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Towards a synthetic osteo-odonto-keratoprosthesis

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Abstract

Osteo-odonto-keratoprostheses (OOKP) is a unique form of keratoprosthesis involving surgical removal of a tooth root and surrounding bone from the patient which are then used to construct an osteo-odonto lamina into which an optical cylinder is cemented. The OOKP procedure is successful and capable of withstanding the very hostile ocular environments found in severe Stevens–Johnson syndrome, pemphigoid, chemical burns, trachoma and multiple corneal graft failure. The existing procedure is complex and time consuming in terms of operative time, and additionally involves sacrifice of the oral structures. This paper discusses the rational search for a "synthetic" analogue of the dental lamina, capable of mimicking those features of the natural system that are responsible for the success of OOKP. In this study the degradation of selected commercial and natural bioceramics was tested in vitro using a purpose-designed resorption assay. Degradation rate was compared with tooth and bone, which are currently used in OOKP lamina. At normal physiological pH the degradation of bioceramics was equivalent to tooth and bone; however, at pH 6.5–5.0, associated with infectious and inflamed tissues, the bioceramics degrade more rapidly. At lower pH the degradation rate decreased in the following order: calcium carbonate corals > biphasic calcium phosphates > hydroxyapatite. Porosity did not significantly influence these degradation rates. Such degradation is likely to compromise the stability and viability of the synthetic OOKP. Consequently more chemically stable materials are required that are optimized for the surrounding ocular environment.

Keywords: Keratoprosthesis; In vitro resorption; Corals; Ceramics

1. Introduction

The general treatment for serious corneal disease is corneal graft by penetrating keratoplasty (PK). Such transplants are common and have a success rate in excess of 90% in ordinary patients. However, PK failure is virtually certain when the ocular surface severely compromised. This includes patients suffering from corneal alkali burn (a serious industrial hazard), Stevens–Johnson syndrome or recurrent graft failure, and is a distinct possibility with dry eye, abnormal intraocular pressure (i.e. glaucoma) or ongoing ocular inflammation. Keratoprosthesis represents the only viable option for restoring sight in these patients. However, various forms of ocular surface epithelial transplantation procedures are now available for ocular surface diseases not amenable to conventional PK, e.g. limbal transplants, stem cell or ex vivo cultured epithelial transplants using autologous limbal, conjunctival or oral mucosal epithelium. These new emerging procedures have limited long-term follow up and differing success rates. For example in the dry eye limbal stem cell transplantation

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and other forms of ocular surface transplantation may not perform optimally [1–3].

Keratoprostheses are penetrating total replacements of the cornea and therefore require the maintenance of a clear visual window whilst allowing sufficient cellular invasion to fix the implant firmly in place. This represents a very considerable biomaterials challenge. Extrusion of the keratoprosthesis as a result of internal globe pressure is a common problem, resulting from a failure to promote wound healing at the implant–tissue interface. Although the concept of a keratoprosthesis can be traced back to 1789 and is attributed to the French ophthalmologist Guillaume Pellier de Quengsy, the first functional keratoprosthesis was not fabricated until nearly two centuries later. This device, produced by Cardona and co-workers [4], used a PMMA "nut and bolt" design to allow the device to be secured into the ocular surface by means of a trepanned "bolt hole".

It is apparent that since Guillaume Pellier de Quengsy's speculative proposal, the artificial cornea has had a very chequered developmental history. Some 300 designs of artificial cornea have been suggested, but success in implementation has been extremely low. Additionally, success rates vary widely; data published in 1988 indicated that between 8% and 53% of inserted artificial corneas fail completely within 3 months to 5 years [5]. This contrasts with a 95% success rate for donor corneas in the first 5 years after implantation. In the succeeding decade and beyond, better surgical techniques and materials with enhanced properties have improved the success of more recent keratoprostheses, such as those developed by Legeais et al. [6], Pintucci et al. [7] and Chirila et al. [8].

The level of interest and considerable level of difficulty in creating a universal replacement for severely damaged corneas continues. There are still many long-standing complications to be completely addressed following the implantation of the artificial cornea. They include bacterial infection, enzyme degradation of surrounding tissue, proliferation of membranes, raised intraocular pressure and poor stabilization.

A unique approach to the artificial cornea problem, the osteo-odonto-keratoprosthesis (OOKP), was developed in Italy by Strampelli in 1963 [9]. In examining the use of various autologous biological tissues to act as a frame for a polymethyl methacrylate (PMMA) optical cylinder, Strampelli found the tooth root most effective. Strampelli's device used a lamina prepared from a single-root tooth with surrounding bone sawn from the patient's jawbone, into which the PMMA optic was cemented. The device was implanted in a subcutaneous pocket below the eye in the patient's cheek for 3 months after which the device was removed and surgically inserted into the cornea below a covering of buccal mucosa. Despite recent advances in the keratoprosthesis field, OOKP surgery as pioneered by Strampelli not only provides effective control of most of the biological complications, but remains the most successful approach for the keratinized eye.

Following the pioneering work of Strampelli, Falcinelli [10–13] made stepwise improvements to the original technique, ensuring good long-term visual and retention: 75% of his patients achieved 6/12 vision or better. Long-term follow up has shown good retention results (85% in 18 years). As a consequence, this is currently the only procedure used in the UK and, because of its cost and complexity, is carried out in only one centre, which has a dedicated ophthalmologist working in conjunction with an experienced dental surgeon [14].

Modern OOKP surgery is usually performed in two stages, spaced 2–4 months apart. The first stage involves ocular surface reconstruction and fashioning of an osteo-odonto lamina and its optical cylinder. The ocular surface is reconstructed by suturing a piece of explanted buccal mucosa to the patient's sclera. A tooth root and surrounding bone is surgically removed from the patient and worked into a lamina with dentine on one side and bone on the other. A hole is drilled through the dentine to accommodate a PMMA optical cylinder, which is cemented in place. The resultant osteo-odonto lamina is placed into a sub-muscular pocket under the lower lid of the fellow eye, in order to acquire a soft tissue covering and to allow the lamina to recover from any thermal damage caused by the drilling. Any infections introduced from the oral cavity can be treated whilst the lamina is sub-muscular prior to implantation in the eye. Longer sub-muscular implantation periods have the potential to lead to significant resorption of the lamina. The second stage of the OOKP surgery essentially involves the retrieval of the osteo-odonto lamina from its sub-muscular pocket and implantation under the buccal mucosa. The optic is fitted through a trephined hole in the patient's cornea and the lamina is sutured onto the cornea and sclera. The procedure is completed by cutting a hole in the overlying buccal mucosa to allow the protrusion of the anterior part the optical cylinder.

The physiological environment where the OOKP is implanted is quite complex and depends partly on the medical history of the patient. The lateral and anterior sides of the OOKP support frame are in contact with the buccal mucous membrane graft, allowing integration due to growth of the soft tissue into the pores of the bone enabling improved fixation of the implant. The lower part of the support frame is in contact with the cornea and possible with aqueous humour, which could percolate round the posterior part of the optical cylinder. In seeking to build on and improve the performance of current OOKPs, it is important to examine the advantages, unique features and shortcomings of the procedure. The particular structural features of the OOKP that might explain its success are the porosity of the bone and the suspensory periodontal ligament linking it to the tooth, thereby forming a semi-rigid block into which is anchored the optical cylinder. This composite structure of tooth and bone is called the osteo-odonto or dental lamina. The peripheral interconnected pore spaces of the bone provide fixation of supporting tissue and is the key issue, whilst the periodontal ligament

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