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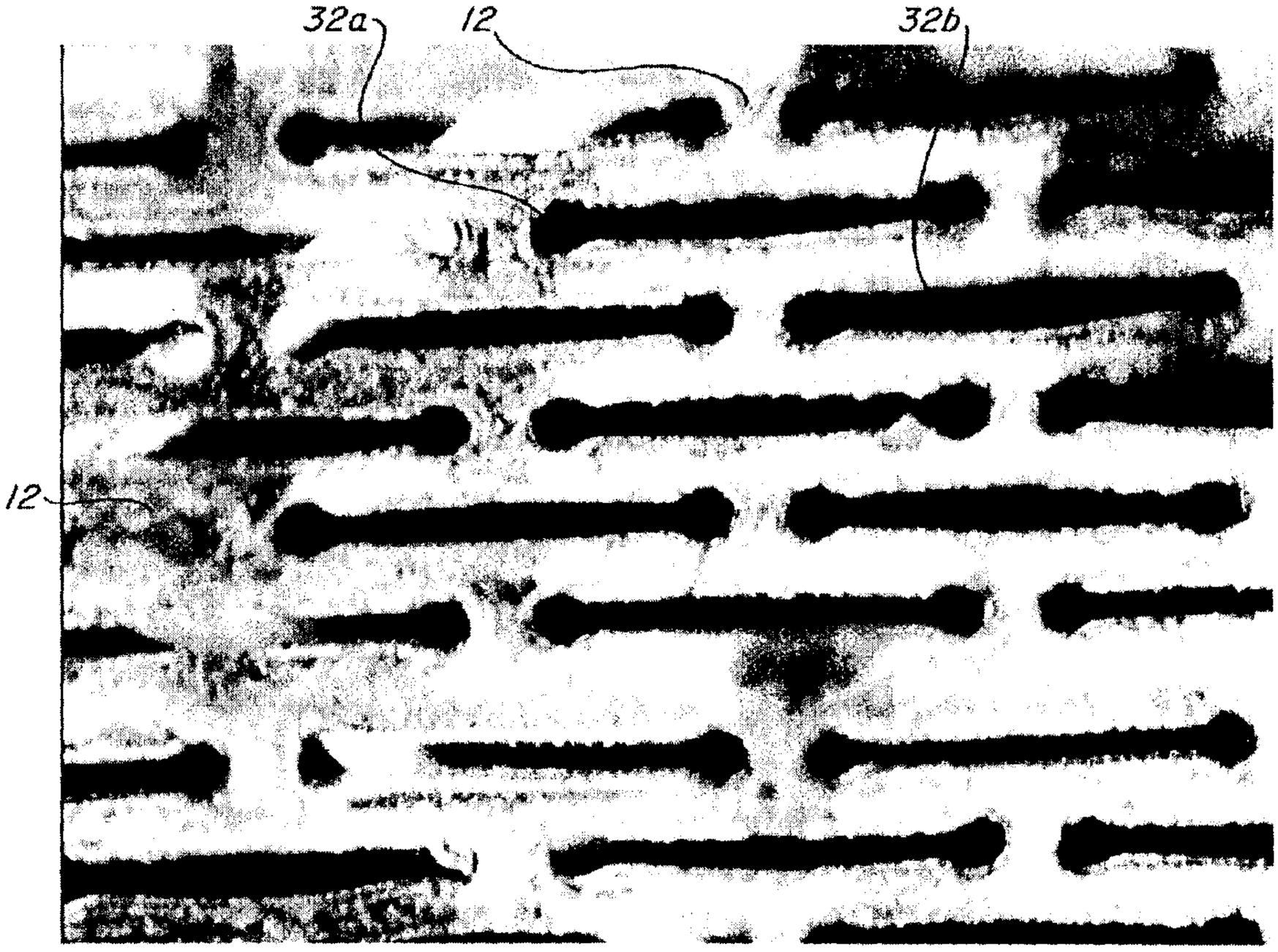
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(54) Titre : GREFFONS IMPLANTABLES METALLIQUES AUTOPORTEURS, IMPLANTS MEDICAUX CONFORMES ET PROCEDES DE FABRICATION

(54) Title: SELF-SUPPORTING METALLIC IMPLANTABLE GRAFTS, COMPLIANT IMPLANTABLE MEDICAL DEVICES AND METHODS OF MAKING SAME



(57) Abrégé/Abstract:
Implantable medical grafts (10) fabricated of metallic or pseudometallic films of biocompatible materials having a plurality of microperforations (20) passing through the film in a pattern that imparts fabric-like qualities to the graft or permits the geometric

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(57) Abrégé(suite)/Abstract(continued):
deformation of the graft. The implantable graft is preferably fabricated by vacuum deposition of metallic and/or pseudometallic materials into either single or multi-layered structures with the plurality of microperforations either being formed during deposition or after deposition by selective removal of sections of the deposited film. The implantable medical grafts are suitable for use as endoluminal or surgical grafts and may be used as vascular grafts, stent-grafts, shunts, bone grafts, surgical patches, non-vascular conduits, valvular leaflets, filters, occlusion membranes, artificial sphincters, tendons and ligaments.

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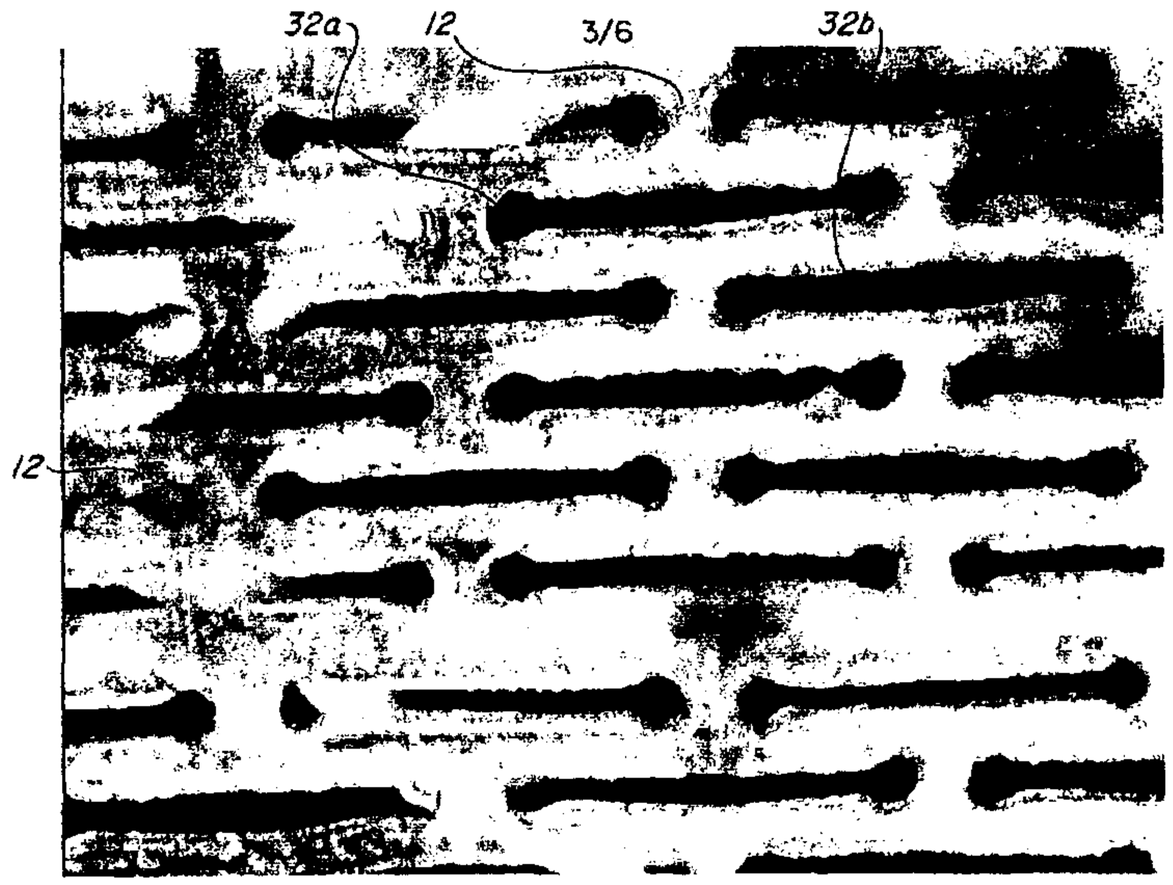
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(54) Title: MEDICAL GRAFTS HAVING PLURALITY OF MICROPERFORATIONS



(57) Abstract: Implantable medical grafts (10) fabricated of metallic or pseudometallic films of biocompatible materials having a plurality of microperforations (20) passing through the film in a pattern that imparts fabric-like qualities to the graft or permits the geometric deformation of the graft. The implantable graft is preferably fabricated by vacuum deposition of metallic and/or pseudometallic materials into either single or multi-layered structures with the plurality of microperforations either being formed during deposition or after deposition by selective removal of sections of the deposited film. The implantable medical grafts are suitable for use as endoluminal or surgical grafts and may be used as vascular grafts, stent-grafts, shunts, bone grafts, surgical patches, non-vascular conduits, valvular leaflets, filters, occlusion membranes, artificial sphincters, tendons and ligaments.

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Title Of The Invention

[0001] SELF-SUPPORTING METALLIC IMPLANTABLE GRAFTS, COMPLIANT IMPLANTABLE MEDICAL DEVICES AND METHODS OF MAKING SAME

Background of the Invention

[0002] The present invention relates generally to implantable metallic medical devices. More specifically, the present invention relates to implantable medical devices, including, for example, surgical and endoluminal vascular grafts, stent grafts, skin grafts, shunts, bone grafts, surgical patches, non-vascular conduits, valvular leaflets, filters, occlusion membranes, sphincters, artificial tendons and ligaments. More specifically, the present invention relates to implantable medical grafts fabricated of metallic or pseudometallic films of biocompatible materials having a plurality of microperforations passing through the film. The plurality of microperforations may serve multiple purposes, including, for example, permitting geometric deformation of the film, imparting a fabric-like quality to the film, and imparting flexibility to the film. The term "fabric-like" is intended to mean a quality of being pliable and/or compliant in a manner similar to that found with natural or synthetic woven fabrics.

[0003] The inventive implantable grafts are fabricated entirely of self-supporting films made of biocompatible metals or biocompatible pseudometals. Heretofore in the field of implantable medical devices, it is unknown to fabricate an implantable medical device that comprises a graft at least as one of its elements, such as a stent graft, entirely of self-supporting metal or pseudometal materials. As used herein the term "graft" is intended to indicate any type of device or part of a device that comprises essentially a material delimited by two surfaces where the distance between said surfaces is the thickness of the graft and that exhibits integral dimensional strength and that has microperforations that pass through the thickness of the graft. The inventive grafts may be formed in planar sheets, toroids, and in other shapes as particular applications may warrant. However, for purposes of illustration only, the present application will refer to tubular grafts. For purposes of this application, the terms "pseudometal" and "pseudometallic" are intended to mean a biocompatible material which exhibits biological response and material characteristics substantially the same as biocompatible metals. Examples of pseudometallic materials include, for example, composite

materials and ceramics. Composite materials are composed of a matrix material reinforced with any of a variety of fibers made from ceramics, metals, carbon, or polymers.

[0004] When implanted into the body, metals are generally considered to have superior biocompatibility than that exhibited by polymers used to fabricate commercially available polymeric grafts. It has been found that when prosthetic materials are implanted, integrin receptors on cell surfaces interact with the prosthetic surface. The integrin receptors are specific for certain ligands *in vivo*. If a specific protein is adsorbed on a prosthetic surface and the ligand exposed, cellular binding to the prosthetic surface may occur by integrin-ligand docking. It has also been observed that proteins bind to metals in a more permanent fashion than they do to polymers, thereby providing a more stable adhesive surface. The conformation of proteins coupled to surfaces of most medical metals and alloys appears to expose greater numbers of ligands and preferentially attract endothelial cells having surface integrin clusters to the metal or alloy surface relative to leukocytes. Finally, metals and metal alloys exhibit greater resistance to degradation of metals relative to polymers, thereby providing greater long-term structural integrity and stable interface conditions.

[0005] Because of their relatively greater adhesive surface profiles, metals are also susceptible to short-term platelet activity and/or thrombogenicity. These deleterious properties may be offset by administration of pharmacologically active antithrombogenic agents in routine use today. Surface thrombogenicity usually disappears 1-3 weeks after initial exposure. Antithrombotic coverage is routinely provided during this period of time for coronary stenting. In non-vascular applications such as musculoskeletal and dental, metals have also greater tissue compatibility than polymers because of similar molecular considerations. The best article to demonstrate the fact that all polymers are inferior to metals is van der Giessen, WJ. *et al.* Marked inflammatory sequelae to implantation of biodegradable and non-biodegradable polymers in porcine coronary arteries, *Circulation*, 1996:94(7):1690-7.

