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— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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(54) Title: DEVICES AND INJECTABLE OR IMPLANTABLE COMPOSITIONS FOR INTERVERTEBRAL FUSION

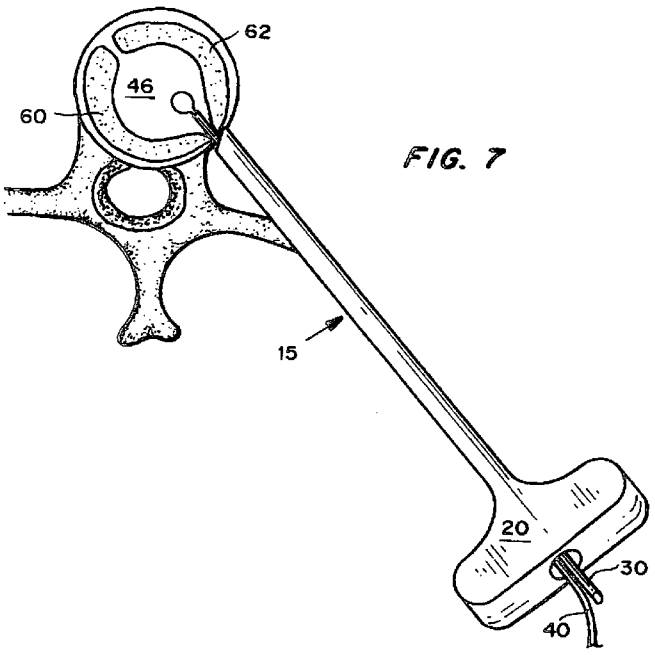

FIG. 7

(57) Abstract: A device for injecting materials for intervertebral fusions, kits containing the device, injectable and implantable modified poly(methyl methacrylate) (mPMMA) materials, and methods of use thereof, particularly in interverterbral fusions or intravertebral structural fortification, are described herein. The device contains an outer canula (20), an inner canula (30) that is in telescoping relation with respect to the outer canula (20) and removable therefrom, and one or more barrier forming materials, preferably two balloons. When the mPMMA material is cured, it produces a cement with a sufficient porosity to allow for bone growth through the cement to connect one vertebral endplate to the adjacent endplate. The mPMMA cement has sufficient compressive strength to withstand physiologic loads of the body during weight bearing activity and exhibits a Young's modulus of elasticity which is slightly less than cortical bone. Additionally, the mPMMA is able to bind to calcium phosphate and/or BMP.

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DEVICES AND INJECTABLE OR IMPLANTABLE COMPOSITIONS FOR INTERVERTEBRAL FUSION

CROSS-REFERENCE TO RELATED APPLICATION

This application claims priority under 35 U.S.C. §119 to provisional application U.S.S.N. 61/166,406, filed April 3, 2009, which is incorporated herein by reference.

FIELD OF THE INVENTION

The present invention is in the field of improved materials, devices and methods for intervertebral fusions and intravertebral stabilization.

BACKGROUND OF THE INVENTION

Poly (methyl methacrylate) or poly(methyl 2-methylpropenoate) ("PMMA") is currently used to "cement" and stabilize vertebral compression fractures (VCF). A VCF is a fracture in the body of a vertebra, which causes it to collapse. In turn, this causes intense pain, induced by the movement of the fracture fragments, and the spinal column above it may develop an abnormal forward curve called a kyphotic deformity. Additionally, kyphosis often causes fatigue related muscular back pain as result of the abnormal biomechanical alignment.

PMMA cement is surgically administered to a patient during a surgical technique, such as vertebroplasty or kyphoplasty.

Vertebroplasty involves the percutaneous injection of PMMA into a fractured vertebral body via a trocar and canula system. The targeted vertebrae are identified under fluoroscopy. A needle is introduced into the vertebrae body under fluoroscopic control, to allow radiographic visualization. A bilateral transpedicular approach is typical but the procedure can also be done unilaterally. Since the PMMA needs to be forced into the cancellous bone, the techniques may require high pressures and fairly low viscosity cement. Since the cortical bone of the targeted vertebra may have a recent fracture, there is the risk of PMMA leakage.

Kyphoplasty (Kyphon®) is a modification of percutaneous vertebroplasty. Kyphoplasty involves, as a preliminary step, the percutaneous placement of an inflatable balloon tamp in the vertebral body.

Inflation of the balloon creates a cavity in the bone prior to injection of the PMMA cement. The kyphoplasty technique generally allows for application of the PMMA cement at lower pressures than are needed for application using the vertebroplasty technique.

Leakage of PMMA during vertebroplasty or kyphoplasty can result in serious complications, including compression of adjacent structures that necessitate emergency decompressive surgery. *See* Groen, R. *et al*, "Anatomical and Pathological Considerations in Percutaneous Vertebroplasty and Kyphoplasty: A Reappraisal of the Vertebral Venous System", *Spine*, 29(13): 1465-1471 (2004). The PMMA leakage could lead to serious adjacent tissue injury, such as a compressive or thermal neural injury. It has been found that leakage of PMMA is related to various clinical factors such as the vertebral compression pattern, and the extent of the cortical fracture, bone mineral density, the interval from injury to operation, the amount of PMMA injected and the location of the injector tip. Leakage or extravasion of PMMA includes paravertebral leakage, venous infiltration, epidural leakage and intradiscal leakage.

PMMA cement is formed by combining powdered PMMA with liquid methyl methacrylate (MMA) at the time of surgery in the operating room. Typically, the surgical "scrub" technician mixes the materials while the patient is asleep on the operating table. Temperature and humidity affect the time for the PMMA to cure and form the solid PMMA cement. Typical cure times range from 2 to 10 minutes following mixing the powdered PMMA with liquid MMA. This variability places a time constraint upon the surgeon during the surgery. The surgeon must time the use and implantation of the cement appropriately in order for it to be injected into the body and placed in the appropriate location and in an appropriate volume. If it cures too fast, not enough PMMA is able to be injected or the PMMA is not delivered to the desired location, and the operation is compromised. Additionally, if the PMMA is injected under pressure when it is not sufficiently viscous, the risk of cement embolization is increased compared to if the injected material has a higher viscosity. Cement embolization results when PMMA cement enters the vascular system and travels to the

lungs or even the brain and becomes lodged into blood vessels of either of these organs. The time constraints occur as the surgeon attempts to inject this polymer carefully into the fractured vertebral body in a short period of time between when the material's viscosity increases from when it is considered "too runny" to when it is considered "too thick" where it becomes difficult to inject and may actually harden to the point that further injection of PMMA is not possible or requires higher pressure to inject and possibly increases the risk for extravasation from the vertebral body.

Another risk related to using PMMA is due to the exothermic reaction of PMMA. During curing, PMMA undergoes an exothermic reaction, which carries potential catastrophic consequences if thermal damage extends to the dural sac, spinal cord, and/or nerve roots. However, some clinicians speculate that the thermal curing process may desensitize the pain fibers from the fractured vertebral body, yet this has not been proven.

Intervertebral or spinal fusion is a surgical procedure used to correct problems with the vertebrae of the spine. The spine is stabilized by fusing together two or more vertebrae, typically using intervertebral cages, bone grafts and metal rods and screws. Spinal implant, such as interbody bone grafts or synthetic cages, are known in the art and are routinely used by spine surgeons to keep adjacent vertebrae in a desired spaced-apart relation while interbody bone ingrowth and fusion takes place. Such spinal fusion devices are also used to provide weight bearing support between adjacent vertebral bodies and thereby correct clinical problems. Such spinal fusion devices are indicated for medical treatment of conditions, such as degenerative disc disease, discogenic low back pain and spondylolisthesis. These conditions have been treated by using constructs, typically made from metals such as titanium or cobalt chrome alloys such as used in orthopedic implants, and allograft (from a third party donor) or autograft (from the patient) bone to promote bone ingrowth and fusion between two or more vertebrae.

