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ORIGINAL ARTICLE

Modular Endoprosthesis for Mandibular Reconstruction – A Thematic Research Study at the National Dental Centre Singapore

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ABSTRACT

Introduction: A thematic research project was undertaken by the National Dental Centre Singapore to study the feasibility of using a novel modular endoprosthesis for reconstruction of the mandible. Successful application of this technique potentially eliminates the need for a donor site.

Methods: Three sub-projects done in a monkey model are presented. In the first two sub-projects, a titanium modular endoprosthesis was inserted in surgically created defects for reconstruction of the ascending ramus and condyle; and body of the mandible respectively. In the third sub-project, a polycaprolactone scaffold with calcium phosphate (CaP) surface coating modular endoprosthesis was used for reconstruction of the body of the mandible. The animals were sacrificed at three to six months. Microcomputed tomographic and histologic analyses were done.

Results: At the time of sacrifice, signs of infection were present in a few animals treated either with the titanium or the polycaprolactone endoprosthesis for replacement of the body of the mandible. None of the animals who received the ascending ramus and condyle titanium endoprosthesis had an infection. New bone formation was noted around the stems of the titanium devices and inflammatory reaction was much reduced from three to six months. For the polycaprolactone device, more de novo bone formation was seen in the group using Human-BMP-2.

Conclusion: The use of a modular endoprosthesis for mandibular reconstruction seemed to result in a physiologic replacement of the lost part of the mandible, although the biomechanics of the system need further evaluation so as to improve its long term stability.

Keywords: Jaw, Prosthesis, Tissue engineering

INTRODUCTION

Surgeons have been reconstructing mandibles for more than a century. Despite the enormous progress made particularly over the last 40 years, the ideal solution has not yet been achieved. The introduction of microvascular surgery and its subsequent application in the transposition of bone grafts brought about a revolution in mandibular reconstructive surgery. For the first time, a free tissue graft can be transferred together with its blood vessels and a blood supply is re-established by microvascular anastomosis at the recipient site. Provided the graft is properly fixed, it will heal primarily at the site of the ostectomies. In principle, healing time will be short and complications like resorption and infection are greatly reduced as compared to non-vascularized grafts[1]. McKee[2] was the first to describe the use of a microvascular free rib graft, for mandibular reconstruction in 1971. Since then, various donor sites have been employed

for free flap reconstruction of the mandible, including the radial forearm, scapula and iliac crest but the fibula is currently the most popular and has the widest application. First described by Taylor et al[3] in 1975 and later adapted for mandibular reconstruction by Hidalgo[4] in 1989, the fibula flap is based on the peroneal artery and associated veins. Blood supply to the fibula is both intraosseous and segmental and, therefore, multiple osteotomies can be made so as to match the contour of the mandible. It can provide up to 30cm of bone length which is sufficient for reconstructing any length of the mandible. The height of bone is, however, usually inadequate relative to a dentate mandible which can be a problem when dental implants are planned for occlusal rehabilitation. To overcome this problem, the use of a "double barrel" flap[5] and vertical distraction of the fibular flap[6] have been described. At present, mandibular reconstruction using microvascular free flaps is the gold standard in that it provides in most cases a functional reconstruction.

However, despite the many advantages of microvascular free flap reconstruction, it is time-consuming and associated with varying degrees of donor site morbidity. A study done in a Medical Centre in the United States employing a two-team approach for mandibular resection and reconstruction with the free fibula flap reported a mean operating room time of 8.3 hours, a mean hospital stay of 12.9 days of which 5.1 days were in the Intensive Care Unit[7]. These may not be acceptable in elderly patients whose health is often compromised by the primary disease and other medical conditions. The procedures require specialised surgical expertise and hospital infrastructure which may not be available everywhere in the world.

In recent years, new techniques for mandibular reconstruction are being tested, with the common aim of eliminating the need for harvesting bone from a donor site. These include Transport Disc Distraction Osteogenesis (TDDO) and bone regeneration using tissue engineering methods. These techniques are still in the experimental stage and reported results have been inconsistent.