[0006] Normally, endothelial cells (EC) migrate and proliferate to cover denuded areas until confluence is achieved. Migration, quantitatively more important than proliferation, proceeds under normal blood flow roughly at a rate of 25 μm/hr or 2.5 times the diameter of an EC, which is nominally 10μm. EC migrate by a rolling motion of the cell membrane, coordinated by a complex system of intracellular filaments attached to clusters of cell membrane integrin receptors, specifically focal contact points. The integrins within the focal contact sites are expressed according to complex signaling mechanisms and eventually

couple to specific amino acid sequences in substrate adhesion molecules. An EC has roughly 16-22% of its cell surface represented by integrin clusters. Davies, P.F., Robotewskyi A., Griem M.L. Endothelial cell adhesion in real time. *J.Clin.Invest.*1993; 91:2640-2652, Davies, P.F., Robotewski, A., Griem, M.L., Qualitiative studies of endothelial cell adhesion, *J.Clin.Invest.*1994; 93:2031-2038. This is a dynamic process, which implies more than 50% remodeling in 30 minutes. The focal adhesion contacts vary in size and distribution, but 80% of them measure less than 6 μm^2, with the majority of them being about 1 μm^2, and tend to elongate in the direction of flow and concentrate at leading edges of the cell. Although the process of recognition and signaling to determine specific attachment receptor response to attachment sites is incompletely understood, availability of attachment sites will favorably influence attachment and migration. It is known that materials commonly used as medical grafts, such as polymers, do not become covered with EC and therefore do not heal after they are placed in the arteries. It is therefore an object of this invention to replace polymer grafts with metal grafts that can potentially become covered with EC and can heal completely. Furthermore, heterogeneities of materials in contact with blood flow are preferably controlled by using vacuum deposited materials.

[0007] There have been numerous attempts to increase endothelialization of implanted medical devices such as stents, including covering the stent with a polymeric material (U.S. Patent No. 5,897,911), imparting a diamond-like carbon coating onto the stent (U.S. Patent No. 5,725,573), covalently binding hydrophobic moieties to a heparin molecule (U.S. Patent No. 5,955,588), coating a stent with a layer of blue to black zirconium oxide or zirconium nitride (U.S. Patent No. 5,649,951), coating a stent with a layer of turbostratic carbon (U.S. Patent No. 5,387,247), coating the tissue-contacting surface of a stent with a thin layer of a Group VB metal (U.S. Patent No. 5,607,463), imparting a porous coating of titanium or of a titanium alloy, such as Ti-Nb-Zr alloy, onto the surface of a stent (U.S. Patent No. 5,690,670), coating the stent, under ultrasonic conditions, with a synthetic or biological, active or inactive agent, such as heparin, endothelium derived growth factor, vascular growth factors, silicone, polyurethane, or polytetrafluoroethylene, U.S. Patent No. 5,891,507), coating a stent with a silane compound with vinyl functionality, then forming a graft polymer by polymerization with the vinyl groups of the silane compound (U.S. Patent No. 5,782,908), grafting monomers, oligomers or polymers onto the surface of a stent using infrared radiation, microwave radiation or high voltage polymerization to impart the property of the

monomer, oligomer or polymer to the stent (U.S. Patent No. 5,932,299). However, all these approaches do not address the lack of endothelialization of polymer grafts.

[0008] It is, therefore, desirable to fabricate the inventive graft of metallic and/or pseudometallic materials. The inventive metal devices may be fabricated of pre-existing conventional wrought metallic materials, such as stainless steel or nitinol hypotubes, or may be fabricated by thin film vacuum deposition techniques. In accordance with the present invention, it is preferable to fabricate the inventive implantable devices by vacuum deposition. Vacuum deposition permits greater control over many material characteristics and properties of the resulting formed device. For example, vacuum deposition permits control over grain size, grain phase, grain material composition, bulk material composition, surface topography, mechanical properties, such as transition temperatures in the case of a shape memory alloy. Moreover, vacuum deposition processes will permit creation of devices with greater material purity without the introduction of large quantities of contaminants that adversely affect the material, mechanical or biological properties of the implanted device. Vacuum deposition techniques also lend themselves to fabrication of more complex devices than those susceptible of manufacture by conventional cold-working techniques. For example, multi-layer structures, complex geometrical configurations, extremely fine control over material tolerances, such as thickness or surface uniformity, are all advantages of vacuum deposition processing.

[0009] In vacuum deposition technologies, materials are formed directly in the desired geometry, *e.g.,* planar, tubular, etc. The common principle of vacuum deposition processes is to take a material in a minimally processed form, such as pellets or thick foils, known as the source material and atomize them. Atomization may be carried out using heat, as is the case in physical vapor deposition, or using the effect of collisional processes, as in the case of sputter deposition, for example. In some forms of deposition, a process, such as laser ablation, which creates microparticles that typically consist of one or more atoms, may replace atomization; the number of atoms per particle may be in the thousands or more. The atoms or particles of the source material are then deposited on a substrate or mandrel to directly form the desired object. In other deposition methodologies, chemical reactions between ambient gas introduced into the vacuum chamber, *i.e.*, the gas source, and the deposited atoms and/or particles are part of the deposition process. The deposited material includes compound species that are formed due to the reaction of the solid source and the gas source, such as in the case of chemical vapor deposition. In most cases, the deposited

material is then either partially or completely removed from the substrate, to form the desired product.

[0010] A first advantage of vacuum deposition processing is that vacuum deposition of the metallic and/or pseudometallic films permits tight process control and films may be deposited that have regular, homogeneous atomic and molecular pattern of distribution along their fluid-contacting surfaces. This avoids the marked variations in surface composition, creating predictable oxidation and organic adsorption patterns and has predictable interactions with water, electrolytes, proteins and cells. Particularly, EC migration is supported by a homogeneous distribution of binding domains that serve as natural or implanted cell attachment sites, in order to promote unimpeded migration and attachment.

[0011] Secondly, in addition to materials and devices that are made of a single metal or metal alloy, henceforth termed a layer, the inventive grafts may be comprised of a layer of biocompatible material or of a plurality of layers of biocompatible materials formed upon one another into a self-supporting multilayer structure because multilayer structures are generally known to increase the mechanical strength of sheet materials, or to provide special qualities by including layers that have special properties such as superelasticity, shape memory, radio-opacity, corrosion resistance etc. A special advantage of vacuum deposition technologies is that it is possible to deposit layered materials and thus films possessing exceptional qualities may be produced (*cf.*, H. Holleck, V. Schier: Multilayer PVD coatings for wear protection, *Surface and Coatings Technology*, Vol. 76-77 (1995) pp. 328-336). Layered materials, such as superstructures or multilayers, are commonly deposited to take advantage of some chemical, electronic, or optical property of the material as a coating; a common example is an antireflective coating on an optical lens. Multilayers are also used in the field of thin film fabrication to increase the mechanical properties of the thin film, specifically hardness and toughness.

[0012] Thirdly, the design possibilities for possible configurations and applications of the inventive graft are greatly enhanced by employing vacuum deposition technologies. Specifically, vacuum deposition is an additive technique that lends itself toward fabrication of substantially uniformly thin materials with potentially complex three dimensional geometries and structures that cannot be cost-effectively achieved, or in some cases achieved at all, by employing conventional wrought fabrication techniques. Conventional wrought metal fabrication techniques may entail smelting, hot working, cold working, heat treatment, high temperature annealing, precipitation annealing, grinding, ablation, wet etching, dry

etching, cutting and welding. All of these processing steps have disadvantages including contamination, material property degradation, ultimate achievable configurations, dimensions and tolerances, biocompatibility and cost. For example conventional wrought processes are not suitable for fabricating tubes having diameters greater than about 20mm diameter, nor are such processes suitable for fabricating materials having wall thicknesses down to about 5 μm with sub-μm tolerances.

[0013] While the inventive self-supporting metal or pseudometal graft may be fabricated of conventionally fabricated wrought materials, in accordance with the best mode contemplated for the present invention, the inventive graft is preferably fabricated by vacuum deposition techniques. By vacuum depositing the metal and/or pseudometallic film as the precursor material for the inventive graft, it is possible to more stringently control the material, biocompatibility and mechanical properties of the resulting film material and graft than is possible with conventionally fabricated graft-forming materials. The inventive self-supporting graft may be used alone, *i.e.*, the whole implantable device may be made of a single graft, or it may be a part of a structure where the graft is used in conjunction either with other grafts, or in conjunction with other structural elements, such as scaffolds, stents, and other devices. The term "in conjunction" may mean actual connection, such as that made by welding, fusing, or other joining methods, as well as being made from the same piece of material by forming some area of the piece into a graft and some other area of the piece into another member or part of the device.

Summary of the Invention

[0014] In accordance with a preferred embodiment of the invention, there is provided a self-supporting graft member having a plurality of microperforations passing through the wall thickness of the graft. The graft member may assume virtually any geometric configuration, including sheets, tubes or rings. The plurality of microperforations may serve to impart geometric compliance to the graft, geometric distendability to the graft and/or limit or permit the passage of body fluids or biological matter through the graft, such as facilitating transmural endothelialization while preventing fluid flow through the wall of the graft under normal physiological conditions. The plurality of microperforations may also impart a fabric-like quality to the graft by imparting pliability and/or elastic, plastic or superelastic

compliance to the graft, such as that required for longitudinal flexibility in the case of a vascular graft.

[0015] In a first embodiment, the graft may be made from plastically deformable materials such that upon application of a force, the microperforations geometrically deform to impart permanent enlargement of one or more axes of the graft, such as length in the case of a planar graft, *e.g.*, a surgical patch graft, or diameter, such as in the case of a tubular graft, *e.g.*, a vascular graft. In a second embodiment, the graft may be fabricated of elastic or superelastic materials. Elastic and/or superelastic materials will permit the microperforations to geometrically deform under an applied force in a manner that allows for a recoverable change in one or more axes of the graft.

[0016] In each of the first and second embodiments of the invention, the graft may be fabricated in such a manner as to have fabric-like qualities by controlling the film thickness, material properties and geometry of the plurality of microperforations. Furthermore, in such cases where minimally invasive delivery is required, such as for endoluminal delivery of vascular grafts, the first and second embodiments allow for delivery using balloon expansion and self-expansion, respectively, or a combination of both. Minimally invasive delivery may also be accomplished by folding the graft for delivery similar to the manner in which an angioplasty balloon is creased and fluted or folded. The graft may be delivered by unfolding the device *in vivo* either by assistance such as by using a balloon, or by the graft material's plastic, elastic or superelastic properties or by a combination thereof. After delivery, the plurality of microperforations may be patterned in such a manner as to allow for additional dimensional enlargement of the graft member by elastic or plastic deformation such as a radially expansive positive pressure.

[0017] For some applications it is preferable that the size of each of the plurality of microperforations be such as to permit cellular migration through each opening, without permitting fluid flow there through. In this manner, for example, blood cannot flow through the plurality of microperforations (in their deformed or un-deformed state), but various cells or proteins may freely pass through the plurality of microperforations to promote graft healing *in vivo*. For other applications, moderate amounts of fluid flow through the plurality of deformed or un-deformed microperforations may be acceptable. For example, endoluminal saphenous vein grafts may be fabricated with microperforations that serve the dual function of permitting transmural endothelialization while also excluding biological debris, such as thrombus from passing through the wall thickness of the graft, effectively excluding

detrimental matter from entering the circulation. In this example, each of the plurality of microperforations in either their deformed or undeformed state, may exceed several hundred microns.

[0018] Those skilled in the art will understand that a direct relationship exists between the size of pores and the overall ratio of expansion or deformability of an implantable graft. Generally, therefore, it is appreciated that pore sizes must increase in order to increase the effective attainable degree of expansion or deformation of the graft.

[0019] For applications where large deformation and small pore size are both requirements, in accordance with another aspect of the inventive graft embodiment, it is contemplated that two or more graft members are employed such as diametrically concentric grafts for tubular configurations. The two or more graft members have a pattern of a plurality of microperforations passing there through, with the plurality of patterned microperforations being positioned out of phase relative to one another such as to create a tortuous cellular migration pathway through the wall of the concentrically engaged first and second graft members as well as a smaller effective pore size. In order to facilitate cellular migration through and healing of the first and second graft members *in vivo*, it may be preferable to provide additional cellular migration pathways that communicate between the plurality of microperforations in the first and second graft members. These additional cellular migration pathways, if necessary, may be imparted as 1) a plurality of projections formed on either the luminal surface of the second graft or the abluminal surface of the first graft, or both, which serve as spacers and act to maintain an annular opening between the first and second graft members that permits cellular migration and cellular communication between the plurality of microperforations in the first and second graft members, 2) a plurality of microgrooves, which may be random, radial, helical, or longitudinal relative to the longitudinal axis of the first and second graft members, the plurality of microgrooves being of a sufficient size to permit cellular migration and propagation along the groove, the microgrooves serve as cellular migration conduits between the plurality of microperforations in the first and second graft members, or 3) where the microperforations are designed to impart an out of plane motion of the graft material upon deformation, thereby keeping a well defined space between the planes originally defining the facing surfaces of the grafts.

[0020] The graft member or members may be formed as a monolayer film, or may be formed from a plurality of film layers formed one upon another. The particular material used to form each layer of biocompatible metal and/or pseudometal is chosen for its

biocompatibility, corrosion-fatigue resistance and mechanical properties, *i.e.*, tensile strength, yield strength. The metals include, without limitation, the following: titanium, vanadium, aluminum, nickel, tantalum, zirconium, chromium, silver, gold, silicon, magnesium, niobium, scandium, platinum, cobalt, palladium, manganese, molybdenum and alloys thereof, such as zirconium-titanium-tantalum alloys, nitinol, and stainless steel. Additionally, each layer of material used to form the graft may be doped with another material for purposes of improving properties of the material, such as radiopacity or radioactivity, by doping with tantalum, gold, or radioactive isotopes.

