Arquivos Brasileiros de
Oftalmologia

ORIGINAL ARTICLE

A three-dimensional printed photopolymer resin implant for orbital rehabilitation for evisceration

Implante de resina fotocurável para evisceração produzido por impressora tridimensional

Rodrigo Beraldi Kormann[1], Ricardo Mörschbächer[2,3], Hamilton Moreira[4], Patricia Akaishi[5]

1. Department of Ophthalmology, Hospital de Olhos do Paraná, Curitiba, PR, Brazil.
2. Hospital Banco de Olhos de Porto Alegre, Porto Alegre, RS, Brazil.
3. Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, RS, Brazil.
4. Department of Ophthalmology; Hospital de Olhos do Paraná, Curitiba, Paraná, Brazil.
5. Department of Ophthalmology, Otorhinolaryngology and Head and Neck Surgery, Escola de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.

ABSTRACT | Purpose: To evaluate the biocompatibility of three-dimensional (3D) printed orbital spheres for evisceration. **Materials:** A total of 10 consecutive patients (eight females and two males; mean age, 46.8 ± 14.2 years) underwent evisceration of blind painful eyes. 3D spherical implants produced by a rapid prototype machine were used to restore orbital volume. The implants were produced from a commercially available photocurable resin (Fullcure®). Systemic toxicity was evaluated by comparing serum biochemical measurements (creatine phosphokinase, aspartate aminotransferase, alanine aminotransferase, albumin, creatinine, urea, alkaline phosphatase, and C-reactive protein) before and at 12 months after surgery. Local toxicity was assessed by the evaluation of signs of socket inflammation at the first postoperative month. Changes in implant size were determined by computed tomography scans at 2 and 12 months after surgery. **Results:** The postoperative evaluations were uneventful. The biochemical evaluation showed no significant changes after surgery. None of the patients presented signs of orbital implant inflammation, infection, exposure, or extrusion. Computed tomography scan evaluations revealed no changes in implant size. **Conclusion:** To the best of our knowledge, this is the first phase-1 clinical study to certify the biocompatibility of the Fullcure resin for orbital implants in humans. The 3D printing technology permits fast and accurate production of implants for this purpose.

Submitted for publication: September 24, 2018
Accepted for publication: January 22, 2019

Funding: No specific financial support was available for this study.

Disclosure of potential conflicts of interest: None of the authors have any potential conflicts of interest to disclose.

Corresponding author: Patricia Akaishi.

Departamento de Oftalmologia, Otorrinolaringologia e Cirurgia de Cabeça e Pescoço Hospital das Clínicas - Campus, Escola de Medicina de Ribeirão Preto, Universidade de São Paulo
Av. Bandeirantes, 3900 - Ribeirão Preto – SP - 14049-900 - Brazil
E-mail: patriciamitiko@gmail.com

Approved by the following research ethics committee: Sociedade Evangélica Beneficente de Curitiba (CAAE: 10006013.8.0000.0103).

Keywords: Orbit evisceration; Orbital diseases/rehabilitation; Orbit/surgery; Printing, three-dimensional; Acrylic resins/therapeutic use; Biocompatible materials; Orbital implants

RESUMO | Objetivos: Avaliar a biocompatibilidade das esferas produzidas por impressora tridimensional em evisceração. **Pacientes e métodos:** Evisceração por olho cego doloroso foi realizada em 10 pacientes consecutivos (8 mulheres, idade média: 46.8 ± 14.2 anos). Os implantes esféricos foram produzidos pelo sistema de prototipagem rápida utilizando dados tridimensionais computadorizados. O material utilizado para produção dos implantes foi a resina fotocurável Fullcure®. A avaliação da toxicidade sistêmica do material foi realizada por meio da dosagem de marcadores bioquímicos (creatina fosfoquinase, aspartato aminotransferase, alanina aminotransferase, albumina, creatinina, ureia, fosfatase alcalina, e proteína C-reactiva) antes da cirurgia e aos 12 meses de pós-operatorio. A avaliação da toxicidade local foi realizada por meio do registro qualitativo dos sinais inflamatórios no lado operado durante o primeiro mês de pós-operatório. O tamanho dos implantes foi medido em tomografias computadorizadas (CT) aos 2 e 12 meses de pós-operatório. **Resultados:** A avaliação bioquímica mostrou que os marcadores estudados não sofreram alterações significativas após a cirurgia. Nenhum paciente apresentou sinais de inflamação atípica, infecção, exposição ou extrusão. A avaliação tomográfica não demonstrou mudanças nos tamanhos dos implantes. **Conclusão:** O presente trabalho é o primeiro estudo clínico realizado para atestar a biocompatibilidade dos implantes orbitais de resina fotocurável Fullcure. A produção dos implantes pela técnica de impressão tridimensional, utilizando essa resina, permite a disponibilização rápida e acurada do produto final

