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Original article

Computed tomographic evaluation of novel custom-made artificial bones, “CT-bone”, applied for maxillofacial reconstruction

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ABSTRACT

Introduction: We fabricated custom-made artificial bones using three-dimensionally layered manufacturing (3D printing) process, and have applied them to patients with facial deformities. We termed this novel artificial bone the “CT-bone”. The aim of the present study was to evaluate the middle- and long-term safety and effectiveness of the CT-bones after transplantation.
Methods: The subject areas involved were 23 sites of 20 patients with facial bone deformities due to congenital abnormality, tumor, or trauma. The CT-bones were used for augmentation; they were evaluated by CT images, minimally for 1 year and maximally for 7 years and 3 months (3 years and 1 month on average) after transplantation.
Results: No serious systemic events due to the CT-bone graft were found during the observation period (1 year postoperatively). In 4 sites of 4 patients, the CT-bones were removed due to local infection of the surgical wounds at 1–5 years postoperatively. Compatibility of the shapes between the CT-bone and the recipient bone was confirmed to be good during the operation in all of the 20 cases, implying that the CT-bones could be easily installed onto the recipient sites. During the CT evaluation (<7 years and 3 months), no apparent chronological change was seen in the shape of the CT-bones. Sufficient bone union was confirmed in 19 sites. The inner CT values of the CT-bones increased in all the sites. The longer the postoperative period, greater increases in the CT values of the CT-bones tended to be observed.
Conclusions: The CT-bone showed maintenance of the original shape and good bone replacement, based on the middle- and long-term follow-ups. In the future, we would make an intelligent type of artificial bones in which bone regeneration is induced by gradually releasing angiogenesis-inducing factors and/or bone-regeneration-inducing factors at the three-dimensionally controlled positions.

1. Introduction

Treatments for facial deformities include dermal fat graft, silicone implant, autologous bone graft, and artificial bone graft [1]. Especially, for facial bone deformities and defects, the autologous bone graft has currently been the gold standard as the treatment. However, it has problems such as invasiveness to the donor site and a restriction in volume of the bones that can be harvested from the patients [2]. Moreover, the resorption of transplanted bone is known. Although allogenic bone graft has been clinically used all over the world, it is not popular in Japan, which may reflect the

Abbreviation: TCP, tricalcium phosphate; CT, computed tomography; HA, hydroxyapatite; IPCAB, inkjet-printed custom-made artificial bone; DICOM, digital imaging and communications in medicine; STL, stereolithography; MRSA, methicillin-resistant *Staphylococcus aureus*; CAD, computer aided design.

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cultural and religious differences between Japan and other countries. There are also concerns about problems such as infectious diseases and ethical issues associated with the use of another person's bones [3]. In addition, both the autologous bone graft and the allogenic one have to be shaped to fit the recipient sites during surgery. It takes a long time to make a complicated shape [4].

In order to solve these problems, artificial bones using HA and/or calcium phosphate have been developed [5]. These are not applicable to sites subject to pressure from the skin and/or the mucosa after the transplantation, when they are supplied as granules or paste. To maintain their shape, they must be block-shaped, which also requires caving during surgery, leading to a substantial prolongation of the operation time and the difficulty in making complicated shapes.

Staffa et al. [6,7] reported a method of engrafting a customized artificial bone preoperatively fabricated by a matching center in repair for a cranial bone defect, with satisfactory medium- and long-term outcomes. In this method, an artificial bone is formed in a shape compatible to the defect referring to a full size of three-dimensional model fabricated by rapid prototyping technology based on CT images. However, these artificial bones are likely to require a considerably long time to be replaced by host bones, because they are sintered porous HA blocks with a high crystallinity. Moreover, it is impossible to provide internal structures such as interconnecting pores for blood vessel and cell migration. Cao et al. [8] also reported the clinical application of custom-made artificial bones fabricated from HA and methacrylate resins to the cranio-maxillofacial region. They applied rapid prototyping technology for the fabrication. However, it is impossible to provide internal structures because the bones are formed by casting a mixture of HA and methacrylate resins in a mold. In addition, replacement by autologous tissues cannot be expected due to the remaining resins.

In order to enable to replace artificial bones to host's own bones and to provide internal structures within the artificial bones, we fabricated custom-made artificial bones using a new technique by a three-dimensionally layered manufacturing (3D printing) process, and applied them to patients with facial deformities [9–11]. We called this novel artificial bone IPCAB in our previous report [9]; we currently term it “CT-bone”.