Brief Description of the Drawings

[0021] Figure 1 is a perspective view of the inventive graft.

[0022] Figure 2A is a fragmentary plan view depicting a first pattern of microperforations useful in the present invention.

[0023] Figure 2B is a fragmentary plan view depicting a second pattern of microperforations useful in the present invention.

[0024] Figure 2C is a fragmentary plan view depicting a third pattern of microperforations useful in the present invention.

[0025] Figure 2D is a fragmentary plan view depicting a fourth pattern of microperforations useful in the present invention.

[0026] Figure 3A is photomicrograph depicting the inventive graft having the first pattern of microperforation depicted in Figure 2A in a geometrically undeformed state.

[0027] Figure 3B is a photomicrograph of the inventive graft illustrated in Figure 3A showing the microperforations in a geometrically deformed state.

[0028] Figure 4 is a diagrammatic illustration depicting geometric deformation of the fourth pattern of microperforations in Figure 2D.

[0029] Figure 5 is a diagrammatic cross-sectional view illustration depicting the inventive graft assuming a folded condition suitable for endoluminal delivery.

[0030] Figure 6 is a photographic illustration of the inventive graft used as a stent covering.

[0031] Figure 7 is a photographic illustration of the inventive graft deformed approximately 180 degrees along its longitudinal axis illustrating the fabric-like quality of the graft.

[0032] Figure 8A is a photographic illustration of the inventive graft circumferentially covering a braided expansion member and mounted on an expansion jig that exerts a compressive force along the longitudinal axis of the braided expansion member and which radially expands the braided expansion member.

[0033] Figure 8B is a photographic illustration of the inventive graft radially exhibiting radial compliance under the influence of a radially expansive force.

[0034] Figure 9 is a flow diagram depicting alternate embodiments of making the inventive graft.

[0035] Figure 10A is a histology slide, stained with hematoxylin and eosin, from a 28 day explanted swine carotid artery having the inventive graft implanted therein.

[0036] Figure 10B is a histology slide, stained with hematoxylin and eosin, from a 28 day explanted swine carotid artery having the inventive graft implanted therein.

Detailed Description of the Preferred Embodiments

[0037] With the foregoing as background, we turn now to a description of the present invention with reference the preferred embodiments thereof and with reference to the accompanying figures. As noted above, the inventive microporous metallic implantable devices may assume a wide number of geometric configurations, including, for example, planar sheets, tubes or toroids. For ease of reference, however, the accompanying figures and the following description of the invention will refer to tubular implantable graft members. Those skilled in the art, however, will understand that this is merely an exemplary geometric configuration and is not intended to limit the scope of the invention to tubular members or be limited in application to graft members.

[0038] With particular reference to Figure 1, the inventive implantable medical device is illustrated as a graft 10. Graft 10 consists generally of a body member 12 having a first surface 14 and a second surface 16 and a thickness 18 intermediate the first surface 14 and the second surface 16. A plurality of microperforations 20 is provided and pass through the thickness 18 of the body member 12 with interperforation regions 22 of the body member 12

between adjacent microperforation 20. The plurality of microperforations 20 each preferably have a geometric configuration that is susceptible of geometric change, such that the open surface area of each microperforation 20 may change under an externally applied load. Each of the plurality of microperforations 20 in the undeformed state preferably has an open surface area less than about 2 mm^2, with the total open surface area of the graft in the undeformed state being between 0.001 to 99%. The open surface area of the plurality of microperforations and the open surface area of the graft may change considerably upon deformation of the plurality of microperforations 20. Both the size of the microperforations 20 in the deformed and undeformed state and the total open area of the graft 12 in the deformed and undeformed state may be selected in view of the following non-exclusive factors based on the graft application: 1) the desired compliance of the graft 10, 2) the desired strength of the graft 10, 3) desired stiffness of the graft 10, 4) the desired degree of geometric enlargement of the microperforations 20 upon deformation and 5) in some cases, such as with vascular grafts, the desired delivery profile and post delivery profile.

[0039] In accordance with a preferred embodiment of the present invention, the plurality of microperforations 20 is patterned in such a manner as to define deformation regions of the body member 12. The thickness 18 is between 0.1μm and 75μm, preferably between 1μm and 50μm. When fabricated within these thickness ranges, the graft 10 has a thickness 18 which is thinner than the wall thickness of conventional non-metallic implantable grafts and that of conventional metal endoluminal stents.

[0040] . The plurality of microperforations is patterned in a regular array forming a regular array of microperforations 20 in both the longitudinal and circumferential axes of the body member 12. For purposes of reference, the pattern of microperforations 20 will, hereinafter, be described with reference to a planar X-Y axes, which in a tubular member will correspond to the longitudinal or circumferential axes of the tubular member. Those of ordinary skill in the art will understand that reference to X-axis or Y-axis when applied to a tubular member may be used such that the term "X-axis" may correspond to either the longitudinal axis or circumferential direction of the tubular member and the term "Y-axis" may refer to the corresponding circumferential direction or longitudinal axis or the tubular member.

[0041] It will be appreciated by those of ordinary skill in the art that individual different geometric patterns may have associated intended uses, function or mechanical requirements of a particular device. Thus, the particular intended use of the implantable member 12 will be

a consideration in the selection of the particular geometric pattern for the plurality of microperforations 20. For example, where the implantable member 12 has an intended use as a free-standing implantable endoluminal vascular graft, a large circumferential expansion ratio and longitudinal flexibility may be desirable. Thus, a particular geometry of the plurality of microperforations 20 that offers these properties will be selected. The plurality of microperforations 20 also affect the material properties of the implantable member 10. For example, the geometry each microperforation 20 may be altered so that each microperforation 20 exhibits stress-strain relief capabilities or the microperforations 20 may control whether geometric deformation of the microperforations 20 are plastic, elastic or superelastic deformation. Thus, both the geometry of the individual microperforations 20, the orientation of the microperforations 20 relative to the X-Y axis of the implantable member 10 and the pattern of the microperforations 20 may be selected to directly impart, affect or control the mechanical and material properties of the implantable member 10.

[0042] Different geometric patterns for the plurality of microperforations 20 in accordance with the preferred embodiments of the invention are illustrated in Figures 2A-2C. Figure 2A illustrates a first geometry for each of the plurality of microperforations 30. In accordance with this first geometry, each of the plurality of microperforations 30 consist of generally elongated slots 32a, 32b. Each of the generally elongated slots 32a, 32b preferably include terminal fillets 34 on opposing ends of each elongated slot 32a, 32b. The terminal fillets 34 serve a strain relief function that aids in strain distribution through the interperforation regions 22 between adjacent slots 32. Figure 2A further illustrates a first geometric pattern for the plurality of microperforations 32a, 32b, wherein a first row of a plurality of microperforations 32a is provided with adjacent microperforations 32a being arrayed in end-to-end fashion along a common axis, and a second row of a plurality of microperforations 32b is provided with adjacent microperforations 32b being arrayed in end-to-end fashion along a common axis with one another and with the microperforations 32a. The first row of microperforations 32a and the second row of microperforations 32b are offset or staggered from one another, with an end of a microperforation 32a being laterally adjacent to an intermediate section of a microperforation 32b, and an end of microperforation 32b being laterally adjacent an intermediate section of a microperforation 32a.

[0043] The first geometry 30 of the plurality of microperforations 32a, 32b illustrated in Figure 2A permits a large deformation along an axis perpendicular to a longitudinal axis of the slots. Thus, where the longitudinal axis of slots 32a, 32b is co-axial with the longitudinal

axis of the implantable member 10, deformation of the slots 32a, 32b will permit circumferential compliance and/or expansion of the implantable member 10. Alternatively, where the longitudinal axis of the slots 32a, 32b is parallel to the circumferential axis of the implantable member 10, the slots 32a, 32b permit longitudinal compliance, flexibility and expansion of the implantable member 10.

[0044] Figure 2B illustrates a second geometry 40 for the plurality of microperforations 20 and consists of a plurality of microperforations 42a, 44b, again having a generally elongate slot-like configuration like those of the first geometry 30. In accordance with this second geometry 40, individual microperforations 42a and 44b are oriented orthogonal relative to one another. Specifically, a first microperforation 42a is oriented parallel to an X-axis of the implantable member 10, while a first microperforation 44b is positioned adjacent to the first microperforation 44a along the X-axis, but the first microperforation 44b is oriented perpendicular to the X-axis of the implantable member 10 and parallel to the Y-axis of the implantable member 10. Like the first geometry, each of the plurality of microperforations 42a, 44b may include a terminal fillet 44 at opposing ends of the slot of each microperforation in order to serve a strain relief function and transmit strain to the interperforation region 22 between adjacent microperforations. This second geometry 40 offers a balance in both compliance and degree of expansion in both the X and Y-axes of the implantable device 12

[0045] In each of Figures 2A and 2B, each of the microperforations 32a, 32b, 42a, 44b has a generally longitudinal slot configuration. Each of the generally longitudinal slots may be configured as a generally linear or curvilinear slot. In accordance with the preferred embodiments of the invention, however, it is preferred to employ generally linear slots.

[0046] Figure 2C illustrates a third preferred geometry 50 for the plurality of microperforations. In accordance with this third geometry 50, each of the plurality of microperforations 52 has a generally trapezoidal or diamond-like shape with interperforation graft regions 56 between adjacent pairs of microperforations 52. It will be appreciated that the third geometry 50 may be achieved by geometrically deforming the first geometry 30 along an axis perpendicular to the longitudinal axis of the plurality of microperforations 32a, 32b. Similarly, the first geometry 30 may be achieved by deforming microperforations 52 in the third geometry 50 along either an X-axis or a Y-axis of the implantable member 10.

[0047] Figures 3A and 3B are photomicrographs illustrating the inventive implantable device 12 having a plurality of microperforations formed as generally longitudinal slots 32a, 32b in accordance with the first geometry depicted in Figure 2A. Each of the plurality of microperforations were formed with an orientation parallel to the longitudinal axis of the implantable device 12. The implantable device 12 consists of a 6 mm inner diameter NiTi shape memory tubular graft member having a wall thickness of 5 μm. Figure 3A depicts the plurality of microperforations 32a and 32b in their undeformed state, while Figure 3B depicts the plurality of microperforations 32a and 32b in their geometrically deformed state under the influence of stain applied perpendicular to the longitudinal axis of the implantable graft 12. It may be clearly understood that geometric deformation of the plurality of microperforations 32a, 32b permitted circumferential expansion of the inventive graft. The dimensions of each of the plurality of microperforations in their undeformed state depicted in Figures 3A and 3B was 430 μm in length, 50 μm width, with the terminal fillets having a 50 μm diameter.

[0048] In accordance with a fourth geometry of the plurality of microperforations 20 illustrated in Figures 2D and 4, each of the plurality of microperforations 20 have a generally tri-legged or Y-shaped configuration. The Y-shaped configuration of each of the plurality of microperforations 20 has three co-planar radially projecting legs 31a, 31b, 31c, each offset from the other by an angle of about 120 degrees thereby forming a generally Y-shape. Each of the three co-planar radially projecting legs 31a, 31b, 31c may be symmetrical or asymmetrical relative to one another. However, in order to achieve uniform geometric deformation across the entire graft body member 12, it is preferable that each of the plurality of microperforations 20 has geometric symmetry. Those skilled in the art will recognize that beyond the two particular patterns described here any number of different patterns may be used without significantly departing from the inventive graft concept described in the present patent.

[0049] Those skilled in the art will understand that each of the microperforations 20 are capable of undergoing deformation upon application of a sufficient force. In a tubular geometry, the graft 12 may deform both circumferentially and longitudinally. As is illustrated in Figure 3a, each of the plurality of elongated slots may deform into opened microperforations which assume a generally rhomboidal shape. Similarly, Y-shaped microperforations 20 shown in 4 are capable of deformation into generally circular or oval open microperforations 21. The deformation regions 22 between adjacent microperforations

20 facilitate deformation of each of the plurality of microperforations 20 by deforming to accommodate opening of each of the plurality of microperforations 20.

[0050] As depicted in Figure 5, the inventive graft 12 may be folded to assume a smaller diametric profile for endoluminal delivery. In order to facilitate folding, the pattern of the plurality of microperforations 20 may be fashioned to create a plurality of folding regions 23, that constitute relatively weakened regions of the graft 12, to permit folding the graft 12 along folding regions 23.

[0051] Figure 6 is a photographic illustration of the inventive microporous graft 12 circumferentially mounted onto an endoluminal stent 5. It may be readily seen that the microporous graft 12 exhibits mechanical properties of high longitudinal flexibility and both radial and circumferential compliance.

[0052] Figure 7 is a photographic illustration of the inventive microporous graft 12 mounted onto mandrel and flexed approximately 180 degrees along its longitudinal axis. Upon longitudinal flexion, the inventive graft 12 undergoes a high degree of folding with a plurality of circumferentially oriented folds 7, characteristic of its fabric-like qualities.

[0053] Figures 8A and 8B are photographic reproductions illustrating the high degree of circumferential compliance of the inventive microporous graft 12. A 6mm microporous graft having a 5 μm wall thickness was mounted concentrically over a braided pseudostent. An axial force was applied along the longitudinal axis of the braided pseudostent causing the pseudostent to radially expand and exert a circumferentially expansive force to the inventive graft 12. As is clearly depicted in Figures 8A and 8B the plurality of micropores in the inventive graft 12 geometrically deform thereby permitting circumferential expansion of the graft 12.

