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(54) Title: A SELF-INFLATING ANISOTROPIC COMPOSITION, METHODS OF MANUFACTURING SAID COMPOSITION AND USES THEREOF

(57) Abstract: The present invention relates to a self-inflating anisotropic composition, said composition comprising a compressed copolymer. The present invention also relates to methods of manufacturing and uses of the self-inflating anisotropic composition.

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A self-inflating anisotropic composition, methods of manufacturing said composition and uses thereof

The present invention relates to a self-inflating anisotropic composition, which composition comprises a compressed copolymer. The composition is preferably a tissue expander. The present invention also relates to methods of manufacturing and uses of the self-inflating anisotropic composition.

Tissue expansion is a widely used technique in reconstructive plastic surgery. It has a host of applications ranging from the correction of burn alopecia of the scalp to breast reconstruction post mastectomy. Conventional expanders are based on silicone balloons (Figure 1a) which, via a filling port, are sequentially inflated with saline solution over a period of time.

The application of traditional balloon-type silicone tissue expanders to certain applications (such as craniofacial or cleft palate surgery) has been limited. This is in part related to the physical constraints of the device, which often preclude their use in discrete anatomical locations, but also due to the requirement for regular percutaneous inflation, which can be poorly tolerated by the patient, particularly in the paediatric setting.

Initial self-inflating tissue expanders were relatively crude, consisting of a semipermeable membrane shell containing hypertonic sodium chloride solution. Once implanted subcutaneously, osmotically driven device swelling occurs with concomitant tissue expansion. However, limitations existed both in the rate and extent of expansion and the inherent risk of catastrophic soft tissue necrosis in the event of device rupture.

Subsequently, hydrogels were investigated for use in tissue expanders. This led to the development of an osmotically active polymer-based tissue expander for the treatment of congenital anophthalmia. US5496368 describes a tissue expander of this type.

However, significant limitations are associated with the surgical application of these self-inflating hydrogel tissue expanders. Primarily, the problem is that their expansion is isotropic (it occurs to a similar extent, in all directions). This isotropic characteristic limits the extent to which such tissue expanders can be manipulated for different applications within the body. In particular, it makes these tissue expanders unsuitable for use in small and/or irregularly shaped areas of the body. The development of a tissue expander capable of controlled self-inflating anisotropic expansion significantly increases the clinical indications for which this material could be used. For example, closure of a transverse anatomical defect (e.g. a cleft palate deformity) could be achieved without the attendant risks of anteroposterior expansion and device extrusion. Specifically a self-inflating anisotropic tissue expander would allow controlled physiological inflation over a pre-determined period hence reducing the risk of device extrusion.

US6228116 describes an anisotropic tissue expander. However, this tissue expander is not capable of self-inflation. A self-inflating device has numerous advantages over the tradition balloon-type tissue expander. The absence of a filling port and the ability for the hydrogel to be machined or shaped to virtually any configuration enables the expander to be used in practically any anatomical site desired. Furthermore, the device does not require regular, painful percutaneous inflation; a property which is particularly beneficial in the paediatric population. Whereas traditional expanders necessitate healthcare professional-led inflation on a regular (usually weekly) basis, cost savings would be expected with a hydrogel device as this intervention, with its associated complications, would no longer be required.

The first aspect of the invention provides a self-inflating anisotropic composition, which composition comprises a compressed copolymer. The composition of the first aspect is thus a self-inflating anisotropic expanding composition.

Herein, anisotropic means having properties that differ according to the direction of measurement i.e. not isotropic. The anisotropic composition of the present invention expands more in one direction (plane), than in any other.

Herein, a copolymer means a combination of two or more different polymers or monomers. The composition of the present invention is preferably in the form of a hydrogel (a gel in which water is the dispersion medium). The copolymer of the present invention may also be a biocompatible hydrogel copolymer

Herein, xerogel means the copolymer without water.

The copolymer is formed by standard polymerisation techniques.

For example, the polymerisation technique can be a method known as "chain-growth polymerisation". The method involves three stages comprising initiation, propagation and termination (see, for example, Chapter 5, Fundamentals of Polymers (Kumar and Gupta, McGraw-Hill, 1998)). The copolymer is produced by copolymerising two or more monomers together. An initiator such as azobisisobutyronitrile can be used to initiate the polymerisation and the copolymer cross-linked using a cross-linker such as alkyl methacrylate.

Either during or following the polymerisation process, antibiotics, analgesics, anti-microcidal agents, anti-fungicidal agents, drugs including anti-inflammatory drugs, and any other appropriate or useful substance can be added. Furthermore, polylactic acid could be incorporated comprising any of these substances.

The expander of the present invention will comprise at least two polymers and may include others. The proportion of the first and second or further polymers in the copolymer can be varied depending on the exact application of the expander. Varying the proportion of each polymer will result in different characteristics. For example, to increase the amount of expansion achieved, higher proportions of a hygroscopic

polymer such as poly vinylpyrrolidone (PVP) should be used, as illustrated in Example 2.

As part of the self-inflating anisotropic expanding composition, the copolymer will consist of at least a first hygroscopic polymer. The second polymer will provide a building block/backbone for the composition. The first hygroscopic polymer will be at least one polymer made of at least one of the following: vinylpyrrolidone, acrylamide, vinyl alcohol, *N*-cyclopropylacrylamide, *N*-*n*-propylacrylamide, *N*-isopropylacrylamide, acrylic acid, ethylene oxide, methacrylic acid, gelatin, collagen, cellulose, agar or any polymer or monomer comprising a –COOH, =C=O, =COH, or -NH_2 group or their moieties. The second polymer may be either another hygroscopic polymer formed from those listed above or may be an acrylate. In particular, the second polymer may be at least one polymer synthesised from the following: methyl methacrylate, hydroxyethyl methacrylate, ethyl methacrylate, *n*-butyl methacrylate, *i*-*b*utyl methacrylate, *n*-hexyl methacrylate, 2-ethylhexyl methacrylate, isodecyl methacrylate, dodecyl methacrylate, methacrylic ester, octadecyl methacrylate, cyclohexyl methacrylate, isobornyl methacrylate, benzyl methacrylate, trimethylcyclohexyl methacrylate, isotridecyl methacrylate, methacrylic acid, methacrylic anhydride, maleinic acid, isobornyl acrylate, urethane, and (ethylene-co-vinyl acetate). A preferred copolymer is a copolymer of poly methyl methacrylate and poly vinylpyrrolidone.

The hydrogel may be composed of or also include a polyrotaxane (such as poly(oxyethylene-rotaxa-cyclodextrin). The polyrotaxane may replace one or both of the first and second polymers described above or be present in addition.

Preferably, the composition of the first aspect of the invention is a tissue expanding composition. Such a self-inflating tissue expander is unknown in the art and solves a variety of problems as hereinbefore described. The use of the composition of the present invention as a tissue expander provides benefits in a variety of clinical needs, such as the closure of cleft palate defects, the release of congenitally fused fingers (syndactyly) or to dilate strictures in visceral lumens or vascular structures.

Alternatively, the composition of the first aspect of the invention finds use as an environmentally responsive industrial switch. In this type of embodiment, the hydrogel copolymer swells in response to water and contracts in response to increased temperature. These properties enable use as mechanical/electrical switches to trigger a particular function at a pre-specified parameter (e.g. a sensor that triggers a pump in the event of flooding, triggering the opening and closing of greenhouse windows, use in plant watering/irrigation systems and use as water level monitors). When the environmental situation has been corrected or returned to an acceptable level, the device shrinks (in the case of drying) or expands (in the case of cooling) to its initial state and the system is then re-set. This cycle is entirely repeatable.

The composition of the first aspect of the invention also finds use as an osmotic lifting device. The device can be used as an osmotic lifting device as the forces generated by the swelling hydrogel composition can be considerable.