This artificial bone is directly fabricated by a three-dimensionally layered manufacturing process using an inkjet printer, allowing us to provide complicated shapes such as overhangs and internal structures. Therefore, this is likely to be very suitable for the reproduction of the complicated shapes of the maxillofacial region [12]. Moreover, rapid replacement by living bone can be expected because unsintered calcium phosphate, α-TCP, is the major component. No method has been reported up to date except for our technology, which directly forms artificial bones for clinical use using the rapid prototyping technology [9–11,13].

This study aimed to evaluate the medium- and long-term safety and effectiveness of the CT-bones after transplantation. The CT-bones were used in the augmentation of facial bone deformities, while they were evaluated by the CT images for maximum of 7 years and 3 months after transplantation.

2. Methods

2.1. Patients

The subject areas involved were 23 sites of 20 patients with non weight bearing facial bone deformities (e.g., maxilla, mandible, chin, frontal bone) due to a congenital abnormality, tumor, or trauma. As subjects of this clinical trial and study, they underwent CT-bone grafts in our department between March 2006 and September 2009 (Table 1).

All patients were provided with informed consent and understood the risks of the study and the potential for no benefit. The study was approved by the Ethical Committee of the Faculty of Medicine at the University of Tokyo (approval no. 1310), and Clinical Research Support Center at the University of Tokyo (approval code: 3DB-01/CT-1).

2.2. Design and fabrication of CT-bone

The CT-bones were fabricated according to our previous reports [9–11,13,14]. All of the CT images were generated by a helical CT scanner (Aquilion®, Toshiba, Tokyo, Japan) with unified parameters; reconstruction interval of 1 mm; tube current of 300 mA at 120 kV.

Using the pre-surgical CT scanning data, a three-dimensional model was fabricated from plaster. On this three-dimensional model, the surgeon performed a surgical simulation using wax provided with radiopacity for a better contrast (PCT/JP2007/000885) [15]. To increase the radiopacity without affecting the good handling, dental paraffin wax was mixed with rutile-type titanium oxide at the ratio of 80:3. Next, to extract the design data of the CT-bone from this simulation model, the model underwent a CT scan again. The DICOM data were acquired from the CT images and converted to STL files. The CT-bone was then designed with internal structures such as holes for fixation by absorbable sutures using CAD. This final design was output to a 3D inkjet printer (Z406 3D color printer, Z-Corporation, Burlington, MA, USA), which sprayed hardening liquid onto the α-TCP powder (Taihei Chemical Industrial, Osaka, Japan). This method can manufacture an approximate 0.1 mm thick thin layer at each step. This step was repeated to overlay the thin layers for the fabrication of the specified CT-bone design. The hardening liquid is composed of 5% sodium chondroitin sulfate (Seikagaku, Tokyo, Japan), 12% disodium succinate (Wako, Osaka, Japan), and 83% distilled water (Otsuka Pharmaceuticals, Tokyo, Japan). The CT-bones fabricated by the three-dimensionally layered manufacturing process were immersed in the hardening liquid for an additional 6 h to increase their mechanical strength.

The CT-bones were sterilized by autoclaving (121 °C, 30 min). After the sterilization, the bones were dried for 6 h at 75 °C.

2.3. Surgical procedures and follow-ups

The CT-bone grafting was performed using an intraoral or extraoral approach under general anesthesia in all cases. An oral mucosa or skin incision was made, followed by subperiosteal dissection (or dissection under the periosteum-like tissue) for exposure of the recipient bone. The CT-bone was engrafted in the designated position and fixed onto the host bone using absorbable sutures (2-0 Vicryl®, Johnson & Johnson, USA) when possible. For closing of the incision, the oral mucosa or skin was sutured after suturing the periosteum (or periosteum-like tissue). All of the surgical procedures were only grafts for augmentation purposes.

The presence or absence of any adverse event and the level of satisfaction (yes or no) were surveyed using interviews and examinations by a physician. The CT scan was also performed preoperatively, immediately postoperatively, at half a year and at 1 year postoperatively. As observation period, we primarily evaluated clinical results of the CT-bone at 1 year. Even 1 year after the operation, patients who could attend our hospital underwent outpatient medical examination for follow-up and, when required, CT scans, in order to check safety or adverse events.