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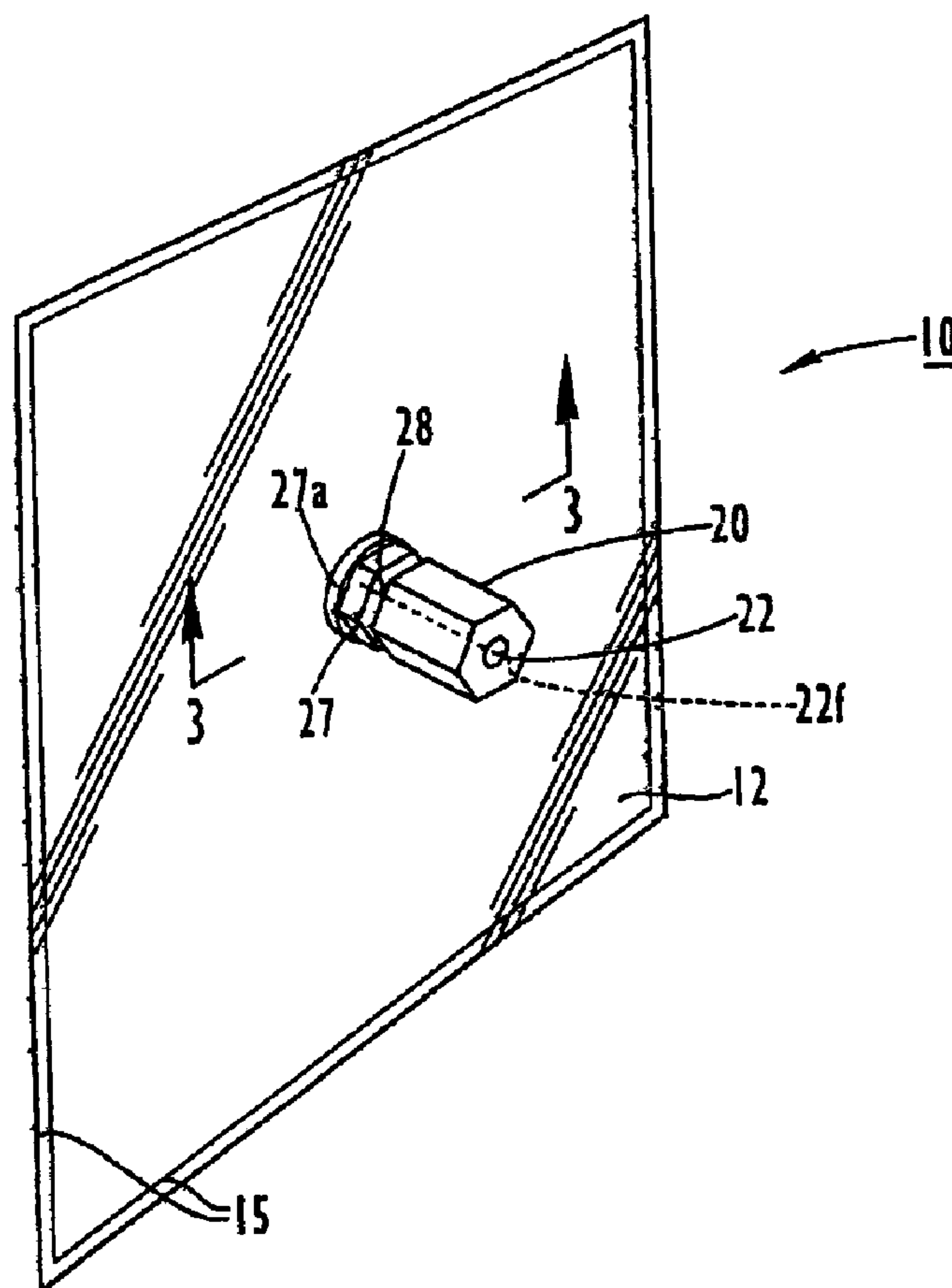
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(54) Title: RESILIENT CONTAINERS FOR HYPERPOLARIZED GASES



(57) Abrégé/Abstract:

A resilient multi-layer container is configured to receive a quantity of hyperpolarized noble fluid such as gas and includes a wall with at least two layers, a first layer with a surface which minimizes contact-induced spin-relaxation and a first or second layer which is

(57) Abrégé(suite)/Abstract(continued):

substantially impermeable to oxygen. The container is especially suitable for collecting and transporting ^3He . The resilient container can be formed of material layers which are concurrently responsive to pressure such as polymers, deuterated polymers, or metallic films. The container can include a capillary stem and/or a port or valve isolation means to inhibit the flow of gas from the main volume of the container during transport. The resilient container can be configured to directly deliver the hyperpolarized noble gas to a target interface by deflating or collapsing the inflated resilient container. In addition, single layer resilient containers with T_1 's of above 4 hours for ^{129}Xe and above 6 hours for ^3He include materials with selected relaxivity values. In addition, a bag with a port fitting or valve member and one or more of a capillary stem and port isolation means is configured to minimize the depolarizing effect of the container valve or fitting(s). Also disclosed is a method for determining the gas solubility in an unknown polymer or liquid using the measured relaxation time of a hyperpolarized gas.

ABSTRACT

A resilient multi-layer container is configured to receive a quantity of hyperpolarized noble fluid such as gas and includes a wall with at least two layers, a first layer with a surface which minimizes contact-induced spin-relaxation and a first
5 or second layer which is substantially impermeable to oxygen. The container is especially suitable for collecting and transporting ^3He . The resilient container can be formed of material layers which are concurrently responsive to pressure such as polymers, deuterated polymers, or metallic films. The container can include a capillary stem and/or a port or valve isolation means to inhibit the flow of gas from
10 the main volume of the container during transport. The resilient container can be configured to directly deliver the hyperpolarized noble gas to a target interface by deflating or collapsing the inflated resilient container. In addition, single layer resilient containers with T_1 's of above 4 hours for ^{129}Xe and above 6 hours for ^3He include materials with selected relaxivity values. In addition, a bag with a port fitting
15 or valve member and one or more of a capillary stem and port isolation means is configured to minimize the depolarizing effect of the container valve or fitting(s). Also disclosed is a method for determining the gas solubility in an unknown polymer or liquid using the measured relaxation time of a hyperpolarized gas.

RESILIENT CONTAINERS FOR HYPERPOLARIZED GASES

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Field of the Invention

The present invention relates to processing, storage, transport and delivery containers for hyperpolarized noble gases.

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Background of the Invention

Conventionally, Magnetic Resonance Imaging ("MRI") has been used to produce images by exciting the nuclei of hydrogen molecules (present in water protons) in the human body. However, it has recently been discovered that polarized noble gases can produce improved images of certain areas and regions of the body which have heretofore produced less than satisfactory images in this modality. Polarized Helium-3 (^3He) and Xenon-129 (^{129}Xe) have been found to be particularly suited for this purpose. Unfortunately, as will be discussed further below, the polarized state of the gases are sensitive to handling and environmental conditions and, undesirably, can decay from the polarized state relatively quickly.

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Hyperpolarizers are used to produce and accumulate polarized noble gases. Hyperpolarizers artificially enhance the polarization of certain noble gas nuclei (such as ^{129}Xe or ^3He) over the natural or equilibrium levels, *i.e.*, the Boltzmann polarization. Such an increase is desirable because it enhances and increases the MRI signal intensity, allowing physicians to obtain better images of the substance in the body. See U. S. Patent No. 5,545,396 to Albert et al.

In order to produce the hyperpolarized gas, the noble gas is typically blended with optically pumped alkali metal vapors such as rubidium ("Rb"). These optically pumped metal vapors collide with the nuclei of the noble gas and hyperpolarize the noble gas through a phenomenon known as "spin-exchange". The "optical pumping" of the alkali metal vapor is produced by irradiating the alkali-metal vapor with circularly polarized light at the wavelength of the first principal resonance for the alkali metal (*e.g.*, 795 nm for Rb). Generally stated, the ground state atoms become excited, then subsequently decay back to the ground state. Under a modest magnetic field (10 Gauss), the cycling of atoms between the ground and excited states can yield nearly 100% polarization of the atoms in a few microseconds. This polarization is generally carried by the lone valence electron characteristics of the alkali metal. In the presence of non-zero nuclear spin noble gases, the alkali-metal vapor atoms can collide with the noble gas atoms in a manner in which the polarization of the valence electrons is transferred to the noble-gas nuclei through a mutual spin flip "spin-exchange".

After the spin-exchange has been completed, the hyperpolarized gas is separated from the alkali metal prior to introduction into a patient to form a non-toxic or sterile composition. Unfortunately, during and after collection, the hyperpolarized gas can deteriorate or decay (lose its hyperpolarized state) relatively quickly and therefore must be handled, collected, transported, and stored carefully. The " T_1 " decay constant associated with the hyperpolarized gas's longitudinal relaxation time is often used to describe the length of time it takes a gas sample to depolarize in a given container. The handling of the hyperpolarized gas is critical, because of the sensitivity of the hyperpolarized state to environmental and handling factors and the potential for undesirable decay of the gas from its hyperpolarized state prior to the planned end use, *i.e.*, delivery to a patient. Processing, transporting, and storing the

hyperpolarized gases -- as well as delivery of the gas to the patient or end user -- can expose the hyperpolarized gases to various relaxation mechanisms such as magnetic gradients, ambient and contact impurities, and the like.

Typically, hyperpolarized gases such as ^{129}Xe and ^3He have been collected in relatively pristine environments and transported in specialty glass containers such as rigid PyrexTM containers. However, to extract the majority of the gas from these rigid containers, complex gas extraction means are typically necessary. Hyperpolarized gas such as ^3He and ^{129}Xe has also been temporarily stored in single layer resilient Tedlar[®] and Teflon[®] bags. However, these containers have produced relatively short relaxation times.

One way of inhibiting the decay of the hyperpolarized state is presented in U. S. Patent No. 5,612,103 to Driehuys et al. entitled "Coatings for Production of Hyperpolarized Noble Gases." Generally stated, this patent describes the use of a modified polymer as a surface coating on physical systems (such as a PyrexTM container) which contact the hyperpolarized gas to inhibit the decaying effect of the surface of the collection chamber or storage unit.

However, there remains a need to address and reduce dominant and sub-dominant relaxation mechanisms and to decrease the complexity of physical systems required to deliver the hyperpolarized gas to the desired subject. Minimizing the effect of one or more of these factors can increase the life of the product by increasing the duration of the hyperpolarized state. Such an increase is desired so that the hyperpolarized product can retain sufficient polarization to allow effective imaging at delivery when transported over longer transport distances and/or stored for longer time periods from the initial polarization than has been viable previously.

Objects of Aspects and Summary of the Invention

In view of the foregoing, it is an object of an aspect of the present invention to process and collect hyperpolarized gas in improved resilient containers which are configured to inhibit depolarization in the collected polarized gas and to provide a longer T_1 for ^3He and ^{129}Xe than has been achieved in the past.

It is another object of an aspect of the present invention to provide an improved container which can be configured to act as both a transport container and a delivery mechanism

to reduce the amount of handling or physical interaction required to deliver the hyperpolarized gas to a subject.

It is a further object of an aspect of the present invention to provide an improved, relatively non-complex and economical container which can prolong the polarization life
5 of the gas in a container and reduce the amount of polarization lost during storage, transport, and delivery.

It is yet another object of an aspect of the invention to provide methods, surface materials and containers which will minimize the depolarizing effects of the hyperpolarized state of the gas (especially ^3He) attributed to one or more of paramagnetic
10 impurities, oxygen exposure, and surface relaxation.

It is an additional object of an aspect of the present invention to provide a method to determine the gas solubility in polymers or liquids with respect to hyperpolarized ^{129}Xe or ^3He .

These and other objects of aspects of the invention are satisfied by the present
15 invention which is directed to resilient containers which are configured to reduce surface or contact-induced depolarization by forming an inner contact surface of a first material (of a predetermined thickness) which acts to minimize the associated surface or contact depolarization. In particular, a first aspect of the invention is directed to a container for receiving a quantity of hyperpolarized gas. The container includes at least one wall
20 comprising inner and outer layers configured to define an enclosed chamber for holding a quantity of hyperpolarized gas. The inner layer has a predetermined thickness and an associated relaxivity value which inhibits contact-induced polarization loss of the hyperpolarized gas. The outer layer defines an oxygen shield overlying the inner layer. Of course, the two layers can be integrated into one, if the material chosen acts as a
25 polarization-friendly contact surface and is also resistant to the introduction of oxygen molecules into the chamber of the container. The container also includes a quantity of hyperpolarized noble gas and a port attached to the wall in fluid communication with the chamber for capturing and releasing the hyperpolarized gas therethrough.

Preferably, the container material(s) are selected to result in effective T_1 's of
30 greater than 6 hours for ^3He and greater than about 4 hours for ^{129}Xe due to the material alone. It is also preferred that the oxygen shield is configured to reduce the migration of oxygen into the container to less than about 5×10^{-6} amgt/min, and more

preferably to less than about 1×10^{-7} amgt/min. It is additionally preferred that the inner layer thickness ("L_{in}") is at least as thick as the polarization decay length scale ("L_p") which can be determined by the equation:

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$$L_p = \sqrt{T_p D_p}$$

where T_p is the noble gas nuclear spin relaxation time in the polymer and D_p is the noble gas diffusion coefficient in the polymer.

Advantageously, using a contact surface which has a thickness which is larger
 10 than the polarization decay length scale can minimize or even prevent the hyperpolarized gas from sampling the substrate (the material underlying the first layer). Indeed, for hyperpolarized gases which can have a high diffusion constant (such as ³He), surfaces with polymer coatings substantially thinner than the polarization decay length scale can have a more detrimental effect on the polarization
 15 than surfaces having no such coating at all. This is because the polarized gas can be retained within the underlying material and interact with the underlying or substrate material for a longer time, potentially causing more depolarization than if the thin coating is not present.

An additional aspect of the present invention is directed to a container with a
 20 wall formed of a single or multiple layers of materials which defines an expandable chamber. The inner surface of the wall is formed of a material which has a low relaxivity value for the (non-toxic) hyperpolarized fluid (hyperpolarized gas which is at least partially dissolved or liquefied) held therein. The wall is configured to define an oxygen shield to inhibit the migration of oxygen into the chamber. The T₁ of the
 25 hyperpolarized fluid held in the container is greater than about 6 hours.

In a preferred embodiment, the container of the instant invention is configured to receive hyperpolarized ³He and the inner layer is at least 16-20 microns thick. In another preferred embodiment, the container is an expandable polymer bag. Preferably, the polymer bag includes a metallized coating positioned over the polymer
 30 which suppresses the migration of oxygen into the polymer and ultimately into the polarized gas holding chamber. In another preferred embodiment, a third layer is added onto the metallized layer (opposite the polymer chamber) for puncture resistance. Advantageously, the captured hyperpolarized gas can be delivered to the

inhalation interface of a subject by exerting pressure on the bag to collapse the bag and cause the gases to exit the chamber. This, in turn, removes the requirement for a supplemental delivery mechanism. It is additionally preferred that the container use seals such as O-rings which are substantially free of paramagnetic impurities. The proximate position of the seal with the hyperpolarized gas can make this component a dominant factor in the depolarization of the gas. Accordingly, it is preferred that the seals or O-rings be formed from substantially pure polyolefins such as polyethylene, polypropylene, copolymers and blends thereof. Of course, fillers which are friendly to hyperpolarization can be used (such as substantially pure carbon black and the like). Alternatively, the O-ring or seal can be coated with a surface material such as LDPE or deuterated HDPE or other low-relaxivity and property material and/or also preferably materials which have a low permeability for the hyperpolarized gas held in the chamber. In addition, the container can be configured such that once the gas is captured in the container to isolate a major portion of the hyperpolarized gas in the container away from potentially depolarizing components (such as fittings, valves, and the like) during transport and/or storage.

Similar to the preferred embodiment discussed above, another aspect of the present invention is a multi-layer resilient container for holding hyperpolarized gas. The container comprises a first layer of a first material configured to define an expandable chamber to hold a quantity of hyperpolarized gas therein. Preferably, the first layer has a predetermined thickness sufficient to inhibit surface or contact depolarization of the hyperpolarized gas held therein wherein the first layer material has a relaxivity value "Y". It is also preferred that the relaxivity value "Y" is less than about 0.0012cm/min for ^3He and less than about 0.01cm/min for ^{129}Xe . The container also includes a second layer of a second material positioned such that the first layer is between the second layer and the chamber, wherein the first and second layers are concurrently responsive to the application of pressure and one or both of the first and second layers acts as an oxygen shield to suppress oxygen permeability into the chamber.

Additional layers of materials can be positioned intermediate the first layer and the second layer. In one preferred embodiment, hyperpolarized gas has a low relaxivity value in the first layer material and the second layer preferably comprises a material which can shield the migration of the oxygen into the first layer. In another

preferred embodiment, the resilient container has a first layer formed of a metal film (which can act both as an oxygen shield and contact surface). In this embodiment, it is preferred that the relaxivity values are less than about .0023 cm/min and .0008 cm/min for ^{129}Xe and ^3He respectively. Stated differently, it is preferred that the hyperpolarized gas have a high mobility on the metal surface or small absorption energy relative to the metal contact surface such that the T_1 of the gas in the container approaches > 50% of its theoretical limit.

An additional aspect of the present invention is directed to a method for storing, transporting, and delivering hyperpolarized gas to a target. The method includes introducing a quantity of hyperpolarized gas into a multi-layer resilient container. The container has a wall comprising at least one material which provides an oxygen shield (*i.e.*, is resistant to the transport of oxygen into the container). Preferably, the container is expanded to capture the quantity of hyperpolarized gas. The container is sealed to contain the hyperpolarized gas therein. The container is transported to a site remote from the hyperpolarization site. The hyperpolarized gas is delivered to a target by compressing the chamber and thereby forcing the hyperpolarized gas to exit therefrom. Preferably, in order to maintain the hyperpolarized state, the container is substantially continuously, from the time of polarization to the delivery, shielded and/or exposed to a proximately maintained homogeneous magnetic field to protect it from undesired external magnetic fields and/or field gradients. It is further preferred that the container be configured to be re-useable (after re-sterilization) to ship additional quantities of hyperpolarized gases.

Similarly, a further aspect of the present invention is configuring single or multi-layer resilient bags as described above with a capillary stem. The capillary stem is configured to restrict the flow of the hyperpolarized gas from the container when the valve is closed. The capillary stem is preferably positioned intermediate the container port and a valve member and, as such, forms a portion of the hyperpolarized gas (or liquid) entrance and exit path. The capillary stem is preferably configured with an inner passage which is sized and configured to inhibit the flow of the hyperpolarized gas and includes a gas contact surface formed of a polarization-friendly material. The capillary stem is preferably operably associated with a valve for the resilient container to allow the gas to be releasably captured and yet protected from any potentially depolarizing affect of the gas when the valve is closed.

Similarly, a further aspect of the present invention is configuring single or multi-layer resilient bags as described above with an isolation means for directing the gas or fluid away from the bag port during transport and storage. As such the isolation means inhibits a major portion of the hyperpolarized gas or fluid from
5 contacting selected components (fittings, valves, O-rings) operably associated with the bag. In a preferred embodiment, the isolation means is provided by a clamp positioned to compress the portion of the bag proximate to the port to inhibit the movement of gas thereabove.

An additional aspect of the present invention is a method for preparing an
10 expandable storage container for receiving a quantity of hyperpolarized gas. The method includes providing a quantity of substantially pure purge gas such as nitrogen or helium (preferably Grade 5 or better) into the hyperpolarized gas container and expanding the hyperpolarized gas container. The container is then collapsed to remove the purge gas. The oxygen in the container walls is outgassed by decreasing
15 the oxygen partial pressure in the container, thereby causing a substantial amount of the oxygen trapped in the walls of the container to migrate into the chamber of the container in the gas phase where it can be removed. Preferably, after the outgassing step, the container is filled with a quantity of storage gas such as nitrogen (again, preferably Grade 5 or better). The gas is introduced into the container at a pressure
20 which reduces the pressure differential across the walls of the container to inhibit further outgassing of the container. Preferably, the container is then stored for future use (the use being spaced apart in time from the point of preconditioning). The storage nitrogen and outgassed oxygen are removed from the container before filling with a quantity of hyperpolarized gas. Preferably, after removal from storage and
25 prior to use, the nitrogen is removed by evacuating the container before filling with a quantity of hyperpolarized gas.

Another aspect of the present invention is directed to a method for determining the hyperpolarized gas (^{129}Xe or ^3He) solubility in a (unknown) polymer or a particular fluid. The method includes introducing a first quantity of hyperpolarized
30 noble gas into a container having a known free volume and measuring a first relaxation time of the hyperpolarized gas in the container. A substantially clean sample of desired material is positioned into the container and a second quantity of hyperpolarized noble gas is introduced into the container. A second relaxation time of

the second hyperpolarized gas is measured in the container with the sample material. The gas solubility of the sample is determined based on the difference between the two measured relaxation times. The material sample can be a structurally rigid sample (geometrically fixed) with a known geometric surface area/volume which is
5 inserted into the free volume of the chamber or container. Alternatively, the material sample can be a liquid which partially fills chamber.

Advantageously, the methods and containers of the present invention can improve the relaxation time (lengthen T_1) of the hyperpolarized gas or liquid or combinations of same held therein. The containers are configured such that the
10 surface contacting the hyperpolarized gas (the hyperpolarized gas contact surface) has a minimum depth or thickness of a low-relaxivity value material relative to the hyperpolarized noble gas. Further, the containers are configured to also inhibit oxygen migration into the gas chamber of the container. In addition, the container itself can define the contact surface by forming the container out of a resilient material
15 such as a metallic or polymer bag. Preferably, the bags are configured to inhibit the hyperpolarized gas from contacting potentially depolarizing components associated with the bag during transport or storage.

The container is preferably a multi-layer container wherein each material layer provides one or more of strength, puncture resistance, and oxygen resistance to the
20 container. Further, at least the inner surface is configured to provide a polarization friendly contact surface. This resilient configuration provides a relatively non-complex container and increased T_1 's and can conveniently be re-used. The gas contact surface is preferably formed of either a polymer or a high purity metal.

Additionally, the resilient or collapsible containers can be used to deliver the
25 gas into the patient interface without the need for additional delivery vehicles/equipment. This can reduce the exposure, handling, and physical manipulation of the hyperpolarized gas which, in turn, can increase the polarization life of the hyperpolarized gas. Resilient containers with high purity contact surfaces can be extremely advantageous for both ^{129}Xe and ^3He as well as other hyperpolarized gases;
30 however, the expandable (polymer) container and coatings/layers are especially suited for hyperpolarized ^3He . Further, the instant invention preferably positions the container with the hyperpolarized gas in a homogenous magnetic field within a

shipping container to shield the gas from stray magnetic fields, especially deleterious oscillating fields which can easily dominate other relaxation mechanisms.

Additionally, the present invention can be used to determine the gas solubility in polymers or fluids which in the past has proven difficult and sometimes inaccurate,
 5 especially for helium.

Advantageously, one aspect of the present invention now provides a way to model the predictive behavior of surface materials and is particularly suited to determining the relaxation properties of polymers used as contact materials in physical systems used to collect, process, or transport hyperpolarized gases. For example, the present invention
 10 successfully provides relaxation properties of various materials (measured and/or calculated). These relaxation values can be used to determine the relaxation time (T_1) of hyperpolarized gas in containers corresponding to the solubility of the gas, the surface area of the contact material, and the free gas volume in the container. This information can be advantageously used to extend the hyperpolarized life of the gas in containers over
 15 those which were previously achievable in high-volume production systems.

According to an aspect of the present invention, there is provided a method of preparing an expandable storage container for receiving a quantity of hyperpolarized gas, comprising the steps of:

providing a quantity of purge gas into the hyperpolarized gas container;
 20 expanding the hyperpolarized gas container by directing a quantity of purge gas therein;

collapsing the hyperpolarized gas container by removing purge gas therefrom;

outgassing the oxygen in the container walls by decreasing the oxygen
 25 partial pressure in the container thereby causing a substantial amount of the oxygen trapped in the walls of the container to migrate into the chamber of the container in the gas phase;

filling a container with a quantity of storage nitrogen after said outgassing step to a pressure which minimizes the pressure differential across the walls of the
 30 container to minimize further outgassing of the container;

storing the container for future use; and

removing the storage nitrogen and outgassed oxygen from the container before filling with a quantity of hyperpolarized gas.

According to another aspect of the present invention, there is provided a method of determining the hyperpolarized gas solubility in a material such as a polymer or fluid, comprising the steps of:

- 5 introducing a first quantity of hyperpolarized gas into a container;
- measuring a first longitudinal spin relaxation rate of the hyperpolarized gas in the container;
- positioning a sample of a desired material in the container;
- introducing a second quantity of the hyperpolarized noble gas into the
- 10 container;
- measuring a second longitudinal spin relaxation rate of the hyperpolarized gas in the container; and
- determining the gas solubility of the sample based on the difference between the first and second relaxation rates.
- 15 The foregoing and other objects of aspects of the present invention are explained in detail herein.

Brief Description of the Drawings

Figure 1 is a schematic diagram of a spin-down station used to measure relaxation times according to one aspect of the present invention.

20 **Figure 2** is a graph showing the polarization level of a gas associated with the distance x the gas moves into a polymer.

Figure 3 is a graph showing the results of the standardized relaxation times plotted against solubility (measured and theoretical) for various materials (T_1^{cc} representing the relaxation time for ^{129}Xe hyperpolarized gas in a one cubic centimeter

25 sphere).

Figure 4 is a graph similar to Figure 3 showing the results of standardized relaxation times for ^3He .

Figure 5 is a detailed chart of experimental material values for Xenon and Helium.

Figure 6 is a detailed chart of predicted material values for Xenon and Helium.

Figure 7 is a perspective view of a hyperpolarized gas container according to one embodiment of the present invention in a deflated state.

5 Figure 8 is a perspective view of the container of Figure 7, shown in an inflated state.

Figure 9 is a sectional view of an alternate embodiment of a container according to the present invention.

10 Figure 10 is an enlarged partial cutaway section view of the container wall according to another embodiment of the present invention.

Figure 11 is an enlarged partial cutaway section view of an additional embodiment of a container wall according to the present invention.

Figure 12 is an enlarged partial cutaway section view of yet another embodiment of a container wall according to the present invention.

15 Figure 13 is a perspective view of a preferred embodiment of a container with a seal according to the present invention.

Figure 14 illustrates the container of Figure 13 with an alternative external seal according to an additional embodiment of the present invention.

20 Figure 15 illustrates another container with an alternative seal arrangement according to another embodiment of the present invention.

Figure 15A is an exploded view of the container shown in Figure 15.

Figure 16 is a side perspective view of a shielded shipping receptacle configured to receive the container according to one embodiment of the present invention.

25 Figure 17 is a schematic illustration of the resilient container of Figure 13 shown attached to a user interface adapted to receive the container for delivering the hyperpolarized gas therein to the user according to one embodiment of the present invention.