Many spinal fusion implants are made from titanium alloy and allograft (donor) bone. However, the former implant devices exhibit poor radiolucency characteristics, presenting difficulties in post-operative monitoring and evaluation of the fusion process due to the artifact produced

by metals. Additionally, while these implant devices are load bearing, they are not osteoconductive. Use of allograft bone in implants has risks, such as transmission of infectious diseases or bioresorption and collapse prior to the patient developing a solid intervertebral fusion. Although, allograft bone implants exhibit good osteoconductive properties, they have variable materials properties and are in limited supply.

In response to these problems some developers, such as Zimmer®, Inc., are attempting to use porous tantalum-based metal constructs (*e.g.* Trabecular Metal® implants, which are fabricated of elemental tantalum metal using a vapor deposition technique to create a metallic strut configuration that is similar to trabecular bone), conferring osteoconductivity, but these have met with limited success owing to the metal artifact which occurs with postoperative imaging. Additionally, these implants are prefabricated in particular shapes that can be surgically placed through an open or mini-open surgical exposure technique. There is a need for a less invasive method for spinal fusions.

Further, there is a need for improved materials and devices for treating disorders of the spine.

It is an object of the present invention to provide improved materials and/or devices for use in intervertebral fusions.

It is a further object of the invention to provide improved methods for intervertebral fusions.

SUMMARY OF THE INVENTION

A device for injecting materials for intervertebral fusions, kits containing the device, injectable and implantable modified poly(methyl methacrylate) (mPMMA) materials, and methods of use thereof, particularly in interverterbral fusions or intravertebral structural fortification, are described herein. The device contains an outer canula (20), an inner canula (30) that is in telescoping relation with respect to the outer canula (20) and removable therefrom, and one or more barrier forming materials, preferably two balloons. When the mPMMA material is cured, it produces a cement with a sufficient porosity to allow for bone growth through the cement to connect one vertebral endplate to the adjacent endplate. The mPMMA

cement has sufficient compressive strength to withstand physiologic loads of the body during weight bearing activity and exhibits a Young's modulus of elasticity which is slightly less than cortical bone. Additionally, the mPMMA is able to bind to calcium phosphate and/or BMP. In yet another embodiment, the mPMMA is a preformed, pre-cured implant.

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A-1D illustrate a system for administering an injectable material into the intervertebral space in a spinal fusion. Figures 1A and 1B illustrate a canula/trocar assembly, assembled and disassembled, respectively. Figures 1C and 1D illustrate a preferred embodiment for a device for administering an injectable material into the intervertebral space in a spinal fusion. Figure 1C shows the syringe, inner canula, which is inserted into the outer canula when the device is assembled, and the barrier forming materials (i.e. 2 deflated balloons). Figure 1D shows the outer canula with the inner canula inserted inside the outer canula.

Figures 2A-2D illustrate a preferred embodiment for a device for administering an injectable material into the intervertebral space in a spinal fusion. Figure 2A shows the device with the balloon in a deflated position. Figure 2B shows the device with the balloons in the inflated position to form the barrier. Figure 2C is a side view of the device with the balloons in the inflated position. Figure 2D shows the device with the injectable material in the center of and surrounded by the barrier.

Figures 3A-C are illustrations of the shaped of an implant designed for lateral intervertebral fusions. Figure 3A is a side view; Figure 3B is a top plan view; and Figure 3C is a front view.

Figures 4A and B are illustrations of the shape of an implant designed for transforaminal interbody fusions (TLIF). Figure 4A is a side view and Figure 4B is a top plan view.

Figures 5A and B are illustrations of the shape of an implant designed for posterior lateral interbody fusions (PLIF). Figure 5A is a side view and Figure 5B is a top plan view.

Figures 6A and B are illustrations of the shape of an implant designed for anterior intervertebral fusions. Figure 6A is a side view and Figure 6B is a top plan view.

Figure 7 is a cross-sectional illustration of a patient's spine showing the relationship of the barrier relative to the patient's spine.

Figure 8 is an illustration of the percutaneous insertion a canula/trocar into a patient via using an extra-pedicular approach.

DETAILED DESCRIPTION OF THE INVENTION

I. Definitions

As used herein "modified poly(methyl methacrylate" or "mPMMA" means a material containing poly(methyl methacrylate) (PMMA) and other comonomers, additives, and/or fillers, and/or PMMA that is chemically modified such as with different functional groups, where the material has at least the following properties: (1) curable upon demand and activated by ultraviolet light and (2) an isothermic curing reaction to prevent thermal tissue injury, and where, when the material is cured, it produces a cement with a sufficient porosity to allow for bone growth onto and through the cement.

II. Compositions for Intervertebral Fusions

Compositions for intervertebral or spinal fusions are described herein. The compositions primarily contain a modified poly (methyl methacrylate) (mPMMA). Optionally, the compositions may contain additional materials, such bioactive agents, additives, or fillers. In one embodiment, the mPMMA is an injectable material. In another embodiment, the mPMMA is an implantable material with prefabricated shapes. Preferably the mPMMA is used in a spinal fusion technique. However, optionally, the mPMMA can be designed to be suitable for other medical applications, such as to stabilize a vertebral compression fracture (VCF). The porosity and other modifications of PMMA are useful in both scenarios.

A. Injectable Materials

An injectable form of the mPMMA can be delivered via injection to the intervertebral space or within the vertebral body (*i.e.* intravertebral delivery). The injectable material is particularly preferred for use in

percutaneous or mini-open intervertebral fusions. Suitable methods for delivery of the injectable mPMMA to the intervertebral space include using a posterior percutaneous approach (such as the technique used to access the disc for discography) or a percutaneous or mini-open lateral transpsoas approach. These surgical approaches are particularly useful for intervertebral fusions. Alternatively, the mPMMA can be injected into the vertebral body for intravertebral applications, such as the treatment of vertebral compression fractures. A suitable method for injection into a vertebral body includes using a percutaneous transpedicular surgical approach, such as by using a canulated trocar technique.

The injectable form of the mPMMA preferably has the following properties: a putty consistency; and a curing time which is preselected, preferably longer than ten (10) minutes. Preferably, the curing time is regulated by the surgeon by exposing the mPMMA to UV light.

Optionally, the injectable mPMMA also contains a material selected for its relatively high osteoconductive and osteoinductive properties, such as a hydroxyapatite or a calcium phosphate material. Alternatively, such osteoconductive and osteoinductive materials can be administered separately from the injectable mPMMA, such as before or after the mPMMA is injected into the desired location. Following injection into the intervertebral space, preferably using the device described herein, the mPMMA is cured, preferably by exposure to UV light, and thereby solidifies forming a mPMMA cement with a sufficient porosity to allow for bone growth onto and through the implant, forming a fusion of adjacent vertebral endplates. Additionally, the mPMMA cement has sufficient compressive strength to withstand physiologic loads of the body during weight bearing or activity. The compressive strength typically ranges from about 50 MPa, *i.e.* a typical compressive strength for trabecular or cancellous bone, to about 150 MPa, *i.e.* a typical compressive strength for cortical bone; preferably the compressive strength ranges from about 50 MPa to about 150 MPa. Further, the mPMMA cement generally has a Young's modulus of elasticity ranges from 0.8 GPa, *i.e.* the Young's modulus of elasticity for trabecular bone, to 15 GPa, *i.e.* the Young's modulus of elasticity for allograft cortical bone, or a

Young's modulus of elasticity which is greater than the Young's modulus of elasticity for cancellous bone but similar to or slightly less than the Young's modulus of elasticity for cortical bone. Preferably the Young's modulus of elasticity for the mPMMA is about 3 GPa. However, the mPMMA may be modified, as needed, to provide a material with the desired compressive strength and Young's modulus of elasticity. Preferably, the Young's modulus of elasticity is selected to correspond with the modulus of elasticity for a patient's bone. The modulus of elasticity of a patient's bone is a function of the bone's density. For example, for an osteoporotic patient, the Young's modulus of elasticity for the mPMMA is lower than the Young's modulus of elasticity of mPMMA used for a typical healthy individual. This reduces the risk of the cement itself inducing a compression fracture as a result of a "modulus mismatch" of the mPMMA and the patient's bone.