Descritores: Exenteração orbitária; Doenças orbitárias/reabilitação; Órbita/cirurgia; Impressão tridimensional; Resinas acrílicas/uso terapêutico; Materiais biocompatíveis; Implantes orbitários

INTRODUCTION

FullCure 720® resin is a photocurable, translucent, durable acrylic-based material, without hypersensitivity properties that can easily be obtained in Brazil, with an accessible cost to the local population. The FullCure 720® acrylic resin spherical orbital implant is a non-integrable, rigid, durable, light (1.19 g/cm³ density), transparent, yellow-colored, and photosensitive material.

Alloplastic porous and non-porous implants are routinely used to restore orbital volume after evisceration or enucleation. In developing countries, cost is an important factor that limits the use of porous implants. Non-porous implants composed of acrylic and silicone are inexpensive, but not always commercially available. Additive manufacturing or three-dimensional (3D) printing is a relatively new and inexpensive technique that allows the production of virtually any type of object[1]. Printable customized surgical instruments and medical devices are now being tested for surgical planning, training, and education[2-4].

In a previous study, we experimentally analyzed the biocompatibility of a 3D printed orbital implant made with a photopolymer (FullCure 720® resin) in 16 rabbit eyes. Our results showed that FullCure® resin did not induce any abnormal inflammatory reaction in the anophthalmic sockets of the rabbits[5].

The purpose of the present study was to evaluate the safety of printed FullCure 720® resin orbital implants for eviscerated human eyes.

METHODS

The study cohort consisted of 10 patients (eight females and two males; mean age: 46.8 ± 14.2 years) with a diagnosis of a blind painful eye, who underwent evisceration at the Evangelic Hospital of Curitiba and the Eye Hospital of Paraná, Brazil, from 2013 to 2014. The study protocol was approved by the Ethical Review Board of Evangelic University of Parana and informed consent was obtained from all the patients prior to participation in this study. No grant was received from any funding agency for this research.

All the patients underwent a comprehensive laboratory investigation, which included the determination of blood levels of creatine phosphokinase (CPK), aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, creatinine, urea, alkaline phosphatase (ALP), and C-reactive protein (CRP) before and 12 months after surgery. These tests were chosen according to the ISO 10993-11 guidelines (international biocompatibility standards, part 11) to assess potential remote adverse effects of medical devices.

Implant production

FullCure 720® orbital implant is produced with the use of rapid prototyping technology (material addition as successive plain layers). Initially, the implant was developed in a computer-aided design-3D format and then converted to a stereolithography (STL) format to enable rapid prototyping via PolyJet technology. SLT 3D printing is a well-known additive manufacturing technology in which photopolymers (liquid resin) are converted into highly complex solid objects with great accuracy and fine details. Specifically, the printer releases a certain amount of resin, part of which is cured by ultraviolet light. Once the initial layer of the object has hardened, the platform moves away from the surface and builds another layer of liquid resin. Again, the laser traces a cross-section of the object being printed, which instantly bonds to the hardened section beneath it. At the end of this process, the final product is delivered.

FullCure 720® resin has been used to produce solid spherical implants of three different diameters of 14 mm (2 patients), 16 mm (7 patients), and 18 mm (1 patient), similar to those of conventional commercial polymethyl methacrylate (PMMA) spheres. At the end of the printing process, the implants were sent to a proper facility for polishing of the surface (Figure 1) and sterilization with ethylene oxide.

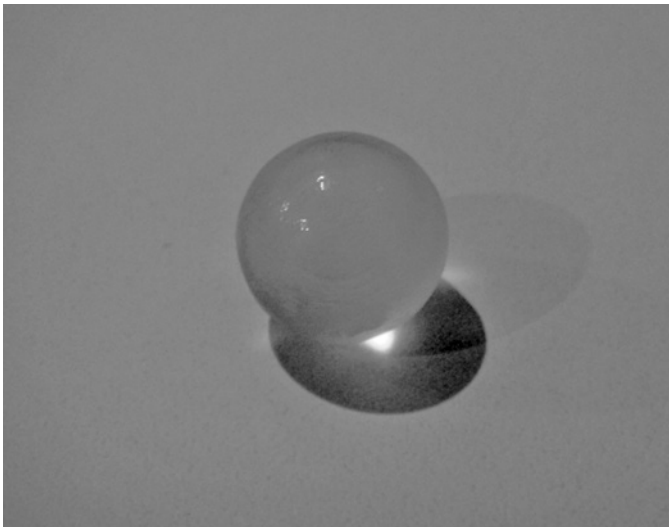

Figure 1. Polished surface of a FullCure 720® resin orbital implant.