In 2006, a thematic research project was launched at the National Dental Centre Singapore to study the feasibility of using a novel prosthetic device for reconstruction of the mandible. The device is a modular endoprosthesis, adapted from those used by orthopaedic surgeons for more than two decades in limb salvage surgery. In orthopedics, the surgery involves removal of all diseased bone and immediate replacement by the metallic device. Instead of using screw fixation, the device is fixed internally into the medullary space of the remaining, healthy bone stump. A modular system consists of several components of varying lengths that are assembled so as to fit the size of the defect at the time of surgery, thus obviating the need for customisation, reducing cost, presurgical planning and waiting time[8]. Although this technique is proven to be highly successful in orthopaedics, it has to be recognised that the mandible is significantly different from long bones in terms of morphology, function and biomechanics. Our research study therefore aimed to assess the feasibility of applying this device in the mandible. The hypothesis was that the use of a modular endoprosthesis for reconstruction of the mandible would result in a stable and physiologic replacement with minimal complications. Successful application of this technique for mandibular reconstruction potentially eliminates the need for a donor site, shortens operating time and hospital stay and allows earlier rehabilitation of the patient.

The five sub-projects under this thematic research programme are:

1) Replacement of the condyle and ascending ramus of the mandible by a metallic modular endoprosthesis in Macaca fascicularis

2) Replacement of the body of the mandible by a metallic modular endoprosthesis in Macaca fascicularis

3) Replacement of the body of the mandible by a polycaprolactone (PCL) scaffold with calcium phosphate (CaP) surface coating modular endoprosthesis in Macaca fascicularis

4) Cementation considerations of a modular endoprosthesis for mandibular reconstruction

5) Biomechanics of reconstructed mandibles with the modular endoprosthesis

Sub-projects 1 to 3 were clinical animal studies. Permission to carry out the study was granted by the Institutional Animal Care and Use Committee



(a) (b) (c)

Fig. 1. Ti-6Al-4V modular endoprosthesis for reconstruction of the ascending ramus and condyle in Macaca fasicularis (a) 2-piece modular system (disassembled) (b) Radiograph showing an implanted modular endoprosthesis for reconstruction of the right ascending ramus and condyle in Macaca fascicularis (c) Histology section of the stem region showing new bone formation adjacent to the bone-cement interface.

of SingHealth in Singapore. A summarised report of these three sub-projects is presented in this paper.

1) REPLACEMENT OF THE CONDYLE AND ASCENDING RAMUS OF THE MANDIBLE BY A METALLIC MODULAR ENDOPROSTHESIS IN MACACA FASCICULARIS

Methods

Eight male, adult monkeys (Macaca fascicularis) were used in this study. The device, made of a titanium alloy (Ti-4Al-6V), was a two-piece modular system. The first module consisted of a stem, which was made to fit as closely as possible the medullary space of the mandibular stump. The second module was shaped to replace the ascending ramus and condyle. The two modules were held together with a screw (Fig. 1a). Under general anaesthesia, the right mandible was exposed via a submandibular approach. The mandibular segment, including the ascending ramus and condyle, posterior to the second molar was resected. The marrow cavity of the distal mandibular stump was prepared using a fissure bur, to create a space for the stem of the prosthesis. A polymethylmethacrylate bone cement, Palacos® (Heraeus Kulzer GmbH, Hanau, Germany), was mixed and brought into the marrow cavity with a spatula . The cement was also applied to the stem of the first module which was then inserted into the marrow cavity. Next, the ascending ramus and condyle module was inserted and then connected to the stem module with a screw. The wound was then closed in layers. The monkeys were put on a soft diet for the first two weeks postoperatively and received appropriate postoperative analgesics and antibiotics. Four monkeys were sacrificed at three months and another four monkeys at six months postoperatively. The reconstructed mandibular segment was harvested en-bloc.

Microcomputed tomographic (Micro-CT) scanning was performed to analyse the bone volume (BV) at the bone-cement interface. Sections were then made at the stem, prosthetic ramus and temporomandibular joint regions and stained with methylene blue and basic fuchsin for histologic analysis.

Results

All eight monkeys functioned well with good intercuspidation, without significant change in interincisal opening and the temporomandibular joints were able to move freely. At the time of sacrifice, no fistulae, dehiscences or mobility of the endoprostheses was observed. Radiographs showed the endoprostheses to be in good position and new bone growth was seen at the lower border of the prosthesis adjacent to the bone stump (Fig. 1b).