30 Figure 18 shows the container of Figure 17 in a deflated condition after forces on the container cause the hyperpolarized gas to exit the container and enter the target.

Figure 19 is a schematic illustration of the container of Figure 15 shown attached to a user interface according to one embodiment of the present invention.

Figure 20 is a block diagram of a method for determining gas solubility in a polymer according to one embodiment of the present invention.

Figures 21A-21C are perspective views of an alternative embodiment of a container with a port isolation means according to the present invention.

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Detailed Description of the Preferred Embodiments

The present invention will now be described more fully hereinafter with reference to the accompanying figures, in which preferred embodiments of the invention are shown. This invention may, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth herein. Like numbers refer to like elements throughout. Layers and regions may be exaggerated for clarity. For ease of discussion, the term "hyperpolarized gas" will be used to describe a hyperpolarized gas alone, or a hyperpolarized gas which contacts or combines with one or more other components whether gaseous, liquid, or solid. Thus, the hyperpolarized gas described herein can be a hyperpolarized gas composition/ mixture (non-toxic such that it is suitable for *in vivo* introduction) such that the hyperpolarized noble gas can be combined with other noble gases and/or other inert or active components. Also, as used herein, the term "hyperpolarized gas" can include a product where the hyperpolarized gas is dissolved into another liquid (such as a carrier) or processed such that it transforms into a substantially liquid state, *i.e.*, "a liquid polarized gas". Thus, although the term includes the word "gas", this word is used to name and descriptively track the gas produced via a hyperpolarizer to obtain a polarized "gas" product. In summary, as used herein, the term "gas" has been used in certain places to descriptively indicate a hyperpolarized noble gas which can include one or more components and which may be present in one or more physical forms.

Preferred hyperpolarized noble gases (either alone or in combination) are listed in Table I. This list is intended to be illustrative and non-limiting.

TABLE I

Hyperpolarizable Noble Gases		
Isotope	Natural Abundance (%)	Nuclear Spin
^3He	$\sim 10^{-6}$	1/2
^{21}Ne	0.27	3/2
^{83}Kr	11.5	9/2
^{129}Xe	26.4	1/2
^{131}Xe	21.2	3/2

Hyperpolarization

5 Various techniques have been employed to polarize, accumulate and capture polarized gases. For example, U.S. Patent No. 5,642,625 to Cates et al. describes a high volume hyperpolarizer for spin polarized noble gas and U.S. Patent No. 5,809,801 to Cates et al. describes a cryogenic accumulator for spin-polarized ^{129}Xe .

10 As used herein, the terms "hyperpolarize" and "polarize" are used interchangeably and mean to artificially enhance the polarization of certain noble gas nuclei over the natural or equilibrium levels. Such an increase is desirable because it allows stronger imaging signals corresponding to better MRI images of the substance and a targeted area of the body. As is known by those of skill
15 in the art, hyperpolarization can be induced by spin-exchange with an optically pumped alkali-metal vapor or alternatively by metastability exchange. See U.S. Patent No. 5,545,396 to Albert et al. The alkali metals capable of acting as spin exchange partners in optically pumped systems include any of the alkali metals. Preferred alkali metals for this hyperpolarization technique include Sodium-23,
20 Potassium-39, Rubidium-85, Rubidium-87, and Cesium-133. Alkali metal isotopes, and their relative abundance and nuclear spins are listed in Table II, below. This list is intended to be illustrative and non-limiting.

TABLE II

Alkali Metals Capable of Spin Exchange		
Isotope	Natural Abundance (%)	Nuclear Spin
^{23}Na	100	$3/2$
^{39}K	93.3	$3/2$
^{85}Rb	72.2	$5/2$
^{87}Rb	27.8	$3/2$
^{133}Cs	100	$7/2$

Alternatively, the noble gas may be hyperpolarized using metastability exchange. (See e.g., Scheerer, L. D., *Phys. Rev.*, 180:83 (1969); Laloe, F. et al., AIP ConfProx #131 (Workshop on Polarized ^3He Beams and Targets) (1984)). The technique of metastability exchange involves direct optical pumping of, for example, ^3He without need for an alkali metal intermediary. The method of metastability exchange usually involves the excitation of ground state ^3He atoms (1^1S_0) to a metastable state (2^3S_1) by weak radio frequency discharge. The 2^3S_1 atoms are then optically pumped using circularly polarized light having a wavelength of $1.08\ \mu\text{m}$ in the case of ^3He . The light drives transitions up to the 2^3P states, producing high polarizations in the metastable state to which the 2^3S atoms then decay. The polarization of the 2^3S_1 states is rapidly transferred to the ground state through metastability exchange collisions between metastable and ground state atoms.

Metastability exchange optical pumping will work in the same low magnetic fields in which spin exchange pumping works. Similar polarizations are achievable, but generally at lower pressures, e.g., about 0-10 Torr.

Generally described, for spin-exchange optically pumped systems, a gas mixture is introduced into the hyperpolarizer apparatus upstream of the polarization chamber. Most xenon gas mixtures include a buffer gas as well as a lean amount of the gas targeted for hyperpolarization and is preferably produced in a continuous flow system. For example, for producing hyperpolarized ^{129}Xe , the pre-mixed gas mixture is typically about 85-89% He, about 5% or less ^{129}Xe , and about 10% N_2 . In contrast,

for producing hyperpolarized ^3He , a mixture of 99.25% ^3He and 0.75% N_2 is pressurized to 8 atm (810KPa) and heated and exposed to the optical laser light source in a batch mode system. In any event, once the hyperpolarized gas exits the pumping chamber it is directed to a collection or accumulation container.

5 A 5-20 Gauss (0.5-2mT) alignment field is typically provided for the optical pumping of Rb for both ^{129}Xe and ^3He polarization. The hyperpolarized gas is collected (as well as stored, transported, and preferably delivered) in the presence of a magnetic field. It is preferred for solid (frozen) ^{129}Xe that the field be on the order of at least 500 Gauss (0.05T), and typically about 2 kilo Gauss (0.2T), although higher
10 fields can be used. Lower fields can potentially undesirably increase the relaxation rate or decrease the relaxation time of the polarized gas. As regards ^3He , the magnetic field is preferably on the order of at least 5-30 gauss (0.5-3mT) although, again, higher (homogeneous) fields can be used. The magnetic field can be provided by electrical or permanent magnets. In one embodiment, the magnetic field is provided
15 by a plurality of permanent magnets positioned about a magnetic yoke which is positioned adjacent the collected hyperpolarized gas. Preferably, the magnetic field is homogeneously maintained around the hyperpolarized gas to minimize field induced degradation.

20 Polarized Gas Relaxation Processes

Once hyperpolarized, there is a theoretical upper limit on the relaxation time (T_1) of the polarized gas based on the collisional relaxation explained by fundamental physics, i.e., the time it takes for a given sample to decay or depolarize due to collisions of the hyperpolarized gas atoms with each other absent other depolarizing
25 factors. For example, ^3He atoms relax through a dipole-dipole interaction during ^3He - ^3He collisions, while ^{129}Xe atoms relax through N-I spin rotation interaction (where N is the molecular angular momentum and I designates nuclear spin rotation) during ^{129}Xe - ^{129}Xe collisions. Stated differently, the angular momentum change associated with flipping a nuclear spin over is conserved by being taken up by the rotational
30 angular momentum of the colliding atoms. In any event, because both processes occur during noble gas-noble gas collisions, both resulting relaxation rates are directly proportional to gas pressure (T_1 is inversely proportional to pressure). At one atmosphere, the theoretical relaxation time (T_1) of ^3He is about 744-760 hours, while for ^{129}Xe the corresponding relaxation time is about 56 hours. See Newbury et al.,

"Gaseous ^3He - ^3He Magnetic Dipolar Spin Relaxation," 48 Phys. Rev. A., No. 6, p.
 4411 (1993); Hunt et al., Nuclear Magnetic Resonance of ^{129}Xe in Natural Xenon, 130
 Phys. Rev. p. 2302 (1963). Unfortunately, other relaxation processes prevent the
 realization of these theoretical relaxation times. For example, the collisions of
 5 gaseous ^{129}Xe and ^3He with container walls ("surface relaxation") have historically
 dominated most relaxation processes. For ^3He , most of the known longer relaxation
 times have been achieved in special glass containers having a low permeability to
 helium. In the past, a fundamental understanding of surface relaxation mechanisms
 has been elusive which has made the predictability of the associated T_1 difficult.

10 U.S. Patent No. 5,612,103 to Driehuys et al. describes using coatings to inhibit
 the surface-induced nuclear spin relaxation of hyperpolarized noble gases, especially
 ^{129}Xe .

Driehuys et al. recognized that nuclear spin relaxation of ^{129}Xe on a
 polydimethoxysiloxane ("PDMS") surface coating can be dominated by dipolar
 15 coupling of the ^{129}Xe nuclear spin to the protons in the polymer matrix. Thus, it was
 demonstrated that paramagnetic contaminants (such as the presence of paramagnetic
 molecules like oxygen) were not the dominant relaxation mechanism in that system
 because the inter-nuclear dipole-dipole relaxation was found to dominate the system
 under investigation. This was because ^{129}Xe substantially dissolved into the particular
 20 polymer matrix (PDMS) under investigation. See Bastiaan Driehuys et al., "Surface
 Relaxation Mechanisms of Laser-Polarized ^{129}Xe ," 74 Phys. Rev. Lett., No. 24, pp.
 4943-4946 (1995).

One aspect of the instant invention now provides a more detailed
 understanding of noble gas depolarization on polymer surfaces. Indeed, as will be
 25 explained further below, noble gas solubility in large numbers of polymer systems
 (not just PDMS) can cause inter-nuclear dipole-dipole relaxation to dominate the
 polarization decay rate. Notably, this insight now indicates that polymers can be
 especially effective for the suppression of ^3He relaxation. In addition, a predictive
 explanation of noble gas relaxation on polymer surfaces is discussed below.

30 Advantageously, it is now possible to calculate and measure the relaxation properties
 of various materials. This information can be advantageously used with other
 parameters such as free gas volume and surface area of containers to provide more
 effective and advantageous surface configurations and material characteristics which

can facilitate, preserve, and further improve the polarization life of the noble gas. This is especially useful in providing containers which can yield reliable, repeatable, and predictable high-volume polarization production and maintenance which in the past has been difficult to achieve outside the pristine conditions of a small production
 5 laboratory.

Generally stated, magnetic interactions can alter the time constant of relaxation, referred to as the longitudinal relaxation time (T_1), and typically occur when different atoms encounter one another. In the case of hyperpolarized noble gases held in containers, the nuclear magnetic moments of the gas atoms interact with
 10 the surface materials to return the gas to the equilibrium or non-hyperpolarized state. The strength of the magnetic moment can be a determinative factor in determining the relaxation rate associated with the surface material. Since different atoms and molecules have different magnetic moments, relaxation rates are material-specific.

15 Relaxivity of Materials

In order to compare the characteristic information of certain materials concerning their respective relaxing effects on hyperpolarized noble gases, the term "relaxivity" is used. As used herein, the term "relaxivity" (" γ ") is used to describe a material property associated with the rate of depolarization (" $1/T_1$ ") of the
 20 hyperpolarized gas sample. For a container having a chamber volume " V_c " capable of holding a quantity of hyperpolarized gas and for a material sample with a surface area " A " in the container chamber, each time a polarized gas atom contacts the container surface, it has a probability (" p ") of depolarizing. The rate of depolarization ($1/T_1$) of this gas sample in the chamber can then be described by p times the rate at which gas
 25 atoms collide with the surface (" R ").

$$\frac{1}{T_1} = Rp \quad (2.1)$$

The average surface collision rate (R) per gas atom is known from statistical mechanics, R. Reif, *Fundamentals of Statistical and Thermal Physics*, McGraw-Hill,
 30 Ch. 12-14, pp. 461-493 (1965):

$$R = \frac{vA}{4V} \quad (2.2)$$

In this equation, " v " is the mean thermal velocity of the gas atoms. For the case of a one cubic centimeter ("1 cc") sphere of ^{129}Xe the area is $A=4\pi r^2$ and the volume is $V=4\pi r^3/3$. Thus, for $v=154$ m/s, equation (2.2) yields a collision rate $R=800$ s $^{-1}$. In
 5 other words, each atom of Xe is contacting the surface of the sphere 800 times in 1 second. Therefore, according to equation (2.1) long T_1 times must have a minute probability for depolarization during each collision ($p \ll 1$). Substituting equation (2.2) back into equation (2.1) yields:

$$\frac{1}{T_1} = \frac{Avp}{4V} \quad (2.3)$$

10

Since measurements for this study are performed at room temperature, " v " will not vary. Therefore, the relaxivity term, (" Y ") which is defined as $Y=vp/4$, results in:

$$\frac{1}{T_1} = \frac{A}{V} Y \quad (2.4)$$

15 Thus, relaxivity (" Y ") is a material property that can describe the depolarizing effect that a specific material has on a hyperpolarized gas sample.

When considering hyperpolarized gas containers, it is important to notice the relationship between the $1/T_1$ and A/V terms in Equation 2.4. Thus, the ratio " A/V " for a sphere with a radius " r ", the ratio reduces to $3/r$. Therefore, a one liter sphere
 20 (1000 cc, $r=6.2$ cm) has a T_1 that is 10 times longer than a sphere with a one cubic centimeter volume (1cc, $r=.62$ cm) made of the same material. Therefore, preferably, in order to improve the T_1 of hyperpolarized gas in the containers, the containers are configured and sized to decrease the value of the ratio A/V -- i.e., to increase the volume relative to the area of the container, as will be discussed further below.

25

Determining Relaxivity

Equation 2.4 can be used to calculate relaxivity of the gas if surface relaxation is the only (dominant) depolarizing effect at work. In the case of practical material studies, this is not the case. The surfaces of the test chamber, the chamber seal, and

other impurities also contribute to the relaxation of the gas. However, by using the relaxation time differences between hyperpolarized gas in an empty test chamber and the hyperpolarized gas in the chamber containing a material sample positioned to contact the hyperpolarized gas, the characteristic relaxivity of the material can be
 5 determined.

Note that the relaxation rates are additive in the following form:

$$\frac{1}{T_1} = \frac{1}{T_1^a} + \frac{1}{T_1^b} + \frac{1}{T_1^c} \dots \quad (2.5)$$

In general form, T_1^a can represent the relaxation effect of the test chamber surface, T_1^b can represent the effect of the hyperpolarized gas atoms colliding with one another, and so on. Assuming that surface relaxation is the dominant relaxation
 10 effect, the relaxation rate can be described by adding the surface effects of the material sample and the test chamber.

$$\frac{1}{T_1} = \frac{A_m \gamma_m}{V} + \frac{A_c \gamma_c}{V} \quad (2.6)$$

15 where A_m and γ_m describes the area and relaxivity respectively of the material sample and A_c and γ_c correspond to the area and relaxivity of the container or chamber. "V" is the free gas volume in the chamber. In this case, $V = V_c - V_m$, where "V_c" is the volume of the chamber and "V_m" is the volume of the container occupied by the material sample. In relaxivity studies for new materials (where the material sample is
 20 small) the free volume "V" can be reasonably approximated as equal to V_c, i.e., $V = V_c$. Substituting back into (2.6):

$$\frac{1}{T_1} = \frac{A_m \gamma_m}{V_c} + \frac{A_c \gamma_c}{V_c} \quad (2.7)$$

Note that for a chamber without a material sample, this equation reduces to:
 25

$$\frac{1}{T_{lc}} = \frac{A_c \gamma_c}{V_c} \quad (2.8)$$

where T_{lc} is the characteristic relaxation rate of the container or empty chamber.

Substituting (2.8) into (2.7) yields:

$$\frac{1}{T_l} = \frac{A_m \gamma_m}{V_c} + \frac{1}{T_{lc}} \quad (2.9)$$

- 5 Solving equation (2.9) gives an expression for the relaxivity γ_m associated with a specific material sample with a measured T_l in a chamber with known volume and observed T_{lc} :

$$\gamma_m = \frac{V_c}{A_m} \left(\frac{1}{T_l} - \frac{1}{T_{lc}} \right) \quad (2.10)$$

- 10 The relaxivity of a given material can easily be translated back into a more intuitive characteristic relaxation time. One method of comparison, in keeping with past surface relaxation rate studies, is to describe the relaxation rate as if there were a 1 cc spherical cell made of the material in question. Knowing the volume and surface area of such a cell ($A=4\pi r^2$, $V=4\pi r^3/3$, $r=.62$ cm) and substituting back into (2.8):

15

$$T_l^{cc} = \frac{0.207 \text{ cm}}{\gamma_c} \quad (2.11)$$

Again, this container geometry is for illustration as it standardizes the relaxation term for comparison with past data. For reference, observed T_l values from ^{129}Xe studies in the past showed ultra clean Pyrex with a Rb monolayer surface to have an associated $T_l^{cc} = 30$ minutes.

20

Experimental Determination of Relaxivity

The hyperpolarized gas samples were used in a materials testing center known as the Spin Down Station. This apparatus was constructed to test various material samples in a controlled environment. The system consists of a materials testing

chamber, a Pulse-NMR Spectrometer, and a LabView user interface. The flexible system allows various chambers or bags to be cleaned and filled with polarized ^{129}Xe or ^3He . The Pulse-NMR system then charts the deterioration of signal from these containers over time.

5

Equipment Layout

Figure 1 is a schematic diagram of the Spin Down Station. This apparatus consists of a Helmholtz pair generating a stable Helmholtz magnetic field 151 around the glass test chamber labeled the Spin Down Chamber 152. The signal response frequency (f) is proportional to the applied magnetic field (B_0) expressed by the equation $f = \gamma B_0 / 2\pi$. This proportionality constant is known as the gyromagnetic ratio ($\gamma_{\text{He}} = 7400 \text{ s}^{-1}\text{G}^{-1}$, $\gamma_{\text{Xe}} = 26700 \text{ s}^{-1}\text{G}^{-1}$). If the applied magnetic field remains constant, the coil must be tuned to switch between the two gases. As an alternative to retuning, the field strength was adjusted to result in the same frequency response for both gases. A current of 1.0 A (7 G field) for ^3He and 2.5 A (21 G field) for ^{129}Xe was applied to the Helmholtz pair noted by the Helmholtz field shown in Figure 1.

In the center of Helmholtz field 151 rested one of the two spin down chambers 152 used in these tests. Both chambers were valved to evacuate (base pressure ~30 milliTorr) and fill the chamber with hyperpolarized gas. Each chamber could be opened to insert polymer samples (typically 10mmx20mmx1mm). As shown, the NMR coil 153 rests beneath the chamber in the center of the Helmholtz field 151.

The first spin down chamber was made of PyrexTM coated with dimethyl dichlorosilane (DMDCS) and used a TeflonTM coated rubber O-ring as the vacuum seal. This chamber had a 110 minute characteristic $T_{1\rho}$ suitable for observing the surface relaxation effects of various polymer samples 154. Notably, after numerous tests, the $T_{1\rho}$ would often decrease. A thorough cleaning with high-purity ethanol restored the chamber to the baseline value. Unfortunately, the $T_{1\rho}$ for the PyrexTM chamber with ^3He was not long enough to distinguish good from bad materials for ^3He . Tests of various glasses in the PyrexTM spin down chamber showed that a chamber made of 1724 aluminosilicate glass would have a sufficiently long $T_{1\rho}$ for ^3He .

The 1724 ^3He chamber was constructed with a ground seal requiring ApiezonTM vacuum grease. The chamber had a characteristic $T_{1\rho}$ of 12 hours on

average. The Apiezon™ grease used to seal both the chamber and the entry valve caused the chamber T_{1c} to fluctuate significantly more than the Pyrex™ chamber. To restore the chamber to baseline T_{1c} , the grease was removed by cleaning the chamber with high-purity Hexane.

5

Testing Procedure

Using the Spin Down Station, seven polymer samples were tested using hyperpolarized ^{129}Xe or ^3He . These polymers were purchased from Goodfellow, Inc., Berwyn, Pennsylvania.

10

Material	Density	Thickness (mm) (T_1 study)	Thickness (mm) (Sorption study)
Polyamide (Nylon 6)	1.13	1	0.012*
Silicone Elastomer	1.1-1.3	1	1
High Density Polyethylene (HDPE)	0.95	1	0.01
Low Density Polyethylene (LDPE)	0.92	1	0.05
Polyimide (Kapton)	1.42	1	0.025
Polypropylene (PP)	0.9	1	0.01
Polytetrafluoroethylene (PTFE)	2.2	1	0.01

*Sample provided by DuPont.

The particular polymers were chosen to represent a wide range of solubilities to ^{129}Xe and ^3He gases. Each polymer sample was cleaned with ethanol and cut to a specific size and shape to provide a known volume and surface area of the polymer sample (normally $V=2\text{ cm}^3$, $SA=42.6\text{ cm}^2$) for each T_1 study.

15

The following steps were taken for each material measurement:

1. Clean the testing chamber
2. Polarize ^{129}Xe or ^3He
- 20 3. Perform a T_1 study to establish the chamber baseline (T_{1c})
4. Place polymer sample in chamber

5. Polarize ^{129}Xe or ^3He
6. Perform a T_1 study of the chamber containing polymer sample (T_{1s})
7. Use T_{1c} and T_{1s} to find relaxation rate due to specific polymer

5 The Polymer Sorption Model

The ability to measure and calculate relaxivity can result in an understanding of the physical characteristics that differentiate materials. An initial study of a wide range of materials confirmed conventional rigid containers of glass are much better than containers of materials containing paramagnetic or ferrous constituents such as stainless steel. Notably, this test also showed a wide range of relaxivities within different material groups. In particular, different polymer materials were observed across the relaxivity spectrum. Manufacturing concerns such as durability and reliability make polymer materials an excellent alternative to the glass storage containers that are typically used for hyperpolarized gases. Scientifically, substantially pure samples of these materials allow for relatively less complex models of surface relaxation.

For discussion purposes, assume there is a polymer container of hyperpolarized gas in a homogeneous magnetic field. Since polymers are permeable materials, some quantity of gas dissolves in the container walls. The only dominant relaxation mechanism in this system is that of the hyperpolarized gas atoms interacting with the protons or contaminants in the surface and bulk of the polymer container. Driehuys et al. demonstrated that relaxation of hyperpolarized ^{129}Xe in a specially coated glass sphere was dominated by the dipolar coupling between the protons in the surface and the ^{129}Xe nuclear spin. See Driehuys et al., "High-volume production of laser-polarized ^{129}Xe ," 69 App. Phys. Lett. (12), p. 1668 (1996). Since Xe-Xe collisions have a 56 hour T_1 and typical conventional material T_1 times are 2 hours or less, the relaxation rate of the free gas can be neglected. Gas dissolved in the polymer surface relaxes quickly (<1 second), so most of the hyperpolarized gas in the container is in the free gas form. Therefore, relaxation of this gas occurs through continual exchange between the free gas and the gas dissolved in the polymer. In material quantities, the rate of this gas exchange can be described by the "sorption parameters" - solubility ("S"), diffusion coefficient ("D"), and permeability ("P"). Permeability is the transmission of atoms or molecules through a polymer film. It

depends on chemical and physical structure of the material as well the structure and physical characteristics of the permeant molecules. Permeability can be defined as the product of solubility and the diffusion coefficient. ("P=SxD"). Solubility ("S") is a measure of how much permeant can be dissolved in a given material. Diffusion
 5 coefficient ("D") is a measure of the random mobility of the atoms in the polymer. The polymer sorption parameters can be used to characterize the relaxation of hyperpolarized gases in the presence of permeable surfaces.

Relaxation in the Presence of Polymer Surfaces

10 Magnetization ("M") is defined as the product of the gas polarization "P" and the gas number density "[G]", $M=[G]P$. The equation governing relaxation of magnetization in the presence of a surface diffusion

$$\frac{\partial}{\partial t} M(x,t) = D \frac{\partial^2}{\partial x^2} M(x,t) - \Gamma M(x,t) \quad (2.12)$$

15 where ("M(x,t)") is magnetization, ("D") is the diffusion coefficient of the gas in the surface material, and ("Γ") is the relaxation rate of the gas. See W. Happer et al., Hyp. Int. 38, pp. 435-470 (1987). As is customary, the solution is written as a product of spatial and time dependent components:

20 $M(x,t)=m(x)e^{-\Gamma t}$ (2.13)

where ("m(x)") is the spatial distribution of magnetization on the surface. Substituting (2.15) into (2.13) yields the spatial equation:

$$\frac{\partial^2}{\partial x^2} m(x) = \frac{1}{D} \left(\Gamma - \frac{1}{T_1} \right) m(x) \quad (2.14)$$

25 This differential equation describes the spatial distribution of magnetization in the presence of diffusion and relaxation. The distribution of magnetization in a one-dimensional chamber is shown in Figure 2.

The chamber is a gas volume of width "2a" bounded on each side by infinite polymer walls. The polarization of gas in this chamber has two specific regions of interest. In the free gas portion of the container, the polarization is relatively homogenous with respect to spatial variable x. In contrast, polarization drops exponentially with distance x into the polymer surface. This profile reflects a much faster relaxation rate inside the polymer as opposed to in free space.

Equation (2.14) can be used to solve for the spatial magnetization of the gas and polymer regions independently. For a gas phase with diffusion coefficient D_g and intrinsic relaxation rate $\Gamma_g=0$, equation (2.14) becomes:

10

$$\frac{\partial^2}{\partial x^2} m_g(x) = -\frac{1}{D_g T_1} m_g(x) \quad (\text{Region I}) \quad (2.15)$$

The first order symmetric solution to this equation is:

$$m_g(x) = A \cos(k_g x) \quad k_g^2 = \frac{1}{T_1 D_g} \quad (\text{Region I})$$

15 Similarly, the polymer region has diffusion coefficient " D_p " and relaxation rate Γ_p :

$$\frac{\partial^2}{\partial x^2} m_p(x) = \frac{1}{D_p} (\Gamma_p - \frac{1}{T_1}) m_p(x) \quad (\text{Region II}) \quad (2.16)$$

One simplifying assumption is that the relaxation rate in the polymer is much faster than the observed relaxation rate ($\Gamma_p \gg 1/T_1$). Thus neglecting $1/T_1$ term in (2.16) yields a solution of the form:

20

$$m_p(x) = B e^{-k_p(x-a)} \quad k_p^2 = \frac{\Gamma_p}{D_p} \quad (\text{Region II})$$

These two solutions in conjunction with the appropriate boundary conditions can be used to solve for the observed T_1 of the gas in the polymer chamber. The first

boundary condition ("BC") maintains continuity of polarization across the polymer gas boundary. Recalling that magnetization is the product of polarization and gas number density yields:

$$5 \quad BC_1 : \quad S m_g(a) = m_p(a)$$

where ("S") is defined as the ratio of gas number densities, or the Ostwald Solubility "S=N_p/N_g". The secondary boundary condition ("BC2") arises because the exchange of magnetization across the gas-polymer boundary is equal on both sides. This
 10 exchange, known as the magnetization current, is defined as J_m= - D∇m(x), yielding the boundary condition:

$$BC2: \quad D_g \frac{d}{dx} m_g(a) = D_p \frac{d}{dx} m_p(a)$$

Applying the boundary conditions to the solutions for magnetization in each of
 15 the two regions yields the following transcendental equation:

$$\tan k_g a = \frac{D_p k_p}{D_g k_g} S \quad (2.17)$$

This equation can be solved numerically, although a reasonable approximation is that k_ga << 1, so that tan k_ga ≈ k_ga. In physical terms, this implies that the
 20 magnetization is spatially uniform across the gas phase. It also considers only the slowest of multiple diffusion modes. In order for this assumption to be false, the relaxation rate at the walls would have to be fast compared to the time it takes for the gas to diffuse across the chamber. Diffusion times are typically a few seconds, while common T₁ values are several minutes. Applying this assumption yields:

$$k_g^2 = S \frac{D_p k_p}{D_g a} \quad (2.18)$$

25

Substituting in k_g and k_p from the solutions to (2.15) and (2.16) gives:

$$\frac{1}{T_1} = \frac{S}{a} \sqrt{\Gamma_p D_p} \quad (2.19)$$

The relaxation rate in the polymer terms can be rewritten in terms of $\Gamma_p = 1/T_{1p}$.

