CUSTOMIZEDBONE SERVICE

PATIENT SPECIFIC CRANIAL/CRANIOFACIAL IMPLANT

INSTRUCTIONS for USE

CAUTION:
FEDERAL LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN

DESCRIPTION

Hydroxyapatite is contained in human bones in percentage close to 70% and is one of the most important elements of human bone structure. CustomizedBone Service patient specific implants for the reconstruction of cranial/craniofacial defects are made of porous bio-mimetic hydroxyapatite with a chemical composition and structure that resembles the mineral component of human bones. This biomaterial is highly porous with trabecular structure and is composed of pores with the following characteristics:

- ✓ macro-pores,
- ✓ interconnecting pores,
- ✓ micro-pores.

This material is completely biocompatible.
The implants are designed and produced by Fin-Ceramica Faenza according to the surgeon's specifications and based on the patient's CT scan data, obtained through a standardized protocol. During the pre-operative planning phase, the surgeon must approve the final implant design. All the implants are accompanied by the patient's identification code.

INDICATIONS FOR USE

CustomizedBone Service (CustomizedBone) is intended to replace bony voids in the cranial and/or craniofacial skeleton (frontal bone including the brow ridge) . This device is indicated for both adult and pediatric use (for children 7 years of age and above).
CustomizedBone implants are suitable for reconstructing cranial and/or craniofacial defects resulting from:

- ✓ trauma and vascular pathologies, either associated or non-associated to cranial decompression;
- ✓ removal of tumours;
- ✓ reabsorption of autologous bone;
- ✓ rejection of other prosthetic materials;
- ✓ congenital malformations.

AVAILABLE FORMATS

CustomizedBone implants are patient specific; the devices are designed based upon the prescription of a qualified surgeon and based upon patient CT scan data. Each patient-specific implant is supplied with an equivalent secondary back-up device. The implants are supplied sterile. The CustomizedBone Service Implants are MR safe.

INSTRUCTIONS for USE

These instructions are intended as guidelines for the use of CustomizedBone implants; they are not designed to replace or change the standard procedures for the treatment of cranial defects.
Clinical results of implants used for the reconstruction of cranial defects depend on several factors. When choosing an implant and the surgical technique to be used, the following factors need to be considered: patient's age and general clinical conditions, and bone quality. Moreover, the possibility of achieving good contact between the implant and the vital host bone, complete defect filling and correct and sufficient primary stabilization of the implant need to be evaluated.
Prior to the surgical intervention, ensure that the implant identification data match those of the patient as detailed in the patient's documents and medical records. In addition, all documents related to the implant have to be carefully checked so as to make sure that the implant is an exact match to the bone gap which is to be treated.

Pre-operative treatment

As per surgical practice prior to the surgery, the patient should be administered standard antibiotic treatment. In patients that are allergic to specific antibiotic, an alternative treatment should be considered. It is necessary to carefully verify that no infection or inflammation is present at the surgical site.

Intra-operative aspects

Once the cranial defect has been exposed, it is necessary to remove any fibrotic or dural tissues from the host bone edges to ensure maximum surface contact between the vital host bone and the implant. CustomizedBone healing is highly favored when the implant is in contact with the greatest amount of vital bone tissue. Avoid exerting excessive pressure on the implant while positioning it; incorrect handling could lead to implant damage. Prepare the suture holes on the edges of the bone to align with those on the edges of the prosthesis. Then secure the implant using suture thread with a diameter less than 2 mm. Do not use absorbable sutures or any screws for implant fixation. Prepare holes along the edge at a distance of 0.5-1.0 cm from the defect area to align with the suture holes on the edges of the prosthesis.
Some holes could also be present in the central part of the implant to allow for dural suspension; the decision to perform a dura suspension is left to the surgeon's discretion. Once the implant fixation is completed, the surgical site should be closed according to standard procedures.

Post-operative procedure

In accordance with standard post-surgical procedures, a peri-operative antibiotic therapy should be administered.
The surgeon must provide the patient with all the indications for a correct post-operative recovery in relation to the localisation and entity of the defect as well as the overall clinical picture. The patient should be advised to avoid direct traumas to the implant area.

CONTRAINDICATIONS

Use of a CustomizedBone implant is contraindicated in the presence of inflammatory conditions and/or infection of the surgical area to be treated; in insufficiently vascularized sites; if dura mater wounds/lacerations are present; and in areas in which the patient's skin tissue is not sufficient to cover the implant entirely.