In addition, the composition of the first aspect of the invention can be used in orthodontic braces, gaskets and actuators, for example.

The copolymer composition of the invention is a compressed composition. The compression is at least partial and is in at least in one direction (or plane). The plane of compression is the plane of predominant expansion. The compression ratio can be altered to manipulate the specific characteristics of the anisotropic expander. The compression ratio is the ratio of the thickness of the uncompressed copolymer to the compressed copolymer. For example, if an amount of copolymer is compressed to a third of the original amount, the compression ratio is 3:1. The compression ratio alters the final degree of overall copolymer expansion. The greater the compression ratio, the greater the overall copolymer expansion. Preferable ratios may include from 2:1, 3:1, 4:1. 5:1 through to 14:1. Varying the ratio enables the expander to increase in dimension to a varying extent. The present invention enables expansion up to approximately 1500% in size.

The resultant expander can be machined or shaped into any desired configuration and thus anatomically tailored for any application either within the human or animal body or otherwise.

An alternative method of forming the anisotropic composition, is to fully hydrate the initial copolymer composition and then hold or constrain the copolymer in a fixed position in at least one plane (e.g. by clamping or by means of an adhesive). The copolymer is then gradually desiccated or dried in order to return it to the xerogel state, at which point it can be removed from the holding or constraining device. This results in the polymer shrinking preferentially in one direction such that on re-expansion on subsequence contact with water, it swells in an anisotropic manner.

The anisotropic composition of the invention self-inflates by osmotic diffusion of fluid into the expander. The present invention has the particular advantage of being relatively cheap, as both the copolymer and labour costs are low.

Methacrylic acid or some similar agent or chemical may be used during the polymerisation process to partially ionize the expander thus increasing the osmotic potential of the copolymer and thus augments the degree of swelling.

When the composition is being used as a surgical implant, it is beneficial that the composition is sterile. The composition of the invention enables this. Sterilisation may be by gamma irradiation or by another method of sterilisation that does not cause the tissue expander to absorb water and expand prematurely. The tissue expander can be surgically implantable in a human or an animal, preferably under anaesthetic (local, regional or general).

Gamma irradiation can reduce the final degree of overall polymer expansion. This understood to be due to increasing the degree of molecular cross-linking.

The anisotropic composition of the invention may further comprise a coating. The purpose of the coating can be to "label" the composition in some way (e.g. for X-ray

identification) or to vary the expansion rate of the composition. The coating can be semi-permeable. The coating can vary, such as silicone rubber of varying thickness (Figure 1c) (including 100 microns or less), lightly cross-linked polyvinyl alcohol, cellulose acetate, polybutadiene or silver or any other appropriate material including radiologically active and/or anti-bacterial materials. The coating can be perforated or semi-permeable. The type of coating and the presence or number of perforations can be manipulated to alter the rate of diffusion into the tissue expander and hence the rate at which it expands.

The ability to control the expansion rate by means of a semi-permeable membrane coating further increases the functionality of the device. The device can be further enhanced by the incorporation of drugs, growth factors or radio-opacifiers in order to tailor the device to specific clinical or non-clinical indications.

A second aspect of the invention is a device comprising the anisotropic composition of the present invention and a radio-opaque (radiologically active) component. The radio-opaque component may be a coated polymer component or a strip. Preferably, the device is a tissue expander, for use as a surgical implant.

A radiologically active component is any component, material, part or aspect that can be detected by an X-ray imaging machine.

The device of the second aspect may comprise at least one tissue expander. Preferably the device has at least one tissue expander arranged on a backbone, optionally of a radiologically active component and may comprise a number (two, three, four, five, six, seven, eight, nine, ten or more) of tissue expanders. The backbone may be in any appropriate shape, for example, a thread, rod or plate. The backbone of the radiologically active component may represent one continuous component running through all of the tissue expanders comprised in the device or may be distinct separate units in each or some of the tissue expanders. In a particular embodiment for use as a surgical implant in areas of the body which are curved (e.g. for cleft palate repair), the device may be in the form of a "necklace", which

comprises two or more distinct anisotropic expanders (as subunits), which are situated and spaced apart on a backbone of polymer which may optionally contain a radio-opaque material such as barium sulphate (see Figure 1b). The backbone may be fashioned from surgical-grade silver wire which is both radio-opaque and anti-bacterial. The "necklace" embodiment further allows the surgeon to tailor the length of the device for a specific surgical site by simply removing the requisite number of "redundant" subunits until the "necklace" is of the desired length.

The device of the invention may additionally comprise a means of attaching the device to another component. The means of attaching can be screws, bolts, or adhesives, for example. The component to which the device of the invention can be attached can be another device of the invention, part of a gasket or part of an actuator, for example.

A third aspect of the present invention is a method of making the anisotropic composition of the first aspect of the invention, which method comprises the following steps;

a) heating a copolymer composition above its glass transition temperature,
b) compressing the composition,
c) allowing the composition to cool.

The compression step is in at least one direction. The compression may be carried out above the transition temperature of the copolymer composition. The compression may be carried out using any compression means, such as a hand or machine operated hydraulic press, preferably modified to contain a thermostatically-controlled heating element. The pressure required depends on the level of compression to be achieved.

The method may further comprise a step of adding a radio-opaque (radiologically active) component. The radio-opaque component may be a strip. In addition, the method may further comprise a step of coating the tissue expander with the radio-

opaque component or a different component. The coating can control the expansion rate. Accordingly, the present invention provides a method of making the second aspect of the invention.

Preferably, the copolymer is heated above the glass transition temperature of the copolymer for at least 30 minutes. The heated copolymer is then compressed. A suitable pressure is at least 10 kPa for at least 10 minutes. It is preferable to maintain the temperature during compression above the glass transition temperature of the copolymer. The copolymer is then allowed to cool to below the glass transition temperature of the copolymer, preferably while maintaining the load

The invention also relates to the composition manufactured according to the methods of the invention.

A fourth aspect of the invention provides a method of expanding tissue in the human or animal body using the anisotropic composition of the first or second aspects of the invention.

The method is preferably applicable to mammals, in particular humans, but also for use in companion and show animals, in particular cats and dogs, as well as sporting animals, such as horses.

Since the tissue expansion is for the purposes of plastic and reconstructive surgery, the methods may be considered to be cosmetic or may, alternatively, be considered as method of treatment including reconstructive treatment in respect of congenital anomalies or acquired tissue defects.

A fifth aspect of the invention provides the anisotropic composition or device of the first and second aspects for use in medicine. In particular, the anisotropic composition or device is for expanding tissue.

The anisotropic composition can be used to expand soft tissue and improve the function and/or appearance of a wide variety of congenital and acquired tissue defects. Congenital anomalies include craniofacial or palatal clefts and syndactyly (congenitally fused fingers or toes). Acquired tissue defects including burns and other traumatic injuries to the skin (including leg ulcers) and soft tissue defects resulting from the surgical resection of a benign, malignant or other lesions. Anatomical regions where this technique would be particularly advantageous include the ears, nose, eyelids, lips, scalp, hands and feet. Accordingly, the tissue expander can be used to expand soft tissue and therefore reconstruct a wide range of defects to the head and neck, limbs and torso.

The tissue expander can also be used in benign or malignant strictures of the bowel, ureter, bile duct or any other anatomical lumen including the vascular and lymphatic systems (e.g. for arterial occlusion due to atheromatous disease). Here, the tissue expander is manipulated into a substantially central hollow core in order to allow the passage of the luminal contents and thus prevent obstruction whilst the expansion process occurs. Once inserted, the device gradually expands and returns the lumen of the viscus to the desired aperture, thus alleviating the physical obstruction.