5 Solving for the relaxation time T_1 :

$$T_1 = \frac{a}{S} \sqrt{\frac{T_1^p}{D_p}} \quad (2.20)$$

This analysis can be extended into three dimensions, yielding:

$$T_1 = \frac{V_c}{A_p S} \sqrt{\frac{T_1^p}{D_p}} \quad (2.21)$$

10 where V_c is the internal volume of the chamber, A is the exposed surface area of the polymer and S is the solubility of the gas in the polymer.

The inverse relationship between T_1 and S is a key observation from this development. Because He solubilities are typically many orders of magnitude lower than corresponding Xe solubilities, T_1 times for ^3He should be significantly longer
15 than for ^{129}Xe . There is also an apparent inverse square root dependence on the diffusion coefficient D_p . However, the relaxation time in the polymer $1/T_p$ also depends on D_p , canceling the overall effect on T_1 . This leaves solubility as the dominant sorption characteristic in determining T_1 .

Despite canceling out of (2.21) the diffusion coefficient plays a significant role
20 in another quantity of interest, the length scale of the gas and polymer interaction. The exponential decay length scale of the polarization $L_p = 1/k_p$ is given by the solution to (2.16):

$$L_p = \sqrt{D_p T_1^p} \quad (2.22)$$

Importantly, this scale describes the depth into the polymer that the gas travels in the relaxation time period. In order to compare theoretical predictions to experimental data, it is preferred that material samples be at least several length scales thick. This ensures that the surface model developed here which assumes infinite polymer thickness is an accurate approximation of the diffusion process. For reference, LDPE has a diffusion constant of $6.90 \times 10^{-6} \text{ cm}^2/\text{s}$ for helium gas and hyperpolarized ^3He has a relaxation time in the polymer of about .601s ($T_1^P=0.601$ seconds). The resulting length scale is about $20 \text{ }\mu\text{m}$, many times smaller than the 1mm polymer samples used in the study described herein.

Predicting T_1 Values Using Sorption Model

Using equation (2.21) to predict T_1 values for hyperpolarized gases in the presence of various polymer surfaces requires knowledge of the test environment (V_c, A_p), as well as parameters linking the specific gas and polymer (T_1^P , S and D).

Unfortunately, the solubility and diffusion data linking gas and polymers is scattered and sometimes nonexistent. On the other hand, the test environment is typically known. Advantageously, this data can be used to calculate the T_1^P .

As discussed earlier, the relaxation mechanism that dominates hyperpolarized gas relaxation in polymers is the interaction with the nuclear magnetic moments of the hydrogen nuclei (in hydrogen based polymers). Generally stated, in the absence of paramagnetic contaminants, the ^1H nuclei are the only source of magnetic dipoles to cause relaxation. Based on this interaction, Huang and Freed developed an expression for the relaxation rate of spin 1/2 gas diffusing through a polymer matrix. See L.P. Hwang et al., "Dynamic effects of pair correlation functions on spin relaxation by translational diffusion in liquids," 63 J. Chem. Phys. No. 9, pp. 4017-4025 (1975); J.H. Freed, "Dynamic effects of pair correlation functions on spin relaxation by translational diffusion in liquids. II. Finite jumps and independent T_1 processes," 68 J. Chem. Phys. Vol. 9, pp. 4034-4037 (1978); and E.J. Cain et al., "Nuclear Spin Relation Mechanisms and Mobility of Gases in Polymers," 94 J. Phys. Chem. No. 5, pp. 2128-2135 (1990). This results in the following expression in a low magnetic field B regime ($B < 1000 \text{ Gauss}$) (0.1 T).

$$T_1^p = \frac{405}{32\pi} \frac{D_p^b}{s(s+1)\gamma_g^2\gamma_H^2 h^2 N_a [^1H]} \quad (2.23)$$

In this formula, γ_g is the gyromagnetic ratio of the noble gas, γ_H is the gyromagnetic ratio of the protons, s is the proton spin number (1/2), N_a is Avogadro's number, $[^1H]$ is the molar density of protons in the matrix, and b is the distance of closest approach of the noble gas to a proton. The dipole interaction equations have an inverse square dependence on the gyromagnetic ratios γ_g and γ_H . As noted before, substituting this form into Equation (2.21) cancels D_p from the relaxation expression. This leaves only solubility (S) to effect the T_1 in various polymers. The other significant factor in (2.23) is the $[^1H]^{-1}$ dependence. As such, since protons in the polymer are the dominant relaxation mechanism, high concentrations will adversely affect T_1^p .

Implementing this expression for T_1^p requires the appropriate physical parameters in CGS units. Table 2.1 shows an example of the approximate values used for this calculation performed for relaxation of ^{129}Xe in low-density polyethylene (LDPE):

γ_g ($\text{G}^{-1}\text{s}^{-1}$)	=	7.40e03
γ_H ($\text{G}^{-1}\text{s}^{-1}$)	=	2.68e04
h (erg s)	=	6.63e-27
$[^1H]$ (mol/L)	=	131.43
b (cm)	=	2.40e-08
D_g (cm^2s^{-1})	=	6.90e-08
T_1^p (s)	=	0.0653

*One of few available literature values (Polymer Handbook)

Table 2.1: Sample Data for T_1^p of ^{129}Xe in LDPE

Confirmation of Predictive Model

The development of the sorption based relaxation model along with the experimental apparatus to test relaxivity allows the comparison of a theoretical model of surface relaxation with experimental results. Confirmation of this model enables quantitative predictions of surface relaxation for selecting appropriate and preferred materials to contact hyperpolarized gases. The spin down station was used to measure

the relaxation effects of 7 different polymers on hyperpolarized ^{129}Xe and ^3He . In order to compare this experimental data with the theoretical, solubility of both gases in each polymer was measured. These sorption measurements are described below as well as a discussion of results from the ^{129}Xe and ^3He polymer studies.

5

Solubility Measurements

Solubility ("S") is the only remaining unknown in the formula to predict T_1 of hyperpolarized gases in polymers (2.21). The equation is restated here for reference:

$$T_1 = \frac{V_c}{A_p S} \sqrt{\frac{T_1^p}{D_p}}$$

10

Sorption data for various polymers is tabulated in sources such as the Polymer Handbook. S. Pauly, *Permeability and Diffusion Data*, The Polymer Handbook VI/435. Unfortunately, while data for helium is widely available (although prone to error), there has not been a need to measure sorption characteristics of Xe in different polymers. The lack of published xenon solubilities resulted in a search for equipment to measure these quantities. The polymer group at the Chemical Engineering Department at North Carolina State University measured the solubility of both xenon and helium gases in the 7 polymers that were to be used to verify the polymer relaxation theory. The results of helium and xenon solubility measurements are compared to the available literature values in Table 4.1 below (note that some data was not available).

20

	S(Xe) (lit.)	S(Xe) (meas.)	S(He) (lit.)	S(He) (meas.)
LDPE	0.59	0.68±	0.0055	0.006±
HDPE	-	0.42±	0.0028	0.004±
PP	-	0.70±	0.0002	0.020±
PTFE	0.75	0.70±	0.1104	0.003±
Nylon 6	-	.31	0.0043*	0.003
Silicone	3.99	1.93±	0.0430	0.034±
PI	-	4.00±0.1	0.0056	0.030±

*Literature value for Nylon 11.

Table 4.1: Results of Solubility Measurements

The measurements were obtained by placing polymer samples in an evacuated chamber. A known pressure of gas was then introduced into the chamber. As the gas dissolved into the polymer, the decrease in chamber pressure was recorded. By
 5 knowing the volume of the test chamber and carefully maintaining the temperature of the apparatus, the solubility of the gas in the polymer can be calculated from the pressure vs. time data. However, there are many intrinsic difficulties in polymer sorption measurements. Because of the low diffusion coefficients in some polymers such as polyimide, it can take a long time for gas to permeate the entire sample and
 10 establish equilibrium. Even the thinnest samples available must be allowed to remain in the chamber for many days. Another problem, evident in He measurements, is that pressure differences observed for materials with low solubilities are extremely small, resulting in significant measurement uncertainty. In addition these to problems, density values play an important role in the solubility calculation. While the
 15 manufacturer provides density estimates for the material samples, laboratory measurements confirmed that these values were often inaccurate. This discrepancy can be responsible for dramatic changes in the final solubility value. It should therefore be noted that relative to the sorption measurements, more reliable results could be obtained. However, the values provided are sufficient to confirm the
 20 solubility based relaxation theory.

^{129}Xe Materials Study

The majority of this materials study was performed using hyperpolarized ^{129}Xe . A much greater sensitivity of ^{129}Xe to surface effects resulted in shorter T_1
 25 times and allowed for more rapid testing of materials. More dramatic relaxation effects eliminate the need for an extremely long chamber T_1 as is the case for ^3He studies. This fact alone resulted in more reliable results for ^{129}Xe materials testing.

Figure 3 is a plot of T_1^{cc} vs. the product $S[1H]^5$, representing the two significant terms in the expression for T_1 (2.21) developed in the polymer sorption
 30 relaxation model. For the experimental data points, the y error bars on the graph represent the cumulative error in the relaxation measurement. The x error bars are associated with the solubility measurements described above. The data confirms that solubility can be used to predict T_1 for hyperpolarized ^{129}Xe on polymer surfaces.

While the experimental data points follow the trend predicted by the theoretical model remarkably well, certain discrepancies merit further discussion.

Lower than predicted T_1 measurements as in the case of silicone can be explained in several ways. Paramagnetic impurities in the material sample or test chamber are the primary suspect. Recall that only protons were assumed to have a depolarizing effect on the hyperpolarized gas. In order for this assumption to hold true, the composition of the material sample would have to be extremely pure. For example, given that the gyromagnetic ratios of Fe and protons are related $\gamma_{Fe} \sim 1000\gamma_{1H}$, a one part per thousand presence of Fe in the material sample can double the relaxation rate. Although the sample surfaces were cleaned with high-purity ethanol prior to testing in the Spin Down Station, paramagnetic impurities can be trapped in the polymer matrix during the curing process. One possible contaminant is Pt metal (which is paramagnetic) that can be used in the mold forming silicone polymers.

When considering factors that cause the measured T_1 results to be higher than predicted as in the case of polyimide (PI) and PTFE, the diffusion coefficient becomes an important parameter. For polyimide, the diffusion of Xe into the polymer is so slow that it takes weeks for the Xe to equilibrate completely. This time scale is much longer than the 1-2 hour time scale of the relaxation measurements. Since the T_1^p of ^{129}Xe in PI is on the order of 100 ms (based on LDPE), the ^{129}Xe atoms only sample a tiny layer ($\sim 5 \mu\text{m}$, based on a diffusion coefficient $D \sim 10^{-8} \text{ cm}^2/\text{s}$), of the surface of the polymer sample. This surface layer may have different sorption characteristics than the bulk polymer that was used in the solubility measurements. While solubility can typically only be measured for the bulk sample, the region of interest is only $0.5 \mu\text{m}$ out of 1 mm, or $0.5 \times 10^{-6} / 1.0 \times 10^{-3}$ (about 1/2000) of the actual sample.

A summary comparison of the predicted and measured results for ^{129}Xe is presented in Table 4.2. More detailed results from the theoretical and experimental calculations are tabulated in Figures 5 and 6.

	S	Pred. Υ (cm/min)	Pred. T_1^{cc} (min)	Measured Υ (cm/min)	Measured T_1^{cc} (min)
LDPE	0.68	0.0419	4.94	0.0370 ± 0.0039	5.59 ± 0.59
HDPE	0.42	0.0263	7.87	0.0362 ± 0.0025	5.71 ± 0.39
PP	0.70	0.0427	4.85	0.0540 ± 0.0035	3.83 ± 0.25
PTFE	0.75	0.0356	5.82	0.0249 ± 0.0016	8.30 ± 0.54
Nylon 6	.31	.0166	12.5	0.0104 ± 0.0016	19.91 ± 2.99
Silicone	1.93	0.1066	1.94	0.3112 ± 0.0072	0.67 ± 0.02
PI	4.10	0.1345	1.54	0.0212 ± 0.0017	9.78 ± 0.78

Table 4.2: Results of Polymer Relaxation Study for ^{129}Xe

5 ^3He Material Studies

The study of ^3He surface relaxation on polymers is much more challenging than the study of ^{129}Xe . Figure 4 shows the results of this study in the T_1^p vs. $S[1H]^{.5}$ form as discussed for the ^{129}Xe presented in Figure 3. The various errors associated with the ^3He study make direct comparison with the ^{129}Xe difficult. However, there are trends linking the two studies worth noting.

The results for LDPE and PTFE agree extremely well with theory. However, the other materials in the ^3He study fall short of predicted T_1 relaxation times. Of these materials, silicone, PP and HDPE are consistent with short results observed in the ^{129}Xe study.

This trend points to paramagnetic impurities in the material samples. These contaminants can include dust, fingerprints, Apiezon grease, and ferrous impurities that may be trapped in the polymer material. Unfortunately, higher diffusion coefficients for He result in much longer length scales ($\sim 20 \mu\text{m}$ ^3He vs. $\sim 1 \mu\text{m}$ ^{129}Xe , Equation 2.23) for polymer gas interaction. The greater mobility of gas atoms in the polymer results in much deeper sampling of the polymer. This sampling could significantly increase the probability of interaction with paramagnetic impurities if their distribution in the polymer is non-uniform. For example, gas in silicone has a large diffusion coefficient ($D_{\text{He}} \sim 4e-5$, $D_{\text{Xe}} \sim 5e-6$) relative to other polymers in the study. While the measured T_1 for silicone, PP, and HDPE was lower than predicted in

both ^{129}Xe and ^3He studies, the ^3He has a length scale roughly 3 times that of ^{129}Xe .

This contaminant concern magnifies the importance of sample preparation in the study of surface effects as well as the preparation of containers used for hyperpolarized gases. As discussed with the ^{129}Xe study, sample preparation included
 5 only a surface cleaning, leaving any contaminants contained within the polymer matrix. One alternative can be to use acid baths to clean containers or container materials to remove or minimize at least surface and proximate sub-surface impurities potentially embedded in the polymer matrix.

Of the remaining polymers in the ^3He study, only polyimide (PI) and nylon 6
 10 show markedly different results between the two studies. One distinction that might explain this result is the difference between amorphous and semicrystalline polymers. LDPE, HDPE, and PP are amorphous polymers that should exhibit uniform solubility. Alternatively, semicrystalline polymers such as PTFE, nylon 6, and PI might exhibit spatial diffusion and thus exhibit regional solubilities that differ from the bulk
 15 solubility measured in the polymer lab.

A summary comparison of the predicted and measured results for ^3He is presented in Table 4.3. (Detailed results in Figures 5 and 6).

	S	Pred. Υ (cm/min)	Pred. T_1^{∞} (min)	Measured Υ (cm/min)	Measured T_1^{∞} (min)
LDPE	0.0060	0.0012	170.98	0.0012 ± 0.00015	170.80 ± 21.22
HDPE	0.0040	0.0008	252.40	0.0056 ± 0.00055	36.65 ± 3.66
PP	0.0067	0.0013	154.81	0.0211 ± 0.00156	9.80 ± 0.77
PTFE	0.1104	0.0158	13.09	0.0150 ± 0.00071	13.72 ± 0.65
Nylon 6	.003	.0005	395	0.0026 ± 0.00034	79.98 ± 11.17
Silicone	0.0340	0.0061	33.69	0.0386 ± 0.00169	5.36 ± 0.22
PI	0.0300	0.0032	64.30	0.0055 ± 0.00054	37.58 ± 3.78

20 Table 4.3: Results of Polymer Relaxation Study for ^3He

O₂ Contamination

Impurities introduced into the test environment could also account for measurement errors. Dust, fingerprints, and other contaminants may be introduced

into the test chamber when the chamber is opened to insert the sample. All of these contaminants have a depolarizing effect that is not included in the sorption model. The most significant confirmed contaminant in the test environment is the presence of O₂ in the test chamber.

5 Because O₂ has a magnetic moment, it can relax hyperpolarized gases in the same manner as protons. While O₂ affects ¹²⁹Xe and ³He similarly, the longer T₁ times associated with the ³He study magnify any O₂ contamination. For example, 1 Torr of O₂ in the chamber would generally not be noticed on the time scale of the ¹²⁹Xe study but would have a radical impact on ³He studies. The effect of O₂ in the
10 test chamber was observed on several occasions. It resulted in a nonexponential decay rate many times faster than the predicted T₁ of the sample.

While in storage, oxygen from the atmosphere diffuses and sorbs into the polymer sample. In order to remove this O₂ from the polymer, the sample is preferably left under vacuum for a period of time before testing. The time period
15 necessary for this degassing to take place can be calculated if diffusion coefficients are available. Table 4.5 shows the degassing calculations for 1 mm thick polymer samples with available O₂ diffusion coefficients, assuming $t \approx (Z)^2/D$ (Z= sample thickness).

Material	D(O ₂) cm ² /s	Volume O ₂ in Polymer cc (STP)	Vacuum Time Hr
LDPE	6.80e-06	0.0201	0.41
HDPE	3.07e-06	0.0077	0.90
PP	1.95e-05	*	0.14
PTFE	8.11e-07	0.0893	3.43
Silicone	4.10e-05	0.1302	0.07

*no S(O₂) available for PP

Table 4.5: O₂ Degassing Time for ³He Relaxation Studies

In determining the relaxation time (T₁) of a hyperpolarized noble gas in a polymer container, equation 2.21 can be restated as:

$$T_1 = \frac{V}{AS} \sqrt{\frac{T_1^p}{D_p}} \quad (2.21)$$

where "V" is the container volume, "A" is the container surface area, "S" is the Ostwald solubility of the noble gas in the polymer, " T_1^p " is the relaxation time of the noble gas dissolved in the polymer matrix, and " D_p " is the diffusion coefficient of the noble gas in the polymer. This quantitative analysis reveals that the relaxation time of the noble gas is inversely proportional to noble gas solubility in the polymer. Indeed, and surprisingly, as noted above, the surface induced relaxation time is believed to be proportional to the *square root* of the noble gas relaxation time in the polymer matrix.

Restating the multiple constants of equation 2.23 into a factor "C" results in:

$$C = \frac{32\pi h^2 Na}{4.05 \times 10^5} \quad (2.23a)$$

Thus, the relaxation rate of a noble gas in the polymer can be expressed as stated in

$$\frac{1}{T_1^p} = \frac{C \gamma_G^2 \gamma_H^2 I(I+1)}{b D_p} [^1H] \quad (2.23b)$$

equation (2.23b (I=proton spin)).

Inserting this relaxation rate expression into equation (2.21) shows that the dependence on diffusion coefficient disappears and results in a surface relaxation time " T_1 " which can be expressed by equation (2.23c).

$$T_1 = \frac{V}{AS \gamma_G \gamma_H} \sqrt{\frac{b}{CI(I+1)[^1H]}} \quad (2.23c)$$

This expression can be used to predict the relaxation time of hyperpolarized noble gases such as either ^3He or ^{129}Xe on any polymer surface. As was pointed out in U.S. Patent Number 5,612,103, perdeuteration of the polymer should lead to improvement in the noble gas relaxation time. However, this improvement appears to be less than what was previously predicted. The gyromagnetic ratio γ_D of deuterium

is 6.5 times smaller than for hydrogen, and the spin " I " is 1. A comparison of the relaxation time of the noble gas in the perdeuterated polymer matrix versus its normal counterpart shows the following:

$$\frac{T_p(D)}{T_p(H)} = \frac{(1/2)(1/2+1)(26750)^2}{(1)(1+1)(4106)^2} = 15.9 \quad (2.30)$$

5

However, this improvement in T_p translates into an overall improvement in relaxation time of about 4 (the square root of 15.9). Thus, deuteration is still desired but perhaps is not as impressive as was previously expected.

A comparison of ^3He relaxation with ^{129}Xe relaxation on a given polymer surface can now be made using equation (2.23c) assuming that " b " does not vary substantially for the two gases as expressed in equation (2.31).

10

$$\frac{T_1(^3\text{He})}{T_1(^{129}\text{Xe})} = \frac{S_{Xe}\gamma_{Xe}}{S_{He}\gamma_{He}} \quad (2.31)$$

For example, in low-density polyethylene ("LDPE"), the ratio of xenon solubility to helium solubility is 107 and the ratio of $\gamma_{Xe}/\gamma_{He}=0.37$. Thus, the relaxation time of ^3He on a LDPE surface will be nearly 40 times longer than for ^{129}Xe .

Further, as noted above, the noble gas polarization level is not spatially uniform in the polymer. The polarization is constant for the gaseous phase but falls off exponentially with distance into the polymer.

20

Therefore, it is important to note that especially in the case of polymer coatings, the thickness of the coating preferably exceeds the polarization decay length scale " L_p " (equation 2.22) in order for the gas depolarization time to depend on the polymer properties in a predictable way. For a coating thickness less than " L_p ", polarized gas can sample the substrate underneath the polymer, and potentially undergo undesirably fast relaxation. Because " T_p " also depends linearly on " D_p ," the depolarization length scale is proportional to the gas diffusion coefficient. Thus, especially for ^3He , which tends to have a high diffusion constant, the polymer contact

25

layer, or the thickness of the coating or film is preferably several times the critical length scale. Preferably, the thickness is above about 16 micrometers and more preferably at least 100-200 micrometers thick in order to be effective. In fact, coatings that are substantially thinner than " L_p " can be more deleterious than having
 5 no coating at all, because the mobility of the noble gas once into the coating is reduced. As such, a noble gas dissolved in a thin coating can interact with the surface underneath for a much longer period of time than if the coating were not present. Indeed, the probability of depolarization appears to increase as the *square* of the interaction time.

10 The relatively long relaxation times achievable with polymers (coatings or container materials) make the development of polymer bags for hyperpolarized gas storage appealing. Further, bags are a desirable storage and delivery device for magnetic resonance imaging using inhaled hyperpolarized ^3He because the gas can be completely extracted by collapsing the bag. In contrast, a rigid container typically
 15 requires a more sophisticated gas extraction mechanism.

O_2 Induced Relaxation

When bags with long surface relaxation times are used, other relaxation mechanisms can become important. One of the most important additional relaxation
 20 mechanisms is due to collisions of the noble gas with paramagnetic oxygen as noted above. Saam *et al.* have shown that the relaxation time of ^3He due to collisions with paramagnetic oxygen can be expressed as stated in equation (2.32).

$$T_1[\text{O}_2] = 2.27s \text{ amgt} \quad (2.32)$$

(Note amagat is abbreviated as "amgt") (1 amagat = 2.689×10^{19} atoms/cm³, the
 25 density of an ideal gas at 273K and 1 atm.). See B. Saam et al., "Nuclear relaxation of ^3He in the presence of O_2 ," Phys. Rev. A, 52, p. 862 (1995). Thus, a pressure of oxygen as small as 1/1000 of an atmosphere can result in a ^3He relaxation time of only 38 minutes even with perfect surfaces. Given this problem, tremendous care should be taken to reduce the oxygen content in the storage container through careful
 30 preconditioning of the container, such as by pumping and pure gas purging methods. However, even with preconditioning, a bag is susceptible to permeation of oxygen

through the polymer which can disadvantageously build substantial oxygen concentration over time. The volume of oxygen transmitted through the polymer material depends on several factors, including the polymer-specific oxygen permeability coefficient " Q_{O_2} ". For small quantities of oxygen transfer, the rate of oxygen concentration build-up in the bag is nearly constant, and can be expressed by equation (2.33).

$$\frac{d}{dt}[O_2] = \frac{A\Delta P_{O_2}}{V_{bag}\Delta x} Q_{O_2} \quad (2.33)$$

" $[O_2]$ " is the oxygen concentration in the bag, " A " is the polymer surface area, " ΔP_{O_2} " is the oxygen pressure difference across the bag surface, " V_{bag} " is the volume of the bag, " Δx " is the polymer thickness, and " Q_{O_2} " is the oxygen permeability coefficient. Using equation (2.33) and a bag having the following characteristics (area = 648 cm², volume = 1000 cm³, Δx = 0.01cm, $P = 2 \times 10^5$ Pa, Q_{O_2} (LDPE) = 2.2×10^{-13} cm²/s Pa) gives a $d/dt(O_2)$ value of about 2.8×10^{-7} amgt/s. Thus, a one hour duration (3600 seconds) will give 1×10^{-3} amgt, which corresponds to a T_1 of about 38 minutes. For Tedlar™, the O_2 permeability is smaller (0.139×10^{-13} cm²/s Pa- 158 times less permeable than LDPE). Thus, in this material, one hour of permeation will give an O_2 induced T_1 of about 99 hours, but after 10 hours the T_1 drops to only 10 hours. Thus, as an alternative to an O_2 shield placed over the inner layer, the contact surface layer itself can be formed as a polymer having reduced permeability to O_2 and/or with increased thickness Δx .

Accordingly, oxygen-induced relaxation can quickly dominate surface relaxation even when careful gas handling techniques are employed. Therefore, in order to make polymer bags a viable storage medium, another layer of material is preferably used to suppress oxygen permeability. So long as the thickness of polymer in contact with the polarized gas is greater than L_p , the secondary material used for oxygen permeability suppression does not need to be non-depolarizing. A metal film such as aluminum can be very effective in such an application.

Materials

A comparison of the experimentally measured relaxation times to the theoretical values reveals remarkable agreement for the polymer systems for which ^{129}Xe solubilities are known. Theoretical relaxation times are also calculated for ^3He on a variety of polymer surfaces/systems. The results are summarized in Figures 5 and 6. The relaxation times have been scaled to a 1 cm^3 spherical container.