In addition, CustomizedBone Service is contraindicated for used in the following patient categories:

- patients suffering from a proven hypersensitivity to calcium phosphates
- patients affected by bone demineralization diseases,
- patients with chronic brain hypertension or coagulation disorders,
- patients with an ongoing bacterial or viral infection(s),
- patients on steroid therapy

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WARNINGS and PRECAUTIONS

- The use of CustomizedBone implant is reserved exclusively to qualified medical specialists.
- In pre- and intra-operative phases the device must be handled with the greatest care, avoiding any manoeuvres that might damage or contaminate the device.
- Hydroxyapatite-based cranioplasty devices have been shown in pre-clinical and clinical studies to potentially result in implant fractures in <2% of cases. The fracture rates and explantation rates are higher in children and shown below in the adverse effects section.
- The device is patient-specific and manufactured exclusively for the patient indicated on the physician's prescription. Thus do not modify the patient-specific device in any way. Any modification to the supplied device shall be the sole and exclusive responsibility of the surgeon. IIf during surgery a modification of the implant is deemed necessary by the surgeon, however, it should be made with extreme caution, only by using low speed diamond drills under water irrigation.
- In order to help achieve adequate device fixation, surgeons are recommended to carefully evaluate the device, both during design validation and during surgery including any condition leading to elevated intracranial pressure or brain herniation which may hinder proper implant positioning
- In cases of frontal sinus reconstruction, to prevent any possible risk of post-op bacterial contamination, it is necessary to assure the implant is not directly exposed to the open nasal tracts/airways.
- The implant should be fixed to the host bone by non-absorbable suture (diameter smaller than 2 mm). Do not use absorbable sutures or metallic screws for implant fixation.
- A skin expander or similar techniques to generate additional skin,should no be used concurrently with implantation of the CustomizedBone device.
- The indications and warnings given to the patient by the surgeon for the post-operative period are extremely important; in particular, patients should be warned to avoid direct traumas in the implant area. Violent blows to the implant area might lead to complications such as implant mobilisation and/or fracture. During the first post-operative year any stress on the implanted area should be avoided. CustomizedBone implants are single-use products; any unused devices or post-operative device residue must be disposed off as per local regulations. The product may not be re-sterilised.
- The product should not be used if the internal packaging has been opened or damaged. Do not use the product if it has expired.
- Prior to surgery, it is imperative to check the labels on the implant and to make sure all the patient's labels are present and matching the traceability information on the implant and on all the packaging parts. The package contains additional labels with the product's traceability details.
- If, during the surgery, the device is accidentally damaged or contaminated, surgery should be completed using the back-up implant. The back-up implant could be used also in case of re-operation but only under surgeon discretion after evaluation of the congruence between the new cranial void and the device.
- No specific, product-related adverse events have been reported when CustomizedBone implants have been used in oncological patients. Nonetheless, patients implanted with a CustomizedBone implant following brain tumour removal should be carefully monitored post-surgically.
- According to available post-marketing surveillance data, there may be a greater chance of adverse events and/or device explantation in pediatric patients 7-12 years of age as compared to pediatric patients older than 13 years of age.
- The safety and effectiveness of CustomizedBone Service has not been evaluated for defect sizes greater than 250 cm^2.

ADVERSE EFFECTS

Procedure Related:
As with all surgical procedures and as for craniotomy and cranioplasty, complications may be expected. These complications include, but are not limited to: headache, nausea, device contamination during surgery, surgical site infection or dehiscence, scar tissue formation, incisional discomfort or pain, intracranial hemorrhage, hydrocephalus, fever, pain, inflammation, seizures, brain swelling, implant malposition, nerve damage, paresthesia, cerebrospinal fluid leak, deep vein thrombosis, neurological injury and/or death.

Device Related:
Complications and adverse events can occur when using any synthetic, customized cranioplasty device. For CustomizedBone implants, complications could include, but are not limited to:

- Implant infection;
- implant mobilization;
- implant fracture.

Some minor adverse events could be conservatively treated, while severe conditions could require reoperation or implant removal.

