. For example, one may dissolve zinc oxide in sulfuric acid, thereby forming a sulfate. One may dissolve nickel oxide in hydrochloric acid, thereby forming a chloride. Other means of providing the desired cation(s) will be readily apparent to those skilled in the art.

In general, as long as the desired cation(s) are present in the solution, it is not significant how the solution was prepared.

30 As long as the metals present in the desired ferrite material are present in solution 9 in the desired stoichiometry, it does not matter whether they are present in the form of a salt, an oxide, or in another form. In one embodiment, however, it is preferred to have the solution contain either the salts of such metals, or their oxides.

The solution 9 of the compounds of such metals preferably will be at a concentration of from
35 about 0.01 to about 1,000 grams of said reagent compounds per liter of the resultant solution. As used in this specification, the term liter refers to 1,000 cubic centimeters.

In one embodiment, it is preferred that solution 9 have a concentration of from about 1 to about 300 grams per liter and, preferably, from about 25 to about 170 grams per liter. It is even more preferred that the concentration of said solution 9 be from about 100 to about 160 grams per liter. In an even more preferred embodiment, the concentration of said solution 9 is from about 140 to about 160 grams per liter.

Referring again to Figure 2, and to the preferred embodiment depicted therein, the solution 9 in misting chamber 11 is preferably caused to form into an aerosol, such as a mist.

The term aerosol, as used in this specification, refers to a suspension of ultramicroscopic solid or liquid particles in air or gas, such as smoke, fog, or mist. See, e.g., page 15 of "A dictionary of mining, mineral, and related terms," edited by Paul W. Thrush (U.S. Department of the Interior, Bureau of Mines, 1968).

As used in this specification, the term mist refers to gas-suspended liquid particles which have diameters less than 10 microns.

The aerosol/mist consisting of gas-suspended liquid particles with diameters less than 10 microns may be produced from solution 9 by any conventional means that causes sufficient mechanical disturbance of said solution. Thus, one may use mechanical vibration. In one preferred embodiment, ultrasonic means are used to mist solution 9. As is known to those skilled in the art, by varying the means used to cause such mechanical disturbance, one can also vary the size of the mist particles produced.

As is known to those skilled in the art, ultrasonic sound waves (those having frequencies above 20,000 hertz) may be used to mechanically disturb solutions and cause them to mist. Thus, by way of illustration, one may use the ultrasonic nebulizer sold by the DeVilbiss Health Care, Inc. of Somerset, Pennsylvania; see, e.g., the "Instruction Manual" for the "Ultra-Neb 99 Ultrasonic Nebulizer, publication A-850-C (published by DeVilbiss, Somerset, Pa., 1989).

In the embodiment shown in Figure 2, the oscillators of ultrasonic nebulizer 13 are shown contacting an exterior surface of misting chamber 11. In this embodiment, the ultrasonic waves produced by the oscillators are transmitted via the walls of the misting chamber 11 and effect the misting of solution 9.

In another embodiment, not shown, the oscillators of ultrasonic nebulizer 13 are in direct contact with solution 9.

In one embodiment, it is preferred that the ultrasonic power used with such machine is in excess of one watt and, more preferably, in excess of 10 watts. In one embodiment, the power used with such machine exceeds about 50 watts.

During the time solution 9 is being caused to mist, it is preferably contacted with carrier gas to apply pressure to the solution and mist. It is preferred that a sufficient amount of carrier gas be introduced into the system at a sufficiently high flow rate so that pressure on the system is in excess of atmospheric pressure. Thus, for example, in one embodiment wherein chamber 11 has a volume of

about 200 cubic centimeters, the flow rate of the carrier gas was from about 100 to about 150 milliliters per minute.

In one embodiment, the carrier gas 15 is introduced via feeding line 17 at a rate sufficient to cause solution 9 to mist at a rate of from about 0.5 to about 20 milliliters per minute. In one
5 embodiment, the misting rate of solution 9 is from about 1.0 to about 3.0 milliliters per minute.

Substantially any gas that facilitates the formation of plasma may be used as carrier gas 15. Thus, by way of illustration, one may use oxygen, air, argon, nitrogen, and the like. It is preferred that the carrier gas used be a compressed gas under a pressure in excess 760 millimeters of mercury. In this
10 embodiment, the use of the compressed gas facilitates the movement of the mist from the misting chamber 11 to the plasma region 21.

The misting container 11 may be any reaction chamber conventionally used by those skilled in the art and preferably is constructed out of such acid-resistant materials such as glass, plastic, and the like.

The mist from misting chamber 11 is fed via misting outlet line 19 into the plasma region 21 of
15 plasma reactor 25. In plasma reactor 25, the mist is mixed with plasma generated by plasma gas 27 and subjected to radio frequency radiation provided by a radio-frequency coil 29.

The plasma reactor 25 provides energy to form plasma and to cause the plasma to react with the mist. Any of the plasmas reactors well known to those skilled in the art may be used as plasma reactor 25. Some of these plasma reactors are described in J. Mort et al.'s "Plasma Deposited Thin Films" (CRC
20 Press Inc., Boca Raton, Fla., 1986); in "Methods of Experimental Physics," Volume 9--Parts A and B, Plasma Physics (Academic Press, New York, 1970/1971); and in N. H. Burlingame's "Glow Discharge Nitriding of Oxides," Ph.D. thesis (Alfred University, Alfred, N.Y., 1985), available from University Microfilm International, Ann Arbor, Mich.

In one preferred embodiment, the plasma reactor 25 is a "model 56 torch" available from the
25 TAFA Inc. of Concord, N.H. It is preferably operated at a frequency of about 4 megahertz and an input power of 30 kilowatts.

Referring again to Figure 2, and to the preferred embodiment depicted therein, it will be seen that into feeding lines 29 and 31 is fed plasma gas 27. As is known to those skilled in the art, a plasma can be produced by passing gas into a plasma reactor. A discussion of the formation of plasma is
30 contained in B. Chapman's "Glow Discharge Processes" (John Wiley & Sons, New York, 1980)

In one preferred embodiment, the plasma gas used is a mixture of argon and oxygen. In another embodiment, the plasma gas is a mixture of nitrogen and oxygen. In yet another embodiment, the plasma gas is pure argon or pure nitrogen.

When the plasma gas is pure argon or pure nitrogen, it is preferred to introduce into the plasma
35 reactor at a flow rate of from about 5 to about 30 liters per minute.

When a mixture of oxygen and either argon or nitrogen is used, the concentration of oxygen in the mixture preferably is from about 1 to about 40 volume percent and, more preferably, from about 15

to about 25 volume percent. When such a mixture is used, the flow rates of each gas in the mixture should be adjusted to obtain the desired gas concentrations. Thus, by way of illustration, in one embodiment that uses a mixture of argon and oxygen, the argon flow rate is 15 liters per minute, and the oxygen flow rate is 40 liters per minute.

5 In one embodiment, auxiliary oxygen 34 is fed into the top of reactor 25, between the plasma region 21 and the flame region 40, via lines 36 and 38. In this embodiment, the auxiliary oxygen is not involved in the formation of plasma but is involved in the enhancement of the oxidation of the ferrite material.

10 Radio frequency energy is applied to the reagents in the plasma reactor 25, and it causes vaporization of the mist.

In general, the energy is applied at a frequency of from about 100 to about 30,000 kilohertz. In one embodiment, the radio frequency used is from about 1 to 20 megahertz. In another embodiment, the radio frequency used is from about 3 to about 5 megahertz.

15 As is known to those skilled in the art, such radio frequency alternating currents may be produced by conventional radio frequency generators. Thus, by way of illustration, said TAPA Inc. "model 56 torch" may be attached to a radio frequency generator rated for operation at 35 kilowatts which manufactured by Lepel Company (a division of TAPA Inc.) and which generates an alternating current with a frequency of 4 megahertz at a power input of 30 kilowatts. Thus, e.g., one may use an induction coil driven at 2.5-5.0 megahertz that is sold as the "PLASMOC 2" by ENI Power Systems, Inc. of Rochester, New York.

20 The use of these type of radio-frequency generators is described in the Ph.D. theses entitled (1) "Heat Transfer Mechanisms in High-Temperature Plasma Processing of Glasses," Donald M. McPherson (Alfred University, Alfred, N.Y., January, 1988) and (2) the aforementioned Nicholas H. Burlingame's "Glow Discharge Nitriding of Oxides."

25 The plasma vapor 23 formed in plasma reactor 25 is allowed to exit via the aperture 42 and can be visualized in the flame region 40. In this region, the plasma contacts air that is at a lower temperature than the plasma region 21, and a flame is visible. A theoretical model of the plasma/flame is presented on pages 88 et seq. of said McPherson thesis.

30 The vapor 44 present in flame region 40 is propelled upward towards substrate 46. Any material onto which vapor 44 will condense may be used as a substrate. Thus, by way of illustration, one may use nonmagnetic materials such alumina, glass, gold-plated ceramic materials, and the like. In one embodiment, substrate 46 consists essentially of a magnesium oxide material such as single crystal magnesium oxide, polycrystalline magnesium oxide, and the like.

35 In another embodiment, the substrate 46 consists essentially of zirconia such as, e.g., yttrium stabilized cubic zirconia.

In another embodiment, the substrate 46 consists essentially of a material selected from the group consisting of strontium titanate, stainless steel, alumina, sapphire, and the like.

The aforementioned listing of substrates is merely meant to be illustrative, and it will be apparent that many other substrates may be used. Thus, by way of illustration, one may use any of the substrates mentioned in M. Sayer's "Ceramic Thin Films . . ." article, supra. Thus, for example, in one embodiment it is preferred to use one or more of the substrates described on page 286 of

5 "Superconducting Devices," edited by S. T. Ruggiero et al. (Academic Press, Inc., Boston, 1990).

One advantage of this embodiment of applicants' process is that the substrate may be of substantially any size or shape, and it may be stationary or movable. Because of the speed of the coating process, the substrate 46 may be moved across the aperture 42 and have any or all of its surface be coated.

10 As will be apparent to those skilled in the art, in the embodiment depicted in Figure 2, the substrate 46 and the coating 48 are not drawn to scale but have been enlarged to the sake of ease of representation.

Referring again to Figure 2, the substrate 46 may be at ambient temperature. Alternatively, one may use additional heating means to heat the substrate prior to, during, or after deposition of the

15 coating.

In one embodiment, illustrated in Figure 2A, the substrate is cooled so that nanomagnetic particles are collected on such substrate. Referring to Figure 2A, and in the preferred embodiment depicted therein, a precursor 1 that preferably contains moieties A, B, and C (which are described elsewhere in this specification) are charged to reactor 3; the reactor 3 may be the plasma reactor depicted in Figure 2, and/or it may be the sputtering reactor described elsewhere in this specification.

20 Referring again to Figure 2A, it will be seen that an energy source 5 is preferably used in order to cause reaction between moieties A, B, and C. The energy source 5 may be an electromagnetic energy source that supplies energy to the reactor 3. In one embodiment, there are at least two species of moiety A present, and at least two species of moiety C present. The two preferred moiety C species are oxygen and nitrogen.

25 Within reactor 3 moieties A, B, and C are preferably combined into a metastable state. This metastable state is then caused to travel towards collector 7. Prior to the time it reaches the collector 7, the ABC moiety is formed, either in the reactor 3 and/or between the reactor 3 and the collector 7.

30 In one embodiment, collector 7 is preferably cooled with a chiller 99 so that its surface 111 is at a temperature below the temperature at which the ABC moiety interacts with surface 111; the goal is to prevent bonding between the ABC moiety and the surface 111. In one embodiment, the surface 111 is at a temperature of less than about 30 degrees Celsius. In another embodiment, the temperature of surface 111 is at the liquid nitrogen temperature, i.e., about 77 degrees Kelvin.

After the ABC moieties have been collected by collector 7, they are removed from surface 111.

35 Referring again to Figure 2, and in one preferred embodiment, a heater (not shown) is used to heat the substrate to a temperature of from about 100 to about 800 degrees centigrade.

In one aspect of this embodiment, temperature sensing means (not shown) may be used to sense the temperature of the substrate and, by feedback means (not shown), adjust the output of the heater (not shown). In one embodiment, not shown, when the substrate 46 is relatively near flame region 40, optical pyrometry measurement means (not shown) may be used to measure the temperature near the substrate.

In one embodiment, a shutter (not shown) is used to selectively interrupt the flow of vapor 44 to substrate 46. This shutter, when used, should be used prior to the time the flame region has become stable; and the vapor should preferably not be allowed to impinge upon the substrate prior to such time.

The substrate 46 may be moved in a plane that is substantially parallel to the top of plasma chamber 25. Alternatively, or additionally, it may be moved in a plane that is substantially perpendicular to the top of plasma chamber 25. In one embodiment, the substrate 46 is moved stepwise along a predetermined path to coat the substrate only at certain predetermined areas.

In one embodiment, rotary substrate motion is utilized to expose as much of the surface of a complex-shaped article to the coating. This rotary substrate motion may be effectuated by conventional means. See, e.g., "Physical Vapor Deposition," edited by Russell J. Hill (Temescal Division of The BOC Group, Inc., Berkeley, Calif., 1986).

The process of this embodiment of the invention allows one to coat an article at a deposition rate of from about 0.01 to about 10 microns per minute and, preferably, from about 0.1 to about 1.0 microns per minute, with a substrate with an exposed surface of 35 square centimeters. One may determine the thickness of the film coated upon said reference substrate material (with an exposed surface of 35 square centimeters) by means well known to those skilled in the art.

The film thickness can be monitored in situ, while the vapor is being deposited onto the substrate. Thus, by way of illustration, one may use an IC-6000 thin film thickness monitor (also referred to as "deposition controller") manufactured by Leybold Inficon Inc. of East Syracuse, N.Y.

The deposit formed on the substrate may be measured after the deposition by standard profilometry techniques. Thus, e.g., one may use a DEKTAK Surface Profiler, model number 900051 (available from Sloan Technology Corporation, Santa Barbara, California).

In general, at least about 80 volume percent of the particles in the as-deposited film are smaller than about 1 micron. It is preferred that at least about 90 percent of such particles are smaller than 1 micron. Because of this fine grain size, the surface of the film is relatively smooth.

In one preferred embodiment, the as-deposited film is post-annealed.

It is preferred that the generation of the vapor in plasma reactor 25 be conducted under substantially atmospheric pressure conditions. As used in this specification, the term "substantially atmospheric" refers to a pressure of at least about 600 millimeters of mercury and, preferably, from about 600 to about 1,000 millimeters of mercury. It is preferred that the vapor generation occur at about atmospheric pressure. As is well known to those skilled in the art, atmospheric pressure at sea level is 760 millimeters of mercury.

The process of this invention may be used to produce coatings on a flexible substrate such as, e.g., stainless steel strips, silver strips, gold strips, copper strips, aluminum strips, and the like. One may deposit the coating directly onto such a strip. Alternatively, one may first deposit one or more buffer layers onto the strip(s). In other embodiments, the process of this invention may be used to produce
5 coatings on a rigid or flexible cylindrical substrate, such as a tube, a rod, or a sleeve.

Referring again to Figure 2, and in the embodiment depicted therein, as the coating 48 is being deposited onto the substrate 46, and as it is undergoing solidification thereon, it is preferably subjected to a magnetic field produced by magnetic field generator 50.

In this embodiment, it is preferred that the magnetic field produced by the magnetic field
10 generator 50 have a field strength of from about 2 Gauss to about 40 Tesla.

It is preferred to expose the deposited material for at least 10 seconds and, more preferably, for at least 30 seconds, to the magnetic field, until the magnetic moments of the nano-sized particles being deposited have been substantially aligned.

As used herein, the term "substantially aligned" means that the inductance of the device being
15 formed by the deposited nano-sized particles is at least 90 percent of its maximum inductance. One may determine when such particles have been aligned by, e.g., measuring the inductance, the permeability, and/or the hysteresis loop of the deposited material.

Thus, e.g., one may measure the degree of alignment of the deposited particles with an impedance meter, an inductance meter, or a SQUID.

In one embodiment, the degree of alignment of the deposited particles is measured with an
20 inductance meter. One may use, e.g., a conventional conductance meter.

When measuring the inductance of the coated sample, the inductance is preferably measured using an applied wave with a specified frequency. As the magnetic moments of the coated samples align, the inductance increases until a specified value; and it rises in accordance with a specified time
25 constant in the measurement circuitry.

In one embodiment, the deposited material is contacted with the magnetic field until the inductance of the deposited material is at least about 90 percent of its maximum value under the measurement circuitry. At this time, the magnetic particles in the deposited material have been aligned to at least about 90 percent of the maximum extent possible for maximizing the inductance of the
30 sample.

By way of illustration and not limitation, a metal rod with a diameter of 1 micron and a length of 1 millimeter, when uncoated with magnetic nano-sized particles, might have an inductance of about 1 nanohenry. When this metal rod is coated with, e.g., nano-sized ferrites, then the inductance of the coated rod might be 5 nanohenries or more. When the magnetic moments of the coating are aligned,
35 then the inductance might increase to 50 nanohenries, or more. As will be apparent to those skilled in the art, the inductance of the coated article will vary, e.g., with the shape of the article and also with the frequency of the applied electromagnetic field.

One may use any of the conventional magnetic field generators known to those skilled in the art to produce such as magnetic field.

In one embodiment, the magnetic field is 1.8 Tesla or less. In this embodiment, the magnetic field can be applied with, e.g., electromagnets disposed around a coated substrate.

5 For fields greater than about 2 Tesla, one may use superconducting magnets that produce fields as high as 40 Tesla.

In one embodiment, no magnetic field is applied to the deposited coating while it is being solidified. In this embodiment, as will be apparent to those skilled in the art, there still may be some alignment of the magnetic domains in a plane parallel to the surface of substrate as the deposited
10 particles are locked into place in a matrix (binder) deposited onto the surface.

In one embodiment, depicted in Figure 2, the magnetic field 52 is preferably delivered to the coating 48 in a direction that is substantially parallel to the surface 56 of the substrate 46. In another embodiment, depicted in Figure 1, the magnetic field 58 is delivered in a direction that is substantially perpendicular to the surface 56. In yet another embodiment, the magnetic field 60 is delivered in a
15 direction that is angularly disposed vis-à-vis surface 56 and may form, e.g., an obtuse angle (as in the case of field 62). As will be apparent, combinations of these magnetic fields may be used.

Figure 3 is a flow diagram of another process that may be used to make the nanomagnetic compositions of this invention. Referring to Figure 3, and to the preferred process depicted therein, it will be seen that nano-sized ferromagnetic material(s), with a particle size less than about 100
20 nanometers, is preferably charged via line 60 to mixer 62. It is preferred to charge a sufficient amount of such nano-sized material(s) so that at least about 10 weight percent of the mixture formed in mixer 62 is comprised of such nano-sized material. In one embodiment, at least about 40 weight percent of such mixture in mixer 62 is comprised of such nano-sized material. In another embodiment, at least about 50 weight percent of such mixture in mixer 62 is comprised of such nano-sized material.

25 In one embodiment, one or more binder materials are charged via line 64 to mixer 62. In one embodiment, the binder used is a ceramic binder. These ceramic binders are well known. Reference may be had, e.g., to pages 172-197 of James S. Reed's "Principles of Ceramic Processing," Second Edition (John Wiley & Sons, Inc., New York, New York, 1995). As is disclosed in the Reed book, the binder may be a clay binder (such as fine kaolin, ball clay, and bentonite), an organic colloidal particle
30 binder (such as microcrystalline cellulose), a molecular organic binder (such as natural gums, polysaccharides, lignin extracts, refined alginate, cellulose ethers, polyvinyl alcohol, polyvinylbutyral, polymethyl methacrylate, polyethylene glycol, paraffin, and the like.). etc.

In one embodiment, the binder is a synthetic polymeric or inorganic composition. Thus, and referring to George S. Brady et al.'s "Materials Handbook," (McGraw-Hill, Inc., New York, New York
35 1991), the binder may be acrylonitrile-butadiene-styrene (see pages 5-6), an acetal resin (see pages 6-7), an acrylic resin (see pages 10-12), an adhesive composition (see pages 14-18), an alkyd resin (see page 27-28), an allyl plastic (see pages 31-32), an amorphous metal (see pages 53-54), a biocompatible

material (see pages 95-98), boron carbide (see page 106), boron nitride (see page 107), camphor (see page 135), one or more carbohydrates (see pages 138-140), carbon steel (see pages 146-151), casein plastic (see page 157), cast iron (see pages 159-164), cast steel (see pages 166-168), cellulose (see pages 172-175), cellulose acetate (see pages 175-177), cellulose nitrate (see pages 177), cement (see page 178-180), ceramics (see pages 180-182), cermets (see pages 182-184), chlorinated polyethers (see pages 191-191), chlorinated rubber (see pages 191-193), cold-molded plastics (see pages 220-221), concrete (see pages 225-227), conductive polymers and elastomers (see pages 227-228), degradable plastics (see pages 261-262), dispersion-strengthened metals (see pages 273-274), elastomers (see pages 284-290), enamel (see pages 299-301), epoxy resins (see pages 301-302), expansive metal (see page 313), ferrosilicon (see page 327), fiber-reinforced plastics (see pages 334-335), fluoroplastics (see pages 345-347), foam materials (see pages 349-351), fusible alloys (see pages 362-364), glass (see pages 376-383), glass-ceramic materials (see pages 383-384), gypsum (see pages 406-407), impregnated wood (see pages 422-423), latex (see pages 456-457), liquid crystals (see page 479), lubricating grease (see pages 488-492), magnetic materials (see pages 505-509), melamine resin (see pages 5210-521), metallic materials (see pages 522-524), nylon (see pages 567-569), olefin copolymers (see pages 574-576), phenol-formaldehyde resin (see pages 615-617), plastics (see pages 637-639), polyarylates (see pages 647-648), polycarbonate resins (see pages 648), polyester thermoplastic resins (see pages 648-650), polyester thermosetting resins (see pages 650-651), polyethylenes (see pages 651-654), polyphenylene oxide (see pages 644-655), polypropylene plastics (see pages 655-656), polystyrenes (see pages 656-658), proteins (see pages 666-670), refractories (see pages 691-697), resins (see pages 697-698), rubber (see pages 706-708), silicones (see pages 747-749), starch (see pages 797-802), superalloys (see pages 819-822), superpolymers (see pages 823-825), thermoplastic elastomers (see pages 837-839), urethanes (see pages 874-875), vinyl resins (see pages 885-888), wood (see pages 912-916), mixtures thereof, and the like.

Referring again to Figure 3, one may charge to line 64 either one or more of these "binder material(s)" and/or the precursor(s) of these materials that, when subjected to the appropriate conditions in former 66, will form the desired mixture of nanomagnetic material and binder.

Referring again to Figure 3, and in the preferred process depicted therein, the mixture within mixer 62 is preferably stirred until a substantially homogeneous mixture is formed. Thereafter, it may be discharged via line 65 to former 66.

One process for making a fluid composition comprising nanomagnetic particles is disclosed in United States patent 5,804,095, "Magnetorheological Fluid Composition," of Jacobs et al. In this patent, there is disclosed a process comprising numerous material handling steps used to prepare a nanomagnetic fluid comprising iron carbonyl particles. One suitable source of iron carbonyl particles having a median particle size of 3.1 microns is the GAF Corporation.

The process of Jacobs et al, is applicable to the present invention, wherein such nanomagnetic fluid further comprises a polymer binder, thereby forming a nanomagnetic paint. In one embodiment,

the nanomagnetic paint is formulated without abrasive particles of cerium dioxide. In another embodiment, the nanomagnetic fluid further comprises a polymer binder, and aluminum nitride is substituted for cerium dioxide.

There are many suitable mixing processes and apparatus for the milling, particle size reduction, and mixing of fluids comprising solid particles. For example, e.g., iron carbonyl particles or other ferromagnetic particles of the paint may be further reduced to a size on the order of 100 nanometers or less, and/or thoroughly mixed with a binder polymer and/or a liquid solvent by the use of a ball mill, a sand mill, a paint shaker holding a vessel containing the paint components and hard steel or ceramic beads; a homogenizer (such as the Model Ytron Z made by the Ytron Quadro Corporation of Chesham, United Kingdom, or the Microfluidics M700 made by the MFIC Corporation of Newton, Ma.), a powder dispersing mixer (such as the Ytron Zyclon mixer, or the Ytron Xyclon mixer, or the Ytron PID mixer by the Ytron Quadro Corporation); a grinding mill (such as the Model F10 Mill by the Ytron Quadro Corporation); high shear mixers (such as the Ytron Y mixer by the Ytron Quadro Corporation), the Silverson Laboratory Mixer sold by the Silverson Corporation of East Longmeadow, Ma., and the like. The use of one or more of these apparatus in series or in parallel may produce a suitably formulated nanomagnetic paint.

Referring again to Figure 3, the former 66 is preferably equipped with an input line 68 and an exhaust line 70 so that the atmosphere within the former can be controlled. One may utilize an ambient atmosphere, an inert atmosphere, pure nitrogen, pure oxygen, mixtures of various gases, and the like. Alternatively, or additionally, one may use lines 68 and 70 to afford subatmospheric pressure, atmospheric pressure, or superatmospheric pressure within former 66.

In the embodiment depicted, former 66 is also preferably comprised of an electromagnetic coil 72 that, in response from signals from controller 74, can control the extent to which, if any, a magnetic field is applied to the mixture within the former 66 (and also within the mold 67 and/or the spinnerette 69).

The controller 74 is also adapted to control the temperature within the former 66 by means of heating/cooling assembly.

In the embodiment depicted in Figure 3, a sensor 78 preferably determines the extent to which the desired nanomagnetic properties have been formed with the nano-sized material in the former 66; and, as appropriate, the sensor 78 imposes a magnetic field upon the mixture within the former 66 until the desired properties have been obtained.

In one embodiment, the sensor 78 is the inductance meter discussed elsewhere in this specification; and the magnetic field is applied until at least about 90 percent of the maximum inductance obtainable with the alignment of the magnetic moments has been obtained.

The magnetic field is preferably imposed until the nano-sized particles within former 78 (and the material with which it is admixed) have a mass density of at least about 0.001 grams per cubic centimeter (and preferably at least about 0.01 grams per cubic centimeter), a saturation magnetization

of from about 1 to about 36,000 Gauss, a coercive force of from about 0.01 to about 5,000 Oersteds, and a relative magnetic permeability of from about 1 to about 500,000.

When the mixture within former 66 has the desired combination of properties (as reflected, e.g., by its substantially maximum inductance) and/or prior to that time, some or all of such mixture may be discharged via line 80 to a mold/extruder 67 wherein the mixture can be molded or extruded into a desired shape. A magnetic coil 72 also preferably may be used in mold/extruder 67 to help align the nano-sized particles.

Alternatively, or additionally, some or all of the mixture within former 66 may be discharged via line 82 to a spinnerette 69, wherein it may be formed into a fiber (not shown).

As will be apparent, one may make fibers by the process indicated that have properties analogous to the nanomagnetic properties of the coating 135 (described elsewhere in this specification), and/or nanoelectrical properties of the coating 141 (described elsewhere in this specification), and/or nanothermal properties of the coating 145 (also described elsewhere in this specification). Such fiber or fibers may be made into fabric by conventional means. By the appropriate selection and placement of such fibers, one may produce a shielded fabric which provides protection against high magnetic voltages and/or high voltages and/or excessive heat. Such shielded fabric may comprise the polymeric material 14 (see Figure 1).

Thus, in one embodiment, nanomagnetic and/or nanoelectrical and/or nanothermal fibers are woven together to produce a garment that will shield from the adverse effects of radiation such as, e.g., radiation experienced by astronauts in outer space. Such fibers may comprise the polymeric material 14 (see Figure 1).

Alternatively, or additionally, some or all of the mixture within former 66 may be discharged via line 84 to a direct writing applicator 90, such as a MicroPen applicator manufactured by OhmCraft Incorporated of Honeoye Falls, NY. Such an applicator is disclosed in United States patent 4,485,387, the disclosure of which is incorporated herein by reference. The use of this applicator to write circuits and other electrical structures is described in, e.g., United States patent 5,861,558 of Buhl et al, "Strain Gauge and Method of Manufacture", the disclosure of which is incorporated herein by reference.

In one preferred embodiment, the nanomagnetic, nanoelectrical, and/or nanothermal compositions of the present invention, along with various conductor, resistor, capacitor, and inductor formulations, are dispensed by the MicroPen device, to fabricate the circuits and structures of the present invention on devices such as, e.g. catheters and other biomedical devices.

In one preferred embodiment, involving the writing of nanomagnetic circuit patterns and/or thin films, the direct writing applicator 90 (as disclosed in U.S. patent 4,485,387) comprises an applicator tip 92 and an annular magnet 94, which provides a magnetic field 72. The use of such an applicator 90 to apply nanomagnetic coatings is particularly beneficial because the presence of the magnetic field from magnet 94, through which the nanomagnetic fluid flows serves to orient the magnetic particles in situ as such nanomagnetic fluid is applied to a substrate. Such an orienting effect is described in United

States patent 5,971,835, the disclosure of which is incorporated herein by reference. Once the nanomagnetic particles are properly oriented by such a field, or by another magnetic field source, the applied coating is cured by heating, by ultraviolet radiation, by an electron beam, or by other suitable means.

5 In one embodiment, not shown, one may form compositions comprised of nanomagnetic particles and/or nanoelectrical particles and/or nanothermal particles and/or other nano-sized particles by a sol-gel process. Thus, by way of illustration and not limitation, one may use one or more of the processes described in United States patents 6,287,639 (nanocomposite material comprised of inorganic particles and silanes), 6,337,117 (optical memory device comprised of nano-sized luminous
10 material), 6,527,972 (magnetorheological polymer gels), 6,589,457 (process for the deposition of ruthenium oxide thin films), 6,657,001 (polysiloxane compositions comprised of inorganic particles smaller than 100 nanometers), 6,666,935 (sol-gel manufactured energetic materials), and the like.

Nanomagnetic compositions comprised of moieties A, B, and C

15 The aforementioned process described in the preceding section of this specification, and the other processes described in this specification, may each be adapted to produce other, comparable nanomagnetic structures, as is illustrated in Figure 4.

Referring to Figure 4, and in the preferred embodiment depicted therein, a phase diagram 100 is presented. As is illustrated by this phase diagram 100, the nanomagnetic material used in this
20 embodiment of the invention preferably is comprised of one or more of moieties A, B, and C. The moieties A, B, and C described in reference to phase 100 of Figure 4 are not necessarily the same as the moieties A, B, and C described in reference to phase diagram 2000 described elsewhere in this specification..

In the embodiment depicted, the moiety A depicted in phase diagram 100 is preferably comprised of a magnetic element selected from the group consisting of a transition series metal, a rare
25 earth series metal, or actinide metal, a mixture thereof, and/or an alloy thereof. In one embodiment, the moiety A is iron. In another embodiment, moiety A is nickel. In yet another embodiment, moiety A is cobalt. In yet another embodiment, moiety A is gadolinium. In another embodiment, the A moiety is selected from the group consisting of samarium, holmium, neodymium, and one or more other members of the Lanthanide series of the periodic table of elements.

30 In one preferred embodiment, two or more A moieties are present, as atoms. In one aspect of this embodiment, the magnetic susceptibilities of the atoms so present are both positive.

In one embodiment, two or more A moieties are present, at least one of which is iron. In one aspect of this embodiment, both iron and cobalt atoms are present.

When both iron and cobalt are present, it is preferred that from about 10 to about 90 mole
35 percent of iron be present by mole percent of total moles of iron and cobalt present in the ABC moiety. In another embodiment, from about 50 to about 90 mole percent of iron is present. In yet another

embodiment, from about 60 to about 90 mole percent of iron is present. In yet another embodiment, from about 70 to about 90 mole percent of iron is present.

As is known to those skilled in the art, the transition series metals include chromium, manganese, iron, cobalt, and nickel. One may use alloys of iron, cobalt and nickel such as, e.g., iron--aluminum, iron--carbon, iron--chromium, iron--cobalt, iron--nickel, iron nitride (Fe_3N), iron phosphide, iron-silicon, iron-vanadium, nickel-cobalt, nickel-copper, and the like. One may use alloys of manganese such as, e.g., manganese-aluminum, manganese-bismuth, MnAs, MnSb, MnTe, manganese-copper, manganese-gold, manganese-nickel, manganese-sulfur and related compounds, manganese-antimony, manganese-tin, manganese-zinc, Heusler alloy W, and the like. One may use compounds and alloys of the iron group, including oxides of the iron group, halides of the iron group, borides of the transition elements, sulfides of the iron group, platinum and palladium with the iron group, chromium compounds, and the like.

One may use a rare earth and/or actinide metal such as, e.g., Ce, Pr, Nd, Pm, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu, La, mixtures thereof, and alloys thereof. One may also use one or more of the actinides such as, e.g., the actinides of Th, Pa, U, Np, Pu, Am, Cm, Bk, Cf, Es, Fm, Md, No, Lr, Ac, and the like.

These moieties, compounds thereof, and alloys thereof are well known and are described, e.g., in the text of R.S. Tebble et al. entitled "Magnetic Materials."

In one preferred embodiment, illustrated in Figure 4, moiety A is selected from the group consisting of iron, nickel, cobalt, alloys thereof, and mixtures thereof. In this embodiment, the moiety A is magnetic, i.e., it has a relative magnetic permeability of from about 1 to about 500,000. As is known to those skilled in the art, relative magnetic permeability is a factor, being a characteristic of a material, which is proportional to the magnetic induction produced in a material divided by the magnetic field strength; it is a tensor when these quantities are not parallel.

The moiety A of Figure 4 also preferably has a saturation magnetization of from about 1 to about 36,000 Gauss, and a coercive force of from about 0.01 to about 5,000 Oersteds.

The moiety A of Figure 4 may be present in the nanomagnetic material either in its elemental form, as an alloy, in a solid solution, or as a compound.

It is preferred at least about 1 mole percent of moiety A be present in the nanomagnetic material (by total moles of A, B, and C), and it is more preferred that at least 10 mole percent of such moiety A be present in the nanomagnetic material (by total moles of A, B, and C). In one embodiment, at least 60 mole percent of such moiety A is present in the nanomagnetic material, (by total moles of A, B, and C.)

In one embodiment, the nanomagnetic material has the formula $A_1A_2(B)_xC_1(C_2)_y$, wherein each of A_1 and A_2 are separate magnetic A moieties, as described above; B is as defined elsewhere in this specification; x is an integer from 0 to 1; each of C_1 and C_2 is as described elsewhere in this specification; and y is an integer from 0 to 1.

In this embodiment, there are always two distinct A moieties, such as, e.g., nickel and iron, iron and cobalt, etc. The A moieties may be present in equimolar amounts; or they may be present in non-equimolar amount.

In one aspect of this embodiment, either or both of the A₁ and A₂ moieties are radioactive.

5 Thus, e.g., either or both of the A₁ and A₂ moieties may be selected from the group consisting of radioactive cobalt, radioactive iron, radioactive nickel, and the like. These radioactive isotopes are well known.

In one preferred embodiment, at least one of the A₁ and A₂ moieties is radioactive cobalt. Complex metal chelate compounds containing radioactive metal isotopes have been known and utilized
10 in the prior art. For example, "tagged" Vitamin B12, that is Vitamin B12 containing a radioactive isotope of cobalt, has been used in the diagnosis of pernicious anemia and has been prepared via biochemical synthesis, wherein microbes are cultured in the presence of a cobalt-57 salt and produce Vitamin B12 containing cobalt-57 isotopes which must then be purified by lengthy chromatographic separations. A method is provided for labeling a complex metal chelate with a radioactive metal
15 isotope via isotopic exchange in the solid state between the metal atom of the complex metal chelate and the radioactive metal isotope. Any metal chelate compound, including cyanocobalamin, cobaltocene, aquocobalamin, porphyrins, phthalocyanines and other macrocyclic compounds, may be labeled with a radioactive isotope of either the same metal as that present in the complex metal chelate compound or a different metal than that present in the complex metal chelate compound....Typical of
20 the radioactive metal isotopes are 57 Co+2, 60 Co+2, 52 Fe+2, 52 Fe+3, 48 Cr+3, 95 Tc+4, 97 Tc+4 and 99 Tc+4.

As is also disclosed in United States patent 3,936,440, "In accordance with the present invention, one preferred embodiment provides a method for labeling Vitamin B12, that is cyanocobalamin, with 57 Co+2, a radioactive isotope of cobalt. It is to be understood, however, that it
25 is fully within the purview of the present invention to substitute other radioactive isotopes of cobalt, such as 60 Co+2, or radioactive isotopes of other metals within the scope of the present invention."

In one embodiment, at least one of the A₁ and A₂ is radioactive iron (e.g., radioactive iron isotope 59 Fe, which is a strong gamma emitter having peaks of 1.1 and 1.3 MeV

Referring again to Figure 4, and to the preferred embodiment depicted therein, in this
30 embodiment, there may be, but need not be, a B moiety (such as, e.g., aluminum). There preferably are at least two C moieties such as, e.g., oxygen and nitrogen. The A moieties, in combination, comprise at least about 80 mole percent of such a composition; and they preferably comprise at least 90 mole percent of such composition.

When two C moieties are present, and when the two C moieties are oxygen and nitrogen, they
35 preferably are present in a mole ratio such that from about 10 to about 90 mole percent of oxygen is present, by total moles of oxygen and nitrogen. It is preferred that at least about 60 mole percent of

oxygen be present. In one embodiment, at least about 70 mole percent of oxygen is so present. In yet another embodiment, at least 80 mole percent of oxygen is so present.

One may measure the surface of the nanomagnetic material, measuring the first 8.5 nanometers of material. When such surface is measured, it is preferred that at least 50 mole percent of oxygen, by total moles of oxygen and nitrogen, be present in such surface. It is preferred that at least about 60 mole percent of oxygen be present. In one embodiment, at least about 70 mole percent of oxygen is so present. In yet another embodiment, at least 80 mole percent of oxygen is so present.

By comparison, and in one preferred embodiment (see Figures 38 and 39), in the "bottom half" of the nanomagnetic coating (i.e., that portion of the coating that is connected to the substrate), more than 1.5 times as much of the "A moiety" appears as does in the "top half" (i.e., that portion of the coating closest to the sputtering machine). Without wishing to be bound to any particular theory, applicants believe that this differential in the concentration of the A moiety in the coating is caused by the attraction of the A moiety to both the surface of the substrate, and to the magnetron used in sputtering. The more than a film is deposited upon a coating, and the further away that the sputtered particles are from the surface of the substrate, the less attraction surface has for the sputtered particles, and the more such sputtered particles are attracted backward towards the magnetron. Consequently, the closer the coating is to the surface of the substrate, the greater its concentration of A moiety or moieties.

Without wishing to be bound to any particular theory, applicants believe that the presence of two distinct A moieties in their composition, and two distinct C moieties (such as, e.g., oxygen and nitrogen), provides better magnetic properties for applicants' nanomagnetic materials.

In the embodiment depicted in Figure 4, in addition to moiety A, it is preferred to have moiety B be present in the nanomagnetic material. In this embodiment, moieties A and B are admixed with each other. The mixture may be a physical mixture, it may be a solid solution, it may be comprised of an alloy of the A/B moieties, etc.

The squareness of the nanomagnetic particles of the invention

As is known to those skilled in the art, the squareness of a magnetic material is the ratio of the residual magnetic flux and the saturation magnetic flux density. Reference may be had to page 1802 of the McGraw-Hill Dictionary of Scientific and Technical Terms, Fourth Edition (McGraw-Hill Book Company, New York, New York, 1989). At such page 1802, the "squareness ratio" is defined as "The magnetic induction at zero magnetizing force divided by the maximum magnetic indication, in a symmetric cyclic magnetization of a material."

In one embodiment, the squareness of applicants' nanomagnetic material is from about 0.05 to about 1.0. In one aspect of this embodiment, such squareness is from about 0.1 to about 0.9. In another aspect of this embodiment, the squareness is from about 0.2 to about 0.8. In applications where a large residual magnetic moment is desired, the squareness is preferably at least about 0.8.

Referring again to Figure 4, and in the preferred embodiment depicted therein, the nanomagnetic material may be comprised of 100 percent of moiety A, provided that such moiety A has

the required normalized magnetic interaction (M). Alternatively, the nanomagnetic material may be comprised of both moiety A and moiety B. In one embodiment, the A moieties comprise at least about 80 mole percent (and preferably at least about 90 mole percent) of the total moles of the A, B, and C moieties.

When moiety B is present in the nanomagnetic material, in whatever form or forms it is present, it is preferred that it be present at a mole ratio (by total moles of A and B) of from about 1 to about 99 percent and, preferably, from about 10 to about 90 percent.

The B moiety, in one embodiment, in whatever form it is present, is preferably nonmagnetic, i.e., it has a relative magnetic permeability of about 1.0; without wishing to be bound to any particular theory, applicants believe that the B moiety acts as buffer between adjacent A moieties. One may use, e.g., such elements as silicon, aluminum, boron, platinum, tantalum, palladium, yttrium, zirconium, titanium, calcium, beryllium, barium, silver, gold, indium, lead, tin, antimony, germanium, gallium, tungsten, bismuth, strontium, magnesium, zinc, and the like.

In one embodiment, the B moiety has a relative magnetic permeability that is about equal to 1 plus the magnetic susceptibility. The relative magnetic susceptibilities of silicon, aluminum, boron, platinum, tantalum, palladium, yttrium, zirconium, titanium, calcium, beryllium, barium, silver, gold, indium, lead, tin, antimony, germanium, gallium, tungsten, bismuth, strontium, magnesium, zinc, copper, cesium, cerium, hafnium, iodine, iridium, lanthanum, lithium, lutetium, manganese, molybdenum, potassium, sodium, strontium, praseodymium, rhenium, rhodium, rubidium, ruthenium, scandium, selenium, tantalum, technetium, tellurium, chromium, thallium, thorium, thulium, titanium, vanadium, zinc, yttrium, ytterbium, zirconium, and the like. Reference may be had, e.g., to pages E-118 through E-123 of the aforementioned CRC Handbook of Chemistry and Physics.

In one embodiment, the nanomagnetic particles may be represented by the formula $A_xB_yC_z$ wherein $x + y + z$ is equal to 1. In this embodiment the ratio of x/y is at least 0.1 and preferably at least 0.2; and the ratio of z/x is from 0.001 to about 0.5.

In one embodiment, and without wishing to be bound to any particular theory, it is believed that B moiety provides plasticity to the nanomagnetic material that it would not have but for the presence of such B moiety. In one aspect of this embodiment, it is preferred that the bending radius of a substrate coated with both A and B moieties be no greater than 90 percent of the bending radius of a substrate coated with only the A moiety.

The use of the B material allows one, in one embodiment, to produce a coated substrate with a springback angle of less than about 45 degrees. As is known to those skilled in the art, all materials have a finite modulus of elasticity; thus, plastic deformation is followed by some elastic recovery when the load is removed. In bending, this recovery is called springback. See, e.g., page 462 of S. Kalparjian's "Manufacturing Engineering and Technology," Third Edition (Addison Wesley Publishing Company, New York, New York, 1995).

In one preferred embodiment, the B material is aluminum and the C material is nitrogen, whereby an AlN moiety is formed. Without wishing to be bound to any particular theory, applicants believe that aluminum nitride (and comparable materials) are both electrically insulating and thermally conductive, thus providing an excellent combination of properties for certain end uses.

5 Referring again to Figures 4 and 5, when an electromagnetic field 110 is incident upon the nanomagnetic material comprised of A and B (see Figure 4), such a field will be reflected to some degree depending upon the ratio of moiety A and moiety B. In one embodiment, it is preferred that at least 1 percent of such field is reflected in the direction of arrow 112 (see Figure 5). In another
10 embodiment, it is preferred that at least about 10 percent of such field is reflected. In yet another embodiment, at least about 90 percent of such field is reflected. Without wishing to be bound to any particular theory, applicants believe that the degree of reflection depends upon the concentration of A in the A/B mixture.

Referring again to Figure 4, and in one embodiment, the nanomagnetic material is comprised of moiety A, moiety C, and optionally moiety B. The moiety C is preferably selected from the group
15 consisting of elemental oxygen, elemental nitrogen, elemental carbon, elemental fluorine, elemental chlorine, elemental hydrogen, and elemental helium, elemental neon, elemental argon, elemental krypton, elemental xenon, elemental fluorine, elemental sulfur, elemental hydrogen, elemental helium, the elemental chlorine, elemental bromine, elemental iodine, elemental boron, elemental phosphorus, and the like. In one aspect of this embodiment, the C moiety is selected from the group consisting of
20 elemental oxygen, elemental nitrogen, and mixtures thereof.

In one embodiment, the C moiety is chosen from the group of elements that, at room temperature, form gases by having two or more of the same elements combine. Such gases include, e.g., hydrogen, the halide gases (fluorine, chlorine, bromine, and iodine), inert gases (helium, neon, argon, krypton, xenon, etc.), etc.

25 In one embodiment, the C moiety is chosen from the group consisting of oxygen, nitrogen, and mixtures thereof. In one aspect of this embodiment, the C moiety is a mixture of oxygen and nitrogen, wherein the oxygen is present at a concentration from about 10 to about 90 mole percent, by total moles of oxygen and nitrogen.

It is preferred, when the C moiety (or moieties) is present, that it be present in a concentration
30 of from about 1 to about 90 mole percent, based upon the total number of moles of the A moiety and/or the B moiety and the C moiety in the composition. In one embodiment, the C moiety is both oxygen and nitrogen.