Furthermore the tissue expander can be used for internal distraction osteogenesis. That is lengthening of bone, such as the mandible. Normally the bone is cut by the surgeon ('osteotomised'), an external distracting device applied, and the bone slowly distracted (i.e. stretched/lengthened) over a period of time until it is of the correct proportion (at which point the device is removed and the bone allowed to heal; rigid internal fixation may be required). However, the same function is performed by the hydrogel.

A sixth aspect of the invention is the use of a hygroscopic polymer and a polymer which provides a building block/backbone in the manufacture of a self-inflating anisotropic expanding composition or device, according to the first or second aspects, for treating a physical abnormality. The physical abnormality may be any of those which are described earlier or later in this text.

A seventh aspect of the invention is the use of the anisotropic composition according to the first aspect of the invention in the manufacture of the device according to the second aspect for treating a physical abnormality.

Preferred features of each aspect of the invention are as for each of the other aspects *mutatis mutandis*.

The present invention is described with references to the drawings, in which:

Figure 1a illustrates a traditional balloon-type silicone tissue expander with filling port.

Figure 1b illustrates a device according to the second aspect of the invention.

Figure 1c illustrates a device with a semi-permeable silicone coating thus limiting the expansion rate.

Figure 2 illustrates the appearance of 99:1 PVP:PMMA composition in differing states: aerial view in left column, cross section along the axis depicted by the broken line in the right column. A: xerogel state, B: fully hydrated isotropic state i.e. expanded in all directions (xerogel size as in A) and C: fully hydrated anisotropic state i.e. expands predominantly along one plane (xerogel size as in A). A compression ratio of 3:1 was used.

Figure 3 illustrates the aerial view of a birefringence pattern of a xerogel disc as viewed by polarised light microscopy. Disc diameter is approximately 25mm.

Figure 4 illustrates the anisotropic weight change of the 90:10 PVP:PMMA composition and the 99:1 PVP:PMMA composition at equilibrium in various physiological solutions at 37°C. The rightmost bars represent swelling of gamma

irradiated 90:10 PVP:PMMA composition and the 99:1 PVP:PMMA composition in Hartmann's solution.

Figure 5 illustrates the effect of compression ratio (C) on swelling behaviour for (*a*) the 90:10 PVP:PMMA composition and (*b*) the 99:1 PVP:PMMA composition. The first sample (far left on x axis) is the isotropic hydrogel; the other samples are all anisotropic hydrogels (with the compression ratio denoted on the x axis).

Figure 6 illustrates the mean swelling pressure (n=5) for the 90:10 PVP:PMMA composition hydrogel (mmHg). The pressure is displayed as a function of the diameter of the hydrogel disc (solid line; solid squares; error bars included), as a function of unit mass (dash line; solid triangles) (ie. mmHg/g), as a function of unit volume (solid line, open circles) (ie. $mmHg/cm^3$) and as a function of unit surface area (solid line; cross) (ie. $mmHg/cm^2$).

Figure 7 illustrates the mean swelling pressure (n=5) for the 99:1 PVP:PMMA composition hydrogel (mmHg). The pressure is displayed as a function of the diameter of the hydrogel disc (solid line; solid squares; error bars included), as a function of unit mass (dash line; solid triangles) (ie. mmHg/g), as a function of unit volume (solid line, open circles) (ie. $mmHg/cm^3$) and as a function of unit surface area (solid line; cross) (ie. $mmHg/cm^2$).

Figure 8 illustrates the mean increase in palatal tissue elements (epidermis, dermis, subcutis and periosteum) expressed as volume (mm^3) post tissue expansion in the control (stippled bars) versus experimental (hatched bars) sides of the palate (n=4 pigs).

Figure 9 illustrates a light micrograph of post mortem porcine palatal tissue stained with Hematoxylin and Eosin (H & E) at x 200 magnification. The central component (identified by an arrow) is a tiny fragment of imbedded polymer (uncoated).

Figure 10 illustrates a CT scan of a Plaster of Paris palatal cast taken from a pig with a palatal implant. The dashed circle demonstrates the position of the tissue expander in situ as compared with the unexpanded (control) side (solid black arrow).

The present invention is described with reference to the following non-limiting examples:

Examples

Example 1

Isotropic hydrogel was used as the starting composition. The isotropic hydrogel was supplied by Polymeric Sciences Ltd (New Ash Green, Longfield, Kent, UK) and consisted of pharmaceutical grade (ISO 13488) poly (methyl methacrylate) and poly (vinylpyrrolidone) with a cross-linkage density of 0.2%. Alkyl methacrylate (0.2 wt %) was used as the cross-linking agent and azobisisobutyronitrile (AZDN) (0.2 wt %) as the initiator in the addition polymerization reaction. Hydrogel compositions (weight ratios) of 90:10 and 99:1 PVP:PMMA were prepared and investigated. The hydrogel was used in the dehydrated phase without further chemical modification.

Anisotropy was achieved by annealing discs of isotropic copolymer under pressure for a specified time period using a hand-operated hydraulic press (Specac Ltd, Orpington, Kent, UK) modified so as to contain a thermostatically-controlled heating element. The hydrogel was heated to approximately 160°C (for the 90:10 PVP:PMMA composition) or 165°C (for the 99:1 PVP:PMMA composition) for 60 minutes and then compressed at approximately 300 MPa for a further 60 minutes. The heating cycle was then terminated and the polymer was allowed to cool to room temperature whilst being maintained at that load throughout. The ratio of the thickness of the uncompressed hydrogel to the compressed hydrogel (the compression ratio) was controlled by means of a brass mould of a pre-defined thickness.

The hydrogel samples were turned by lathe and then ground with 600 grit sandpaper (Kemet International, Maidstone, Kent, UK) into a cylinder 10mm in diameter and 2 mm thick and weighing approximately 0.2g (Figure 2a). The samples were stored in an inert nitrogenous atmosphere in airtight packages until use.

Figure 3 illustrates a xerogel disc as viewed by polarised light microscopy. The presence of the central Maltese Cross pattern confirms the anisotropy in the material and the presence of intrinsic stresses relating to the manufacturing process.

Example 2

Hydrogel anisotropic expansion was investigated by hydrating the 90:10 PVP:PMMA composition and the 99:1 PVP:PMMA composition and determining the percentage weight increase.

The proportion of PVP within the copolymer has a critical influence on hydrogel expansion. When fully hydrated, the 90:10 PVP:PMMA composition has a maximal weight increase of approximately 600%; this is approximately doubled in the 99:1 PVP:PMMA composition , with a maximal weight increase of approximately 1200%. Figure 4 illustrates the weight change of the two compositions in various physiological solutions at 37°C.

The effect of the compression ratio on the degree of anisotropic expansion was also investigated (Figure 5a and 5b). For both the 90:10 PVP:PMMA composition and the 99:1 PVP:PMMA composition the greater the compression ratio, the greater the degree of anisotropy. The degree of change in thickness of the sample at high compression ratios occurs at the expense of sample width. At compression ratios of 14:2 or greater, significant gel fragmentation occurred, possibly as a result of excessive disruption of polymer cross-linking, thus reducing the mechanical stability of the polymer.

Example 3

The *in vitro* swelling pressure was measured using a pressure registration unit, following a design described by Weise (J Craniomaxillofac Surg. 21(7): 309-313 (1993)). A 1g cylinder of anisotropic xerogel (compression ratio 3:1) was sealed within the expansion chamber which was separated from the measuring chamber by means of a diaphragm. The xerogel was then bathed in Hartmann's solution which is added to the adjacent reservoir; the two were in continuity by means of a perforated plate. As the xerogel absorbed fluid from the adjoining reservoir and swells, it deflected the diaphragm thus compressing the oil contained within the measuring chamber. The increase in pressure within the measuring chamber was detected by a pressure transducer (0-1 Bar, 5 Volt output RS Components Ltd, Northampshire, UK) which was zeroed immediately after the addition of the Hartmann's solution. The entire pressure registration apparatus was housed within a warming oven calibrated to 37°C (± 1°C). The electrical output from the pressure transducer was recorded using data acquisition software (Pico Data Logger, Pico Technology Limited, St Neots, Cambridgeshire, UK). The maximum *in vitro* swelling pressure for the uncoated copolymer was measured at approximately 100 kPa (approximately 700 mmHg).