[0054] Thus, one embodiment of the present invention provides a new metallic and/or pseudometallic implantable graft that is biocompatible, geometrically changeable either by folding and unfolding or by application of a plastically, elastically or superelastically deforming force, and capable of endoluminal delivery with a suitably small delivery profile. Suitable metal materials to fabricate the inventive graft are chosen for their biocompatibility, mechanical properties, *i.e.*, tensile strength, yield strength, and their ease of fabrication. The compliant nature of the inventive graft material may be employed to form the graft into complex shapes by deforming the inventive graft over a mandrel or fixture of the appropriate

design. Plastic deformation and shape setting heat treatments may be employed to ensure the inventive implantable members 10 retain a desired conformation.

[0055] According to a first preferred method of making the graft of the present invention, the graft is fabricated of vacuum deposited metallic and/or pseudometallic films. With particular reference to Figure 9, the fabrication method 100 of the present invention is illustrated. A precursor blank of a conventionally fabricated biocompatible metal or pseudometallic material may be employed at step 102. Alternatively, a precursor blank of a vacuum deposited metal or pseudometallic film may be employed at step 104. The precursor blank material obtained either from step 102 or step 104 is then preferably masked at step 108 leaving exposed only those regions defining the plurality of microperforations. The exposed regions from step 108 are then subjected to removal either by etching at step 110, such as by wet or dry chemical etching processing, with the etchant being selected based upon the material of the precursor blank, or by machining at step 112, such as by laser ablation or EDM. Alternatively, when employing the vacuum deposition step 104, a pattern mask corresponding to the plurality of microperforations may be interposed at step 106 between the target and the source and the metal or pseudometal deposited through the pattern mask to form the patterned microperforations. Further, when employing the vacuum deposition step 104, plural film layers maybe deposited to form a multilayer film structure of the film prior to or concurrently with forming the plurality of microperforations.

[0056] Thus, the present invention provides a new metallic and/or pseudometallic implantable graft that is biocompatible, compliant, geometrically changeable either by folding and unfolding or by application of a plastically, elastically or superelastically deforming force, and, in some cases, capable of endoluminal delivery with a suitably small delivery profile and suitably low post-delivery profile. Suitable metal materials to fabricate the inventive graft are chosen for their biocompatibility, mechanical properties, *i.e.*, tensile strength, yield strength, and in the case where vapor deposition is deployed, their ease of deposition include, without limitation, the following: titanium, vanadium, aluminum, nickel, tantalum, zirconium, chromium, silver, gold, silicon, magnesium, niobium, scandium, platinum, cobalt, palladium, manganese, molybdenum and alloys thereof, such as zirconium-titanium-tantalum alloys, nitinol, and stainless steel. Examples of pseudometallic materials potentially useful with the present invention include, for example, composite materials and ceramics.

[0057] The present invention also provides a method of making the inventive expandable metallic graft by vacuum deposition of a graft-forming metal or pseudometal and formation of the microperforations either by removing sections of deposited material, such as by etching, EDM, ablation, or other similar methods, or by interposing a pattern mask, corresponding to the microperforations, between the target and the source during deposition processing. Alternatively, a pre-existing metal and/or pseudometallic film manufactured by conventional non-vacuum deposition methodologies, such as wrought hypotube or sheet, may be obtained, and the microperforations formed in the pre-existing metal and/or pseudometallic film by removing sections of the film, such as by etching, EDM, ablation, or other similar methods. An advantage of employing multilayer film structures to form the inventive graft is that differential functionalities may be imparted in the discrete layers. For example, a radiopaque material such as tantalum may form one layer of a structure while other layers are chosen to provide the graft with its desired mechanical and structural properties.

[0058] In accordance with the preferred embodiment of fabricating the inventive microporous metallic implantable device in which the device is fabricated from vacuum deposited nitinol tube, a cylindrical deoxygenated copper substrate is provided. The substrate is mechanically and/or electropolished to provide a substantially uniform surface topography for accommodating metal deposition thereupon. A cylindrical hollow cathode magnetron sputtering deposition device was employed, in which the cathode was on the outside and the substrate was positioned along the longitudinal axis of the cathode. A cylindrical target consisting either of a nickel-titanium alloy having an atomic ratio of nickel to titanium of about 50-50% and which can be adjusted by spot welding nickel or titanium wires to the target, or a nickel cylinder having a plurality of titanium strips spot welded to the inner surface of the nickel cylinder, or a titanium cylinder having a plurality of nickel strips spot welded to the inner surface of the titanium cylinder is provided. It is known in the sputter deposition arts to cool a target within the deposition chamber by maintaining a thermal contact between the target and a cooling jacket within the cathode. In accordance with the present invention, it has been found useful to reduce the thermal cooling by thermally insulating the target from the cooling jacket within the cathode while still providing electrical contact to it. By insulating the target from the cooling jacket, the target is allowed to become hot within the reaction chamber. Two methods of thermally isolating the cylindrical target from the cooling jacket of the cathode were employed. First, a plurality of wires having a

diameter of 0.0381mm were spot welded around the outer circumference of the target to provide an equivalent spacing between the target and the cathode cooling jacket. Second, a tubular ceramic insulating sleeve was interposed between the outer circumference of the target and the cathode cooling jacket. Further, because the Ni-Ti sputtering yields can be dependant on target temperature, methods which allow the target to become uniformly hot are preferred.

[0059] The deposition chamber was evacuated to a pressure less than or about 2-5 x 10^{-7} Torr and pre-cleaning of the substrate is conducted under vacuum. During the deposition, substrate temperature is preferably maintained within the range of 300 and 700 degrees Centigrade. It is preferable to apply a negative bias voltage between 0 and -1000 volts to the substrate, and preferably between -50 and -150 volts, which is sufficient to cause energetic species arriving at the surface of the substrate. During deposition, the gas pressure is maintained between 0.1 and 40 mTorr but preferably between 1 and 20 mTorr. Sputtering preferably occurs in the presence of an Argon atmosphere. The argon gas must be of high purity and special pumps may be employed to reduce oxygen partial pressure. Deposition times will vary depending upon the desired thickness of the deposited tubular film. After deposition, the plurality of microperforations are formed in the tube by removing regions of the deposited film by etching, such as chemical etching, ablation, such as by excimer laser or by electric discharge machining (EDM), or the like. After the plurality of microperforations are formed, the formed microporous film is removed from the copper substrate by exposing the substrate and film to a nitric acid bath for a period of time sufficient to remove dissolve the copper substrate.

Example

[0060] A 5μm thick NiTi graft having a pattern of microperforations consisting of parallel staggered longitudinally oriented linear slots, each slot being 430 μm length, 25 μm width, and having 50 μm diameter fillets on each end of each linear slot, was mounted onto a 6 mm NiTi stent and delivered endoluminally to the left carotid artery of a swine. After 28 days, the swine was euthanized, and the graft explanted from the left carotid artery. Samples were prepared using standard hematoxylin and eosin staining procedures, and microscope slides prepared. As illustrated in Figures 10A histology of the explanted samples revealed complete endothelialization around the graft 12, negligible neointimal proliferation with the

absence of trauma to the internal elastic lamina. Figure 10B is a sample indicating cross-talk between the arterial superficial and deep layers with the transmural formation of small capillaries.

[0061] While the present invention has been described with reference to its preferred embodiments, those of ordinary skill in the art will understand and appreciate that variations in materials, dimensions, geometries, and fabrication methods may be or become known in the art, yet still remain within the scope of the present invention which is limited only by the claims appended hereto.

Claims:

1. An implantable medical graft, comprising:

a) a tubular graft member comprising a vacuum deposited metal film having a first surface, a second surface and a thickness intermediate the first surface and the second surface wherein said thickness is between 0.1 and 75 µm; and,

b) a plurality of slot microperforations formed in and passing through the thickness of the vacuum deposited metal film and communicating between the first surface and the second surface, wherein the plurality of slot microperforations include a geometry to undergo geometric deformation.

2. The implantable medical graft according to claim 1, wherein the vacuum deposited metal film is made of a metallic material selected from the group consisting of titanium, vanadium, aluminum, nickel, tantalum, zirconium, chromium, silver, gold, silicon, magnesium, niobium, scandium, platinum, cobalt, palladium, manganese, molybdenum and alloys thereof.

3. The implantable graft according to any claim 1 or 2, wherein each of the plurality of microperforations includes a terminal fillet on opposing ends of the slot microperforations to relieve and distribute strain between adjacent slot microperforations.

4. The implantable graft according to any one of claims 1 to 3, wherein the plurality of microperforations are arrayed in at least one pattern that imparts at least one of compliance and pliability to the graft member.

5. The implantable graft according to any one of claims 1 to 4, wherein the plurality of slot microperforations is arrayed in at least one pattern sufficient to permit dimensional change of at least a portion of the device.

6. The implantable graft according to claim 5, wherein the dimensional change comprises at least one of elastic, plastic, shape memory and superelastic compliance.

7. The implantable medical graft according to any one of claims 1 to 6, wherein the first surface further comprises a luminal surface and the second surface including an abluminal surface of the tubular graft member.

8. The implantable medical graft according to any one of claims 1 to 7, wherein the tubular graft member is configured as a generally planar member.

9. The implantable medical graft according to any one of claims 1 to 8, wherein the plurality of slot microperforations each further comprise a generally co-planar tri-leg configuration.

10. An implantable covered stent, characterized by the implantable medical graft according to any one of claims 1-9 concentrically covering and coupled to the stent.

11. The implantable medical graft of claim 1, wherein each of the plurality of slot microperforations having an open surface area less than about 2 mm^2 when the graft member is in a non-diametrically enlarged state.

12. The implantable medical graft according to claim 11, wherein the vacuum deposited metal film is made of a metallic material selected from the group consisting of titanium, vanadium, aluminum, nickel, tantalum, zirconium, chromium, silver, gold, silicon, magnesium, niobium, scandium, platinum, cobalt, palladium, manganese, molybdenum and alloys thereof.

13. The implantable medical graft according to any one of claims 11 to 12, wherein each of the plurality of microperforations includes a terminal fillet on opposing ends of the slot microperforations to relieve and distribute strain between adjacent slot microperforations.

14. The implantable medical graft according to any one of claims 11 to 13, wherein the plurality of slot microperforations are arrayed in at least one pattern that imparts at least one of compliance and pliability to the graft member.

15. The implantable medical graft according to any one of claims 11 to 14, wherein the plurality of slot microperforations is arrayed in at least one pattern sufficient to permit dimensional change of at least a portion of the device.

16. The implantable medical graft according to claim 15, wherein the dimensional change comprises at least one of elastic, plastic, shape memory and superelastic compliance.

17. The implantable medical graft according to any one of claims 11 to 16, wherein the graft member further comprises a tubular member, the first surface further comprises a luminal surface of the tubular member and the second surface further comprises an abluminal surface of the tubular member.

18. The implantable medical graft according to any one of claims 11 to 17, wherein the graft member further comprises a generally planar member having conjoined ends to form the generally tubular shape.

19. The implantable medical graft according to any one of claims 11 to 18, wherein the plurality of slot microperforations each further comprise a generally co-planar tri-leg configuration.