Note that the results for ^{129}Xe in the fluoropolymer PTFE (TeflonTM) are also shown in Figures 5 and 6. For this case, for a one cubic centimeter (" cm^3 ") spherical container, the calculated T_1 was 5.65 min and the observed relaxation time was 8.3 min. The calculations are identical to those discussed previously except for the substitutions in the equations and a subtle change in "b" due the larger size of the fluorine atom compared to the hydrogen atom. The composition of the atomic structure of the material is different (*i.e.*, fluorine versus a hydrogen atom). In fact, with the possible exception of TedlarTM (polyvinylfluoride), most fluoropolymers are not preferred for the preservation of ^3He hyperpolarization. For example, the predicted T_1 for ^3He on PTFE is only 13.1 minutes in a 1 cm^3 sphere. This is due to a relatively high solubility of helium in most fluropolymers due to that larger void space in the polymer resulting from the large fluorine atoms. Furthermore, most common gasket materials such as VitonTM, Kel-FTM, and KalrezTM, are fluropolymers with fillers and can potentially be substantially depolarizing to ^3He as compared to pure hydrocarbon gaskets such as those containing polyolefins. Examples of preferred seal materials include polyolefins such as polyethylene, polypropylene, and copolymers and blends thereof.

Because the shape of the container (the gas holding chamber area) can impact the rate of depolarization, it is preferred that container configurations be selected to maximize the free-gas volume of the container (V) while minimizing the surface area (A) which contacts the hyperpolarized gas (that is, to decrease the value of the ratio A/V). More preferably, the container is sized and configured to provide a A/V ratio of about less than 1.0 cm^{-1} , and even more preferably less than about 0.75 cm^{-1} . In one embodiment, the container is substantially spherical, such as a round balloon-like container.

Preferred polymers for use in the inventions described herein include materials which have a reduced solubility for the hyperpolarized gas. For the purposes of the

inventions herein, the term "polymer" is broadly construed to include homopolymers, copolymers, terpolymers and the like. Similarly, the term "blends and mixtures thereof" includes both immiscible and miscible blends and mixtures. Examples of suitable materials include, but are not limited to, polyolefins (e.g., polyethylenes, polypropylenes), polystyrenes, polymethacrylates, polyvinyls, polydienes, polyesters, polycarbonates, polyamides, polyimides, polynitriles, cellulose, and cellulose derivatives and blends and mixtures thereof. It is more preferred that the coating or surface of the container comprise one or more of a high-density polyethylene, low density polyethylene, polypropylene of about 50% crystallinity, polyvinylchloride, polyvinylflouride, polyamide, polyimide, or cellulose and blends and mixtures thereof.

Of course, the polymers can be modified. For example, using halogen as a substituent or putting the polymer in deuterated (or partially deuterated) form (replacement of hydrogen protons with deuterons) can reduce the relaxation rate associated with same. Methods of deuterating polymers are known in the art. For example, the deuteration of hydrocarbon polymers is described in U.S. Patent Nos. 3,657,363, 3,966,781, and 4,914,160.

Typically, these methods use catalytic substitution of deuterons for protons. Preferred deuterated hydrocarbon polymers and copolymers include deuterated paraffins, polyolefins, and the like. Such polymers and copolymers and the like may also be cross-linked according to known methods.

It is further preferred that the polymer be substantially free of paramagnetic contaminants or impurities such as color centers, free electrons, colorants, other degrading fillers and the like. Any plasticizers or fillers used should be chosen to minimize any magnetic impurities contacting or positioned proximate to the hyperpolarized noble gas.

Alternatively, the first layer or contact surface can be formed with a high purity (and preferably non-magnetic) metal surface such as a metallic film. The high purity metal surface can provide advantageously low relaxivity/depolarization-resistant surfaces relative to hyperpolarized noble gases. Preferred embodiments will be discussed further below. Of course, the high purity metal film can be combined with the materials discussed above or can be used with other materials to form one or

more layers to provide a surface or absorption region which is resistant to contact-induced depolarization interactions.

As noted above, any of these materials can be provided as a surface coating on an underlying substrate or formed as a material layer to define a polarization friendly contact surface. If used as a coating, the coating can be applied by any number of techniques as will be appreciated by those of skill in the art (*e.g.*, by solution coating, chemical vapor deposition, fusion bonding, powder sintering and the like). Hydrocarbon grease can also be used as a coating. As noted above, the storage vessel or container can be rigid or resilient. Rigid containers can be formed of Pyrex™ glass, aluminum, plastic, PVC or the like. Resilient vessels are preferably formed as collapsible bags, preferably collapsible multi-layer bags comprising several secured material layers. The multiple layer configuration can employ material layers formed of different materials, *i.e.*, the material layers can be selected and combined to provide a collapsible bag which is oxygen resistant, moisture resistant, puncture resistant, and which has a gas contacting surface which inhibits contact-induced depolarization. As used herein, the term "oxygen resistant" means that the bag is configured to inhibit the migration of oxygen into the gas holding portion of the bag. Preferably, the bag is configured to provide an oxygen leak rate or oxygen permeability rate of less than about 5×10^{-6} amgt/min, more preferably less than 5.2×10^{-7} amgt/min, and still more preferably less than about 1×10^{-7} amgt/min at one atmosphere of pressure.

Containers

Turning again to the drawings, Figures 7 and 8 illustrate a preferred embodiment of a resilient container 10 for hyperpolarized gas according to the instant invention. Figure 7 shows the container 10 in the collapsed (empty or void) position and Figure 8 shows the container 10 when inflated (filled). As shown, the container 10 includes a front wall 12 and a rear wall 13 and a gas (or liquid) holding chamber 14 formed between the walls 12, 13. As shown, the walls 12, 13 are co-joined by a perimeter seal 15.

As shown in Figure 7, in a preferred embodiment, the container 10 includes an outwardly extending port connector 20 in fluid communication with the port 22. The port connector 20 is preferably attached to the container 10 via a fitting 28. The fitting 28 can be heat sealed to the inside of the wall 12 to secure the fitting 28 to the

inside of the container wall 12 in an airtight manner. Alternatively, as shown in Figure 7, a gasket or O-ring 27a can be used to seal the fitting 28 to the container 10.

As shown in Figure 9, the fitting 28 extends up through the container wall 12 and is secured against the outside of the container wall 12 via compression with a nut coupling member 27 and an intermediately positioned O-ring 27a. As is also shown, the nut coupling member 27 is positioned opposite the multi-layer container wall 12 and is configured such that it includes an aperture with internal threads which is positioned over and threadably mates with the external threads of the fitting 28c. Again, the seal provided by the nut coupling member 27, the associated O-ring 27a, and the fitting 28 are preferably configured to withstand up to about 3 atm of pressure and also are preferably configured to provide a vacuum-tight seal. In the embodiment shown in Figures 7 and 13, the port connector 20 is configured to define a portion of the fluid flow path 22f.

An alternate embodiment is shown in Figure 9. In this embodiment, the port connector 20' is configured to function as a second top coupling nut which threadably engages with the fitting 28 separate from the nut coupling member 27. As shown, the port connector 20' includes an O-ring 20a positioned intermediate a bottom portion of the port connector 20b and a portion of the fitting 28b. As before, it is preferred that this seal between the fitting 28 and the port connector 20' also be configured in an airtight arrangement and be configured to withstand pressures up to about 3 atm (and is also preferably leak-tight at vacuum pressures used to condition the container, as will be discussed further below).

In a preferred embodiment, the container 10 includes a capillary stem 26s and a valve member 26. As shown in Figure 9, the port connector 20' is configured to engage the capillary stem 26s which extends away from the chamber of the container 14 and which is in fluid communication with the valve member 26. The valve member 26 is operably associated with the chamber 14 such that it releasably controls the intake and release of the fluid. That is, in operation, the valve 26 is opened and hyperpolarized gas (or liquid) is directed through the outlet 29 through the body of the valve 26 and through the capillary stem 26s into the chamber 14, thereby forcing the container 10 to expand (Figure 8) and capture the hyperpolarized gas (or liquid). The capillary stem 26s can be formed as an integral part of the valve member 26, or as a separate component. For example, the valve member 26 can include a body portion

formed of glass such as Pyrex or the like, and the capillary stem 26s can be directly formed onto an end portion thereof as a glass such as Pyrex or an aluminosilicate, or other material to extend therefrom as a continuous body co-joined to the lower portion of the valve member 26. The valve illustrated in Figure 9 includes a plug portion 26p
5 with an O-ring 26o which longitudinally translates to engage with the lower nozzle end of the valve chamber 26n to close the flow path 22f in the valve closed position. In the reverse, the valve plug 26p moves away from the nozzle end 26n to allow the gas to flow through the port 22, the capillary stem 26s, and the valve body 26b and in (or out) the valve outlet 29.

10 Operationally, still referring to Figure 9, the capillary stem 26s is configured such that a major portion of the hyperpolarized gas, once in the chamber 14, remains therein when the valve member 26 is closed. That is, the dimensions and shape of the capillary stem 26s are such that diffusion of the hyperpolarized gas away from the container chamber 14 is inhibited. Thus, the capillary stem 26s can reduce the
15 amount of exposure for a major portion of the hyperpolarized gas with the valve 26 and any potentially depolarizing components operably associated therewith. In addition, the capillary stem 26s also provides a portion of the gas flow path 22f therethrough. As such, the capillary stem 26s includes an internal passage which is preferably sized and configured in a manner which inhibits the flow of gas from the
20 chamber during storage or transport while also allowing the gas to exit the chamber 14 at its ultimate destination without undue or significant impedance.

 Preferably, as discussed above the capillary stem 26s is operably associated with the valve member 26 and is configured to retain a major portion of the gas in the bag chamber 14, and away from the valve body 26b when the valve member 26 is
25 closed. In the reverse, when the valve member 26 is opened, the gas exits the chamber 14 into the flow path 22f to the outlet 29. Thus, in operation, when the valve member 26 is closed, the capillary stem 26s helps keep a majority of the hyperpolarized gas away from the valve member 26 (such as retained at least below the O-ring in the nozzle end of the valve designated by the stepped down portion of
30 the valve body in Figure 9) to thereby inhibit any contact-induced depolarization which may be attributed thereto. In one embodiment, the capillary stem 26s has a length which is at least about 2.0 inches (5.1cm) with a 1/8 inch (0.3cm) inner diameter and a 0.2 inch (0.5cm)

outer diameter. For a 7x7 inch (18cm x 18cm) bag (or approximately one liter) container, this length is greater than about 20% the length or width of the container 10.

As shown in Figure 9, the valve member 26 includes an externally accessible adjustment knob 26a which rotates to open and close the valve member 26. As is also shown, the valve member 26 includes a plurality of O-rings 26o therein. A suitable glass valve is available from Kimble Kontes Valves located in Vineland, NJ.

As is also shown in Figure 9, the capillary stem 26s is positioned intermediate the valve member 26 and the container chamber 14 to inhibit the migration of the hyperpolarized substance into the valve member 26 to reduce the exposure to any potentially depolarizing materials therein (which potentially includes one or more of the O-rings 26o). Preferably, all sealing and structural materials associated with the container 10 and other container assembly components which come into contact with hyperpolarized gas are selected or formed of materials which are preferably substantially non-depolarizing.

Preferably, the capillary stem 26s is formed with a substantially rigid body. As used herein, the term "rigid" means that it can structurally help support the weight of a valve member 26 when assembled to the container 10 to minimize the stress/strain which may be introduced onto the juncture of the fitting 28. For example, the rigid body of the capillary stem 26s can be provided by a rigid substrate, such as a plastic, a PVC material, a glass, Pyrex, or aluminosilicate material, a metal, and the like. Of course, the hyperpolarized gas or fluid contacting surfaces of the capillary stem 26s are preferably formed with a material or coating which is substantially non-depolarizing to the hyperpolarized gas or liquid held therein (low relaxivity and or solubility for the hyperpolarized gas). It should also be noted, that, as shown, the capillary stem 26s is an elongated cylindrical stem, but other configurations are also possible. Preferably, whatever the configuration, the inner passage (shown as a diameter) of the capillary stem 26s is configured to inhibit or restrict the flow of fluid from the chamber of the bag 14 when the valve member 26 is closed.

Referring again to Figure 9, the valve member 26 is configured with an end portion which holds the outlet 29 away from the capillary stem 26s which forms the hyperpolarized gas inlet and outlet port. Preferably, the outlet 29 is configured with a sealing means 25 which allows the container to mate and engage with an external

device at the ultimate destination or delivery point (in an air tight manner) to facilitate the delivery of the gas or liquid without exposure to atmosphere. As shown, this sealing means 25 includes an O-ring 25a which is configured to sealably engage with the external device. In operation, the sealing means 25 compresses the O-ring 25a to

5 matably engage with the delivery or input device (not shown). As such, the container chamber 14, the fitting 28, the capillary stem 26s, a portion of the valve member 26, and the end portion of the valve member 29 define the hyperpolarized fluid flow path 22f. Thus, in the embodiment shown in Figure 9, when the valve member 26 is open, the fluid flow path 22f extends from the container chamber 14 through the capillary

10 stem 26s to an external device or source such as a hyperpolarizer dispensing port (such as during filling) or patient delivery interface (such as at a gas delivery clinical use point). That is, a clinician or physician can merely turn the knob 26a to open the valve member 26 and compress the walls of the bag to release or expel the hyperpolarized gas from the chamber 14. In a preferred embodiment, as shown in

15 Figures 17-19, the chamber 14 is engaged with a destination interface. As shown, the container 10, when compressed, expels the gas directly into a patient interface mask 90 so that a patient can inhale or breathe the gas therefrom.

Of course, other flow path configurations can be used (with and without the capillary stem 26s and/or valve member 26) such that the hyperpolarized fluid flow

20 path 22f is defined by other components such as intermediate, distal, or proximate tubing or conduit (relative to the chamber of the bag). An example of the use of conduit 70 without a capillary stem 26s is illustrated in Figure 17. For the conduit or tubing embodiment, various materials can be used for the conduit. An example of one suitable material alternative is polymer tubing attached to the fitting 28 and/or

25 connector 20 and in fluid communication with the chamber 14. The tubing is formed such that at least the inner surface comprises a polarization friendly material with a suitable relaxivity or solubility value to provide a sufficiently long T_1 and the outer layer material comprises a mechanically stable (*i.e.*, self supporting), oxygen resistant flexible polymer matrix. Of course, depending on the material selection, the tubing

30 can be formed as a unitary single layer body wherein the inner surface and outer layer material are the same, or the tubing can include a coated inner surface and a different material outer surface or wall layer.

Figures 21A, 21B, and 21C illustrate yet another preferred embodiment of a container 10. As shown, this embodiment is similar to that shown in Figure 7, except that the fitting 28 can be further isolated from the main volume of gas (or liquid) held in the chamber 14 as shown in Figure 21B. As shown, the container is configured to position the port 22 at an edge portion of the container body. In addition, it is also preferred that an isolation means 31 is positioned intermediate the port and main volume of the chamber to isolate the port 22 and port fittings 28 or other components from the gas or liquid in the container during transport and storage. As such the gas or liquid's exposure to the port 22 or port fittings 28 is reduced. In operation, the container is in an unfilled (deflated position) as shown in Figure 21A. Flexible tubing such as tygon® is attached to the container as shown in Figure 21B. It is also preferred that the tubing be operably associated with a sealing means such as a clamp, valve or the like as discussed herein for other embodiments. As shown in Figure 21B, a quantity of hyperpolarized gas or fluid is directed into the container through the aperture 22a as schematically indicated by the arrows. As shown in Figure 21C, when the resilient container is sufficiently full (but below full capacity), an isolation means 31i is attached or formed onto the bag to pinch or enclose the bag portion with the port 22 and/or fitting 28 in a manner which will inhibit the contact of the main volume of hyperpolarized gas or liquid with this region of the bag or container. As shown, the isolation means 31i is a clamp having opposing clamping bars 31, 32 compressed together by fastener 33. Of course, other isolation means can also be used such as heat sealing, tying, restrictive (pinching) with bag configurations or holding fixtures and the like. For example, the bag container can be sized and configured with the port on an edge portion, preferably, proximate to a corner, and the container partially filled so that the corner can be folded against the body of the container and held in place simply by attaching a portion of the external wall to an opposing wall such as via an adhesive attachment means, velcro™, hook, and the like. The fold line acts to "pinch" off the main chamber of the container from the port (not shown) in a manner which is substantially air tight. Of course, a fold bar or other device can be used to facilitate a tight fold line between the port region and the major volume of the bag.

A multi-layer (3 ply) resilient container 10 having a capillary stem 26s and valve member 26, as shown in Figure 9, can provide a corrected T_1 (taking into

account the material properties alone) for hyperpolarized ^3He gas of at least about 450 minutes (7.5 hours), and more preferably a corrected T_1 of at least about 600 minutes (10 hours) and an associated oxygen permeability rate of about 5.2×10^{-7} amgt/min (at one atmosphere of pressure).

5 In a preferred embodiment, as shown in Figure 12, the walls 12, 13 are configured with two layers 41, 44. The first layer 41 includes the inner contact surface 12a of the chamber 14 that holds and thus contacts the hyperpolarized gas. As such, the hyperpolarized noble gas is susceptible to contact-induced depolarization depending on the type of material and the depth of the material used to form this
10 layer. Thus, this surface is preferably formed by a coating or a material layer with a sufficient thickness for preventing the hyperpolarized gas from sampling the underlying substrate. Also, the surface should have a low relaxivity relative to the hyperpolarized gas. As such, both the material and the thickness are chosen and configured to inhibit the surface-induced depolarization of the gas. As regards the
15 thickness, it is preferred that the thickness be greater than the critical decay scale length L_p and more preferably greater than a plurality of the decay length scale. For example, for ^3He and HDPE, the critical length scale is about $8 \mu\text{m}$ so a preferred material layer depth is greater than about 16-20 μm .

Further, as regards the "low relaxivity", it is preferred that for ^3He the material
20 have a relaxivity value less than about .0013 cm/min and more preferably less than .0008 cm/min. For ^{129}Xe , it is preferred that the material have a relaxivity value less than about .012 cm/min and more preferably less than about .0023 cm/min. "Reduced solubility" is meant to describe materials for which the hyperpolarized gas has a reduced solubility. Preferably, as regards ^{129}Xe , the solubility is less than about 0.75,
25 and more preferably less than about 0.4. For ^3He , the solubility is preferably less than about 0.03, and more preferably less than about 0.01.

The second layer 44 includes the external surface 12b that is exposed to air which includes components which can be potentially degrading to the hyperpolarized gas in the chamber. For example, as discussed above, paramagnetic oxygen can cause
30 depolarization of the gas if it migrates into the contact surface 12a or the chamber 14. As such, it is preferred that the second layer 44 be configured to suppress oxygen migration. The second layer 44 can be formed as an oxygen-resistant substrate, a metal layer, or metallized deposit or coating formed over another layer. Preferably,

the second layer 44 (alone or in combination with other layers) prevents de-
magnetizing amounts of O₂ from entering into the chamber at a rate greater than 5×10^{-6} amgt/min, and more preferably at a rate which is less than about 1×10^{-7} amgt/min. More preferably, for a desired T₁ of about 24 hours and after 24 hours of permeation,
5 it is preferred that the O₂ concentration be less than about 2.6×10^{-5} amgt. Thus, at 1 atm, for a 1 liter bag, it is preferred that the container be configured to maintain the O₂ concentration in the chamber below .003% of the total gas concentration. Of course, the second layer can be alternatively chosen or configured to shield other environmental contaminants such as moisture. For example, in this embodiment, a
10 first layer may have a very low permeability for O₂ but may be sensitive to moisture. The second layer 44 can be configured with a protective polyethylene coating to compensate for this property and provide an improved T₁ container.

In yet another alternative embodiment, the inner surface 12a can be configured as a high purity (non-magnetic) metal film applied to an underlying substrate,
15 polymer, or other container material. High purity metal surfaces can provide even better protection against depolarization relative to other surfaces. Because the hyperpolarized gas contacts the metal, the underlying material is not required to have a low solubility for the hyperpolarized gas. In a preferred embodiment, the container is resiliently configured as a collapsible bag with the inner surface 12a formed from a
20 high purity metal film (preferably a thickness within the range of about 10nm to about 10 microns). As such, in this embodiment, the first layer 41 is the metallized layer and can provide the oxygen resistance/shield as well as protection against contact depolarization. Preferred metals include those that are substantially paramagnetically pure (*i.e.*, they do not introduce magnetic moments) and resistant to contact
25 depolarization of the hyperpolarized gases. Stated differently, the metal used should be chosen to minimize the adsorption time of the gas on the metal surface, *i.e.*, such that the noble gas has a low adsorption energy on the metal surface. Examples of suitable materials include, but are not limited to, aluminum, gold, silver, indium, beryllium copper, copper, and mixtures and blends thereof. As used herein, "high
30 purity" includes materials which have less than 1 ppm ferrous or paramagnetic impurities and more preferably less than 1 ppb ferrous or paramagnetic impurities.

In an additional embodiment, the inner surface 12a can be formed as a hybrid surface (a blend or side by side disposition of high purity metal film and polymer) or

as a high purity metal formed over a polymer substrate. As such, a metal film can be layered over a polymer with good relaxivity properties to compensate for cracks or gaps which may develop in the metal film layer.

In another preferred embodiment, as shown in Figure 12, the inner surface
 5 12a is formed directly by the inner wall of a polymer bag and the outer or intermediate surface is formed by a metallized coating or material positioned over and directly contacting the polymer bag. However, as illustrated in Figures 10 and 11, intermediate layers 42, 43 positioned between the inner layer 41 and outer layer 44 can also be used. For example, in a preferred embodiment, the container has three
 10 layers 41, 42, 44. The first layer 41 is 0.004" linear LDPE; the second layer 42 is 0.0005" aluminum foil, and the third layer 44 is 48 gauge polyester. Advantageously, the first LDPE layer provides a polarization-friendly surface with a relatively long T_1 , the second aluminum foil layer inhibits oxygen permeation, and the polyester layer provides strength and puncture resistance. The outer layers 41 and 44 are secured to
 15 the middle layer 42 with urethane adhesive. Typically the layers are cemented or bonded together but other joining or securing means can be used as will be recognized by those of skill in the art. A container 10 with this three-layer configuration has been observed to have a corrected T_1 (due to material only) for ^3He of about 490 minutes (over 8 hours) and an oxygen leak rate of about 3.9×10^{-5} amgt/min. This T_1 is
 20 contrast to that obtained in the single layer bag used in the past. For example, the T_1 for ^3He in a conventional 1 liter single layer Tedlar® bag (pre-conditioned such as described hereinbelow) has been estimated to be under about 4 hours.

In Figure 10, the container 10 has four layers 41, 42, 43, 44. As shown, the inner layer 41 is not a coating but is defined by the expandable polymer (or modified
 25 polymer) bag having a thickness sufficient to inhibit contact depolarization. In this embodiment the intermediate layers can be formed from any number of alternative materials, preferably resilient materials so as to contract and expand with the inner layer 41. In a preferred embodiment, the inner layer 41 is about 0.0025" (inches) (6.4×10^{-3} cm) of linear LDPE (LLDPE); the second layer 42 is about 0.003 inches (8×10^{-3} cm) of Al; the third layer 43 is 7lb PE, and the outer layer 44 is 48 gauge PET. A
 30 bag container with this multi-layer configuration has been shown to have a corrected T_1 (due to material alone) of about 14 hours and an oxygen leak rate substantially less than about 3×10^{-8} amgt/min at one atmosphere (101 KPa).

In one embodiment (not shown) a bag with five layers is used: the first layer is 35 μm of HDPE; the second layer 42 is 35 μm of polyamide; the third layer 43 is 1 μm of aluminum; the fourth layer 44 is 35 μm of polyvinylidene chloride; and the fifth layer (not shown) is 35 μm of polyester. Advantageously, the multiple layers can provide additional strength and/or puncture and pressure resistance. Of course, alternative materials and numbers of layers can also be employed according to the present invention.

In one embodiment (not shown), a coating can be placed on the inner surface 12a of the polymer bag to define the proper depth of the contact layer either alone or in combination with the thickness of the polymer bag. Of course, the two layers can be formed as one layer if the container material employed has a low-relaxivity for the hyperpolarized gas and if the material is sufficiently impermeable to environmental contaminants such as O_2 . Examples of such materials include but are not limited to PET (polyethylene terephthalate), PVDC (polyvinylidene dichloride), cellophane and polyacrylonitrile.

As shown in Figures 9 and 13-15, the container 10 also includes a sealing means operably associated with the entry port 22 and used to capture the hyperpolarized gas within the chamber 30. Generally described, the sealing means closes off the passage 22a in communication with the bag entry port 22 (Figure 7), thereby retaining the hyperpolarized gas substantially within the chamber 14 of the container. The sealing means can be configured in a number of ways, either with valves integrated with the bag (Figure 9) and or with clamps or other devices which are positioned onto the flow path of the container. In the configuration shown in Figure 13, the coupling member 20 includes a conduit 70 extending outwardly therefrom in the flow path, and the sealing means is a clamp or heat seal applied to the conduit. Examples of suitable sealing means include, but are not limited to, a clamp 72 (Figure 13) a heat seal 74 (Figure 14) and a membrane seal 76 (Figure 15). Alternatively, the valve 26 (Figure 9), a stop-cock, and other fittings and/or seals (gaskets, hydrocarbon grease, O-rings) (not shown) can be used to control the release of the hyperpolarized gas. Preferably, care is taken to insure all fittings, seals, and the like which contact the hyperpolarized gas or which are located relatively near thereto are manufactured from materials which are friendly to polarization or which do not substantially degrade the polarized state of the hyperpolarized gas. For example, as

noted above, many commercially available seals include fluoropolymers or fillers and the like which are not particularly good for the preservation of ^3He hyperpolarized gases because of the solubility of the material with the hyperpolarized gas.

Inasmuch as many common gasket materials are fluoropolymers or contain
5 undesirable fillers, they can potentially have a substantially depolarizing effect on the gas. This can be especially acute with respect to ^3He . This can be attributed to a relatively high solubility of helium in most fluoropolymers due to the larger void space in the polymer attributable to the large fluorine atoms. Indeed, preliminary tests indicate that materials of common O-rings (such as VitonTM, Kel-FTM, ethylene-
10 propylene, Buna-NTM, and silicone) exhibit far worse relaxation properties than would be expected from the relaxation rate of pure polymers. Most conventional O-rings are so depolarizing that they can dominate the relaxation of an entire hyperpolarized gas chamber. Indeed, commercial ethylene propylene O-rings exhibit 1/3 - 1/2 the relaxation time compared to pure LDPE with ^{129}Xe . The faster relaxation rate can be
15 explained because magnetic impurities in the O-rings can be introduced by such things as colorants and fillers and the like. Therefore, it is preferred that the containers of the present invention employ seals, O-rings, gaskets and the like with substantially pure (substantially without magnetic impurities) hydrocarbon materials such as those containing polyolefins. Examples of suitable polyolefins include
20 polyethylene, polypropylene, copolymers and blends thereof which have been modified to minimize the amount of magnetically impure fillers used therein. Additional suitable seals include hydrocarbon grease and hydrocarbon gaskets and O-rings made from polyethylene and the like. Thus, if a valve is used to contain the gas in the chamber 30, it is preferably configured with a magnetically pure (at least the
25 surface) O-ring and/or with hydrocarbon grease. Of course, because fillers and plasticizers are employed, then it is preferred that they be selected to minimize the magnetic impurities such as substantially pure carbon black.