Referring again to Figure 4, and in the embodiment depicted, the area 114 produces a composition which optimizes the degree to which magnetic flux are initially trapped and/or thereafter
35 released by the composition when a magnetic field is withdrawing from the composition.

Without wishing to be bound to any particular theory, applicants believe that, when a composition as described by area 114 is subjected to an alternating magnetic field, at least a portion of

the magnetic field is trapped by the composition when the field is strong, and then this portion tends to be released when the field lessens in intensity.

Thus, e.g., it is believed that, when the magnetic field 110 is applied to the nanomagnetic material, it starts to increase, in a typical sine wave fashion. After a specified period of time, a magnetic moment is created within the nanomagnetic material; but, because of the time delay, there is a phase shift.

The time delay will vary with the composition of the nanomagnetic material. By maximizing the amount of trapping, and by minimizing the amount of reflection and absorption, one may minimize the magnetic artifacts caused by the nanomagnetic shield.

Thus, and referring again to Figure 4, one may optimize the A/B/C composition to preferably be within the area 114. In general, the A/B/C composition has molar ratios such that the ratio of A/(A and C) is from about 1 to about 99 mole percent and, preferably, from about 10 to about 90 mole percent. In one preferred embodiment, such ratio is from about 40 to about 60 molar percent.

The molar ratio of A/(A and B and C) generally is from about 1 to about 99 molar percent and, preferably, from about 10 to about 90 molar percent. In one embodiment, such molar ratio is from about 30 to about 60 molar percent.

The molar ratio of B/(A plus B plus C) generally is from about 1 to about 99 mole percent and, preferably, from about 10 to about 40 mole percent.

The molar ratio of C/(A plus B plus C) generally is from about 1 to about 99 mole percent and, preferably, from about 10 to about 50 mole percent.

In one embodiment, the composition of the nanomagnetic material is chosen so that the applied electromagnetic field 110 is absorbed by the nanomagnetic material by less than about 1 percent; thus, in this embodiment, the applied magnetic field 110 is substantially restored by correcting the time delay.

By utilizing nanomagnetic material that absorbs the electromagnetic field, one may selectively direct energy to various cells within a biological organism that are to be treated. Thus, e.g., cancer cells can be injected with the nanomagnetic material and then destroyed by the application of externally applied electromagnetic fields. Because of the nano size of applicants' materials, they can readily and preferentially be directed to the malignant cells to be treated within a living organism. In this embodiment, the nanomagnetic material preferably has a particle size of from about 5 to about 10 nanometers.

In one embodiment of this invention, there is provided a multiplicity of nanomagnetic particles that may be in the form of a film, a powder, a solution, etc. This multiplicity of nanomagnetic particles is hereinafter referred to as a collection of nanomagnetic particles.

The collection of nanomagnetic particles of this embodiment of the invention is generally comprised of at least about 0.05 weight percent of such nanomagnetic particles and, preferably, at least about 5 weight percent of such nanomagnetic particles. In one embodiment, such collection is

comprised of at least about 50 weight percent of such magnetic particles. In another embodiment, such collection consists essentially of such nanomagnetic particles.

When the collection of nanomagnetic particles consists essentially of nanomagnetic particles, the term "compact" will be used to refer to such collection of nanomagnetic particles.

5 The average size of the nanomagnetic particles is preferably less than about 100 nanometers. In one embodiment, the nanomagnetic particles have an average size of less than about 20 nanometers. In another embodiment, the nanomagnetic particles have an average size of less than about 15 nanometers. In yet another embodiment, such average size is less than about 11 nanometers. In yet another embodiment, such average size is less than about 3 nanometers.

10 In one embodiment of this invention, the nanomagnetic particles have a phase transition temperature of from about 0 degrees Celsius to about 1,200 degrees Celsius. In one aspect of this embodiment, the phase transition temperature is from about 40 degrees Celsius to about 200 degrees Celsius.

As used herein, the term phase transition temperature refers to temperature in which the magnetic order of a magnetic particle transitions from one magnetic order to another. Thus, for example, when a magnetic particle transitions from the ferromagnetic order to the paramagnetic order, the phase transition temperature is the Curie temperature. Thus, e.g., when the magnetic particle transitions from the anti-ferromagnetic order to the paramagnetic order, the phase transition temperature is known as the Neel temperature.

20 The nanomagnetic particles of this invention may be used for hyperthermia therapy. The use of small magnetic particles for hyperthermia therapy is discussed, e.g., in United States patents 4,136,683; 4,303,636; 4,735,796; and 5,043,101 of Robert T. Gordon.

The nanomagnetic material of this invention is well adapted for hyperthermia therapy because, e.g., of the small size of the nanomagnetic particles and the magnetic properties of such particles, such as, e.g., their Curie temperature.

25 As used herein, the term "Curie temperature" refers to the temperature marking the transition between ferromagnetism and paramagnetism, or between the ferroelectric phase and paraelectric phase. This term is also sometimes referred to as the "Curie point."

30 As used herein, the term "Neel temperature" refers to a temperature, characteristic of certain metals, alloys, and salts, below which spontaneous magnetic ordering takes place so that they become antiferromagnetic, and above which they are paramagnetic; this is also known as the Neel point.

Neel temperature is also discussed at page F-92 of the "Handbook of Chemistry and Physics," 63rd Edition (CRC Press, Inc., Boca Raton, Florida, 1982-1983). As is disclosed on such page, ferromagnetic materials are "those in which the magnetic moments of atoms or ions tend to assume an ordered but nonparallel arrangement in zero applied field, below a characteristic temperature called the Neel point. In the usual case, within a magnetic domain, a substantial net magnetization results form

the antiparallel alignment of neighboring nonequivalent sublattices. The macroscopic behavior is similar to that in ferromagnetism. Above the Neel point, these materials become paramagnetic.”

Without wishing to be bound to any particular theory, applicants believe that the phase temperature of their nanomagnetic particles can be varied by varying the ratio of the A, B, and C moieties described hereinabove as well as the particle sizes of the nanoparticles.

In one embodiment, the magnetic order of the nanomagnetic particles of this invention is destroyed at a temperature in excess of the phase transition temperature. This phenomenon is illustrated in Figures 4A and 4B.

Referring to Figure 4A, it will be seen that a multiplicity of nano-sized particles 91 are disposed within a cell 93 which, in the embodiment depicted, is a cancer cell. The particles 91 are subjected to electromagnetic radiation 95 which causes them, in the embodiment depicted, to heat to a temperature sufficient to destroy the cancer cell but insufficient to destroy surrounding cells. The particles 91 are preferably delivered to the cancer cell 93 by one or more of the means described elsewhere in this specification and/or in the prior art.

In the embodiment depicted in Figure 4A, the temperature of the particles 91 is less than the phase transition temperature of such particles, “ $T_{\text{transition}}$.” Thus, in this case, the particles 91 have a magnetic order, i.e., they are either ferromagnetic or superparamagnetic and, thus, are able to receive the external radiation 95 and transform at least a portion of the electromagnetic energy into heat.

When the temperature of the particles 91 exceeds the “ $T_{\text{transition}}$ ” temperature (i.e., their phase transition temperature), the magnetic order of such particles is destroyed, and they are no longer able to transform electromagnetic energy into heat. This situation is depicted in Figure 4B.

When the particles 91 cease transforming electromagnetic energy into heat, they tend to cool and then revert to a temperature below “ $T_{\text{transition}}$ ”, as depicted in Figure 4A. Thus, the particles 91 act as a heat switch, ceasing to transform electromagnetic energy into heat when they exceed their phase transition temperature and resuming such capability when they are cooled below their phase transition temperature. This capability is schematically illustrated in Figure 3A.

In one embodiment, the phase transition temperature of the nanoparticles is higher than the temperature needed to kill cancer cells but lower than the temperature needed to kill normal cells. As is disclosed in, e.g., United States patent 4,776,086 “The use of elevated temperatures, i.e., hyperthermia, to repress tumors has been under continuous investigation for many years. When normal human cells are heated to 41°-43° C., DNA synthesis is reduced and respiration is depressed. At about 45° C., irreversible destruction of structure, and thus function of chromosome associated proteins, occurs. Autodigestion by the cell's digestive mechanism occurs at lower temperatures in tumor cells than in normal cells. In addition, hyperthermia induces an inflammatory response which may also lead to tumor destruction. Cancer cells are more likely to undergo these changes at a particular temperature. This may be due to intrinsic differences, between normal cells and cancerous cells. More likely, the difference is associated with the low pH (acidity), low oxygen content and poor nutrition in tumors as a

consequence of decreased blood flow. This is confirmed by the fact that recurrence of tumors in animals, after hyperthermia, is found in the tumor margins; probably as a consequence of better blood supply to those areas.”

In one embodiment of this invention, the phase transition temperature of the nanomagnetic material is less than about 50 degrees Celsius and, preferably, less than about 46 degrees Celsius. In one aspect of this embodiment, such phase transition temperature is less than about 45 degrees Celsius.

The nanomagnetic particles of this invention preferably have a saturation magnetization (“magnetic moment”) of from about 2 to about 3,000 electromagnetic units (emu) per cubic centimeter of material. This parameter may be measured by conventional means.

In one embodiment, the saturation magnetization of the nanomagnetic particles is measured by a SQUID (superconducting quantum interference device).

In one preferred embodiment, the saturation magnetization of the nanomagnetic particle of this invention is at least 100 electromagnetic units (emu) per cubic centimeter and, more preferably, at least about 200 electromagnetic units (emu) per cubic centimeter. In one aspect of this embodiment, the saturation magnetization of such nanomagnetic particles is at least about 1,000 electromagnetic units per cubic centimeter.

In another embodiment, the nanomagnetic material of this invention is present in the form a film with a saturation magnetization of at least about 2,000 electromagnetic units per cubic centimeter and, more preferably, at least about 2,500 electromagnetic units per cubic centimeter. In this embodiment, the nanomagnetic material in the film preferably has the formula $A_1A_2(B)_xC_1(C_2)_y$, wherein y is 1, and the C moieties are oxygen and nitrogen, respectively.

Without wishing to be bound to any particular theory, applicants believe that the saturation magnetization of their nanomagnetic particles may be varied by varying the concentration of the “magnetic” moiety A in such particles, and/or the concentrations of moieties B and/or C.

In one embodiment of this invention, the composition of one aspect of this invention is comprised of nanomagnetic particles with a specified magnetization. As is known to those skilled in the art, magnetization is the magnetic moment per unit volume of a substance.

In this embodiment, and in one aspect thereof, the nanomagnetic particles are present within a layer that preferably has a saturation magnetization, at 25 degrees Centigrade, of from about 1 to about 36,000 Gauss, or higher. In one embodiment, the saturation magnetization at room temperature of the nanomagnetic particles is from about 500 to about 10,000 Gauss. As will be apparent to those skilled in the art, the saturation magnetization of thin films is often higher than the saturation magnetization of bulk objects.

In one embodiment, it is preferred to utilize a thin film with a thickness of less than about 2 microns and a saturation magnetization in excess of 20,000 Gauss. The thickness of the layer of nanomagnetic material is measured from the bottom surface of the layer that contains such material to the top surface of such layer that contains such material; and such bottom surface and/or such top

surface may be contiguous with other layers of material (such as insulating material) that do not contain nanomagnetic particles. In one preferred embodiment, the bottom surface of such layer (and the material within about 1 nanometer of such bottom surface) contains at least 150 percent as much of the A moiety (and preferably at least 200 percent as much of the A moiety) as does the top surface of such layer (and the material within about 1 nanometer of such top surface). An illustration how to obtain such a structure by sputtering with a magnetron is illustrated in Figures 38 and 39.

Thus, e.g., one may make a thin film in accordance with the procedure described at page 156 of Nature, Volume 407, September 14, 2000, that describes a multilayer thin film that has a saturation magnetization of 24,000 Gauss.

By the appropriate selection of nanomagnetic particles, and the thickness of the films deposited, one may obtain saturation magnetizations of as high as at least about 36,000.

In one preferred embodiment, the thin film/coating made by the process of this invention has a magnetization under magnetic resonance imaging (MRI) conditions of from about 0.1 to about 10 electromagnetic units per cubic centimeter. Such MRI conditions typically involve a direct current field of 2.0 Tesla. When exposed to such direct current magnetic field, the magnetization of one preferred coating of the invention is from about 0.2 to about 1 electromagnetic units per cubic centimeter and, more preferably, from about 0.2 to about 0.8 electromagnetic units per cubic centimeter. In one aspect of this embodiment, the thin film/coating contains from about 2 to about 20 moles of the aforementioned A moiety or moieties (such as, e.g., iron and/or cobalt) by the total number of moles of such A moiety or moieties and the B moiety or moieties (such as aluminum); in another aspect, from about 5-10 mole percent of the A moiety (and more preferably from about 6 to about 8 mole percent of the A moiety) is used by total number of moles of the A moiety and the B moiety.

One may produce the aforementioned thin film by conventional sputtering techniques using a target that is, e.g., comprised of from about 1 to about 20 weight percent of iron by total weight of iron and aluminum, and by using as a gaseous reactant a mixture of nitrogen and oxygen. The product produced via this process will have the formula $\text{FeAl}_x\text{N}_y\text{O}_z$, wherein the iron is preferably present in a concentration of from about 9 to about 11 weight percent of iron by total weight of iron and aluminum. When the iron is in the form of nanomagnetic particles disposed in a dielectric matrix, it is preferred that more of such iron appears closer to the substrate than away from the substrate.

In one embodiment, the nanomagnetic materials used in the invention typically comprise one or more of iron, cobalt, nickel, gadolinium, and samarium atoms. Thus, e.g., typical nanomagnetic materials include alloys of iron and nickel (permalloy), cobalt, niobium, and zirconium (CNZ), iron, boron, and nitrogen, cobalt, iron, boron, and silica, iron, cobalt, boron, and fluoride, and the like. These and other materials are described in a book by J. Douglas Adam et al. entitled "Handbook of Thin Film Devices" (Academic Press, San Diego, California, 2000). Chapter 5 of this book, beginning at page 185, describes "magnetic films for planar inductive components and devices;" and Tables 5.1 and 5.2 in this chapter describe many magnetic materials.

In one embodiment, the nanomagnetic material has a saturation magnetization of from about 1 to about 36,000 Gauss. In one embodiment, the nanomagnetic material has a saturation magnetization of from about 200 to about 26,000 Gauss.

In one embodiment, the nanomagnetic material also has a coercive force of from about 0.01 to about 5,000 Oersteds. The term coercive force refers to the magnetic field, H , which must be applied to a magnetic material in a symmetrical, cyclically magnetized fashion, to make the magnetic induction, B , vanish; this term often is referred to as magnetic coercive force.

In one embodiment, the nanomagnetic material has a coercive force of from about 0.01 to about 3,000 Oersteds. In yet another embodiment, the nanomagnetic material 103 has a coercive force of from about 0.1 to about 10.

In one embodiment, the nanomagnetic material preferably has a relative magnetic permeability of from about 1 to about 500,000; in one embodiment, such material has a relative magnetic permeability of from about 1.5 to about 260,000. As used in this specification, the term relative magnetic permeability is equal to B/H , and is also equal to the slope of a section of the magnetization curve of the magnetic material.

In one embodiment, best illustrated in Figure 37, when the nanomagnetic material is in the form of a thin film disposed upon a nonmagnetic substrate, the relative magnetic permeability (i.e., the slope of the plot 7020) increases from an alternating current frequency of 10 hertz to a frequency at which the magnetic resonance frequency occurs (at point 7002 in Figure 37), which generally is at a frequency in excess of 1 gigahertz.

Reference also may be had to page 1399 of Sybil P. Parker's "McGraw-Hill Dictionary of Scientific and Technical Terms," Fourth Edition (McGraw Hill Book Company, New York, 1989). As is disclosed on this page 1399, permeability is "...a factor, characteristic of a material, that is proportional to the magnetic induction produced in a material divided by the magnetic field strength; it is a tensor when these quantities are not parallel.

In one preferred embodiment, the coating of this invention, which preferably is comprised of the aforementioned nanomagnetic material, has a relative alternating current magnetic permeability of at least 1.0 and, more preferably, at least 1.1 (see, e.g., Figure 37) within the alternating current frequency range of from about 10 megahertz to about 1 gigahertz. In one embodiment, the relative alternating current magnetic permeability of the coating within the aforementioned a.c. frequency range is at least about 1.2 and, more preferably, at least about 1.3. As this term is used in this specification, the relative alternating current magnetic permeability is the relative magnetic permeability of the coating when such coating is subjected to a radio frequency of from about 10 megahertz to about 1 gigahertz.

In one embodiment, the nanomagnetic material has a relative magnetic permeability of from about 1.5 to about 2,000.

In one embodiment, the nanomagnetic material preferably has a mass density of at least about 0.001 grams per cubic centimeter; in one aspect of this embodiment, such mass density is at least about 1 gram per cubic centimeter. As used in this specification, the term mass density refers to the mass of a give substance per unit volume. See, e.g., page 510 of the aforementioned "McGraw-Hill Dictionary of Scientific and Technical Terms." In another embodiment, the material has a mass density of at least about 3 grams per cubic centimeter. In another embodiment, the nanomagnetic material has a mass density of at least about 4 grams per cubic centimeter.

In one embodiment, it is preferred that the nanomagnetic material, and/or the article into which the nanomagnetic material has been incorporated, be interposed between a source of radiation and a substrate to be protected therefrom.

In one embodiment, the nanomagnetic material is in the form of a layer that preferably has a saturation magnetization, at 25 degree Centigrade, of from about 1 to about 36,000 Gauss and, more preferably, from about 1 to about 26,000 Gauss. In one aspect of this embodiment, the saturation magnetization at room temperature of the nanomagnetic particles is from about 500 to about 10,000 Gauss.

In one embodiment, the nanomagnetic material is disposed within an insulating matrix so that any heat produced by such particles will be slowly dispersed within such matrix. Such matrix may be made from, e.g., ceria, calcium oxide, silica, alumina, and the like. In general, the insulating material preferably has a thermal conductivity of less than about 20 (calories centimeters/square centimeters-degree Kelvin second) x 10,000. See, e.g., page E-6 of the 63rd. Edition of the "Handbook of Chemistry and Physics" (CRC Press, Inc. Boca Raton, Florida, 1982).

In one embodiment, there is provided a coating of nanomagnetic particles that consists of a mixture of aluminum oxide (Al_2O_3), iron, and other particles that have the ability to deflect electromagnetic fields while remaining electrically non-conductive. In one aspect of this embodiment, the particle size in such a coating is approximately 10 nanometers. Preferably the particle packing density is relatively low so as to minimize electrical conductivity. Such a coating, when placed on a fully or partially metallic object (such as a guide wire, catheter, stent, and the like) is capable of deflecting electromagnetic fields, thereby protecting sensitive internal components, while also preventing the formation of eddy currents in the metallic object or coating. The absence of eddy currents in a metallic medical device provides several advantages, to wit: (1) reduction or elimination of heating, (2) reduction or elimination of electrical voltages which can damage the device and/or inappropriately stimulate internal tissues and organs, and (3) reduction or elimination of disruption and distortion of a magnetic-resonance image.

Determination of the heat shielding effect of a magnetic shield

In one preferred embodiment, the composition of this invention minimizes the extent to which a substrate increases its heat when subjected to a strong magnetic field. This heat buildup can be

determined in accordance with A.S.T.M. Standard Test F-2182-02, "Standard test method for measurement of radio-frequency induced heating near passive implant during magnetic resonance imaging."

In this test, the radiation used is representative of the fields present during MRI procedures. As is known to those skilled in the art, such fields typically include a static field with a strength of from about 0.5 to about 2 Teslas, a radio frequency alternating magnetic field with a strength of from about 20 microTeslas to about 100 microTeslas, and a gradient magnetic field that has three components (x, y, and z), each of which has a field strength of from about 0.05 to 500 milliTeslas.

During this test, a temperature probe is used to measure the temperature of an unshielded conductor when subjected to the magnetic field in accordance with such A.S.T.M. F-2182-02 test.

The same test is then performed upon a shielded conductor assembly that is comprised of the conductor and a magnetic shield.

The magnetic shield used may comprise nanomagnetic particles, as described hereinabove. Alternatively, or additionally, it may comprise other shielding material, such as, e.g., oriented nanotubes (see, e.g., United States patent 6,265,466).

In one embodiment, the shield is in the form of a layer of shielding material with a thickness of from about 10 nanometers to about 1 millimeter. In another embodiment, the thickness is from about 10 nanometers to about 20 microns.

In one preferred embodiment the shielded conductor is an implantable device and is connected to a pacemaker assembly comprised of a power source, a pulse generator, and a controller. The pacemaker assembly and its associated shielded conductor are preferably disposed within a living biological organism.

In one preferred embodiment, when the shielded assembly is tested in accordance with A.S.T.M. 2182-02, it will have a specified temperature increase (" dT_s "). The " dT_c " is the change in temperature of the unshielded conductor using precisely the same test conditions but omitting the shield. The ratio of dT_s/dT_c is the temperature increase ratio; and one minus the temperature increase ratio ($1 - dT_s/dT_c$) is defined as the heat shielding factor.

It is preferred that the shielded conductor assembly have a heat shielding factor of at least about 0.2. In one embodiment, the shielded conductor assembly has a heat shielding factor of at least 0.3.

In one embodiment, the nanomagnetic shield of this invention is comprised of an antithrombogenic material.

Antithrombogenic compositions and structures have been well known to those skilled in the art for many years. Some of these compositions are described, e.g., in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

A process for preparation of an iron-containing thin film

In one preferred embodiment of the invention, a sputtering technique is used to prepare an AlFe thin film or particles, as well as comparable thin films containing other atomic moieties, or particles,

such as, e.g., elemental nitrogen, and elemental oxygen. Conventional sputtering techniques may be used to prepare such films by sputtering. See, for example, R. Herrmann and G. Brauer, "D.C.- and R.F. Magnetron Sputtering," in the "Handbook of Optical Properties: Volume I -- Thin Films for Optical Coatings," edited by R.E. Hummel and K.H. Guenther (CRC Press, Boca Raton, Florida, 1955).

5 Reference also may be had, e.g., to M. Allendorf, "Report of Coatings on Glass Technology Roadmap Workshop," January 18-19, 2000, Livermore, California; and also to United States patent 6,342,134, "Method for producing piezoelectric films with rotating magnetron sputtering system."

Although the sputtering technique is advantageously used, the plasma technique described elsewhere in this specification also may be used. Alternatively, or additionally, one or more of the
10 other forming techniques described elsewhere in this specification also may be used.

One may utilize conventional sputtering devices in this process. By way of illustration and not limitation, a typical sputtering system is described in United States patent 5,178,739. As is disclosed in this patent, "...a sputter system 10 includes a vacuum chamber 20, which contains a circular end sputter target 12, a hollow, cylindrical, thin, cathode magnetron target 14, a RF coil 16 and a chuck 18, which
15 holds a semiconductor substrate 19. The atmosphere inside the vacuum chamber 20 is controlled through channel 22 by a pump (not shown). The vacuum chamber 20 is cylindrical and has a series of permanent, magnets 24 positioned around the chamber and in close proximity therewith to create a multiple field configuration near the interior surface 15 of target 12. Magnets 26, 28 are placed above end sputter target 12 to also create a multipole field in proximity to target 12. A singular magnet 26 is
20 placed above the center of target 12 with a plurality of other magnets 28 disposed in a circular formation around magnet 26. For convenience, only two magnets 24 and 28 are shown. The configuration of target 12 with magnets 26, 28 comprises a magnetron sputter source 29 known in the prior art, such as the Torus-10E system manufactured by K. Lesker, Inc. A sputter power supply 30 (DC or RF) is connected by a line 32 to the sputter target 12. A RF supply 34 provides power to RF coil
25 16 by a line 36 and through a matching network 37. Variable impedance 38 is connected in series with the cold end 17 of coil 16. A second sputter power supply 39 is connected by a line 40 to cylindrical sputter target 14. A bias power supply 42 (DC or RF) is connected by a line 44 to chuck 18 in order to provide electrical bias to substrate 19 placed thereon, in a manner well known in the prior art."

By way of yet further illustration, other conventional sputtering systems and processes are
30 described in United States patents 5,569,506 (a modified Kurt Lesker sputtering system), 5,824,761 (a Lesker Torus 10 sputter cathode), 5,768,123, 5,645,910, 6,046,398 (sputter deposition with a Kurt J. Lesker Co. Torus 2 sputter gun), 5,736,488, 5,567,673, 6,454,910, and the like.

By way of yet further illustration, one may use the techniques described in a paper by Xingwu Wang et al. entitled "Technique Devised for Sputtering AlN Thin Films," published in "the Glass
35 Researcher," Volume 11, No. 2 (December 12, 2002).

In one preferred embodiment, a magnetron sputtering technique is utilized, with

a Lesker Super System III system. The vacuum chamber of this system is preferably cylindrical, with a diameter of approximately one meter and a height of approximately 0.6 meters. The base pressure used is from about 0.001 to 0.0001 Pascals. In one aspect of this process, the target is a metallic FeAl disk, with a diameter of approximately 0.1 meter. The molar ratio between iron and aluminum used in this aspect is approximately 70/30. Thus, the starting composition in this aspect is almost non-magnetic. See, e.g., page 83 (Figure 3.1aii) of R.S. Tebble et al.'s "Magnetic Materials" (Wiley-Interscience, New York, New York, 1969); this Figure discloses that a bulk composition containing iron and aluminum with at least 30 mole percent of aluminum (by total moles of iron and aluminum) is substantially non-magnetic.

In this aspect, to fabricate FeAl films, a DC power source is utilized, with a power level of from about 150 to about 550 watts (Advanced Energy Company of Colorado, model MDX Magnetron Drive). The sputtering gas used in this aspect is argon, with a flow rate of from about 0.0012 to about 0.0018 standard cubic meters per second. To fabricate FeAlN films in this aspect, in addition to the DC source, a pulse-forming device is utilized, with a frequency of from about 50 to about 250 MHz (Advanced Energy Company, model Sparc-le V). One may fabricate FeAlO films in a similar manner but using oxygen rather than nitrogen.

In this aspect, a typical argon flow rate is from about $(0.9 \text{ to about } 1.5) \times 10^{-3}$ standard cubic meters per second; a typical nitrogen flow rate is from about $(0.9 \text{ to about } 1.8) \times 10^{-3}$ standard cubic meters per second; and a typical oxygen flow rate is from about $(0.5 \text{ to about } 2) \times 10^{-3}$ standard cubic meters per second. During fabrication, the pressure typically is maintained at from about 0.2 to about 0.4 Pascals. Such a pressure range has been found to be suitable for nanomagnetic materials fabrications. In one embodiment, it is preferred that both gaseous nitrogen and gaseous oxygen are present during the sputtering process.

In this aspect, the substrate used may be either flat or curved. A typical flat substrate is a silicon wafer with or without a thermally grown silicon dioxide layer, and its diameter is preferably from about 0.1 to about 0.15 meters. A typical curved substrate is an aluminum rod or a stainless steel wire, with a length of from about 0.10 to about 0.56 meters and a diameter of from $(\text{about } 0.8 \text{ to about } 3.0) \times 10^{-3}$ meters. The distance between the substrate and the target is preferably from about 0.05 to about 0.26 meters.

In this aspect, in order to deposit a film on a wafer, the wafer is fixed on a substrate holder. The substrate may or may not be rotated during deposition. In one embodiment, to deposit a film on a rod or wire, the rod or wire is rotated at a rotational speed of from about 0.01 to about 0.1 revolutions per second, and it is moved slowly back and forth along its symmetrical axis with a maximum speed of about 0.01 meters per second.

In this aspect, to achieve a film deposition rate on the flat wafer of 5×10^{-10} meters per second, the power required for the FeAl film is 200 watts, and the power required for the FeAlN film is 500 watts. The resistivity of the FeAlN film is approximately one order of magnitude larger than that of the

metallic FeAl film. Similarly, the resistivity of the FeAlO film is about one order of magnitude larger than that of the metallic FeAl film.

Iron containing magnetic materials, such as FeAl, FeAlN and FeAlO, FeAlNO, FeCoAlNO, and the like, may be fabricated by sputtering. The magnetic properties of those materials vary with stoichiometric ratios, particle sizes, and fabrication conditions; see, e.g., R.S. Tebble and D.J. Craik, "Magnetic Materials", pp. 81-88, Wiley-Interscience, New York, 1969 As is disclosed in this reference, when the iron molar ratio in bulk FeAl materials is less than 70 percent or so, the materials will no longer exhibit magnetic properties.

However, it has been discovered that, in contrast to bulk materials, a thin film material often exhibits different properties.

In one embodiment, the magnetic material A is dispersed within nonmagnetic material B. This embodiment is depicted schematically in Figure 5.

Referring to Figure 5, and in the preferred embodiment depicted therein, it will be seen that A moieties 102, 104, and 106 are preferably separated from each other either at the atomic level and/or at the nanometer level. The A moieties may be, e.g., A atoms, clusters of A atoms, A compounds, A solid solutions, etc. Regardless of the form of the A moiety, it preferably has the magnetic properties described hereinabove.

In the embodiment depicted in Figure 5, each A moiety preferably produces an independent magnetic moment. The coherence length (L) between adjacent A moieties is, on average, preferably from about 0.1 to about 100 nanometers and, more preferably, from about 1 to about 50 nanometers.

Thus, referring again to Figure 5, the normalized magnetic interaction between adjacent A moieties 102 and 104, and also between 104 and 106, is preferably described by the formula $M = \exp(-x/L)$, wherein M is the normalized magnetic interaction, exp is the base of the natural logarithm (and is approximately equal to 2.71828), x is the distance between adjacent A moieties, and L is the coherence length. M, the normalized magnetic interaction, preferably ranges from about 3×10^{-44} to about 1.0.

In one preferred embodiment, M is from about 0.01 to 0.99. In another preferred embodiment, M is from about 0.1 to about 0.9.

In one embodiment, and referring again to Figure 5, x is preferably measured from the center 101 of A moiety 102 to the center 103 of A moiety 104; and x is preferably equal to from about 0.00001 times L to about 100 times L.

In one embodiment, the ratio of x/L is at least 0.5 and, preferably, at least 1.5.

In one embodiment, the "ABC particles" of nanomagnetic material also have a specified coherence length. This embodiment is depicted in Figure 5A.

As is used with regard to such "ABC particles," the term "coherence length" refers to the smallest distance 1110 between the surfaces 113 of any particles 115 that are adjacent to each other. It is preferred that such coherence length, with regard to such ABC particles, be less than about 100

nanometers and, preferably, less than about 50 nanometers. In one embodiment, such coherence length is less than about 20 nanometers.

Figure 6 is a schematic sectional view, not drawn to scale, of a shielded conductor assembly 130 that is comprised of a conductor 132 and, disposed around such conductor, a film 134 of nanomagnetic material. The conductor 132 preferably has a resistivity at 20 degrees Centigrade of from about 1 to about 100-microohm-centimeters.

The film 134 is comprised of nanomagnetic material that preferably has a maximum dimension of from about 10 to about 100 nanometers. The film 134 also preferably has a saturation magnetization of from about 200 to about 26,000 Gauss and a thickness of less than about 2 microns. In one embodiment, the magnetically shielded conductor assembly 130 is flexible, having a bend radius of less than 2 centimeters.

As used in this specification, the term flexible refers to an assembly that can be bent to form a circle with a radius of less than 2 centimeters without breaking. Put another way, the bend radius of the coated assembly is preferably less than 2 centimeters.

Without wishing to be bound to any particular theory, applicants believe that the use of nanomagnetic materials in their coatings and their articles of manufacture allows one to produce a flexible device that otherwise could not be produced were not the materials so used nano-sized (less than 100 nanometers).

Referring again to Figure 6, and in the preferred embodiment depicted therein, one or more electrical filter circuit(s) 136 are preferably disposed around the nanomagnetic film 134. These circuit(s) may be deposited by conventional means.

In one embodiment, the electrical filter circuit(s) are deposited onto the film 134 by one or more of the techniques described in United States patents 5,498,289 (apparatus for applying narrow metal electrode), 5,389,573 (method for making narrow metal electrode), 5,973,573 (method of making narrow metal electrode), 5,973,259 (heated tool positioned in the X, Y, and Z-directions for depositing electrode), 5,741,557 (method for depositing fine lines onto a substrate), and the like.

Referring again to Figure 6, and in the preferred embodiment depicted therein, disposed around electrical filter circuit(s) 136 is a second film of nanomagnetic material 138, which may be identical to or different from film layer 134. In one embodiment, film layer 138 provides a different filtering response to electromagnetic waves than does film layer 134.

Disposed around nanomagnetic film layer 138 is a second layer of electrical filter circuit(s) 140. Each of circuit(s) 136 and circuit(s) 140 comprises at least one electrical circuit. It is preferred that the at least two circuits that comprise assembly 130 provide different electrical responses.

As is known to those skilled in the art, at high frequencies the inductive reactance of a coil is great. The inductive reactance (X_L) is equal to $2\pi FL$, wherein F is the frequency (in hertz), and L is the inductance (in Henries).

At low-frequencies, by comparison, the capacitive reactance (X_C) is high, being equal to $1/2\pi fC$, wherein C is the capacitance in Farads. The impedance of a circuit, Z , is equal to the square root of $(R^2 + [X_L - X_C]^2)$, wherein R is the resistance, in ohms, of the circuit, and X_L and X_C are the inductive reactance and the capacitive reactance, respectively, in ohms, of the circuit.

Thus, for any particular alternating frequency electromagnetic wave, one can, by the appropriate selection of values for R , L , and C , pick a circuit that is purely resistive (in which case the inductive reactance is equal to the capacitive reactance at that frequency), is primarily inductive, or is primarily capacitive.

Maximum power transfer occurs at resonance, when the inductance reactance is equal to the capacitive reactance and the difference between them is zero. Conversely, minimum power transfer occurs when the circuit has little resistance in it (all circuits have some finite resistance) but is predominantly inductive or predominantly capacitive.

An LC tank circuit is an example of a circuit in which minimum power is transmitted. A tank circuit is a circuit in which an inductor and capacitor are in parallel; such a circuit appears, e.g., in the output stage of a radio transmitter.

An LC tank circuit exhibits the well-known flywheel effect, in which the energy introduced into the circuit continues to oscillate between the capacitor and inductor after an input signal has been applied; the oscillation stops when the tank-circuit finally loses the energy absorbed, but it resumes when a new source of energy is applied. The lower the inherent resistance of the circuit, the longer the oscillation will continue before dying out.

A typical tank circuit is comprised of a parallel-resonant circuit; and it acts as a selective filter. As is known to those skilled in the art, and as is disclosed in Stan Gibilisco's "Handbook of Radio & Wireless Technology" (McGraw-Hill, New York, New York, 1999), a selective filter is a circuit designed to tailor the way an electronic circuit or system responds to signals at various frequencies (see page 62).

The selective filter may be a bandpass filter (see pages 62-63 of the Gibilisco book) that comprises a resonant circuit, or a combination of resonant circuits, designed to discriminate against all frequencies except a specified frequency, or a band of frequencies between two limiting frequencies. In a parallel LC circuit, a bandpass filter shows a high impedance at the desired frequency or frequencies and a low impedance at unwanted frequencies. In a series LC configuration, the filter has a low impedance at the desired frequency or frequencies, and a high impedance at unwanted frequencies.

The selective filter may be a band-rejection filter, also known as a band-stop filter (see pages 63-65 of the Gibilisco book). This band-rejection filter comprises a resonant circuit adapted to pass energy at all frequencies except within a certain range. The attenuation is greatest at the resonant frequency or within two limiting frequencies.

The selective filter may be a notch filter; see page 65 of the Gibilisco book. A notch filter is a narrowband-rejection filter. A properly designed notch filter can produce attenuation in excess of 40 decibels in the center of the notch.

5 The selective filter may be a high-pass filter; see pages 65-66 of the Gibilisco book. A high-pass filter is a combination of capacitance, inductance, and/or resistance intended to produce large amounts of attenuation below a certain frequency and little or no attenuation above that frequency. The frequency above which the transition occurs is called the cutoff frequency.

10 The selective filter may be a low-pass filter; see pages 67-68 of the Gibilisco book. A low-pass filter is a combination of capacitance, inductance, and/or resistance intended to produce large amounts of attenuation above a certain frequency and little or no attenuation below that frequency.

In the embodiment depicted in Figure 6, the electrical circuit is preferably integrally formed with the coated conductor construct. In another embodiment, not shown in Figure 6, one or more electrical circuits are separately formed from a coated substrate construct and then operatively connected to such construct.

15 Figure 7A is a sectional schematic view of one preferred shielded assembly 131 that is comprised of a conductor 133 and, disposed around such conductor 133, a layer of nanomagnetic material 135.

As is used with regard to such "ABC particles," the term "coherence length" refers to the smallest distance 1110 between the surfaces 113 of any particles 115 that are adjacent to each other. It is preferred that such coherence length, with regard to such ABC particles, be less than about 100 nanometers and, preferably, less than about 50 nanometers. In one embodiment, such coherence length is less than about 20 nanometers. The layer 135 of nanomagnetic material 137 preferably is comprised of nanomagnetic material that may be formed, e.g., by subjecting the material in layer 137 to a magnetic field of from about 10 Gauss to about 40 Tesla for from about 1 to about 20 minutes. The layer 135 preferably has a mass density of at least about 0.001 grams per cubic centimeter (and preferably at least about 0.01 grams per cubic centimeter), a saturation magnetization of from about 1 to about 36,000 Gauss, and a coercive force of from about 0.01 to about 5,000.

25 In one embodiment, the B moiety is added to the nanomagnetic A moiety, preferably with a B/A molar ratio of from about 5:95 to about 95:5 (see Figure 3). In one aspect of this embodiment, the resistivity of the mixture of the B moiety and the A moiety is from about 1 micro-ohm-cm to about 10,000 micro-ohm-cm.

35 Without wishing to be bound to any particular theory, applicants believe that such a mixture of the A and B moieties provides two mechanisms for shielding the magnetic fields. One such mechanism/effect is the shielding provided by the nanomagnetic materials, described elsewhere in this specification. The other mechanism/effect is the shielding provided by the electrically conductive materials.

In one particularly preferred embodiment, the A moiety is iron, the B moiety is aluminum, and the molar ratio of A/B is about 70:30; the resistivity of this mixture is about 8 micro-ohms-cm.

Figure 7B is a schematic sectional view of a magnetically shielded assembly 139 that is similar to assembly 131 but differs therefrom in that a layer 141 of nanoelectrical material is disposed around layer 135.

The layer of nanoelectrical material 141 preferably has a thickness of from about 0.5 to about 2 microns. In this embodiment, the nanoelectrical material comprising layer 141 has a resistivity of from about 1 to about 100 microohm-centimeters. As is known to those skilled in the art, when nanoelectrical material is exposed to electromagnetic radiation, and in particular to an electric field, it will shield the substrate over which it is disposed from such electrical field.

As is disclosed in United States patent 4,963,291, one may produce electromagnetic shielding resins comprised of electroconductive particles, such as iron, aluminum, copper, silver and steel in sizes ranging from 0.5 to 50 microns.

The nanoelectrical particles used in this aspect of the invention preferably have a particle size within the range of from about 1 to about 100 microns, and a resistivity of from about 1.6 to about 100 microohm-centimeters. In one embodiment, such nanoelectrical particles comprise a mixture of iron and aluminum. In another embodiment, such nanoelectrical particles consist essentially of a mixture of iron and aluminum.

It is preferred that, in such nanoelectrical particles, and in one embodiment, at least 9 moles of aluminum are present for each mole of iron. In another embodiment, at least about 9.5 moles of aluminum are present for each mole of iron. In yet another embodiment, at least 9.9 moles of aluminum are present for each mole of iron.

In one embodiment, and referring again to Figure 7D, the layer 141 of nanoelectrical material has a thermal conductivity of from about 1 to about 4 watts/centimeter-degree Kelvin.

In one embodiment, not shown, in either or both of layers 135 and 141 there is present both the nanoelectrical material and the nanomagnetic material. One may produce such a layer 135 and/or 141 by simultaneously depositing the nanoelectrical particles and the nanomagnetic particles with, e.g., sputtering technology such as, e.g., the sputtering technology described elsewhere in this specification.

Figure 7C is a sectional schematic view of a magnetically shielded assembly 143 that differs from assembly 131 in that it contains a layer 145 of nanothermal material disposed around the layer 135 of nanomagnetic material. The layer 145 of nanothermal material preferably has a thickness of less than 2 microns and a thermal conductivity of at least about 150 watts/meter-degree Kelvin and, more preferably, at least about 200 watts/meter-degree Kelvin. It is preferred that the resistivity of layer 145 be at least about 10^{10} microohm-centimeters and, more preferably, at least about 10^{12} microohm-centimeters. In one embodiment, the resistivity of layer 145 is at least about 10^{13} microohm-centimeters. In one embodiment, the nanothermal layer is comprised of AlN.

In one embodiment, depicted in Figure 7C, the thickness 147 of all of the layers of material coated onto the conductor 133 is preferably less than about 20 microns.

In Figure 7D, a sectional view of an assembly 149 is depicted that contains, disposed around conductor 133, layers of nanomagnetic material 135, nanoelectrical material 141, nanomagnetic material 135, and nanoelectrical material 141.

In Figure 7E, a sectional view of an assembly 151 is depicted that contains, disposed around conductor 133, a layer 135 of nanomagnetic material, a layer 141 of nanoelectrical material, a layer 135 of nanomagnetic material, a layer 145 of nanothermal material, and a layer 135 of nanomagnetic material. Optionally disposed in layer 153 is antithrombogenic material that is biocompatible with the living organism in which the assembly 151 is preferably disposed.

In the embodiments depicted in Figures 7A through 7E, the coatings 135, and/or 141, and/or 145, and/or 153, are disposed around a conductor 133. In one embodiment, the conductor so coated is preferably part of medical device, preferably an implanted medical device (such as, e.g., a pacemaker). In another embodiment, in addition to coating the conductor 133, or instead of coating the conductor 133, the actual medical device itself is coated.

A preferred sputtering process

On December 29, 2003, applicants filed United States patent application 10/747,472, for "Nanoelectrical Compositions."

U.S.S.N. 10/747,472, at pages 10-15 thereof (and by reference to its Figure 9), described the "...preparation of a doped aluminum nitride assembly." It is also described below, by reference to Figure 8, which is similar to the Figure 9 of U.S.SN. 10/747,472 but utilizes different reference numerals.

The system depicted in Figure 8 may be used to prepare an assembly comprised of moieties A, B, and C (see Figure 4). Figure 8 will be described hereinafter with reference to one of the preferred ABC moieties, i.e., aluminum nitride doped with magnesium.

Figure 8 is a schematic of a deposition system 300 comprised of a power supply 302 operatively connected via line 304 to a magnetron 306. Disposed on top of magnetron 306 is a target 308. The target 308 is contacted by gas 310 and gas 312, which cause sputtering of the target 308. The material so sputtered contacts substrate 314 when allowed to do so by the absence of shutter 316.

In one preferred embodiment, the target 308 is mixture of aluminum and magnesium atoms in a molar ratio of from about 0.05 to about 0.5 Mg/(Al + Mg). In one aspect of this embodiment, the ratio of Mg/(Al + Mg) is from about 0.08 to about 0.12. These targets are commercially available and are custom made by companies such as, e.g., Kurt Lasker and Company of Pittsburgh, Pa.

The power supply 302 preferably provides pulsed direct current. Generally, power supply 302 provides power in excess of 300 watts, preferably in excess of 500 watts, and more preferably in excess of 1,000 watts. In one embodiment, the power supplied by power supply 302 is from about 1800 to about 2500 watts.

The power supply preferably provides rectangular-shaped pulses with a duration (pulse width) of from about 10 nanoseconds to about 100 nanoseconds. In one embodiment, the pulse width is from about 20 to about 40 nanoseconds.

5 In between adjacent pulses, preferably substantially no power is delivered. The time between adjacent pulses is generally from about 1 microsecond to about 10 microseconds and is generally at least 100 times greater than the pulse width. In one embodiment, the repetition rate of the rectangular pulses is preferably about 150 kilohertz.

One may use a conventional pulsed direct current (d.c.) power supply. Thus, e.g., one may purchase such a power supply from Advanced Energy Company of Colorado, and/or from ENI
10 Company of Rochester, New York.

The pulsed d.c. power from power supply 302 is delivered to a magnetron 306, that creates an electromagnetic field near target 308. In one embodiment, a magnetic field has a magnetic flux density of from about 0.01 Tesla to about 0.1 Tesla. The magnetic flux tends to attract particles (such as particles 320) that also are magnetic.

15 As will be apparent, because the energy provided to magnetron 306 preferably comprises intermittent pulses, the resulting magnetic fields produced by magnetron 306 will also be intermittent. Without wishing to be bound to any particular theory, applicants believe that the use of such intermittent electromagnetic energy yields better results than those produced by continuous radio-frequency energy.

20 Referring again to Figure 8, it will be seen that the process depicted therein preferably is conducted within a vacuum chamber 118 in which the base pressure is from about 1×10^{-8} Torr to about 0.000005 Torr. In one embodiment, the base pressure is from about 0.000001 to about 0.000003 Torr.

The temperature in the vacuum chamber 318 generally is ambient temperature prior to the time sputtering occurs.

25 In one aspect of the embodiment illustrated in Figure 8, argon gas is fed via line 310, and nitrogen gas is fed via line 312 so that both impact target 308, preferably in an ionized state. In another embodiment of the invention, argon gas, nitrogen gas, and oxygen gas are fed via target 312.