B. Implantable Materials

The mPMMA may be in the form of an implantable material, such as a putty. The implantable mPMMA may be implanted using a minimally open surgical approach.

In one embodiment, the mPMMA material is a prefabricated structural graft. The graft is also cured prior to implantation. Prefabricated structural grafts can be formed in a various sizes and shapes for implantation in the intervertebral space, typically using an open surgical approach. Suitable methods include an anterior, posterior or lateral intervertebral approach.

The grafts may be of a suitable size and shape for anterior lumbar interbody fusion (ALIF) surgery. The grafts may be designed to be used as anterior cervical interbody grafts, such as for anterior cervical discectomy and fusion surgery. Banana or crescent-shaped grafts may be implanted in a patient for transforaminal lumbar interbody fusion (TLIF). Straight grafts may be implanted in a patient for posterior lumbar interbody fusion (PLIF) surgery. Grafts with a generally rectangular shape may be used in minimally invasive, open transpsoas implantation in the intervertebral space. Alternatively, rectangular grafts, built with lordotic angulation and to

conform to the lumbar and thoracic vertebral endplates may be used for implantation for intervertebral fusions.

Exemplary shapes for the implantable materials are illustrated in Figures 3-6. Preferred shapes include a generally rectangular implant with a tapered or lordotic cross section to suit the required curvature of the intervertebral space (*see* Figures 3A-3C), in the case of a spinal fusion device. For example, this implant would be used in a lateral intervertebral fusion. Another preferred shape is a crescent shape (also referred to as "banana-shaped") implants, optionally with a tapered or lordotic cross section for improved fit into the inter-vertebral space (*see* Figures 4A and 4B). This implant can be used in transforaminal interbody fusions (TLIF). Another preferred shape is a generally oblong, rectangular implant, optionally with a tapered or lordotic cross section for improved fit into the inter-vertebral space (*see* Figures 5A and 5B). This implant can be used for posterior lateral interbody fusions (PLIF). Another preferred shape is a generally circular implant (*see* Figures 6A and 6B). This implant can be used for anterior intervertebral fusions.

The prefabricated implants typically are lordotic to restore the vertebral alignment as needed, for example used commonly in the lumbar or cervical spine. Other areas of the spine, such as the thoracolumbar section, are more likely to require a neutral alignment, thus parallel or neutral prefabricated grafts are better suited than the above-described shapes when implanted in the thoracolumbar section.

In one embodiment, the implantable material has a coefficient of friction which is suitable for preventing the material from moving out of the site of implantation as the spine experiences physiologic loads. For example, the implantable material may have a coefficient of friction that ranges from 0.58 to 0.86, which is generally a suitable coefficient of friction to prevent dislocation of the graft from the site of implantation as the spine experiences physiologic loads.

In a preferred embodiment the implantable material contains one or more means for attaching to tissue (*e.g.* vertebral end plate), such as points, hooks or spikes. The one or more means for attaching to tissue are generally

suitable for preventing the implant material from moving out of the site of implantation (*i.e.* dislocation) as the spine experiences physiologic loads.

In one embodiment, the prefabricated structural graft is coated with or contains within and/or throughout the graft a material that has relatively high osteoconductive and osteoinductive properties, such as a hydroxyapatite or a calcium phosphate material.

The mPMMA implant is cured prior to implantation. The mPMMA implant has a sufficient porosity to allow for bone growth through the implant. The mPMMA implant has the same compressive strength and Young's modulus of elasticity as described above with respect to the injectable mPMMA material.

C. Bioactive agents

In a preferred embodiment, the injectable or implantable material contains one or more bioactive agents, preferably the injectable or implantable material contains the one or more bioactive agents in an effective amount to enhance bone fusion and/or bone ingrowth at the site of treatment. Suitable bioactive agents include natural or synthetic osteoconductive, osteoinductive, osteogenic agents, and other fusion enhancing agents or beneficial therapeutic agents, such as bone morphogenic proteins (BMPs), growth factors, bone marrow aspirate, stem cells, progenitor cells, and antibiotics.

Other suitable bioactive agents include agents that preferentially bind to bone morphogenic proteins (BMPs),calcium phosphate outer surface area covering, FORTEO® (Eli Lilly and Company) (teriparatide (rDNA origin) injection, which contains recombinant human parathyroid hormone (1-34), agents that bind to rhPTH(1-34), or stem cells.

In one embodiment, the bioactive agent is encapsulated in micro- or nano-particles within the mPMMA material. The bioactive agent may be delivered locally to the site at which the pMMA is delivered via injection or implantation. Typically the bioactive agents are delivered to the tissue surrounding the mPMMA when the micro- or nanoparticles rupture and/or degrade. Preferably, the micro- or nano-particles are biodegradable and release the bioactive agent as they degrade. Alternatively, the spheres may

be fractured after the polymer is cured, such as following exposure to UV light, and thereby release the bioactive agent.

In a preferred embodiment, the injectable or implantable material contains one or more osteobiologic materials, such as bone morphogenetic proteins (BMP), such as, recombinant BMP-2 (rhBMP-2) (*e.g.* INFUSE® Bone Graft by Medtronic®, Memphis, TN), LIM mineralization protein-1 (LMP-1), demineralized bone matrix (DBM), growth differentiation factors (GDF), transforming growth factors (TGF), hydroxyapatite, tri-calcium phosphate (TCP), bioactive glass, calcium phosphate, calcium sulfates, collagen, or alginate. In one embodiment, the osteobiologic material comprises a calcium mineral, such as hydroxyapatite, calcium phosphate or calcium sulphate. Suitable materials include biodegradable porous mixtures of hydroxyapatite and tricalciumphosphate, such as TRICOS® from Biomatlante (France) or CAMCERAM® from Cam Implants, Leiden (Netherlands). Nonporous hydroxyapatite/tricalcium phosphate granules, pure hydroxyapatite granules (porous or nonporous), tricalcium phosphate granules (porous or nonporous), calcium sulfate granules, bone chips (either autograft or allograft) or xenograft bone chips may also be used.

D. Additives, Fillers, and/or Excipients

Optionally, the implantable or injectable material contains one or more additives, fillers or excipients. In one embodiment, the implantable or injectable material contains one or more radio-opaque agents in order to track the material, and in the case of the injectable material, detect any possible leakage.

Radio-opaque agents are commercially available and can be readily synthesized, as is well-known to the man skilled in the art. Monitoring of the radio-opaque agent may be accomplished with the methods generally used in the art, for example by X-ray imaging.

Suitable radio-opaque agents include standard X-ray contrast agents such as barium sulfate ($BaSO_4$), zirconium oxide (ZrO_2), gold, or titan. In a preferred embodiment the radio-opaque agent is barium sulphate ($BaSO_4$). Alternatively, iodinated radio-opaque agents may also be used. Exemplary non-ionic, iodinated contrast agents include iodixanol, iohexol, iopamidol,

iopentol, iopromide, iorneprol, iosimide, iotasul, iotrolan, ioversol, ioxilan, and metrizamide. Examplary ionic, iodinated contrast agents include diatrizoate, iobenzamate, iocarmate, iocetamate, iodamide, iodipamide, iodoxamate, ioglicate, ioglycamate, iopanoate, iophendylate, iopronate, ioserate, iothalamate, iotroxate, ioxaglate, ioxithalamate, and metrizoate.