In an alternative embodiment, the O-ring seal can be configured with the exposed surface coated with a high purity metal as discussed for the container surface.
30 Similarly, the O-ring or seal can be coated or formed with an outer exposed layer of a polymer at least " L_p " thick. For example, a layer of pure polyethylene can be positioned over a commercially available O-ring. One preferred commercially available O-ring material for ^{129}Xe is a TeflonTM-coated rubber O-ring or a low-

relaxivity polymer as discussed above. The void spaces in Teflon™, although a fluoropolymer, do not affect ^{129}Xe as much as it does ^3He because ^{129}Xe is much larger than fluorine, which is much larger than ^3He . As discussed previously, fluoropolymers can be used as seals with ^{129}Xe but are not preferable for use with
 5 arrangements where the seal may contact the hyperpolarized ^3He .

In operation, after delivery to a use site, the technician or patient can open the valve member 26 (Figure 9) and breathe in, or halt the flow by placing a temporary clamp 72 on the conduit 20 (Figure 13). Figures 13 and 14 illustrate preferred embodiments of a seal arrangement used to ship or store the filled container. Each
 10 acts to seal the fluid passage 22a by pinching the conduit 70 shut in at least one position therealong. Figure 13 shows the use of an external clamp 72 and Figure 14 shows the use of a redundant heat seal 74. In operation, each is easily employed with little impact on the polarization of the gas in the container 10. For example, for the embodiment shown in Figure 14, after the container 10 is filled with hyperpolarized
 15 gas, an in-process clamp (not shown) is inserted over the conduit 70 such that it closes off the passage 22a. Heat is applied to the conduit 70 as the conduit wall is collapsed to provide a heat seal 74 to at least one side of the in-process clamp. The bag is then ready to transport. Once at the desired delivery location site, the heat seal 74 can be cut away and a temporary clamp can be placed on the conduit 70. As shown in
 20 Figure 17, the conduit 70 can be directly engaged with a breathing apparatus or patient interface 90. As illustrated in Figure 18, the hyperpolarized gas can be forced out of the bag and into the interface 90 such as by externally depressing/compressing the walls of the container 10. Alternatively, the patient 92 can simply inhale thereby directing the gas 100 into the inhalation pathway 105.

Turning now to Figure 15, in another embodiment, a membrane seal 76 is positioned directly over the external portion of the entry port 22. The membrane seal 76 can be attached by heat, or an anchoring member such as a polymer washer threadably attached over the peripheral portion of the coupling member 22, preferably leaving the central portion 76a externally accessible. In this embodiment, as shown in
 30 Figure 19, the container 10 can be transported to the use site and inserted directly into a patient interface 90'. Preferably, the membrane seal 76 is inserted into the interface 90' such that it is positioned internal to the air tight coupling provided by the joint 130 between the coupling member 20 and the interface 90'. Advantageously, the interface

90' can include a puncture 79 recessed within the receiving area to open the central portion of the membrane seal 76 after the coupling member 20 forms the external joint 120 such that the container is sealed to the interface 90'. This allows the gas in the container to be easily released and directed to the patient. The gas can be easily
 5 extracted or forced out of the container 10 by depressing the walls 12, 13 of the container 10 or via inhalation. Advantageously, such a configuration removes the requirement for relatively complex or sophisticated gas extraction mechanisms and also reduces the amount of physical manipulation and/or interfaces required to deliver the gas to the subject.

10 As shown in Figure 16, a shipping box 80 is preferably used to hold the bag 10 during transport. This can help protect the bag from physical hazards. In addition, it is preferred that the box 80 include magnet means to provide a desired static magnetic (substantially homogeneous) field around the hyperpolarized gas. In addition, or alternatively, the box 80 can be configured to form a shield from
 15 undesirable stray magnetic fields as will be discussed further below.

In summary, the present invention provides containers which improve on the relaxation time of the hyperpolarized gas. Preferably, the container is sized and configured and the contact surface formed from a suitable material such that the hyperpolarized gas in the container has a relaxation time greater than about 6 hours
 20 and more preferable greater than about 20 hours for ^3He . Similarly, the container is preferably sized and configured such and the contact surfaces formed from a suitable material that the ^{129}Xe hyperpolarized gas in the container has a relaxation time greater than about 4 hours, preferably more than about 6 hours, and more preferably greater than about 8 hours.

25

Shielding

The present invention recognizes that unless special precautions are taken, relaxation due to external magnetic fields (static and/or time dependent) can dominate all other relaxation mechanisms. Both gradients in the static field and (low
 30 frequency) oscillating magnetic fields experienced by the hyperpolarized gas can cause significant relaxation.

Advantageously, an (externally) applied substantially static magnetic holding field " B_H " can substantially protect the hyperpolarized gas from depolarizing effects

attributed to one or more of the EMI and gradient fields during transport. The instant
 invention employs a magnetic holding field which raises the Larmor frequency of the
 hyperpolarized gas above the region of noise ($1/f$), *i.e.* the region where the intensity
 of ambient electromagnetic noise is typically high (this noise is typically under about
 5 5 kHz). Further, a magnetic holding field is also preferably selected such that it raises
 the frequency of the hyperpolarized gas to a level which is above those frequencies
 associated with large acoustic vibrations (these acoustic vibrations are typically less
 than about 20 kHz). As will be discussed below, the increased frequency associated
 with the applied magnetic holding field advantageously allows a transport unit
 10 (Figure 16) to have greater electromagnetic shielding effectiveness for a given
 housing thickness (the housing used to hold the hyperpolarized gas therein during
 transport and/or storage). The skin depth " δ " of a conductive shielding material is
 inversely proportional to the square root of the frequency. Thus, at 25 kHz, an
 exemplary skin depth for aluminum is about 0.5 mm, as compared to about 2.0 mm at
 15 1.6 kHz.

Preferably, the magnetic holding field of the instant invention is selected so
 that any external field-related fluctuations are small in magnitude compared to the
 field strength of the holding field; in this way the holding field can minimize the
 hyperpolarized gas's response to unpredictable external static field gradient-induced
 20 relaxation. This can be accomplished by applying to the hyperpolarized gas a
 proximately positioned magnetic holding field which is sufficiently strong and
 homogeneous so that it minimizes the unpredictable static field-related relaxation
 during transport and storage. A sufficiently homogeneous holding field preferably
 includes (but is not limited to) a magnetic holding field which has homogeneity which
 25 is on the order of about at least 10^{-3} cm^{-1} over the central part of the holding field (*i.e.*,
 the part in which the gas resides). More preferably, the magnetic holding field
 homogeneity is about at least $5 \times 10^{-4} \text{ cm}^{-1}$. Further, the magnetic holding field should
 be positioned, sized, and configured relative to the hyperpolarized gas such that it also
 minimizes the EMI or oscillating magnetic field depolarization effects. The
 30 depolarizing effect of EMI is preferably (substantially) diminished by applying the
 magnetic holding field (B_H) proximate to the gas so that the resonant frequency of the
 hyperpolarized gas is preferably above or outside the bandwidth of prevalent time-
 dependent fields produced by electrically powered or supplied sources.

Alternatively, or additionally, the external interference can be shielded by positioning a substantially continuous shield or shipping container having at least one layer formed of a conductive material such as metal around the hyperpolarized gas in the container. The preferred shielding thickness is related to the spatial decay constant of an electromagnetic wave or skin depth δ . The skin depth δ at an angular frequency ω is given by $\delta = c/(2\pi\mu\sigma\omega)^{1/2}$, where μ is the magnetic permeability and σ is the electrical conductivity of the material. At these frequencies, the Larmor radiation wavelength is long (~10 km), and is much larger than the container size. The shielding effectiveness is therefore dependent upon the container geometry as well as the shielding thickness. For a thin spherical conductor of radius a and thickness t , the shielding factor for wavelengths $\lambda \gg a$ is given approximately by

$$F = (1 + (2at/3\delta^2)^2)^{1/2}$$

Interestingly, the shielding effectiveness increases as the size (radius) of the shield is increased. It is therefore preferred that a metallic enclosure used to shield or surround the hyperpolarized gas be configured to define an internal volume which is sufficient to provide increased shielding effectiveness. Stated differently, it is preferred that the walls of the enclosure are spaced apart a predetermined distance relative to the position of the gas container.

Alternatively, or additionally, a transport unit can be configured with at least one layer formed from about 0.5 mm thick of magnetically permeable material, such as ultra low carbon steel soft iron, or mu-metals (by virtue of their greater magnetic permeability). However, these materials may significantly influence the static magnetic field and must be designed accordingly not to affect the homogeneity adversely.

Irrespective of the skin depth of the materials (types of materials and number of layers) used to form a shipping container enclosure, application of a homogeneous magnetic holding field proximate to the hyperpolarized gas can help minimize the gas depolarization by virtue of decreasing the skin depth δ , which is inversely proportional to the square root of the frequency. Further, it helps by pushing the resonant frequency of the gas outside the bandwidth of common AC fields. It is

preferred that the resonant frequency of the hyperpolarized gas be raised such that it is above about 10 kHz, and more preferably be raised such that it is between about 20-30 kHz. Stated differently, it is preferred that for shielding, the applied magnetic holding field have a field strength of about 2 to 35 Gauss (0.2-3.5mT). It is more preferred that for ^{129}Xe , the magnetic holding field is preferably at least about 20 Gauss; and for ^3He , the magnetic holding field is preferably at least about 7 Gauss (0.7mT). See co-pending and co-assigned provisional U. S. Patent Application No. 60/121,315 for additional shielding method details and preferred transport unit configurations.

10

Preconditioning the Container

Preferably, due to susceptibility of the hyperpolarized to paramagnetic oxygen as noted above, the storage container 10 is preconditioned to remove contaminants. That is, it is processed to reduce or remove the paramagnetic gases such as oxygen from within the chamber and container walls. For containers made with rigid substrates, such as Pyrex™, UHV vacuum pumps can be connected to the container to extract the oxygen. However, a roughing pump can also be used which is typically cheaper and easier than the UHV vacuum pump based process for both resilient and non-resilient containers. Preferably, the bag is processed with several purge/pump cycles, e.g., pumping at or below 20 mtorr (2.7Pa) for one minute, and then directing clean buffer gas (such as Grade 5 or better nitrogen) into the container at a pressure of about one atm (101KPa) or until the bag is substantially inflated. The oxygen partial pressure is then reduced in the container. This can be done with a vacuum but it is preferred that it be done with nitrogen. Once the oxygen realizes the partial pressure imbalance across the container walls, it will outgas to re-establish equilibrium. Stated differently, the oxygen in the container walls is outgassed by decreasing the partial pressure inside the container chamber. Typical oxygen solubilities are on the order of .01-.05; thus, 95-99% of the oxygen trapped in the walls will transition to a gas phase. Prior to use or filling, the container is evacuated, thus harmlessly removing the gaseous oxygen. Unlike conventional rigid containers, polymer bag containers can continue to outgas (trapped gases can migrate to the chamber because of pressure differentials between the outer surface and the inner surface) even after the initial purge and pump cycles. Thus, care should be taken to minimize this behavior especially when the final filling

is not temporally performed with the preconditioning of the container. Preferably, a quantity of clean filler gas (such as Grade 5) is directed into the bag (to substantially equalize the pressure between the chamber and ambient conditions) and sealed for storage in order to minimize the amount of further outgassing that may occur when the bag is stored and exposed to ambient conditions. This should substantially stabilize or minimize any further outgassing of the polymer or container wall materials. In any event, the filler gas is preferably removed (evacuated) prior to final filling with the hyperpolarized gas. Advantageously, the container of the instant invention can be economically reprocessed (purged, cleaned, etc.) and reused to ship additional quantities of hyperpolarized gases.

It is also preferred that the container or bag be sterilized prior to introducing the hyperpolarized product therein. As used herein the term "sterilized" includes cleaning containers and contact surfaces such that the container is sufficiently clean to inhibit contamination of the product such that it is suitable for medical and medicinal purposes. In this way, the sterilized container allows for a substantially sterile and non-toxic hyperpolarized product to be delivered for *in vivo* introduction into the patient. Suitable sterilization and cleaning methods are well known to those of skill in the art.

20 Measuring Gas Solubility in a Polymer or Liquid

In the past, measuring gas solubilities of most polymers has been time consuming and difficult, and in the case of helium, usually inaccurate. However, as discussed above, the hyperpolarized gas relaxation time, T_1 , is now determined to be proportional to gas solubility. Advantageously, due to the recognition and determination of the relationships discussed above, hyperpolarized noble gases such as ^3He and ^{129}Xe can be used to determine or measure the gas solubility in a polymer or liquid. This information can be valuable for quickly assessing the structures of the polymer. In addition, a given polymer sample can be evaluated using both ^{129}Xe and ^3He gases, as each can give complimentary information. For example, ^3He will sample a greater depth of the polymer based on its greater diffusion coefficients.

Preferably, as shown in Figure 20, a first quantity of a hyperpolarized gas is introduced into a container (Block 300). A first relaxation time is measured of the hyperpolarized gas in the container (Block 310). A selected material sample is

positioned in the container (Block 320). A second quantity of a hyperpolarized noble gas is introduced into the container (Block 330). A second relaxation time is measured associated with the sample and the gas in the container (Block 340). The gas solubility is determined based on the difference between the two relaxation times
 5 (Block 350). Preferably this is determined according to equation (2.23c). The material sample can be a physical or solid sample or a liquid as described above.

Although the sample used above was a geometrically fixed polymer sample, the method can also be used to determine gas solubilities in liquids or fluids. For example, instead of placing a polymer sample into the chamber, a liquid can be
 10 introduced. The liquid will preferably be introduced in a quantity which is less than the free volume of the chamber as it will conform to the shape of the chamber to define an associated volume and surface area. The polarized gas can then be directed into the chamber with the liquid and the relaxation rate determined due to the specific liquid. This can be especially helpful in formulating carrier substances for injection
 15 formulations of hyperpolarized ^{129}Xe and ^3He .

EXAMPLES

In the examples provided below, the polymer contact surface is assumed to be present at a depth corresponding to a plurality of critical length scales as discussed
 20 above.

EXAMPLE 1: ^3He LDPE/HDPE Bag

An exemplary one liter patient delivery bag, such as is shown in Figure 7, is a 7 inch x 7 inch square. The expected T_1 for ^3He can be determined using (Equation
 25 2.4) and the theoretical relaxivity of LDPE for ^3He quoted in Table 4.3. The associated area ($A=2*18\text{cm}*18\text{cm}$) is 648cm^2 , the volume is 1000 cubic centimeters, and the relaxivity is 0.0012cm/min. Equation 2.4 leads to a T_1 of about 1286 min or 21.4 hours for an LDPE bag configured and sized as noted above (absent other relaxation mechanisms). For a bag made of HDPE, which has a lower relaxivity
 30 value of about 0.0008 cm/min (attributed to the lower ^3He solubility), the T_1 is estimated at 32 hours. In deuterated HDPE, the T_1 is expected to be about 132 hours.

EXAMPLE 2: ^{129}Xe LDPE/Nylon Bag

The same 1 liter LDPE patient delivery bag as described in Example 1 contains hyperpolarized ^{129}Xe . Volume and surface area are the same but the theoretical relaxivity is 0.0419 cm/min (Table 4.2) for ^{129}Xe on LDPE. The relaxivity is much higher because of the higher solubility of ^{129}Xe in LDPE compared to He ($S_{\text{Xe}}=0.68$ vs $S_{\text{He}}=0.006$). For this configuration, T_1 is estimated at 36.8 minutes. Similarly, for the measured relaxivity for Nylon-6 of 0.0104 cm/min, predict T_1 is predicted to be about 148 min or about 2.4 hours. This value is close to what has been measured for the presently used TedlarTM bags.

10

EXAMPLE 3: Metal Film Surface

In this example, metal film coatings are used as the contact surface. The 7" x 7" square (18cm x 18cm) bag described in Example 1 is employed but coated or formed with high purity aluminum on its internal contact surface (the surface in contact with the hyperpolarized gas). The relaxivity of high purity aluminum for ^{129}Xe has been recently measured to be about 0.00225 cm/min. (One readily available material suitable for use is Reynold'sTM heavy duty freezer foil). Doing the calculation, one can obtain a container with an extended T_1 for xenon of about 11.43 hours. This is a great improvement in T_1 for Xe. Similarly, the use of such metal film surfaces for ^3He can generate T_1 's in the range of thousands of hours (the container no longer being a limiting factor as these T_1 's are above the theoretical collisional relaxation time described above). Metals other than aluminum which can be used include indium, gold, zinc, tin, copper, bismuth, silver, niobium, and oxides thereof. Preferably, "high purity" metals are employed (*i.e.*, metals which are substantially free of paramagnetic or ferrous impurities) because even minute amounts of undesirable materials or contaminants can degrade the surface. For example, another high purity aluminum sample tested had a relaxivity of about 0.049 cm/min, a full 22 times worse than the sample quoted above. This is most likely due to the presence of ferrous or paramagnetic impurities such as iron, nickel, cobalt, chromium and the like. Preferably, the metal is chosen such that it is well below 1ppm in ferrous or paramagnetic impurity content.

30

EXAMPLE 4: Multiple Materials

Using the bag configured as noted in Example 1, one can determine the effects of the addition of multiple materials. For example, a 5cm² silicone gasket positioned on the 1 liter deuterated HDPE bag (described in Example 1 (for ³He)) with a starting

5 T₁ of 132 hours will reduce the container's associated relaxation time. As pointed out in Equations 2.5, 2.6, relaxation rates are additive. Thus, to properly determine the container or equipment relaxation time, the relaxivities and corresponding surface areas of all the materials adjacent the free volume should be evaluated. The hypothetical silicone gasket, with an exemplary area "A" of 5cm², the measured

10 relaxivity of 0.0386cm/min (p. 47, table 4.3), and free volume still at 1000cc, gives a relaxation rate of about 1.9x 10⁻⁴/min. Adding the rate due to the bag itself (1.3x10⁻⁴/min) yields a total rate of about 3.2x10⁻⁴/min which is inverted to get a T₁ of about 52 hours. Therefore, it is apparent that adding a very small surface area of a poor material can drastically shorten the T₁ despite the fact that most of the container

15 material is good. Indeed, many commercially used O-ring materials can have relaxivities an order of magnitude higher than the one described, making the situation even worse. Thus, it is important to use substantially pure (impurity free) materials. The relaxivity for an available "off the shelf" silicone O-ring for ¹²⁹Xe was measured at about 0.2-0.3 cm/min. For example, using the measured ¹²⁹Xe relaxivity numbers

20 for the ³He deuterated HDPE container will reduce the 132 hour bag down to just 15 hours (a full order of magnitude deterioration). The key is that every gasket, coupling, valve, tubing or other component that is added to the bag or container (especially those that are in fluid communication with the hyperpolarized gas) is preferably made of the friendliest possible material relative to the hyperpolarized

25 state.

EXAMPLE 5: Measurement of Specific Material Properties

Measurement of specific material properties such as the relaxivities of materials is described above. For example, as noted in equation 2.5, relaxation rates

30 attributed to various relaxation mechanisms are additive. Therefore, in order to measure the specific material property, a spin-down chamber such as that described herein can be used to determine two relaxation times for a hyperpolarized gas. Using the chamber consisting of two hemispheres sealed with an O-ring, the chamber is

closed, HP ("hyperpolarized gas") is introduced therein, and the relaxation time T_1 is measured. Then the chamber is opened, a sample of known surface area is inserted, and the process is repeated to measure a new T_1 . The new T_1 will be less than the old because a new relaxing surface has been added while keeping the free volume roughly the same. The difference between the two relaxation times is attributed to the relaxivity of the added material specimen. Thus, the difference can be used to calculate the material relaxivity using equation (2.10).

EXAMPLE 6: Validation of the Sorption Model

Figures 4.1 and 4.2 show the calculated and experimental T_1 values for ^{129}Xe and ^3He , respectively, in a 1 cc sphere for different surface materials as plotted against the product of solubility (S) and the square root of the molar density of protons in the material matrix $[\text{H}]^{.5}$. The 1cc sphere value incorporates both volume and surface area and is a useful T_1 metric corresponding to conventional evaluations, and as such is typically more readily descriptive than the relaxivity parameters described herein. The T_1 value according to equation (2.23c) depends on a number of fixed constants and then depends inversely on gas solubility and the square root of the proton concentration. Experimental values of the measured one cubic centimeter sphere T_1 (T_1^{cc}) for all the polymers are plotted as well and show substantial agreement between theory and experiment, thus validating the sorption model described herein.

The foregoing is illustrative of the present invention and is not to be construed as limiting thereof. Although a few exemplary embodiments of this invention have been described, those skilled in the art will readily appreciate that many modifications are possible in the exemplary embodiments without materially departing from the novel teachings and advantages of this invention. Accordingly, all such modifications are intended to be included within the scope of this invention as defined in the claims. In the claims, means-plus-function clause are intended to cover the structures described herein as performing the recited function and not only structural equivalents but also equivalent structures. Therefore, it is to be understood that the foregoing is illustrative of the present invention and is not to be construed as limited to the specific embodiments disclosed, and that modifications to the disclosed embodiments, as well

as other embodiments, are intended to be included within the scope of the appended claims. The invention is defined by the following claims, with equivalents of the claims to be included therein.

THAT WHICH IS CLAIMED IS:

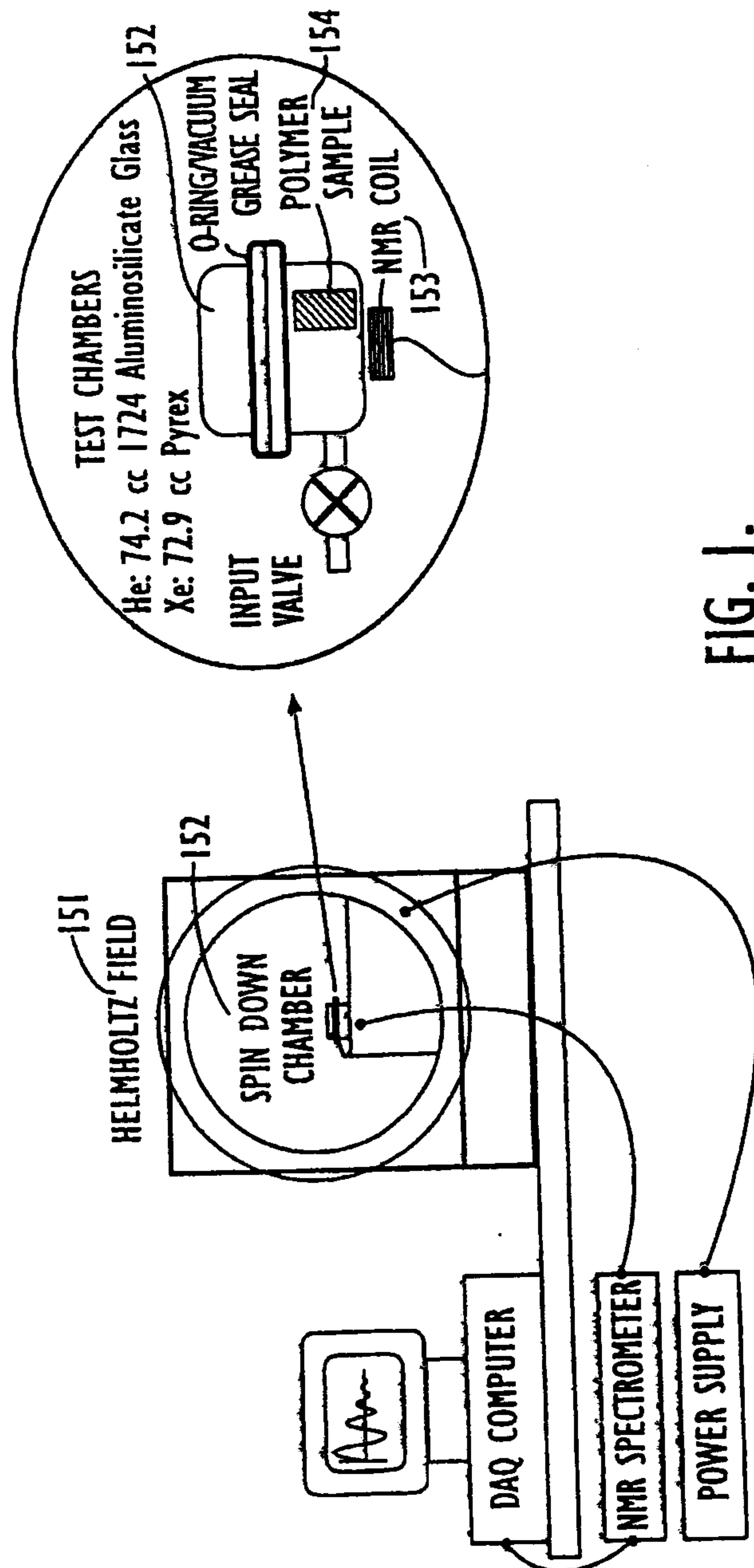
1. A method of preparing an expandable storage container for receiving a quantity of hyperpolarized gas, comprising the steps of:
 - 5 providing a quantity of purge gas into the hyperpolarized gas container;
 - expanding the hyperpolarized gas container by directing a quantity of purge gas therein;
 - collapsing the hyperpolarized gas container by removing purge gas
 - 10 therefrom;
 - outgassing the oxygen in the container walls by decreasing the oxygen partial pressure in the container thereby causing a substantial amount of the oxygen trapped in the walls of the container to migrate into the chamber of the container in the gas phase;
 - 15 filling a container with a quantity of storage nitrogen after said outgassing step to a pressure which minimizes the pressure differential across the walls of the container to minimize further outgassing of the container;
 - storing the container for future use; and
 - removing the storage nitrogen and outgassed oxygen from the
 - 20 container before filling with a quantity of hyperpolarized gas.