The same experiment was conducted with the 90:10 PVP:PMMA composition (see Figure 6 for the swelling pressures that can be achieved) and the 99:1 PVP:PMMA composition (See Figure 7 for the swelling pressures that can be achieved).

Example 4

The ease of surgical application and functionality of the device has been demonstrated *in vivo* during a non-cleft pig model. Under UK Home Office Licence, the device was implanted in the palates of normal non-cleft Large White pigs whilst under general anaesthetic. The surgical site was cleaned and the proposed site of insertion of the device was marked out and infiltrated with local anaesthetic. A small transverse anterior incision was made in the hard palate and a longitudinal pocket was fashioned in a subperiosteal plane. The device was then inserted into the pocket with ease and having ensured adequate haemostasis, the incision was closed by means of an

absorbable suture. Peri-operative prophylactic antibiotics were administered. The pigs were recovered and returned to the housing pen and allowed to eat and drink as normal. The animals were examined under general anaesthetic at intervals in order to monitor the device expansion. Anisotropic tissue expansion was achieved.

Figure 8 illustrates the significant increase in the palatal tissue elements. This tissue may be used for surgical reconstruction of a cleft palate defect for example.

The implanted polymer has been illustrated as causing minimal inflammatory reaction of the host tissue to the foreign body (see Figure 9). Thus the polymer is highly biocompatible.

A CT scan was taken of a Plaster of Paris palatal cast taken from a pig with a palatal implant (see Figure 10). This demonstrated that the anisotropic expander is capable of producing an increase in palatal volume in a vertical plane only (without the risks of anteroposterior expansion and thus device extrusion).

Claims

1. A self-inflating anisotropic expanding composition, which composition comprises a compressed copolymer.

2. A self-inflating composition, as claimed in claim 1, wherein the copolymer comprises a first hygroscopic polymer and a second polymer which provides a backbone for the composition.

3. The composition of claim 1 or claim 2, wherein the first hygroscopic polymer is vinyl pyrrolidone.

4. The composition, as claimed in any one of claims 1 to 3, wherein the second polymer is an acrylate or a hygroscopic polymer.

5. The composition of any one of claims 1 to 4, which is a tissue expanding composition.

6. The composition, as claimed in any one of claims 1 to 5, further comprising a coating.

7. The composition as claimed in claim 6, wherein the coating is perforated or semi-permeable.

8. A device comprising a composition of any one of claims 1 to 7 and a radio-opaque component.

9. A device according to anyone of claims 1 to 8, comprising at least two of the self-inflating compositions which are arranged in a linked but spaced apart configuration.

10. The device of claim 8 or claim 9 wherein the device further comprises means for attaching the device to at least one other component.

11. A method of manufacturing a composition of any one of claims 1 to 7 comprising the following steps;

a) heating a copolymer above its glass transition temperature,

b) compressing the copolymer,

c) allowing the copolymer to cool.

12. The method of claim 11, further comprising the step of adding a radio-opaque component.

13. A composition manufactured according to the method of claim 11 or claim 12.

14. A method of expanding tissue using the composition of any one of claims 1 to 7 or the device of claim 8 or claim 9.

15. The composition or device according to any one of claims 1 to 9 for use in medicine.

16. The composition or device according to any one of claims 1 to 9 for expanding tissue.

17. Use of a hygroscopic polymer and a polymer which provides a backbone in the manufacture of a self-inflating anisotropic expanding composition or device, according to any one of claims 1 to 9, for treating a physical abnormality.

18. Use of the composition of any one of claims 1 to 7 in the manufacture of the device of claim 8 or claim 9 for treating a physical abnormality.

Fig. 1a.

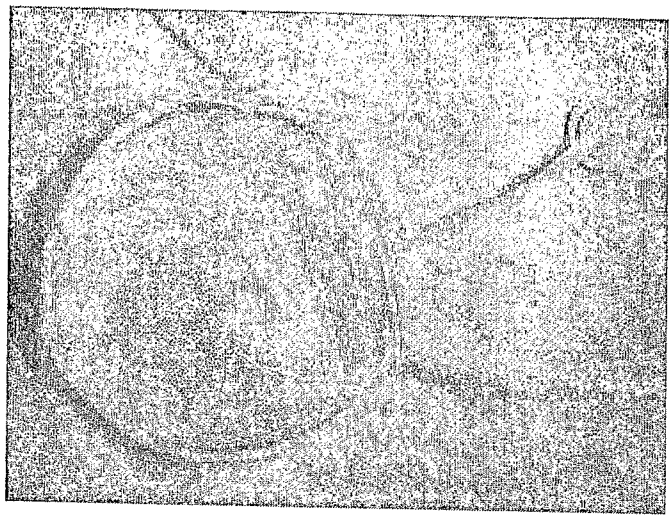


Fig. 1b.

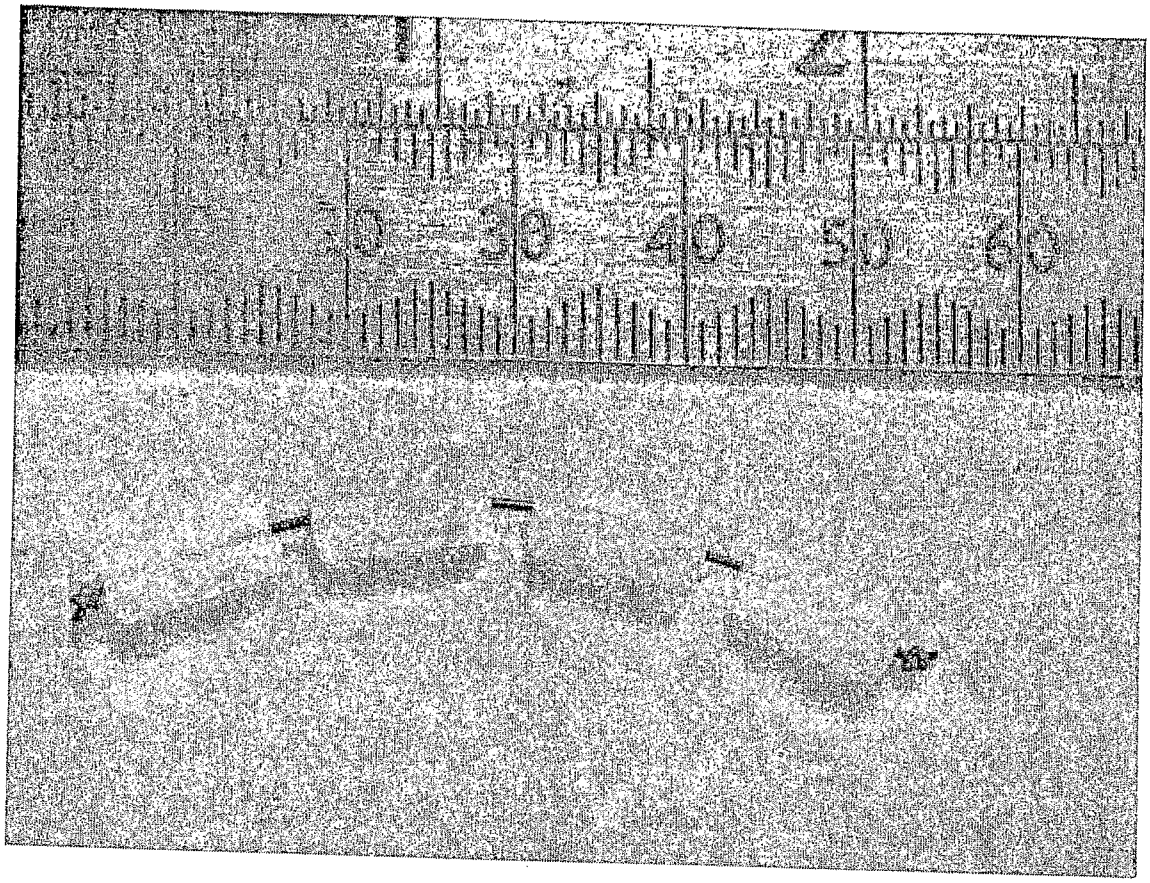


Fig. 1c.