Preferably the implantable or injectable material contains an effective amount of a radiopaque agent to provide a uniform radiopaque background under X-ray radiation.

Optionally the injectable or implantable material contains one or more fillers, such as silica, zirconium oxide and barium sulfate. The addition of fillers result in an increase of the mechanical properties (*e.g.*, compressive strength and Young's modulus E) of the resulting cement compared to the mechanical properties of the same cement in the absence of the fillers.

In one embodiment, the injectable material contains one or more thixotropic agents. The thixotropic agent can contain organic (*e.g.* hydroxypropylcellulose) or inorganic materials, such as hydrophilic or hydrophobic silica, smectite and hormite clay.

III. System and Device for Administration of mPMMA

A system for administering injectable materials in the intervertebral space, such as in an intervertebral fusion, is described herein.

As shown in Figures 1A-D, the system (10) contains (i) a canula-trocar assembly (26), which contains an outer canula (20) and an inner trocar (25), which is used to place the outer canula in the desired site; (ii) an inner canula (30), (iii) a catheter (40), (iv) one or more barrier forming materials that form a barrier (50) when inflated, and (v) a syringe (60).

a. Canula/Trocar Assembly

In a first step, the system contains a canula-trocar assembly (26), which contains an outer canula (20) and an inner trocar (25). The canula-trocar assembly (26) is inserted percutaneously into the patient, typically via a posterior-lateral approach, to gain access to the disc space using an extra-pedicular approach (*see* Fig. 1A and B). Once the desired site in the disc space is reached, the inner trocar (25) is removed, leaving the outer canula (20) in place, which provides canula access to the intervertebral disc space.

i. Outer Canula

The outer canula (20) is formed from any suitable biocompatible material. Preferably the outer canula is formed from a radio-opaque material, such as a metal, to facilitate imaging. The outer canula (20) has a proximal end (22) and a distal end (24). The outer canula has an inner diameter of at least 4 to 5 mm and does not exceed 10 mm and typically has an outer diameter of 6mm, where the outer diameter ranges from 5mm to 12 mm. Suitable canulas are available from a variety of manufacturers, including Medtronic®.

ii. Inner Trocar

The inner trocar (25) is formed from any suitable biocompatible material. The diameter of the inner trocar is less than the inner diameter of the outer canula so that the trocar is slidable within the outer canula and slidably removable therefrom. Suitable trocars are available from a variety of manufacturers, including Medtronic®.

b. mPMMA injection Device

In the next step, the mPMMA injection device (15) is assembled. This device (15) is illustrated in Figures 1C and D and 2A-2D and contains the outer canula (20), an inner canula (30), a catheter (40), one or more barrier forming materials that form a barrier (50) when inflated, and a first syringe (60).

i. Inner Canula

The inner canula (30) is formed of any suitable inert, biocompatible material. Preferably the inner canula is formed from a clear plastic. The inner canula contains two delivery portions (36 and 38) in the shape of tubes. The outer diameter of the inner canula is less than the inner diameter of the outer canula. The inner canula is inserted into the outer canula so that it is in telescoping relation to thereto and can be slidably removed therefrom.

A first delivery portion (36) is designed to deliver a fluid to inflate the one or more barrier forming materials. Typically, the first delivery portion has an inner diameter of about 2 mm, and may range from 1mm to 5 mm. The second delivery portion (38) is designed to deliver the injectable mPMMA to the desired site in the patient. Typically, the second delivery

portion has the same inner diameter as the first delivery portion, such as an inner diameter of about 2 mm, and may range from 1mm to 5 mm.

The first delivery portion has a proximal end (42) and a distal end (44). The second delivery portion (38) has a proximal end (32) and a distal end (34). The location of the proximal end (42) of the first delivery portion and the proximal end (32) of the second delivery portion (38) are pre-selected so that opening (39) in the proximal end of the second delivery portion (38) is in the hollow portion (46) of the barrier (50) that forms when the barrier forming materials are inflated.

The barrier forming material(s), typically one or more balloons, are attached to the distal end (42) of the first delivery portion (36) of the inner canula (30). The proximal end (44) of the first delivery portion (36) is attached to a catheter (40), which is attached to a first syringe (60).

A second syringe (not shown in figures) is filled with a suitable volume of the mPMMA to form the bone cement. The syringe is connected via a suitable connector to the proximal end (34) of the second delivery portion (38) of the inner canula. In one embodiment, the syringe is pre-filled with the mPMMA. In another embodiment, the mPMMA is mixed and then placed into the syringe.

ii. Catheter

The catheter (40) is designed to deliver a fluid, preferably saline, to the first delivery portion (36) of the inner canula.

iii. First Syringe

The first syringe (60) stores and delivers a fluid, preferably saline, to the catheter (40) to inflate the barrier forming materials and thereby form a barrier having the desired size. The volume of fluid that is delivered is suitable for inflating the barrier forming materials to the necessary height to restore the intervertebral disc height and sagittal balance. Typically the syringe able to contain at least 5 cc of fluid. Preferably the syringe is a 5 cc syringe.

Typically, the catheter attaches to a syringe via a valve, or other suitable attachment device at its distal end (45). In the preferred embodiment, the attachment device is a 3-way stopcock (48), which is used

to regulate the amount of fluid that is delivered to fill the barrier forming materials.

iv. Barrier

a. Size and Shape

The barrier (50) may be formed by inflating one or more balloons. The barrier has a suitable shape and size to restore the disc height and alignment and retain the cement at the desired location. In the preferred embodiment, the barrier is in the shape of an asymmetric ring, where one portion is higher than the opposite portion on the ring (*see e.g.* Fig. 2C and 2D). Within a patient, the higher portion of the barrier corresponds with the anterior portion of the patient's spine, while the lower portion of the barrier corresponds with the posterior portion of the spine. As shown in Figure 7, in the preferred embodiment, when the barrier is formed, the posterior portion (60) of the barrier protects the neural elements within the spinal canal, and the anterior portion (62) inflates to a height that is greater than the height of the posterior portion, thereby introducing lordosis where needed in the lumbar spine. The height of the barrier varies based on the level of inflation. In some embodiments, the highest portion of the barrier typically has a height ranging from 6 to 14 mm, with preferred heights of 6, 8, 10, 12 and 14 mm. The lowest portion of the barrier typically has a height ranging from 3 to 8 mm.

The barrier is typically about 6 to 10 mm thick (*i.e.*, the difference between the inner and the outer diameters of the resulting barrier), however, the thickness varies based on the level of inflation.

The outer diameter for the barrier will generally correspond with the width of the vertebrae at its widest dimension. Standard dimensions for the barrier are: an outer diameter ranging from 15 to 25 mm (measured anterior to posterior) and from 20 to 30 mm (measured side to side).

b. Materials

The barrier is formed from any biocompatible, inflatable material. Suitable materials are strong enough to resist the high pressures required for inflation of the balloon in the intervertebral space and include, but are not limited to, non-elastic materials, such as polyethylene terephthalate (PET),

nylon, and Kevlar®. (E. I. du Pont de Nemours and Co.) or other medical balloon materials (*see e.g.* U.S. Patent No. 7,261,720 to Stevens *et al.*). The balloon can also be made of semi-elastic materials, such as silicone, rubber, thermoplastic rubbers and elastomers or elastic materials such as latex or polyurethane, if appropriate restraints are incorporated. The restraints can be continuous or made of discrete elements of a flexible, inelastic high tensile strength material including, but not limited to, the materials described in U.S. Patent No. 4,706,670, which is incorporated herein by reference.