Evisceration

Conventional evisceration, in which the cornea is removed without posterior sclerotomy, was performed for all the patients under peribulbar and monitored anesthesia[6]. In most patients, 16-mm implants were introduced into the scleral sac. Polyglactin sutures were employed to close the sclera. The Tenon's capsule and conjunctiva were closed independently with 6-0 polyglactin sutures. A medium-sized conformer was then placed and topical antibiotics were applied.

Postoperative evaluation

Inflammatory signs of hyperemia, chemosis, and discharge were weekly categorized as 1 (minimal) to 3+ (intense) during the first postoperative month. Computed tomography was used to evaluate reabsorption of the sphere by linear measurement of the implant at 2 and 12 months after surgery. Biochemical marker measurements were made at postoperative month12 and compared to preoperative values.

RESULTS

Postoperative evaluation was uneventful, as none of the patients presented with signs of orbital implant inflammation, infection, exposure, or extrusion (Figure 2). Biochemical evaluations revealed no significant changes after surgery (Table1).

Mean linear measurements of the implant were 15.8 ± 1.13 mm before surgery, 15.97 ± 1.21 mm at 2 months after surgery, and 15.99 ± 1.15 after 12 months (one-way analysis of variance: F=0.08, p=0.92). Ocular prostheses were adapted during the third month of follow-up, when the socket was completely healed with no signs of inflammation or infection (Figure 3).

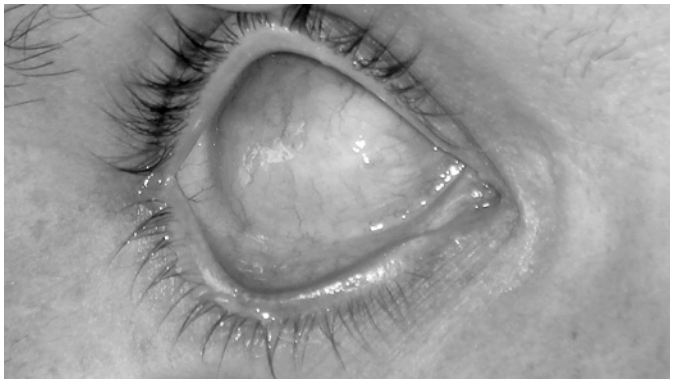

Figure 2. Right socket with the Fullcure implant at 3 months after evisceration.

DISCUSSION

The technology used to print 3D objects has become increasingly affordable. For surgeons, 3D printing has been useful for research, surgical training, and preoperative planning[2]. Callahan et al.[7] recently demonstrated the use of 3D implant molds for orbital fracture repairs. In 2013, a 3D object was successfully implanted for the first time in a patient, during which a printed splint was introduced in the trachea of an infant with localized tracheobronchomalacia[8].

Several implants have been developed for volume replacement after evisceration and enucleation. Although both time-tested and new materials are currently available in many countries, occasionally production cannot be certified by local health surveillance agencies. In Brazil, the only certified product currently available for orbital implant after evisceration is a porous polyethylene product distributed under the trade name Medpore® (Porex Surgical, Inc., Fairburn, GA, USA). However, the high cost of this implant material has prevented its use in most public hospitals.

We chose to produce the implants from a low-molecular weight (density=1.19 g/cm³) acrylic-based, low-cost, monomer resin, sold under the trade name FullCure 720®. The final product was similar to acrylic implants. The weight of an 18-mm diameter FullCure 720® implant was 3.56 g, while a PMMA implant of the same size weighs 3.61 g[9].

After the introduction of FullCure 720® resin implants into the scleral shell, no systemic toxic effects were detected. All biochemical tests remained within normal ranges during the postoperative period, with the exception of CRP values, which had slightly increased (up to 10 mg/dL) from preoperative levels. Many conditions, such as obesity, diabetes, hypertension, sedentary lifestyle, and alcohol consumption, can cause an increase in CRP levels. As these variables were evaluated and the CRP level did not increase further throughout the postoperative period, this abnormality was not considered a systemic effect of the implant.

The results of our previous experimental study demonstrated that a fibrous capsule between the sclera and the implant surface prevented long-term interactions between the implant and sclera[5]. Postoperative conjunctival hyperemia and other inflammatory signs were within expected ranges for this procedure with current non-porous implants[10].