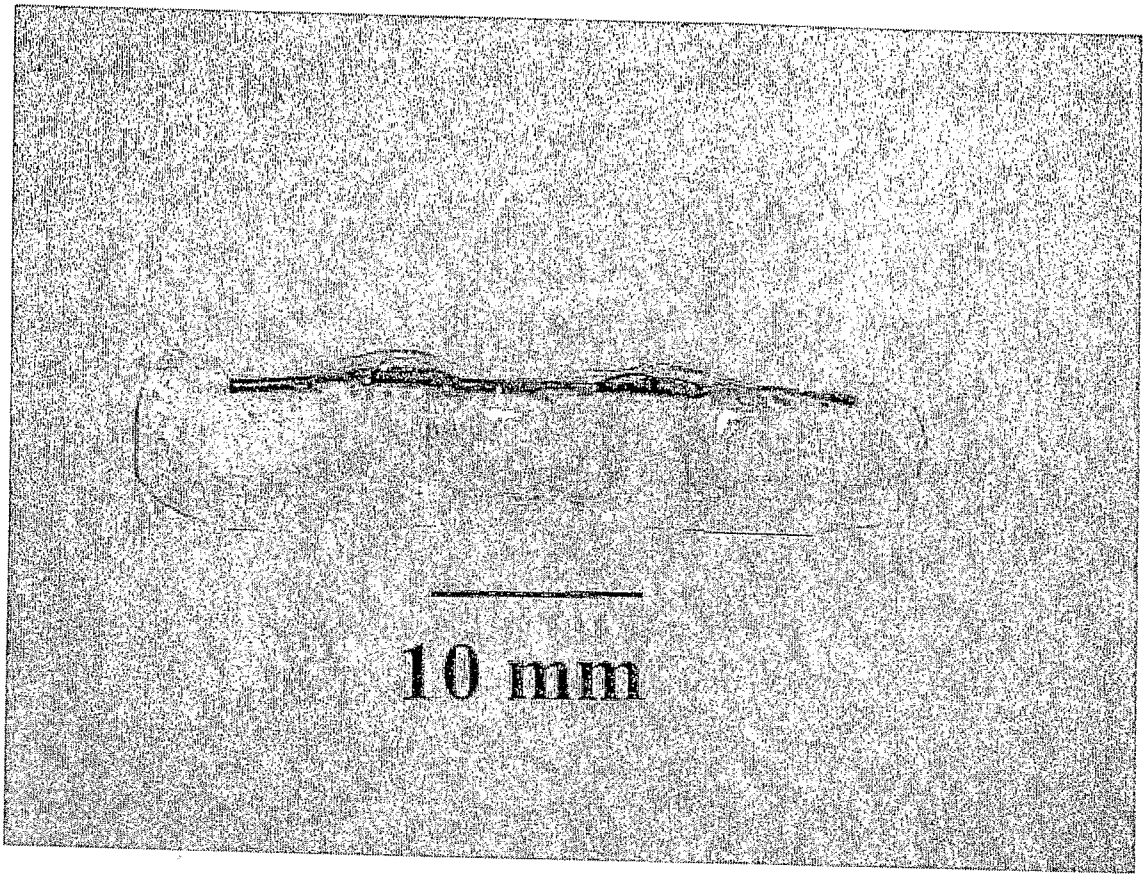
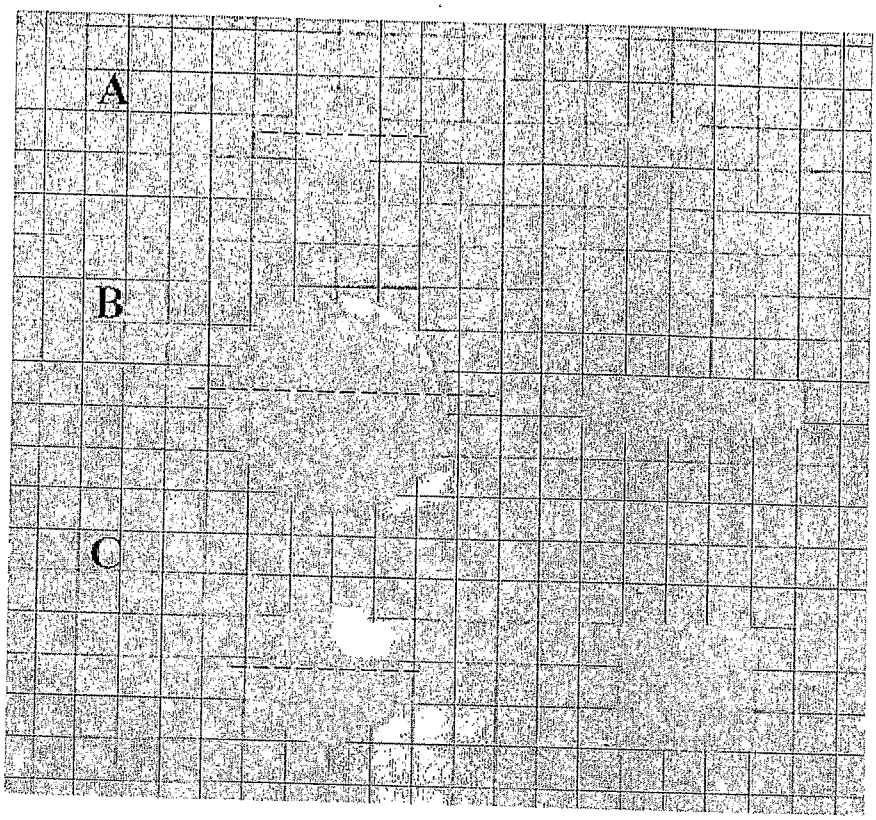


Fig. 2.



