J Stomatol Oral Maxillofac Surg xxx (2017) xxx–xxx

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Original Article

Histological and radiological evaluation of subcutaneous implants in mouse of a 3D-printable material (Fulcure 720) and experimental application in mandibular reconstruction

J. Megías Barrera [a,*], L. García-Consuegra [a], A. Novoa [a], S. Costilla [b], S. Junquera [c], G. Ascani [d]

[a] Oral and Maxillofacial Surgery Department, Central University Hospital of Asturias, Oviedo, Spain
[b] Radiology Department, Central University Hospital of Asturias, Spain
[c] Radiology Department, University Hospital of Santiago de Compostela, Spain
[d] Oral and Maxillofacial Surgery Department, Ospedale Civile dello Spirito Santo di Pescara, Italy

ARTICLE INFO

Article history:
Received 12 September 2017
Accepted 2 November 2017

Keywords:
FullCure
Biocompatibility
Implant biomaterial
3D-printing
Mandibular reconstruction

ABSTRACT

Introduction: The aim of this study was to evaluate the bioactivity of Fullcure compared to porous polyethylene implants (Medpor) in rats prior to custom-made scaffold support manufacturing for mandible segmental defects (MSD) reconstruction in sheep.
Methods: Twelve Fullcure and Medpor laminaes were implanted in the left and right dorsum respectively of six wistar rats. Toxicity was assessed by skin, kidney and liver histopathology three months post-implantation. Computed Tomography (CT) was carried out in order to assess radiological differences between implants. Fullcure containers were subsequently manufactured by CAD/CAM to hold scaffold cylinders for MSD reconstruction in sheep.
Results: No statistical differences were observed in tissue response between implants. Fullcure radiodensity was higher than Medpor ($P < 0.05$). Fullcure manufactured support was successfully used for mandible repair in sheep. Nevertheless, the manufactured container did not accomplish the goal of guiding new bone formation according to the mandible shape.
Conclusions: Fullcure showed similar biocompatibility and stronger radiodensity than Medpor. Despite its cheaper price and endless 3D-printing possibilities as scaffold holder for mandible reconstruction, further animal studies are needed to ensure Fullcure biocompatibility as implantable biomaterial.

1. Introduction

There are four different classes of biomaterials available for surgeons: metals, composites, ceramics and polymers [1,2]. Among the different polymers, FullCure 720 is an acrylic photopolymer with transparent appearance, used in 3-Dimensional Printing Systems for the manufacturing of stereolithographic models by rapid prototyping system. Rapid prototyping is a procedure of producing models. There are various methods of rapid prototyping. The main advantage lies in the speed of producing physical prototypes as well as almost unlimited complexity of geometry [3].

Polyjet Fullcure 720 (Objet Geometries Ltd., Sint-Stevens-Woluwe, Belgium) is a translucent resin, epoxy-acrylic based, that supports up to 20% tensile strain, holding its accuracy and shape up to 50 °C and can be handled directly after construction. The PolyJet printing system consists on a print head that applies a photo-curable resin layer that is cured immediately after its building with a ultraviolet lamp. Once cured it becomes solidified, thus allowing for further overlapping process. This printing system showed higher accuracy than conventional systems of rapid manufacturing such as selective laser sintering or conventional 3-Dimensional printing [4]. According to the thickness of the layer it is possible to print in High Quality (HQ, 16 μm) or High Speed (HS, 32 μm).

The aim of this study is the histological and radiological evaluation of Fullcure 720 in wistar rats and to compare the foreign body response with a porous ultra-high density polyethylene broadly used in the surgical management of orbital defects

* Corresponding author. Escuela de Estomatología, Catedrático José Serrano, 33009 Oviedo, Spain.
E-mail address: dr.megias@yahoo.es (J. Megías Barrera).

https://doi.org/10.1016/j.jormas.2017.11.004
2468-7855/

(Medpor, Porex Surgical, USA) prior to CAD/CAM manufacturing of custom-made polymer containers of scaffold cylinders for mandible reconstruction in sheep.

2. Materials and methods

In order to analyse the bioactivity of Fullcure compared to porous polyethylene implants (Medpor), twelve Fullcure laminae were implanted on the left side of the dorsum of six wistar rats (average 290 g weight) whereas the same number of Medpor laminae in the right side were placed.

All animal manipulations were carried out according to the European directive for protection of animals used for experimental and other scientific purposes 86/609/EEC, Spanish directive BOE 67/8509-12 and with the approval of the Animal Care and Handling Committee of the University of Oviedo.

Surgery consisted on the subcutaneous inset of two 5 mm diameter round implants in each side of the dorsum of six wistar rats. Implants were obtained after drilling with a 5 mm diameter trephine Fullcure and one ultrathin sheet of Medpor (Fig. 1). On the left dorsum, two round Fullcure implants were placed in subcutaneous sockets as well as two Medpor round implants of the same size were equally placed in the right side (see video 1, supplementary data). The rats were sacrificed after three months and local microscopic tissue response at the implanted site and systemic toxicity in both liver and kidneys histologic samples were evaluated by a pathologist using hematoxilin/eosin (H.E). To asses implant site histopathologic changes, foreign body response was graded into four levels according to Duranti et al. [5] were 0 corresponded to no visible reaction and 4 was granuloma and encapsulated implant-clear foreign body reaction. After grading all skin samples mean value was calculated and Wilcoxon test for paired variables was used to assess differences of foreign body reaction between both implants.