In one embodiment, the barrier is formed from a bioresorbable material, such as poly hydroxyl acids or blends or copolymers thereof. Preferred poly hydroxyl acids include poly lactic acid, poly glycolic acid, and copolymers (*e.g.* poly(lactide-co-glycolide)) and blends thereof. In one embodiment, if the barrier is formed from one balloon, the barrier is preferably bioresorbable, and preferably degrades in less than six months, more preferably less than one month, following insertion into the patient's body.

c. Inflation of the Barrier forming Material(s)

The one or more barrier forming materials are deflated prior to insertion into the patient. The barrier forming materials can be inflated by any suitable means, such as filling with an inert gas or mixture of gases, such as air, or by injecting a liquid into the balloon, such as water or saline. Preferably the barrier forming materials are balloons, which are inflated by injecting saline into the balloons, more preferably the saline contains a radio-opaque material, such as barium sulfate ($BaSO_4$).

d. Two Balloons for the Barrier

In a preferred embodiment, the barrier is formed by inflating two balloons. One balloon forms the left side (52) (referred to herein as "left balloon") of the barrier and the other balloon forms the right side (54) of the barrier (referred to herein as "right balloon") which meet to form a ring when they are inflated. Each balloon has a distal end (51 and 53) which attaches to one side of the proximal end (42) of the first portion (36) of the inner canula

(30). The proximal ends (55 and 56) of the inflated right and left balloons meet to form the barrier (50). In this embodiment, the barrier (50) is a discontinuous ring that surrounds a hollow center portion (46).

Each of the left balloon and the right balloon are preferably asymmetrical, such that each of each inflated balloon has a greater height at its proximal end (55 and 56) than at its distal end (51 and 53) (*see e.g.* Fig. 2C).

V. Kits

In one embodiment the above-described device for administration of mPMMA is included in a kit. In one embodiment, the kit contains (a) powdered mPMMA precursor material, (b) the canula trocar assembly, (c) the inner canula (30), catheter (40), and or more barrier forming materials to form a barrier (50) when inflated, to form the mPMMA injection device and (d) instructions for use thereof. Preferably the kit also contains a first syringe (60) to inflate the barrier forming material(s) and, optionally, a second syringe for delivering the mPMMA. More preferably the kit also contains a plunger to administer the mPMMA to the desired site.

In another embodiment, the kit contains (a) the canula trocar assembly, (b) the inner canula (30), catheter (40), and the one or more barrier forming materials to form a barrier (50) when inflated, to form the mPMMA injection device, (c) instructions for use thereof, and (d) a pre-filled syringe which contains a suitable volume of the injectable mPMMA to form the desired bone cement.. Preferably the kit also contains a first syringe (60) to inflate the barrier forming material(s). More preferably the kit also contains a plunger.

The kit may ensure that the above-describe device is a single-use device and protect patients from the potential adverse consequences occasioned by multiple use, which include disease transmission, or material stress and instability, or decreased or unpredictable performance.

The kit may include at least one wrap, which is peripherally sealed by heat or the like, to enclose the above-listed components of the kit and prevent contact with the outside environment. One end of the inner wrap, preferably includes a conventional peal-away seal, to provide quick access to the above-

listed components of the kit upon instance of use, which preferably occurs in a sterile environment, such as within an operating room.

Preferably at least one portion of the wrap, e.g. a top sheet, is made of transparent plastic film, such as polyethylene or MYLAR® material, to allow visual identification of the contents of the kit. Preferably at least one portion of the wrap, e.g. a bottom sheet, is made from a material that is permeable to EtO sterilization gas, e.g., TYVEC® plastic material (available from DuPont).

The sterile kit preferably contains a label or insert, which includes the statement "For Single Patient Use Only" (or comparable language) to affirmatively caution against reuse of the contents of the kit. The label also preferably instructs the physician or user to dispose of the entire contents of the kit upon use in accordance with applicable biological waste procedures.

The presence of the contents packaged in the kit verifies to the physician or user that device is sterile and has not be subjected to prior use.

VI. Methods of Using Materials and/or Device

1. Delivery of Injectable mPMMA

A. Cleaning the intervertebral space

In the first step, the intervertebral space is cleaned using standard methods. In this step the system contains a canula/trocar assembly (26). The canula/trocar assembly is advanced into the intervertebral space via an oblique posterior approach (also referred to as the "discogram approach").

In a posterior lateral interbody fusion, the canula/trocar assembly (26) is inserted percutaneously into the patient, typically via a posterior-lateral approach, to gain access to the disc space using an extra-pedicular approach (*see* Fig. 8).

In a lateral interbody fusion, a mini-open technique may be used. In this embodiment, the canula/trocar assembly is advanced into the intervertebral space via a lateral transpsoas approach.

Once the desired site in the disc space is reached, the inner trocar (25) is removed, leaving the outer canula (20) in place, which provides canula access to the intervertebral disc space.

Then the intervertebral disc material is evacuated using standard procedures and the effacing vertebral endplates are prepared for fusion by scraping the cartilaginous disc attachments to the bone. Any suitable technique for performing the discectomy may be used. For example, instruments that fit through the outer canula and that can curette and aspirate within the disc space can be inserted into the canula to curette and aspirate within the disc space. Examples of suitable instruments for removing the intervertebral disc material include, but are not limited to, HydroCision®'s instruments (*e.g.* HydroCision®'s HydroSurgery system, such as SpineJet®), which use a high pressure, pulsatile means for evacuating the disc, and nitinol brushes, etc.

B. Assembly of the Device for delivering mPMMA

Upon completion of the endplate preparation, the barrier forming materials, preferably deflated or collapsed balloons (52 and 54), are advanced through the outer canula (20) into the intervertebral space by pushing the inner canula (30) into and through the outer canula (20) (*see* Fig. 2A). The inner canula (30) is pushed through the outer canula until the proximal end (42) of the first delivery portion (36) and the proximal end (32) of the second delivery portion (38) are beyond the proximal end (12) of the outer canula (20).

After the barrier forming materials, preferably deflated or collapsed balloons (52 and 54), reach the desired site, the barrier forming materials are inflated, such as by depressing the syringe device. In the preferred embodiment, the syringe contains a normal saline solution, preferably containing a radio-opaque material, which is injected into the one or more, and preferably two, balloons to the desired fill level. The barrier forming materials, preferably balloons (52 and 54), are inflated to a sufficient height to restore the intervertebral height and alignment in both the coronal and sagittal planes. Thus, the barrier forming materials can be inflated to restore lumbar lordosis. The barrier forming materials form a barrier (50) that is suitable for retaining the mPMMA cement in the desired site, thereby preventing cement extravasation.

In a lateral interbody fusion, the shape of the resulting barrier is a hollow rectangle and side view of the barrier generally corresponds with the shape of the side view of the implant illustrated in Figure 3A.

The desired fill level and location of the barrier (50) is determined by intraoperative fluoroscopic imaging. Typically the location of the barrier is confirmed, and adjusted, if necessary by the surgeon, prior to delivery of the injectable mPMMA. The fill level of the barrier forming materials can also be increased, or decreased, if necessary, prior to delivery of the injectable mPMMA. In a posterior lateral interbody fusion, the balloons are filled with a sufficient amount of fluid to restore the intervertebral disc height and sagittal balance (*see* Fig. 2C). In a lateral interbody fusion, the balloons are filled with a sufficient amount of fluid to restore the anatomic reduction of the disc height and sagittal and coronal balance.

C. Delivery of Injectable material

After the barrier is formed via inflation of the barrier forming materials, and preferably after its location, shape and size are confirmed, the injectable mPMMA can be delivered percutaneously into the intervertebral space guided by fluoroscopy (intraoperative x-ray).

