

DESCRIPTION

5 The invention relates to an alloplastic implant on the basis of a histocompatible solid. Said implant is used in particular to even out irregularities of the skin. It can, however, be used for any other purpose in the plastic surgery.

10 It has been tried for a long time and in many ways to "restore" by surgical methods elements of the human body which are pathologically changed or have been destroyed by an accident. If necessary, said elements are replaced by foreign bodies. In particular implants are used more and more in the area of plastic surgery and cosmetic surgery.

15 It is very often desired to even out irregularities of the skin of any origin permanently and without side effects. One has already used different materials for this purpose and of course also for other purposes in plastic surgery.

20 For instance, collagen has been used already very often. Collagen is however a xenogeneic protein product which is degraded in the body. In case an irregularity of the skin has been evened out with collagen, for instance by an  
25 injection under the skin (intracutaneously or subcutaneously) then it is normally necessary to have further injections in order to restore the results originally obtained after the first injection.

30 Furthermore collagen causes allergies so that allergic reactions can be observed in at least 3% percent of the cases. Said phenomenon is in particular then very strong when a couple of injections, which is normally the case, are required for obtaining the desired result.

It is furthermore known to use gelatine for the above given purpose. However, gelatine has similar drawbacks as collagen. In addition it is much more difficult to inject gelatine.

5

Also silicone or silicone oils, respectively, have been used already. However, silicone oils cause a severe reaction of the tissue at the site of the injection (siliconome). In addition the silicone oils are rather badly kept in place by the tissue at the site where it has been injected so that, as a consequence, the silicone oils are transmitted to more or less distant parts of the body, for instance lymphatic nodules and liver.

10

15

An implant, more particularly for breast enlargement, is known from FR-A 2 287 210. This implant consists of a small soft sack of histocompatible material, more particularly solid silicone. The dimensions of this implant must be selected according to requirements.

20

It is also known to perform an injection of fat by using endogenous fat for the purpose mentioned above. It has been observed, however, that such a measure very often causes injection. Furthermore the endogenous fat is rapidly and strongly absorbed by the body so that normally only 10% of the injected fat remain immobilised at the desired site.

25

30

It is therefore the object of the present invention to provide an alloplastic implant which can easily be injected, remains immobilised at the site where it has been injected and is tolerated by the tissue so that no side effects are caused.

Said object is solved by the teaching of claim 1.

35

According to the present invention a histocompatible solid in the form of a powder is used as an implant. The solid particles forming said solid, which may be incorporated into a suspension agent, are injected for instance with an injection needle to the desired site.

The solid particles used according to the present invention have a smooth surface and are free from corners, edges and so on. In other words, said particles are not allowed to have sharp transitions at their surface. Said transitions are for instance found at such corners and edges. In addition they are not allowed to have peaks of any kind or tapered projections. Furthermore the surface should not have pores.

Consequently the transition from one outer surface to the other outer surface of the solid particles as used according to the present invention has to take place in a continuous manner. If such transitions are present, as is the case for the edges of a cube, they have to be smoothed off.

According to the present invention it is therefore not possible to use solid particles which are crystallites (for instance needle-shaped) or particles which have been obtained by mechanically breaking up (eg grinding) greater units into small pieces since said particles possess the above mentioned sharp edges and corners.

Due to said smooth and smoothed off surface structure no cells or other tissue structures are damaged. In addition the danger of causing reactions of the tissue, which are followed by infections, is minimised.

Preferably rotationally symmetrical solid particles and in particular particles having an elliptic or spherical form

are used. In addition, it is possible to use solid particles of a different geometrical form if all said particles have a smooth and smoothed off surface.

5 Said solid particles which are present as a dust or powder, respectively, possess an average diameter of  $\geq 10$  to  $200 \mu\text{m}$ . Said solid particles are too great to be "eaten" by monocytes.

10 Said solid particles have preferably an average diameter of about  $15$  to about  $200 \mu\text{m}$  and more preferred from about  $15$  to about  $60 \mu\text{m}$ .

15 In this case said solid particles are also small enough to be injected through the cannula of an injection syringe to the desired site.

20 Particles having the diameters specified above can also not be identified by touch as a single foreign body in or under the skin.

25 The solid particles have preferably such a diameter that they are not washed away through lymph tracts or other tissue tracts from the site to which they have been brought.

If the solid particles do not have a spherical form, then the diameter as used in the present documents refers to the greatest diameter of the smallest cross sectional area.