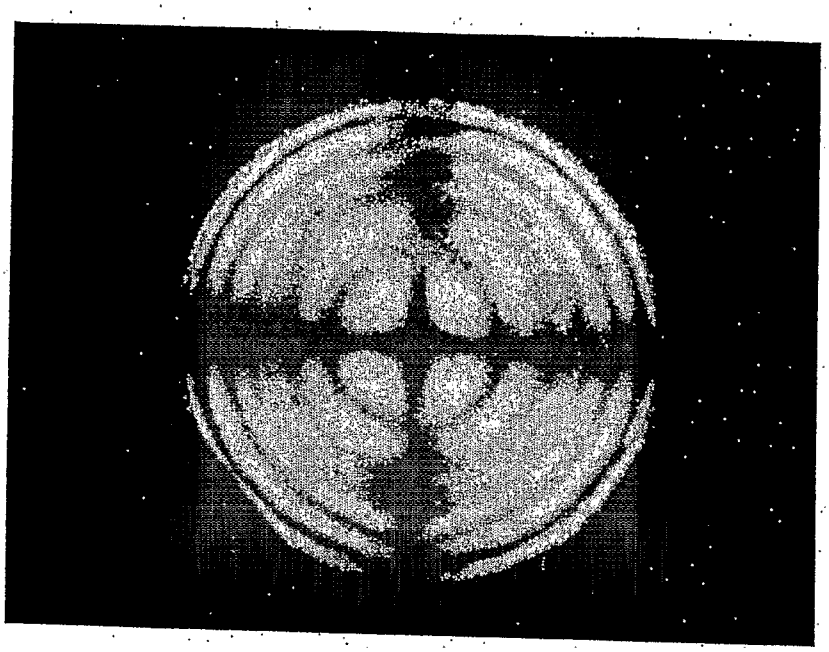


FIG 3

Fig. 4

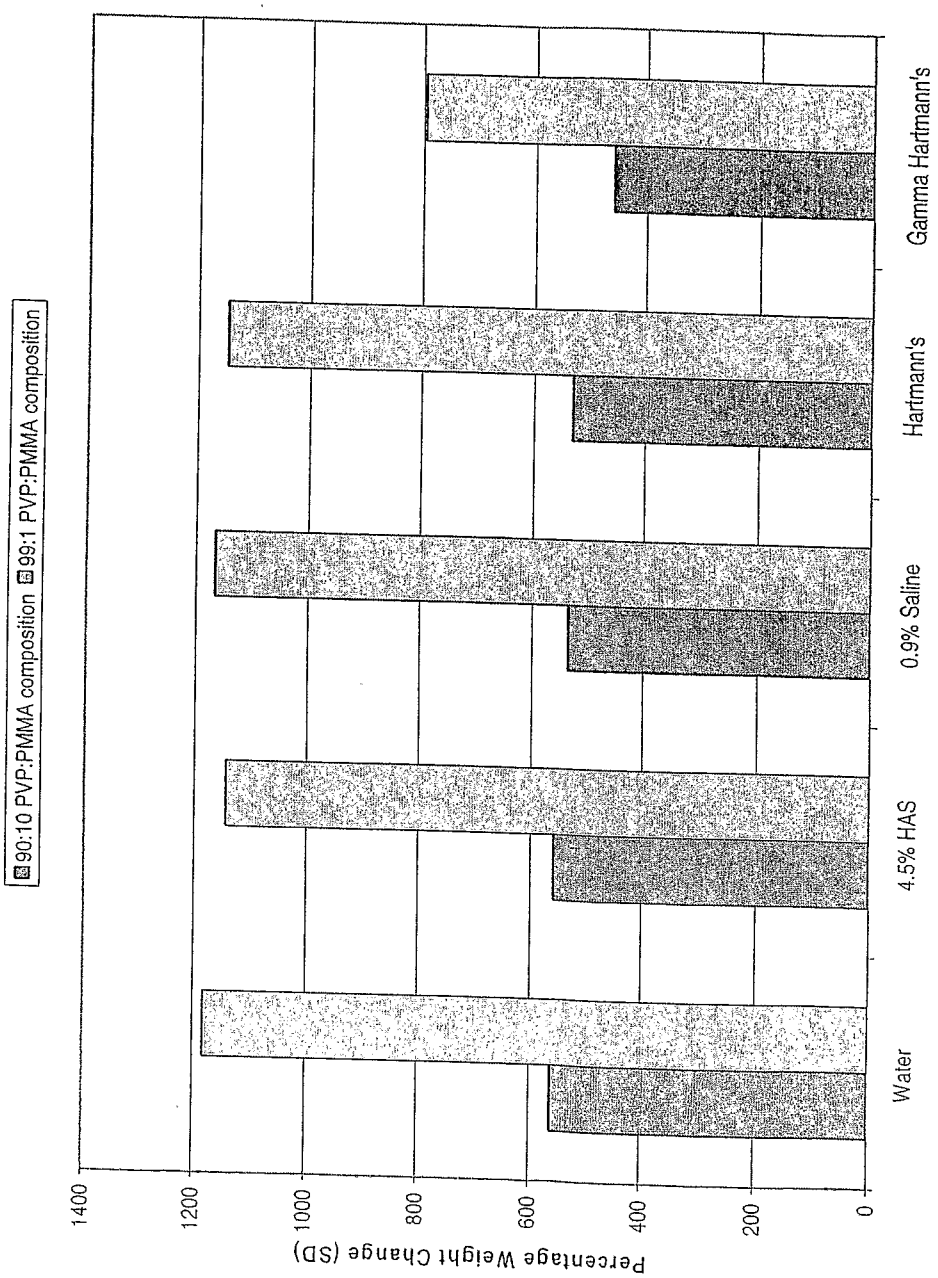

90:10 PVP:PMMA composition
99:1 PVP:PMMA composition
Percentage Weight Change (SD)
0
200
400
600
800
1000
1200
1400
Water
4.5% HAS
0.9% Saline
Hartmann's
Gamma Hartmann's

