Polydioxanone Polymers for Annuloplasty in Valve Repair

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Summary: The Kalangos biodegradable ring® was recently developed fpr mitral and tricuspid annuloplasty to allow for flexibility, remodeling and preservation of growth potential of the native annulus. In this article, the results of the experimental trials carried out to assess its safety and potential advantages will be discussed.

Keywords: annuloplasty; biodegradable ring; polydioxanone; valve repair

Introduction

Annuloplasty rings are artificial prostheses aimed at correcting the dilatation of mitral and tricuspid valve orifices, remodeling their shape, and improving coaptation between their leaflets during systole. Since the first human rigid prosthetic mitral ring implantation in 1968[1], annuloplasty technology has evolved from the planar, complete, rigid ring to a flexible and then semi-rigid ring over time.[2–4] The Kalangos biodegradable ring® (Bioring Co., Lonay, Switzerland) was recently developed to allow mitral and tricuspid annuloplasty associating remodelling, flexibility and preservation of the growth potential of the native annulus in pediatric population.

Characteristics of The Biodegradable Ring

The Kalangos biodegradable annuloplasty ring® has a curved «C» segment comprised of a poly-1, 4-dioxanone polymer colored with a blue dye, and suture material extensions equiped with a stainless steel needle at each extremity. Remodeling of the posterior mitral annulus or anteroposterior tricuspid annulus is achieved by progressive fibrous tissue formation during biodegradation of the ring by hydrolysis. Its specific molecular weight provides structural memory to protect it from subsequent deformity. The suture material equiped with needles at each extremity allows for the ring to be implanted inside the native annulus to be remodeled – as opposed to traditional rings which are implanted on the native annulus.

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Ring Selection and Surgical Technique

Rings are available in sizes 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36 in mitral and tricuspid positions. Selection of the correct ring size is based on the sizer which approximates to the anterior leaflet surface area.

Experimental

Animals in which a tricuspid biodegradable ring was implanted, were sacrificed by lethal injection of pentobarbital (0.1 to 0.3 g/kg intravenously) at 1, 3, 6, 9 and 12 months after surgery. After the sacrifice, each ring implantation site was harvested with the neighbouring tricuspid annulus, leaflets and the adjacent right atrial and ventricular walls. Qualitative and semi-quantitative histological evaluation of each slide were performed to assess the local tolerance (inflammatory cells, degenerative or necrotic changes, neovessels, etc) and the degradation of the implant. A particular attention was given to the quality of the fibrous tissue induced by the ring.

At 1 week, 1, 2, 3, 4, 5 and 6 months after implantation, the transthoracic echocardiographic examination did not show neither tricuspid insufficiency, nor transvalvular gradient in any of the animals. The right ventricular contractility was normal.

All macroscopic observations were carried out at the time of sacrifices after having harvested the heart of each animal. The leaflets of the tricuspid valve were normal with no evidence of thickening, necrosis or thrombus formation. The annuloplasty ring degradation appeared to be progressive over time, being degraded at its midpoint at 1 month after its implantation, its two segments being attached to each other by a fibrous bundle at 3 months, and being completely degraded and replaced by a marked fibrous tissue at 6 months. At 9 and 12 months sacrifices, this marked fibrous tissue was macroscopically visible and a leathery consistency was palpable on hand examination compared to the annulus segment without ring implantation. The fibrous tissue was only at the annulus level without any sign of invasion into the anterior and posterior leaflets tissue.

At 1 month the antero-septal, anterior and postero-septal resin slides showed the Kalangos annuloplasty ring® with a blueish staining and a rounded shape. Its diameter was between 1600 and 1700 μm. Signs of surface erosion and limited amounts of material debris were observed around the ring. The inflammatory tissue observed around the ring was constituted of macrophages, polymorphonucleated cells, multinucleated giant cells, lymphocytes, neovessels, fibrin and proliferating fibroblastic cells and collagen production. On the paraffin section performed in the midpoint degraded area of the ring, a fibro-inflammatory tissue was observed with few residus of the implant. The mean tickness of the fibrous tissue around the ring was 550 μm.