30 Due to the form, surface and size of the particles used they are not detected by the endogenous macrophages as foreign bodies so that no defensive reactions take place.

35 The particles having a spherical form or a spherical like form have the advantage that they form a closely packed

arrangement at the site to which they have been brought.

5 The solid particles used according to the present invention consist of an inert, histocompatible material. Such material can be for instance glass which is present in the form of glass beads or glass pellets having a smooth and smoothed off surface.

10 The solid particles used according to the present invention consist preferably of a plastics and in particular of a completely cured and fully polymerised plastics so that no remaining monomers, which may be toxic or may cause cancer, are incorporated into the body of the treated patient.

15 In principle it is possible to use any inert histocompatible plastics for producing the plastics particles used according to the present invention. Preferably polymethacrylates and in particular polymethylmethacrylate (PMMA) are used as plastics. Fully polymerised PMMA is histocompatible and can  
20 be incorporated in the human body without fear so that it can be considered as chemically and physically inert. Due to this reason said plastics has already been used for manufacturing implants, for instance for the plastic covering of bone defects in the face and in the cranium or  
25 as an arthroplasty. Said plastics is also being used for manufacturing artificial teeth, as suture material and for manufacturing intraocular lenses and dialysis membranes.

30 In order to be able to inject the solid particles or plastics particles, respectively, used according to the present invention as an implant in or under the skin said particles are preferably suspended in a kind of suspending agent. For instance water, alcohols, in particular ethyl alcohol, as well as mixtures thereof can be used as  
35 suspending agents.

5 The suspending agents used according to the present invention contain preferably also a tenside, for instance Tween 80, since such a tenside changes the surface tension of water so that the solid particles and in particular the plastics particles float better.

10 The mixing ratio of the components of the suspending agent can be chosen according to the needs and in particular according to the size of the syringe used for the injection. A suitable mixture consists of 0.5 ml ethylalcohol, 0.5 ml Tween 80 and 9 ml water. The term "Tween" is a trademark of ICI Americas Inc. Polyoxyethylene derivatives of sorbitan esters are distributed under this nomination. Tween 80 is a polyethoxysorbitanoleate. It is not only possible to use 15 the said Tween type (Tween 80) but also other Tween types for the purposes of the present invention.

20 For the application or injection, respectively, of the solid particles used according to the present invention said particles are suspended or slurried, respectively, in a fluid inert medium. It has been found advantageous to choose a ratio of two volume parts of the suspending agent and one volume part of the solid particles or plastics particles, respectively.

25 A gel which is known per se and is degraded within the body, for instance on the basis of gelatine, is preferably used as the suspending agent.

30 By using a suspending agent it is easier to inject the solid particles as used according to the present invention with the help of an injection syringe for instance intracutaneously. It is for instance possible to use a 20 G to 27 G cannula for such an injection.

35

Animal experiments have been performed in order to investigate which tissue reactions take place after the exogenous materials used according to the present invention have been injected.

5

For said experiments PMMA-beads with a smooth, smoothed off surface having different diameters, for instance from 40 to 80  $\mu\text{m}$  as well as from 15 to 60  $\mu\text{m}$ , have been used. A mixture of 0.5 ml ethylalcohol, 0.5 ml Tween and 9 ml water has been used as suspending agent. Such PMMA-beads or pellets, respectively, are known per se and are commercially available.

10

Said suspending agent, which prevents the small beads from settling down in the injection syringe due to the gravitation so that an injection would be impossible, are mixed with the PMMA-beads before the injection in a ratio of about 1 volume part beads and 2 volume parts suspending agent.

20

Said alloplastic implant according to the invention was injected into male wistar rats, weighing 200 to 250 g and being completely anaesthetised with Nembutal, at four places in an amount of 0.5 ml with the help of a 20 G cannula intracutaneously into the peritoneal skin of the animals since it is much softer and more flexible than the skin on the backside. After the injection small weals formed at the injection site due to the injected volume. This, however, was also the case when the suspending agent was injected alone.

30

The alloplastic implant of the present invention was injected into 39 animals. At days 3, 6, 9, 12, 15, 21 and 28 as well as 8, 12, 16, 20, 24 and 28 weeks after the injection three of the test animals were sacrificed. The

35

peritoneal skin was then shaved with the help of a depilatory cream. At the injection site the beads, which were still visible but did not project anymore, were cut out together with a part of the peritoneal skin and investigated.