2. A method of determining the hyperpolarized gas solubility in a material such as a polymer or fluid, comprising the steps of:
 - introducing a first quantity of hyperpolarized gas into a container;
 - 25 measuring a first longitudinal spin relaxation rate of the hyperpolarized gas in the container;
 - positioning a sample of a desired material in the container;
 - introducing a second quantity of the hyperpolarized noble gas into the container;
 - 30 measuring a second longitudinal spin relaxation rate of the hyperpolarized gas in the container; and

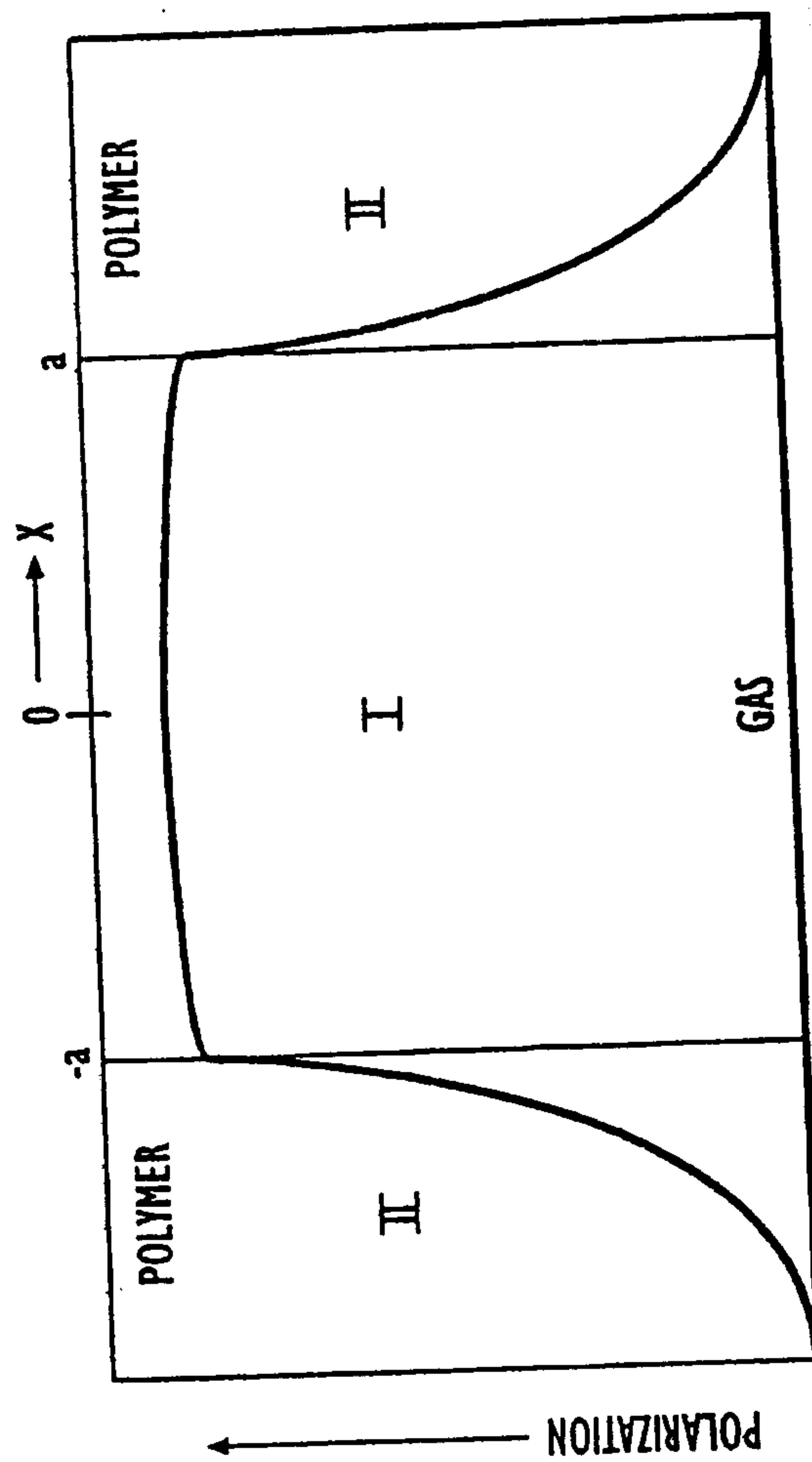
determining the gas solubility of the sample based on the difference between the first and second relaxation rates.

- 5 3. A method according to Claim 2, wherein said sample is a structurally fixed sample having a known geometric shape with a surface formed of the desired material.
4. A method according to Claim 2, wherein said sample is a quantity of
- 10 fluid filling a portion of the free volume in the container.

1/14



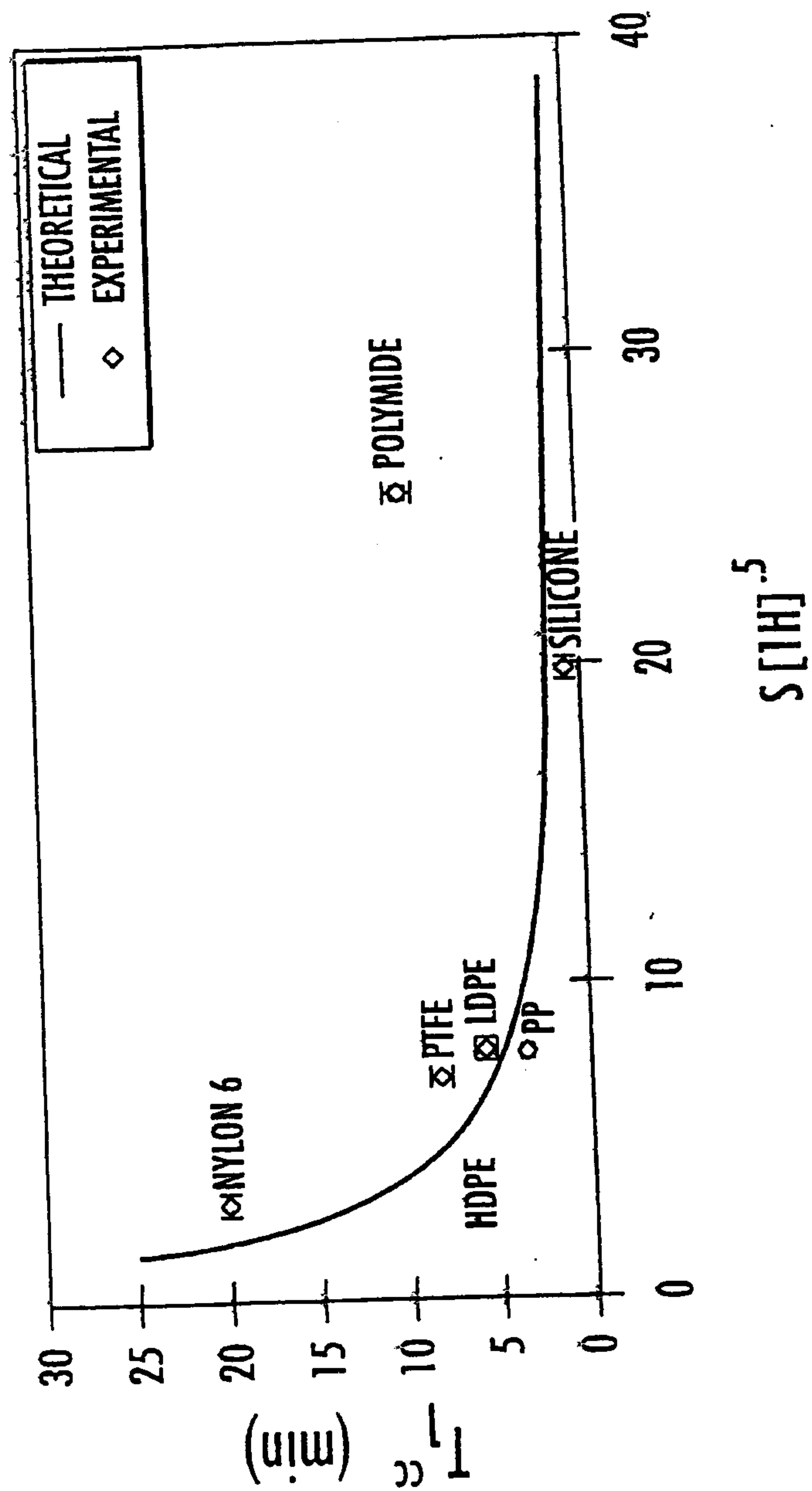
2/14

FIG. 2.

3/14

FIG. 3.

T_1^c vs SOLUBILITY S
POLYMERS IN HYPERPOLARIZED ^{129}Xe



4/14

T_1^{cc} vs SOLUBILITY S POLYMERS IN HYPERPOLARIZED ^3He

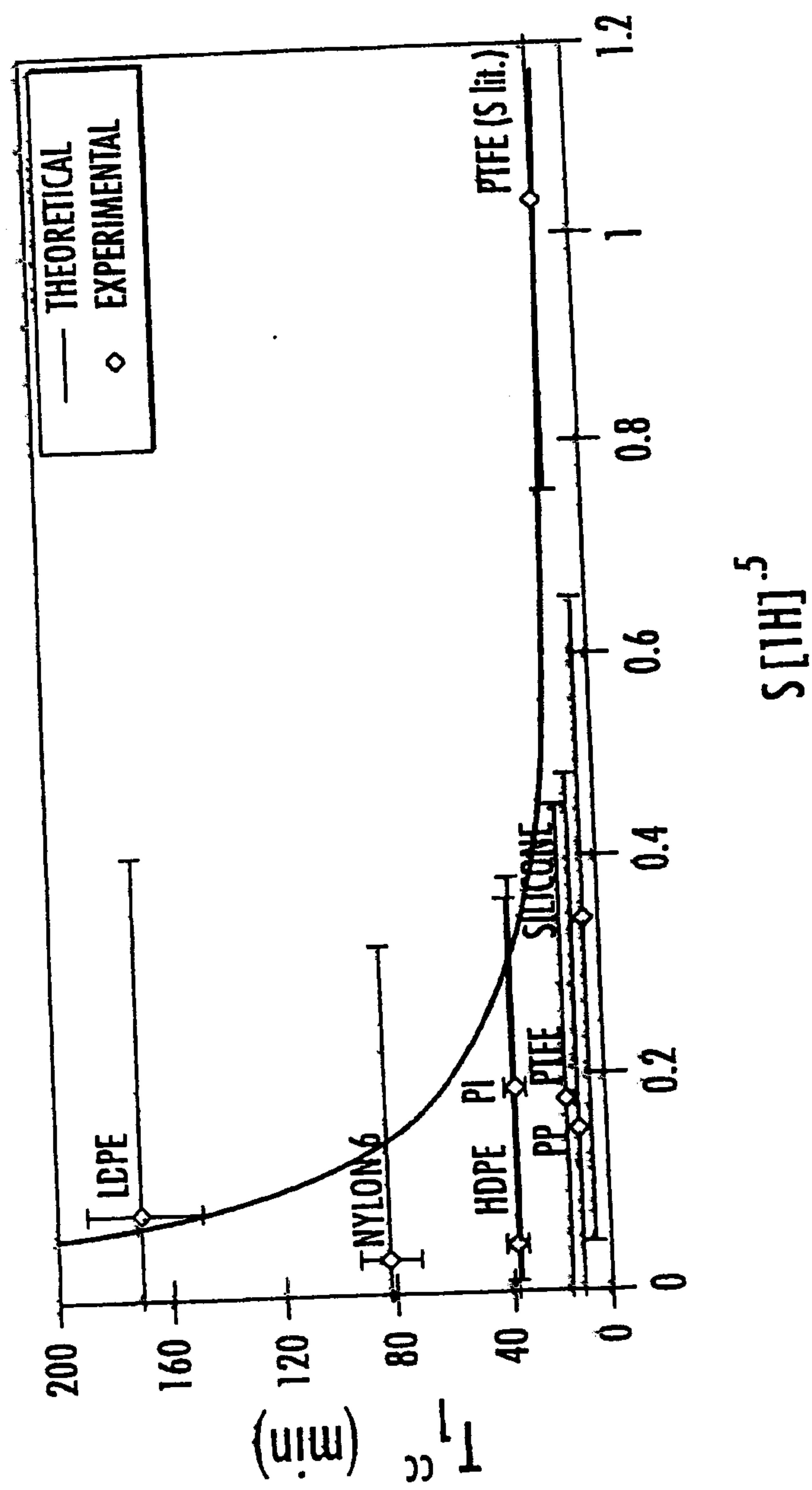


FIG. 4.

5/14

EXPERIMENTAL RESULTS

	MATERIAL	DATE	T _{1c} min	ERROR T _{1c} min	T _{1p} min	ERROR T _{1p} min	RELAXIVITY cm/min	ERROR RELAXIVITY cm/min	T _{1cc} min	ERROR T _{1cc} min
XENON										
	POLYETHYLENE (LDPE)	11.18.97	102	7.32	31.7	1.23	0.0370	0.00391	5.59	0.59
	POLYETHYLENE (HDPE)	11.18.97	113	4.96	33.2	2.18	0.0362	0.00246	5.71	0.39
	POLYPROPYLENE (PP)	11.20.97	123	6.18	25.1	1.35	0.0540	0.00349	3.83	0.25
	POLYTETRAFLUOROETHYLENE (PTFE)	11.25.97	107	3.67	41.7	2.12	0.0249	0.00162	8.30	0.54
	POLYAMIDE - NYLON 6	11.25.97	118	6.96	68.6	2.55	0.0104	0.00156	19.91	2.99
	SILICONE ELASTOMER	12.17.97	118	2.58	5.23	0.299	0.3112	0.00717	0.67	0.02
	POLYIMIDE (PI)	12.18.97	126	5.98	49.1	1.33	0.0212	0.00169	9.78	0.78
HELIUM										
	POLYETHYLENE (LDPE)	3.31.98	700	28.1	470	5.16	0.0012	0.00015	170.80	21.22
	POLYETHYLENE (HDPE)	5.10.98	681	45.98	213.4	2.9	0.0056	0.00055	37.11	3.66
	POLYPROPYLENE (PP)	5.4.98	681	45.98	75.2	0.5	0.0205	0.00156	10.09	0.77
	POLYTETRAFLUOROETHYLENE (PTFE)	4.3.98	700	28.1	98.7	3.28	0.0151	0.00071	13.72	0.65
	POLYAMIDE - NYLON 6	5.11.98	681	45.98	342.3	2.3	0.0025	0.00034	82.18	11.17
	SILICONE ELASTOMER	3.18.98	700	28.1	41.1	1.01	0.0397	0.00169	5.21	0.22
	POLYIMIDE (PI)	5.10.98	681	45.98	217.1	2.7	0.0054	0.00054	38.05	3.78

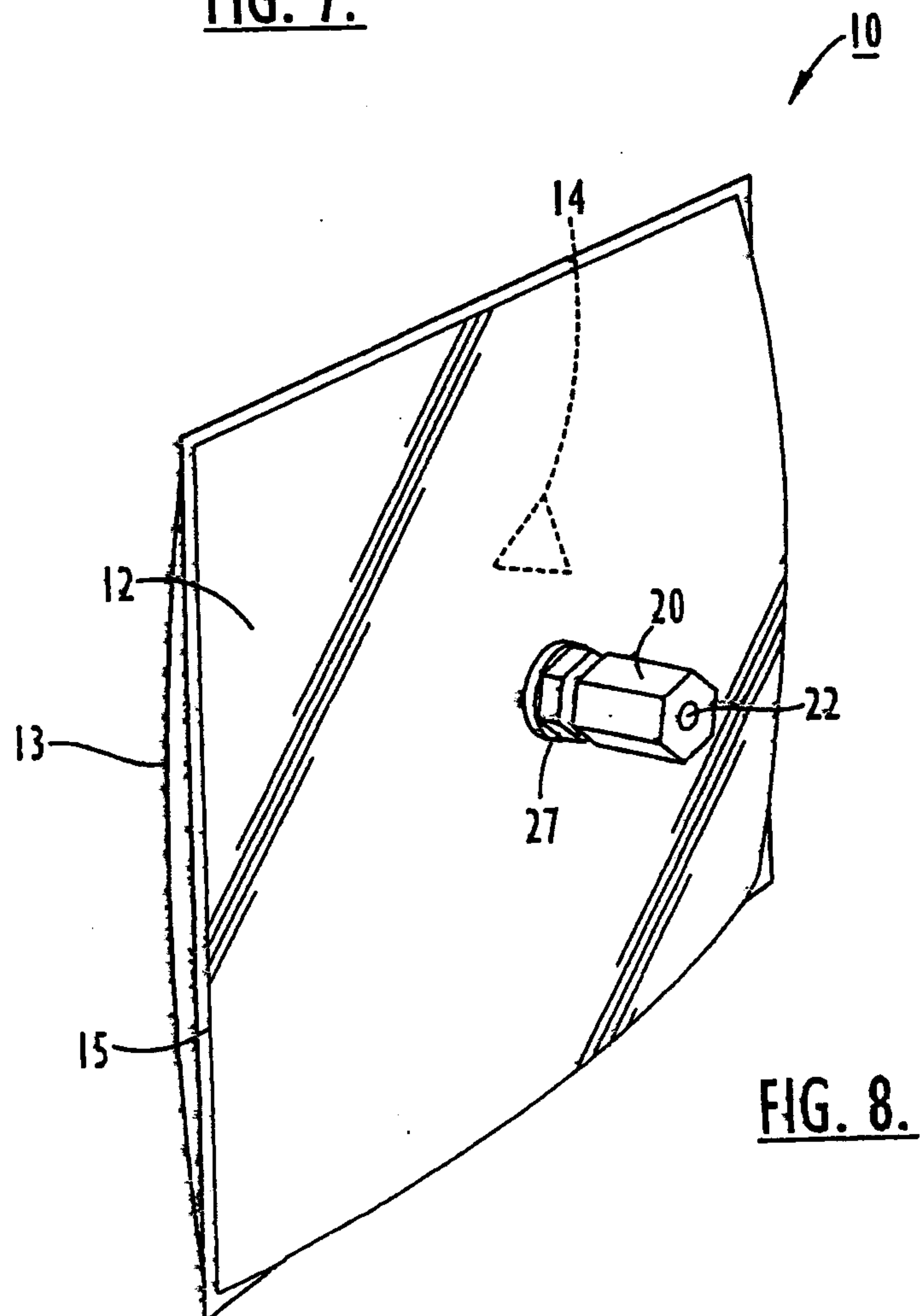
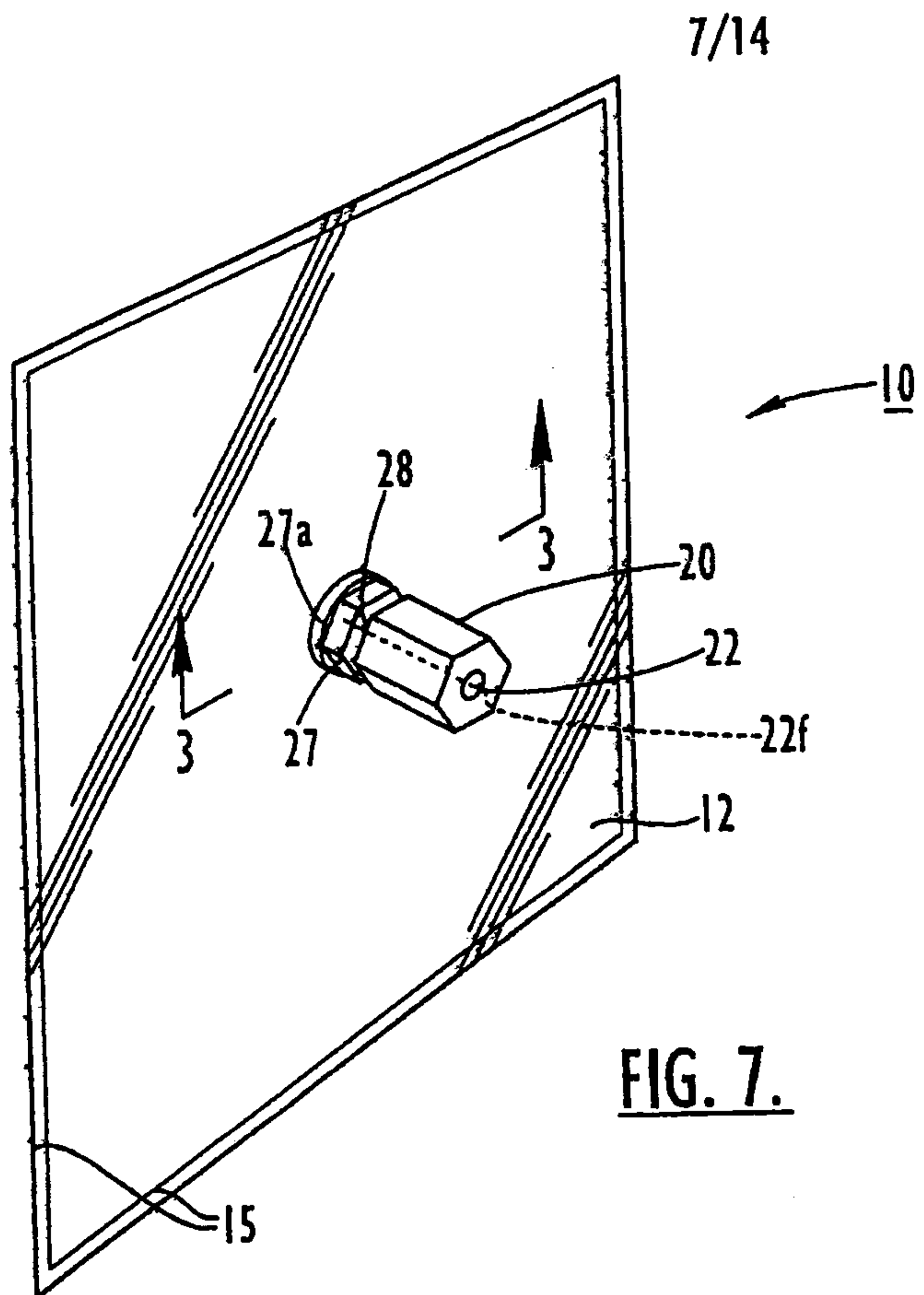
FIG. 5.

6/14

PREDICTED RESULTS

	MATERIAL	S		[1H]	D	T _{1p}	RELAXIVITY	T _{1cc}	LENGTH/SCALE
		(MEASURED)	(LITERATURE)						
XENON									
	POLYETHYLENE (LDPE)	0.683	0.5896	131.43	6.90E-08	0.065	0.0421	4.91	0.67
	POLYETHYLENE (HDPE)	0.424	-	135.71	-	-	0.0266	7.79	-
	POLYPROPYLENE (PP)	0.682	-	128.57	-	-	0.0416	4.98	-
	POLYTETRAFLUOROETHYLENE (PTFE)	0.726	0.7496	88.00	4.00E-09	0.006	0.0366	5.65	0.05
	POLYAMIDE - NYLON 6	0.310	-	98.74	-	-	0.0166	12.49	-
	SILICONE ELASTOMER	1.930	3.9912	105.41	4.80E-06	5.666	0.1066	1.94	52.15
HELIUM	POLYIMIDE (PI)	4.200	-	37.17	-	-	0.1377	1.50	-
	POLYETHYLENE (LDPE)	0.0069	0.0055	131.43	6.80E-06	0.601	0.0014	148.68	20.22
	POLYETHYLENE (HDPE)	0.0035	0.0028	135.71	3.07E-06	0.263	0.0007	288.45	8.98
	POLYPROPYLENE (PP)	0.0130	0.0001	128.57	1.95E-05	1.763	0.0026	79.79	58.63
	POLYTETRAFLUOROETHYLENE (PTFE)	0.0190	0.1104	88.00	8.11E-07	0.126	0.0029	71.57	3.20
	POLYAMIDE - NYLON 6	0.0030	0.0043	98.74	-	-	0.0005	394.53	-
	SILICONE ELASTOMER	0.0340	0.0430	105.41	4.10E-05	4.521	0.0061	33.69	136.14
	POLYIMIDE (PI)	0.0310	-	37.17	-	-	0.0033	62.23	-

FIG. 6.



8/14

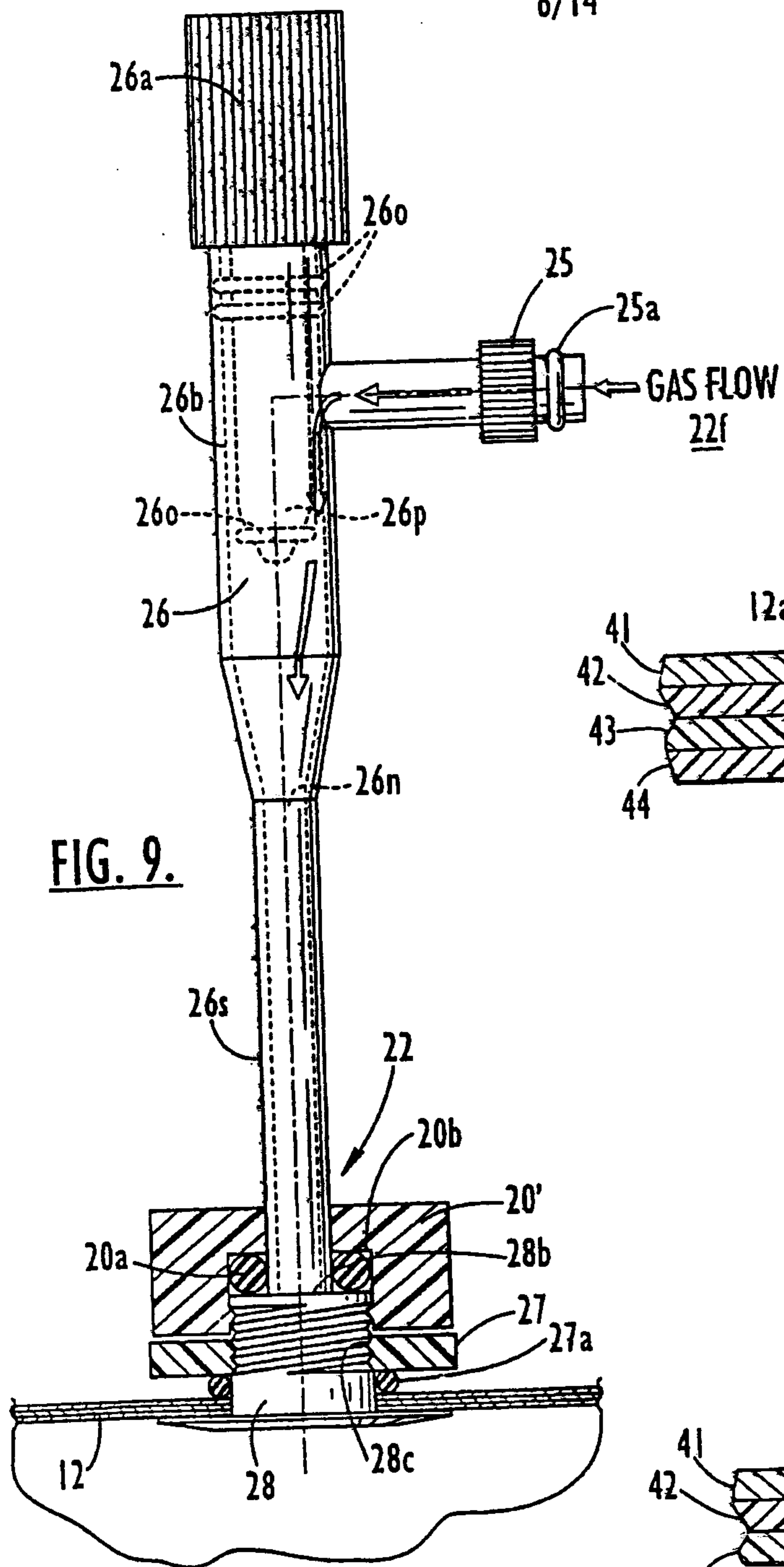


FIG. 9.