The opening (39) at the proximal end (32) of the second delivery portion (38) of the inner canula (30) is located in the hollow portion (46) of the barrier (50), and the injectable mPMMA is forced out of the second syringe and through the inner canula (30) by depressing the second syringe. Typically, the injectable mPMMA is forced out of the inner canula (30) by pushing a plunger (not shown in figures) through the second delivery portion (38) the inner canula (30). The plunger is in telescoping relation to the second delivery portion (38) of the inner canula and removable therefrom. The mPMMA is pushed out of the second delivery portion (38) of the inner canula and into the area within the intervertebral space that corresponds with the hollow portion (46) of the barrier. Thus, the injected mPMMA is surrounded by the barrier (50), which prevents cement extravasation.

The placement of the mPMMA is verified radiographically using intraoperative fluoroscopy. In the preferred embodiment, the amount of contrast agent in the mPMMA is different than the amount of contrast agent

in the saline to facilitate distinguishing the mPMMA from the barrier (50) and thereby determining the location of the mPMMA. Preferably the mPMMA has a greater concentration of contrast agent than the concentration of contrast agent in the saline. This difference in concentrations of contrast agents allows the surgeon to distinguish the barrier from the mPMMA using fluoroscopic imaging.

D. Curing of mPMMA to form Cement

Following delivery of a suitable amount of injectable mPMMA to the desired site, the mPMMA is cured. In one embodiment, the curing occurs by merely waiting a sufficient period of time, preferably greater than 10 minutes following mixing the powder MMA with the liquid to form the injectable mPMMA.

In another preferred embodiment, the mPMMA is exposed to UV light for a sufficient period of time to cure the mPMMA, typically a few seconds or less, preferably for about one second. In this embodiment, the plunger is removed from the second delivery portion (38) of the inner canula (30) after the mPMMA is delivered to the desired site. Then a UV light source (not shown in figures) is passed down the second delivery portion (38) of the inner canula until it reaches the proximal end (32) of the second delivery portion (38) and is located proximal to the mPMMA material in the hollow portion (46) of the barrier. Alternatively, the plunger may contain a UV light source at its proximal end, which is located inside the proximal end (32) of the second delivery portion (38), or a UV light source may be located at the distal end (34) of the second delivery portion (38) of the inner canula.

After the mPMMA is cured, the barrier (50) is deflated by aspirating the fluid via the syringe. The inner canula (30) along with the one or more deflated barrier forming materials are withdrawn and removed from the distal end (24) of the outer canula (20). Finally, the outer catheter (20) is removed from the patient.

1. Delivery of Implantable mPMMA

Implantable mPMMA materials, such as prefabricated interbody grafts may be implanted into the intervertebral space in need of treatment via open surgical procedures using the traditional anterior, posterior or lateral

surgical approaches. Typical surgical approaches include posterior approaches such as the transforaminal lumbar interbody fusion (TLIF) and posterior lateral interbody fusion (PLIF). Alternatively, an anterior approach may be used, such as the anterior lumbar interbody fusion (ALIF). Finally, the lateral transpsoas approach may be used to place a lateral intervertebral graft.

After the intervertebral space has been cleaned as described above with respect to the injectable mPMMA material, the implantable mPMMA material can be implanted using a standard open or mini-open approach.

The placement of the prefabricated implantable mPMMA is verified by direct visualization by the surgeon.

The prefabricated implants contain cured mPMMA. The implant may be formed into a variety of shapes. These implants are porous, with a trabecular network of channels that allows fluids to flow through easily (*e.g.*,, blood or BMP). The mPMMA may then be able to bind to BMP or calcium hydroxyapetite or calcium phosphate prior to implantation. In the case of BMP, the implant can be bathed in a solution of BMP at the time of surgery prior to implantation.

Typically, a variety of different shapes and sizes of each graft are stocked for use in the operating room. Trial size implants are used by the surgeon to determine the final size and shape to implant intraoperatively.

A Treatment of the Thoracic Spine using Implantable mPMMA

The device described herein may be used in a lateral, mini- open approach to treat not only the lumbar spine, but also the thoracic spine

The surgical approach for this use is a lateral mini-thoracotomy, which is used to access the thoracic spine. A retractor system which fixes to the operating table is used to protect the lung parenchyma and major vessels (inferior vena cava and thoracic aorta). Examples of this existing technology are NuVasive XLIF, Medtronic DLIF or Synthes Oracle instrumentation sets.

After the discectomy is performed using traditional techniques, templating of the final implant is performed using any of various existing technologies noted above.

The final mPMMA implant is tamped across the intervertebral disc space using anterior-posterior and lateral fluoroscopic imaging to guide the placement. These implants are similar in shape to the implants illustrated in Figures 6A and 6B for the anterior lumbar intervertebral fusion (ALIF), however the end of the shape of the implant is parallel rather than lordotic. Further typical sizes for these implants are: from 6 to 14 mm in height, from 30 to 50 mm in length.

The mPMMA prefabricated implants would exhibit the same properties as those described for the lumbar and cervical spine.

B. Treatment of the Cervical Spine using Implantable mPMMA

The implantable mPMMA can be implanted in a patient's neck by using the standard Smith Robinson approach for the access to the cervical spine. Preferably the implant also contains a radio-opaque material to allow for fluoroscopic imaging.

Upon gaining access to the appropriate treatment level of the cervical spine, the standard techniques for performing a discectomy and osteophyte and disc decompression of the spinal cord and neural foraminal can be performed prior to implanting the prefabricated mPMMA graft.

Trial sizing is performed to determine the appropriate implant size prior to selecting the implant. Implant sizes range from 5 to 8 mm in height, 10 to 13 mm in depth, to 8 to 12 mm in width in lordotic configuration to restore or maintain the normal lordotic sagittal alignment of the cervical spine.

Implants are shaped to match the typical endplate shapes of the adjacent vertebrae to the treatment disc level. The appropriate sized and shaped implant is then tamped into position under direct visualization and can be imaged fluoroscopically to verify positioning.

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of skill in the art to which the disclosed invention belongs.

I claim:

1. A device for injecting a curable material in an intervertebral fusion, comprising an outer canula, an inner canula, wherein the inner canula comprises a first delivery portion and a second delivery portion, wherein each delivery portion has a proximal end and a distal end, and one or more barrier forming materials, wherein the one or more barrier forming materials are attached to the proximal end of the first delivery portion, and wherein the one or more barrier forming materials form a barrier upon inflation.

2. The device of claim 1, wherein the one or more barrier forming materials are balloons.

3. The device of claim 2, comprising two balloons.

4. The device of claim 3, wherein the balloons form an asymmetric, discontinuous ring upon inflation, wherein the proximal ends of the balloons are sufficiently close following inflation to prevent release of an injectable modified poly(methyl methacrylate) material from the center of the ring.

5. The device of claim 4, wherein one portion of the ring is higher than the portion on the opposite side of the ring.

6. The device of claim 1, further comprising a first syringe and a catheter, wherein the first syringe is attached to the distal end of the catheter, and the proximal end of the catheter is attached to the distal end of the first delivery portion.

7. The device of claim 1, further comprising a second syringe, wherein the second syringe is in fluid communication with the distal end of the second delivery portion, and wherein the second syringe comprises a injectable, curable modified poly(methyl methacrylate).

8. A method for injecting a curable material into an intervertebral space in need of treatment, comprising

(i) inserting the device of any one of claims 1 to 7 into the intervertebral space,

(ii) inflating the one or more barrier forming materials to form a barrier surrounding a hollow portion,

(iii) injecting the curable material into the hollow portion, and

(iv) curing the material to form a porous cement via an isothermic reaction.