At 3 months, the ring was significantly degraded with signs of bulk erosion. In anteroseptal and posteroseptal sections the implanted ring was only partially degraded with signs of superficial erosion and limited material fragmentation. The foreign body reaction observed around the ring decreased with respect to the one month observation. Cellular degeneration and myolysis were significantly diminished compared to the previous time point, suggesting that these findings were surgery related rather than material related. The fibrous tissue reached the mean value of 578 μm and showed signs of fibrous remodelling. The control group animal showed a normal histology of the tricuspid annulus.

At 6 months, marked signs of implant degradation were observed and only few signs of residual material debris were still visible. The fibrous tissue thickened and filled the space left by the degraded implant material to reach a mean thickness of 950 μm. The fibrous tissue was dense and the intensity of the macrophagic and giant cells foreign body reaction decreased with regard to the previous time point analysis. In the single control group animal no fibrous tissue was observed.

At 9 months, marked to complete signs of implant material degradation were observed and only few signs of residual material particles with foamy material were still visible. The inflammatory reaction was mainly characterized by the presence of macrophages, multinucleated giant cells and lymphocytes and was slightly reduced in intensity as compared to the 6 months observation. The fibrous tissue of dense aspect filled the space left by the degraded implant material and represented an average diameter of 1250 μm increasing the amount of fibrous scar tissue developed around the ring material as compared to the previous 6 months examination. The control specimen showed the presence of normal fibroconnective annulus tissue.

At 12 months, degradation of the annuloplasty ring material progressed as compared to the 9th month period and only little foamy material was observed. The inflammatory reaction decreased in all animals. A thicker and dense fibrous tissue (1772 μm in diameter) replaced the degraded annuloplasty ring. The thickness of the formed annular fibrous tissue was comparable to the initial ring prosthesis thickness.

In this experimental study, the most important finding was continuation of fibrous tissue thickness despite complete ring degradation by hydrolysis at 6 months, which prevents the annulus against redilatative stretch. This fibrous tissue apparently behaves like an autologous ring remodeling the annulus which does not interfere with its dynamic physiological motion.

Results and Discussions

Ring technology is evolving from planar, complete, and rigid rings to flexible and semi-rigid rings as a result of increased understanding of annular remodeling and the dynamic physiological structure of the mitral annulus. The pioneering canine experiments of Tsakiris[2], who first described the dynamic structure and physiologic behavior of the mitral annulus during the cardiac cycle in terms of contractility, constituted the key study that triggered the concept of flexible rings, that unlike rigid rings, preserve the anatomical non-plane configuration and normal dynamics of the mitral annulus.[3–7] Although traditional rings available in the market respond to the needs of the adult population, no annuloplasty ring has thus far been designed for children in whom preservation of the growth potential of the native annulus is an important issue in terms of long term stability of valve repair procedures. Lack of available pediatric sizes below 26 in the traditional rings which could not allow for growth of the native mitral annulus, is due to the induction of a stenotic effect in a growing child which could be worsening with time.[5] Being encouraged by some annuloplasty techniques which have been described in the pediatric population using different biodegradable suture materials and especially by polymers of poly-diaxanone largely used in pediatric cardiovascular interventions[8–10], we started in 1994 to develop the Kalangos annuloplasty ring® capable of preserving the growth potential of native mitral and tricuspid annuli. In the experimental trial, echocardiographic controls performed at monthy intervals showed no signs of valve dysfunction, preserved ventricular contractility and physiological growth of the valve orifice with no transvalvular gradients. Moreover, macroscopic measures of the valve orifices in the sacrificed animals confirmed the preserved annulus growth potential at each time period in these animals which had increased their body weights from 30–43 kg to 190–200 kg over a year.

The implantation of the ring within the native annulus – contrary to the other traditional rings that are inserted on the native annulus – prevents it from being in contact with blood, and therefore avoiding thromboembolic complications. Anticoagulation is therefore not necessary, unlike with other rings for which anticoagulation is preferable during the first postoperative 3 months until the endocardium covers the synthetic material of the ring. In addition, the Kalangos ring® does not contain any synthetic material and can theoretically be used during the acute phase of cases suffering from infectious valve disorders.

In conclusion, the concept of annulus remodeling using a biodegradable ring which preserves growth potential of the native annulus and maintains the three dimensional dynamic motion of the mitral and tricuspid valves opens new perspectives for valve repair procedures.

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