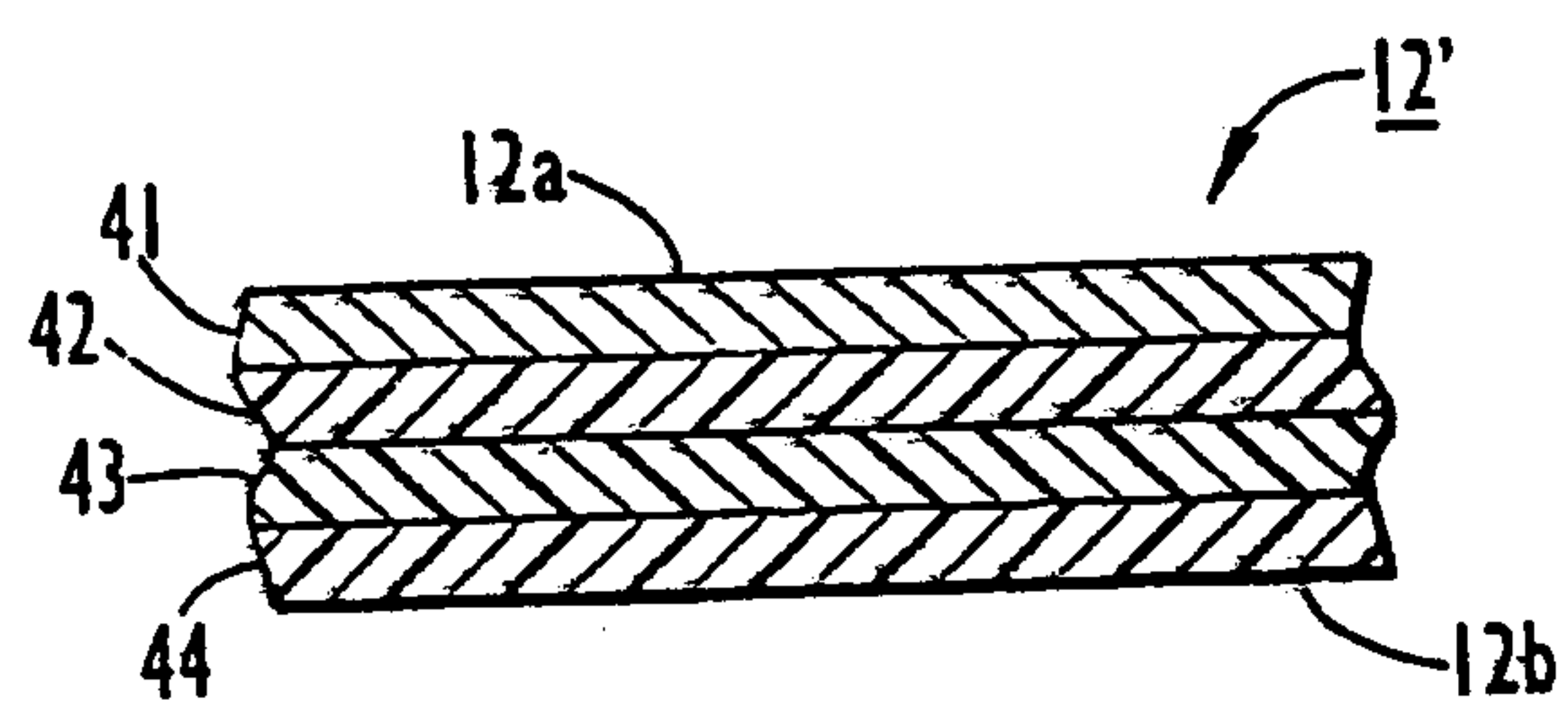


FIG. 10.

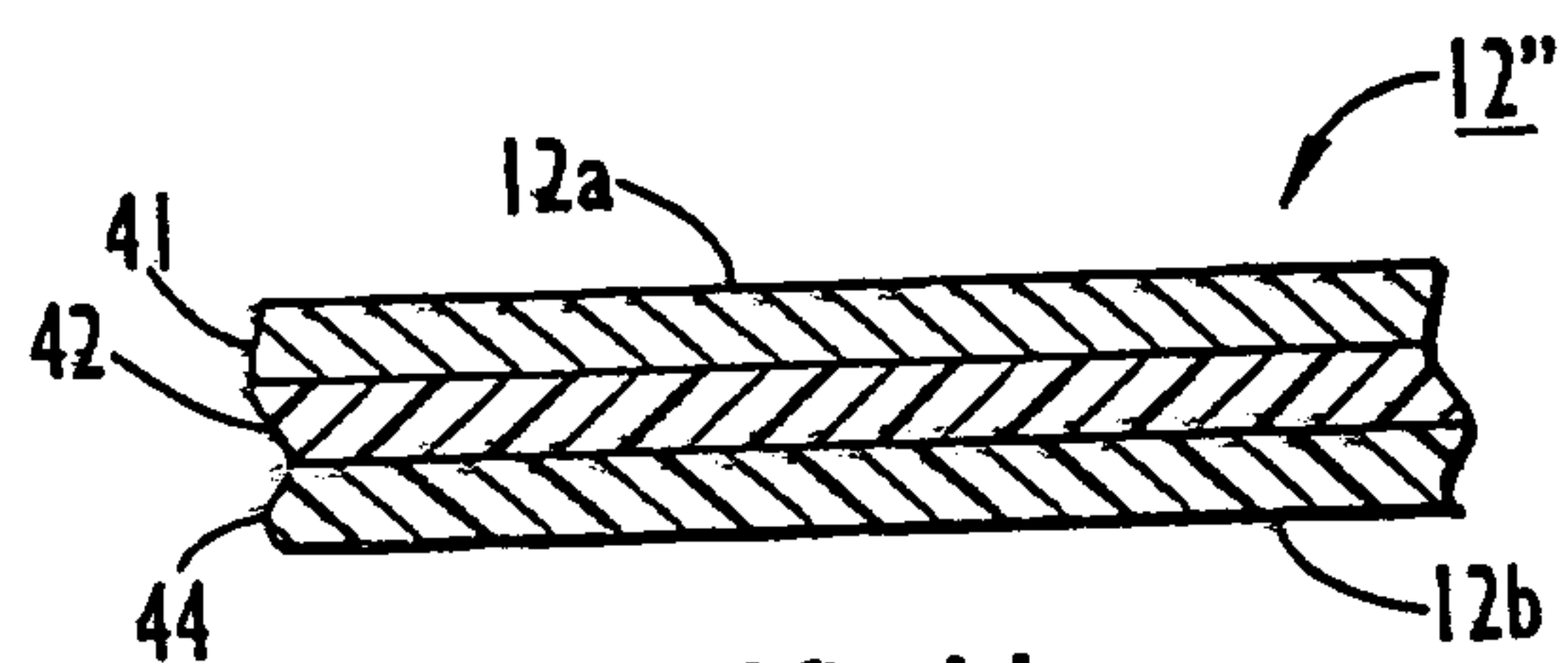


FIG. 11.

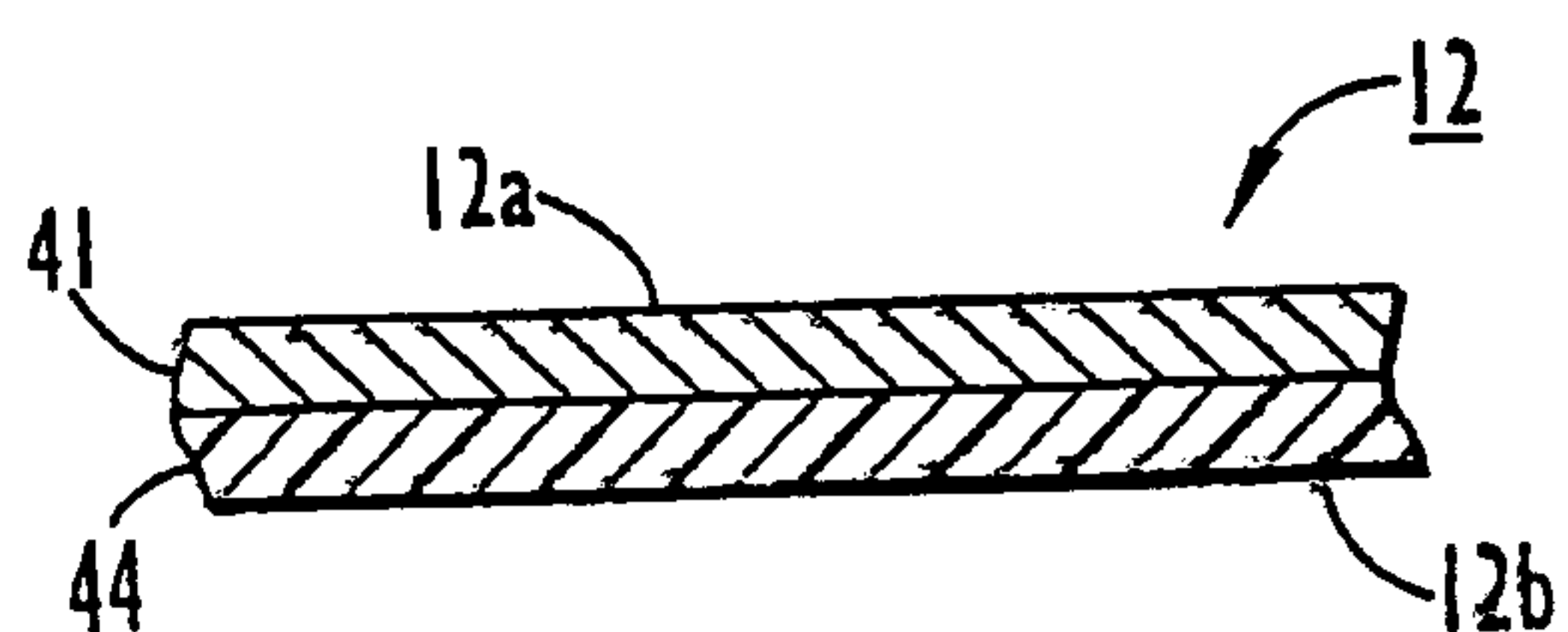


FIG. 12.

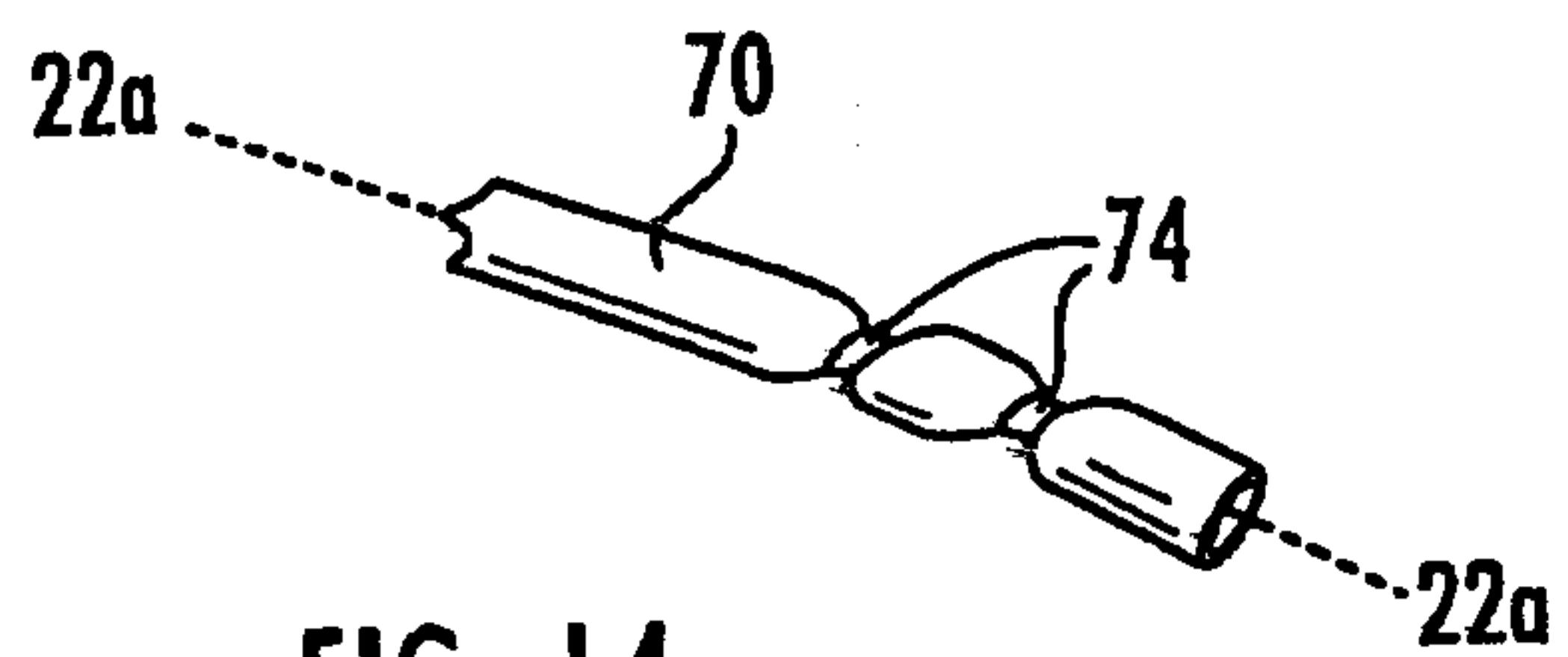
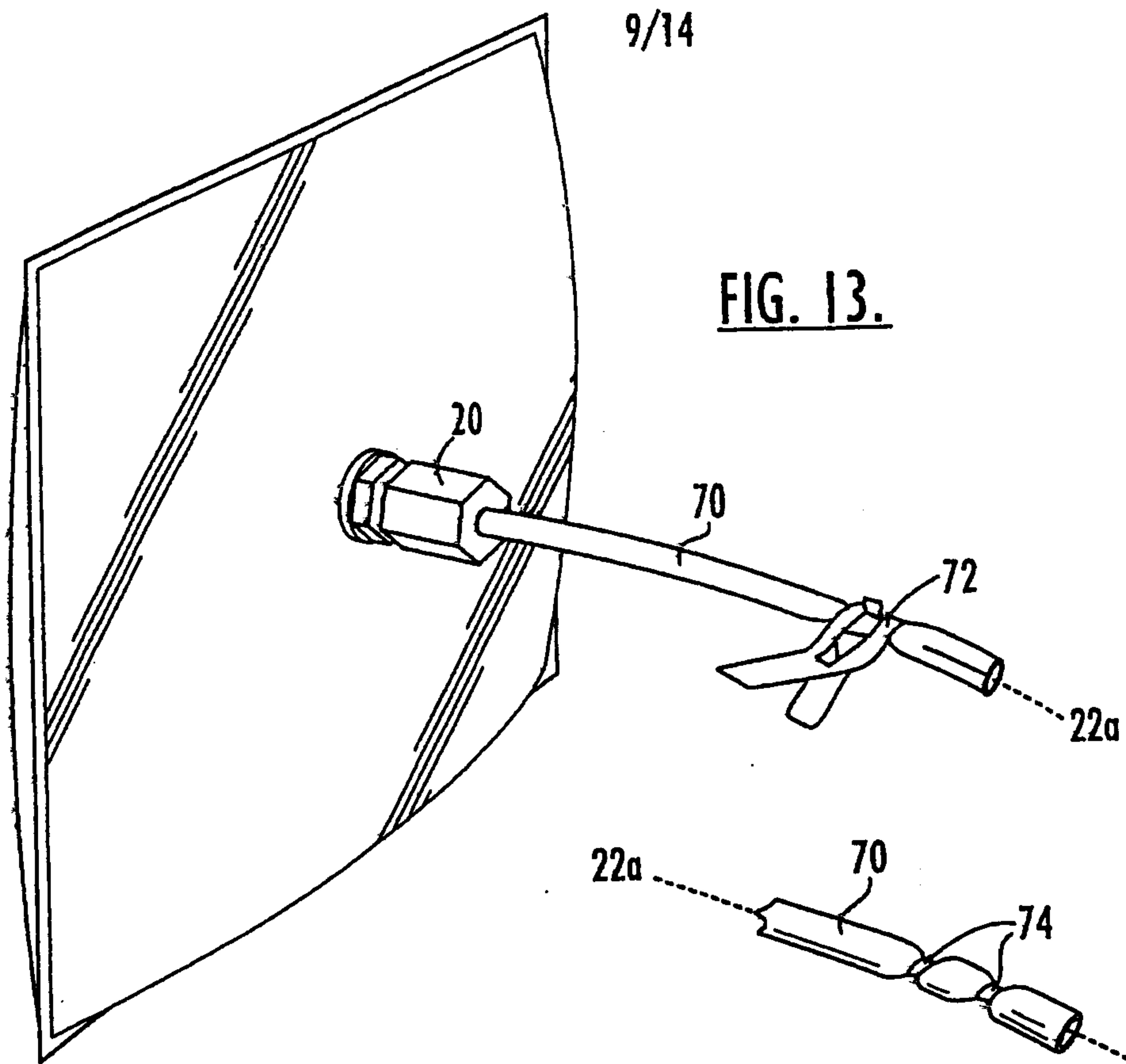


FIG. 14.

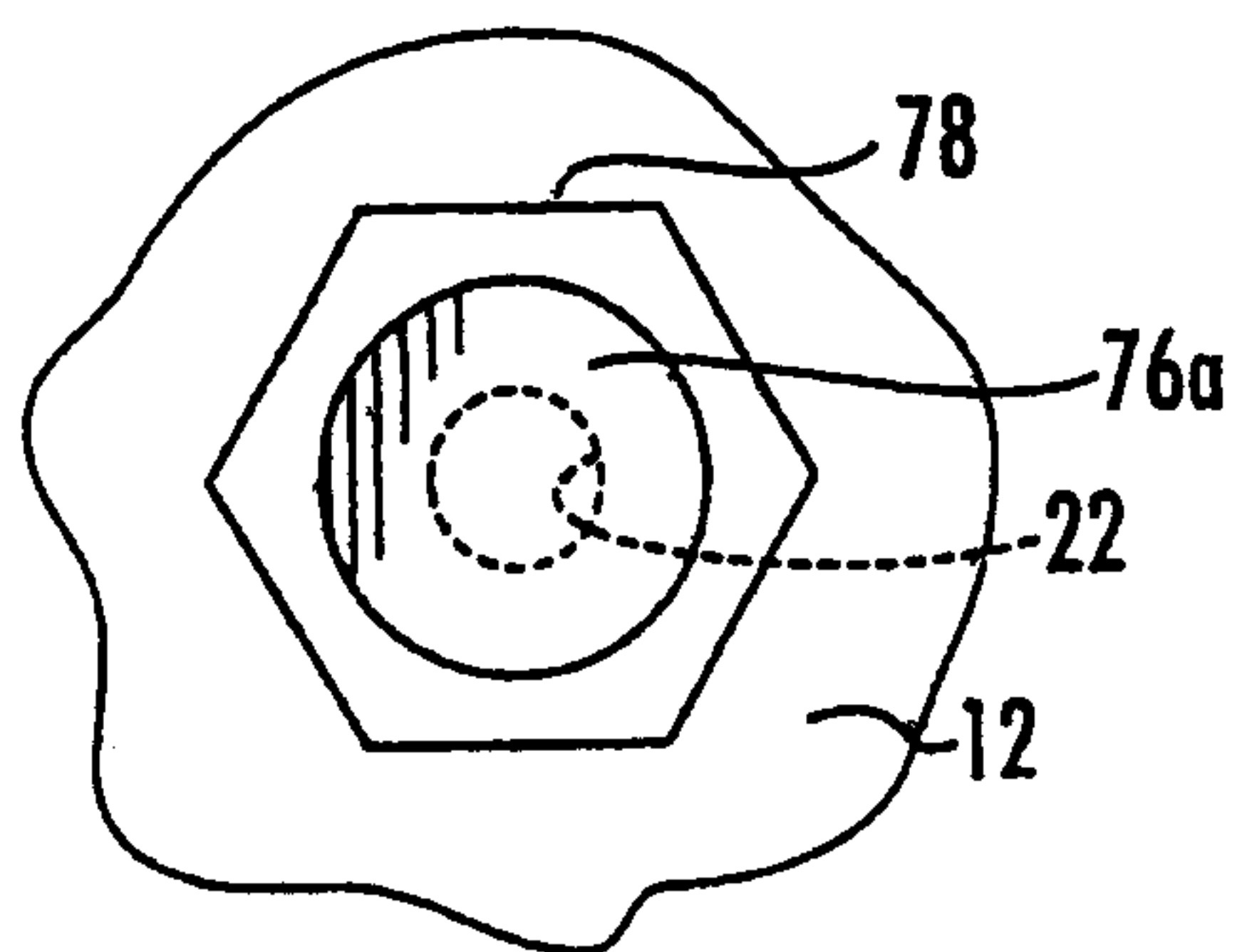
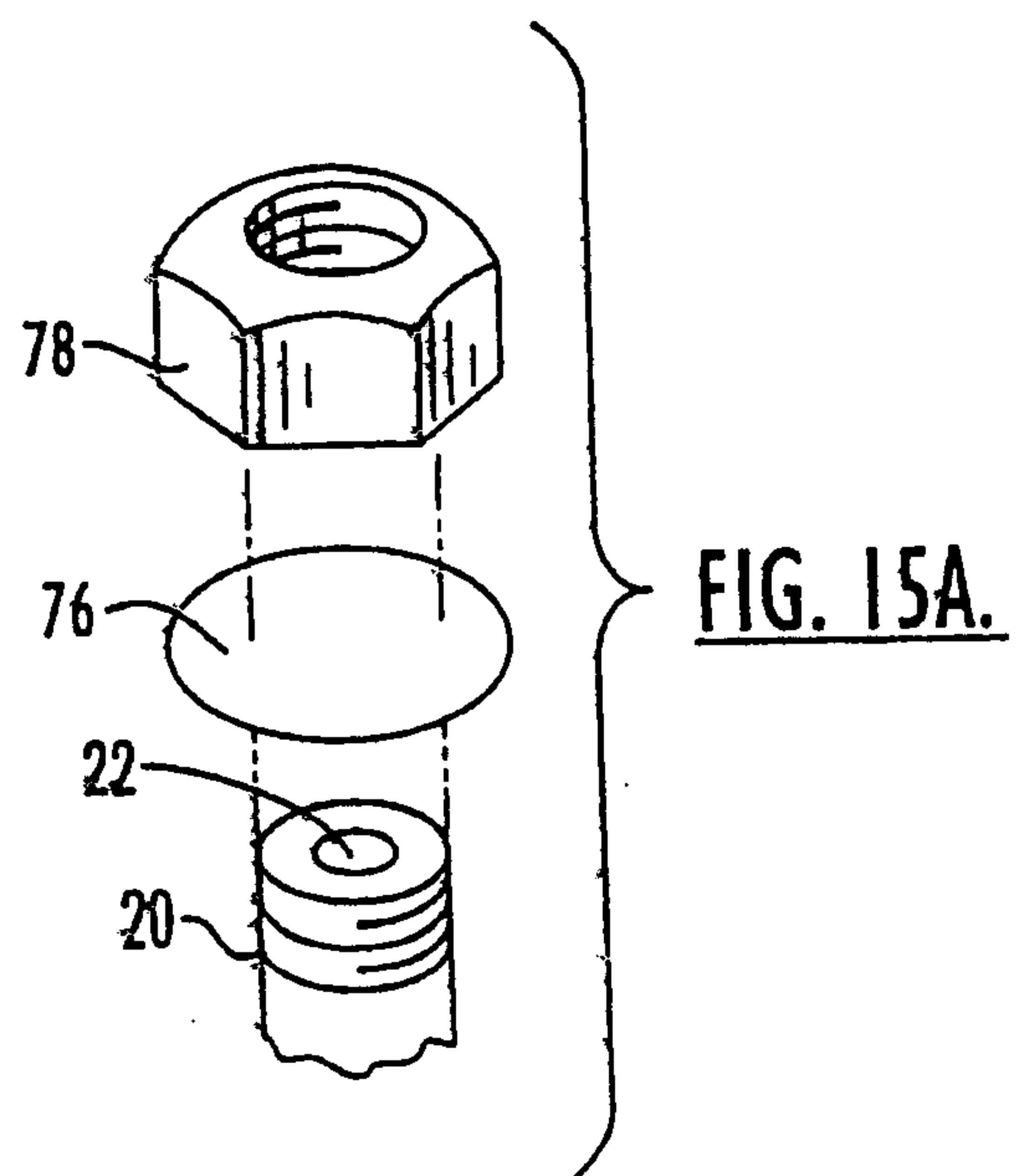


FIG. 15.



10/14

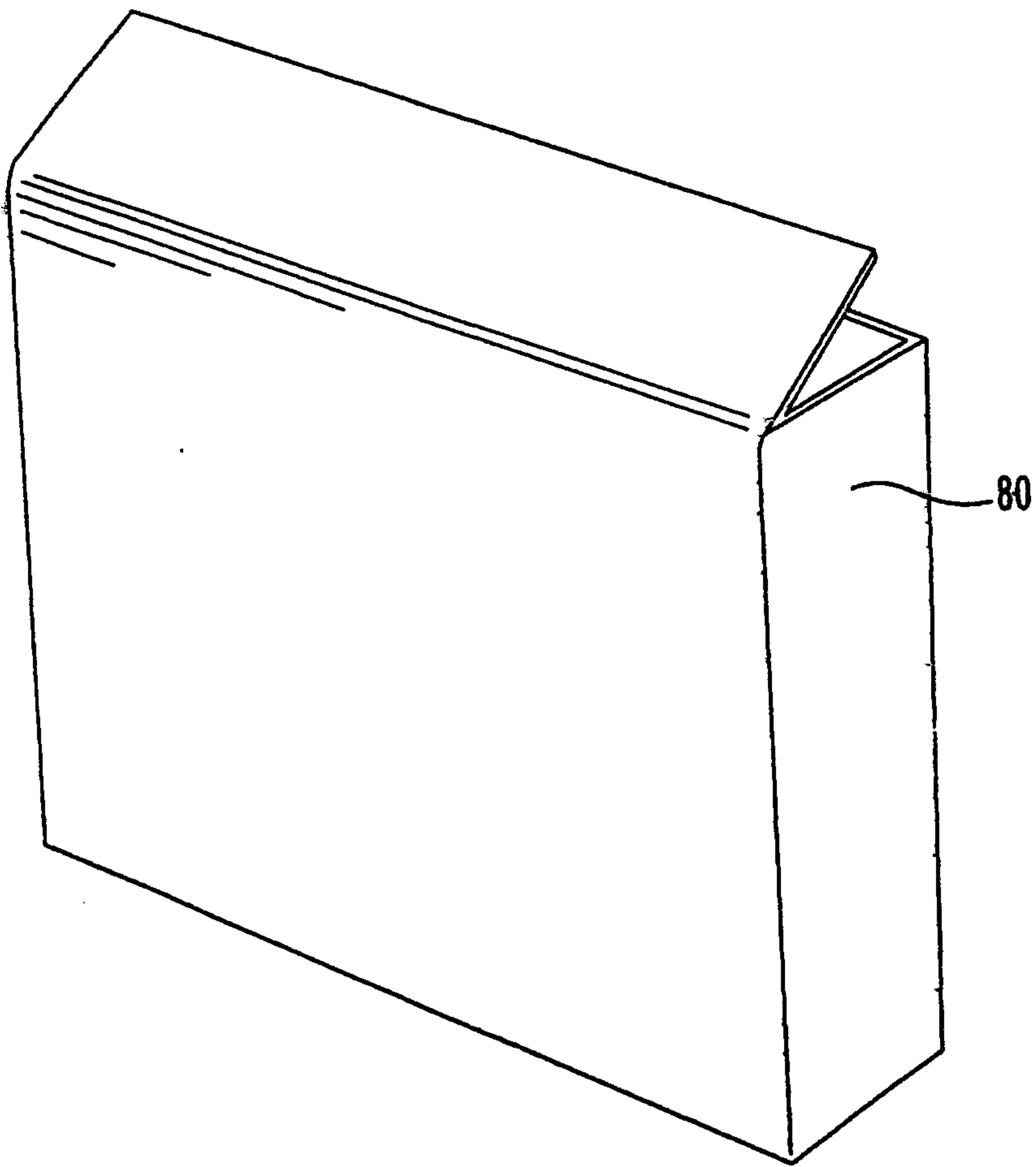


FIG. 16.