The argon gas, and the nitrogen gas, are fed at flow rates such that the flow rate of the argon gas divided by the flow rate of the nitrogen gas preferably is from about 0.6 to about 1.2. In one
30 aspect of this embodiment, such ratio of argon to nitrogen is from about 0.8 to about 0.95. Thus, for example, the flow rate of the argon may be 20 standard cubic centimeters per minute, and the flow rate of the nitrogen may be 23 standard cubic feet per minute.

The argon gas, and the nitrogen gas, contact a target 308 that is preferably immersed in an electromagnetic field. This field tends to ionize the argon and the nitrogen, providing ionized species of
35 both gases. It is such ionized species that bombard target 308.

In one embodiment, target 308 may be, e.g., pure aluminum. In one preferred embodiment, however, target 308 is aluminum doped with minor amounts of one or more of the aforementioned moieties B.

In the latter embodiment, the moieties B are preferably present in a concentration of from about 1 to about 40 molar percent, by total moles of aluminum and moieties B. It is preferred to use from about 5 to about 30 molar percent of such moieties B.

The ionized argon gas, and the ionized nitrogen gas, after impacting the target 308, creates a multiplicity of sputtered particles 320. In the embodiment illustrated in Figure 8 the shutter 316 prevents the sputtered particles from contacting substrate 314.

When the shutter 316 is removed, however, the sputtered particles 320 can contact and coat the substrate 314. Depending upon the amount of kinetic energy each of such sputtered particles have, some of such particles are attracted back towards the magnetron 306.

In one embodiment, illustrated in Figure 8 the temperature of substrate 314 is controlled by controller 322 that can heat the substrate (by means such as a conduction heater or an infrared heater) and/or cool the substrate (by means such as liquid nitrogen or water).

The sputtering operation increases the pressure within the region of the sputtered particles 320. In general, the pressure within the area of the sputtered particles 320 is at least 100 times, and preferably 1000 times, greater than the base pressure.

Referring again to Figure 8 a cryo pump 324 is preferably used to maintain the base pressure within vacuum chamber 318. In the embodiment depicted, a mechanical pump (dry pump) 326 is operatively connected to the cryo pump 324. Atmosphere from chamber 318 is removed by dry pump 326 at the beginning of the evacuation. At some point, shutter 328 is removed and allows cryo pump 324 to continue the evacuation. A valve 330 controls the flow of atmosphere to dry pump 326 so that it is only open at the beginning of the evacuation.

It is preferred to utilize a substantially constant pumping speed for cryo pump 324, i.e., to maintain a constant outflow of gases through the cryo pump 324. This may be accomplished by sensing the gas outflow via sensor 332 and, as appropriate, varying the extent to which the shutter 328 is open or partially closed.

Without wishing to be bound to any particular theory, applicants believe that the use of a substantially constant gas outflow rate insures a substantially constant deposition of sputtered nitrides.

Referring again to Figure 8 and in one embodiment thereof, it is preferred to clean the substrate 314 prior to the time it is utilized in the process. Thus, e.g., one may use detergent to clean any grease or oil or fingerprints off the surface of the substrate. Thereafter, one may use an organic solvent such as acetone, isopropyl alcohol, toluene, etc.

In one embodiment, the cleaned substrate 314 is presputtered by suppressing sputtering of the target 308 and sputtering the surface of the substrate 314.

As will be apparent to those skilled in the art, the process depicted in Figure 8 may be used to prepare coated substrates 314 comprised of moieties other than doped aluminum nitride.

Figure 9 is a schematic, partial sectional illustration of a coated substrate 400 that, in the preferred embodiment illustrated, is comprised of a coating 402 disposed upon a stent 404. As will be apparent, only one side of the coated stent 404 is depicted for simplicity of illustration. As will also be apparent, the direct current magnetic susceptibility of assembly 400 is equal to the mass of stent (404) x (the susceptibility of stent 404) + the (nmass of the coating 402) x (the susceptibility of coating 402).

In the preferred coated substrate depicted in Figure 9, the coating 402 may be comprised of one layer of material, two layers of material, or three or more layers of material.

Regardless of the number of coating layers used, it is preferred that the total thickness 410 of the coating 402 be at least about 400 nanometers and, preferably, be from about 400 to about 4,000 nanometers. In one embodiment, thickness 410 is from about 600 to about 1,000 nanometers. In another embodiment, thickness 410 is from about 750 to about 850 nanometers.

In the embodiment depicted, the substrate 404 has a thickness 412 that is substantially greater than the thickness 410. As will be apparent, the coated substrate 400 is not drawn to scale.

In general, the thickness 410 is less than about 5 percent of thickness 412 and, more preferably, less than about 2 percent. In one embodiment, the thickness of 410 is no greater than about 1.5 percent of the thickness 412.

The substrate 404, prior to the time it is coated with coating 402, has a certain flexural strength, and a certain spring constant.

The flexural strength is the strength of a material in bending, i.e., its resistance to fracture. As is disclosed in ASTM C-790, the flexural strength is a property of a solid material that indicates its ability to withstand a flexural or transverse load. As is known to those skilled in the art, the spring constant is the constant of proportionality k which appears in Hooke's law for springs. Hooke's law states that: $F = -kx$, wherein F is the applied force and x is the displacement from equilibrium. The spring constant has units of force per unit length.

Means for measuring the spring constant of a material are well known to those skilled in the art.

Referring again to Figure 9, the flexural strength of the uncoated substrate 404 preferably differs from the flexural strength of the coated substrate 404 by no greater than about 5 percent.

Similarly, the spring constant of the uncoated substrate 404 differs from the spring constant of the coated substrate 404 by no greater than about 5 percent.

Referring again to Figure 9, and in the preferred embodiment depicted, the substrate 404 is comprised of a multiplicity of openings through which biological material is often free to pass. As will be apparent to those skilled in the art, when the substrate 404 is a stent, it will be realized that the stent has a mesh structure.

Figure 10 is a schematic view of a typical stent 500 that is comprised of wire mesh 502 constructed in such a manner as to define a multiplicity of openings 504. The mesh material is typically

a metal or metal alloy, such as, e.g., stainless steel, Nitinol (an alloy of nickel and titanium), niobium, copper, etc.

Typically the materials used in stents tend to cause current flow when exposed to a field 506. When the field 506 is a nuclear magnetic resonance field, it generally has a direct current component, and a radio-frequency component. For MRI (magnetic resonance imaging) purposes, a gradient component is added for spatial resolution.

The material or materials used to make the stent itself has certain magnetic properties such as, e.g., magnetic susceptibility. Thus, e.g., niobium has a magnetic susceptibility of 1.95×10^{-6} centimeter-gram-second units. Nitinol has a magnetic susceptibility of from about 2.5 to about 3.8×10^{-6} centimeter-gram-second units. Copper has a magnetic susceptibility of from -5.46 to about -6.16×10^{-6} centimeter-gram-second units.

The total magnetic susceptibility of an object is equal to the mass of the object times its susceptibility. Thus, assuming an object has equal parts of niobium, Nitinol, and copper, its total susceptibility would be equal to $(+1.95 + 3.15 - 5.46) \times 10^{-6}$ cgs, or about 0.36×10^{-6} cgs.

In a more general case, where the masses of niobium, Nitinol, and copper are not equal in the object, the susceptibility, in c.g.s. units, would be equal to $1.95 M_n + 3.15 M_{ni} - 5.46 M_c$, wherein M_n is the mass of niobium, M_{ni} is the mass of Nitinol, and M_c is the mass of copper.

When any particular material is used to make the stent, its response to an applied MRI field will vary depending upon, e.g., the relative orientation of the stent in relationship to the fields (including the d.c. field, the r.f. field, and the gradient field).

Any particular stent implanted in a human body will tend to have a different orientation than any other stent implanted in another human body due, in part, to the uniqueness of each human body. Thus, it cannot be predicted a priori how any particular stent will respond to a particular MRI field.

The solution provided by one aspect of applicants' invention tends to cancel, or compensate for, the response of any particular stent in any particular body when exposed to an MRI field.

Referring again to Figure 10, and to the uncoated stent 500 depicted therein, when an MRI field 506 is imposed upon the stent, it will tend to induce eddy currents. As used in this specification, the term eddy currents refers to loop currents and surface eddy currents.

Referring to Figure 10, the MRI field 506 will induce a loop current 508. As is apparent to those skilled in the art, the MRI field 506 is an alternating current field that, as it alternates, induces an alternating eddy current 508. The radio-frequency field is also an alternating current field, as is the gradient field. By way of illustration, when the d.c. field is about 1.5 Tesla, the r.f. field has frequency of about 64 megahertz. With these conditions, the gradient field is in the kilohertz range, typically having a frequency of from about 2 to about 200 kilohertz.

Applying the well-known right hand rule, the loop current 508 will produce a magnetic field 510 extending into the plane of the paper and designated by an "x." This magnetic field 510 will tend to oppose the direction of the applied field 506.

Referring again to Figure 10, when the stent 500 is exposed to the MRI field 506, a surface eddy current will be produced where there is a relatively large surface area of conductive material such as, e.g., at junction 514.

The stent 500 should be constructed to have certain desirable mechanical properties. However, the materials that will provide the desired mechanical properties generally do not have desirable magnetic and/or electromagnetic properties. In an ideal situation, the stent 500 will produce no loop currents 508 and no surface eddy currents 512; in such situation, the stent 500 would have an effective zero magnetic susceptibility. Put another way, ideally the direct current magnetic susceptibility of an ideal stent should be about 0.

A d.c. ("direct current") magnetic susceptibility of precisely zero is often difficult to obtain. In general, it is sufficient if the d.c. susceptibility of the stent is plus or minus 1×10^{-3} centimeter-gram-seconds (cgs) and, more preferably, plus or minus 1×10^{-4} centimeter-gram-seconds. In one embodiment, the d.c. susceptibility of the stent is equal to plus or minus 1×10^{-5} centimeter-gram-seconds. In another embodiment, the d.c. susceptibility of the stent is equal to plus or minus 1×10^{-6} centimeter-gram-seconds.

In one embodiment, discussed elsewhere in this specification the d.c. susceptibility of the stent in contact with bodily fluid is plus or minus plus or minus 1×10^{-3} centimeter-gram-seconds (cgs), or plus or minus 1×10^{-4} centimeter-gram-seconds, or plus or minus 1×10^{-5} centimeter-gram-seconds, or plus or minus 1×10^{-6} centimeter-gram-seconds. In this embodiment, the materials comprising the nanomagnetic coating on the stent are chosen to have susceptibility values that, in combination with the susceptibility values of the other components of the stent, and of the bodily fluid, will yield the desired values.

The prior art has heretofore been unable to provide such an ideal stent. Applicants' invention allows one to compensate for the deficiencies of the current stents, and/or of the current stents in contact with bodily fluid, by canceling the undesirable effects due to their magnetic susceptibilities, and/or by compensating for such undesirable effects.

Figure 11 is a graph of the magnetization of an object (such as an uncoated stent, or a coated stent) when subjected to an electromagnetic field, such as an MRI field. It will be seen that, at different field strengths, different materials have different magnetic responses.

Thus, e.g., it will be seen that copper, at a d.c. field strength of 1.5 Tesla, is changing its magnetization as a function of the composite field strength (including the d.c. field strength, the r.f. field strength, and the gradient field strength) at a rate (defined by Δ -magnetization/ Δ composite field strength) that is decreasing. With regard to the r.f. field and the gradient field, it should be understood that the order of magnitude of these fields is relatively small compared to the d.c. field, which is usually about 1.5 Tesla.

Referring again to Figure 11, it will be seen that the slope of line 602 is negative. This negative slope indicates that copper, in response to the applied fields, is opposing the applied fields. Because the

applied fields (including r.f. fields, and the gradient fields), are required for effective MRI imaging, the response of the copper to the applied fields tends to block the desired imaging, especially with the loop current and the surface eddy current described hereinabove. The d.c. susceptibility of copper is equal to the mass of the copper present in the device times its magnetic susceptibility.

Referring again to Figure 11, and in the preferred embodiment depicted therein, the ideal magnetization response is illustrated by line 604, which is the response of the coated substrate of one aspect of this invention, and wherein the slope is substantially zero. As used herein, and with regard to Figure 11, the term substantially zero includes a slope will produce an effective magnetic susceptibility of from about 1×10^{-7} to about 1×10^{-8} centimeters-gram-second (cgs).

Referring again to Figure 11, one means of correcting the negative slope of line 602 is by coating the copper with a coating which produces a response 606 with a positive slope so that the composite material produces the desired effective magnetic susceptibility of from about 1×10^{-7} to about 1×10^{-8} centimeters-gram-second (cgs) units. In order to do so, the following equation must be satisfied: (magnetic susceptibility of the uncoated device) (mass of uncoated device) + (magnetic susceptibility of copper) (mass of copper) = from about 1×10^{-7} to about 1×10^{-8} centimeters-gram-second (cgs).

Figure 9 illustrates a coating that will produce the desired correction for the copper substrate 404. Referring to Figure 9, it will be seen that, in the embodiment depicted, the coating 402 is comprised of at least nanomagnetic material 420 and nanodielectric material 422.

In one embodiment, the nanomagnetic material 420 preferably has an average particle size of less than about 20 nanometers and a saturation magnetization of from 10,000 to about 26,000 Gauss.

In one embodiment, the nanomagnetic material used is iron. In another embodiment, the nanomagnetic material used is FeAlN. In yet another embodiment, the nanomagnetic material is FeAl. Other suitable materials will be apparent to those skilled in the art and include, e.g., nickel, cobalt, magnetic rare earth materials and alloys, thereof, and the like.

The nanodielectric material 422 preferably has a resistivity at 20 degrees Centigrade of from about 1×10^{-5} ohm-centimeters to about 1×10^{13} ohm-centimeters.

Referring again to Figure 9, and in the preferred embodiment depicted therein, the nanomagnetic material 420 is preferably homogeneously dispersed within nanodielectric material 422, which acts as an insulating matrix. In general, the amount of nanodielectric material 422 in coating 402 exceeds the amount of nanomagnetic material 420 in such coating 402. In general, the coating 402 is comprised of at least about 70 mole percent of such nanodielectric material (by total moles of nanomagnetic material and nanodielectric material). In one embodiment, the coating 402 is comprised of less than about 20 mole percent of the nanomagnetic material, by total moles of nanomagnetic material and nanodielectric material. In one embodiment, the nanodielectric material used is aluminum nitride.

In another embodiment, not shown, substantially more nanomagnetic material 420 is disposed in the bottom half of such coating than in the top half of such coating; in general, the bottom half of such coating has at least about 1.5 times as much nanomagnetic material 420 as does such top half.

Referring again to Figure 9, one may optionally include nanoconductive material 424 in the coating 402. This nanoconductive material generally has a resistivity at 20 degrees Centigrade of from about 1×10^{-6} ohm-centimeters to about 1×10^{-5} ohm-centimeters; and it generally has an average particle size of less than about 100 nanometers. In one embodiment, the nanoconductive material used is aluminum.

Referring again to Figure 9, and in the embodiment depicted, it will be seen that two layers are preferably used to obtain the desired correction. In one embodiment, three or more such layers are used. This embodiment is depicted in Figure 9A.

Figure 9A is a schematic illustration of a coated substrate that is similar to coated substrate 400 but differs therefrom in that it contains two layers of dielectric material 405 and 407. In one embodiment, only one such layer of dielectric material 405 issued. Notwithstanding the use of additional layers 405 and 407, the coating 402 still preferably has a thickness 410 of from about 400 to about 4000 nanometers

In the embodiment depicted in Figure 9A, the direct current susceptibility of the assembly depicted is equal to the sum of the (mass)x (susceptibility) for each individual layer.

As will be apparent, it may be difficult with only one layer of coating material to obtain the desired correction for the material comprising the stent (see Figure 11). With a multiplicity of layers comprising the coating 402, which may have the same and/or different thicknesses, and/or the same and/or different masses, and/or the same and/or different compositions, and/or the same and/or different magnetic susceptibilities, more flexibility is provided in obtaining the desired correction.

Figure 11 illustrates the desired correction in terms of magnetization. Figure 12 illustrates the desired correction in terms of reactance.

Referring again to Figure 11, in the embodiment depicted a correction is shown for a coating on a substrate. As will be apparent, the same correction can be made with a mixture of at least two different materials in which each of the different materials retains its distinct magnetic characteristics, and/or any composition containing at least two different moieties, provided that each of such different moieties retains its distinct magnetic characteristics. Such correction process is illustrated in Figure 11A.

Figure 11A illustrates the response of different species within a composition (such as, e.g., a particle) to magnetic radiation, wherein each such species retains its individual magnetic characteristics. The graph depicted in Figure 11A does not illustrate the response of different species alloyed with each other, wherein each of the species does not retain its individual magnetic characteristics.

As is known to those skilled in the art, an alloy is a substance having magnetic properties and consisting of two or more elements, which usually are metallic elements. The bonds in the alloy are

usually metallic bonds, and thus the individual elements in the alloy do not retain their individual magnetic properties because of the substantial "crosstalk" between the elements via the metallic bonding process.

By comparison, e.g., materials that are covalently bond to each other are more likely to retain their individual magnetic characteristics; it is such materials whose behavior is illustrated in Figure 11A. Each of the "magnetically distinct" materials may be, e.g., a material in elemental form, a compound, an alloy, etc.

Referring again to Figure 11A, the response of different, "magnetically distinct" species within a composition (such as particle compact) to MRI radiation is shown. In the embodiment depicted, a direct current (d.c.) magnetic field is shown being applied in the direction of arrow 701. The magnetization plot 703 of the positively magnetized species is shown with a positive slope.

As is known to those skilled in the art, the positively magnetized species include, e.g., those species that exhibit paramagnetism, superparamagnetism, ferromagnetism, and/or ferrimagnetism.

Paramagnetism is a property exhibited by substances which, when placed in a magnetic field, are magnetized parallel to the field to an extent proportional to the field (except at very low temperatures or in extremely large magnetic fields). Paramagnetic materials are well known to those skilled in the art.

Superparamagnetic materials are also well known to those skilled in the art. Reference may be had, e.g., to United States patent 5,238,811, the entire disclosure of which is hereby incorporated by reference into this specification, it is disclosed (at column 5) that: "The superparamagnetic material used in the assay methods according to the first and second embodiments of the present invention described above is a substance which has a particle size smaller than that of a ferromagnetic material and retains no residual magnetization after disappearance of the external magnetic field. The superparamagnetic material and ferromagnetic material are quite different from each other in their hysteresis curve, susceptibility, Mesbauer effect, etc. Indeed, ferromagnetic materials are most suited for the conventional assay methods since they require that magnetic micro-particles used for labeling be efficiently guided even when a weak magnetic force is applied. On the other hand, in the non-separation assay method according to the first embodiment of the present invention, it is required that the magnetic-labeled body alone be difficult to guide by a magnetic force, and for this purpose superparamagnetic materials are most suited." The preparation of these superparamagnetic materials is discussed at columns 6 et seq. of United States patent 5,238,811, wherein it is disclosed that: "The ferromagnetic substances can be selected appropriately, for example, from various compound magnetic substances such as magnetite and gamma-ferrite, metal magnetic substances such as iron, nickel and cobalt, etc. The ferromagnetic substances can be converted into ultramicro particles using conventional methods excepting a mechanical grinding method, i.e., various gas phase methods and liquid phase methods. For example, an evaporation-in-gas method, a laser heating evaporation method, a coprecipitation method, etc. can be applied. The ultramicro particles produced by the gas phase

methods and liquid phase methods contain both superparamagnetic particles and ferromagnetic particles in admixture, and it is therefore necessary to separate and collect only those particles which show superparamagnetic property. For the separation and collection, various methods including mechanical, chemical and physical methods can be applied, examples of which include centrifugation, liquid chromatography, magnetic filtering, etc. The particle size of the superparamagnetic ultramicro particles may vary depending upon the kind of the ferromagnetic substance used but it must be below the critical size of single domain particles. Preferably, it is not larger than 10 nm when the ferromagnetic substance used is magnetite or gamma-ferrite and it is not larger than 3 nm when pure iron is used as a ferromagnetic substance, for example."

Ferromagnetic materials may also be used as the positively magnetized species. As is known to those skilled in the art, ferromagnetism is a property, exhibited by certain metals, alloys, and compounds of the transition (iron group), rare-earth, and actinide elements, in which the internal magnetic moments spontaneously organize in a common direction; this property gives rise to a permeability considerably greater than that of a vacuum, and also to magnetic hysteresis.

Ferrimagnetic materials may also be used as the positively magnetized species. As is known to those skilled in the art, ferrimagnetism is a type of magnetism in which the magnetic moments of neighboring ions tend to align nonparallel, usually antiparallel, to each other, but the moments are of different magnitudes, so there is an appreciable, resultant magnetization.

A discussion of certain paramagnetic, superparamagnetic, ferromagnetic, and/or ferromagnetic materials is presented in United States patent 5,238,811.

By way of yet further illustration, and not limitation, some suitable positively magnetized species include, e.g., iron; iron/aluminum; iron/aluminum oxide; iron/aluminum nitride; iron/tantalum nitride; iron/tantalum oxide; nickel; nickel/cobalt; cobalt/iron; cobalt; samarium; gadolinium; neodymium; mixtures thereof; nano-sized particles of the aforementioned mixtures, where super-paramagnetic properties are exhibited; and the like.

By way of yet further illustration, some of suitable positively magnetized species are listed in the "CRC Handbook of Chemistry and Physics," 63rd Edition (CRC Press, Inc., Boca-Raton, Florida, 1982-1983). As is discussed on pages E-118 to E-123 of such CRC Handbook, materials with positive susceptibility include, e.g., aluminum, americium, cerium (beta form), cerium (gamma form), cesium, compounds of cobalt, dysprosium, compounds of dysprosium, europium, compounds of europium, gadolinium, compounds of gadolinium, hafnium, compounds of holmium, iridium, compounds of iron, lithium, magnesium, manganese, molybdenum, neodymium, niobium, osmium, palladium, plutonium, potassium, praseodymium, rhodium, rubidium, ruthenium, samarium, sodium, strontium, tantalum, technetium, terbium, thorium, thulium, titanium, tungsten, uranium, vanadium, ytterbium, yttrium, and the like.

By way of comparison, and referring again to Figure 11A, plot 705 of the negatively magnetized species is shown with a negative slope. The negatively magnetized species include those

materials with negative susceptibilities that are listed on such pages E-118 to E-123 of the CRC Handbook. By way of illustration and not limitation, such species include, e.g.: antimony; argon; arsenic; barium; beryllium; bismuth; boron; calcium; carbon (dia); chromium; copper; gallium; germanium; gold; indium; krypton; lead; mercury; phosphorous; selenium; silicon; silver; sulfur; tellurium; thallium; tin (gray); xenon; zinc; and the like.

Many diamagnetic materials also are suitable negatively magnetized species. As is known to those skilled in the art, diamagnetism is that property of a material that is repelled by magnets. The term "diamagnetic susceptibility" refers to the susceptibility of a diamagnetic material, which is always negative. Diamagnetic materials are well known to those skilled in the art.

By way of further illustration, the diamagnetic material used may be an organic compound with a negative susceptibility. Referring to pages E-123 to pages E-134 of the aforementioned CRC Handbook, such compounds include, e.g.: alanine; allyl alcohol; amylamine; aniline; asparagines; aspartic acid; butyl alcohol; cholesterol; coumarin; diethylamine; erythritol; eucalyptol; fructose; galactose; glucose; D-glucose; glutamic acid; glycerol; glycine; leucine; isoleucine; mannitol; mannose; and the like.

Referring again to Figure 11A, when a positively magnetized species is mixed with a negatively magnetized species, and assuming that each species retains its magnetic properties, the resulting magnetic properties are indicated by plot 707, with substantially zero magnetization. In this embodiment, one must insure that the positively magnetized species does not lose its magnetic properties, as often happens when one material is alloyed with another. The magnetic properties of alloys and compounds containing different species are known, and thus it readily ascertainable whether the different species that make up such alloys and/or compounds have retained their unique magnetic characteristics.

Without wishing to be bound to any particular theory, applicants believe that, when a positively magnetized species is mixed with a negatively magnetized species, and assuming that each species retains its magnetic properties, the plot 707 (zero magnetization) will be achieved when the volume of the positively magnetized species times its positive susceptibility is substantially equal to the volume of the negatively magnetized species times its negative susceptibility. For this relationship to hold, however, each of the positively magnetized species and the negatively magnetized species must retain the distinctive magnetic characteristics when mixed with each other.

Thus, for example, if element A has a positive magnetic susceptibility, and element B has a negative magnetic susceptibility, the alloying of A and B in equal proportions may not yield a zero magnetization compact.

Without wishing to be bound to any particular theory, nano-sized particles, or micro-sized particles (with a size of at least about 0.5 nanometers) tend to retain their magnetic properties as long as they remain in particulate form. On the other hand, alloys of such materials often do not retain such properties.

With regard to reactance (see Figure 12) the r.f. field and the gradient field are treated as a radiation source which is applied to a living organism comprised of a stent in contact with biological material. The stent, with or without a coating, reacts to the radiation source by exhibiting a certain inductive reactance and a certain capacitive reactance. The net reactance is the difference between the inductive reactance and the capacitive reactance; and it desired that the net reactance be as close to zero as is possible. When the net reactance is greater than zero, it distorts some of the applied MRI fields and thus interferes with their imaging capabilities. Similarly, when the net reactance is less than zero, it also distorts some of the applied MRI fields.

Nullification of the susceptibility contribution due to the substrate

As will be apparent by reference, e.g., to Figure 11, the copper substrate depicted therein has a negative susceptibility, the coating depicted therein has a positive susceptibility, and the coated substrate thus has a substantially zero susceptibility. As will also be apparent, some substrates (such as niobium, nitinol, stainless steel, etc.) have positive susceptibilities. In such cases, and in one preferred embodiment, the coatings should preferably be chosen to have a negative susceptibility so that, under the conditions of the MRI radiation (or of any other radiation source used), the net susceptibility of the coated object is still substantially zero. As will be apparent, the contribution of each of the materials in the coating(s) is a function of the mass of such material and its magnetic susceptibility.

The magnetic susceptibilities of various substrate materials are well known. Reference may be had, e.g., to pages E-118 to E-123 of the "Handbook of Chemistry and Physics," 63rd edition (CRC Press, Inc., Boca Raton, Florida, 1974).

Once the susceptibility of the substrate material is determined, one can use the following equation: $\chi_{\text{sub}} + \chi_{\text{coat}} = 0$, wherein χ_{sub} is the susceptibility of the substrate, and χ_{coat} is the susceptibility of the coating, when each of these is present in a 1/1 ratio. As will be apparent, the aforementioned equation is used when the coating and substrate are present in a 1/1 ratio. When other ratios are used other than a 1/1 ratio, the volume percent of each component (or its mass) must be taken into consideration in accordance with the equation: (volume percent of substrate x susceptibility of the substrate) + (volume percent of coating x susceptibility of the coating) = 0. One may use a comparable formula in which the weight percent of each component is substituted for the volume percent, if the susceptibility is measured in terms of the weight percent.

By way of illustration, and in one embodiment, the uncoated substrate may either comprise or consist essentially of niobium, which has a susceptibility of $+ 195.0 \times 10^{-6}$ centimeter-gram seconds at 298 degrees Kelvin.

In another embodiment, the substrate may contain at least 98 molar percent of niobium and less than 2 molar percent of zirconium. Zirconium has a susceptibility of -122×10^{-6} centimeter-gram seconds at 293 degrees Kelvin. As will be apparent, because of the predominance of niobium, the net susceptibility of the uncoated substrate will be positive.

The substrate may comprise Nitinol. Nitinol is a paramagnetic alloy, an intermetallic compound of nickel and titanium; the alloy preferably contains from 50 to 60 percent of nickel, and it has a permeability value of about 1.002. The susceptibility of Nitinol is positive.

Nitinols with nickel content ranging from about 53 to 57 percent are known as "memory alloys" because of their ability to "remember" or return to a previous shape upon being heated.. which is an alloy of nickel and titanium, in an approximate 1/1 ratio. The susceptibility of Nitinol is positive.

The substrate may comprise tantalum and/or titanium, each of which has a positive susceptibility.

When the uncoated substrate has a positive susceptibility, the coating to be used for such a substrate should have a negative susceptibility. Referring again to said CRC handbook, it will be seen that the values of negative susceptibilities for various elements are -9.0 for beryllium, -280.1 for bismuth (s), -10.5 for bismuth (l), - 6.7 for boron, - 56.4 for bromine (l), -73.5 for bromine(g), -19.8 for cadmium(s), -18.0 for cadmium(l), -5.9 for carbon(dia), -6.0 for carbon (graph), -5.46 for copper(s), - 6.16 for copper(l), -76.84 for germanium, -28.0 for gold(s), -34.0 for gold(l), -25.5 for indium, -88.7 for iodine(s), -23.0 for lead(s), -15.5 for lead(l), -19.5 for silver(s), -24.0 for silver(l), -15.5 for sulfur(alpha), -14.9 for sulfur(beta), -15.4 for sulfur(l), -39.5 for tellurium(s), -6.4 for tellurium(l), -37.0 for tin(gray), -31.7 for tin(gray), -4.5 for tin(l), -11.4 for zinc(s), -7.8 for zinc(l), and the like. As will be apparent, each of these values is expressed in units equal to the number in question x 10^{-6} centimeter-gram seconds at a temperature at or about 293 degrees Kelvin. As will also be apparent, those materials which have a negative susceptibility value are often referred to as being diamagnetic.

By way of further reference, a listing of organic compounds that are diamagnetic is presented on pages E123 to E134 of the aforementioned "Handbook of Chemistry and Physics," 63rd edition (CRC Press, Inc., Boca Raton, Florida, 1974).

In one embodiment, and referring again to the aforementioned "Handbook of Chemistry and Physics," 63rd edition (CRC Press, Inc., Boca Raton, Florida, 1974), one or more of the following magnetic materials described below are preferably incorporated into the coating.

The desired magnetic materials, in this embodiment, preferably have a positive susceptibility, with values ranging from $+1 \times 10^{-6}$ centimeter-gram seconds at a temperature at or about 293 degrees Kelvin, to about 1×10^7 centimeter-gram seconds at a temperature at or about 293 degrees Kelvin.

Thus, by way of illustration and not limitation, one may use materials such as Alnico (see page E-112 of the CRC handbook), which is an alloy containing nickel, aluminum, and other elements such as, e.g., cobalt and/or iron. Thus, e.g., one may use silicon iron (see page E113 of the CRC handbook), which is an acid resistant iron containing a high percentage of silicon. Thus, e.g., one may use steel (see page 117 of the CRC handbook). Thus, e.g., one may use elements such as dysprosium, erbium, europium, gadolinium, hafnium, holmium, manganese, molybdenum, neodymium, nickel-cobalt, alloys of the above, and compounds of the above such as, e.g., their oxides, nitrides, carbonates, and the like.

Referring to Figure 12, and to the embodiment depicted therein, it will be seen that the uncoated stent has an effective inductive reactance at a d.c. field of 1.5 Tesla that exceeds its capacitive reactance, whereas the coating 704 has a capacitive reactance that exceeds its inductive reactance. The coated (composite) stent 706 has a net reactance that is substantially zero.

5 As will be apparent, the effective inductive reactance of the uncoated stent 702 may be due to a multiplicity of factors including, e.g., the positive magnetic susceptibility of the materials which it is comprised of it, the loop currents produced, the surface eddy produced, etc. Regardless of the source(s) of its effective inductive reactance, it can be "corrected" by the use of one or more coatings which provide, in combination, an effective capacitive reactance that is equal to the effective inductive
10 reactance.

Referring again to Figure 9, and in the embodiment depicted, plaque particles 430,432 are disposed on the inside of substrate 404. When the net reactance of the coated substrate 404 is essentially zero, the imaging field 440 can pass substantially unimpeded through the coating 402 and the substrate 404 and interact with the plaque particles 430/432 to produce imaging signals 441.

15 The imaging signals 441 are able to pass back through the substrate 404 and the coating 402 because the net reactance is substantially zero. Thus, these imaging signals are able to be received and processed by the MRI apparatus.

Thus, by the use of applicants' technology, one may negate the negative substrate effect and, additionally, provide pathways for the image signals to interact with the desired object to be imaged
20 (such as, e.g., the plaque particles) and to produce imaging signals that are capable of escaping the substrate assembly and being received by the MRI apparatus.

United States patent application U.S.S.N. 10/303,264 (and also United States patent 6,713,671) discloses a shielded assembly comprised of a substrate and, disposed above a substrate, a shield comprising from about 1 to about 99 weight percent of a first nanomagnetic material, and from about
25 99 to about 1 weight percent of a second material with a resistivity of from about 1 microohm-centimeter to about 1×10^{25} microohm centimeters; the nanomagnetic material comprises nanomagnetic particles, and these nanomagnetic particles respond to an externally applied magnetic field by realigning to the externally applied field. Such a shielded assembly and/or the substrate thereof and/or the shield thereof may be used in the processes, compositions, and/or constructs of this
30 invention.

As is disclosed in United States patent 6,713,617, in one embodiment the substrate used may be, e.g., comprised of one or more conductive material(s) that have a resistivity at 20 degrees Centigrade of from about 1 to about 100 microohm-centimeters. Thus, e.g., the conductive material(s) may be silver, copper, aluminum, alloys thereof, mixtures thereof, and the like.

35 In one embodiment, the substrate consists essentially of such conductive material. Thus, e.g., it is preferred not to use, e.g., copper wire coated with enamel in this embodiment..

In the first step of the process preferably used to make this embodiment of the invention, (see step 40 of Figure 1 of U.S. patent 6,713,671), conductive wires are coated with electrically insulative material. Suitable insulative materials include nano-sized silicon dioxide, aluminum oxide, cerium oxide, yttrium-stabilized zirconia, silicon carbide, silicon nitride, aluminum nitride, and the like. In general, these nano-sized particles will have a particle size distribution such that at least about 90 weight percent of the particles have a maximum dimension in the range of from about 10 to about 100 nanometers.

In such process, the coated conductors may be prepared by conventional means such as, e.g., the process described in United States patent 5,540,959. Alternatively, one may coat the conductors by means of the processes disclosed in a text by D. Satas on "Coatings Technology Handbook" (Marcel Dekker, Inc., New York, New York, 1991). As is disclosed in such text, one may use cathodic arc plasma deposition (see pages 229 et seq.), chemical vapor deposition (see pages 257 et seq.), sol-gel coatings (see pages 655 et seq.), and the like.

Figure 2 of United States patent 6,713,671 is a sectional view of the coated conductors 14/16. In the embodiment depicted in such Figure 2, it will be seen that conductors 14 and 16 are separated by insulating material 42. In order to obtain the structure depicted in such Figure 2, one may simultaneously coat conductors 14 and 16 with the insulating material so that such insulators both coat the conductors 14 and 16 and fill in the distance between them with insulation.

Referring again to such Figure 2 of United States patent 6,713,671, the insulating material 42 that is disposed between conductors 14/16, may be the same as the insulating material 44/46 that is disposed above conductor 14 and below conductor 16. Alternatively, and as dictated by the choice of processing steps and materials, the insulating material 42 may be different from the insulating material 44 and/or the insulating material 46. Thus, step 48 of the process of such Figure 2 describes disposing insulating material between the coated conductors 14 and 16. This step may be done simultaneously with step 40; and it may be done thereafter.

Referring again to such Figure 2, and to the preferred embodiment depicted therein, the insulating material 42, the insulating material 44, and the insulating material 46 each generally has a resistivity of from about 1,000,000,000 to about 10,000,000,000,000 ohm-centimeters.

Referring again to Figure 2 of United States patent 6,713,671, after the insulating material 42/44/46 has been deposited, and in one embodiment, the coated conductor assembly is preferably heat treated in step 50. This heat treatment often is used in conjunction with coating processes in which the heat is required to bond the insulative material to the conductors 14/16.

The heat-treatment step may be conducted after the deposition of the insulating material 42/44/46, or it may be conducted simultaneously therewith. In either event, and when it is used, it is preferred to heat the coated conductors 14/16 to a temperature of from about 200 to about 600 degrees Centigrade for from about 1 minute to about 10 minutes.

Referring again to Figure 1A of United States patent 6,713,67, and in step 52 of the process, after the coated conductors 14/16 have been subjected to heat treatment step 50, they are allowed to cool to a temperature of from about 30 to about 100 degrees Centigrade over a period of time of from about 3 to about 15 minutes.

5 One need not invariably heat treat and/or cool. Thus, referring to such Figure 1A, one may immediately coat nanomagnetic particles onto the coated conductors 14/16 in step 54 either after step 48 and/or after step 50 and/or after step 52.

Referring again to Figure 1A of United States patent 6,713,67, in step 54, nanomagnetic materials are coated onto the previously coated conductors 14 and 16. This is best shown in Figure 2 of
10 such patent, wherein the nanomagnetic particles are identified as particles 24.

In general, and as is known to those skilled in the art, nanomagnetic material is magnetic material which has an average particle size less than 100 nanometers and, preferably, in the range of from about 2 to 50 nanometers.

In general, the thickness of the layer of nanomagnetic material deposited onto the coated
15 conductors 14/16 is less than about 5 microns and generally from about 0.1 to about 3 microns.

Referring again to Figure 2 of United States patent 6,713,671, after the nanomagnetic material is coated in step 54, the coated assembly may be optionally heat-treated in step 56. In this optional step 56, it is preferred to subject the coated conductors 14/16 to a temperature of from about 200 to about 600 degrees Centigrade for from about 1 to about 10 minutes.

20 In one embodiment, illustrated in Figure 3 of United States patent 6,713,671, one or more additional insulating layers 43 are coated onto the assembly depicted in Figure 2 of such patent. This is conducted in optional step 58 (see Figure 1A of such patent).

Figure 4 of United States patent 6,713,671 is a partial schematic view of the assembly 11 of Figure 2 of such patent, illustrating the current flow in such assembly. Referring again to Figure 4 of
25 United States patent 6,713,671, it will be seen that current flows into conductor 14 in the direction of arrow 60, and it flows out of conductor 16 in the direction of arrow 62. The net current flow through the assembly 11 is zero; and the net Lorentz force in the assembly 11 is thus zero. Consequently, even high current flows in the assembly 11 do not cause such assembly to move.

Referring again to Figure 4 of United States patent 6,713,67, conductors 14 and 16 are
30 substantially parallel to each other. As will be apparent, without such parallel orientation, there may be some net current and some net Lorentz effect.

In the embodiment depicted in such Figure 4, and in one preferred aspect thereof, the conductors 14 and 16 preferably have the same diameters and/or the same compositions and/or the same length.

35 Referring again to Figure 4 of United States patent 6,713,671, the nanomagnetic particles 24 are present in a density sufficient so as to provide shielding from magnetic flux lines 64. Without

wishing to be bound to any particular theory, applicant believes that the nanomagnetic particles 24 trap and pin the magnetic lines of flux 64.

In order to function optimally, the nanomagnetic particles 24 preferably have a specified magnetization. As is known to those skilled in the art, magnetization is the magnetic moment per unit volume of a substance.

Referring again to Figure 4 of United States patent 6,713,671, the entire disclosure of which is hereby incorporated by reference into this specification, the layer of nanomagnetic particles 24 preferably has a saturation magnetization, at 25 degrees Centigrade, of from about 1 to about 36,000 Gauss, or higher. In one embodiment, the saturation magnetization at room temperature of the nanomagnetic particles is from about 500 to about 10,000 Gauss.

In one embodiment, it is preferred to utilize a thin film with a thickness of less than about 2 microns and a saturation magnetization in excess of 20,000 Gauss. The thickness of the layer of nanomagnetic material is measured from the bottom surface of the layer that contains such material to the top surface of such layer that contains such material; and such bottom surface and/or such top surface may be contiguous with other layers of material (such as insulating material) that do not contain nanomagnetic particles.

Thus, e.g., one may make a thin film in accordance with the procedure described at page 156 of Nature, Volume 407, September 14, 2000, that describes a multilayer thin film has a saturation magnetization of 24,000 Gauss.

Referring again to Figure 4 of United States patent 6,713,671, the nanomagnetic particles 24 are disposed within an insulating matrix so that any heat produced by such particles will be slowly dispersed within such matrix. Such matrix, as indicated hereinabove, may be made from ceria, calcium oxide, silica, alumina. In general, the insulating material 42 preferably has a thermal conductivity of less than about 20 (caloriescentimeters/square centimeters—degree second) x 10,000. See, e.g., page E-6 of the 63rd Edition of the “Handbook of Chemistry and Physics” (CRC Press, Inc., Boca Raton, Florida, 1982).

The nanomagnetic materials 24 typically comprise one or more of iron, cobalt, nickel, gadolinium, and samarium atoms. Thus, e.g., typical nanomagnetic materials include alloys of iron and nickel (permalloy), cobalt, niobium, and zirconium (CNZ), iron, boron, and nitrogen, cobalt, iron, boron, and silica, iron, cobalt, boron, and fluoride, and the like. These and other materials are described in a book by J. Douglas Adam et al. entitled “Handbook of Thin Film Devices” (Academic Press, San Diego, California, 2000). Chapter 5 of this book beginning at page 185, describes “magnetic films for planar inductive components and devices;” and Tables 5.1 and 5.2 in this chapter describe many magnetic materials.

Figure 5 of United States patent 6,713,671 is a sectional view of the assembly 11 of Figure 2 of such patent. The device of such Figure 5 is preferably substantially flexible. As used in this specification, the term flexible refers to an assembly that can be bent to form a circle with a radius of

less than 2 centimeters without breaking. Put another way, the bend radius of the coated assembly 11 can be less than 2 centimeters.

In another embodiment, not shown, the shield is not flexible. Thus, in one aspect of this embodiment, the shield is a rigid, removable sheath that can be placed over an endoscope or a biopsy probe used inter-operatively with magnetic resonance imaging.

In another embodiment of the invention of United States patent 6,713,671, there is provided a magnetically shielded conductor assembly comprised of a conductor and a film of nanomagnetic material disposed above said conductor. In this embodiment, the conductor has a resistivity at 20 degrees Centigrade of from about 1 to about 2,000 micro ohm-centimeters and is comprised of a first surface exposed to electromagnetic radiation. In this embodiment, the film of nanomagnetic material has a thickness of from about 100 nanometers to about 10 micrometers and a mass density of at least about 1 gram per cubic centimeter, wherein the film of nanomagnetic material is disposed above at least about 50 percent of said first surface exposed to electromagnetic radiation, and the film of nanomagnetic material has a saturation magnetization of from about 1 to about 36,000 Gauss, a coercive force of from about 0.01 to about 5,000 Oersteds, a relative magnetic permeability of from about 1 to about 500,000, and a magnetic shielding factor of at least about 0.5. In this embodiment, the nanomagnetic material has an average particle size of less than about 100 nanometers.

In one preferred embodiment of this invention, and referring to Figure 6 of United States patent 6,713,671, a film of nanomagnetic material is disposed above at least one surface of a conductor. Referring to such Figure 6, and in the schematic diagram depicted therein, a source of electromagnetic radiation 100 emits radiation 102 in the direction of film 104. Film 104 is disposed above conductor 106, i.e., it is disposed between conductor 106 of the electromagnetic radiation 102.

Referring again to Figure 6 of United States patent 6,713,671, the film 104 is adapted to reduce the magnetic field strength at point 108 (which is disposed less than 1 centimeter above film 104) by at least about 50 percent. Thus, if one were to measure the magnetic field strength at point 108, and thereafter measure the magnetic field strength at point 110 (which is disposed less than 1 centimeter below film 104), the latter magnetic field strength would be no more than about 50 percent of the former magnetic field strength. Put another way, the film 104 has a magnetic shielding factor of at least about 0.5.

Referring again to Figure 6 of United States patent 6,713,671, in one embodiment, the film 104 has a magnetic shielding factor of at least about 0.9, i.e., the magnetic field strength at point 110 is no greater than about 10 percent of the magnetic field strength at point 108. Thus, e.g., the static magnetic field strength at point 108 can be, e.g., one Tesla, whereas the static magnetic field strength at point 110 can be, e.g., 0.1 Tesla. Furthermore, the time-varying magnetic field strength of a 100 milliTesla would be reduced to about 10 milliTesla of the time-varying field.

Referring again to Figure 6 of United States patent 6,713,671, in one embodiment of the invention of this patent application it is desired to allow as much as the MRI radiation through the stent

as is possible so that it can interact with material within the stent. In this embodiment, and by the appropriate choice of the A,B, and C moieties, the preferred film 104 has a magnetic shielding factor of less than about 0.1, i.e., the magnetic field strength at point 110 is at least 90 percent of the magnetic field strength at point 108

5 Referring again to Figure 6 of United States patent 6,713,671, the nanomagnetic material 103 in film 104 has a saturation magnetization of from about 1 to about 36,000 Gauss. In one embodiment, the nanomagnetic material 103 a saturation magnetization of from about 200 to about 26,000 Gauss.

Referring again to Figure 6 of United States patent 6,713,671, the nanomagnetic material 103 in film 104 also has a coercive force of from about 0.01 to about 5,000 Oersteds. The term coercive force
10 refers to the magnetic field, H, which must be applied to a magnetic material in a symmetrical, cyclically magnetized fashion, to make the magnetic induction, B, vanish; this term often is referred to as magnetic coercive force.

Referring again to Figure 6 of United States patent 6,713,671, in one embodiment, the nanomagnetic material 103 has a coercive force of from about 0.01 to about 3,000 Oersteds. In yet
15 another embodiment, the nanomagnetic material 103 has a coercive force of from about 0.1 to about 10.