There was no instance of implant exposure or extrusion within the 12-month evaluation period, which may

Table 1. Mean, median, minimum, and maximum values of biochemical markers before and 12 months after surgery

Variable	Time	Mean	Median	Minimum	Maximum	SD	Reference value	*p*
CPK (U/l)	Pre	111.2	89.0	49.0	361.0	93.3	40–150 (female)	
	Post	140.1	105.0	40.0	434.0	116.3	60–400	
	Post-Pre	28.9	5.0	-11.0	119.0	43.0		0.062
AST (U/l)	Pre	28.9	27.0	17.0	54.0	11.7	0–35	
	Post	24.3	23.0	17.0	35.0	6.0		
	Post-Pre	-4.6	1.0	-28.0	4.0	11.2		0.227
ALT (U/l)	Pre	30.9	29.0	19.0	53.0	9.9	0–35	
	Post	28.6	28.0	14.0	54.0	10.8		
	Post-Pre	-2.3	1.0	-15.0	5.0	7.1		0.33
Albumin (g/dl)	Pre	4.2	4.2	3.9	4.8	0.3		
	Post	4.4	4.5	3.8	4.8	0.3	3.5–5.5	
	Post-Pre	0.2	0.3	-0.4	0.6	0.3		0.109
Creatinine (mg/dl)	Pre	0.9	0.9	0.7	1.1	0.1		
	Post	0.9	0.9	0.7	1.2	0.2	<1.5	
	Post-Pre	0.0	0.0	-0.3	0.4	0.2		0.751
Urea (mg/dl)	Pre	30.8	26.0	10.0	59.0	16.4	15–45	
	Post	36.6	36.0	16.0	81.0	19.1		
	Post-Pre	5.8	2.0	-9.0	30.0	11.8		0.154
ALP (U/l)	Pre	75.1	66.0	47.0	110.0	20.0		
	Post	85.0	79.0	41.0	121.0	28.9	30–120	
	Post-Pre	9.9	9.0	-35.0	55.0	25.1		0.244
CRP (mg/dl)	Pre	7.2	4.0	0.3	24.0	8.3		
	Post	5.4	6.0	0.3	17.0	4.8	0.8–3.1	
	Post-Pre	-1.9	0.0	-15.0	2.0	5.2		0.500

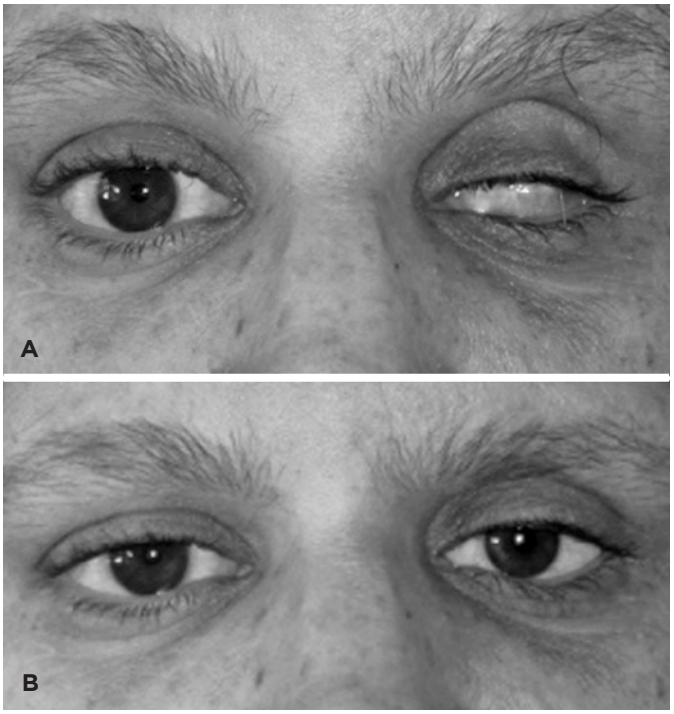

Figure 3. Clinical aspect of a patient at 3 months after implantation of the Fullcure sphere; (A) without an external ocular prosthesis (B) with the prosthesis in place.

be considered as good clinical tolerance similar to that obtained with other non-porous implants[11].

The relatively small size of the implant allowed intrascleral placement without scleral modification, thus, preventing contact of the implant with the orbital tissue. Nonetheless, further studies are necessary to determine whether exposure of the implant to the orbital tissues could lead to different outcomes. Intrascleral implant placement also avoids implant migration, but prevents the use of larger implants, which can lead to a lack of orbital volume. In this series, no patient complained about the final cosmetic result.

3D technology allows for customization of the implant format and size according to the patient's anophthalmic socket. In this study, to minimize the influence of multiple factors on biocompatibility analysis, all the implants were spherical.

To determine if the stability of this new implant is comparable to that of currently available non-porous implants, long-term follow-up is necessary. However, to the best of our knowledge, this phase-1 study is the first to apply 3D technology to produce a spheri-

cal implant for orbital volume replacement following evisceration.

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