The tables below provide information on the expected device use outcomes by summarizing adverse events observed in pediatric and adult patients (Table 1) and as relate to device size (Table 2):

Table 1

Patient Age	Adverse Events (Rate)	Fractures (Rate)	Infection (Rate)	Mobilization (Rate)	Explantations (Rate)
Children 7 – 12 years	19 (9.5%)	9 (4.5%)	4 (2.0%)	3 (1.5%)	11 (5.5%)
Children 13 – 21 years	35 (5.7%)	19 (3.1%)	13 (2.1%)	1 (0.2%)	24 (3.9%)
Adults >21 years	156 (3.8%)	34 (0.8%)	80 (1.9%)	13 (0.3%)	111 (2.7%)

Rates based on 812 pediatric and 4,087 adults cases

Table 2

Device Size	Number of cases	Adverse Events (Rate)	Fractures (Rate)	Infection (Rate)	Mobilization (Rate)	Explantations (Rate)
≤100 cm^2	605	14 (2.3%)	3 (0.5%)	7 (1.2%)	3 (0.5%)	8 (1.3%)
101 – 150 cm^2	703	21 (3.0%)	5 (0.7%)	9 (1.3%)	1 (0.1%)	14 (2.0%)
151 – 200 cm^2	257	9 (3.5%)	3 (1.2%)	4 (1.6%)	0 (0.0%)	6 (2.3%)
201 – 250 cm^2	37	3 (8.1%)	1 (2.7%)	2 (5.4%)	0 (0.0%)	2 (5.4%)
Total	1602	47 (2.9%)	12 (0.8%)	22 (1.4%)	4 (0.3%)	30 (1.9%)

Rates based on 1,602 devices

STERILIZATION

All CustomizedBone products are supplied sterile (i.e sterilized with steam). The products are single-use and may not be re-sterilised. This product is intended for single use and must not be re-sterilized. Its reuse, in whole or in part, may involve the risk of cross contamination and the danger of infection at the implant site.

STORAGE

The product must be stored in a cool, dry area, and should be protected from direct light and heat sources (+ 10° C /+ 40°C)

SYMBOLS GLOSSARY

Symbol	Standard Reference	Standard Title	Symbol Title	Explanatory Text
	ISO 15223-1, Clause 5.1.1	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Manufacturer	Indicates the medical device manufacturer.
	ISO 15223-1, Clause 5.1.5	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Batch code	Indicates the manufacturer's batch code so that the batch or lot can be identified.
	ISO 15223-1, Clause 5.7.1	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Patient number	Indicates a unique number associated with an individual patient.
	ISO 15223-1, Clause 5.1.6	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Catalogue number	Indicates the manufacturer's catalogue number so that the medical device can be identified.
	ISO 15223-1, Clause 5.2.6	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Do not resterilize	Indicates a medical device that is not to be resterilized.
	ISO 15223-1, Clause 5.4.2	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Do not re-use	Indicates a medical device that is intended for one use, or for use on a single patient during a single procedure.
	ISO 15223-1, Clause 5.2.8	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Do not use if package is damaged	Indicates a medical device that should not be used if the package has been damaged or opened.
	ISO 15223-1, Clause 5.4.3	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Consult instruction for use	Indicates the need for the user to consult the instructions for use.
	ISO 15223-1, Clause 5.4.4	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Caution	Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device itself.
	ISO 15223-1, Clause 5.2.5	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Sterilized using steam or dry heat	Indicates a medical device that has been sterilized using steam or dry heat.

Symbol	Standard Reference	Standard Title	Symbol Title	Explanatory Text
	ISO 15223-1, Clause 5.3.2	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Keep away from sunlight	Indicates a medical device that needs protection from light sources
	ISO 15223-1, Clause 5.1.4	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Use-by date	Indicates the date after which the medical device is not to be used.
	ISO 15223-1, Clause 5.3.4	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Keep dry	Indicates a medical device that needs to be protected from moisture.
	ISO 15223-1, Clause 5.3.7	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Temperature limit	Indicates the temperature limits to which the medical device can be safely exposed.
	ISO 15223-1, Clause 5.3.1	Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements	Fragile; handle with care	Indicates a medical device that can be broken or damaged if not handled carefully.
	ISO 7000 - 0623	Graphical symbols for use on equipment – Registered Symbols	This way up	Indicates correct upright position of the transport package.
	ASTM F2503	Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment	MR Safe	Safe for use in magnetic resonance imaging.
	N/A	N/A	Pieces number	The number of pieces within the package.
	21 CFR 801.15(c)(1)(i)(F)	Labeling - Medical devices; prominence of required label statements; use of symbols in labeling.	Prescription use only	Requires prescription in the United States.
	21 CFR 801.109(b)(1)	Labeling - Prescription devices.		

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