The results of the microscopic and macroscopic investigations performed can be summarised as follows.

None of the test animals died within the test time of 28 weeks. After the injection no defensive reactions or inflammations, respectively, were observed which were greater than those which are caused by an injury (insertion of the cannula). Such reactions were also not observed later on. No tumors could be found, neither in the area of the injection nor in the complete organism. No pathological changes of the peritoneal skin could be observed from the outside. After a couple of days the fur started growing again. The lymph tracts and the lymph nodules in the vicinity were without an pathological findings.

Monocytes migrate during the first three days after the injection of the PMMA-beads used into the area of the injection. Then a differentiation of the monocytes takes place. The different forms of said differentiation can be recognised after about 6 d after the application of the foreign bodies. It is possible to recognise the macrophages, foreign body-giant cells and fibrocytes. Said process of differentiation lasts until about the 16th week after the implant of the invention has been injected. The process of differentiation is however, limited mainly to the fibrocytes which, after a further transformation to fibrin fibres, shield the PMMA-beads against the animal body. Thereby a certain physical stability towards the interior and the exterior is imparted to the accumulation of balls.

Due to the size and the physical stability of the PMMA-beads they cannot be phagocytised or lysed, respectively. In order to "remove" the foreign body the animal body can only fibriotically encapsulate said foreign bodies. Such a process takes place with almost any foreign body which cannot be destroyed by the animal body.

The fibrotic growth of connective tissue is a natural reaction to the lesion of the tissue caused by the injection cannula. Said fibrotic reaction breaks down completely already after a couple of weeks due to the smooth surface and the chemical inertness of the PMMA-beads. From then on said beads remain in the tissue without reaction.

It can therefore be summaried that the PMMA-beads, which have been inserted into the body, are encapsulated by a delicate capsule of connective tissue or are embedded into connective-tissue fibers, respectively, and remain stationary in the tissue. The histologically established foreign body reaction was minimal and was also conditioned through the mechanical wounding of the tissue during injection.

The use of the above described suspending agent is moreover not mandatory since the above described PMMA-beads can be injected also without a suspending agent into the body.

In order to investigate the reaction of the test animals with respect to the incorporation of PMMA-beads without a suspending agent the peritoneal skin of the test animals was opened by a stab incision. Then the PMMA-powder was scattered into the opening. The wound was then closed by a single button suture.

The same course of reaction as in the case of the above

described tests could be observed. A delicate connective-tissue capsule was formed which enclosed the PMMA-beads.

5 It should, however, be advisable to use a suspending agent if an intracutaneous or subcutaneous injection under the skin of a human being shall be performed since in this case the implant of the invention can be more easily injected with syringe.

10 If it is desired that the beads used float better in the suspending agent it is also possible to replace the tenside mentioned in the beginning by charging the beads in the same sense. Then they repel mutually and float better in the medium of the suspending agent which can consist in this  
15 case exclusively of water, alcohol or a mixture thereof.

For charging the PMMA-beads in the same sense said beads can be treated in such a way that the beads already completely cured are molten once again at the surface and then charged  
20 in an electric field.



PATENT CLAIMS

1. Alloplastic implant based on a histocompatible solid, characterised in that the solid is in powder form and is composed of solid particles with a diameter of 10 to 200  $\mu\text{m}$  on average and having a smooth surface free from corners and edges.
2. Implant according to claim 1, characterised in that the solid particles are rotationally symmetrical and have in particular an elliptical or spherical form.
3. Implant according to claim 1 or 2, characterised in that the solid particles have a diameter of 15 to 60  $\mu\text{m}$ .
4. Implant according to at least one of claims 1 to 3, characterised in that the solid is a plastics, in particular a cured plastics.
5. Implant according to claim 4, characterised in that the plastics is a polymethacrylate, in particular polymethylmethacrylate.
6. Implant according to at least one of the claims 1 to 5, characterised in that the solid particles or plastics particles, respectively, are present in a physiologically acceptable suspending agent.
7. Implant according to claim 6, characterised in that the suspending agent is a gel, degradable in the body, in particular on the basis of gelatine.
8. Implant according to claim 6, characterised in that the suspending agent is liquid and consists in particular



of water or an alcohol, in particular ethylalcohol, or of a mixture thereof and is optionally admixed with a tenside.

- 5      9. Use of the powderlike solid particles according to one of claims 1 to 8 as an alloplastic implant, more particularly to even out irregularities of the skin.

10