The combined (buccal, lingual and inferior regions) mean BV of the six-month group was significantly higher than that of the three-month group ($P<0.05$). Histology sections containing the stem revealed a space between the stem and surrounding tissues. This area was previously occupied by bone cement, which had degraded during the fixation and dehydation processes of the histological preparation. A thin fibrous tissue capsule surrounded the bone cement space completely. Inflammatory cells were observed at the "cement surface" but were generally less pronounced in the six-month than the three-month specimens. Newly formed bone was noted adjacent to the interface (Fig. 1c). A fibrous capsule of varying thickness was also noted surrounding the metal ramus. There were abundant inflammatory cells in this region in the three-month specimens but were very much reduced in the six-month specimens. Bone resorption in the glenoid fossa



(a) (b) (c)

Fig. 2. Ti-6Al-4V modular endoprosthesis for reconstruction of the body of the mandible in Macaca fascicularis (a) 3-piece modular system (assembled) (b) Radiograph showing an implanted modular endoprosthesis for reconstruction of the right body of mandible in Macaca fascicularis (c) Micro-CT scan of the anterior stem within the medullary space of the mandibular bone stump.

and pathologic changes in the articular disc (fissuring, splitting or perforation) were noted in the temporomandibular joint on the reconstructed side in most specimens[9-11].

2) REPLACEMENT OF THE BODY OF THE MANDIBLE BY A METALLIC MODULAR ENDOPROSTHESIS IN MACACA FASCICULARIS

Methods

Eight male, adult Macaca fascicularis were used in this study. The device, also made of titanium alloy, consisted of three modules: two stem modules which will be inserted into the mandibular stumps on either side of the resection and a centre body module, to which the stem modules will be attached by screws (Fig. 2a). During surgery, resection of a segment of the right body of the mandible including the first and second permanent molars was done via an intraoral approach. Techniques for preparation of the bony stumps and cementation of the endoprosthesis were similar to those described above.

Four monkeys were sacrificed after three months and the remaining four monkeys were sacrificed after six months. Micro-CT and histologic evaluations were performed using a similar protocol as described above.

Results

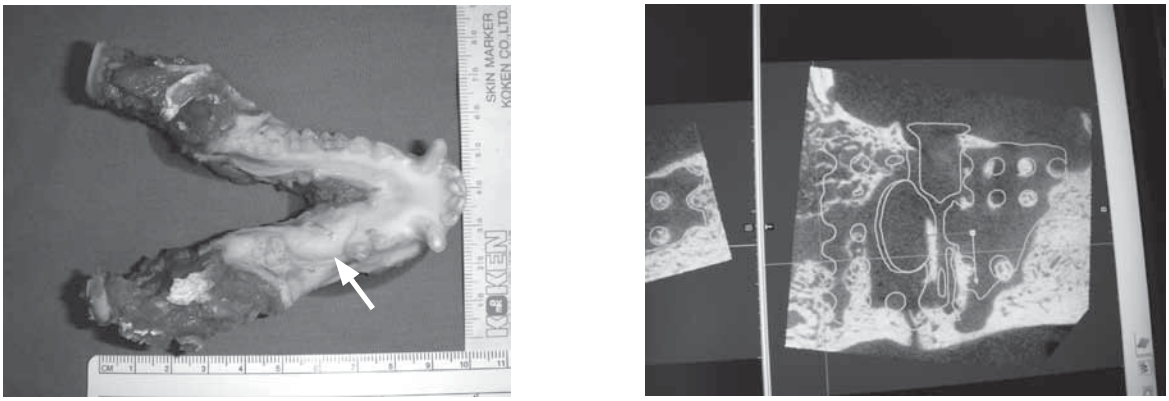
At sacrifice, none of the monkeys showed appreciable mobility at the interface of the bone stumps and endoprosthesis. Occlusion was also found to be satisfactory and there was no soft tissue dehiscence noted in any of the animals. Three monkeys had intra-oral fistulas at sacrifice. One also had a fistula at the right submental region. At exploration, it was found that all 4 fistulas were leading to loose screws of the endoprostheses. Radiographs at sacrifice, however, showed no dislodged screws and the endoprostheses seemed to be in good position with no displacement (Fig. 2b). Micro-CT analyses showed no significant difference in mean BV at the bone-cement interface between the three-month and six-month groups (Fig. 2c).