Fig 5a Key: ▼ = percentage weight change

● = percentage thickness change

○ = percentage width change

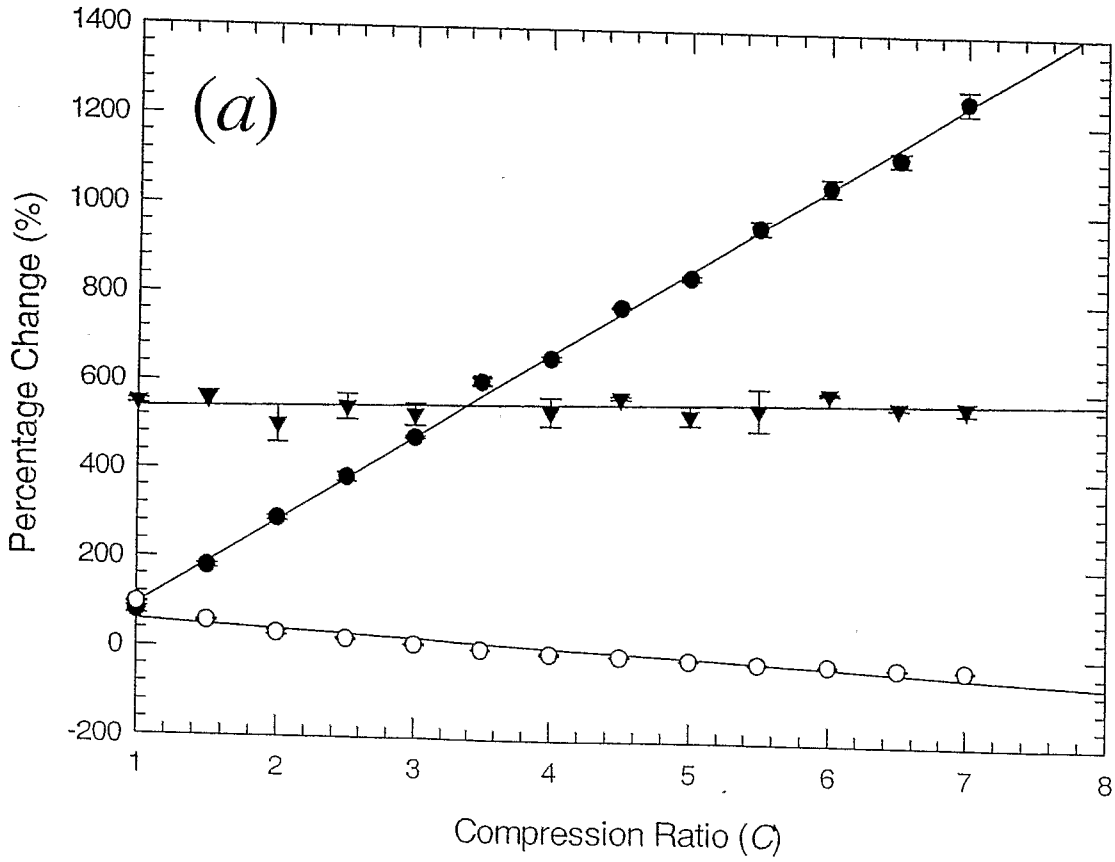
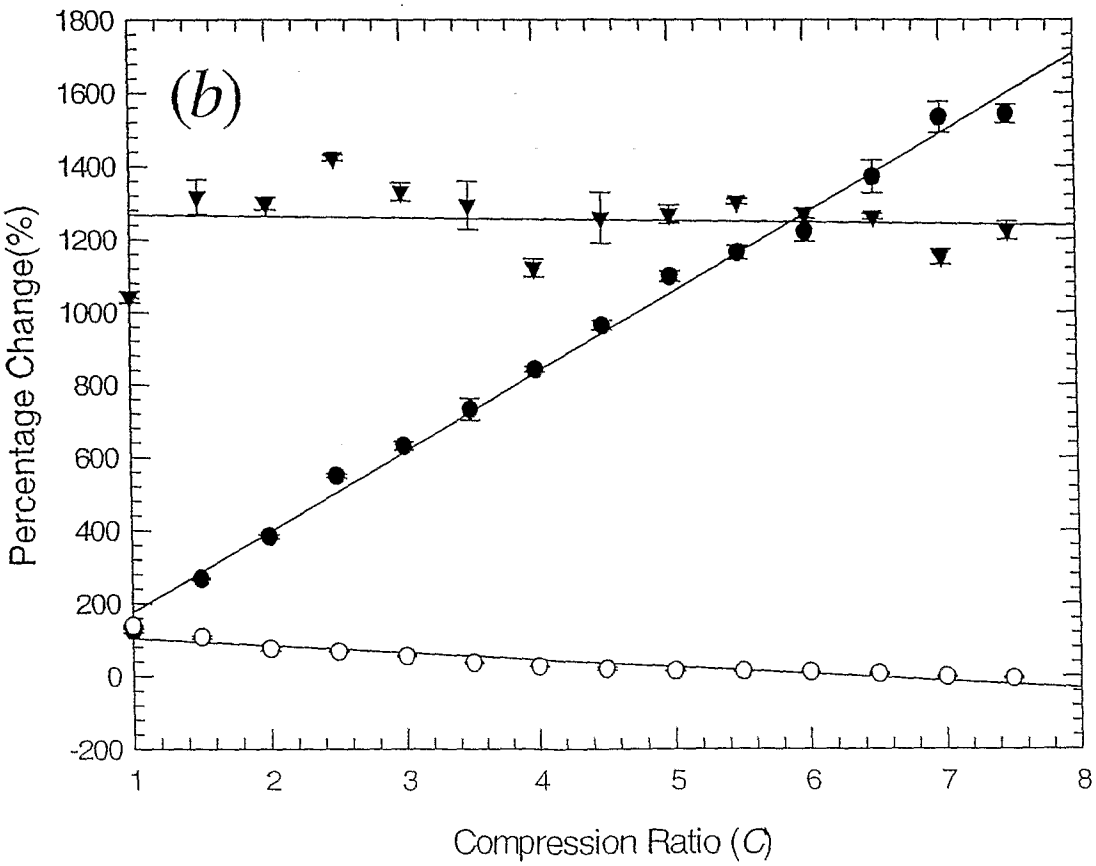


Fig 5b Key: ▼ = percentage weight change

● = percentage thickness change

○ = percentage width change



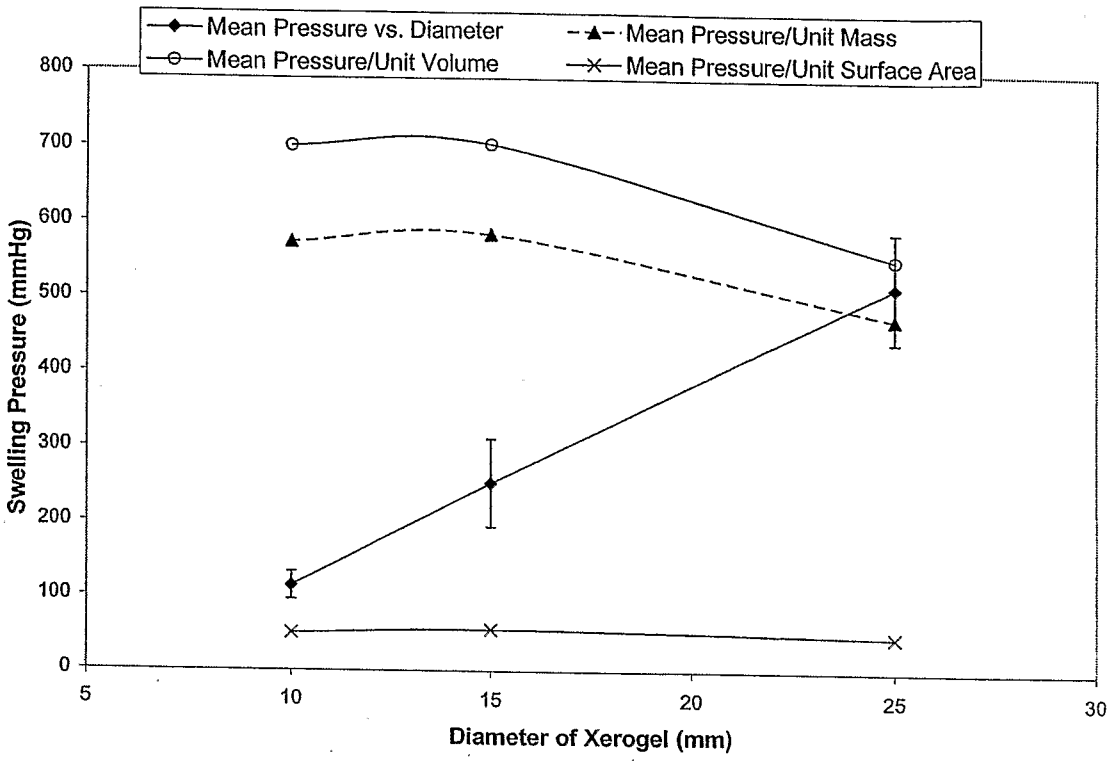

Mean Pressure vs. Diameter
Mean Pressure/Unit Mass
Mean Pressure/Unit Volume
Mean Pressure/Unit Surface Area
Swelling Pressure (mmHg)
800
700
600
500
400
300
200
100
0
5
10
15
20
25
30
Diameter of Xerogel (mm)