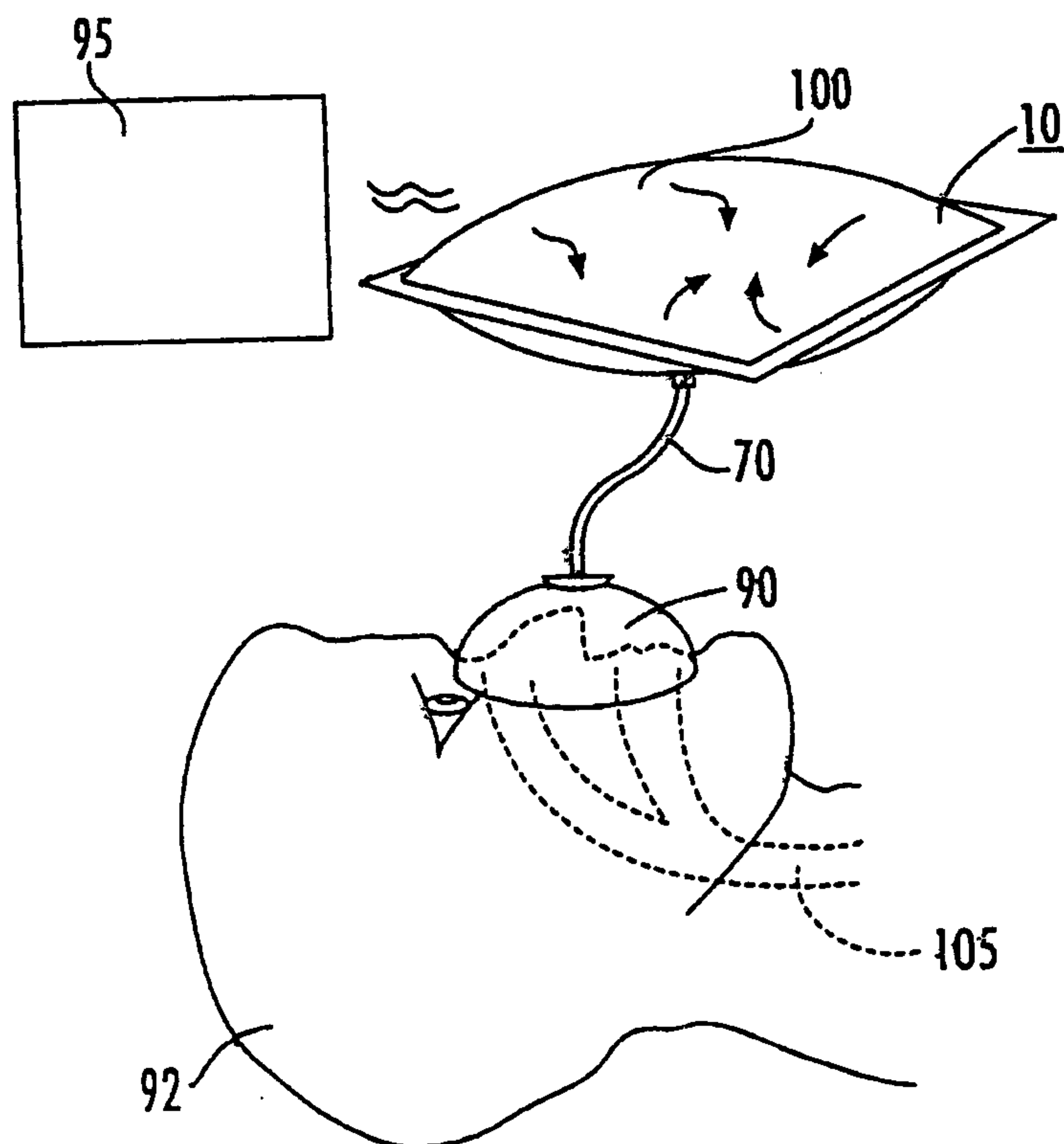


FIG. 17.

11/14

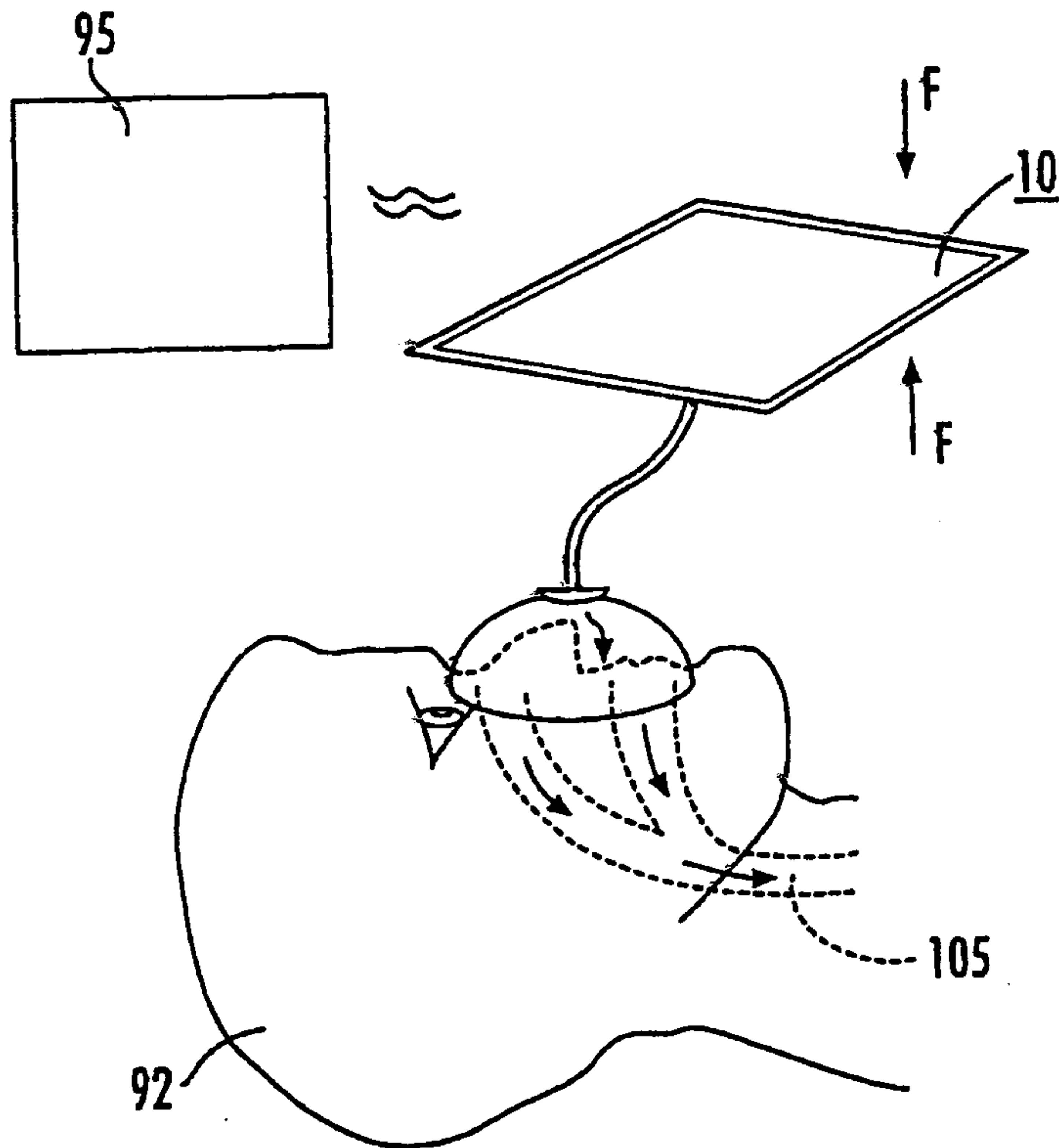


FIG. 18.

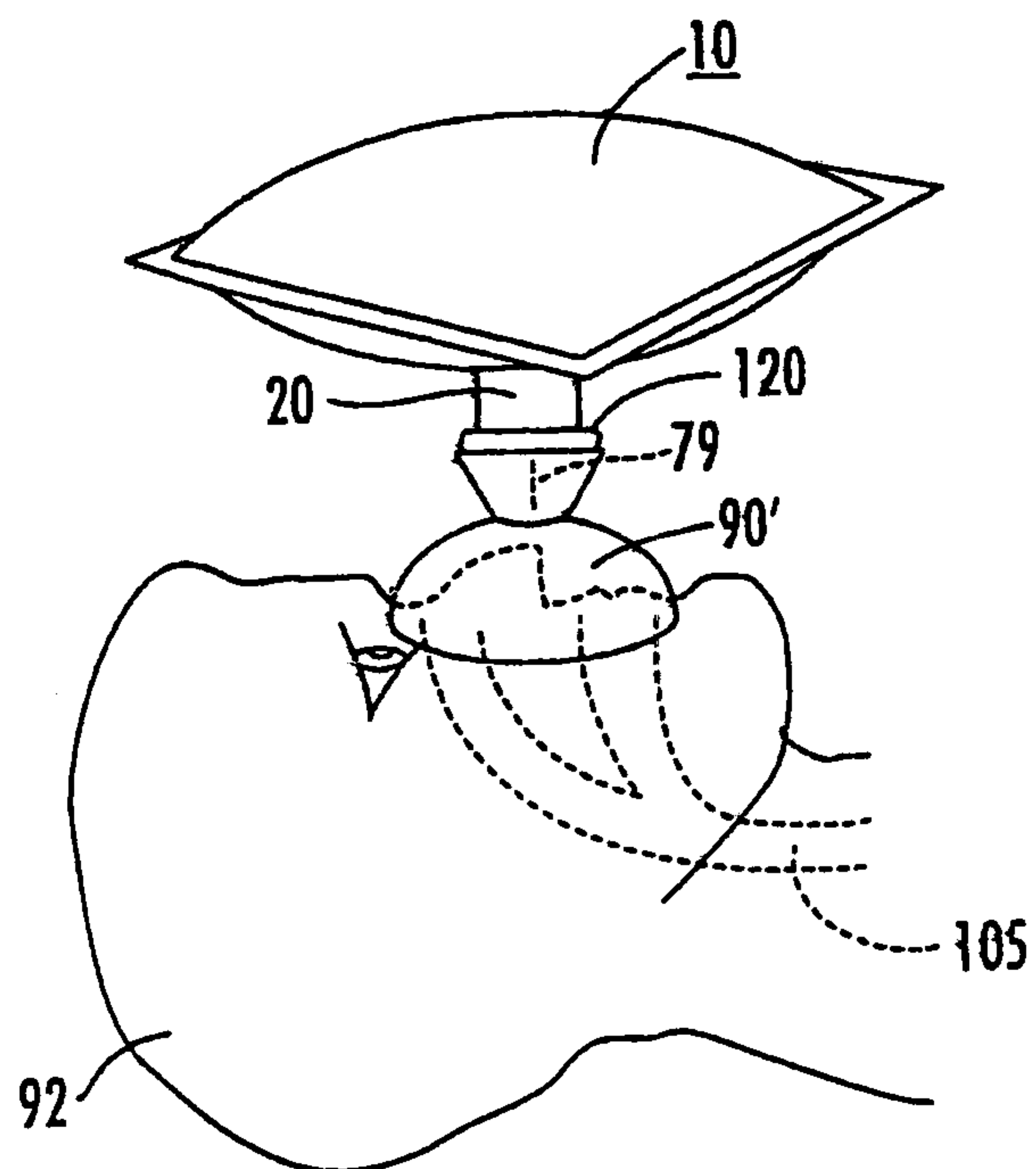
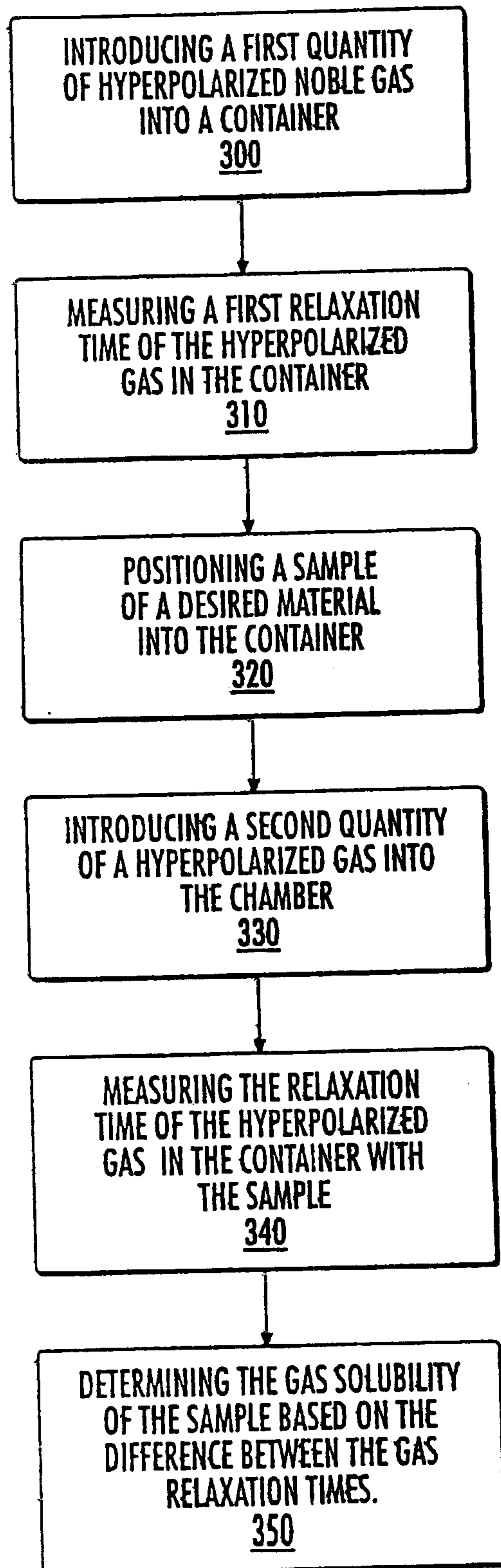


FIG. 19.

12/14

FIG. 20.

13/14

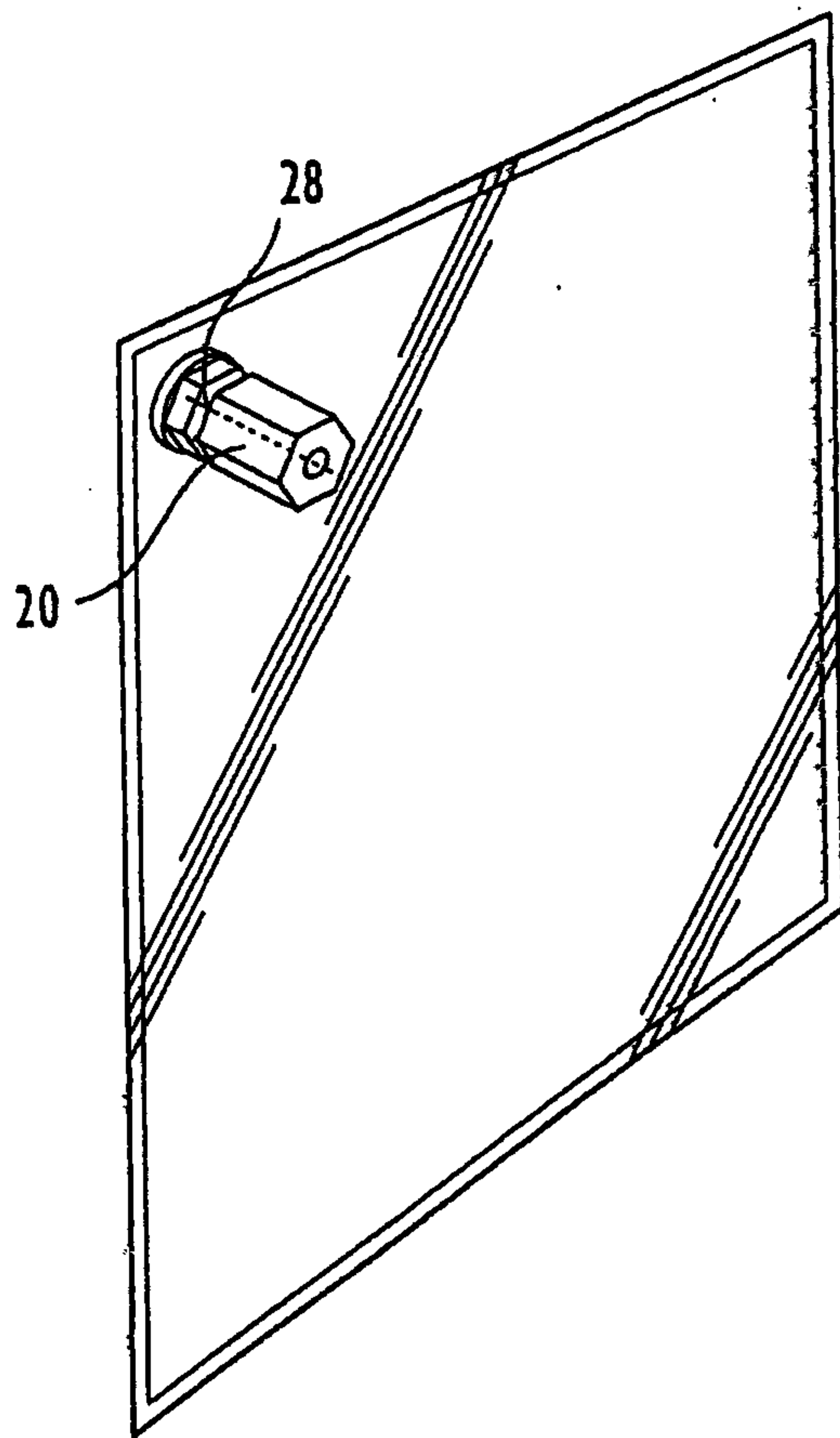
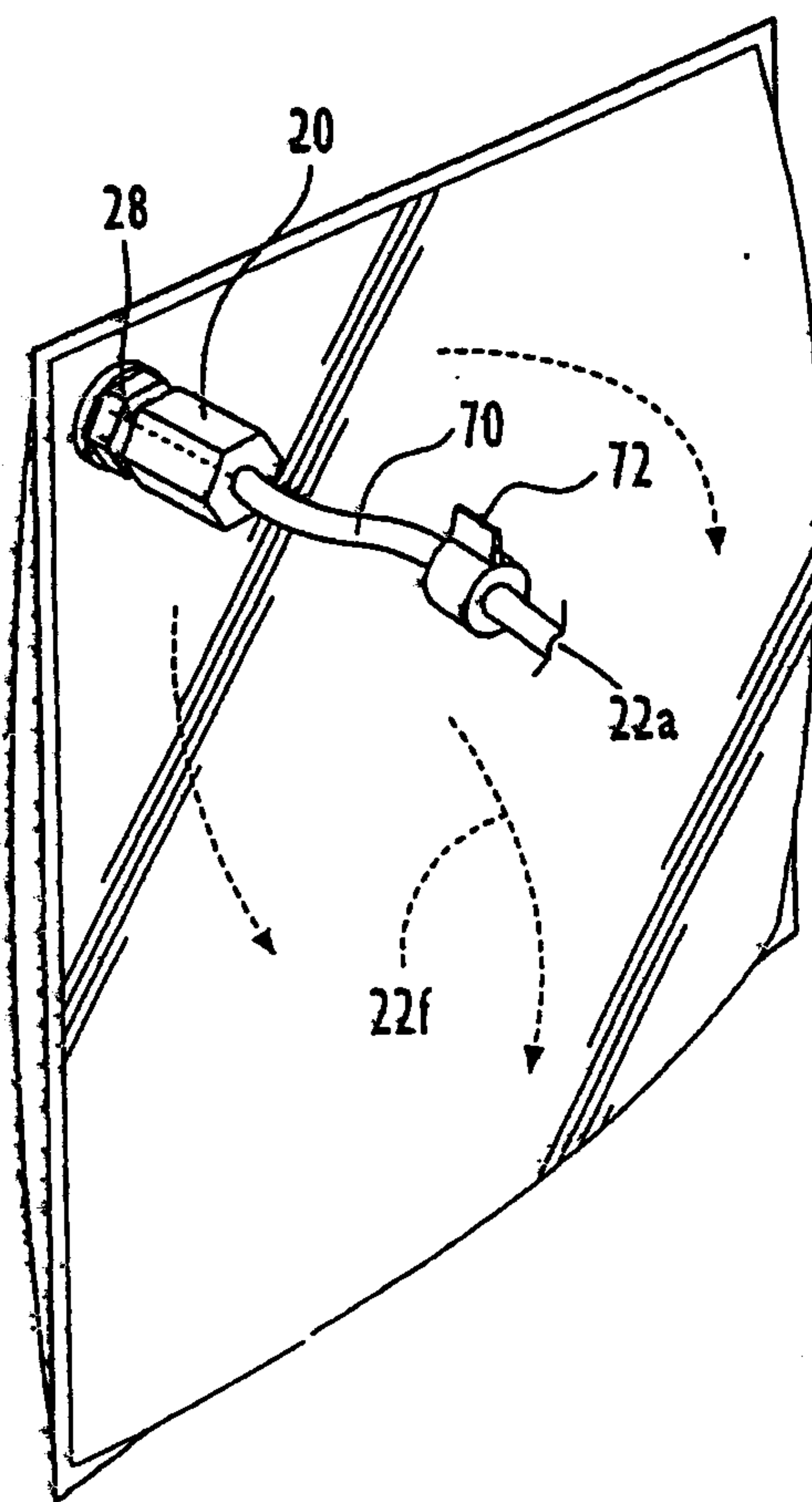


FIG. 21A.

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FIG. 21B.

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14/14

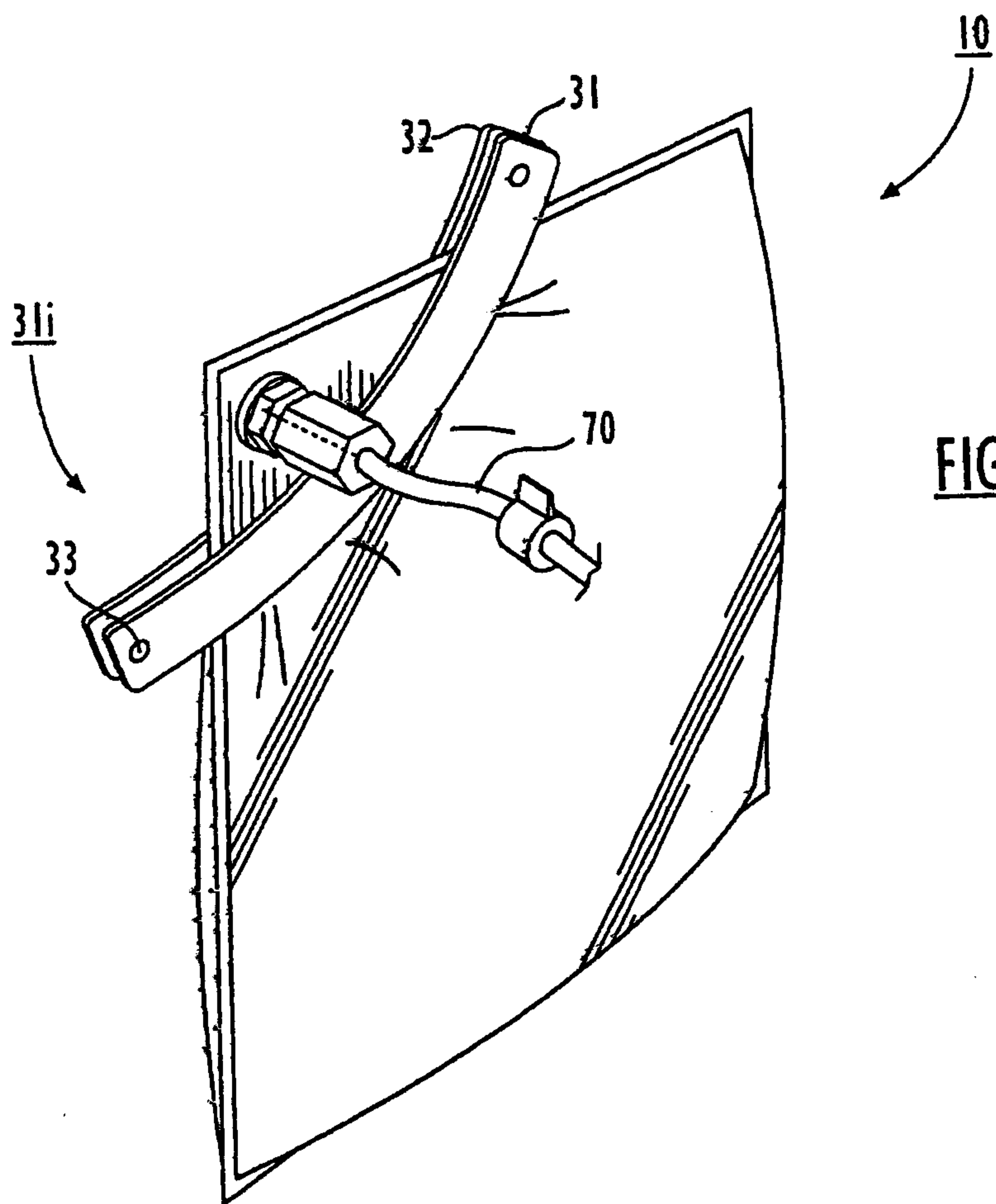


FIG. 21C.