At three months, histological examination showed a thick fibrous capsule and an abundance of inflammatory cells at the bone-cement interface around both the anterior and posterior stems. At six months, the fibrous capsule was reduced in thickness for both the anterior and posterior stems. Inflammatory cells were still present at the bone-cement interface in some specimens, but to a lesser extent as compared to the three-month group[12].

3) REPLACEMENT OF THE BODY OF THE MANDIBLE BY A POLYCAPROLACTONE (PCL) SCAFFOLD WITH CALCIUM PHOSPHATE (CaP) SURFACE COATING MODULAR ENDOPROSTHESIS IN MACACA FASCICULARIS

Methods

Twenty-four male, adult Macaca fascicularis were used in this study. The device used was a modular endoprosthesis made of an engineered integrated polycaprolactone (PCL) scaffold with calcium phosphate surface coating. The 3D porous scaffolds consisting of two stem modules were fabricated to replace a 1.5-cm body segment of the mandible. In this study, the modular endoprosthesis PCL scaffolds were implanted in 24 monkey mandibular body segmental defects. No cementation was used but instead the stems were stabilised mechanically within the marrow space of the mandible by friction-fit. The animals



(a) (b)

Fig. 3. PCL scaffold with calcium phosphate (CaP) surface coating modular endoprosthesis for reconstruction of the body of the mandible in Macaca fascicularis. (a) Mandible specimen of Macaca fascicularis (arrow indicates the reconstruction site) (b) Micro-CT scan showing some regenerated bone inside the PCL scaffold (with Human-BMP-2 group) after six months.

were divided into three groups (eight animals per group); 1) empty PCL scaffold as a control, 2) PCL scaffold with autogenous bone marrow cells and 3) PCL scaffold with Human-BMP-2. The mandible was then stabilised with two titanium miniplates placed across the reconstruction due to the inadequate rigidity and mechanical strength of the PCL scaffold. Upon sacrifice at six months postoperatively, the reconstructed sites (Fig. 3a) were evaluated by plain radiographs, micro-CT scans (Fig. 3b), mechanical testing and histologic analyses.

Results

All monkeys survived the experimental period. Two animals in the control group (empty PCL scaffold), five animals in the group reconstructed with PCL scaffold with autogenous bone marrow cells and five animals in the group using PCL with Human-BMP-2 were sacrificed and the mandibular specimens harvested. The rest of the animals presented with infection at the reconstructed sites and were removed from the investigation. Radiographs and micro-CT scans showed more de novo bone formation at the reconstructed sites in the group using PCL with Human-BMP-2 compared with the rest of the groups. The results of the mechanical testing and histology studies are currently being analysed.

DISCUSSION

Endoprostheses anchored with bone cement has proven to achieve long term stability with good function in long bones, with 15-year survival rates of 94% reported[13]. When applying this reconstructive method to the mandible, however, several unique challenges had to be addressed. The mandible is a curved bone with a flat, tear-drop-shaped cross-section unlike the long bone which is straight with a concentric cross-section. This difference in morphology necessitated a different design of the prosthetic stem. The stem in the mandible device had to be flat, like a plate, rather than concentric, like a rod as in long bone devices. The stem was also comparatively shorter in the mandible prosthesis because the mandible is curved and a longer stem would encounter the curvature during placement into the medullary space, making insertion more difficult or impossible. A shorter stem would mean that the length of the lever arm was much greater with the mandibular endoprosthesis. Functional forces in the mandible are significantly lower than those in the weight-bearing long bones of the lower limbs. Moreover, following partial resection and reconstruction of the mandible, Maurer et al.[14] found a reduction in bite force of about 76% in the molar region and 59% in the incisor region. Despite the lower forces, however, the mandible has to withstand a lot of lateral forces unlike in long bones where the forces are mainly axial to the endoprosthesis. During function, the mandible is subjected to forces produced by the muscles of mastication and by reaction forces acting through the teeth and temporomandibular joint. Champy and co-workers[15] described a zone of tension in the alveolar part of the mandible and a zone of compression in the lower border. During unilateral molar loading, deformation of the mandible can be described as a combination of sagittal bending, torsion and lateral transverse bending[16]. Any