Referring again to such Figure 6, the nanomagnetic material 103 in film 104 preferably has a relative magnetic permeability of from about 1 to about 500,000; in one embodiment, such material 103 has a relative magnetic permeability of from about 1.5 to about 260,000. As used in this specification, the term relative magnetic permeability is equal to B/H , and is also equal to the slope of a section of
20 the magnetization curve of the film. Reference may be had, e.g., to page 4-28 of E.U. Condon et al.'s "Handbook of Physics" (McGraw-Hill Book Company, Inc., New York, 1958). The relative alternating current magnetic permeability is the permeability of the film when it is subjected to an alternating current of 64 megahertz.

Reference also may be had to page 1399 of Sybil P. Parker's "McGraw-Hill Dictionary of
25 Scientific and Technical Terms," Fourth Edition (McGraw Hill Book Company, New York, 1989). As is disclosed on this page 1399, permeability is "...a factor, characteristic of a material, that is proportional to the magnetic induction produced in a material divided by the magnetic field strength; it is a tensor when these quantities are not parallel."

In one embodiment, the nanomagnetic material 103 in film 104 has a relative magnetic
30 permeability of from about 1.5 to about 2,000.

Referring again to Figure 6 of United States patent 6,713,671, the nanomagnetic material 103 in film 104 preferably has a mass density of at least about 0.001 grams per cubic centimeter; in one embodiment, such mass density is at least about 1 gram per cubic centimeter. As used in this specification, the term mass density refers to the mass of a give substance per unit volume. See, e.g.,
35 page 510 of the aforementioned "McGraw-Hill Dictionary of Scientific and Technical Terms." In one embodiment, the film 104 has a mass density of at least about 3 grams per cubic centimeter. In another

embodiment, the nanomagnetic material 103 has a mass density of at least about 4 grams per cubic centimeter.

Referring again to Figure 6 of United States patent 6,713,671, and in the embodiment depicted in such Figure 6, the film 104 is disposed above 100 percent of the surfaces 112, 114, 116, and 118 of the conductor 106. In the embodiment depicted in Figure 2, by comparison, the nanomagnetic film is disposed around the conductor.

Yet another embodiment is depicted in Figure 7 of United States patent 6,713,671. In the embodiment depicted in Figure 7, the film 104 is not disposed in front of either surface 114, or 116, or 118 of the conductor 106. Inasmuch as radiation is not directed towards these surfaces, this is possible.

What is essential in this embodiment, however, is that the film 104 be interposed between the radiation 102 and surface 112. It is preferred that film 104 be disposed above at least about 50 percent of surface 112. In one embodiment, film 104 is disposed above at least about 90 percent of surface 112.

Referring again to Figure 8A of United States patent 6,713,671, and in the preferred embodiment depicted in Figure 8A, the nanomagnetic material 202 may be disposed within an insulating matrix (not shown) so that any heat produced by such particles will be slowly dispersed within such matrix. Such matrix, as indicated hereinabove, may be made from ceria, calcium oxide, silica, alumina, and the like. In general, the insulating material 202 preferably has a thermal conductivity of less than about 20 (calories centimeters/square centimeters-degree second) x 10,000. See, e.g., page E-6 of the 63rd. Edition of the "Handbook of Chemistry and Physics" (CRC Press, Inc. Boca Raton, Florida, 1982).

Referring again to Figure 8A of United States patent 6,713,67, and in the preferred embodiment depicted therein the nanomagnetic material 202 typically comprises one or more of iron, cobalt, nickel, gadolinium, and samarium atoms. Thus, e.g., typical nanomagnetic materials include alloys of iron, and nickel (permalloy), cobalt, niobium and zirconium (CNZ), iron, boron, and nitrogen, cobalt, iron, boron and silica, iron, cobalt, boron, and fluoride, and the like. These and other materials are described in a book by J. Douglass Adam et al. entitled "Handbook of Thin Film Devices" (Academic Press, San Diego, California, 2000). Chapter 5 of this book beginning at page 185 describes "magnetic films for planar inductive components and devices;" and Tables 5.1 and 5.2 in this chapter describes many magnetic materials.

Figure 11 of United States patent 6,713,671 is a schematic sectional view of a substrate 401, which is part of an implantable medical device (not shown). Referring to such Figure 11, and in the preferred embodiment depicted therein, it will be seen that substrate 401 is coated with a layer 404 of nanomagnetic material(s). The layer 404, in the embodiment depicted, is comprised of nanomagnetic particulate 405 and nanomagnetic particulate 406. Each of the nanomagnetic particulate 405 and nanomagnetic particulate 406 preferably has an elongated shape, with a length that is greater than its diameter. In one aspect of this embodiment, nanomagnetic particles 405 have a different size than nanomagnetic particles 406. In another aspect of this embodiment, nanomagnetic particles 405 have

different magnetic properties than nanomagnetic particles 406. Referring again to such Figure 11, and in the preferred embodiment depicted therein, nanomagnetic particulate material 405 and nanomagnetic particulate material 406 are designed to respond to an static or time-varying electromagnetic fields or effects in a manner similar to that of liquid crystal display (LCD) materials. More specifically, these
5 nanomagnetic particulate materials 405 and nanomagnetic particulate materials 406 are designed to shift alignment and to effect switching from a magnetic shielding orientation to a non-magnetic shielding orientation. As will be apparent, the magnetic shield provided by layer 404, can be turned "ON" and "OFF" upon demand. In yet another embodiment (not shown), the magnetic shield is turned on when heating of the shielded object is detected.

10 In one embodiment of the invention, also described in United States patent 6,713,671, there is provided a coating of nanomagnetic particles that consists of a mixture of aluminum oxide (Al_2O_3), iron, and other particles that have the ability to deflect electromagnetic fields while remaining electrically non-conductive. Preferably the particle size in such a coating is approximately 10
15 nanometers. Preferably the particle packing density is relatively low so as to minimize electrical conductivity. Such a coating when placed on a fully or partially metallic object (such as a guide wire, catheter, stent, and the like) is capable of deflecting electromagnetic fields, thereby protecting sensitive internal components, while also preventing the formation of eddy currents in the metallic object or coating. The absence of eddy currents in a metallic medical device provides several advantages, to wit:
20 (1) reduction or elimination of heating, (2) reduction or elimination of electrical voltages which can damage the device and/or inappropriately stimulate internal tissues and organs, and (3) reduction or elimination of disruption and distortion of a magnetic-resonance image.

In one portion of United States patent 6,713,671, the patentees described one embodiment of a composite shield. This embodiment involves a shielded assembly comprised of a substrate and, disposed above a substrate, a shield comprising from about 1 to about 99 weight percent of a first
25 nanomagnetic material, and from about 99 to about 1 weight percent of a second material with a resistivity of from about 1 microohm-centimeter to about 1×10^{25} microohm centimeters.

Figure 29 of United States patent 6,713,671 is a schematic of a preferred shielded assembly 3000 that is comprised of a substrate 3002. The substrate 3002 may be any one of the substrates illustrated hereinabove. Alternatively, or additionally, it may be any receiving surface which it is
30 desired to shield from magnetic and/or electrical fields. Thus, e.g., the substrate can be substantially any size, any shape, any material, or any combination of materials. The shielding material(s) disposed on and/or in such substrate may be disposed on and/or in some or all of such substrate.

Referring again to Figure 29 of United States patent 6,713,671, and by way of illustration and not limitation, the substrate 3002 may be, e.g., a foil comprised of metallic material and/or polymeric
35 material. The substrate 3002 may, e.g., comprise ceramic material, glass material, composites, etc. The substrate 3002 may be in the shape of a cylinder, a sphere, a wire, a rectilinear shaped device (such as a box), an irregularly shaped device, etc.

Referring again to Figure 29 of United States patent 6,713,671, and in one embodiment, the substrate 3002 preferably a thickness of from about 100 nanometers to about 2 centimeters. In one aspect of this embodiment, the substrate 3002 preferably is flexible.

Referring again to Figure 29 of United States patent 6,713,671, and in the preferred
5 embodiment depicted therein, it will be seen that a shield 3004 is disposed above the substrate 3002. As used herein, the term "above" refers to a shield that is disposed between a source 3006 of electromagnetic radiation and the substrate 3002.

The shield 3004 is comprised of from about 1 to about 99 weight percent of nanomagnetic material 3008; such nanomagnetic material, and its properties, are described elsewhere in this
10 specification. In one embodiment, the shield 3004 is comprised of at least about 40 weight percent of such nanomagnetic material 3008. In another embodiment, the shield 3004 is comprised of at least about 50 weight percent of such nanomagnetic material 3008.

Referring again to Figure 29 of such United States patent 6,713,671, and in the preferred embodiment depicted therein, it will be seen that the shield 3004 is also comprised of another material
15 3010 that preferably has an electrical resistivity of from about 1 microhm-centimeter to about 1×10^{25} microhm-centimeters. This material 3010 is preferably present in the shield at a concentration of from about 1 to about 1 to about 99 weight percent and, more preferably, from about 40 to about 60 weight percent.

In one embodiment, the material 3010 has a dielectric constant of from about 1 to about 50
20 and, more preferably, from about 1.1 to about 10. In another embodiment, the material 3010 has resistivity of from about 3 to about 20 microhm-centimeters.

In one embodiment, the material 3010 preferably is a nanoelectrical material with a particle size of from about 5 nanometers to about 100 nanometers.

In another embodiment, the material 3010 has an elongated shape with an aspect ratio (its
25 length divided by its width) of at least about 10. In one aspect of this embodiment, the material 3010 is comprised of a multiplicity of aligned filaments.

In one embodiment, the material 3010 is comprised of one or more of the compositions of United States patent 5,827,997 and 5,643,670.

Thus, e.g., the material 3010 may comprise filaments, wherein each filament comprises a metal
30 and an essentially coaxial core, each filament having a diameter less than about 6 microns, each core comprising essentially carbon, such that the incorporation of 7 percent volume of this material in a matrix that is incapable of electromagnetic interference shielding results in a composite that is substantially equal to copper in electromagnetic interference shielding effectiveness at 1-2 gigahertz.

In another embodiment, the material 3010 is a particulate carbon complex comprising: a
35 carbon black substrate, and a plurality of carbon filaments each having a first end attached to said carbon black substrate and a second end distal from said carbon black substrate, wherein said particulate carbon complex transfers electrical current at a density of 7000 to 8000 milliamperes per

square centimeter for a Fe+2/Fe+3 oxidation/reduction electrochemical reaction couple carried out in an aqueous electrolyte solution containing 6 millmoles of potassium ferrocyanide and one mole of aqueous potassium nitrate.

In another embodiment, the material 3010 may be a diamond-like carbon material. As is known to those skilled in the art, this diamond-like carbon material has a Mohs hardness of from about 2 to about 15 and, preferably, from about 5 to about 15. Reference may be had, e.g., to United States patents 5,098,737 (amorphous diamond material), 5,658,470 (diamond-like carbon for ion milling magnetic material), 5,731,045 (application of diamond-like carbon coatings to tungsten carbide components), 6,037,016 (capacitively coupled radio frequency diamond-like carbon reactor), 6,087,025 (application of diamond like material to cutting surfaces), and the like.

In another embodiment, material 3010 is a carbon nanotube material. These carbon nanotubes generally have a cylindrical shape with a diameter of from about 2 nanometers to about 100 nanometers, and length of from about 1 micron to about 100 microns.

These carbon nanotubes are well known to those skilled in the art. Reference may be had, e.g., to United States patent 6,203,864 (heterojunction comprised of a carbon nanotube), 6,361,861 (carbon nanotubes on a substrate), 6,445,006 (microelectronic device comprising carbon nanotube components), 6,457,350 (carbon nanotube probe tip), and the like.

In one embodiment, material 3010 is silicon dioxide particulate matter with a particle size of from about 10 nanometers to about 100 nanometers.

In another embodiment, the material 3010 is particulate alumina, with a particle size of from about 10 to about 100 nanometers. Alternatively, or additionally, one may use aluminum nitride particles, cerium oxide particles, yttrium oxide particles, combinations thereof, and the like; regardless of the particle(s) used, it is preferred that its particle size be from about 10 to about 100 nanometers.

Referring again to Figure 29 of United States patent 6,713,671, and in the embodiment depicted in such Figure 29, the shield 3004 is in the form of a layer of material that has a thickness of from about 100 nanometers to about 10 microns. In this embodiment, both the nanomagnetic particles 3008 and the electrical particles 3010 are present in the same layer.

In the embodiment depicted in Figure 30 of United States patent 6,713,671, by comparison, the shield 3012 is comprised of layers 3014 and 3016. The layer 3014 is comprised of at least about 50 weight percent of nanomagnetic material 3008 and, preferably, at least about 90 weight percent of such nanomagnetic material 3008. The layer 3016 is comprised of at least about 50 weight percent of electrical material 3010 and, preferably, at least about 90 weight percent of such electrical material 3010.

Referring to Figure 30 of United States patent 6,713,671, and in the embodiment depicted therein, the layer 3014 is disposed between the substrate 3002 and the layer 3016. In the embodiment depicted in Figure 31, the layer 3016 is disposed between the substrate 3002 and the layer 3014. Each of the layers 3014 and 3016 preferably has a thickness of from about 10 nanometers to about 5 microns.

Referring again to Figure 30 of United States patent 6,713,671, and in one embodiment, the shield 3012 has an electromagnetic shielding factor of at least about 0.9, i.e., the electromagnetic field strength at point 3020 is no greater than about 10 percent of the electromagnetic field strength at point 3022.

Referring again to Figure 31 of United States patent 6,713,671, and in one preferred embodiment, the nanomagnetic material preferably has a mass density of at least about 0.01 grams per cubic centimeter, a saturation magnetization of from about 1 to about 36,000 Gauss, a coercive force of from about 0.01 to about 5000 Oersteds, a relative magnetic permeability of from about 1 to about 500,000, and an average particle size of less than about 100 nanometers.

In one embodiment, the medical devices described elsewhere in this specification are coated with a coating that provides specified "signature" when subjected to the MRI field, regardless of the orientation of the device. Such a medical device may be the sealed container 12 (see Figure 1), a stent, etc. For the purposes of simplicity of description, the coating of a stent will be described, it being understood that the same technology could be used to coat other medical devices. The effect of such coating is illustrated in Figure 13.

Figure 13 is a plot of the image response of the MRI apparatus (image clarity) as a function of the applied MRI fields. The image clarity is generally related to the net reactance.

Referring to Figure 13, plot 802 illustrates the response of a particular uncoated stent in a first orientation in a patient's body. As will be seen from plot 802, this stent in this first orientation has an effective net inductive response.

Figure 13, and in particular plot 804, illustrates the response of the same uncoated stent in a second orientation in a patient's body. As has been discussed elsewhere in this specification, the response of an uncoated stent is orientation specific. Thus, plot 804 shows a smaller inductive response than plot 802.

When the uncoated stent is coated with the appropriate coating, as described elsewhere in this specification, the net reactive effect is zero, as is illustrated in plot 806. In this plot 806, the magnetic response of the substrate is nullified regardless of the orientation of such substrate within a patient's body.

In one embodiment, illustrated as plot 808, a stent is coated in such a manner that its net reactance is substantially larger than zero, to provide a unique imaging signature for such stent. Because the imaging response of such coated stent is also orientation independent, one may determine its precise location in a human body with the use of conventional MRI imaging techniques. In effect, the coating on the stent 808 acts like a tracer, enabling one to locate the position of the stent 808 at will.

In one embodiment, if one knows the MRI signature of a stent in a certain condition, one may be able to determine changes in such stent. Thus, for example, if one knows the signature of such stent with plaque deposited on it, and the signature of such stent without plaque deposited on it, one may be able to determine a human body's response to such stent.

Preparation of coatings comprised of nanoelectrical material

In this portion of the specification, coatings comprised of nanoelectrical material will be described. In accordance with one aspect of this invention, there is provided a nanoelectrical material with an average particle size of less than 100 nanometers, a surface area to volume ratio of from about 0.1 to about 0.05 1/nanometer, and a relative dielectric constant of less than about 1.5.

The nanoelectrical particles of aspect of the invention have an average particle size of less than about 100 nanometers. In one embodiment, such particles have an average particle size of less than about 50 nanometers. In yet another embodiment, such particles have an average particle size of less than about 10 nanometers.

The nanoelectrical particles of this invention have surface area to volume ratio of from about 0.1 to about 0.05 1/nanometer.

When the nanoelectrical particles of this invention are agglomerated into a cluster, or when they are deposited onto a substrate, the collection of particles preferably has a relative dielectric constant of less than about 1.5. In one embodiment, such relative dielectric constant is less than about 1.2.

In one embodiment, the nanoelectrical particles of this invention are preferably comprised of aluminum, magnesium, and nitrogen atoms. This embodiment is illustrated in Figure 14.

Figure 14 illustrates a phase diagram 2000 comprised of moieties A, B, and C. Moiety A is preferably selected from the group consisting of aluminum, copper, gold, silver, and mixtures thereof. It is preferred that the moiety A have a resistivity of from about 2 to about 100 microhm-centimeters. In one preferred embodiment, A is aluminum with a resistivity of about 2.824 microhm-centimeters. As will apparent, other materials with resistivities within the desired range also may be used.

Referring again to Figure 14, C is selected from the group consisting of nitrogen and oxygen. It is preferred that C be nitrogen, and A is aluminum; and aluminum nitride is present as a phase in system.

Referring again to Figure 14, B is preferably a dopant that is present in a minor amount in the preferred aluminum nitride. In general, less than about 50 percent (by weight) of the B moiety is present, by total weight of the doped aluminum nitride. In one aspect of this embodiment, less than about 10 weight percent of the B moiety is present, by total weight of the doped aluminum nitride.

The B moiety may be, e.g., magnesium, zinc, tin, indium, gallium, niobium, zirconium, strontium, lanthanum, tungsten, mixtures thereof, and the like. In one embodiment, B is selected from the group consisting of magnesium, zinc, tin, and indium. In another especially preferred embodiment, the B moiety is magnesium.

Referring again to Figure 14, and when A is aluminum, B is magnesium, and C is nitrogen, it will be seen that regions 2002 and 2003 correspond to materials which have a low relative dielectric constant (less than about 1.5), and a high relative dielectric constant (greater than about 1.5), respectively.

Figure 15 is a schematic view of a coated substrate 2004 comprised of a substrate 2005 and a multiplicity of nanoelectrical particles 2006. In this embodiment, it is preferred that the nanoelectrical particles 2006 form a film with a thickness 2007 of from about 10 nanometers to about 2 micrometers and, more preferably, from about 100 nanometers to about 1 micrometer.

5 A coated substrate with a dense coating

Figure 16A and 16B are sectional and top views, respectively, of a coated substrate 2100 assembly comprised of a substrate 2102 and, disposed therein, a coating 2104.

In the embodiment depicted, the coating 2104 has a thickness 2106 of from about 400 to about 2,000 nanometers and, in one embodiment, has a thickness of from about 600 to about 1200
10 nanometers.

Referring again to Figures 16A and 16B, it will be seen that coating 2104 has a morphological density of at least about 98 percent. As is known to those skilled in the art, the morphological density of a coating is a function of the ratio of the dense coating material on its surface to the pores on its surface; and it is usually measured by scanning electron microscopy.

15 By way of illustration, published United States patent application US 2003/0102222A1 contains a Figure 3A that is a scanning electron microscope (SEM) image of a coating of "long" single-walled carbon nanotubes on a substrate. Referring to this SEM image, it will be seen that the white areas are the areas of the coating where pores occur.

The technique of making morphological density measurements also is described, e.g., in a M.S. thesis by Raymond Lewis entitled "Process study of the atmospheric RF plasma deposition system for oxide coatings" that was deposited in the Scholes Library of Alfred University, Alfred, New York in
20 1999 (call Number TP2 a75 1999 vol. 1., no. 1.).

Figures 16A and 16B schematically illustrate the porosity of the side 2107 of coating 2104, and the top 2109 of the coating 2104. The SEM image depicted shows two pores 2108 and 2110 in the
25 cross-sectional area 2107, and it also shows two pores 2212 and 2114 in the top 2109. As will be apparent, the SEM image can be divided into a matrix whose adjacent lines 2116/2120, and adjacent lines 2118/2122 define square portion with a surface area of 100 square nanometers (10 nanometers x 10 nanometers). Each such square portion that contains a porous area is counted, as is each such square portion that contains a dense area. The ratio of dense areas/porous areas, x 100, is preferably at least
30 98. Put another way, the morphological density of the coating 2104 is at least 98 percent. In one embodiment, the morphological density of the coating 2104 is at least about 99 percent. In another embodiment, the morphological density of the coating 2104 is at least about 99.5 percent.

One may obtain such high morphological densities by atomic size deposition, i.e., the particles sizes deposited on the substrate are atomic scale. The atomic scale particles thus deposited often
35 interact with each other to form nano-sized moieties that are less than 100 nanometers in size.

In one embodiment, the coating 2104 (see Figures 16A and 16B) has an average surface roughness of less than about 100 nanometers and, more preferably, less than about 10 nanometers. As is

known to those skilled in the art, the average surface roughness of a thin film is preferably measured by an atomic force microscope (AFM).

Alternatively, or additionally, one may measure surface roughness by a laser interference technique. This technique is well known.

5 In one embodiment, the coated substrate of this invention has durable magnetic properties that do not vary upon extended exposure to a saline solution. If the magnetic moment of a coated substrate is measured at "time zero" (i.e., prior to the time it has been exposed to a saline solution), and then the coated substrate is then immersed in a saline solution comprised of 7.0 mole percent of sodium chloride and 93 mole percent of water, and if the substrate/saline solution is maintained at atmospheric pressure
10 and at temperature of 98.6 degrees Fahrenheit for 6 months, the coated substrate, upon removal from the saline solution and drying, will be found to have a magnetic moment that is within plus or minus 5 percent of its magnetic moment at time zero.

In another embodiment, the coated substrate of this invention has durable mechanical properties when tested by the saline immersion test described above.

15 In one embodiment, the coating 2104 is biocompatible with biological organisms. As used herein, the term biocompatible refers to a coating whose chemical composition does not change substantially upon exposure to biological fluids. Thus, when the coating 2104 is immersed in a 7.0 mole percent saline solution for 6 months maintained at a temperature of 98.6 degrees Fahrenheit, its chemical composition (as measured by, e.g., energy dispersive X-ray analysis [EDS, or EDAX]) is
20 substantially identical to its chemical composition at "time zero."

A preferred process of the invention

In one embodiment of the invention, best illustrated in Figure 9, a coated stent is imaged by an MRI imaging process. As will be apparent to those skilled in the art, the process depicted in Figure 9 can be used with reference to other medical devices such as, e.g., a coated brachytherapy seed (see, e.g.,
25 Figure 1).

In the first step of this process, the coated stent described by reference to Figure 9 is contacted with the radio-frequency, direct current, and gradient fields normally associated with MRI imaging processes; these fields are discussed elsewhere in this specification. They are depicted as an MRI imaging signal 440 in Figure 9

30 In the second step of this process, the MRI imaging signal 440 penetrates the coated stent 400 and interacts with material disposed on the inside of such stent, such as, e.g., plaque particles 430 and 432. This interaction produces a signal best depicted as arrow 441 in Figure 9.

In one embodiment, the signal 440 is substantially unaffected by its passage through the coated stent 400. Thus, in this embodiment, the radio-frequency field that is disposed on the outside of the
35 coated stent 400 is substantially the same as the radio-frequency field that passes through and is disposed on the inside of the coated stent 400.

It is preferred that at least about 90 percent of such r.f. field pass through to the inside of the coated stent 400. In such a case, the stent is said to have a radio frequency shielding factor of less than about ten percent.

By comparison, when the stent (not shown) is not coated with the coatings of this invention, the characteristics of the signal 440 are substantially varied by its passage through the uncoated stent. Thus, with such uncoated stent, the radio-frequency signal that is disposed on the outside of the stent (not shown) differs substantially from the radio-frequency field inside of the uncoated stent (not shown). In some cases, because of substrate effects, substantially none of such radio-frequency signal passes through the uncoated stent (not shown).

In the third step of this process, and in one embodiment thereof, the MRI field(s) interact with material disposed on the inside of coated stent 400 such as, e.g., plaque particles 430 and 432. This interaction produces a signal 441 by means well known to those in the MRI imaging art.

In the fourth step of the preferred process of this invention, the signal 441 passes back through the coated stent 400 in a manner such that it is substantially unaffected by the coated stent 400. Thus, in this embodiment, the radio-frequency field that is disposed on the inside of the coated stent 400 is substantially the same as the radio-frequency field that passes through and is disposed on the outside of the coated stent 400.

By comparison, when the stent (not shown) is not coated with the coatings of this invention, the characteristics of the signal 441 are substantially varied by its passage through the uncoated stent. Thus, with such uncoated stent, the radio-frequency signal that is disposed on the inside of the stent (not shown) differs substantially from the radio-frequency field outside of the uncoated stent (not shown). In some cases, because of substrate effects, substantially none of such signal 441 passes through the uncoated stent (not shown).

Another preferred process of the invention

Figures 17A, 17B, and 17C illustrate another preferred process of the invention in which a medical device (such as, e.g., a stent 2200) may be imaged with an MRI imaging process. In the embodiment depicted in Figure 17A, the stent 2200 is comprised of plaque 2202 disposed inside the inside wall 2204 of the stent 2200.

Figure 17B illustrates three images produced from the imaging of stent 2200, depending upon the orientation of such stent 2200 in relation to the MRI imaging apparatus reference line (not shown). With a first orientation, an image 2206 is produced. With a second orientation, an image 2208 is produced. With a third orientation, an image 2210 is produced.

By comparison, Figure 17C illustrates the images obtained when the stent 2200 has the nanomagnetic coating of this invention disposed about it. Thus, when the coated stent 400 of Figure 9 is imaged, the images 2212, 2214, and 2216 are obtained.

The images 2212, 2214, and 2216 are obtained when the coated stent 400 is at the orientations of the uncoated stent 2200 the produced images 2206, 2208, and 2210, respectively. However, as will be noted, despite the variation in orientations, one obtains the same image with the coated stent 400.

Thus, e.g., the image 2218 of the coated stent (or other coated medical device) will be identical regardless of how such coated stent (or other coated medical device) is oriented vis-a-vis the MRI imaging apparatus reference line (not shown). Thus, e.g., the image 2220 of the plaque particles will be the same regardless of how such coated stent is oriented vis-a-vis the MRI imaging apparatus reference line (not shown).

Consequently, in this embodiment of the invention, one may utilize a nanomagnetic coating that, when imaged with the MRI imaging apparatus, will provide a distinctive and reproducible imaging response regardless of the orientation of the medical device.

Figures 18A and 18B illustrate a hydrophobic coating 2300 and a hydrophilic coating 2301 that may be produced by the process of this invention.

As is known to those skilled in the art, a hydrophobic material is antagonistic to water and incapable of dissolving in water. A hydrophobic surface is illustrated in Figure 18A.

Referring to Figure 18A, it will be seen that a coating 2300 is deposited onto substrate 2302. In the embodiment depicted, the coating 2300 an average surface roughness of less than about 1 nanometer. Inasmuch as the average water droplet has a minimum cross-sectional dimension of at least about 3 nanometers, the water droplets 2304 will tend not to bond to the coated surface 2306 which, thus, is hydrophobic with regard to such water droplets.

One may vary the average surface roughness of coated surface 2306 by varying the pressure used in the sputtering process described elsewhere in this specification. In general, the higher the gas pressure used, the rougher the surface.

Figure 18BB illustrates water droplets 2308 between surface features 2310 of coated surface 2312. In this embodiment, because the surface features 2310 are spaced from each other by a distance of at least about 10 nanometers, the water droplets 2308 have an opportunity to bond to the surface 2312 which, in this embodiment, is hydrophilic.

The bond formed between the substrate and the coating

Applicants believe that, in at least one preferred embodiment of the process of their invention, the particles in their coating diffuse into the substrate being coated to form an interfacial diffusion layer. This structure is best illustrated in Figure 19 which, as will be apparent, is not drawn to scale.

Referring to Figure 19, the coated assembly 3000 is preferably comprised of a coating 3002 disposed on a substrate 3004. The coating 3002 preferably has a thickness 3008 of at least about 150 nanometers.

The interlayer 3006, by comparison, has a thickness of 3010 of less than about 10 nanometers and, preferably, less than about 5 nanometers. In one embodiment, the thickness of interlayer 3010 is less than about 2 nanometers.

The interlayer 3006 is preferably comprised of a heterogeneous mixture of atoms from the substrate 3004 and the coating 3002. It is preferred that at least 10 mole percent of the atoms from the coating 3002 are present in the interlayer 3006, and that at least 10 mole percent of the atoms from the substrate 3004 are in the interlayer 3006. It is more preferred that from about 40 to about 60 mole percent of the atoms from each of the coating and the substrate be present in the interlayer 3006, it being apparent that more atoms from the coating will be present in that portion 3012 of the interlayer closest to the coating, and more atoms from the substrate will be present in that portion 3014 closest to the substrate.

In one embodiment, the substrate 3004 will consist essentially of niobium atoms with from about 0 to about 2 molar percent of zirconium atoms present. In another embodiment, the substrate 3004 will comprise nickel atoms and titanium atoms. In yet another embodiment, the substrate will comprise tantalum atoms, or titanium atoms.

The coating may comprise any of the A, B, and/or C atoms described hereinabove. By way of way of illustration, the coating may comprise aluminum atoms and oxygen atoms (in the form of aluminum oxide), iridium atoms and oxygen atoms (in the form of iridium oxide), etc.

A coated substrate with a specified surface morphology

Figure 20 is a sectional schematic view of a coated substrate 3100 comprised of a substrate 3102 and, bonded thereto, a layer 3104 of nano-sized particles that may comprise nanomagnetic particles, nanoelectrical particles, nanoinsulative particles, nanothermal particles. These particles, the mixtures thereof, and the matrices in which they are disposed have all been described elsewhere in this specification. Depending upon the properties desired from the coated substrate 3100 and/or the layer 3104, one may use one or more of the coating constructs described elsewhere in this specification. Thus, e.g., depending upon the type of particle(s) used and its properties, one may produce a desired set of electrical and magnetic properties for either the coated substrate 3100, the substrate 3200, and/or the coating 3104..

In one embodiment, the coating 3104 is comprised of at least about 5 weight percent of nanomagnetic material with the properties described elsewhere in this specification. In another embodiment, the coating 3104 is comprised of at least 10 weight percent of nanomagnetic material. In yet another embodiment, the coating 3104 is comprised of at least about 40 weight percent of nanomagnetic material..

Referring again to Figure 20, and to the preferred embodiment depicted therein, the surface 3106 of the coating 3104 is comprised of a multiplicity of morphological indentations 3108 sized to receive drug particles 3110.

In one embodiment, the drug particles are particles of an anti-microtubule agent.

As is known to those skilled in the art, paclitaxel is an anti-microtubule agent. As that term is used in this specification, the term "anti-microtubule agent" includes any protein, peptide, chemical, or other molecule which impairs the function of microtubules, for example, through the prevention or

stabilization of polymerization. Many of these anti-microtubule agents are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

In the process of this invention, the anti-microtubule agent may be utilized by itself, and/or it may be utilized in a formulation that comprises such agent and a carrier. The carrier may be either of
5 polymeric or non-polymeric origin; it may, e.g., be one or more of the polymeric materials 14 (see Figures 1 and 1A) described elsewhere in this specification.. Many suitable carriers for anti-microtubule agents are disclosed at columns 6-9 of such United States patent 6,333,347.

The anti-microtubule agents used in one embodiment of the process of this invention may be formulated in a variety of forms suitable for administration; and they may be formulated to contain
10 more than one anti-microtubule agents, to contain a variety of additional compounds, to have certain physical properties such as, e.g., elasticity, a particular melting point, or a specified release rate.

Anti-microtubule agents with a magnetic moment

In one embodiment of the process of this invention, the drug particles 3110 used (see Figure 20) are particles of an anti-microtubule agent with a magnetic moment. Some of these "magnetic
15 moment anti-microtubule agents" are disclosed in applicants' copending United States patent application U.S.S.N. 60/516,134, filed on October 31, 2003. Other of these "magnetic moment anti-microtubule agents" are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

In one embodiment, paclitaxel is bonded to the nanomagnetic particles of this invention in the
20 manner described in United States patent 6,200,547.

Referring again to Figure 20 of the instant specification, and to the preferred embodiment depicted therein, the morphologically indented surface 3106 may be made by conventional means.

Referring again to Figure 20, and in one preferred embodiment thereof, the size of the indentations 3108 is preferably chosen such that it matches the size of the drug particles 3110. In one
25 embodiment, depicted in Figure 36A, the surface 3112 of the indentations 3108 is coated with receptor material 3114 adapted to bind to the drug particles 3110.

Receptor material 3114 is comprised of a "recognition molecule". As is known to those skilled in the art, recognition is a specific binding interaction occurring between macromolecules. These "recognition molecules" and "recognition systems" are described in copending patent application
30 U.S.S.N. 10/887,521, filed on July 7, 2004.

Referring again to Figure 20, and in the embodiment depicted, an external electromagnetic field 3116 is shown being applied near the surface 3106 of the coated substrate 3100. In the embodiment depicted, this applied field 3116 is adapted to facilitate the bonding of the drug particles 3110 to the indentations 3108. As long as such indentations are not totally filled, and as long as the
35 appropriate electromagnetic field is applied, then the drug molecules 3110 will continue to bond to such indentations 3108. In one embodiment, not depicted in Figure 20, instead of drug particles 3110 or in

addition thereto, one or more of the nanomagnetic particles of this invention may be caused to bind to a specific site within a biological organism.

The external attachment electromagnetic field 3116 may, e.g., be ultrasound. It is known that ultrasound can be used to greatly enhance the rate of binding between members of a specific binding pair. Other ultrasound devices and processes are discussed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

In one embodiment, the electromagnetic radiation used in the process of this invention is a magnetic field with a field strength of at least about 6 Tesla. It is known, e.g., that microtubules move linearly in magnetic fields of at least about 6 Tesla.

In this embodiment, the focusing of the magnetic field onto an in vivo site within a patient may be done by conventional magnetic focusing means. Some of these magnetic focusing means are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

Figure 20B is a schematic of an electromagnetic coil set 3160 and 3162, aligned to an axis 3164, and which in combination create a magnetic standing wave 3166. The excitation energy delivered to the two coils 3160 and 3162 comprises a set of high frequency sinusoidal signals that are determined via well known Fourier techniques, to create a first zone 3168 having a positive standing wave magnetic field 'E', a second zone 3170 having a zero or near-zero magnetic field, and a third zone 3172 having a positive magnetic field 'E'. It should be noted that the two zones 3168 and 3172 need not have exactly matched waveforms, in frequency, phase, or amplitude; it is sufficient that the magnetic fields in both are large with respect to the near-zero magnetic field in zone 3170. The fields in zones 3168 and 3172 may be static standing wave fields or time-varying standing waves. It should be noted that in order to create a zone 3170 of useful size (1 to 5 cm at the lower limit) and having reasonably sharp 'edges', the frequencies of the Fourier waveforms used to create standing wave 3166 may be in the gigahertz range. These fields may be switched on and off at some secondary frequency that is substantially lower; the resulting switched-standing-wave fields in zones 3168 and 3172 will impart vibrational energy to any magnetic materials within them, while the near-zero switched field in zone 3170 will not impart substantial energy into magnetic materials within its boundaries. This secondary switching frequency may be adjusted in concert with the amplitude of the standing wave field to tune the vibrational energy to impart an optimal level of thermal energy to a specific molecule (e.g. paclitaxel) by virtue of the natural resonant frequency of that molecule. The energy imparted to an individual molecule will follow the relationship $E_T = C \times M \times A \times F^2$, where E_T is the thermal energy imparted to an individual molecule, C is a constant, M is the magnetic moment of the molecule and any bound magnetic particles, A is the amplitude of the time-varying magnetic field, and F is the frequency of field switching.

Figure 20C is a three-dimensional schematic showing the use of three sets of magnetic coils arranged orthogonally. Each of the axes, 'X', 'Y', and 'Z' will impart either positive thermal energy (E) in its outer zones that correspond to zones 3168 and 3172 (from Figure 20B), or zero thermal

energy, in its central zone which corresponds to zone 3170 (from Figure 20B). It may be seen from Figure 20C that there will be a small volume at the centroid of the overall 3-D volume that will have overall zero magnetically-induced thermal energy. The notations '1 x E', '2 x E', and '3 x E' denote the relative magnetically-induced thermal energy in other regions. Since the overall volume is made up of three zones in each of three dimensions, the overall volume will have 27 sectors. Of these sectors one (the centroid) will have near-zero magnetically-induced thermal energy, (6) sectors will have a '1 x E' energy level, (12) sectors will have a '2 x E' energy level, and (8) sectors will have a '3 x E' energy level.

If the energy imported to any individual molecule (e.g. paclitaxel bound to one or more nanomagnetic particles) is sufficiently larger than the binding energy of that molecule to its target (e.g. tubulin in the case of paclitaxel) to account for thermal losses in coupling magnetically-induced energy into the molecule, then binding between the paclitaxel molecule and the tubulin target will not occur. Thus if we define the binding energy between the two (e.g. paclitaxel to tubulin) as E_B , and D as a constant that compensates for damping losses due to a molecule that is not purely elastic, then the equation $E_T > D \times E_B$ will have been satisfied, and chemical binding (in this case between paclitaxel and tubulin) will not occur.

In one embodiment, a device having matched coil sets as shown in Figure 20B, but in three orthogonal axes, creates an overall operational volume that imparts an relatively low energy in the above-described centroid ($E_T < D \times E_B$), and imparts a relatively higher energy in the other surrounding (26) segments ($E_T > D \times E_B$); and if the centroid volume corresponds to the site under treatment, then a high degree of binding will occur in the centroid and no binding will occur in the exterior regions. The size of the non-binding centroid region may be adjusted via alterations to the Fourier waveforms, relative energy levels may be adjusted via amplitude and frequency of field switching, and the region may be aligned to correspond to the volume of the tumor under treatment. One preferred method for use is to place the patient in the device as disclosed herein, administer either native paclitaxel (or other drug having an innate magnetic characteristic) or magnetically-enhanced Paclitaxel (nanomagnetic or other magnetic particles either chemically or magnetically bound), maintain the patient in the controlled fields for a period of time necessary for the drug to pass out of the patient's excretory system, and then remove the patient from the device.

In another embodiment, the three fields in the X, Y, and Z directions are selectively activated and deactivated in a predetermined pattern. For example, one may activate the field in the X axis, thus causing the therapeutic agent to align with the X axis. A certain time later the field along the X axis is deactivated and the field corresponding to the Y axis is activated for a predetermined period of time. The agent then aligns with the new axis. This may be repeated along any axis. By rapidly activating and deactivating the respective fields in a predetermined pattern, one imparts thermal and/or rotational energy to the molecule. When the energy imparted to the therapeutic agent is greater than the binding energy necessary to bring about a biological effect, such binding is drastically reduced.

In another embodiment, the Fourier techniques are selected so as to create a near-zero magnetic field zone external to the tissue to be treated, while a time-varying standing wave is generated within the centroid region. A therapeutic agent that is weakly attached to a magnetic carrier particle (a carrier-agent complex) is introduced into the body. In one embodiment, the carrier particle acts to inhibit the biological activity of the therapeutic agent. When the carrier-agent complex enters the region of variable magnetic field located at the centroid, the thermal energy imparted to the carrier-agent complex the agent is liberated from its carrier and is no longer inhibited by the presence of that carrier. The region external to the centroid is a near-zero magnetic field, thus minimizing any premature dissociation of the carrier-agent complex.

In one embodiment the carrier particles are organic moieties that are covalently attached to the therapeutic agent. By way of illustration and not limitation, one may covalently attach a nitroxide spin label to a therapeutic agent. As is known to those skilled in the art, a nitroxide spin label is a persistent paramagnetic free radical. Biomolecules are routinely modified by the attachment of such labeling compounds, thus generating paramagnetic biomolecules. Reference may be had to United States patent 6,271,382, the entire disclosure of which is hereby incorporated by reference into this specification.

In another embodiment the carrier particles are magnetic encapsulating agents that surround the therapeutic agent. By way of illustration and not limitation, one may encapsulate a therapeutic agent within magnetosomes or magnetoliposomes described elsewhere in this specification. The agent exhibits minimal biological activity when in a near-zero magnetic field as the agent is at least partially encapsulated. When the carrier-agent complex is exposed to a variable magnetic field of sufficient intensity, the carrier particle releases the agent at or near the desired location.

Referring again to Figures 20 and 36A, it will be seen that Figure 20A is a partial sectional view of an indentation 3108 coated with a multiplicity of receptors 3114 for the drug molecules.

Figure 21 is a schematic illustration of one process for preparing a coating with morphological indentations 3108. In this process, a mask 3120 is disposed over the film 3014. The mask 3120 is comprised of a multiplicity of holes 3122 through which etchant 3124 is applied for a time sufficient to create the desired indentations 3108.

One may use conventional etching technology to prepare the desired indentations 3108. Some of these processes are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

Referring again to Figure 21, and to the process depicted therein, after the indentations 3108 have been formed, the etchant is removed from the holes 3122 and the indentations 3108 by conventional means, such as, e.g., by rinsing, and then receptor material 3114 is used to form the receptor surface. The receptor material 3114 may be deposited within the indentations by one or more of the techniques described elsewhere in this specification.

Figure 22 is a schematic illustration of a drug molecule 3130 disposed inside of a indentation 3108. Referring to Figure 22, and to the preferred embodiment depicted therein, it will be seen that a

multiplicity of nanomagnetic particles 3140 are disposed around the drug molecule 3130. In the embodiment depicted, the forces between particles 3140 and 3130 may be altered by the application of an external field 3142. In one case, the characteristics of the field are chosen to facilitate the attachment of the particles 3130 to the particles 3140. In another case, the characteristics of the field are chosen to cause detachment of the particles 3130 from the particles 3140.

In one embodiment, the drug molecule 3130 is an anti-microtubule agent. Thus, and referring to United States patent 6,333,347, the anti-microtubule agent is preferably administered to the pericardium, heart, or coronary vasculature.

As is known to those skilled in the art, most physical and chemical interactions are facilitated by certain energy patterns, and discouraged by other energy patterns. Thus, e.g., electromagnetic attractive force may be enhanced by one applied electromagnetic field, and electromagnetic repulsive force may be enhanced by another applied electromagnetic field. One, thus, by choosing the appropriate field(s), can determine the degree to which the one recognition molecule will bind to another, or to which a drug will bind to a implantable device, such as, e.g., a stent.

In one process, illustrated in Figure 23, paclitaxel is administered into the arm 3200 of a patient near a stent 3202, via an injector 3204. During this administration, a first electromagnetic field 3206 is directed towards the stent 3202 in order to facilitate the binding of the paclitaxel to the stent. When it has been determined that a sufficient amount of paclitaxel has bound to the stent, a second electromagnetic field 3208 is directed towards the stent 3202 to discourage the binding of paclitaxel to the stent. The strength of the second electromagnetic field 3208 is sufficient to discourage such binding but not necessarily sufficient to dislodge paclitaxel particles already bound to the stent and disposed within indentations 3208.

A preferred binding process

Figure 24 is a schematic illustration of a preferred binding process of the invention. As will be apparent, Figure 24 is not drawn to scale, and unnecessary detail has been omitted for the sake of simplicity of representation.

In the first step of the process of Figure 24, a multiplicity of drug particles, such as drug particles 3130, are brought close to or contiguous with a coated substrate 3103 comprised of receptor material 3114 disposed on its top surface. The drug particles 3130 are near and/or contiguous with the receptor material 3114. They may be delivered to such receptor material 3114 by one or more of the drug delivery processes discussed elsewhere in this specification.

In the second step of the process depicted in Figure 24, the substrate 3102/coating 3104/receptor material 3114/drug particles 3130 assembly is contacted with electromagnetic radiation to affect, e.g., the binding of the drug particles 3130 to the receptor material 3114. This may be done by, e.g., the transmission of ultrasonic radiation, as is discussed elsewhere in this specification. Alternatively, or additionally, it may be done by the use of other electromagnetic radiation that is known to affect the rate of binding between two recognition moieties and/or other biological processes.

The electromagnetic radiation may be conveyed by transmitter 3132 in the direction of arrow 3134. Alternatively, or additionally, the electromagnetic radiation may be conveyed by transmitter 3136 in the direction of arrows 3138. In the embodiment depicted in Figure 40, both transmitter 3132 and/or transmitter 3136 are operatively connected to a controller 3140. The connection may be by
5 direct means (such as, e.g., line 3142), and/or by indirect means (such as, e.g., telemetry link 3144).

Referring again to Figure 24, and in the preferred embodiment depicted therein, transmitter 3132 is comprised of a sensor (not shown) that can monitor the radiation 3144 retransmitted from the surface 3114 of assembly 3103.

One may use many forms of electromagnetic radiation to affect the binding of the drug moieties
10 3130 to the receptor surface 3114. By way of illustration, and referring to United States patent 6,095,148, the growth and differentiation of nerve cells may be affected by electrical stimulation of such cells. As is disclosed in column 1 of such patent, "Electrical charges have been found to play a role in enhancement of neurite extension in vitro and nerve regeneration in vivo. Examples of conditions that stimulate nerve regeneration include piezoelectric materials and electrets, exogenous
15 DC electric fields, pulsed electromagnetic fields, and direct application of current across the regenerating nerve. Neurite outgrowth has been shown to be enhanced on piezoelectric materials such as poled polyvinylidenedifluoride (PVDF) (Aebischer et al., Brain Res., 436:165 (1987); and R. F. Valentini et al., Biomaterials, 13:183 (1992)) and electrets such as poled polytetrafluoroethylene (PTFE) (R. F. Valentini et al., Brain. Res. 480:300 (1989)). This effect has been attributed to the
20 presence of transient surface charges in the material which appear when the material is subjected to minute mechanical stresses. Electromagnetic fields also have been shown to be important in neurite extension and regeneration of transected nerve ends. R. F. Valentini et al., Brain. Res., 480:300 (1989); J. M. Kerns et al., Neuroscience 40:93 (1991); M. J. Politis et al., J. Trauma, 28:1548 (1988); and B. F. Siskin et al., Brain. Res., 485:309 (1989). Surface charge density and substrate wettability have also
25 been shown to affect nerve regeneration. Valentini et al., Brain Res., 480:300-304 (1989)."