9. The method of claim 8, wherein the material is a modified poly(methyl methacrylate).

10. The method of any one of claims 8 or 9, further comprising deflating the one or more barrier forming materials after step (iv).

11. The method of any one of claims 8 to 10, wherein step (iv) comprises exposing the material to a UV light source to initiate the curing step.

12. The method of any one of claims 8 to 11, wherein the resulting porous cement has a sufficient porosity to allow blood to pass through from one endplate to the adjacent vertebral endplate and to allow for sufficient bone growth through the cement to create an endplate-to-endplate fusion.

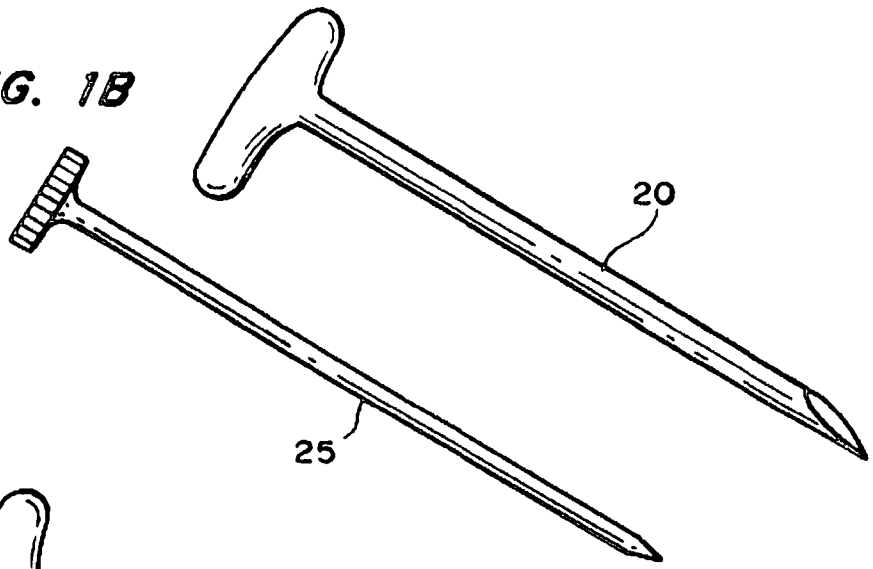
13. A method of forming an intervertebral fusion in a patient in need of treatment comprising implanting into the intervertebral space in need of treatment a modified poly(methyl methacrylate) implant, wherein the implant is a porous cement with a sufficient porosity to allow blood to pass through from one endplate to the adjacent vertebral endplate and to allow for sufficient bone growth through the cement to create an endplate-to-endplate fusion.

14. The method of claim 13, wherein the implant has a shape selected from the group consisting of rectangular implant with a tapered or lordotic cross section; crescent shape with a tapered or lordotic cross section; oblong, rectangular implant with a tapered or lordotic cross section; and circular.

15. A kit comprising (i) a powdered precursor for a modified poly(methyl methacrylate) (mPMMA) or an injectable mPMMA, (ii) a trocar, and (iii) the device of any one of claims 1 to 7.

16. The kit of claim 15 further comprising a plunger and a second syringe for administration of the mPMMA.

FIG. 1B



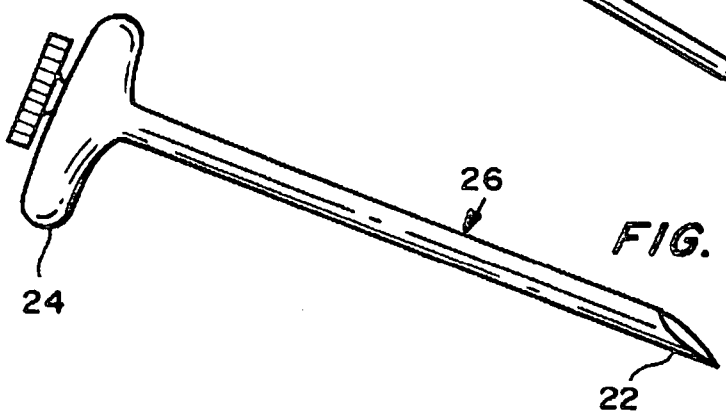


FIG. 1A

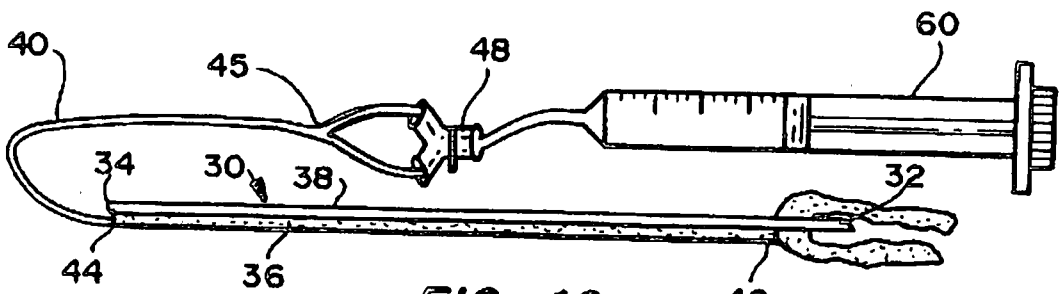


FIG. 1C

FIG. 1D

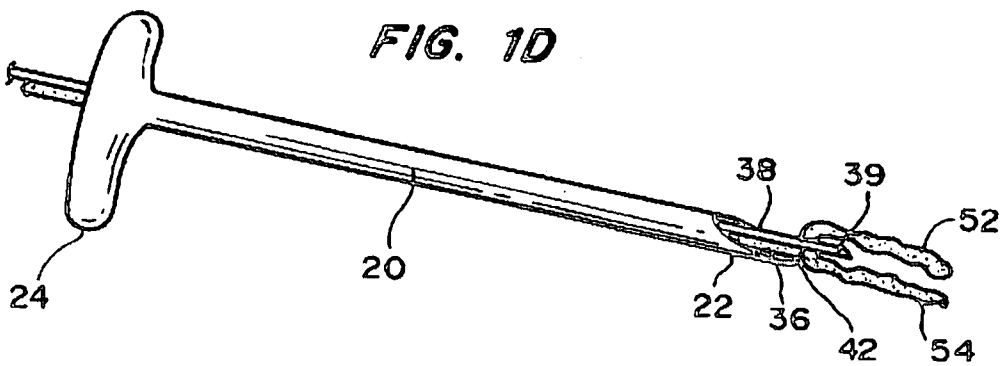


FIG. 2A

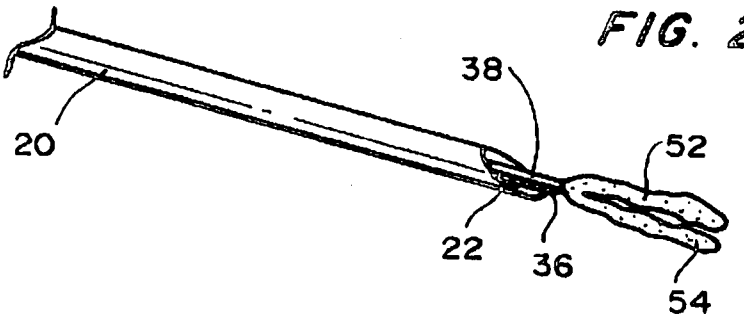
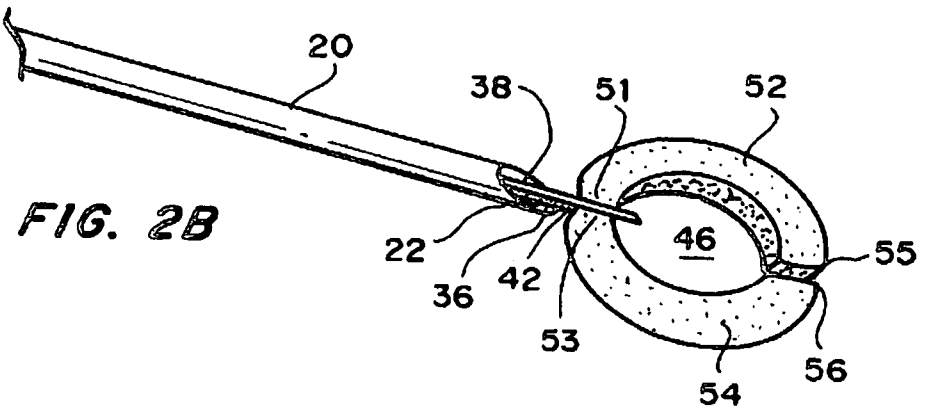