Computed Tomography (CT) analysis was done in the flat panel CT component of small animals PET/CT (Argus PET/CT, SEDECAL, Madrid, Spain) with radiodensity measuring and 3D volume rendering was carried out using Osirix (Pixmeo, Geneva, Switzerland) to evaluate radiologic features between Fullcure and Medpor implants. Radiodensity mean values of each implant in Hounsfield Units (HU) were obtained using region of interest (ROI) tool in the soft tissue window and statistical differences were calculated (t-test). All statistical analysis was performed using SPSS 20 (IBM, Armonk, NY) and $P < 0.05$ was considered for statistically significant differences.

After implantation in rats, Fullcure was subsequently used to manufacturing a custom-made support to hold a scaffold cylinder for mandible reconstruction of segmental defects (30 mm) in a 15 months old female sheep (“Latxa” Asturian sheep, 59 kg weight). The albumin-derived scaffold cylinder was elaborated from sheep blood according to Gallego et al. [6] technique. CAD/CAM was used to scan the sheep mandible and to virtually perform 30 mm long segmental ostectomy and manufacture the Fullcure support for the scaffold to reconstruct the defect. The polymer construct was expected to stabilize the scaffold with the osteosynthesis plate fixed with three bicortical screws at each side of the defect and to guide new bone formation into an anatomic mandibular shape following the contour of the Fullcure container. After 32 weeks the sheep was sacrificed. The mandibular bone repair was analyzed by computed tomography (Toshiba Aquilion 16; Toshiba Medical Systems Corporation, Tochigi, Japan).

3. Results

During the immediate postoperative period no acute complications were observed, and any of the animals died after implantation. Before the sacrifice no any extrusion or infection on the implanted site occurred, and no systemic toxicity in liver or kidney histologic samples was found (Fig. 2). Macroscopically, Medpore implants showed stronger capsule and fibrosis formation subcutaneously compared to Fullcure. Microscopically, FullCure showed marked biocompatibility and both implants were well integrated into the tissues with newly formed collagen bands around the implants and no granulomas were detected. FullCure implants showed low inflammatory cell infiltration, without significant differences with respect to Medpor implants (Fig. 3). Mean values for inflammatory response for Fullcure and Medpore were 1.67 and 2.17 respectively, and no statistical differences were observed.

Radiological evaluation showed no local signs of cellulitis in any sample. Stronger radiodensity of Fullcure in all specimens was observed (Fig. 4). Using OsiriX (Pixmeo, Ginebra, Switzerland) 3D volume reconstruction tool Fullcure showed bony-like radiodensity. For each sample, Medpor and Fullcure areas were used to calculate their radiodensity in the soft tissue window. To this, each material area was marked to calculate mean radiodensity area for each sample using region of interest tool (ROI), which provided us lineal graphic with all values for Medpor and Fullcure. Fullcure showed a statistically significant higher radiodensity than Medpor in all samples ($P < 0.0001$, t-test), showing a mean value of 140.68 ± 46.93 compared to -180.72 ± 54.24 of Medpor.

Finally, after no toxicities observed in any of the rats implanted, the custom-made Fullcure support was manufactured to hold the albumin-derived scaffold to reconstruct the 30 mm segmental

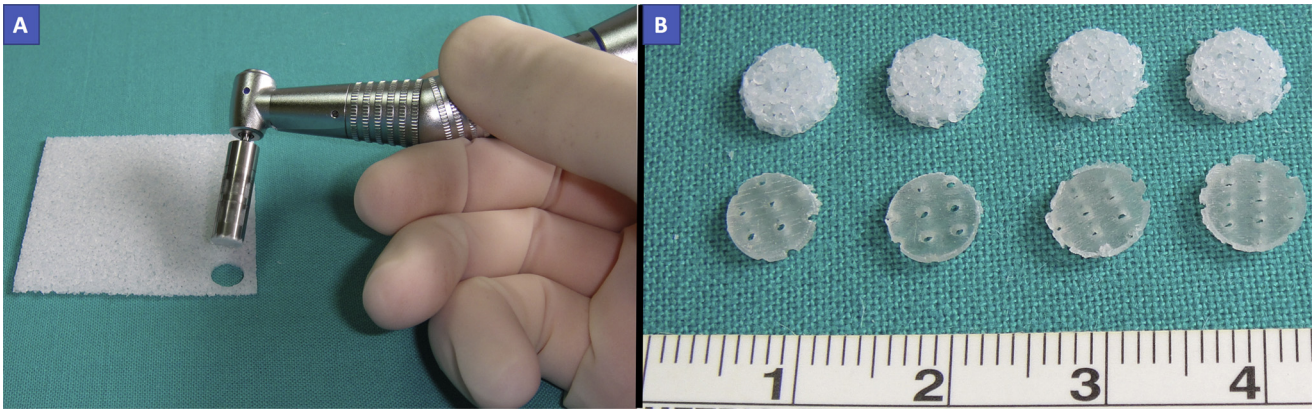

Fig. 1. A. A 5 mm diameter trephine for botton-shaped implant obtention in a Medpor laminae. B. Paired botton-like 5 mm diameter implants of Medpor (bottom up) and Fullcure (bottom down).

Please cite this article in press as: Megías Barrera J, et al. Histological and radiological evaluation of subcutaneous implants in mouse of a 3D-printable material (Fulcure 720) and experimental application in mandibular reconstruction. J Stomatol Oral Maxillofac Surg (2017), https://doi.org/10.1016/j.jormas.2017.11.004