By way of further illustration, and again referring to United States patent 5,566,685, extremely low frequency electromagnetic fields may be used to cause, e.g., "...changes in enzyme activities...", "...stimulation of bone cell growth...", "...suppression of nocturnal melatonin...", "...quantative changes in transcripts...", "changes in "...gene expression of regenerating rate liver...", "changes in "...gene
30 expression...", "changes in "...gene transcription...", "changes in "...modulation of RNA synthesis and degradation...", "...alterations in protein kinase activity...", "changes in "...growth-related enzyme ornithine decarboxylase...", "changes in embryological activity, "...stimulation of experimental endochondral ossification...", "...suppression of nocturnal melatonin...", "changes in "...human pineal gland function...", "changes in "...calcium binding...", etc. Reference may be had, in particular, to columns 2
35 and 3 of United States patent 5,566,685.

Referring again to Figure 24, and to the preferred embodiment depicted therein, the transmitter 3132 preferably has a sensor to determine the extent to which radiation incident upon, e.g., surface

3146 is reflected. Information from transmitter 3132 may be conveyed to and from controller 3140 via line 3148.

In the embodiment depicted in Figure 24, a sensor 3150 is adapted to sense the degree of binding on surface 3146 between the drug molecules 3130 and the receptor molecules 3114. This sensor 3150 preferably transmits radiation in the direction of arrow 3152 and senses reflected radiation traveling in the direction of arrow 3154. Information from and to controller 3140 is fed to and from sensor 3150 via line 3156.

There are many sensors known to those skilled in the art which can determine the extent to which two recognition molecules have bound to each other. Some of these sensors are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

Figure 25 is a schematic view of a preferred coated stent 4000 of the invention; as will be apparent, other coated medical devices may also be used.. Referring to Figure 25, and to the preferred embodiment depicted therein, it will be seen that coated stent 4000 is comprised of a stent 4002 onto which is deposited one or more of the nanomagnetic coatings 4004 described elsewhere in this specification. Disposed above the nanomagnetic coatings 4004 is a coating of drug-eluting polymer 4006.

One may use any of the drug eluting polymers known to those skilled in the art to produce coated stent 4000. Alternatively, or additionally, one may use one or more of the polymeric materials 14 described elsewhere in this specification. Many of these drug-eluting polymeric compositions are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

Referring again to Figure 25, and to the preferred embodiment depicted therein, disposed on the surface 4008 of the drug eluting polymer are a multiplicity of magnetic drug particles, such the magnetic drug particle 3130 (see Figure 22).

Figure 26 is a graph of a typical response of a magnetic drug particle, such as magnetic drug particles 3130 (see, e.g., Figure 22) to an applied electromagnetic field. As will be seen by reference to Figure 26, as the magnetic field strength 4100 of an applied magnetic field is increased along the positive axis, the magnetic moment 4102 of the magnetic drug particle(s) also continuously increases along the positive axis. As will be apparent, a decrease in the magnetic field strength also causes a decrease in magnetic moment. Thus, when the polarity of the applied magnetic field changes (see section 4106 of the graph), the magnetic moment also decreases. Thus, one may affect the magnetic moment of the magnetic drug particles by varying either the intensity of the applied electromagnetic field and/or its polarity.

Figures 27A and 27B illustrate the effect of applied fields upon the nanomagnetic coating 4004 (see Figure 25) and the magnetic drug particles 3130. Referring to Figure 27A, when the applied magnetic field 4120 is sufficient to align the drug particle 3130 in a north(up)/south(down) orientation (see Figure 27A), it will also tend to align the nanomagnetic material in such an orientation. However, because the magnetic hardness of the nanomagnetic material will be chosen to substantially exceed the

magnetic hardness of the drug particles 3130, then the applied magnetic field will not be able to realign the nanomagnetic material.

In the ensuing discussion relating to the effects of an applied electromagnetic field, certain terms (such as, e.g., "magnetization saturation") will be used. These terms (and others) have the meaning set forth in several of applicants' published patent applications and patents, including (without limitation) published patent application US20030107463, 6,700,472, 6,673,999, 6,506,972, 5,540,959, and the like.

Thus, by way of illustration, reference is made to the term "magnetization." As is disclosed in applicants' publications, magnetization is the magnetic moment per unit volume of a substance.

Thus, by way of further illustration, reference is made to the term "saturation magnetization." As is disclosed in applicants' publications, for a discussion of the saturation magnetization of various materials, reference may be had, e.g., to U.S. Pat. numbers 4,705,613, 4,631,613, 5,543,070, 3,901,741 (cobalt, samarium, and gadolinium alloys), and the like. As will be apparent to those skilled in the art, especially upon studying the aforementioned patents, the saturation magnetization of thin films is often higher than the saturation magnetization of bulk objects.

By way of further illustration, reference is made to the term "coercive force." As is disclosed in applicants' publications, the term coercive force refers to the magnetic field, H, which must be applied to a magnetic material in a symmetrical, cyclically magnetized fashion, to make the magnetic induction, B, vanish; this term often is referred to as magnetic coercive force.

In one embodiment, the nanomagnetic material 103 has a coercive force of from about 0.01 to about 3,000 Oersteds. In yet another embodiment, the nanomagnetic material 103 has a coercive force of from about 0.1 to about 10.

By way of yet further illustration, reference is made to the term relative magnetic permeability. As is disclosed in applicants' publications, the term relative magnetic permeability is equal to B/H , and is also equal to the slope of a section of the magnetization curve of the film. Reference may be had, e.g., to page 4-28 of E. U. Condon et al.'s "Handbook of Physics" (McGraw-Hill Book Company, Inc., New York, 1958). Reference also may be had to page 1399 of Sybil P. Parker's "McGraw-Hill Dictionary of Scientific and Technical Terms," Fourth Edition (McGraw Hill Book Company, New York, 1989). As is disclosed on this page 1399, permeability is "... a factor, characteristic of a material, that is proportional to the magnetic induction produced in a material divided by the magnetic field strength; it is a tensor when these quantities are not parallel.

Referring again to Figure 27, and in the preferred embodiment depicted therein, the magnetic hardness of the nanomagnetic material 4104 is preferably at least about 10 times as great as the magnetic hardness of the drug particles 3130. The term "magnetic hardness" is well known to those skilled in the art.

Figure 28 is graph of a preferred nanomagnetic material and its response to an applied electromagnetic field, in which the applied field is applied against the magnetic moment of the nanomagnetic material.

As will be apparent from this Figure 28, a certain amount of the applied electromagnetic force is required to overcome the remnant magnetization (M_r) and to change the direction of the remnant magnetization from $+M_r$ to $-M_r$. Thus, e.g., the point $-H_c$, at point 4130, indicates how much of the field is required to make the magnetic moment be zero.

Referring again to Figures 27A and 27B, and in the preferred embodiments depicted therein, the H_c values of the nanomagnetic material chosen will be sufficient to realign to magnetic drug particles 3130 but insufficient to realign the nanomagnetic material. The resulting situation is depicted in Figures 27A and 27B.

In Figure 27A, with the appropriate applied magnetic field, the magnetic drug particle 3130 is attached to the nanomagnetic material 4104 and thus will tend to diffuse into the polymer 4106. By comparison, in the situation depicted in Figure 27B, the magnetic drug particles will be repelled by the nanomagnetic material. Thus, and as will be apparent, by the appropriate choice of the applied magnetic field, one can cause the magnetic drug particles either to be attracted to the layer of polymer material 4106 or to be repelled therefrom.

Figure 29 illustrates the forces acting upon a magnetic drug particle 3130 as it approaches the nanomagnetic material 4104. Referring to Figure 29, and in the preferred embodiment depicted therein, a certain hydrodynamic force 4140 will be applied to the particle 3130 due to the force of flow of bodily fluid, such as blood. Simultaneously, a certain attractive force 4142 will be created by the attraction of the nanomagnetic material 4104 and the particle 3130. The resulting force vector 4144 will tend to be the direction the particle 3130 will travel in. If the surface of the polymeric material is preferably comprised of a multiplicity of pores 4146, the entry of the drug particles 3130 will be facilitated into such pores.

Figure 30 illustrates the situation that occurs after the drug particles 3130 have migrated into the layer of polymeric material and when one desires to release such drug particles. In this situation (see Figure 27B), the applied magnetic field will be chosen such that the nanomagnetic material will tend to repel the drug particles 3130 and cause their departure into bodily fluid in the direction of arrow 4148.

Figure 31 illustrates the situation that occurs after the drug particles 3130 have migrated into the layer of polymeric material 4106 but when no external electromagnetic field is imposed. In this situation, there will still be an attraction between the nanomagnetic material 4104 and the magnetic drug particles 3130 that will be sufficient to keep such particles bound.. However, the attraction will be weak enough such that, when hydrodynamic force 4140 is applied (see Figure 45), the particles 3130 will elute into the bodily fluid (not shown). As will be apparent, the degree of elution in this case is less than the degree of elution in the case depicted in Figure 43B. Thus, by the appropriate choice of

electromagnetic field 4120, one can control the rate of deposition of the drug particles 3130 onto the polymer 4106, or from the polymer 4106.

Magnetic drug compositions

In this section of the specification, applicants will describe certain magnetic drug compositions 3130 that may be used in their preferred process. Each of these drug compositions preferably is comprised of at least one therapeutic agent and has a magnetic moment so that it can be attracted to or repelled from the nanomagnetic coatings upon application of an external electromagnetic field.

Many of these magnetic drug compositions 3130 are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

In one embodiment of the instant invention, an anti-microtubule agent (such as, e.g., paclitaxel), is adsorbed onto the surfaces of the nanoparticles. In one aspect of this embodiment, the release rate of the paclitaxel is varied by cross-linking the carbohydrate matrix after crystallization. Reference may be had, e.g., to column 4 of United States patent 4,501,726.

In one embodiment, the coercive force and the remnant magnetization of applicants' nanomagnetic particles are preferably adjusted to optimize the magnetic responsiveness of the particles so that the coercive force is preferably from about 1 Gauss to about 1 Tesla and, more preferably, from about 1 to about 100 Gauss.

In one embodiment of this invention, an anti-microtubule agent (such as, e.g., paclitaxel) is incorporated into the vesicle of United States patent 4,652,257 and delivered to the situs of an implantable medical device, wherein the paclitaxel is released at a controlled release rate. Such a situs might be, e.g., the interior surface of a stent wherein the paclitaxel, as it is slowly released, will inhibit restenosis of the stent.

The use of externally applied energy to affect an implanted medical device

The prior art discloses many devices in which an externally applied electromagnetic field (i.e., a field originating outside of a biological organism, such as a human body) is generated in order to influence one or more implantable devices disposed within the biological organism. Some of these devices are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

Other compositions comprised of nanomagnetic particles

In addition to the compositions already mentioned in this specification, other compositions may advantageously incorporate the nanomagnetic material of this invention. Thus, by way of illustration and not limitation, one may replace the magnetic particles in prior art compositions with the nanomagnetic materials of this invention.

In many of the prior art patents, the term "comprising magnetic particles" appears in the claims; some of these patents are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

By way of yet further illustration, one may replace "magnetic particles" described in the medical device claimed in published United States patent application 2004/0030379 with applicants' nanomagnetic particles.

A preferred container coated with magnetostrictive material

Figure 32 is a partial view of a coated container 5000 comprised of a container 12 (see Figure 1) over which is disposed a layer 5002 of material which changes its dimensions in response to an applied magnetic field. The material may be, e.g., magnetostrictive material, and/or it may be electrostrictive material. The direct current susceptibility of coated container 5000 is equal to the (mass of layer 5002) x (the susceptibility of layer 5002) + (the mass of container 12)x (the susceptibility of container 12).

As is known to those skilled in the art, magnetostriction is the dependence of the state of strain (dimensions) of a ferromagnetic sample on the direction and extent of its magnetization. Magnetostriction is discussed, e.g., at page 1106 of the McGraw-Hill Concise Encyclopedia of Science and Technology, Third Edition (McGraw Hill Book Company, New York, New York, 1994), wherein it is defined as "The change of length of a ferromagnetic substance when it is magnetized. More generally, magnetostriction is the phenomenon that the state of strain of a ferromagnetic sample depends on the direction and extent of magnetization. The phenomenon has an important application in devices known as magnetostriction transducers." The phenomenon of magnetostriction has been widely discussed, and used in various devices, in the patent literature. This patent literature is discussed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

Referring again to Figure 1, and to the preferred embodiment depicted therein, in one aspect of such embodiment the magnetostrictive materials 5006, 5010, and 5014 do not have uniform properties. Means for varying the properties of one or more coatings of magnetostrictive material are well known and are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

Referring again to Figure 32, and to the preferred embodiment depicted therein, preferably disposed on the outer surface 5004 of the container 12, is a multiplicity of coatings, including a first coating of magnetostrictive material 5006 in which is disposed a first drug eluting polymer 5008, a second coating of magnetostrictive material 5010 in which is disposed a second drug eluting polymer 5012, and a third coating of magnetostrictive material 5014 in which is disposed a third drug eluting polymer 5016.

Referring again to Figure 32, disposed between coatings 5006 and 5008 is 5018 of nanomagnetic material; and disposed between 5008 and 5010 is nanomagnetic material 5019.

The coated device 5000 may be made, e.g., in substantial accordance with the procedure used to make semiconductor devices with different patterns of material on their surfaces. Thus, e.g., one can

first mask the surface 5004, deposit the magnetostrictive material 5006, deposit the polymeric material on and in said magnetostrictive material, and thereafter, by changing the masking and the coatings, deposit the rest of the components.

Figure 33 is a partial view of magnetostrictive material 5006 prior to the time an orifice has been created in it. In the embodiment depicted, a mask 5020 with an opening 5022 is disposed on top of the magnetostrictive material 5006, and an etchant (not shown) is disposed in said opening 5022 to create an orifice 5024, shown in dotted line outline. Thereafter, a drug-eluting polymer (such as, e.g., polymer 5008) is contacted with said etched surface and disposed within the orifice 5024. The resulting structure is shown in Figure 34.

Figure 34 shows the magnetostrictive material 5006 bounded by nanomagnetic material 5018/5019, and it illustrates how such assembly responds when the magnetostrictive material is subjected to one or more magnetic fields adapted to cause distortion of the material.

In the embodiment depicted in Figure 34, a first direct current magnetic field 5026 causes force to act in the direction of arrow 5028, thereby causing distortion of the polymeric material 5024 in the direction of arrow 5030. When a second varying magnetic field 5032 (nominal direction) is applied, it causes force to act in the direction of arrow 5034. These fields, and others, may act simultaneously or sequentially to pump the material 5025 within orifice 5024 out of such orifice. The material 5025, in one embodiment, is caused to move in the direction of arrow 5027, to cause a layer of material 5029 (which may be the same as or different than material 5025) to distend, and to thus rupture pressure rupturable seal 5030.

The pressure rupturable seal 5030 illustrated in Figure 34 may be any of the pressure rupturable seals known to those skilled in the art. Some of these seals are disclosed in applicants' copending patent application U.S.S.N. 10/887,521, filed on July 7, 2004.

An implantable medical device with minimal susceptibility

Figure 35 presents a solution to a problem posed in published United States patent application 2004/0030379. This published patent application discloses (at page 1 thereof) that: " In the medical field, magnetic resonance imaging (MRI) is used to non-invasively produce medical information. The patient is positioned in an aperture of a large annular magnet, and the magnet produces a strong and static magnetic field, which forces hydrogen and other chemical elements in the patient's body into alignment with the static field. A series of radio frequency (RF) pulses are applied orthogonally to the static magnetic field at the resonant frequency of one of the chemical elements, such as hydrogen in the water in the patient's body. The RF pulses force the spin of protons of chemical elements, such as hydrogen, from their magnetically aligned positions and cause the electrons to precess. This precession is sensed to produce electromagnetic signals that are used to create images of the patient's body. In order to create an image of a plane of patient cross-section, pulsed magnetic fields are superimposed on the high strength static magnetic field."

Published United States patent application US2004/0093075 also discloses that: "While researching heart problems, it was found that all the currently used metal stents distorted the magnetic resonance images of blood vessels. As a result, it was impossible to study the blood flow in the stents and the area directly around the stents for determining tissue response to different stents in the heart region.

Published United States patent application 2004/0093075 also discloses that: "A solution, which would allow the development of a heart valve which could be inserted with the patients only slightly sedated, locally anesthetized, and released from the hospital quickly (within a day) after a procedure and would allow the in situ magnetic resonance imaging of stents, has long been sought but yet equally as long eluded those skilled in the art." Such a solution is disclosed in Figure 35 of the instant application.

The device 6000 depicted in Figure 35, in one embodiment, is an assembly comprised of a device and material within which such device is disposed, wherein the direct current magnetic susceptibility of such assembly is plus or minus 1×10^{-3} .

Referring to Figure 35, there is disclosed an assembly 6000 comprised of a first material 6002 (with a first mass $[M_1]$ and a first magnetic susceptibility $[S_1]$) that, in the embodiment depicted, is contiguous with a substrate 6004 (with a second mass $[M_2]$ and a second magnetic susceptibility $[S_2]$).

In one preferred embodiment, the substrate 6004 is an implantable medical device. Thus, and as is disclosed in published United States patent application 2004/0030379, the implanted medical device may be a stent. Thus, and referring to page 4 of such published patent application, "Medical devices which are particularly suitable for the present invention include any kind of stent for medical purposes, which are known to the skilled artisan. Suitable stents include, for example, vascular stents such as self-expanding stents and balloon expandable stents. Examples of self-expanding stents useful in the present invention are illustrated in U.S. Pat. Nos. 4,655,771 and 4,954,126 issued to Wallsten and U.S. Pat. No. 5,061,275 issued to Wallsten et al. Examples of appropriate balloon-expandable stents are shown in U.S. Pat. No. 4,733,665 issued to Palmaz, U.S. Pat. No. 4,800,882 issued to Gianturco, U.S. Pat. No. 4,886,062 issued to Wiktor and U.S. Pat. No. 5,449,373 issued to Pinchasik et al. A bifurcated stent is also included among the medical devices suitable for the present invention."

As is also disclosed in published United States patent application 2004/0030379. "The medical devices suitable for the present invention may be fabricated from polymeric and/or metallic materials. Examples of such polymeric materials include polyurethane and its copolymers, silicone and its copolymers, ethylene vinyl-acetate, poly(ethylene terephthalate), thermoplastic elastomer, polyvinyl chloride, polyolephines, cellulotics, polyamides, polyesters, polysulfones, polytetrafluoroethylenes, acrylonitrile butadiene styrene copolymers, acrylics, polyactic acid, polycyclic acid, polycaprolactone, polyacetal, poly(lactic acid), polylactic acid-polyethylene oxide copolymers, polycarbonate cellulose, collagen and chitins. Examples of suitable metallic materials include metals

and alloys based on titanium (e.g., nitinol, nickel titanium alloys, thermo-memory alloy materials), stainless steel, platinum, tantalum, nickel-chrome, certain cobalt alloys including cobalt-chromium-nickel alloys (e.g., Elgiloy® and Phynox®) and gold/platinum alloy. Metallic materials also include clad composite filaments, such as those disclosed in WO 94/16646."

5 In one preferred embodiment, the substrate 6004 is a conventional drug-eluting medical device (such as, e.g., a drug eluting stent) to which the nanomagnetic material of this invention has been added as described herein below. One may use, and modify, any of the prior art self-eluting medical devices.

By way of illustration, and as is disclosed in United States patents 5,591,227, 5,599,352, and 6,597,967, the medical device may be "...a drug eluting intravascular stent comprising: (a) a generally
10 cylindrical stent body; (b) a solid composite of a polymer and a therapeutic substance in an adherent layer on the stent body; and (c) fibrin in an adherent layer on the composite." In the device of United States patent 5,591,227, the fibrin was used to provide a biocompatible surface. In the device 6000 depicted in Figure 35, it may be used as, or in place of barrier layer 6006 and/or barrier layer 6008.

By way of yet further illustration, and as is disclosed in United States patent 6,623,521, the
15 medical device may be an expandable stent with sliding and locking radial elements. This patent discloses many "prior art" stents, whose designs also may be modified by the inclusion of nanomagnetic material. Thus as is disclosed at columns 1-2 of this patent, "Examples of prior developed stents have been described by Balcon et al., "Recommendations on Stent Manufacture, Implantation and Utilization," European Heart Journal (1997), vol. 18, pages 1536-1547, and Phillips,
20 et al., "The Stenter's Notebook," Physician's Press (1998), Birmingham, Mich. The first stent used clinically was the self-expanding "Wallstent" which comprised a metallic mesh in the form of a Chinese fingercuff. This design concept serves as the basis for many stents used today. These stents were cut from elongated tubes of wire braid and, accordingly, had the disadvantage that metal prongs from the cutting process remained at the longitudinal ends thereof. A second disadvantage is the inherent rigidity
25 of the cobalt based alloy with a platinum core used to form the stent, which together with the terminal prongs, makes navigation of the blood vessels to the locus of the lesion difficult as well as risky from the standpoint of injury to healthy tissue along the passage to the target vessel. Another disadvantage is that the continuous stresses from blood flow and cardiac muscle activity create significant risks of thrombosis and damage to the vessel walls adjacent to the lesion, leading to restenosis. A major
30 disadvantage of these types of stents is that their radial expansion is associated with significant shortening in their length, resulting in unpredictable longitudinal coverage when fully deployed."

As is also disclosed in United States patent 6,623,521 "Among subsequent designs, some of the most popular have been the Palmaz-Schatz slotted tube stents. Originally, the Palmaz-Schatz stents consisted of slotted stainless steel tubes comprising separate segments connected with articulations.
35 Later designs incorporated spiral articulation for improved flexibility. These stents are delivered to the affected area by means of a balloon catheter, and are then expanded to the proper size. The disadvantage of the Palmaz-Schatz designs and similar variations is that they exhibit moderate

longitudinal shortening upon expansion, with some decrease in diameter, or recoil, after deployment. Furthermore, the expanded metal mesh is associated with relatively jagged terminal prongs, which increase the risk of thrombosis and/or restenosis. This design is considered current state of the art, even though their thickness is 0.004 to 0.006 inches."

5 As is also disclosed in United States patent 6,623,521, "Another type of stent involves a tube formed of a single strand of tantalum wire, wound in a sinusoidal helix; these are known as coil stents. They exhibit increased flexibility compared to the Palmaz-Schatz stents. However, they have the disadvantage of not providing sufficient scaffolding support for many applications, including calcified or bulky vascular lesions. Further, the coil stents also exhibit recoil after radial expansion."

10 As is also disclosed in United States patent 6,623,521, "One stent design described by Fordenbacher, employs a plurality of elongated parallel stent components, each having a longitudinal backbone with a plurality of opposing circumferential elements or fingers. The circumferential elements from one stent component weave into paired slots in the longitudinal backbone of an adjacent stent component. By incorporating locking means within the slotted articulation, the Fordenbacher stent may
15 minimize recoil after radial expansion. In addition, sufficient numbers of circumferential elements in the Fordenbacher stent may provide adequate scaffolding. Unfortunately, the free ends of the circumferential elements, protruding through the paired slots, may pose significant risks of thrombosis and/or restenosis. Moreover, this stent design would tend to be rather inflexible as a result of the plurality of longitudinal backbones."

20 As is also disclosed in United States patent 6,623,521, "Some stents employ "jelly roll" designs, wherein a sheet is rolled upon itself with a high degree of overlap in the collapsed state and a decreasing overlap as the stent unrolls to an expanded state. Examples of such designs are described in U.S. Pat. No. 5,421,955 to Lau, U.S. Pat. Nos. 5,441,515 and 5,618,299 to Khosravi, and U.S. Pat. No. 5,443,500 to Sigwart. The disadvantage of these designs is that they tend to exhibit very poor
25 longitudinal flexibility. In a modified design that exhibits improved longitudinal flexibility, multiple short rolls are coupled longitudinally. See e.g., U.S. Pat. No. 5,649,977 to Campbell and U.S. Pat. Nos. 5,643,314 and 5,735,872 to Carpenter. However, these coupled rolls lack vessel support between adjacent rolls."

30 As is also disclosed in United States patent 6,623,521, "Another form of metal stent is a heat expandable device using Nitinol or a tin-coated, heat expandable coil. This type of stent is delivered to the affected area on a catheter capable of receiving heated fluids. Once properly situated, heated saline is passed through the portion of the catheter on which the stent is located, causing the stent to expand. The disadvantages associated with this stent design are numerous. Difficulties that have been encountered with this device include difficulty in obtaining reliable expansion, and difficulties in
35 maintaining the stent in its expanded state."

As is also disclosed in United States patent 6,623,521, "Self-expanding stents are also available. These are delivered while restrained within a sleeve (or other restraining mechanism), that

when removed allows the stent to expand. Self-expanding stents are problematic in that exact sizing, within 0.1 to 0.2 mm expanded diameter, is necessary to adequately reduce restenosis. However, self-expanding stents are currently available only in 0.5 mm increments. Thus, greater selection and adaptability in expanded size is needed."

5 The stent design claimed in United States patent 6,623,521 is: An expandable intraluminal stent, comprising: a tubular member comprising a clear through-lumen, and having proximal and distal ends and a longitudinal length defined there between, a circumference, and a diameter which is adjustable between at least a first collapsed diameter and at least a second expanded diameter, said tubular member comprising: at least one module comprising a series of radial elements, wherein each
10 radial element defines a portion of the circumference of the tubular member and wherein no radial element overlaps with itself in either the first collapsed diameter or the second expanded diameter; at least one articulating mechanism which permits one-way sliding of the radial elements from the first collapsed diameter to the second expanded diameter, but inhibits radial recoil from the second expanded diameter; and a frame element which surrounds at least one radial element in each module."

15 By way of yet further illustration, one may use the multi-coated drug-eluting stent described in United States patent 6,702,850. This patent describes and claims: "... a stent body comprising a surface; and a coating comprising at least two layers disposed over at least a portion of the stent body, wherein the at least two layers comprise a first layer disposed over the surface of the stent body and a second layer disposed over the first layer, said first layer comprising a polymer film having a
20 biologically active agent dispersed therein, and the second layer comprising an antithrombogenic heparinized polymer comprising a macromolecule, a hydrophobic material, and heparin bound together by covalent bonds, wherein the hydrophobic material has more than one reactive functional group and under 100 mg/ml water solubility after being combined with the macromolecule."

Referring again to Figure 35, and to the preferred embodiment depicted therein, the substrate
25 6004 (such as, e.g., an implantable stent) is disposed within material 6002. The material is preferably biological material, such as the biological material disclosed in published United States patent application 2004/0030379. Thus, and as is disclosed in such published patent application, "The present invention provides a method of treatment to reduce or prevent the degree of restenosis or hyperplasia after vascular intervention such as angioplasty, stenting,
30 atherectomy and grafting. All forms of vascular intervention are contemplated by the invention, including, those for treating diseases of the cardiovascular and renal system. Such vascular intervention include, renal angioplasty, percutaneous coronary intervention (PCI), percutaneous transluminal coronary angioplasty (PTCA); carotid percutaneous transluminal angioplasty (PTA); coronary by-pass grafting, angioplasty with stent implantation, peripheral percutaneous transluminal intervention of the
35 iliac, femoral or popliteal arteries, carotid and cranial vessels, surgical intervention using impregnated artificial grafts and the like. Furthermore, the system described in the present invention can be used for treating vessel walls, portal and hepatic veins, esophagus, intestine, ureters, urethra, intracerebrally,

lumen, conduits, channels, canals, vessels, cavities, bile ducts, or any other duct or passageway in the human body, either in-born, built in or artificially made. It is understood that the present invention has application for both human and veterinary use."

Thus, in one embodiment, the material 6002 is biological material such as, e.g., blood, fat cells, muscle, etc.

Referring again to Figure 35, and to the preferred embodiment depicted therein, a layer of magnetoresistive material 6016 is disposed over the substrate 6004. As is known to those skilled art, magnetoresistance is the change in electrical resistance produced in a current-carrying conductor or semi-conductor upon the application of a magnetic field.

Without wishing to be bound to any particular theory, applicants believe that the presence of the magnetoresistive material 6004 helps minimize the presence of eddy currents in substrate 6004 when the assembly 6000 is subjected to a magnetic resonance imaging (MRI) field 6020.

In one preferred embodiment, illustrated in Figure 35, layers of barrier material 6006 and 6008 are disposed over drug eluting polymer materials 6020 and 6018, respectively. This barrier material is described in United States patent 6,716,444.

In one preferred embodiment, the diffusivity of the drug through the barrier layer is affected by the application of an external electromagnetic field. The external magnetic field (such as, e.g., field 6020) may be used to heat the nanomagnetic material 6010 and/or the nanomagnetic material 6012 and/or the magnetoresistive material 6016, which in turn will tend to heat the drug eluting polymer 6018 and/or the drug eluting polymer 6020 and/or the barrier layer 6008 and/or the barrier layer 6006. To the extent that such heating increases the diffusion of the drug from the drug-eluting polymer, one may increase the release of such drug from such drug-eluting polymer.

In one embodiment, illustrated in Figure 35, The heating of the nanomagnetic material 6010 and/or 6012 decreases the effectiveness of the barrier layers 6006 and/or 6008 and, thereby, increases the rate of drug delivery from drug-eluting polymers 6020 and/or 6018.

Referring again to Figure 35, when an MRI field 6020 is present, the entire assembly 6000, including the biological material 6020, presents a direct current magnetic susceptibility that preferably is plus or minus 1×10^{-3} centimeter-gram-seconds (cgs) and, more preferably, plus or minus 1×10^{-4} centimeter-gram-seconds. In one embodiment, the d.c. susceptibility of the stent is equal to plus or minus 1×10^{-5} centimeter-gram-seconds. In another embodiment, the d.c. susceptibility of the stent is equal to plus or minus 1×10^{-6} centimeter-gram-seconds.

Referring again to Figure 35, each of the components of assembly 6000 has its own value of magnetic susceptibility. The biological material 6002 has a magnetic susceptibility of S_1 . The substrate 6012 has a magnetic susceptibility of S_2 . The magnetoresistive 6016 material has a magnetic susceptibility of S_3 . The drug-eluting polymeric materials 6018 and 6020 have magnetic susceptibilities of S_9 and S_{10} , respectively.

Each of the components of the assembly 6000 makes a contribution to the total magnetic susceptibility of such assembly, depending upon (a) whether its magnetic susceptibility is positive or negative, (b) the amount of its positive or negative susceptibility value, and (c) the percentage of the total mass that the individual component represents.

5 In determining the total susceptibility of the assembly 6000, one can first determine the product of M_c and S_c , wherein M_c is the weight fraction of that component (the weight of that component divided by the total weight of all components in the assembly 6000).

10 In one preferred process, the $M_c S_c$ values for the nanomagnetic material 6016 and the nanomagnetic material 6012 are chosen to, when appropriate, correct for the total $M_c S_c$ values of all of the other components (including the biological material 6002 such that, after such correction(s), the total susceptibility of the assembly 6000 is plus or minus 1×10^{-3} centimeter-gram-seconds (cgs) and, more preferably, plus or minus 1×10^{-4} centimeter-gram-seconds. In one embodiment, the d.c. susceptibility of the assembly 6000 is equal to plus or minus 1×10^{-5} centimeter-gram-seconds. In another embodiment, the d.c. susceptibility of the assembly 6000 is equal to plus or
15 minus 1×10^{-6} centimeter-gram-seconds.

As will be apparent, there may be other materials/components in the assembly 6000 whose values of positive or negative susceptibility, and/or their mass, may be chosen such that the total magnetic susceptibility of the assembly is plus or minus 1×10^{-3} centimeter-gram-seconds (cgs) and, more preferably, plus or minus 1×10^{-4} centimeter-gram-seconds. Similarly, the configuration of the
20 substrate may be varied in order to vary its magnetic susceptibility properties and/or other properties. One of these variations is depicted in Figure 36.

As is known to those skilled in the art, many stents comprise wire. See, e.g., United States patents 6,723,118 (flexible metal wire stent), 6,719,782 (flat wire stent), 6,525,574 (wire stent coated with a biocompatible fluoropolymer), 6,579,308, 6,375,660, 6,161,399 (wire reinforced monolayer
25 fabric stent), 6,071,308 (flexible metal wire stent), 6,056,187 (modular wire band stent), 5,999,482 (flat wire stent), 5,906,639 (high strength and high density intraluminal wire stent), and the like.

Figure 36 is a sectional view of a wire 6100 which may be used to replace the wire used in conventional metal wire stents. The wire 6100 preferably has a sheath/core arrangement, with sheath 6102 disposed about core 6104.

30 In one embodiment, the materials chosen for the sheath 6102 and/or the core 6104 afford one both the desired mechanical properties as well as a magnetic susceptibility that, in combination with the other components of the assembly (and of the biological tissue), produce a magnetic susceptibility of plus or minus 1×10^{-3} cgs.

35 In another embodiment, the materials chosen for the sheath 6102 and/or the core 6104 are preferably magnetoresistive and produce a high resistance when subjected to MRI radiation.

Figure 37 is a graph 7000 of the relative permeability of a coating 7002 (depicted by triangles in the plot), and a bulk ceramic material 7004 (depicted by squares in the plot), versus the frequency

that each of such coatings 7002/7004 interacts with. The term "relative permeability" is well known to those skilled in the art.

The coating 7002 is preferably a coating of the nanomagnetic material described elsewhere in this specification. This material preferably has a magnetization at 2.0 Tesla of from about 0.1 to about 10 electromagnetic units per cubic centimeter. The particle size of the nanomagnetic particles in the coating are preferably from about 3 to about 20 nanometers. Additionally, it is preferred that the concentration of the nanomagnetic particles in the coating be less at the surface of the coating than at its bottom surface, adjacent to the substrate. This is illustrated in Figure 38.

Figure 38 is a schematic of a sputtering process 7100 in which a target 7102 is emitting particles 7104 of nanomagnetic material as well as particles 7106 of nonmagnetic material (such as, e.g., aluminum, nitrogen, etc.). The sputtering process 7100 is similar to the sputtering processes discussed elsewhere in this specification.

Referring again to Figure 38, when the first nanomagnetic particles 7104a approach the substrate 7108, they are attracted by two competing sets of forces. The top surface 7110 of the substrate 7108 provides nucleation centers (not shown) that facilitate the binding of many of the nanomagnetic particles 7104a; and these nucleation centers are sufficient to overcome, at least for these particles 7104a, the attractive forces provided by the magnetic field 7112 of the magnetron 7114.

As the particles 7104a tend to bind to the substrate at the nucleation centers, the new surfaces provided for such binding are not the substrate surface 7110, but the coating of the particles 7104a (and other particles). The coating provides fewer nucleation sites than did the surface 7110; and the more material 7104a (and other material) that is deposited, the weaker the attraction is between the substrate surface 7110 and the nanomagnetic particles 7104a.

Thus, and referring again to Figure 38, when nanomagnetic particles 7104b are being propelled towards the substrate surface 7110, they are attracted less to such surface 7110 than were the particles 7104a; more of these particles 7104b are attracted back towards the magnetron 7114, and fewer of them are deposited onto the substrate surface 7110.

Similarly, when nanomagnetic particles 7104c are being propelled towards the substrate surface 7110, more of these particles are attracted back towards the magnetron 7114 than were particles 7104b (or 7104a), and fewer of them are deposited onto the substrate surface.

Accordingly, there is a concentration gradient for the nanomagnetic particles 7104. This is best illustrated in Figure 39, which is a depth profile 8000 of a typical coating 7120 (see Figure 38), plotting the concentration of the nanomagnetic material 7104 on the surface 7110 (see Figure 38), and working upwardly from such surface 7110 towards the top surface 8002 of the coating 7120 (see Figure 38). The

depth profile 8000 compares, e.g., the concentration of the magnetic material at the surface 7110 (see point 8004) versus the concentration of the magnetic material at the surface 8002 (see point 8006).

Referring to Figure 39, it will be seen that the concentration value "A" (which corresponds to the concentration of the magnetic material at or near the surface 7110) is greater than the concentration value "C" (which corresponds to concentration of the magnetic material at or near the top surface 8002 of the coating 7120). The ratio of A/C is preferably at least about 1.5 and, more preferably, is at least about 2.0. As used herein, the term "at or near" refers to the concentration of the material either at the surface in question and/or within the first 0.5 nanometers thereof.

Referring again to Figure 37, and to the preferred embodiment depicted therein, plots of coated assembly 7020 are presented. Coated assembly 7020 is comprised of a substrate (which preferably is nonmagnetic), nanomagnetic particles, and the coating that such particles comprise.

The plot for coated assembly 7020 shows a relative permeability (plotted on the vertical axis 7010) that increases from a finite value at point 7012 (which corresponds to an a.c. frequency of 0 [or d.c.] at point 7012), up to a maximum relative permeability at point 7014, which corresponds to a critical frequency of the coating 7120; beyond this critical frequency, the ferromagnetic resonance frequency of the coating 7120 will be reached. It will be seen that the ferromagnetic resonance frequency of such coating 7120 on the substrate (which is preferably nonmagnetic) is at least 1 gigahertz (see decreased trend of the curve after point 7014), and more preferably is at least about 5 gigahertz. As is known to those skilled in the art, the precise definition of the ferromagnetic resonance frequency is the frequency at which the real part of the permeability is near 1.

As is known to those skilled in the art, ferromagnetic resonance is the magnetic resonance of a ferromagnetic material. Reference may be had, e.g., to page 7-98 of E.U. Condon et al.'s "Handbook of Physics," (McGraw-Hill Book Company, New York, New York, 1958).

As noted above, the ferromagnetic resonance frequency of the nanomagnetic material is at least 1 gigahertz. By comparison, a bulk ceramic material (such as iron oxide/ferrite material) will have a ferromagnetic resonance frequency that is generally less than about 100 megahertz (see point 7016). The plot 7018 of this ferrite material represents the plot of a material with an average particle size greater than 1 micron. As used in this specification, the term "bulk" refers to a material with an average particle size greater than about 1 micron.

The plot 7018 is a plot of a film comprised of ferrite material that is preferably formed by conventional means, such as plasma spraying. The film has a thickness of about 1 micrometer, as does the nanomagnetic coating 7120.

Thus, the graph 7000 shows the responses of two coatings disposed on substantially identical substrates (which are preferably nonmagnetic) with substantially identical film thicknesses,

substantially identical magnetizations at 2.0 Tesla, and substantially identical molar percentages of magnetic material in the films. Both of these samples, at 0 frequency, have the same relative permeability (at point 7012); but their behaviors diverge radically as the alternating current frequency is increased from zero hertz to greater than 1 gigahertz.

5 Referring to the plot 7020 of the nanomagnetic film, it will be seen that the relative permeability increases at a rate defined by $\Delta \text{permeability} / \Delta \text{frequency}$; see, e.g., the slope of the triangle 7022, which indicates that the increase in permeability per hertz is from about 1×10^{-14} to about 1×10^{-6} , and preferably is from about 1×10^{-10} to about 1×10^{-7} . By comparison, and referring to plot 7018 (and to triangle 7024), the permeability of the "bulk" ceramic material decreases at a rate of at
10 least about -1×10^{-8} .

Figure 40 is a schematic of a preferred process 9000 in which, when coated stent assembly 9002 is contacted with electromagnetic radiation 9022, images of biological material 9024, 9026, and 9028 are obtained without substantial image artifacts and with good resolution.

The electromagnetic radiation 9022 is preferably radio-frequency alternating current radiation
15 with a frequency of from about 10 to about 300 megahertz. In one preferred embodiment, the frequency is either 64 megahertz, 128 megahertz, or 256 megahertz.

The frequency is preferably in the form of a sine wave with a maximum amplitude 9024 (see Figure 40). The energy in such electromagnetic radiation 9022 is proportional to the square of the amplitude 9024.

20 In the preferred embodiment depicted in Figure 40, the coated stent assembly 9002 is comprised of a stent 9006 on which is disposed a coating 9004. The coating 9004 is similar to the coating 7120 depicted in Figure 38, and it contains substantially more magnetic particles 9008 (such as, e.g., particles of iron) near the surface 9010 of the stent 9006 than near the top surface 9012 of the coating. There is preferably at least about 1.5 times as many particles of "moiety A" near surface 9010
25 than near top surface 9012. Without wishing to be bound to any particular theory, applicants believe that this concentration differential along the depth of the coating 9004 facilitates the entry of energy into the interior 9014 of the stent 9006, and it also facilitates the exit of energy from the interior 9014 of the stent 9006 to exterior 9016 of such stent.

Referring again to Figure 40, and to the preferred embodiment depicted therein, it will be seen
30 that a sensor 9018 is disposed outside of the stent assembly 9002, and that another sensor 9020 is disposed within the interior of the stent 9006. These sensors 9018/9020 are adapted to measure the amount of electromagnetic energy, and the frequency of the electromagnetic energy, that exists at a given spatial point both without and within the stent assembly 9002.

In one preferred embodiment, the stent assembly 9002 has a radio frequency shielding factor of less than about 10 percent and, more preferably, less than about 5 percent. The radio frequency shielding factor is a function of the amount of energy that is blocked from entering the interior 9104 of the stent.

5 The radio frequency shielding factor can be calculated by first determining the amount of energy in electromagnetic wave 9022. As is known to those skilled in the art, this energy is dependent upon the amplitude 9024 of the energy 9022, being directly dependent upon the square of such amplitude.

10 After the initial energy of the electromagnetic wave 9022 is determined (and measured by sensor 9018), the amount of such initial energy that passes unimpeded to the interior 9014 of stent assembly 9002 is then determined. Only that energy that has a frequency that is within plus or minus 5 percent of the initial energy of electromagnetic wave 9022 is considered. In one embodiment, only that energy that has a frequency that is within plus or minus two percent of the initial energy of electromagnetic wave 9022 is considered. In an even more preferred embodiment, the frequency of the
15 energy that passes unimpeded into the interior of the stent is within plus or minus one percent of the initial energy.

The "interior energy" is measured by one or more of the sensors 9020; it is also dependent upon the square of the amplitude 9024.

20 Referring again to Figure 40, the exterior energy 9030 passes through the stent assembly 9002 (wherein it is identified as energy 9032) until it reaches the interior 9014 of the stent (wherein it is identified as energy 9034). The energy 9034 interacts with biological matter 9024 disposed within the interior of the stent. Depending upon the type and characteristics of the biological matter 9024, a signal 9048 is generated (and measured by sensor 9020); and then this signal passes back through the stent assembly (wherein it is identified as signal 9050) and to the outside of the stent assembly (wherein it is
25 identified as signal 9052).

30 Without wishing to be bound to any particular theory, applicants believe that the presence of the concentration gradient in coating 9004 of the moiety A (discussed elsewhere in this specification) facilitates the substantially unimpeded exit of signal 9048 through the stent assembly 9002 (wherein it is identified as signal 9050) and to the exterior of the stent assembly (wherein it is identified as signal 9052). The term "substantially unimpeded" refers to the fact that the signal 9052 contains at least 90 percent (and preferably at least 95 percent) of the energy of signal 9048 and has a frequency which is within plus or minus 5 percent (and preferably plus or minus 2 percent) of the frequency of signal 9048.

Referring again to Figure 40, the exterior energy 9036 passes through the stent assembly 9002 (wherein it is identified as energy 9038) until it reaches the interior 9014 of the stent (wherein it is

identified as energy 9040). The exterior energy 9036 and the interior energy 9040 are preferably substantially identical to the exterior energy 9030 and the interior energy 9034, and also to the exterior energy 9042 and to the interior energy 9046.

Referring again to Figure 40, the energy 9040 interacts with biological matter 9026 disposed within the interior of the stent. Depending upon the type and characteristics of the biological matter 9026, a signal 9054 is generated (and measured by sensor 9020). This signal 9054 will differ from signal 9048 (and also from signal 9056) in that biological matter 9026 differs from biological matter 9024 and biological matter 9028 in either its size, composition, shape, etc.

Referring again to Figure 40, the signal 9054 passes back through the stent assembly (wherein it is identified as signal 9058) and to the outside of the stent assembly (wherein it is identified as signal 9062).

Without wishing to be bound to any particular theory, applicants believe that the presence of the concentration gradient in coating 9004 of the moiety A (discussed elsewhere in this specification) facilitates the substantially unimpeded exit of signal 9054 through the stent assembly 9002 (wherein it is identified as signal 9058) and to the exterior of the stent assembly (wherein it is identified as signal 9062). The term "substantially unimpeded" refers to the fact that the signal 9062 contains at least 90 percent (and preferably at least 95 percent) of the energy of signal 9040 and has a frequency which is within plus or minus 5 percent (and preferably plus or minus 2 percent) of the frequency of signal 9040.

Referring again to Figure 40, the exterior energy 9042 passes through the stent assembly 9002 (wherein it is identified as energy 9044) until it reaches the interior 9014 of the stent (wherein it is identified as energy 9046). The exterior energy 9042 and the interior energy 9046 are preferably substantially identical to the exterior energy 9030 and the interior energy 9036.