device and cement interfaces in the mandible must be able to withstand such multi-directional forces to prevent loosening and ultimate failure of the system in the long term. The results of our studies showed better stability with the ascending ramus-condyle endoprosthesis (Sub-project 1) as compared to the body endoprosthesis (Sub-project 2), as the latter presented with several cases of loosened screws. The presence of a "free" end at the temporomandibular joint in the ascending ramus-condyle reconstruction probably allowed dissipation of the transmitted stresses, whereas in the body design, where both ends were fixed to the bone stumps, stresses were borne by module connection. The screws used for stabilising the modules appeared to be a weakness in the system, especially when they were placed in the lateral aspect, as Dechow and Hylander[17] showed in primate studies that the magnitude of bone stress and strains was larger on the buccal than on the lingual cortex of the mandible during mastication. The possibility of re-locating the connection screws or using an alternative screw-less locking system is being investigated. Another challenge that is unique to the mandible endoprosthesis is that it is comparatively superficial when implanted, being surrounded only by thin oral mucosa unlike the orthopaedic device which is surrounded by thick vascular muscles and skin. This may imply a higher potential of soft tissue dehiscence and exposure of the mandibular device. The superior aspect of the body of the prosthesis was therefore designed to be lower than the adjacent mandibular stumps to prevent this complication. Research to improve soft tissue adhesion by surface modification of the titanium alloy prosthesis is being done.

The early inflammatory response seen in the three-month specimens of the metallic devices was an expected reaction to surgery and implantation of a foreign body i.e. bone cement and endoprosthesis. Signs of resolution of the inflammatory response over time support the notion that the components of the system, including the cement, were rather biocompatible. The fibrous tissue bone-cement interface noted in our specimens has also been similarly documented in orthopedic endoprostheses and has not been known to compromise stability in the long-term provided it remains within 2mm thickness[18]. Histology of the ascending ramus/ condyle replacement described is clearly indicating that adaptive changes took place in the fossa up to six months postoperatively, which seemed to suggest overloading. One has to bear in mind, however, that the chewing pattern of monkeys is rather different from human beings, in that, because of the large canines, lateral movements are minimal as compared to humans[19]. Further studies are needed to evaluate the long-term effects of the remodelling process.

Sub-project 3 combined the concept of the modular endoprosthesis with bone regeneration techniques for mandibular reconstruction. Instead of a foreign metallic device, the reconstruction would ultimately consist of the host's own regenerated bone. This was tested in our study by implanting a degradable osteoconductive scaffold that delivered osteoinductive factors directly to the mandibular defect site. In the literature, Warnke et al[20,21] reported a clinical case whereby an engineered graft was allowed to heal in the latissimus dorsi muscle and subsequently transplanted to the mandibular resection site, using microvascular anastomosis. In principle, engineering a graft at the site of the defect would be more of an advantage in that the transplantation microvascular surgery may be avoided. It would, however, require a period of healing during which the mandible should be immobilised. It would also require adequate soft tissue conditions as to protect the engineered bone during its healing phase. Inadequate immobilisation or a breakdown of the soft tissue cover can ultimately lead to failure of the entire construct as seen in several of our cases where infection occurred. In our study, the results of the BMP-2 group showed good potential of bone regeneration within the boundaries of the degradable osteoconductive scaffold and also presented with the best load-bearing capability at six months. The predictability of this method, however, in reconstructing defects of a larger size and in conditions where vascularity is compromised by surgery and irradiation, will continue to be a challenge.

CONCLUSION

The results of our study seemed to support the hypothesis that a modular endoprosthesis for mandibular reconstruction would result in a physiologic replacement of the lost part of the mandible, although the biomechanics of the system need further evaluation so as to improve its long-term stability.

This thematic research undertaken by our Centre

aims to introduce a system that is simple to use and does not require sub-specialised training in micro-vascular surgery. It should be readily available as an "off-the-shelf" pre-fabricated product which eliminates the need for customisation, thereby reducing cost and production time. The modular design will mean minimal preoperative planning and greater intra-operative flexibility. The modular endoprosthesis, in our opinion, has a potential in reconstructive surgery of the mandible, especially for the older and medically compromised patient. Advantages to the patient include reduced operation time and no donor site morbidity which translate to shorter hospital stay, reduced medical costs and earlier functional and aesthetic rehabilitation of the occlusion. With these benefits, we hope that the quality of life of our patients will be improved.

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