FIG. 6

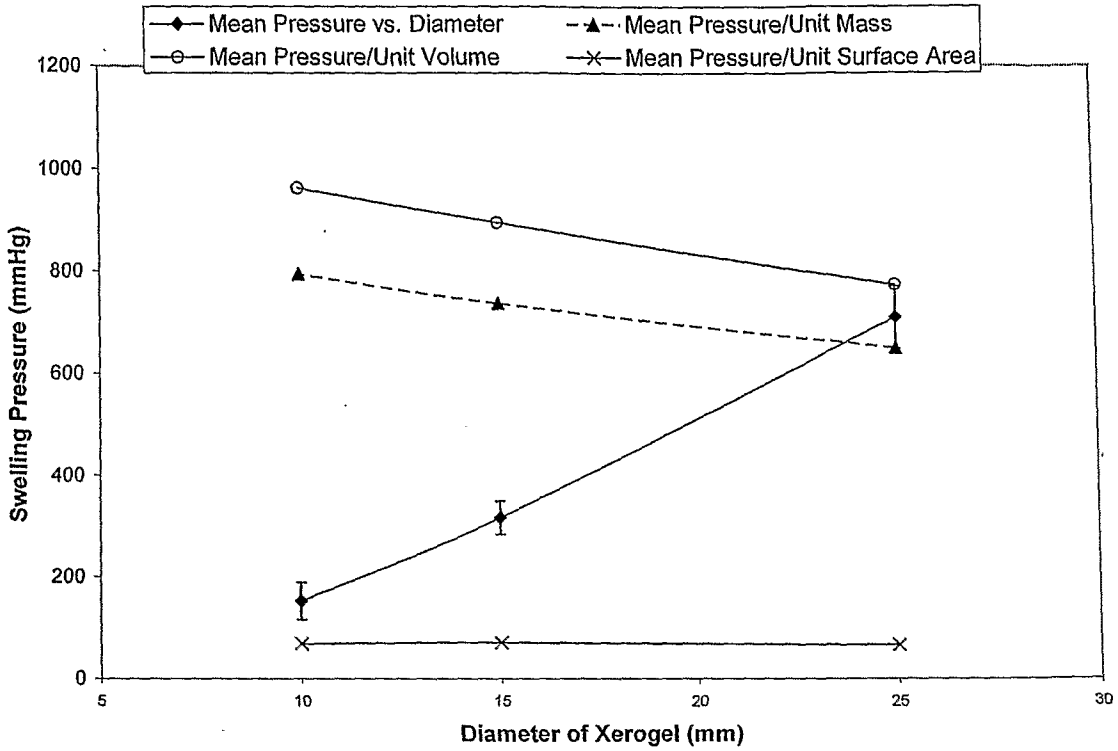

Mean Pressure vs. Diameter
Mean Pressure/Unit Mass
Mean Pressure/Unit Volume
Mean Pressure/Unit Surface Area
Swelling Pressure (mmHg)
1200
1000
800
600
400
200
0
5
10
15
20
25
30
Diameter of Xerogel (mm)

FIG. 7

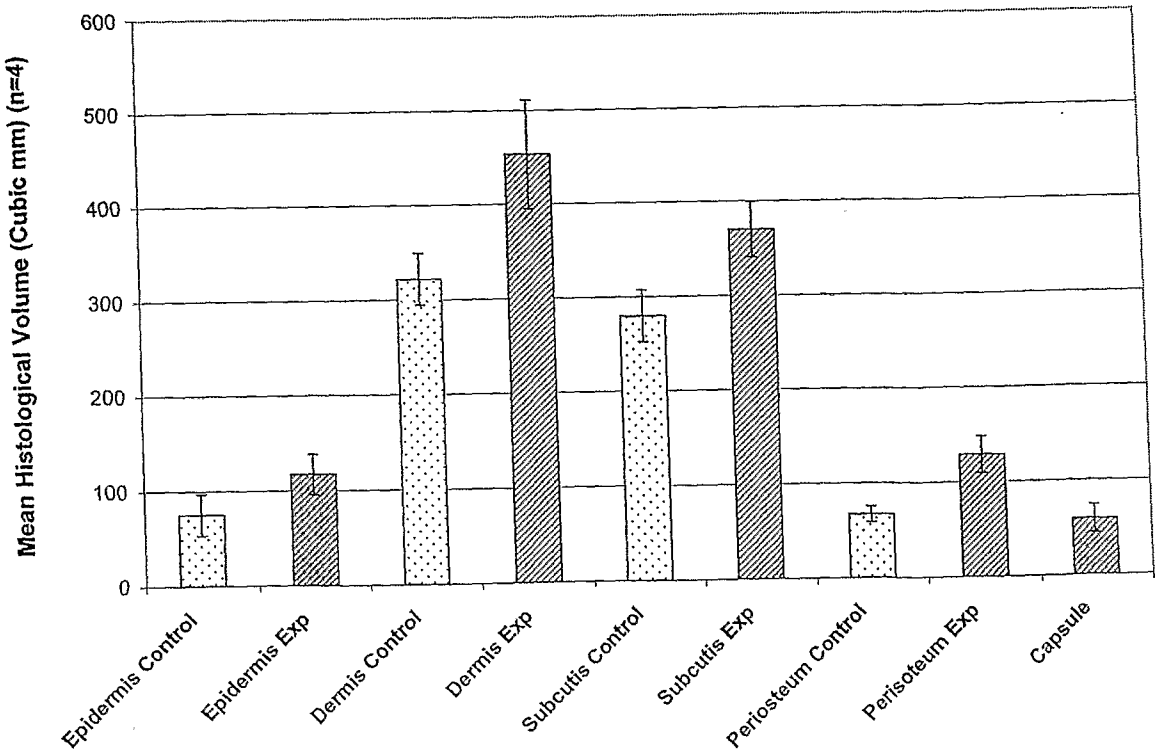

Mean Histological Volume (Cubic mm) (n=4)
600
500
400
300
200
100
0
Epidermis Control
Epidermis Exp
Dermis Control
Dermis Exp
Subcutis Control
Subcutis Exp
Periosteum Control
Perisoteum Exp
Capsule

FIG. 8

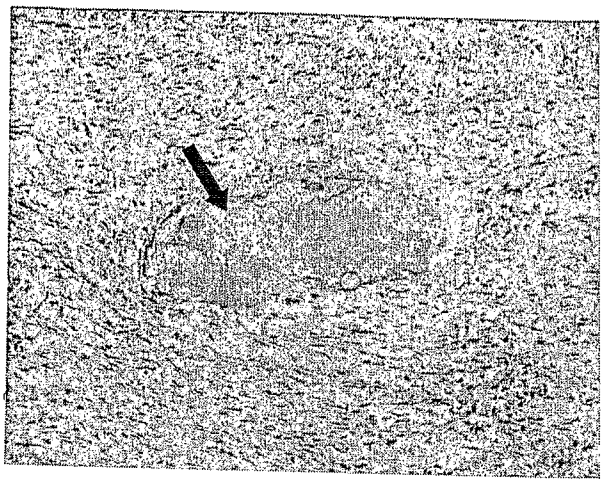
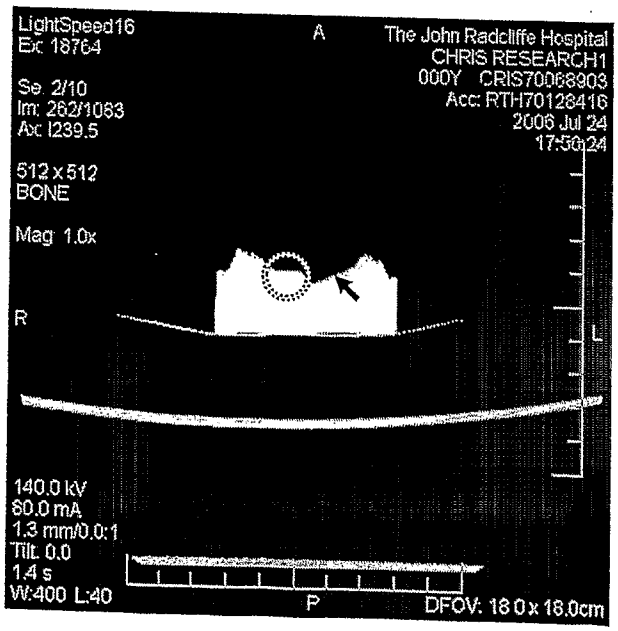


FIG. 9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Se: 2/10
Im: 262/1083
Ax: I239.5
512 x 512
BONE
Mag: 1.0x
R
A
The John Radcliffe Hospital
CHRIS RESEARCH1
000Y CRIS70068903
Acc: RTH70128416
2006 Jul 24
17:50:24
140.0 kV
80.0 mA
1.3 mm/0.0:1
Tilt: 0.0
1.4 s
W:400 L:40
P
DFOV: 18.0 x 18.0cm

FIG. 10