Referring again to Figure 40, the energy 9046 interacts with biological matter 9028 disposed within the interior of the stent. Depending upon the type and characteristics of the biological matter 9028, a signal 9056 is generated (and measured by sensor 9020). This signal 9056 will differ from signal 9048 (and also from signal 9054) in that biological matter 9028 differs from biological matter 9024 and biological matter 9026 in either its size, composition, shape, etc.

Referring again to Figure 40, the signal 9056 passes back through the stent assembly (wherein it is identified as signal 9060) and to the outside of the stent assembly (wherein it is identified as signal 9064).

Without wishing to be bound to any particular theory, applicants believe that the presence of the concentration gradient in coating 9004 of the moiety A (discussed elsewhere in this specification) facilitates the substantially unimpeded exit of signal 9056 through the stent assembly 9002 (wherein it

is identified as signal 9060) and to the exterior of the stent assembly (wherein it is identified as signal 9064). The term "substantially unimpeded" refers to the fact that the signal 9064 contains at least 90 percent (and preferably at least 95 percent) of the energy of signal 9056 and has a frequency which is within plus or minus 5 percent (and preferably plus or minus 2 percent) of the frequency of signal 9056.

5 The "exterior energies" 9030, 9036, and 9042 will all be substantially identical to each other, as will their corresponding "intermediate energies" 9032/9038/9044 and "interior energies" 9034/9040/9046. However, because each of biological materials 9024, 9026, and 9028 differs from the others, the interaction of these biological matters with interior energies 9034/9040/9046 will produce differing interior signals 9048/9054/9056, differing intermediate signals 9050/9058/9060, and differing
10 exterior signals 9052/9062/9064.

However, although the process 9000 produces differing interior signals 9048/9054/9056, differing intermediate signals 9050/9058/9060, and differing exterior signals 9052/9062/9064, it produces a substantially uniform response along the length of the stent assembly 9002. The ratio of the energy of signal 9052 to signal 9048 (their frequencies being within plus or minus 5 percent of each
15 other), and the ratio of the energy of signal 9062 to signal 9058 (their frequencies being within plus or minus 5 percent of each other), and the ratio of the energy of signal 9064 to signal 9056 (their frequencies being within plus or minus 5 percent of each other), will each be substantially identical to each other, and all of them will be within the range of from 0.9 to 1.0, as described above.

Without wishing to be bound to any particular theory, applicants believe that this uniformity of
20 imaging response is due to the substantially uniform nature of the coating 9004 disposed on the stent 9006. Because the concentration differential of the moiety A is substantially identical along the length of the stent 9006, the imaging response of the stent is also substantially identical along its entire length. This is schematically illustrated by graph 9027.

Figure 41 is a schematic of a coated stent 9102 on which is disposed a nanomagnetic coating
25 9104 and within which is disposed biological materials 9106, 9108, and 9110. In the embodiment depicted, the images produced of these materials when they are subjected to MRI imaging with a 64 megahertz radio frequency source and 1.5 Tesla d.c. field are shown as 9116, 9118, and 9120. Similar images will be produced with 128 megahertz and 256 megahertz radio frequency fields.

When the coating 9104 is not disposed on the stent 9102, a "smeared" set of images 9122 is
30 produced that makes it difficult for, e.g., a physician to clearly distinguish the images 9116, 9118, and 9120. When, however, the coating 9104 is disposed on the stent 9102, the images 9116, 9118, and 9120 are presented with good resolution.

As is known to those skilled in the art, resolution is the ability of a system to reproduce the points, lines, and surfaces in an object as separate entities in the image. A substantial amount of patent

literature has been devoted to the resolution of, e.g., MRI images. Reference may be had, e.g., United States patents 4,684,891 (rapid magnetic resonance imaging using multiple phase encoded spin echoes in each of plural measurement cycles), 4,857,846 (rapid MRI using multiple receivers), 4,881,034 (switchable MRI RF coil arrangement), 4,888,552 (magnetic resonance imaging), 4,954,779 (correction for eddy current caused phase degradation), 5,361,764 (magnetic resonance imaging foot coil assembly), 5,399,969 (analyzer of gradient power usage for oblique MRI imaging), 5,438,263 (method of selectable resolution magnetic resonance imaging), 5,646,529 (system for producing high-resolution magnetic resonance images), 5,818,229 (correction of MR imaging pulse sequence), 6,317,620 (method and apparatus for rapid assessment of stenosis severity), 6,425,864 (method and apparatus for optimal imaging of the peripheral vasculature), 6,463,316 (delay based active noise cancellation for magnetic resonance imaging), 6,556,845 (dual resolution acquisition of magnetic resonance angiography data), 6,597,173 (method and apparatus for reconstructing zoom MR images), 6,603,992 (method and system for synchronizing magnetic resonance image acquisition to the arrival of a signal-enhancing contrast agent), 6,720,766 (thin film phantoms and phantom systems), 6,741,880 (method and apparatus for efficient stenosis identification and assessment using MR imaging), and the like.

Referring again to Figure 41, and in the preferred embodiment depicted, the objects 9106, 9108, and 9110 preferably have maximum dimensions of about 1 millimeter. These objects are accurately imaged with the coated stent of this invention; thus, such coated stent is said to have a resolution of at least about 1 millimeter. In one embodiment, the resolution is at least about 0.5 millimeters.

The process and apparatus of this invention allows one to avoid the well known Faraday cage effects that limit the visibility of images of objects within a stent. If the stent 9102 did not have the coating 9104, it is likely that, at best, a smeared image would be produced because of the Faraday cage effects. Such a smeared image is indicated as 9122, and it is substantially useless in helping one to accurately determine what objects are disposed within the stent.

In one preferred embodiment, phase imaging is used with the coated stent 9100. The phase imaging process 9200 is schematically illustrated in Figure 42.

The phase imaging process is well known to those skilled in the art and widely described in the patent literature. Reference may be had, e.g., to United States patents 4,878,116 (vector lock-in imaging system), 5,335,602 (apparatus for all-optical self-aligning holographic phase modulation and motion sensing), 5,447,159 (optical imaging for specimens having dispersive properties), 5,633,714 (preprocessing of image amplitude and phase data for CD and OL measurement), 5,760,902 (method and apparatus for producing an intensity contrast image from phase detail in transparent phase objects), 5,995,223 (apparatus for rapid phase imaging interferometry), 6,809,845 (phase imaging using multi-

wavelength digital holography), 6,853,191 (method of removing dynamic nonlinear phase errors from MRI data), and the like.

Referring again to Figure 42, in step 9202 the real part 9201 and the imaginary part 9203 are processed in computer 9202. These parts are discussed in Figure 13-18 of Ray H. Hashemi's "MRI The Basics," (Lippincott Williams & Wilkins, Philadelphia, Pennsylvania, 2004) at page 158, wherein it is disclosed that "The FTs of the real and imaginary k-spaces provide the real and imaginary images, respectively." At pages 156-157 of the Hashemi et al. text, it is disclosed that "We discussed two components of the data space, namely, the real and imaginary components. Their respective Fourier transforms provide the real and imaginary components of the image (Fig. 13-18)."

The Hashemi et al. text also discloses that (at page 157) "Recall that a given complex number $c = a + ib$, with a being the real and b the imaginary component....This concept can be applied to the real and imaginary components of the image (Fig. 13-18) to generate the magnitude and the phase images. The magnitude image (modulus) is what we deal with most of the time in MR imaging. The phase image is used in cases in which the direction is important. An example is phase contrast MR angiography....."

Referring again to Figure 42, and in step 9204 thereof, the magnitude image 9208 is derived by calculating the square root of the $[(\text{real image})^2 + (\text{imaginary image})^2]$. By comparison, the phase image 9210 is derived by calculating the arc tangent of the $[\text{imaginary image}/\text{real image}]$.

Without wishing to be bound to any particular theory, applicants' believe that their nanomagnetic coating is ideally suited for phase imaging. Some of the reasons for this suitability are illustrated in Figure 43.

Referring to Figure 43, plot 9300 represents the energy input to the device to be imaged; this energy is often 64 megahertz radio frequency energy.

Plot 9302 is the output signal generated from a stent with biological matter disposed therein, wherein the stent is not coated with the nanomagnetic material of this invention. As will be apparent, this output signal has a loss of coherence (see points 9304 and 9306) due to the Faraday cage effect..

Plot 9308 shows the image from a coated stent with biological matter disposed therein, wherein the coating is the nanomagnetic material of this invention.the bottom shows the signal out with nanomagnetic coating. This is a coherent image (compare image 9302) whose phase is shifted by less than about 90 degrees and, more preferably, less than about 45 degrees. In one preferred embodiment, depicted in Figure 43, the phase angle 9310 is preferably less than about 30 degrees.

Referring again to Figure 43, the coherent signal 9308 is preferably substantially identical to the input signal, except for its phase shift 9310. . It has substantially the same amplitude, substantially the same frequency, and substantially the same shape.

5 In one embodiment of the process of this invention, using the phase shift 9310, one can reconstruct the image of the actual object inside the stent by reference to the stent and with the use of phase imaging.

10 Figure 44 is a schematic of a coated stent assembly 9400 comprised of a coating 9402 disposed circumferentially around a stent 9404. Without wishing to be bound to any particular theory, applicants believe that, in order to "choke" any particular section of the stent 9404 (such as, e.g., section 9405), the coating 9402 should preferably be circumferentially disposed around the entire periphery of such section of the stent. Applicants also believe that such circumferential coating effectively blocks the flow of induced eddy currents or loop currents through the section of sections in question.

15 Referring again to Figure 44, and in the preferred embodiment depicted therein, it will be seen that coating 9402 is comprised of a first section 9406, a second section 9408, and a third section 9409. Each of these sections has different physical properties.

The first section 9406 has a thickness 9410 that preferably is from about 50 to about 150 nanometers. In one preferred embodiment, the thickness 9410 is from about 5 to about 15 percent of the total thickness 9412 of the coating, which often is in the range of from about 400 to about 1500 nanometers.

20 The third (top) section 9409 preferably has a thickness 9411 that is at least 10 nanometers and, more preferably, from about 10 to about 100 nanometers. In one embodiment, the thickness 9411 is from about 0.5 to about 15 percent of the total thickness 9412.

25 Magnetic material, such as the "moiety A" described elsewhere in this specification, is disposed throughout the entire thickness 9412 of the coating 9402, but more of it is disposed on a fractional mole per unit volume basis in the first coating than in the third coating. The first section 9406 preferably has at least 1.5 times as greater the number of fractional moles of moiety A per cubic centimeter than does the middle section 9408; and the first section 9406 preferably has at least 2.0 times as great the number of fractional moles of moiety A than does the top section 9409.

30 The relative permeability of the first section 9406 is preferably greater than about 2. The relatively permeability of the third section 9409 preferably is less than about 2 and, more preferably, less than about 1.5.

35 The resistivity of the third section 9409 is at least 10 times as great as the combined average resistivity of sections 9406 and 9408. In one embodiment, the resistivity of section 9409 is at least 100 times as great as the combined average resistivity of sections 9406 and 9408. In one embodiment, the combined average resistivity of sections 9406 and 9408 is from about 10^8 to about 10^{-3} . In another

centimeter than does the middle section 9408; and the first section 9406 preferably has at least 2.0 times as great the number of fractional moles of moiety A than does the top section 9409.

The relative permeability of the first section 9406 is preferably greater than about 2. The relatively permeability of the third section 9409 preferably is less than about 2 and, more preferably, less than about 1.5.

The resistivity of the third section 9409 is at least 10 times as great as the combined average resistivity of sections 9406 and 9408. In one embodiment, the resistivity of section 9409 is at least 100 times as great as the combined average resistivity of sections 9406 and 9408. In one embodiment, the combined average resistivity of sections 9406 and 9408 is from about 10^8 to about 10^3 . In another embodiment, the resistivity of section 9409 is from about 10^{10} to about 10^3 and, more preferably, from about 10^9 to about 10^7 .

In one embodiment, the section 9408 has a relative dielectric constant that is at least 1.2 times as great as the relative dielectric constant from section 9406, and is also at least 1.2 times as great as the relative dielectric constant 9409.

The patents, patent applications and patent application publications referenced herein, are hereby incorporated into this Specification as if fully written out below.

Although the invention has been described herein with respect to certain preferred embodiments, numerous modifications and alterations may be made to the described embodiment without departing from the spirit and intended scope of the invention. It is intended to include any and all such modifications and alterations within the scope of the following claims and/or the equivalents thereof.

We claim:

1. A coated substrate assembly comprised of a substrate and a coating disposed thereon, wherein said coating has a magnetization at 2.0 Tesla of from about 0.1 to about 10 electromagnetic units per cubic centimeter, wherein said coating is comprised of magnetic particles with a particle size in the range of from about 3 to about 20 nanometers, and wherein said coating has a ferromagnetic resonance frequency of at least 1 gigahertz.
2. A coated substrate assembly comprised of a substrate and a coating disposed thereon, wherein said coating has a magnetization at 2.0 Tesla of from about 0.1 to about 10 electromagnetic units per cubic centimeter, wherein said coating is comprised of magnetic particles with a particle size in the range of from about 3 to about 20 nanometers, wherein said coating has a top surface and a bottom surface, wherein said bottom surface is contiguous with said substrate, and wherein at least 1.5 times as many of said magnetic particles are disposed near said bottom surface of said substrate than near said top surface of said substrate.
3. A coated stent assembly comprised of a substrate, a coating disposed thereon, a lumen, and biological material disposed within said lumen, wherein said coating has a magnetization at 2.0 Tesla of from about 0.1 to about 10 electromagnetic units per cubic centimeter, and wherein, when said stent is exposed to radio frequency electromagnetic radiation with a frequency of from 10 megahertz to about 200 megahertz, said coated stent assembly has a radio frequency shielding factor of less than about 10 percent, at least 90 percent of said electromagnetic radiation penetrating said stent and contacting said biological material.
4. The coated stent assembly as recited in claim 3, wherein said stent has a substantially constant radio frequency shielding factor along the length of said stent.
5. A coated assembly comprised of a substrate on which a coating is disposed, said coating has a relative permeability of at least 1.1 over the range of frequencies of from about 10 megahertz to about 200 megahertz, an increase of such relative permeability over such range of from about 1×10^{-14} to about 1×10^{-6} per hertz, and a magnetization, when measured at a direct current magnetic field of 2 Tesla, of from about 0.1 to about 10 electromagnetic units per cubic centimeter.
6. The coated assembly as recited in claim 5, wherein said substrate is a stent.
7. The coated assembly as recited in claim 6, wherein said coating is comprised of particles of nanomagnetic material.
8. The coated assembly as recited in claim 7, wherein said particles of said nanomagnetic material are at least triatomic, being comprised of a first distinct atom, a second distinct atom, and a third distinct atom.
9. The coated assembly as recited in claim 8, wherein said first distinct atom is an atom selected from the group consisting of atoms of actinium, americium, berkelium, californium, cerium, chromium, cobalt, curium, dysprosium, einsteinium, erbium, europium, fermium, gadolinium, holmium, iron,

lanthanum, lawrencium, lutetium, manganese, mendelevium, nickel, neodymium, neptunium, nobelium, plutonium, praseodymium, promethium, protactinium, samarium, terbium, thorium, thulium, uranium, and ytterbium, and mixtures thereof; wherein said second distinct atom is selected from the group consisting of silicon, aluminum, boron, platinum, tantalum, palladium, yttrium, zirconium, titanium, calcium, cerium, beryllium, barium, silver, gold, indium, lead, tin, antimony, germanium, gallium, tungsten, bismuth, strontium, magnesium, zinc, and mixtures thereof.

10. The coated assembly as recited in claim 8, wherein from about 2 to about 20 mole percent of said first distinct atom is present in said coating, by combined moles of said first distinct atom and said second distinct atom.

11. The coated assembly as recited in claim 5, wherein said coating has a relative permeability when measured at a radio frequency of 64 megahertz of at least 1.2.

12. The coated assembly as recited in claim 8, wherein said particles of nanomagnetic material are comprised of a said first distinct atom, said second distinct atom, said third distinct atom, and a fourth distinct atom.

13. The coated assembly as recited in claim 7, wherein said particles of nanomagnetic material have a squareness of from about 0.1 to about 0.9.

14. The coated assembly as recited in claim 7, wherein said particles of nanomagnetic material have an average size of less than about 50 nanometers.

15. The coated assembly as recited in claim 7, wherein said particles of nanomagnetic material have a phase transition temperature of less than about 50 degrees Celsius.

16. The coated assembly as recited in claim 7, wherein said nanomagnetic material has a coercive force of from about 0.1 to about 10 Oersteds.

17. The coated assembly as recited in claim 7, wherein said particles of nanomagnetic material have a saturation magnetization of at least 100 electromagnetic units per cubic centimeter.

18. The coated assembly as recited in claim 7, wherein said particles of nanomagnetic material have a coercive force of from about 0.01 to about 5,000 Oersteds.

19. The coated assembly as recited in claim 7, wherein said particles of nanomagnetic material are disposed within a film that has a heat shielding factor of at least 0.2.

20. The coated assembly as recited in claim 1, wherein said coated assembly is a coated medical device.

21. The coated assembly as recited in claim 1, wherein said coated assembly has a magnetic susceptibility within the range of plus or minus 1×10^{-3} centimeter-gram-seconds.

22. The coated assembly as recited in claim 1, wherein said coated assembly is an implantable assembly.

23. The coated assembly as recited in claim 7, wherein the average coherence length between adjacent nanomagnetic particles is less than 100 nanometers

24. The coated assembly as recited in claim 7, wherein said nanomagnetic material has a saturation magnetization of at least 2,000 electromagnetic units per cubic centimeter.
25. The coated assembly as recited in claim 7, wherein said particles of nanomagnetic material have a mass density of at least about 3 grams per cubic centimeter.
- 5 26. The coated assembly as recited in claim 12, wherein said fourth distinct atom is an atom selected from the group consisting of argon, bromine, carbon, chlorine, fluorine, helium, helium, hydrogen, iodine, krypton, oxygen, neon, nitrogen, phosphorus, sulfur, and xenon.
27. The coated assembly as recited in claim 7, wherein said particles of nanomagnetic material are disposed within an insulating matrix.
- 10 28. The coated assembly as recited in claim 2, wherein said coating has a thickness of from about 400 to about 2000 nanometers.
29. The coated assembly as recited in claim 2, wherein said coating has a morphological density of at least about 99 percent.
30. The coated assembly as recited in claim 2, wherein said coating has an average surface roughness
15 of less than about 10 nanometers.
31. The coated assembly as recited in claim 2, wherein said coating is biocompatible.
32. The coated assembly as recited in claim 2, wherein said coating is hydrophobic.
33. The coated assembly as recited in claim 2, wherein said coating is hydrophilic.
34. The coated assembly as recited in claim 3, wherein said assembly is comprised of magnetostrictive
20 material.
35. The coated assembly as recited in claim 7, wherein said nanomagnetic particles are disposed within an insulating matrix, wherein at least about 90 weight percent of said nanomagnetic particles have a maximum dimension of from about 10 to about 100 nanometers, wherein said insulating matrix has a resistivity of from about 1,000,000,000 to about 10,000,000,000,000 ohm-centimeter, the nanomagnetic
25 material has an average particle size of less than about 100 nanometers,.
36. The coated assembly as recited in claim 3, wherein said coated assembly has a springback angle of less than about 45 degrees.
37. The coated assembly as recited in claim 7, wherein said particles of nanomagnetic material have a coherence length less than about 50 nanometers.
- 30 38. The coated assembly as recited in claim 2, wherein said coated assembly has a direct current magnetic susceptibility of plus or minus 1×10^{-3} centimeter-gram-seconds.
39. The coated assembly as recited in claim 2, wherein said substrate is selected from the group consisting of, stents, surgical staples, catheters, guidewires, balloons, vena cava filters, cannulas, cardiac pacemaker leads or lead tips, cardiac defibrillator leads or lead tips,
35 vascular access ports, and stent grafts.
40. The coated assembly as recited in claim 2, wherein said stent is selected from the group consisting of self-expanding stents, balloon expandable stents, and bifurcated stents.

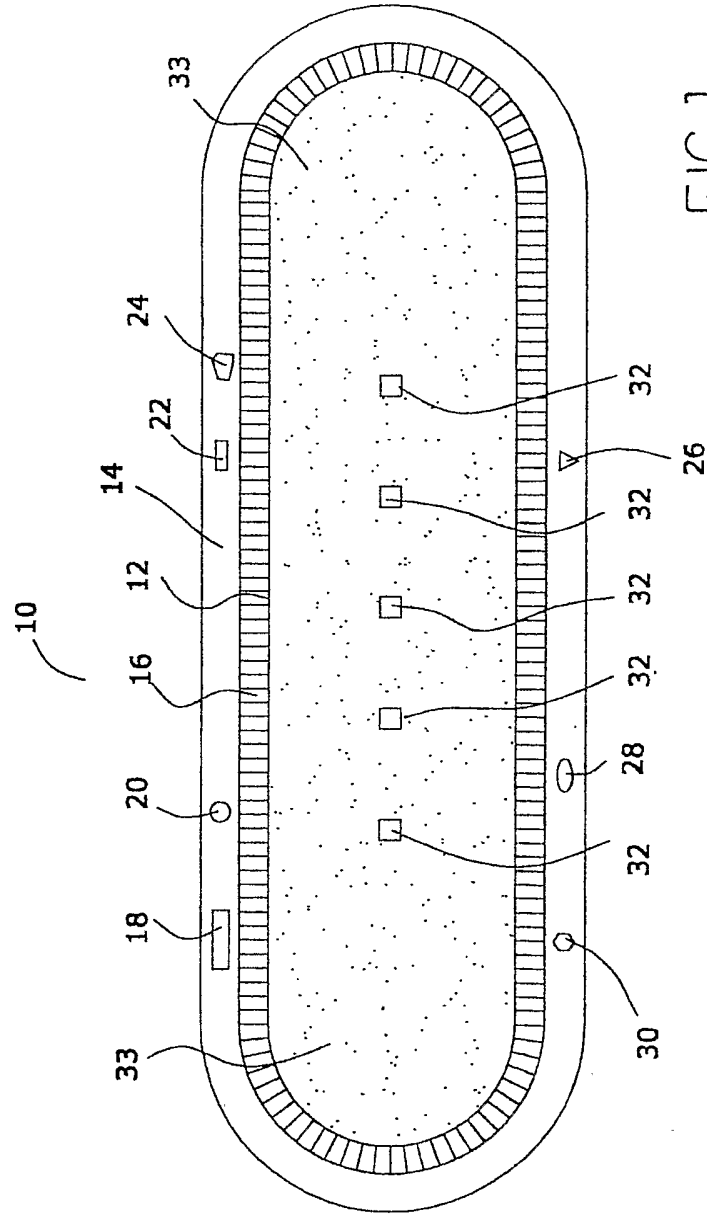


FIG. 1

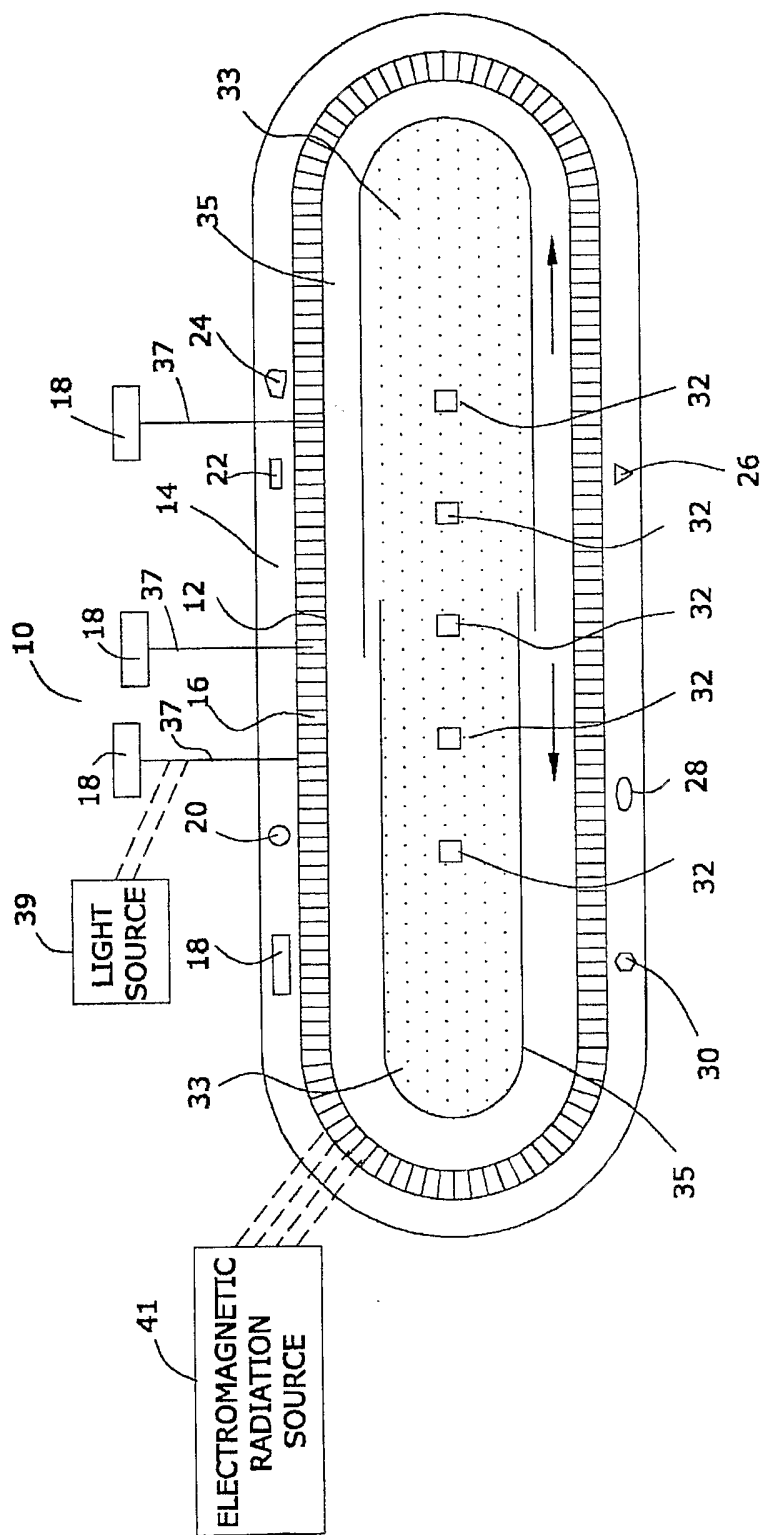
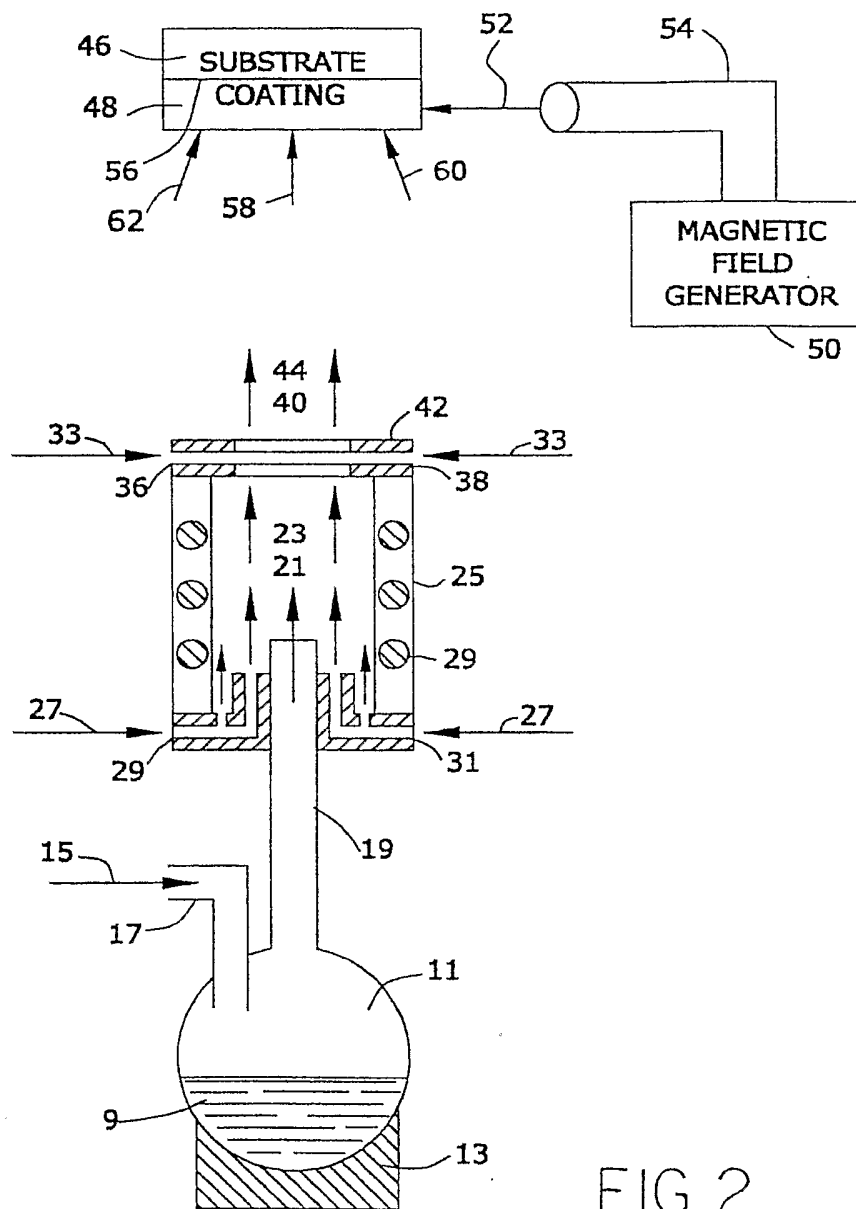
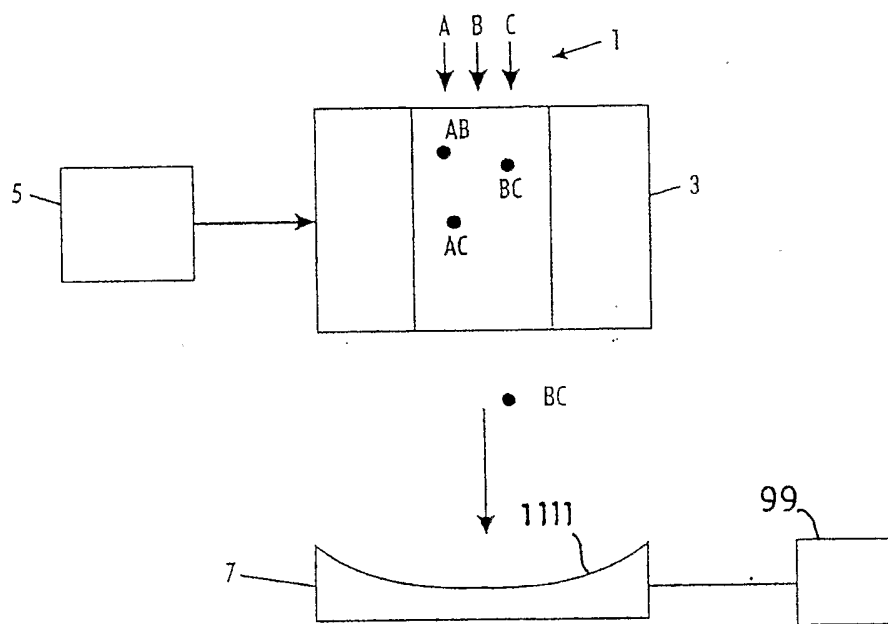


FIG.1A

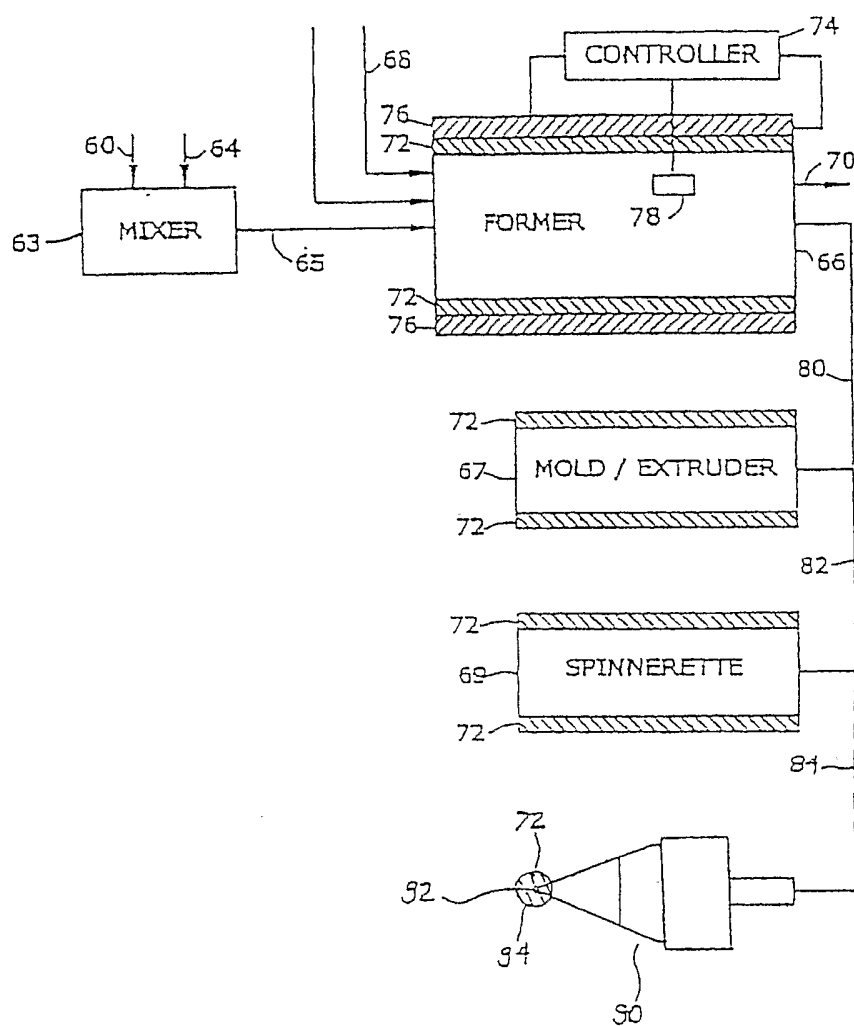
3/50

FIG. 2

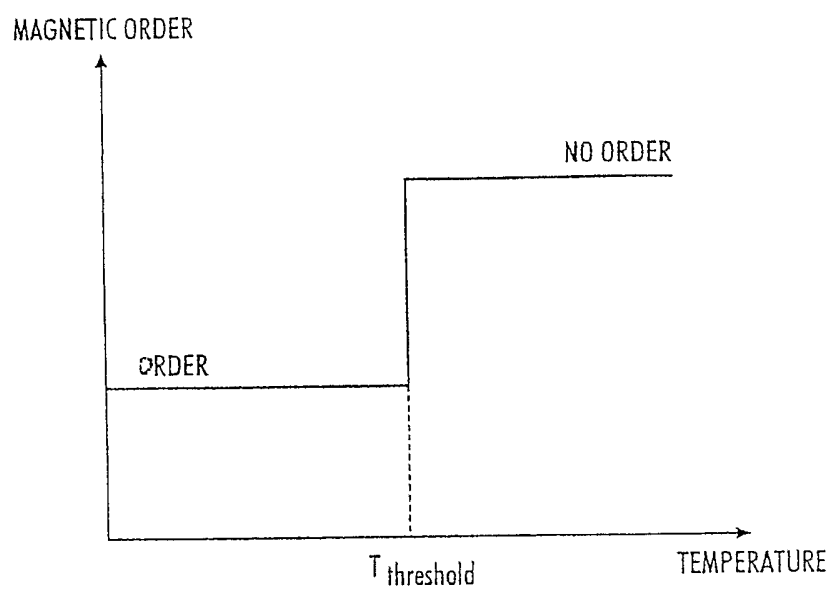
4/50

FIG.2A

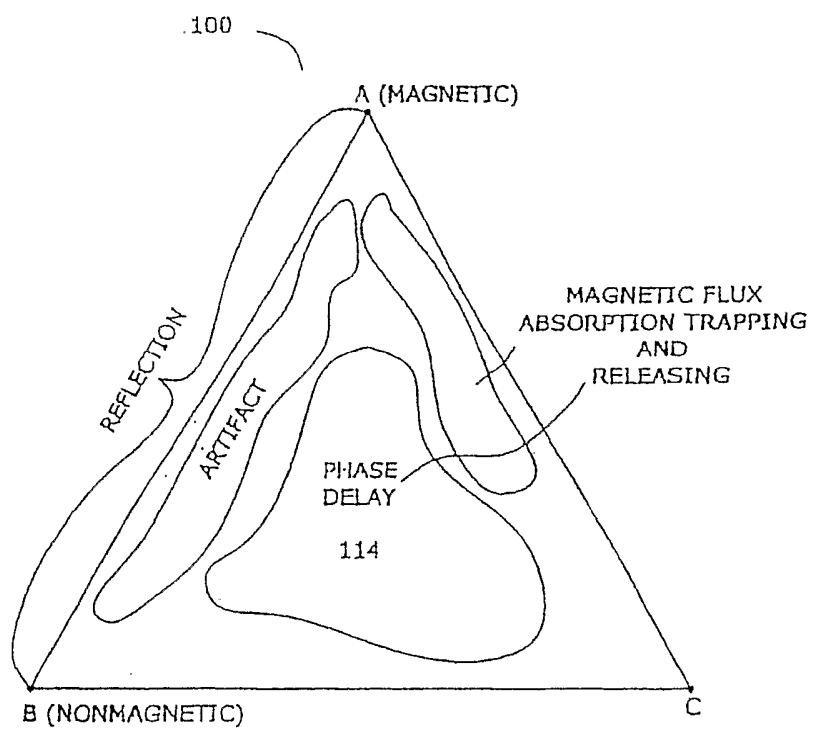
5/50

FIG. 3

6/50

FIG. 3A

7/50

FIG. 4

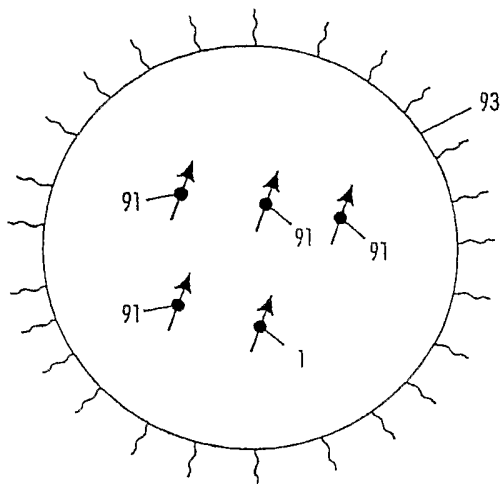


FIG. 4A

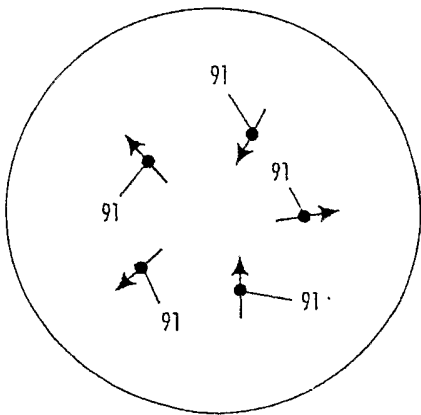
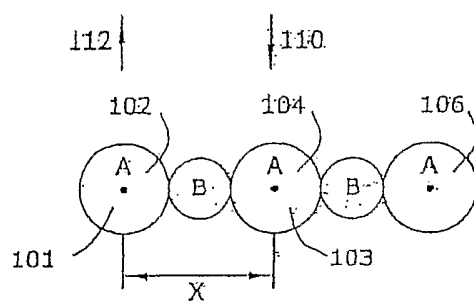
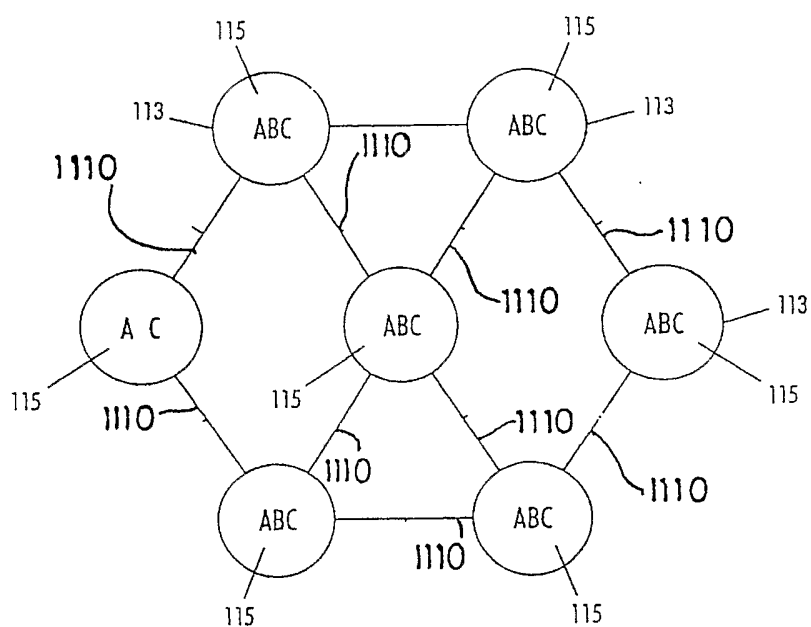


FIG. 4B

9/50

FIG. 5

10/50

FIG. 5A

11/50

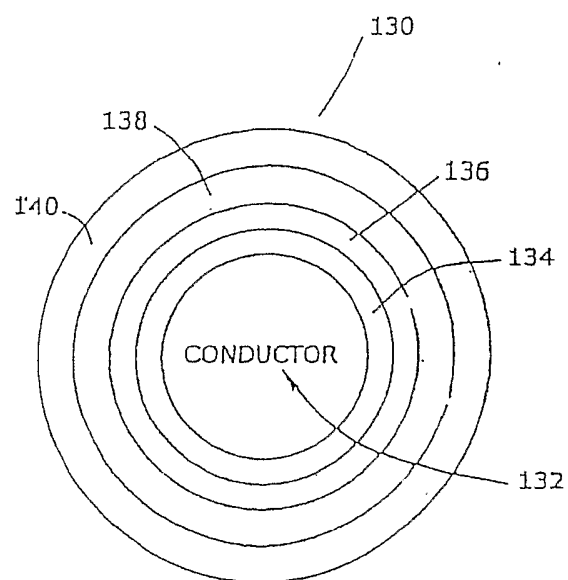


FIG. 6

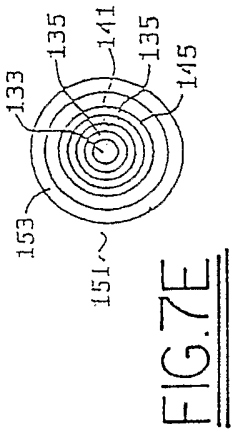
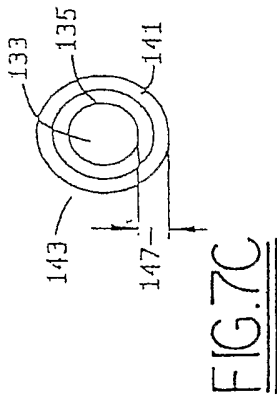
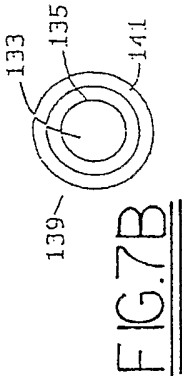
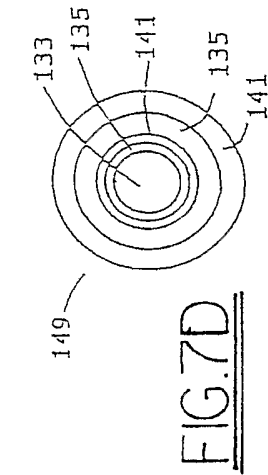