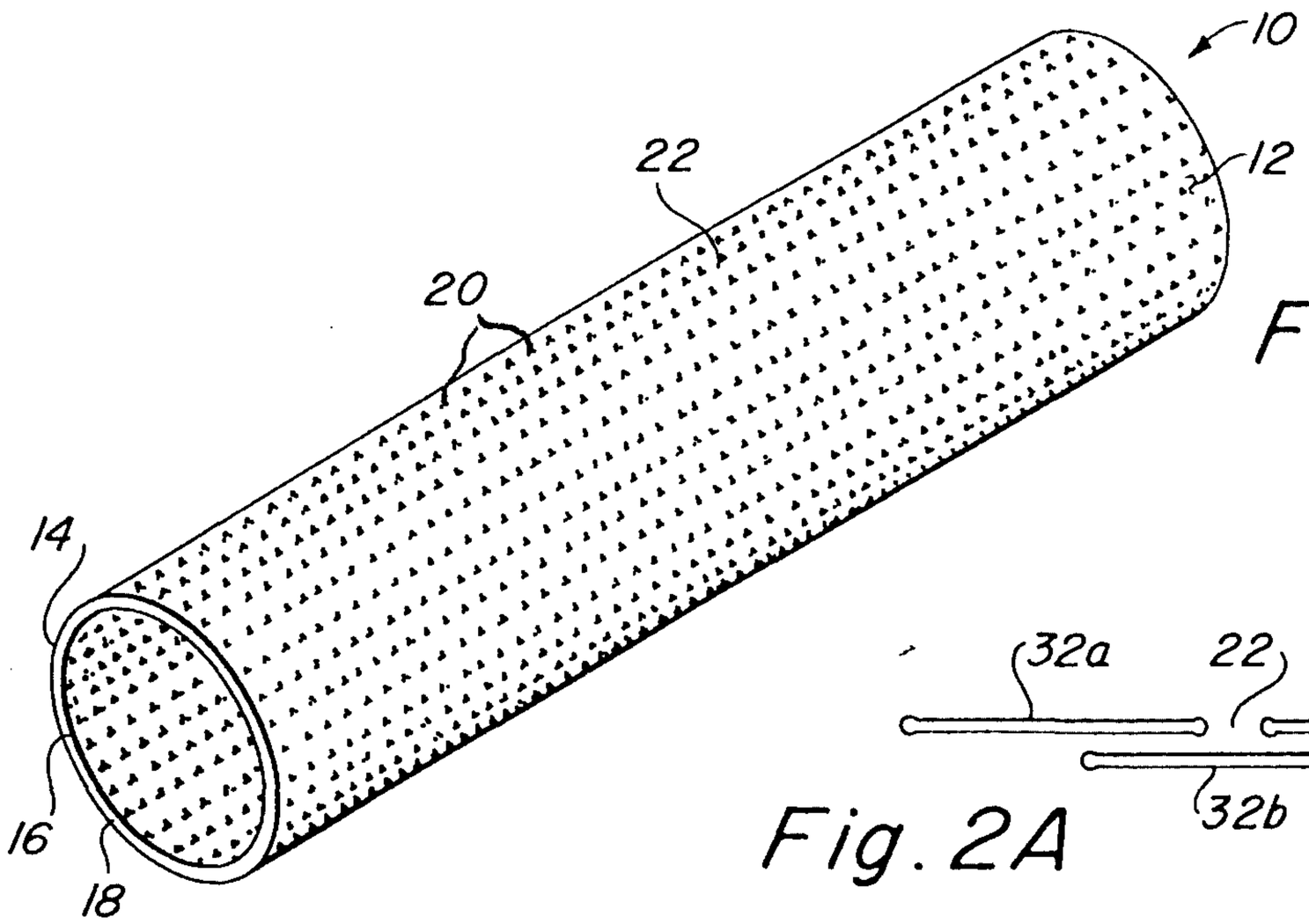


Fig. 1

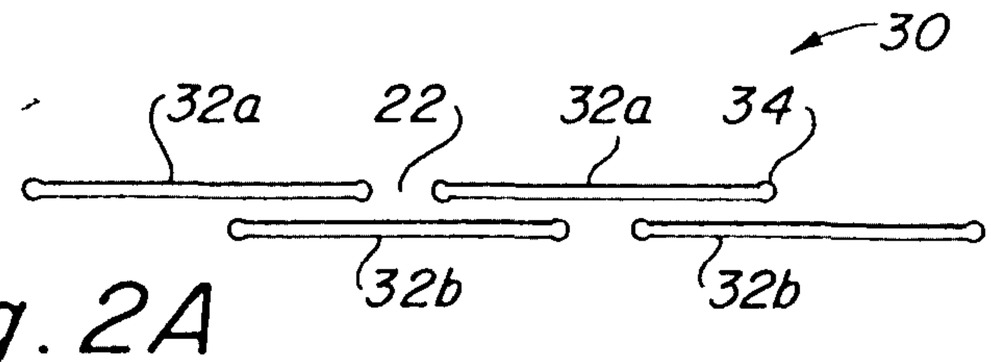


Fig. 2A

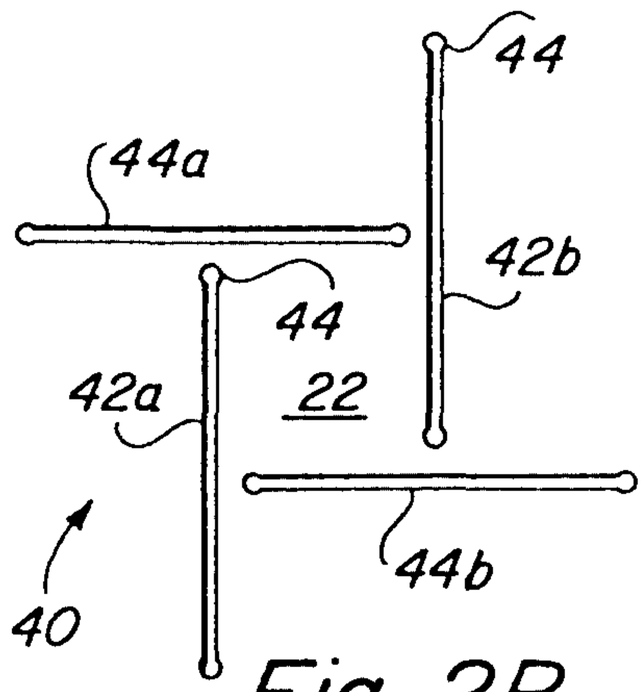


Fig. 2B

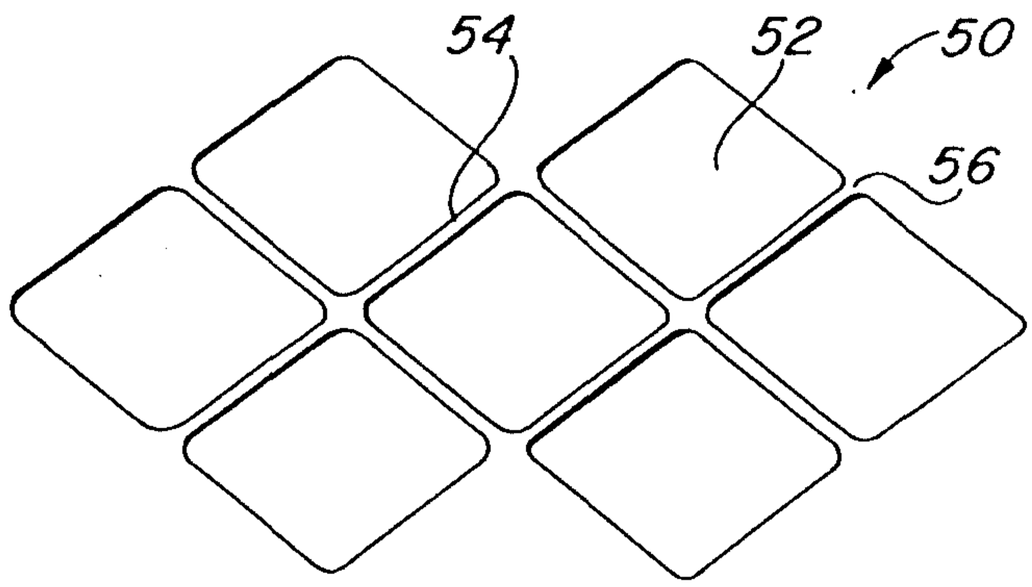


Fig. 2C

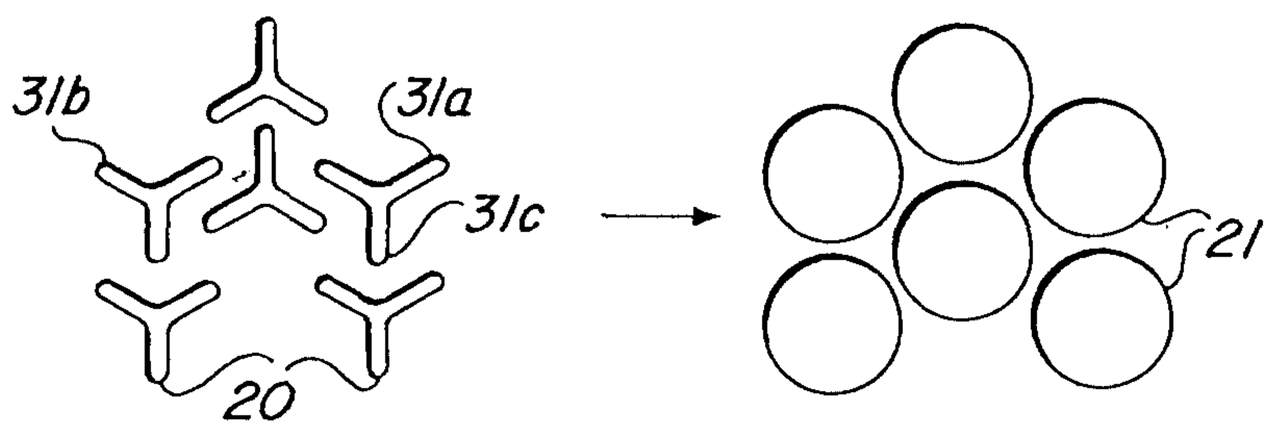


Fig. 4

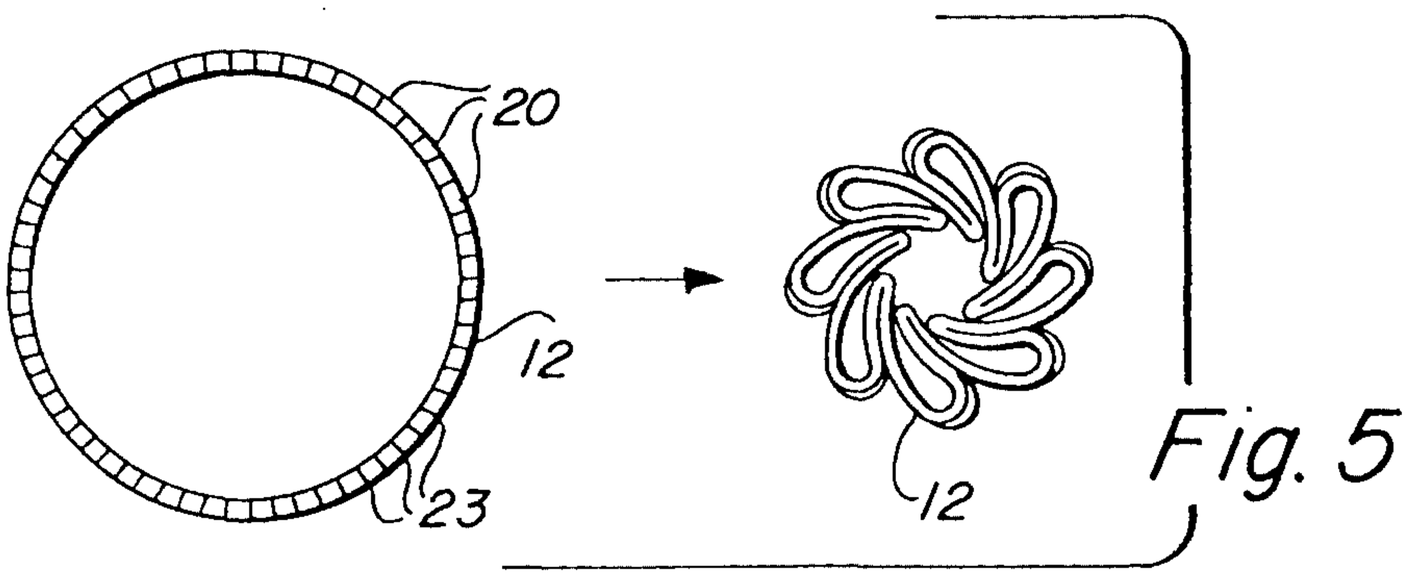


Fig. 5

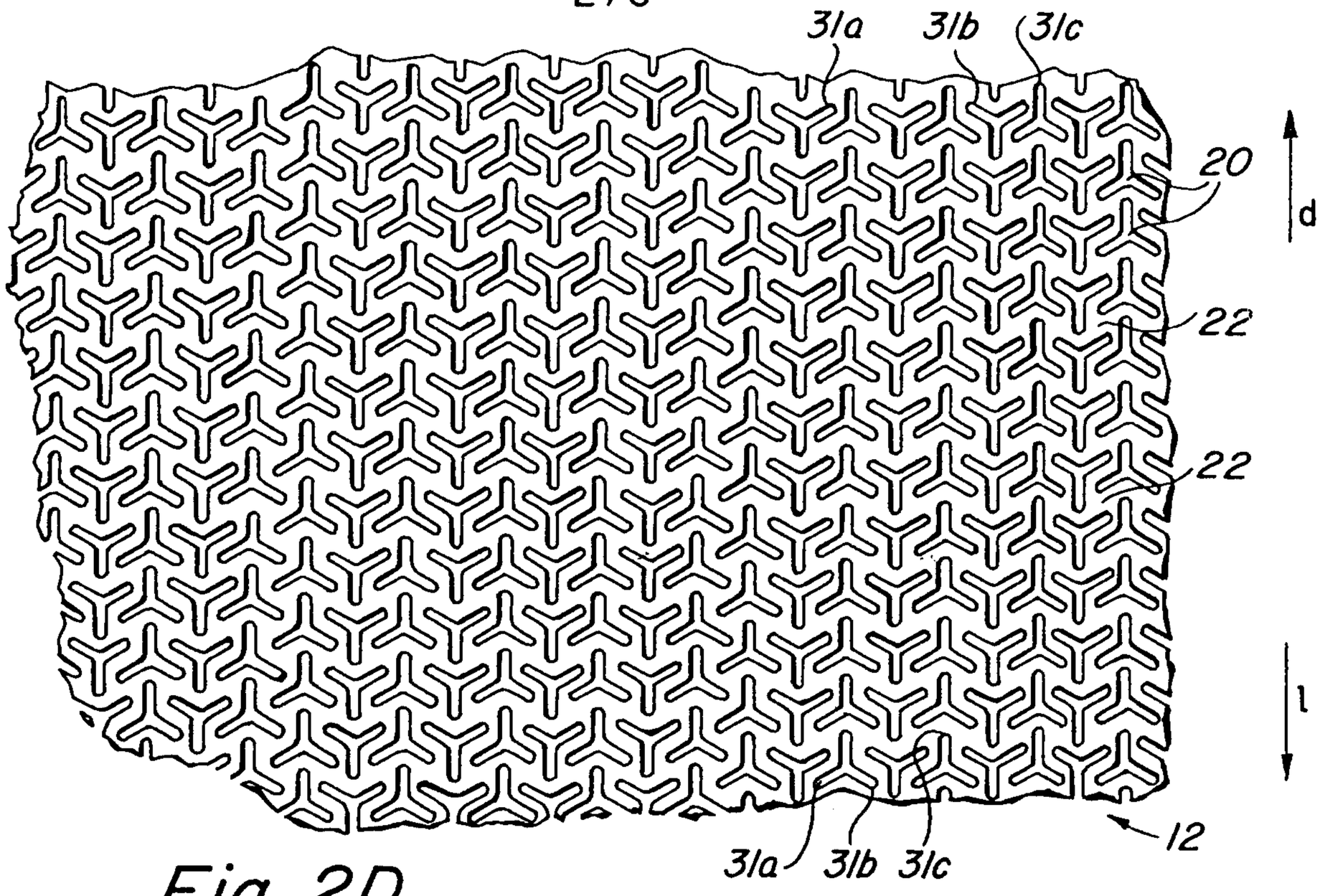

31a
31b
31c
20
d
22
22
l
12
31a
31b
31c

Fig. 2D

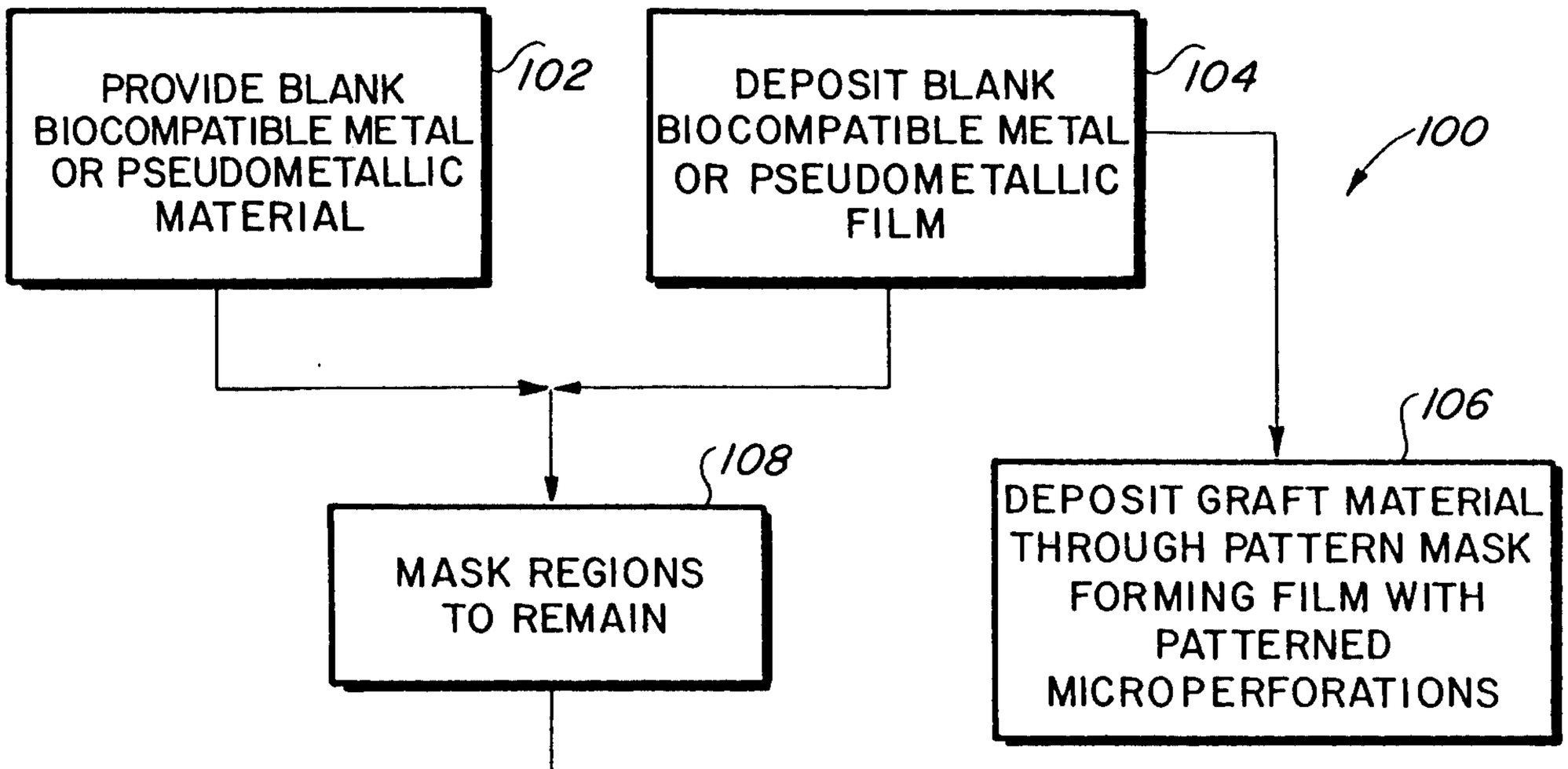