FIG. 2B



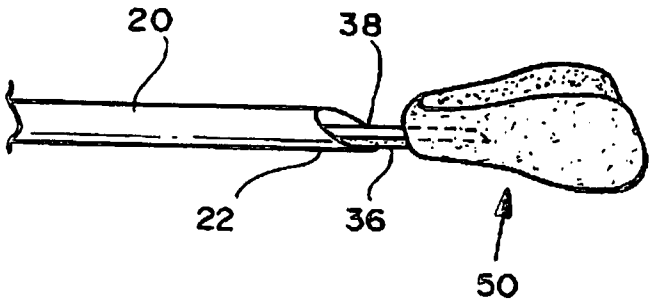


FIG. 2C

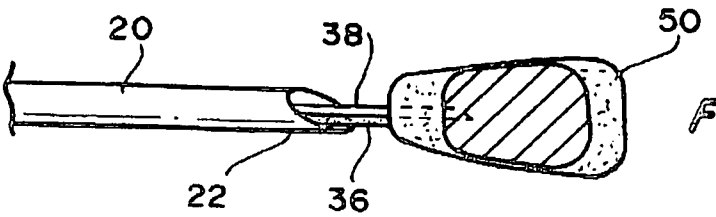


FIG. 2D

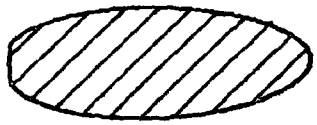


FIG. 3A

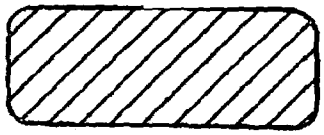


FIG. 3B

FIG. 3C

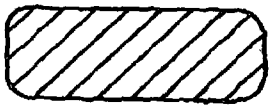


FIG. 4A

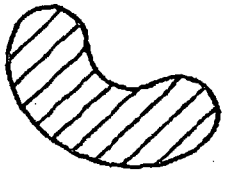


FIG. 4B

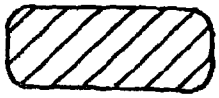


FIG. 5A

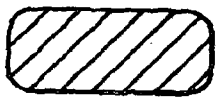


FIG. 5B

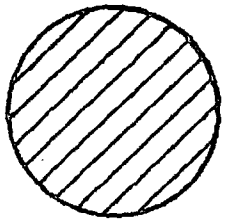


FIG. 6A

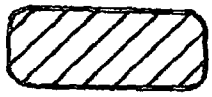


FIG. 6B

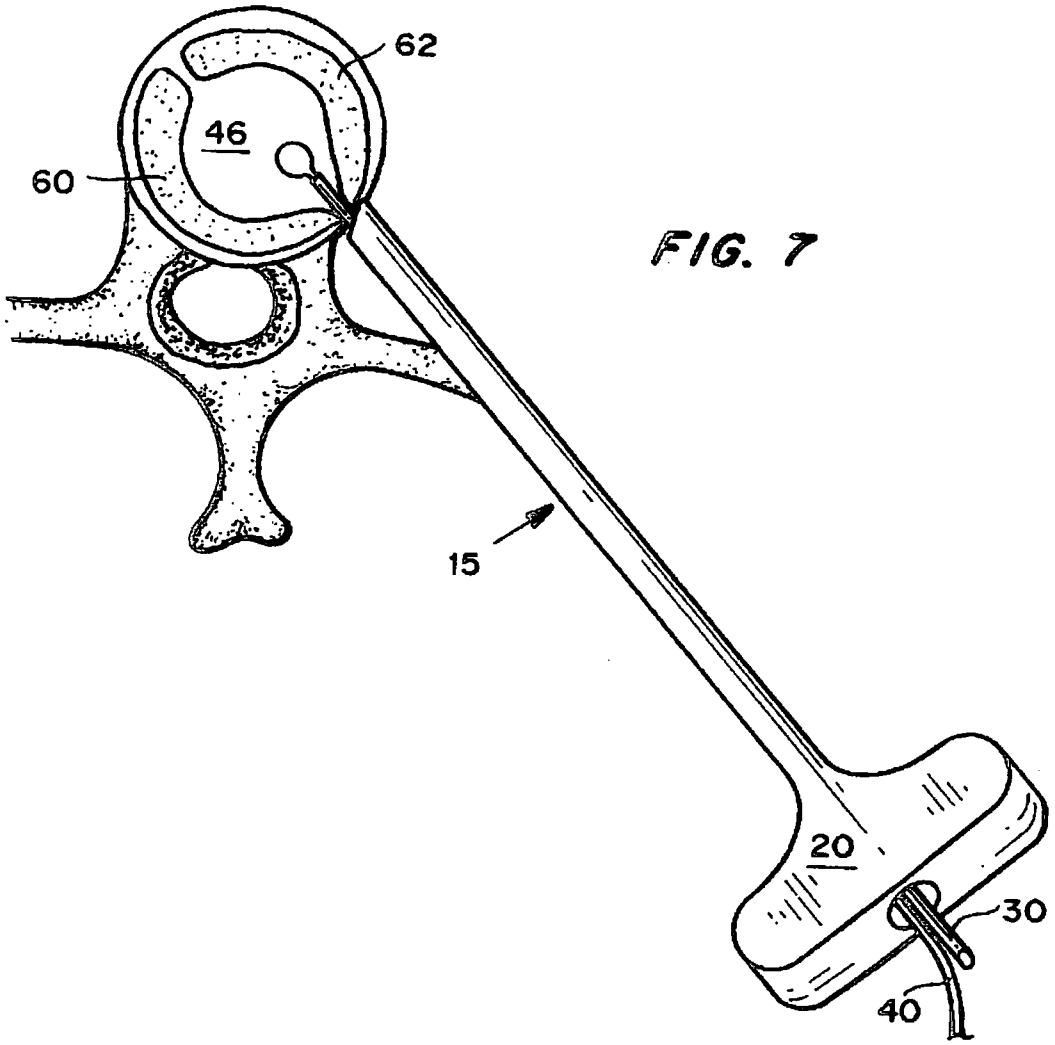


FIG. 7

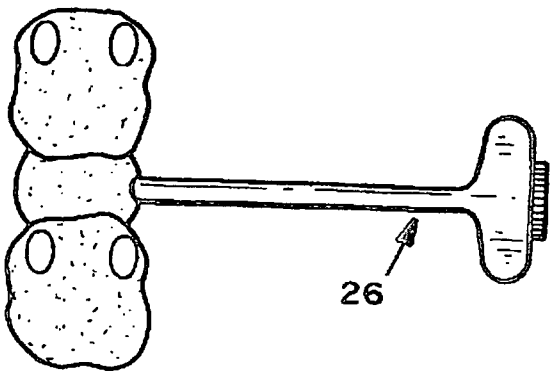


FIG. 8