FIG. 7A

FIG. 7B

FIG. 7C

FIG. 7D

FIG. 7E

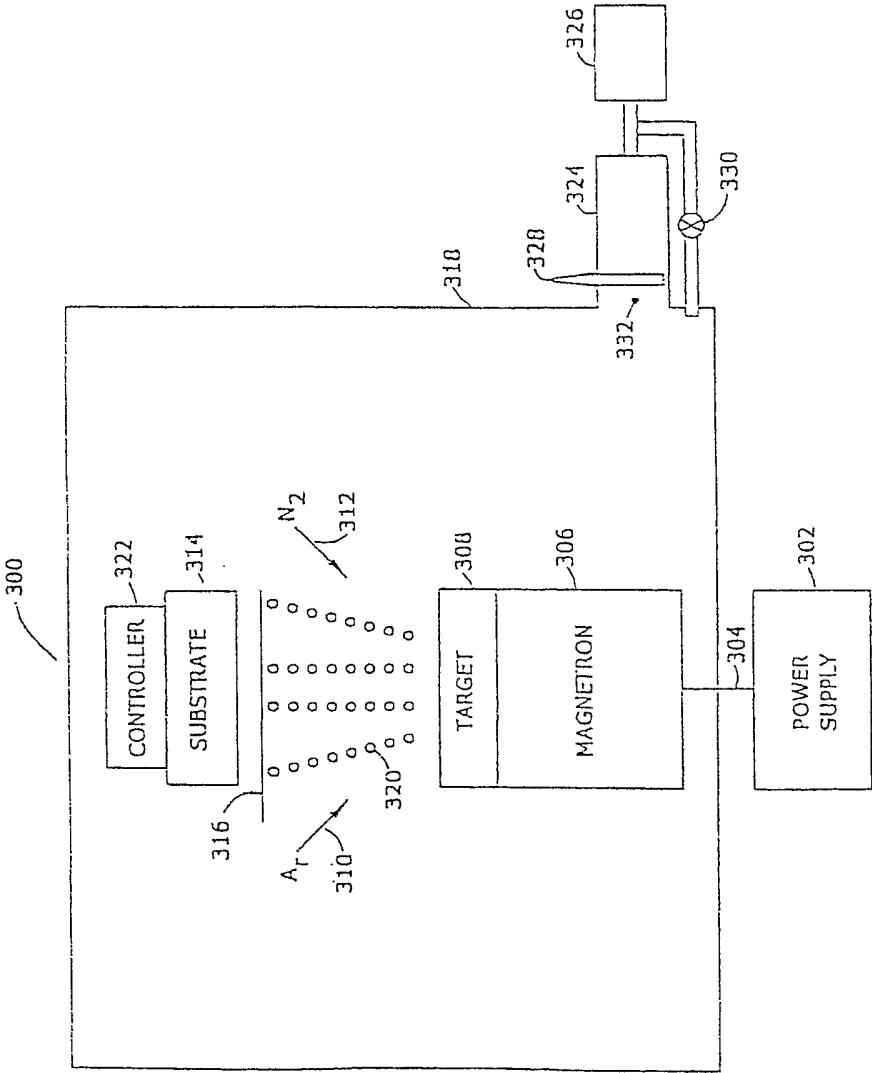


FIG.8

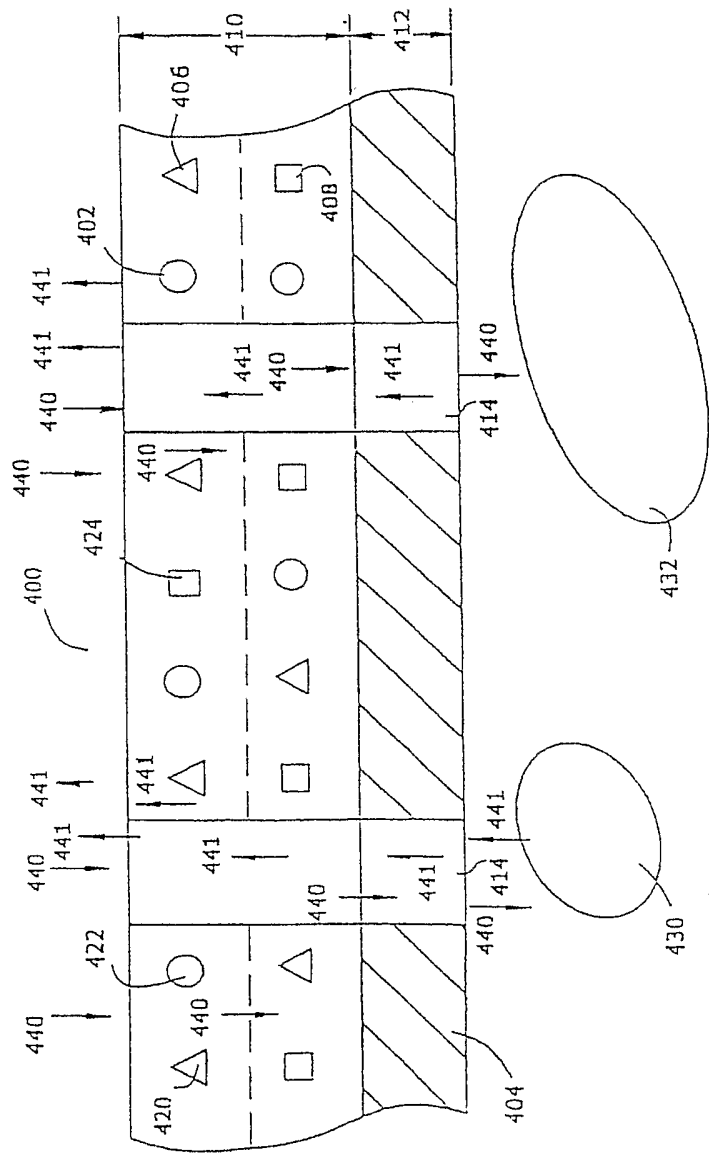


FIG. 9

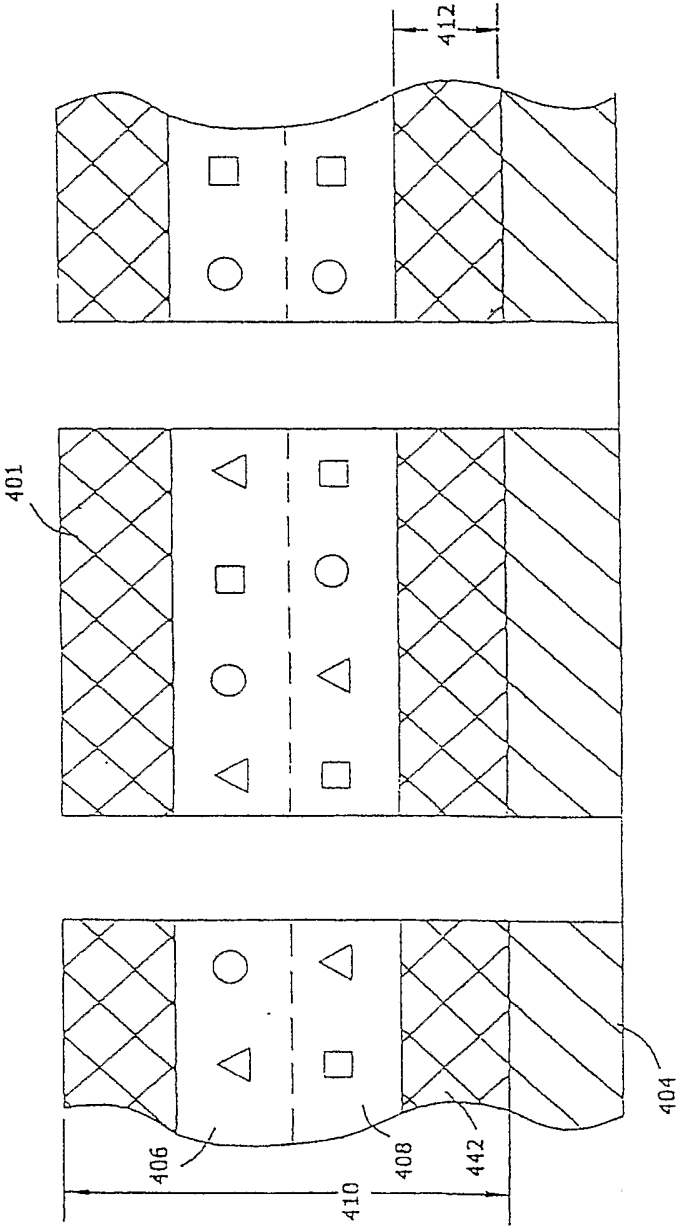


FIG. 9A

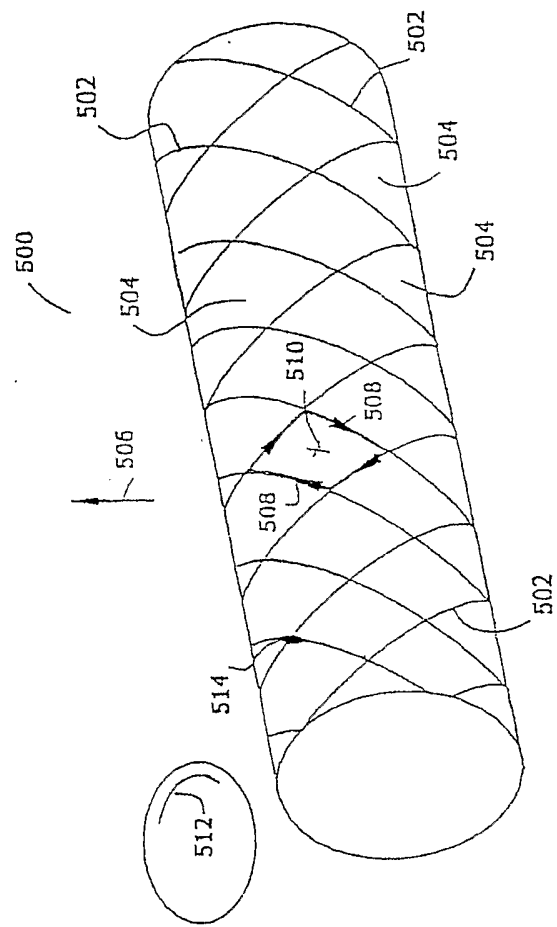


FIG. 10

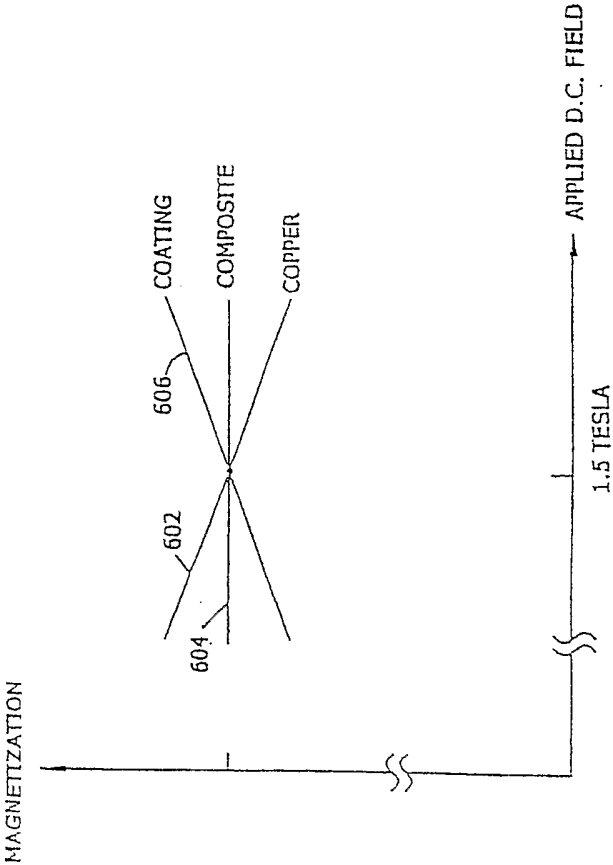


FIG. 11

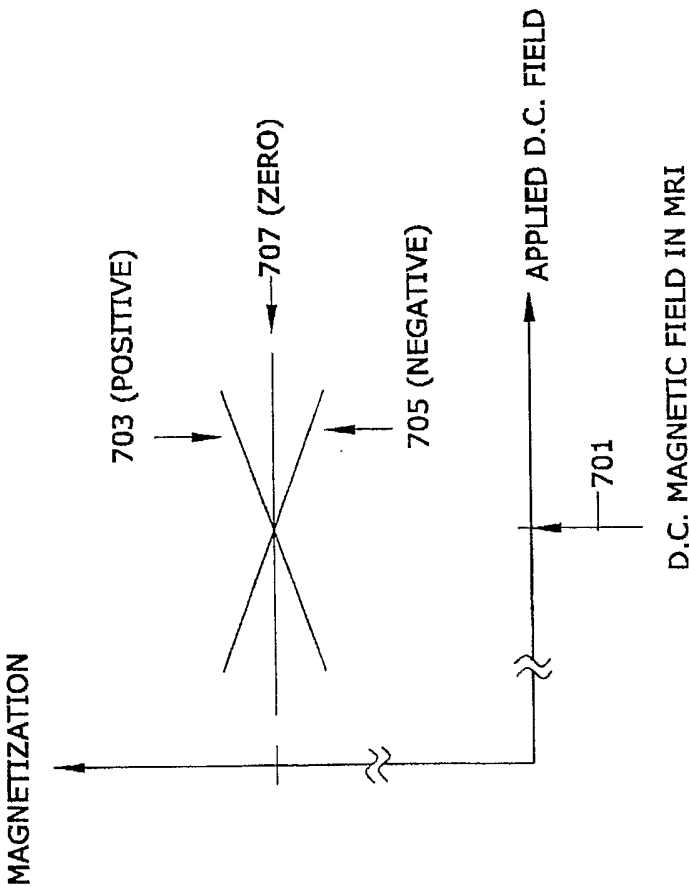


FIG.11A

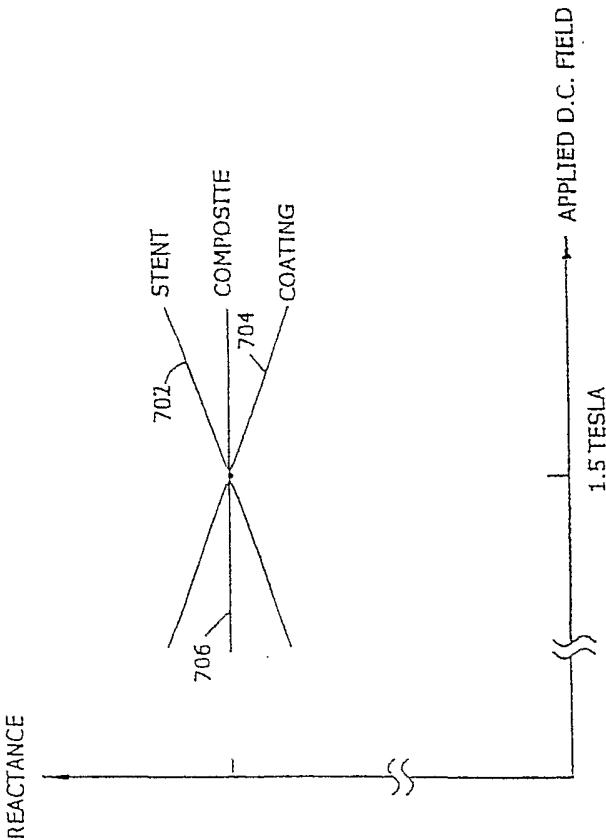


FIG. 12

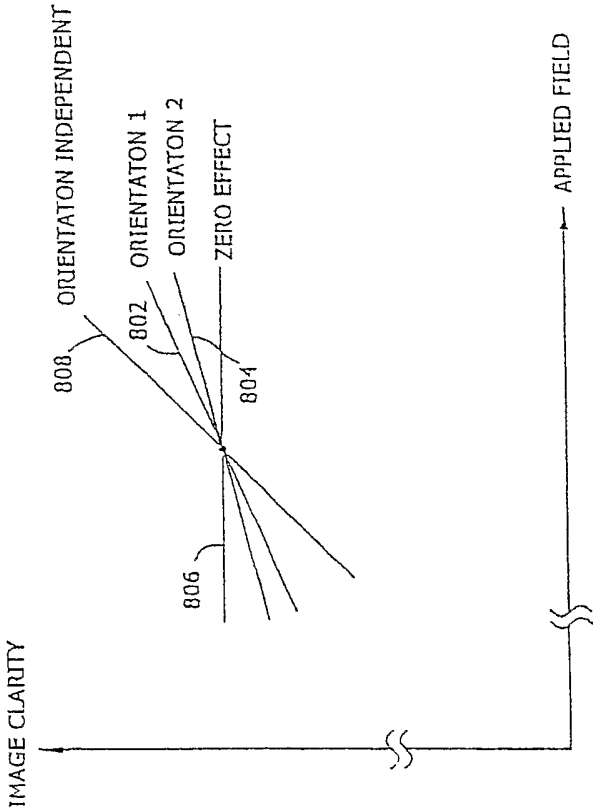
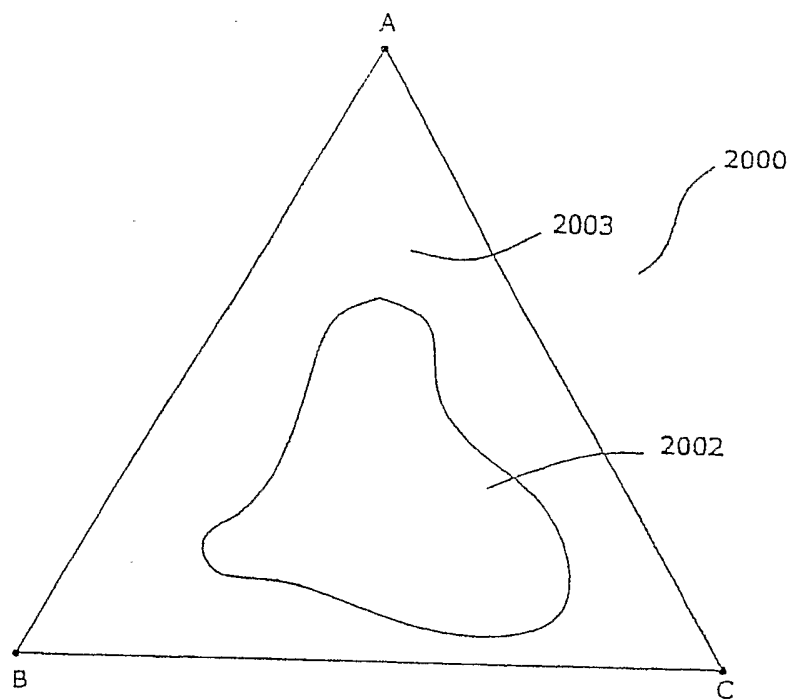


FIG.13

21/50

FIG. 14

22/50

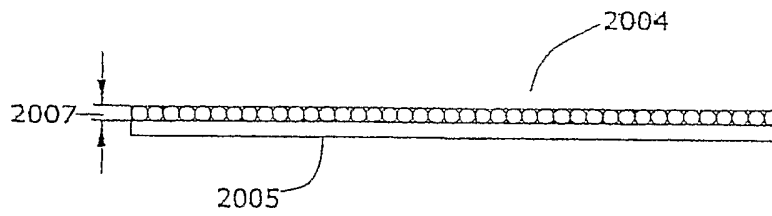


FIG. 15

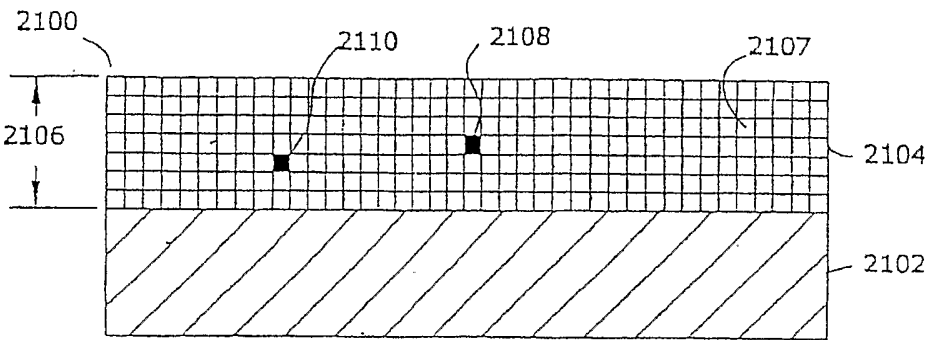


FIG. 16A

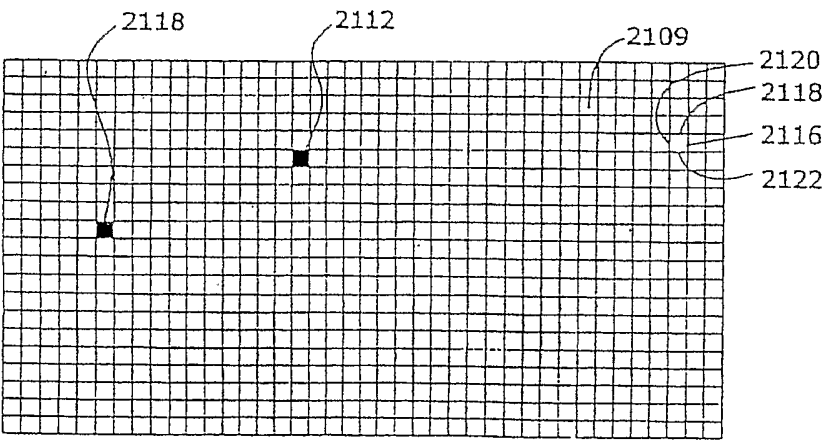


FIG. 16B

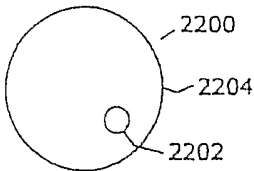


FIG. 17A

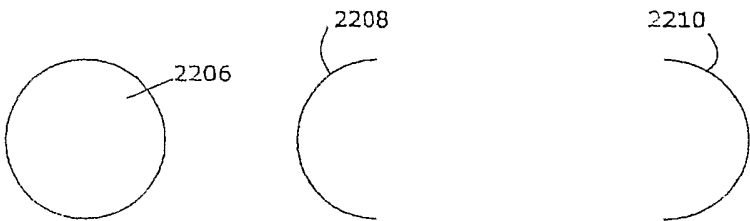


FIG. 17B

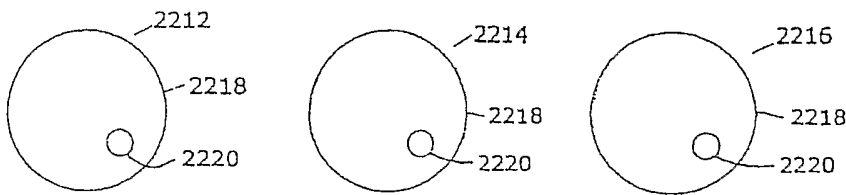


FIG. 17C

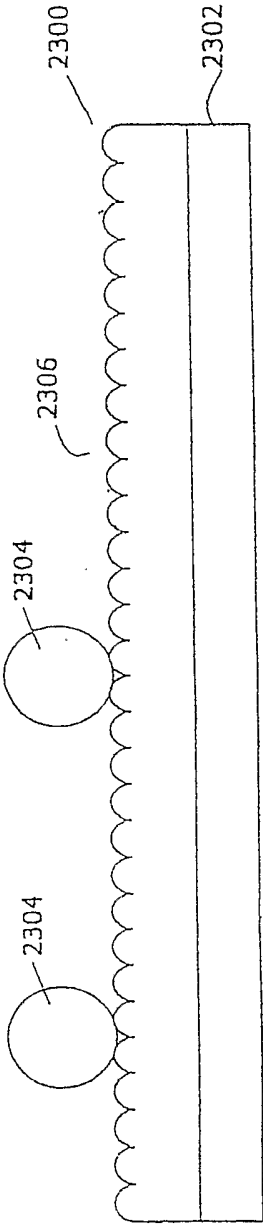


FIG. 18A

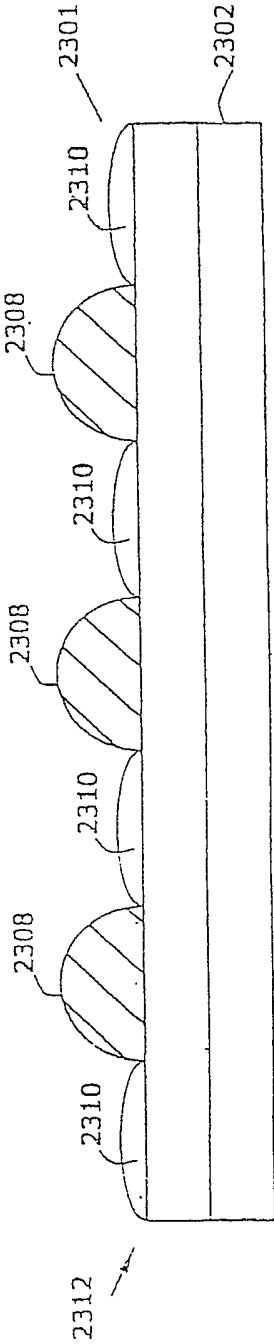


FIG. 18B

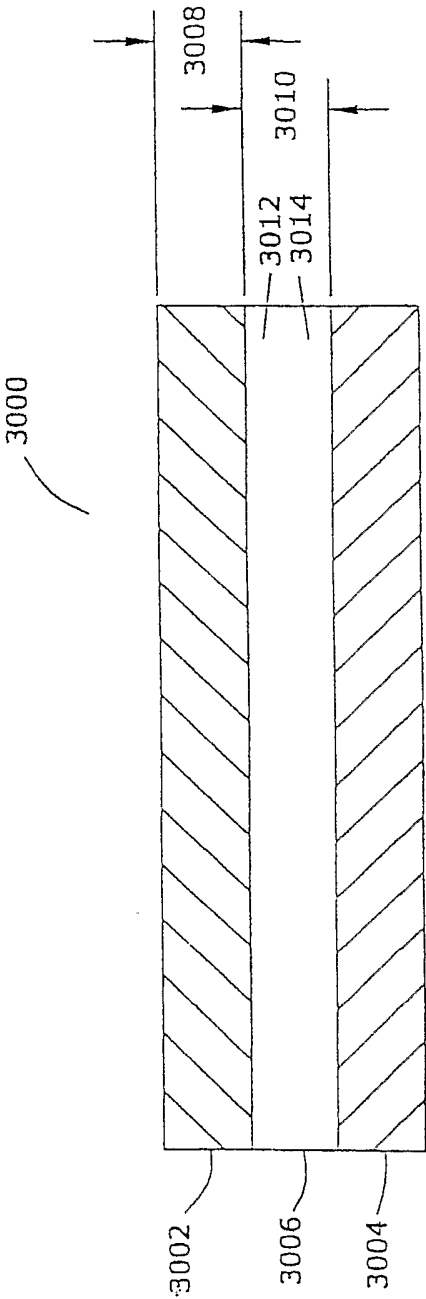
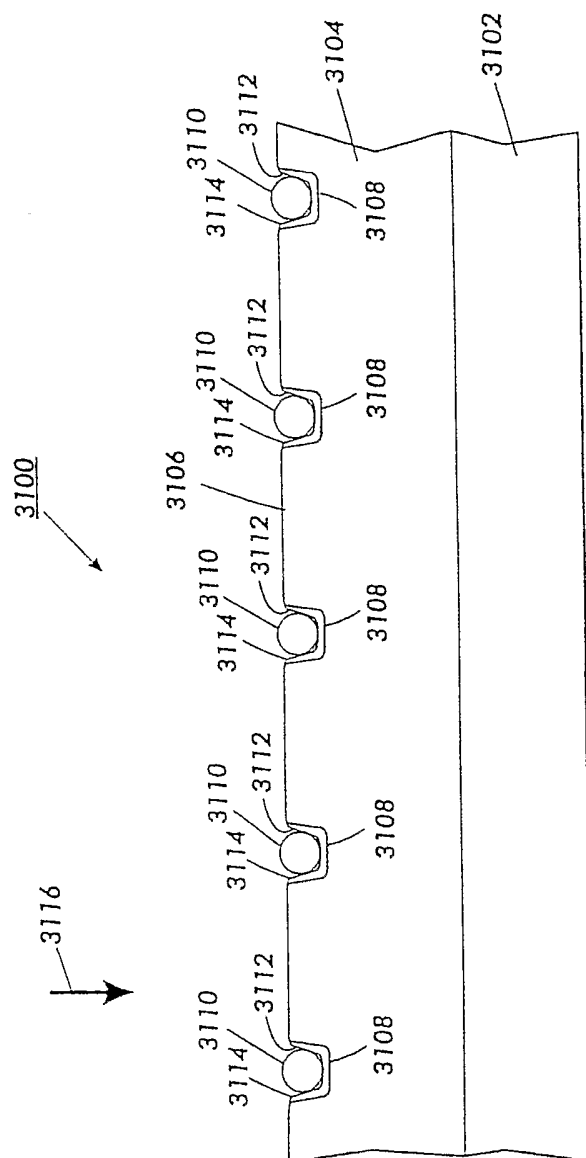


FIG. 19

27/50

FIG. 20

28/50

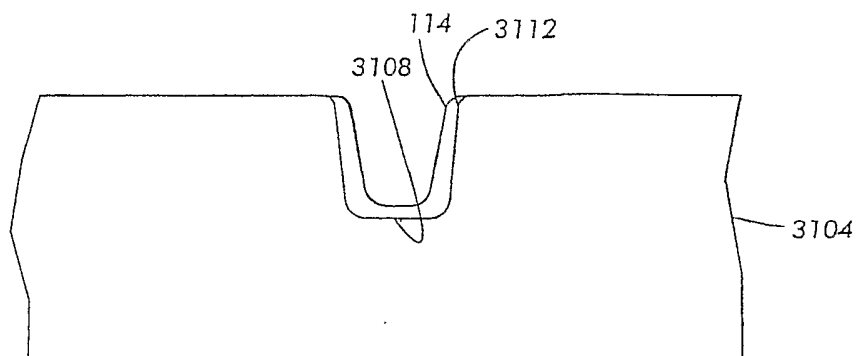


FIG. 20A

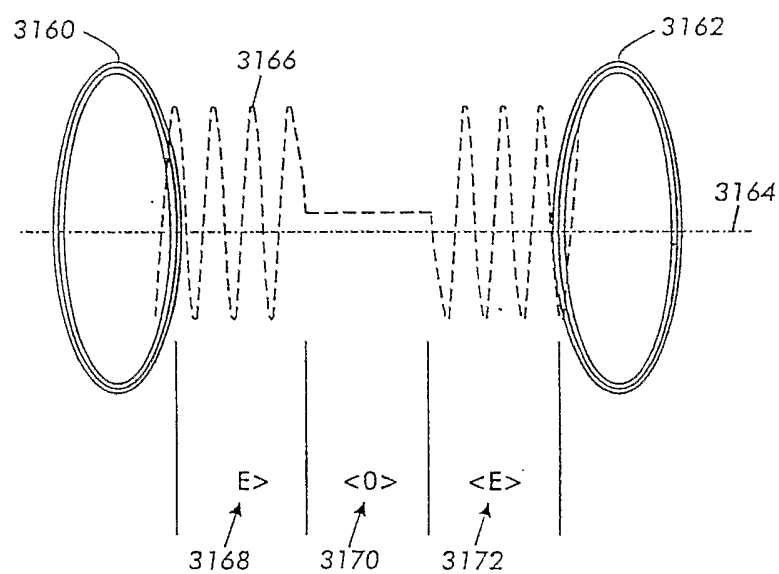


FIG. 20B

29/50

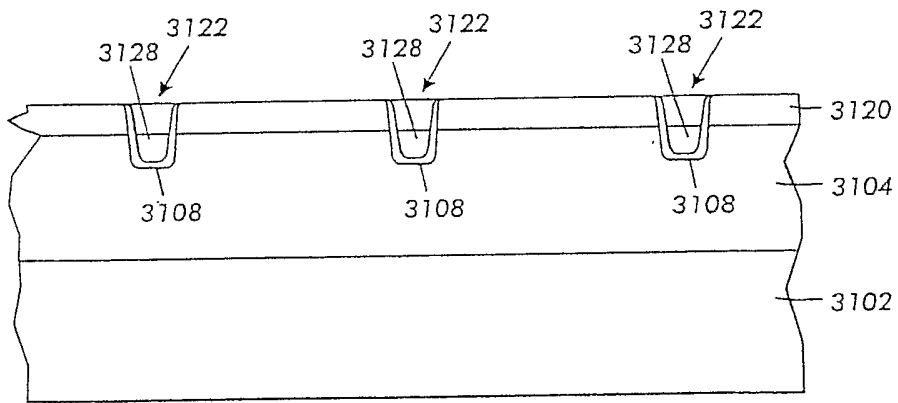
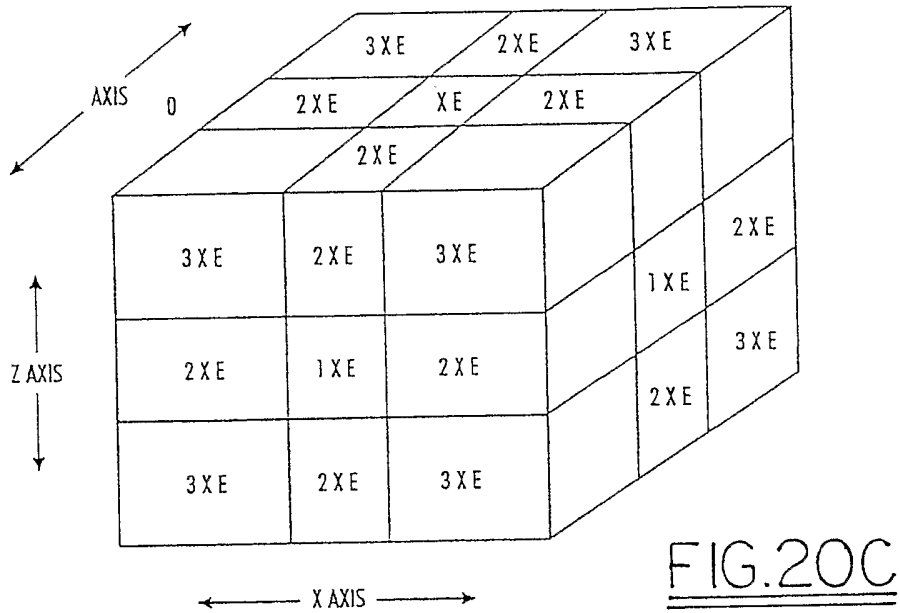


FIG. 21

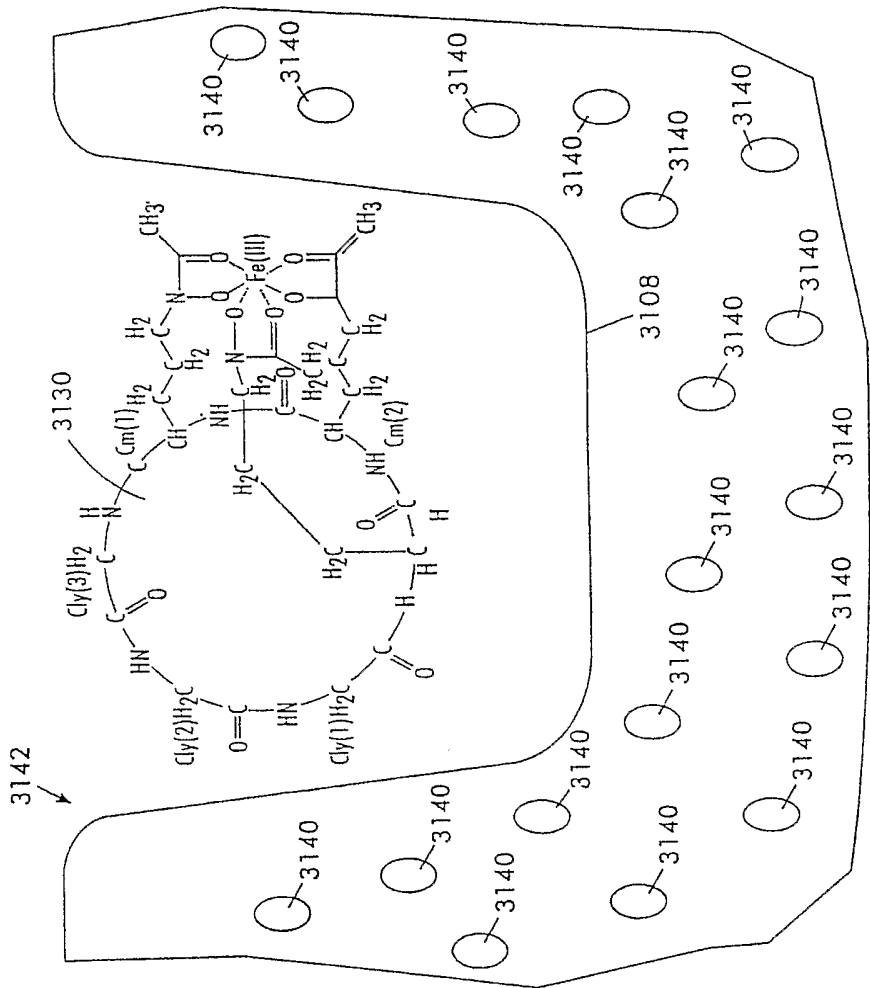


FIG. 22

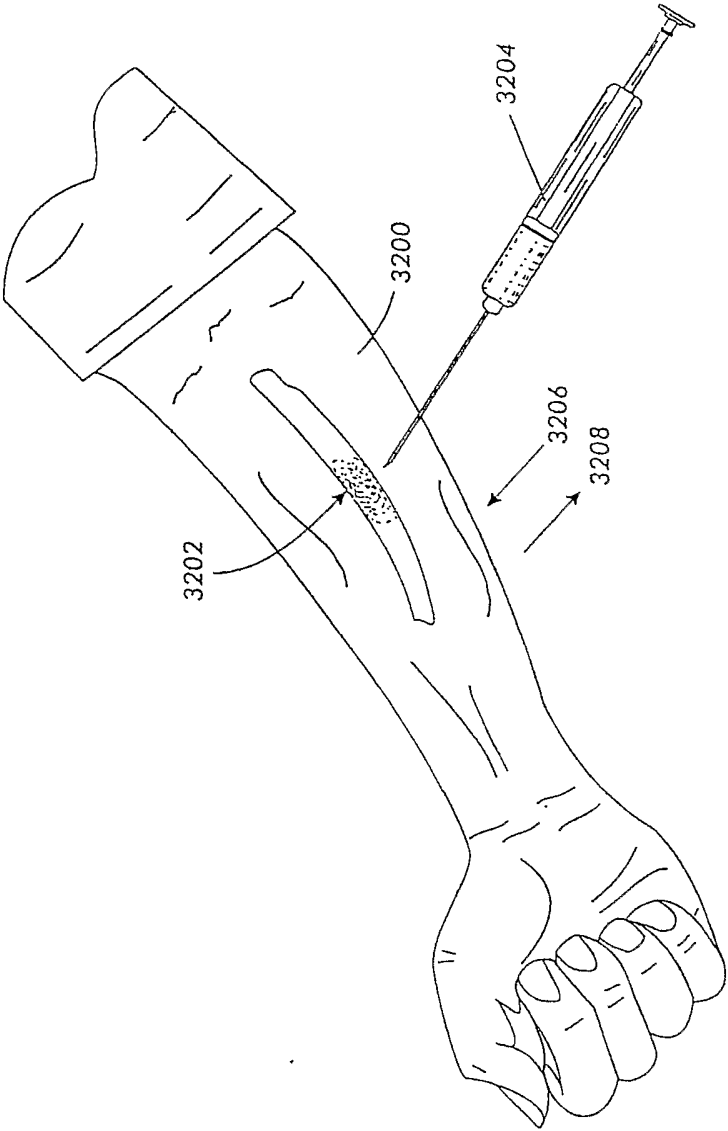
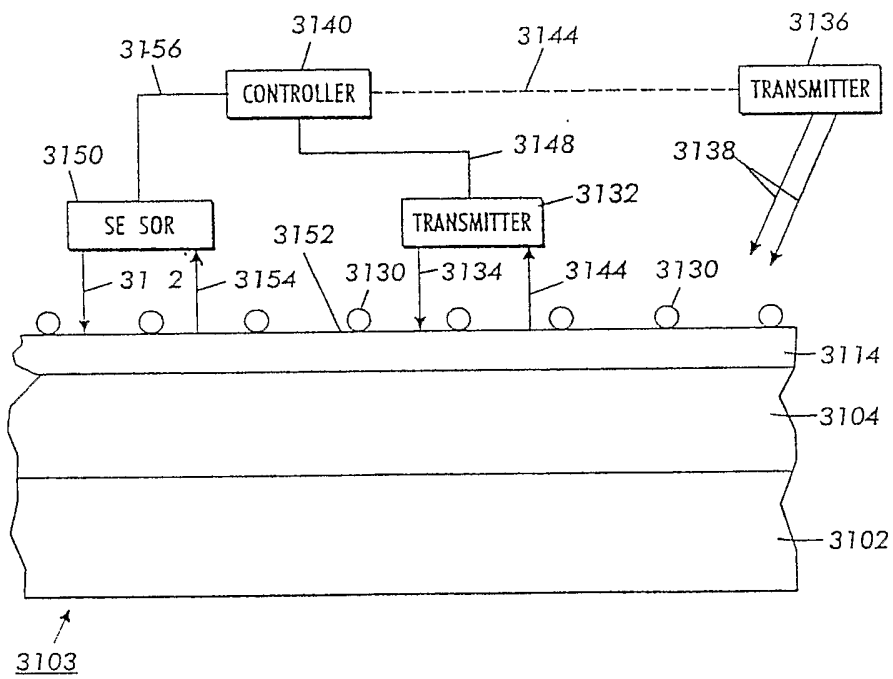


FIG. 23

32/50

FIG.24

33/50

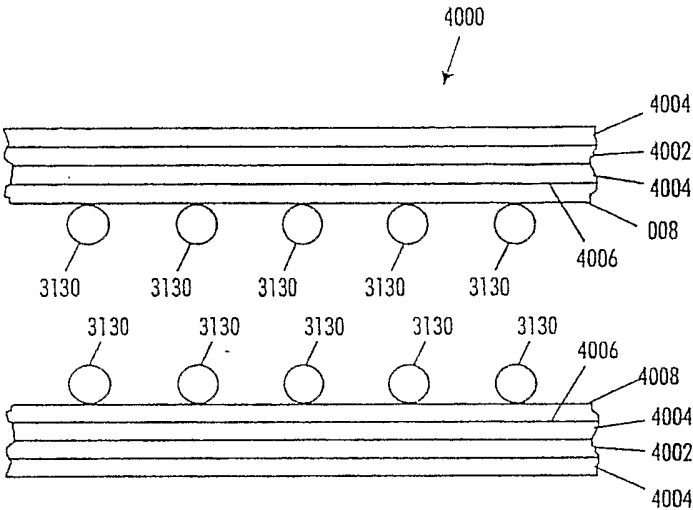


FIG.25

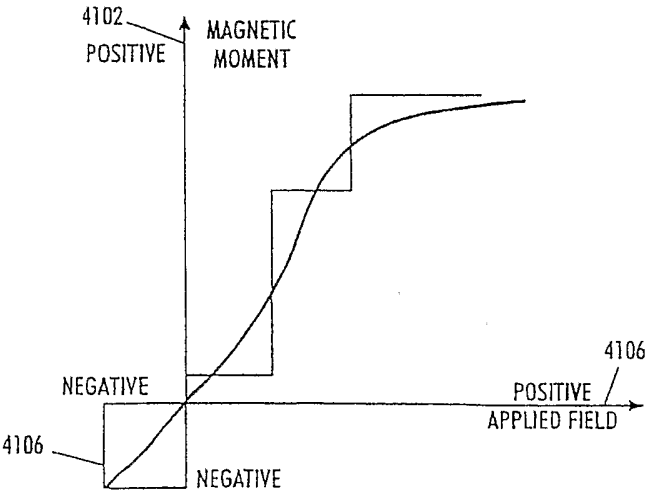


FIG.26

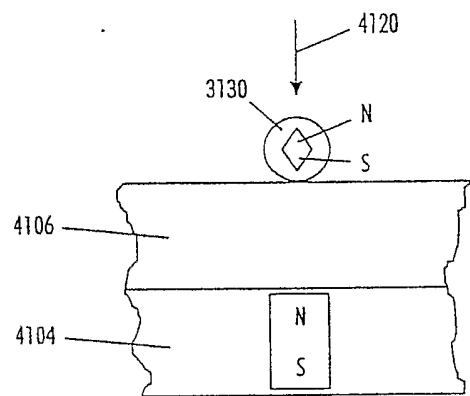


FIG. 27A

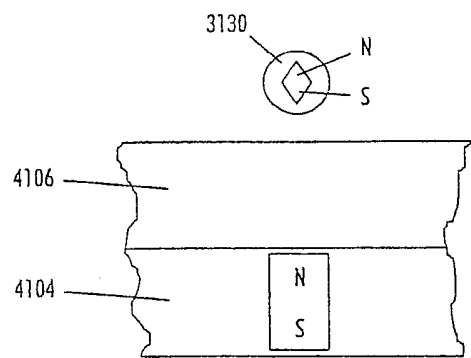
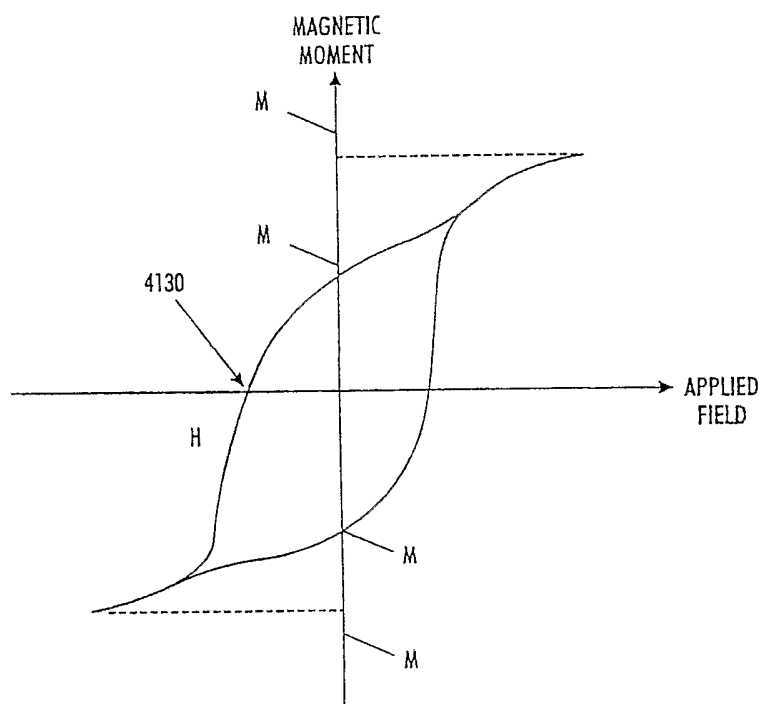