PROVIDE BLANK BIOCOMPATIBLE METAL OR PSEUDOMETALLIC MATERIAL
102
DEPOSIT BLANK BIOCOMPATIBLE METAL OR PSEUDOMETALLIC FILM
104
100
106
MASK REGIONS TO REMAIN
108
DEPOSIT GRAFT MATERIAL THROUGH PATTERN MASK FORMING FILM WITH PATTERNED MICROPERFORATIONS
110
ETCH UNMASKED REGIONS TO FORM MICROPERFORATIONS
112
MACHINE REMOVAL OF MATERIAL TO FORM MICROPERFORATIONS, e.g., LASER ABLATION, EDM

Fig. 9

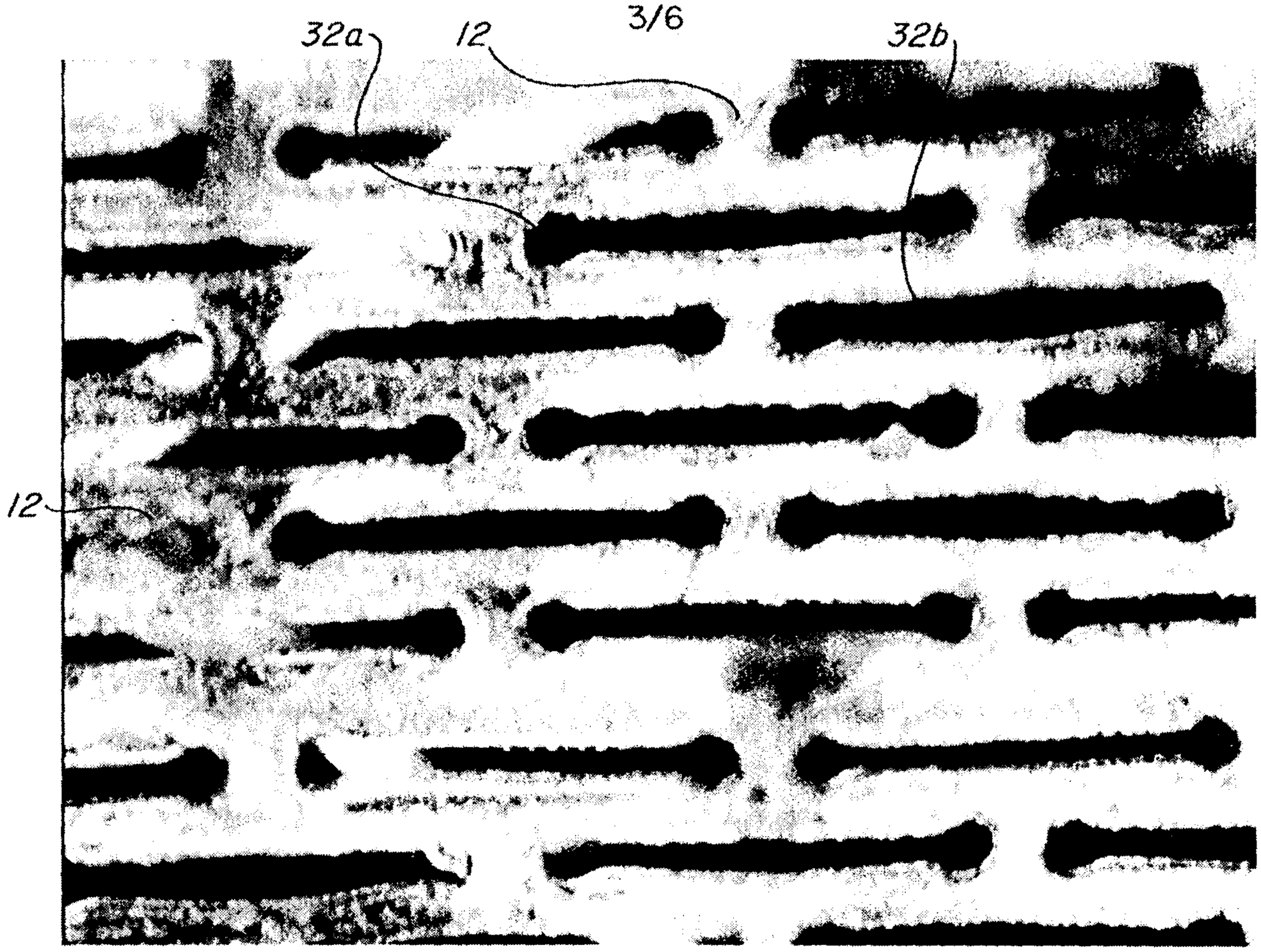
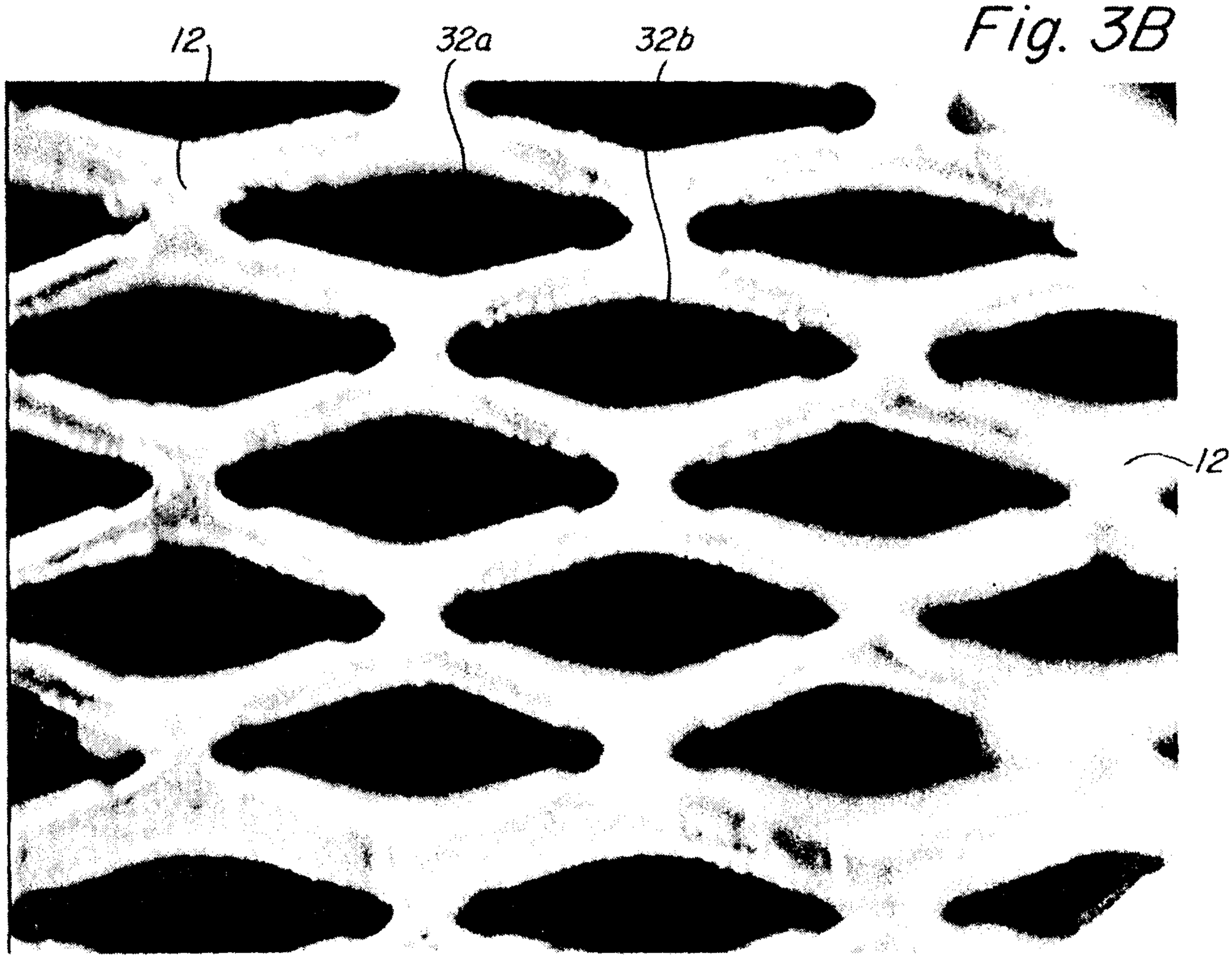


Fig. 3A

Fig. 3B



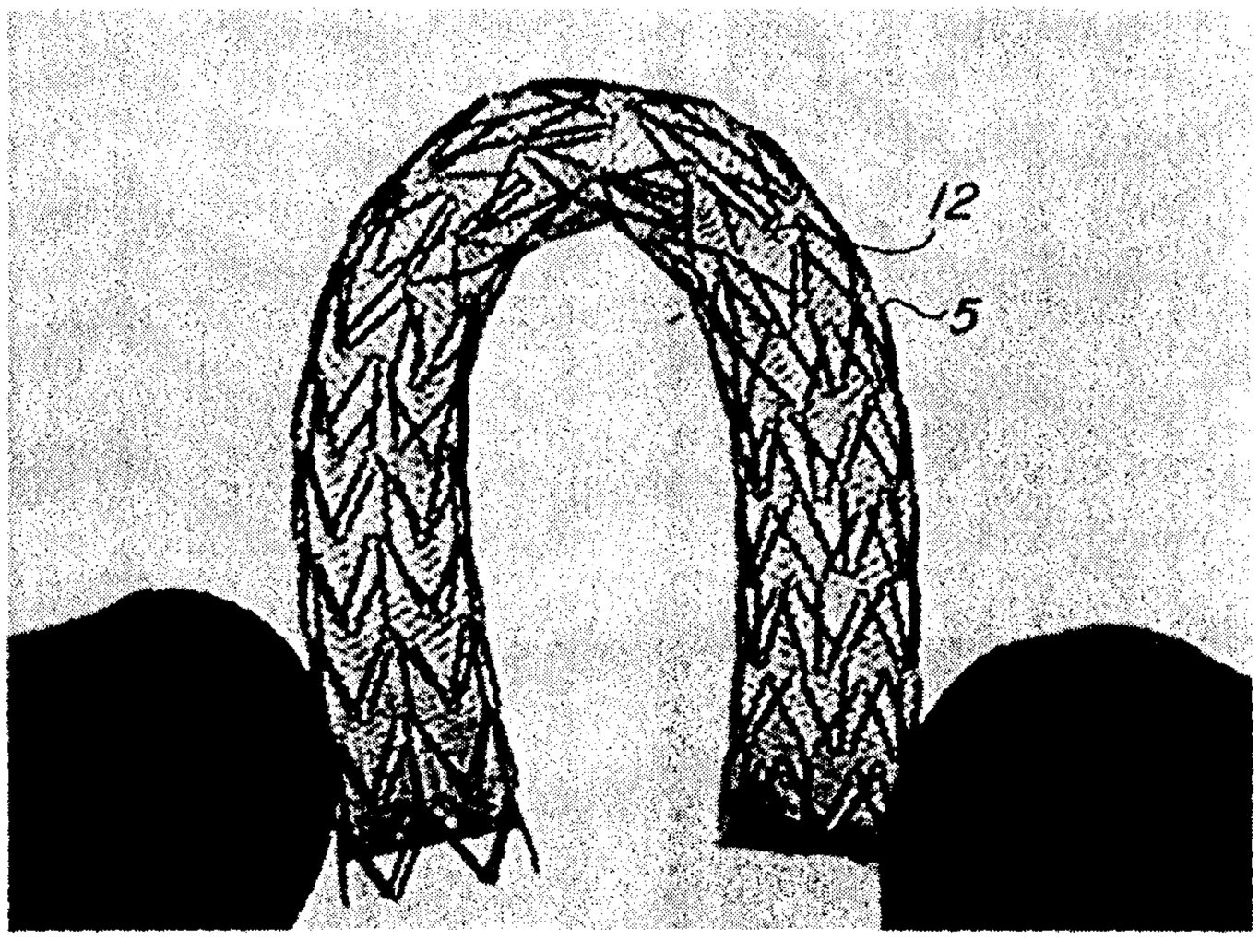


Fig. 6

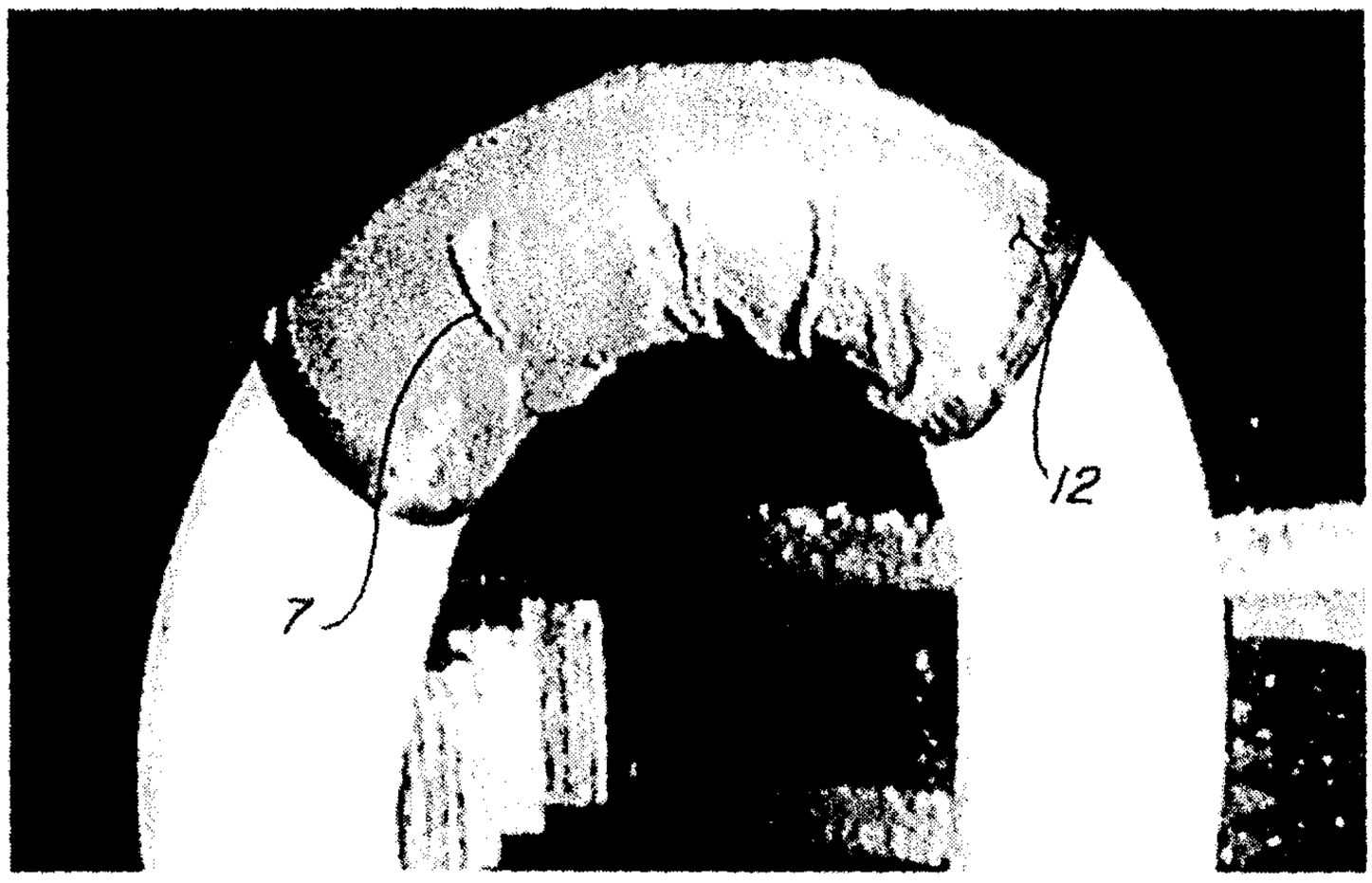


Fig. 7

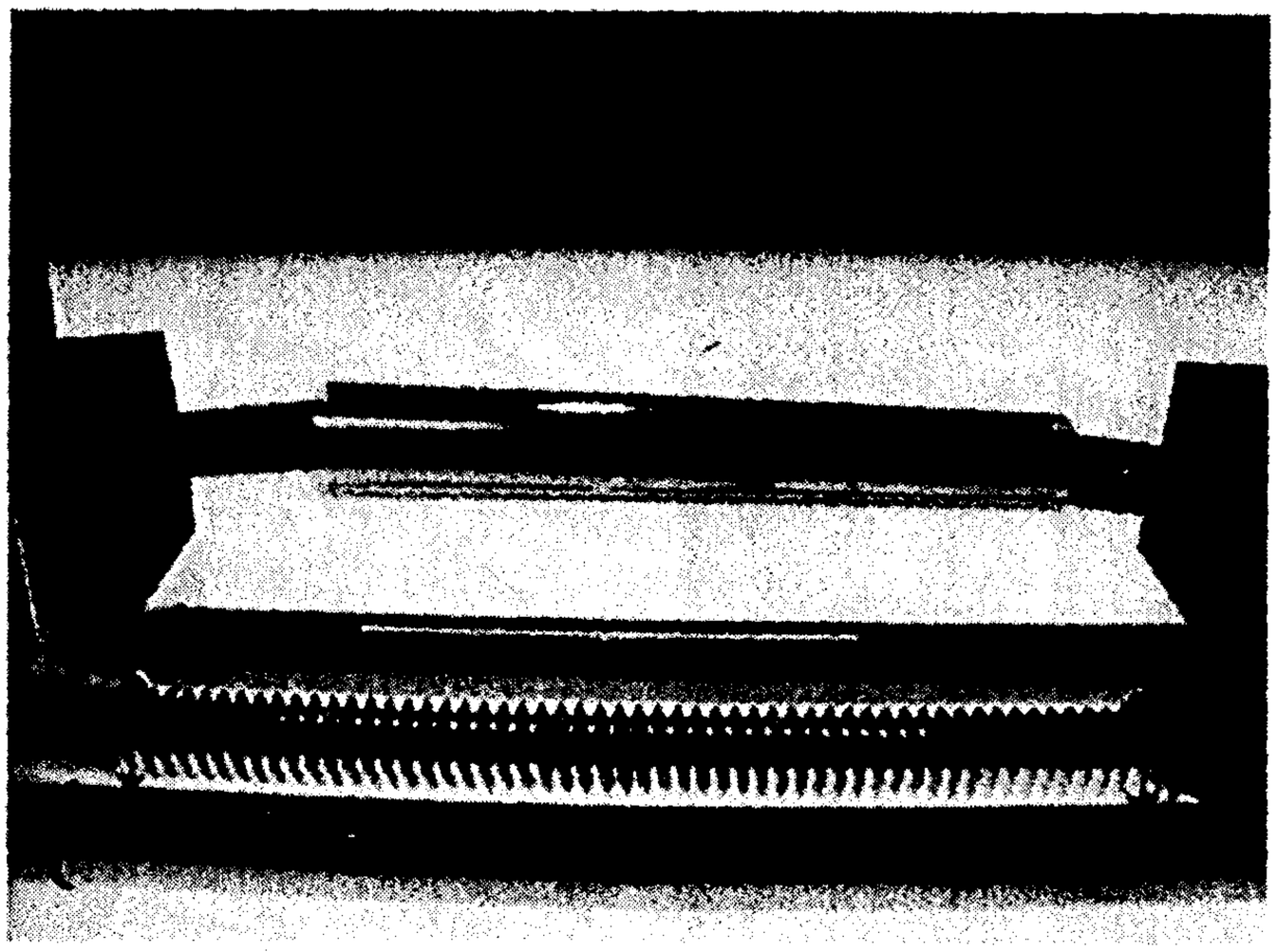


Fig. 8A