FIG. 27B

35/50

FIG. 28

36/50

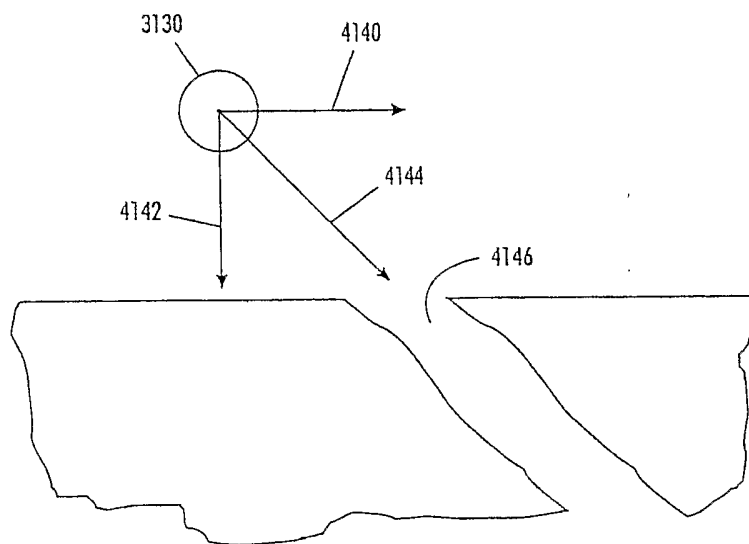


FIG. 29

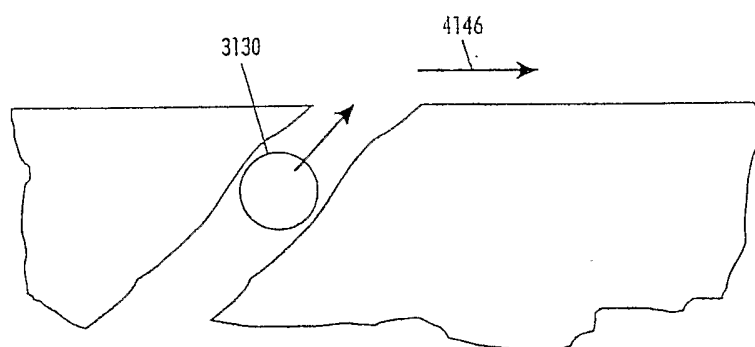


FIG. 30

37/50

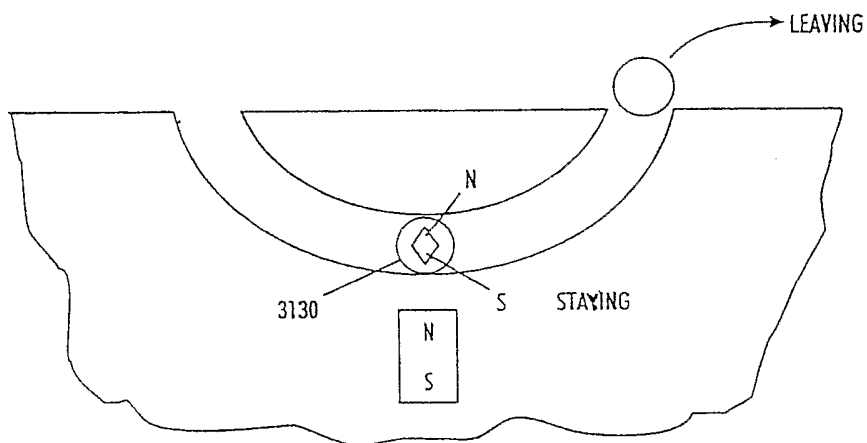


FIG. 31

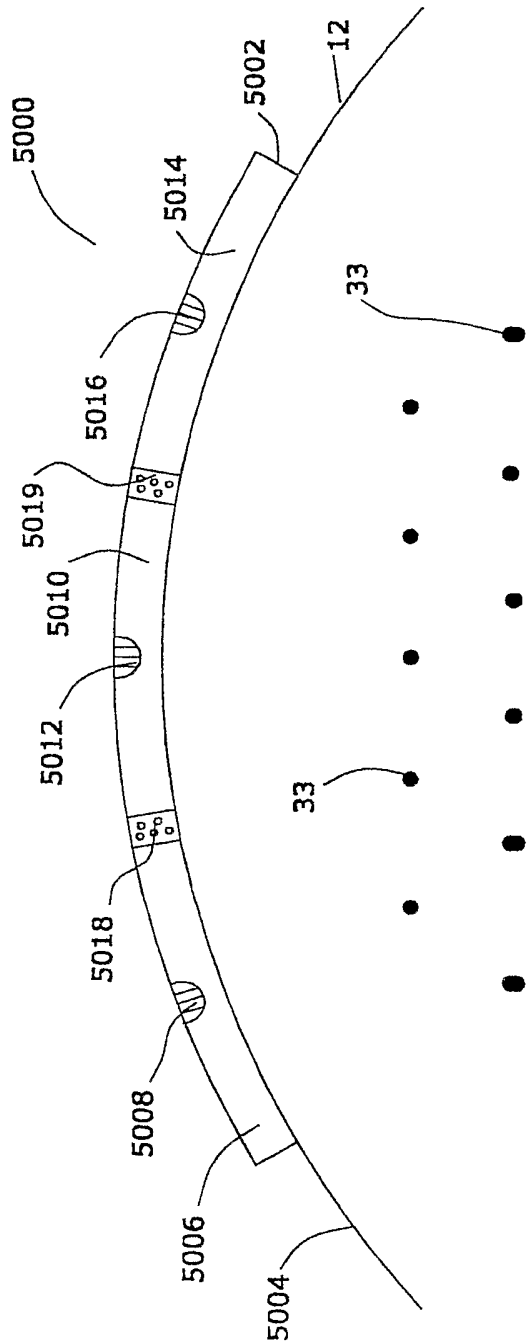


FIG. 32

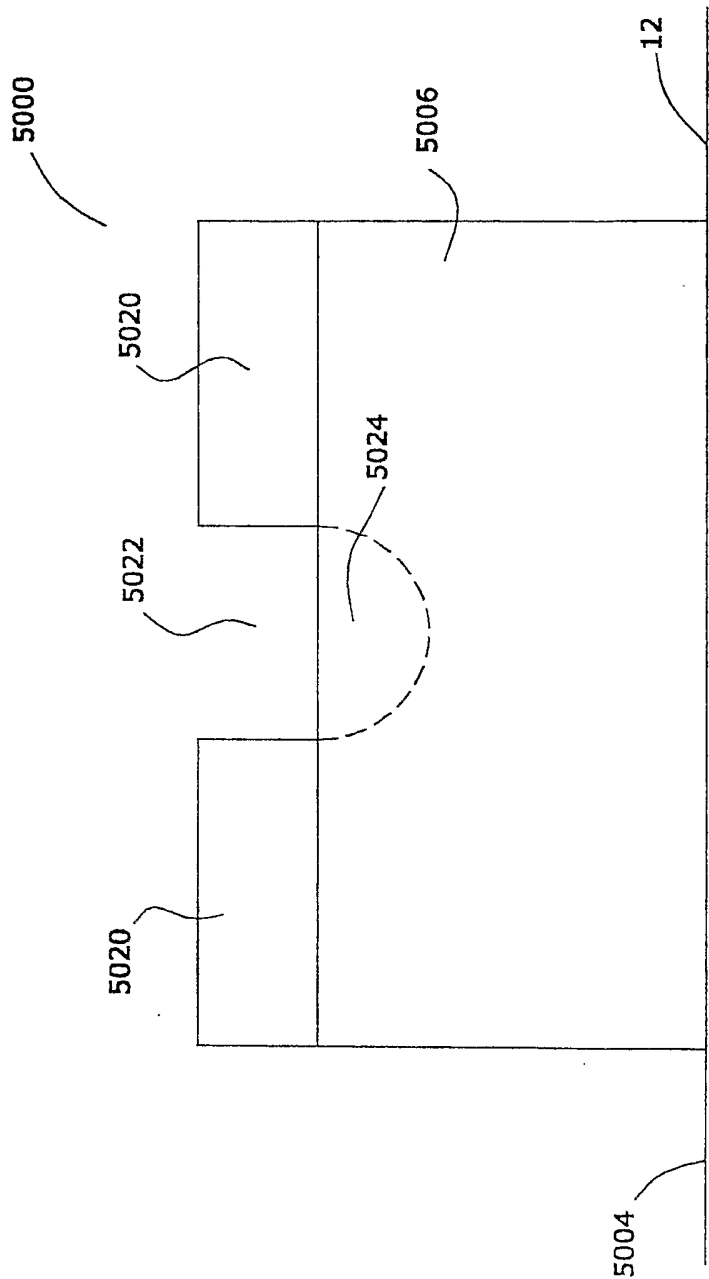


FIG. 33

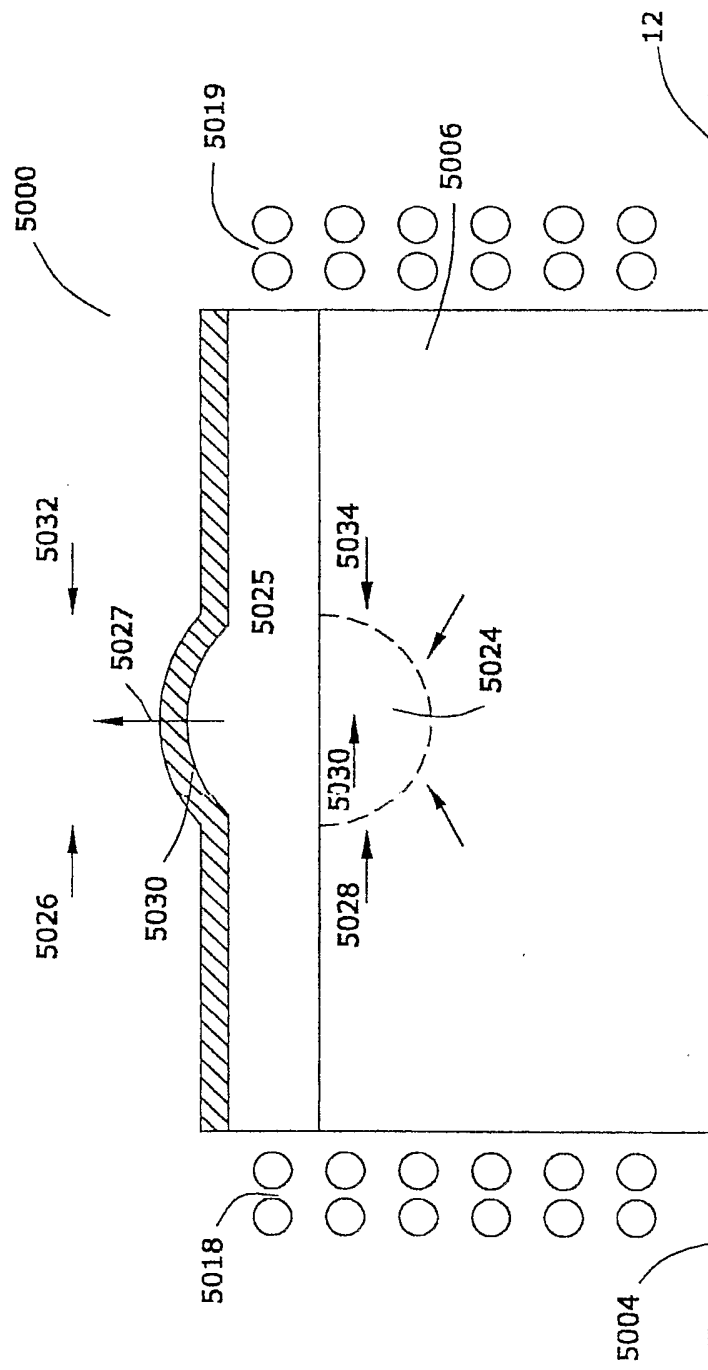


FIG. 34

41/50

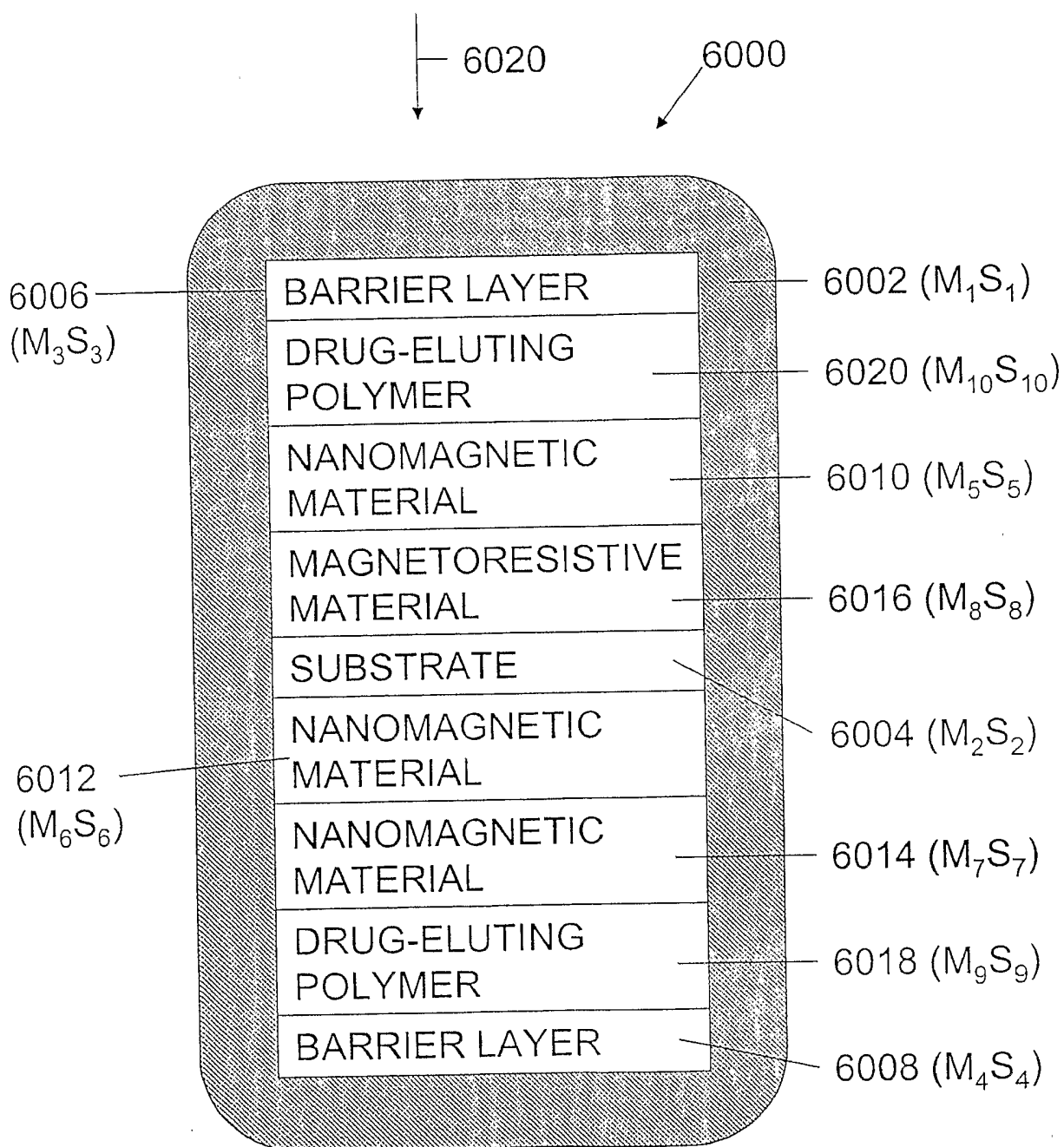


FIG. 35

42/50

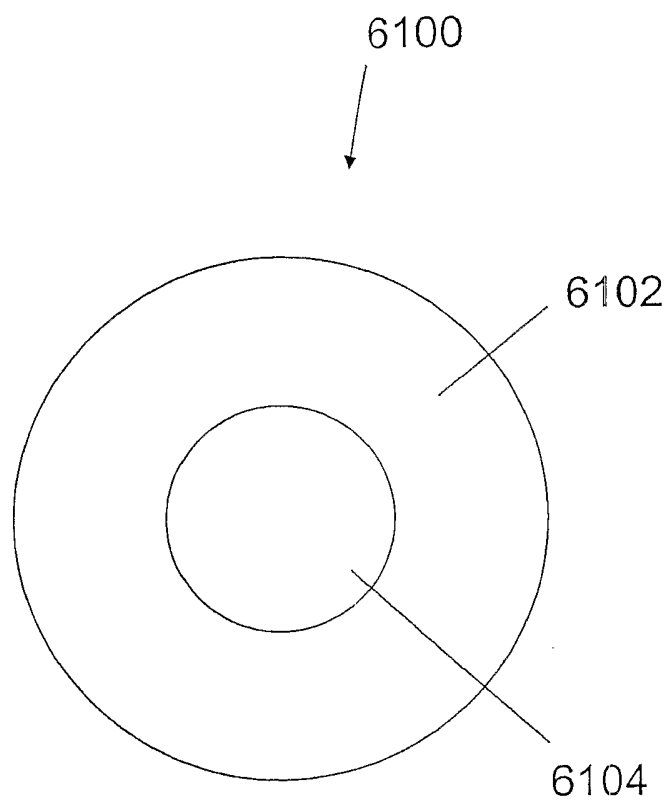


FIG. 36

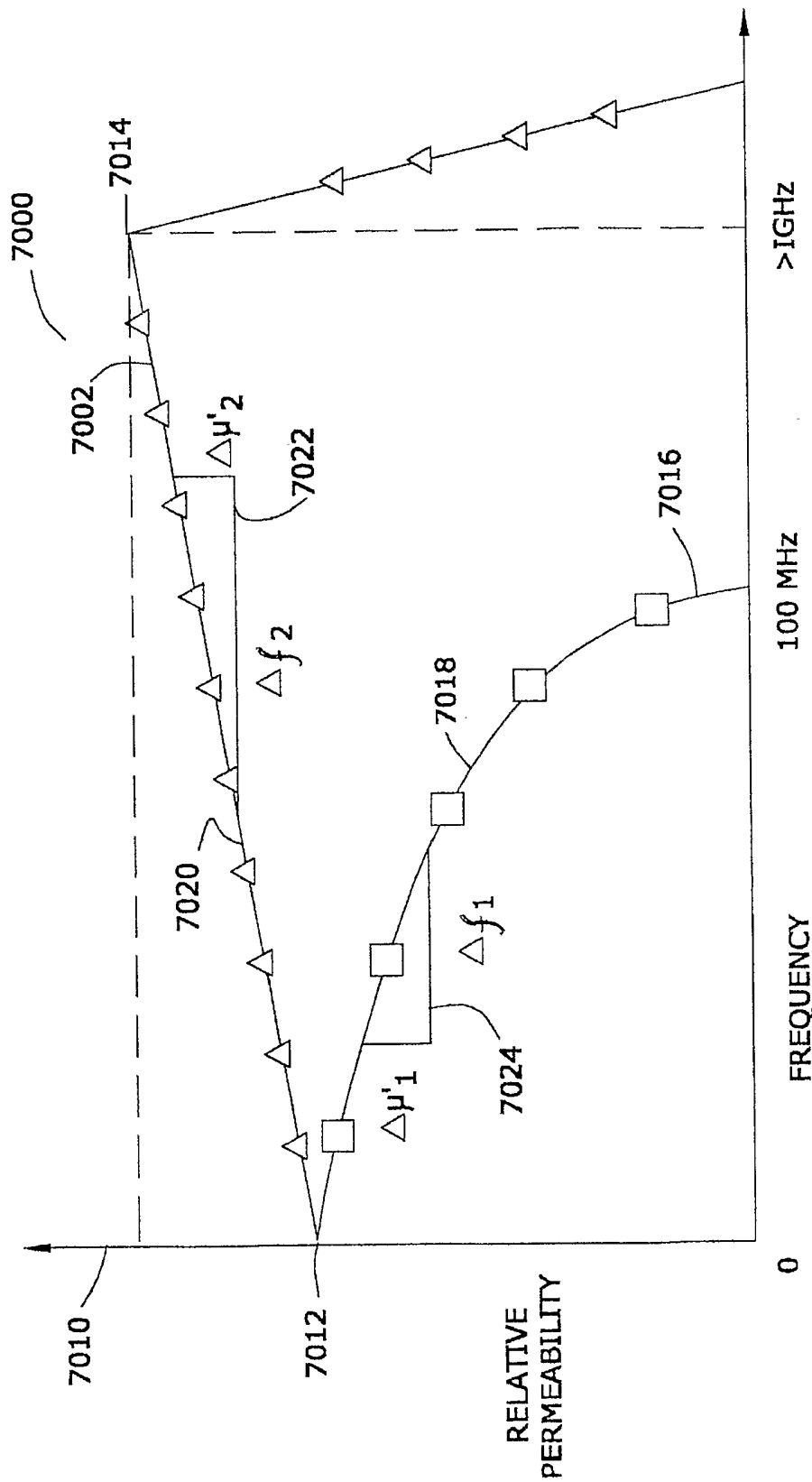


FIG.37

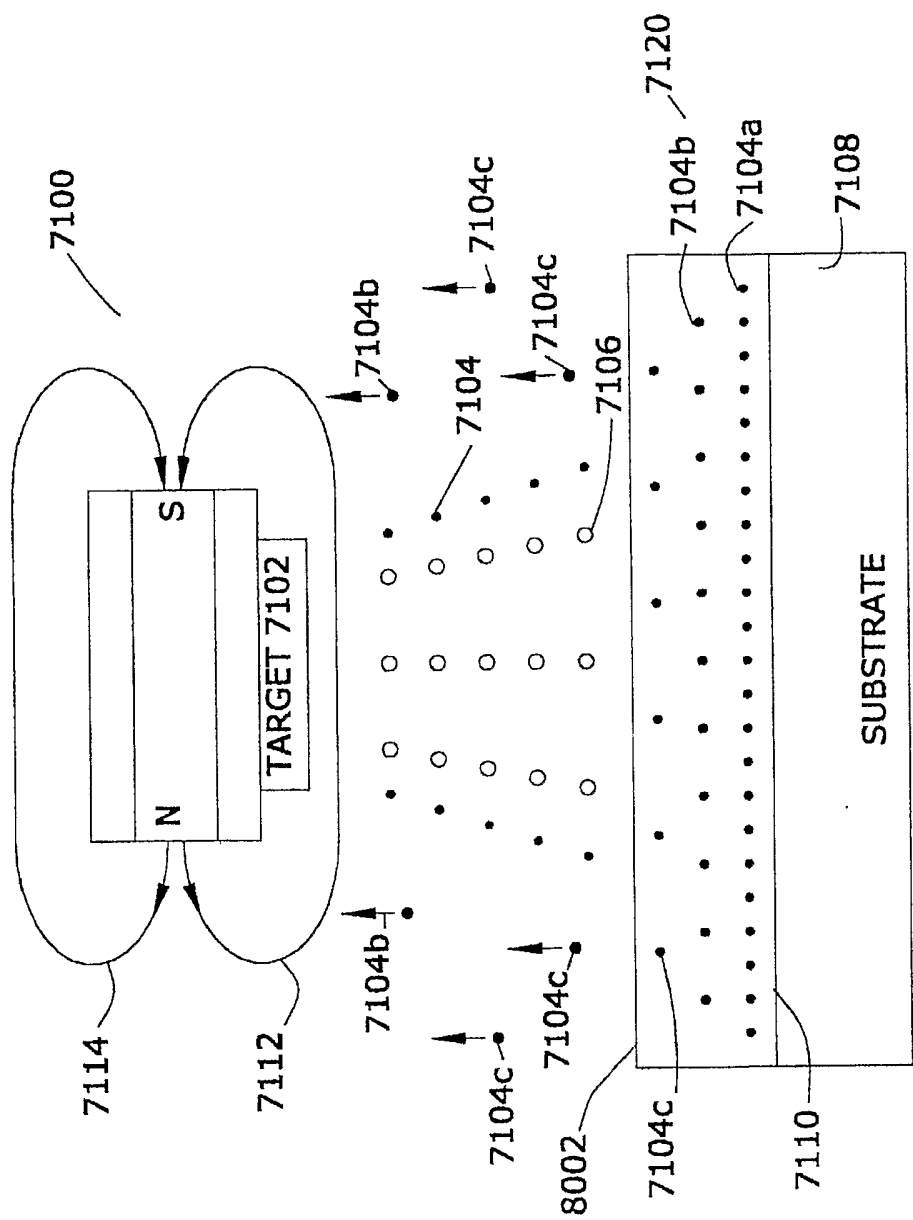


FIG.38

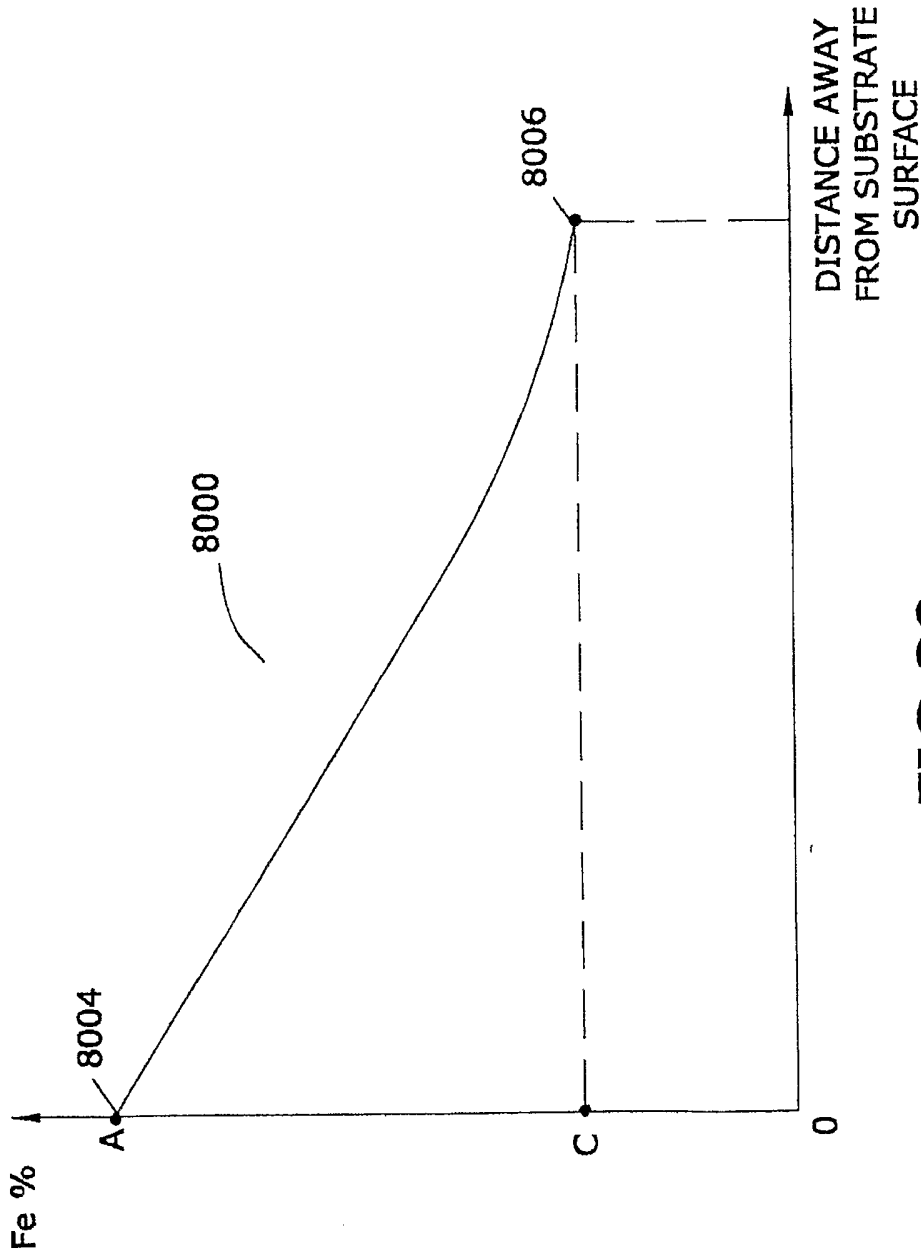


FIG. 39

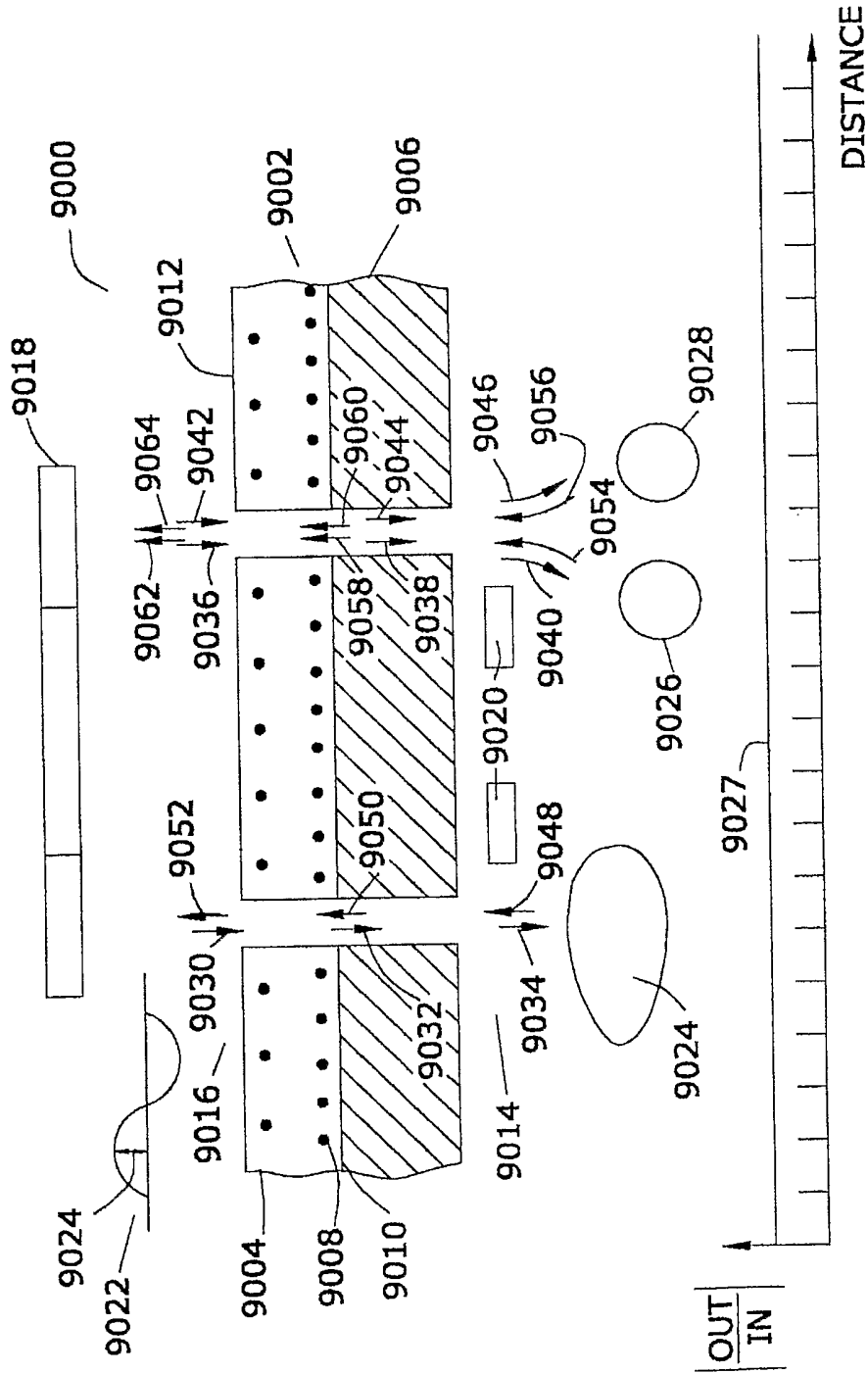


FIG. 40

47/50

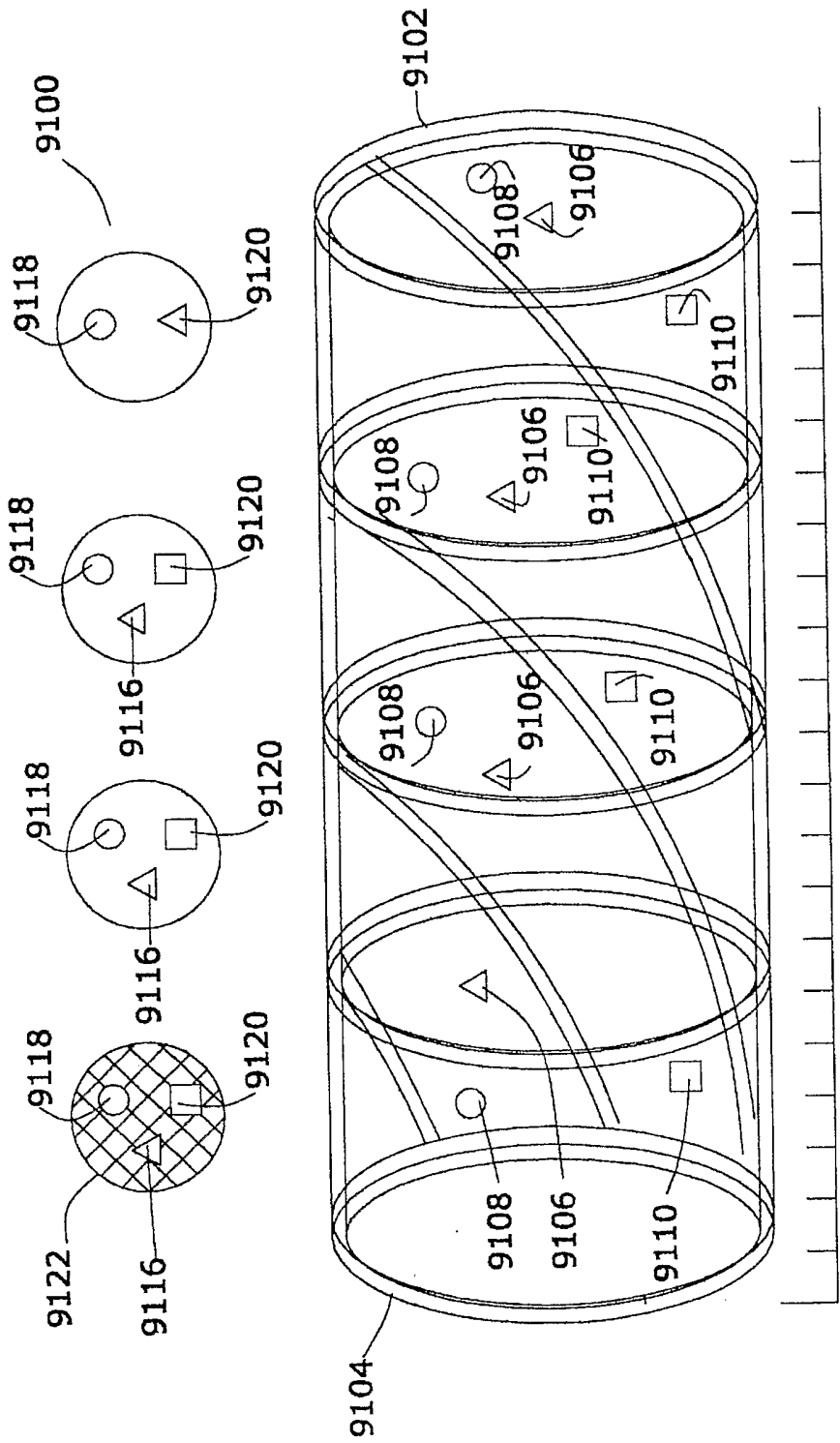


FIG. 41

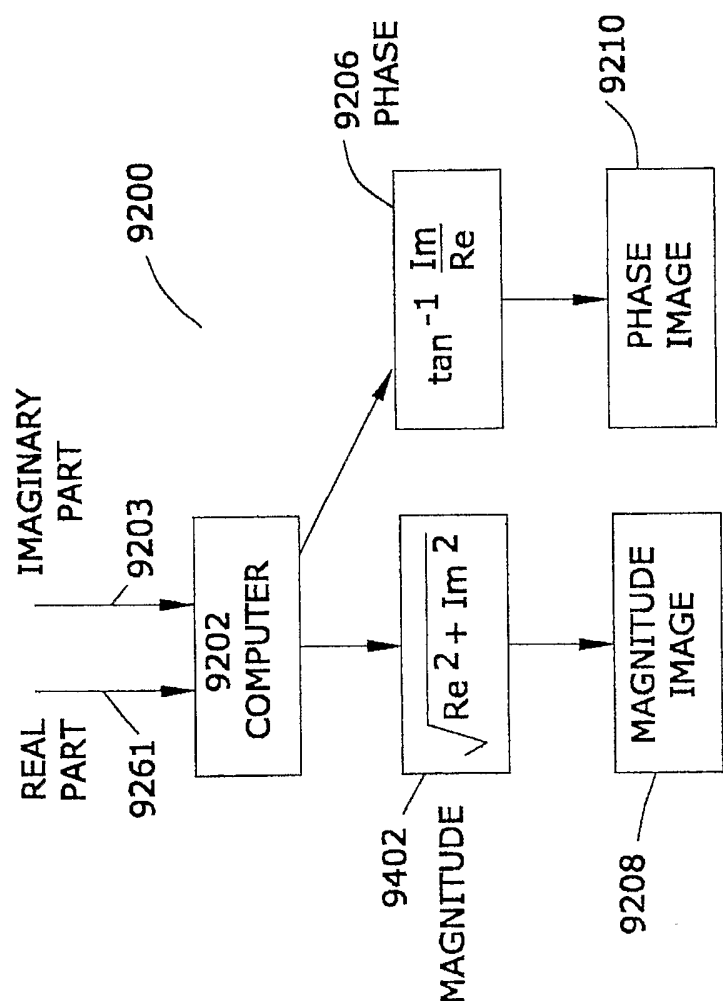


FIG.42

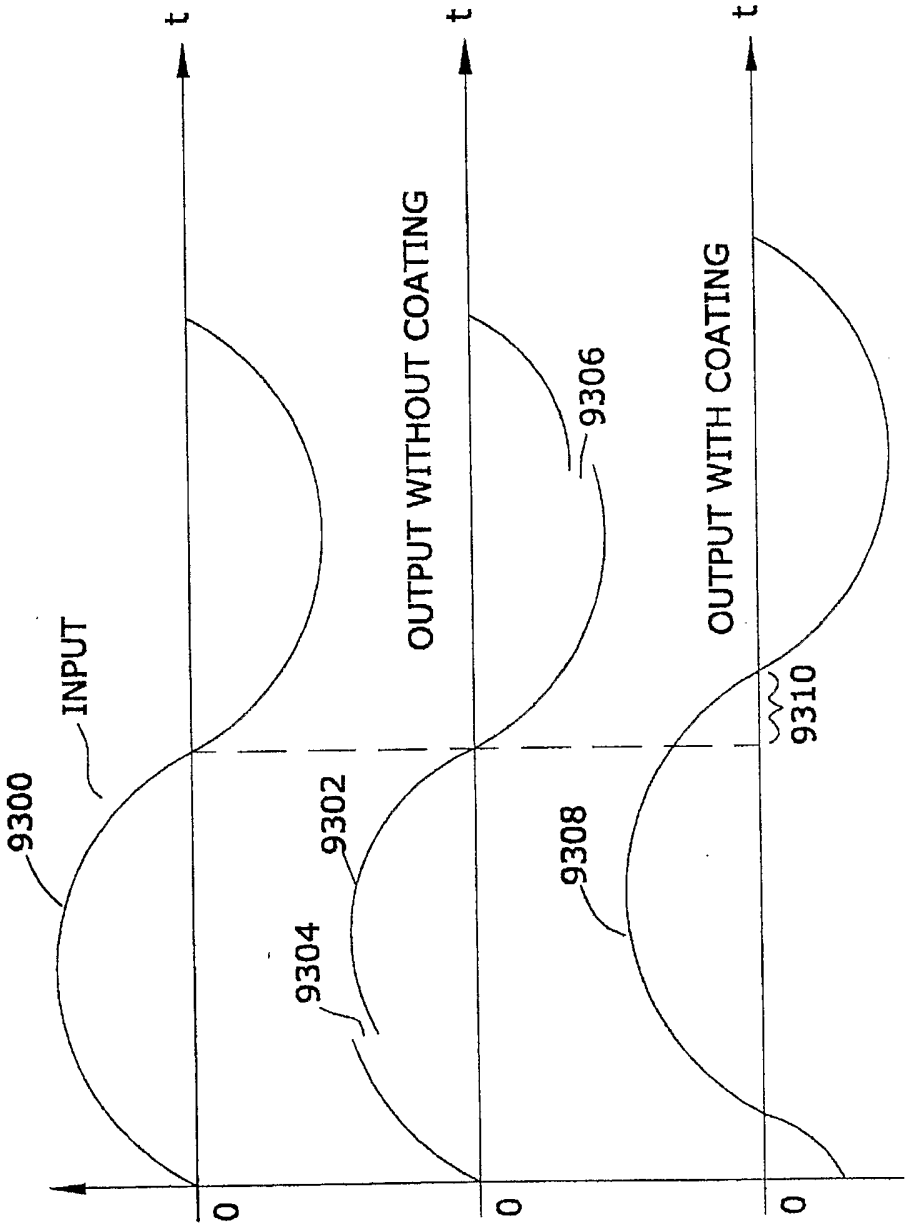


FIG.43

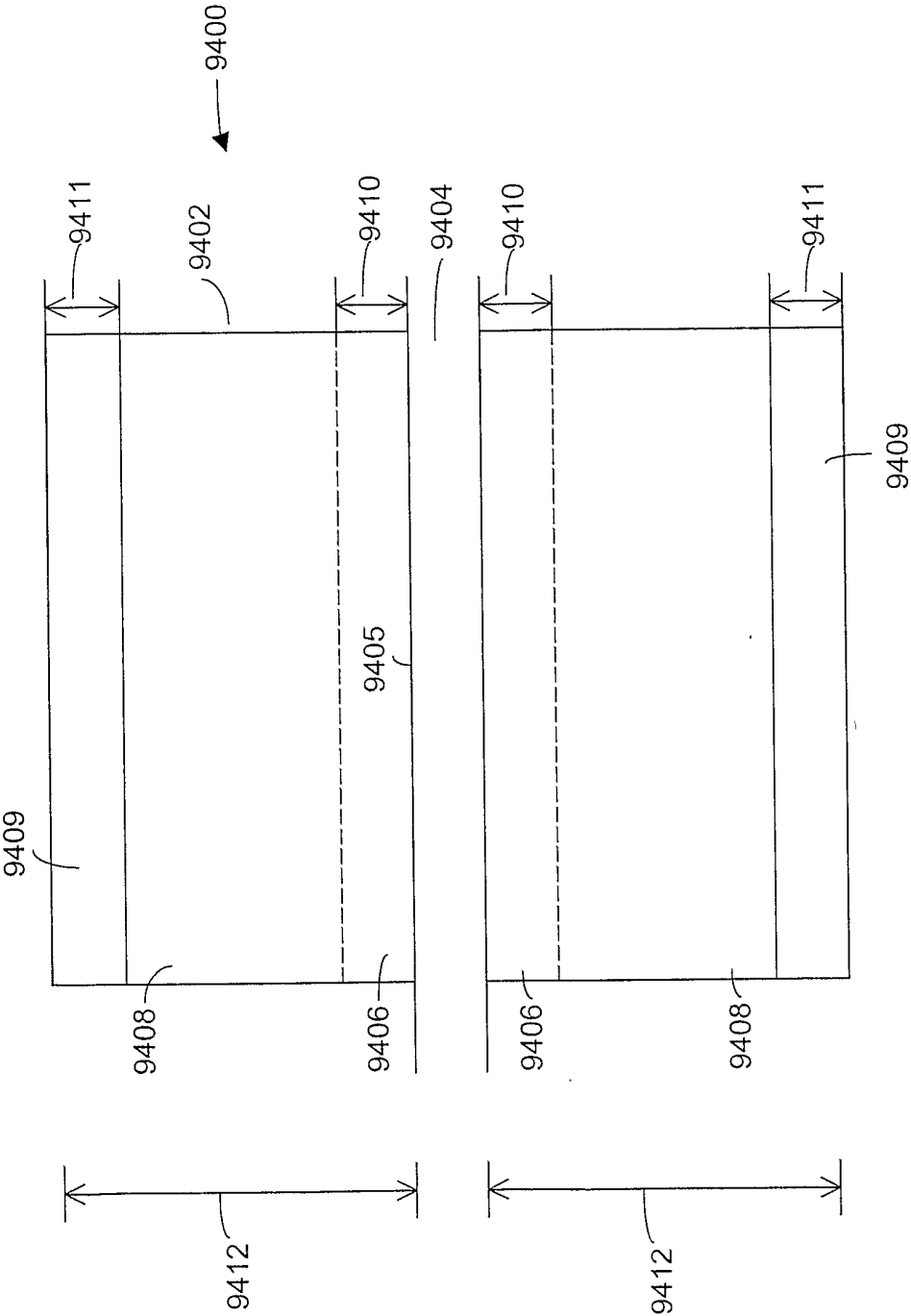


FIG. 44