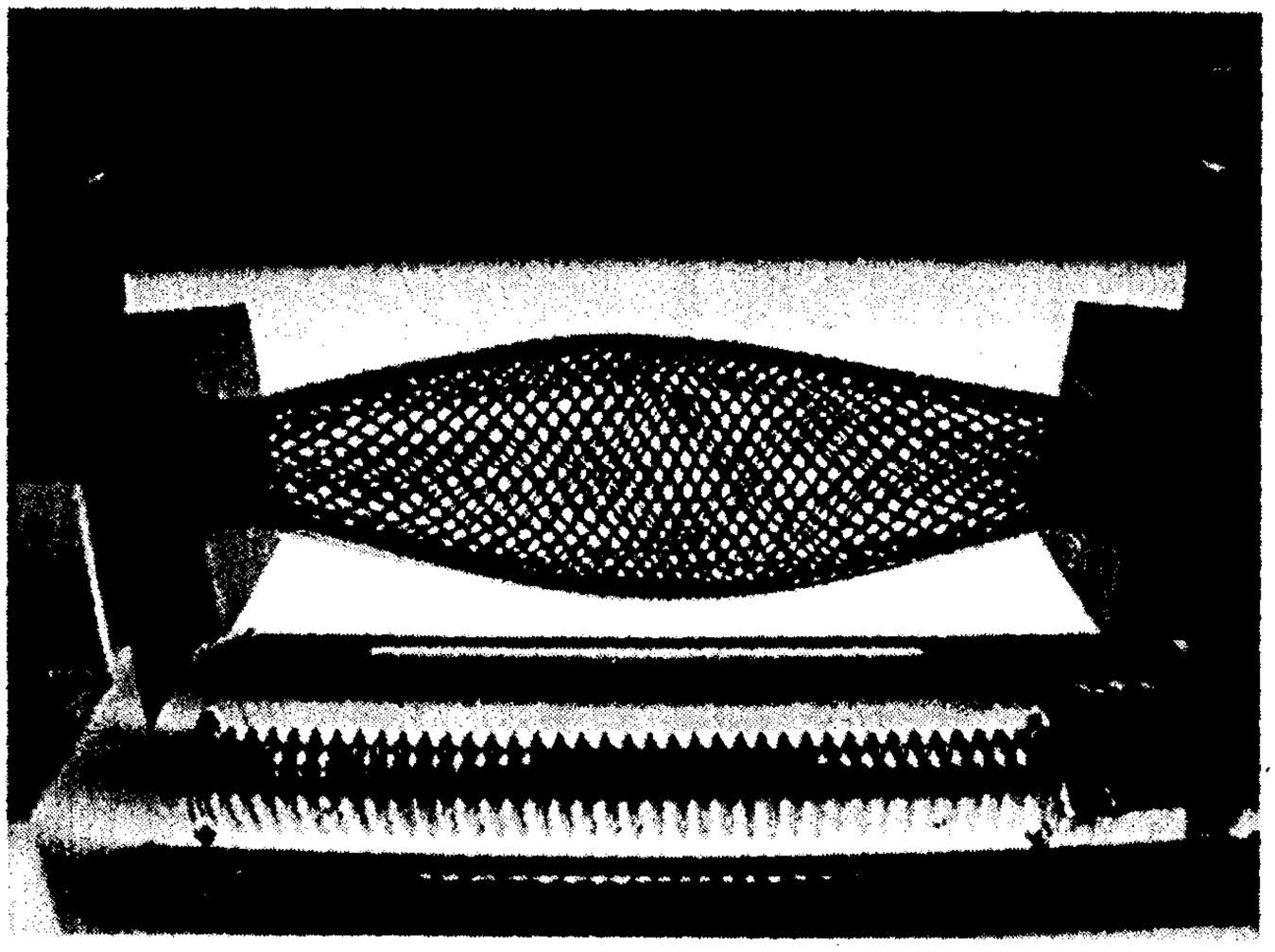


Fig. 8B

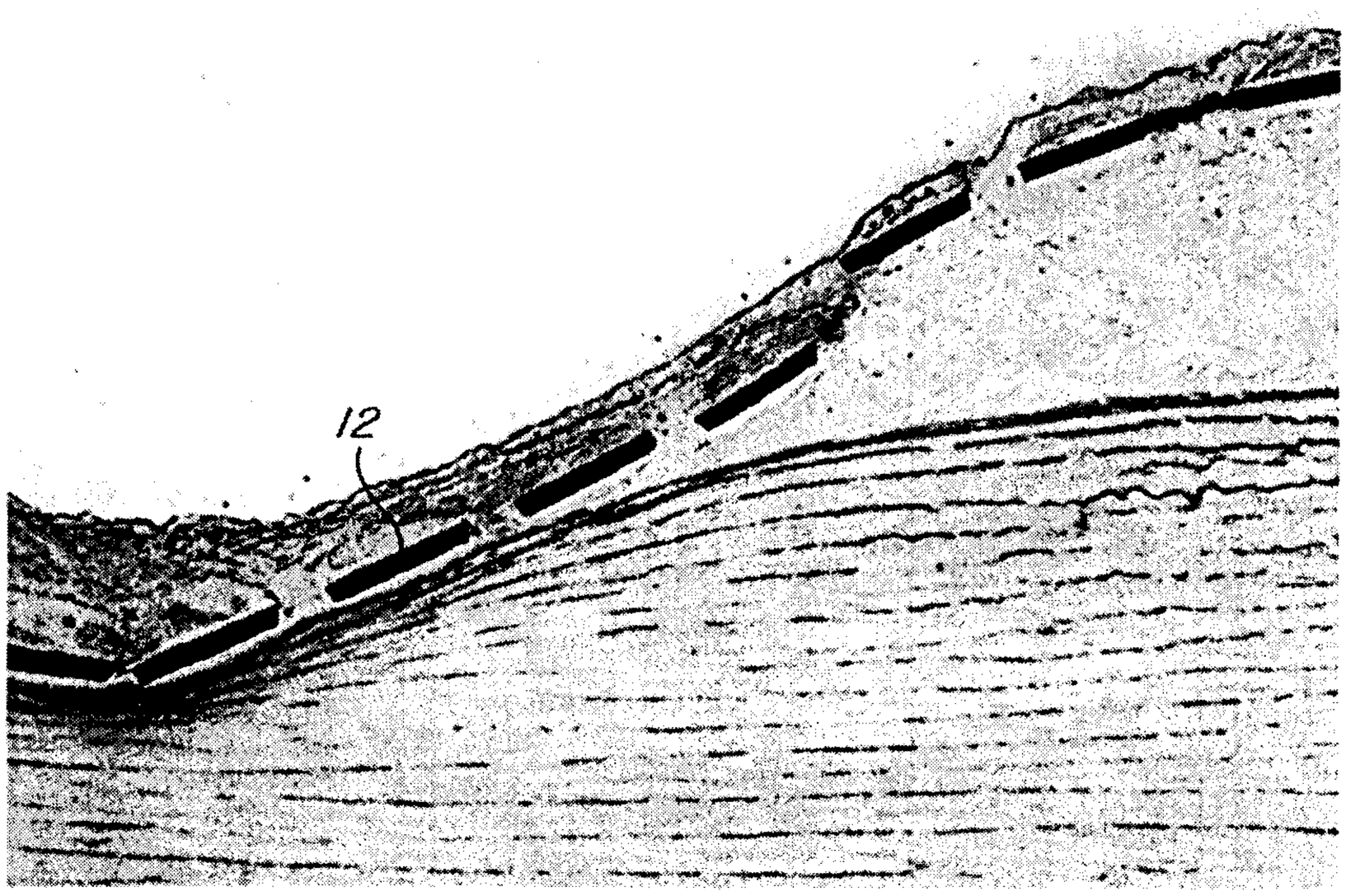


Fig. 10A

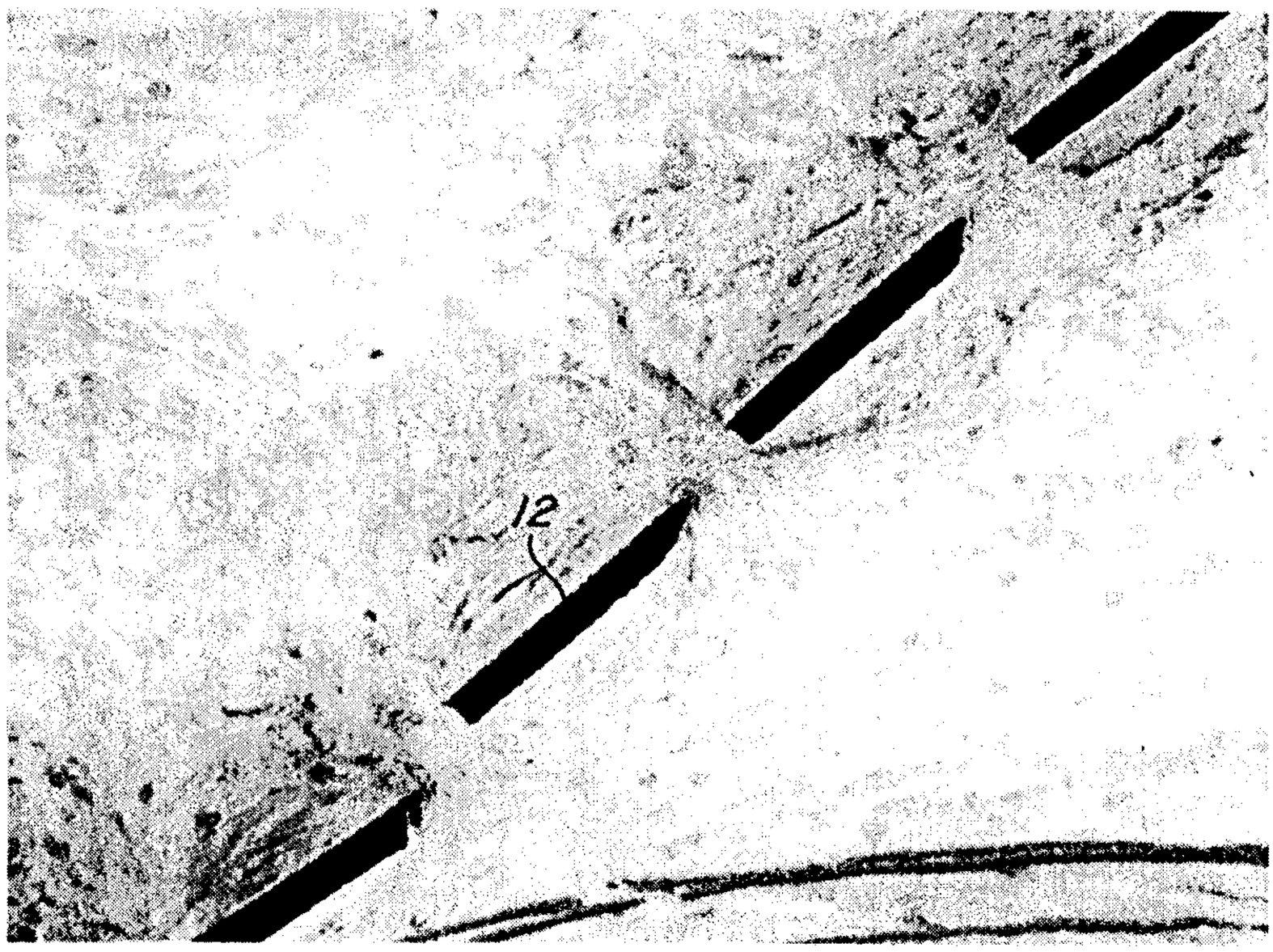
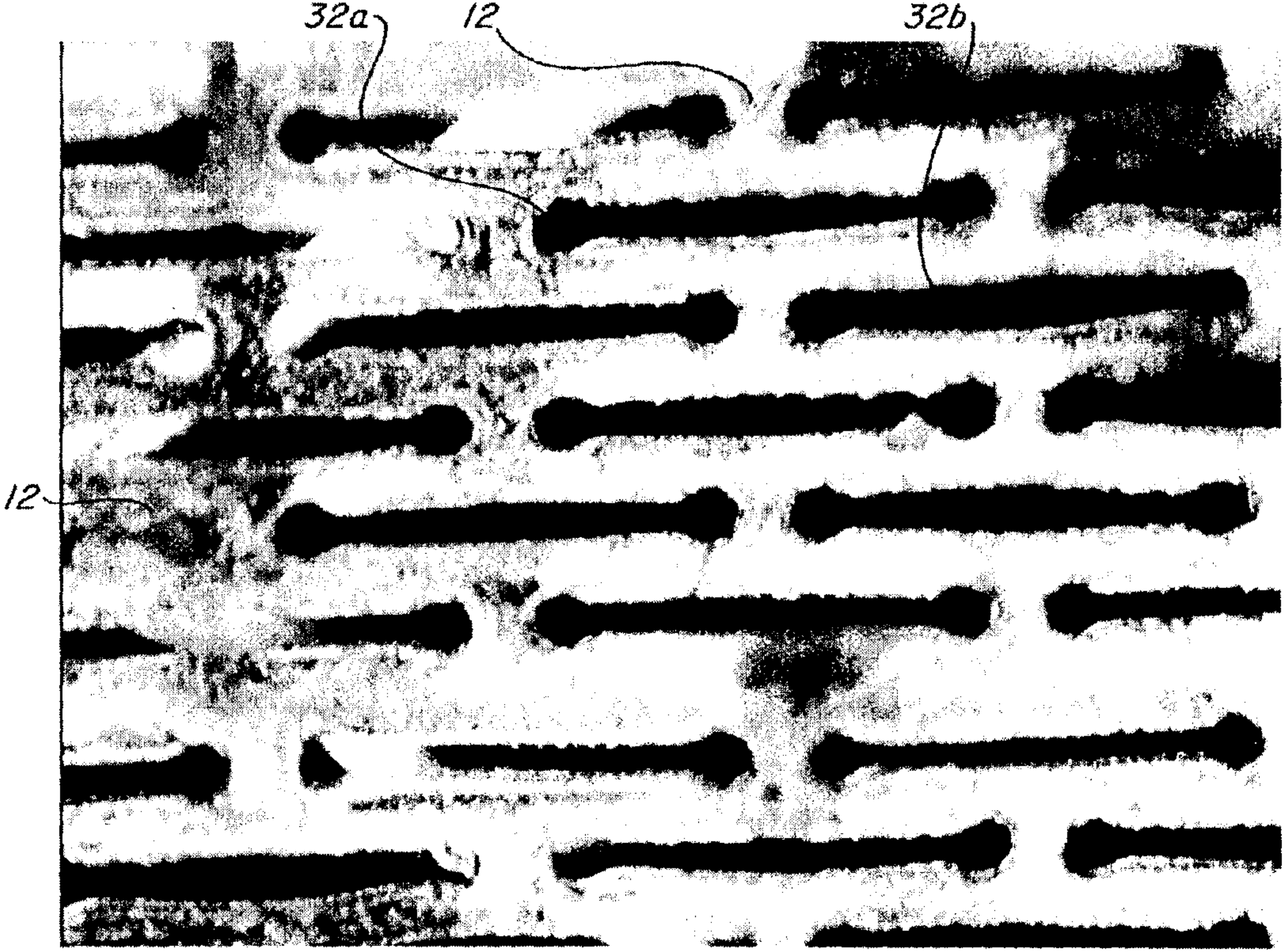


Fig. 10B


32a
12
32b
12